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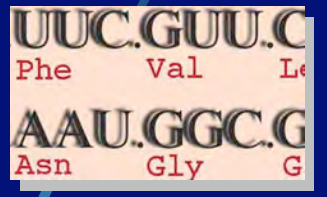

Is the computer metaphor relevant to describe living organisms?

(Functional Selective Stabilization and Epigenesis)

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Mass media speak of gene and genomes as if there was a one to one correspondence between an individual and its genome

We also hear about “good” or “bad” genes, and some would like to screen for better humans

Is this compatible with what we know about what life is?

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The originality of Life

- Physics: *matter, energy, time*
- Biology: Physics + *information, coding, control...*

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What is Life?

Three processes cooperate to create Life:

- **Information transfer (Living Turing Machines)**

This involves a coding process and an algorithmic way of processing the data (a "programme")

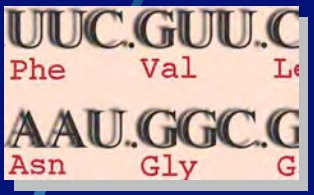
Driving force for a coupling between the genome structure and the structure of the cell (not discussed today):

- **Metabolism (Internal organisation)**
- **Compartmentalization (General structure)**

Function: a central concept an extension of Cuvier's view...

- Physical stability ([cyto]skeleton)
- Reproduction
- Respiration
- Locomotion
- Perception
- Transport (import / export)
- Circulation (internal fluxes)
- Digestion and recycling
- Assimilation
- Accommodation (regulation)
- Communication
- Maintenance (repair)….

A general *a posteriori* rule



Functional selective stabilisation

creates structures and processes that exist *a posteriori* because, when expressed, they survived challenges from the environment

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Empedocle / Maupertuis / Malthus / Darwin

Variation / Selection / Amplification

Stabilisation

Evolution

↓ *creates*

Function

↓ *recruits*

Structure

↕ *coding process*

Sequence

http://www.pasteur.fr/recherche/unites/REG/vision_en.html

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Three processes overlap to create the ultimate individual living entity

- ***Phylogenesis*** **(shaping the genotypes)**
- ***Ontogenesis*** **(shaping the 3D forms)**
- ***Epigenesis*** **(shaping the individual in context)**

Each one is stabilized under the selective pressure of events acting on the corresponding functions

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Three (interrelated) levels carve an image of the world

- Evolution (phylogenesis)
- Differentiation (ontogenesis)
- Individuation (epigenesis)

The alphabetic metaphor

As is the case when building up a machine, one needs a book of recipe to build up a cell

This asks for changing the text of the recipe into something concrete: this transfers « information ».

Naturally, the book of recipe is not the dish!

In a cell, information transfer is managed by the genetic programme represented as an alphabetical text

Copying the text implies introducing errors

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Information transfer

- **Replication** (law "complementarity")
- **Transcription** (law "complementarity")
- **Translation** (law, a cipher, the "genetic code")

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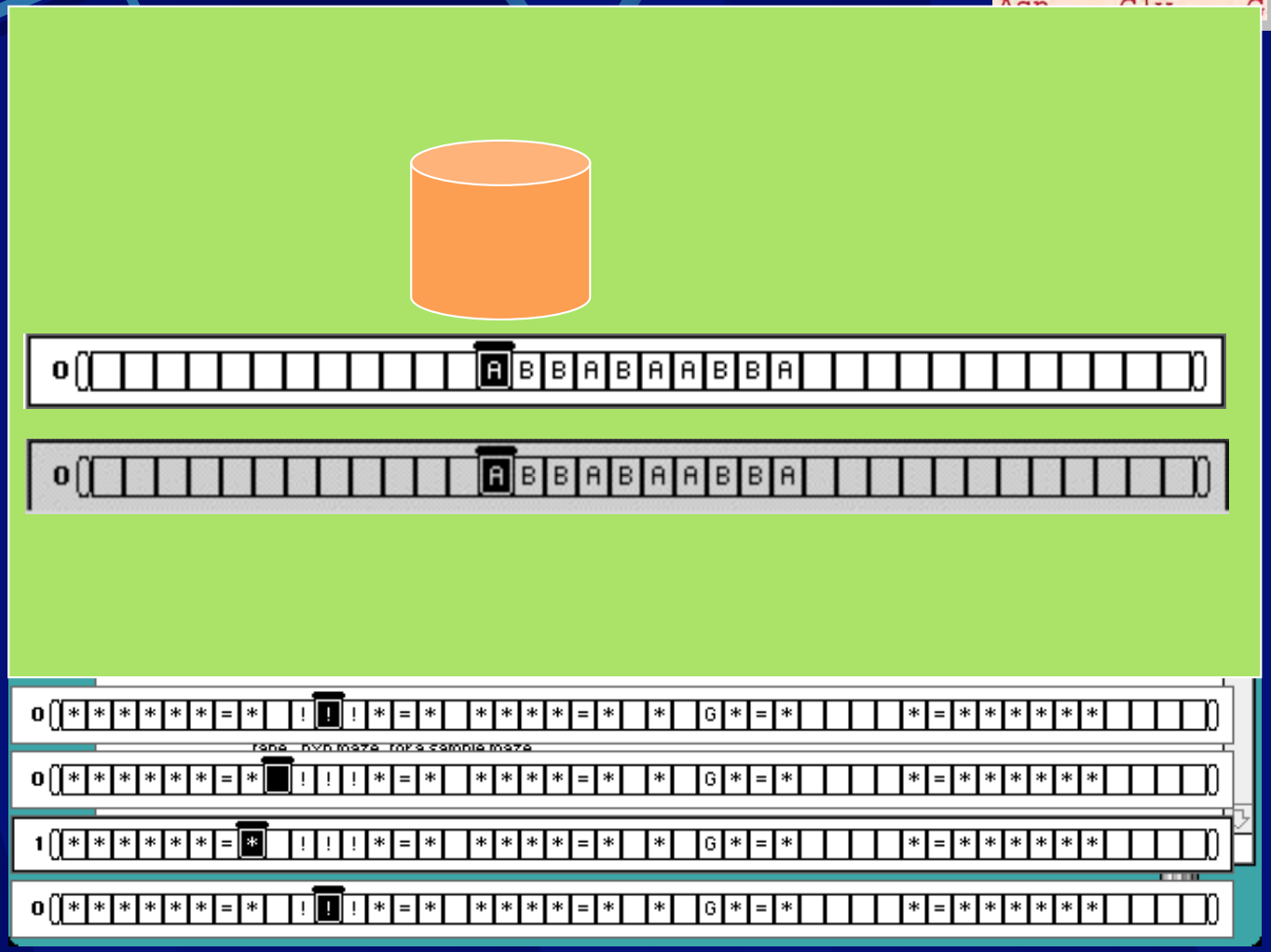
A genetic Turing machine

- In a Turing machine the machine is separated from the data, and the program
- Data and program play the same role (*i.e.* they can be thought of as ‘ declarations ’); they can be modified by the machine (Pol IV, Pol V...)
- General reflection (theoretical insights) considers the actions of the machine, but not the way it is constructed

A genetic Turing machine

programme (≈ data)

The machine can modify the programme/data, represented as a string of symbols (a sequence)



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Cells as Turing Machines

Genomics rest on description of genomes as texts written with a four-letter alphabet. Conjecture: do cells behave as Turing Machines? How far goes the metaphor?

Genetic engineering

Viruses => the example of hepatitis C reconstruction

Horizontal gene transfer

Cloning animal cells

all point to separation between

Machine

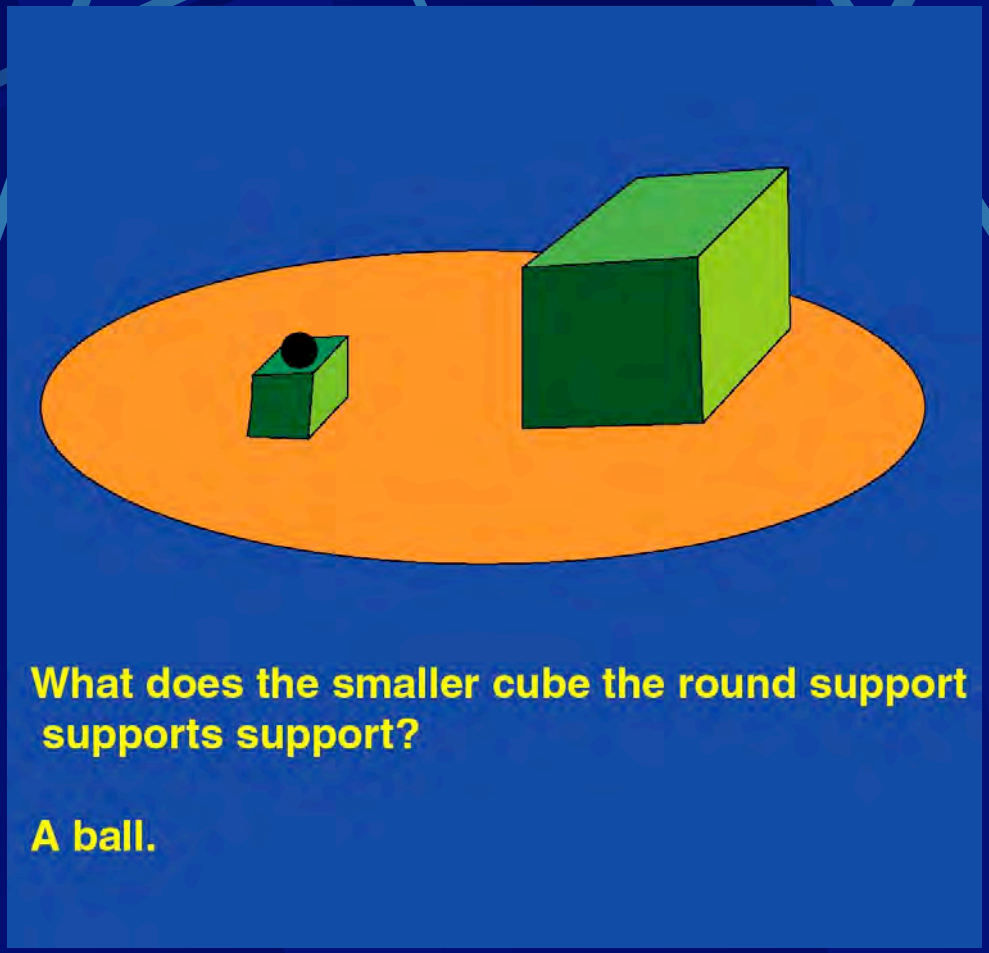
Data +

Programme

Algorithmic complexity

- Shannon's « entropy » does not care about the meaning (replication)
- Kolmogorov and others proposed to define randomness of one sequence by stating that it cannot be described by a program with a length shorter than the sequence
- This provides us a research program: in order to approach algorithmic complexity of a sequence, we need to describe how it has been constructed (in the real physical world)
- Prokaryotic genomes look « random »; eukaryotic genomes look « repeated »

Caveat:
Repeats can be meaningful



Remember also:

This clock has a minute minute hand

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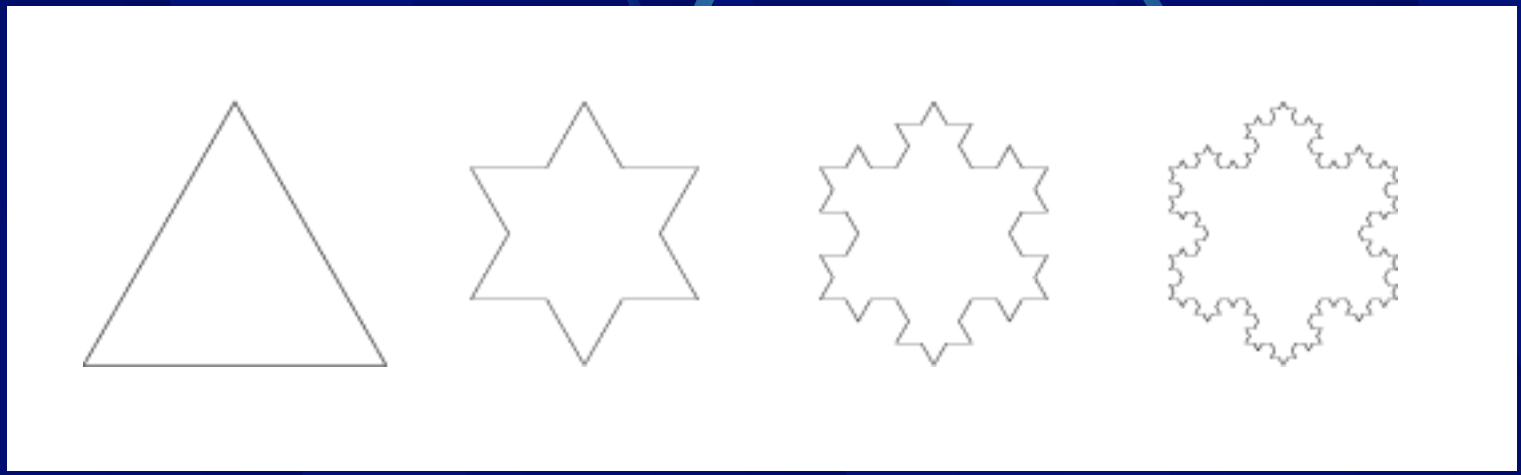
Logical Depth

A very short program (low algorithmic complexity) can describe a simple repeated sequence, but also a fractal figure such as Koch 's snowflake



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Logical Depth

A remarkable consequence of logical depth is that, when a program is complicated enough (branching and recursive), it becomes impossible to predict its outcome in a reasonable time. The only way to know it is to run the program….

Evolution has evolved DNA from DNA from DNA in such a way that every single base has a certain « depth », that makes that living organisms are, in principle and by construction, poised to be ultimately unpredictable…

This allows them to create some progeny that can survive in an unpredictable future.

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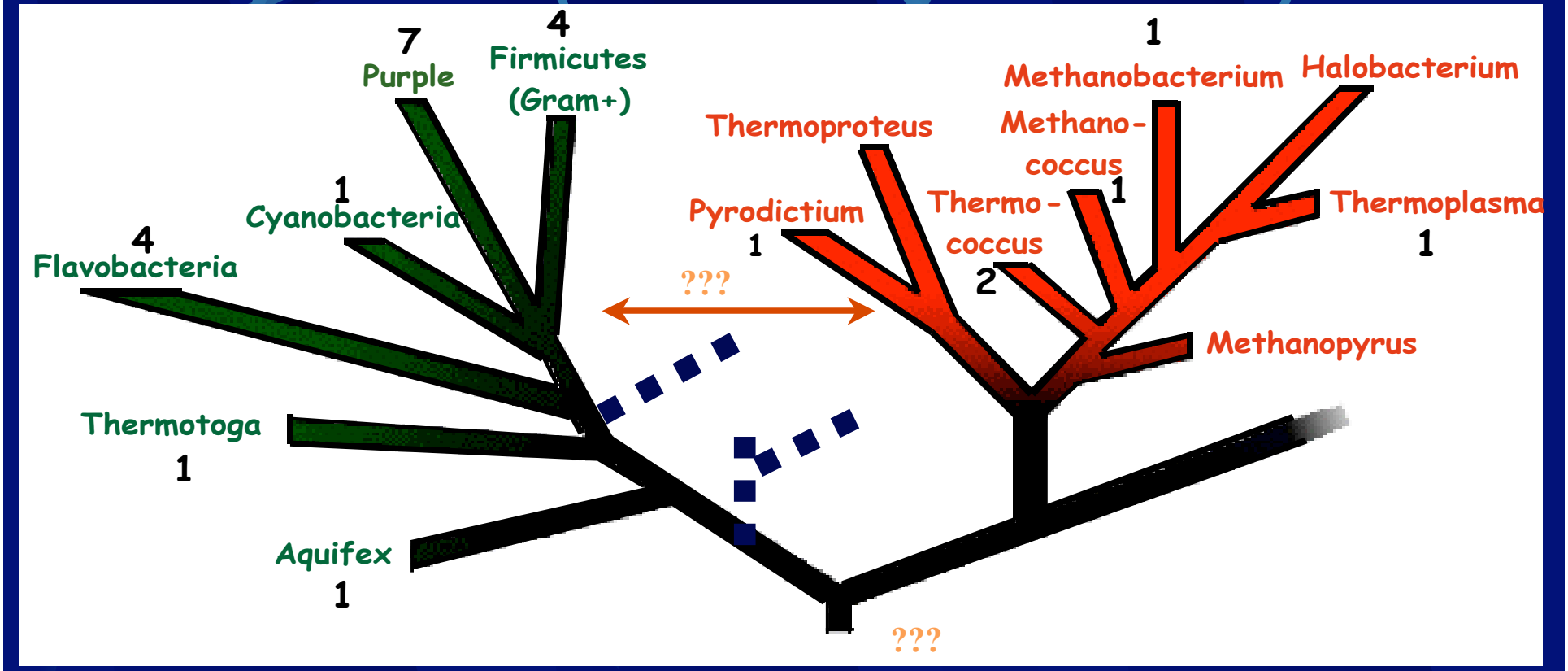
A phylogenetic view of the world

- Living systems evolve by mutations (sometimes simple rearrangements, without changing the genome « text »)
- Those that are not totally unable to survive and multiply create a progeny: survival implies that the local conditions of the environment carve an image of the world in the genomes that are retained
- This process creates, through assessment of the concrete functioning of a living organism its stability in the environment where it happened to be born

Phylogenesis



(Woese, 1990)

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Three (interrelated) levels carve an image of the world

- Evolution (phylogenesis)
- Differentiation (ontogenesis)
- « Individuation » (epigenesis)

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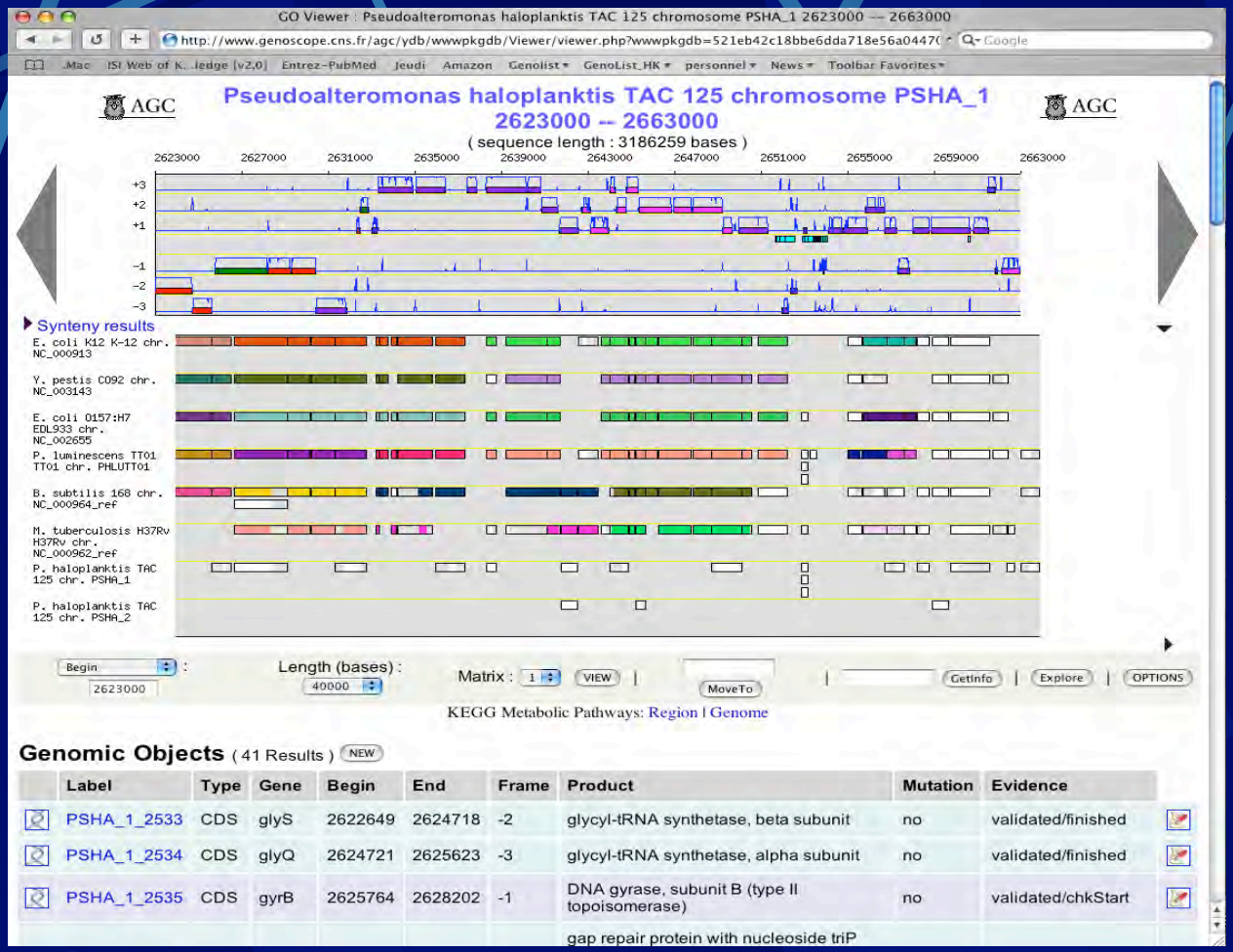
Ontogenesis

If the machine not only has to behave as a Turing machine but also to construct the machine, one must find a geometrical programme somewhere in the machine (J. von Neumann)

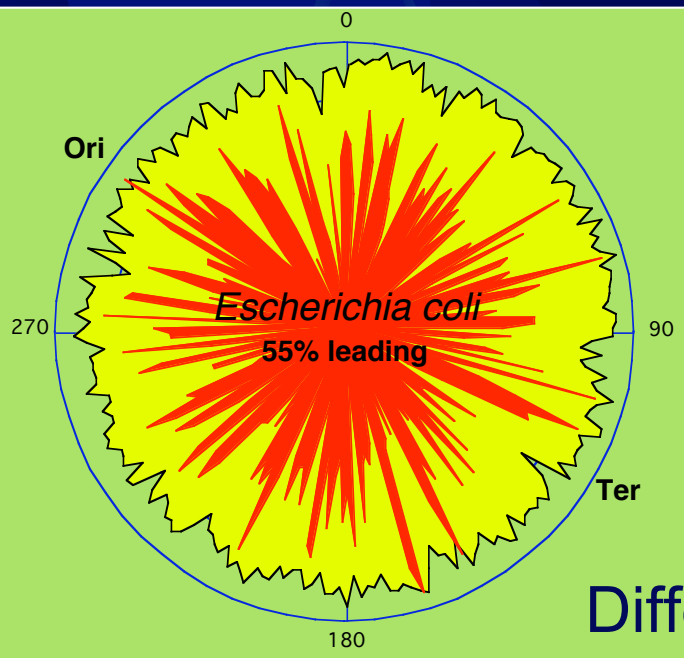
Is the gene order random in bacterial genomes?

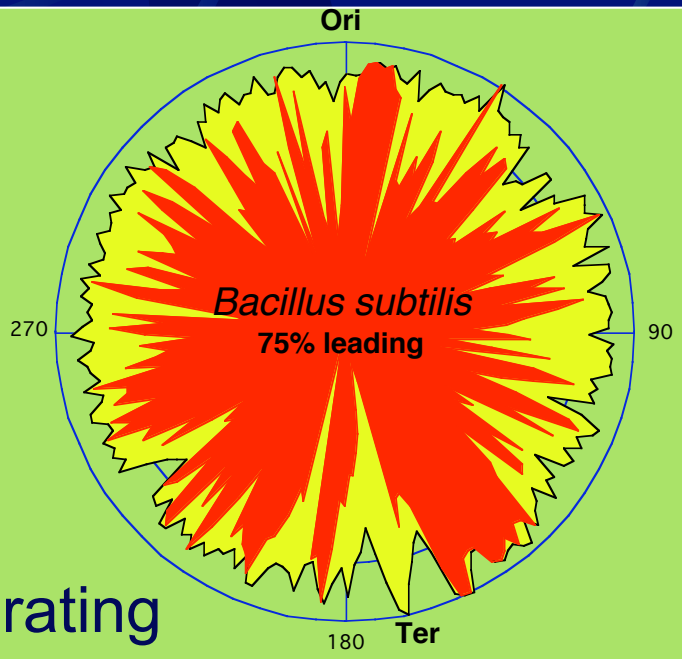
Many living organisms are multicellular: they grow from an egg to an adult form. How is this organized within the « alphabetic metaphor -Turing machine » paradigm?

Gene vicinity: synteny

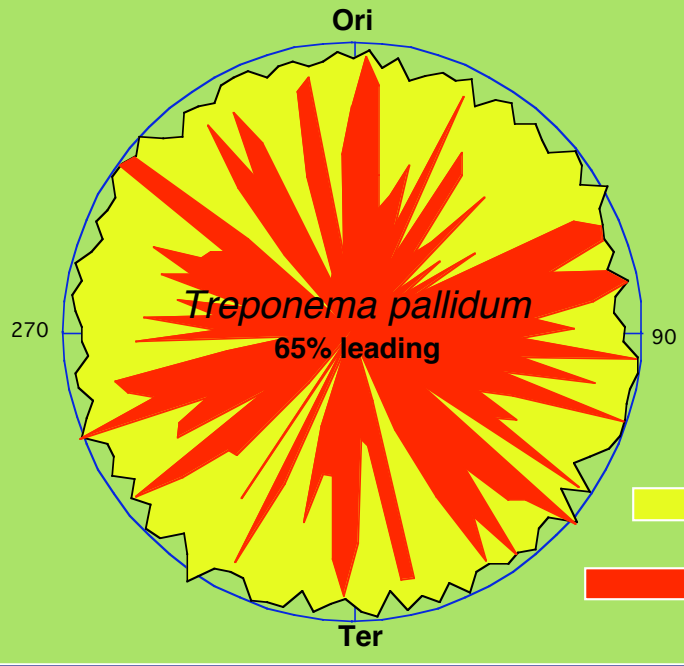


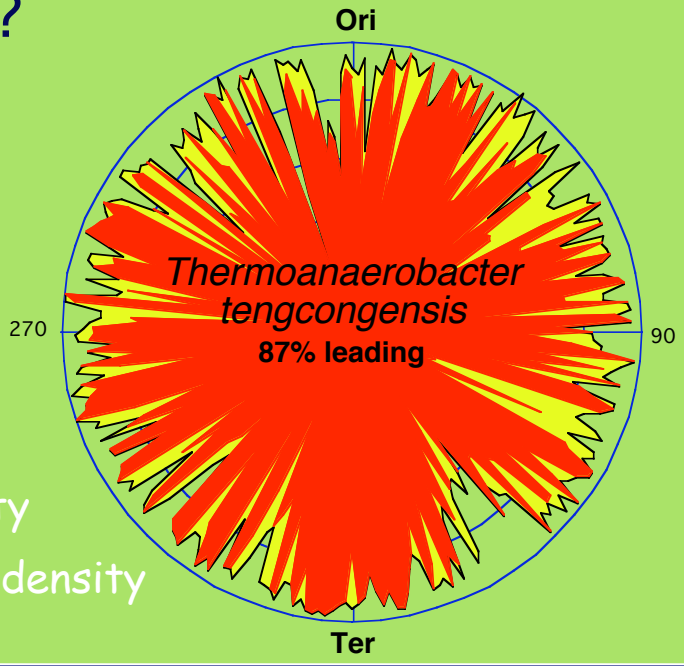
Label	Type	Gene	Begin	End	Frame	Product	Mutation	Evidence
PSHA_1_2533	CDS	glyS	2622649	2624718	-2	glycyl-tRNA synthetase, beta subunit	no	validated/finished
PSHA_1_2534	CDS	glyQ	2624721	2625623	-3	glycyl-tRNA synthetase, alpha subunit	no	validated/finished
PSHA_1_2535	CDS	gyrB	2625764	2628202	-1	DNA gyrase, subunit B (type II topoisomerase)	no	validated/chkStart
						gap repair protein with nucleoside triP		





Different "Operating Systems"?





CDS density

Leading CDS density

(updated from Kunst *et al* , Nature, 97)

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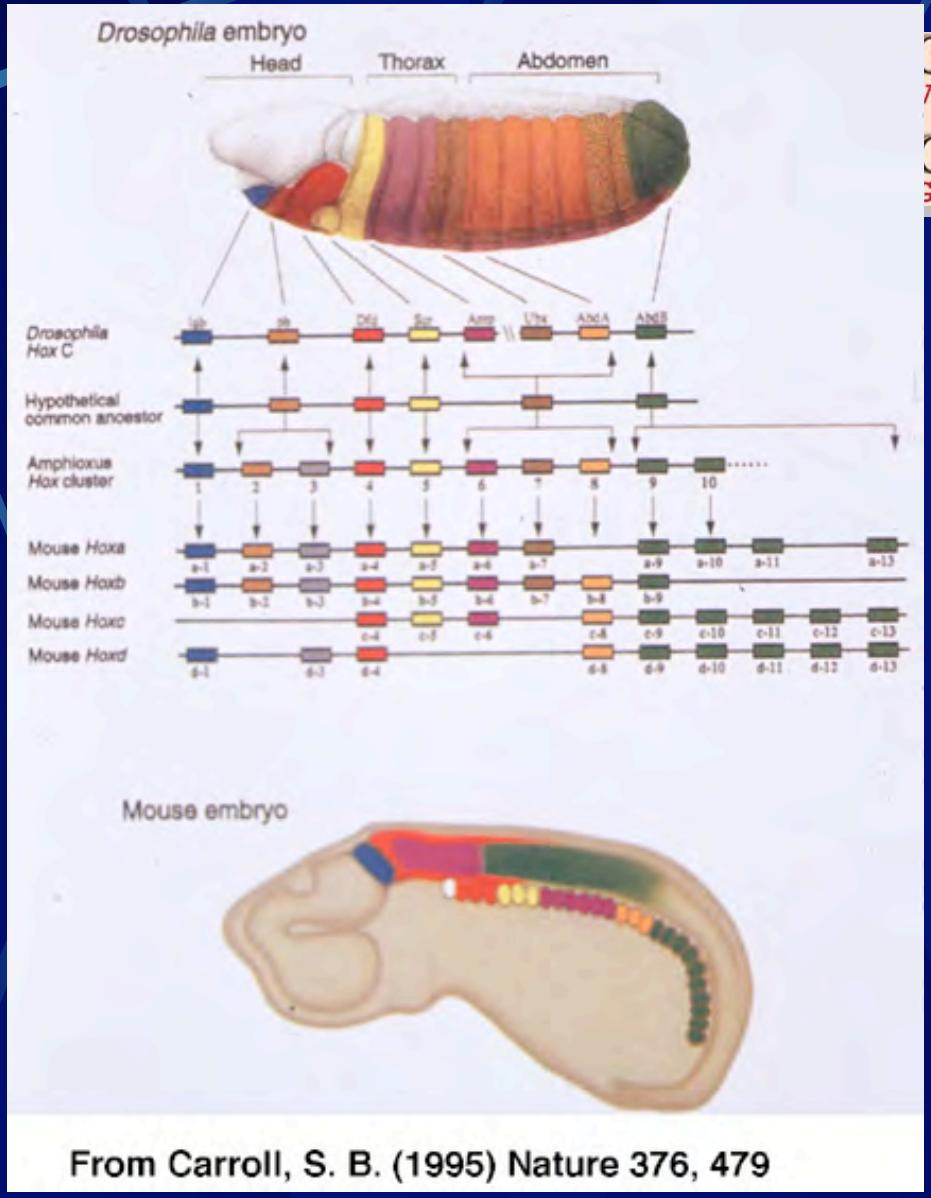
Drosophiloculus,

Homunculus ?



From Carroll, S. B. (1995) Nature 376, 479

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Three (interrelated) levels carve an image of the world

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Epigenesis: the ultimate level of identity

Heredity is not necessarily of genetic origin: language or fortune can be transmitted from generation to generation, this is the case of epigenetic heredity

Epigenesis summarizes processes that express the genetic programme in a variety of ways according to the environment of the cell or the organism. At the level of the Central Nervous System, learning is an epigenetic process

Neuronal network connections are often unstable, and become stabilized when triggered to function. This carves an epigenetic image of the world in the brain by functional stabilization of neuronal connections (synapses).

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Epigenesis

Shaping the animal that started as a more or less spherical egg requires systematic cell migrations as well as cell death (apoptosis).

Apoptosis is the functional stabilization process that retains only those cells that are adjusted to their local environment (taking into account the functioning of neighboring cells as well as global and environmental signals). This creates a particular level of identity, that begins to carve a particular image of the world in the organism.

The role of the genes here is to learn how to learn, not to tell what will be the exact outcome.

This can be illustrated for example by seasonal dimorphism (**Araschnia levana)**.

The “genetic envelope”

The genetic programme provides rules for the construction of an individual organism and its development and survival in a family of environments. Its role can be perceived by analyzing a population of individuals with the same genome: all characters present are within the « genetic envelope » provided by the genome text

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Back to "Identity"

- Belonging to a community, a population, a species, thus similar to the others….
- Being an individual irreducible to the others…

This is the difficult paradox that creates the misunderstanding on the nature of genes and genomes and that of the person

And for possible questions: two more slides!

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Unexpected properties of strings of symbols

- The DNA « text » can be considered as a string of symbols
- Many theories know how to deal with such objects

- In particular they can play the role of « programmes » that have remarkable properties (for example they can be « recursive », i.e. they can call themselves as routines). A machine run by a recursive programme usually does not have standard mechanistic (i.e. predictable) properties

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Gestalt and Algorithms

« Start from the top, middle

Go down from right to left

Accelerate

Turn right

etc.