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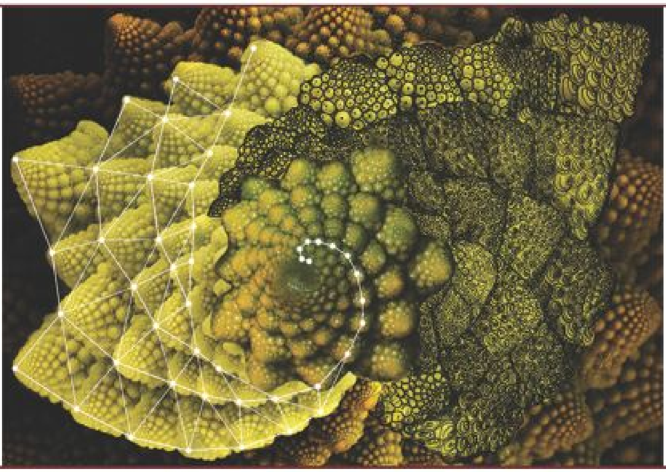
Predictability and the Unpredictable

Life, Evolution and Behaviour

Editors
David Ceccarelli
Giulia Frezza



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Sconfinamenti tra i saperi umanistici e le scienze della vita
Crossing borders between the humanities and the life sciences

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Crossing borders between the humanities and the life sciences

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Introduction. The Culture of Predictability and the Nature of the Unpredictable: Life Sciences at the Crossroad

David Ceccarelli
Giulia Frezza

Prediction in science relies on the capacity of generalizing the repeated observation of phenomena and forecasting their dynamics. In modern Western science, the emphasis on prediction became an essential part of the so-called "deterministic trend" epitomized by classical Newtonian-Laplacian physics, which claimed the in-principle possibility of determining the global behaviour of the system under study as the sum of its local parts, i.e. the individual behaviours and their interactions (P.S. Laplace 1995). In this way, a general trend was further established according to which it would be possible to predict organisms' behaviour by applying a physical analysis to living beings. As emphasized by the American physicist and historian of science Evelyn Fox-Keller, what counts as an explanation of a phenomenon is defined by the temporal, disciplinary and cultural needs of a specific "epistemological culture" (E. Fox Keller 2002). We propose therefore to refer to such deterministic trend in Western science in terms of the "culture of predictability".

However, especially from the beginning of the XX century onwards, limits affecting scientific determinism, and the culture of predictability in general, have been discussed in relation both to epistemic restrictions in the study of living beings (epistemic determination) and to the specificity of the objects of analysis (ontological determination) (P. Suppes 1985; R.C. Bishop; N. Rescher 1998). The first, epistemic determination, especially refers to the possibility that a *cognitive agent* could at least in principle capture natural processes and behaviours through predictive algorithms (P. Suppes 1974).

As to the second, ontological determination, the dichotomy between predictability and unpredictability turned out to be a fundamental tool in the study of the *boundaries* between the state of the inert and the living matter (M. Buiatti and G. Longo 2013).

Since the second half of the XX century, the study of living beings within the "culture of predictability" has increasingly shown weak points. A more specific characterization of biological specificity and unpredictability, indeed, resulted from the evolutionary gaze fostered by the modern synthesis and its later developments (G.G. Simpson 1944; T. Dobzhansky 1973; E. Mayr 1982; S.J. Gould 1989). Since its emancipation from the traditional Newtonian-Laplacian physical determinism, and along the lines of the new developments in physics, the study of biological complexity and self-organization has advanced the idea that biological phenomena represent the main challenge to strong determinism (M. Eigen and P. Schuster 1979; S.A. Kauffman 1993; S. Sarkar 1996; S. Oyama, P.E. Griffiths, R.D. Gray 2001; N. Gontier 2015). Such approach especially countered the new epistemological culture of predictability based on a reviewed version of determinism that spread in the life sciences since the 1950s, conveyed by means of reifying metaphors borrowed from the informational domain and applied to the biological field, such as the metaphor of the "genetic code" (R.C. Lewontin *et al.* 1984; S. Oyama 1985; E. Fox Keller 1995; J. Maynard Smith 2000). Since the 1970s, however, the theoretical trend focusing on the characteristic unpredictability of life evolution took centre stage in the scientific debate, especially in the form expressed by the American evolutionary biologist Stephen J. Gould's "evolutionary contingency thesis" (J. Beatty 2006).

Such epistemological shift frames a counterculture opposed to the "culture of predictability" by underlining its strong focus on "the nature of the unpredictable" in living beings.

Recent developments in theoretical biology have extensively highlighted the radical difference between the processes of determination in physics vs. biology, contrasting the previous theoretical trend expressed by the culture of predictability. Scholars indeed emphasize the substantially different meaning between the two domains of the main parameters of observation (time and energy), thus criticizing the physical approach to "objectification" applied to the "instable" biological objects (J. Dupré 2012; G. Longo and M. Montévil 2014). According to such views, when it comes to predictability, the notion of randomness applied to the inert and to the living matter diverges. In physics randomness is unpredictability (deterministic or not deterministic) within an intended space of phases, by contrast, in biology, randomness – though being a fundamental factor enhancing variability and bio-diversity – may not be measurable by probabilities (Longo and Montévil 2014; C.S. Calude and G. Longo 2016). The state of living matter and the biological indeterminacy appear as the outcome of the blend of stochasticity, multilevel interactions and historicity that pervade living beings (Buiatti and Longo 2013). The study of the living matter in its dynamics entails the analysis of different levels of variation processes and their interactions: DNA mutations, crossing-over, gametic selection, mate selection, random drift of gene frequencies, stochastic perturbations, as well as patterns of evolutionary changes, and organisms' more complex systems of feedbacks and homeostatic devices, till the emergence of unexpected novelties at higher hierarchical levels such as cognition and behaviour (B. Rensch 1960; Mayr 1982; R. Lewontin 2000; F. Capra and P.L. Luisi 2014).

Each of these phenomena outlines what we aim to present in this volume as "the nature of the unpredictable", a specific variety of biological unpredictability that scholars have differently described over the last decades by referring to categories such as "chance" and "historical contingency" (J. Monod 1970; Gould 1989; M. Travisano *et al.* 1995; Beatty 2006). The notion of chance, originally framed in physics, has been traditionally extended to such inherently unpredictable phenomena like DNA mutations, genetic recombination and drift. Within the Darwinian theory of evolution, the relationship between individual variations and the adaptation of organisms has been considered as product of "randomness" (C. Johnson 2015). Especially in respect to larger-scale phenomena, such as in the case of macroevolution, scholars have regarded biological change rather as a phenomenon to be described in terms of the "historical explanation" which, in Gould's words, rests on the unpredictable sequences of antecedent states, «where any major change in any step of the sequence would have altered the final result» (Gould 1989, p. 283).

As highlighted in this volume, the debate on the culture of predictability vs the nature of the unpredictable is complex and far from exhibiting a unified framework. The predictability of biological processes is still under discussion from different perspectives and at different levels: from genetics, epigenetics, systems biology, evo-devo theories, ecology to ethological, cognitive and behavioural studies, medicine and within the new trends of evolutionary anthropology and ethics (P. Bateson 1991; P.E. Griffiths and R.D. Gray 1994; L. Alberghina and H.V. Westeroff 2005; Burian

2005; C. Caroll 2008; P. Huneman and D.M. Walsh 2017). Scholars are increasingly highlighting the need to better analyse and frame living beings' processes and therefore gaining insight into their specific form of causality too (Dupré 2012; J. Dupré and Woodward 2013).

The predictability vs. unpredictability dichotomy has recently come to the fore in conceptualizing developmental and epigenetic mechanisms along with the revision of the evolutionary theory. By favouring a multilevel causality, «postmodern evolutionists» (J. Whitfield 2008; G.B. Müller 2007) have increasingly fostered a critical redefinition of the boundaries between predictable and unpredictable phenomena in morphogenesis, development, and evolution. In particular, new studies of repeated and parallel evolution have helped to reassess the instance of predictability at specific levels of evolution (P.M. Brakefield 2006). At the same time, the employment of sophisticated mathematical models and data-intensive techniques in the study of biological events at various scales (from cell and individual behaviour to complex ecological dynamics) outline a new scenario which calls into question again the notions of uncertainty and randomness.

Lately, optimism towards prediction in biosciences came to the fore in "data-intensive science", which emphasizes how new statistics methods and techniques, as well as "big data" and "big programs" of data collection, can generate reliable predictions.

This new epistemological turn has been described as the "fourth paradigm", after experimental, theoretical and computational science, and can be seen as a new revised expression of the culture of predictability (T. Hey 2009). It is based on data capture, data curation (organization and preservation of data through time) and analysis and points to the possibility of establishing a direct relation between intensive-data production and prediction (through data mining), i.e. generating prediction by simply looking at how large amounts of data statistically capture existing patterns and behaviours. "Big Data" approach was hailed as a substitute of the "obsolete" scientific method, by means of its presumed self-standing approach to data mining and data set, i.e., data presenting themselves as self-evidence, under the slogan "correlation is enough" (C. Anderson 2008). By regarding data evidence as an unbiased and self-explanatory epistemic tool, the claim of «evidence-based policy making» is at the centre of a transdisciplinary debate (T. Koch 2016). Considering its «dream of establishing a "sensors everywhere" data infrastructure to support new modes of scientific research» (Hey 2009, p. XV), such an approach is being questioned as to its multi-level implications, especially because of its use as a powerful framing tool for shaping institutional, political and everyday life practices from education, information to healthcare (R. Kitchin 2014; D. Beer 2016). Here the power of the culture of predictability seems to have gained its acme when it exhibited its most controversial aspect, as shown in the second section of the volume.

The predictability vs. unpredictability debate impinges on philosophical and ethical issues in contemporary cognitive theories, in the neurosciences and in their application in the medical field. Strong criticisms arise, for instance, against traditional deterministic framings of the brain, centred on the mechanistic metaphors generally used to describe brain-machine functioning and its impairment, as well as against the new simulation methodology and its wide application to public health, as in the "Big Brain" projects (H.P. Lane *et. al* 2013; S. Reardon 2016; M. Wadman 2016). In spite of this, new approaches contrast such deterministic culture of predictability which tends to conflate organisms' behaviours with the functioning of their brain (D. Bates and N. Bassiri 2016). Neural plasticity and environmental enrichment models are providing a complex image of the brain and the mind, focused on the ongoing relations within and across different environment(s) (A. Sale, N. Berardi, L. Maffei 2014). The paradigmatic image of brain's functioning and its predictability based on the traditional behaviourist scheme of "the black box", where behaviour used to be described as the chain of inputs and outputs, is overturned by a more dynamic image, based on neural connectivity and on brain's continuous interaction with the environment(s). Moreover, when applied to the medical field, such models lead to a multifactorial analysis of the global determinants of health and on a person-centred approach in healthcare, rather than on traditional mono-causal explanations (C. Clarke and E. Wolverson 2016; G. Frezza 2016).

This shift in the approach to brain and behaviour acquires a new meaning also from an evolutionary perspective, where brain, mind and behaviour are described from radically new interactionist, interdisciplinary, and trans-specific perspectives in ethological studies (from cognition to language use and narratology). New evolution-informed perspectives (D. Parfit 2011) are on the brink of reshaping inter-specific cultural approaches also in the ethical field, stressing the need of an ecological view in the study of the relationship between humans and non-human animals.

Currently, the question whether life sciences can rigorously generate predictive models in genetics, developmental biology, micro- and macroevolution, neurosciences, as well as in environmental sciences and biomedicine, such as for the evaluation of risk and health prevention, is therefore a highly topical subject. At the same time, the predictability vs. unpredictability dichotomy, as underlined, derives from and conveys longstanding conceptual, historical and epistemological issues.

In this new scenario, two main issues arise: whether groundbreaking studies in life sciences are informing a new "culture of prediction", and consequently the need of an up-to-date definition of the status of predictability and unpredictability in the biosciences. To answer these questions, an encompassing epistemological as well as historical reflection is needed. This book proposes an updated review from both viewpoints addressing the issues raised by new ground-breaking researches within a coherent theoretical framework. We expect this approach to make a significant contribution to outline the state of the art on the matter as well as new directions of research, tackling how the conceptual borders between predictability and unpredictability changed, and are still changing, through time.

The volume consists of fifteen essays, each of which focuses on a different scale of biological complexity and a different unit of analysis (from genes and cells to organisms' complex behaviour, to ecosystems). Far from any epistemological and ontological reductionist commitment, all the authors highlight both the singularities that characterise each level and unit of analysis, and their mutual connections. This necessarily calls for an interdisciplinary framework aimed at developing new theoretical and methodological tools for describing the complex dynamics of organisms.

Aiming to display this encompassing and interdisciplinary view, the book discusses three fundamental issues on the matter:

(i) How the predictability-vs-unpredictability dichotomy is nowadays discussed at different levels of the complexity of the living beings', from cells to populations and communities (section one);

(ii) How the current debate on predictability vs. unpredictability triggered by new paradigm shifts can be better understood against a critical and historical-epistemological framework (section two);

(iii) How the predictability vs. unpredictability dichotomy is driving traditional theoretical issues in evolutionary theory along innovative interdisciplinary directions of research: from behavioural, cognitive, and linguistic fields to the crossed study of animal and human ethos (section three).

The book, therefore, is the result of a highly interdisciplinary effort, comprising different viewpoints that we do not wish to dismantle by artificial divisions and sub-divisions. However, to help the reader orient herself in the volume we set out the predictability vs. unpredictability dichotomy in three thematically related sections: *1. Forms of stochasticity between physical and life sciences*, which explores recent conceptualizations of the predictability vs. unpredictability dichotomy across different scales of the hierarchical organization of living beings; *2. Predictability from biology to neuroscience and biomedicine: are they so predictable after all?*, which provides a critical theoretical standpoint and a historical-epistemological framework to discuss recent paradigm shifts from Big Data to brain plasticity, and *3. The evolutionary unpredictability: past and future*, which shows the potential of traditional evolutionary approaches in their broad application from contemporary biological issues to ethology and ethics. This division allows the readers to understand how each area of research deals with a different variety of unpredictability, and helps getting a consistent view of the relation between the culture of prediction and the nature of unpredictability within and across different domains.

The first section, *Forms of stochasticity between physical and life sciences*, frames the recent epistemological discussion on randomness in physics, cellular studies, population genetics, and ecology. Attention is devoted to the mathematical modelling at the intersection between such levels of analysis, starting from the article «From Predictability to the Theories of Change», where Ignazio Licata addresses the issue of epistemic uncertainty in complex systems modelling, drawing a parallelism between the emergentist model and the advances in Quantum Mechanics and Quantum Field Theory. By specifying how the study of processes and change in systems requires overcoming the *ideal models* centred on univocal descriptions and predictability, the author highlights that in complex systems descriptions become plural, thus setting an extreme limit for predictability. In this regard, the *Theories of Change* aim at setting *multi-model strategies* focused on the observational and computational investigation of the events under consideration.

At the level of cellular behaviour, the prediction and contingency dichotomy is investigated by Luigi Preziosi in «Determinism and Stochasticity in Mathematical Modelling for Cell Migration». Through an in-depth analysis of cell migration phenomena, the contribution highlights how even slight changes in parameter space can induce dramatic bifurcations in cell behaviour. System's dynamics can drastically depend on simple changes in the history of stimuli, and it is thus possible to have cells behaving differently for the same value of the stimulus depending on the recent history of the system. Furthermore, due to randomness in signal reception and transmission, as well as to the modelling procedure and to the response parameters, the uncertainty of the system increases. Thus, the use of mathematical models can be helpful to find cells in their migration state as well as to figure out the main parameters determining cell migration.

At a further level of analysis, Fabio Sterpetti's essay «On the Nature of Natural Selection» analyses the discussion on evolutionary stochasticity triggered by the current epistemological debate between "statisticalism"and "causalism" about whether or not the explanations provided by population g*enetics* are genuine instances of causal explanations. Such a debate intersects the more general discussion on whether or not mathematical explanations can be understood as genuine causal explanations, and thus explanations that may be acceptable from a naturalist viewpoint. The author shows aspects of the debate by focusing on the concept of *genetic drift*. This allows to highlight how, in the causalist view, predictability or unpredictability in evolution is a matter of complete knowledge or lack thereof, while, from statisticalist standpoint, there is no way to fill in the gap between predictions and actual frequencies since the mathematical models used to make predictions deal with infinite quantities.

In «Predicting the Genetic Loci of Past Evolution», Virginie Courtier-Orgogozo and Arnaud Martin delve into the causal relationship between multiple stochastic events (mutations, unpredictable environmental changes) and reiterations in distinct taxa through independent mutations in the same genes. Dealing with examples of retrodictions, inferences on events that occurred in the past, and not deductions on the future, they show how the causal mutations of specific evolutionary changes become predictable: for a given phenotypic change that occurred in the past the underlying mutations can be consistently guessed. As already outlined by the authors in the study of repeated evolution (Courtier-Orgogozo 2016), here predictions about life evolution rely on knowledge of certain parameters of the final state, and thus they do not require the causal understanding of repeatability.

The section closes with a broad ecological reflection by Philippe Huneman in the chapter «Contingency, Laws and Random Events: Epistemic Specificities of the Neutral Theory in Ecology». By considering Hubbel's theory in ecology and biogeography (1979), the author re-evaluates the role of neutral models in ecology and evolution – i.e. models where selection plays no causal role – focusing on the relation between scales of biological change and the weight of neutral processes.

The second section of the book, *Predictability from biology to neuroscience and biomedicine: are they so predictable after all?*, outlines a historical and theoretical view as to the "Big Data approach" and the recent theoretical shifts in biology, neuroscience and their potential application in healthcare.

The epistemological nature of Big Data approaches is analysed by Barbara Continenza in the chapter «Uncompromising Empiricism Once Again? Big data and the case of Numerical Taxonomy». After presenting a useful historical reconstruction of the Big Data sciences as to their technical and epistemological impact on life sciences, the author proposes a historical parallelism between Big Data studies and phenetic taxonomy. This parallelism emphasizes the recurrence of the empiricist attitudes of data-driven paradigms parallelism in the history of various fields of XX Century biological research.

A major analysis of the heuristic power and potential biases of massive data analysis applied to the study of living organisms is presented by Maël Montévil and Giuseppe Longo in the chapter «Big Data and Biological Knowledge». Particular attention is devoted to the analysis of how generalizations drawn from big data set might derive from chance and foster a "deluge of spurious correlations". As a solution, or rather as a fundamental criticism of such approaches, the authors point to the need of considering the organisms from a theory-laden approach providing a crystal-clear view of what we can and cannot predict *in principle*. Understanding living beings entails to target their specific form of causality, i.e., constrains that are only limitedly stable in time and that can be considered as invariants only at a given time scale. Variation is the "rule" that shapes real living organisms and not generic objects that potentially would all have the same state of organization.

In the chapter «Epigenetics and Development in Cognitive Functions. Literacy as a Case-Study», Carmela Morabito shows neuronal processes involved in literacy as a case study for addressing the importance of contingency in the development of cerebral pathways, portraying the brain as an intrinsically dynamic and plastic organ. In particular, the author outlines how learning to read involves a "neural exaptation" process whereby pre-existing cortical systems (cortical mechanisms for visual recognition) have been functionally reconverted to the novel task of recognizing written words. Such issue sheds light on the role of causal-dependent contingency (Beatty 2006) in biological and cultural evolution.

Moving to the application of such neuroscientific researches in the field of health communication, in «"Decline" vs. "Plasticity": Conflicting Narratives in the Dementia Tsunami», Giulia Frezza, in a crossed view (discourse analysis and historical-epistemological), discusses two metaphorical models of the brain ("decline" and "plasticity") used in dementia public discourse to frame two conflicting narratives: a global descendent trajectory leading to a hopeless neurodegeneration of the individual in the decline narrative and a local, less predictable, trajectory of brain decline in the plasticity narrative. The potential risks and the ethical responsibilities of metaphorical language use in dementia are outlined by considering the potential impact on therapeutic outcomes as well as the ethical backlashes related to each narrative.

In the last section, *Evolutionary unpredictability: past and future*, the book provides a coherent historical-epistemological study of the predictability vs. unpredictability dichotomy in evolutionary biology and its most recent application to other domains of research. Ranging from the post-Darwinian debate to the contemporary scenario, the authors of this section focus on traditional questions in theoretical biosciences as well as on new directions of research relative to animal and human behaviour from cognition to language and ethics. First, authors look at past and present conceptualizations of "repeated evolution" and their implications as to the claim for prediction ranging from traditional theoretical biology to ethology and evolutionary ethics. In «Orthogenetic Predictability: Orderliness and Symmetry in Early Macroevolutionary Explanations», David Ceccarelli reconstructs the historical and epistemological foundations of such claims in the late nineteenth-century orthogenetic theories. Special attention is given to the emphasis on homoplasy within orthogenetic paleontology, with a particular focus on the works of the American paleontologists Alpheus Hyatt, Edward Drinker Cope, William Berryman Scott and Henry Fairfield Osborn. The author highlights how orthogenetic theories could be reconsidered as the outcome of the epistemological mismatch between Darwin's notion of chance and the prevailing nineteenth-century uniformitarian epistemology, a view that allowed orthogenesists to see natural history as a set of tapes regularly replayed over time.

Sara Campanella's chapter «Synthesis and Behaviour: A New Role for Selection», focuses on one of the most controversial topics of evolutionary biology: grasping the action of natural selection. Campanella choses to focus on the Synthetic theory in the late 1950s, in the work of George Gaylord Simpson and his wife the psychologist Anne Roe, to show the historical roots of the debate on the relationship between behaviour, development and contingency as factors of evolution. Jean Piaget's work and his 'genetic epistemology' are then presented as a crucial epistemological reflection on the macro-evolutionary impact of the selective dynamics within the organisms and on their behaviour. This reflection lead Piaget to challenge the emerging metaphor of the "program" and to extend the concept of heredity beyond the role played by genes.

In connection to the recent studies of repeated evolution brought about by comparative genomics, systems biology and evo-devo studies, Silvia Caianiello explores in «*Seinesgleichen geschieht*: Contemporary Challenges to Evolutionary Contingency» how the studies of repeated and parallel evolution have recently raised claims that evolutionary biology is on the brink of becoming a more predictive science. In particular, the author highlights how the case of repeated evolution not only affects the retrodictive destiny of evolutionary theory entailed by Gould's "evolutionary contingency thesis", but also challenges the frozen view of conservation in favour of a different approach that aims at studying the systemic conditions that enable the *dynamic reiteration* of the same at different levels of the biological complexity.

The application of the evolutionary theory to other fields of research is then evaluated along with the advances in trans-specific behavioural studies, as well as in the evolutionary approach to philosophical and normative dilemmas in the ethical domain. Along the lines of a cross-field challenge, Marco Celentano addresses the biological and social functions performed by singing in different animal species, and some converging aspects they present, in his «Interspecific Cultural Studies (ICS) and Interspecific Cultural Convergences (ICC). From the only human towards a comparative history of animal uses and traditions». In particular, the author analyses the interspecific evolution of singing in terms of "Cultural Convergent Evolution", thus highlighting how the spread of singing in clades and environments is the result of mutually independent, but in some aspects similar, evolutionary processes and selective pressures. Such recent progresses in the study of the syntactic complexity and richness of intraspecific differentiations in animal singing has extended our understanding of what we may consider predictable or unpredictable in animal behaviours.

In the chapter «On the Contingency of What Matters: Predictability and Evolutionary Ethics» Eleonora Severini, criticising the core of Derek Parfit's realist conception, rethinks what really matters morally in the light of evolutionary contingency. In a review of anti-realists' and realists' positions, from Parfit's to Street's and Lecaldano's view on normativity, the author argues that a clearer understanding of contingency framed within an evolutionary approach points to an alternative framework for moral normativity than the realist one: where *unpredictable* things are relevant from a moral perspective.

«Estimations, Plans, Narratives: how Non-Human Animals Deal with the Future and "Possible Worlds"» is the book's concluding chapter. Dario Martinelli critically discusses the cutting-edge debate about the capability of imagining and planning the future as being a human uniqueness, i.e. human species-specific trait. Humans are traditionally considered the only species where three distinctive characteristics of language are found: i. distant space-time semiosis (the ability to deal with both recent and remote past events and places, as well as with expectations in immediate and remote places and future events), ii. narrativeness and iii. linking signs to create meaningful relations among them. By proposing an operationalization of these concepts within a more interdisciplinary ground from semiotics to ethology and narratology, Martinelli sets forth a not anthropocentrically-biased approach.

More than ever, the impact of the culture of predictability vs. the nature of the unpredictable debate on theoretical and applied biosciences is multifarious and far removed from a systematic understanding. The manifold character of such debate is mirrored in the variety of the contributions: we cannot expect such variation – informing different levels, units of analysis, and disciplines – to be extrapolated from one level of analysis to explain other levels while keeping the specificity of the described phenomenon. However, from genes to cells and ecosystems, as well as from normal to pathologic phenomena, we gain a more accurate and appropriate gaze on organisms' complexity by considering both unpredictability and predictability as entangled parts of the same discourse.

We believe such controversial issue will benefit from the multi-level and interdisciplinary analysis informed by the historical-epistemological approach offered in this volume, which is also result of a peculiar gaze on the biosciences arisen from twenty years of discussions within the activities of *Res Viva* Italian interuniversity association to which this volume wishes to pay a tribute. Despite and beyond such variety, this view may contribute to the development of an encompassing theoretical interdisciplinary framework (from evolutionary to semiotic, cognitive, behavioural, ethical, medical, ethological, linguistic and narratological researches), fostering a refined and critical view on the mutable borders between predictability and unpredictability when applied to living beings' evolution and behaviour.

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I

Scales of Stochasticity Between Physical and Life Sciences

From Predictability to the Theories of Change

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Introduction: The scientific explanation and the Causality-Determinism-Predictability triad

Predictability is still considered as a crucial ingredient in scientific explanations. Likely, this close association depends on the historical fortunes of Determinism, a peculiar trait of many physical theories from Classical Mechanics to Relativity up to Quantum Mechanics. However, the understanding of predictability has changed its features and range over time. As it is well known, a physical system is described by deterministic laws when, given the dynamic laws and the initial conditions, the "mathematical crank" (differential equations) univocally fixes a state of the system in a future or past instant. The success of Rational Mechanics confirms the philosophical triumph of *Laplace's demon* (R. HAHN 2005). For a long time, the huge complications linked – for example – to the three-body general problem were considered as computational problems or just a matter of inexact data. It will be an 1887 work by Poincare to clarify that the problem actually pertains to a *new typology*, an insight which prefigured the modern theory of dynamical systems based on chaos and non-linearity. In this new framework, the sensitive dependence on the initial conditions limits very quickly the predictability in a range strictly connected to the system's non-linearity (*Lyapunov time*). In addition, it can be demonstrated that a non-linear system is an information amplifier – it can, for example, "amplify" a fluctuation – whereby the connection between determinism and predictability completely falls down (M. CENCINI *et al.* 2009; I. LICATA 2008a). The qualitative theory of dynamical systems has developed since the 1930s in order to solve these situations by proposing a concept of predictability no longer based on the detail of the specific trajectories, but on the global behaviour of the system, i.e. its stability and asymptotic states (Y.A. KUZNESTOV 2004). We find this situation also in General Relativity, the difference – and some subtler problems more, see the specialized bibliography – lying in the fact that there is no background, actually the space-time itself is generated by the initial data and the evolutionary equations (J. Barrow 1982).

The case of Quantum Mechanics is a completely different one. Actually, if evolutionary dynamics **U** (for example, the Schrödinger's equation) are strictly deterministic, any predictability on a single event (**R**, reduction of the state vector) is impossible for reasons of principle, linked to the very nature of quantum systems. The whole debate on foundations can be seen as different attempts to find a synthesis between **U** and **R**, or, at least, the "ontological" elimination of one of the two sides.

Despite its "erosion" within the hard fabric of theoretical physics, predictability seems to preserve a special position. Actually, it is considered that determinism distils the scientific features of causality, a long debated notion in philosophy. Clearly such idea does not stand to a careful examination. The possibility to connect two events in a temporal framework (for example in the light cone structure in relativity) does not guarantee by itself a causal relation (S. Mumford and R.L. Anjun 2014; P. Illari and F. Russo 2014). Moreover, the local features of Quantum Mechanics would make the question much more problematic (P.M. Nager 2016; M. Ringbauer *et al.* 2016; D.T. Pegg 2006; I. Popescu and D. Rohrlich 1997).

Thus, it is more natural to connect the notion of "cause" with the global structure of a scientific explanation, considered as the configuration of theories and models providing a picture of *how things work*! Predictability is rather a feature of some classes of models. We can easily realize this fact by a simple example. Just consider the classical double slit experiment for electrons by C. J. Davisson and L.H. Germer in 1927, which R. Feynman correctly considered as the archetypal QM experiment (R.P. Feynman 1985). Let us imagine we could collect all the data of electron impacts on the screen and process them statistically. In the end, we can get a very good probabilistic evaluation of the areas where we can find an electron, no more, no less than by using wave-function. Anyway, such prediction does not explain the phenomenon. In order to have an exhaustive picture of the situation we have to turn to Schrödinger equation; moreover, our statistics cannot be exported to other phenomena. The Schrödinger equation, instead, is an explanation connecting scales, objects and dynamics for non-relativistic quantum systems.

The separation between explanation and predictability becomes far more evident in the study of complex and emergent systems. Without going into technical details, we remind that, in an emergent process, modifications of the internal structure of the system and of its relationship with the environment lead to the emergence of new properties which, generally, cannot be ascribable to the level of its constituents, in a way that reminds us of the universal aspects of phase transitions (I. Licata, 2008b; 2008c; 2011). This can imply different levels of description, and the manifestation of some forms of coherence on some levels and not in other ones. In general, *intrinsic* emergence is related to the appearance of properties or phenomena compatible with the models which describe those phenomena. Yet – in principle – they are unpredictable considering that the models, under the same conditions, admit different behaviours and that the new properties or phenomena can modify irreversibly the nature of the system itself (P.V. Anderson and D.L. Stein 1985; E.M.A. Ronald, M. Sipper, M.S. Capcarrére 1999; J. Goldstein 1999; E. Pessa 2006, 2008; M.A. Bedau and P. Humphreys 2008). Thus, the problem is to understand the physical and mathematical reasons why some classes of models admit a strong predictive apparatus as a consequence of their descriptions and others not, and – in this case – what evaluations and interventions are possible.

Ideal Models, Phase Space and Boundary Conditions

Predictability is a mathematical feature of a model and corresponds, all in all, to a series of physical conditions satisfied by the system under consideration. We will focus here on these conditions, by taking into consideration some essential features that constrain the building of the so-called ideal models, that is the models susceptible either of closed analytical solutions or, anyway, of approximations that ensure broad predictability, if not a local one, at least on its asymptotic states. Such wide class of models covers a quite big theoretical range from Newton Mechanics to Quantum Field Theory (QFT).

Differently from what is often stated, reductionism – i.e. the exclusive attention for constituents and explicative downward arrows – is not an essential requirement for predictability. This assumption derives from classical trajectories, but it is easy to realize that it is not correct at the example of a perfect gas in a jar. If we open the jar, the gas will diffuse in the environment; this will fix a time arrow based on entropy. However, the level of gas particles is always ruled by a reversible dynamics that does not change if we “rewind the film”: indeed, it is ruled by the Boltzmann *Stosszahlansatz*. Anyway, the evolution of the system can be represented by means of a diffusion equation applied to the whole statistic ensemble. This exemplary case demonstrates that the key to predictability is related to the interplay between different micro, meso and macro levels rather than reductionist assumptions. In this case, it is statistical physics that, by bridging Newtonian mechanics and thermodynamics, allows establishing the physics and mathematics of the phenomenon (C. Cercignani 2006; D. Lindley 2001).

The case of molecular chaos is interesting because it allows introducing some further important elements. The "identity" of particles and forces at play is always well defined and fixed. Moreover, at the microscopic level, temporal reversibility is conserved, and the environment plays the role of a very elementary and "passive" scenario. The "before" and the "after" of the phenomenon are determined by the modifications of the boundary conditions of the gas when the jar is opened. Neglecting the decisive importance of the boundary conditions has been one of the reasons, which contributed in creating a reductionist-deterministic mythology. If we forget them – and the environmental influence as well – physical laws turn into *good for all season* mere algorithms, which are, above all, indifferent to the level under consideration. That is not so! Our example reminds us that a level of analysis does not guarantee its portability to other levels. For molecular chaos, we can, at least, connect macro and micro levels thanks to the statistical interpretation of thermodynamic quantities; but this is impossible for most of the real interesting complex systems. On the contrary, emergent processes suggest that the creation of new models and the "convergence" of different approaches into a "super-model" cannot be guaranteed. The complementarity between laws and conditions is well described by D. Bohm (D. Bohm 1957) when he states that a physical law is a *frame of possibilities*. It is a matter of chance (in etymological sense) which phenomenon will take place. This may sound obvious for quantum systems and inappropriate for an aseptic world of Newtonian balls, but it is not for systems where noise, fluctuations, non-linearity and the strong variability ruling the system-environment relations make the system greatly sensitive to chance when modifications of boundary conditions occur. Complex systems can be defined as systems where the variation of boundary conditions is more important than laws, because they modify the role of the laws involved – by a drastic complexification of the phase space – and the nature itself of the "objects" into play (I. Licata 2012; I. Licata and G. Minati 2016).

There is a very general and powerful theorem by Shaw, on the behaviour of non-linear systems from the informational viewpoint (R. Shaw 1981). Suffice it to remind that the system's volume in the phase space (i.e. the space of the *behaviours* in relation to a set of observables) modifies its information content at a rate dependent on the peculiar type of non-linearity of the system. Thus, such theorem can be considered as a non-linear filiation of the Liouville Theorem. A notion deserving special attention is the system's volume. Even without any mathematical lingo, it easy to see that it is closely connected to boundary conditions. In other words, if we assume that the system/environment relationships can be clearly described by a handful of fixed parameters, it is possible to monitor the information exchange. Many interesting systems are included in this classification[1]. *Information amplifying systems* are particularly interesting for the topic of predictability. A first category is the *polynomial amplifiers,* which include the well-known dissipative structures (G. Nicolis and I. Prigogine, 1989). These systems evolve towards *self-organization* states by means of a balancing feedback between outgoing entropy and ingoing energy. Such approaches have been welcomed with great enthusiasm, as they were considered at first able to provide a general framework for the *order out of chaos* program. Soon, however, many limiting theorems (N. Kopell and D. Ruelle 1986) have showed that the complexity of these structures is rather poor. The expectations raised by H. Haken's Synergetics (H. Haken 2012) met the same destiny. Synergetics treats the emergence of some order parameters on mesoscopic regime that lead the system toward more organized states, by taking control of the microscopic variables. In spite of the interesting analogies that such scenarios have stimulated for systems very far from physics or chemistry, their importance in biology is limited and, in socioeconomic fields, purely metaphoric.

What is worth noticing is that, in all the above-mentioned cases, the hypotheses on the system's openness are such that it is possible to apply some mathematical techniques corresponding to a careful mapping of the information in the phase space. With dissipative and synergetic systems, non-linearity provides a simplified situation in the transition form the microscopic to the mesoscopic, by merging many lower level disordered dynamics into an ordered scenario. This procedure warrants high predictability. Also in the case of *exponential amplifier systems* – the chaotic system in the strict sense –, there are many different techniques to monitor the transition to chaos and the asymptotic states (at least for low dimensional systems). We find ourselves here at the extreme borders of predictability, whose essential condition seems to be the possibility to make models able to follow the system's phase space.

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[1] Maturana and Varela's emphasis on the system/environment coupling for living systems suffices to show how little this assumption can be generalized (H. Maturana and F. Varela 1980).

This condition can be met by applying a series of hypotheses related to symmetries, balancing laws and constraints about the system-environment relationship to the system. These hypotheses give way to the possibility of developing an analytical treatment with strong predictive features (S. Vakulenko 2014).

Another possibility is to use the *Quantum Field Theory* (QFT) formalism as a general framework to study formally the dynamics of phase transition with intrinsic emergence. In these systems, emergence is introduced as symmetry breaking and there new types of long-range correlations are created. Despite some interest-worthy cases, such as the *Quantum Brain* by G. Vitiello, everyone agrees that these approaches are quite far from the actual complexity of a biological system (E. Pessa 2002; G. Vitiello 2002).

Recalcitrant Systems and Configurational Variables

There is, thus, a problem in fixing some common features for *recalcitrant systems.* In fact, they defy mathematic formalization and, in any case, do not offer foothold for the traditional notion of predictability. The very concept of equilibrium state does not make sense for these phenomena. Such systems are continuously evolving, often very fast, and cannot be "zipped" within a model because their nature is essentially that of a *process.* In these cases, neither the system's nature nor the environment can be regarded as fixed and characterized by few parameters. The attention, instead, has to be focused on the kind of coupling in order to grasp the aspects that can influence the system's evolutionary characteristics, which continuously undergo a multi-level plurality of metastable adapting situations. Strictly speaking, we should no longer speak about a system-environment distinction, but about *classes of events*. In particular, there has been lately an intense work on networks – a *strategic* architecture in natural as well as artificial systems – that has shown clearly another important difference: the one between *dynamics* and *history*. In networks, the dynamic behaviours can lead to the disappearing/creating or reinforcing of some *hubs*, thus completely modifying how the system manages information (L. Barabasi 2016; S. Boccaletti *et al.* 2006; L.F. Costa *et al.* 2007). In this situation, some *frozen* components can come out; they mark the system's history in the form of stratified constraints that act on temporal scales much longer than the ones of other nodes. In a much more radical way than is the case of the gas in the jar, the system's global history develops on a different level from the individual dynamics. Moreover, such transitions do not take place near a critical point, as it happens in the traditional phase transition theory. Therefore the analysis of these systems diverges radically from the one of ideal models. The changes linked to the complex structures of the internal constraints tend to make this kind of system autonomous and its relation with environment is *highly selective*, thus introducing a *semantic dimension* in the informational flux. This is, maybe, the current strongest limit for the mathematical modeling in providing some sort of predictability. It is clear that in these situations the conservation of energy, for example, (as well as the microscopic syntactic information) is naturally compatible, but it does not say anything about the global semantic choices. Actually, this is merely true also in "simple" systems: a physical description of the energy dissipated by a computer hardware does not say anything about the characteristics and the complexity of its software. A strong evidence of the global importance of semantics has come from the study of biological neurons. It has been found that the electrical activity of the same neuron crucially depends on the global functions performed by the neuron network in which it is immersed (A. Sahasranamam *et al.* 2016).

We can realize, even from these few lines, that the majority of interesting complex systems – for example, the socio-economic ones – are *recalcitrant* to ideal modeling. This is the big challenge of the *theories of change*, which do not refer to a formal structure such as the T theory and M model – axiomatic or semi-axiomatic – of theoretical physics, but to a set of *multi-model strategies* focused on the observational and computational investigation of the events under consideration. It is not so much predictability at stake, but rather the understanding of the change factors and – above all – of the possible *intervention* on an actual process.

The good news is that the *extremely recalcitrant* systems – i.e. living in pure disorder and perfect randomness – are very rare and, anyway, not so interesting to study. An authentic casual sequence, according to Kolmogorov, is an infinite sequence that cannot be zipped in a string shorter than the sequence itself; we can only observe its evolution *step by step*. Actually, stating that for any finite sequence it is always possible to find a rule or interpolation connecting the values of the sequence does not solve any *empirical* problem. What is really interesting in a network of events is to identify *information*, at least as *meaningful* configurations for an observer. The 300-years-old implicit assumption of theoretical physics is that our descriptions correspond to something *in the World out there*. While this is surely true, we must not forget that we are the ones who *build* such descriptions. We can do it as long as the systems ruled by ideal models are *simple*. The challenge is raised by the systems between order and disorder, where «at the edge of chaos, the boundaries of change fluctuate endlessly between a sluggish status quo and the anarchy of perpetual destruction» (B. Cohen 1997). In these systems, it is almost always impossible to bridge the microscopic and the macroscopic levels in a simple way; nonetheless, configurations emerge that make possible to identify some mesoscopic variables which mediate between the two levels and characterize the metastable state of the change. These are not "observables" in a traditional sense, but rather a choice among patters individuated by an observer as the expression of change. Here, we will focus neither on the available analytical tools nor on the formidable problems of quasi-ergodicity (C.S. Bertuglia and F. Vaio 2005; C.C. Moore 2015); we will try instead to fix some conceptual aspects relevant for the study of these systems.

Metastructures and Big Data Forecasting

Metastructures are a general framework for the study of change. They answer the question, common to cognitive sciences (observer) and Physics (observed): *how can a change in a process be detected?* Since the very beginning, an observer is called to choose what to observe and how to do it, by trying to spot interesting characteristics which occur quite regularly. This is the notion of *intuitive* emergence, according to the famous classification by Crutchfield (J. Crutchfield 1994). However, considering that we are dealing with processes that are quite far from ideal models, we can detect only their emergence, because there aren't any available mathematical structures to study the dissipative forms or intrinsic emergence. Thus, the investigation of metastructures is not only focused on emergent features and how a system changes objectively, but also on the dynamic relationship between an observer and an observed system (for the technical aspects see I. Licata and G. Minati 2013; G. Minati and I. Licata 2013b).

The procedure is based on building one or more *mesoscopic vectors*, whose values are chosen by an observer. In the "pedagogic" flock example, the typical values can be velocity, directions, habits, distance – maximum and minimum – between two "constituents", the instantaneous value in a time interval of the flock surface of volume, and so on. In this way, it is possible to draw information from the system to detect change, its phases, sequences and modalities. For example, what elements play the same role at different instants or different roles at the same instant. In other words, the mesoscopic vector is an active "grid" that probes the system by means of computational procedures in search of meaningful signals for the observer/model builder. Such scenario offers some reflections about *Big Data*.

In Jeff Jonas' words (J. Jonas 2012), it is true that *data did not become big overnight*, and we can add that science has always strongly needed data not only to build theories, but to correct and delimit them, as well as to make them operative. The Navier Stokes equations would just be a conceptual scenario for meteorologists, if it were not for a thick network of sensors, and it surely does not depend on their mathematical status of *Millennium Clay Problem*! Actually, the debate about Big Data has become hot, especially as far as its epistemological and ethical implications are concerned (D. Cardon 2015; V. Mayer-Schöberger and K.N. Cikier 2013). Chris Anderson's provocative paper for Wired (C. Anderson 2008) has triggered many relevant answers. One of the most relevant answers is Calude and Longo's one (C. Calude and G. Longo 2016), which shows that in general, and for very good mathematical reasons, data do not speak for themselves, and most of the correlation are spurious. It happens only if we look at correlations as "objective", and – above all – if we limit our research to correlations! If we accept that this is a brand new field, and that data have first to be investigated in order to speak, then we will find ourselves in a world of possibilities similar to the one described by Ermanno Bencivenga:

> So there you have it. Big Data enthusiasts are (unwittingly) advocating a new definition of what it is to know. Their agenda is (unwittingly) semantical. Except that it is not worked out, and any attempt at developing it in the semantical terms that have been current (and antagonistic) for the past two millennia is hopeless (E. Bencivenga 2017).

If we try to look beyond the simple correlations and consider Big Data as something more than a passive object of multivariate statistics, we can see an extraordinary number of patterns with formidable theoretical implications, such as the power law, non-Gaussian behaviours, scenery of criticality, fat fractals, and so on[2]. This does not mean that the processes under consideration can-

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[2] For a general textbook on these techniques see J.P. Sethna 2006; for a class of exemplary problems see S.V. Buldyrev *et al.* 2010.

not be included within the old theoretical boundaries; but that we have to do theory in progress, reframing the historical baggage within a new style of work which involves testing heuristic hypotheses following the process, according to an abductive line.

The current classification of Big Data in the so-called 6Vs model (volume, velocity, variety, veridicity, variability and value) is still much too tied to the quantitative data flux and to an objectivist conception. It is advisable, and greatly plausible, that the structures *analytics* (descriptive/predicative) point more and more towards the search of the *secret life* of Big Data. In order to do that, we have to realize that analytics directly express the specific meaning that the process has for the agent observing it. It is not a matter of building up the robot-scientist, dear to the old AI, but to acknowledge that, in the same way as high speed and the extremely small changed theoretical physics, the extreme complexity will modify our concept of *Physis* in an even more radical way.

Conclusions

In the history of theoretical physics, predictability has established itself within deterministic explanations, and then it has extended, in its different forms, to the class of ideal models, which allow a univocal description of a system. In complex systems at high emergence, univocity breaks down and the descriptions become plural, thus setting an extreme limit for predictability in the strict sense. Many strategies and tools for *forecasting* a process have been developed, which are connected to the meaning that a class of events has for the observer or agent. However, in many complex systems more than an abstract forecasting, it is the actual awareness about the possibilities among which a guess can be made that better solves the problem. This strengthens the insight by Bruno de Finetti (1906 - 1985):

> Knowing how things will go, as if they were occurring on their own [...] it is a problem of decision, not prevision […]. Shouldn't the exceptional dimension of our empiric world lead to a completely new awareness? How can we expect that logic chains end with certainties, just like a good old syllogism? (B. de Finetti 1972).

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Determinism and Stochasticity in Mathematical Modelling for Cell Migration

Luigi Preziosi

Bi-stability and Multi-stability

Cell behaviour and eventually cell fate is determined by the chemistry inside the cell, which involves thousands of proteins functionally connected through promoting and inhibiting reactions. Their alternative over-expression or under-expression determines the actions undertaken by the cell: activating to produce some signals or products, moving or staying attached to the environmental substratum, undergoing mitosis or going to quiescence, differentiating or not, surviving or committing suicide, and so on.

As can be noted, the main common characteristic of the just mentioned processes is that hesitation is not allowed: a cell cannot do things by halves. A cell will either divide or not. It cannot "partially divide". A heart muscle cell will either contract or not because it is useless to have a weakly beating heart. A neuron will either fire an electric impulse or not. The commitment is so strong that in many cases if a decision is taken the cell will persist in it with very little space, if any at all, to reconsideration, even if in the meantime the environmental conditions have changed. A crucial role in embryogenesis is played by the organisation and the related collective movement of cells to the right places. This is a very fascinating subject that has attracted the attention of a lot of researchers, also because it represents a benchmark to understand cell migration processes that are relevant for important physiological functions, such as immune response and wound healing, and in the pathological development of several diseases, such as the diffusion of cancer metastasis.

Regarding cell migration, a very nice visible example of the type of commitment mentioned above is given by the experiment performed by Verkhovsky et al. (A.B. Verkhovsky, M. Svitkina, G.G. Borisy 1999) on a fragment of the cytoplasm of a keratocyte. Initially, the part of the cell (that does not contain a nucleus) is immobile and non-polar. However, it is enough to mechanically perturb it with a micro-pipette to spontaneously trigger a polarization and give rise to a transition to a migratory state that has the characteristic speed and the shape of a whole keratocyte. Even though the mechanical stimulus has ceased and the environmental conditions are the same as when the cell fragment was standing still, the motion will continue until the available energy exhausts. This represents a go decision in response to a temporary mechanical stimulus.

Referring to Te Baekhorst et al. (V. te Baekhorst, L. Preziosi, P. Friedl 2016) for a more detailed biological discussion, from the biological point of view it is well known that the proteins present in the cells react with each other through a network of interactions that it is useful to sub-divide in several functional modules. Each chemical module reacts to some inputs that can come either from the environment through suitable receptors and interface modules or from other chemical modules. In this way, a "cause" will determine an "effect". However, the relation between cause and effect is not a linear one, that is, it is not true that doubling the input stimulus gives rise to a doubling of the output response. In some cases the input-output relations lead to nonlinear behaviour characterized by smooth phase transitions. But in most cases, they might not even be continuous. They might present jumps corresponding biologically to an all-or-none response like that happening in the keratocyte fragment described above.

From the point of view of dynamical systems, the qualitative description above can be schematized and generalized saying that each module is characterized by the presence of chemically-activated switches due to the presence of feedback loops. In fact, it can be shown that the presence of mutually inhibitory feedback loops and positive feedback loops might generate on-off responses. Referring to the top inset of **Figure 1**, the basic mechanism is very simple: if A is over-expressed because of the stimulus S, it will inhibit B. The presence of B would control the amount of A, but if it is inhibited, then A can grow even more because of the lack of its inhibitor.

Referring to **Figure 1**, the main characteristic brought in the chemical dynamics is the fact that the equilibrium of the system is not unique and it is not possible to progress smoothly from a situation of under-expression of a protein to a situation of over-expression of the same protein: Vice versa, there are jumps (represented by the grey arrows in **Figure 1**) in the response that might be eventually related to transitions in cell behaviours, e.g., neuron firing, heart beat, polarization or loss of polarization, cell stemness or differentiation, epithelial-mesenchymal transition and viceversa, ameboid-mesenchymal transition and viceversa, go-or-grow, attachment to or detachment from the substratum, and so on.

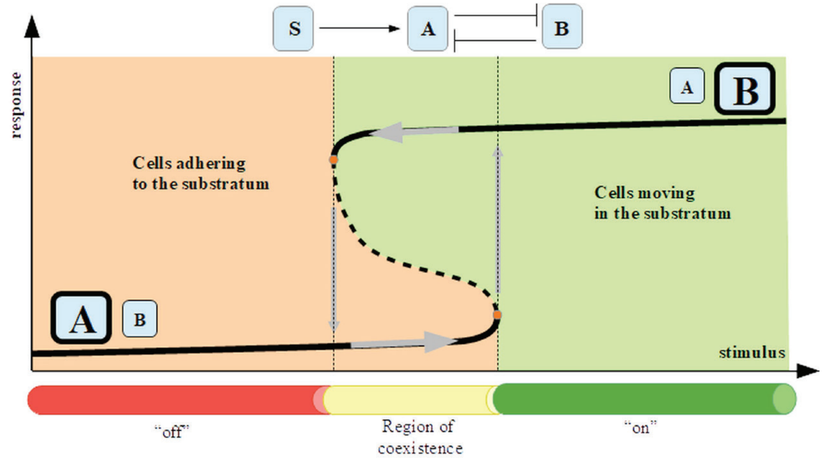

Figure 1 – On the top a schematization of a mutually inhibitory feedback loop involving two molecules B and A that is stimulated by S. The lower curve corresponds to an equilibrium with over-expression of A and under-expression of B. The upper curve to the opposite situation. Red circles indicate the turning points dividing stable equilibria (full lines) from unstable equilibria (dashed line). The orange and pale green regions depict the basins of attraction of the two equilibrium configurations.

This situation is named bi-stability because of the presence of two equilibrium configurations in the same range of stimulus named *region of co-existence*, coloured in yellow in **Figure 1**, but can be easily generalized to multi-stability when even more equilibrium configurations might be present for the same value of the parameter referring to the stimulus. The region of co-existence is characterized at its extrema by the presence of two turning points such that following the curve the equilibrium ceases to be stable to become unstable. In the region of co-existence, each equilibrium configuration has its own region of attraction, so that if the system falls in the region of attraction of an equilibrium configuration it will move toward it and if it falls in the other region of attraction it will move toward the other equilibrium configuration. This implies, for instance, that the output will be also determined by the history of the stimulus. Still referring to **Figure 1**,

(i) If the stimulus is increasing up to the co-existing region from a situation with over-expression of the protein A, it will be still over-ex-

pressed till the limit to the right of the region of co-existence is reached. After that it will suddenly jump to the equilibrium situation with over-expression of the protein B (following the upward arrow);
(ii) Vice versa, if the stimulus is decreasing down to the co-existing region from a situation with over-expression of the protein B, it will be still over-expressed till the limit to the left of the region of co-existence is reached. After that it will suddenly jump to the equilibrium situation with over-expression of the protein A (following the downward arrow).

This means that, like the keratocyte fragment, it is possible to have cells behaving differently for the same value of the stimulus depending on the recent history of the system, i.e., whether the chemical module started from a situation with an over-expression of the protein A or of the protein B.

In its simplicity, this very simple dynamical system contains the essence of the phenomenon and illustrates how the realization of a system can drastically depend on a simple change in the history of stimuli, if it gets too close to some critical values.

For sake of completeness, we remark that in biological systems another important characteristic of such stimulus-response dynamics can be observed. Namely, as long as the level of stimulus stays away from critical values, the response of the system is almost independent from the level of the stimulus. This leads to a sort of robustness of the system that is another important feature of biological systems.

So, in presence of such dynamics it is living dangerously close to criticality that can dramatically amplify the effect of a contingent event. Staying away from criticality will lead to qualitatively the same response regardless of the environmental stimulus.

Determinism and Stochasticity

In principle, in the discussion above, if the history of the stimulus is completely known, the state of the system could be accurately predicted. So, generalizing, even though the path of cell life might be characterized by a sequel of forks and the final behaviour will depend on what happens at such intersections, the knowledge of the history of the stimulus would lead to a fully deterministic response. However, knowing the entire history of the system is impossible and so we are left with an uncertainty, which can have big effects if at some point the cell history has come close to criticality. We remark that this uncertainty is a *deterministic uncertainty* because casuality has not entered the game yet.

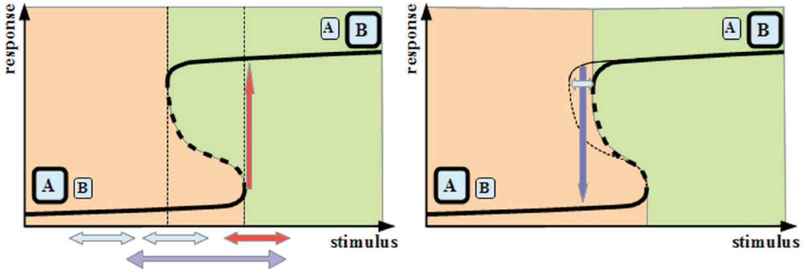

Figure 2 - On the left, effect of uncertainty in the environmental stimulus. If the system is in the equlibrium with over-expression of A the two pale blue actions will barely give any effect. The red one might cause a jump to a state with over-expression of B. The blue lower arrow might give rise to histeresis loops between the two states. On the right, the effect of randomness in the response parameters.

On the other hand, biological phenomena are characterized by the lack of microscopic determinism, making the situation more complicated. In fact, several sources of uncertainties can be identified. The first one has a biological origin and consists in a randomness present in the signal reception or in its transmission to the chemical module inside the cell. In this case, nothing happens if the basic level of stimulus is far from the critical values and the randomness is not too strong (see the leftmost arrow in **Figure 2** or even the central one if the system is in the equilibrium state with over-expression of A). On the other hand, if the stimulus is dangerously close to the value corresponding to the turning point, the stimulus strength can stochastically fall beyond the co-existence region changing dramatically the cell response (see the red rightmost arrow in **Figure 2**). Actually, referring to the lower arrow, a sufficiently strong randomness might even cause the system to jump randomly and hectically between the two extreme configurations.

The second source of randomness is introduced by the modelling procedure used in both biology and mathematics. It is related to the need of minimizing the number of possible modules from a large number of combinations and of identifying which are the key mechanisms. This modelling process aims at simplifying reality while retaining its main features. The strategy consists in monitoring which state variables have the strongest effects on the output of the model. This discriminates important from negligible connections between the main modules and simplifies context-dependent input-output relations. However, as a shortcoming, the simplification procedure introduces stochastic noise into the system, which acts as a random perturbation since not all the causes (input) determining the effects (output) are taken into account. In fact, eliminated variables retain certain degrees of background activity and may affect the outcome in unpredictable ways, particularly when a supposedly weak interaction is relevant. In this category we can also include the fact that unfortunately not all reactions and reaction kinetics parameters are known.

The third source of randomness consists in a stochasticity in the response parameters, which graphically corresponds to perturbing and changing the curve in **Figure 2** (right). This can be for instance caused by the fact that the parameters themselves depend on other variables, which might be very easily influenced by other chemical modules or by the activation/de-activation of signalling receptors. The behaviour is then not very different from the ones above, though in this case it is the curve that randomly moves, rather than the environmental stimulus. Actually, in real situations they are both affected simultaneously by random behaviours and contribute to the evolution.

The just mentioned situation is the simplest example of how the interaction of different chemical modules can generate a combined response according to the ensemble of input types, rather than according to a single input. In reality the number of chemical modules that interact to determine, for instance, the migration mode of a cell, is not at all small and each one is influenced by the activation of several receptors with each element affected by stochastic noise. Hence, one can speak of multi-stochasticity. In addition, migration mode is characterized by a joint and coordinated combination of different cell properties.

Summarizing, referring to **Figure 3**, the cell is subject to all sorts of environmental input types that feed on a receptor repertoire to give rise to a *reception fingerprint*, that includes the activation of ion channels and of metalloproteinases, the expression of adhesion molecules, such as integrins and cadherins, of Rac1 and Rho/Rock related receptors, of several growth factor receptors. The receptor fingerprint acts like a safety-key of a secret code, activating several protein cascades downstream that are interlinked giving rise to an integrated cell response. The output of this process eventually determines, among other things, the final migration mode.

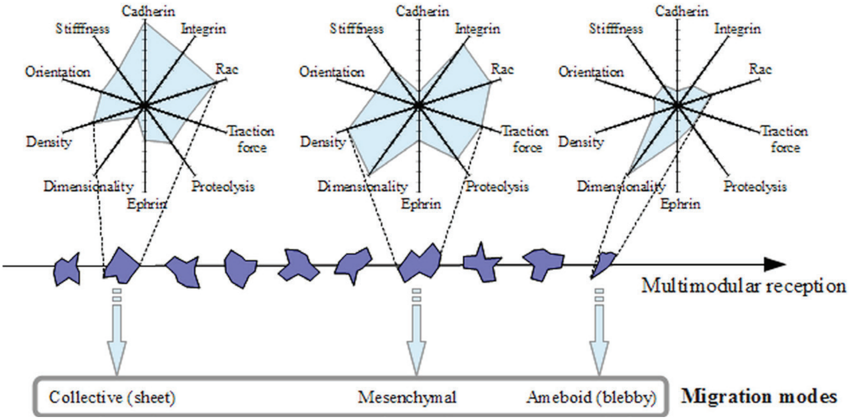

Figure 3 - Schematization of the link between the ensemble of signal inputs and migration mode. The wind-rose diagrams on the top depict the intensity of several external signalling that form a sort of receptor fingerprint. Different migration modes correspond to different fingerprints, i.e. different ensembles of inputs.

It is then evident that any alteration along the information processing cascade, including environmental cues, their perception by the cell, and the information processing inside the cell, might yield different realizations and even a possible range of varying migration outputs for the same basic set of parameters. The overall output can then be described by a probabilistic distribution characterized by a mean probability.

Modelling cases

As an example, we consider the process of tubulogenesis. This is a spontaneous phenomenon regarding some cell lines that, by migrating and aggregating, give rise to the spontaneous formation of vascular networks from dispersed distributions of cells. Using an individual cell-based model (M. Scianna, L. Munaron, L. Preziosi 2011), it is possible to study the relationship between the proper formation of a vascular network and some morphogens such as vascular endothelial growth factor (VEGF) and calcium-dependent downstream pathways, which involve a number of intracellular messengers, such as nitric oxide and arachidonic acid. It was found that interfering with such pathways might prevent the formation of a proper vascular network with dramatic consequences because of the lack o a proper percolating structure (see **Figure 4**). It is also possible to rank the importance of the different aspects involved in the process. This, for instance, highlights that VEGF and calcium are more relevant than nitric oxide and arachidonic acid.

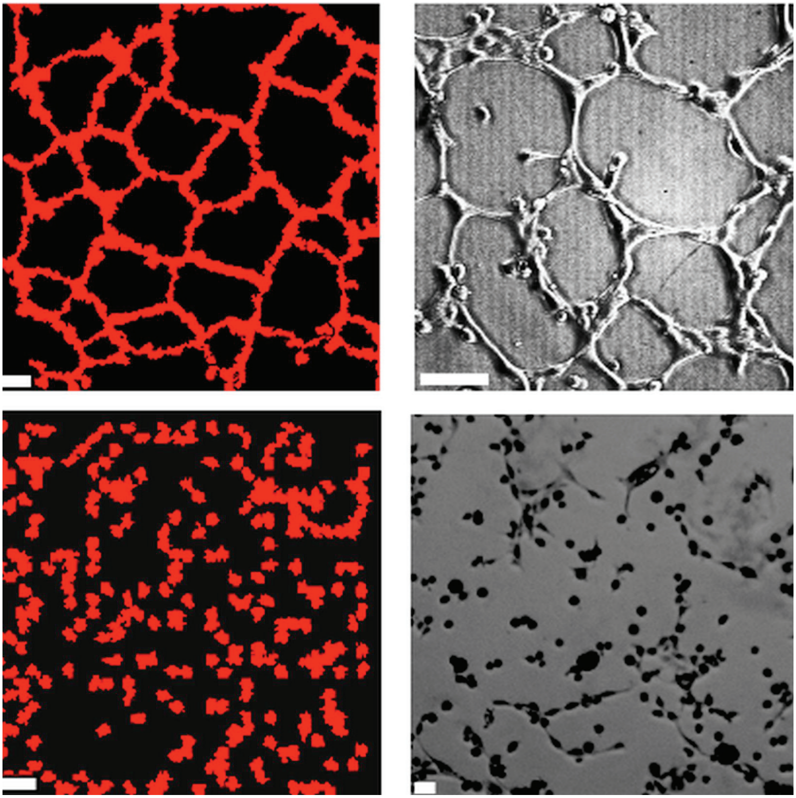

Figure 4 – Tubulogenesis in physiological conditions (top) and interphering with VEGF and the related downstream calcium pathways (the result of the experiments are given on the right and those of the mathematical model to the left).

As another example, consider the migration of a cell in a micro-channel, mimicking the real motion of a cell in the network of fibers it lives in. Experiments show that in such situations whilst the cytoplasm is very flexible and is able to accommodate nearly any pore size, the cell nucleus, being the stiffest organelle of the cell, has difficulties in being deformed. Hence, if the pores in the extracellular matrix are big enough the cell is able to migrate in it, possibly deforming the nucleus, but if the network of fibers is too tight, then even if the cell protrudes in the extracellular matrix, the nucleus lags behind and can not be deformed enough to pass through the narrow pores, blocking cell motion.

Using continuum mechanics methods (C. Giverso, A. Grillo, L. Preziosi 2014; C. Giverso, A. Arduino, L. Preziosi 2017) it is possible to study the deformations of the nucleus and of the cell, the energy required to achieve such deformations and the work that traction forces can perform. On this basis, it is possible to identify a criterion of penetration based on an energetic argument. The criterion involves a mechanical parameter (namely, the ratio of quantities related to the adhesion forces exerted by the cells and the stiffness of the nuclear membrane and of the genetic material within the nucleus) and a geometrical parameter (namely, a function of the ratio of the pore size of the fiber network with respect to the nucleus diameter). In particular, it was demonstrated that if the size ratio is too restrictive, then the cell cannot penetrate into the fiber network. Nevertheless, keeping the same geometrical characteristics, cell clones with higher traction abilities or softer nuclei might be able to invade the surrounding extra-cellular environment and then give rise to the formation of metastasis. Hence, we have a threshold-like behaviour according to some geometrical and mechanical cell parameters. In principle, the criterion is deterministic, but stochastic behaviours within the cell population or in the environment might generate a probabilistic output, even a non-vanishing probability of the formation of metastases for mean parameter values that would imply no invasion.

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On the Nature of Natural Selection

Fabio Sterpetti

1. Introduction

The causal nature of natural selection has been a very debated issue in the last years in philosophy of biology, and it is still a controversial issue. Some philosophers, known as *statisticalists*, claim that the concept of natural selection, as it is normally presented in population genetics, is statistical in character and cannot be construed in causal terms (see e.g. M. Matthen and A. Ariew 2009; D.M. Walsh, T. Lewens, A. Ariew 2002; D.M. Walsh, M. Ariew, A. Matthen 2017). On the contrary, other philosophers, known as *causalists*, argue against the statistical view and reaffirm the causal interpretation of natural selection (see e.g. E. Sober 1984; R. Millstein, R.A.J. Skipper, M.R. Dietrich 2009; J. Otsuka 2016a, 2016b).

Statisticalists started questioning the causal interpretation of natural selection because «most, if not all, principles of evolutionary theory [...] are expressed by purely statistical terms such as variances or covariances» (Otsuka 2016b, p. 248). In order to avoid any misunderstanding, it is worth specifying that the debate between causalists and statisticalists *is not* about whether genetic variations in a given population are due to causal factors. No one doubts this fact. The debate between causalists and statisticalists is about whether or not the explanations provided by population genetics are genuine causal explanations.

There are many issues involved in the debate between causalists and statisticalists. It is impossible to give here an exhaustive treatment of such debate. We will present just some aspects of the debate between statisticalists and causalists by focusing especially on genetic drift (for a survey on drift, see R. Millstein 2017). Indeed, a key element in the debate between causalists and statisticalists is the dispute on the nature of drift and whether drift is really distinguishable from natural selection (see e.g. Millstein, Skipper, Dietrich 2009; M. Matthen 2009, 2010; V.J. Luque 2016). Drift is supposed to be a sort of measure of contingency in evolution. Thus, drift can be thought as affecting predictability in evolutionary biology. If drift is a cause of evolution, uncertainty in population genetics is due to some processes that make a population deviate from predicted outcomes. But while causalists see drift as a distinct natural phenomenon originated by some set of physical processes, statisticalists claim that there is no process that accounts for this uncertainty, since the uncertainty lies not in the events but in the fact that natural selection in population genetics is modeled by a statistical theory.

This article does not aim at taking side on the debate between statisticalists and causalists. Rather, it aims to illustrate the debate between causalists and statisticalists in order to present a challenge that statisticalists need to address if they wish to take a naturalist stance. Indeed, the debate on the nature of natural selection intersects the more general debate on whether or not non-causal explanations, and more precisely mathematical explanations, are genuine scientific explanations, and so explanations that may be acceptable from a naturalist viewpoint. Since evolutionism is essential for a naturalist perspective to be defined as such (R.N. Giere 2006), and natural selection is central to evolutionism, an inquiry on what kind of explanations is provided by population genetics is crucial to assess the coherence of any naturalist stance.

2. The Force Analogy

To better appreciate the criticisms moved by statisticalists to the traditional view, it may be useful to briefly present one of the most controversial formulation of this view, namely the so-called “Force Analogy” (see Luque 2016; C. Hitchcock and J. Velasco 2014). The idea is to present evolution as if it were driven by forces that behave analogously to the forces in Newtonian mechanics. The most developed use of the Newtonian analogy to illustrate evolutionary theory is made by Sober in his famous book *The Nature of Selection* in 1984: «In evolutionary theory, the forces of mutation, migration, selection and drift constitute causes that propel a population through a sequence of gene frequencies. To identify the causes of the current state […] requires describing which evolutionary forces impinged» (Sober 1984, p. 141).

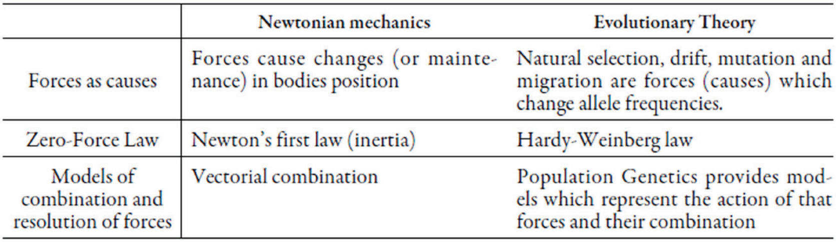
The force analogy has been widely used to expose the causal structure of the evolutionary theory. More precisely, three main features of evolution have been characterized by using the Force Analogy to interpret population genetics in causal terms: (1) evolution is driven by forces (namely: natural selection, drift, mutation, and migration) which act (and so they are causes) by modifying allele frequencies; (2) the Hardy-Weinberg principle is the “zero-force law" in population genetics; (3) population genetics gives us models that show how evolutionary forces act and combine with each other. The Force Analogy mainly rests on the idea that as forces in mechanics are usually taken to be causes of motion, so evolutionary forces in population genetics should be taken to be causes of change in gene frequencies.

Consider (2), the analogy between the Hardy-Weinberg principle in population genetics and zero-force law in mechanics. The adoption of a zero-force law tells us how the system would behave if forces were not acting on it. For instance, the first law of Newtonian mechanics functions to establish that a body continues in its state of rest, or of uniform motion in a straight line, unless it is compelled to change that state by forces impressed upon it. Many authors claim that the Hardy-Weinberg principle can be regarded as the zero-force law in population genetics. According to the Hardy-Weinberg principle, in a diploid and infinite population, where there is random mating, genotype frequencies will remain stable if no cause acts on it, since Mendelian inheritance alone cannot change the allele frequencies. In this view, the equation:

$$p^2 + 2pq + q^2 = 1$$

can be interpreted as representing the Hardy-Weinberg principle. Consider one locus with two alleles, *A* and *a*. *A* has a frequency p, while *a* has a frequency q. The values p^2, 2pq, and q^2 represent the proportions that *AA*, *Aa*, and *aa* will maintain (respectively) in the population from generation to generation (Millstein, Skipper, Dietrich 2009).

Luque has clearly summarized how the Force Analogy has been exploited through the following scheme:



	Newtonian mechanics	Evolutionary Theory
Forces as causes	Forces cause changes (or maintenance) in bodies position	Natural selection, drift, mutation and migration are forces (causes) which change allele frequencies.
Zero-Force Law	Newton's first law (inertia)	Hardy-Weinberg law
Models of combination and resolution of forces	Vectorial combination	Population Genetics provides models which represent the action of that forces and their combination

Figure 1. Drawn from: Luque 2016, p. 398.

But the Force Analogy implies some disputable consequences. Two of the most relevant difficulties that the supporters of the Force Analogy have to face are the following: (a) if we take the Force Analogy seriously, we have to consider evolutionary forces as *distinct* forces, i.e. forces amenable to be separately defined and investigated; (b) if evolutionary forces are regarded as causes of change in gene frequencies, then they should be able to *directly* modify gene frequencies.

3. Statisticalists' Criticism on the Force Analogy

Let us consider firstly the second difficulty described above, i.e. (b) proving that evolutionary forces modify gene frequencies directly. The difficulty of supporting such a claim derives from the fact that such claim seems to imply a disputable ontological commitment. For example, Sober holds that natural selection is evolution due to heritable variation in fitness. In this line of reasoning, an evolutionary force such as selection would be not merely the sequence of events that lead from variation in heritable fitness to a new gene frequency, but a force that appears when organisms have heritable differences that lead to differential reproductive success (Matthen and Ariew 2009). In this view, evolution does not occur merely because types of organism reproduce and die in differing amounts. Rather evolution is driven by natural selection. If selection is a force in the same way in which a Newtonian force is a force, then we should assume that it is natural selection that *acts* on gene frequencies.

According to the statisticalists, this construal of selection is unacceptable, since it implies a sort of reification of the concept of natural selection, which illegitimately leads to an inflation of our ontology. Matthen and Ariew make clear this point by illustrating how the causal diagram of evolution by natural selection diverges depending on whether one adopts Sober's or their own interpretation of natural selection. According to Sober, evolution by selection would go something like this: «heritable variation in trait T → selection of magnitude proportionate to variance in heritable fitness due to heritable variation in T → birth and death of animals → evolution» (Matthen and Ariew 2009, p. 206). On the contrary, according to Matthen and Ariew, the causal diagram goes like this: heritable variation in trait T → birth and death of animals → evolution. No extra cause is needed to account for how gene frequencies change at the population level besides those natural events that are responsible for the survival or the death of organisms at the individual level.

So, according to the statisticalists, the Force Analogy is unacceptable because natural selection in population genetics does not really cause any variance in gene frequencies, it is just a statistical abstraction of the events that are the real causes of gene frequencies, i.e.: births, deaths, and matings, which occur at the individual level. Natural selection «is ontologically derivative on individual-level events such as births, deaths, and mutations [...]. It occurs in ensembles as a mathematical consequence of events that involve members of those ensembles» (Matthen and Arew 2009, p. 216). In this view, natural selection in population genetics should be merely regarded as an abstract mathematical description of the accumulation of reproduction events.

4. Drift

Let us now consider the first difficulty mentioned above (section 2) that causalists have to face, i.e. (a) proving that evolutionary forces are distinct forces. The difficulty of supporting such claim becomes particularly evident if one considers drift. The question is: Is drift *really* an independent cause of evolution? More precisely: Can drift be really distinguished from natural selection? This issue is deeply related to the criticism moved to the causalist view illustrated in the previous section. Indeed, if one accepts the traditional view, each evolutionary force has to be regarded as an independent "fact of nature". On the contrary, if one adopts statisticalism, one cannot neatly distinguish natural selection from drift. To see this, it may be useful to recapitulate what drift is. In population genetics, drift is usually understood as departures from expected gene frequencies that arise in finite populations. Briefly, when one kind of individuals is better endowed than another for reproduction, from a statistical viewpoint, one might expect that the better endowed kind will increase, but this expectation can be frustrated by actual outcomes. Departures from expected values are what population geneticists call "drift" (Matthen 2010).

An analogy with coin tossing may be of use to illuminate random drift. If one has a fair coin and one tosses it ten times, the expected outcome is 5 heads and 5 tails; but it well may be the case that one gets 6 heads and 4 tails or 8 heads and 2 tails. If one increases the number of tosses (say one tosses the coin 1,000 times), the frequencies obtained will approximate to the expected outcome. If one increases further the number of tosses (say one tosses the coin 1,000,000 times), the frequencies obtained will approximate to the expected outcome even better.

So, we can say that the magnitude of this sampling error (i.e. drift) is inversely proportional to sample size: the smaller the population, the bigger the deviation from the expected outcome.

Coming to population genetics, the basic model of drift is the Wright-Fisher model, a binomial sampling process in a diploid population in which a new generation is formed as a sample of $2N$ alleles. The transition matrix for i copies of allele A at generation t to j copies of allele A at generation $t + 1$ is given by:

$$P_{ij} = \binom{2N}{j}\left(\frac{i}{2N}\right)^{j}\left(1-\frac{i}{2N}\right)^{2N-j}$$

It is easy to see that the transition matrix is determined only by the initial allele frequencies and the population size N. Since in population genetics scientists are usually interested in allele frequencies, we define:

$$f_t = \frac{i}{2N}$$

to be the frequency of A in generation t. Using the properties of the binomial distribution, we see that:

$$\mathbb{E}\left[f_{t+1} \mid f_t = f\right] = f$$

$$\mathrm{Var}\left(f_{t+1} \mid f_t = f\right) = \frac{f(1-f)}{2N}$$

So, according to this model, while average allele frequencies will remain constant from one generation to the next one ($\mathbb{E}$), since there are no other evolutionary forces at work, the actual allele frequencies will change at a rate that is inversely proportional to population size (Var). These fluctuations in allele frequencies constitute drift. As the Wright-Fisher model suggests, drift is stronger in smaller populations. And this explains why drift is often compared with coin tossing (Luque 2016).

Turning back to the issue at stake, i.e. how drift should be interpreted, for the causalists drift is a natural fact or process in which heritable differences between entities are causally irrelevant to differences in reproductive success. For instance, C. Stephens (2004) suggests that drift acts on populations, causing sampling error. In this view, drift is a force with a greater strength in small populations. Consider again the coin tosses example: according to Stephens, drift «plays a larger role in flipping a fair coin 10 times than it does in flipping a coin 10,000 times» (Stephens 2004, p. 556). On the contrary, according to the statistical interpretation, drift is a departure from expected values attributable to the statistical uncertainty that is inherent in any series of births, deaths, and matings. It is not a separate natural process over and above the individual-level causes of such events. The only relevant feature in drift explanations is population size. And, in this perspective, it is just this feature that distinguishes selection explanations from drift explanations.

5. Drift and Predictability

It is important to appreciate the different consequences that these two interpretations of drift imply with respect to the issue of predictability in evolution. Drift is usually supposed to be connected to the uncertainty of evolutionary outcomes (Matthen 2009). Indeed, genetic drift is often associated with randomness (A. Wagner 2012), and randomness is deeply related to unpredictability (A. Eagle 2005). Nevertheless, despite in both causalists' and statisticalists' interpretations of drift, drift can be regarded as deviation from prediction, causalists and statisticalists provide radically divergent answers to the following question: What, in the ultimate analysis, is the source of drift? In other words, if drift is deviation from predictions, then «a fundamental understanding of drift requires one to give an account of the source(s) of this deviation» (Ramsey 2013, p. 3912).

According to the causalists there are natural facts or processes that are responsible for the deviation of actual frequencies from predictions. Drift, in this view, is an objective feature of the world, and the source of drift are objective (i.e. independent from the epistemic subject) worldly processes or facts that make frequencies deviate from their expected values. Thus, the source of drift should be amenable to scientific inquiry as any other natural phenomenon. On the contrary, according to the statisticalists, drift is a merely statistical fact, i.e. it is a mathematical consequence of the mathematical tools that we use to model genetic dynamics. This means that in this view the source of drift is in some sense epistemic. Epistemic here does not imply "subjectiveness" or "arbitrariness". Mathematics is widely held to be objective. Nevertheless, in natural sciences mathematics is usually seen as a tool used by the epistemic subject to model a worldly phenomenon. So, epistemic here has to be understood as implying that the source of drift is not the worldly phenomenon itself, but the tool used to model such phenomenon. Drift is in a sense a feature of the model, not of the world. For instance, according to Walsh, causalist models aim at «carving evolutionary change at its causal joints», while in the statisticalist view «one and the same episode of population change could conceivably be explained exclusively as selection *or* exclusively as drift», depending on how we choose to describe such episode, since selection and drift are «ways of characterising population level change *relative to a description*» (D.M. Walsh 2013, p. 303).

These different ways to construe drift have implications also for how one explains one's failure to predict evolutionary outcomes. If one takes the causalist view, then one can see deviation from prediction as due to a lack in one's knowledge of some relevant aspects of the population one wishes to model. If actual frequencies deviate from predictions, there must be somewhere in the world a process which is responsible for such deviation. Obviously, we are not denying that lack of knowledge of some relevant aspects in actual observations or experiments may be unavoidable *in practice*. What we are focused on here is what *in principle* can be regarded as the source of predictability or unpredictability in population genetics. In the causalist view, predictability or unpredictability in evolution would be a matter of complete knowledge or lack thereof. On the contrary, if one takes the statisticalist view, there is no way to fill in the gap between predictions and actual frequencies by enlarging one's knowledge of relevant aspects of a given population, because such deviation derives from the fact that one compares a finite actual population with predictions made by using models that deal with infinite quantities to calculate their outcomes, i.e. predictions. In infinite populations drift cannot occur (Ramsey 2013). For instance, Strevens states that «in an infinite population, there is no drift», and this is the reason why biologists so often develop their models assuming infinite populations. Indeed, drift «cannot be set to zero directly, […], but it can zeroed indirectly by taking population size, another parameter in stochastic models, to be infinitely large» (M. Strevens 2017, p. 6). Since there is wide consensus that there cannot be actual infinite worldly elements of any kind, it will not be the case that drift will fail to emerge when one deals with actual populations. Predictability or unpredictability in this view is not merely a matter of complete knowledge or lack thereof, neither is it a matter of developing better, i.e. more accurate, models; rather, it is a matter deeply related to some intrinsic feature of the very tool that allows us to make predictions in the first place, i.e. mathematics.

6. Population Genetics and Non-Causal Explanations

It is important to clarify some points in order to avoid any misunderstanding. First of all, it is worth stressing that statisticalists do not deny that population genetics models explain some relevant and objective aspects of the modeled population. They agree that those models do that. The point is that statisticalists deny that population genetics explanations are *causal* explanations. As we already noted above, this claim is mainly motivated by the fact that most, if not all, «principles of evolutionary theory […] are expressed by purely statistical terms such as variances or covariances» (Otsuka 2016b, p. 248).

To better see this crucial point, consider Price's Equation and Fisher's Fundamental Theorem of Natural Selection (FTNS). Price's Equation is a central result in population genetics, and can be written in the following form:

$$\Delta\bar{z} = \mathrm{Cov}\,(\omega, z) + E_w(\Delta z)$$

where $\Delta\bar{z}$ is the change in average value of a given character from one generation to the next; $\mathrm{Cov}\,(\omega, z)$ represents the covariance between relative fitness (ω)[1] and the value character (z), i.e. the action of selection; and $E_w(\Delta z)$ represents the fitness-weighted average of transmission bias Δz, which is defined as the difference between the character value of the i^{th} entity (zi) and the average for its offspring ($\bar{z}$) (S. Okasha 2006, sec. 1.2). The FTNS can be regarded as a special case of Price's Equation. Indeed, Price's Equation tells us exactly how much of a character will exist in the population in the next period. If we let the character equal fitness itself, then we get Fisher's theorem:

$$\Delta\bar{w} = \mathrm{Var}_{add}(g)/\bar{w}$$

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[1] The relative fitness of the i^{th} entity (ω) is defined as the fitness of the i^{th} entity (w_i) divided by the average fitness of the population ($\bar{w}$).

which can be read as: the change in average fitness from one generation to another ($\Delta\overline{w}$) equals the additive genetic variance in the first generation ($\mathrm{Var}_{\mathrm{add}}(g)$), divided by mean fitness ($\overline{w}$). The additive genetic variance, i.e. $\mathrm{Var}_{\mathrm{add}}(g)$, measures the fitness variation in the population that is due to the additive, i.e. independent, action of the genes. In other words, it measures any gene's effect on fitness which is independent of its "genetic background". Indeed, in this perspective, it is possible to see the total genetic variance as the sum of the additive genetic variance and the non-additive genetic variance.

Since its formulation, the FTNS has received different interpretations. This is mainly due to the unclear formulation of the FTNS given by Fisher in his writings (S. Okasha 2008). Fisher himself describes the FTNS as follows: «the rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time» (R.A. Fisher 1930, p. 35). This formulation of the FTNS induced many authors to compare the FTNS to the second law of thermodynamics, according to which entropy, on average, can never decrease. In this interpretation, the FTNS is able to give a formal representation (and explanation) of the directionality of evolution, i.e. to give a proof of the fact that fitness, on average, will never decrease. If such interpretation were correct, the FTNS would have been able to explain the course of evolution and the development of forms ever more complex without any reference to any kind of design or teleological explanation. This last point clarifies why the analogy between the FTNS and the second law of thermodynamics is relevant to the issue of whether or not the explanations provided by populations genetics are causal explanations. Indeed, if the analogy between the FTNS and the second law of thermodynamics holds, the FTNS would be able to account for a relevant asymmetry in evolution, i.e. complexification of living forms, in a way which is analogous to the way in which the second law of thermodynamics is able to account for relevant asymmetries in physics.

Thus, the reasoning goes, as statistical mechanics, although it is cast in statistical terms, may be understood as bearing on the causal structure of the physical world, so the FTNS, despite it is cast in statistical terms, can be understood as bearing on the causal structure of biological evolution. For instance, French says that one could take Price equation (of which, as stated, the FTNS can be regarded as a special case) «as characterizing a certain fundamental – if, perhaps, abstract – and 'high-level' feature of biological structure» (S. French 2014, p. 338). According to French, this covariance equation can be regarded as able to represent the «modal, relational structure of the evolutionary process […]. Just as the laws and symmetries of physics ‘encode’ the relevant possibilities, so Price’s equation encodes how the average values of certain characters changes between generations in a given biological population» (*ibidem*).

The problem with the analogy between the FTNS and the second law of thermodynamics is that «it is *simply untrue that the average fitness of a population undergoing natural* selection never decreases, so the rate of change of average fitness *cannot always* be given by the additive genetic variance» (Okasha 2008, p. 328). Okasha clarifies that «Fisher was not talking about the rate of change of average fitness at all, but rather the *partial rate of change which results from* [the direct action of] *natural selection* altering gene frequencies in the population, *in a constant environment*» (Okasha 2008, p. 329)[2]. This means that it is more adequate to say that, according to the FTNS, when natural selection is the only force in operation, average fitness can never decrease. The problem is now that «by Fisher’s lights, natural selection will almost never be the *only force in operation; for by causing gene frequencies to change, selection* almost always induces environmental change, which is itself a force affecting average fitness» (Okasha 2008, p. 344). In fact, «the environment in Fisher’s sense will *not remain fixed, for selection itself alters it*» (Okasha 2008, p. 347). Details are not relevant here, the basic idea is that for Fisher, when natural selection operates, this fact directly alters both the mean fitness $\bar{w}$, and the “environment”, which in its turn alters the mean fitness $\bar{w}$. Thus, if the FTNS holds only when natural selection is the only force to operate in a constant environment, and if when natural selection operates, the environment cannot remain constant, then we should conclude that the FTNS can never hold. For example, Okasha states that the «theorem tells us that in a constant environment, selection can only drive average fitness up; but since the environment, in Fisher’s sense, is always changing, nothing follows about whether average fitness will actually increase or not» (Okasha 2008, p. 345). Thus, the analogy between fitness and entropy seems to fail.

The biological import of the FTNS is still controversial. G.R. Price (1972) and W.J. Ewens (1989) felt that the FTNS, though mathematically correct, did not have the biological significance that Fisher claimed for it. On the contrary, A.W.F. Edwards (1994) and A. Grafen (2003) are much more

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[2] To understand Fisher’s understanding of the FTNS, we have to accept Fisher’s view of “environment”: any change in the average effects constitutes an environmental change.

sympathetic to Fisher's view. We cannot develop this issue here for reasons of space. What we wish to point out here is that, despite no-one doubts that the FTNS is a sound mathematical theorem, the possibility of interpreting the explanations provided by such theorem in causal terms in analogy with how explanations provided by certain equations are interpreted in physics, has been fiercely disputed by the statisticalists.

Matthen and Ariew, for instance, state that the reason «for reifying natural selection [...] lies in a[n] [. . .] analogy between equations of population genetics – such as Fisher's Theorem – and certain equations of physics» (Matthen and Ariew 2009, p. 208). But in their view this analogy is not well founded, because, unlike that in physics, the description of natural selection «rendered by population genetics models are in general neither predictive nor explanatory», since «population genetics models are, in general, noncausal models» (B. Glymour 2006, pp. 369, 383). Moreover, as we have seen, in this view natural selection itself is not a genuine feature of the world, it is just «ontologically derivative on individual-level events such as births, deaths, and mutations» (Matthen and Ariew 2009, p. 216).

In this perspective, the FTNS does not tell us anything about the causal structure of the evolutionary process, firstly because such theorem refers to something which, being ontologically derivative, is not a causal concept (i.e. natural selection), and secondly, because such theorem itself is not intrinsically related to anything which is biological in character. For example, Matthen and Ariew state that natural selection «is not even a biological phenomenon as such. It holds in any history in which the terms of the theory can be jointly interpreted in a way that accords with the abstract requirements of the theory» (Matthen and Ariew 2009, p. 222).

As already noted, our aim here is not to take side on the dispute over the nature of natural selection, rather we just wish to point out a possible difficulty for the statisticalists which has so far (at least to the best of our knowledge) gone quite unnoticed, a difficulty which might derive from their claim that population genetics explanations are non-causal explanations.

7. Mathematical Explanations and Naturalism

A possible challenge that the statisticalists may have to address is the following: if the explanations provided by population genetics are regarded by statisticalists as non-causal explanations of a certain kind, then statisticalism risks being incompatible with a naturalist stance. This may be a relevant problem because many statisticalists view themselves as naturalists. Moreover, as evolution is central to naturalism in general, for all those who proclaim themselves naturalists it is of relevance what kind of explanations population genetics provides.

According to a widespread view, scientific explanations need to be causal explanations in order to be genuinely scientific (for a survey see J. Woodward 2017). This is mainly due to the fact that models of scientific explanation which made no reference to causation, because they were developed by positivists «motivated by the apparent appearance within legitimate science of explanations that didn't seem causal in nature» (L. Sklar 2009, p. 661), were shown to count various non-explanations as explanatory, i.e. they were unable to account for the so-called explanatory asymmetry. Indeed, if A is correlated with B, and A explains B, we usually think that it cannot be the case that B explains A. There is an asymmetry between the explanans and the explanandum, despite their being correlated. And an adequate account of scientific explanation must be able to account for such asymmetry. To face the asymmetry problem, in the last decades philosophers thought that causal notions should be introduced in our models of scientific explanations to distinguish between regularities that are genuinely explanatory and those that are not. So, despite issues as what is the metaphysical nature of causality, or whether causality finds room in fundamental physics, are very debated issues in philosophy of science and metaphysics (for a survey see T. Blanchard 2016), there is still a wide consensus that causation is relevant when dealing with a philosophical account of scientific explanations in order to account for the explanatory asymmetry.

In recent years, the debate on the nature of non-causal scientific explanations flourished. Some philosophers maintain that there are several genuinely scientific non-causal explanations, while other philosophers either deny that those explanations are genuine explanations, or they deny that those explanations are genuinely non-causal explanations (see A. Reutlinger 2017 for a survey).

For our purposes, it is not relevant to take side on this debate. We just wish to underline that, given that statisticalists claim that natural selection and drift are not really causes of evolution, the statisticalist faces a sort of dilemma: (1) either she maintains that population genetics explanations are not genuine instances of scientific explanations; (2) or she maintains that scientific explanations can also be non-causal, and that populations genetic explanations are non-causal explanations. Obviously, the first horn of the dilemma, i.e. (1), is unacceptable, and, as we have already stressed, no statisticalist would be interested in taking it, since no statisticalist denies that population genetics *do* provide explanations. So, the statisticalist seems to be committed to the claim that (at least some) non-causal explanations are genuine scientific explanations, and that explanations provided by populations genetics are explanations of that kind.

The problem now is to determine what kind of non-causal explanations the explanations provided by populations genetics are. Apparently, several kinds of non-causal explanations can be distinguished (Reutlinger 2017). It is beyond the scope of this paper to investigate whether every kind of non-causal explanations is problematic from a naturalist point of view. What is less contentious and easiest to show is that at least one kind of non-causal explanations, namely Mathematical Explanations of Natural Phenomena (MENP), is potentially highly problematic for those who wish to take a naturalist stance. So, as we will try to show, if the explanations provided by population genetics are regarded as MENP, statisticalists have to face the challenge described above.

Briefly, MENP are those non-causal scientific explanations in which an indispensable explanatory role is played by a mathematical result (see e.g. A. Baker 2009). As an example, consider the following question: Why do hive-bee honeycombs have a hexagonal structure? Part of the explanation depends on evolutionary facts. But the explanation is completed by pointing out that the hexagonal tiling is optimal with respect to dividing the plane into equal areas and minimizing the perimeter. This geometrical fact, known as the honeycomb conjecture, was finally proved by Hales in 2001 (T.C. Hales 2001). Thus, for the supporters of the MENP claim, the explanation of the biological fact that hive-bee honeycombs have a hexagonal structure seems to depend *essentially* on a mathematical result. Such a dependency on mathematical results makes MENP non-causal explanations, since mathematical results/facts/objects are usually regarded as non-causal, better they are usually regarded as non-spatiotemporally located and causally inert (M. Balaguer 2009). This last point is crucial: it is indeed the causal inertness of the explanans in a non-causal explanation of the MENP-kind that is at the core of the difficulty of making this kind of explanations compatible with a naturalist stance.

Two clarifications are in order here: (1) it is important not to confound alleged instances of MENP with scientific explanations that merely use mathematics for representational purposes, i.e. explanations where mathematical results are not playing an *indispensable* explanatory role; (2) MENP are not non-causal explanations in the mere sense that they do not explicitly cite causes. Indeed, there are abstract explanations which do not explicitly cite causes, or which do not clearly specify any mechanism or process responsible for the explanandum, but which, despite their "abstractness", cannot be regarded as genuine MENP (see A. Reutlinger and H. Andersen 2016).

Another example of MENP is provided by M. Lange (2013b): a mother tries to divide twenty-three strawberries evenly among three children without cutting any strawberry and fails. What explains her failure? According to Lange, the explanation of her failure involves crucially the following assumption: it is a mathematical fact that twenty-three cannot be divided evenly by three. In this view, this mathematical fact is both non-causal and explanatory, so this explanation can be regarded as a genuine MENP. According to Lange, mathematical explanations explain in virtue of the extra modal force they have compared to the necessity associated with causal laws, i.e. ordinary physical laws.

As regard the compatibility between MENP and naturalism, the main problem derives from the difficulty of giving a justification of the claim that mathematical facts constrain natural phenomena which can be acceptable for a naturalist. We will not be concerned here with any specific view of naturalism, nor we will survey the many criticisms that have been moved to this view so far. For the purpose of this paper, naturalism can be understood as the metaphilosophical stance according to which we should refuse explanations that appeal to non-natural entities, faculties or events, where "non-natural" has to be understood as indicating that those entities, faculties or events cannot *in principle* be investigated and accounted for in the way we usually do in science (for a survey, see D. Papineau 2016).

Although such a characterization of naturalism is quite broad, it nevertheless retains the idea that every naturalist view requires both (1) an ontological and (2) an epistemological commitment. This means that, in order to naturalize a domain D, it is insufficient to merely specify what kind of entities we can admit in our ontology of D. We have also to provide a naturalistic (i.e. a scientific adequate and reliable) account of how we can acquire knowledge of those D-entities. In other words, one needs to justify the claim that there is a sort of connection between the mathematical domain and the worldly domain.

The difficulty of providing a naturalist account for mathematics and modality derives from the fact that both mathematics and modality have to face the access problem. The access problem, first raised in the philosophy of mathematics by P. Benacerraf 1973, is now thought to arise in many other domains (see e.g. S. Jonas 2017). It is the problem of justifying the claim that our D-beliefs align with the D-truths of a given domain D, if D is regarded as an a priori domain, i.e. a domain whose objects cannot *in principle* be empirically investigated. Both mathematics and modality are usually regarded as a priori domains, i.e. inaccessible domains, or better *in principle* empirically inaccessible domains, domains which cannot be investigated by the means of empirical sciences. Since naturalism claims that we should regard as knowledge only what is knowable by the same means by which we acquire scientific knowledge (M. Devitt 1998), it is easy to see why there are no satisfactory naturalist accounts of how it is that we can have knowledge of those a priori domains.

Turning to the issue at stake, the point now is: If one adopts statisticalism, is one committed to accept the claim that the explanations provided by population genetics are genuine MENP? This issue is controversial. As already said, if a statisticalist embraces the idea that population genetics explanations are genuine MENP, she has to face a dilemma: either she tries to reconcile her view with naturalism, a goal which might be very difficult to reach, or she has to submit to an anti-naturalist stance, an option which might be unpalatable to many statisticalists.

To avoid this dilemma, the statisticalist should deny that the explanations provided by population genetics are genuine MENP. But, obviously, she should also maintain that such explanations are nevertheless non-causal explanations, since statisticalists deny that population genetics provides us with causal explanations. It is not clear whether the statisticalist may find a way out. However, this seems not an easy task. Indeed, in order to achieve this goal, since supporters of MENP usually claim that the explanations provided by population genetics are genuine instances of MENP, the statisticalist has to prove that (at least some of) the claims made by the supporters of MENP are ungrounded or do not apply to the explanations provided by population genetics.

Consider, for instance, how Lange conceives of drift explanations. According to Lange, drift explanations in population genetics are what he calls Really Statistical (RS) explanations. In Lange's view, a RS explanation «does not proceed from the particular chances of various results […]. It exploits merely the fact that some process is chancy, and so an RS explanation shows the result to be just 'a statistical fact of life'» (M. Lange 2013a, p. 173). RS explanations are instances of MENP, since it can be shown that they are both (1) genuine non-causal explanations, i.e. they are not explanations that merely fail to cite causes; and (2) genuine mathematical explanations, i.e. they are not explanations that merely use mathematics for representational purposes.

As regard (1), in order to explain why RS are non-causal explanations, Lange considers explanations by regression to the mean. Regression to the mean is, roughly, the phenomenon that if a variable is extreme on its first measurement it will tend to be closer to the average on its second measurement. This kind of explanations «is not causal. It depicts the result as fallout from the statistical character of the case» (*ibidem*). Indeed, the point of this kind of explanation is «to exhibit the result as arising from the fact that successive runs have a statistical relation – regardless of that precise relation or its […] causes or, indeed, whether it has any causes at all» (Lange 2013a, p. 177).

As regard (2), in order to explain why RS are genuine mathematical explanations, Lange points out that RS explanations do not appeal to any particular aspects of what needs to be explained, «but merely to the fact that there are chances. Consequently, instead of subsuming the result to be explained under a statistical law of nature, an RS explanation exploits a theorem of the probability calculus» (*ibidem*). This last point is crucial, since insofar as «mathematical facts alone are emphasized as doing the explaining, the explanation is properly characterized as distinctively mathematical» (Lange 2013b, p. 507), i.e. as a MENP. So, if RS explanations depend indispensably on theorems of probability calculus, i.e. on mathematical results, then such explanations are genuine MENP.

Lange's line of reasoning, although it may be disputable to many, seems sound and so worth being taken seriously. Thus, if a statisticalist wishes to deny that drift explanations in population genetics are RS explanations, and so can be regarded as genuine MENP, she has to provide reason for either (a) the claim that drift explanations are not really non-causal, or (b) the claim that in drift explanations it is not some mathematical result that is really indispensably doing the explaining. Both options may be problematic for the statisticalist. As regard (a), it is easy to see that a statisticalist cannot take it, since statisticalists claim precisely that drift explanations in population genetics are non-causal explanations. So (b) appears to be the only option that a statisticalist can take in order to deny that drift explanations are MENP. Now, the problem is that taking (b) may be impervious. Indeed, denying that in a scientific explanation mathematics is indispensably doing the explaining amounts to claim that such explanation is an ordinary scientific explanation which uses mathematics for representational purposes. But when one deals with an explanation in which mathematics is used for merely representational purposes, it is more difficult for one to claim that such explanation is non-causal. It is hard to say whether it is merely difficult or rather impossible. Certainly, it is a big issue to deal with. It seems fair to conclude by saying that the statisticalist who wishes to take a naturalist stance should at least clarify whether she thinks that the explanations provided by population genetics are genuine MENP, and, in the affirmative case, whether she thinks that MENP are compatible with a naturalist stance.

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Predicting the Genetic Loci of Past Evolution

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Introduction

Evolution reveals itself by the changes in observable characteristics of biological populations over successive generations. Here we focus on the DNA mutations underlying phenotypic changes that have occurred during natural evolution of populations or species, as well as through domestication and experimental evolution. The search for the mutations responsible for evolutionary changes started with iconic case studies such as the ABO blood group gene (F.I. Yamamoto *et al.* 1990) or hemoglobin for drepanocytosis and malaria resistance (V.M. Ingram 1957). As instances of genes causing phenotypic changes between populations and species started to accumulate, some researchers noticed that the mutations causing evolution did not appear to be randomly distributed across the genomes. Intriguing cases of repeated evolution at the genetic level were reported, with recurrent genetic changes involved in the evolution of similar phenotypes in distant taxa (A.H. Paterson *et al.* 1908; N. Gompel and B. Prud'homme 2009; A. Kopp 2009; P.A. Christin *et al.* 2010; A.E. Lobkovsky and E.V. Koonin 2012; G.L. Conte *et al.* 2012; A. Martin and V. Orgogozo 2013; D.L. Stern 2013; T. Lenser and G. Theissen 2013). Furthermore, certain types of phenotypic changes seemed to be preferentially associated with certain broad categories of mutations (S.B. Carroll 2000; E.H. Davidson 2006; G.A. Wray 2007; B. Prud'homme; N. Gompel and S.B. Carroll 2007; S.B. Carroll 2008; D.L. Stern and V. Orgogozo 2008; V.J. Lynch and G. Wagner 2008; G. Wagner and V.J. Lynch 2008; M.A. Streisfeld and M.D. Rausher 2011; D.L. Stern 2011). For example, morphological evolution in animals was suggested to preferentially involve cis-regulatory mutations rather than coding changes. Please note that "preferentially" refers here to the final consequence of selection and of other population genetics processes and does not necessarily mean that mutations occur in a non-random fashion. Genetic variations occur throughout the genome, some of them being gradually eliminated while others are maintained, thus allowing enrichments in certain types of mutations when one looks at the result of selection and of other population genetics processes over multiple generations.

Observation of consistent patterns in the genetic loci of evolution has had two main consequences on evolutionary biology research. First, it prompted the elaboration of various explanatory hypotheses. Second, it led some biologists to propose that the genetic loci of evolution are partly predictable, in the sense that for a given phenotypic change that occurred in the past the underlying mutations can be guessed with reasonable confidence. What is predicted here is the genetic causes of evolutionary events that occurred in the past (V. Orgogozo 2015; V. Orgogozo, B. Morizot, A. Martin 2015), and not the mutations that will occur in the future (for such cases see Lobkovsky and Koonin 2012; R.E. Lenski 2017; M. Lässing, V. Mustonen and A.M. Walczak 2017).

In this paper we examine the predictions regarding the genetic loci of past evolution: what kinds of predictions are they? What are they based on? How accurate are they?

Nature of the Predictions

Published predictions about the genetic loci of evolution do not arise from complex mechanistic models. They simply derive from the observation of repeated cases of genetic evolution and the identification of the context and the hypothetical causes that lead to repetitions. For example, the loss of larval trichomes in *Drosophila sechellia* was found to be caused by multiple mutations in five distinct enhancers of the *svb* gene, with each enhancer regulating trichome development in a specific body part (N. Frankel *et al.* 2010). Such recurrent evolution at the same locus, together with the special “hub” position of *svb* in the gene network for trichome development, suggested that *svb* was a hotspot gene for trichome evolution in flies (A.P. McGregor *et al.* 2007; Stern and Orgogozo 2008; Stern 2011). The independent loss of trichomes in *Drosophila ezoana* was thus inferred to involve cis-regulatory mutations in *svb*, as in *D. sechellia*, and indeed this was found to be true (N. Frankel, S. Wang, D.L. Stern 2012). Agricultural pests and mosquitoes have repeatedly evolved resistance to pyrethroid insecticides such as DDT via coding mutations in the *para voltage-gated sodium channel* gene (*syn. para, vgsC*) (D.M. Soderlund 2008). Weston et al. predicted that pyrethroids may also affect non-pest organisms that populate sprayed areas (D.P. Weston *et* *al.* 2013). Not only they found that pyrethroid resistance had evolved in populations of freshwater crustaceans exposed to agricultural run-off, but they also uncovered typical mutations in *para* gene, mirroring the evolutionary mechanisms previously observed in the targeted pests. Thus, a specific evolutionary pressure left a predictable genetic signature in the environment that can now be detected. In principle, comparable predictions could be done in other situations where human activity has chemically modified the environment.

Predictions rely on the assumption that the set of already known loci of evolution on which predictions are based are identified via an unbiased approach. Linkage mapping studies and association studies screen the entire genome sequence and are thus supposed to be unbiased in their detection of the genetic loci. However, one should keep in mind that once a genomic region is narrowed down to a few candidate genes through linkage mapping or association mapping, knowledge from past studies might favor for validation tests the candidate genes that are already known to be involved in a similar phenotypic change. As a result, even genome-wide mapping studies carry some bias towards already known genes.

Predictions are usually formulated along the following lines: "For a given phenotypic change, it is predicted that the causal mutations are such and such". Formulations can also be relatively more complex. For evolution of red flowers in *Penstemon barbatus*, *Wessinger* and Rausher not only predicted the causal genes (*F35'H* or *F3'H*) and the fact that the mutations should create loss-of-function alleles but also provided gene-specific details about the expected mutations: "when it involves elimination of F3′5′H activity, functional inactivation or deletion of this gene tends to occur; however, when it involves elimination of F3′H activity, tissue-specific regulatory substitutions occur and the gene is not functionally inactivated" (C.A. Wessinger and M.D. Rausher 2014).

Predicting the genetic loci of evolution is a retrodiction

Predictions are usually inferences about the future, based on current knowledge about the past. When the causal temporality is reversed, some authors prefer to use the term retrodiction. Retrodicting can be defined as making an inference about an event that occurred in the past (A. Love, personal communication; J. Fetzer 2017). If this past event is already known, then retrodiction is the act of providing a *post hoc* explanation for it. For example, Darwin retrodicted why species similar to those found on oceanic islands are usually found on the nearest mainland (C. Darwin 1859). In other cases, retrodiction can produce facts that are yet unknown and that we should observe. For example, Darwin retrodicted from the existence of orchids with very long nectaries that we should discover moths with equally long proboscis (Darwin 1859). Predictions are not always explanatory: they do not necessarily rely on a model or on causal explanations. For example, a prehistorical astronomer without a heliocentric theory who accumulates observations such as "the sun always rises above that hill" would predict that the sun will rise above the hill again, simply by noticing the repetitions. In our case, published predictions about the genetic loci of evolution do not arise from complex mechanistic models, they instead derive from the observation of repeated cases of genetic evolution. In this sense, evolutionary geneticists resemble prehistorical astronomers without a heliocentric theory. Using repetitions among the known loci of evolution to make predictions about the past is thus a retrodiction. Moreover, predictions about past genetic loci concern a genetic difference that exists today between two living taxa (a property of the present state). Predictions about the genetic loci of past evolution are thus retrodictions about the past and the present.

Predictions at various genetic levels

Predictions can be made at the gene level, as for *svb* or the *para* sodium channel gene, but also at higher and lower genetic levels: at the level of a nucleotide, of part of a coding region, of a specific enhancer, of a group of genes, and also for broader categories of genetic changes (Table 1).

Table 1. Repetitions can be detected and predicted at various genetic levels, from specific nucleotides to general classes of mutations

Genetic Level	Example of prediction or of repeated evolution

Nucleotide	Resistance to cyclodiene insecticides was successfully predicted to be associated with amino acid substitutions at a single residue (A302) within the gamma-aminobutyric acid (GABA) receptor sub-unit named Rdl in the cat flea *Ctenocephalides felis* for 8 of the 9 laboratory strains that were tested (C. Bass *et al.* 2004).
Part of a coding region	Various amino acid substitutions in the DIII and DIV pore loops of the sodium channel Nav1.4 explain tetrodotoxin resistance in newts, snakes, pufferfishes (G. Toledo *et al.* 2016) and to red tide toxin-resistance in clams (V.M. Bricelj *et al.* 2005).
Enhancer	Pelvic loss in sticklebacks originating from 13 different lakes is due to various deletions with distinct breakpoints of the same *pitx1* enhancer region in 9 cases and to other yet unknown genetic change(s) in 4 cases (Y.F. Chan *et al.* 2010).
Gene	The gene *svb* was successfully predicted to cause an evolutionary loss of trichomes in *Drosophila ezoana* (N. Frankel, S. Wang, D.L. Stern 2012). The gene *WntA* was successfully predicted to cause wing color pattern variation across many *Heliconius* species and populations (A. Martin *et al.* 2012), and beyond (J.R. Gallant *et al.* 2014).
Gene Family, Gene Paralogs	Interspecific changes in anthocyanin pigment intensity in flowers was successfully predicted to involve preferentially mutations in transcription factor genes of the MYB family (M.A. Streisfeld and M.D. Rausher 2011).
Genetic Pathway	It was successfully predicted that flower color evolution in *Penstemon barbatus* was caused by the inactivation of one of the candidate anthocyanin pathway genes, *F3'H*, *F3'5'H* and *DFR* (C.A. Wessinger and M.D. Rausher 2014).

Gene Ontology	Animal morphological evolution is predicted to involve preferentially signaling ligand encoding genes, i.e. genes associated with the gene ontology (GO) terms "extracellular region" and "receptor binding" (A. Martin V. and Orgogozo 2017).
Broader Class of Mutation	Cis-regulatory mutations are the predominant mechanism underlying the evolution of morphology in animals (S.B. Carroll 2008; D.L. Stern,V. Orgogozo 2008).

Some predictions carry more information than others. Predicting the impact of a projectile within 1 m is better than within 1 km. In a first approximation, the *inference gain* can be estimated by the inverse of the probability of the predicted outcome according to the null model. In most cases, the null model considers that mutations can occur with equal probability at all nucleotide positions within a genome (Orgogozo 2015), or with equal probability in all genes of a genome. The prediction that trichome pattern evolution in *Drosophila* is likely to involve the *svb* gene (McGregor *et al.* 2007) has an inference gain of approximately 17,500 (*svb* is one gene out of the total of 17,737 genes present in the genome of *D. melanogaster* (FlBase FB2017_04). In contrast, the prediction that morphological evolution is likely to involve signaling ligand encoding genes (A. Martin and V. Orgogozo 2017) has a lower inference gain, estimated to be about 180 in the stickleback fish, as the proportion of genes associated with gene ontology (GO) terms "extracellular region" and "receptor binding" in the stickleback *G. aculeatus* (BROADS1) is 115/20,787 (Martin and Orgogozo 2017). Predictions at the level of the gene or at the nucleotide level have a higher inference gain than predictions about broader classes of mutations.

The causes of genetic repetition

In general, authors put forward several arguments for the over-representation of certain genetic loci for phenotypic traits of interests and suggest that their combination explains repeated evolution. Arguments for the importance of cis-regulatory mutations versus coding changes are not reviewed here and can be found in Carroll 2000, Carroll 2008, Davidson 2006, Wray 2007, Stern and Orgogozo 2008, D.L. Stern and V. Orgogozo 2009, B.-Y. Liao, M.-P. Weng and J. Zhang 2010, Stern 2011.

Several non-exclusive hypotheses have been proposed to explain why some genetic changes repeatedly drive certain phenotypic changes or adaptations during evolution (Table 2).

Table 2. Non-exhaustive list of arguments that have been proposed to explain hotspot genes

Argument	Example
Mutation bias	*Pitx-1* is located within a fragile chromosome region, which exhibits a higher rate of breakage and is thus prone to deletions caused by DNA break repair by non-homologous end joining (NHEJ) (Y.F. Chan *et al.* 2010). Primate chimeric genes involved in retroviral defense have evolved multiple times through the transposition of *CypA*, encoding a protein with high affinity for viral proteins, with a *Trim5alpha*, encoding a protein involved in virus degradation. Such an event seems intuitively unlikely but it did occur several times, probably because *CypA* is prone to retrotransposition and formation of hybrid genes by exon shuffling (R. Malfavon-Borja. 2013; Z. Zhang. 2003).
Large target size	The *Mc1R* coding region contains a large number of sites which, when mutated, yield a viable phenotypic change (N. Gompel and B. Prud'homme 2009). *Oca2* is a large gene: in humans it contains 24 exons spanning 345 kb (N. Gompel and B. Prud'homme 2009).

Intragenic modularity	In the mouse *Peromyscus* the *Agouti* gene harbors a large cis-regulatory region decomposed into several modules, allowing many nucleotide sites to be tweaked to generate precise and specific pigmentation changes in various parts of the body (C.R. Linnen. 2009).
Genetic potentiality	The reduced content of amylose, a characteristics of cereals with sticky texture, can only arise via mutations within the *Waxy* gene, which encodes a granule-bound starch synthase (T. Lenser and G. Theissen 2013). No other mutations than coding mutations in opsin genes can lead to change in light wavelength sensitivity (S.C. Morris 2003).
Architecture of Gene Networks	The *svb* gene sits at a “hub” position in the gene network for trichome development (A.P. McGregor. 2007).
Optimal Pleiotropy	Interspecific changes in anthocyanin pigment intensity in flowers is more likely to involve transcription factor genes of the MYB family than basic helix-loop-helix (bHLH) or WD40 repeat family members because MYB genes usually have more tissue-specific functions and thus fewer pleiotropic effects (M.A. Streisfeld and M.D. Rausher 2011; A. Kopp 2009).
Mutational Path	A mutation in tuberculosis strains providing resistance to a first antibiotic acted as a preliminary condition and strong predictor for the secondary evolution of multidrug resistance on five continents (A. Manson 2017).

Hemiplasy: Standing Variation, Introgression, and Horizontal Gene Transfer	The non-shattering allele *sh4* in rice was already present at low frequency within wild populations, so that independent selection has probably driven the same allele to fixation in distinct varieties (T. Lenser and G. Theissen 2013). Adaptation to high altitude in dogs evolved via an allele of *EPAS1* that was already present in highland wolves, by interbreeding (Z. Fan, D. Ortega-Del Vecchyo, R.K. Wayne 2017).

A first category of explanation can be attributed to mutational bias: certain mutations are more likely to occur than others. For instance, a region that is prone to structural variation or transposon insertion is likely to undergo repeated rearrangements, thus facilitating certain gene-to-phenotype changes (Y.F. Chan *et al.* 2010). Adaptation to high-altitude in *Andean* house wrens and hummingbirds has been associated with single point mutations in the β*A-globin* gene and these mutations appear to lie within CpG sites, which are known to be chemically instable and highly mutable (S.C. Galen *et al.* 2015; A. Stoltzfus and D.M. McCandlish 2015; M. Lynch and B. Walsh 2007). A recent study of various high-altitude species (C. Natarajan *et al.* 2016) discovered other mutations in β*A-globin* that increase affinity for oxygen, indicating that other genetic paths are theoretically possible. In Andean house wrens the spontaneous mutation rate appears to have biased evolution towards certain genetic paths. Spontaneous mutation rates are higher for transitions (A↔G or C↔T) than for transversions (Lynch and Walsh 2007). Using this property as a test case for investigating the role of mutation biases, Stoltzfus and McCandlish compiled from existing literature a list of putatively adaptive amino-acid changes that have evolved in parallel in natural or experimental contexts. They found a fourfold excess of transitions over transversions (A. Stoltzfus and D.M. McCandlish 2017), suggesting that the repeatability of adaptive coding changes is at least partly explained by biases in the mutations. This is consistent with a "first come, first served" model where even if a number of possible mutational paths to adaptation exist, the ones that are more likely to emerge in the first place are more accessible to selection, and are thus repeatedly observed when the environmental challenge is replicated.

Two other categories of explanations (named "Intragenic Modularity" and "Large Target Size" in Table 2) are related to the fact that compared to other loci that may provide mutational paths to the considered phenotypic change, a given gene may be favored because of its properties at the DNA sequence level: a large intergenic region that can provide relatively more possibilities for a modular control, or a large coding region allowing many amino-acid sites to be tweaked.

A third category of explanation deals with gene function itself rather than just the physical properties of the stretch of DNA hosting their information. Kopp used the term "Optimal Pleiotropy" to propose that only certain genes may host the potential for tuning a given phenotype without deleterious effects. In this concept, the emphasis is on the capacity of certain genes to yield specific effects, whether they simply have a limited number of roles, or on the contrary, a large number of roles but sufficient modularity to allow genetic uncoupling of these roles (A. Kopp 2009). Similarly, the "Architecture of Gene Networks" may highlight "hub" or "input/output" genes that are more likely to coordinate a cascade of changes and thus, drive effects accessible to selection (McGregor *et al.* 2007; Stern and Orgogozo 2008).

A fourth mechanism deals with "Permissive Mutations" that may relax the constraints preventing a given change and thus open a new valley in the adaptive landscape. This phenomenon was reviewed recently (J.F. Storz 2016) and has been mostly studied in the framework of protein evolution (R.D. Tarvin *et al.* 2017; J.D. Bloom, L.I. Gong, D. Baltimore 2010; A. Manson *et al.* 2017; T.N. Starr, L.K. Picton, J.W. Thornton 2015). The predictability is of the form "if change A has happened, then change B is likely as well because we observed that A is often followed by B". In principle, such phenomenon could also apply to genome-wide epistasis, with mutational paths being contingent on allelic states present at distant loci on the genome, as has been observed in "Evolve and Resequence" experiments (J.B. Anderson *et al.* 2010; A. Long *et al.* 2015).

Finally, another explanation underlines the higher capacity of certain derived alleles to circulate among the branches of a species phylogeny, due to various mechanisms such as incomplete lineage sorting or standing genetic variation (*e.g.* C.T. Miller *et al.* 2007), genetic introgressions in intermixing populations or closely related species (*e.g.* J. Enciso-Romero *et al.* 2017; Z. Fan, D. Ortega-Del Vecchyo, R.K. Wayne 2017; L.T. Dunning *et al.* 2017), or even horizontal gene transfers between distant branches of the tree of life (*e.g.* F.W. Li *et al.* 2014; J.A. Metcalf *et al.* 2014; J. Ropars *et al.* 2015). These cases, named "collateral evolution" or "hemiplasies" (reviewed in Stern 2013; Martin and Orgogozo 2013) contrast with *stricto sensu* occurences of genetic parallelism (R.W. Scotland 2011; Stern 2013; J.F. Storz 2016) because the alleles are identical-by-descent rather than identical-by-state. The derived phenotypes may be "convergent", i.e. show a pattern of homoplasy due to a discontinuity on a phylogeny, but the genotypes are not, hence representing a so-called "hemiplasy" (J.C. Avise and T.J. Robinson 2008). As our understanding of gene flow is rapidly improving in the phylogenomic era, it is likely that the *a priori* observation of connectivity between two lineages will increase our capacity to make predictions on causal mechanisms of gene-to-phenotype change (R.W. Wallbank *et al.* 2016).

In summary, predictable genetic changes may be 1) under the influence of a mutational bias (site-specific rates of mutation); 2) in a large locus, more prone to change due to a sequence size parameter (narrow mutational target size, independently of genetic function – large target size, intragenic modularity); 3) in a gene that is inherently poised to tweak a given trait due to properties of its molecular function or regulatory interactions (narrow mutational target size, due to the structure of the genotype-phenotype map; genetic potentiality; architecture of gene networks; optimal pleiotropy); 4) contingent upon the pre-existence of other changes in the genome (mutational path); 5) a by-product of allele sorting or transfer processes (hemiplasy).

Prediction accuracy

Good predictions are not only the ones with high inference gain, but also the ones with high *accuracy*. As a matter of fact, the prediction that tomorrow will be a sunny day is better with 95% accuracy than with 50% accuracy. Accuracy corresponds to the ratio of correct predictions to the total number of cases evaluated. How accurate are the predictions about the genetic loci of evolution? Some appear to be 100% accurate whereas others are not. Pigmentation evolution in flies was predicted to involve mostly cis-regulatory mutations (Carroll 2008). A recent review compiles 32 cases of pigmentation evolution in various *Drosophila* species: all of them are caused by cis-regulatory mutations and none are caused by coding changes (J.H. Massey and P.J. Wittkopp 2016). If we suppose that existing approaches are not biased towards cis-regulatory changes, then it means that so far the prediction for cis-regulatory evolution is 100% accurate. Resistance to trimethoprim in *Escherichia coli* was correctly predicted to be associated with genes encoding dihydrofolate reductase enzymes in 308 of the 320 tested resistant strains, thus giving an accuracy of 96% (A. Brolund *et al.* 2010). An examination of 192 worldwide populations of *Arabidopsis thaliana* exhibiting natural variation in flowering time found that approximately 70% of the early-flowering strains carried deleterious mutations in the hotspot gene *FRIGIDA* (C. Shindo *et al.* 2005). The prediction that variation in flowering time in *A. thaliana* should involve deleterious mutations in *FRIGIDA* has thus an estimated accuracy of 70%. In tetrapods, the *MC1R* receptor and its antagonist *Agouti* together account for 54% of the 206 published cases of pigmentation variation (Martin and Orgogozo 2017). This percentage is inflated by a "caveman effect", which is a type of sampling bias: these two genes might be called "pigmentation hotspot genes" because there are precisely the loci researchers look at first when digging for genetic changes driving pigment variation. Nonetheless, the 54% value gives a maximum estimate of the accuracy of the prediction for a commonly studied trait.

The prediction that genes encoding signaling ligands should be responsible for morphological evolution is one of the less accurate predictions that have been presented. According to experimental data, about 20% of the cases where an animal morphological difference has been mapped to a gene involve a signaling ligand gene (80/391, Martin and Orgogozo 2017, www.gephebase.org). In sticklebacks, 14 genome-wide QTL studies ended with the identification of the causal gene and 4 of them identified a secreted ligand gene, thus giving an estimated accuracy of 28%. The ligand prediction is still better that the null model of each gene having an equal probability of being responsible for the phenotypic change, as ligand genes represent less than 5% of the total number of genes in a genome (Martin and Orgogozo 2017). A more accurate formulation of the ligand prediction is thus that for animal morphological evolution signaling ligand genes are over-represented compared to their proportion in genomes.

Interestingly, the accuracy of actual predictions does not appear to be determined by the strength of the arguments that have been proposed to substantiate them. A wealth of arguments have been proposed for the importance of cis-regulatory mutations in morphological evolution (Carroll 2000; B. Prud'homme, N. Gompel, S.B. Carroll 2007; Wray 2007) and yet this prediction does not appear to be accurate for plant morphological evolution (M.A. Streisfeld and M.D. Rausher 2011).

Inference gain varies with phenotypes

Certain phenotypic traits are associated with predictions of high inference gain while other phenotypic changes call for low inference gain predictions. Predictions about metabolic activity or resistance to particular molecules appear to have more inference gain than predictions about morphological differences. For example, evolution of C4 photosynthesis can be associated with a few specific amino acid changes in the *PEPC* gene (P.A. Christin *et al.* 2007) and antifolate resistance in *Plasmodium falciparum* with only 6 mutations in the dihydrofolate reductase (*DHFR*) locus (M.S. Costanzo and D.L. Hartl 2011).

In contrast, pigmentation pattern evolution can be caused by mutations in at least 10 genes in *Drosophila* flies and 13 genes in vertebrates (Table 3).

Table 3. Non-exhaustive list of genes responsible for evolution of pigmentation pattern in natural populations in Vertebrates and Drosophila flies. See www.gephebase.org for details

Vertebrates	Drosophila flies
Agouti *Atrn* *BCO2* *CYP2J2* *EIF2F2* *HERC2* *KITL* *MC1R* *MGRN1* *Oca2* *SLC45A2* *Taqpep* *TPCN2*	*bab1, bab2* *Dat* *Dll* *ebony* *omb* *pdm3* *tan* *yellow* *wg*

Importantly, additional data about the phenotypic change of interest can help narrow down the number of candidate genetic loci. Coat-darkening phenotypes in natural populations of vertebrates have been associated to only two of these pigmentation genes, the *Agouti* signaling protein (*Agouti*) and melanocortin-1 receptor (*Mc1r*). So these are the best candidates genes for natural coat-darkening phenotypes. Of note, spontaneous coat-darkening phenotypes in mice have also been associated with mutations in two other genes, *attractin* (*Atrn*), and *mahogunin* (*Mgrn*) (E.P. Kingsley *et al.* 2009). Moreover, knowing whether the coat-darkening phenotype is dominant or recessive reduces the number of candidate mutations further: a gain-of-function in *Mc1R* is inferred for dominant phenotypes and a loss-of-function in *Agouti* for recessive traits (E. Eizirik *et al.* 2003). The better characterized the phenotypic change, the more inference gain one can have. For example, pelvic-reduced sticklebacks were found to exhibit a left-right directional asymmetry of pelvic bones, as in P*itx1*-null mice, thus strengthening the prediction that the underlying gene should be *Pitx1* (M.D. Shapiro *et al.* 2004, Y.F. Chan *et al.* 2010).

Rockman and others have argued in favor of a polygenic model behind complex traits (R.A. Fisher 1918; M.V. Rockmann 2012; E.A. Boyle, Y.I. Li and J.K. Pritchard 2017), suggesting that the genetic loci underlying certain complex traits may not be predictable. We do not doubt the generality of this view, but it is useful to stress that traits assumed to be multigenic are sometimes found to be oligogenic (S. Makvandi-Nejad *et al.* 2012). Focusing on large-effect loci can facilitate the discovery and identification of some of the genetic causes of phenotypic variation. This said, it remains critical to look for alternative mutations and avoid the pitfall of ascertainment bias. The power of contemporary association mapping in naturally variable populations and of genome-wide genotyping for QTL analysis shall facilitate our escape from the low-hanging large-effect loci and help us draw a balanced view of genetic predictability in the next decades.

Does prediction accuracy vary with time scale and taxonomic range?

As the taxon of interest becomes more distant from the set of species from which genetic knowledge is available and from which predictions are elaborated, predictions may be less likely. For example, table 3 shows that genes involved in pigmentation evolution in vertebrates cannot be used as candidate genes for pigmentation evolution in flies. C4 photosynthesis evolved many times independently in grasses and sedges through mutations in phosphoenolpyruvate carboxylase (PEPC) via a limited number of amino acid positions and the distribution of sites that have repeatedly mutated differ significantly between grasses and sedges, indicating that the genetic basis of C4 photosynthesis evolution is slightly different between taxa (Christin *et al.* 2007). A meta-analysis of ~25 cases (G.L. Conte *et al.* 2012) suggested that probability of gene reuse declines with divergence time between the two taxa under consideration. However, this trend was not reproduced with a larger dataset (118 cases, Fig. 6 in J.R.Gallant *et al.* 2014). Therefore, we cannot conclude from current data that independent evolution of the same phenotype is more likely to involve mutations in the same genetic locus when taxa are closely related than when they are distantly related.

Conclusion

Even though predictions about the loci of past evolution do not rely on advanced theoretical models, they have proved relatively accurate so far. Predicting the mutations of the past can help not only to understand the mechanisms of evolution, but also to genetically-engineer domesticated species and to infer the mutations that will occur in pathogenic microorganisms.

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Contingency, Laws and Random Events: Epistemic Specificities of the Neutral Theory in Ecology

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In a famous 1999 paper John Lawton argued that ecology is but a set of descriptions of intertwining contingent facts. His challenge triggered many responses and discussions (J.H. Lawton 1999). In this paper, I will consider the neutral theory in ecology and biogeography put forth by Hubbell, as a way to make sense of ecology in a lawful way, through the stochastic modeling of random events at various scales.

I will first situate the neutral ecology in the context of community ecology and of the general distinction between 'niche models', which revolve around a law-like "competitive exclusion principle" (M. Weber 1999) and "dispersal assembly models".

Then I will look at the major controversy among community ecologists that occurred in the 1970s, between Jared Diamond on one side and Edward Connor and Daniel Simberloff on the other, about the possibility of detecting patterns hinting at competition as the driver of biodiversity. This controversy paved the way for the acknowledgment of the key role of neutral models (namely models where selection plays no causal role) in ecology. This will lead me to address the neutral models designed by Stephen Hubbell and their relation with the "island biogeography" models by Robert MacArthur and Edward Wilson (R.H. MacArthur and E.O. Wilson 1967) as their immediate ancestor. I will show how Hubbell's models promote unification between biogeographical and community scales, and describe a specific relation between dispersal models and niche models.

Finally, I will specify the epistemic features of Hubbell's theory, and the way they allow stochasticity to give rise to null hypotheses and alternative hypotheses that answer Lawton's challenge. Taking into account the explicit parallel between the neutral theory in ecology and Kimura's neutral theories in evolution, I will conclude by viewing more generally the role of neutrality in ecology and evolution, and focus on the relation between scales of biological change and the weight of neutral processes.

Introduction

The status of scientific ecology has constantly been controversial, given that it deals with complex phenomena occurring at various scales, and involves regularities usually studied by distinct disciplines: geology, biochemistry, thermodynamics, physiology, evolutionary biology. As S.E. Kingsland 1986 emphasized, «while the rest of biology had become specialized in research and education, ecologists still believed in the value of grappling with the complexities of nature as a whole». Hence, it has been asserted on a regular basis that ecology could not satisfy the highest standards of scientificity – namely, providing causal explanations, laws or mechanisms. Therefore, a constant concern has been to rebuild ecology on firm bases, taking as an objective the scientific structure of another discipline. This was the goal of Odum's systematic book on ecosystems ecology (P.E. Odum 1953); this was also the goal of the "theoretical ecology" movement initiated by Robert McArthur, a very influential ecologist, who used to reconvene with his friends Richard Lewontin, Richard Levins and E.O. Wilson in the early 1960s to wholly rethink ecology and evolutionary biology on the bases of population biology and mathematical modeling. MacArthur was a student of Hutchinson, who mentored many of the fathers of modern ecology (N. Slack 2010) and formulated the influential concept of ecological niche. McArthur indeed, and most recently Mark Vellend, have proposed to structure ecology around an explanatory scheme inspired by population genetics and the Modern Synthesis theory of evolution (M. Vellend 2016).

The recurrence of those attempts indicates clearly that there is a foundational problem with the status of ecology. A very influential formulation of the critique against scientific ecology was the 1999 paper by the ecologist John Lawton. He argued that because of the pervasiveness of contingency in ecology – due to the amount of different scales and levels intertwined – there are no universal laws in ecology.

> General ecological patterns emerge most clearly from this glorious diversity when systems are not too complicated, that is when the contingencies are manageable (as in the population dynamics of single species, or very small numbers of interacting species), and at very large scales. When a kind of statistical order emerges from the scrum. The middle ground is a mess. It is fascinating to study, and rich in wonderful biology. But by studying it, do not expect universal rules, even simple contingent general rules to emerge (Lawton 1999, p. 188).

In this paper, I will consider the so-called neutral theory of ecology, put forth by S.P. Hubbell in his 2001 book but elaborated by him during two decades. This theory confers a key role to stochasticity, randomness and therefore contingent events. I will show how modeling such stochasticity allows Hubbell to propose a strong theoretical framework for ecology, and therefore, supersede the critiques about the lawlessness of ecology. In the first section I will sketch some main research question of ecology, and the most important family of theories that address them, namely 'niche theories' or 'limiting similarity theories', based on competition; in the second section I will consider a controversy about the explanatory role of competition in ecology that saw the emergence of the notion of 'neutral model'. In the third section I will describe the neutral theory of ecology, and especially explain the parallel with neutral evolution *sensu* Kimura.

1. What is scientific ecology about?

There are many subfields in ecology – even leaving aside "behavioural ecology", which mostly focuses on the traits of organisms explained as the result of selection for 'strategies' (J. Krebs and N. Davis 1995). Biogeography, functional ecology, community ecology, population ecology and landscape ecology all consider the distribution, stability, regulation, succession of populations of animal and plant species at various time and spatial scales. In this paper I will focus on the question raised by Lawton in his paper, about communities, distribution of diversity and coexistence of species.

A general concern in ecology is explaining the composition of communities: why do these animals and plant live together? This question may extend to the question Hutchinson raised: why are there so many animals (G.E. Hutchinson 1961)?

A major issue raised by biogeography and community ecology concerns the *patterns of biodiversity*. An important one, studied by biogeography, is the "*species area curve*", which relates the *area of a territory* to the amount of species it includes. MacArthur and Wilson's *Theory of Island Biogeography* (1967) proposed an "island–mainland model", which models according to few parameters the biodiversity dynamics yielding species area curves.

In turn, traditional community ecology asks: how are species distributed *according to their abundances*? Such distributions, called "species abundance distributions" (SAD) can also be expressed as the relative rank in abundance of each species. What processes account for these patterns? It's known since

Fisher that many of the species-abundance distributions (SAD) are log-series; yet some are also log-normal curves, as advocated against him by Preston (1948), but mainly at a smaller scale. This regularity calls for explanations, as well as for an explanation of the differences (Figure 1).

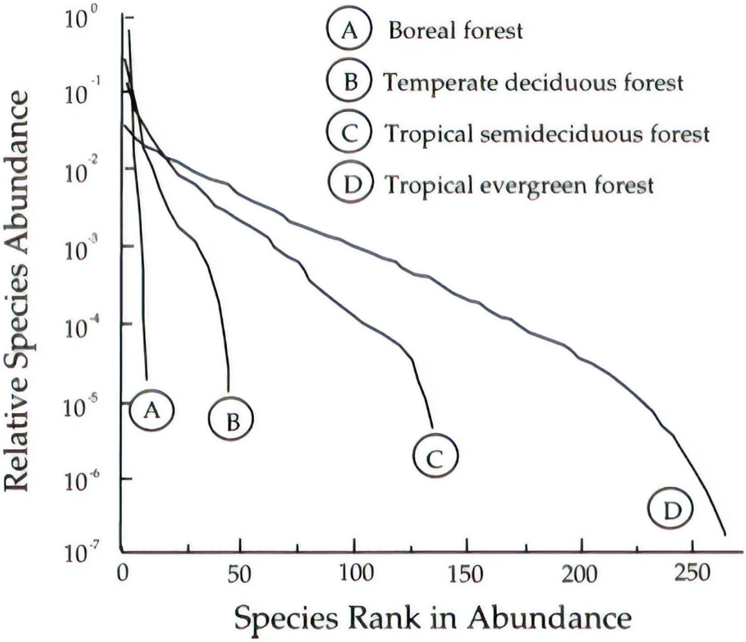

Figure 1. Some species abundance distributions in various ecological regions (from UNTB)

A major family of answers to the coexistence question invokes competition. The Russian ecologist Gause introduced in the 1930s the "competitive exclusion principle", which states that two species having the same requirements and predators will compete until one gets extinct (G.F. Gause 1932, 1934). At equilibrium, states the principle, there is only one species on one "niche", understood as the set of resources and predators. Gause's experiments, however, were not as neat as that and showed some fluctuations in abundances rather than the equilibrium exclusion (S.E. Kingsland 1995; A. Pocheville 2015). The riddle of those fluctuations triggered constant interest from ecologists.

In 1957, Hutchinson reassessed the competitive exclusion principle in a modern form redefining "niche" as the subspace of the hyperspace of environmental parameters in which a given species is capable to live. Then, if there are two species on overlapping fundamental niches, the best competitor on the part of the fundamental niches that is overlapped will occupy it. Therefore, competitive exclusion finally partitions species into a set of discrete non-overlapping environmental niches. Hutchinson's idea of a niche yielded a set of families of theories that explain coexistence in terms of the partition of the hyperspace of environmental parameters; it is called "limiting similarity".

But, as Hutchinson immediately noticed, the competitive exclusion and parsing of fundamental niches is not the last word on diversity. Actually, the amount of extant coexisting species results far higher than what the partition of the environmental parameter space would predict. Hutchinson – a limnologist and marine ecologist, familiar with the many species of plankton – famously named this the "paradox of the plankton". The surprising fact is that even though the environmental parameters in deep ocean are rare and vary poorly, there are many species of plankton – thousands – which diverge from the prediction of the competitive exclusion model.

A possible explanation of this divergence is that in fact the direction of competition alternates regularly, so that the equilibrium – namely, the complete partition of the parameter space into realized niches – is never reached and many species coexist outside this equilibrium. Another option, also considered by Hutchinson at the time, is that there are many tiny variations of parameters that are not significant or detectable but still play a role in determining niches (G.E. Hutchinson 1959). The first option is an out-of-equilibrium, the latter is an equilibrium one. In any case, what is shown here is that the pure limiting similarity modeling does not grasp the reasons for coexistence. Even if it's a law, and, as M. Weber 1999 argued – against philosophers like Smart (J.J. Smart 1963) or later on Brandon (R. Brandon 1997) or Rosenberg (A. Rosenberg 2001), who claimed there are no laws in biology – perhaps the only law in biology, this law is challenged by many counterexamples, fluctuations, irregularities and particular cases: a point that would further support Lawton's (1999) conclusion.

Many sophisticated variants of limiting similarity theory were consequently elaborated in order to account for those apparent falsifications of the predicted outcome – a bit like the Ptolemean system of the orbits of planets gave rise to extremely smart variants of the system, with ecliptic planes etc. Finally, inspired by R.H. MacArthur and R. Levins 1964 paper on patchy environments, a very sophisticated variant of niche theory called R* ("resource-ratio") theory was proposed in the 1980s. In D. Tilman's 1982 formulation, it asserts that "when resources are heterogeneously distributed, the number of species can be larger than the number of limiting resources, thereby resolving Hutchinson's paradox of the plankton. R* theory is a conceptual advance over previous phenomenological-competition theories, such as the Lotka-Volterra predator-prey model, because it predicts the outcome of competition experiments before they are performed" (P. Marquet *et al.* 2014).

Ecologists strove to find the laws of coexistence, but the cost was the extreme sophistication of the mathematical theory. But what happened to the coexistence problem, interestingly, also affected the understanding of some specific patterns of coexistence and diversity, as shown below.

2. Checkerboard patterns and neutral models

It's in the context of the assessment of the competition-based theory of coexistence that the notion of neutrality and stochasticity came first to the fore in ecology. The issue was the explanation of the distribution of species in communities, and not of pure coexistence per se, as targeted by the competitive exclusion principle.

The so-called "null models war" broke out in 1977. Jared Diamond argued that competition is the cause of the checkerboard distribution of species, or the case in which, for instance in an archipelago, species are present on an island only when another is absent locally and reciprocally (J.M. Diamond 1975). Ecologists Daniel Simberloff and Edward Connor challenged Diamond's method, arguing that under a rigorous statistical procedure for computing the probability of the checkerboard distribution no significant conclusion could be drawn on the effects of competition from a checkerboard-like attested pattern (E.F. Connor and D.S. Simberloff 1979, 1983; D.S. Simberloff 2014). It was a rude controversy (W. Dritschilo 2008), all the harsher because of the significant impact of the diverging conclusions on conservation practices. The side of Simberloff, apparently more technically refined, was accused of being oblivious to actual biology (and conservation needs). The war culminated in an issue of *The American Naturalist* devoted to "A Round Table on Research in Ecology and Evolutionary Biology" (G.W. Salt 1984), with the contributions of some of these authors. Here, J. Roughgarden 1983 for instance stated: «No biological processes are exhibited that produce the distributions predicted by the null models. Hence, we do not learn anything by falsifying these hypotheses», adding: «the neutrality hypothesis is about real processes».

Ironically, in the very same years Stephen Hubbell, an ecologist working in the Barro Colorado Forest in Panama, an ecological station and lab monitored by the Smithsonian Institution (J. Sapp 2016), published a paper on the distribution of trees in tropical forest that hinted towards the idea that a neutral model with purely random events underlying the dynamics might explain the biodiversity patterns in trees.

> Suppose that forests are saturated with trees, each of which individually controls a unit of canopy space in the forest and resists invasion by other trees until it is damaged or killed. Let the forest be saturated when it has K individual trees, regardless of species. Now suppose that the forest is disturbed by a wind, storm, landslide, or the like, and some trees are killed. Let D trees be killed, and assume that this mortality is randomly distributed across species, with the expectation that the losses of each species are strictly proportional to its current relative abundance. Next let D new trees grow up, exactly replacing the D "vacancies" in the canopy created by the disturbance, so that the community is restored to its predisturbance saturation until the next disturbance comes along. Let the expected proportion of the replacement trees contributed by each species be given by the proportional abundance of the species in the community after the disturbance. Finally, repeat this cycle of disturbance and resaturation over and over again. In the absence of immigration of new species into the community, or of the re-colonization of species formerly present but lost through local extinction, this simple stochastic model leads in the long run to complete dominance by one species. In the short run, however, the model leads to lognormal relative abundance patterns, and to geometric patterns in the intermediate run (S.P. Hubbell 1979, p. 1306).

Hubbell didn't publish almost anything on neutrality, in part because he did not want to get involved in the speculations on neutral models that were so harsh at the time (pers. comm.), or also because of the possible hostility the use of neutral or null models in ecology could trigger at those times among some field ecologists. The publication of the *Unified Neutral Theory of Ecology and Biogeography* (Hubbell 2001, hereafter UNTB), the book that brought to the fore the "neutral theory" as the most serious alternative to the niche models emphasizing the key role of competition in shaping biodiversity patterns, had to wait for the null models war to calm down a bit.

The stochastic model sketched in the 1979 paper was the germ of the whole neutral theory book Hubbell published in 2001. It explains 'in the short term' the lognormal patterns seen by Fisher. In the long run, it leads to dominance and that's a shortcoming of the model Hubbell will supersede later on in the 'neutral theory' completed. In the neutral theory, the key idea is the 'ecological equivalence', namely the identical birth and death rates per capita of all species. It is implicit that the probability of replacement of a tree by trees of all other species is proportional to their frequency, so the "choice" of the replacing individual (of its species) is random.

When MacArthur and Wilson elaborated in 1967 their *Theory of island biogeography*, they also thought in terms of equivalent fitness of species. In their island-mainland model, species that occupy a mainland randomly colonize islands, and the amount of species to be found on each island depends upon the mainland population size, its distance to the island, the number of species on the mainland and on the other islands, and it is given at the equilibrium between extinction and immigration. This simple model allows predicting the species area-curves, their different profiles in continuous mainlands and in archipelagoes, as well as the evolutionary fate of some characters of those species (convergence or divergence). In their island biogeography, selection intervenes only later on in the models.

For this reason Hubbell considered *Island biogeography* as the first of a family of models explaining diversity that contrasts with limiting similarity and what he calls 'niche assembly' models. Here, dispersal is the key of the assembly, niche and competition don't play a major explanatory role. The neutral theory is a more elaborated form of dispersal assembly model, and Hubbell intends to show that his understanding of ecological equivalence allows to explain not only species area curves at the scale of biogeography, as MacArthur and Wilson were doing, but also biodiversity patterns such as SAD at the local scale of community.

Granted, UNTB can appear as a null model (B.J. McGill *et al.* 2006): testing whether niches determine species coexistence seems to require that this particular coexistence cannot be due to chance (see also N.J. Gotelli and G.R. Graves 1996, arguing that null is not neutral). However, even if viewed as a null model, Hubbell's neutral theory does not correspond to Simberloff's or the later Gotelli and Graves 1996 null models: it is not built by randomly reshuffling the extant data, but by starting with some processes – migration, speciation, dispersal, ecological drift –, then considering their outcomes, and comparing them to what would happen through niche effects. As Bell indicates:

> The weak version [of neutrality] recognizes that the neutral theory is capable of generating patterns that resemble those arising from survey data, without acknowledging that it correctly identifies the underlying mechanism responsible for generating these patterns. The role of the neutral theory is then *restricted* to providing the *appropriate null hypothesis* when evaluating patterns of abundance and diversity. […] statistical null hypotheses based on randomization are not appropriate for evaluating ecological patterns that stem from species distributions, because local dispersal readily gives rise to spatial patterns (G. Bell 2001).

Yet the times when ecologists designed null models like Simberloff and Connor's correspond exactly to the emergence of neutral models in another field – paleobiology. A major event in the advent of this new discipline was in fact the MBL model by Gould, Raup, Schopf and Simberloff (himself involved in the null models controversy in ecology), simulating shape of clades at a very long timescale (D.M. Raup *et al.* 1973; J. Huss 2009). Biologists' interest for neutral modeling is confirmed by *Neutral models in biology* (M.H. Nitecki and A. Hoffman 1987), which includes sections on paleobiology, on ecology, and on genetics (by Jim Crow). UNTB appears to have maturated in such an atmosphere of neutrality-friendly biology, but emerged genuinely when it was over; possibly, after the null model wars in ecology made people more acquainted with neutral models and less reluctant to selection-free models.

3. The unified neutral theory of ecology: project and characteristics

3.1. Ecological equivalence and randomness in ecology.

In Hubbell's UNTB, random events happen at each step. His model develops the insight of the 1977 paper: it features a community, and even a metacommunity, of *n* species in which at each time step an individual of a species in the focal community dies and is replaced by another one. The traditional, limiting similarity view would understand the substitution of the dead individual in Hubbell's model as not random, and the key for the overall replacement would be the 'competitive exclusion principle'. On the contrary, Hubbell's theory assumes a "hypothesis of ecological equivalence": each individual in each species has the same birth and death rates, which means that everything works as if we had no selection. In effect, when an individual of a given species dies, in the Hubbellian model there is no reason that an individual of species X rather than of species Y replaces it, so it is a random choice of X or Y that determines which individual replaces it. The model understands each step of random substitution as a Markov process; and the replacement of dead individuals occurs in a zero-sum game, limited by the population size (Figure 2). Hubbell's theory is *neutralist* because differences between species are by definition irrelevant and do not explain biodiversity patterns.

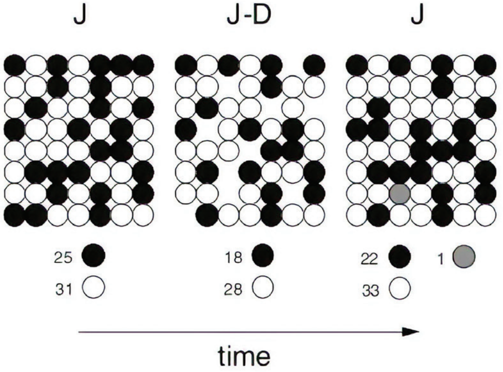

Figure 2. Simulation of the Markov process of a zero sum game in a community (from UNTB).

Nonetheless, the theory has been very predictive of many biodiversity patterns (coral reefs, tropical forests), exactly like Kimura's neutralism for nucleotide composition of genomes (McGill *et al.* 2006). This predictive ability has been the most surprising feature, since the ecological equivalence assumption seems highly unrealistic: species have of course biological differences and it seems intuitive that those differences should play an explanatory and causal role in their distribution. This predictive and therefore explanatory ability of the neutral models have been the chief epistemic problem of the theory (e.g. S.P. Hubbell 2006; R.D. Holt 2006; F. Munoz and P. Huneman 2016). A major issue raised about the status of the theory, in the wake of the checkerboard controversy, was indeed the *place for null hypotheses*. Some ecologists indeed consider that the neutral theory is a null hypothesis (McGill *et al.* 2006), against which any hypothesis about species coexistence or SAD should be measured, but not a hypothesis by itself. Others tried either to understand the emergence of ecological equivalence, and show that even though niche processes rule populations of each species, ecological equivalence can be expected at higher levels, as a result of the intertwining of local and regional ecological processes (Hubbell 2006; Munoz and Huneman 2016). But for us here the lesson is that a theory putting contingent events at the forefront of its modeling method seems to succeed in explaining patterns, and therefore provide ecology with some law-likeness, against Lawton's pessimistic diagnosis.

3.2. Neutral ecology in 2001: metacommunity and speciation.

Hubbell's 2001 book is hugely different from the first 1979 insight quoted above. One major new concept in the formulation of the theory is the *metacommunity*. In fact, Hubbell's 1979 prediction that in the long run the community would undergo the monodominance of one randomly chosen species did not hold true. Therefore, he adds in UNTB the level of metacommunity to this first formulation of ecological neutralism. Since individuals to be replaced may also be replaced by individuals from other communities in the metacommunity, the community dominance at the limit no longer happens in the model, allowing a better fit with the data. But the overall dynamics is now of course more complex, since it combines the community (local) and the metacommunity (regional) scales.

Notice that, by emphasizing the articulation between regional and local dynamics regarding biodiversity, Hubbell shares the general concern about the epistemic value of community as a unit of ecological analysis that came to the fore in the 2000s. At this time in fact the traditional focus on the rules for the constitution of the community (assemblage and succession) shifted toward the metacommunity and metapopulation level. Ricklefs, a fierce critique of the neutral theory, in his paper on the “Disintegration of the community” (R.E. Ricklefs 2008), argues that focusing on the community misses the major determinants of the dynamics, since what happens within it mostly hinges around other communities. Lawton’s paper in 1999 can be regarded as a first manifestation of this skepticism regarding the very project of community ecology as a law. But while Lawton lamented the impossibility of a rigorous science, Hubbell took up the challenge by elaborating a theoretical framework that enlarged community ecology and articulated levels. In this sense, Hubbell’s UNTB, a powerful response to the community ecology crisis, is driven by a concern for unification. In fact, the assumption of ecological equivalence entailed in his neutral theory is likely to be construed across all the scales involved in the dynamics of biodiversity, and therefore is likely to provide a unifying theoretical framework for ecology.

Another missing concept in Hubbell’s early version of his theory with respect to UNTB is *speciation*. Hubbell admits to have been driven to introduce speciation by a student in tropical ecology courses in Princeton (pers. comm.). He introduced it in UNTB as point speciation, which made indeed the parallel with the neutral theory in genetics more salient. One of Hubbell’s latest challenges consists in considering a more realist view of speciation, accounting for the fact that for several generations individuals from new species are not readily distinguishable from individuals of the prior species. This “proctracted” speciation models yields in many cases fitter predictions than the classical neutral model (J. Rosindell *et al.* 2010).

Encompassing speciation is crucial because it allows Hubbell to embed his early insights of neutrality into the metacommunity dynamics, since it turns metacommunity into a reserve of potentially new species likely to bypass the absorbing character of the metacommunity under drift. Then, «adding speciation unexpectedly resulted in a unification of the theories of island biogeography and relative species abundance-theories that heretofore have had almost completely separate intellectual histories» (UNTB, p. 5).

But a major feature of the UNTB is its explicit reference to Kimura’s theory of neutral evolution, which challenged traditional Modern Synthesis thinking in population genetics in the 1960s (J. Crow 2008). I will consider in more detail the implications of this parallelism.

3.3. *Parallelism with neutral evolutionary genetics*

Generally speaking, Kimura and Hubbell have elaborated the same kind of model: assuming neutrality – i.e., fitness invariance for species, or relative fitness equality for alleles – they infer the diversity patterns exhibited by the varying alleles in the genome or species in the community. The parallel holds in a very detailed way: species (in ecology) correspond to allele types (in genetics), population corresponds to gene pool, speciation corresponds to mutation, dispersal corresponds to migration, niche effect corresponds to selection, and ecological drift corresponds to random genetic drift. Moreover, Hubbell introduced the "fundamental biodiversity number", namely a parameter Θ governing biodiversity dynamics, where earlier Kimura has shown that, despite all the complexity of molecular interactions and evolutionary dynamics, a unique parameter, called also Θ by geneticists, and similarly made up by effective population size and mutation rate, governs neutral evolution.

This evolution/ecology parallel was actually missing in Hubbell's early formulations of his ideas. It has been introduced in 2001 with the elaboration of the sampling formula in metacommunities, which appears to be equivalent in the field of community ecology to Ewens' sampling formula in molecular evolution. This formula, used by Warren Ewens in population genetics, concerns sampling selectively neutral alleles in the infinite allele case (W.J. Ewens 1972). It is the same employed for sampling individuals from various species in an infinite metacommunity.

One could philosophically argue against the ecological neutral theory by emphasizing that, in evolution, drift is a process distinct from selection (e.g. D.M. Beatty 1994; J.Walsh 2010): each time there is selection, there is also drift as sampling error proportional to the smallness of the population. Hubbell's idea that ecological drift can occur in communities with no niche effects therefore contradicts this unity between selection and drift in evolutionary theory. Actually, drift in evolution covers two kinds of cases, (a) the fittest does not go to fixation, which indeed is always possible in a token population since fitness describes only probabilities possibly not actualized; (b) cases of equal fitness so that selection doesn't occur, but random pick of the one that goes to fixation. Hubbell's drift is equivalent to the latter case only.

At the same time, fitness invariance is itself yielded by the logics of niche differences: «niche differences obey life-history trade-off rules that maintain per capita fitness equivalence among the niche-differentiated species» (UNTB,

p. 327) Thus, as in evolution, in ecology the *conditions* for drift (i.e. ecological equivalence) are yielded by the fact of selection (i.e. by niche differentiation).

4. Epistemic status of the theory: what stochasticity, what laws?

What kind of epistemological attitude did the elaboration of Hubbell's UNTB allow? What solution does this attitude bring to Lawton's challenge?

4.1 Paradigm shifts?

In some way Hubbell's idea of an extensively equivalent nature was entrenched in potentialities that were already mainstream: neutral genetics, of course, outside ecology, and island biogeography within ecology. Yet two paradigm shifts characterize this view. First, change occurs regarding the paradigmatic ecological object: the *Theory of island biogeography* had introduced the "island", then finally ecological thinking came to detect islands everywhere; Hubbell put the tropical forest at the center of the stage. Second, very deeply, what emerges with Hubbell is an *ecology of non-equilibrium* – which was already indicated as an empirical result in the 1979 paper: «the available circumstantial evidence suggests that the forest is in a nonequilibrium state». Yet major theories in ecology were equilibrium theory, considering the state of affairs from the viewpoint of equilibrium reached: competitive exclusion, equilibrium between immigration and extinction in *Theory of Island Biogeography*, optimal strategies reached by selection in behavioural ecology (e.g. R.H. MacArthur and R.E. Pianka 1966). In many cases, natural selection brings about those equilibria, which entitles biologists to consider traits and phenotypes from the viewpoint of achieved selection. This is not available in UNTB; on the contrary, the zero-sum game models a system that is not oriented towards equilibrium (as would do fitness maximization).

4.2 Epistemic attitudes: lawlikeness, mathematics and chance.

For Lawton, ecology is a gerrymandered patchwork of generalizations at all scales. This plainly contrasts with Hubbell's unifying intent, which could be so defined: «starting first from principles and then asking what patterns in nature we expect to see based on the action of elementary processes» (M. Vellend 2010). Hubbell starts with generality. On the basis of simple assumptions, one constructs a model and then reflects upon the plausibility of the assumptions. Neutral theory is to some extent the most parsimonious hypothesis: parameters such as niches differences are set to 0, and then one builds the model, computes outcomes – and compares them to data[1]. Where this parsimonious theory fails, it shows that biological difference (niches and competition abilities) should play an explanatory role – and not before, otherwise the model will face testability problems. «Exactly when and how a good formal neutral theory fails should be as interesting, if not more so, as when and how it succeeds» (UNTB, p. 311).

Neutral theory in ecology appears therefore as an attempt to systematize the simplest explanatory framework for pervasive pattern generalities in ecology: log-series or log-normal shapes of SAD, species area curves such as the Arrhenius law, which proves very robust. Hubbell's gambit is that a single theory can account those seemingly universal patterns – and that this theory should minimize its amount of parameters. Especially, it should rather derive key parameter values from a few parameters such as m (migration rate), J (metacommunity size) and Θ, rather than assume them in advance. Extinction rates were assumed in *Theory of Island Biogeography*, but derived in UNTB; community ecology assumes species richness in order to investigate SAD, and biogeography also assumes it to explain species area curves; and in general, niche theories assume the set of niches, in order to apply competitive exclusion principles. In contrast, the neutral theory derives SAD and species area curves, as well as the amount of species, from its basic parameters. If the predictions fit the data, then it has a legitimate pretension to be taken seriously.

This is why the neutral theory claims an epistemic superiority to limiting similarity theories like the R* theory. However, it includes a high amount of free parameters, whereas the neutral theory in fact has only three or four depending upon the models (Θ, m, J). Considering that they yield the same predictions, one should then favor the neutral theory for parsimony reasons. Moreover, the epistemic cost of the sophistications of the R* theory is that it

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[1] Compare with *Theory of Island Biogeography*: «From these a priori mathematical considerations, a biological portrait of the superior colonist is drawn, and matched against an empirical description of superior colonising species made by previous biogeographers» (MacArthur and Wilson 1967, p. 93).

is very hard to falsify it, since one can set the parameters in the correct way to yield the expected results. Inversely, estimating the value of parameters is highly difficult, given their amount, which is an advantage of the neutral theory, because calibrating models is easy since it has only three parameters.

Simplicity and testability are therefore the key epistemic values claimed by Hubbell, added to simplicity, unifying character and parsimony, even though the latter are not explicitly discussed[2]. The concern for parsimony and hypothetico-deductive reasoning allowed a new hope for an integrated and unified theory in ecology, in which patterns could be systematically explained. To this extent, the contrast between Lawton's pessimistic view, inspired by the failures of inductive approaches to pattern-explanatory mechanisms, and Hubbell's strongly mathematical and deductive approach, provides us with two diverging perspectives on the chances of ecology as a science.

Yet the most important point to make here is that while Hubbell strives for generalization and a completely local-regional unified explanation of various recurring patterns, his ability of reaching such goals relies on the major features of UNTB, namely ecological equivalence – or, in other words, the non-relevance of biological species differences in their relative abundances, which ultimately involve stochastic success, i.e. chance.

4.3. Chance and scale differences an ecology and biology

Hubbell's success in elaborating a unified theory likely to supersede the flaws of limiting similarity or niche-based theories suggest a few insights about biological laws and biology *generaliter*. First, if both neutral theories – Kimura's and Hubbell's, evolution and ecology – are taken as true, a picture of ecology and evolution emerges in which stochasticity seems to rule the highest and the lowest levels of the hierarchy of biological domain. Communities on the one hand, alleles on the other hand are mostly driven by stochastic dynamics, whereas intermediary levels – organisms, groups, species – seem to be mostly governed by natural selection. This is just an untested hypothesis, but the picture arguably deserves some consideration.

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[2] Notwithstanding the fact that epistemological considerations have been vindicated by him and coauthors in the 2014 paper, and also that controversies around UNTB have been quickly revolving around deep epistemic issues: model testing, statistics, parameter estimations, null hypotheses, etc.

And this picture could be even more general. As it is well known, S.J. Gould 1989 emphasized that contingency may have played a major role in the history of life at the highest time scale. Even if selection plausibly determines the outcomes of microevolution, which makes evolution at this scale quite predictable and not much contingent – since selection is a directional process, increasing adaptedness in general – considering megaevolution, the appearance of clades, lineages, new body plans and their disappearance, confronts us with mass extinctions due to contingent events (with respect to biological conditions) that have contingent outcomes (e.g. up to 70-80% of the species went extinct in each of the five major mass extinctions, in a quick lapse of time which suggests that the 'choice' of those getting extinct was chancy). Thus, Gould suggests that contingency rules also at the highest time scales of paleontology (P. Huneman 2017). Hubbell expressed this notion of a parallelism between paleobiological scales and biogeography scales with respect to chance and even suggested that a common explanation might be possible. S.P. Hubbell (2005) indicated that paleobiology, with all the data regarding the phylogenies of biodiversity, may provide a set of evidences even more reliable for the neutral theory than ecological data. In fact, a fundamental level of unification lurks behind the overall theory, namely unification between ecology and evolution, sought ever since Hutchinson[3], but never reached. Indeed, metacommunity drift dynamics, governed by a parameter Θ which is very large, proves very slow (common species tend to dominate for a very long time), so that «ecological and evolutionary rates of change will become commensurate on large landscape scales» (UNTB, p.149). To this extent, neutral ecology directly pertains to macroevolution, hence to paleobiology.

The overall picture would be that, even if Darwinian evolution governs the origin of species and microevolution, as well as most of the phenotypes of organisms, chance is overwhelmingly explanatory at both the extreme spatial scales – genome composition (Kimura), and metacommunities (Hubbell) – and the largest timescale – megaevolution (Gould). The explanatory importance of chance at each time and spatial scale is not at all homogeneously distributed: on the contrary, chance appears as negligible at all intermediate space/timescales, and crucial at extreme ones. This is of course a sort of meta-

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[3] He authored the *Ecological Theater and Evolutionary Play*, a title that indicates both the need and difficulty of unification between both.

physical hypothesis, justified by the successes of neutral theories in ecology, evolution and paleobiology.

But the major lesson of the neutral ecology is that chance is not in principle an obstacle to understanding and science: on the contrary, modeling chance is what allows us to overcome the feeling that ecological communities have no rules, follow no laws, and are just a mess which is only susceptible to be described but not explained.

Surely, Hubbell's model is not providing us with laws, in the sense of what philosophers of science debate under this name: counterfactual-supporting generalizations, necessary connections between universals, etc. Nonetheless, a shift in the modeling, putting chance and stochasticity, hence contingent events, at the center, allowed him to answer Lawton's challenge about ecology. Even if it is not shown that 'laws' govern ecology, neutral theory suggests that 'absence of laws' or lawlessness is not a correct depiction of the scientific status of community ecology and biogeography.

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II

Predictability from Biology to Neuroscience and Biomedicine: Are They So Predictable after All?

Uncompromising Empiricism Once Again? Big Data and the Case of Numerical Taxonomy

Barbara Continenza

> In that Empire, the craft of Cartography attained such Perfection that the Map of a Single province covered the space of an entire City, and the Map of the Empire itself an entire Province. In the course of Time, these Extensive maps were found somehow wanting, and so the College of Cartographers evolved a Map of the Empire that was of the same Scale as the Empire and that coincided with it point for point. Less attentive to the Study of Cartography, succeeding Generations came to judge a map of such Magnitude cumbersome, and, not without Irreverence, they abandoned it to the Rigours of sun and Rain.
>
> Borges, *A Universal History of Infamy*

Big Data are pervasive and ubiquitous. The expression evokes exactly what it states: massive amounts of data – a "deluge" of data is the most recorrent commonplace – destined to further proliferate thanks to the increasing spread of digital devices such as smartphones, labtops, personal sensors and so on (D. Bollier 2010). The Cisco, worldwide leader in Information Tecnology and networking, estimates that, over the past five years, global Internet traffic has increased fivefold, and it will triple again in 2019. In the same year, the number of Internet-connected devices is expected to reach 24 billion (14 billion in 2015). There are already «more data […] being generated every week than in the last millennia», and at a rate that is likely to accelerate» (G. Rieder and J. Simon 2017, p. 86).

Lots of "Big Data scientists" are already collecting, processing, analyzing and managing these immense amounts of data for the most diverse purposes: from business to government agencies, from marketing to social networks, from educational institutions to scientific laboratories.

From the point of view of their training and skills, Big Data scientists are transversal figures. They are statisticians, computer scientists, mathematicians, engineers, bioinformatics (D. Boyd and K. Crawford 2012): new professionals increasingly required for their ability to apply analytical power to huge masses of messy data. The number of degree courses offered both from private providers and universities is now very high for «the sexiest work of the 21st century» (T.H Davenport and D.J. Patil 2012).

It should be stressed from the start that Big Data are not raw data or, as some claims, simple tools. They convey «a profound change at the levels of epistemology and ethics. Big Data reframes key questions about the constitution of knowledge, the processes of research, how we should engage with information, and the nature and the categorization of reality» (Boyd and Crawford 2012, p. 665).

We will firstly introduce from a historical and epistemological perspecive the debate about the claims of the "new science" of data, heralded by Jim Gray, the creator of Google Earth, as the "fourth paradigm", a new stage in the development of science after the stages of experimentation, induction and simulation. Secondly, we will investigate a historical antecedent of the actual debate, by comparing these claims with the ones raised by Numerical Taxonomy, or Phenetics, in the second half of the tweentieth century.

As Gray stated in 2007:

> Originally, there was just experimental science and then there was theoretical science, with Kepler's Laws, Newton's Laws of Motion, Maxwell's equations, and so on. Then, for many problems, the theoretical models grew too complicated to solve analytically, and people had to start simulating. These simulations have carried us through much of the last half of the last millennium. At this point, these simulations are generating a whole lot of data, along with a huge increase in data from the experimental sciences. People now do not actually look through telescopes. Instead, they are "looking" through large-scale, complex instruments which relay data to datacenters, and only then do they look at the information on their computers» (J. Gray 2009, pp. XVIII-XIX).

Thus, according to Gray, science has undeniably changed and the new data-intensive science, or e-Science, uses methods and technologies different from former computational science. Its purpose is «to have a world in which all of the science literature is online, all of the science data is online, and they interoperate with each other. Lots of new tools are needed to make this happen» (Gray 2009, p. XXX).

The problem is, however, neither the vast amount of data nor the tools and procedures used to manipulate and analyze them, but rather the alleged and acclaimed paradigmatic turn: «a cultural, technological, and scholarly phenomenon that [...] provokes extensive utopian and dystopian rhetoric» and that goes with «the widespread belief that large data sets offer a higher form of intelligence and knowledge that can generate insights that were previously impossible, with the aura of truth, objectivity, and accuracy» (Boyd and Crawford 2012, p. 663).

Indeed, thanks to the proclaimed all sufficiency of numbers, a kind of new, uncompromising empiricism (R. Kitchin 2014) is emerging. In the name of a radical re-foundation of knowledge esclusively based on data, it announces the dismissal of old theories and disciplines, as well as the marginalization of previous research methods for the identification of causal links.

In 2008, Dhanurjay Patil and Jeff Hammerbacher, who at the time were rispectively leaders of data and analytics efforts at LinkedIn and Facebook, coined the term *data scientists*, «those who use both data and science to create something new» (D.J. Patil 2011). In the same 2008, the British American Chris Anderson – physicist by training, journalist and essayist, considered one of the ten most influential minds of the American media – also published a provocative article entitled *The End of Theory. The Data Deluge Makes the Scientific Method Obsolete*. This article is recurrently quoted when it comes to discussing the epistemological issues of the Big Data Science, whose conceptual and philosophical complexity deserves attention since it involves the statute of science itself as well as its methodologies.

The End of Theory

For Anderson, the traditional scientific approach, which has lasted for centuries and is based on hypothesis, models and tests, is no longer tenable in the Petabyte Age, the «most measured age in history». The champion of this new age is rather Google, which «conquered the advertising world with nothing more than applied mathematics. Anything about the culture and conventions of advertising – it just assumed that better data, with better analytical tools, would win the day. And Google was right» (C. Anderson 2008).

According to the traditional approach, simple correlations of data are suspicious, because they may represent mere coincidences. An effective explanation is only achieved by identifying the underlying causal mechanisms, and can only be obtained through a model that allows to reliably connect the data. For this view of science, Anderson emphasizes, «data without a model is just noise» (Anderson 2008). With the rise of Big Data, however, all this is out of date. No hypothesis, no models, no tests, and, above all, no theory are needed. Anderson's claims are «with enough data, the numbers speak for themselves» and «correlation is enough» (*ibidem*).

Physics would already have faced with the inadequacy of its procedures in the field of quantum mechanics which, though on a statistical basis, still uses a model «and as such, too, is flawed, no doubt a caricature of a more complex underlying reality. The reason physics has drifted into theoretical speculation about n-dimensional grand unified models over the past few decades [...] is that we do not know how to run the experiments that would falsify the hypotheses – the energies are too high, accelerators too expensive, and so on» (*ibidem*).

Biology also abandoned the oversimplification of reality entailed by the Mendelian model, and has embarked on a different pathway. Postgenomic biology embraced data-driven science for the unbiased discovery of gene-protein interactions and other aspects of epigenetics, opening to unexpected interpretations. Thus it «challenged the view of DNA as a destiny and even introduced evidence that the environment can influence inherited traits, something once considered a genetic impossibility» (*ibidem*). DNA sequencing by Craig Venter through supercomputers and statistical analysis of data is the emblematic example of this «new way of understanding the world» for which correlation is enogh.

"Googling Your Genes"

Craig Venter is the American biochemist-geneticist universally known for having announced, in 2000, the sequencing of human genome, not to mention the clamorous results achieved by sampling the biodiversity of whole ecosystems through the method of "whole-genome shotgun sequencing" of microbial populations collected en masse. In 2003, he started mapping the Ocean's DNA, and this first pilot study was followed by a further expedition, the Sorcerer II Global Ocean Sampling, on the routes of the famous nineteenth-century expedition of the Challenger (1872-1876), during which about 4,700 new marine species had been discovered. In the *Report of the Scientific Results of the Exploring Voyage of H.M.S. Challenger*, in 50 volumes, supervised by John Murray (J. Murray 1873-1876), these amazing results are described as «the greatest advance in the knowledge of our planet since the celebrated discoveries of the fifteenth and sixteenth centuries» (J. Murray and J. Hjort 1912).

The results of the environmental metagenomics project achieved by the Sorcerer Expedition on the genetic and biochemical microbial diversity as well as on the role of marine microbes by sequencing their DNA certainly are not less sensational. «The resulting 7.7 million sequencing reads provide an unprecedented look at the incredible diversity and heterogeneity in naturally occurring microbial populations» (D.B. Rusch *et al.* 2007).

The J. Craig Venter Institute (JCVI) has also embarked in the Air Genome Project applying the same techniques of 'shotgun' to characterize the genomic spectrum of microorganisms through the air filtering. Moreover, after 15 years of research on the synthesis of large DNA molecules and chromosomes «to build a minimal cell that contains only essential genes» (D.G. Gibson *et al.* 2010, p. 52), in 2010, the Craig Venter Institute successfully achieved the construction of the first self-replicating, synthetic bacterial cell.

The applicative expectation in terms of synthetic biology and artificial life are extraordinarily high (bacteria programmed to produce biofuels, green fertilizers, vaccines, new ways to counter environmental pollution), but above all, the DNA sequencing is now considered as the driving force of a new era of medicine and personalized medicine.

Indeed it is precisely on digital biology that a strategic convergence has been achieved between Venter and Google, that is, respectively, the largest genomics sequencing facility and the huge computing power to process enormous amounts of data. Google's Calico (California Life Company, founded in 2014) and Venter's HLI (Human Longevity Inc., launched in 2014) share the intent of extending healthier, high performing, lifespan to change the perspectives of aging using large-scale genome sequencing.

It is a really exciting project with a very high impact made possible by the increasingly cheaper genome sequencing technology, although the financial commitment is still extraordinarily high. The latest Illumina technology, the famous "thousand-dollar genome" instrument, HiSeq X, capable of sequencing five human genomes in a single day, is the fastest sequencer in existence, which costs a million dollars (Krol 2014). HLI bought twenty of them to sequence tens of thousands of genomes every year.

It's just data?

Venter's achievements realize Anderson's expectation: by analyzing data with Google-quality computing resources, «Venter has advanced biology more than anyone else of his generation». As he had explained: «we can stop looking for models. We can analyze the data without hypotheses about what it might show. We can throw the numbers into the biggest computing clusters the world has ever seen and let statistical algorithms find patterns where science cannot» (Anderson 2008). In 2008, Venter's sequencing of entire ecosystems discovered «thousands of previously unknown species of bacteria and other life-forms» (*ibidem*). As Anderson emphasized, however, the expression "discovering new species" must not be associated to Darwin, that is to «the old way of doing science». Venter, in fact, «can tell you almost nothing about the species he found. He doesn't know what they look like, how they live, or much of anything else about their morphology. He doesn't even have their entire genome. All he has is a statistical blip - a unique sequence that, being unlike any other sequence in the database, must represent a new species» (*ibidem*). Correlation is enough, indeed!

Actually, "discovering new species" has always represented one of the most critical issue in the knowledge of the living beings. "Discovering new species" means, broadly speaking, to classify reality and organize it into categories. And, in this sense, defining the "concept" of species and constructing taxonomies of the living beings in biology was the inescapable requirement «to convey and store information about the biological world» (J. Dupré 2001, p. 208). Originally the leading criterion of classifications was the morphological resemblance, which ignited the great classical debates between essentialism and nominalism and those on the naturalness or artificiality of systems and methods of classification (B. Continenza 1996). Since Darwin «the hidden link that the naturalists are unconsciously seeking» has been instead identified in the common descent, which is «the one certainly known cause of similarity in organic beings» (C. Darwin 1859, pp. 369, 403). However, understanding and explaining the resemblances through the identification of causal connections is exactly "the old way of doing science" that Anderson sets aside. The "new knowledge" presents itself as radically different and, in fact, it does not relate to Darwin at all. The "datification" of life that is at the heart of Big Data is «a way of accessing reality through bringing interactions and relationships to the surface and making them visible, readable and thereby governable, rather than seeking to understand hidden laws of causality (D. Chandler 2015).

Numerical Taxonomy

It may be useful to recall that the opposition between such approaches to biological classification, i.e. data-driven classification and theory-driven classification, is not new in the history of taxonomy. We refer, in particular, to Numerical Taxonomy, or Phenetics, which, in the 1960s and 1970s, produced a longstanding controversy with the other two systematic schools that, so to speak, already occupied the field: Evolutionary Systematics and Cladistics.

Its two best known exponents, Robert R. Sokal, a biostatistician and entomologist, and P. H. A. Sneath, a bacterial geneticist and biochemist, published in 1963 their pioneering book on the subject, *Principles of Numerical Taxonomy*. Ten years later, in 1973, the updated and expanded version, *Numerical Taxonomy. The Principles and Practice of Numerical Classification* appeared.

At its debut, in the late 1950s, Numerical Taxonomy is presented strictly associated to the development of computers.

> Even though the principles and many of the mathematical ideas underlying modern classificatory methods antedate the appearance of the electronic computer, the recent great increase in classificatory work is intimately related to the development of this new tool. It is difficult to assess the degree to which the acceleration of work in classification is due to the simultaneaous rapid increase in the avalaibility and capability of computers […] An unprecedented number of scientists is at work and new, automated methodologies are yielding information on many properties of numerous objects […]. Without computers it is inconceivable how such development could be implemented (R.R. Sokal 1974, p. 1115).

Thus, computer science was undoubtedly fundamental for the development of Numerical Taxonomy in the 1960s (cfr. B. Sterner 2018), although, as stressed by K. Vernon 1988, its deeper causes are related to the current state of taxonomy and to the rejection of phylogenetic speculation.

Numerical Taxonomy is based on the numerical evaluation of the affinity – or *overall similarity* – among taxonomic units, and on the ordering of these units into taxa according to their affinities (R.R. Sokal and P.H. Sneath

1963). The method consists in identifying a large number of morphological characters attributing equal weight to each of them and in constructing taxa on the basis of the correlations of the characters without considering the genetic and phylogenetic aspects of the organisms. The Numerical Taxonomy thus makes use of large numbers of unweighted characters, of statistical techniques to cluster the similarity values among organisms forming taxonomic groups, and of computers to process the large numbers of required calculations. Moreover, it ignores any phylogenetic information to construct the classification (K. Vernon 1988; Continenza 1996).

In fact, for the phenetists, classifications built on genetic or phylogenetic criteria are based on inferences and generalizations too much speculative and theory-based to guarantee any scientific reliability. «Our current ideas of species and speciation – Sokal claimed in 1975 – are undergoing renewed inquiry and possible change. It would therefore seem a dubious practice to rest a classificatory philosophy so heavily on a preconceived model of speciation» (R.R. Sokal 1975, p. 261). The use of formal and quantitative criteria to establish coefficients of association between so called "Operational Taxonomic Units" (OTU) has the purpose of automating the manipulation of data through an operational system that guarantees the classification repeatability, objectivity and stability. Thanks to its reliability, the applications of numerical taxonomy – expecially conducted on bacteria and, in part, plants – can go further than just biological systematics, including, as its exponents explicitly supported, several other fields ranging «from archaeology to political science, from materials classification to linguistics, from television programming to biogeography» (P.H. Sneath and R.R. Sokal 1973, p. XIV).

As Sokal had clearly stated as early as 1962:

> *A priori* weighting or preference of some characters over others, based on either presumed phylogenetic importance or logical or functional primacy, is an unjustifiable procedure. Equal weighting and use of all characters leads directly into an empirical approach, which attempts to classify organisms on the basis of all available evidence, without preconceived notions about their arrangement (R.R. Sokal 1962, p. 230).

In 1995, more than thirty years after the debut of numerical taxonomy, Sneath reiterated that the early aims and assumptions of numerical taxonomy were «(1) the aims of repeatability and objectivity, (2) the use of quantitative measures of resemblance from numerous equally weighted characters, (3) the construction of taxa from character correlations leading to groups of high information content, and (4) the separation of phenetic and phylogenetic considerations. The subject was viewed as an empirical science» (P.H. Sneath 1995, p. 283). Sokal regards Numerical Taxonomy as the most notable example of the empirical approach in recent years.

David Hull asserted that «the key notion in the empiricist philosophy is the claim that, ideally, a priori weighting is to be completely expunged from taxonomic practice» (D. Hull 1970, p. 33). Phenetists' belief in a purely descriptive, non-theoretical classification is rooted, according to Hull, in empiricist epistemology. Therefore he ascribes to phenetists a kind of «metaphysical compulsion to believe that such a reduction must be possible, and with it, the notion of a purely phenetic classification» (Hull 1970, p. 34).

The claim of an empirical approach actually dates back right at the beginnings of Numerical Taxonomy, in an article by Sneath (1957) on the classification of bacteria. After having established that «Scientific classification is virtually a branch of mathematics which describes the overall similarities of organisms», and that simple mathematical methods are usefull in bacterial classification, Sneath identifies in the eighteenth-century systematist and botanist Michel Adanson (M. Adanson 1763) the first taxonomist «who conceived of the use of every feature impartially and with equal weight. His views were far ahead of his time». The attempt to build a natural system through the consideration of all the parts of the plant would have, in fact, placed Adanson in conflict with his contemporaries who, on the other hand, considered some characteristics more important than others for the purposes of classification. Yet, «Adanson seems to me to have been right, for the concept of 'importance' seems to play little part in the concept of 'greatest content of information'» (P.H. Sneath 1957, pp. 184, 195-196).

In 1963, Sneath delivered an extensive and detailed lecture on "The Mathematics and Classification from Adanson to the Present" at the Congress for the celebration of the bicentennial of Adanson's two volumes *Familles des plantes* (1763-1764). It was an opportunity to reiterate that «Adanson›s Universal or Natural Method was remarkably similar to the first few steps of numerical taxonomy» (P.H. Sneath 1964, p. 483).

On that same occasion, however, the Dutch botanist and historian of botany Frans Stafleu countered Sneath claiming that «it is not true that all properties or characteristics had equal weight for Adanson. To say this is a misinterpretation of his insistence to take all parts of the plants into consideration in order to find a natural order [...] To compare everything and so be open-minded about additional characters, is not the same as giving equal weight to them» (F.A. Stafleu 1964, p. 185). Further polemics were raised on the frequent use of the expression "adansonian" or "neo-adansonian" referred to the Numerical Taxonomy (Sokal and Sneath 1963; Sneath and Sokal 1973; M. Jacobs 1966; D. Hull 1988; Stafleu 1964, K. Vernon 2001). M.P. Winsor (2001) also conducted an articulated historical analysis both on the most recent sources from which Sneath drew his first references to Adanson (J.S.L. Gilmour 1940; F.A. Bather 1927), and on the complicated interweaving of interpretations that characterized the debate on classification. Indeed, Adanson is right in that theoretical and philosophical clash that has repeatedly resorted. As Sloan explains,

Only with those biologists heavily influenced by the empiricism of Locke and Condillac - Buffon, Michel Adanson, and Lamarck - will we see a revival in the late eighteenth century of a challenge to the weighting of characters, in this case directed against Linnaeus and his followers, only once again to be eclipsed by the authority of Cuvier and Antoine Laurent de Jussieu. With the twentieth century, the challenge will again be raised, this time against Darwin himself, with the outcome and consequences as yet undecided (P.R. Sloan 1972, p. 52).

Sloan writes in the 1970s, and the twentieth century challenge he refers to as the «contemporary replay of the eighteenth-century dispute» (Sloan 1972, p. 56), is the one that pushed by Numerical Taxonomy. Numerical Taxonomy was then fully involved in a reorganization of classificatory work and centered on a universalist methodology based on essentially statistical tools as well as on the application of clustering algorithms through the use of computers.

The present scope in not to assess the validity of the historical and theoretical reference established between the Numerical Taxonomy and Adanson. That Adanson was «the patron saint of numerical taxonomy in the early days» (Hull 1988, p. 362) and that Sneath's excursion into history was «part of his effort to shape the future of taxonomic theory and practice» (Winsor 2001, p. 2) is relatively manifest. It is not even relevant to determine whether it makes sense to attribute to Adanson «the elaboration of tables of comparison between each organism and every other which would have been, in effect, a similarity matrix» (Sneath 1964, p. 483). Sneath himself has admitted that it is very doubtful that Adanson had proceeded in this way: «the number of parwise comparison between the 1615 genera in the *Familles des Plantes* total over a milion. It is more likely that he counted the disagreement for some of the comparison only, but did enough to obtain a fair idea of the salient relations between the organisms» (*ibidem*). Stafleu, on the other hand, explicitly denied that Adanson research had been based on statistics, concluding that «it is extremely doubtful whether Adanson really acted as a computer *avant lettre*» (Stafleu 1964, p. 201).

It is not even a matter of determining whether the origins of Numerical Taxonomy are inseparably connected to the use of computers. The fact that computers played an indispensable role in Numerical Taxonomy is evident as well as claimed by its own exponents. More than fifty years ago, numerical taxonomists were part of the first generation of scientists to use computers. This obviously does not mean considering them as "precursors" of the Big Data scientists, though there are many aspects that they seem to share: their claim of inductive reasoning; the "overall similarity" used to identify more formalized exemplars through the use of statistics and character correlations in data matrices; the construction of classifications that are free from theory; repeatability, objectivity and stability considered as distinctive characteristics of their method.

In 1966, Michael Ghiselin wrote a long article where he criticized Numerical Taxonomy on several fronts. In particular, he referred to a recent "turning point" which made the comparison between the different taxonomic schools even more complex (Continenza 1996). In a series of articles published in 1965, Sokal and Camin had indeed stated that their thesis that «phyletic information was generally unknown and unknowable and that therefore, *faute de mieux*, only phenetic classifications are available» and called for «a reconsideration of the entire issue of phenetics and phyletics in systematics» (R.R. Sokal and J.H. Camin 1965, p. 177). Recognizing at this point the usefulness and complementarity of both approaches, the authors regarded their method, programmed for computer processing, as «not substantially different from the conventional cladistic approaches of phylogenists. It simply quantifies and systematizes these procedures, making them objective in the process and permitting them to be put on a computer» (J.H. Camin and R.R. Sokal 1965, p. 324). They also reiterated that the weighting procedure remained consistent with the principles of Numerical Taxonomy, «it is automatic and a posteriori, based on the entire available evidence rather than on a priori or character-by-character weighting as employed in conventional phylogenetic procedures» (*ibidem*).

The articulated and analytical discussion of Ghiselin ranges from the inadequacy of similarity as an objective basis for a natural classification, «as if it corresponded to an intrinsic property of organisms» (M. Ghiselin 1966, p. 212), to the "induction metaphysics", to the misleading idea that quantifying procedures can constitute a foundation of objectivity. The use of computers may also make easier to carry out the traditional logical steps, but it will not modify the underlying theoretical principles, which, according to Ghiselin, were misunderstood by numerical taxonomy because of «a failure to grasp the distinction between induction by simple enumeration and the modern, hypothetico-deductive scientific method» (M. Ghiselin 1966, p. 207).

There is no doubt, however, that by advocating computerization and mathematization, Sokal and Sneath have opened «a contentious and still ongoing debate in the field about the relative epistemic value of mechanical objectivity» (Sterner 2018, p. 59). The opposition between knowledge-driven science and data-driven science resurfaces in the debate about Big Data science. A similar challenge appears to be raised again. Perhaps it is a revival of traditional and returning oppositions, which, at least in part, the criticisms by Ghiselin seem to apply to, so to speak *ante litteram*.

To re-emerge is, in Kitchin's words, an "empiricism reborn", which sees the data-driven-science strongly committed to pursue to the so-called "end of the theory". Data and their correlations would be able to speak for themselves by disclosing, through exclusively inductive procedures, interpretations and predictions that would be otherwise invisible and inaccessible to the deductive approach.

In *Big Data* (2013), one of the most popular texts on data science, we read: «the correlations may not tell us precisely *why* something is happening, but they alert us that it is happening» (V. Mayer-Schönberger and K.N. Cukier 2013, p. 21). Whether it is "a revolution that will transform how we live, work, and think", as the subtitle emphasizes, or a «chimera» (M. Frické 2015), or instead «disruptive innovations» (Kitchin 2014), or just «a reinvention of natural history» (B.J. Strasser 2012), or even a «modern myth» and «a matter of faith», and «some sort of today's oracle, a voice revealing insights and predictions from an abundant yet obscure source that is claimed to be the world itself» (B. Gransche 2016, pp. 58-60), there is however no doubt on the big impact of Big Data on the social and material conditions of research as well as on the epistemological models of knowledge. The great challenge that they have launched to the theory-centric way of thinking (S. Leonelli 2016), beyond any rhetoric, cannot be minimized in any way.

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Big Data and Biological Knowledge[1]

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1.Introduction

Biology is a domain where variation has a fundamental theoretical role. Biological variation is profound and qualitative, and we have defended elsewhere the idea that variation justifies that biology requires its own epistemology. Notably, this variation is expression of the historicity and the contextual nature of living things (G. Longo and M. Montévil 2014; M. Montévil *et al.* 2016) and it is at the core of the adaptivity and diversity of life. Variation is, in part, due to random phenomena at different levels of organization, and to the many forms of interaction between these levels (bio-resonance, see M. Buiatti and G. Longo 2013), yet it is always canalized by constraints and contexts and may be induced by the context to an extent (M-J. West-Eberhard 2003; Montévil *et al.* 2016; G. Longo 2017). In our perspective, variation is thus an integral component, but not the only component, of diversity and adaptation, both in phylogenesis and ontogenesis, up to having a crucial role in the etiology of cancer (A. Soto, G. Longo, D. Noble 2016; C. Sonnenschein and A.M. Soto 1999).

It finally leads to a peculiar form of unpredictability, proper to biological dynamics, since variation is largely based on random phenomena, at all levels of organization (Buiatti and Longo 2013). As for this issue, note that randomness is not an absolute notion, but it means "unpredictability w.r. to the intended theory" (C. Calude and G. Longo 2016b). And biological randomness deserves its proper treatment as related to the changing phase space (the pertinent observables and parameters or the space of all possible dynamics) and to the role of rare events, in particular along evolution (Montévil *et al.* 2016; G. Longo 2016).

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[1] Extensively revised version of G. Longo and M. Montévil 2017, *Big Data et connaissance biologique*, in *Sciences de la vie, sciences de l'information*, ed. by T. Gaudin, D. Lacroix, M.-C. Maurel *et al.*, ISTE-Editions, Paris.

Biologists are thus confronted with the evolutionary diversity and adaptivity of the living. Moreover, organisms possess an internal heterogeneity which corresponds to their different organs (and organites, in the case of cells): "correlated variations" in the terms used by Darwin, depends both on the internal coherence of each organisms and on the changing eco-systemic conditions. Faced with these two dimensions of biological complexity the human mind sometimes seems disarmed. In this context, the contemporary possibility of developing immense digital databases in collaborative frameworks is regarded as a major opportunity. But this opportunity is not without peril – and analyses lacking biological meaning is not the least of these perils.

All fields of biological sciences are not equally equipped to use these growing databases. Some fields build on robust theoretical thinking. For example, phylogenetic analyses rely on the conceptual framework of the theory of evolution, extensively enriched in the XX century. This theory frames the production of knowledge on the basis of data by relying on non-trivial theoretical structures, in particular Darwin's principles ("descent with modification" and "selection"). By contrast, there is no well-established, unified theory to understand organisms, their physiology and their development, in spite of recent advances (see A. Minelli and T. Pradeu 2014; Soto, Longo, Noble 2016; G. Longo *et al.* 2012). Despite decades of informal use, the traditional notion of a genetic program has never acquired a real theoretical status, for a lack of both biological pertinence and of reference to a rigorous scientific notion (G. Longo *et al.* 2012). This lasting tradition leads to a causal priority assigned to the molecular level, a priority that is embodied in the nature of the data obtained by high throughput techniques. By contrast, many relevant quantities are neglected by the use of Big Data in biology. For example, the modeling of an organ like the heart requires to take simultaneously into account several levels of organization (D. Noble 2006). Similarly, many physicists and biologists emphasize the importance of physical quantities in the determination of biological phenomena. Here physical quantities refer informally to the forces and fields of classical mechanics. For example, the stiffness of a tissue or the forces exerted by cells are fundamental determinant of a tissue. However, these quantities are not associated with high throughput experimental methods. For example, the interplay of forces in a morphogenetic dynamics is not measured neither in genomics, nor proteomics or metabolomics. As a result, we can see that the choice of a theoretical framework impacts directly the quantities that should be measured and analyzed.

Beyond the choice of the quantities relevant to understand a given phenomenon, theoretical frameworks also matter for the analysis of data. Statistical analyses are based on mathematical hypotheses that, in general, correspond to theoretical hypotheses, albeit the latter are sometimes informal or even implicit. The capacity of databases to contribute to the comprehension of phenomena depends on the theoretical view that frames the use of these data and confers meaning to them, as well as on the pertinence of these data in relation to a theoretical frame. In short, there is always a choice, sometimes considered to be "obvious" if not unique, of observables to be measured, of a metric, of criteria of numerical approximation: this choice needs to be made and explicitly so.

The application of Big Data to cancer, for example, is developed in a particular theoretical frame, the somatic mutation theory, where the process of carcinogenesis is conceived as the appearance of cancerous cells by the accumulation of somatic, genetic mutations:

> The story of cancer is a story of how the body's complex coding systems go awry through the creation of self-perpetuating errors in cellular replication and growth (A.R. SHAIKH *et al.* 2014).

However, this theoretical point of view encounters major conceptual and empirical difficulties. These difficulties manifest themselves in translational researches and explain the limited medical outcomes of cancer biology despite significant investments. For example, changes in the proportion of deaths due to cancer are not large except in cases which can be interpreted in terms of prevention (R.L. SIEGEL, K.D MILLER, A. JEMAL 2015). One of the most influential advocates of the somatic mutation theory of carcinogenesis acknowledges the difficulties of this genocentric approach and stresses that we are once again faced with the "endless complexity" of these phenomena (R.A. WEINBERG 2014).

Several scholars analyze the situation as the manifestation of a theoretical problem and propose alternative viewpoints about the nature of carcinogenesis (C. SONNENSCHEIN and A.M. SOTO 1999; 2011; S.G. BAKER 2011). These theoretical viewpoints also come with different research strategies, consider different levels of organization and relevant quantities (M. BERTOLASO 2016). However, most of the community stick to the somatic mutation theory. From their perspective, it is then appealing to consider Big Data analysis as a solution permitting the treatment of cancer while keeping the focus on molecular and more specifically genomic data. This technological solution is called personalized medicine or precision medicine. Precision oncology is advocated by groups such as the Personalized Medicine Coalition and is supported by the US government through the Precision Medecine Initiative program.

More generally, the absence of a theoretical framework for organisms makes particularly seductive a certain rhetoric that goes beyond – if not against – the rational use of data. The omnipotence and autonomy of database analysis is at the center of a contemporary myth. For a decade, several successful articles, including one by Chris Anderson (2008), maintain that the figures speak for themselves:

> We can throw the numbers into the biggest computing clusters the world has ever seen and let statistical algorithms find patterns where science cannot [...] Correlation supersedes causation, and science can advance even without coherent models, unified theories [...] No semantic or causal analysis is required.

The idea is that «data miners» are capable of detecting correlations and orienting decisions without having to perform any theoretical discussion. So it is no longer a matter of enriching the «obsolete» scientific method but instead of replacing it, in particular by bypassing theoretical thinking. This point of view is associated with the slogan that the larger the database, the easier it is to find relations on the basis of which to act.

2. Immense databases, prediction, and chance

The rhetoric that defends the replacement of the scientific method by the analysis of big databases can be assessed by the use of Mathematics. Theorems enable us to demonstrate the limits of these purely algorithmic methods by showing the impossibility of replacing the scientific quest for meaning by pure “data mining”. Theorems at the crossroads of ergodic theory and Ramsey’s Theory, a combinatory theory of numbers born in the 1920s and well-developed since then, permit to contradict this use of Big Data (C. Calude and G. Longo 2016a; H. Hosni and A. Vulpiani 2017).

2.1 The deluge of spurious correlations

Let us first consider "Ramsey-type" theorems, used in Calude and Longo (2016a, b). These theorems show that for any correlation between numbers in a database, there exists a number (let us say *m*) such that any database having at least *m* elements contains the demanded correlation. Therefore, it is just a matter of size, and it is possible to compute a threshold beyond which all databases (sequence of numbers) will contain a regularity with the stipulated characteristics. In other words, be as precise as you wish about the criterion for correlating pairs, triplets, etc., as well as the minimal number of times that you want to observe them, in what space and over what duration and the manner in which you will divide up your database (for example, by correlating proximate values, even iterated according to the preferred criterion). Then the theorems mentioned will tell you how many data to gather in order to achieve those criteria, that is to find some correlation realizing them. More precisely, a regularity in an ensemble of numbers may be established by fixing three parameters, or even more ("arity" of the relation, cardinality of the threshold of interest – how many you wish to have, and the partition of the database...). On the basis of these parameters, we can then calculate a number *m*, such that any ensemble of numbers *A* that contains at least *m* elements will satisfy the required regularity.

We should observe that *A* is any ensemble and that the only requirement is that *A* must be "sufficiently large", enormous in fact, since *m* is growing very rapidly as a function of the given parameters. But being arbitrary, *A* may be engendered by... dice throwing, measurements of an electron's spin-up/spin-down, a random quantum phenomenon, or random phenomena of any kind (physical, biological, social...). The bigger the database the better, the credulous propagandists of Big Data tell us. Is this number *m* too big to be encountered in our Universe for a correlation between a sufficient number of elements? Then not all sets of numbers of a cardinality below the Ramsey threshold need to contain the pre-given regularity, yet … lots of them will.

In summary, these results tell us that *any A* that is sufficiently big contains arbitrary, thus potentially "spurious" correlations; moreover, if we ask merely that these correlations appear in a high percentage, but lower than 100% of the ensembles, that is "only" in a reasonably high percentage of ensembles, then we would obtain an *m* attainable by our databases. In short, this hazard in the huge quantities of numbers is by no means rare. Let us explain.

A finite ensemble of numbers may be considered (algorithmically) "random" when it cannot be engendered by a program smaller than its number of elements. This is a notion of "incompressibility" for sequences of numbers, that may be extended to matrices or other organizations of data in finite dimension. It does not correspond exactly to randomness, yet it is a good "symptom" of randomness: that is an incompressible sequence has a high chance to be random; moreover, asymptotically (for sequences tending to infinite length), it does yield a robust notion of randomness for infinite sequences (Calude and Longo 2016b). Now, the percentage of ensembles of random numbers in this weak sense (incompressibility) tends toward 100 % (measure 1, to be more precise) when their cardinality grows toward infinity. Infinity is big, even for "data miners" who are the richest in data, yet as soon as we are dealing with ensembles of numbers that are expressed with 2000 bits, for example – which is not out of reach – we approach 80% of incompressible ensembles (Calude and Longo 2016a). So good luck making any kind of use in terms of prediction or action of data that may derive from chance! In every case where chance dominates, it is out of the question for the regularities found by clever data-exploration programs to be of any help at predicting if not acting, precisely because they are the fruit of chance, and they, therefore, may not be reproduced in time and in space, or derived from any causal relation. Thus, it is due to chance that one finds spurious correlations as illustrated in the eponymous book by T. Vigen (2015, see also the associated website http://www.tylervigen.com/spurious-correlations). Picturesque examples include the correlation between the US spending on science, space and technology and the suicides by hanging, strangulation and suffocation (r=0.99, from 1999 to 2009) or the number of Japanese passenger cars sold in the US which correlates with the suicides by crashing of motor vehicle (r=0.93, from 1999 to 2009). We leave the causal relevance of these correlations to the reader's appreciation. In (C. Calude and G. Longo 2016a), we gave the mathematical arguments that justify these spurious correlations and their high chances to appear.

2.2 Data, prediction and dynamical systems

The analysis of prediction is a central question in meteorology. Hosni and Vulpiani (2017) present an introductory survey of the problems encountered in this scientific area written by two insiders. The first point is that too many data may kill information and forecasting. The issue was understood by von Neumann and Charney since the 1950s. For example, it follows from the nature of hydrodynamic (and thermodynamics) equations that knowledge and description of data concerning waves of too high or too low frequencies may distort the analysis. So data, possibly implicit in the databases, concerning nonpertinent phenomena, may incorrectly affect the forecast. Moreover, the larger the database, the larger the physical space required to organize them; that is, the data may belong to description spaces (the spaces of the pertinent observables and parameters) of large or even huge dimension. If the dynamics happens to generate some "attractors" (a precise mathematical notion[2]), then the dimension of the attractors also matters, since the relative unpredictability of future evolutions of the intended dynamical system *grows exponentially* with both the phase space and attractors' dimensions (F. Cecconi *et al.* 2012).

Finally, Cecconi *et al.* (2012) give a further mathematical argument against the abuses of Big Data rhetoric. In linear and non-linear dynamics, in bounded phase spaces, regularities may appear under the form of "recurring phenomena". That is, patterns of the dynamics such as series of observable values that go very close to already traveled paths, may be proved to recur. That is to say they may – and actually will – appear again, a famous theorem by Poincaré (1892). Yet, as later intuited by Boltzmann and proved by Kac (M. Kac 1947), the recurrence times are immense (see F. Cecconi *et al.* 2012 and H. Hosni 2017 for extensive references). If the a-critical Big Data proponents claim that they do have sufficiently large sets of numbers to accommodate recurrence and thus "predict", then they surely fall under the case analyzed in section 2.1. That is, their database must be so huge as to exceed the cardinality limits given by Ramsey theorems, beyond which one finds a "deluge of spurious correlations" in *any* database. The conditions necessary to use Big Data strategies for these dynamics are exactly the ones which lead to the appearance of spurious correlations. As a result, their use for prediction and action is not a valid strategy: a correlation does not need to recur (i.e. to continue in time) nor to be due to any "causal" structure – beyond certain

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[2] An attractor describes the asymptotic behavior of a dynamical system, that is to say its behavior after the disappearance of short terms behaviors. For example, the attractor of a dynamics which converge to a single state is this state. More complex situations include limit cycles for dynamics which converge towards an oscillatory behavior and strange attractors in the case of chaotic dynamics.

large sizes, today accessible to Big Data, they are "meaningless" or due only to the size of the database.

3. A few remarks on biological unpredictability

In the introduction, we hinted to the idea that biological variation plays a fundamental theoretical role in biology. The principle of variation that we have proposed entails that biological objects cannot be defined theoretically like in physics (M. Montévil *et al.* 2016).

In physics, objects are assumed to follow stable equations which can be found on the basis of quantitative transformations (symmetries) and invariants under these transformations. These transformations define the space of possibilities. Changes are then quantitative changes of state in this predefined state space. By contrast, in biology, we defend the notion that changes also impact these invariants and symmetries (Longo and Montévil 2014). As a result, variation is also a variation of the relevant equations and a biological object cannot be defined by its invariants and symmetries. Accordingly, the space of possibilities is not a biological invariant, instead it can change over time (see F. Bailly and G. Longo 2006 ; Longo 2017). Methodologically, it is not possible to assume the existence of an invariant mathematical structure underlying the biological object of interest and to probe this mathematical structure by experiments.

Nevertheless, there are elements endowed with a restricted stability in biological objects. We call "constraints" these relatively stable elements which play a causal role on the processes that they constrain. Constraints are only stable for a limited time and can only be used as invariants at a given time scale. In an organism, constraints mutually stabilize and reconstruct each other so that the organism can maintain itself over time. With M. Mossio, we call this idea closure of constraints (M. Montévil and M. Mossio 2015) and we have proposed the principle of organization which states that closure of constraints is a hallmark of biological organisms (M. Mossio, M. Montévil, G. Longo 2016). In line with previous work of Rosen, Varela, Kauffman, etc., the principle of organization is a way to understand the mutual dependencies in an organism and to interpret biological functions. A constraint is a part of the closure of an organism when it is maintained by a process under another constraint of the organism and at the same time contributes to maintain at least another constraint of the organism, thus contributing to maintaining the whole and ultimately itself through the whole.

Let us now discuss a few consequences of this framework when considering Big Data approaches. Following the principle of organization, the relations between the parts of the individual is a fundamental notion. Following the principle of variation, the set of relevant constraints and their mutual dependencies may undergo variations. The ubiquity of variations is precisely why we can talk of an individual and not of generic organisms which would all have exactly the same organization. In this context, data analysis cannot unravel a stable structure that would be instantiated in all the data points corresponding to different individuals. Instead, these different data points correspond to individuals that are different to an extent: the constraints involved and their relations are slightly different for different individuals. Of course, data analysis may still help when focusing on a few constraints that are stable enough among the individuals considered. However, analyzing jointly the organization of many individuals leads to mixing different organization together and leveling down their specificity.

4. Conclusion

The results cited in section 2 are technical: they belong to the combinatory theory of numbers and to the theory of algorithms or involve non-trivial aspects of dynamical systems theory and ergodic theory. The defenders of what we define here as "Big Data without Theory" and of data-mining algorithms without analyses of meaning aim to disregard questions pertaining to theoretical frameworks. Another way to look at their aim is to say that they defend the idea of a generic theoretical framework that would apply in all kinds of empirical contexts without the need of a specific elaboration of meaning, from physics to social sciences.

In this context, recall that the Theory of Computability was invented in the 1930s by Gödel, Church and Turing in order to prove the existence of undecidable propositions and incomputable functions. More particularly, in our case, variants of results of Ramsey's Theory are situated in the difficult space of "what is computable" (the set of decidable propositions and computable functions), but such that its "computability cannot be proven" within formal number theory. That is, they allow defining functions that are computable but cannot be proven to be computable within the proper Theory of Computability (Arithmetic) (G. Longo 2011) – one needs to step outside this theory and use infinitary or geometric tools in the proofs. These methods and objects are totally extraneous to effective computability and discrete Data Types. Thus, as a non-obvious consequence of these results, even checking that a correlation is spurious is highly undecidable for a machine. Instead, it happens that we can generally detect the spurious correlations as in the examples above, whenever we have reasonably good, meaningful theories of many aspects of the world: one can give good reasons why the relation between the number of Japanese passenger cars sold in the US and the number of suicides by crashing of motor vehicle are spurious, in principle (or, if it applies, search for a meaningful correlation ...).

Mathematical theories such as computability demonstrate their own limits in the possibilities of computations and prediction by «negative results» that are present at the origin of scientific knowledge and characterize it. Once we have grasped the importance of the limits of the myths that «all is algorithmic» or «all is computable», we may make a better use of these immense quantities of data that computer networks make available, which is a great chance for science in every domain, including biology. Once we clarify the hypotheses that make us choose certain observables and not others, and choose measures suitable to the objectives of the knowledge that we are adopting, then digital information can help conjecture or corroborate a theory or a sketch of it, even produce new understanding. Whether it precedes or is propelled by data analysis, it seems urgent and necessary to develop theoretical frameworks for understanding organisms. In this context, we are engaged in a collaborative and interdisciplinary effort whose latest results are contained in a special issue of *Progress in Biophysics and Molecular Biology: From the century of the genome to the century of the organism: New theoretical approaches* (Longo, Soto, Noble 2016).

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Epigenetics and the Development of Cognitive Functions: Literacy as a Case-Study

Carmela Morabito

Contingency and predictability are at the core of contemporary study of mind and behaviour. In the last three decades, a new "social biology" has developed on the basis of our growing knowledge about the deep entanglement between body, mind and environment. Thus, the classical dichotomous view of biology vs. society and culture appears to inadequately explain the multiple ways in which organisms and their environment coevolve and reciprocally shape each other (C. Morabito 2013).

Especially in the development of human beings and of their cognitive functions, environment – primarily intended as the social, relational and affective environment – deeply penetrates into our skin, our brain, and our genes.

In the postgenomic era, after the completion of the Human Genome Project, genes are no longer conceived as discrete and autonomous factors, powerful drivers of the developmental processes. Today we assume the genome to be a vast reactive system (J. Dupré 2012), a complex and dynamic regulatory network that responds to a broad range of environmental signals, from the cellular dynamics to social and cultural processes, cognitive and affective interactions. In the words of Maurizio Meloni: «There are no genetic factors that can be studied independently of the environment, and there are no environmental factors that function independently of the genome» (M. Meloni 2016, p. 203). Genes are always "genes in context" (F.A. Champagne and R. Mashoodh 2009, p. 127).

The use of the term "epigenetics" in referring to the whole complex of developmental processes goes back to C.H. Waddington, who in the 1940s coined the neologism to designate the branch of biology which studies the causal interactions between genes and their products, which bring the phenotype into being (C.H. Waddington 1942). Since Waddington there has been a long history of epigenetics (R. Costa and G. Frezza 2015), the focus now is on the study of genetic and non-genetic factors acting upon cells that selectively control gene expression, producing an increasing phenotypic complexity during development. Thus, the first goal of the epigenetic approach to living beings is to point at phenotypic variations not attributable to genetic variations, but to genes expression and regulation. Through epigenetic change the genome responds in a dynamical way to environmental cues and produces individual phenotypes. This process is at the core of developmental plasticity, especially in human behavioral and cognitive development. «Epigenetics usually refers to what happens within an individual developing organism» (P. Bateson and P. Gluckman 2011, p. 11).

Studying the neurobiological bases of mind and behaviour clearly emphasises the necessity to look at the neuronal pathways underlying cognitive functions from the point of view of environmental influences operating on the brain during its development. The environment, in the case of humans, is first of all cultural and social. Therefore, contemporary cognitive neurosciences look at the development of the cerebral pathways at the basis of our cognitive functions in terms of "epigenetic landscapes". Further, they emphasise a broad range of environmental cues – «developmental niches» in the words of Stotz (K. Stotz 2008, p. 5) – that shape individual behaviour as well as individual resilience and susceptibility to disease (P. Gluckman 2011).

> The power of genes ensures the perpetuation of broad traits of [cerebral] organization, such as the form of the brain and of its circumvolutions, the organization of its areas and the general architecture of cerebral tissue [...]. But considerable variability [...] remains despite the genes' power (J.P. Changeux 1983, in C. Malabou 2008, p. 8).

The brain has the capacity to reorganize itself continuously, creating new neural pathways in order to let the individual actively interact with his environment. It is an organ continuously molded by individual's history and experience. Conditions in our environment, including social interaction and individual experience, play a crucial role in brain cells survival and in the formation of new synaptic connections. Decades of research have shown that the individual experiential, social and cultural environment can substantially change cortical areas, altering the pattern of neuronal activation in response to experience. Contemporary neuroscientific research clearly indicates that experience can actually change both the physical structure of the brain and its functional organization. «The brain is a work […] we are its subjects-authors and products at once. [...] It's not just that the brain has a history […] but that it *is* a history» (C. Malabou 2008, p. 1).

Therefore, since the nervous system is continuously altered in structure or function throughout the whole individual life *by* development, experience or injury, *plasticity* is the dominant concept of contemporary neurosciences. Our brain is plastic on three levels: it has a "developmental plasticity" (the modelling of neuronal connections in the embryo and the child)[1], a "modulational plasticity" (synaptic modulation in the modification of neuronal connections throughout life), and a "reparative plasticity" (the post-lesional capacity for repair).

The genetic evolution of the human brain is characterized by two main factors: 1) the non-linear increase in the organizational complexity of the brain despite a nearly constant number of genes (as we know, gene sequences have not increased in complexity in parallel with the increase in complexity of the brain: our genome sequence differs only 1,2% from that of the chimpanzee); 2) the long post-natal period of brain maturation (at about fifteen years old humans stabilize their synaptic density; in the rat this happens within a few weeks after birth; Z. PETANJEK *et. al.* 2011). The so-called "porousness" of the brain (M. MELONI 2014b) to social signals and individual experience is grounded in this long maturational period. Its open architecture is the fundamental topic of social and cognitive neurosciences ("interpersonal neurobiology" in the words of D.J. SIEGEL 2014), which encounter – in an epistemological triangulation of sorts – the model of the embodied and extended mind formulated by the new cognitive science and developed in the last decades:

> The brain is increasingly thought of as a tool specifically designed to create social relationships, to reach out for human relationships and company, literally made sick by loneliness and social isolation […]. The emergence of this novel language certifies the success of a discipline like social neuroscience […], with its landscape populated by empathic brain and moral molecules, mirror neurons and plastic synapses (M. MELONI 2014a).

Epigenetic processes may be crucial in the development of important cognitive and emotional abilities: in learning and memory, as well as in response to stress (A. FISCHER *et al.* 2007; F.A. CHAMPAGNE 2008; M.G. MEANEY 2001a, 2001b; V.K. RAKYAN and S. BECK 2006). David Sweatt, studying the

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[1] «Today epigenetics is not restricted to the study of embryonic stages of an organism. Embriological topics like parental imprinting (e.g., inactivation of the X-chromosome in female mammals) still fall under the heading of epigenetics, but the list certainly does not end there» (L. VAN SPEYBROEK 2002, p. 79).

role of epigenetics in the formation and consolidation of memory, has discovered that the metilation of DNA, acting on the hyppocampus, influences long-term spatial as well as episodic memory (D. Sweatt 2010). Obviously, epigenetics acts on memory through neuronal plasticity; we thus need to study the interrelation between genetic plasticity and synaptic plasticity in order to understand the neurobiological basis of learning.

The major mechanism in the production of diversity in neuronal connections beyond their genetic determination is the activity-dependent stabilization and selective elimination of the initially overproduced synapses (J.P. Changeux and A. Danchin 1976). Epigenetic met neurosciences for the first time with the introduction of the Selective Stabilization of Synapses Theory (SSST, or, Synapse Selection Theory) (J.P. Changeux *et al.* 1973). This theory states that the environment affects the organization of connections in an evolving neuronal network through the stabilization or degeneration (pruning) of synapses associated with the state of activity of the network. Starting from the initial exuberance of connections, during childhood we have a clear decline in the synaptic numbers (through the degeneration and then the pruning of connections). In the light of SSST, this complex phenomenon reflects "learning by selection": on the basis of critical and reciprocal interactions between the brain and its physical, social and cultural environment, humans develop a prolonged and extensive post-natal increase in neuronal branching, synaptic connectivity and its modulation by extended epigenetic responses to the environment. To learn is to eliminate (J.P. Changeux 1985). Applying the Darwinian paradigm (selectionism), we can assume that the organism is "shaped" to fit its environment through a selection process in the network of neuronal connections.

The epigenetic selection of synapses – with the elimination of the "unfit" ones and the strengthening of new functional pathways, cultural and experiential pathways – is the neurobiological mechanism at the base of learning and individual variability as well as of almost all our higher brain functions (i.e. writing and learning). Only humans experience a massive expansion of their evolutionary niche through cultural invention and transmission. Cultural objects, such as tools or writing systems, are recent, optional, and acquired by learning (no selective pressure could have shaped the human brain to facilitate reading) (S. Dehaene and L. Cohen 2007). Nevertheless, part of the human cortex is specialized for cultural domains: fundamental elements of human culture, such as reading, are mapped at the cortical level revealing a systematic architecture within different functional areas: reading is "implemented" in the left occipito-temporal cortex.

Literacy – in its neurobiological basis – is an interesting case-study in the dialectic relation established in human evolution between contingency and predictability.

Many neuroimaging studies have clearly shown that in all cultures, the ability to read and write maps onto remarkably invariant brain structures – the neuronal circuits involved in literacy (S. Dehaene *et al*. 2010) – that may be called "cultural maps", with only little cross-cultural variations[2]. Systematic reading activates the left lateral occipito-temporal sulcus, a site that is termed "the visual word form area" (VWFA). By comparing functional brain organization in illiterate-versus-literate adults (Dehaene *et al.* 2010) many meta-analysis have confirmed that the same region of the left lateral occipito-temporal sulcus is always activated, to within a few millimeters, whenever literate humans read (L. Cohen *et al.* 2000; S. Dehaene and H.P. Lamberts 2002). Further, in blind subjects, Braille reading specifically activates the VWFA relative to a tactile control task (L. Reich *et al.* 2011). This area is therefore meta-modal: it may possess a general capacity for identifying shapes, whether visual or tactile, and mapping them onto language areas.

Therefore, the neuronal mechanisms for orthography-to-phonology transformation seem to be domain-universal across different writing systems (C.Y. Lee *et al.* 2004).

The theoretical framework within which it is possible to explain this – at first sight, "paradoxical" – cerebral invariance of cultural maps, is based on epigenetic assumptions about the dialectic link between nature and nurture, neurobiological species-specific features and their plasticity and "porousness" to environment.

Writing – as we know – was invented around 5400 years ago in Mesopotamia. Its invention is too recent and, until the last century, concerned too small a fraction of humanity (able to read) to have influenced the human genome. It is thus logically impossible that human brain regions at the neurobiological basis of literacy may have evolved specifically for the purpose of reading and writing.

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[2] Activation is more bilateral for ideographic Chinese/Kanji scripts than for alphabetic or Kana scripts, and within alphabetic script, activation is also more extended and lateral for English compared to Italian: this can be due to the different gradient of complexity in the respective orthographies (E. Paulesu *et al.* 2000; D.J. Bolger *et al.* 2005; M.A. Changizi *et al.* 2006).

Human genome evolution can not have been influenced by such a recent and culturally variable activity, and the human brain can not have evolved a dedicated mechanism for reading. Learning to read must involve a "neural recycling" (S. Dehaene 2009; S. Dehaene and L. Cohen 2011) process whereby pre-existing cortical systems are functionally reconverted to the novel task of recognizing written words. Literacy activates a complex functional system in our left occipito-temporal lobe: the Visual Word Area (VWA) is the major neural correlate of literacy acquisition. This localization is surprisingly reproducible across cultures that vary greatly in reading direction or type of script (alphabetic, syllabic as in Japanese Kana or morpho-syllabic as in Chinese) (Dehaene and Cohen 2011), and we know that this cortical circuit has a primary functional specialisation for object and face recognition in the ventral visual cortex. In Dehaene's hypothesis, writing evolved as a recycling of the ventral visual cortex's competence for extracting configurations of object contours, asymmetrically in the left hemisphere where the cortical areas controlling language and the use of the right hand are located. The left visual occipito-temporal cortex may have been selected not only because it provides shorter, more direct connections to language areas, but also for purely visual interhemispheric differences as reading requires an analytic, fine-grained mode of recognition for which the left hemisphere seems intrinsically superior[3].

During education, reading processes invade and recycle the cortical spaces devoted to older evolutionary functions. In their neurobiological basis, the major domains of human cultural variability – including writing – are tightly constrained by our prior evolution and brain organization: cortical biases (such as interhemispheric differences) constrain visual word recognition to a specific anatomical site. During the evolution of writing systems, they may even have exerted a powerful constraint on the very form that these systems take, thus reducing the span of cross-cultural variations. Cross-cultural analysis shows that almost all the world's writing and symbol systems make use of the same set of line junctions, with a frequency pattern that matches the frequency profile of natural scenes. Dehaene and Cohen (2011) emphasize the neural constraints of cross-cultural invariants across the world's

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[3] A complex interplay of early biases concurs in making this cortical site in the left hemisphere nearly optimal for written words recognition: 1) a preference for high resolution foveal shapes, 2) sensitivity to lines configurations, 3) a tight proximity, and, presumably, strong reciprocal interconnections to spoken language representations in the lateral temporal lobe.

visual properties of writing systems: 1) in all alphabets letters are consistently composed of an average of about three strokes per character[4], 2) in all writing systems topological intersections of contours (e.g. T,Y, L, Δ, Λ…) recur with a universal frequency distribution. These intersections are not typically observed in random images, but occur with the same frequency in natural images (many of these intersections signals have "non-accidental properties" that denote important and invariant connection and occlusion relations) (I. Biederman 1987).

According to the neuronal recycling hypothesis, in the course of human evolution cultural acquisitions (e.g. reading) could have found their "neuronal niche" through the reuse of an ancient biological mechanism in a different role, to perform a different function. From an evolutionary point of view, they arose by minimal transformation from cortical precursor maps present in other nonhuman species. During individual life, cultural learning shapes the cerebral bases of cultural acquisition as a result of brain plasticity.

The "neuronal recycling" perspective could also explain the ease with which children acquire certain cultural tools as well as the specific difficulties that they occasionally meet. For instance, in dyslexia, the systematic difficulty in discriminating mirror-image letters such as p and q could have its neurobiological basis in the native propensity of our visual object recognition system for mirror-image generalization, due to its evolution in a world where the left-right distinction is largely irrelevant. To learn to write and read, therefore, we need to "silence" one of the basic perceptive ability acquired through evolution, and in doing this, children may encounter many different obstacles.

While the occipito-temporal cortex did not evolve for reading, the symbols' shapes used by our writing systems were submitted to a cultural evolution for faster learnability, by matching the elementary intersections already used in any primate visual system for object and scene recognition. It is a kind of "exaptation" (S.J. Gould and E. Vrba 1982), the change in function of a pre-existing structure during phylogeny under appropriate conditions of selection. A trait, previously shaped by natural selection for a function, may be reused for a new function with evolutionary value. This is the evolutionary process by which an adaptation is co-opted to meet a new requirement set by the environment[5].

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[4] Chinese characters also typically combine two to four functional sub-elements (C. Ding *et al.* 2011).

[5] In the theoretical assumption of neural reuse, whereby neural circuits evolved for one purpose can be exapted for another purpose, also the «mirror neurons could be evolved from a mechanism that

A trait may have initially evolved to be beneficial in one situation, but it may become useless or may evolve (by exaptation) an entirely different function in another environment. Some traits may not be adaptations at all, but rather be the incidental consequence of Darwinian selection on other traits – for which Gould and Lewontin (1979) adopted from architecture the term "spandrels" in a famous essay (P. Bateson and P. Gluckman 2011, p. 19).

> The reproducibility of the cultural maps for reading and arithmetic imply that they ultimately originate from universal cortical biases that may themselves be imputed to two major sources of organization. First, patterns of gene expression may specify an early organization of the cortex into basic "morphogenetic maps". [...] Second, postnatal activity may refine these initial genetic biases and lead to detailed "epigenetic maps" that reflect the constraints and correlation structure of sensory inputs (Dehaene and Cohen 2007, p. 386).

The brain's open architecture reflects the influence of culture and education over spontaneous brain development (J. Heinrich *et al.* 2010); "perceptual learning" induces clear modifications of cortical maps[6]. And literacy as a form of perceptual learning is deeply anchored to the earliest stage of cortical visual processing: i.e. at the VWFA site, learning to read competes primarily with the cortical representation of objects and faces[7]. The hypothesis of a sort of competition for cortical space between the nascent VWFA and the pre-existing neural coding of other categories is compatible with the fact that with increasing literacy a small but significant decrease in responses to faces at the VWFA has been observed. Hence, the connectivity used for reading and writing can be seen as an epigenetic functional remodulation of a pre-existing neuronal circuitry, the cortical mechanisms for visual recognition:

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monitored own hand goal-directed movement and were then exapted to serve additional functions, especially in humans, e.g., understand others' actions and emotional states, social learning» (P.F. Ferrari *et al.* 2013).

[6] In the form of a displacement of map boundaries due to cortical competition (D.B. Polley *et al.* 2006) including sharpened receptive fields and neuronal tuning curves correlated with behavioural improvements (H.W. Mahncke, A. Bronstone, M.M. Merzenich 2006).

[7] Competitive interactions between written words and faces in ventral visual cortex primarily occur when reading is acquired in childhood, when visual maps are known to be highly malleable (G. Golarai *et al.* 2007).

> Literacy, whether acquired in childhood or through adult classes, enhances brain responses in at least three distinct ways. First it boosts the organization of visual cortices, particularly by inducing an enhanced response to the known script at the VWFA site in left occipito-temporal cortex and by augmenting early visual responses in occipital cortex, in a partially retinotopic manner. Second, literacy allows practically the entire left-hemispheric spoken language network to be activated by written sentences. Thus reading, a late cultural invention approaches the efficiency of the human species' most evolved communication channel, namely speech. Third, literacy refines spoken language processing by enhancing a phonological region, the planum temporale, and by making an orthographic code available in a top-down manner (Dehaene *et al.* 2010, pp. 1363-1364).

In summary, literacy education induces five main neural modifications: 1) an increased VWFA response to letter strings, 2) the capacity to activate the spoken language network through reading, 3) a general visual augmentation in early visual responses in occipital cortex, in a partially retinotopic manner, 4) a greater response of area V1 to horizontal checkerboards and written sentences, 5) an enhanced planum temporale and top-down VWFA activation to spoken words.

Coming back to epigenetics, literacy relies on epigenetic cultural transmission from within a robust genetic frame. Education in the social and cultural environment is essential for establishing the neuronal circuits serving culturally acquired behaviours such as writing and reading. The massive postnatal increase in the size of the human brain – the adult brain weights five times more than that of the newborn infant and about 50% of the adult brain's connections develop after birth (J. Bourgeois 2010) – is the condition of possibility for the developing brain to shape itself through intense social and cultural interactions. Here is the strong link between the environment, our social and cultural environment, the human brain and the development of human cognitive capacities. During development plastic neuronal changes, socio-cultural and educational changes occur in the human cortex (without any change in the human genetic dotation) in the context of strong constraints imposed by the prior evolution of the cortex. Here we find the crucial dialectics between contingency and predictability, in the reciprocal moulding of brain and culture (C. Morabito 2017). There are clear bidirectional constraints between brain and culture.

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“Decline” vs. “Plasticity”: Conflicting Narratives in the Dementia Tsunami

GIULIA FREZZA

Introduction

Dementia is an umbrella term used to describe the most frequent, complex and multiple degenerative conditions, especially aged-related (patients older than 65 years). The many different identified types of dementias that include Alzheimer’s, which is the most common (60-70% of cases), Lewy Body dementias (the second most common type in the elderly), frontotemporal dementia and dementia secondary to other disease, are all pathologies for which there is no cure (yet) (K. RITCHIE and S. LOVESTONE 2002). In 2015 dementias were affecting 10.5 million people in Europe, and 46.8 million in the world (M. PRINCE *et al.* 2015).

The ultimate burst of people living with dementia - 9.9 million new cases in the entire world in 2015 (nearly one new case every three seconds), and the prediction of 74.7 million cases in 2030 and 131.5 in 2050 - it is such a titanic number bearing both alarming social and economic costs for which we are totally unprepared that was epitomized with an iconic metaphor by the WHO (World Health Organisation) Director-General, Dr. Margaret Chan, «the tidal wave of dementia that is coming our way» (WHO 2015, p. 9) and was discussed by governments and media as the spreading of a «dementia silent tsunami».

Clearly predictability is one of the key issues: how reliably to predict dementia risk factors, also by means of biomarkers, and therefore identify people who are more likely to be affected in order to increase prevention and strategies to drive optimal intervention and public agendas. Here, predictability and unpredictability are two sides of the same coin. As in most multifactorial noncommunicable diseases such as cancer, predictability is associated to high variability: an association between a number of genetic and environmental factors following a complex inheritance pattern (polygenic effects and environmental exposure) and subject to individual variability (D. GALIMBERTI and E. SCARPINI 2014).

Ethical issues are at the core of dementia discourse (Nuffield Council on Bioethics 2009). The prediction of this epidemic shocked public opinion, raising issues about our capability to come across the "dementia tsunami" and provoked a general call for a better integrated understanding of the clinical, cultural, social, ethical, economic, and political issues, and where the complexity of the lived experience of dementia is not conflated to a simplifying dichotomous rhetoric dementia is positive vs. dementia is negative but within a more encompassing model that directly takes into account the lived experience of people with dementia (C. Clarke and E. Wolverson 2016).

Negative attitudes, lack of awareness – often dementia is considered part of normal aging – social stigma, lack of public policy action and of funding for research are barriers to intervention from health to social care strategies (WHO 2015, p. 25). On the other hand, both research and communication strategies are controversial: WHO's guidelines establishing dementia research priorities sparked criticism (L.S. Schneider 2016) and yet scarce attention is given to bottom-up approaches targeting people living with dementia's opinion to more reliably impact on their positive behaviour and well-being (F. Ingravallo *et al.* 2017).

If everyone must be prepared to cope with the "dementia tsunami", customer-tailored language use becomes a critical factor at play for prevention and communication campaigns, and requires considering how people think and talk about dementia. For doing this we will first proceed by analysing dementia from a discourse analysis viewpoint, highlighting two main metaphorical narratives in use and their framing effect in communication. Next, to better clarify such metaphorical framing and their underlying socio-cultural values, we will outline both narratives against their historical-epistemological roots.

Dementia public discourse and scientific metaphors

A most notable element of dementia public discourse is that it is highly dominated by metaphor use, as mentioned by the Alzheimer's Europe Report-2013's chapter dedicated to dementia ethical issues. As the report stressed, language and metaphor use should be scrutinised for their possible influence on social stigma and ethical issues, and their backlashes on well-being and prevention.

The metaphorical use in dementia discourse is part of scientific communication too: scientific metaphors are commonly used to describe people's functional impairment by the conventional metaphor of *decline* and by the more innovative metaphor of *brain plasticity*. Just briefly note that metaphors in science are conceptual tools used to explain complex or abstract scientific ideas among the scientific community, which can be then echoed, or re-invented, by the media. Especially in the latter "hybrid" form, metaphors spread and become a powerful medium of interpretation bridging cognition and culture, and are used as cultural framing at the crossroad of culture and time, where specific values and assumptions are met (J. Zinken *et al.* 2008).

In health communication, for instance, the framing mechanism was described for war vs. journey metaphors used for talking about cancer (E. Semino *et al.* 2016). The metaphorical frames "disease is a fight" or "disease is a journey" work by setting a determined frame in the discourse proposing the specific viewpoint that the speaker wishes to sell on a subject, like "disease is a fight" or "disease is a journey", which creates expectations (causal, moral, treatment) in communication. Nevertheless, despite metaphors being used as shortcuts to talk about complex concepts in simpler terms, metaphor functioning in discourse is not simple at all, since it can be subject to «blind-spots» and involves ethical issues (B. Nerlich *et al.* 2016; G. Frezza 2017a), also requiring a thorough multilevel analysis of its own (G. Steen 2011).

Methodology

We analysed metaphor in dementia public discourse, confining our attention to scientific metaphors used in the news. We selected two main metaphorical themes, decline and plasticity, that according to the literature mainly characterize the metaphorical framing of dementia discourse in a positive and negative way (e.g. H.P. Lane *et al.* 2013; C. Clarke and E. Wolverson 2016). Next, we described them by analysing the frequency and proportion of words and semantic areas mostly associated to them, exemplifying the semantic characterisation of the two polarised images of dementia in the news media.

By means of corpus analysis – quantitative research into patterns of language use – in dementia public discourse, we aim to show concretely the mirror image of what people think about dementia as expressed in their language use, and hence possibly related to people's intentions and behaviour about it. In particular, we focus on how metaphor language use and dementia are connected in communication and which words and expressions are exactly at play, highlighting the two polarised narratives.

We used the *LexisNexis* academic database to collect textual data in major world newspapers during the last 17 years (from 2000 to 2017) with the word “dementia” in the headline or lead of the article, and we distinguished two different sets identifying the traditional decline metaphorical narrative and the plasticity metaphorical narrative[1].

Item 1-Decline provided an uncountable output of more than 3000 articles that we sorted out through the relevance criterion displaying the first 1000 relevant results which then we refined by selecting namely the categories «newspapers» and «magazines and journals» and as subject «medicine and health», resulting in 921 articles, of which we selected the first group of 200 articles. We refined Item 2-Plasticity with the same criteria used for Item 1-Decline, and this resulted in 51 articles. After filtering out duplicates we obtained a set of 168 articles for item 1-Decline, and of 37 for item 2-Plasticity, for a total number of 205 articles included in our analysis.

Next, we uploaded our data into *WMatrix*, a software tool for corpus analysis and comparison including frequency and semantic field identification (P. Rayson 2008). We first confronted a sample including Item 1-Decline and Item 2-Plasticity against the *BNC sampler written informative*, a subset of the full *British National Corpus* (*BNC*). In this way, we could quantitatively define how the proportion and frequency of our set of words is associated to, and hence characterize, our sample of dementia texts by comparison with a standard sample of informative texts from *BNC*.

Secondly, we applied the same procedure and compared the key words and semantic areas more associated with Item 1-Decline against those associated to Item 2-Plasticity. Eventually we could observe dementia-related words and the associated semantic areas that characterizes dementia public discourse, as well as the specific differences characterising the two conflicting narratives: decline vs. plasticity.

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[1] The search query we used is: HLEAD (Dementia) AND EVERYWHERE 1. (Decline), OR 2. (Plasticity). This is a preliminary analysis of the work carried out at the Metaphor Lab-Amsterdam, University of Amsterdam, during the NWO Visitor’s Grant project «Resistance Risk and Responsibility» awarded to Giulia Frezza and supervised by Gerard Steen. The study is underway and needs further refinement; however, our preliminary results adequately fulfill the aim of this article. For any further information, please, contact the author.

Discussion: two conflicting narratives, decline vs. plasticity

The general picture that emerges from our preliminary analysis of words and semantic domains associated to both narratives is consistent with the ordinary definition of dementia (D. Ames, J.T. O’Brien, A. Burns 2017) as an especially aged-related subject affecting individuals’ and their families’ everyday life and portraying a frail individual: mental and intellectual impairment in attention, recognising, remembering, hearing and communicating hinder the individual interactions with the external world. By contrast, the comparison between words and associated semantic domains of item 1-Decline vs. item 2-Plasticity allowed identifying two distinctive narratives.

First, as mentioned above, the decline sample provided an uncountable number of more than 3000 articles, while plasticity just 51, of which 18 were duplicates. Besides, all the articles about plasticity also contained the word decline – the opposite was not the case. Both things illustrate how the idea of decline is deep-rooted in the cultural framing of dementia representing the standard pervasive narrative, whereas the plasticity narrative is still not much in use.

Moreover, in the two metaphors of decline and plasticity source and target domains work differently, showing a different explaining function of the metaphor. Briefly note that the target domain is the semantic domain containing the complex idea that needs to be explained by using the metaphor, as here dementia intercourse in general. The source domain is the more familiar semantic domain to which we refer to explain complex ideas in metaphorical terms, as here decline or plasticity. The source domain *decline* is applied to different specific *target domains*: cognition, memory, faculties, brain, the individual, and society, framing a global description of dementia. By contrast, the source domain *plasticity* is applied only to the target domain of brain and neural plasticity, depicting a local explanation of dementia. However the *source* domain *plasticity* is ambiguous: people refer to different things when they talk about a «plastic brain», as will be further detailed.

Next, we describe the polarisation between the two narratives. The decline narrative is characterized by the domains of care and death-related problems and outlines a frail individual. The plasticity narrative, by contrast, highlights the power of the brain by means of its skills, capacity of learning and resilience throughout individual life and it is linked to the domains of research and innovation technologies. Although dementia public discourse in general is connected to the semantic domain of research, such domain emerges more in the plasticity narrative. Here we find many references to IT technologies like applications, computer programs and games that were recently developed to keep the aged brain active, to «train the brain» and «fight dementia back».

The polarisation between a negative and a positive view of dementia in the two narratives becomes more straightforward in the domain of time. In Item 1-Decline, «time» was over-represented and characterised by the categories of «Time: Old» and «Time: Ending», referring to terms such as stopping, and ending, representing a category of time that we can define as *passive* by means of the idea of time passing and elapsing. In Item 2-Plasticity «time» was over-represented too, but through different categories including «Time Beginning», «Time: New and young» (with terms like forming, beginning, renew, regeneration, fresh,), «Time: Late» and «Time period: long» (with terms like delay the onset, and never too late, chronic, and long-term, referred to problems to be fought). This characterizes an idea of time that we can define as *active*, opposed to that presented in the decline narrative, outlining a sharp contrast: in the decline narrative people refer to a «passive» conception of time tied to experiencing time passing and elapsing, while in the narrative of plasticity people refer to an «active» counter-time that represents time as beginning and tied to activity.

Two different stories seem to emerge as a result of the framing effect of the two narratives, where the dynamics of prediction and unpredictability play a different role too. One story, decline, seems more conventional and pervasive describing a *global*, predictable, declining trajectory of dementia pathological path: the deterioration of the brain's faculties leads to a predictable linearly progressive pathologic descent of the individual. The other, plasticity, is more innovative and less common. Moreover, it focuses on a *local* explanation of neuroplasticity, foreseeing a less steep predictable trajectory of dementia pathological path which considers the ecological shaping power of the environment where the pathologic descent can be slowed down by «training the brain» and «fight dementia back».

To clarify such contrast and better outline the characteristic framing effect of each narrative – how scientific, cultural, ethical and social issues impinge on them – we will now outline the two metaphorical themes against their own historical-epistemological background. The epistemological-historical analysis of the two conceptual metaphors of decline and plasticity allows to identify their traditional/innovative characteristics against previous and actual scientific paradigms, as well as to shed light on the complex underlying socio-cultural ideas that are constantly evolving throughout them.

Decline

In a brief historical overview, which is necessarily limited here, we could remark that in Western culture since antiquity the idea of decline traditionally framed old age (D. Schäfer 2011). Thorough investigations of old age as conceptualized in early modern and contemporary medicine cannot be discussed at length here (see Schäfer 2011; M. Cambron-Goulet and L. Monteils-Laeng 2018; H.W. Park 2016). We will summarize four major points from Schäfer's book (2011) as introductory for our discussion:

(1) *Lack of definition*. «Old age was classified in ancient and medieval intellectual culture by a process of "definition" […] distinguished from life's earlier phases […] and approximated to impending death; reflects the difficulties still faced by modern geriatrics science and medicine to recognizing and explaining the specific characteristics proper to this phase of life » (Schäfer 2011, p. 16).

(2) *Natural vs. un natural disease*. Aristotle defined old age as a «natural disease», whereas diseases were unnatural (*res praeternaturalis*), because aging is a natural process (*dyskrasia*) which besides can result from illness. This idea was extended by Galen also in medical terms but got simplified in proverbial terms as «senectus ipsa morbus est» (old age is itself a disease).

(3) *Cold temperament and sensus diminutio*. Since Aristotle, the cold and dry temperament of the old explain the aetiopathology in the elderly. Such view was maintained in the humoralist framework: Galen asserts that cold and dry temperament may lead to boldness and brain shrinking («cerebri consumtio/ consumtionem cerebri comminutionem esse», Galen 1965a, p. 5), and to memory loss (*memoriae lesiones*) and idiocy (*stultitiae*), respectively (Galen 1956b, p. 162). The interpretation of old-age as a decline of faculties to the point of their extinction was then supported by the Christian culture, as exemplified by Isidore's *Etymologie* deriving the term *senes* (old, plural) as *sensus diminutione* (lessening of the senses, Isidore of Seville 1911, lib. XI 2, 7). And the Aristotelian lamp metaphor as life-fuel that runs out in the elderly dominated Western medical culture until the 17th century.

(4) *Between physiology and pathology*. Old age throughout antiquity and early modern period has a controversial status in between physiological and pathological decline, which often portrays also a pejorative and derogatory image of the elderly, epitomized by the etymology of senescence as «senes quod sese nesciant», likely dating to the Middle Ages. «The loss of cognitive functions in old age (memory loss, dementia) was also portrayed negatively in poetry […] ignorant, forgetful old people […] act as a counter-image, so to speak, of the much vaunted wisdom of the old age» (Schäfer 2011, p. 17).

In extreme synthesis, antiquity, the Renaissance and the early modern period portray aging as decline with a blurry status between physiology and pathology and with a double image of the elderly: «on the one hand a harsh condemnation of bodily and mental decline, on the other an idealization of special capabilities and freedoms» (Schäfer 2011, p. 18).

Decline and deterioration of the faculties in aging are linked to disease and to the negative character of mental and physical deficiency in the elderly. As observed by Armelle Debru, a similar lexical assimilation happened to the related compound term *neurodegenerative disease* that became commonly used since the middle of the 20th century to indicate those processes that lead to «departing from the original neurological state, an irreversible degradation and finally the destruction or death of neurons» and which can entail a nefarious impact for patients, family and carers (A. Debru 2017, p. 127). However, the term *degeneration* had an older «heavy and dark» history which included negative connotations: from its Latin origin and a quasi-botanical neutral definition it came to represent the moral degradation of the species.

A semantic history links brain degeneration and decline, which are often intended as synonyms, and as both have in medical lexicon a metaphorical reference to «going down» meaning becoming worse. Debru reconstructed the etymology of degeneration from the Latin *degenerare*, de- «to depart from» and as «the movement of going "down", locally and metaphorically, in worse» (Debru 2017, p. 128) and *gens, genus*, the original family group, so that *degenerare* means «to depart from its original genus», and only secondarily may imply a deterioration or degradation (Debru 2017, pp. 129-130).

Debru mapped the evolution of the concept through the French medical dictionaries: starting from early 19th century to the new notion of *dégénérescence* developed by psychiatrists and introduced to medical lexicology through Morel's *Traité des dégénérescensce* (1857) where the term refers to a variety of pathological processes caused by social circumstances (like poverty and incorrect nutrition). Despite the subsequent Littré's proposal (E. Littré 1873) to apply the term «degradation» instead of *dégénérescensce* to the hereditary degeneration of the species – being the shift from normal to pathological only a matter of degree and not of nature – the negative-moral meaning of degeneration was reactivated since the 19th century theories of degeneration, hygienic and eugenics theories. This, maintains Debru, makes us reflect whether such negative connotation can still be found in the «perception of the otherwise objective definition of neurodegenerative disease» (Debru 2017, p. 128).

In the limited space of this chapter, we examine the possible assimilation of the metaphorical meanings of decline and degeneration, which both include negative, moral connotations that have been conflated in the definition of dementia by means of the metaphorical mechanism at play in the narrative of decline.

In the metaphor of decline we compare something that is impaired to something that «goes down». This metaphor is conventionalized in language use: it is lexicalised – it can be found in current language dictionaries. However, in the historical Oxford English Dictionary we can determine that *decline* originates in Late Middle English from Old French *decliner*, from Latin *declinare* (de – (down) + clinare, «to bend») and means to «bend down, to turn aside». It was initially used in antiquity to talk about the descendant trajectories of the celestial bodies in Latin. Archaic forms already included the domain of medicine in which the bodily strength gradually fails, e.g. tuberculosis.

The actual meaning of decline that is «a decrease in the quality, quantity, or importance of something» (*Longman Dictionary of Contemporary English*, 6th Edition) and «to become less or worse» (*MacMillan Dictionary*) is therefore conventionalized; however, it is typically seen metaphorically as a fall: something good becoming smaller, fewer, or less, such as in falling, decreasing or deteriorating. This still refers to a metaphorical «going down», which, besides, has a negative, moral connotation as «becoming worse» in line with the traditional Lakoff's and Johnson's (1980) conceptual metaphor theory (CMT) for which DOWN IS BAD and HIGH is GOOD.

Applying CMT viewpoint, the primary metaphor DOWN IS BAD creates a conceptual link between decline and bad by which decline is intended not only as something going down but also as something going bad and progressively worse. This prime conceptualization, then, may explain the stronger pervasive and persuasive effect of the narrative of decline vs. the narrative of plasticity as described in the first part of the article. The conceptual cultural framing of decline embeds the decline story in an established and extended metaphorical narrative where the source domain is applied to multifarious objects (from cognition, to memory, behaviour and the individual).

The conceptual metaphorical model of aging as decline, portrays a global metaphorical *descendent trajectory* in which the brain, its faculties and the individual from their (figurative) highest point in youth, start to go down, getting bad and worse till the end of the trajectory that ideally corresponds to the individual's death. This is a metaphorical trajectory – nothing and nobody have *literally* gone down anywhere – which represents the brain's and individual capabilities as predictably progressively both decreasing and deteriorating throughout time, as similarly happens under the pressure of dementias.

This interpretation can shed light on the fact that in the Western traditional culture the idea of *decline* is isomorphic to *aging*, the status of which was and still is conflated between physiological and pathological. Such conceptual cultural framing is accepted and conventionalised in our culture as in Western medical lexicology the controversial status of aging still is a conundrum (Schäfer 2011). This calls for a reflection on the potential that such decline-degenerative, and pejorative narrative of aging has to impact negatively on the public "management" of the dementia tsunami and pleas to reassess concepts such as healthy, pathological, and well-being.

Plasticity

The plasticity narrative in dementia is a more recent and «positive» story, focusing on the scientific concepts of neural plasticity, recovery, resilience, and cognitive reserve (Y. Stern 2012; D.V. Buomomano and M.M. Merzenich 1998). These connected concepts generally underline living beings' natural capacity to react to environmental stress, and frame individual autonomy and capacity of recovery.

Longman contemporary language dictionary defines plasticity as follows: «the quality of being easily made into any shape, and of staying in that shape until someone changes it». This literal meaning is not the one used in science to talk about *brain plasticity*: plasticity is a word originally borrowed from ordinary language to talk in science, not *literally* about the brain capacity to bend, to keep a shape or to be pressed into any shape, but *metaphorically* to mean the brain's adaptability and capacity to rewire. In the *Merriam-Webster*

Dictionary of English usage, we find four different meanings: i. the quality or state of being plastic; especially the capacity for being molded or altered; ii. the ability to retain a shape attained by pressure deformation; iii. the capacity of organisms with the same genotype to vary in developmental pattern, in phenotype, or in behavior according to varying environmental conditions; iv. the capacity for continuous alteration of the neural pathways and synapses of the living brain and nervous system in response to experience or injury.

The concept of plasticity is open and multifold, and that of neural plasticity is undergoing a process of definition. Morabito (in this volume) explains the manifold notion of neural synaptic plasticity (developmental, modulational and reparative plasticity) by underlying its link with the notion of learning and contingency that we won't further discuss here. Besides, despite its interest we won't touch the related concepts of behavioural and evolutionary plasticity, as early described by Baldwin (J.M. Baldwin 1905, p. 302-3, see Campanella in this volume) and Edelman's "neural Darwinism"[2].

We cannot provide here a systematic historical overview about the (structural) plastic brain. We would refer to Rees' work *Plastic Reason* (2016) that thoroughly explains the genealogy of the term *plasticity* applied to the embryogenetic and neuroscientific field. Rees underlines how, despite many attempts to trace back the origins of the concept of plasticity to the late 19th century, from James' psychology to Tanzi's, Minea's and Wiedersheim's efforts to describe the brain in cellular terms, before the 1990s plasticity was unusual in the neuronal sciences dictionary where the model of the brain was a fixed entity.

Three paradigmatic shifts emerged before the actual concept of plasticity could become of use: synaptic brain in the early 1950s, synaptic plasticity in the 1970s, and adult embryogenetic growth in the 1990s. Only since the late 1950s was plasticity first used in regeneration studies referring to «the search for which neuronal processes prevent the brain from replacing neurons lost to disease or injury», and since the 1970s also to talk about «the experimental observation that the intensity with which synapses communicate with one another can change» (T. Rees 2016, p. 236). According to Rees both of these uses eventually present a model of the adult human brain as fixed, «an immutable cellular structure», while leaving flexibility and capacity of transformation only to synapses and synaptic communication.

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[2] Special thanks to Sara Campanella who highlighted the concept of plasticity in Baldwin's work.

The «embryogenetic concept of plasticity» (structural plasticity) which refers to the developmental process of cellular growth that doesn't stop with aging, was originally described in the 1990s by Prochiantz, and informed by Gage's study on trophic proteins.

We should add two other ideas related to neuroplasticity. The first focuses on the ecological perspective of the brain in relation to its environment(s) synthetised by the French philosopher Malabou (2016). The second emerged in the field of geriatric neurology by means of an «epistemological exaptation» – a mechanism by which a concept born in a specific domain with a specific meaning is then taken over for use in another domain (G. Frezza 2017b). So, the concept of neuroplasticity was «exapted» and used to mean the capability of the adult brain to reorganise and keep up after injury (Buomomano and Merzenich 1998).

One thing should be brought to the reader's attention. In these studies, the concept of plasticity has often been presented through the mind-machine metaphor, where plastic is referring to the software wiring mechanism, epitomized here by Merzenich's words: «the brain's machinery is being continually rewired and functionally revised, substantially under your control, throughout the course of your natural life» (M.M. Merzenich 2008, p. 1). This aspect of dementia public discourse should be carefully considered, given the attention to machine metaphors in public health communication, which are not always accepted and often resisted.

To conclude with a positive note, we should mention that also in antiquity voices were raised against the established decline narrative. Cicero, with his popular apologetic portrait of the elderly, *De Senectute*, is the most famous among the few supporters of old-age who emphasize a counter-argument in diametric opposition to the standard view: «the possibility of fending off bodily and mental enfeeblement though training and a suitable lifestyle» (Schäfer 2011, p. 18).

Conclusions

The conceptual historical-epistemological analysis of decline vs. plasticity narratives in dementia enabled us to underline the recent epistemological shift in the way the aged brain is conceived, both functionally and structurally: the brain as fixed vs. the brain as an evergreen, transforming matter. It also allowed to frame the traditional/innovative traits characterising the aged brain, linking the traditional Western idea of aging with decline, which comprises also brain degeneration and diseases like dementias.

Moreover, we observed a potential shift in the traditional negative idea of dementia as decline. As corpus and discourse analysis showed, dementia can be seen through the lens of two major polarised views (decline and plasticity). These were analysed by means of their patterns in language use focusing on two opposing characterisations of some semantic domains: care and death-related problems for the decline narrative, activity, exercising and technological apps for the plasticity narrative. The semantic domain of time also resulted in a split in two polarised images: a “passive” time that is passing and elapsing in the decline narrative and an “active” time tied to regeneration and activity in the plasticity narrative.

These patterns present two different stories with two different pathological paths bearing a dissimilar role of predictability and unpredictability. The traditional metaphorical «negative» global narrative of decline as degeneration (both going down and bad) portrays dementia as a descendent linearly progressive trajectory of brain functions, predictably leading to neurodegeneration and decline also of the individual, who is characterised with passive and hopeless traits. The innovative «positive» local narrative of plasticity represents the brain metaphorically as «being malleable», points to the brain’s resilience and motivates individuals to train if they wish to halt their own deterioration.

The contrast in the two opposed pathological paths raises crucial ethical issues, impacting on people’s autonomous capability of well-being (R. Dworkin 1986) and on those who care for them; and it informs health prevention and communication differently. By training the brain, people with dementia should/can keep up: this enhances hope as well as the individual *active* role but also self-responsibility in preventing, and coping, with dementia (E. Peel 2014). While social health needs to be emphasized for «de-stigmatizing dementia and offering an alternative frame for the negative discourse that predominantly surrounds dementia» (M. de Vugt and R.-M. Dröes 2107, p. 1).

Recent studies focused on different cultural representations of dementia, highlighting corresponding different ethical risks (A. Hillman and J. Latimer 2017) and suggesting especially a renewal of metaphors, as people living with dementia may not want to be associated with frailty, loss and decline (e.g. H. Zelig 2014) and propose other framings such as “precarious” life rather than "frail" for referring to elderly and people with dementia (A. Grenier *et al.* 2017).

From our viewpoint it is key to underline that metaphor discourse analysis may further shed light on the possible consequences in real-world scenarios of endorsing one narrative over the other. As a consequence of people's different resistance and expectations to metaphorical framings, the choice of one narrative over another may be crucial especially when aiming to enhance positive health behaviour: for different individuals the two narratives may entail opposed ethical assumptions such as emphasizing personal vs. social responsibility; they can be perceived as hopeless vs. encouraging (Peel 2014), and propose different therapeutic ideas, as pharmacological vs. behaviourally based.

In a lack of a specific ethical framework for healthy aging that is still under construction (WHO 2017), shared decision-making and communication strategies should target an optimal cost-benefit relation between prediction, prevention and ethical issues. We aim to define an operative concept of the relation between the potential risks and the ethical responsibilities involved in dementia public discourse while using a specific metaphor use and endorsing its related narrative. As shown in cancer research, some metaphors and their associated narratives may be helpful for someone while for others are not. The language that professionals, physicians, carers and society use is crucial and impinges on social responsibility (S. Schicktanz *et al.* 2014). Despite people's sociocultural differences and idiosyncrasy, people with dementia are all equally in need of help; institutional public agendas shouldn't risk choosing a language that may be controversial or that risks cutting someone off.

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III

Evolutionary Unpredictability: Past and Future

Orthogenetic Predictability: Orderliness and Symmetry in Early Macroevolutionary Explanations

David Ceccarelli

Introduction

The emphasis on unpredictability deeply characterized the evolutionary debate in the course of the twentieth century. At least two generations of evolutionists have regarded biological change as a phenomenon to be described in terms of historical narratives, and have strongly challenged the possibility of prediction, especially at macroevolutionary scales. Since the incorporation of paleontology within the framework of the Modern Synthesis, scholars have stressed the contingency of large-scale evolutionary phenomena. In the years of the so-called "second synthesis"[1], students of macroevolution traced back fossils "trends" to contingent processes such as orthoselection, according to which phyletic directions are consistent with persistent natural selection (G.G. Simpson 1944, p. 163), and random genetic drift (Simpson 1944; B. Rensch 1960). In many respects, such post-synthetic paleontologists as S.J. Gould and N. Eldredge (1972) and S.M. Stanley (1975, 1979) emphasised even more the contingency and intricacy of evolution. Since the 1970s, the focus on biological unpredictability has taken centre stage in evolutionary debate, especially in the form expressed by Gould's "evolutionary contingency thesis" (J. Beatty 2006).

Both these generations of macroevolutionary scholars highlighted that the fossil record can exhibit law-like patterns (E. Serrelli and N. Gontier 2015, p. 22). Nevertheless, none of them assumed the existence of universal laws driving phylogeny towards fully predictable ends. As stated by George Gaylord Simpson, general laws are unsuitable for historical entities whose properties depend on «the actual state of the universe or of any part of it at

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[1] In their classic account, Ernst Mayr and William B. Provine (1980) recognised two phases of the Modern Synthesis. A first step was the reconciliation of Mendelian genetics with the Darwinian theory of natural selection, dated between the 1910s and 1940s. The "second synthesis" occurred between the 1930s and 1940s, and entailed the inclusion of paleontology, morphology, taxonomy and systematics within the new theoretical framework.

a given time» (G.G. Simpson 1963, pp. 24-25). In 1960, Bernard Rensch pointed out that biologists should rather speak of "rules". Though they allow a degree of prediction, such generalizations must take account of complex interactions which often make results unpredictable (Rensch 1960, p. 97). Ernst Mayr reinforced Rensch's stance adding that "biological rules" cannot be considered predictive if not in a probabilistic sense (E. Mayr 1982, p. 37). Even the work of Gould was motivated by a tension between the search for group-level properties that allow the formulation of laws and the idea that life could have been otherwise (D. Sepkoski 2012; C. Haufe 2015).

However, between the nineteenth and the twentieth century many naturalists had tried to frame macroevolutionary phenomena in terms of universal laws and largely predictable events. Before life's history was considered, in Gould's metaphor, a tape you cannot re-run (S.J. Gould 1989, p. 166), predictability had a pivotal role in early macroevolutionary studies. In particular, the spread of orthogenetic theories fostered various forms of nomothetic evolutionism in paleontology and zoology across these two centuries. This essay aims at exploring the historical and epistemological foundation of such views. Special attention will be devoted to the emphasis on homoplasy within orthogenetic paleontology, with a particular focus on the works of the American paleontologists Alpheus Hyatt, Edward Drinker Cope, William Berryman Scott and Henry Fairfield Osborn. This will enable us to reconsider orthogenetic theories as the outcome of the epistemological mismatch between Darwin's notion of chance and the prevailing nineteenth-century epistemology. Further, it will allow us to highlight the epistemological discontinuities that punctuated the history of macroevolutionary studies.

Orthogenesis and the claim for prediction: a historical review

Orthogenetic theories played a major role in the years of the post-Darwinian debate. Orthogenesists were key actors of the so-called eclipse of Darwinism; they critically questioned the role of randomness in evolution and the very idea that variations may be «isotropic» (S.J. Gould 2002), i.e. that they might occur in every direction. As remarked by Simpson, the term orthogenesis was «employed not simply as the name of a phenomenon», namely the existence of linear series in fossils records, but also as the name of the theory for explaining such linearity (Simpson 1944, p. 150). Wilhem Haacke's original definition of orthogenesis dealt with the genetic factors behind phyletic trends, as he conceived the germplasm to be composed of geometrical elements (*Gemmaria*) whose arrangements were limited by their actual shape (W. Haacke 1893). The term "orthogenesis" gained popularity under Theodor Eimer's (T. Eimer 1897) more general definition: evolution by «definitely directed variation» (P.J. Bowler 1979).

Though the advocates of orthogenesis may not have been driven by a unity of purpose towards a single research program (D. Ceccarelli 2018), almost all of them saw in macroevolution a form of orderliness they could not explain through the Darwinian theory of natural selection operating on random variations[2]. Orthogenesists rejected Darwin's «bigger idea» (C. Johnson 2015, p. XII) that variations were blind with respect to the future shape of organisms. Their theories relied on a law-like conception of nature, which entailed the assumption of a linear causal nexus between individual variability and phyletic trends. This view not rarely turned into claims for evolutionary predictability. Once variation was conceptualized in terms of orderly phenomena due to ontogenetic and structural constraints, as well as to goal-directed efforts and self-oriented germinal changes, evolution appeared as a largely predictable phenomenon (G.S. Levit and L. Olsson 2006, p. 128). In this respect, many orthogenesists were anti-Darwinians not only for their refusal of natural selection, but because they «asserted the regularity, and indeed the predictability, of the process» (P.J. Bowler 1985, p. 646).

The works of the American paleontologists Alpheus Hyatt and Edward Drinker Cope, who both advocated the idea of non-random variability and maintained the neo-Lamarckian theory of use-inheritance, well typify this form of nomothetic evolutionism. Since his famous lecture on Tetrabrachiata delivered at the Boston Society in 1866 (A. Hyatt 1866), Hyatt had been developing the principle of "racial senescence", according to which the modifications in the adults of the retrogressive stage of a phylum «may be predicted from the study of the similar changes that take place in the senile stages of the progressive individuals» (A. Hyatt 1893, in E.D. Cope 1896 p. 191). Cope, who laid the foundations for the American neo-Lamarckian orthogenetic school together with Hyatt (E.J. Pfeifer 1965), proposed in 1871 the "law of the unspecialized" and in 1896 the "rule of the increase of phyletic size". According to the first law, the founders of new phyla would always be the simplest forms. Paleontologists could thus «seek the point of departure

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[2] The soviet orthogenesist Leo Berg defined evolution as «development in accordance with definite laws, and not, as was believed by Darwin, development due to chance» (L. Berg 1926, p. XVII).

of the type which is to predominate in the future, at the lower stages of the line» (E.D. Cope 1871, p. 161). The second generalization, commonly known as "Cope's rule", states that all lines of descent exhibit a general increase of body size over time.

Such lawlike general assertions were based on generalizations drawn from the comparative study of phyletic and embryological stages in different taxa. As an invertebrate paleontologist trained at Harvard under the aegis of Louis Agassiz, Hyatt worked mainly on ammonoids. Cope drew generalizations from the herpetological collections of the Academy of Natural Sciences of Philadelphia and of the Smithsonian Institute, as well as from the fossil specimens he had discovered in the western U.S. lands between the 1870s and the 1880s. Theodore Eimer's *Orthogenesis* (1897) was based on a thorough analysis of evolution of the butterfly *Phyciodes*, while the zoologist Charles Otis Whitman (1919) studied the patterns in the colouration of pigeons. By considering Ernst Haeckel's biogenetic law as a true analytic principle (S.J. Gould 1977; G.E. Allen 1978), these naturalists deduced unknown phyletic and developmental stages from their observations. Yet this nomothetic attitude had often resulted in contentious and arbitrary generalizations (Simpson 1944; Gould 2002). For instance, Cope compared human teeth specialization to the dental trends of Primates, and then predicted that the differential disappearance of wisdom teeth would have led to the emergence of new human genera:

> The very frequent absence of the posterior molars (wisdom teeth) has been recently found to characterize a race in India. Should this peculiarity prove constant, this race would with property be referred to as a new genus of *Hominidae*, as we have many cases of very similar species being referred to different genera (Cope 1871, p. 598).

Whitman ventured to predict the evolution of colour patterns in the Tambourine dove on the basis of the colour trends he had described in pigeon phylogeny. Interestingly, Whitman himself admitted to never having seen any Tambourine species (C.O. Whitman 1919, p. 101). Generalizations sometimes took the shape of cosmic views encompassing the evolution of morals and society. Hyatt's speculations drawn from the law of racial senescence were in this regard emblematic. By assuming that old-age characters always merge with juvenile and unspecialized characteristics, Hyatt opposed the social emancipation of women, which he considered to be a regression in human evolution. And this because he had learnt from cephalopods that any form of sexual homogeneity preludes phyletic extinction (A. Hyatt 1897, p. 89).

Orthogenetic predictability between uniformitarianism and determinism

Criticisms of the law-making effort of orthogenesists have circulated since the 1940s. Among all the orthogenetic "laws", the preferred evolutionists' target has been Cope's rule of the increase of phyletic size. Cope's notion of anagenetic progress has been radically challenged, and size increase has been ascribed to positive directional selection (Simpson 1944; J.H. Brown and B.A. Maurer 1986; A. Hallam 1990; J.G. Kingsolver and D.W. Pfennig 2004), passive departure from ancestral sizes (S.M. Stanley 1973), fallacies in taxonomic classification (S.J. Gould 1997), as well as to morphological paths due to phyletic specialization (P. Raia and M. Fortelius 2013, p. 6).

Especially in paleontology, later scientists have been increasingly highlighting the arbitrariness of the reconstructions carried out by orthogenesists, emphasizing how their empirical evidence was liable to multiple interpretations (G.G. Simpson 1944; 1949; 1951). Similar criticisms were raised also by their contemporaries. In 1895, Darwin's disciple George Romanes considered the facts invoked by Cope and his pupil Henry Fairfield Osborn «not crucial as test-cases between the rival theories» (G.J. Romanes 1895, p. 63). Orthogenetic paleontologists were induction-addicted scientists who framed «spatio-temporally situated general statements» (P. Huneman 2007, p. 64) without considering the amount of contingent events that permeate fossils records (S.J. Gould 1970, p. 88). They imposed teleologically biased constructions on «what a bunch of historical accidents have in common» (Haufe 2015, p. 7), an attitude the American philosopher Chauncey Wright had regarded as the fundamental weakness of the palaeotiological sciences[3].

This epistemological framework rests on the assumptions of methodological uniformitarianism and of nomic spatiotemporal invariance (Haufe

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[3] «The facts of the sciences which Dr. Whewell calls palaetiological, like the various branches of geology, and every actual concrete series of events which together form an object of interest to us, are apt, unless we are fully acquainted with the actual details through observation or by actual particular deductions from well-known particular facts and general laws, to fall into a dramatic procession in our imaginations» (C. Wright 1877, pp. 70–71).

2015). In fact, such a stance had gained ground in early nineteenth-century geological inquiry (S.J. Gould 1965, p. 226). By endorsing a law-like view of nature, uniformitarianists assumed that an adequate observational knowledge should suffice to inductively retrodict the past and predict the future (N. Gontier 2015, p. 254). Therefore uniformitarianism, as a scientific procedure that excluded extra-naturalistic explanations, represented an essential element of nineteenth-century scientific practice, common to different geological and evolutionary theories (Gould 1965, p. 224). Furthermore, the epistemic attitude characteristic of orthogenesists was to endorse, in line with classical mechanics, a strict symmetry between causes and effects in evolution. Evolution appeared orthogenetic as well as predictable to the extent that it could be epistemologically reduced to physical processes (Levit and Olsson 2006, p. 103). Eimer and Haacke advocated the epistemological symmetry between organic and inorganic structures (T. Eimer 1888, 1897; Haacke 1893). Likewise, Whitman emphasized that evolution, like the production of crystals, consisted primarily of automatic self-determination towards a morphological outcome (Whitman 1919, p. 194).

In a Laplacian universe of steady causes and effects, in which organic and inorganic phenomena behave similarly, orthogenesis emerged as a «favored a priori prediction of deterministic science» (Gould 2002, p. 384). As Whitman stated with a grandiloquent attitude,

> Orthogenesis enables us to predict stages yet to come in the evolution of color-patterns; to trace histories of past sequences, and to anticipate the discovery of elements that have been overlooked. It enables us to understand parallel evolution in allied species, even when living under quite unlike conditions. It saves us from the stultification of holding selection sufficient to account for those long and definite lines of evolution revealed by paleontology (Whitman 1919, p. 183).

Paleontology was regarded as an exact science since paleontologists, relying on the «invariability of Nature's operations under identical circumstances» (E.D. Cope 1887a, pp. 6-7), could extend laws obtained by induction to the unknown. So strong was the faith in the symmetry between physical and biological causal determination that, in 1917, the Princeton orthogenesist William Berryman Scott drew a parallel between astronomy and paleontology in the testing of prediction:

> From irregularities in the motion of Uranus […] the astronomers predicted the discovery of another planet beyond, and the prediction was verified when Neptune was discovered with the telescope. […] Similarly, predictions and deductions have been made and subsequently verified concerning "missing links" in genealogical series. I myself had the great pleasure of finding in the rocks of northern Utah a fossil animal with a type of dentation which no man had ever seen, but which had been predicted some time before by dr. Max Schlosser of Munich (W.B. Scott 1917, p. 171).

The subtle relationship between orthogenesis, determinism and uniformitarian epistemology becomes even more evident if we look at the study of homoplasy within the American orthogenetic school. The development of similar phenotypes in not-homologous groups that live in distant geographical areas, or that lived in different geological epochs, represented for many orthogenesists the demonstration that, given the same conditions, the tape of life could actually replay itself. In Cope's terms, homoplasy was the proof that «in biological evolution, as in ordinary mechanics, identical causes produce identical results» (Cope 1896, p. 361). This "motto" became a shared tenet in the study of homoplasy, though the hypothesis on the origin of homoplastic sameness changed along with the evolutionary debate.

«Identical causes produce identical results»: the orthogenetic interpretations of homoplastic sameness

The term "homoplasy" was originally proposed in 1870 by the British zoologist and staunch Darwinian Edwin Ray Lankester. In the attempt to reframe the old dichotomy between homology and analogy, which was rooted in the pre-evolutionary school of morphology led by Richard Owen, Lankester distinguished two classes of homology: *homogeny*, i.e. similarity inherited from a common ancestor, and *homoplasy*, which included those resemblances that occur when «nearly similar forces act on two or more parts of an organism which are exactly alike» (E.R. Lankester 1870, p. 39). In his original formulation, Lankester remarked upon the difference between homoplastic and analogous structures. Whilst homoplasy required «a likeness of material» to begin with, «*any* two organs having the same function» can be considered analogous (Lankester 1870, pp. 41-42). The concept of analogy retained a wider meaning and should be thus considered as a distinct phenomenon resulting from completely independent evolution. However, during the nineteenth century such distinction was anything but clear, and naturalists tended to overlap interpretations tackling phenotypic similarities through inferences based on comparative anatomy (J. Arendt and D. Reznick 2008). In particular, the concept of homoplasy came to include all similarities evolved independently, thus moving from a subcategory of homology to its opposite (O. Haas and G.G. Simpson 1946; B.A. Wood 1999; Gould 2002; B.K. Hall 2007; J.B. Losos 2011; G.R. McGhee 2011).

According to Lankester's original definition, homoplasy resulted from «the common action of evoking causes or moulding environment» on alike parts (Lankester 1870, p. 42). Being close to the classic Darwinian viewpoint, Lankester addressed such causes in terms of natural selection. Yet in the early post-Darwinian debate, many naturalists considered homoplasy as the evidence that evolution was driven by non-Darwinian mechanisms. In particular, neo-Lamarckians saw in homoplasy the demonstration that, if organisms behave similarly under the same environmental conditions, they acquire the same variations. Therefore, the reduction of digits or the development of similar orthogenetically-oriented dental cusps in distinct lineages appeared as the effect of identical «efforts» (Cope 1896, p. 497) tending to a common end.

Edward Drinker Cope was the lead representative of this interpretation of homoplasy. He considered the repetition of the same movements (*kinetogenesis*) to be the prime cause of macroevolutionary trends (Cope 1871, 1887a, 1896). Variations were self-oriented to the extent that organisms, thanks to their physical sensitiveness, reacted to environmental challenges modifying their habits and behaviour. In accordance with the use-inheritance theory, actions performed under similar environmental pressures caused similar mechanical adaptations among independent taxa. «Another reason for believing in use as a cause of structural change», Cope stated, «is the manner in which the same useful structures have appeared on totally distinct stems, as an evident adaptation to the same circumstances in which the different types have been equally placed» (Cope 1887a, p. 25). Cope's account of the evolution of horses between Europe and America is in this sense emblematic. By analysing the limbs and teeth of the ancestors of the modern horse, and considering the rule of the increase of phyletic size, Cope theorized that the genus *Equus* «was born two times» (G. Pinna 1995, p. 143). Its diphyletic origin resulted from the same adaptations occurred in two distinct lines of descent (E.D. Cope 1887b). According to Cope, polyphyletic groups were also the evidence that several taxa had evolved through ontogenetic changes transmissible to offspring. Indeed, the idea that similar shapes had independently evolved through the contingent accumulation of identical random variations in distinct groups was wholly unsuitable in light of the positivist conception of causal determinism. All the variations, Osborn remarked in support of Cope, should have appeared simultaneously and subsequently be selected «at the same rate in the species of the Rocky Mountains, the Thames Valley, and Switzerland!» (H.F. Osborn 1890, p. 111).

Especially among American paleontologists, the neo-Lamarckian explanation of homoplasy continued to be successful until the early 1890s (P.J. Bowler 1983). However, as August Weismann's theory of the separation of germplasm from the somatoplasm gave the so-called «deathblow» to soft heredity (H.F. Osborn 1931, p. 528), advocates of directional evolution began reshaping their account of homoplasy. In spite of this, their main epistemological view remained unchanged, as witnessed by the works of the Princeton paleontologists Henry Fairfield Osborn and William Berryman Scott.

Osborn and Scott had begun their career as Cope's pupils in the mid-1870s (R. Rainger 1991). From the 1890s, they started questioning soft heredity, accepting the argument of experimental biology dismissing neo-Lamarckian conceptions of osteological evolution[4]. Yet even this theoretical shift did not affect their main epistemological stance. Osborn and Scott could not deny the evidence of trends, for instance that mammal evolution had followed parallel lines in Europe, North America and South America. Such phyletic regularities had to deterministically entail linear variations, even if such linearity could no longer be explained through soft heredity. In the attempt to address this issue, Scott and Osborn reframed the notion of homoplasy within a renewed definition of parallelism (Gould 2002).

It was Scott who first pointed out the differences between convergence and parallelism defining this latter as the «independent acquisition of similar structure in forms which are themselves nearly related» (W.B. Scott 1896, p. 185). Six years later, Osborn explained the evolution of mammal teeth from the so-called "tritubercular molar type" (W.K. Gregory 1934) by extending

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[4] In reference to Cope's kinetogenetic explanation of teeth evolution, Osborn stated in 1897: «Determinate evolution in these non-plastic structures at present strikes me as part of the mechanical necessities of development» (H.F. Osborn 1897, p. 951).

Scott's notion of parallelism. The homoplastic evolution of these structures, Osborn now stated, had to be traced back to a remote hereditary kinship he called «latent homology». Curiously, Osborn employed the same argument he had used in 1890 in favour of neo-Lamarckian homoplasy:

> If molar teeth are found independently evolving in exactly similar ways in such remote parts of the world as Switzerland, Wyoming, and Patagonia, it is obvious that the process is not governed by chance but represents the operation of some similar or uniform law deduced from the four following considerations: *firstly*, the teeth differ from all the other tissues and organs of body in being preformed, beneath the gum. […]. *Secondly*, the teeth are, nevertheless, among the most progressive organs in the body […]. *Thirdly*, according to the present paleontological evidence many of the different families and orders of mammals diverged from each other at a time when they possessed three cusps on the upper molar teeth and from three of five cusps on the lower molar teeth. This being the case, only the cusps comparable in different orders of mammals with these original three upper and five lower cusps are […] homogenous. *Fourthly*, it follows that the new cusps of the teeth furnish an example of homoplasy independent of the individual modification. Thus, we may say that in the teeth at least homoplasy involves a law of latent or potential homology (H.F. Osborn 1902, pp. 267-268).

Homoplastic cusps became at this point the manifestation of the same potential changes «evoked under certain somatic and environmental conditions» (H.F. Osborn 1912, p. 277). In turn, natural selection became a mere regulative principle instead of a causative factor in the production of evolutionary novelties.

Concluding remarks

Despite the shift from a neo-Lamarckian functionalist explanation to a renewed internalist conception of evolutionary change, orthogenesists did not change their symmetrical view of evolution. In line with the «complexity-as-design argument» (P. Huneman 2015, p. 115), Osborn and Scott denied natural selection the power of producing isomorphisms, and rather explained homoplastic sameness as the result of similar internally-directed variations. Once again, the repetition of bone patterns in the fossil records appeared as the linear outcome of repeated orderly variants, a view that allowed orthogenesists to see natural history as a set of tapes regularly replayed over time.

It must be stressed that these claims for evolutionary symmetry relied on a vague notion of identity (Huneman 2007), as already highlighted in the early criticism of orthogenesis. In 1890, the English naturalist Frederick W. Hutton attacked Cope's messy notion of structural sameness:

> If we test this hypothesis by Professor Cope's rule — that the same mechanical cause must always produce the same effect — we find it to fail; for fishes have not developed a vertebral column adapted for lateral movements, although they always move their tails laterally and never vertically. […] Again, the lightening of neck is sometimes, as in the swan, due to an increase in the number of vertebrae; while in other case, as in the giraffe, the number of vertebrae in not increased, but each one is greatly elongated. How could the same mechanical cause have brought about such different results? (F.W. Hutton 1890, pp. 152-153).

Similar criticisms targeted Osborn's works on homoplasy. Lankester personally wrote to Osborn and complained the way he had overlapped the expression «likeness of material» and the notion of homology:

> The "likeness" due to "to other reasons" than homogeny […] cannot be homogeny. The "likeness" which clearly enough is included and pointed to in the whole paragraph – favouring the action of homoplasy – is either a likeness of true homogeny (that is of form and relation inherited), or a likeness of similarity in material, in position, or in initial form – not due close homogeny – but possibly a likeness of such general character as the "likeness of material" (not of elaborated form and pasts) in two epidermal surfaces (H.F. Osborn 1907, pp. 238-239).

Prompted by an essentially deterministic framework, the arguments of the orthogenesists were affected by conceptual ambiguities, murky terminologies and biased reconstructions. In spite of this, in the context of nineteenth-century epistemology, the explanations they provided were long considered as more complete than the Darwinian ones (Pfeifer 1965), for they befitted the positivist conception of causal determinism. Orthogenesis, in all its theoretical heterogeneity, represented a response to Darwin's challenge to the prevailing nineteenth-century epistemology. This epistemological rejection of evolutionary contingency cannot be entirely detached from the need to preserve the idea of design that Darwin had strongly challenged (Simpson 1944; P.J. Bowler 1976, 1983; Mayr 1982; M. Ruse 1996). As a matter of fact, orthogenetic theories left room for purposive and even theistic interpretations of evolutionary change[5] which have profoundly undermined their reception since the 1930s.

However, some of the main issues raised by the orthogenesists, such as the critique of panselectionism and the need to theorise built-in limits to individual variability, did survive such criticism. Especially in the last few decades, the evo-devo studies have emphasised the role of structural, developmental, and genetic constraints in evolution. A new theoretical scenario has emerged in evolutionary biology for critically rethinking the contribution of a non-Darwinian tradition (P.J. Bowler 2017, p. 214), whose representatives believed that internally-channeled variations were the major determinants of predictable trends (Gould 2002, pp. 1086-1088). This conceptual shift was made possible by two conditions: (i) the emancipation of orthogenesis from any teleological involvement; (ii) its reconceptualization beyond the traditional deterministic framework which had led orthogenesists to reject Darwin's notion of chance on an epistemological basis. Once the mechanisms theorised by orthogenesists ceased to be used as a way to contrast natural selection, they started to be regarded as operational subjects for a pluralist approach to evolutionary research.

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[5] The historical scenario was however multifaceted. Historian Archibald David (A. David 2014) has recently suggested that orthogenetic explanations involving a strict nexus between directional variations and phyletic regularities composed a wide spectrum of positions that ranged from the materialist stance of Charles Otis Whitman to the metaphysical views of Teilhard de Chardin.

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“Synthesis” and Behavior: A New Role for Selection

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Introduction

In the Darwinian frame, understanding evolutionary trends concerns essentially catching the action of natural selection, whose role is one of the most controversial topics of evolutionary biology, but also one of the major heuristic tools through which to explain the emergence of acquired adaptive responses in a system (G. CORBELLINI 2004).

Does selection act on the genetic endowment, on the whole organism, or on the species (S.J. GOULD, 2002)? And how do these different units of selection emerge? Are they pre-established entities or rather transition processes (J. MAYNARD SMITH and E. SZATHMÁRY 1995)? These questions undermine our predictive ability because of the «*reciprocity* of effects of genetic state on environmental sensitivity and of environmental state on genetic sensitivity of the developing organism» which affect evolution (R. LEWONTIN 2001, p. 62)[1].

Along these lines, I would like to discuss the role played by the organism and its behavior in evolution, taking into account the epistemological reflection on the “possible” proposed by Piagetian epistemology. I intend to show how the active role of the organism in a context could entail an *intra-organic selection* able to regulate the interaction between the organism and the environment, linking individual change and macro-evolutionary effects. This argument allows to emphasize the tension between unpredictable actions as creative forces of living systems and the predictable effects of selection on the species’ constitution. A tension that is mirrored in the Piagetian “genetic

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[1] Some biologists assert that biology has a “units problem” or that it is not possible to univocally individualize such units: «The units of evolution problem resembles other units problems in science. Identification and classification of the subjects of research are necessary steps in theory-building and are also important when assessing whether theoretical descriptions in the science are well formed and accurate.[…] The philosophical challenge in evolutionary theory over the last 30 years has been to convince biologists they even have a units problem». (J. GRIESEMER 2003, p. 169).

epistemology" aimed to explain the formation of the intersubjective cognitive structures and their transformation (J. Piaget 1971).

In which way are living beings open to new evolutionary possibilities – possibilities that are not intrinsic to living beings' starting conditions and that by consequence are not predictable?

I will discuss this topic firstly by highlighting, at a historical level, some key stages in the Synthetic Theory of the late 1950s, when an attempt was made to integrate the role of *behavior* and *development* within evolution. Then, I will discuss some aspects of Jean Piaget's epistemology which, albeit extrinsic to the debate within evolutionary theory, is nevertheless one of the most remarkable among the epistemological approaches that sought to assess the impact of the selective dynamics at work within the organisms and their behavior on macroevolution, extending beyond the genes the concept of heredity too.

I.

At the turn of the 20th century, on one side non-teleological orthogenetic trends in North America (Whitman, Hyatt, Eimer), centered on the dynamics of development as the necessary and sufficient cause for the evolution of a species, and on the other side the rise of biometric and Mendelian analysis in Europe, contributed to marginalize Darwinism and especially its chief tenet: natural selection (P. Bowler 1983).

Natural selection became controversial as agent of change in the evolution of living beings. Different styles of thoughts regarded it as being essentially incapable of explaining life's variability. As the historian of science V. Kellogg said: «Natural selection remains the one causal-mechanical explanation of the large and general progress toward fitness; […] But what Darwinism does not do is to explain the beginnings of change, the modifications in indifferent characters and in indifferent directions» (V. Kellogg 1907, p. 376).

By contrast, the Modern Synthesis from the 1930s represented a crucial stage for Darwinian thought, because of its renewed understanding across different disciplinary fields – first of all population genetics – of natural selection. Such reevaluation of natural selection culminated in the late 1970s, when the evolutionary biologist Stephen Jay Gould denounced the "hardening" of the Modern Synthesis (S.J. Gould 1983) towards an "adaptationist selectionism", unable to recognize further evolutionary processes. The role of selection started to broaden, beyond its action on genes alone: «we need to expand and modify Darwin's world to a hierarchical view of selection operating differently and simultaneously at several levels of nature's individuality – and not segregate natural selection to exclusive operation in a single domain» (S.J. Gould 2003, p. 451).

From the point of view of systematics, E. Vrba and S.J. Gould gave emphasis to the influence of genetic drift and of geo-climatic pressures on speciation (E. Vrba and S.J. Gould 1982). Against the more established study of the environment as an indirect selector of the genetic frequency of a population, the idea of a co-evolutionary interrelation between organisms and their environment was advanced by R. Lewontin (1974), and further developed by the ecological and ethological theories of *niche construction* (F.J. Odling-Smee, K.N. Laland, M.W. Feldman 2003).

Increasing attention was given to the active role of organisms' behavior. In the early 1950s, the paleo-ornithologist George Gaylord Simpson together with his wife, the psychologist Anne Roe, delivered a series of lectures on behavior and evolution, presented at the "American Psychological Association" and at the "Society for the Study of Evolution". In 1953 and 1956 they held two sessions of lectures, funded by the Rockefeller Foundation and the National Science Foundation, focusing on the points of contact between the evolutionary study of behavior and the behavioral study of evolution.

These discussions, which led to the publication of the collected volume *Behavior and Evolution* (G. Simpson and A. Roe 1958), had the merit of exploring for the first time behavioral processes as *causal agents* rather than merely as byproducts of evolution. As Simpson affirmed: «An aspect of the Synthetic theory especially pertinent here is that again brings in behavior as a central element. It not only points the way to evolutionary, historical explanations of existing behavior patterns but also involves behavior as one of the factors that produce or guide evolution» (Simpson and Roe p. 21). In other words, Simpson proposed for the first time a theory capable of accounting for the fact that behavior is at the same time a factor and a product of evolution[2]. «Accepting the geneticists' knowledge of egg-processes, it shows that these are not autonomous but are strongly influenced by hen-processes. The means

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[2] «There are, they [the students] said, no theories of behavior. There are theories, or, at least formal generalizations about particular categories of behavior, such as the theory of imprinting […]. But as to theories in a broader sense, which might apply to and unify the whole field of behavioral studies, they were said simply not to exist» (Simpson and Roe 1958, p. IX).

of that influence is, as Darwin thought, natural selection. […] Natural selection has turned out to be something broader» (Simpson and Roe 1958, p. 9).

Simpson, therefore, acknowledged the reciprocal influence between genetic (the egg-process) and developmental (the hen-process) levels, between the genetic line and the somatic or ontogenetic line (the hen-process), both acted upon by natural selection, which – however – should be understood in broader terms. The cornerstone of Darwinism was thus extended, and new attention was given to the teachings of other evolutionists who had considered further levels of selective processes, such as the psychologist James Mark Baldwin. Simpson published an essay on Baldwin in the journal *Evolution* in 1953, rescuing Baldwin from historical oblivion.

According to Baldwin, organisms are able to actively respond to environmental challenges through "individual adjustment" by means of random movements which, however, can converge in a functional response to the disequilibrium produced by the altered environmental conditions. This response, according to Baldwin, enables the organism to resist to the negative action of natural selection and in some cases, allows the organism to be positively selected by virtue of the plasticity ensured by such process. At the peak of Darwinism's crisis, Baldwin did not question the Darwinian process but suggested "a new factor in evolution" *i.e.* organic selection, which became the object of a famous study published in 1896 (J.M. Baldwin 1896; B. Continenza 1984). This "new factor" was a kind of selection at the individual level, capable of producing functional responses allowing the organism to adapt in accordance to external conditions:

> There is a process by which the theatre of the application of natural selection is transferred from the outside relations of the organism, its relations to its environment, to the inside relations of the organism. It takes the form of the *functional adjustment of the life processes to variations in its own motor responses*, so that beneficial reactions are selected from the entire mass of responses (J.M. Baldwin 1895, p. 176).

By placing the concept of selection within the organism, Baldwin adopted from physiology the notion that a concentration of motor energy, or state of excitement, in the areas critical for the interaction with the environment might trigger responses which, through a beneficial reiteration ("circular reaction"), could give rise to new and advantageous actions that are indirectly inheritable[3]. Through this concentration of motor energy, in fact, the organism is capable of producing a rich variety of *new* responses that are not determined by its "hereditary endowment" and by consequence are not predictable. Nonetheless, selection on these responses represents new and active source of "accommodation" of the individual to external critical conditions. Baldwin, thus, combined the concept of behavior with that of plasticity: the idea that concentrations of energy can give rise to non-deterministic variability of motor reactions, liable to be selected or even "imitated" by the "hereditary" endowment. In Baldwin's view, what can be inherited is *not* the accommodation itself but the conditions of plasticity that have enabled it. Thus, behavior acquires new relevance within the economy of evolutionary thought: «It is the behavior of the organism, therefore, which is important, and not [genetic] variations alone, as in simple natural selection generally – and hence the adjective "organic" » (BALDWIN 1895, pp. 1902, 214).

Behavior becomes a *factor* of evolution, as opposed to a mere outcome, as in the traditional evolutionary account. In fact, it implies the capability of an organism to act and alter its own constitution. If organisms are not just «billiard balls driven toward new positions on the table by external, measurable forces» (S.J. GOULD 1977), then selection does not operate only on given variations but can extend the spectrum of possible variations on the organic level, without any teleological implication. This outcome was also acknowledged by one of the fathers of the Synthesis, namely by Ernst Mayr: «A shift into new niche or adaptive zone is, almost, without exception, initiated by a change in behavior. […] With habitat and food selection – behavioral phenomena – playing a major role in the shift into new adaptive zones, the importance of behavior in initiating new evolutionary events is self-evident. Sibling species, in spite of their morphological similarities, often show remarkable behavioral differences» (E. MAYR 1963, p. 604).

II.

By making the most of the critical debate surrounding the Synthesis (S.J. GOULD 1983), Piaget chose to further develop his early insights regarding

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[3] This physiological process lies at the origin of attention in learning process as the American psychologist had learned from the works of the German physiologist Eduard Pflüger (J.M. BALDWIN 1902, p. 110).

the behavior of freshwater snails and speciation within the framework of his mature epistemology (J. Piaget 1974). According to Piaget, behavior constitutes a source of *new,* unpredictable, adaptive responses in changing environment: it features both as «the expression of the overall dynamics of organization in its interaction with the environment and as source of supersessions and innovations for as long as the environment or environments continue to contain any elements creating obstacles for the organism» (J. Piaget 1978, p. 140). This is an adaptive process emerged from non-deterministic motor responses of the organism, that is only one instance of a broader phenomenon that essentially concerns the "disclosing of new possibilities".

Piagetian "genetic epistemology" rules out any innate or empiric emergence of life structures, notwithstanding his emphasis on the universality of knowledge structures. Indeed, according to Piaget, who was originally trained as a naturalist and continued to pursue his experimental studies on *Limnea* and *Sedum* along his career, to explain the universality of human reason, and hence of its cognitive structure, means considering both the need for stability, coherence and permanence and the instability, transformation and diversification of forms. The development of the concept of "construction" mirrors his firm belief in the inadequacy of innatist and preformist approaches, as well as of the acquired ones in Lamarckian tradition (J. Piaget 1976), as means to understand organic and cognitive development. Piaget sought to understand the relation between subject and object in their actual coming into being without yielding to any external force that might shape their course as was the case in his early philosophical writings concerning the concept of the possible (J.J. Ducret and G. Cellerier 2007). The outcome of this research is the concept of "equilibration" (J. Piaget 1975), which lies at the basis of his notion of behavior as well as of his innovative views on heredity.

The sources of Piaget's thought are multifarious. From his teacher, Arnold Reymond, Piaget learned the Kantian lesson about the constitution of the cognitive categories. At the same time, however, through the influence of Emile Boutroux's doctoral thesis *De la contingence des lois de la nature* (1874; cfr. E. Boutroux 1915), Piaget came to focus on the concept of contingency (J.J. Ducret 1984). Boutroux's thesis questioned Kantian *a priori* synthesis, arguing that the idea of *a priori* synthetic judgement, i.e. a judgement whose predicate is not already included within the subject, is untenable. In fact, for this reason, *a priori* knowledge remains essentially analytical, and expresses identity (A=A). Experience, on the contrary, develops as a relation between facts coordinated by a knowing subject; a relation between facts that is necessary in itself, can only exist as a repetition of the identical – which is not the case of life nor of learning. According to Boutroux, *nature affirms itself through the contingency of its action*: it is open to countless, unpredictable variations that cannot be traced back to necessary and universal laws, but only to simple constant relations that are derived by us inferentially[4].

The first part of Boutroux's doctoral thesis centers on a critique of Positivism, as it challenges the very notion of "linear causality" and the idea of predictability of events on the basis of given laws. According to Boutroux, the existence of what is possible cannot be inferred from some premises as the conclusion of a syllogism, since there is a gap between possibility and existence, whereby the latter cannot be the necessary outcome of the former[5]. Therefore, contingency may be seen to disclose the prospect of unpredictability, sweeping away both preformism and determinism[6].

This attack to Positivism was further reinforced by the influence of Henry Bergson's work, one of the young Piaget's favorite thinkers. In *Creative Evolution* (H. Bergson 1944), the distinction between living and non-living beings revolves precisely around the need for the formers to "endure", tracing a unique and irreversible, and therefore unpredictable, course. Temporality enables life to endure, to take shape in a creative way. In his article *Le possible et le réel* (1930; cfr. H. Bergson 1934), Bergson argues that the possible should not be conceived as something that awaits to be realized on the basis of given conditions: this would be a possible that awaits an "infusion of life"[7]. The possible, according to Bergson, exists after and not before concrete existence, which endures continuously. The priority of action means grasping the actual

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[4] Mayr affirms the importance of the conceptual modelling in biology against universal laws which lack the flexibility and heuristic utility of concepts (E. Mayr 1982, p. 43).

[5] «Faut-il admettre que la distinction du possible et de l'être n'est qu'une illusion causée par l'interposition du temps entre notre point de vue et les choses en soi?» (E. Boutroux 1915, pp. 18-19). In Boutroux's opinion knowledge cannot be *a priori* precisely because nature, its object, cannot be reduced to a closed system in which chains of relations are necessarily formed, creating countless yet finite possibility of transformation.

[6] «Il n'y a pas équivalence, rapport de causalité pure et simple, entre un homme et les élements qui lui ont donné naissance, entre l'être dévéloppé et l'être en voie de formation» (Boutroux 1915, p. 28).

[7] «[…] le possible aurait été là de tout temps, fantôme qui attend son heure; il serait donc devenu réalité par l'addition de quelque chose, par je ne sais quelle transfusion de sang ou de vie » (H. Bergson 1934, p. 111).

giving itself of the living being without tracing it back to past configurations (preformism) or future ones (finalism). It is the real that makes itself possible, and not the possible that becomes real (Bergson 1934, p. 112).

These early readings by Piaget go hand in hand with his study of the behavior of freshwater snails and *Sedum* in unfavorable environmental conditions. Piaget observed that different phenotypes emerging in extreme conditions are inherited even once the original conditions have been re-established. The result of this functional process is called *phenocopy* and serves as the biological model for the concept of "equilibration"[8]. Started in the 1960s, these biological studies and the related reflections on the "possible" (as opening up to something new rather than as recombining existing traits) became crucial in Piaget's work. In 1975 the history and temporality of living processes acquired greater importance: the research came to focus on irreversible processes, processes that shatter temporal symmetry (i.e., that cannot equally be carried out forward and backward but which are non-reversible). The study of the qualitative change implied by the process of equilibration (as opposed to equilibrium), acquired prominence: the functional process that restores a state of equilibrium considering the perturbations that had affected it. In other words, phenocopy, as an equilibration process, expands plasticity.

The challenge that Piaget took up was to avoid the pitfall of Lamarckian empiricism, which – in his opinion (Piaget 1976) – made the subject passive and powerless *vis-à-vis* the environment, while at the same time downplaying the influence of natural selection on aleatory variation. His challenge, in other words, was to reaffirm the element of contingency in the constitution of the life trajectories of the organisms, assigning them a central role with respect to the great structural changes of the species via the inner dynamics of selection.

Conclusions

One of the most interesting consequences of Piaget's reasoning, is the extension of the concept of heredity beyond the emerging metaphor of the

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[8] The phenocopy concept is very close to Baldwin's organic selection (Piaget 1978). Piaget describes phenocopy as «une convergence entre un accommodat (phénotypique) et une mutation (génotypique) qui vient le remplacer et on l'explique ordinairement par l'intervention de processus géniques» (Piaget 1974, p. 2).

"program", proposed in the 1960s. If organic adjustment in developmental and evolutionary processes depends on inner processes of selection (*phenocopy*) that are not completely predictable, then hereditary endowment cannot encompass all possible forms of adaptation; rather, organic activity will promote new forms of adaptation, modifying the genes themselves. Piaget presented this hypothesis at the "Colloque de Royaumont", where it was heavily criticized by Danchin, Jacob and Changeux[9]. However, Piaget defended it by quoting Mayr's paper in *Behavior and Evolution*: «there are at least two different possibilities for the acquisition of a new behavior pattern by a species: 1. the new behavior may have a genetic basis [...]; 2. a new behavior is at first a nongenetic modification of an existing behavior, as a result of learning, conditioning or habituation, and is replaced (by an unknown process) by genetically controlled behavior» (E. Mayr 1958, p. 354).

According to Piaget, acknowledging the centrality of organic activity and of its processes of selection is the only way to approach a "fundamental problem":

> that of understanding in what way the genetic system evolved. Since epigenetic systems are partly (and only partly) determined by the genetic system, broadly conceived, why should we rule out the existence of rebound actions of the former on the latter, given that we are reasoning no longer in terms of a one-way linear causality (J. Piaget 1967, p. 325).

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[9] The criticisms essentially consisted in bringing back the Piagetian concept of phenocopy to phenotypic plasticity, without implying a genetic change. Cf. M. Piattelli-Palmarini 1979, p. 113.

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Seinesgleichen geschieht[1]: Contemporary Challenges to Evolutionary Contingency

Silvia Caianiello

The strongest statement on the overwhelming role of contingency in the evolution of life was uttered by Stephen Jay Gould. His well-known thought experiment that, winding back the tape of life at the Cambrian explosion, the earth will result populated «with a radically different set of creatures» (S.J. Gould 1996) – is still the terminus a quo of the actual debate. As for many other issues, Gould's "evolutionary contingency thesis" set the agenda for a long-standing debate, which has lately experienced an interesting revival.

The climate in which such statement was conceived is very different from the present one. The impact of the Alvarez theory (L.W. Alvarez 1980; but see G. Keller 2011) of the extraterrestrial cause of the Cretaceous-Tertiary Extinction, Gould's work with Schopf instantiating computational simulations of macroevolution as a totally random process (D.M. Raup *et al.* 1973; D. Sepkoski 2016; D.D. Turner 2011), are some of the background conditions of his strategy for opposing Modern Synthesis adaptationism by emphasizing the contingency of evolutionary processes. Actually, it appears that, in the manifold dissections to which Gould's notion of contingency has been fruitfully subjected (J. Beatty 2006; S. Oyama 2000, pp. 116 ff; W. Callebaut *et al.* 2007, pp. 67-68; K. Sterelny and P.E. Griffiths 1996, pp. 296 ff; R. Millstein 2000), the only unifying opposite to his aggregate term is adaptationism. Rather than being the outcome of the optimization power of natural selection, «modern order is largely a product of contingency» (S.J. Gould 1989, p. 288).

How does order arise out of contingent evolutionary processes?

Gould's answer to this issue matches mainly one among the different senses of his contingency notion, the one by now labelled "causal dependency" or "contingency upon" (Beatty 2006). From it follows that singularities, «the unpredictable sequences of antecedent states», are congealed in

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[1] "Seinesgleichen geschieht", "things of the same kind happen again", is the title of the second part of *The Man Without Qualities*, the masterpiece of the Austrian writer Robert Musil. The title typifies the thought style proper of the Austrian Empire, conveying an image of how Kakania – as he calls it – «remained entrapped within its own systemic logic» (T.J. Mehigan 2003, p. 62).

historical constraints, the «unerasable and determining signatures of history» (Gould 1989, p. 283). This notion of contingency as causal dependency of per se singular events has two complementary implications.

The first is a "frozen" view of conservation; a view that, mutatis mutandis, is not that far, at least not as far as one might have expected from Monod's: «hasard capté, conservé, reproduit […] et ainsi converti en ordre, règle, nécessité (J. Monod 1970, p. 112). It was still along this line that Gould, as most in the early evolutionary developmental biology (evo-devo), saluted the discovery of the deep conservation of genetic pathways as a proof that convergent evolution might turn out to be frequently due to «a positive constraint of parallelism»[2] rather than to natural selection.

The other implication is that the only "good science" accessible to evolutionary theory is retrodiction. While «unpredictable in principle from full knowledge of antecedent conditions» – as these are themselves singular, «particulars of history rather than necessary expressions of law» – living complex systems are nonetheless «fully explainable after time's actual unfolding» (S.J. Gould 2002, p. 46; Gould 1989, p. 278). This conclusion shaped his notion of evolutionary explanation as not only historical, «idiographic» (S.J. Gould 2001, p. 196) but also narrative, as a *linear* sequence of states «each crucially dependent upon tiny differences of antecedent states» (Gould 2002, p. 1333; cfr. Gould 1989, p. 178, 283).

A rapid glimpse at the actual debate about predictability in evolution captures a very changed mood, expressed often in direct challenge to Gould's evolutionary contingency thesis (A. de Queiroz 2002, pp. 917, 926; J.C. Conant and A. Wagner 2003, p. 265; P.M. Brakefield 2006, p. 364; D.M. Weinreich *et al.* 2006, p. 113; G.B. Müller 2007, p. 510; A.S. Wilkins 2007, p. 8596; A.E. Lobkovsky and E.V. Koonin 2012, p. 63). The feeling that «evolution might not be as unpredictable as one thought 25 years ago, when Gould formulated his original question» (V. Courtier-Orgogozo 2016, p. 9) is more widespread, as the expectation that evolutionary biology is on the verge of becoming «a more predictive discipline» (B. Papp *et al.* 2011, pp. 599-600).

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[2] «Homologous developmental pathways (*retained from a deep and different past*, whatever the original adaptive context) strongly shape current possibilities "from the inside"» (Gould 2002, p. 1129, cfr. p. 1123, my emphasis).

[3] I am not quoting Simon Conway Morris to support, as his position on predictability was already in place at the time of his open controversy with Gould; see S.C. Morris 1998.

My scope in this paper will be to inquire, at the specific case of *repeated evolution* – or the evolution of similar traits in distinct lineages facing similar environmental conditions but strictly due to mutations in the same genes –, what has changed; and to show how this change affects both of the highlighted aspects of Gould's thesis: the "retrodictive" destiny of evolutionary theory and, more subtly, also the frozen view of conservation.

Beyond the contingency/predictability dichotomy

Whatever the exact meaning of contingency understood, the actual claims of increased predictability do not challenge contingency per se but rather the dichotomy contingency/predictability as proposed by Gould (M. Mahner and M. Bunge 1997, p. 211; R. Powell 2012; V. Courtier-Orgogozo 2016). In fact, especially since the eclipse of the Laplacian universe (R.C. Bishop 2003; L. Vinicius 2010, pp. 5ff, 18), this dichotomy appears infected by a "katabasis eis allo genos", indeterminism having become an utterly ontological notion (independent from the limits of human knowledge), while predictability is an epistemological one (Earman 1986).

Thus, as determinism does not involve predictability – and indeed much before the mediatisation of the chaos revolution (A. Aubin and D. Dalmedico 2002) –, so on the same ground contingency does not preclude the possibility of establishing even for nonlinear systems specific «predictability horizons» or «domains» (J.B. Kadtke and Y.A. Kravtsov 1996, p. 4ff; see Y. Prigogine 1997, Powell 2012), and even more importantly, determine when, at which level and to what degree nontrivial «time, system and purpose dependent» predictions are possible (Bishop 2003, p. 181). One might add that it is exactly because it did not resign to the impotence in front of complexity that the whole history of dynamical systems theory devoted so much effort, since Poincarè's recurrence theorem (A.M. Lesk 2008), to classifying different kinds of system and degrees of probability for predictions of their qualitative behaviour and, when possible, to devising control engineering techniques to steer them to a desired one (Aubin and Dalmedico 2002; cfr. J.N. Weiss *et al.* 1994; E. Schöll and H.G. Schuster 2008); what, unsurprisingly, is being increasingly achieved by reverse engineering the mechanisms evolved to this end by biological systems themselves (M.E. Csete and J.C. Doyle 2002; J.H. Holland 2008).

The American philosopher Sandra Mitchell has baptized "pragmatic" those laws that, without aiming at the logical unification that was the dream of logical positivism, can serve the concrete goals of science by assessing the «*nature* and *degree* characteristic of biological generalizations», and consequently of their predictive power (S. Mitchell 2003, p. 116). This issue is patently crucial for biology, and is the subject of an ongoing debate, which has brought about sophisticated notions such as contingent predictability (de Queiroz 2002) and conditional inevitability (K. Sterelny 2005).

Interestingly, Mitchell's pragmatic approach is corroborated by some contemporary developments in the upcoming epistemology of big data, that emphasize both the power of this "new scientific method" in dealing with complexity and its intrinsic limitations (W. Pietsch 2016; see also S. Leonelli 2012). This method allows, according to Pietsch, beyond a given data threshold, a practice of "horizontal modeling", which attains highly contextualized predictions, and can even reconstruct in detail individual "causal stories". Data intensive models would thus be highly specific and effective in discerning highly context-dependent rules, but would not lead to a higher level, generalized and even less to a unifying explanation. Therefore, such models would be able to predict even without causal understanding: an unexpected consequence of the breaking of the logical-positivist symmetry between explanation and prediction.

This appears to be the case in the predictions about life evolution based on the observation of repeatability, to which I will refer in the following: they «rely on knowledge of certain parameters of the final state (final environment or final phenotype) and they do not require a good understanding of why repeatability exists» (Courtier-Orgogozo 2016).

Predictability can be considered a property of models, and, as reminded before, even Gould's conclusions were influenced by the playing with specific modeling devices. Inquiries about the accountability of models have been rigorously set up in evolutionary biology since the pivotal paper by Richard Levins (R. Levins 1960), and left us with no doubt that a model, as Freud said of consciousness, «it is not worth much, but it is all we have» (S. Freud 1933, p. 102). Unsurprisingly, it is to advancements in the modeling practice that the shift I am trying to highlight is due.

Big data and predictability

The big data revolution looms large in the actual claims of increased predictability, in so far as they rely on data intensive postgenomic high-throughput studies.

Comparative genomics and Systems Biology methods for integrating both "dry" computational simulations of pattern of differential gene expression and their morphogenetic consequences, and "wet" experimental identification of gene networks functional interactions (H. Kitano 2002; M.A. O'Malley and O.S. Soyer 2012) have given unprecedented insights on patterns and process of genome and phenome evolution, based on the measure of the strength and the elucidation of the biological nature of constraints on different classes of genomic sites (E.V. Koonin and Y.I. Wolf 2010; Papp *et al.* 2011). New "big data" tools for the study of genotype-phenotype maps, enhanced by genome-wide high-throughput sequencing technologies coupled with advanced manipulation techniques[4], are part and parcel of the actual claim that replaying the tape of life is no longer a thought experiment, but rather amenable to a quantitative and qualitative analysis (Courtier-Orgogozo 2016).

A crucial role has been played by experimental evolution. The «evolution of organisms with precisely defined genetic backgrounds and known evolutionary histories under controlled laboratory conditions» (Koonin and Wolf 2010, p. 493; cfr. D.L. Stern 2011, pp. 88 ss) has the unprecedented power of offering insights also «into rare events and slow processes» (T.J. Kawecki *et al.* 2012). Since the early experiments by Richard Lenski in the 1990s, experimental evolution was directly committed to test Gould's claim about the effects of "rewinding the tape", although both the resulting wealth of data and their interpretation are not univocal (see Millstein 2000, Beatty 2006, Brakefield 2006). Lenski could rely at the time on the new techniques of rapid DNA sequencing and mutagenesis; nowadays next generation sequencing allows coupling controlled experiments of evolution with high precision genomic sequencing of multiple clones in bacteria as well as in some eukaryote such as yeast.

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[4] Such as Gephebase (http:// www.gephebase.org), a database reporting associations between a mutation and a phenotypic variation.

But even the realism of population genetic models has increased, as new methods allow the mapping of epistatic interactions, as in genome scale metabolic models, which are already allowing «specific and reliable predictions on the outcome of metabolic evolution, both in short-term laboratory evolution and on macroevolutionary time scales» (Papp *et al.* 2011).

Also "generative capacities" and "variational properties" of developmental systems (I. Salazar Ciudad 2008; Müller 2007) have become increasingly amenable to mechanistic analysis. Recent computational simulations have lately achieved unprecedented success in predicting the phenotypic evolution of some morphological traits in specific ecological contexts, matching with astounding precision the macroevolutionary data (K.D. Kavanagh *et al.* 2007; see also I. Salazar Ciudad and J. Jernvall 2010).

The investigation, in comparative genomics, of causal links between genomic changes, phenotypes and fitness, has brought to the identification of so-called *loci of evolution*, genes and mutations associated to evolutionary changes between species and population at different levels of the phenome (N. Gompel and B. Proudhomme 2009; A. Martin and Courtier-Orgogozo 2013; Stern 2011). These new tools and data have brought to the most unexpected finding: the abundance of cases of repeated evolution, or the «multiple instances of adaptation occurring through the increase in frequency of the same segregating alleles or through independent de novo mutations either at the same nucleotide position, in the same gene or affecting the same gene expression profile» (Courtier-Orgogozo 2016).

Thus, not only *seinesgleichen geschieht*, but also events that the huge number of possible paths to the same phenotype, especially in more complex genomes, render highly improbable (J. Arendt and D. Reznick 2008; see S.B. Carroll 2006, chap. 6) do repeat themselves in phenotypic evolution. This hints at the possibility that the design space of life might be highly structured, and consequently that the transitions between states may be less random than previously thought (G.J. Vermeij 2006; Koonin and Wolf 2010).

Convergent – parallel – repeated: On different ways of being the same

Indeed it is has long been known that similar phenotypic traits do appear time and again in evolution. Homoplasy by convergent evolution is maybe the oldest argument in favour of natural selection. However, repeated evolution pinpoints specific comparative criteria of "sameness" which are not covered not only by the old notion of convergence but not even exactly by the more recent one of parallel evolution.

One of the major contributions of evo-devo – actually, of its constitutive subfield of comparative developmental genetics – has been the discovery of the shared genetic toolkit for the development of animal form (S.B. Carroll *et al.* 2001), which corroborated the possibility of establishing homologies across distant taxa at the genetic level, and, more importantly, at the level of the functional organization of gene expression patterns. The widespread conservation of genetic and developmental modules set the ground for an alternative, "internalist" explanation of homoplasy, which challenged the all-sufficiency of natural selection. As Zuckerkandl put it, «the organizational arch-conservatism of living systems has strikingly revealed itself only now» (E. Zuckerkandl 1994). In this early formulation, parallel evolution was consistent with the "frozen" view of constraints, «developmental designs that then congealed, enforcing reiteration and change within their internally directed channels forever after» (Gould 2002, p. 1178; see B.K. Hall 2012).

Nonetheless, further insights in the combinatorial and modular logic of gene regulatory evolution disproved that the conservation of genetic pathways is sufficient to endorse parallelism rather than divergence (Vinicius 2010, p. 19), as conserved expression patterns mostly represent a mere "fractional" homology (Zuckerkandl 1994), parts of machineries that are easily coopted into new contexts and functions. The very notion of homology has consequently become both "combinatorial" (A. Minelli 1998) and irreducibly hierarchical, requiring that homologies are compared and established only at their respective organizational level (S. Caianiello 2015).

Even at a higher organizational level, it has been established that many developmental constraints have been easily escaped on the long run (Vermeij 2015), and, on the other side, that phenomena of "developmental system drift" – by which even in closely related taxa, homologous characters have diverged in their morphogenetic or gene regulatory underpinnings – are ubiquitous (J.R. True *et al.* 2001).

While this body of evidence has strengthened the awareness of the nonlinearity of the mapping between genotype and phenotype (across the multiple biological levels that nowadays span these terms), bringing grist to the mill of evolutionary unpredictability, it also makes the case of repeated evolution, with the specific requirements of sameness it entails, the more intriguing.

The deeper mechanistic understanding of the genotype-phenotype mapping has challenged a too simplistic dichotomization between convergent and parallel evolution, between the "sameness" accomplished by the action of natural selection and the one deriving from the resilience of architectural features at different levels. The distinction between convergent vs parallel evolution would be but a «relics of a time when we could not evaluate the underlying cause of phenotypic similarity and were confined to inferences based on comparative anatomy» (Arendt and Reznick 2008). Convergence and parallelism might be rather held as extremes of a continuum, covering a variety of cases that are partly illustrated in this diagram by Losos (Figure 1). Even in parallelism, mutations in the same genes do not ensure the identity of the evolutionary trajectory. Different kinds of changes in the same genes can bring about the same phenotypic outcome: «parallel phenotypic evolution can result from nonconvergent molecular evolution» (J.B. Losos 2011).

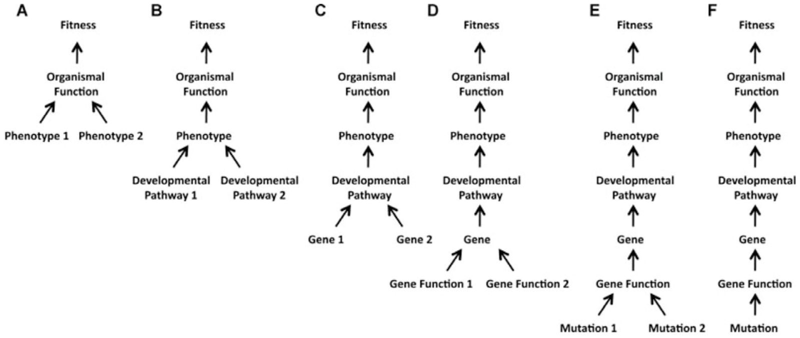

Figure 1. From Losos 2011

Nonetheless, in the continuum of parallel and convergent evolution, the notion of repeated evolution has recently acquired a status in its own right. In fact, the requisites for sameness that come into play in repeated evolution differ from the general definition of both parallel and convergent evolution.

While parallel evolution has come to cover in the literature mostly cases in which independent modifications of the same kind occur in shared (homologous) developmental patterns, and thus has been restricted to closely related species (Arendt and Reznick 2008), convergent evolution is usually referred to cases in which the sameness arises from different developmental pathways, what usually happens in widely distant taxa (Powell 2011). This criterion of taxonomical distance is lost in repeated evolution, which highlights the independent appearance of similar phenotypic traits also in widely distant evolutionary lineages but nonetheless due to identical or similar changes at the same genetic loci.

An important implication of this wider taxonomical range is that repeated evolution is not consistent with a "frozen" view of conservation. In fact, the evolution of parallel genetic trajectories to the same phenotype in distant taxa cannot be ascribed to similar starting points, because they move from different genetic backgrounds. As Vermeij suggests, it would be more proper to speak of «repeated innovations», whose recurrent emergence is the more striking as «genetic instructions […] only predispose the organism toward development of the structure and do not ensure its expression» (Vermeij 2006).

At the same time, unlike parallel evolution, which can be and has been in principle uncoupled from the environment, repeated evolution involves the pressure of a similar ecological challenge, and is thus focused on cases in which a "same" selective pressure has elicited the same genetic trajectory to phenotypic change.

However, while repeated evolution involves, as convergence, the action of the environment, it implies also the recognition that natural selection alone cannot be its sufficient cause. In fact, as already emphasized, natural selection per se would not explain the bias toward a parallel route instead of a convergent one for achieving adaptation – that is why to a similar environmental challenge a similar solution has been preferred.

Why is the independent evolution of a closely similar variation at the same genetic loci eliciting the same phenotype a riddle? Morphological traits usually involve the contribution of a huge set of genes, and would thus allow in principle an equally huge number of possible trajectories for change. That repeated events of change occur at the same genetic loci suggests that their modifications are not as random as it should be expected. Specific sets of bias (such as mutational target size; gene regulatory network architecture, structure and history of gene families, length of mutational pathways and pleiotropic effects of mutations, reviewed in Gompel and Proud'homme 2009; Courtier-Orgogozo and Martin in this volume) appear to characterize the loci which are most likely targets of repeated evolution as endowed with higher *evolvability*, in that they appear biased to generate tolerable phenotypic changes.

The focus on evolvability conveys, even if pinpointed at a strictly genetic level, a systemic perspective both on change and stability, as the differential role of single components is no longer causal in itself, as in the original "factorial hypothesis" at the dawn of genetics (T.H. Morgan 1915). It is instead the outcome of the complex, nonlinear dynamics of the underlying genetic network; an outcome whose constancy reveals rather the *robustness* than the deterministic inevitability of the resulting evolutionary trajectory (S. Caianiello 2018).

A well-established example of repeated evolution is the developmental mutation that results in light colour phenotypes. Coloration is a complex multistep process and involves in mouse more than a hundred genes, largely conserved in all vertebrates. However, even if several genetic paths are available to change coat colour, one particular gene, Mc1r (melanocortin-1 receptor) appears to be an evolutionary "hotspot" for body colour variation. Although body colour changes, in absence of this gene, are realized through different pathways, a specific association between body colour differences and changes in the coding sequence of melanocortin-1 receptor has been detected in quite distant vertebrate species – from birds, cats, bear, humans, mammoth, to lizards, snakes, cave fish, and in some cases the changes arisen in these genes are closely the same, such as in dark pocket mice and arctic skua (Arendt and Reznick 2008; Carroll 2006).

The explanation of the fact that only a small subset of the involved genes is the preferential target for «the repeated occurrence of de novo mutations […] causing similar phenotypic variation» (Martin and Courtier-Orgogozo 2013) is, as already highlighted, far from atomistic. Although the properties that qualify specific genetic loci for being "hotspots" of evolutionary and of developmental change differ, the function and molecular properties of the particular gene or pathway are but one, and not always the most relevant of the factors involved in repeated evolution. A far more relevant property is their position in the genetic network of which they are part, that of "integrative control point" (Stern 2011). It is therefore the evolved architectural structure of the relative regulatory network that confers upon them their specific mark of evolvability, one of the most general being of maximizing adaptation while minimizing the pleiotropic effects of mutations. This does not (and should not) exclude the causal role of further epigenetic organizational levels, but constrains the way they act on genetic architecture. Hotspots composed of a restricted set of loci would offer «paths of least resistance» to genetic change, facilitating the access to «evolutionarily viable regions of the phenotypic landscape» (Martin and Courtier-Orgogozo 2013).

It is also because of this "architectural" properties that mutations at these loci would be more likely fixed given specific selective pressures, which, as Stern highlights, should be equally related to a further crucial "conditionality", population size and structure – a further step in the direction of the much sought after unification of evo-devo and devo-evo, or devgen-popgen (S.F. Gilbert 2003).

Tinkering and beyond

Knowledge of the topological and dynamical properties of genetic networks appears to be part and parcel of the enhanced predictability of evolutionary trajectories. This point has been lately emphasized by Adam Wilkins, a pioneer of evo-devo, in a paper in which he partly challenges Jacob's notion of bricolage, arguing that the "jeu du possible" is much too biased to be defined tinkering. Many of the properties of complex biological systems would not be set by «the unique contingencies of history» (Gould 2001). The complex interaction networks that act as «organizational devices» (Wilkins 2007) at the many different levels of hierarchical organization that intervene between the genotype and the phenotype are not assembled randomly. Rather, the joint action of self-organization and selection appears to have shaped the highly specific topological and dynamical properties that underlie their architecture. What the increasing amount of cases headed under repeated evolution highlights, is that the genome – and maybe the organism as a whole, with all its multiple epigenetic regulatory levels – «runs on stochastic processes and finds ways to channel stochasticity» (E.V. Koonin 2013).

Conclusion

I come back briefly to my original point, to highlight the subtle but not irrelevant shift in the understanding of conservation, by which it ceases to be an *explanans* of long-term stability to become an *explanandum*.

Increasing evidence that «evolution, by constant tinkering, appears to converge again and again on these [same] circuit patterns in different nonhomologous systems» (U. Alon 2003; cfr. Conant and Wagner 2003), or of the differential evolutionary conservation of components according to their location in the spatial hierarchy of developmental gene regulatory networks

(D.H. Erwin and E.H. Davidson 2009) – all clear the ground from an *inertial* view of conservation, and lead to a different approach, focused on the investigation of the specific systemic conditions that enable the *dynamic reiteration* of the same.

This subtle difference could be an important one, if we consider how Gould's challenge has become lately one of the crucial issues of the upcoming philosophy of exobiology, which promises to become the ultimate testing ground for his thought experiment.

The difference has been well synthetized by Vermeij in his recent challenge to Gould's contingency thesis.

> If history flows from singularities, the unique "frozen accidents" of Kauffman and Crick, then all events, interactions, players, and outcomes subsequent to the unique initial state are likewise unreplicable, meaning that we should expect life's properties and deployment elsewhere in the universe to be utterly unlike those on Earth. If, on the other hand, even very rare phenomena can be shown to be iterative and replicable, and if certain pathways and outcomes are strongly favored over others, then similar phenotypes and interactions of life should emerge wherever conditions suitable for life exist (Vermeij 2006, p. 1905).

Or, in the more colourful rhetoric of the exobiologist David Grinspoon:

> There is no way to predict precisely what aliens will look like, but the fractal geometry of life gives us reason to believe that when they do finally land on the White House lawn, whatever walks or slithers down the gangplank may look strangely familiar (A. Grinspoon 2003, p. 273).

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Interspecific Cultural Convergences (ICC) and Interspecific Cultural Studies (ICS): From the Only Human Towards a Comparative History of Animal Uses and Traditions

Marco Celentano

Predictability is a relational, historically and culturally shaped concept. A phenomenon can be defined as predictable in relation to the available knowledge, instruments and methods, as well as the epistemic horizons in which its explanation is located (E. Fox Keller 2002). From this point of view, the last hundred years in the field of comparative study of animal behaviours and minds have led to radical changes in our epistemic horizon by extending our understanding of what we have to consider predictable or unpredictable in animal behaviours. Indeed, this historical phase has seen the discovery of entire classes of phenomena related to the expression of animal thought, languages, societies and cultures, which in the preceding decades would have been considered *impossible* within relevant scientific areas as anthropology, comparative psychology, theoretical and moral philosophy, linguistic and cultural studies.

For instance, new sound analysis technologies developed over the last decades have allowed a decoding of bird songs that, pushing the limits of our sensory and cognitive channels, allowed us to appreciate its syntactic complexity and the richness of its intraspecific differentiations (cultural traditions), radically modifying our views. In the last ten years, the analysis of the cerebral structures of birds has also demonstrated the presence of areas for processing and decoding acoustic communication similar to those found in our central nervous system. The brain of parrots, corvides and sparrows has been shown to have a higher neuronal density than that of mammals, including primates. Higher is also the percentage of neurons that are part of the brain areas destined to the so-called "superior functions" as the bark in mammals and the *Pallium* in birds. A research directed by Clifton W. Ragsdale, of the University of Chicago, has recently confirmed a close affinity between the mammal neocortex and the birds' DVR, or ventricular backbone (J. Dugas-Ford, J.J. Rowell, C.W. Ragsdale 2012). In the last fifty years, the use of microphones suitable for recording in the deep sea, and the computerized analysis of sounds, made us begin to understand the complexity of whale songs, or the amazing analogies of the dolphins' whistling with human names. In the same span of time, progress in the techniques of brain analysis has shown that the cetacean's paralimbic system makes possible a very rapid integration of perceptions and a richness of information which is considered superior to the human one, and that cetacean such as humpback whales and dolphins have brains with even more cortical convolutions than humans (R. D. Fields 2008).

These developments open up new perspectives, making it necessary to overcome, both in scientific training and in research, classical dichotomies such as nature/culture, Natural Sciences/Humanities. They integrate the horizon of the foreseeable, including the expectation of a gradual extension of the class of organisms that we should recognize as "cultural animals", as well as of the phenomena to which this chapter is devoted: the cases of Cultural Convergent Evolution between different species.

From the discovery of animal cultures to the approach of contemporary philosophy of ethology

In the second half of the 20th century the developments of ethology led to one of the most revolutionary discoveries of contemporary science: the existence of animal cultures[1]. It falsified, or empirically refuted, one of the fundamental assumptions of our philosophical and scientific tradition: man as the only "cultural animal". Therefore, it questioned *the very partition of science in Humanities*, conceived as the sciences of culture, *and Natural Sciences*.

Two field studies, which became known to the scientific community in the mid-1960s, prompted this discovery. The first, directed by J. Itani, S. Kawamura and M. Kawai, disciples of the Japanese ethologist K. Imanishi, began in 1948 on the island of Koshima, where a community of macaques (*Macacafuscata*) lived then and still does today. The second, promoted by Louis Leakey, the most authoritative anthropologist of the time, began in 1960 and was carried on by J. Goodall, who was the first scholar to study

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[1] Ethologists broadly agree nowadays on a trans-specific notion of "culture" that implies, as its necessary and sufficient conditions, the existence of systems of transmission of experiences and uses to other individuals and generations, through learning/teaching processes (F. de Waal 2001, p. 11; D. Martinelli 2011, p. 230).

the behaviour of chimpanzees in their natural environment, in the Gombe Stream Chimpanzee Reserve, in Tanzania.

The observation of macaques made Satsue Mito, an inhabitant aide to the three ethologists, the first human witness to the birth of a tradition within a community of non-human animals (de Waal 2001, pp. 179-211) in 1953. The Western scientific community became aware of this discovery in 1965, when Kaway published a paper on the scientific magazine *Primates* (M. Kaway 1965). Meanwhile, in 1960, Jane Goodall had begun studying the chimpanzees at the Gombe Stream Chimpanzee Reserve[2]. She was the first scholar to discover important aspects of the social life and material culture, and of the emotional and cognitive behaviour, of chimpanzees: their ability to build wooden tools and exploit them to obtain food; the techniques used to open coconuts by choosing, carrying and using different stones in the form of anvils and hammers; the existence of cultural differences between groups; the complexity of their social structures and the differences in sensitivity, intelligence, character and preferences in every single individual.

In the 1960s another sub-field of ethological research began to contribute to the birth of cultural ethology: the study of communicative systems in singing birds. It led to the discovery of the existence of "dialects", which are regional and macro-regional differentiations of the songs within a same species. Marler and Tamura, pioneers of this turn, already in the early 1960s discussed «the Song Dialects» (P. Marler and M. Tamura 1962) and «culturally transmitted patterns of vocal behavior» in sparrows (P. Marler and M. Tamura 1964).

The debate on the philosophical and scientific consequences of such discoveries began to develop in the 1970s and intertwined with the discussions on animal minds aroused from some comparative psychologists who studied the ability of higher primates to learn man-made languages as the ASL (R. Fouts 1997; F. Patterson 1999; H.L. Miles 1994) or other techniques of interactive use of human lemmas or symbols (D. Premack 1986; S. Savage Rumbaugh 1977), to recognize themselves in the mirror (G. Gallup 1970; D.J. Povinelli 1987), to solve cognitive problems (de Waal 2016).

Despite their methodology, based on observations in captivity and on anthropocentric assumptions which equated the intelligence of other animals to their ability to acquire and use human language or tools, these experiments

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[2] The site, thanks to Goodall's efforts, has become a protected area since 1968.

opened up a window on a new territory: the translation of thought and experience of other animals, like apes and later parrots (D.K. Patterson and I. Pepperberg 1994), in human languages.

Between the '90s and the next decade a both anti-determinist and anti-anthropocentric oriented *philosophy of ethology* emerged, intersecting with the rising *Animal Studies*. Books like *Visions of Caliban* (D. Peterson and J. Goodall 1993) and *Species of Mind* (C. Allen and M. Bekoff 1997) gave a first significant boost in this direction. Then, philosophers of ethology and zoo-anthropologists as Marchesini (1999), Lestel (2001), de Waal (2001), Wolf (2003), Despret (2004), Martinelli (2007) contributed to set the comparative study of animal minds, cultures and societies on new both post-mechanistic and post-idealistic bases (M. Celentano 2000).

Ethno-ethology and Interspecific Cultural Studies

According to the approach of the contemporary philosophy of ethology, the discovery of animal thought and cultures required an overcoming of the division between Life Science and Humanities, as well as the development of a meta-disciplinary area able to combine biological, ethological and ecological skills with the methods of the modern comparative cultural studies.

This approach, that I will call hereafter *Interspecific Cultural Studies,* is oriented to a comparative study of cultural traditions, uses, expressions and developments that include not just the human, but *all the known and knowable animal cultures*. It can be consolidated only through a reallocation of cultural studies within an inter-specific perspective. To this aim, it is necessary to dispose of traditional mechanist and dualistic Cartesian models, but also of the "psycho-hydraulic" model of classical and early cognitive ethology (R. Marchesini 2016), as well as of the gene-centric "classical sociobiology" (De Waal 2001), and of the deterministic approach dominant in evolutionary psychology (P. Lieberman 2013). The main tasks of *Interspecific Cultural Studies* will be the following:

To upturn traditional forms of human self-representation, and pave the way to post-anthropocentric forms of self-understanding, in which man is *only one of* the cultural animals, and to consequently re-found methodologies, epistemological references, and narrative background of the cultural studies with a post-anthropocentric and inter-specific setting.

To refocus ethology and behavioural science on a post-gene-centric, post-deterministic, and post-mechanist approach, which considers all the organisms, not only as products of an external selection, but also as selective agents, whose explorative activities are part of the driving forces of evolution trough their cognitive and behaviour.

To form new generations of teachers and scholars equipped to compare human and non-human cultures and societies without falling into the traditional opposition between anthropomorphism and anthropodenial;

To collectively construct, through researches, comparisons and debates, a meta-disciplinary lexicon capable of attributing to concepts such as “culture”, “traditions”, “invention”, or “singing” meanings usable in reference not only to a human, but also to a non-human context;

To critically reframe the (chronologically) short history of human cultures into the big history of animal experiences, traditions and cultures which is hundreds of millions of years long.

These tenets appear to reflect the actual trend of ethology at large. Contemporary ethology, assimilating approaches and methodologies already in use in the ethnological field, is increasingly shaping itself as «animal ethnography» (D. Lestel 2006). «The convergence between ethology and ethnography has significantly transformed studies of animal subjectivity and culture» and the future of both fields lies, according to Lestel, «in a cultural zoology that treats animals as subjects partaking in culture» (Lestel 2006, p. 147). These developments have led to the birth of a new interdisciplinary field of research, ethno-ethology, which «can be described as a discipline that studies the dynamics of agents which combine actions and interpretations in an ecological, historical and individual perspective». It is «an ethnography of the way the individual beings perceive and conceive, in the course of their interactions, the behaviors of other living beings and the way they react to these behaviors» (D. Lestel, F. Brunois, F. Gaunet 2006, pp. 166-167). The etho-ethnologic approach aims at a comparative study of animal behaviours, minds, and cultures which considers each animal as «a coherent agent that interprets significations in a homogenous manner […] and attempts to understand it in a historical (which calls on a temporal dimension) and social (an agent always acts in coordination with other agents) perspective» (*ibidem*). This approach implies the adoption of procedures and methods that allow distinguishing each individual as such, within an observed group, and each observable local or regional intraspecific difference in the populations belonging to the same species.

Behaviour as a self-regulative interaction and a driving force of evolution

In the perspective of contemporary ethology, behaviour is framed as *a self-regulative* and *cognitive interaction* of organisms with their inter- and intra-specific environment body. "Self-regulative activity and interaction" means that all organisms, of every species, need at any time to maintain or restore internal processes and physiological states which allow them to stay alive, and perform this function through explorative and energy trading activities, absorbing and transforming matter and energy present in the external environment, and modifying both the latter and themselves.

What does "cognitive" mean here? In the perspective of contemporary ethology, we can call "cognitive" all the activities through which organisms explore their survival chances and test their ability to actively change their physiological and/or perceptual states. Each "cognitive" activity is in this sense *a production of behavioural forms*, or of *self-regulative internal and external interactions*, enabling the performance of the organism's life cycle. In this perspective, cognitive activities are not a prerogative of animals, but of all organisms, because the simple fact that organisms are able to survive constitutes evidence of their ability *to make an object of knowledge out of their own living conditions* (K. Lorenz 1977; R. Riedl 1980; M. Celentano 2000, 2017).

These self-regulating and cognitive activities are obviously channelled and limited through the constraints imposed by the anatomy and morphology of the species, of the intra-specific and inter-specific context, and of individual characteristics and contingencies. Nonetheless, framing behaviour in such terms allows us to understand both the history of each existed and existing species and group, and the history of each body as an active and selective exploration of the environment, and an active construction of the respective ecological and social niche.

This post-mechanical conception of behaviour has assumed, since the '90s, a relevant role in the renewal of models of evolutionary biology derived from the developments of epigenetics and from the introduction of the evo-devo perspective.

Two notions in particular, previously introduced by two scholars of the 20th century, C.H. Waddington and J. Piaget, began to find consensus and corroboration from experimental findings, and to take relevance in evolutionary studies: the notion of «behavior as motor of evolution» (J. Piaget 1976), and of *non-genetic hereditary systems* – nowadays called *Epigenetic Inheritance Systems* (E. Jablonka and M. Lamb 2005) –, able to produce phenotypic modifications much faster than genetic mutations (C.H. Waddington 1975; Piaget 1976).

What does it mean in this new context that behaviour is a "motor of evolution"?

To conceive behaviour as a driving force of the differentiation of organisms means that individuals, populations and species, when they encounter environmental changes that endanger their survival or offer them new growth opportunities, do not passively wait for a favourable genetic mutation that allows some of them to overcome those new obstacles or exploit those new resources. Organisms, in the face of any change, engage all the innate and/or learned cognitive and physiologic resources they possess, to take advantage of the new conditions. Under this perspective, evolutionary divergences start from the sphere of behaviours, from changes in the ethological attitudes, which are active responses to changes in the environmental, social or individual context. Significant genetic mutations, on the contrary, appear only rarely as self-sufficient causes of evolutionary change.

During the last decade, promising research developments made increasingly evident the close correlation between EIS (Epigenetic Inheritance Systems) and BIS (Behavioural Inheritance Systems), leading to the birth of two new interdisciplinary field of inquiry: "behavioural epigenetics" (E. Jablonka 2006, 2013; F.A. Champagne and E.F. Rissman 2011; I. Tavory, S. Ginsburg, E. Jablonka 2012) and "cultural epigenetics" which include «the investigation of the role of behavior in shaping developmental-epigenetic states and the reciprocal role of epigenetic factors and mechanisms in shaping behavior» (E. Jablonka 2017, p. 42).

Interspecific Cultural Convergences (ICC) or cases of Convergent Cultural Evolution (CCE)

In ethology, as in morphology, the cases in which, during phylogeny, different species have developed similar structural and/or functional traits that are not inherited from common ancestors are called *convergent evolutions*, *evolutionary convergences*, or simply *convergences* (A. Heymer 1977, p. 74; D. Mainardi 1992, pp. 221-222). A typical example is the wings in flying insects, bats and birds. I propose to extend the concept of *evolutionary convergence* to the phenomena inherent in *cultural evolution*, defining:
As *Cultural Convergences* or *Cultural Convergent Evolution* (CCE) all (and exclusively) the cases in which it is historically proven that a technique, an invention, a discovery or a use has been developed by different cultures and populations in reciprocal independence[3];
As *Interspecific Cultural Convergences* (ICC) all (and only) the cases in which cultural convergences occur not only between populations of the same species, but also between *societies and traditions of different species*.

The concept of CCE so intended presents some differences from that of "convergent evolution" traditionally adopted in the evolutionary studies. «In the bio-ecological world the term convergence is used in reference to morphological, physiological, ecological and behavioral characteristics exhibited in an indipendent way by individuals belonging to different species» (G. Pigozzi 1992, p. 221) united by the fact of colonizing «environments characterized by relatively similar ecological conditions» (*ibidem*). However, cases of CCE can also occur among species living in very *different* environments.

The case of singing is emblematic in this regard: from a taxonomic point of view, singing is a phenomenon widespread in very distant and different animal clades. It appears in species genetically, phylogenetically and ecologically as different from one another as cetaceans, monkeys as Hylobatidae, Tarsius, Indri and Callicebus, in all the human cultures spread over the planet, the mice, and thousands of species of singing birds (M. Celentano 2016).

The fact that singing is developed in species so distant from each other means that this convergence cannot be explained on the basis of "homologies", understood as characteristics inherited by common ancestor. The ances-

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[3] This concept of CCE should not be confused with that of "Convergence Culture", recently introduced by H. Jenkins (2006), which refers to the effects of interactions between the traditional and the new digital media.

tors common to birds and mammals did not sing, as well as those common to insects and birds did not have wings.

The diffusion of singing in so different clades and environments is the result of mutually independent, but in some aspects similar, evolutionary processes and selective pressures. It can be adequately understood only by identifying and comparing the *functions* that this kind of expression plays, and the *forms* it has assumed in all these animal societies, just as it is normally done in the comparison of the human singing traditions and performances. This approach can be extended to all the fields of the ICC.

The cataloguing of CCE cases and the research on the causes of these evolutionary convergences are still at an early stage. To deepen our knowledge of such phenomena we will need to integrate the methodologies of comparative study of customs and practices, communication systems and expressive forms, social regulation devices and material techniques, as developed by the Humanities, with the observation and intra- and inter-specific comparison methods of contemporary ethology. We also need to construct open databases to set a methodical comparison between products, forms and intra-specific differentiations of all the animal cultures.

I would like to conclude this section by proposing, in Figures 1 and 2, a first provisional mapping of the most common cases of ICC, or CCE, and of the factors that may have contributed to their genesis. It is of course only a first sketch that, with the contributions of other scholars, will be widened and further articulated.

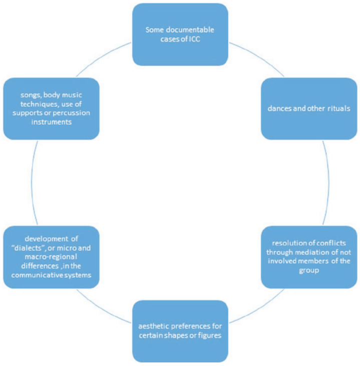

Figure 1. most common cases of ICC or CCE

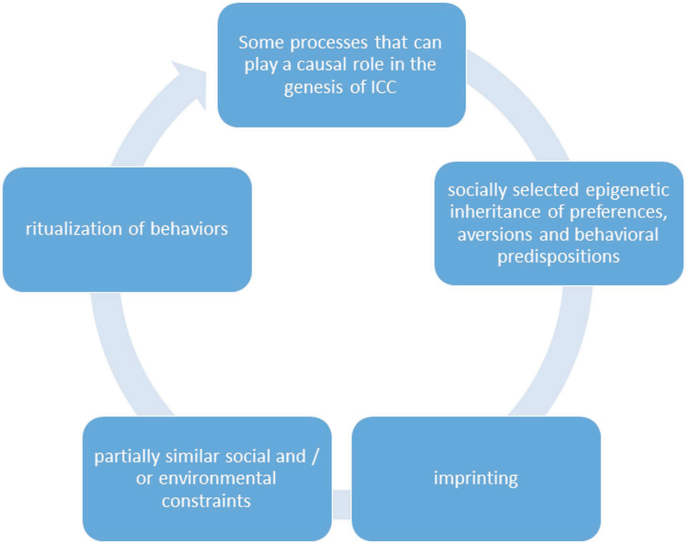

Figure 2. Factors that may contribute to ICC or CCE

CCE: the case of singing

In this final section I will illustrate the biological and social functions performed by singing in different animal species, and some converging aspects they present. I will borrow the method from a somewhat unorthodox source, the traveller, ethnologist and writer B. Chatwin. I will in fact start by comparing the functions of animal songs highlighted by ethologists with the ones that Chatwin ascribed to the «songs of the ancestors» of Australian Aborigines (B. Chatwin 1987). In fact, although some biologically and socially important features of these songs, such as courtship, are not reflected in his descriptions[4], Chatwin's analysis illuminates in a surprising way some characters and uses of songs which can be found also in other animal communities.

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[4] Chatwin privileges, within a rich set of local songs, only a few. He did not aim at an exhaustive cataloging of native songs, yet the existence of courtship serenades in aboriginal traditions is attested by other authors (D. Lockwood 1962; G. Englaro 1998; T. Gioia 2015).

Chatwin ascribes to the Australian songs of ancestors three different functions:

1. Totemic memories of the clan and documents for individual recognition. The songs tell of the familiar and mythical roots from which an individual comes, and thus allow the identification of each member of the group through his affiliation with his "totemic" ancestors (Chatwin 1987, pp. 4, 12-13)[5].
2. Melodic and vocal maps of a territory, travel guides for migration and occasional or cyclical displacements, providing information about territorial features and boundaries that cannot be crossed without risk (Chatwin 1987, pp. 13, 14, 69, 134-135).
3. "Pass": sound attestations that allow to recognize a person as «the owner of that path»; they feature as documents transmitted by cultural inheritance, in order to identify who has the right of transit in a given territory and the right to give or deny to others the transit permission (Chatwin 1987, pp. 14, 70).

It is possible to find equivalents of these three functions in the songs of other species?

1. Songs as individual recognition "documents", informing on the geographical and family roots from which an individual comes, allowing mutual recognition among members of a group or colony.

At the end of the 1950s, J.S. Weeden and J.B. Falls (1959) interpreted some duets between male birds in neighbouring territories as exchanges aimed at making acquaintance, and P. Marler (1960) suggested that melodies of birds could provide information for individual identification. A decade later, two studies conducted in different areas (W.L. Thompson and J. O'Hara Rice 1970; S.T. Emlen 1971), documented this functioning in the song of the male of *Passerina Cyanea*. In fact, in case of a sound intrusion of new neighbours, males modified their singing by adding to the specific sequence of their species some individually differentiated final parts. The songs of all the members of the group were so marked by a different ending. Further studies have shown that there are intermediate layers between the songs of a species and its individual variations. According to F. Feekes (1977), the *Cac-*

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[5] Similar cases of anthroponymic functions of songs are reported by other scholars concerning Australian populations such as Warramunga (R. Bosi 1994, p. 116) and Aranda (Bosi 1994, pp. 95-96).

icuscela emits colony-specific songs that have the function of a colony password and similar functions are found (E.D. Bailey and J.A. Baker 1982) in Virginia quail (*Colinusvirginianus*). Marler and Tamura (1962, 1964), W. Thorphe (1961, 1972), W. Wickler (1988) and many others contributed to the discovery of local and regional dialects. The existence of this «micro-geographic (or local dialects) and macro-geographic differences (regional dialects)» (D. Martinelli 2011, p. 238) was also found in the communicative systems of other animals and it is now regarded as a phenomenon widespread in mammals and birds. For example, studying the songs of the *Batismolitor* in nine different regions of East Africa, ethologists and zoo-musicologists found two kinds of dialectal variations: the presence of a sequence of three descending sounds or of longer sequential sequences, and differences in the order of the three base sounds, in which the middle height may be in the second or third position (Wickler 1988, pp. 76-77).

In many cases, the development of local song traditions is a prerequisite for the invention of personal songs and for their use for identifying individuals and reinforcing parental or couple ties. We find an interesting example thereof in the African *Lanariusaethiopicus major*: Here, the members of a pair learn to perform duets with one another and, while adopting certain phrases and rhythms which are characteristic of the locality, work out between themselves the duets which are sufficiently individualistic to enable the bird to distinguish and keep contact with its mate by singing duets with it – or, to be more exact, singing antiphonally with it – in the dense vegetation in which they usually live (Thorphe 1972, pp. 160–61).

These performances of Ethiopian shrikes revealed, in later studies, more complex interactions which include a dozen of different pair duets, and many duets between competing males and/or neighbours, both divisible, from a formal point of view, into two subgroups: unisons and antiphonal duets. The latter, in the case of male territorial duets, are, in turn, divided into exchanges of identical notes and varied exchanges. There are also cases in which an individual sings by issuing two different voices at the same time and cases where individuals who lost their companion, using this technique, run alone the sequence they used to do together (T. Harris 2000). Finally, there is evidence of the simultaneous running of two different types of duet, one of courting or strengthening the couple's tie, the other as a sort of duet/duel with a rival (Wickler 1988, p. 33). Instances of songs that mix different dialects are also documented (Wickler 1988, p. 43).

2. Songs like melodic and sung maps of the territory, guides for migrations and occasional or cyclical displacements, which transmit information about resources and dangers and on "borders" that cannot be trespassed without risk.

The cases of the Lira bird (*Menuranovaehollandiae*), who includes in its own repertory environmental and animal sounds collected from the surrounding territory, thus offering an acoustic mapping of it (A.H. Dalziell and R.D. Magrath 2012), and that of the Australian magpie which exchanges information on food sources and migratory routes whit conspecifics through songs (L.J. Rogers and G. Kaplan 1998, p. 86) are well known. Well-documented is also the use of vocalizations with information and referential functions in birds such as the northern royal gull (*Larusargentatus*), or the *Indicator indicator*, that uses the song to locate food resources.

With regard to whales, R. Payne was the first to hypothesize that «the humpbacks use their songs a bit like Australian aborigines, whose songs contain descriptions of the road and the points where you are and tell about the characteristics of the scenery you are in» (R. Payne 1995, p. 165). In turn, Martinelli observed that «migratory species of cetaceans use songs as geographic maps, in a way that cannot help but think of Chatwin's songs» (Martinelli 2011, p. 163). Stimpert, Peavey, Friedlaender, and Nowacek (A.K. Stympert *et al.* 2012), conducting a study on ten male individuals of megattera provided with multisensors that allow deep recordings have reinforced this hypothesis. Their research led to the conclusion that the choir repertory of *Megapteran ovaeangliae*'s male does not include only courtship songs and does not only appear in the breeding season. In the vicinity of the migratory season, the individuals they observed were leaving for food, and using songs that were significantly different from those of courtship, to communicate remotely.

3. Songs as "pass" that allow to recognize an individual as "path owner": a person who has "right" of transit on that path, can enjoy the resources that it offers, and can grant or deny to others the transit to such resources.

The words "right" and "owner" that Chatwin chooses to describe this use of songs, and the reference to bargaining practices that take place through songs exchanges, would seem at first glance to preclude a comparisons with non human cultures. However, we are here facing notions of "right" and "property" very different from those used for humans. In fact, they do not sanction the fixed property of a territory, and do not permanently interrupt the other's right of access or of usufruct of its products. They only attest that someone has the privilege of crossing it, practicing hunting, gathering or exchanging without being attacked, and receiving help when needed during this crossing. Sticking to this definition, this type of use of songs presents remarkable analogies with the "territorial" delimitation function that ethologists have found in the song of adult males of many of the singing birds. But, in order to determine whether we can detect analogies or convergences with this use of songs in other animal species, it is necessary to first ascertain whether other animals can, through variations in the intensity intense gradients or formal differentiations of their singing, not only signal the presence of a male x in a territory y, but also send a generic messages of transit prohibition or permit. We should therefore ascertain:

Whether resident male responses depend or not on the ability/inability of the intruder to be individually recognized through its song;
Whether or not we can find any differences in the songs that the resident male performs in presence of intruders depending on their being unknown individuals, new entries, or long-term frequentations;
Whether actual adjustments and bargaining occur between these animals through singing or not.

Recent observations indicate that generally both the bird that enters the territory of another and the one already located in it may adopt various communication strategies that reduce or intensify aggressive reactions. These choices are manifested by variations in the form and intensity of the song, or through options that consist in overlapping or not on the other's emissions. Recently, a study titled *The Social Interaction of Song in Song Sparrows* introduced the concept of «acoustic ownership marker» (J.M. BURT and M.D. BEECHER 2008). The study shows that the songs of resident males can perform the function of deterrent to many varying degrees of intensity, some of which seem to include the possibility of resolving controversies caused by small boundaries trespasses between neighbours without any physical clashes, only through exchange of songs. According to the authors, these interactions appear like a continuous strategic game of escalation and/or de-escalation of aggressive elements driven by different parameters such as overlapping or not of songs, and the repetition or variation of the verse performed. Different dynamics characterize the exchange of songs between «first-year neighbours» and «neighbours of long time» (*ibidem*). The authors suggest that the use of a kind of "conventional matching", which gives rise to an agreement on repertoires that can be paired or alternated (Burt and Beecher 2008, p. 89), can be attested between long time neighbours.

Territorial defence and recognition of the con-specifics that occurs through the exchange of songs are closely linked to the last group of biosocial functions of singing we have mentioned: those related to courtship, mating, and strengthening of the couple's bond. The study on this kind of song functions has been conducted on two main groups: singing birds (P. Marler and H. Slabbekoorn 2004, pp. 39-78; M. Naguib and K. Riebel 2014) and mysticeti (Payne 1995; R. Suzuki, J. Buck, P. Tyack 2006). More recently, more model species have been added. For example, individual differences and local dialects have been identified in the male-female couple duets of the crested gibbon (T. Geissmann 2006, V. Thinh *et al.* 2011). The courtship vocalization of the mice, brought to frequencies that are audible and distinguishable by human ears, revealed melodic qualities comparable, for beauty and complexity, to those of the birds (Chabout *et al.* 2015).

Among the mysticeti, the species whose song has been more studied is *Megapteranovaeangliae*. R. Payne and S. McVay (1971) were the first to decode structures and functions of its songs. Thanks to their efforts, it has been ascertained that the males of humpback whale produce melodies that are differentiated by geographical area and are renewed year after year or, more drastically, in multi-year cycles. They have complex structures, composed by different parts or "themes", consisting of ascending and descending sounds, lasting between 20 and 30 minutes, and can be repeated several times. Recently, R. Suzuki, J. Buck and P. Tyack (2006), examining the songs of 16 male humpbacks and thanks to specially designed software, have analysed their basic structures. The algorithm has mathematically confirmed the hypothesis of Payne and McVay that humpback whales have their own syntax and their song, like human speech, is based on a hierarchical language, consisting of lengthy sound blocks with increasing complexity, inserted into each other as in a system of Chinese boxes. This syntactic system, in many respects analogous to human verbal language with its subdivisions in phonemes, phrases, words, propositions and periods, is actually found in an ever-increasing number of social mammals and birds. The same conclusions have led to the analysis of vocal languages of cetaceans such as dolphins and "killer whales", of mice, and especially of sparrows and other birds, such as the *Parus minor* (T.N. Suzuki, D. Whatcroft, M. Griesser 2016).

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On the Contingency of What Matters: Predictability and Evolutionary Ethics

ELEONORA SEVERINI

1. Introduction: could we predict what matters?

We are evolved creatures who are concerned about many things that we judge as mattering and, accordingly, we make evaluative judgements about what matters[1]. Which is the epistemic status of these judgements is a pivotal question in metaethics and, more precisely, in moral epistemology[2]. On a realist view, when we say that something matters, we are recognizing something as mattering; therefore, there are things in the world that matter insofar as they *necessarily* matter. On an antirealist view, on the other hand, when we say that something matters, we are expressing our concern about that something; therefore, things in the world matter insofar as they are the objects of our concern.

The present work aims at analyzing how evolutionism may contribute to the debate between realism and antirealism in moral epistemology. More precisely, which are the consequences of evolutionism for the epistemic status of our evaluative judgements about what matters will be investigated, and whether predictability may play a role in evolutionary ethics will be assessed. In such a cross-disciplinary and normative field as evolutionary ethics, predictability acquires some peculiar features, and thus it has to be understood in a slightly different way than in the biosciences. More precisely, in the current debate, predictability has been mainly understood as a crucial notion for the descriptive tasks of evolutionary ethics, e.g. to develop evolutionary explanations for moral behavior or adequate accounts for the functioning of moral mind.

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[1] I would like to thank Eugenio Lecaldano for his helpful comments to a previous draft of this work.

[2] On the relation between metaethics and moral epistemology, see M. TIMMONS 1998 who distinguishes metaethics from other forms of inquiry into morality (i.e. normative ethics) and moral epistemology from other areas of metaethics (i.e. from its semantic and ontological components).

Contrary to that, it is argued here, predictability can be relevant not only for the descriptive components of evolutionary ethics but also for the claim of normativity itself. To make this point clearer: (1) normative claims and (2) descriptive claims have to be distinguished; thus, (1) I can predict what matters (e.g., I must keep my promises) (2) whatever I later do (e.g., I don't keep my promise to Rosa). Let us assume that I am a free agent, i.e. the author of actions which I could have chosen to perform differently[3]. In spite of this variety of actions, on a realist view what matters is just what necessarily matters. If what matters is just what necessarily matters, one could argue that we are able to predict what matters. Therefore, the question as to whether we could predict what matters, depends on a more fundamental question: does anything necessarily matter? Moral realists, such as Parfit and Scanlon, answer "yes", while antirealists, such as Street and Lecaldano, answer "no".

In what follows I will try to compare precisely realists and antirealists approaches on normativity. More precisely, I will investigate whether realists are able to secure normativity in the face of evolutionism. Firstly (§2), why evolutionism – and in particular its contingent nature – represents a challenge for normative realism will be clarified and Parfit's realist position illustrated. Then (§3), I will present some antirealist positions (i.e. Street and Lecaldano's view on normativity) which constitute alternative strategies to Parfit; in particular, I will assess whether those strategies are able to avoid normative realism without embracing nihilism. Finally (§4), I will take into account a last realist argument, according to which there is still room for a realist conception of normativity in an evolutionary framework, insofar as certain normative beliefs cannot be accounted by the evolutionary explanation of our dispositions to judge things as mattering.

2. Does anything really matter?

Does anything really matter in the light of evolutionism? The answer depends both on what one means by "really", and on whether evolutionism is taken seriously. Firstly, these claims will be investigated separately; then, they will be joined and some consequences will be drawn.

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[3] Here, I will not dwell on the issue of "free will" and I take for granted that we are free agents insofar as we are responsible of our actions (on this, see T. O'Connor 2010).

2.1 Parfit and what really matters

In his seminal work, *On What Matters* (henceforth, OWM)[4], Derek Parfit argues that to matter has to be intended only in a robustly attitude-independent sense, according to which to matter is to necessarily matter[5]. In other words, according to Parfit, there are some independent irreducibly normative truths, such as truths about what matters, which are in no sense created by us. The concept of "normative truth" is strictly connected to the one of "reason", since normative truths are about what we have reason to believe or do. Thus, for instance, we recognize the truth of *p*, and *if p then q* gives us reason to believe that *q* or to act accordingly. «We are the animals», Parfit writes, «that can both understand and *respond* to reasons» (OWM I, p. 31). These reasons are purely normative and should be distinguished from any psychological account. It is hard to define the concept of a "non-psychological, purely normative reason". Although this question cannot be exhaustively addressed here, it might be useful to refer to Thomas Scanlon's words: «I will take the idea of a reason as primitive. Any attempt to explain what it is to be a reason for something seems to me to lead back to the same idea: a consideration that counts in favor of it. "Counts in favor how" one might ask. "By providing a reason for it" seems to be the only answer. So I will presuppose the idea of a reason […]». (T.M. Scanlon 1998, p. 17).

Reasons are elicited by some external facts; on the other hand, for their part, facts elicit reasons from us when such facts – following Scanlon – count in favor of our believing or acting in some way. It is precisely by understanding and responding to these reasons, that we can form true normative beliefs. We are rational insofar as we correctly respond to reasons. Conversely, according to Parfit, «[o]ur desires and acts are rational when, if our beliefs were true, we would have sufficient reasons to have these desires, and to act in these ways» (OWM I, p. 5). Obviously, Parfit acknowledges, not all normative beliefs are true; and whether our normative beliefs are true depends on the process through which we develop them. Some beliefs, indeed, are formed by an epistemically defective process, such as random thinking, wishful thinking, or hypnosis. In all these cases, learning that a belief was shaped

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[4] Parfit's OWM is made up of three massive volumes. Here, the texts that will be mainly analyzed are Volume I and Volume II (respectively, D. Parfit 2011a and 2011b).

[5] For a useful review and discussion of Parfit's metaethics, see F. Orsi 2013.

by an irrelevant factor, i.e. a factor that doesn't bear on the normative truth of the belief, can reduce or even remove the justification of such a belief (K. Vavova 2016).

2.2 Evolutionary contingency and the modal fragility of what matters

Recently, epistemological worries about normative beliefs have been pressed in the form of arguments relying on evolutionary facts. According to this line of reasoning[6], normative beliefs are the result of the evolutionary process, and given that evolution is a "blind" process insofar as it is indifferent to whichever truth[7], being aware of the evolutionary origins of our normative beliefs can make them unjustified. Showing the justification of our normative beliefs is showing why they are true; moreover, showing the justification of our normative beliefs entails showing that «their truth is not an accident but is rather counterfactually robust» (M. Barkhausen 2016, p. 663). Contrary to this expectation, evolutionary considerations show that our normative beliefs covary with our evolutionary history; since our evolutionary history is independent from any alleged normative truth, the truth of our normative beliefs is not counterfactually robust at all. Therefore, if evolutionism is taken seriously, there are good reasons to think that, contrary to Parfit, our beliefs on what matters are the result of a contingent process, i.e. evolution (S. Oyama *et al.* 2001).

In his famous thought experiment of "replaying life's tape", Stephen Jay Gould claims that if we would press the rewind button of life and then run the tape again, the replay would be totally different from the actual one (S.J. Gould 1991). According to the evolutionary explanation of ethics, our normative beliefs are the result of the evolutionary process which is a contingent process insofar as it could easily have been different. These considerations

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[6] See S. Street 2006, R. Joyce 2006, P. Kitcher 2011.

[7] This blindness of the evolutionary process, i.e. the starting point of each of the skeptical position about normativity quoted above, has been clearly summarized by Stephen Stich, who states that: «natural selection does not care about truth, it cares only about reproductive success» (S. Stich 1990, p. 62). However, whether evolution "cares" or not about truth is a controversial question. I will not tackle this question here, but I just underline that the majority of those authors who maintain that there can be a relation between evolution and truth, are skeptics when it comes to extend such a relation to normative domains (see J.S. Wilkins and P.E. Griffiths 2013).

may be summarized by this counterfactual: if we had evolved under the same conditions as hive-bees, Charles Darwin speculated, «our unmarried females would […] think it a sacred duty to kill their brothers, and mothers would strive to kill their fertile daughters; and no one would think of interfering» (C. Darwin 1871, p. 73). In other words, had things gone differently in our evolutionary history, our normative beliefs would have been correspondingly different. This implies that we would disagree with our counterfactual selves on normative questions[8]: we actually believe that *p* thanks to our evolutionary history, while our counterfactual selves would believe that ¬p thanks to their evolutionary history. Thus, evolutionary considerations show the "modal fragility" of what matters and, more precisely, that there is a possible disagreement between *us-as-we-actually-evolved* and *us-as-we-easily-might-have-evolved* (T. Bogardus 2016). Moreover, given the epistemic symmetry between *us-as-we-actually-evolved* and *us-as-we-easily-might-have-evolved*, a full understanding of evolution teaches us that «we have no independent […] reason to believe that we are in a better epistemic position on moral questions than our many nearby counterfactual selves» (Bogardus 2016, p. 656).

Thus, from an evolutionary perspective, what matters is rooted in our evolutionary history, and it is a matter of pure contingency. Therefore, since what matters does not necessarily matter, it is not possible to predict what matters. Parfit believes that this is unacceptable, since to conclude that nothing really matters in his robust sense, is to conclude that nothing matters at all (OWM II, p. 267), i.e. that nihilism is the only viable route.

3. If nothing matters

The worry that the theory of evolution and nihilism may go hand in hand is far from new (see S. Stewart-Williams 2010). The main idea underlying this worry is that «if we are the products of blind natural selection, then morality and value are merely reflections of our subjective attitudes, and that in that case everything is permitted and *nothing matters*» (G. Kahane 2011, p.

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[8] The phenomenon of moral disagreement has traditionally been taken to entail that realist approaches on normativity are false (J.L. Mackie 1977). More recently, some authors (e.g. F. Tersman 2015, M. Klenk manuscript) have developed promising strategies to connect disagreement and evolutionary considerations.

103, emphasis mine). That the theory of evolution implies skepticism about normativity, can be summarized as follows:

(Premise 1): Nothing matters unless it necessarily matters (see §2.1).
(Premise 2): According to evolutionary considerations, nothing matters in a necessary way (see §2.2).
(Conclusion): Therefore, nothing matters.

Premise 1 is precisely the core idea of Parfit's realism about normativity. Now, if we think that Premise 2 is correct and, at the same time, that the Conclusion (i.e. that nothing matters) is implausible, then what we have to reject is Premise 1, i.e. Parfit's core claim. In other words, we have to show that that evolutionary considerations point out that nothing matters in Parfit's realist sense, does not necessarily amount to say that nothing matters and, moreover, that there is no room to rethink what matters. The attempt to develop an alternative account of what matters has been undertaken, for instance, by Street and Lecaldano. Indeed, they both maintain that it would be wrong to think that evolutionary considerations imply evaluative nihilism.

3.1 Street's response

The antirealist stance (*contra* Parfit) has been supported by Sharon Street. Street argues that the dichotomy between a bold realist account of what matters and nihilism is false. According to her, the evolutionary explanation of morality does not undermine normativity *tout court*, but only the realist conception of it. More precisely, Street writes: «I think that many things matter a very great deal. I just think, of the things that matter, that their mattering ultimately depends on their mattering to beings like us» (S. STREET 2017, p. 147). In other words, what Street upholds is precisely the denial of Premise 1, i.e. nothing matters unless it necessarily matters. Contrary to that, things may matter in a more modest way than the realist one, insofar as their mattering is stance-dependent. This amounts to say that «to matter is to matter from the point of view of someone» (STREET 2017, p. 121). Therefore, Street's view is a form of moral constructivism according to which: «[n]ormativity depends on the attitudes of beings who take things to matter, but that doesn't mean it doesn't exist» (STREET 2017, p. 121). Indeed, following a constructivist approach to normativity, practical reasons are grounded by the valuing attitudes of agents. And, for the constructivist, «there is nothing that must matter to us beyond what does matter to us» (D. Dorsey 2018, p. 576).

It should be noticed that the advantage of Street's position over Parfit's one consists in the fact that the former – unlike the latter – is perfectly consistent with the theory of evolution and, in particular, with its contingent nature (S. Street 2012). Indeed, the framework that Street has in mind is precisely the evolutionary one. Our evaluative attitudes are the results, among other things, of the evolutionary process. However, here, normative truths are not threatened by the fact that evolution is a contingent process. Street construes the evolutionary process to be prior to normative truths, insofar as, first, the evolutionary process caused our having such and such evaluative attitudes; second, those evaluative attitudes represent the starting fund from which we *construe* what matters. Therefore, according to Street, evolution and normative truths can be consistent with each other. To sum up, things are mattering ultimately because we are "normative animals" (N. Roughley forthcoming), not the other way around.

3.2 Lecaldano's response

In his recent book, *Sul senso della vita*, Eugenio Lecaldano (2016) analyses the topic of "what matters" with a special reference to the question of the meaning of life. Before going any further, it ought to be noted that Lecaldano's analysis starts from the recognition that the issue of the meaning of life is distinct, though not entirely independent, from the domain of ethics[9]. According to Lecaldano there can be lives which are highly meaningful although slightly immoral. This is, for instance, the well-known case of a somewhat fictionalized Gauguin[10], who abandons his wife and children to choose a life of painting in Tahiti: even though Gauguin's choice of life can certainly be questioned from a moral point of view, we cannot but recognize that such a life has been meaningful (Lecaldano 2016, p. 56). Therefore, if Lecaldano's arguments certainly discuss the topic of what matters, he does so in a different field than that of ethics which other authors (e.g. Street)

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[9] I am grateful to an anonymous referee for raising my attention to this point.

[10] This example has been first developed by B. Williams 1981.

fully refers to. However, such a distinction between the meaning of life and morality, though extremely significant and capable of notable implications[11], does not affect our argument. Indeed, for the purpose of this work, we can assume that there is an overlap between Lecaldano's quest for the meaning of life and Parfit's analysis about what matters, insofar as they both are dealing with evaluative normativity.

Given that premise, Lecaldano places the discussion about the meaning of life in an evolutionary framework[12]. According to Lecaldano, learning the evolutionary lesson and, then, becoming fully aware of the contingency which characterizes our lives, is the fundamental step to *really* understand what matters. Along this line of reasoning, what matters will be completely contingent; nevertheless, this contingency does not imply skepticism about what matters, but only skepticism about a realist conception of what matters (i.e. skepticism about Parfit's position). Moreover, what is important to stress is that, according to Lecaldano, only in an evolutionary perspective the question about what matters can have any sense. In other words, acknowledging that in our life there is still room for chance and contingency, is the basic condition for an autonomous search for what matters (Lecaldano 2016, pp. 97-98). This search has also to be an individual effort construed on a sentimentalist perspective, according to which the core of human life is made of affective states[13]. On a sentimentalist perspective[14], such as that developed by Lecaldano, emotions and desires play a leading role in the analysis of normativity, insofar as our emotions and desires are the primary source of what matters.

In this way, Lecaldano not only maintains that merely acknowledging that we possess a certain (normative) attitude, does not commit us to the view that there is some external thing (i.e., a normative reason) which corresponds to the attitude in question; but he also argues that the fact that there is no external normative reason is the fundamental precondition for something to matter at all. In this respect, Lecaldano goes beyond Street: if Street describes

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[11] For an interesting and more detailed discussion of this subject, see G. Pellegrino 2017.

[12] See especially Chapter 3.1, "Il contesto evoluzionistico: i valori in un mondo di cause contingenti" (Lecaldano 2016, pp. 95-101).

[13] Lecaldano's argument for an individual search of what matters, has been interestingly discussed and broadened by Botti who emphasizes the importance of the relationship with others in such a construction of what matters to us (see C. Botti 2017).

[14] Contemporary sentimentalism is rooted in the work of 18th Century philosophers as David Hume and Adam Smith. For a review, see A. Kauppinen 2017.

her antirealist view about what matters as a solution to avoid the nihilism that could be implied in the evolutionary explanation of life, Lecaldano, on the other hand, affirms that it is precisely the nihilism implied in the evolutionary explanation of life which makes possible that there is something mattering. In other words, according to Lecaldano, it is precisely the lack of any external normative truth which guarantees an authentic and personal reflection about what matters. We can *still* take into account, or we can take into account even *better*, what matters, by showing the fallacy of the thesis that if nothing matters in a realist sense, we are nothing but condemned to nihilism.

Thus, both Street and Lecaldano develop an antirealist perspective on normativity. Moreover, they both show that, even if evolutionary considerations imply an antirealist perspective on normativity, it is wrong to think that this perspective implies evaluative nihilism. The starting point of every antirealist view is precisely our existing normative attitudes; for this reason, in accounting for those attitudes, antirealist views should leave our first-order normative beliefs exactly as they are or, at least, be in continuity with those beliefs[15]. Therefore, even if we are the products of blind natural selection, and normativity is the result of our subjective attitudes (as, e.g., Street and Lecaldano claim), we are not forced to conclude that everything is permitted and nothing matters; on the contrary, we can embrace an antirealist perspective on normativity which is consistent with both the theory of evolution and our existing, first-order normative beliefs.

4. If something matters

In the light of this discussion, it seems that the realist, such as Parfit, cannot face the evolutionary challenge. Therefore, back to the starting question (i.e., “Does anything really matter in the light of evolutionism?”), it seems that we should conclude that, in the light of evolutionism, nothing matters

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[15] To make this point clearer, we can distinguish between first-order normative claims and second-order ones. A first-order normative belief is a belief about what we ought to do (e.g. the killing of animals for food is impermissible). A second-order, or metaethical, view is an account about the status of first-order normative beliefs (e.g., Can normative beliefs like “the killing of animals for food is impermissible” be true or false? Are they instead mere expressions of approval or disapproval?). Given that the present paper investigates the epistemic status of our beliefs about what matters, it deals only with second-order questions.

in a realist sense. So far, it has also been argued that the antirealist positions, such as those developed by Street or Lecaldano, result more convincing than the realist position, insofar as only the formers are able to give us an account of normativity which is consistent with the evolutionary explanation of our life and, in particular, of our normative attitudes. The realist, however, has a last option at her disposal. The theoretical gain of embracing an antirealist position consists, indeed, in the fact that the antirealist, unlike the realist, is able to find room for normativity within the evolutionary description of the natural world which we inhabit. Given that, what the realist can contest is precisely such an evolutionary description on which is based the antirealist account of normativity. This strategy is endorsed by Parfit, in his realist position, who argues that, if our normative beliefs were caused by evolutionary forces, «we would expect that we would have beliefs that were reproductively advantageous, by making it likely that we would have more descendants» (OWM II, p. 534). Contrary to that expectation, Parfit argues, we have many beliefs about what matters which are not "reproductively advantageous", therefore, not all of our normative beliefs are caused by evolutionary forces. Consider, for instance, the following case from environmental ethics: «One moral ideal that I share with many environmentalists is voluntary childlessness (or that, at most, people should have only one child). In almost every case acting on this principle is to act against one's own biological fitness. How could evolution have produced creatures who act in such a way?» (D. Jamieson 2002, pp. 323-324). A possible answer is that those beliefs, as the voluntary childlessness ideal, are relevant normative beliefs which are grasped through careful reflection and, more importantly, which are very likely not to be caused by evolutionary forces or other distorting processes. Along these lines, the realist may argue, that in the light of evolutionism, there is something that necessarily matters. More precisely, things mattering are those which are not caught by the evolutionary explanation and thus undermined by its contingent nature. In other words, there is something beyond evolution and that is what *really* matters.

Though interesting, this argument is flawed and thus fails in securing a realist conception of what matters in the face of evolutionism. This argument, indeed, relies on a crucial misunderstanding which is due to the fact that it presupposes an extremely rough evolutionary view. According to this rough view, the evolutionary process has to be ultimately explained in terms of its primary factor, i.e. natural selection, and its primary currency, i.e. biological fitness. Now, it is quite obvious that our intuitive idea of what matters cannot be accounted solely in terms of promoting biological fitness. However, this does not automatically mean that (1) there is something that evolution cannot explain, (2) nor that this evolutionary unexplainable something is what really matters, as I will try to explain in what follows.

As regards to argument (1), it should be noticed that we have to distinguish the task of explaining the existence of a certain phenomenon from the task of describing its content; moreover, we have to distinguish both of these tasks from yet another one, the one of justification. In this way, we have to distinguish the task of explaining why we judge some things as mattering from the task of pointing out which are the things that matter; both tasks, finally, do not amount to justify our normative beliefs about what matters. After having recognized these three different tasks, we need to clarify that evolutionism can contribute only to the first one: indeed, it can contribute to explain the existence of a phenomenon like normative judgements. Then, the evolutionary account can be understood just as explaining why our normative attitude evolved, but it cannot be construed as characterizing the content of our normative attitude, i.e. it cannot be construed as determining what matters. In addition, that a certain attitude has evolved cannot count as a justification, i.e. the evolutionary account cannot be construed as distinguishing what matters from what doesn't matter. Therefore, if evolution cannot determine the specific content of our normative beliefs, we should not expect, as Parfit claims, that such a content is necessarily "reproductively advantageous", and we should admit a certain variety regarding the contents of the beliefs that the normative attitude gives rise to. In this way, the normative pluralism that we might easily find across different cultures, ages or, simply, individuals, can be perfectly accounted for within evolutionary ethics.

As regards to argument (2), even admitting, for the sake of the argument, that there is something beyond evolution, the mere fact that this has not been caused by evolutionary forces is not enough to argue that it is what really matters. In other words, that a normative belief has not evolved through natural selection and then is not, strictly speaking, reproductively advantageous, cannot count as an evidence for the truth of such belief. Rather, a plausible account of what matters should be assessed against what science tells us about how human beings think and behave. This does not amount to purport a reductionist approach to the philosophical investigation on what matters; rather, it highlights the idea that a philosophical analysis on what matters cannot be undertaken without a reliable, empirical knowledge of human beings[16]. This is the so-called "principle of minimal psychological realism", according to which we should «[m]ake sure when [...] projecting a moral ideal that the character, decision processing, and behavior prescribed are possible, or are perceived to be possible, for creatures like us» (O. Flanagan 1991, p. 32). In this way, one may argue that those ideals which are allegedly not caused by evolutionary factors (e.g., absolute impartiality) are simply too demanding and, thus, unattainable by evolved creatures like us[17].

5. Conclusions: why plenty of things still matter

Does anything really matter in the light of evolutionism? The paper argued that the dichotomy between a bold realist account of what matters and nihilism is false. Indeed, the evolutionary explanation of our normative attitudes does not undermine normativity *tout court*, but the realist conception of it. The denial of realism can also be construed as the first, inescapable step for an autonomous construction of what matters to us. In other words, it is precisely the denial of realism, i.e. the denial of the claim that there is some normative reason external to us, that makes possible an autonomous and authentic search for what matters and, therefore, that makes possible that something could matter. Moreover, a better understanding of evolutionism seems to strengthen such an alternative framework for normativity than the realist one, and, more precisely, to push us toward a constructivist (e.g. Street) or sentimentalist (e.g. Lecaldano) approach to what matters. If we look at it from a more general and intersubjective point of view, we cannot but notice that the search for what matters takes the form of a normative pluralism. Therefore, in the light of evolutionism, though nothing really matters in Parfit's sense, plenty of *unpredictable* things still matter.

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[16] How the scientific understanding of human beings can improve our capacities for philosophical and ethical reflection, has been addressed by S. Pollo 2017.

[17] It should be stressed that this argument is only hypothetical, and it does not mean that I am admitting that there can be something outside evolution. As I argued (see argument 1), indeed, the only apparent plausibility of this statement relies on a misunderstood view about what evolution is able to tell us about our normative belief.

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Estimations, Plans, Narratives: How Non Human Animals Deal with Future and “Possible Worlds”

Dario Martinelli

Introduction

The relation between humanities and animal studies is becoming more and more relevant in current research. As Francesca Ferrando has correctly noticed, we entered in an age of “post-anthropocentrism”, which is «*post* to the concept of the human and to the historical occurrence of humanism, both based […] on hierarchical social constructs and humancentric assumptions» (F. Ferrando 2013, p. 29). However encouraging such overcoming sounds (at least in the posthumanist program, which is what Ferrando is talking about), many open questions and many challenges remain – and certainly there is a number of topics where the debate can get particularly heated, and the confrontation between the two parties rather controversial (that is, simply put, the party of those who maintain that plenty of animal studies have been affected and impaired by anthropocentric – when not speciesist – biases, versus the party of those who consider that “too generous” animal studies have been affected and impaired by anthropomorphic biases).

One of such topics is certainly the possibility of imagining and planning the future (or, more generally, to create “possible worlds”) – a trait that has often been considered humanly species-specific, when not even a “defining” trait of humankind – a claim that is probably due to the fact that possible worlds production is intrinsically tied with the notion of “language”, which, as we know, is the very topic where – half-ironically speaking – the scholarly “resistance” to post-anthropocentrism is at its most vigorous and belligerent.

Roughly summarizing the existing research on the topic, there seems to be a general agreement on three major common denominators, that is three (again, humanly-exclusive) characteristics of language that make possible worlds production possible. Considering the different terminologies (and methodological contexts) employed to define such denominators, I take the liberty to call them in my own way: a) *distant space-time semiosis*; b) *narrativeness* (as cognitive phenomenon, therefore slightly different from “narrativity"); and c) *linking signs*. Distant space-time semiosis refers to the ability to keep track, transmit and reconstruct both recent and remote past events and places, and to the ability to articulate projects and expectations regarding both immediate and remote places and future events (in a way not dissimilar to what Charles Hockett called "Displacement", in his famous "design features of language" formulation, C. Hockett 1960). Such ability is both direct and indirect, the former being related to the personal experience of the subject, and the latter referring to experiences that the subject has not lived or will hardly live personally. In other words, language allows human beings to talk not only about their childhood and about their intention to live in a country-house when they will finally retire from work, but also to discuss the defeat of Napoleon at Waterloo and to wonder about the day when Martians will finally land on Planet Earth.

Narrativeness refers not only to storytelling (which is still an important feature itself), but mostly to the general capacity of accessing and describing alien *Umwelten* (in Jakob von Uexküll's sense, of course), either imaginary or not. Regardless of whether these descriptions are trustworthy or not, what matters here is the fact that, in principle, any dialectic account of a given context, environment or reality is possible in the human semiosis. The descriptions of the *Umwelten* of both the species Peking Duck *Anas platyrhynchos*, and of the fictional character Donald Duck (inspired by the very same species) are possible only thanks to the existence of such a device like language.

Finally, linking signs (linking words, in particular, since we are talking about language) refer to a specific aspect within the broader concept of syntax, namely those signs that in verbal speech are known as conjunctions, transitions, and prepositions. Linking words are a form of para-signs that do not refer to any other existing entity apart from themselves, and whose function is to create meaningful relations among signs that, by contrast, stand for something else than only themselves. In other words, linking words are yet another confirmation of the capacity of language to create possible worlds, even when those "worlds", as in this case, are simply signs that are untied from tangible entities.

A recent and very good example of this approach (plus, a specifically semiotic one, which allows me to be in my natural element, as a scholar) is the concept of the "Semiotic Animal". I shall commence my argumentation by employing this notion as a point of departure to reach what I would call a "renegotiation" of the terms of this discussion into a theoretical perspective that attempts to avoid its most extreme anthropocentric biases.

On the notion of semiotic animal

Originally developed by Prof. John Deely in 1990[1], the concept of "semiotic animal" departs from the Peircean semio-philosophical tradition, which – within the semiotic paradigm – assumes the stand of "opening" semiotics to the multiple instances of non-human signification, communication and representation, «seeing cultural creation itself as a natural extension of the activities of the semiotic animal according to what is proper to it as part of nature» (J. Deely 2005, p. 26), and therefore fairly leaning towards Ferrando's "post-anthropocentrism". The notion was apparently conceived to overcome the human-animal dualism and create that continuity-discontinuity dialogue envisioned by Giorgio Prodi (G. Prodi 1983, p. 180). The very species-specific characteristic of human beings, Deely argues, is the capability of emancipating their semiosis from the constrictions of their own *Umwelt* and: a) access other organisms' *Umwelten* (also, but not only, at a purely speculative level), and b) create possible worlds, i.e., *Umwelten* that are distant in time, in space, or that are not even existing at all, but are created through language (there is no such a thing like Cyclops, yet *there is* such a thing like Cyclops, at the very moment at least one person linguistically produces a concept, or an idea, of them). Such abilities, Deely points out, do *not* make the human being *something else* than an animal, yet they establish the ground for human biological identity. The bottom line being (as Deely himself pointed out in 2009 during a plenary lecture at the Summer School of Semiotics in Imatra, which I had the pleasure to attend): the human beings, unlike other species, are *semiotic* animals, while non-human animals (NHA, from now on) it appears, are *semiosic* animals – with an *s*. And what chiefly distinguishes semiotic from semiosic cognition is the above-mentioned creation of "possible worlds" – a narratological expression that comprises numerous cognitive activities, future predictions, expectations and planning included. *Semiotic* are those animals that manage to create and access possible worlds, *semiosic* are those that cannot. Virtually, thus, one shall now need to divide semiotics into two sub-fields: the logocentric (or meta-logocentric) "semiotics", and the huge "semiosics", that is, a field that investigates all semiosic processes, except those that lead to the creation of possible worlds. Also, the upper level

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[1] That is, the first edition of J. Deely 2009, in this essay's bibliography. In the latter, we have of course a much more elaborated and updated treatise of the concept, with several questions that pertain specifically to the issue I am discussing in this article.

of the semiotic threshold should be considered as corresponding to the realm of abstract imagination (the one that, indeed, makes possible worlds cognitively possible, if the pun is allowed).

Or should it? Of course, this is not the end of the story: a crucial precondition to this form of imagination is the ability (this also attributed to humans only, in the "semiotic animal" formulation) of using signs and being aware that they are signs. Only with this *metasemiosis*, as Susan Petrilli (S. Petrilli 1998, p. 8) calls it, the human animal becomes aware that "there are signs", and that these signs can be detached from any association and manipulated to create endless new associations, including imaginary ones. It is metasemiosis that makes Cyclops (and unicorns, angels, gods, super-heroes…) possible, and that – indeed – creates what we may call a cognitive "ontology" of the future: this is how expressions like "One day I'll go to Australia", "Maybe it will rain tomorrow", "Monday I start dieting" logical and possible (though, in some cases, unlikely, as it is certainly the case with diets). All this, it is claimed, occurs only among humans.

The whole concept (and the line of reasoning behind it), legitimate as such, seems however to beg the question on at least two levels: the assumption (all to be proven) that such characteristics are exclusive of (human) language, and cannot be produced by other communication and/or modelling systems, and the consequent implication of human uniqueness in the cognitive production of the concepts of possible worlds and future in particular.

A few objections

As a first remark, in order to tie inevitably metasemiosis with possible worlds, one should assume that metasemiosis *only* produces possible worlds. Because, if it produces something else, then it is not just alien *Umwelten* that NHA are not able to access, but a lot more. Indeed, the awareness that "there are signs" is a precondition for a million of other cognitive abilities. Deception, play, symbolic representation, aesthetic semiosis, ritualization, interspecific communication… They all imply (simple or complex) forms of sign manipulation that are possible *only* by being aware that what is being used *is a sign*, and not the actual entity it refers to. There is no doubt, from the present state of animal studies, that NHA are unmistakably capable of all these behavioral patterns: there are differences, of course, across species (and it would be very interesting to finally discuss *those*, rather than posing the problem in a dualistic human-versus-animals way, but few seem to be interested in that).

Back to our topic, would it be right to assert that no animal except the human one is able to cognitively access alien *Umwelten*, particularly the imaginary/future ones? It is an interesting question, with several possible answers (which I have tackled already in D. Martinelli 2010, p. 153, and 2016, p. 47 – I mostly quote from these sources):

1) Following the logics of Peircean abduction, one could quickly state that "As the unavoidable precondition for possible worlds cognition is metasemiosis", and "As metasemiosisis an existing, empirically proven, cognitive condition in many NHA", then there are good reasons to think that many NHA are able to cognitively construct possible worlds. That is: language is not the only condition for metasemiosis. If metasemiosis is equaled with what we may call "possible worlds cognition", there is a *de facto* denial that the latter is produced exclusively by language. And, indeed, there are very good reasons to think so;

2) The concept itself of accessing alien *Umwelten* may be in fact a contradiction in principle. Taking von Uexküll's theories very faithfully, one shall deduce that if we, members of the *Umwelt* A, manage to cognitively access the *Umwelt* B, then we cannot really talk about different *Umwelten* anymore, because the occurrence of this very process would prove that the *Umwelt* B is simply part of the *Umwelt* A, therefore not "alien".

3) Even accepting the language's capacity to create strong dialectical, philosophical and possibly rhetorical configurations of alien *Umwelten*, it is important to remember that dialectics, philosophy and rhetoric do not provide *full* access to another *Umwelt*, even though they certainly allow some reflections and conclusions about it. This is an important point: too often we take for granted that we understand of other animals *all* that is to be understood. For example, we may understand, speculate and dissert about echolocation, but a complete, senso-motorial, psycho-physiological access to a process like echolocation (at least so far) is not possible, and that makes a huge difference (especially when we think of the dominant role that echolocation has in the semiosis of some species). We can *represent* echolocation, but we do not *have* echolocation;

4) Our ability to invent myths, tales and superheroes should not be pushed to the extent of founding a new definition of "human being" upon it, because all the imaginary entities produced by language are *not* untied to our perception. They might not exist, but they are a combination of (mostly visual) percep-

tion-bound elements (a horse plus a horn for a unicorn, a human female plus a fish for a mermaid, etc.).

We know from narratology (see at least G. Genette 1972; J.R. Searle 1975; J. Bruner 1986) that possible worlds are forms of a) *parasitism* and b) *limitation* of the real empirical world (meaning that a possible world presents a limited amount of events and context, as compared to the portion of reality it refers to, or borrows from). We know from logic (see at least D. Lewis 1986; P. Herrick 1999; J. Divers 2002) that their ontological status in relation to reality is not independent, and in particular their modal status completely relies on this relation (even the six propositions that emerge from Aristotelian logic – true, false, possible, contingent, necessary and impossible – are no less than hermeneutic variations applied on empirical reality). We finally know, since the early days of psychoanalysis (S. Freud 1899), that the "true" abstract imagination, i.e., dreams (those we cannot even logically reconstruct after waking up because they escape the cerebral centers for thinking activity, which indeed do not function during dreams), belongs to a realm, the unconscious, which is neither linguistic nor para/pseudo/proto/pre-linguistic: it has simply nothing to do with language, but with cerebral centers for sensorial and nervous activities[2].

5) Even when staying on this particular (perception-bound) case of abstract imagination (focusing only on the possible worlds constructed via linguistic rhetorical-narrative properties), we do not have elements to affirm that these features of human semiosis are *qualitatively* different from other animals. If many experiments in interspecific communication turned out to be a successful attempt to teach human language to other animals (see particularly the Washoe, Koko, Kanzi, Chantek and Alex programs), and if language belongs to the human *Umwelt*, then it follows automatically that those language-trained animals *did* access the human *Umwelt*, in fact they accessed what is commonly regarded as the quintessence of it. An extensive mastering of a powerful device as language, in the human sense, certainly allows a drastic *increase* of this type of semiosis, however, the outcomes of those experiments seriously call into question our exclusivity in this respect.

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[2] Incidentally, dreaming activity in NHA, in the neurological (non speculative) sense, has been already investigated, in various degrees of complexity (i.e., beyond the stereotype that cats simply dream of catching mice): interesting readings, in this respect, are: C. Smith 1995; A.G. Siapas and M.A. Wilson 1998; G.R. Poe *et al.* 2000, and K. Louie and M.A. Wilson 2001.

6) Not before apologizing with my fellow colleagues in humanities for the harshness of the following remark, I have to say that while semioticians and other humanists were busy *speculating* about alien *Umwelten* and possible worlds, a few scholars in natural sciences actually bothered to perform empirical research on these topics (or at least on topics that would allow us to speculate with more ground). We have works like R.W. Mitchell 2002, which presents (for better or for worse) a definition of imagination that is pre-linguistic and closely related to the idea of deception and play. There are studies like S.P. Correia *et al.* 2007, N.S. Clayton *et al.* 2003, N.J. Emery and N.S. Clayton 2008, N.J. Mulcahy and J. Call 2006, and C.R. Raby *et al.* 2007, on alternative future-scenarios in the cognition of species like jays and apes. Then, there are studies like M.P. Shanahan 2006 and M.P. Shanahan and B. Baars 2005, where it is argued that the neurological prerequisites for consciousness, emotion and imagination are typical of the mammalian brain. This model – it has been suggested – can be applied to other animals too (N.J. Emery and N.S. Clayton 2008, p. 135). And finally we have the above-mentioned studies on dreaming and unconscious activities (among those mentioned in the footnotes, I shall particularly single out those performed by the Wilson Lab at MIT, for their particular pertinence to this article's discussion – see for instance A.G. Siapas and M.A. Wilson 1998; K. Louie and M.A. Wilson 2001).

We are extremely far from semiotics or other humanities, here, but then again that is exactly the thesis defended here: when not empirically-grounded, the humanities have *not* the appropriate tools to investigate these issues: speculation is not enough, and most of all it is not fair.

Conclusions

Humanities are probably at their best when they "critically reflect upon" scientific findings, and put them in relation with social, cultural, anthropological and ethical aspects. Therefore, I believe that the only role humanities should take in issues like the one discussed in this article is that of producing reasonably not-too-speculative assessments that are *based on* and *informed by* the scientific findings (and relative gaps). Speculations for speculations' sake are not, to my mind, valuable contributions to the scientific community.

Let us take our case, once again. Part of the scientific gaps concerning the understanding of possible world cognition in NHA is due to an objective difficulty to study matters of this sort ("this sort" actually standing for cognition in general). Even with those NHA that seem to have successfully learned human language the assessment is difficult. It is known that some of them are often caught performing signs at random, for their own entertainment or in front of their trainers. If we proceeded speculatively, we could easily launch the hypothesis that some of those random signs are actually the result of their own imagination. Maybe Kanzi or Koko are accessing imaginary *Umwelten*, and even describing them to us. It sure sounds a ridiculous hypothesis, and maybe it is, but once we are in the field of speculation, all logically-acceptable hypotheses have a similar ontological status. Plus, by far, a hypothesis like this remains less ridiculous than the assumption that NHA do not possess metasemiosis.

Also, there are authoritative speculations on this subject. Jane Goodall, during her very long experience with chimpanzees in their habitat, described a group performance that she called a "rain dance", which may show indications that chimpanzees perceive natural phenomena in a mythical way (J. Goodall 1971, p. 54). Darwin, too, was convinced that traces of belief in supernatural and transcendental entities were present in other animals as well (C. Darwin 1871, pp. 67-68).

The hypothesis that only humans have this kind of imagination is constructed on two points chiefly: a) the fact that humans clearly have (and verbalize about) this ability; and b) the fact that no similar ability is "visible" in NHA. This, within a context of "fair" humanistic speculation, is not enough to allow the affirmation that NHA, *therefore*, are not capable of imagination.

This seems to be the main problem: in most cases, speculations of this sort are delivered without the support of solid knowledge on animal behavior. Finding "empirical evidence" does not necessarily mean that humanists have to design and perform an actual experiment to prove their theories. It would already be remarkable if they could at least base their reflections on the works of those scholars who did perform field work. In other words, speculation for speculation, one prefers to trust Goodall's or Darwin's reflections on NHA's spirituality, since they at least spent a life among NHA, so they may have a clue of what they talk about.

All in all, the lack of specific competences is the most puzzling aspect in this whole enterprise. Nearly every semiotician (or philosopher, linguist, anthropologist, etc.) sooner or later has a go at NHA and at the human qualitative difference with them, yet nearly nobody displays a specific training in animal studies that would entitle them to issue such important statements.

With few exceptions, essays on human uniqueness within the animal kingdom display a remarkable background on human knowledge, humanity and human behavior, and at the same time an impressively poor background on animal studies. They speak of what humans do and are and what other animals do not and are not, but they know only what humans do and are, and display no care in backing their assumptions on what other animals do not or are not[3].

Like a recent Frans De Waal's book title goes: *are we intelligent enough to know how smart animals are?*

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Abstracts

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Seinesgleichen geschieht: Contemporary Challenges to Evolutionary Contingency

"Things of the same kind happen again" in Robert Musil's Kakania. But even in biology, similar claims have been raised since the finding of an unexpected amount of repeated evolution: the evolution of "same" traits in distinct, and even quite distant lineages facing similar environmental conditions but strictly due to mutations in the same genes. Evolutionary biology may be on the verge of becoming a more predictive science than previously suspected. This claim reflects a deeply changed conceptual and biotechnological research framework, issued from the merging of comparative genomics, systems biology and experimental evolution. This new perspective undermines at least some of the implications of Stephen Jay Gould's well-known "evolutionary contingency thesis": firstly, that evolutionary explanations are doomed to be purely retrodictive, and, last but not least, that evolutionary conservation may not depend on "frozen accidents" but on specific systemic conditions that foster the "repeated innovation" (Vermeij 2006) of the same.

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{Synthesis| and Behaviour: a New Role for Selection

Grasping the action of natural selection is one of the most controversial topics of evolutionary biology. A key stage in the debate within the Synthetic Theory of the late 1950s was the attempt to integrate the role of behaviour

and development within evolution. This was also the aim of the Piagetian epistemological reflection on the «possible» since the late 1950s. In Piaget's view, the active role of the organism in a given context would entail an *intra-organic selection* able to regulate the interaction between the organism and the environment, linking individual change and macro-evolutionary effects. This argument allows to emphasize the tension between unpredictable actions as creative forces of living systems and the predictable effects of selection on the species' constitution.

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Orthogenetic Predictability: Orderliness and Symmetry in Early Macroevolutionary Explanations

Between the 1870s and the 1920s, orthogenetic theories spread among paleontologists and zoologists, and led to the proposal of several macroevolutionary "laws" and to hypotheses about the future evolution of taxonomic groups. This paper explores the historical and epistemological foundations of such explanations. By focusing on the interpretations of homoplastic phenomena within orthogenetic paleontology, we will argue that these models were based on a "methodological uniformitarianism", that is, a law-like view of nature, and on the idea, professed by the well-known American paleontologist Edward Drinker Cope, that «in biologic evolution, as in ordinary, *identical causes produce identical results*». This principle became a shared tenet of early orthogenetic views, ranging from the functionalist explanations of homoplasy to the conceptualization of parallelism in terms of "latent homology". This will enable us to reconsider orthogenesists' critiques of Darwin's notion of chance as the outcome of the nineteenth-century uniformitarian epistemology. Further, it will allow us to highlight the epistemological discontinuities that punctuated the history of macroevolutionary studies.

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Interspecific Cultural Convergences (ICC) and Interspecific Cultural Studies (ICS): From the Only Human Towards a Comparative History of Animal Uses and Traditions

During the last century, the comparative study of animal behaviours and minds has made it necessary to overcome such dichotomies as nature/culture, natural sciences/humanities. In particular, the study of animal cultures allowed the development of the *Interspecific Cultural Studies*, which combine biological, ethological and ecological approaches with the methods of the modern comparative cultural studies. Moving from such meta-disciplinary area, this paper aims at analysing the biological and social functions performed by singing in different animal species, and some converging aspects they present. In this regard, I propose to extend the concept of *evolutionary convergence* to the phenomena inherent in *cultural evolution*, defining as *Cultural Convergent Evolution* (CCE) all (and exclusively) the cases in which it is historically proven that a technique, an invention, a discovery or a use has been developed by different cultures and populations in reciprocal independence; and as *Interspecific Cultural Convergences* (ICC) all (and only) the cases in which cultural convergences occur also among societies and traditions of different species.

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Uncompromising Empiricism Once Again: Big Data and the Case of Numerical Taxonomy

Big Data are not rough data or mere tools. They foreshadow epistemological and ethical changes and raise issues as to the nature of knowledge and the categorization of reality. In this paper, we aim to analyse the so-called “data science” from a historical and epistemological perspective. We will first consider how, in the name of a new and uncompromising empiricism, a reconfiguration of the traditional view of causality in science is claimed on the basis of data analytics. Secondly, we will investigate a historical antecedent of the current debate by comparing these claims with the ones raised by Numerical Taxonomy, or Phenetics, in the second half of the twentieth century. This will allow us to highlight how the opposition between knowledge-driven science and data-driven science resurfaces in the debate about Big Data science.

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Predicting the Genetic Loci of Past Evolution

Repetitions in the mutations found to be responsible for independent evolution of similar phenotypes in various taxa have led some biologists to propose that for certain evolutionary changes the causal mutations are predictable. We examine here the nature of the predictions that have been made and their associated arguments. Predictions about the loci of past evolution are retrodictions, i.e. inferences about events that occurred in the past. They are not based on elaborate models and they derive mainly from the observation of repeated cases of genetic evolution. Predictions at the nucleotide level or at the gene level have a higher inference gain than those for broader categories of genetic changes such as cis-regulatory mutations.

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"Decline" vs. "Plasticity": Conflicting Narratives in the Dementia Tsunami

In dementia, the role of predictability is crucial to assess clinical and therapeutic aspects as well as individual and social impacts of such spreading epidemic. The article discusses both from discourse analysis and historical-epistemological view two metaphorical models of the brain, "decline" and "plasticity", informing two polarised narratives about dementia. By means of corpus linguistic analysis of dementia language use in the news media, we describe a different dynamic of predictability vs. unpredictability in the two narratives: the more traditional and negative narrative portrays dementia globally as terminal decline of brain functions predictably leading to neurodegeneration and decline of the whole individual; the more recent and positive narrative of plasticity describes dementia locally pointing to the brain's capability of resilience, and motivates individuals to train the brain if they wish to halt their decline. Different scenarios are at play in such polarised views, and, accordingly, different potential risks and responsibilities from an ethical viewpoint.

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Contingency, Laws and Random Events: Epistemic Specificities of the Neutral Theory in Ecology

In a famous 1999 paper John Lawton argued that ecology is but a set of descriptions of intertwining contingent facts. His challenge triggered many

responses and discussions. In this paper, I will consider the neutral theory in ecology and biogeography put forth by Hubbell, as a way to make sense of ecology in a lawful way, through the stochastic modeling of random events at various scales. I will first situate the neutral ecology in the context of community ecology and of the general distinction between ‘niche models’, which revolve around a law-like “competitive exclusion principle” and ‘dispersal assembly models’. Then I will look at the major controversy among community ecologists that occurred in the 1970s, between Diamond (1975) and Connor and Simberloff (1979) about the possibility of detecting patterns hinting at competition as the driver of biodiversity. This controversy paved the way for the acknowledgment of the key role of neutral models (namely models where selection plays no causal role) in ecology. This will lead me to address the neutral models designed by Hubbell (2001) and their relation with the ‘island biogeography’ models by MacArthur and Wilson (1967) as their immediate ancestor. I will show how Hubbell’s models promote unification between biogeographical and community scales, and describe a specific relation between dispersal models and niche models. Finally, I will specify the epistemic features of Hubbell’s theory, and the way they allow stochasticity to give rise to null hypotheses and alternative hypotheses that answer Lawton’s challenge. Taking into account the explicit parallel between the neutral theory in ecology and Kimura’s neutral theories in evolution, I will conclude by viewing more generally the role of neutrality in ecology and evolution, and focus on the relation between scales of biological change and the weight of neutral processes.

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From Predictability to the Theories of Change

The study of processes and change in systems is a requirement for Theoretical Physics after the development of complexity and emergence theories. This problem is far beyond the ideal models – centred on predictability – which Mathematical Physics usually deals with. The strongly interdisciplinary and systemic issue of Theories of Change implies a careful reconsideration of the essential features of the relationship between the observer/model-builder and the system under study. We delineate here such relationship as the meta-theoretical step wherein it is possible to give a first and partial place to the wide class of not ideal models, and to evaluate the effective predictive possibilities of Big Data.

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Big Data and Biological Knowledge

Some authors assert that the analysis of huge databases could replace the scientific method. On the contrary, we argue that the best way to make these new technologies bear fruits is to frame them with theories concerning the phenomena of interest. Such theories hint to the observable that should be taken into account and the mathematical structures that may link them. In biology, we argue that the community urgently needs an overarching theory of organisms that would provide a precise framework to understand lifecycles. Among other benefits, such a theory should make explicit what we can and cannot predict in principle.

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Estimations, Plans, Narratives: How Non-Human Animals Deal with the Future and "Possible Worlds"

The possibility of imagining and planning the future (or, more generally, to create "possible worlds") has often been considered a human species-specific trait, or – to put it with Peter Singer – one of the «ultimate signs of human distinction». When approached within a humanistic environment (particularly in philosophy, linguistics and semiotics), the main argument brought in support of this assumption is that such a capacity is expressed via three major (and again, supposedly-exclusive of humankind) characteristics of language: 1) Distant space-time semiosis, or the ability to keep track, transmit and reconstruct both recent and remote past events and places, and the ability to articulate projects and expectations regarding both immediate and remote places and future events. 2) Narrativeness, or the general capacity of accessing and describing alien *Umwelten*, either imaginary or not. 3) Linking signs, that is, para-signs that do not refer to any other existing entity apart from themselves, and whose function is to create meaningful relations among signs that, by contrast, stand for something else than only themselves. As reasonable as such argumentation can be, there are at least two major points that expose it to criticism: the assumption that such characteristics are exclusive of human language, and cannot be produced by other communication and/or modelling systems, and the consequent implication of human uniqueness in the cognitive production of the concepts of possible worlds and future in particular. The present article has the methodological goal to systematize these notions into an operative, interdisciplinary framework that is informed of at least semiotic, cognitive-ethological, psychological and narratological research, and – perhaps more importantly – the theoretical goal to renegotiate the terms of this discussion into a more accurate, hopefully not anthropocentrically-biased, perspective.

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Epigenetics and Development in Cognitive Functions: Literacy as a Case-Study

In contemporary cognitive neurosciences contingency refers to the importance of individual experience – sociocultural environment and interpersonal relationships – in the continuous molding of our bodies, brains and individual minds. The so-called “social and cultural neurosciences” (“interpersonal neurobiology” in Siegel’s words) are clearly aimed at studying the essential connection between cognition, brain, body, and environment. Looking at the brain as an intrinsically dynamic and plastic organ, with an open architecture sculpted over the time by the history and experience of the individual, the neurobiological basis of our behaviour, our neuronal pathways, today are viewed in terms of ñepigenetic landscapesò. In fact, the development of many cognitive functions and emotional capacities – from learning and memory to individual resilience and coping with stress – is deeply grounded in epigenetic processes. From within this theoretical framework, we will adopt as case-study *literacy*, a species-specific cognitive function with an essential role in human biological and cultural evolution. We will find the neurobiological foundations of our ability to write and to read the linguistic code in the epigenetic and developmental neuronal pathways and circuits of the brain. Assuming “Neural Darwinism” as a paradigm, one of the fundamental heuristic tools of the proposed analysis will be that of neural recycling, as intended in the context of the contemporary neuroplasticity revolution.

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Determinism and Stochasticity in Mathematical Modelling for Cell Migration

The aim of this contribution is to use well-known characteristics of cell migration to explain the different origin of uncertainties and dramatic bifurcation of cell behaviours. At first the examples develop in a deterministic framework showing how even slight changes in the parameter space can induce dramatic changes in the behaviours of cells. As a second step different sources of uncertainties are introduced which might complicate even further the possible output scenarios. Mathematical models can in this respect help give a panorama of the probability to find a cell in a certain migration state and what are the main parameters determining cell migration. This is an important aspect to understand several phenomena during the embryonic development or in diseases involving for instance immune cells and cancer cells.

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On the Contingency of What Matters: Predictability and Evolutionary Ethics

The paper explores the role that predictability may play in a cross-disciplinary and normative field such as evolutionary ethics. Although predictability is generally understood as a crucial notion for the descriptive components of evolutionary ethics, here, it will be investigated its role for the claim of normativity itself. In particular, it will be assessed the epistemic status of our judgements about what matters in the light of evolutionism. On a realist view about what matters, there are things in the world that matter insofar as they necessarily matter. Contrary to that, if one embraces evolutionism, what matters is rooted in our biological history, and it is a matter of pure contingency; therefore, since what matters does not necessarily matter, it is not possible to predict what matters and nihilism appears to be the only viable route. After having clarified in which sense we may intend predictability in evolutionary ethics, the paper assesses whether a better understanding of contingency in the evolutionary process can point out an alternative conception of normativity than the realist one without being forced to embrace nihilism.

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On the Nature of Natural Selection

Some philosophers, known as statisticalists, claim that the concept of natural selection, as it is normally presented in population genetics, is statistical in character and cannot be construed in causal terms. On the contrary, other philosophers, known as causalists, argue against the statistical view and reaffirm the causal interpretation of natural selection. A key element in this debate is the dispute on the nature of drift. Drift is supposed to be a sort of measure of contingency in evolution. Thus, drift can be thought as affecting predictability in evolutionary biology. If drift is a cause of evolution, uncertainty in population genetics is due to some processes that make a population deviate from predicted outcomes. But, while causalists see drift as a distinct phenomenon originated by some set of natural processes, statisticalists claim that there is no process that accounts for this uncertainty, since the uncertainty lies not in the events but in the fact that natural selection in population genetics is modeled by a statistical theory. This article aims to illustrate the debate between causalists and statisticalists in order to present a challenge that statisticalists need to address if they wish to maintain a naturalist stance. Indeed, the debate on the nature of natural selection intersects the more general debate on whether or not non-causal explanations, and more precisely mathematical explanations, are genuine scientific explanations. Since evolutionism is essential for a naturalist perspective to be defined as such, and natural selection is central to evolutionism, an inquiry on what kind of explanations are provided by population genetics is crucial to assess the coherence of any naturalist stance.

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Filosofia e saperi - 10
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Crossing borders between the humanities and the life sciences

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