Meta-analysis of the genes underlying phenotypic changes

Virginie Courtier-Orgogozo
Institut Jacques Monod, Paris

www.gephebase.org

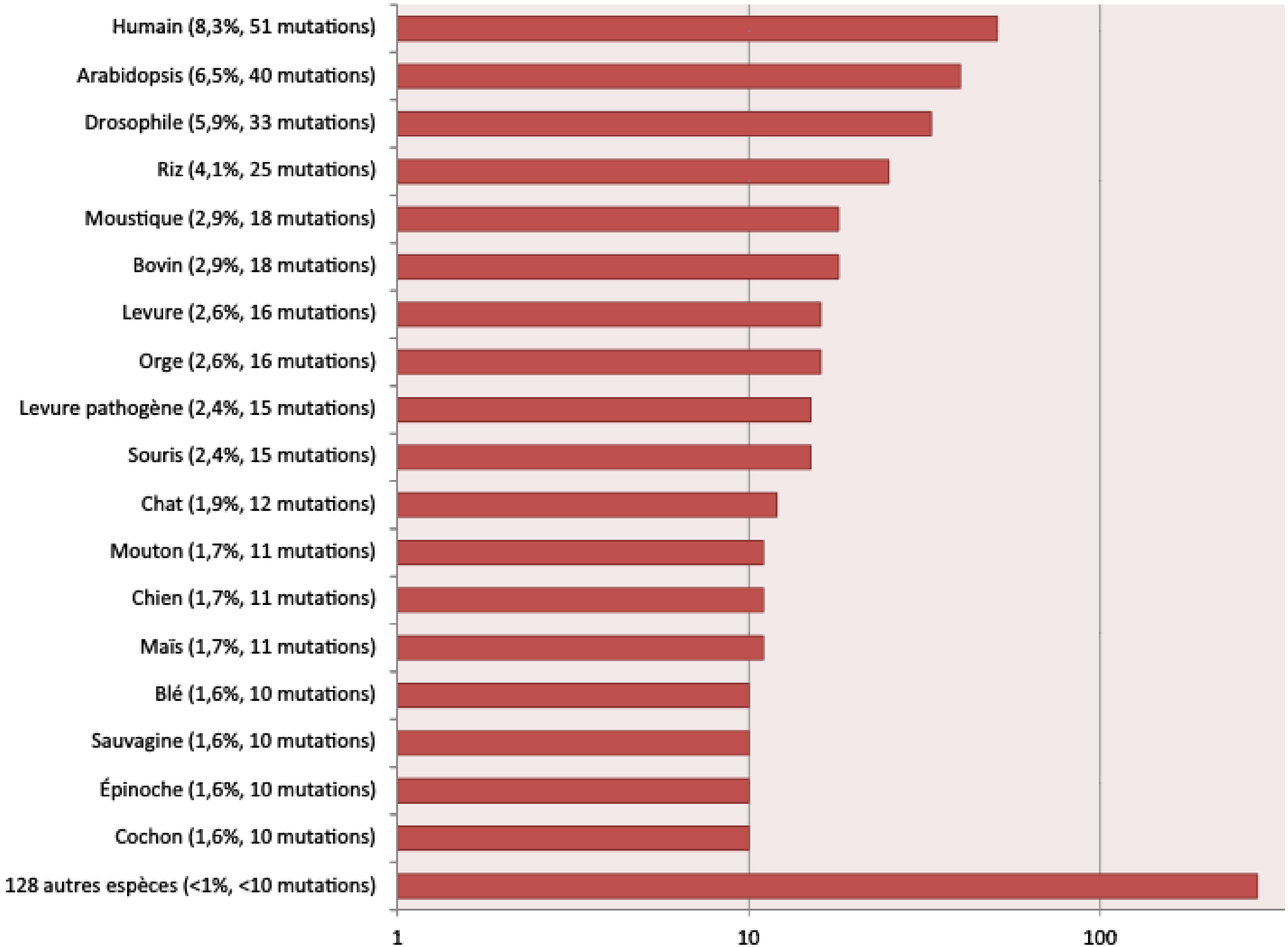
Includes Natural, Domesticated and Experimental Variation
but NO *LAB MUTANTS* and NO *CLINICAL TRAITS*

>1600 genes and mutations associated with natural phenotypic changes in animals and plants

Virginie Courtier-Orgogozo
Arnaud Martin (Washington DC)
Laurent Arnoult (former postdoc)
Stéphane Prigent (former postdoc)

Biases in current data

Bias toward certain species



Arnoult 2014

Coding: global change

OVATE coding region
(Liu 2002)

myostatin coding region
(Grobet 1997)

Mc1r coding region
(Eizirik 2003)

Cis-regulatory: local change

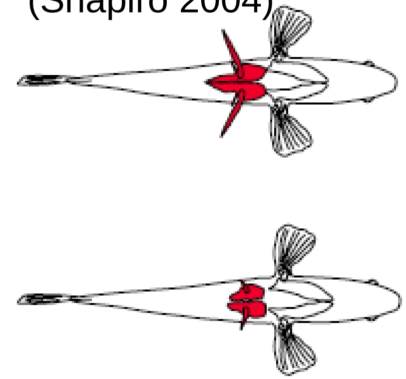
yellow cis-reg. region
(Prud'homme 2006)

luciferase coding region
(Stolz 2003)

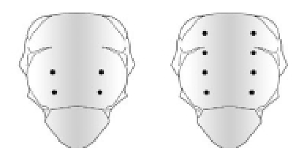
anthocyanin-2 coding region
(Quattrocchio 1999)

spatially

Pitx1 cis-reg. region
(Shapiro 2004)



scute cis-reg. region
(Marcelini 2006)

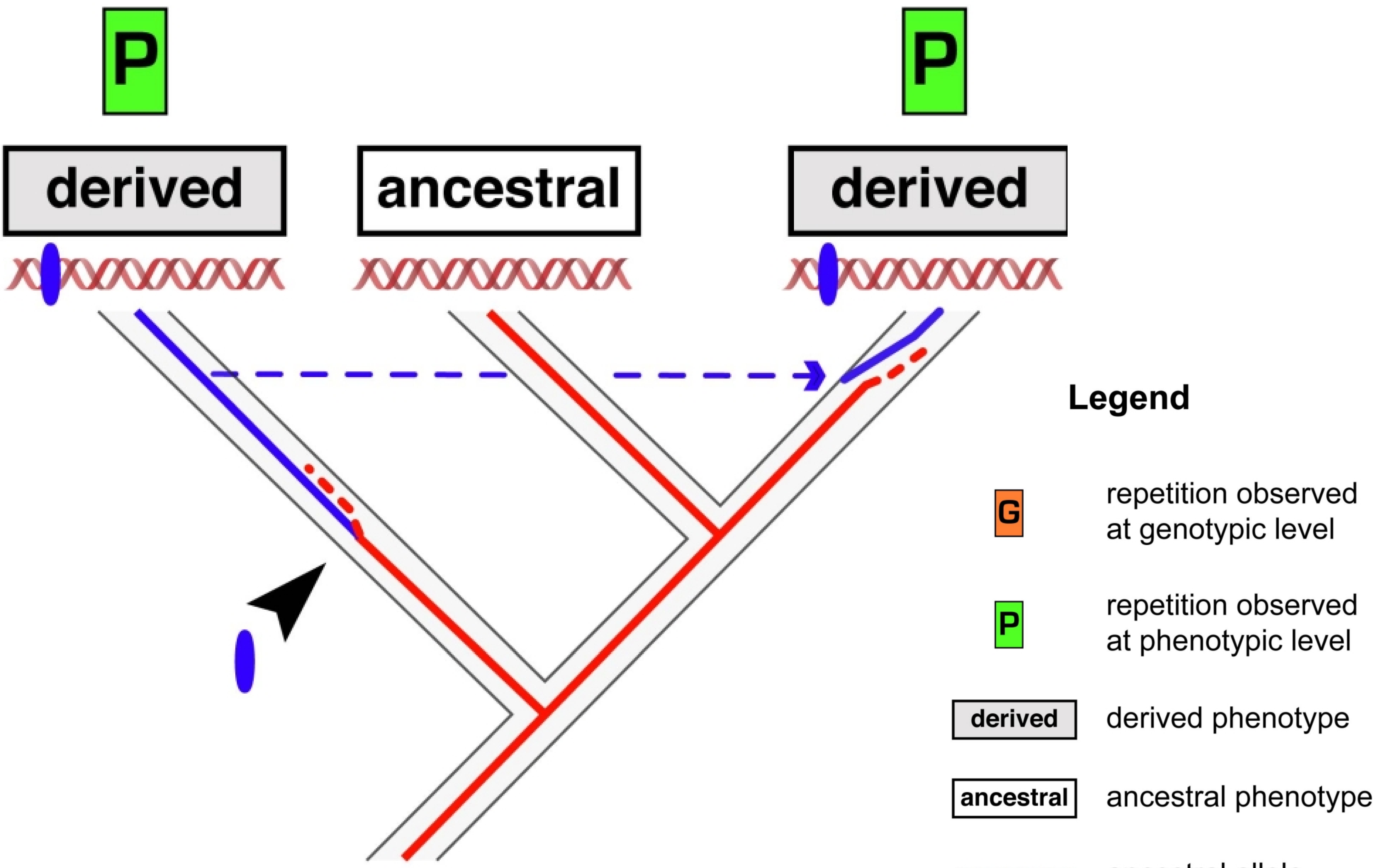


temporarily

agouti cis-reg. region
(Jones 2018)

The tree of life is not a tree

Lateral transfer

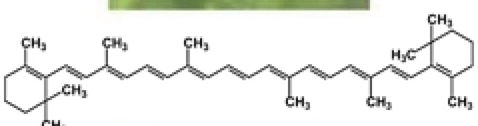



L.S. Mills research photo by Jaco and Lindsey Barnard

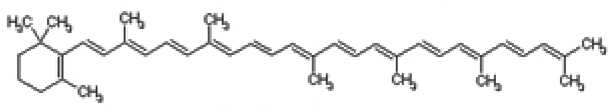
Genetic plagiarism of body color in aphids

Green morph

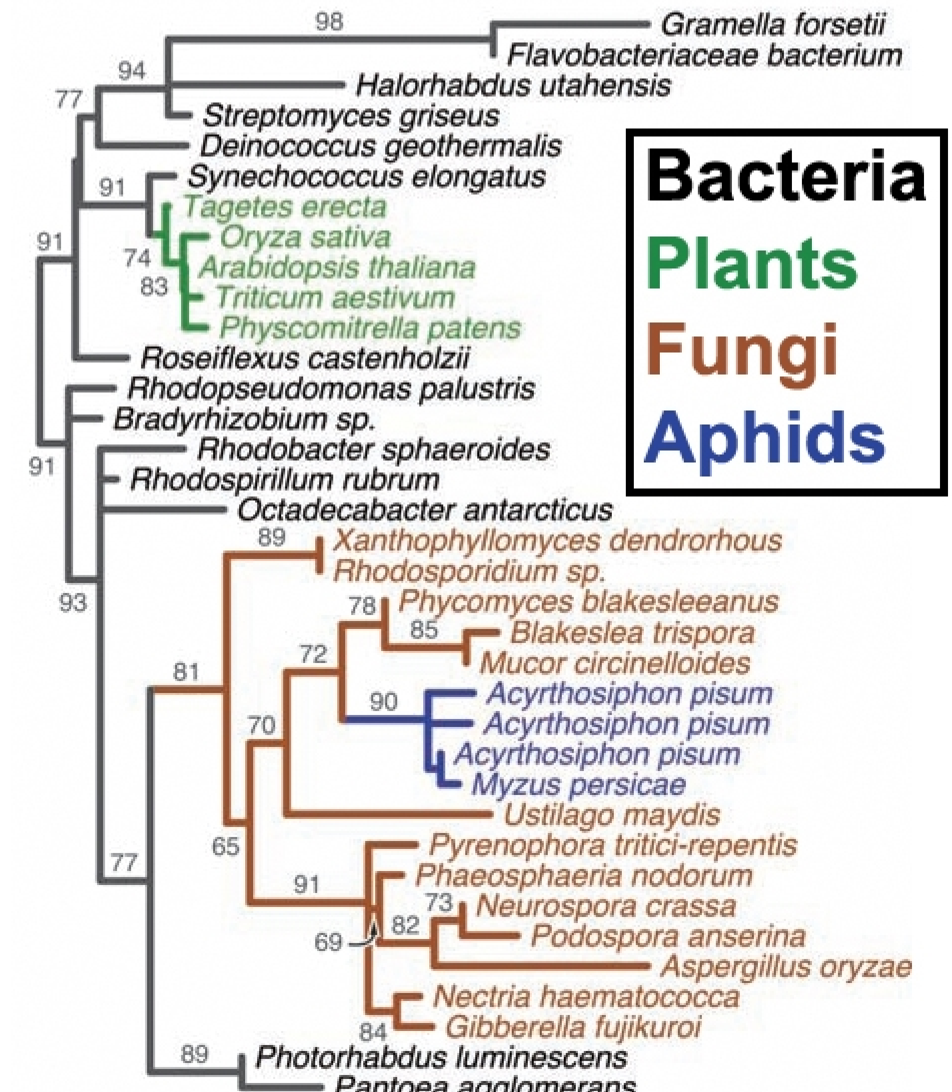
Red morph



Beta-carotene



Torulene

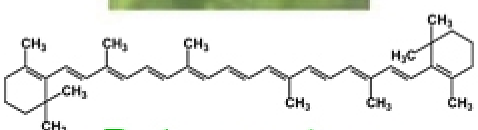


- Moran and Jarvik 2010 Science

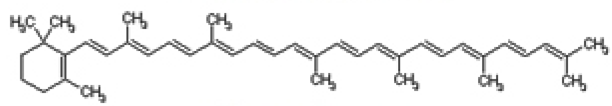
Genetic plagiarism of body color in aphids

Green morph

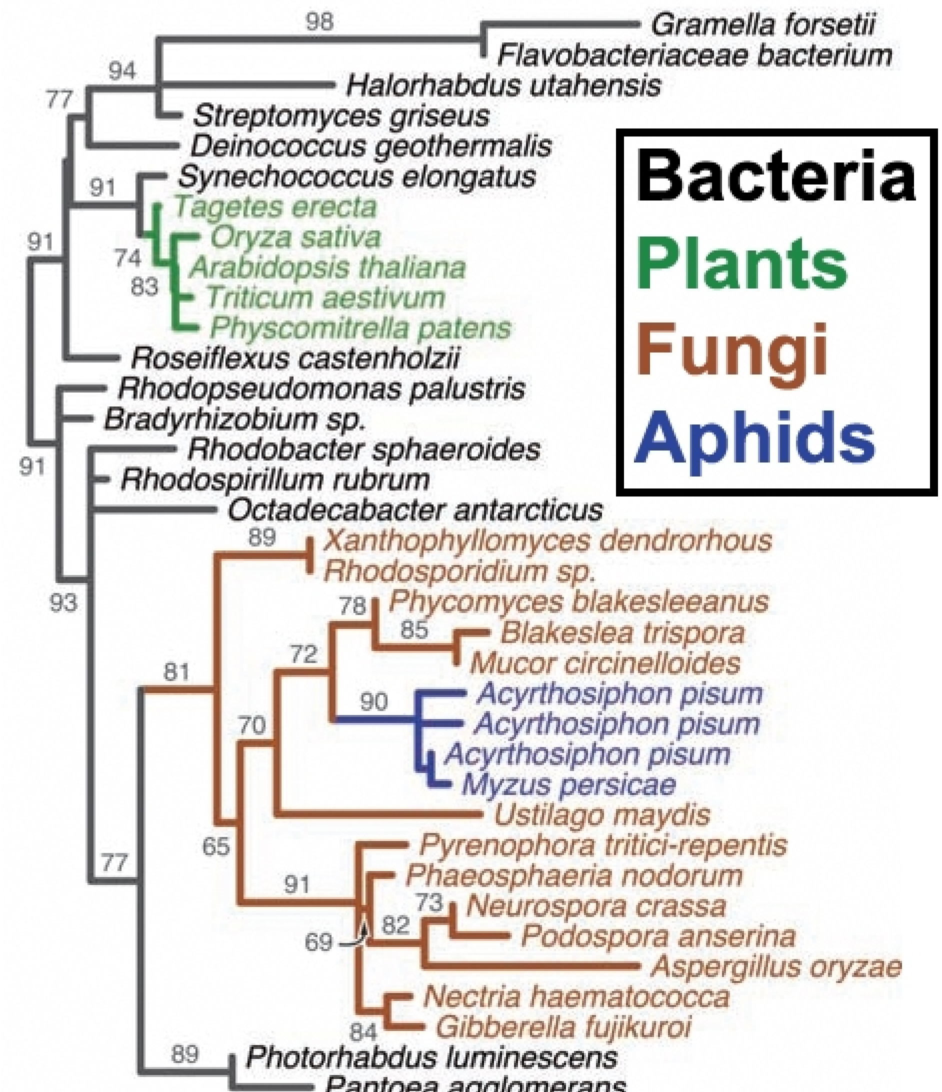
Red morph



Beta-carotene



Torulene

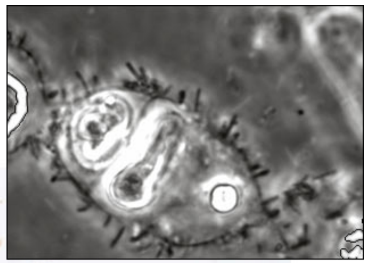


Carotenoid biosynthesis enzymes transferred also from fungi to the two-spotted spider mite (Altincicek 2012)

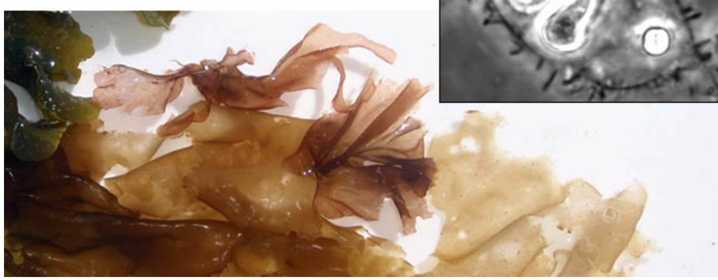
- Moran and Jarvik 2010 Science

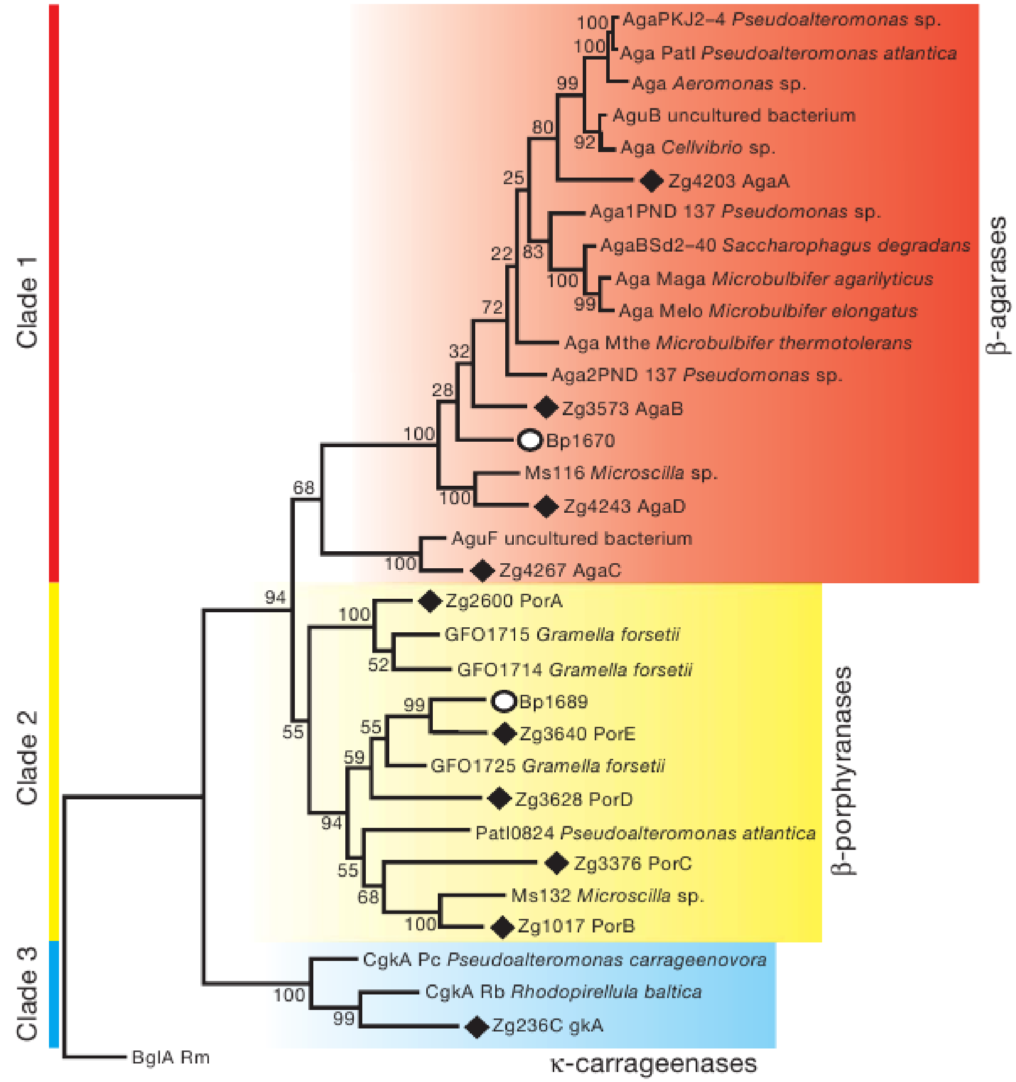
We are what we eat
Seaweed digestion in Japanese people

◆ *Zobellia galactanivorans*



seaweed



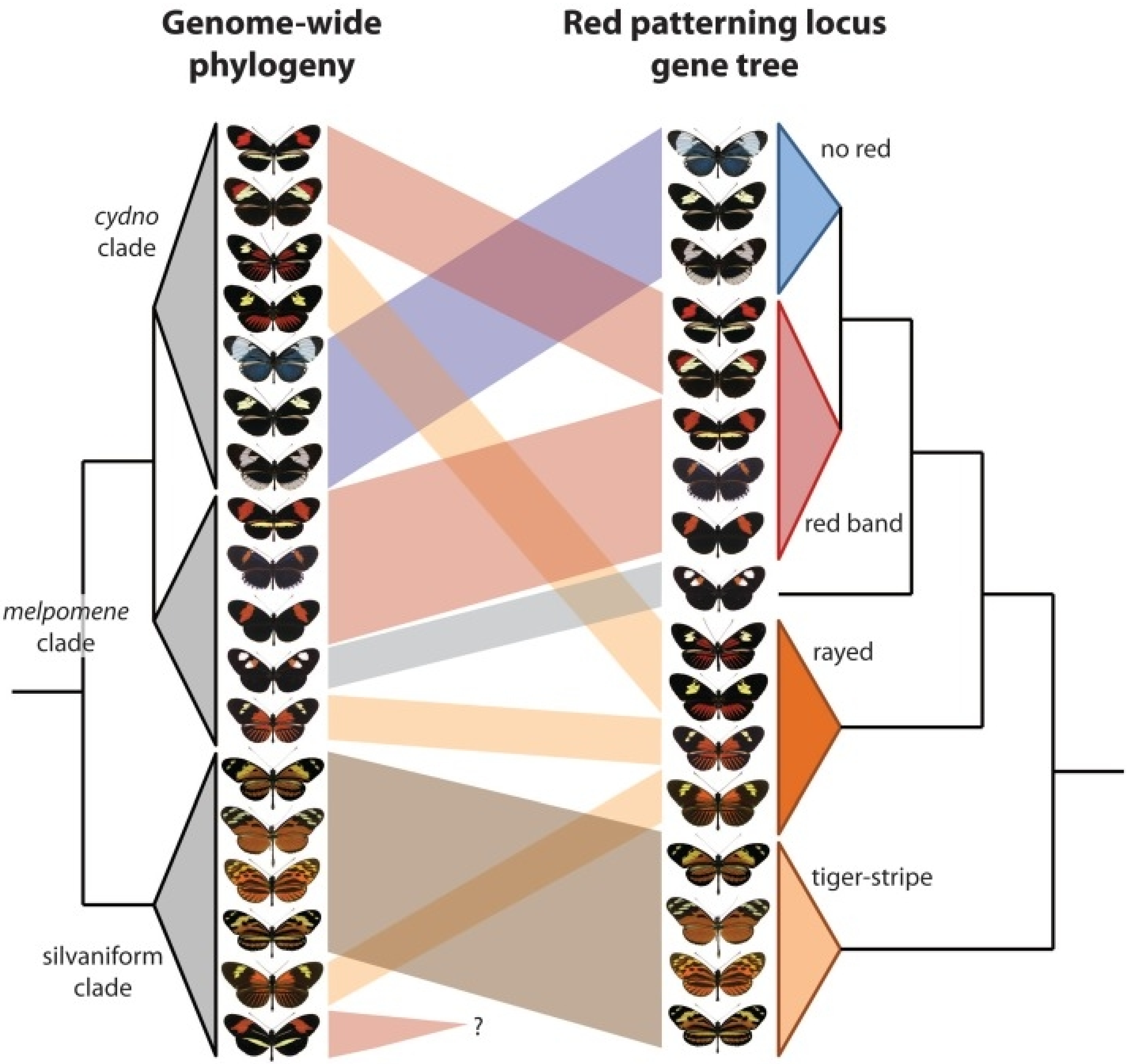


○ *Bacteroides plebeius*

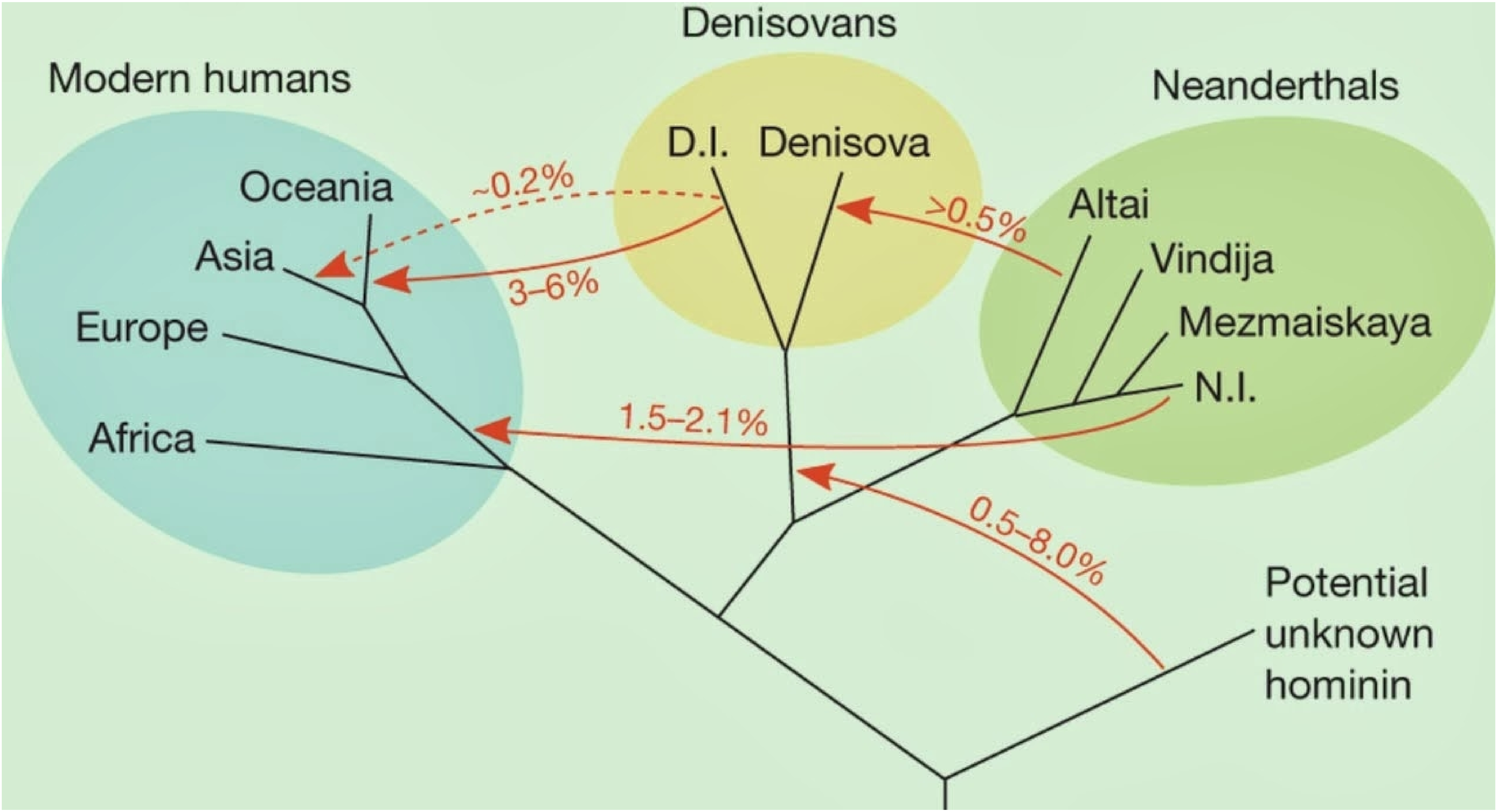
from Japanese microbiome only!

- Hehemann et al 2010 Nature

Genetic plagiarism of the red wing color pattern



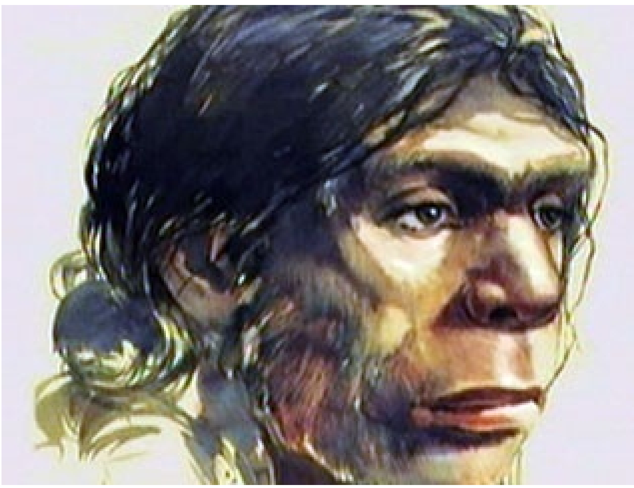
(Reed 2011, Pardo-Diaz 2012, Heliconius Consortium 2012)

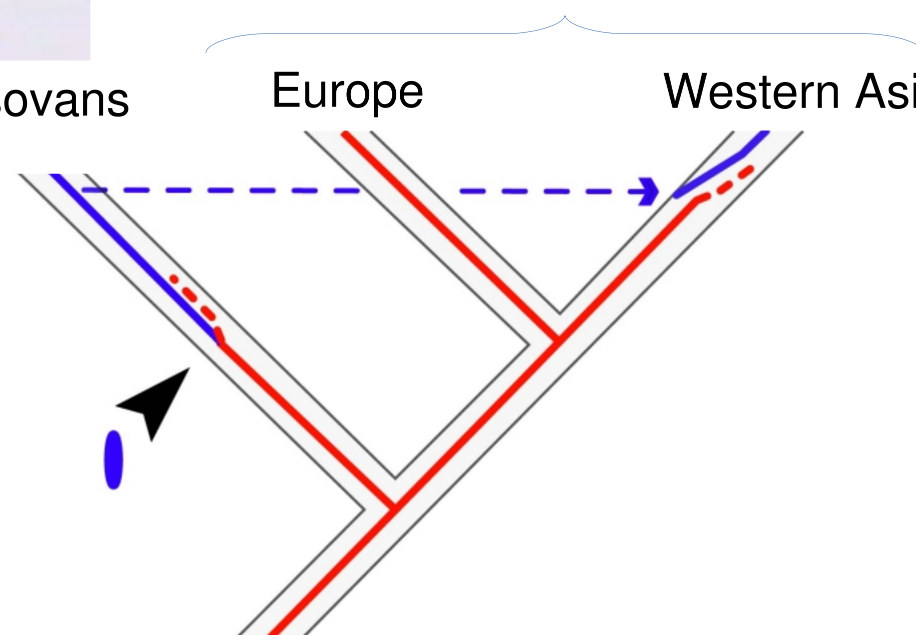


Denisovans
Modern humans
Neanderthals
D.I.
Denisova
Oceania
Asia
Europe
Africa
~0.2%
3–6%
>0.5%
Altai
Vindija
Mezmaiskaya
N.I.
1.5–2.1%
0.5–8.0%
Potential unknown hominin

Genetic plagiarism of immune resistance genes

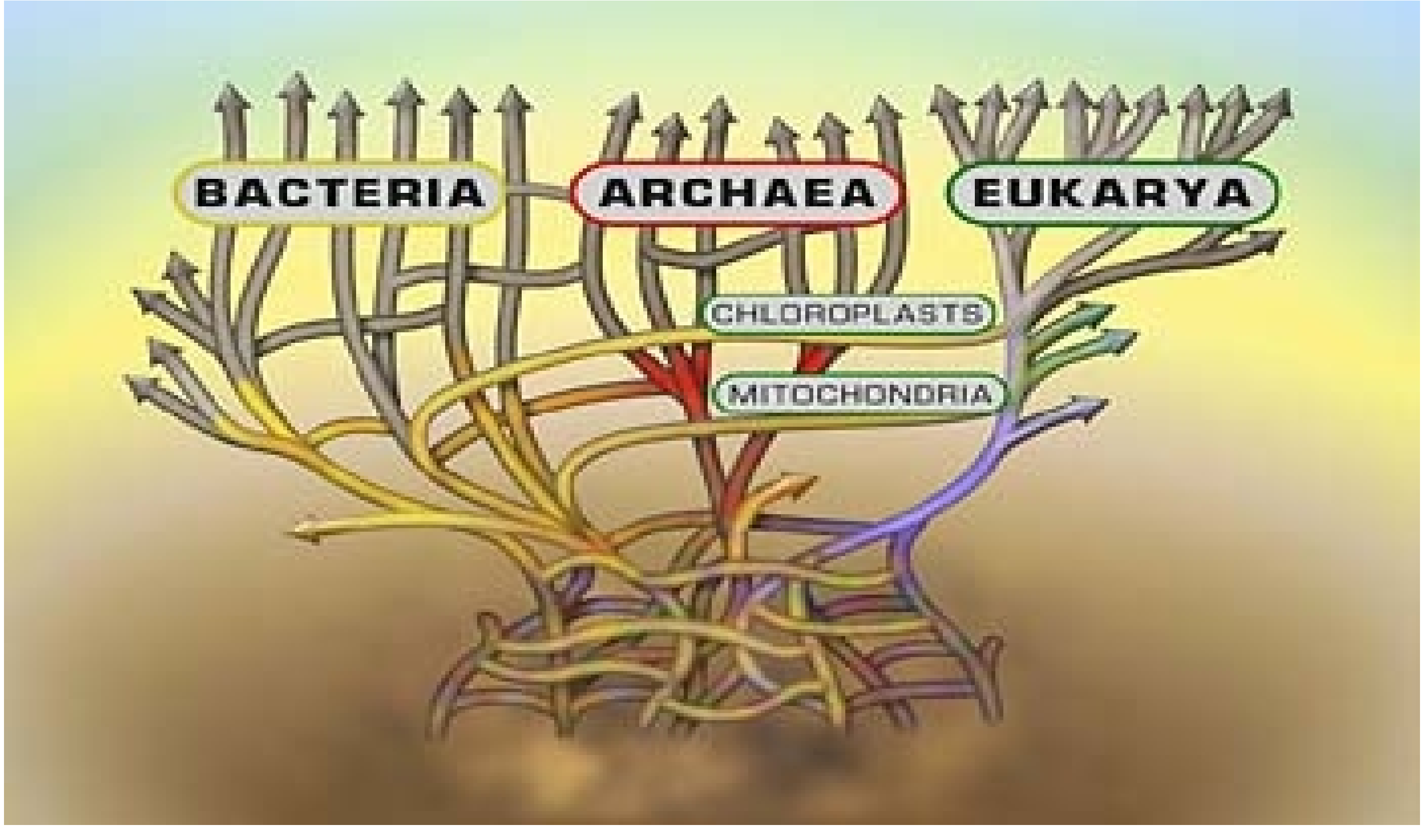
Siberia to Southeast Asia





Abi-Rached et al 2011 Nature

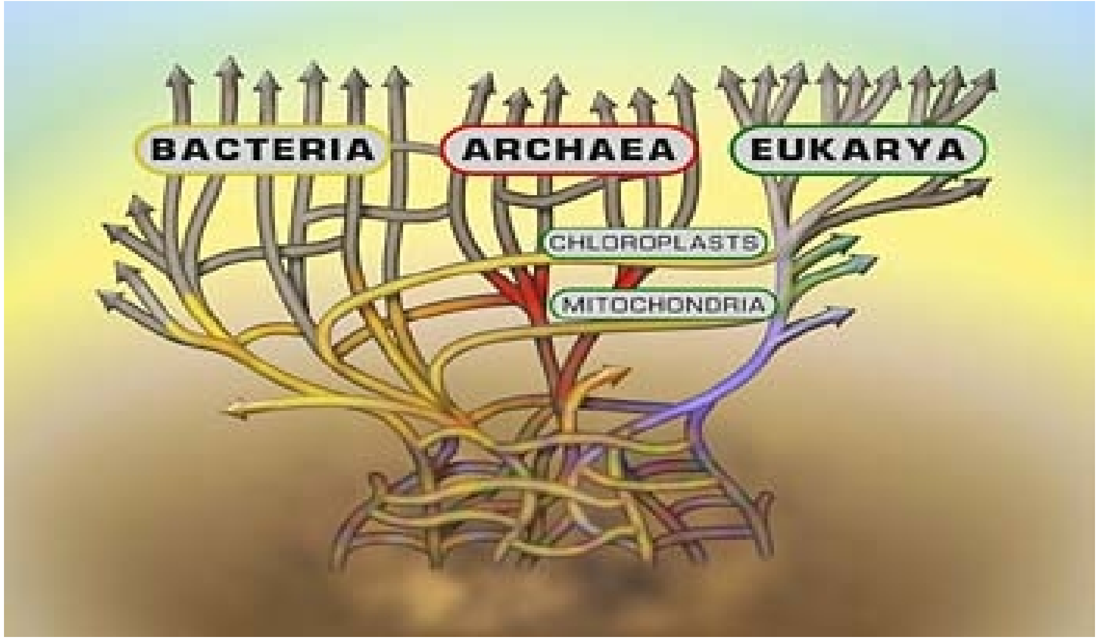
The tree of life is not a tree



Even more interconnections!

Exchange of metabolites throughout the tree of life

Arginine
Histidine
Isoleucine
Leucine
Lysine
Methionine
Phenylalanine
Threonine
Valine
Ascorbic acid (Vitamin C)
Biotin (Vitamin H)
Folic acid (Vitamin M)
Riboflavin (Vitamin B2)
Thiamine (Vitamine B1)
Cobalamin (Vitamin B12)

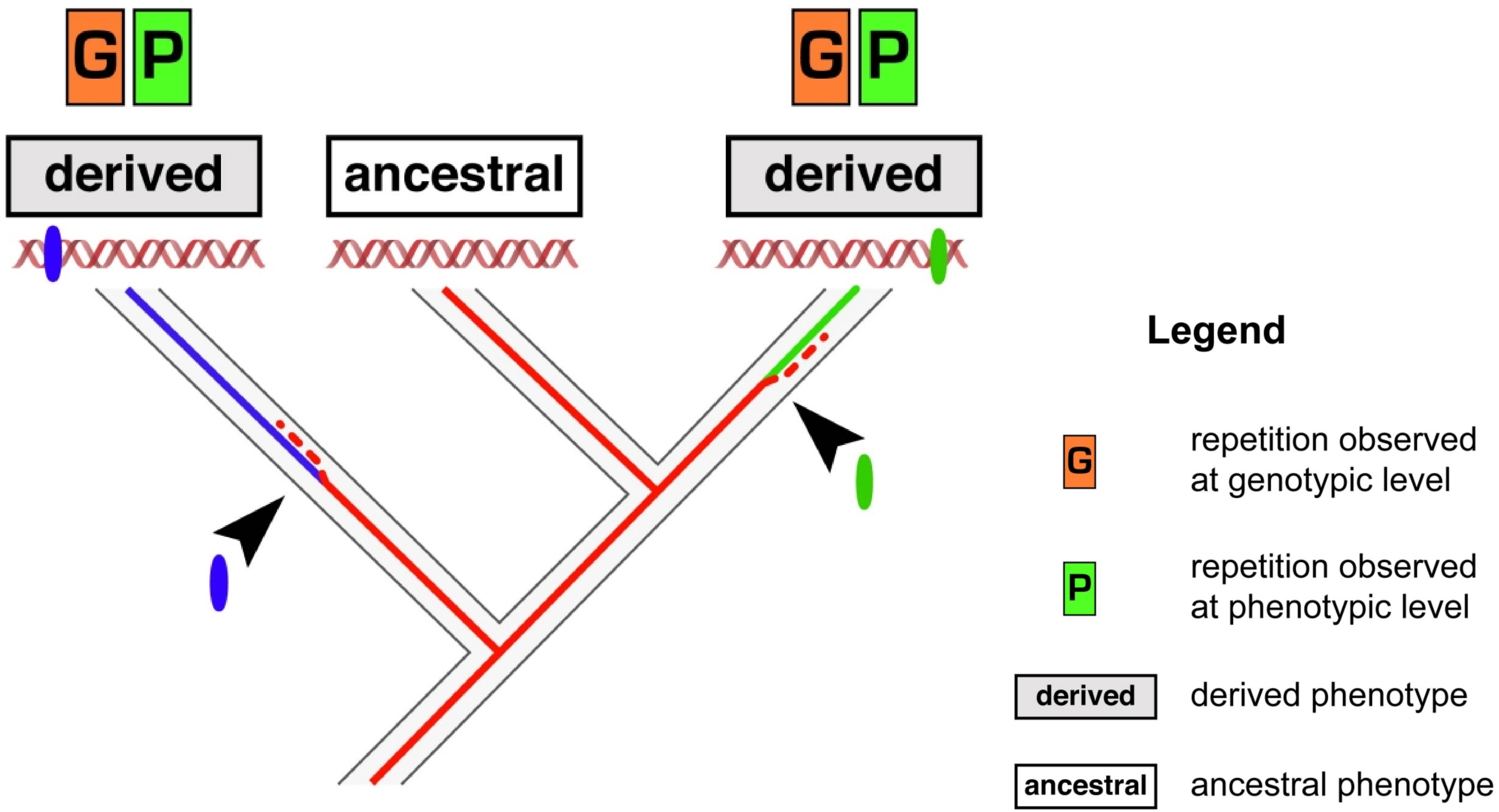


Even more interconnections!

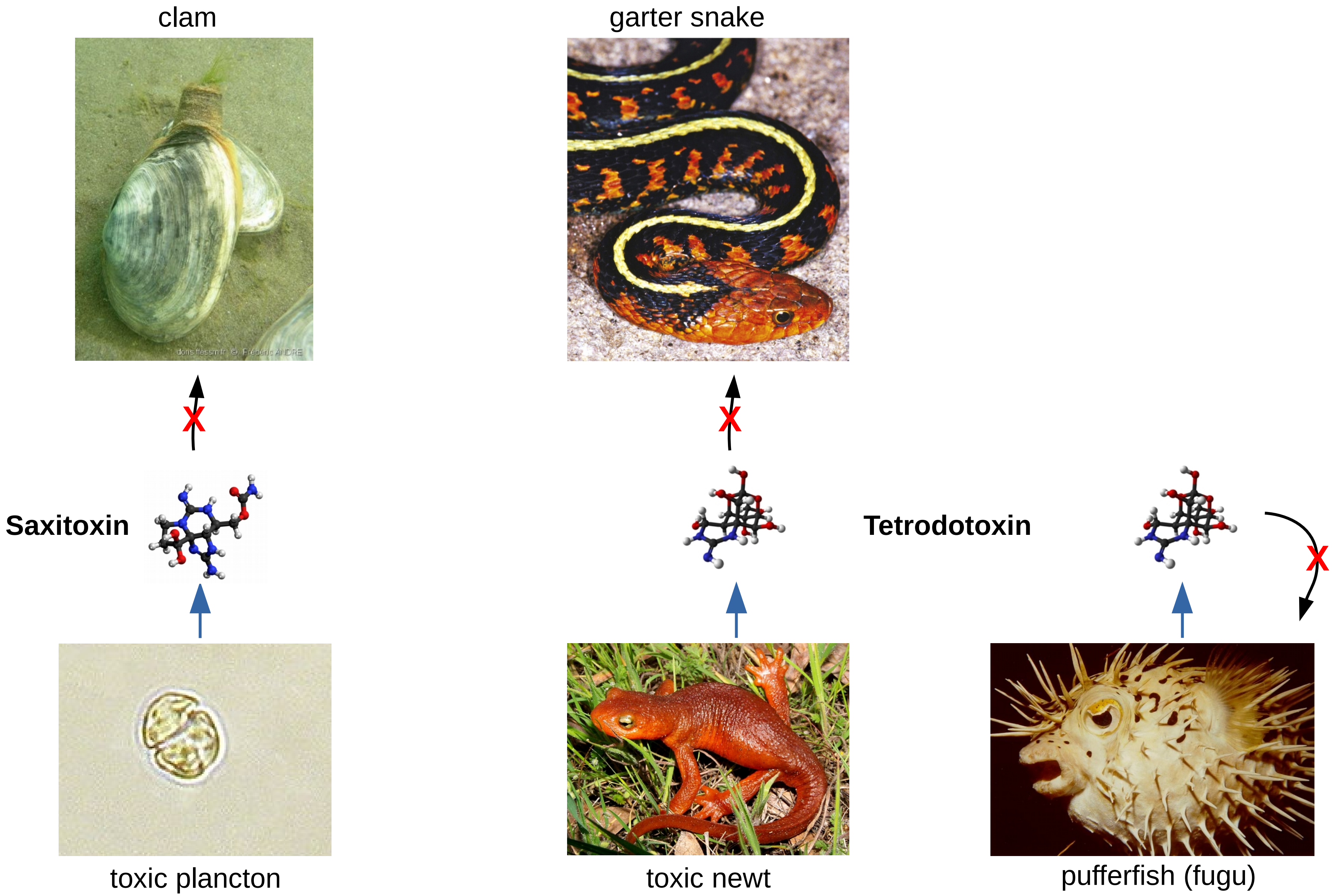
(Romero et al., 2005 Genome Biology)

Few genetic paths to evolution

Repeated evolution sensu stricto

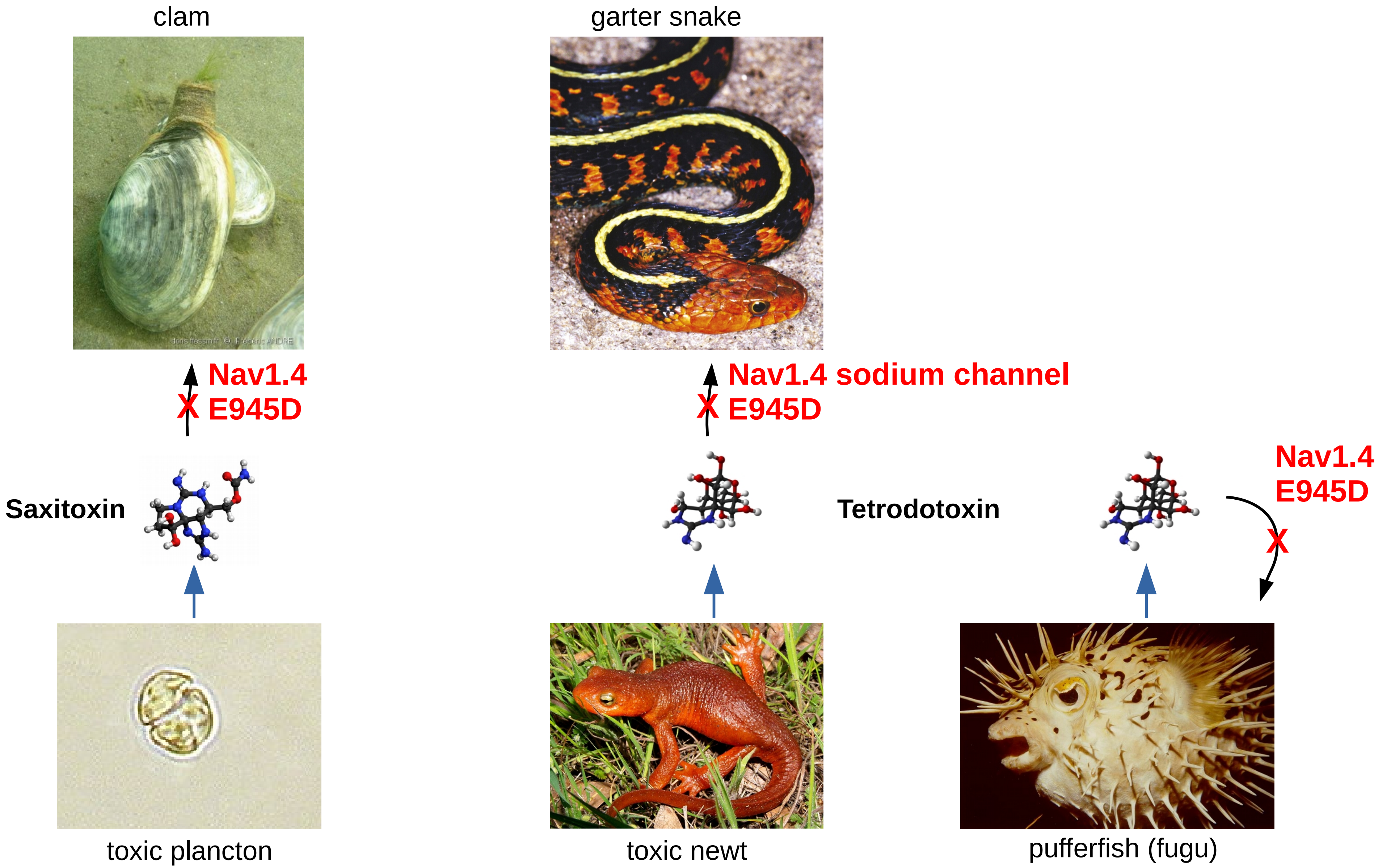


Repeated evolution



Bricelj 2005
Geffeney 2005
Venkatesh 2005

Repeated evolution via the same amino acid change



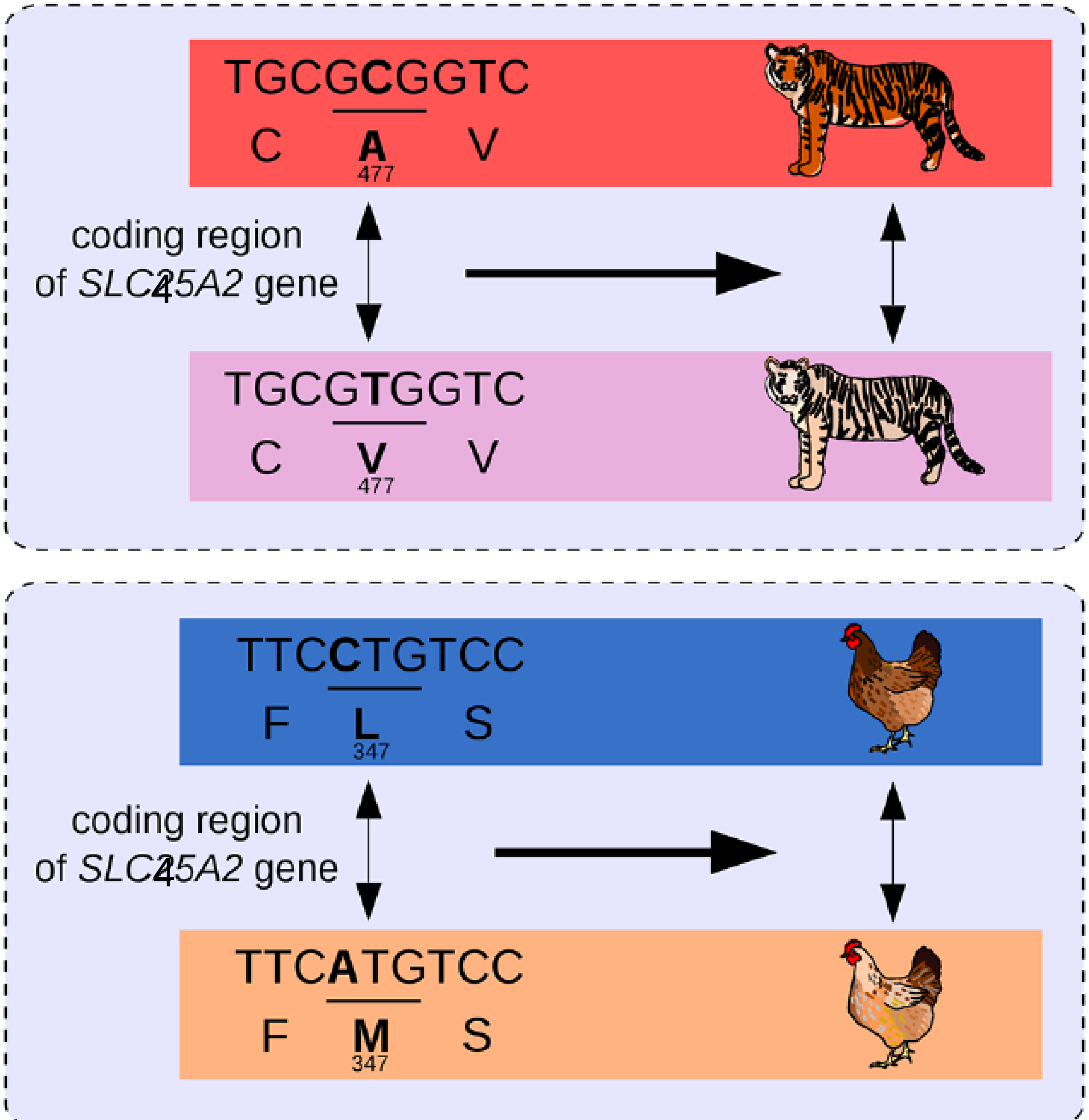
Bricelj 2005
Geffeney 2005
Venkatesh 2005

Repeated evolution via the same amino acid change

Locus	Mutation	Homoplastic lineages	Variation	Xenobiotic
Ace-1	Gly119Ser	5 (insects)	Intraspecific	Insecticides (organophosphorus)
ERG3	Trp205Stop	4 (yeast lines)	Experimental	Fungicide (nystatin)
ERG6	Gln44Stop Gly127Arg Tyr223Stop	3 (yeast lines) 4 (yeast lines) 4 (yeast lines)	Experimental	Fungicide (nystatin)
Esterase E3	Gly137Asp Trp251Leu/Ser	3 (flies) 2 (blowflies)	Intraspecific	Insecticides (diazinon) Insecticides (malathion)
Na,K-ATPase α	Asn122His Glu111Val Glu111Leu Iso315Val Thr797Ala	5 (insects) 3 (insects) 3 (insects) 2 (insects) 2 (insects)	Interspecific	Host plant toxins (cardenolides)
Nav1.4 channel	Glu945Asp Glu945Asp Glu945Asp	1 (pufferfish) 1 (snake) 1 (bivalve mollusk)	Interspecific Interspecific Intraspecific	Endogenous toxin (tetrodoxin) Salamander toxin (tetrodoxin) Plankton toxin (saxitoxin)
para (kdr)	Leu1014His Leu1014Phe Leu1014Ser Met918Thr Thr929Ile	2 (insects) 11 (insects) 2 (mosquitoes) 5 (insects) 3 (2 moths, 1 louse)	Intraspecific	Insecticides (pyrethroids)
Rdl	Ala302Gly Ala302Ser	3 (insects) 11 (insects)	Intraspecific	Insecticides (cyclodienes)
Vkorc1	Leu128Ser/Gln Tyr139Cys	3 (rodents) 2 (rodents)	Intraspecific	Pesticide (warfarin)

Resistance to xenobiotics

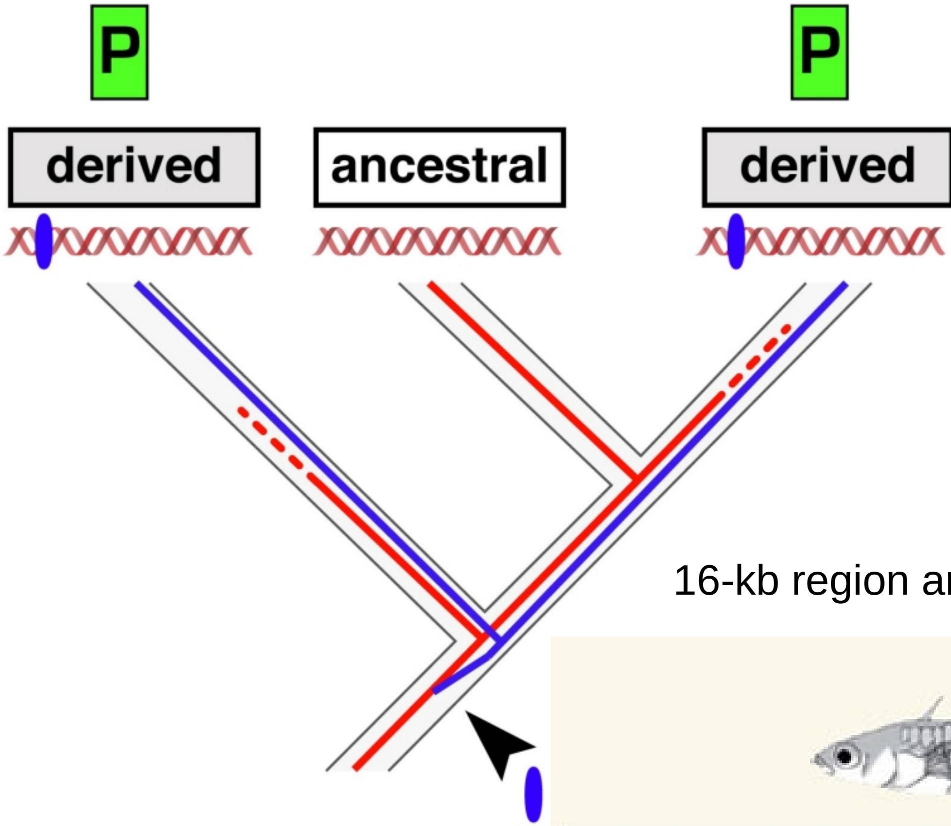
Repeated evolution



Also in:
Humans
Horses
Quails
Chickens
Mice
Pigeons

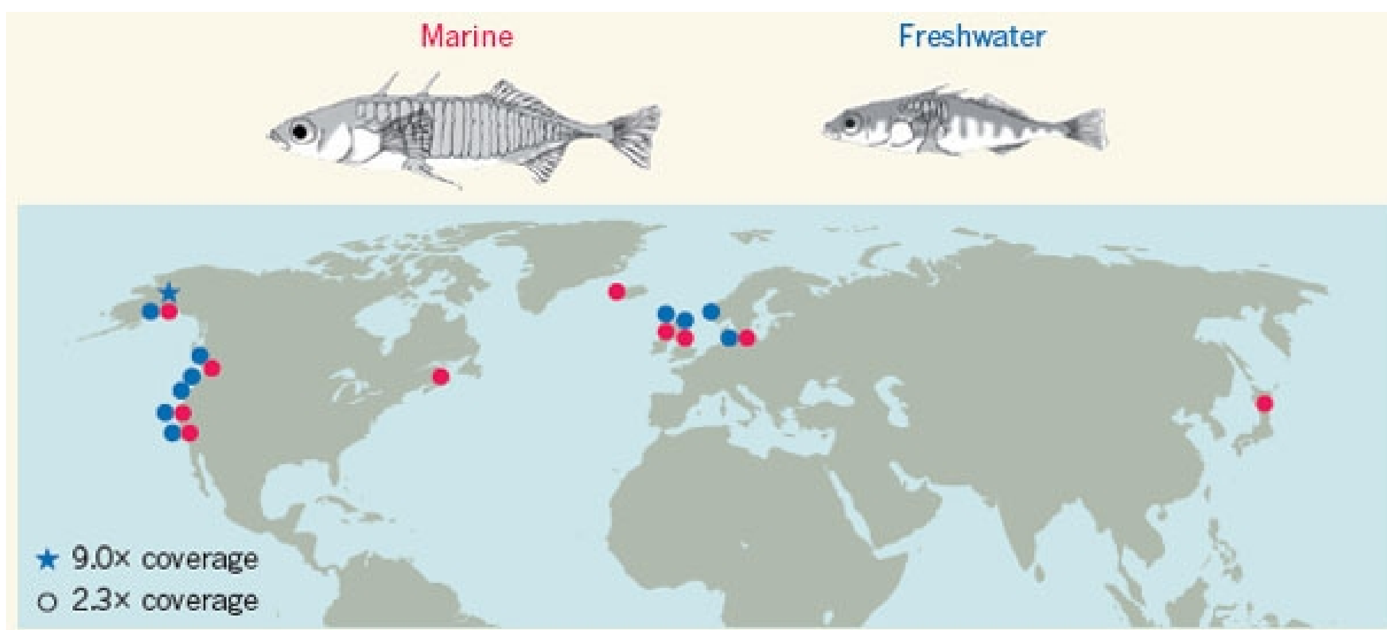
Orgogozo et al 2015 Frontiers Genetics

Repeated evolution via ancestral polymorphisms

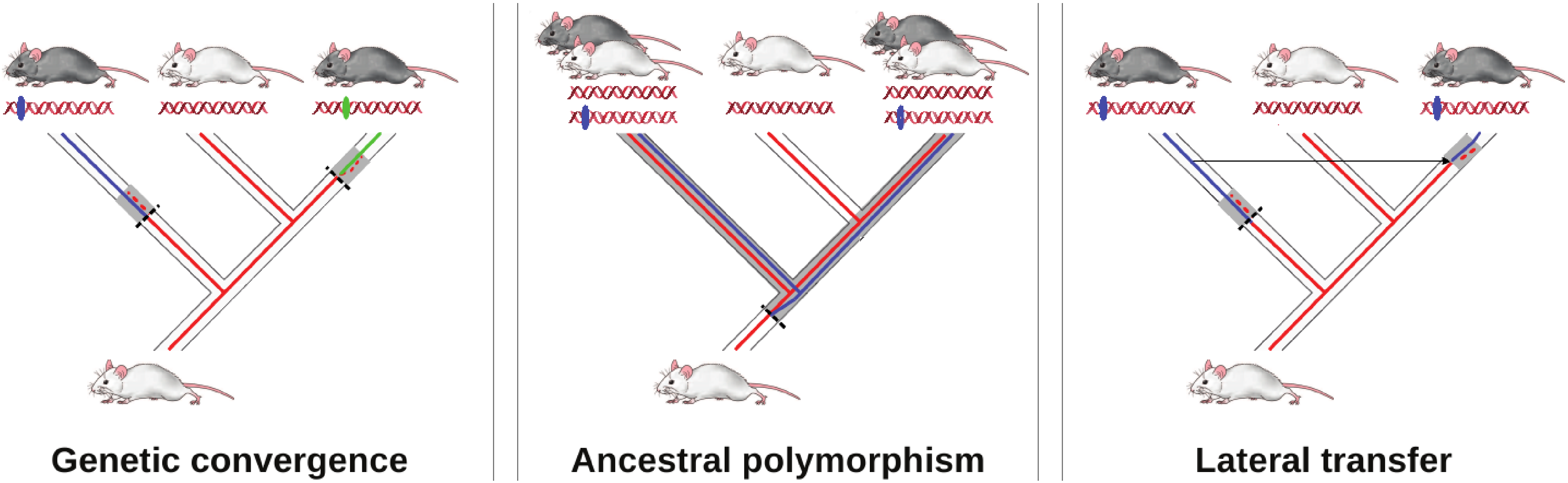


Incomplete lineage sorting
Standing genetic variation

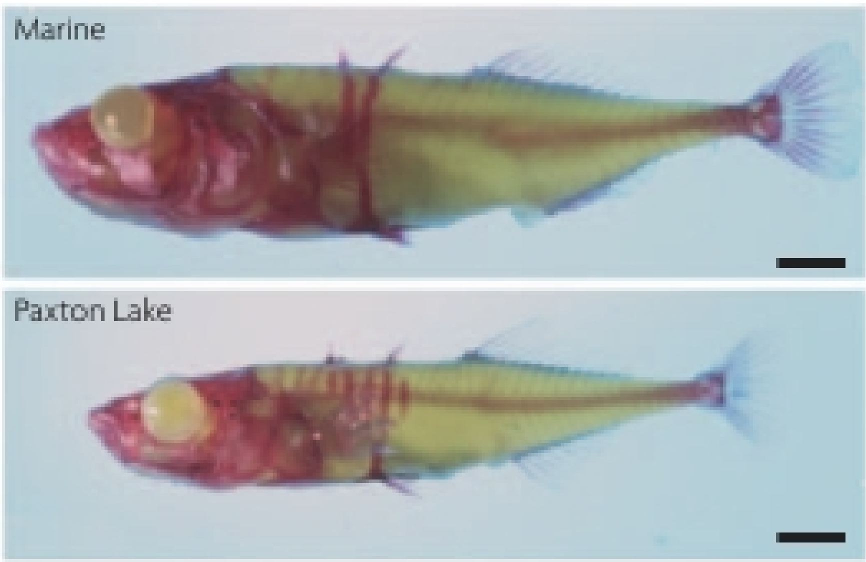
16-kb region around *Eda* shared by all freshwater fishes

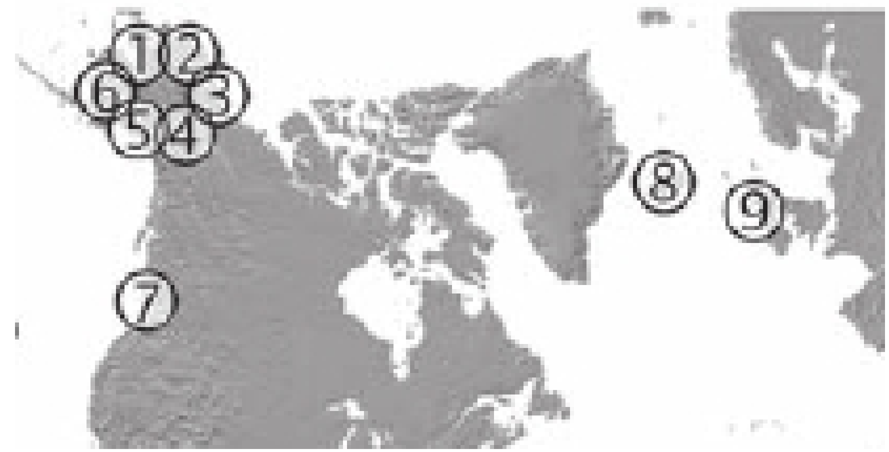


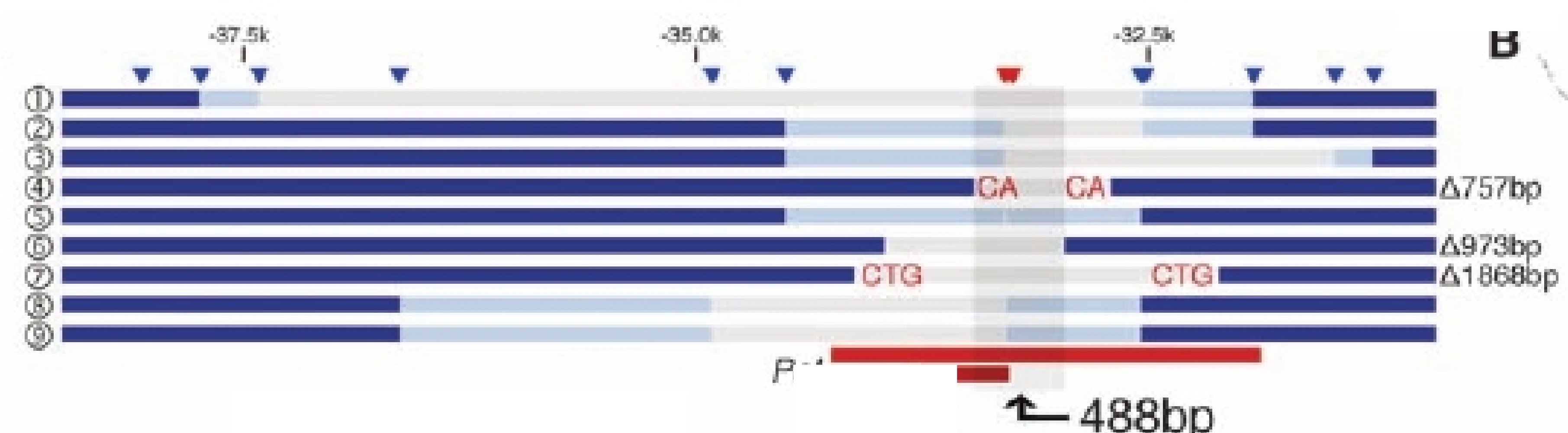
Armor plate
(Colosimo 2005
Jones 2012)


Genetic convergence
Ancestral polymorphism
Lateral transfer

9 independent deletions in the cis-regulatory region of *Pitx1*

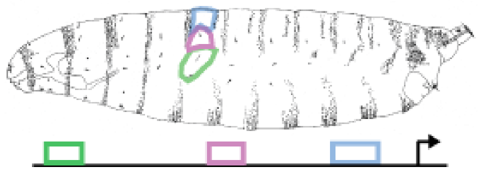






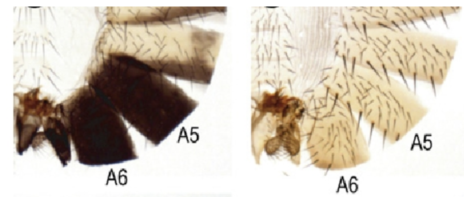
Accumulation of evolutionary-relevant mutations at the same locus

≥ 6 mutations in *svb*



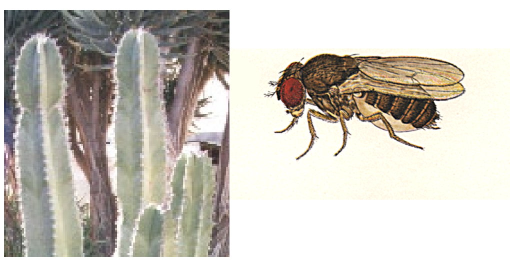
(McGregor, Orgogozo et al. 2007 Nature)

3 mutations in *tan*



(Jeong et al., 2008 Cell)

2-4 mutations in *nvd*

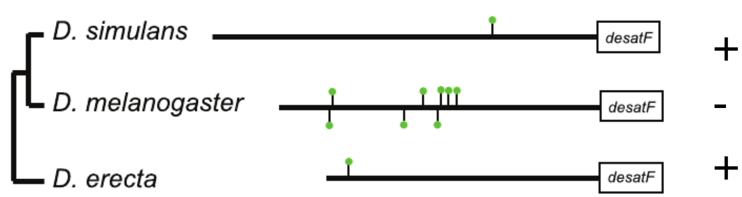


(Lang et al. 2012 Science)

5 mutations in *ebony*

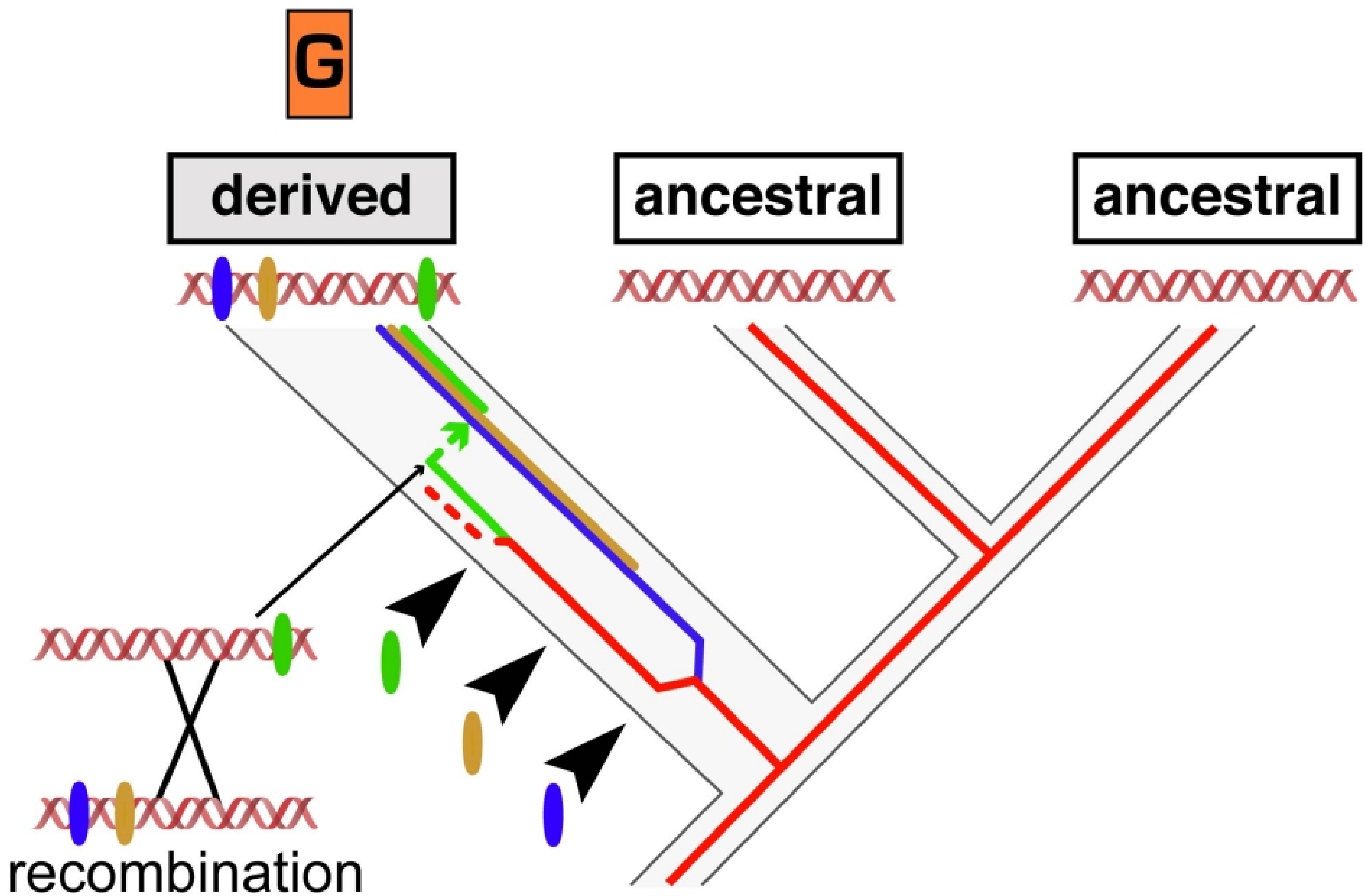
(Rebeiz et al., 2009 Cell)

3 deletions in *desatF*

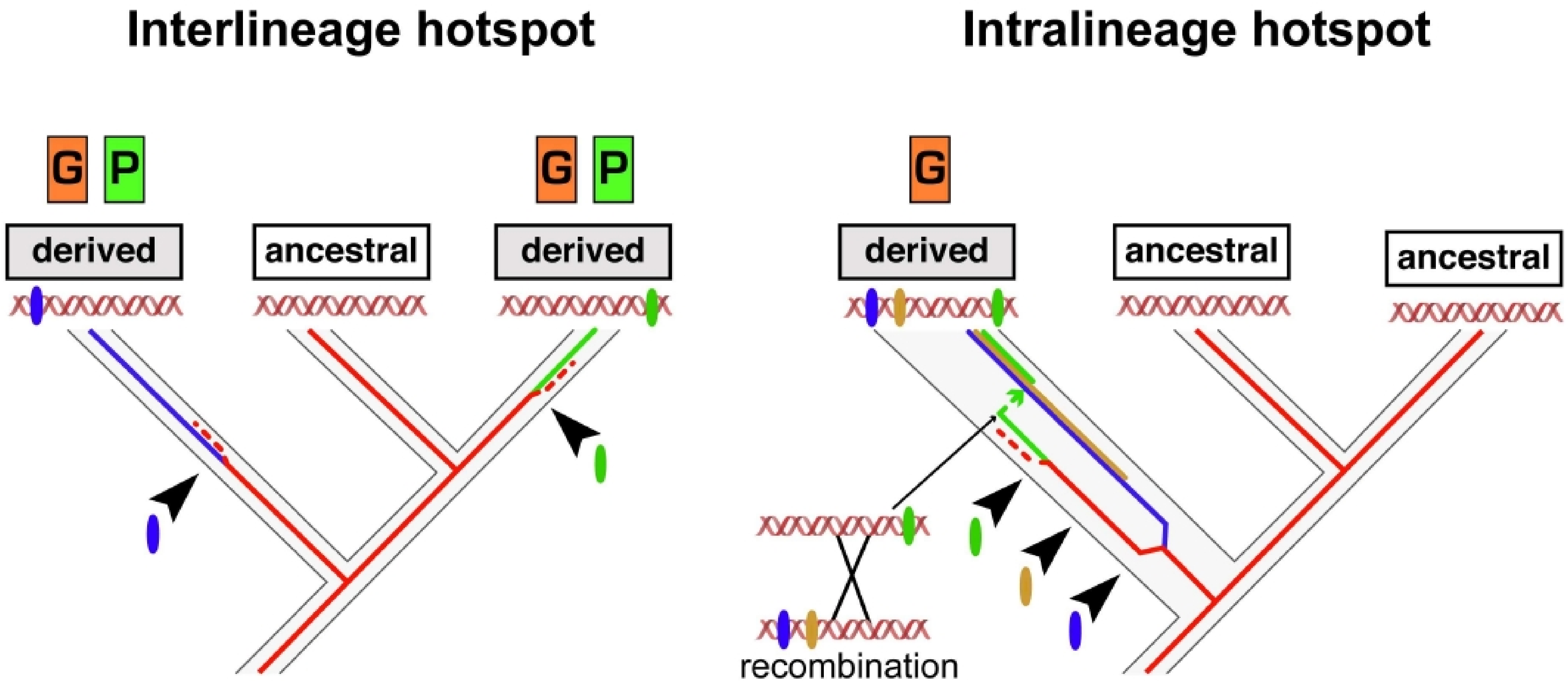


(Shirangi et al., 2009 PloS Biol)

Intralineage hotspot



Hotspot genes: preferred targets of evolution



Martin and Orgogozo,2013

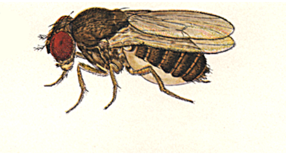
Why is the set of genetic paths limited?

There are specialized genes in a genome

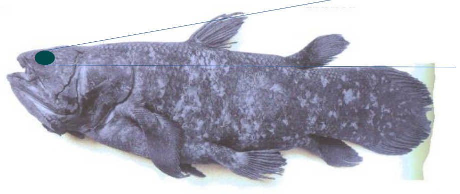
Steroid hormone biosynthesis

a specialized tissue
specialized enzymes

2-4 mutations in *nvd*



Color vision



a specialized tissue
specialized molecules

mutations in *opsin* genes

Hypoxia resistance

a specialized tissue
specialized molecules

mutations in *haemoglobin* genes

McCracken 2009

Specialized genes are usually genes that interact with external parameters

Why is the set of genetic paths limited?

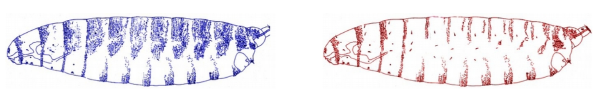
genes with specialized functions

But what about phenotypes involving multifunctional genes?

Evolution appears to use a restricted set of all possible paths

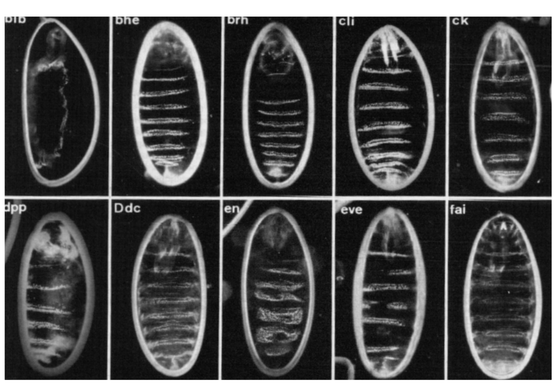
Changes in trichome pattern

EVOLUTION



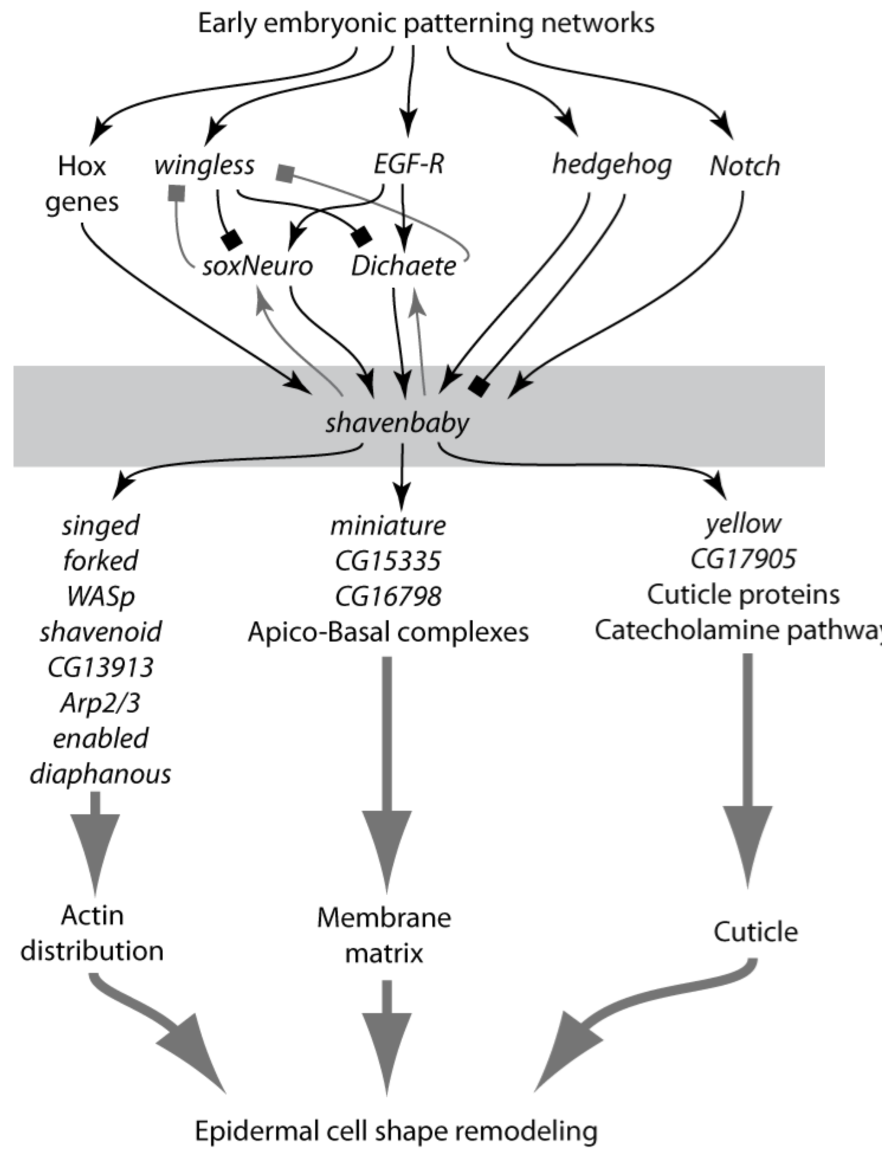
A single gene

MUTAGENESIS



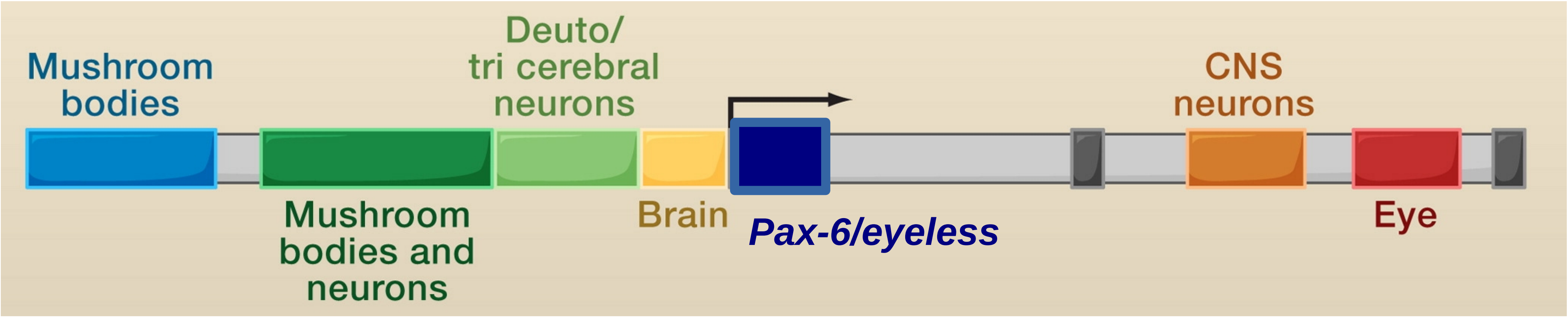
(Nüsslein-Volhard et Weischaus)

~100 genes



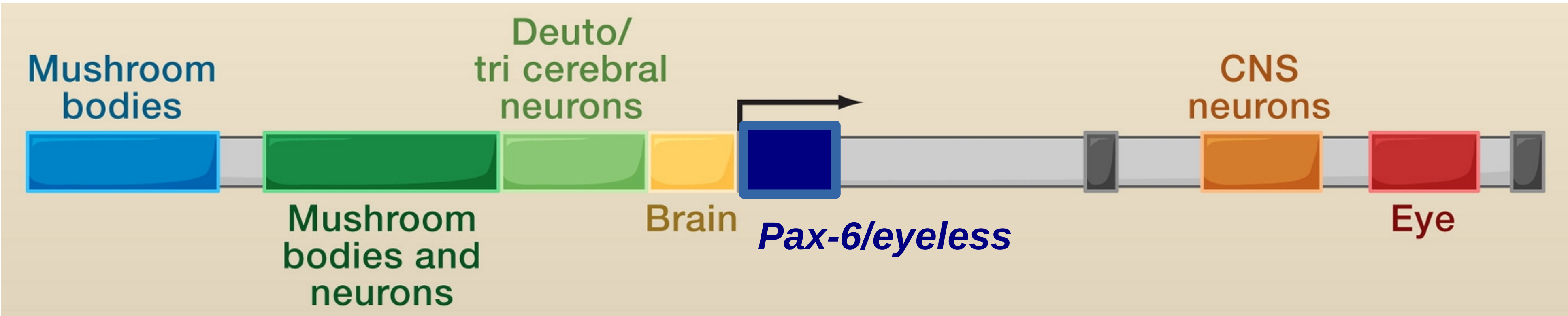
(Stern et Orgogozo, 2008 Evolution – Stern et Orgogozo, 2009 Science)

Specialized loci within multifunctional genes



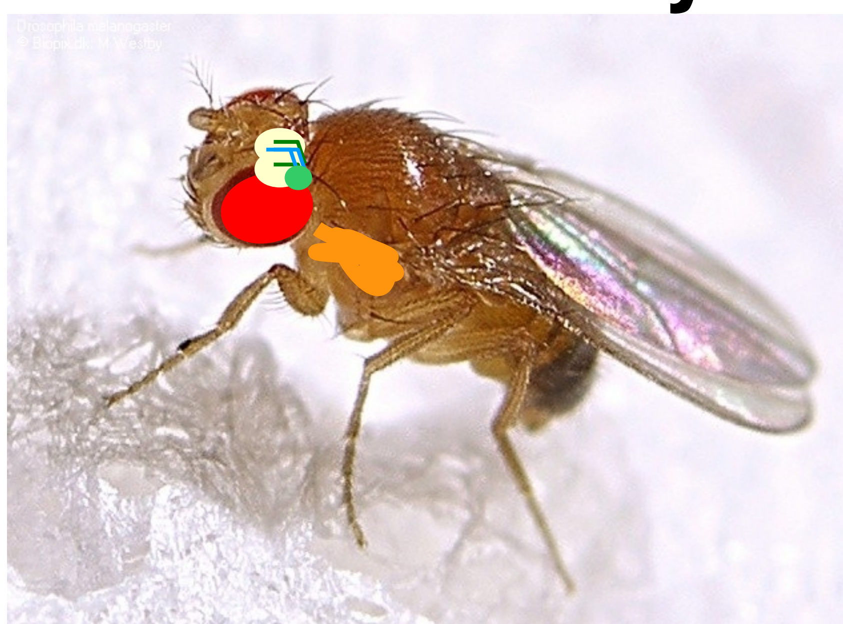
Carroll 2008

Specialized loci within multifunctional genes



Carroll 2008

Modularity of cis-regulatory elements is reflected in modularity of body parts



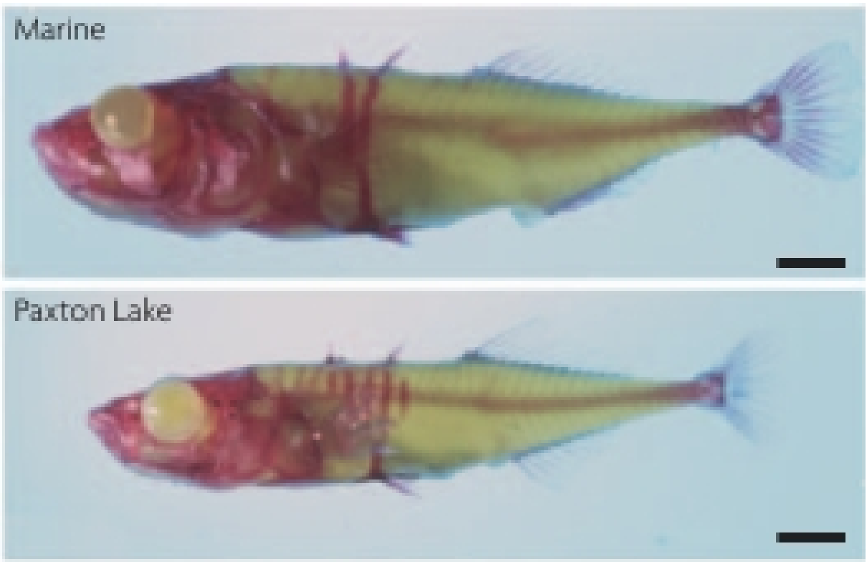
Why is the set of genetic paths limited?

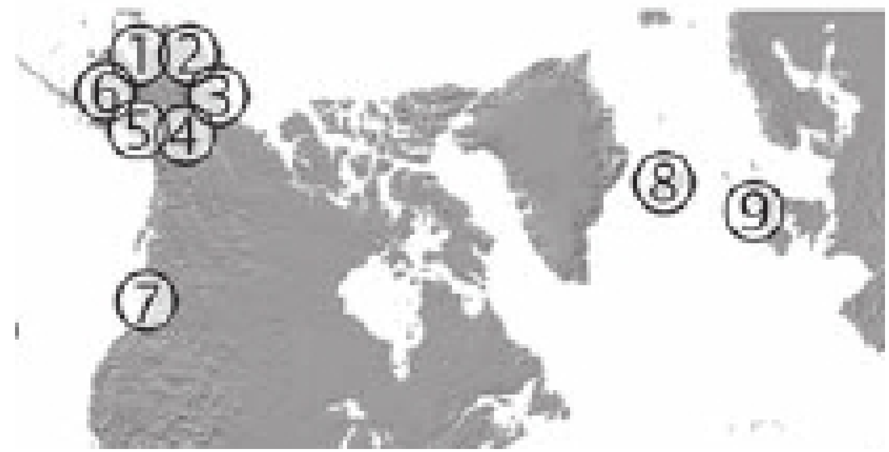
genes with specialized functions

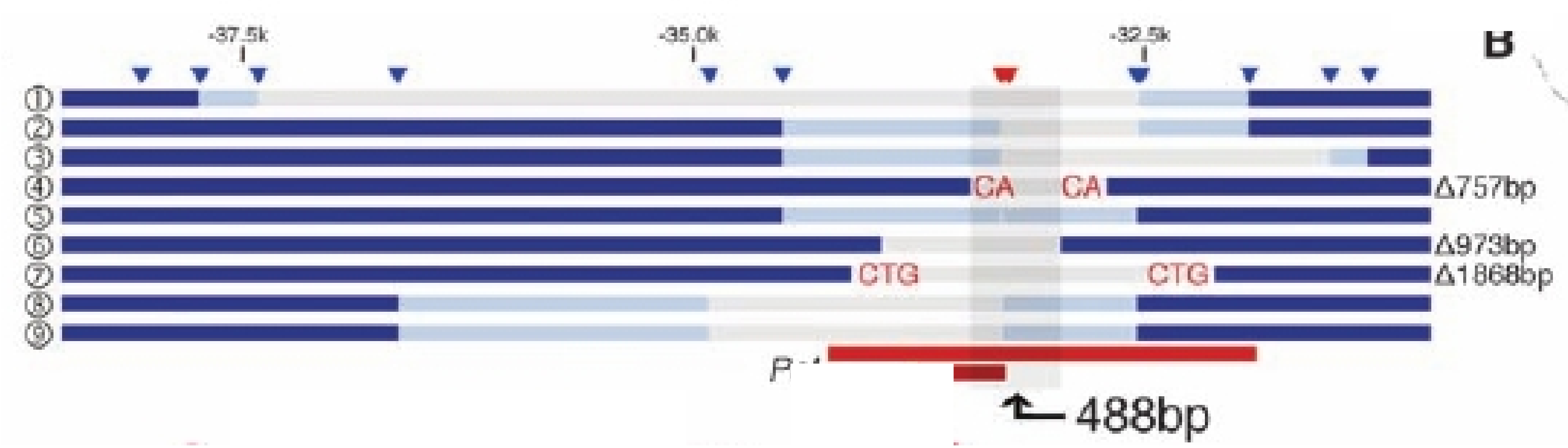
multifunctional genes with specialized regions

mutational bias

9 deletions in the cis-regulatory region of *Pitx1* *due to region sensitive to chromosome breaks*







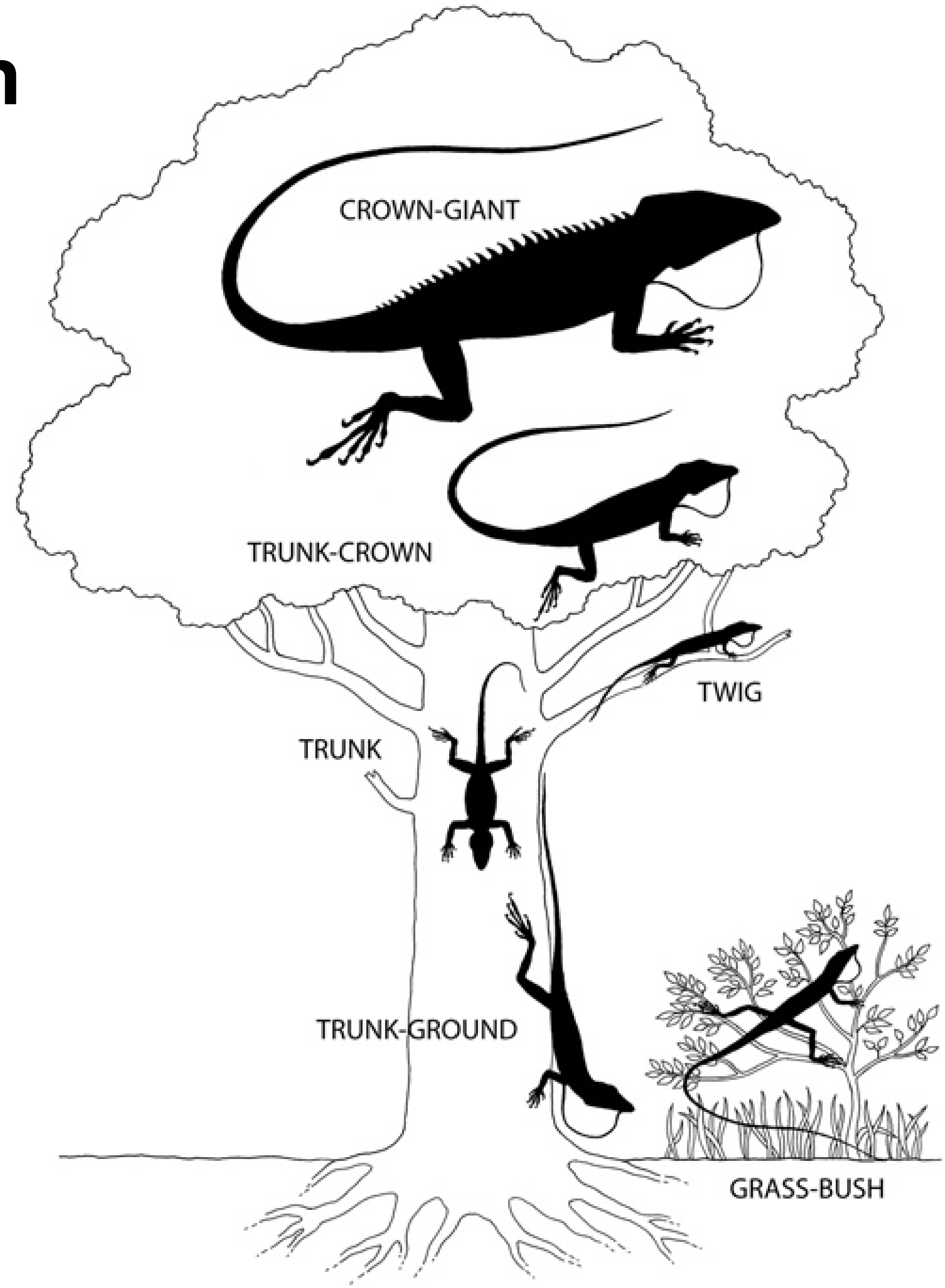
Why is the set of genetic paths limited?

genes with specialized functions

multifunctional genes with specialized regions

mutational bias

Repeated evolution in diverse Caribbean islands



Evolution repeats itself in..

.. the genes responsible for natural evolution

Ex : *hemoglobin* in dogs and humans in Tibet
(Wang et al 2014 GBE)

.. the genes responsible for experimental evolution

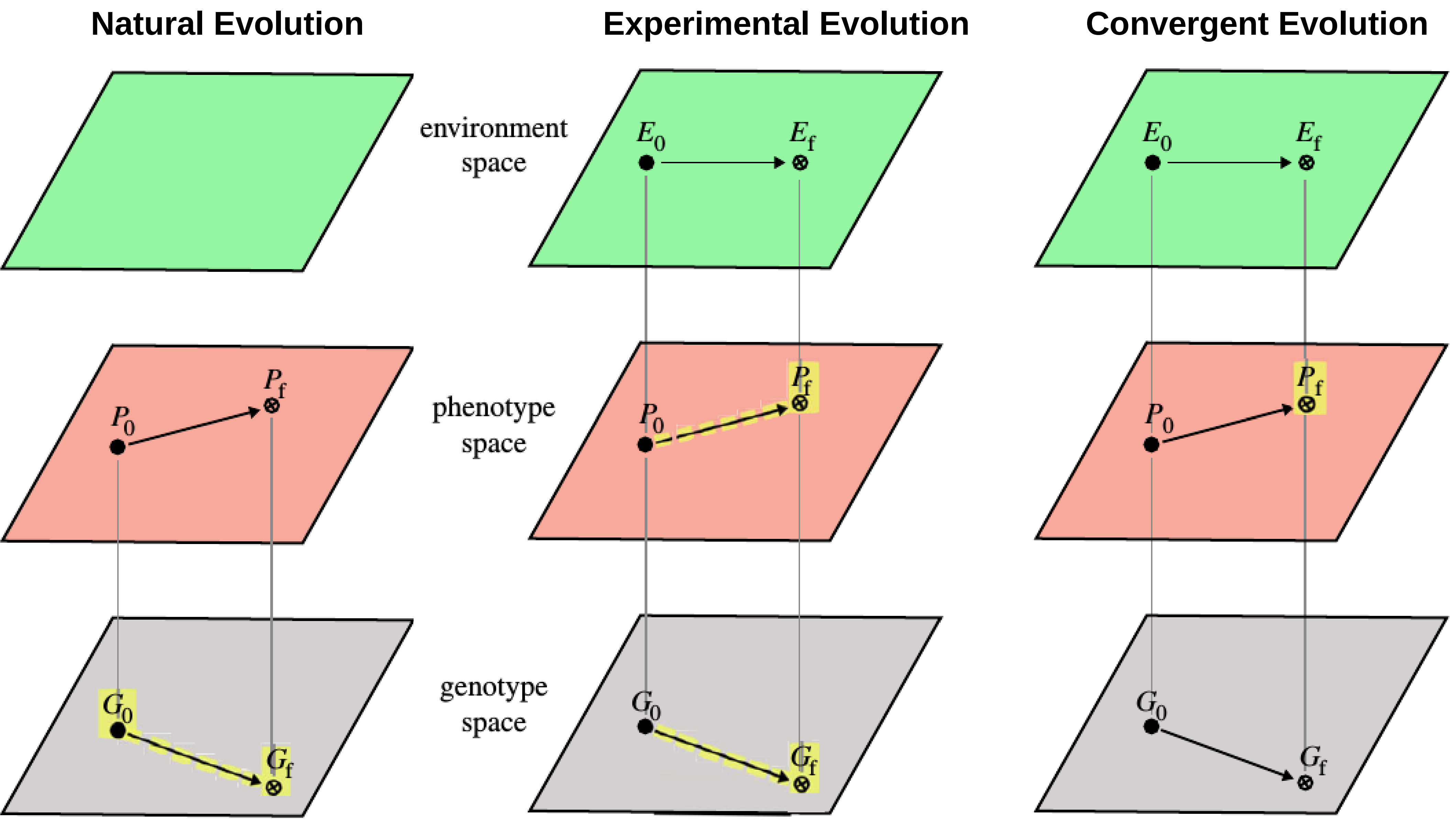
Ex : *sulfate transporter SUL1* in yeasts in low sulfate
(Gresham et al 2008 PloS Genetics)

.. the phenotypes evolving in certain environments

Ex : flying marsupial phalanger and placental flying squirrel

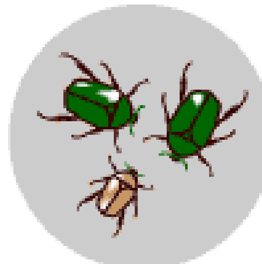
Orgogozo 2015 Interface Focus

Synchronous predictability



Classical Darwinian Evolution

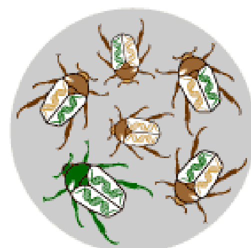
1
Variation



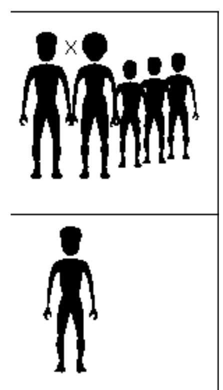
UNPREDICTABLE

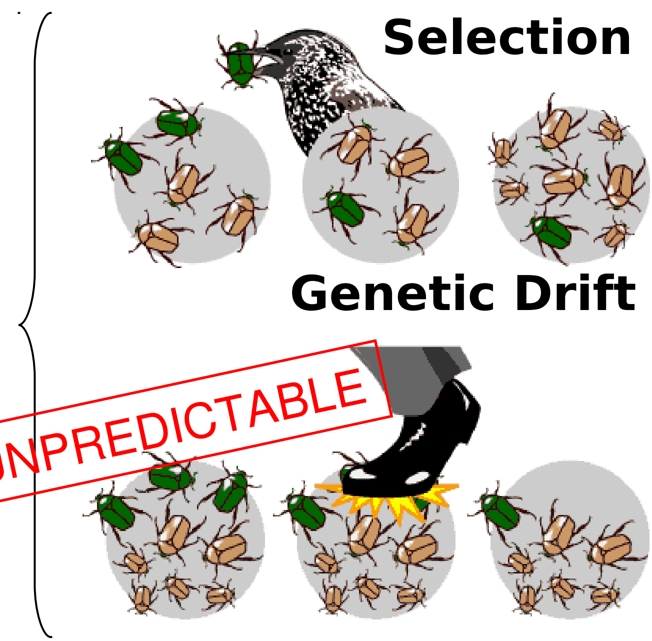
Mutations in DNA

2
Transmission to the next generation



3
Reproduction Variability between individuals





http://evolution.berkeley.edu

Many unpredictable processes
at a low level

?
→

Predictable Evolution
at the genetic level

Mutations in DNA
Chromosome segregation during meiosis
Assortative mating
Gamete competition during fecondation
Life history traits
Genetic linkage
Environmental changes (meteorite, etc.)
...

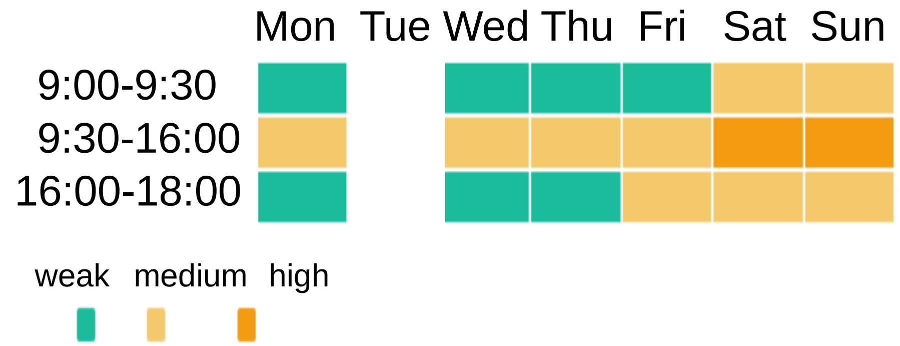
From random processes can emerge predictability

Many unpredictable processes
at a low level

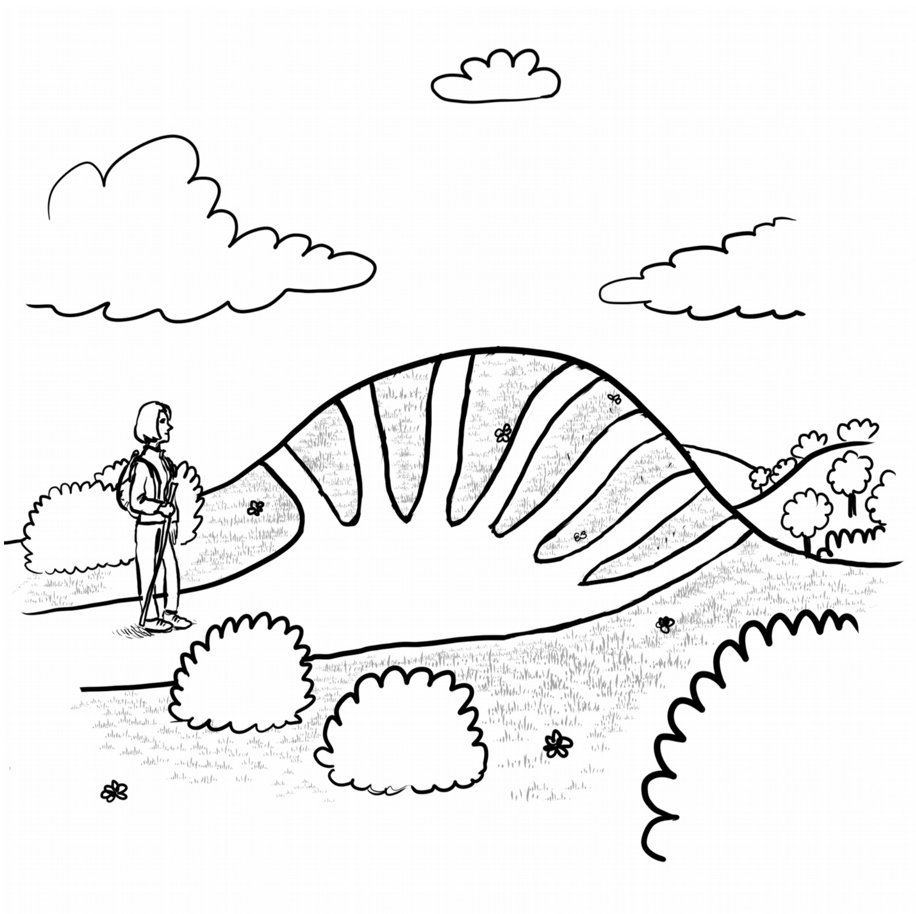
Predictable
at a higher level

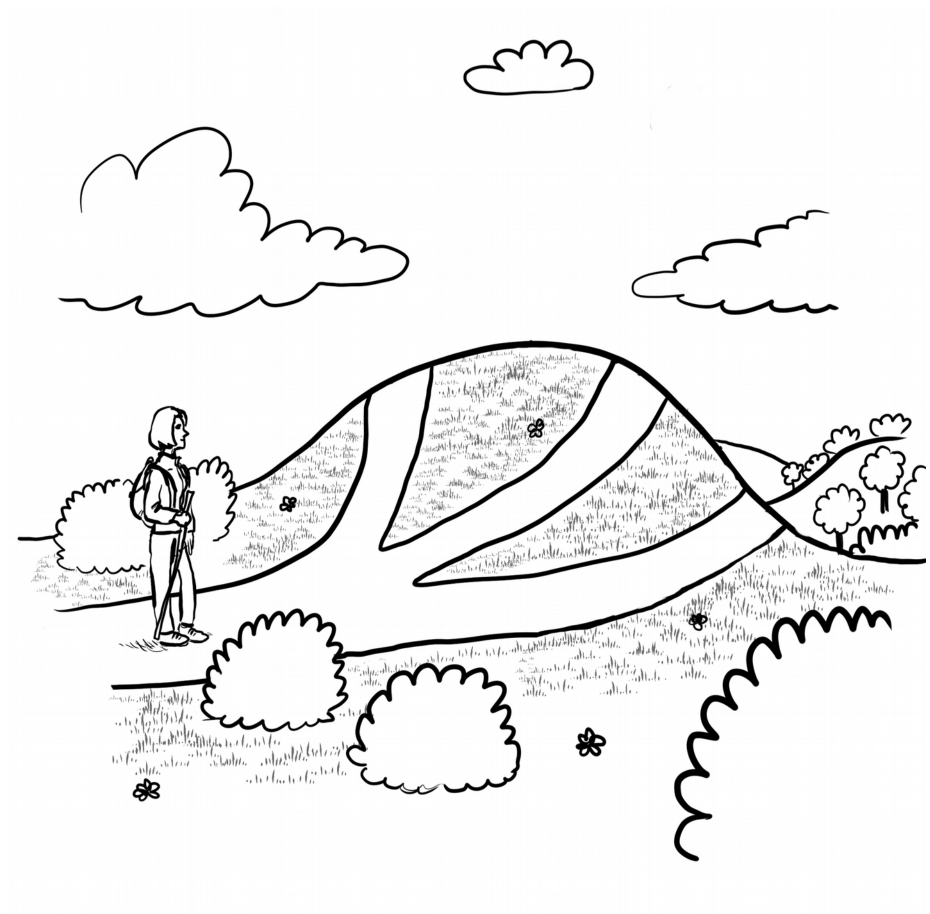
Trajectory of single individuals

Estimated waiting time for Louvre museum



The number of possible paths for evolution is smaller than previously thought





What are all the possible evolutionary paths?

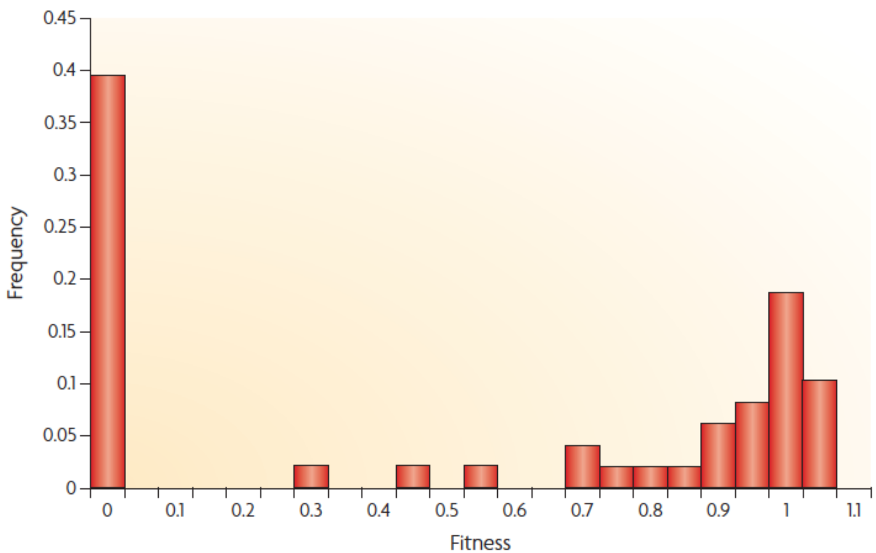
evolution

- **How?**
- **Why?** (1) rather than nothing
- **Why?** (2) rather than another change

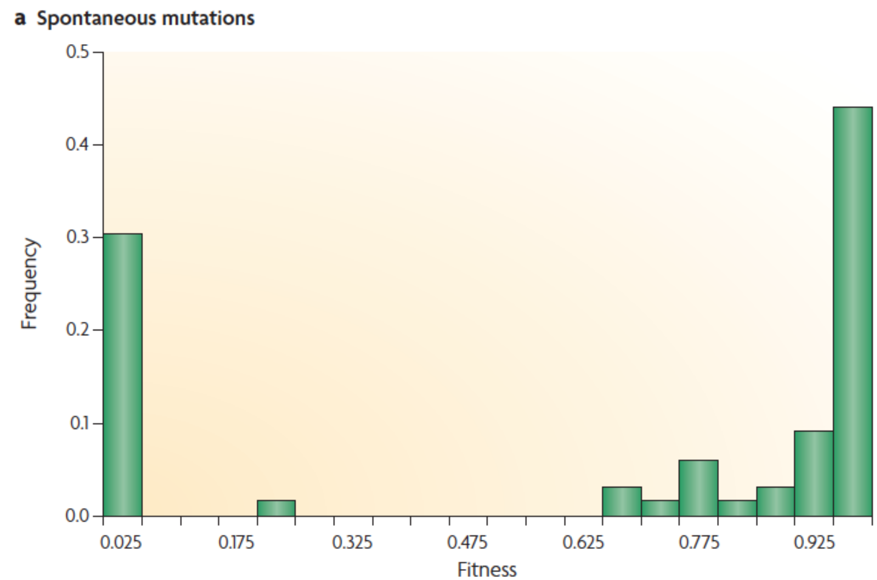
Test all possible paths:

Examine all possible mutations in a protein sequence, in a cis-regulatory sequence, etc.

Mostly deleterious and neutral mutations



Vesicular Stomatitis Virus



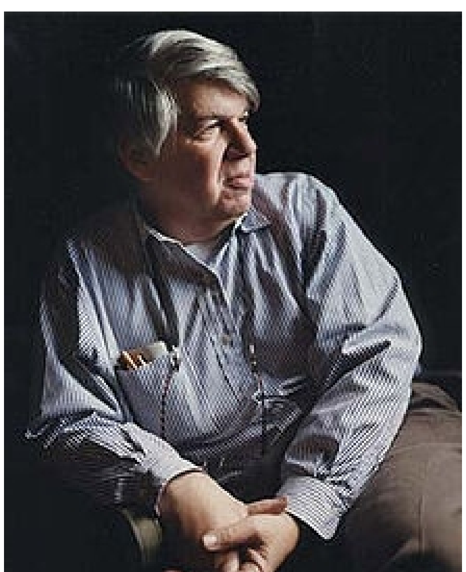
Saccharomyces cerevisiae diploids

Eyre-Walker and Keightley *NRG* 2007

Evolution: unconstrained and unpredictable?

[past and present organisms are] a subset of workable, but basically fortuitous, survivals among a much larger set that could have functioned just as well, but either never arose, or lost their opportunities, by historical happenstance.

Stephen Jay Gould, 2002

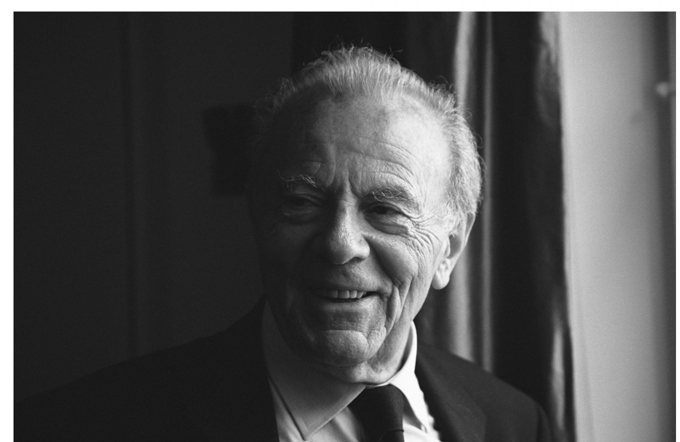


It is hard to realize that the living world as we know it is just one among many possibilities; that its actual structure results from the history of the earth.

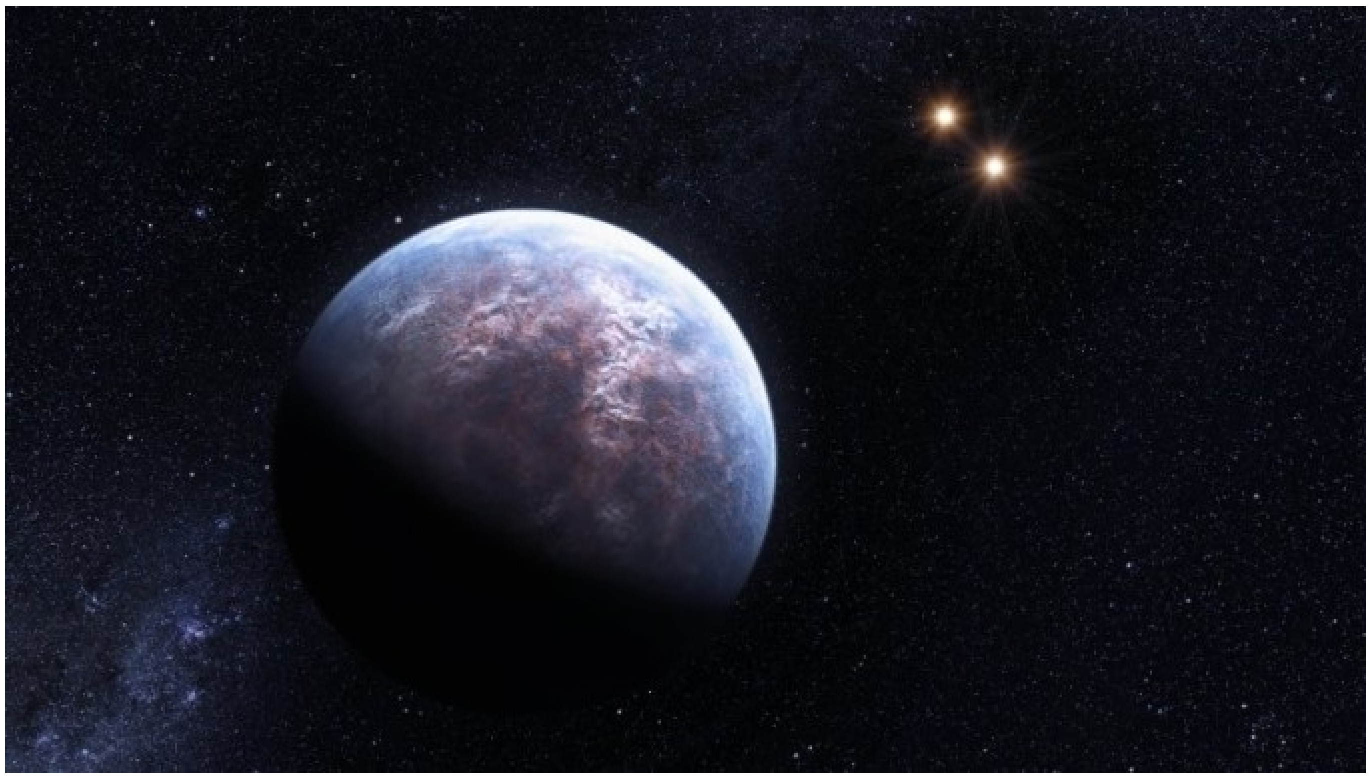
1977

Evolution and Tinkering

François Jacob

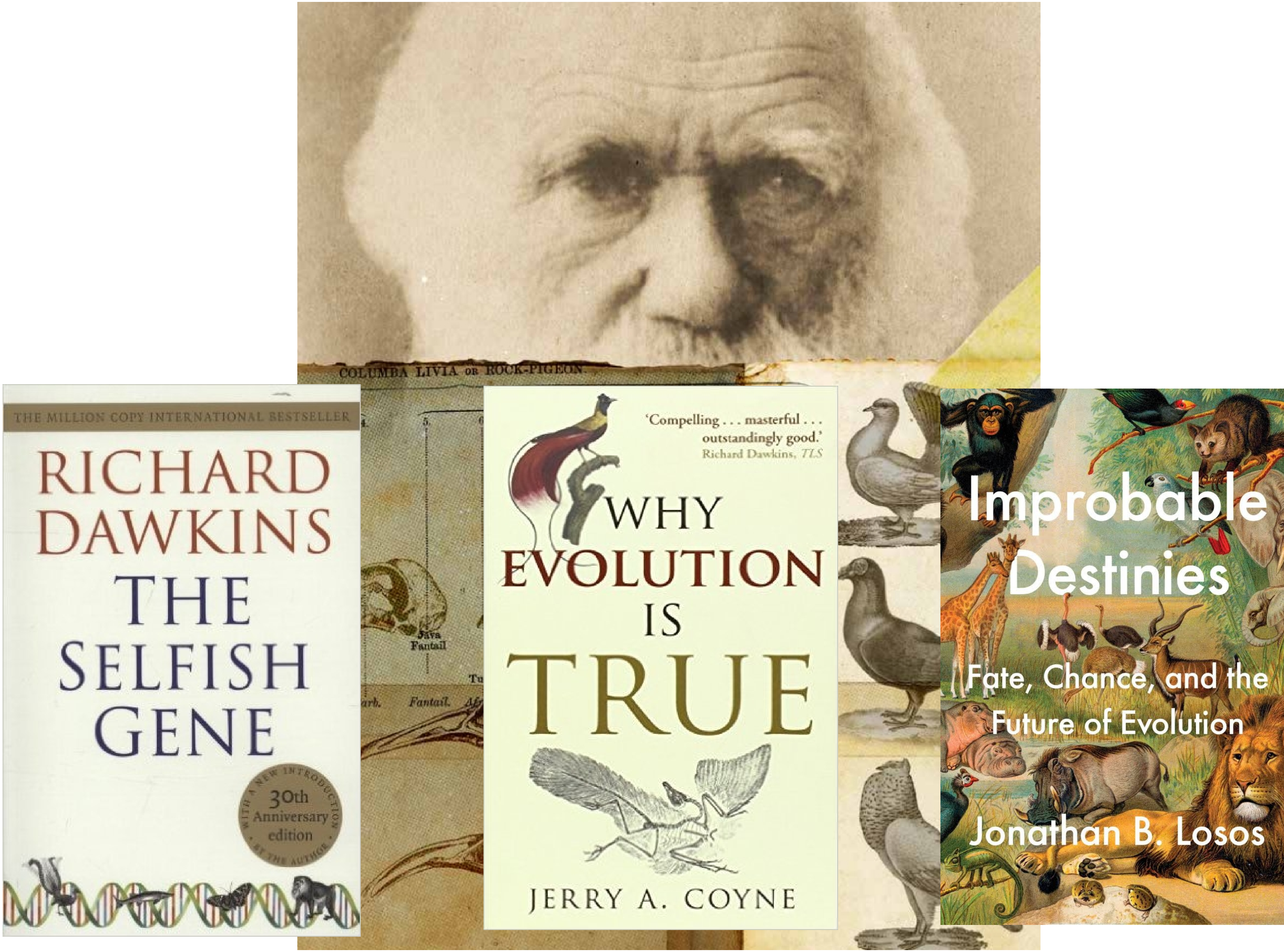


Would life evolve again, would it produce similar living beings?



evolution

- **How?**
- **Why?** (1) rather than nothing
- **Why?** (2) rather than another change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