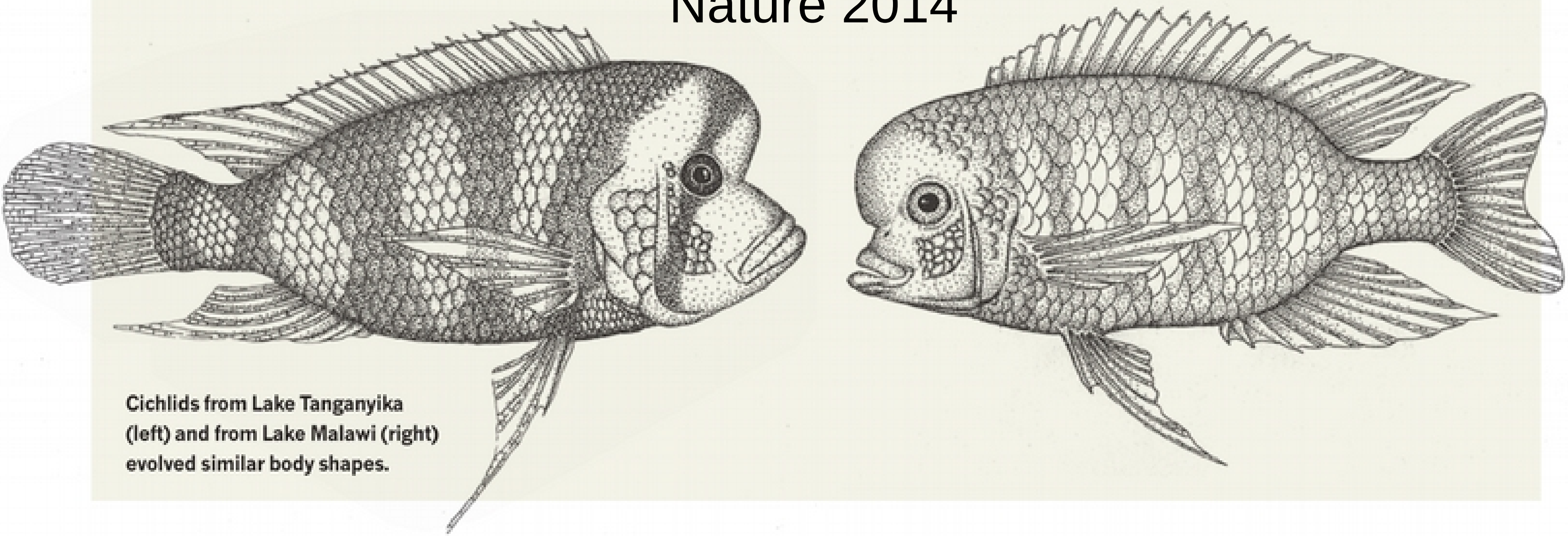
Relations génotype-phénotype et Evolution

Virginie COURTIER-ORGOGOZO

ROBUST

Nature 2014



Cichlids from Lake Tanganyika (left) and from Lake Malawi (right) evolved similar body shapes.

Does evolutionary theory need a rethink?

Researchers are divided over what processes should be considered fundamental.

POINT

Yes, urgently

Without an extended evolutionary framework, the theory neglects key processes, say Kevin Laland *and colleagues.*

COUNTERPOINT

No, all is well

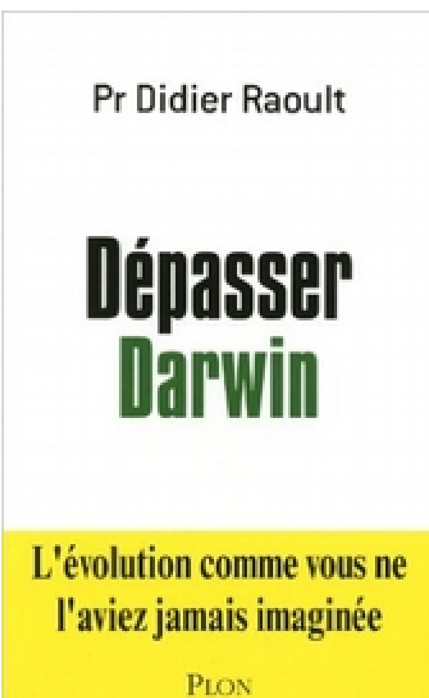
Theory accommodates evidence through relentless synthesis, say Gregory A. Wray, Hopi E. Hoekstra *and colleagues.*

Le Point, Décembre 2016

Didier Raoult dénigre la théorie de l'évolution

Actuellement, la théorie la plus castratrice en science est celle de Charles Darwin, car elle empêche une réanalyse des données contemporaines. C'est juste une théorie de WASP (Anglo-Saxons protestants blancs), ceux qui dominaient le Royaume-Uni

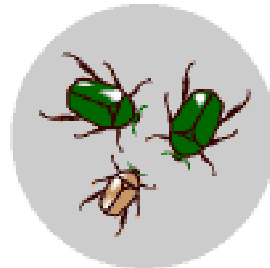
Enfin, Darwin définit la sélection naturelle par analogie à la sélection humaine. Il pense que la nature agit pour trier les espèces comme les hommes l'ont fait pour le bétail, les poules, les chevaux, les chiens et les chats, choisissant les « étalons » les plus capables et ségréguant progressivement les caractères. Mais la nature ne fonctionne pas ainsi, la plupart des évolutions résultent de sélections multiples dues au hasard, les plus capables à un instant ne seront pas les plus fertiles ni les plus performants à l'avenir. Le tri se fait souvent par catastrophe. La nature se développe aussi par imitation et par adaptation à l'environnement, et cette acquisition de compétences est transmissible. C'est ce



Classical Darwinian Evolution

1

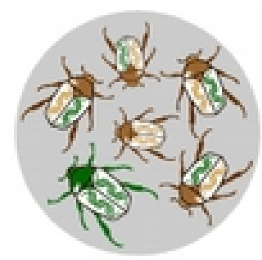
Variation



Mutations de l'ADN

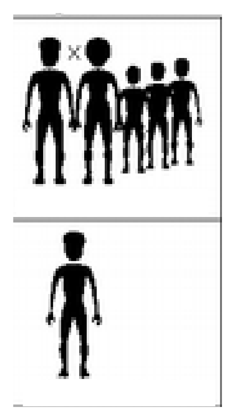
2

Transmission à la génération suivante



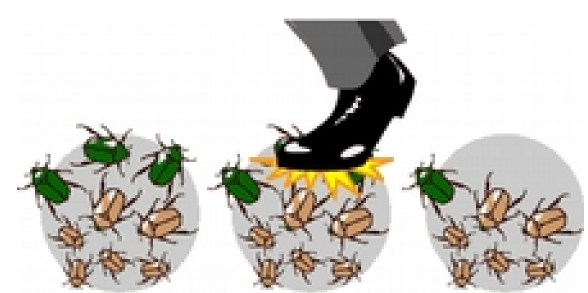
3

Reproduction différente selon les individus



Sélection

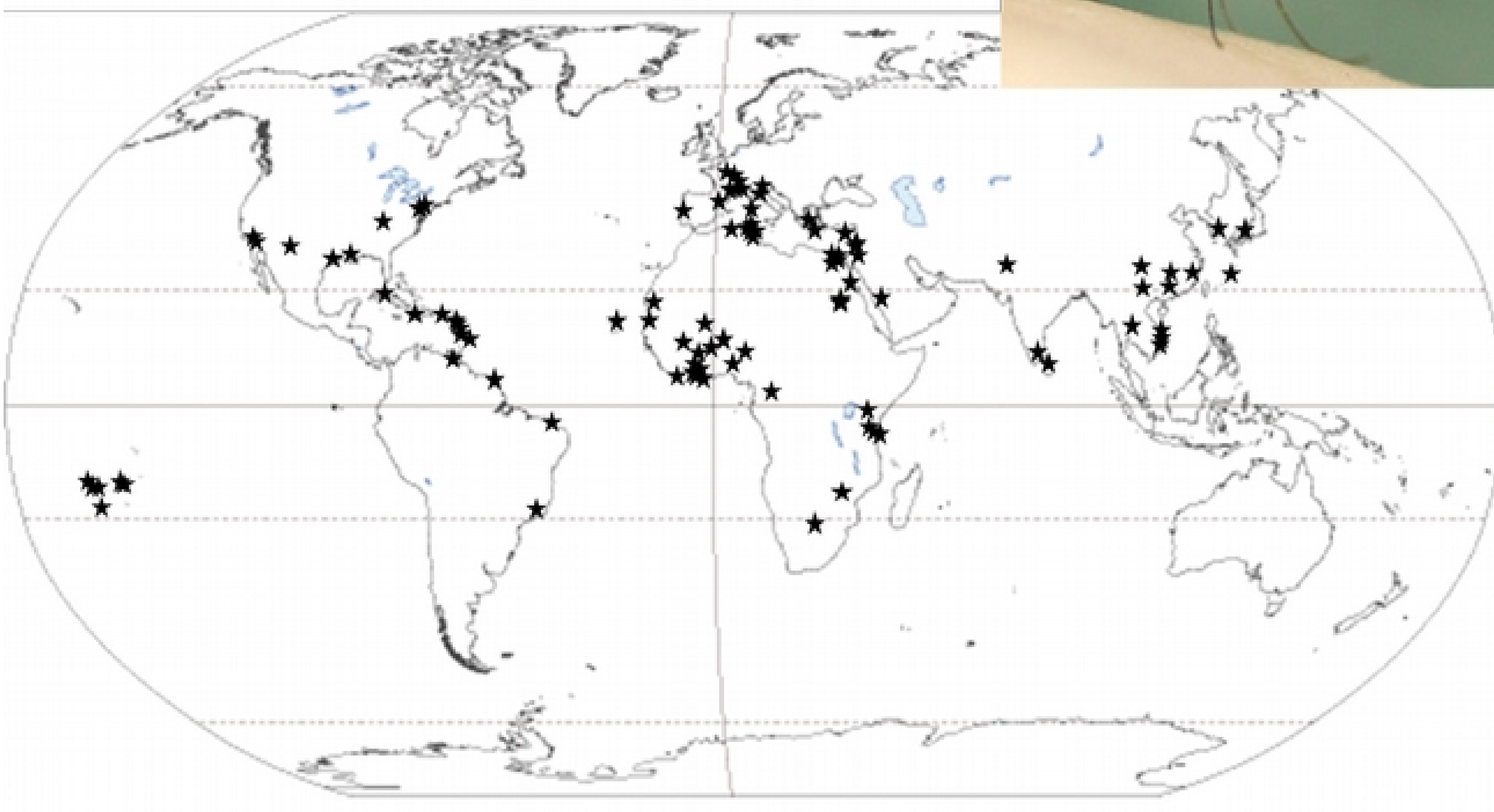
Dérive génétique



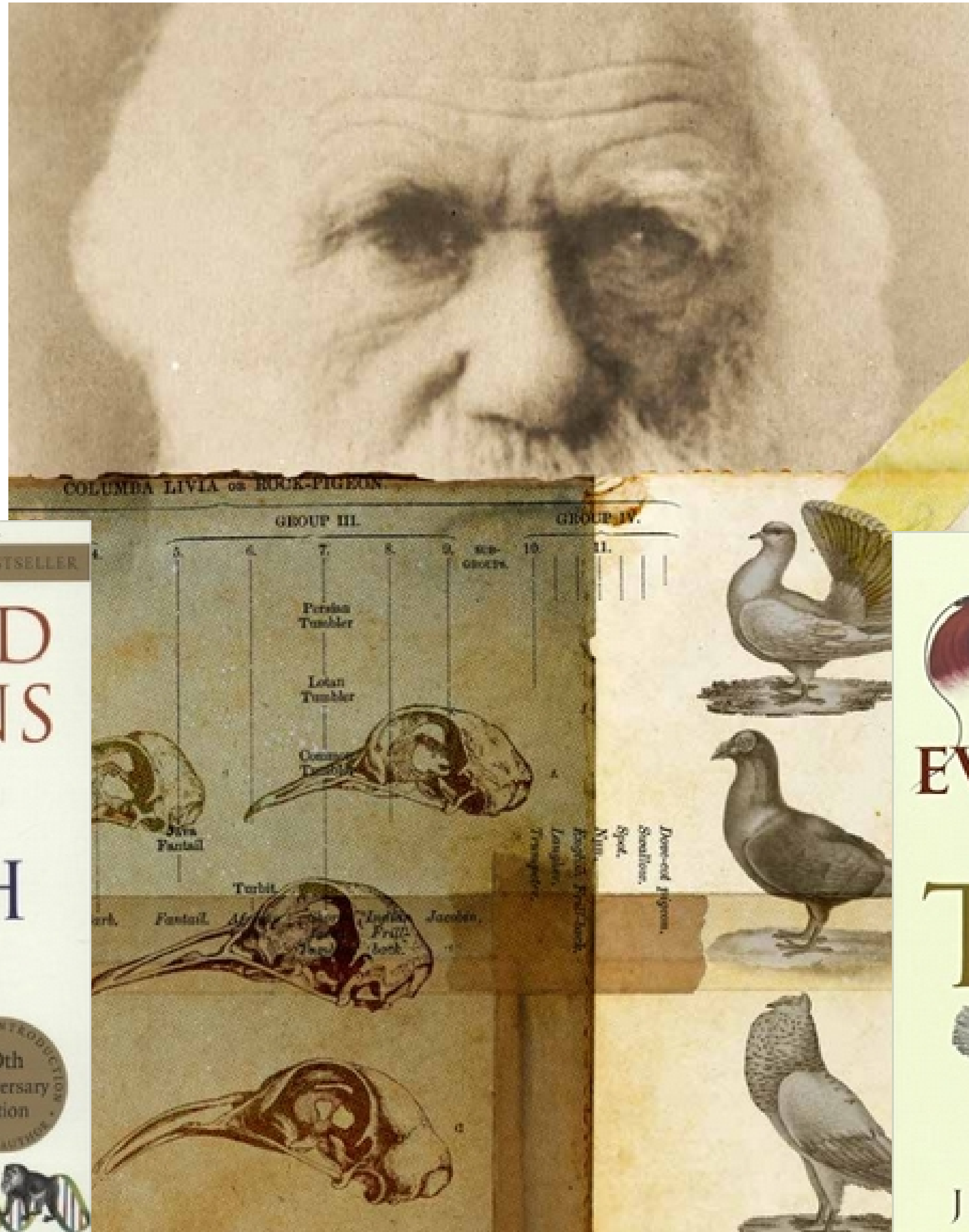
http://evolution.berkeley.edu

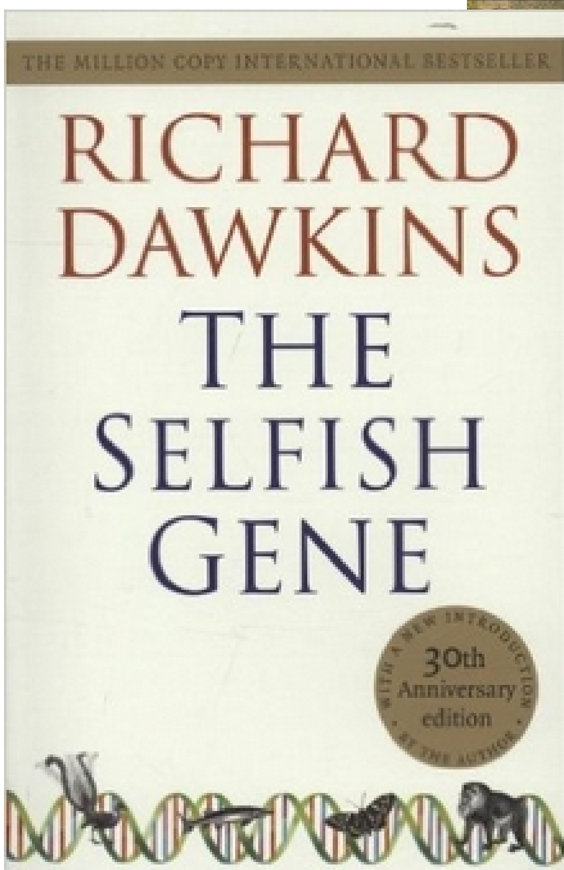
Insecticide resistance in *Culex pipiens*

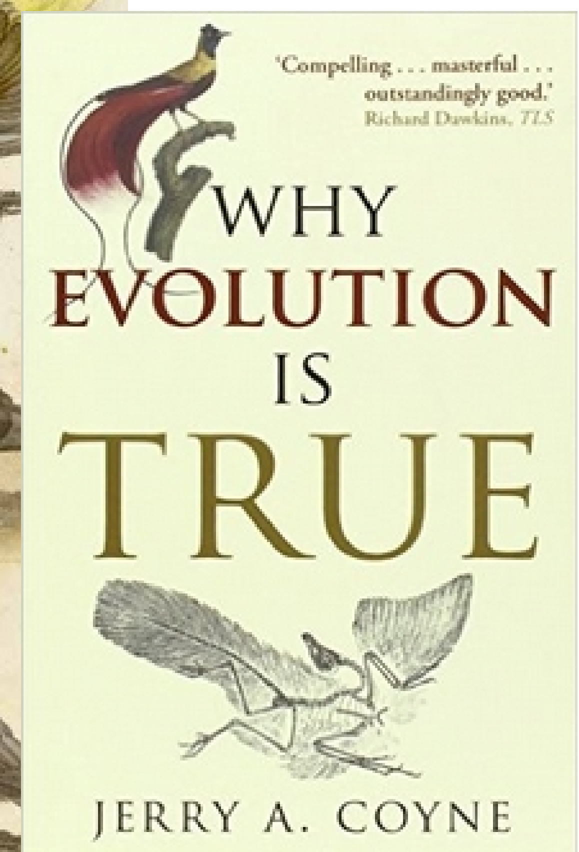
Ester[2]
First detected in Liberia and Nigeria in 1977
and in France in 1986



Labbé 2005 JEB


COLUMBA LIVIA or ROCK-PIGEON
GROUP III.
GROUP IV.
Persian Tumbler
Lotan Tumbler
Turbit
Fantail
Jacobin


THE MILLION COPY INTERNATIONAL BESTSELLER
RICHARD DAWKINS
THE SELFISH GENE
WITH A NEW INTRODUCTION BY THE AUTHOR
30th Anniversary edition


'Compelling . . . masterful . . . outstandingly good.'
Richard Dawkins, TLS
WHY EVOLUTION IS TRUE
JERRY A. COYNE

Current critics

New view = EES = Extended Evolutionary Synthesis

Evolution is not random:

- physical development influences the generation of variation (developmental bias)

- the environment directly shapes organisms' traits (plasticity)

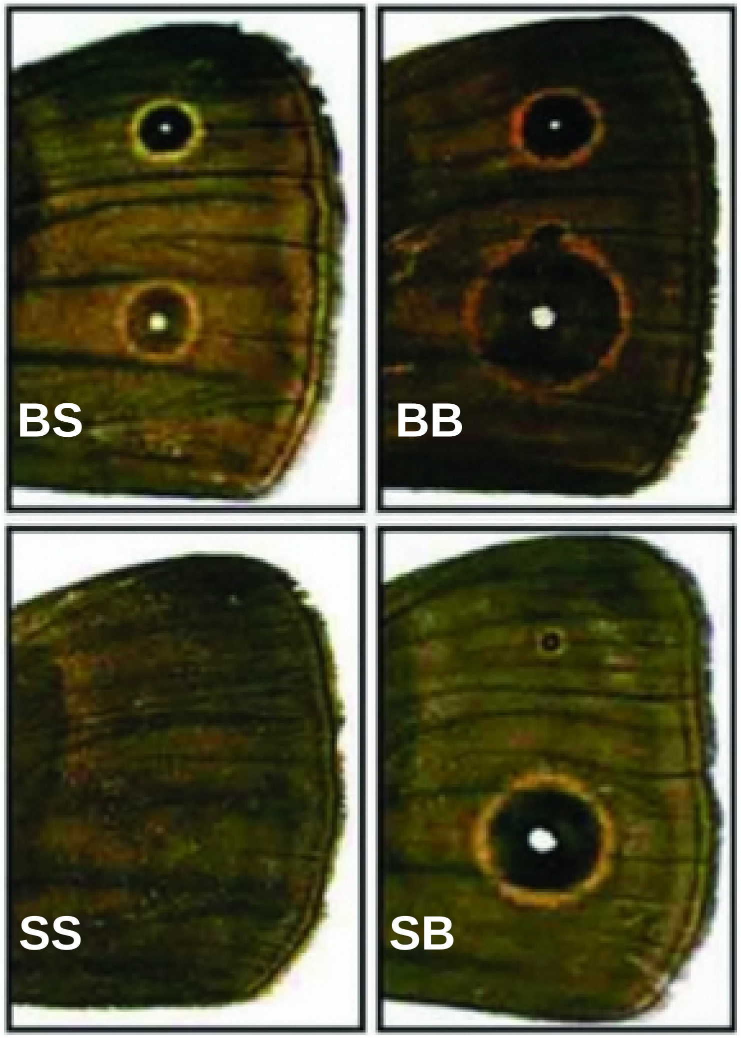
- organisms modify environments (niche construction)

- organisms transmit more than genes across generations (extra-genetic inheritance)

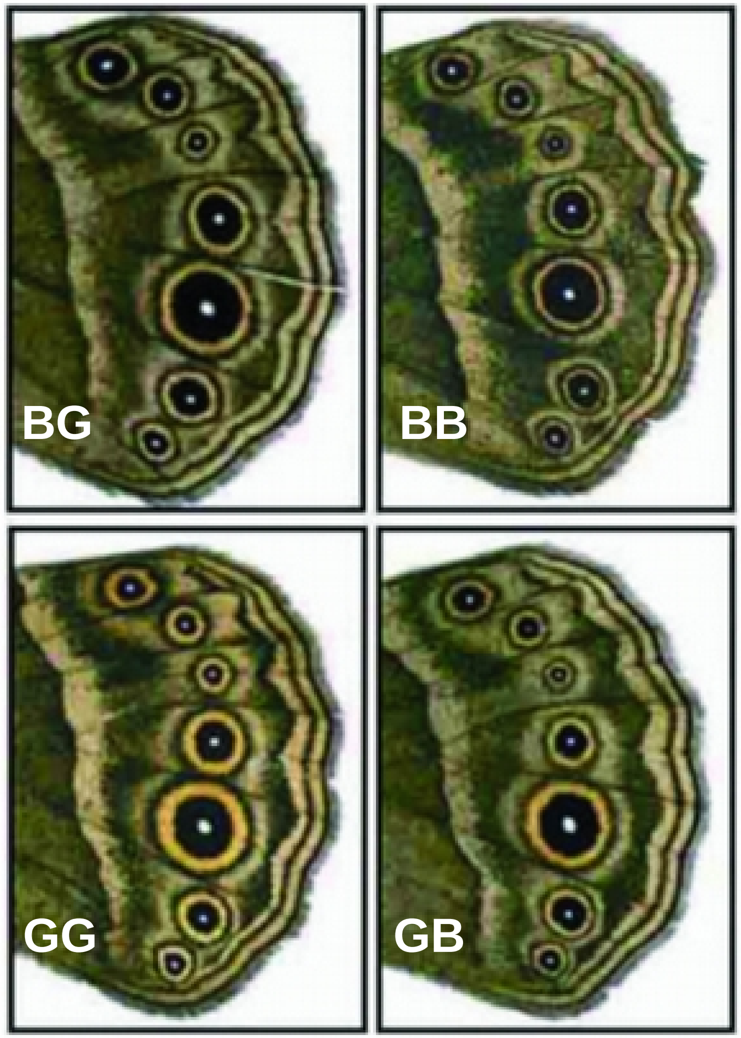
Laland et al. 2014, Laland et al. 2015

Developmental bias

Selection for bigger/smaller spots



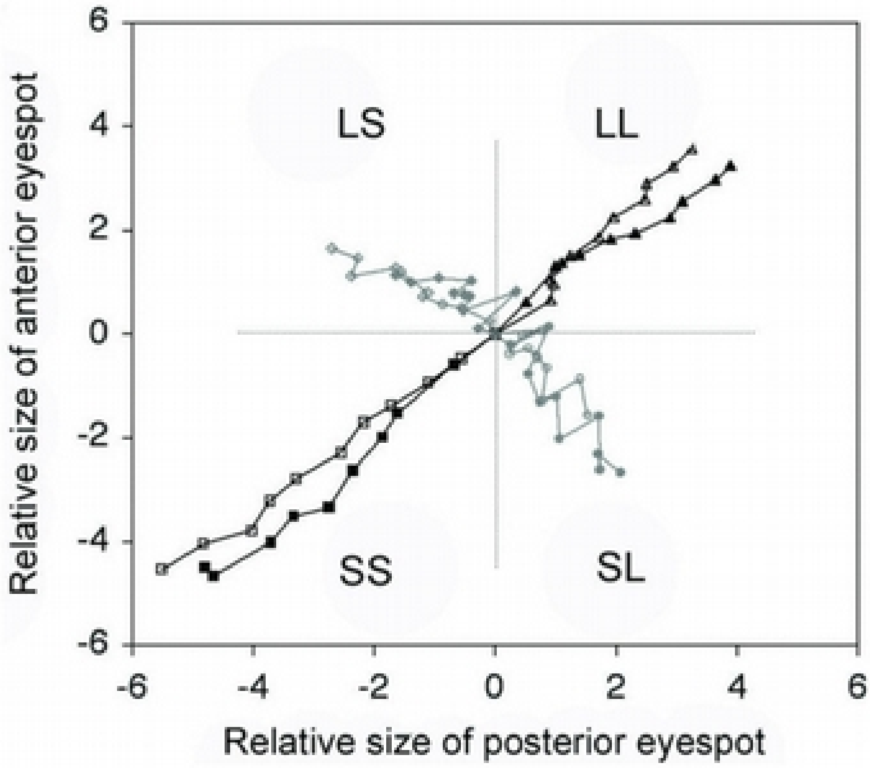
Selection for more black/more gold



Beldade and Brakefield

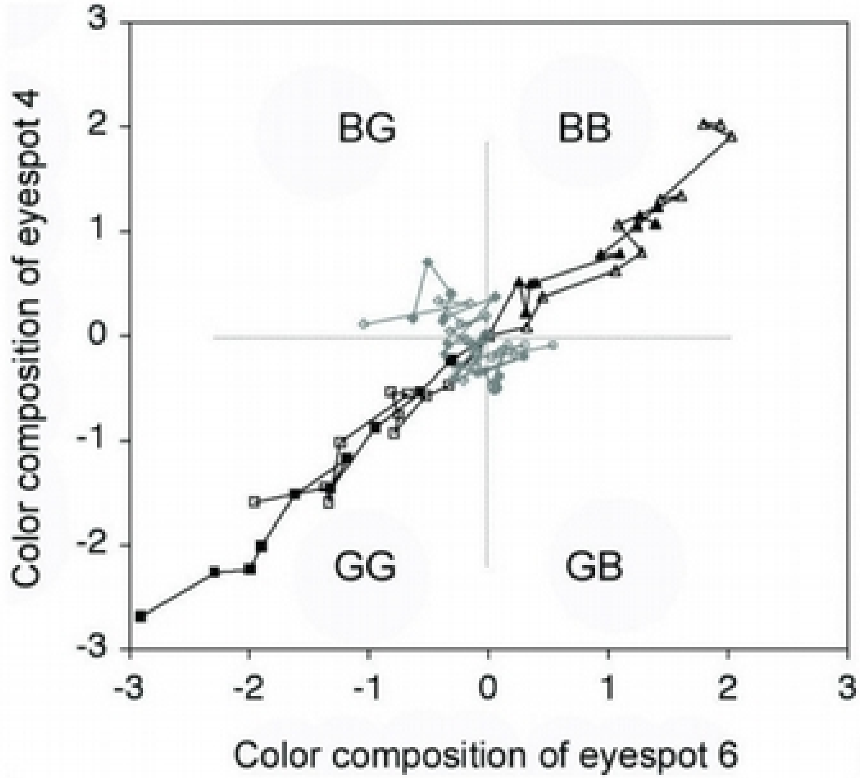
Developmental bias

Eyespot size



L = Large
S = Small

Eyespot colour composition

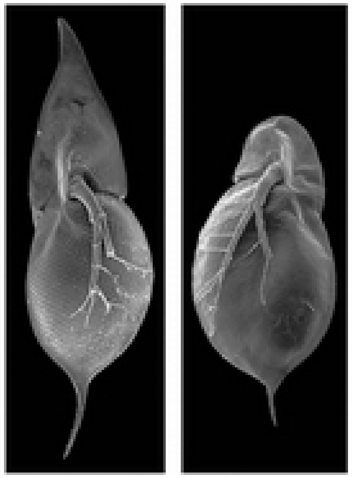


B = Black
G = Gold

Beldade and Brakefield

Plasticity

Daphnia



with helmet | without helmet

Nemoria arizonaria caterillars

spring: caterpillars feed on catkins | summer: caterpillars feed on leaves

Water crowfoot plant

leaves growing above water | leaves growing below water

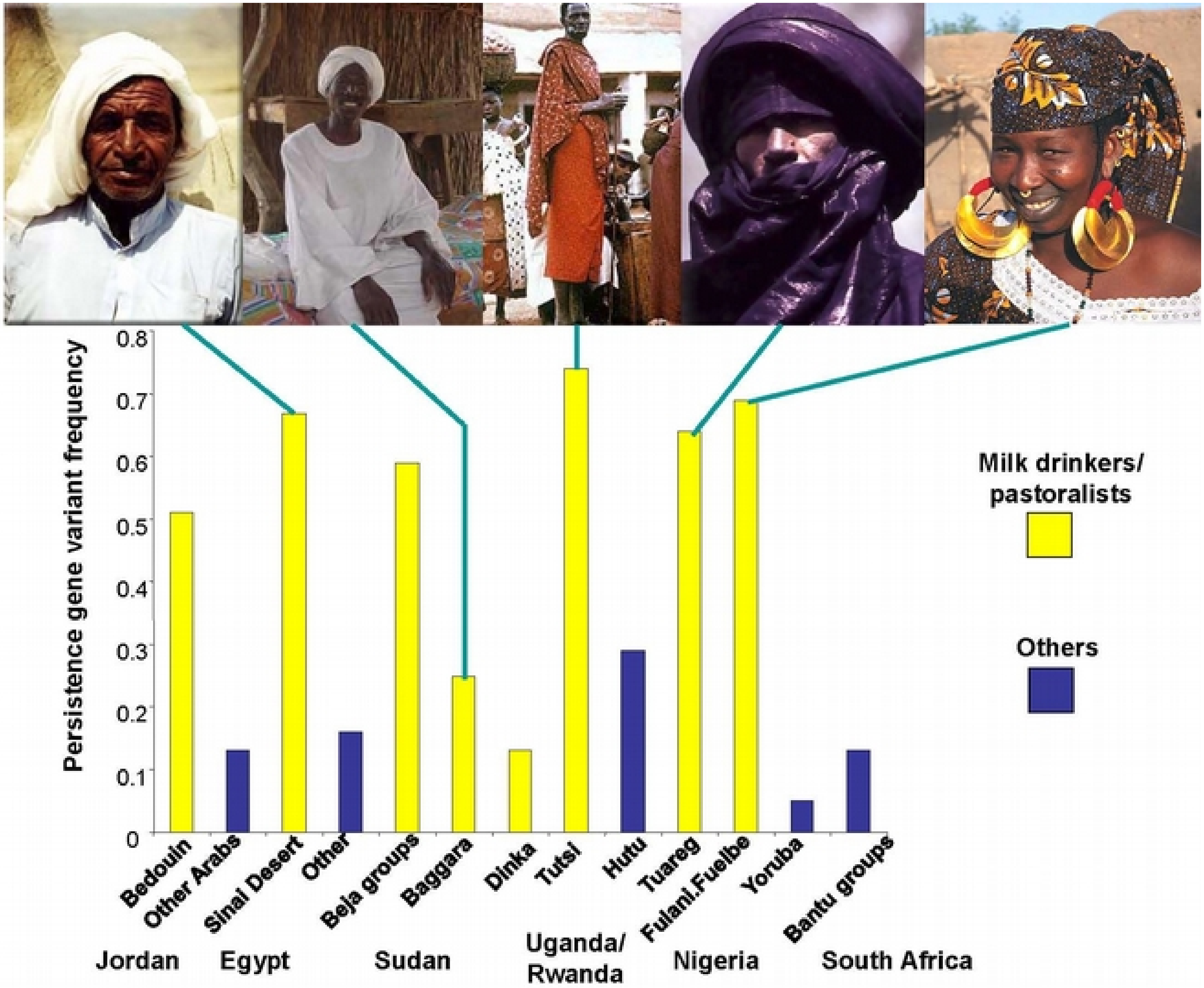
Desert locusts

solitary | gregarious

Commodore butterfly

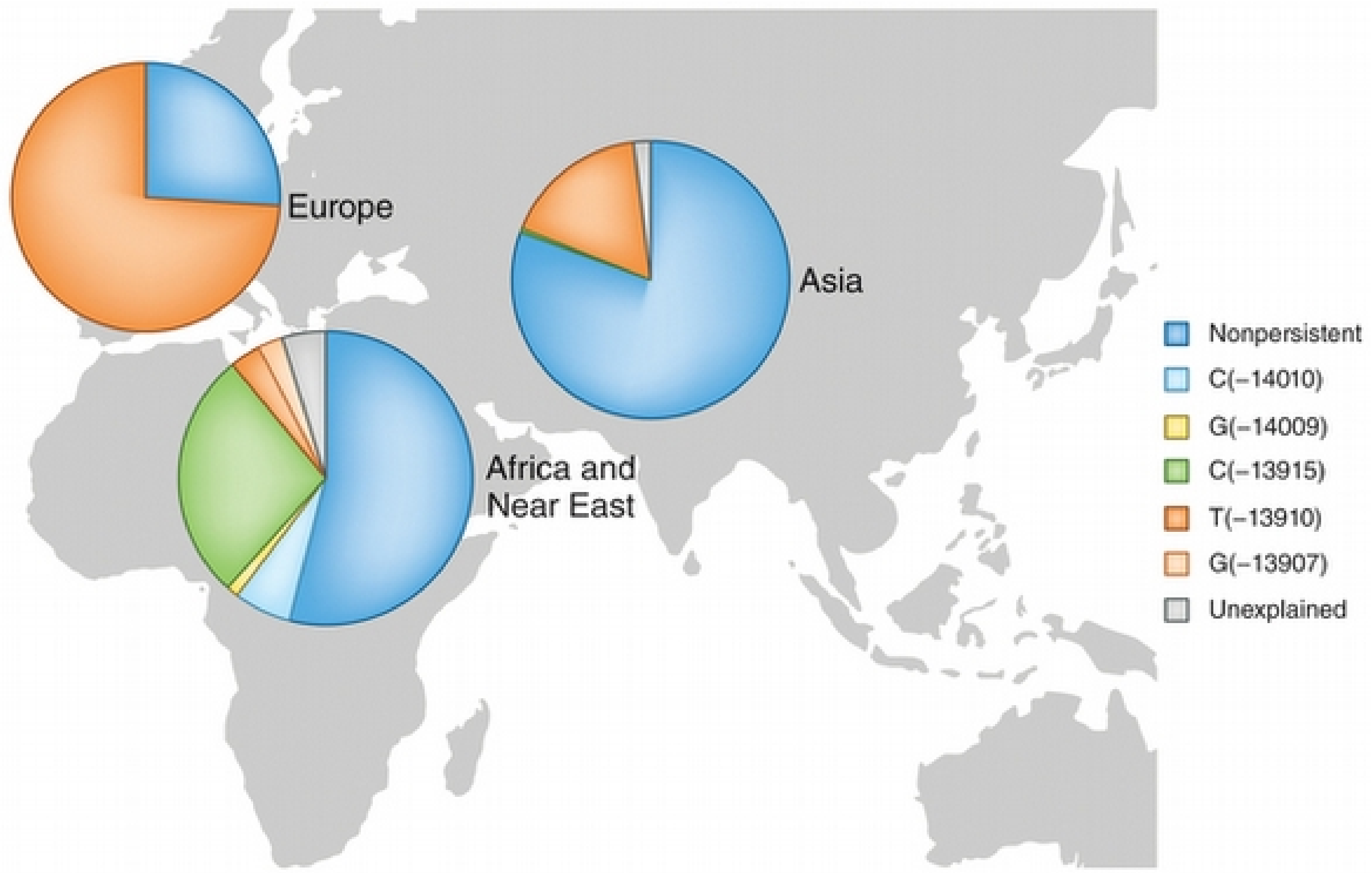
winter | summer

Niche construction



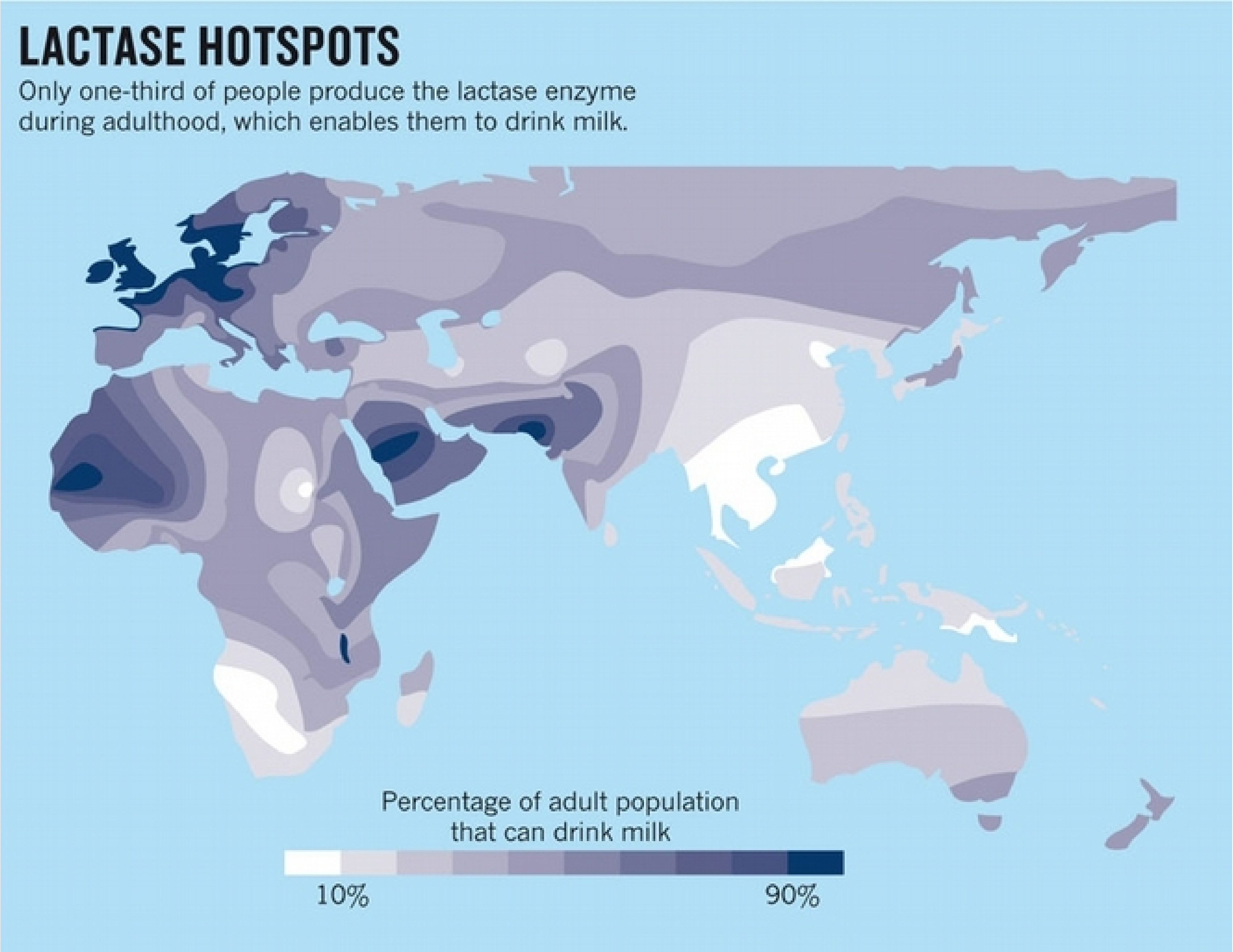
Niche construction

Lactase persistence alleles



Swallow 2016

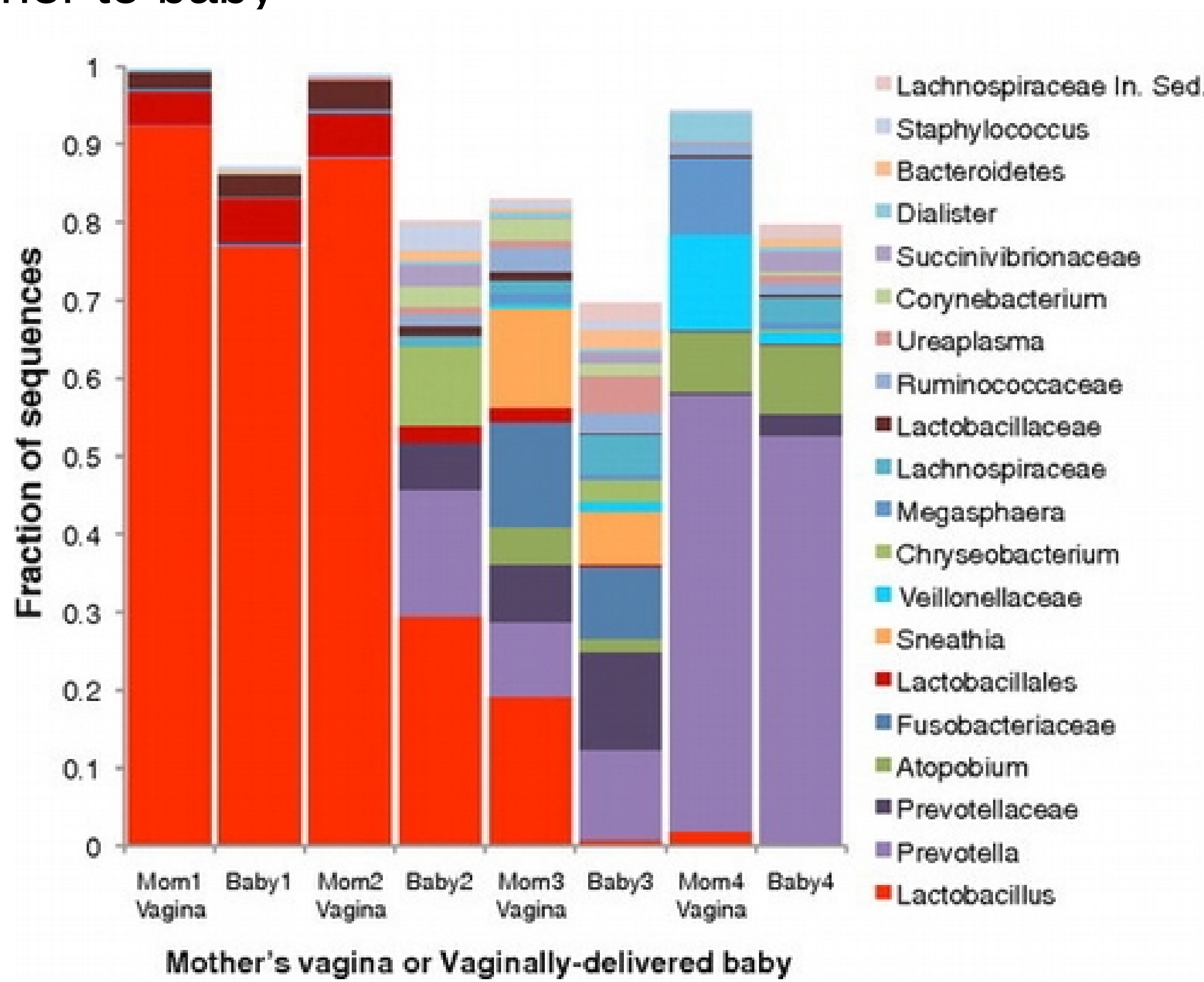
Niche construction



Extra-genetic inheritance

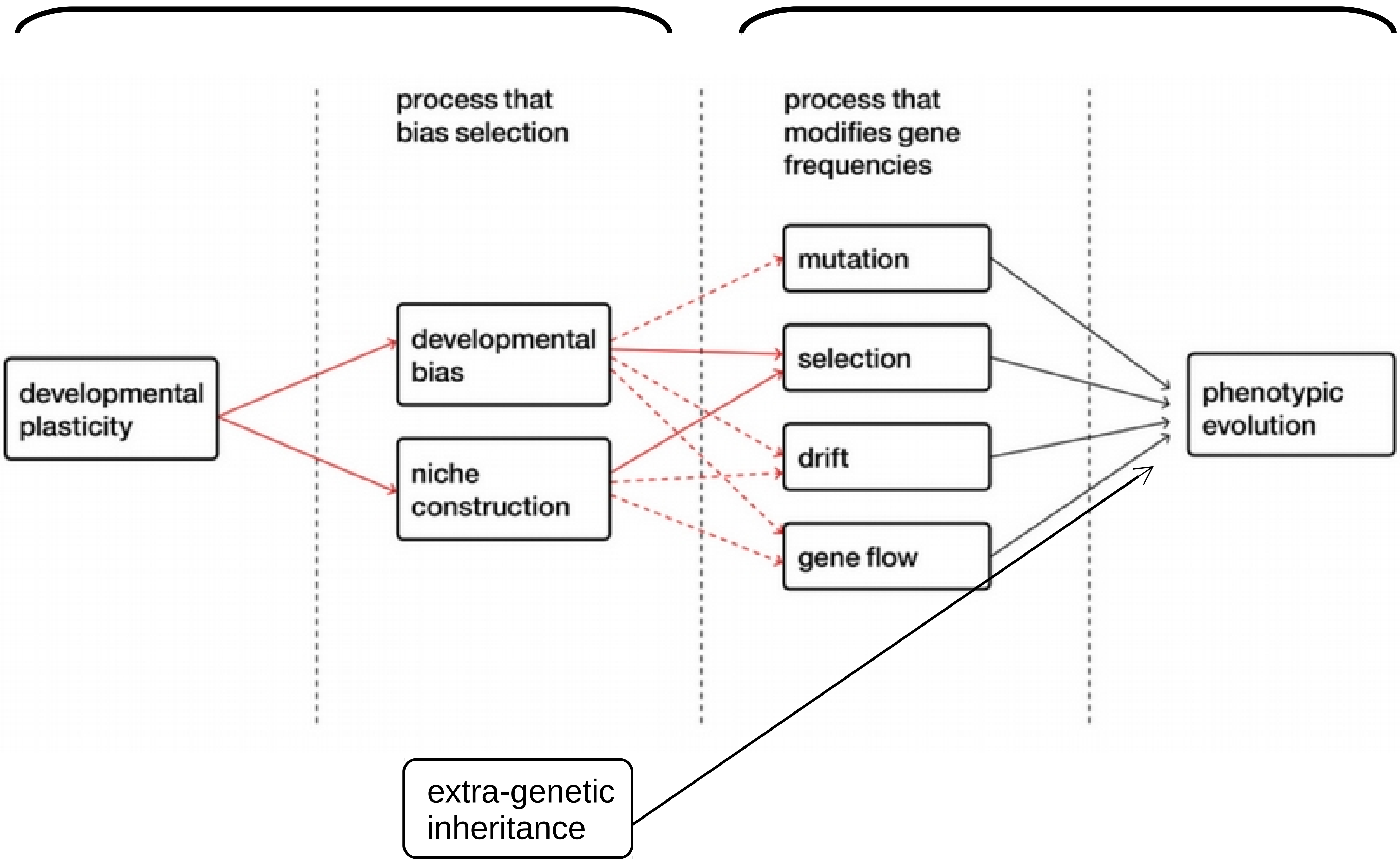
Antibodies from mother to baby's blood
via breast milk and placenta

Microbiome from mother to baby



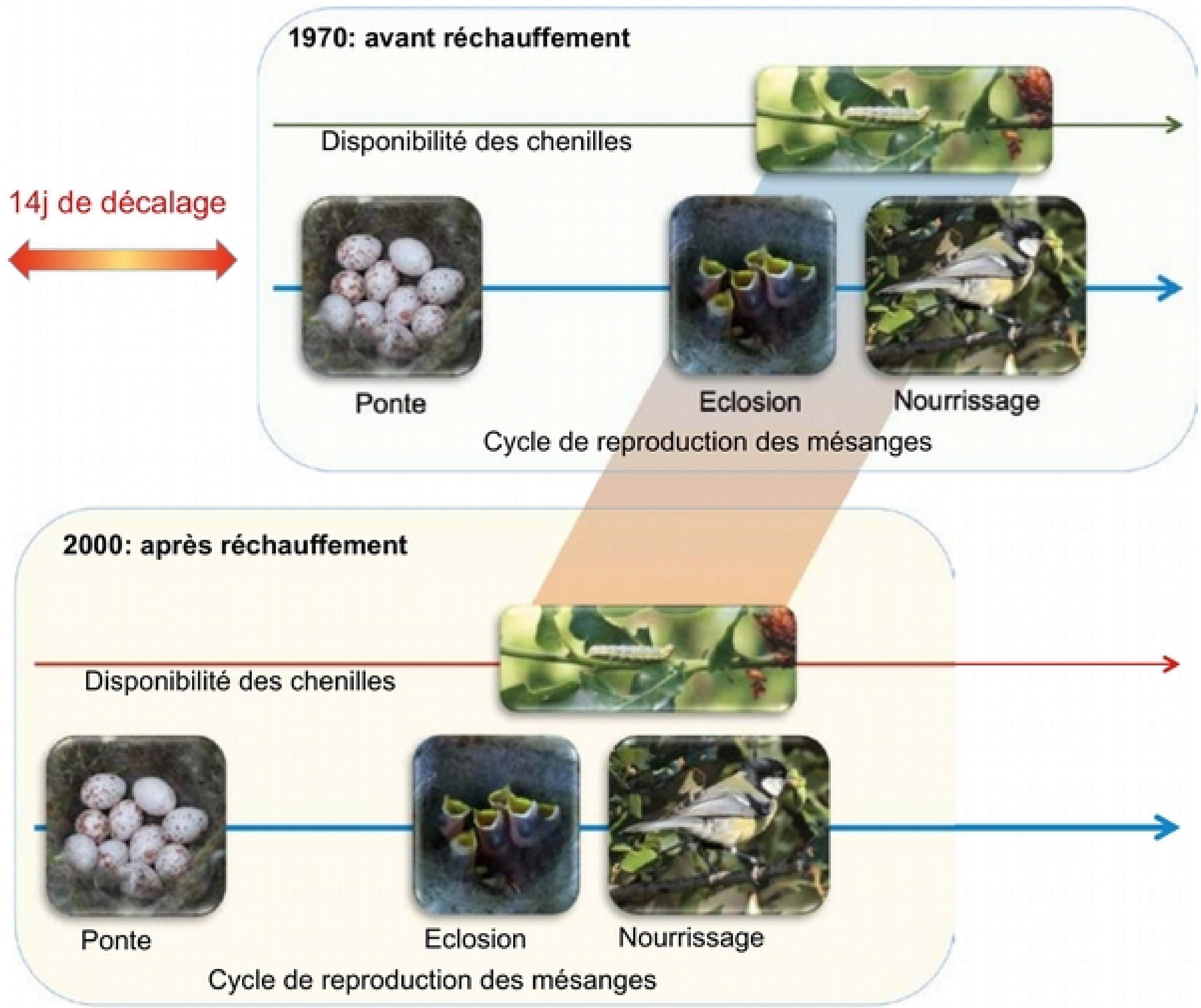
Dominguez-Bello 2010 PNAS

Additions   Classical view



classical MS core assumptions	EES core assumptions
(i) *The pre-eminence of natural selection.* The major directing or creative influence in evolution is natural selection, which alone explains why the properties of organisms match the properties of their environments (adaptation)	(i) *Reciprocal causation (organisms shape, and are shaped by, selective and developmental environments).* Developmental processes, operating through developmental bias and niche construction, share with natural selection some responsibility for the direction and rate of evolution and contribute to organism–environment complementarity
(ii) *Genetic inheritance.* Genes constitute the only general inheritance system. Acquired characters are not inherited	(ii) *Inclusive inheritance.* Inheritance extends beyond genes to encompass (transgenerational) epigenetic inheritance, physiological inheritance, ecological inheritance, social (behavioural) transmission and cultural inheritance. Acquired characters can play evolutionary roles by biasing phenotypic variants subject to selection, modifying environments and contributing to heritability
(iii) *Random genetic variation.* There is no relationship between the direction in which mutations occur—and hence the supply of phenotypic variants—and the direction that would lead to enhanced fitness	(iii) *Non-random phenotypic variation.* Developmental bias, resulting from non-random mutation or phenotypic accommodation, means that some phenotypic variants are more likely than others. Developmental systems facilitate well-integrated, functional phenotypic responses to mutation or environmental induction
(iv) *Gradualism.* Evolution via mutations of large effects is unlikely because such mutations have disruptive pleiotropic effects. Phenotypic transitions typically occur through multiple small steps, leading to gradual evolutionary change	(iv) *Variable rates of change.* Variants of large effect are possible, allowing for rapid evolutionary change. Saltation can occur either through mutations in major regulatory control genes expressed in tissue-, module- or compartment-specific manner, or when developmental processes respond to environmental challenges with change in coordinated suites of traits, or through nonlinear threshold effects
(v) *Gene-centred perspective.* Evolution requires, and is often defined as, *change in gene frequencies*. Populations evolve through changes in gene frequencies brought about through natural selection, drift, mutation and gene flow	(v) *Organism-centred perspective.* Developmental systems can facilitate adaptive variation and modify selective environments. Evolution redefined as a *transgenerational change in the distribution of heritable traits of a population*. There is a broadened notion of evolutionary process and inheritance
(vi) *Macro-evolution.* Macro-evolutionary patterns are explained by micro-evolutionary processes of selection, drift, mutation and gene flow	(vi) *Macro-evolution.* Additional evolutionary processes, including developmental bias and ecological inheritance, help explain macro-evolutionary patterns and contribute to evolvability

Evolution rapide des mésanges charbonnières



Etonnant vivant : découvertes et promesses du XXIe siècle (2017)

Our research approach

The genetic program is dead

Evolution is not as random as previously thought

The tree of life is not a tree

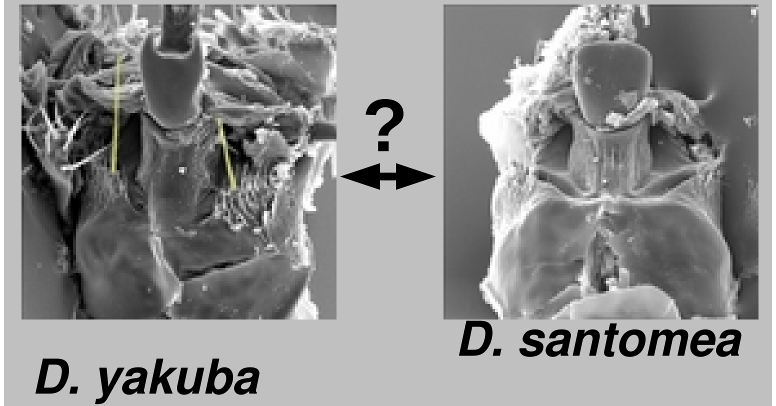
Our research approach

Finding the mutations responsible for evolution

The mutations underlying evolution and diversity of living forms

Our strategy

one phenotypic difference



Causing mutations?

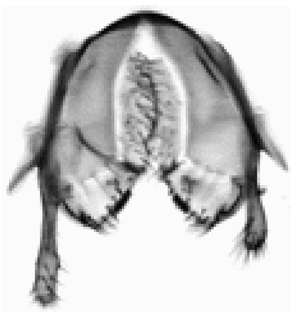
Effect on development?

Effect on reproductive success?

Population dynamics?

How D. pachea became dependent on its host cactus

Lang et al. 2012 Science



How and why asymmetric genitals evolved

Lang and Orgogozo 2012 Cont Zool
Rhebergen et al. 2016 BMC Evol Biol
unpublished

How a new bristle pattern evolved despite pleiotropy

unpublished

Gephebase: The Loci of Evolution

unpublished

Evolution is partly predictable

Orgogozo 2015 Interface Focus

Sex bristles
Alexis Matamoro-Vidal
Isabelle Nuez
Olga Nagy
Alexandre Peluffo

Ventral branches
Alexandre Peluffo

Posterior lobe
Alexis Lalouette

Left-right asymmetry
Michael Lang
Andrea Acurio

Gephebase
Stéphane Prigent
Laurent Arnoult

Collaborators

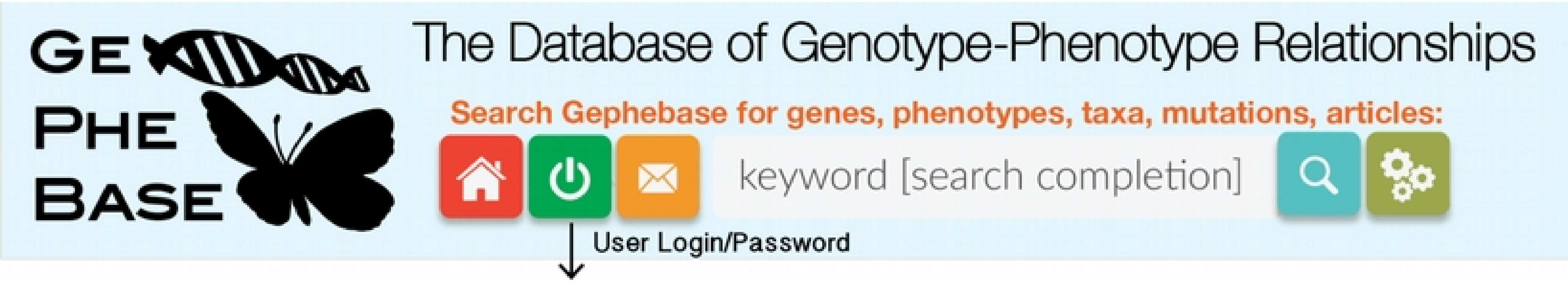
Gephebase
Arnaud Martin
Baptiste Morizot

Fly anatomy
Jean David

Morphometrics
François Graner

Genotyping
David L. Stern

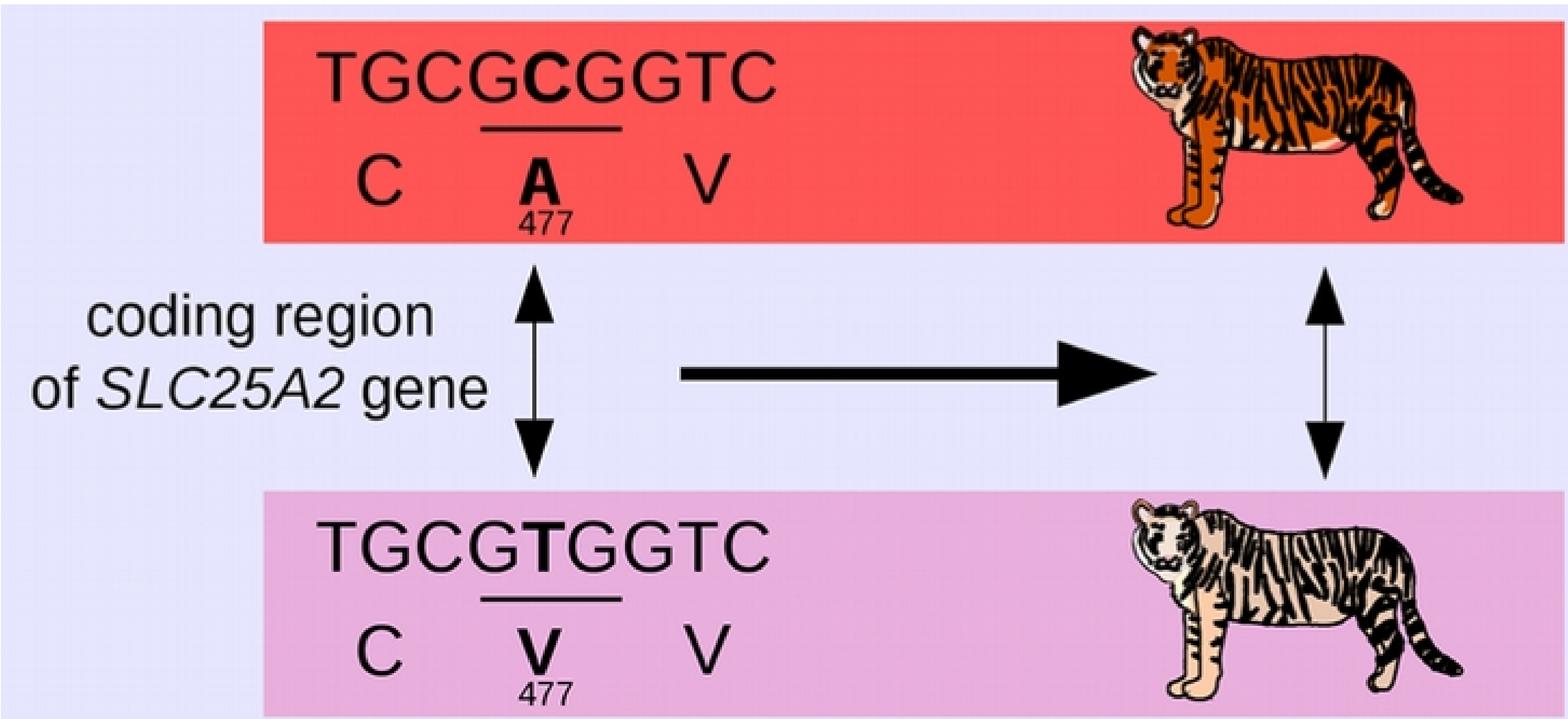
Fly crosses
Daniel Matute



>1400 cases of evolutionary changes
associated to a gene locus
in animals and plants

Martin and Orgogozo 2013 Evolution
Ongoing project

The genotype-phenotype connection



Xu et al 2013 Current Biology

Orgogozo et al 2015 Frontiers Genetics

The genotype-phenotype connection

Report of the National Academy of Sciences on gene drive, 2016

Genotype = "the genetic makeup of an organism that determines a specific phenotype (trait), from one generation to the next, and potentially throughout the population".

NO!

The genetic program is dead

Cunz, 2008, BMC Computational Biology:

“T*he genetic program encoding the morphological identity of a single dendrite remains a mystery*”.

The phenotype is not caused by genes only

The phenotype is not caused by genes only

No carotenoid — Carotenoid restricted diet

Hill 1994 Behav Ecol

Causes of these differences ?

Genetic

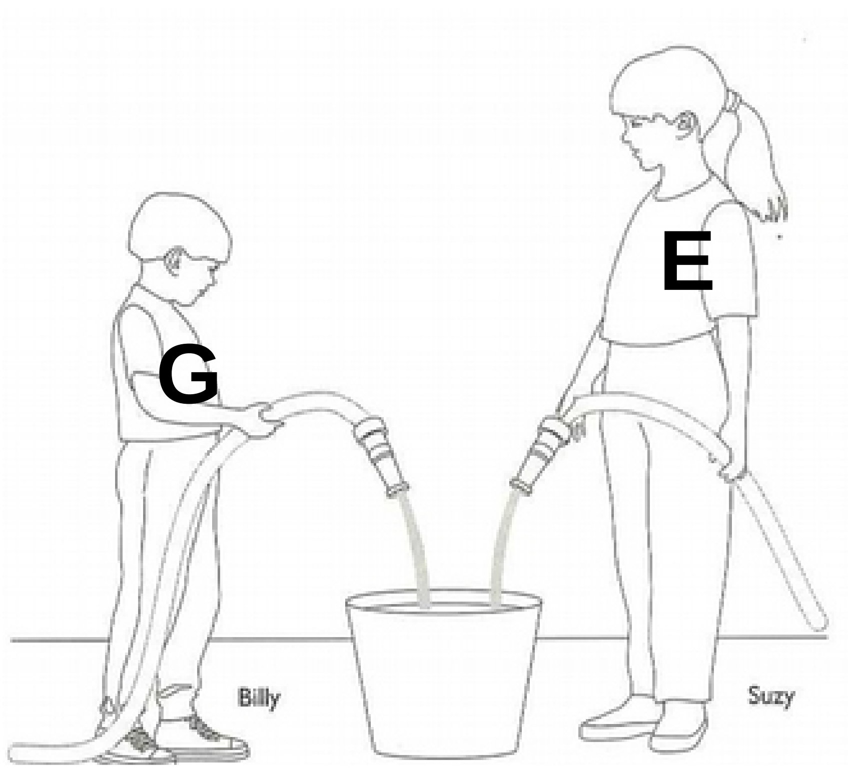
Environment

Phenotype = G + E + GxE

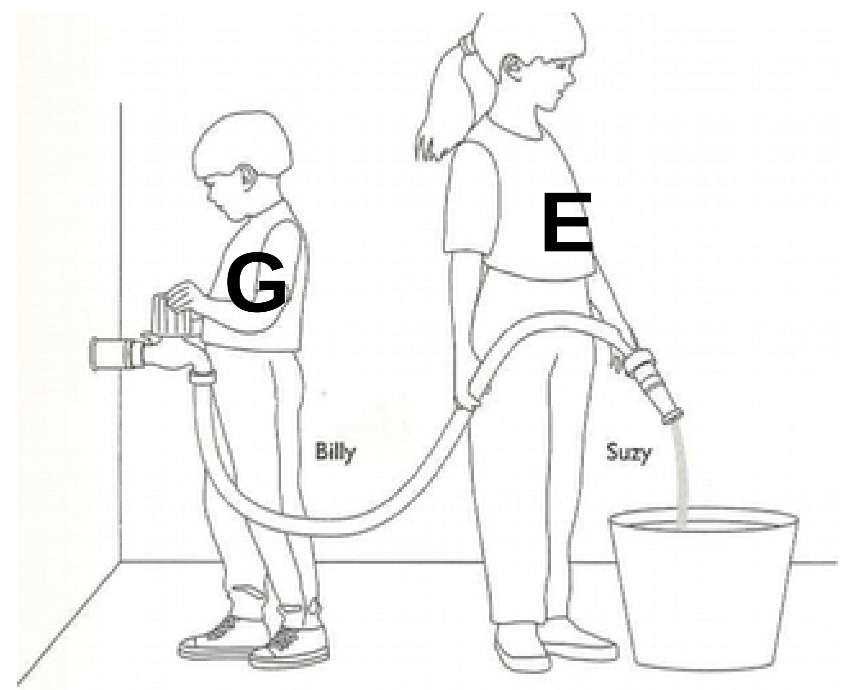
The Siamese cat
An example of GxE

Mutation in *tyrosinase*
Heat-sensitive enzyme
No production of melanin in warm body parts

Contributions of the genotype (G) and the environment (E) to phenotypic variation

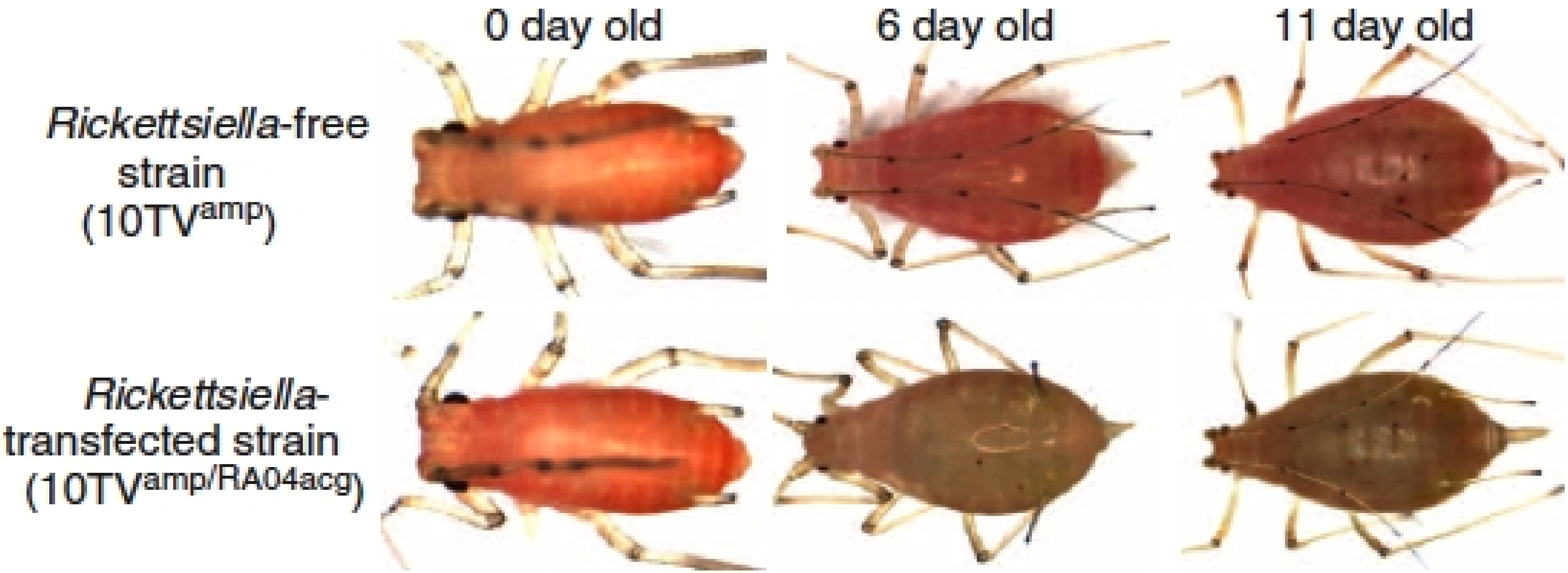


GxE



From Fox Keller (2010)

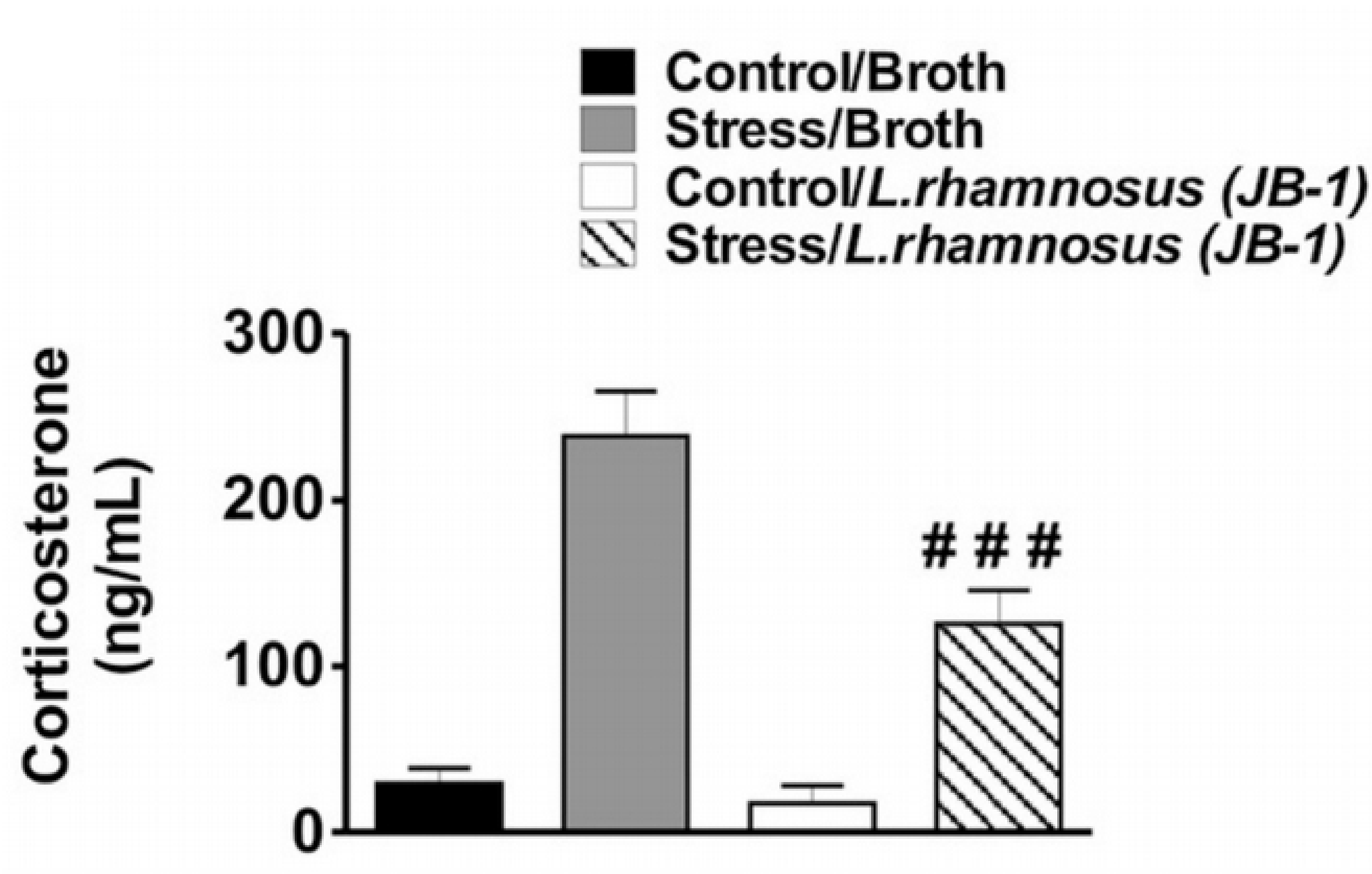
Pea aphid color variation



Without *Rickettsiella*, red aphid newborns become red adults.
With *Rickettsiella*, red aphid newborns become green adults.

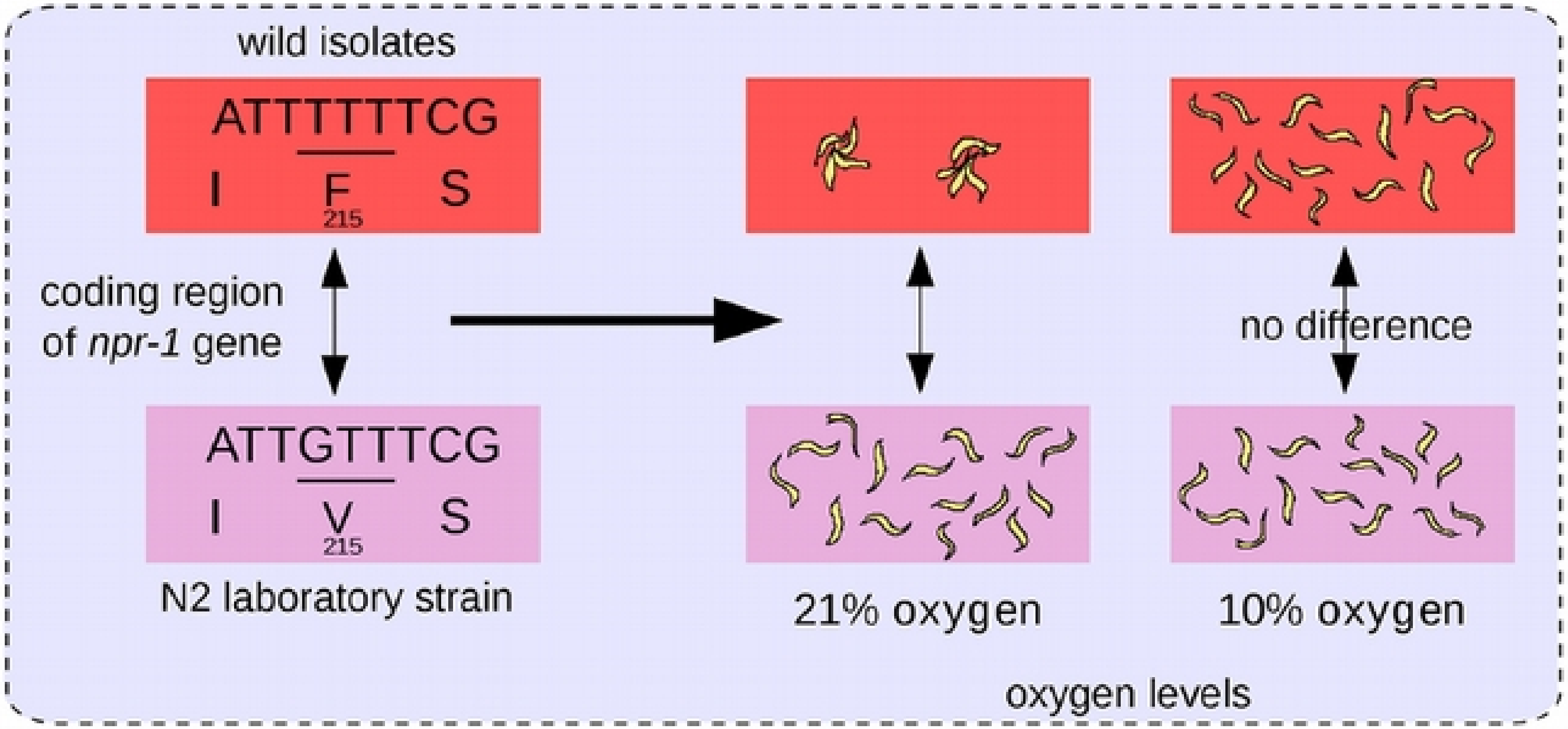
Tsuchida 2011 Science

Mouse emotional behavior modified by presence of *Lactobacillus* bacteria



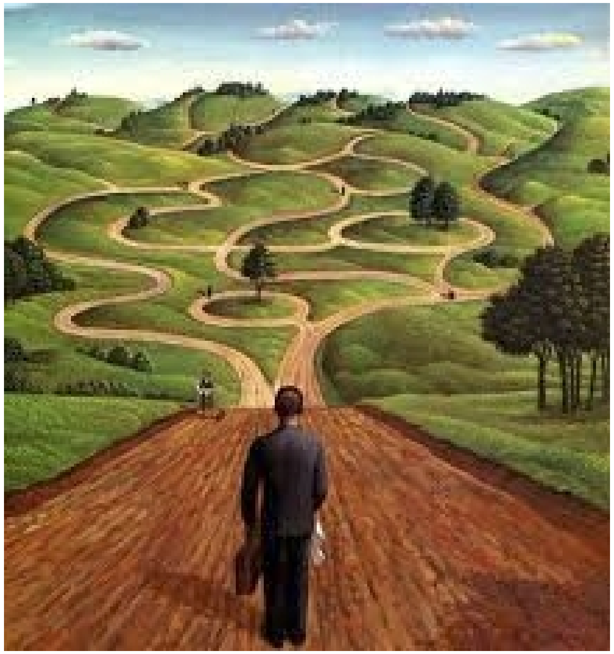
Bravo 2011 PNAS

GxE: a difference within a difference

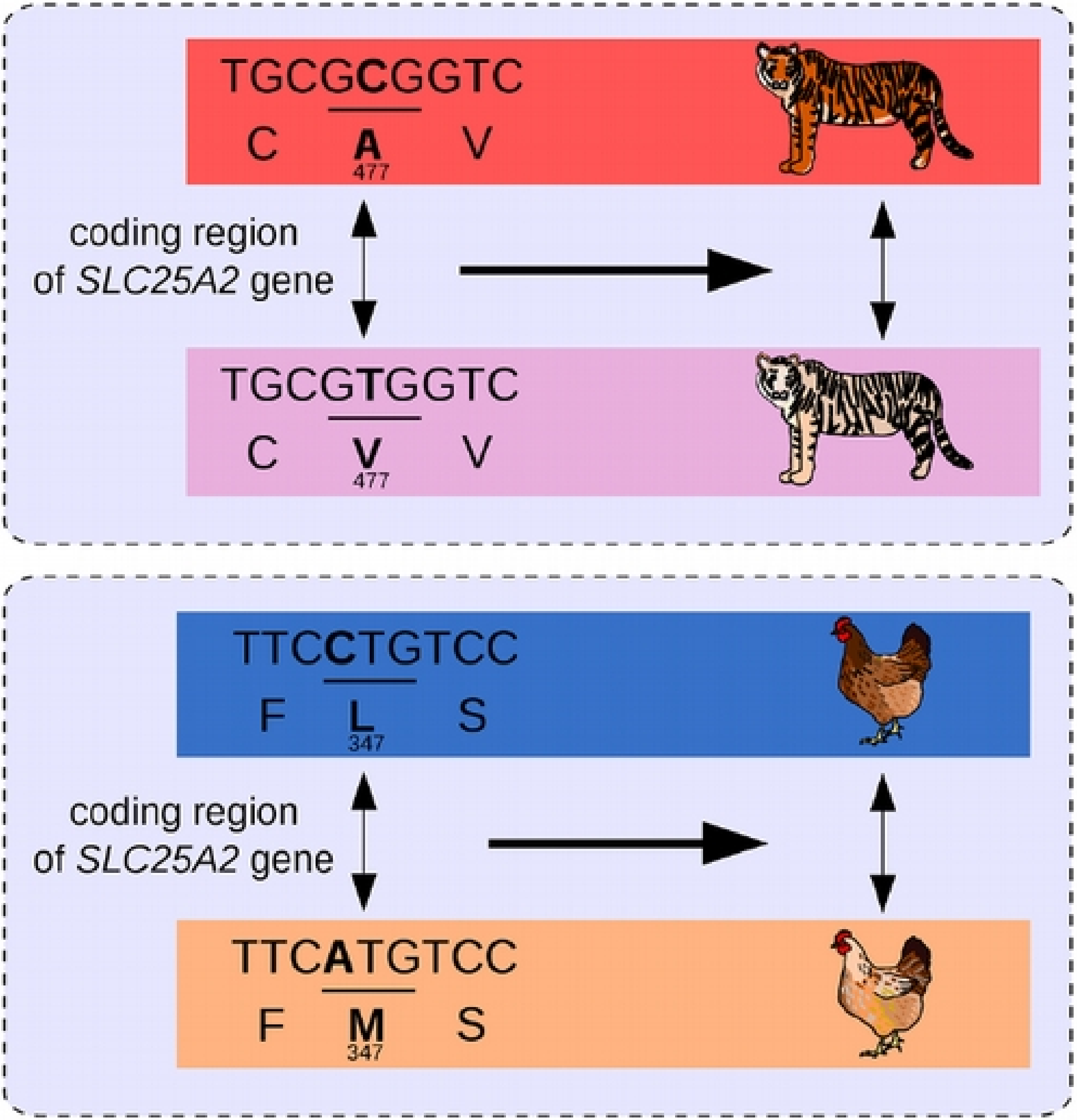


Orgogozo 2015 Frontiers Genetics

Evolution is not as random as previously thought



Repeated evolution



Orgogozo et al 2015 Frontiers Genetics

Repeats 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

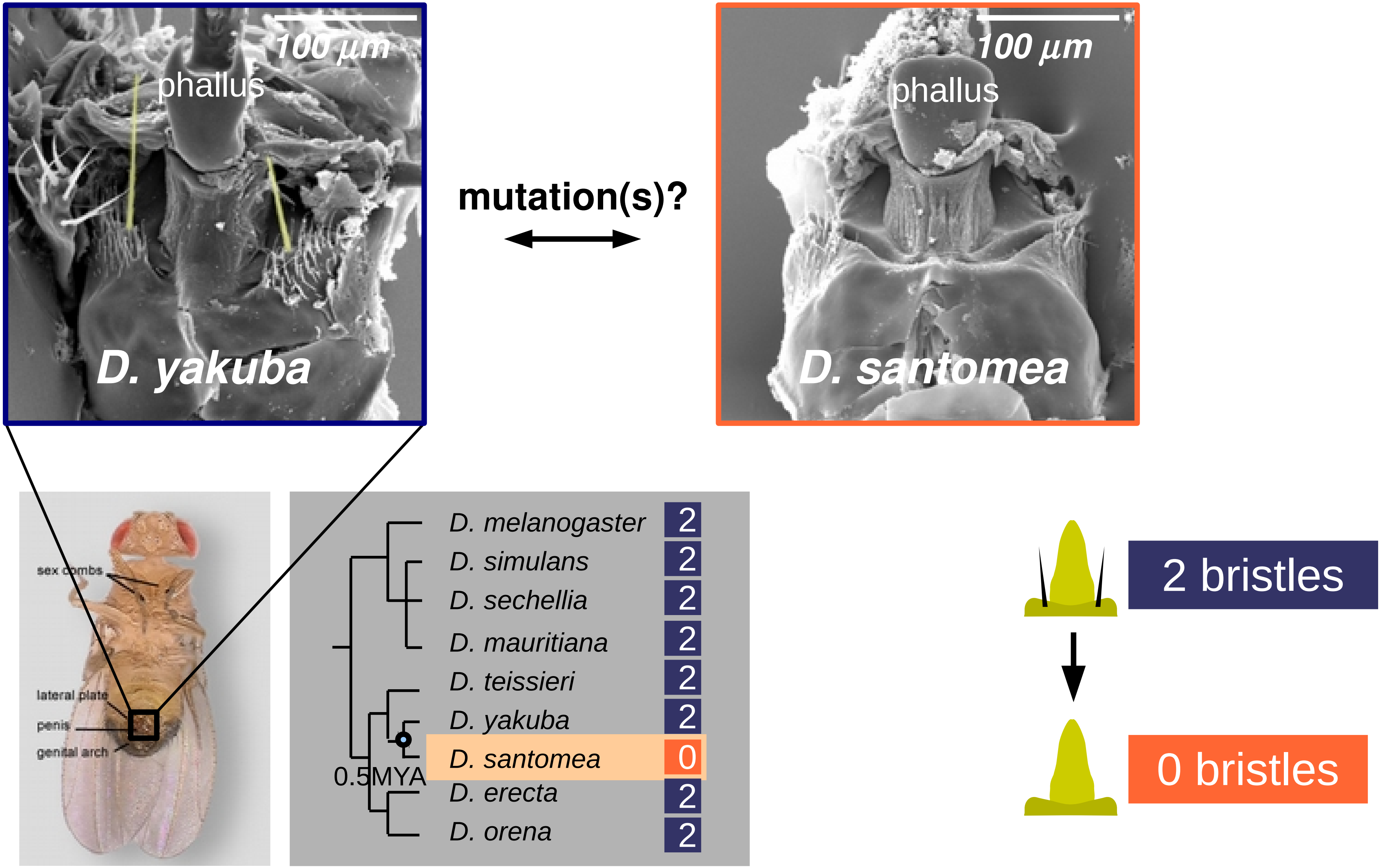
Ex : *sulfate transporter SUL1* in yeasts in low sulfate
(Gresham et al 2008 PloS Genetics)

.. the phenotypes evolving in certain environments

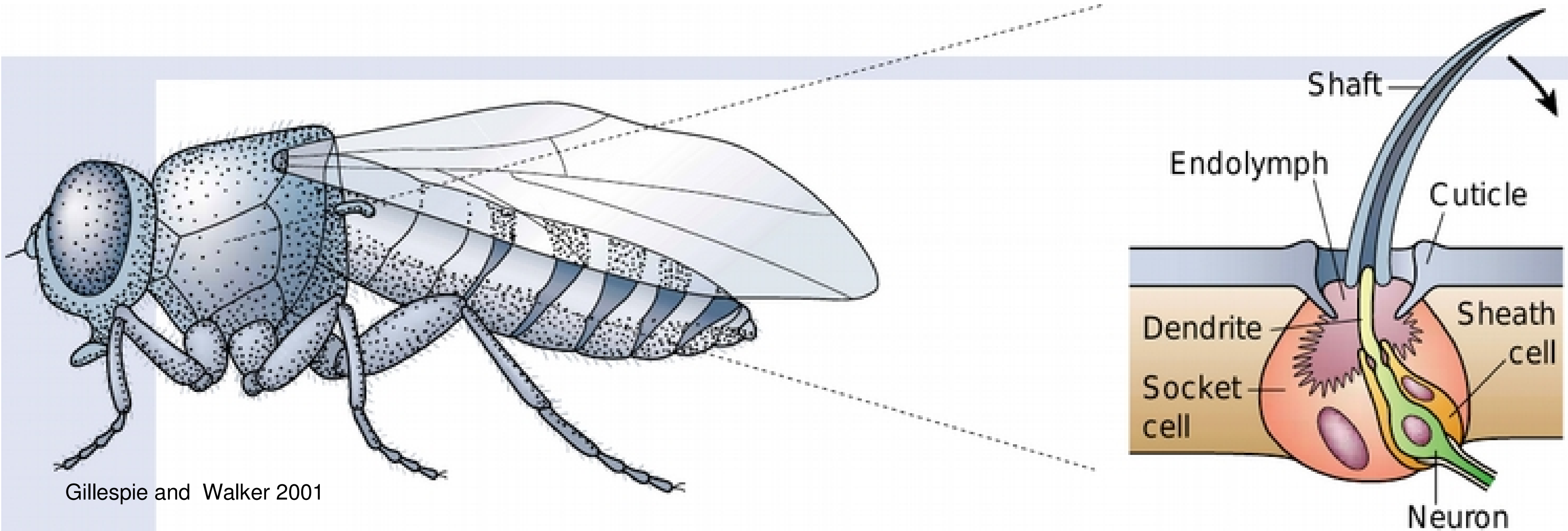
Ex : flying marsupial phalanger and placental flying squirrel

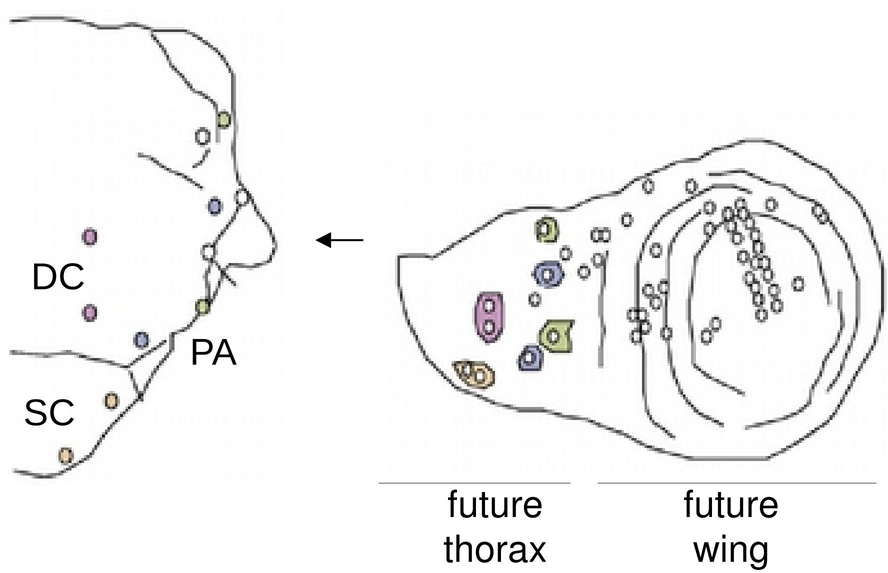
Orgogozo 2015 Interface Focus

What are the mutations responsible for the loss of sex bristles in *D. santomea*?

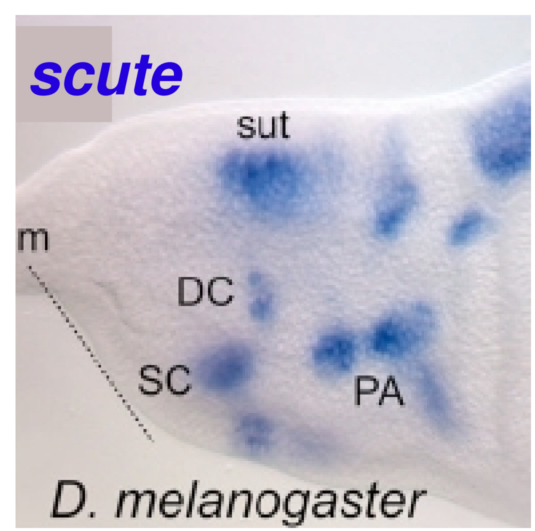


Bristle development

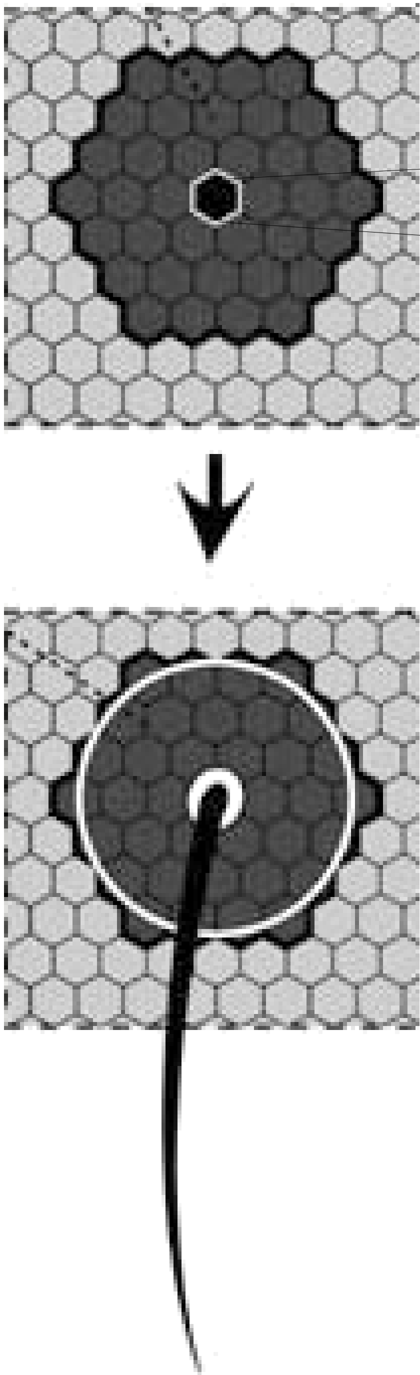


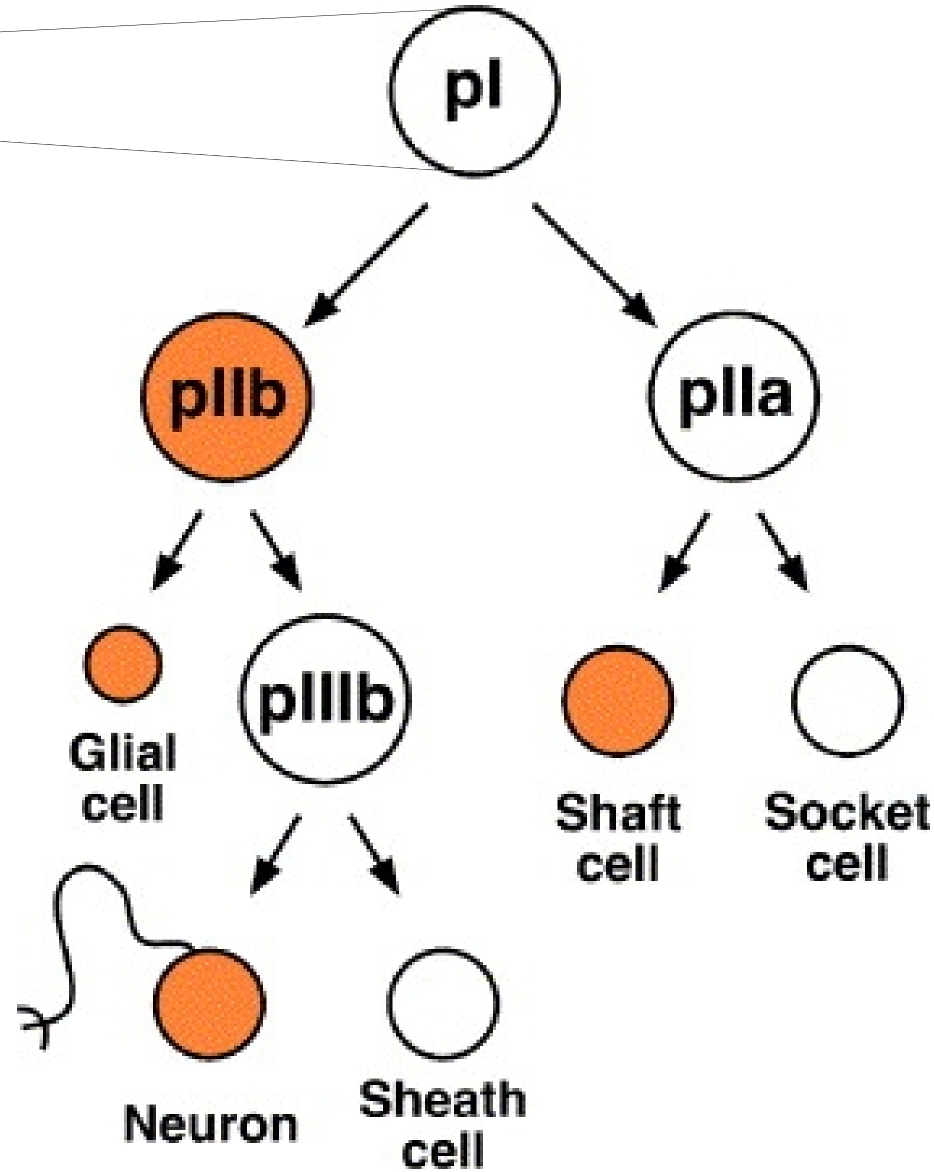


Simpson 2007



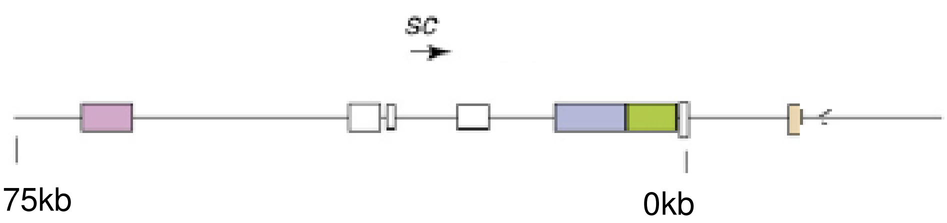
Marcellini 2006 - PloS Biology

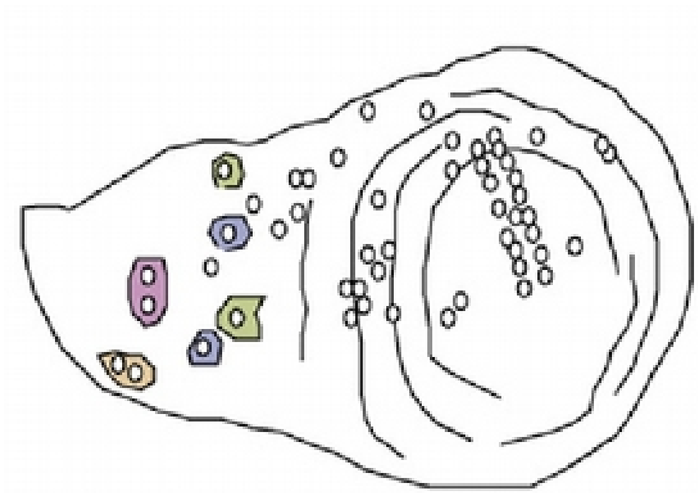




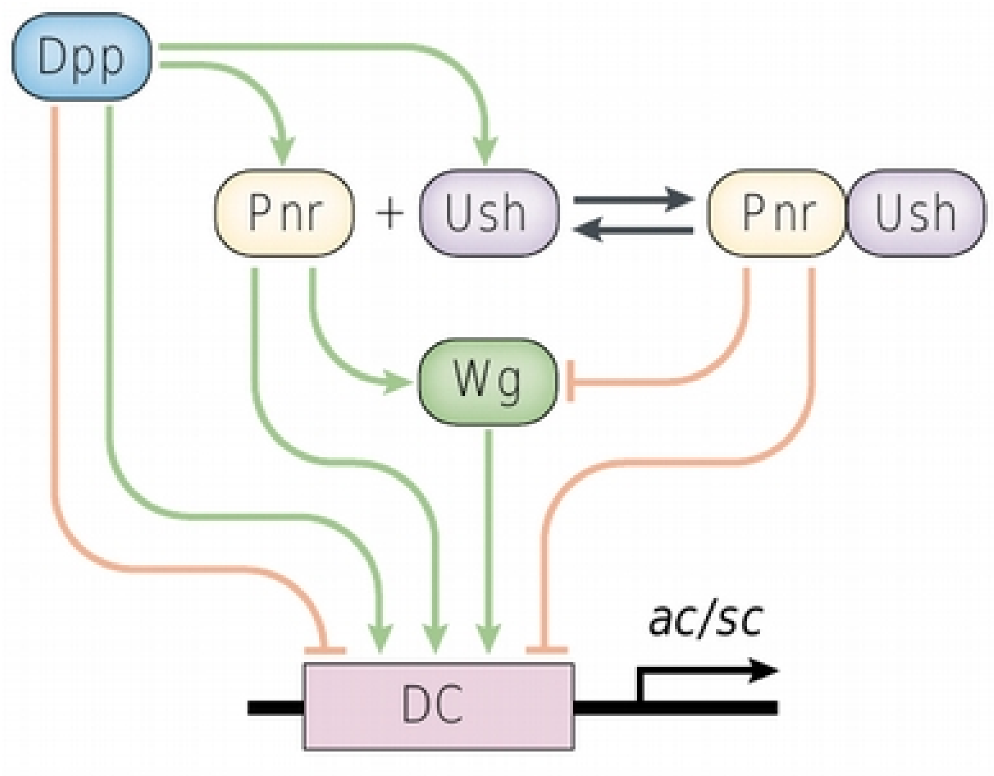
Lewis - Imaginal discs

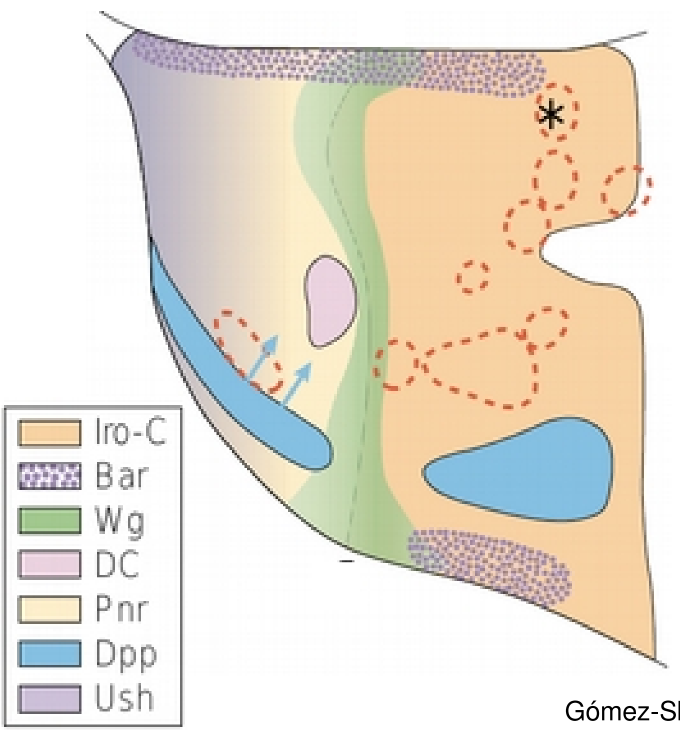
scute cis-regulatory elements are "master switches"





Simpson 2007

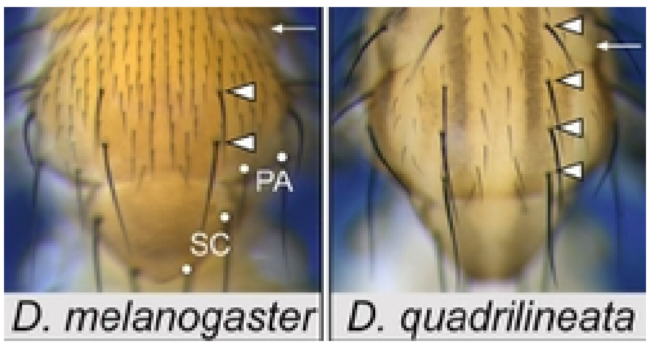


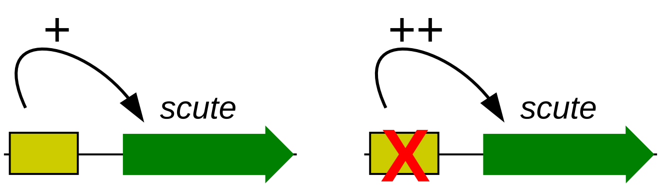


Gómez-Skarmeta 2003

Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*



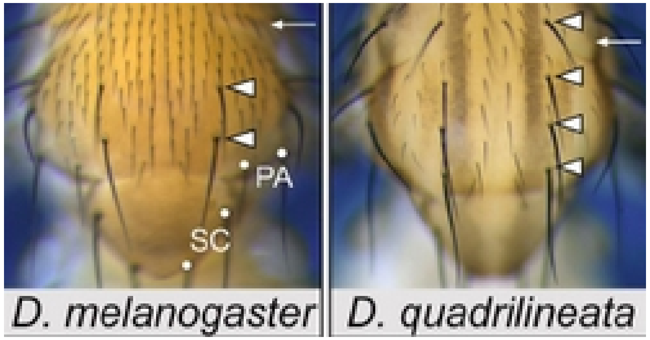


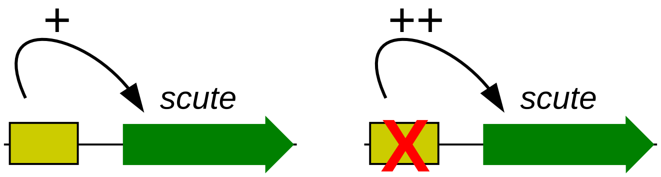
Marcelini and Simpson 2006 PloS Biology

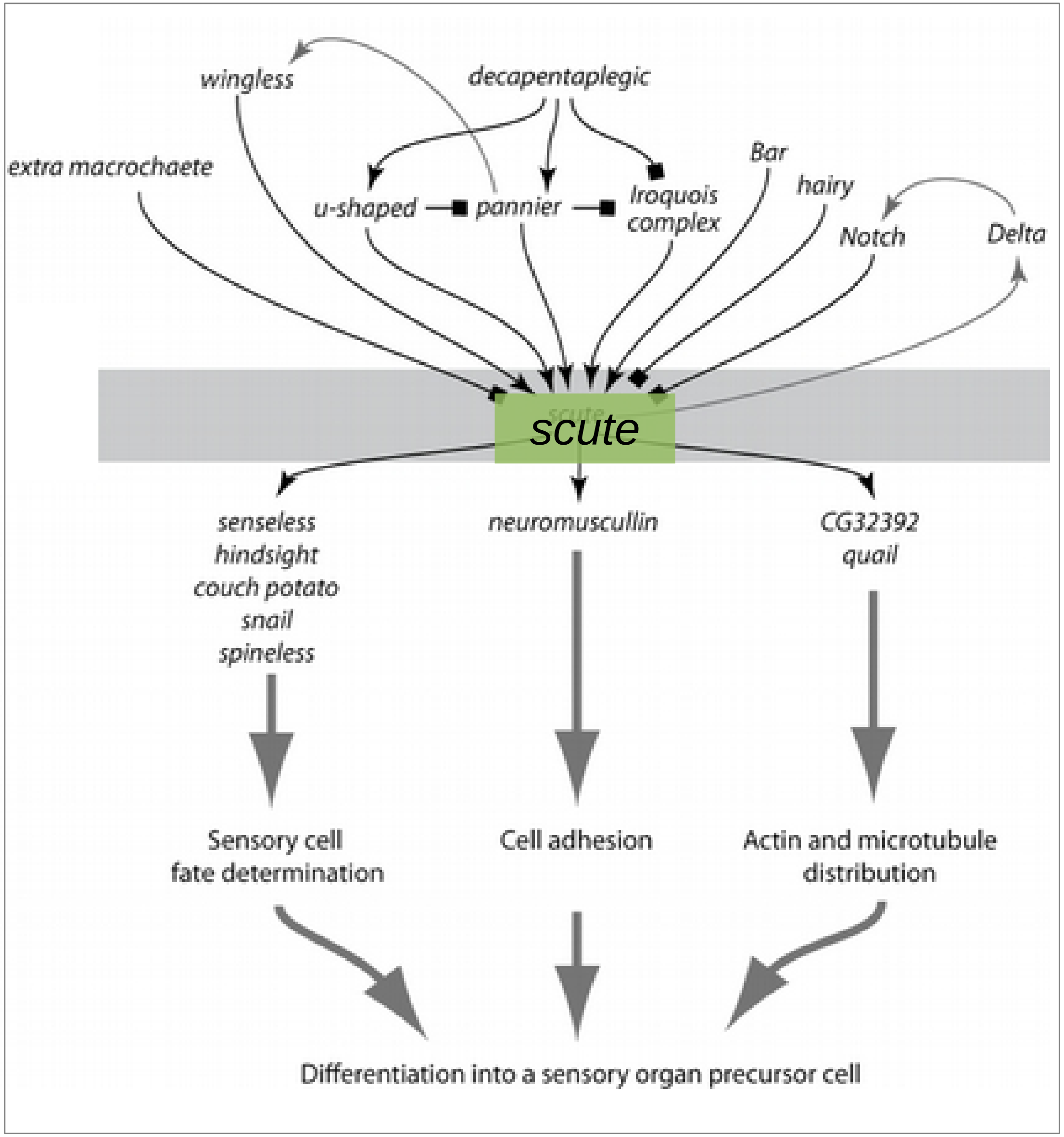
Genetic evolution is predictable

Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*



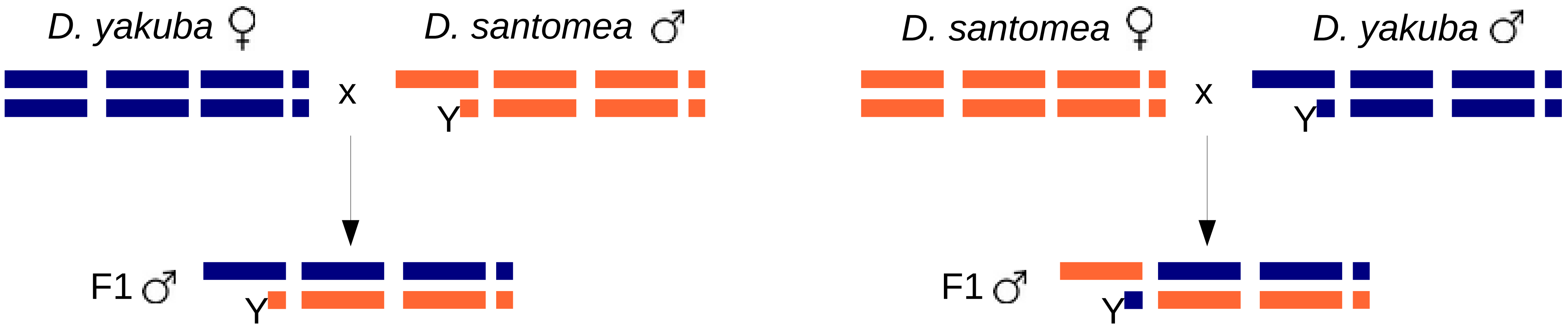




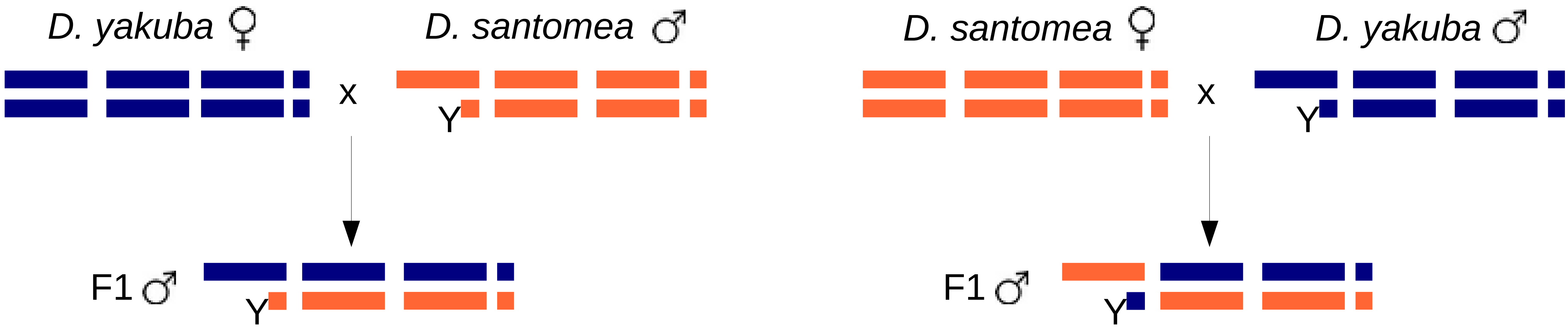
Marcelini and Simpson 2006 PloS Biology

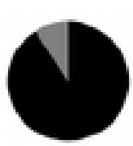
Stern and Orgogozo 2009 Science

Is the causing mutation X-linked?



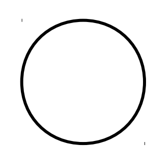
Is the causing mutation X-linked ?





n = 35

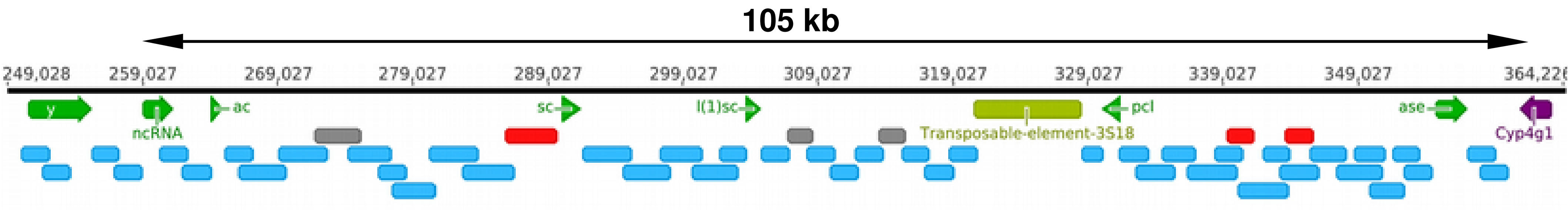
The causing mutation is X-linked



n = 8

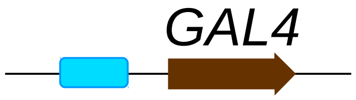
■ 2 bristles
■ 1 bristle
□ 0 bristle

Screening a 100-kb region

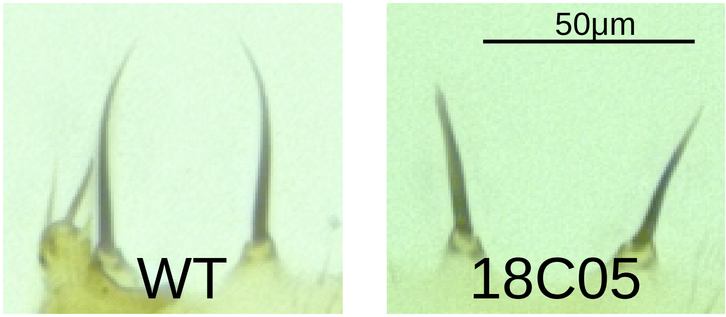


screen of
D. melanogaster
***GAL4* lines**

- drives expression in developing genital bristles
- drives no expression
- not tested yet

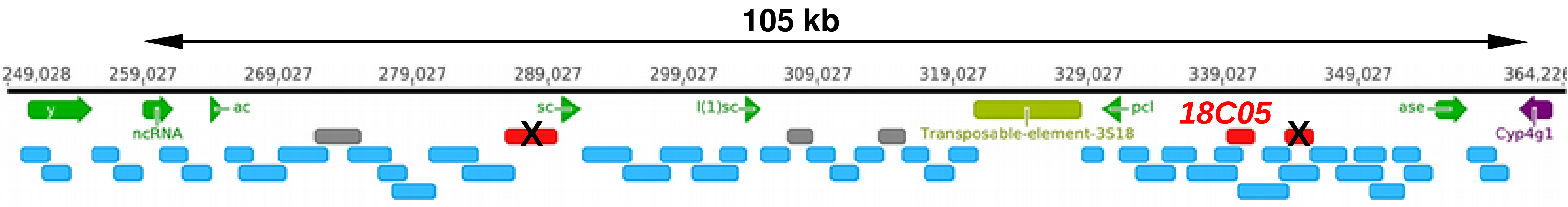


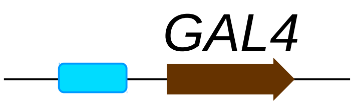
x *UAS-RNAi-singed , UAS-Dicer2*



singed
bristles

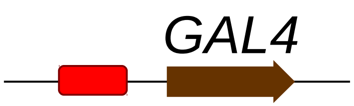
18C05 drives expression independently of *scute*



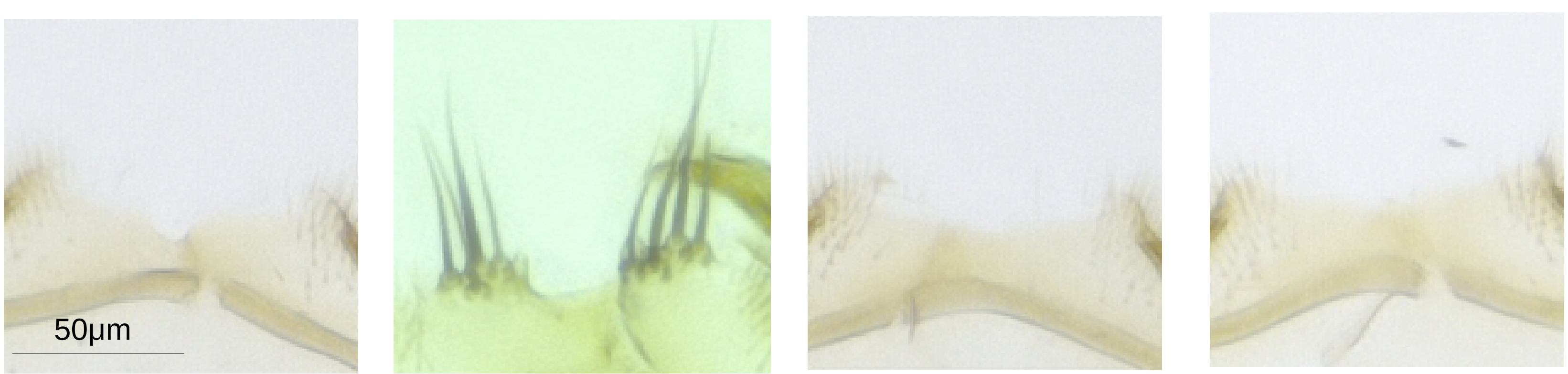


x *UAS-RNAi-singed , UAS-Dicer2*

- drives expression in developing genital bristles (red)
- drives no expression (blue)
- not tested yet (grey)



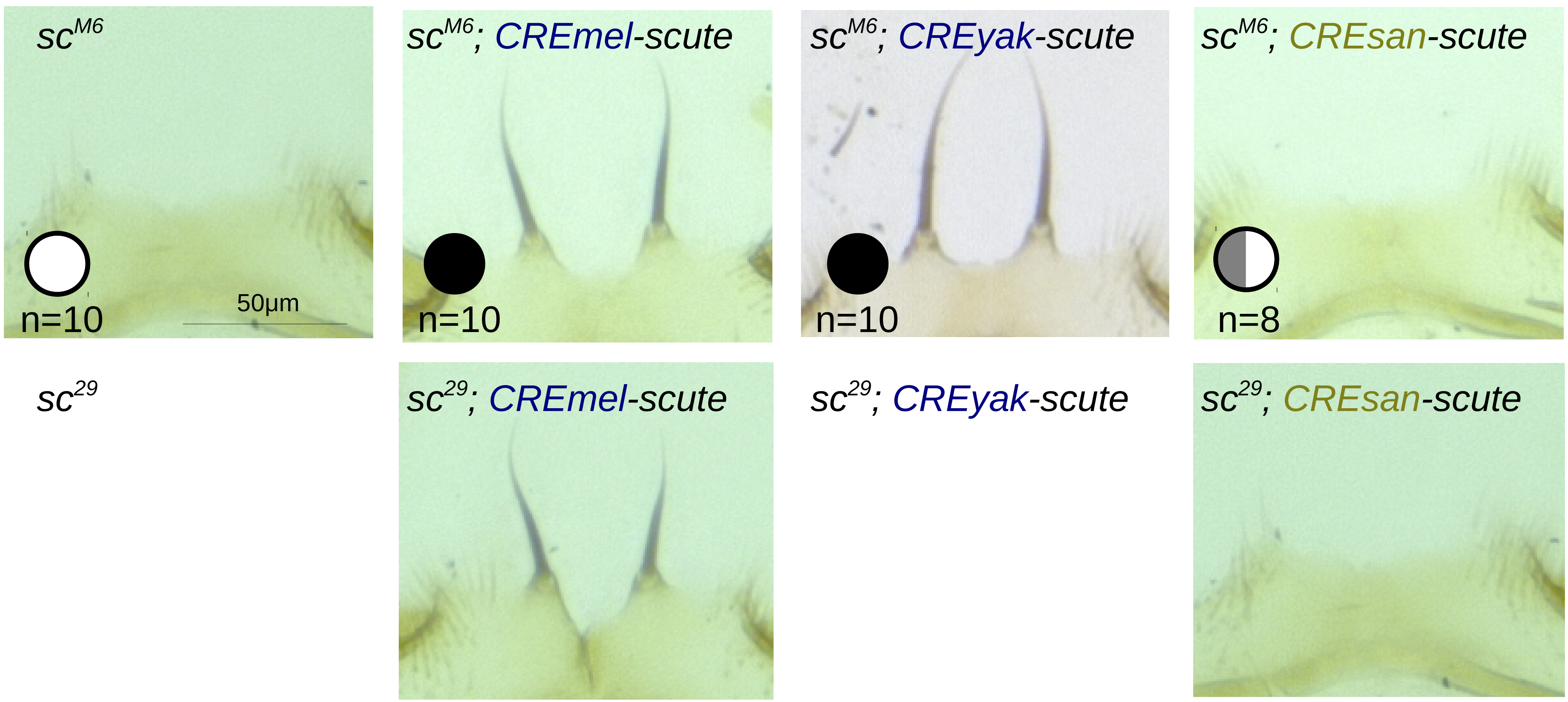
x *sc*^{M6} *; UAS-scute*



- | *18C05* | *15E09* | *054839*

Mutation(s) in *18C05* cause loss of bristles

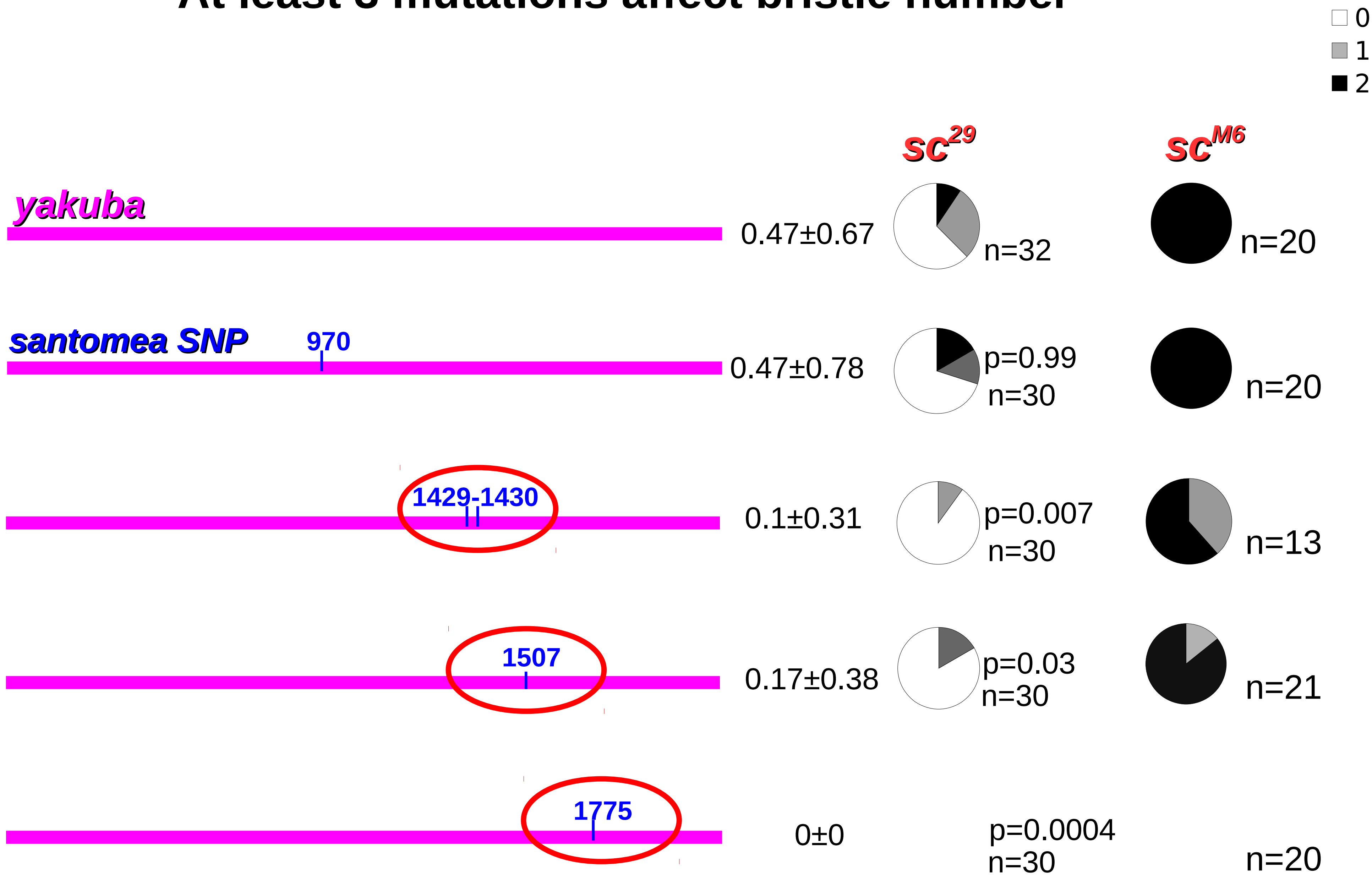
D. melanogaster transgenics



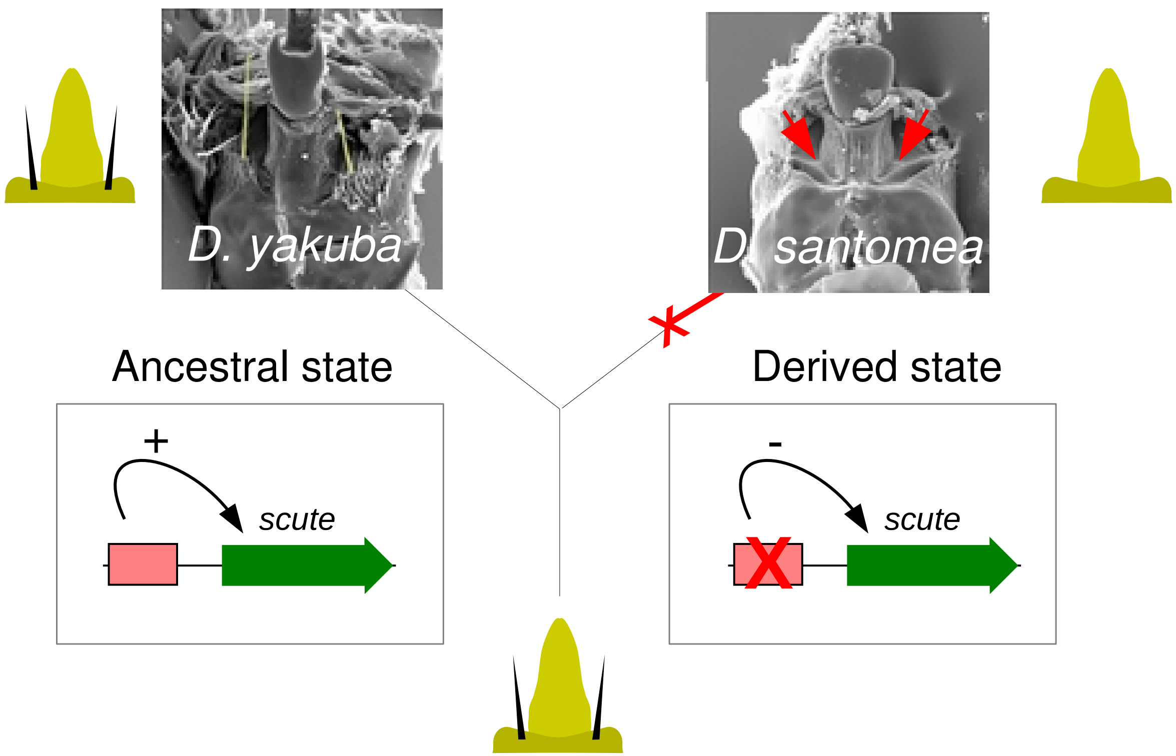
27 SNPs and 3 indels between *D. santomea* and *D. yakuba*

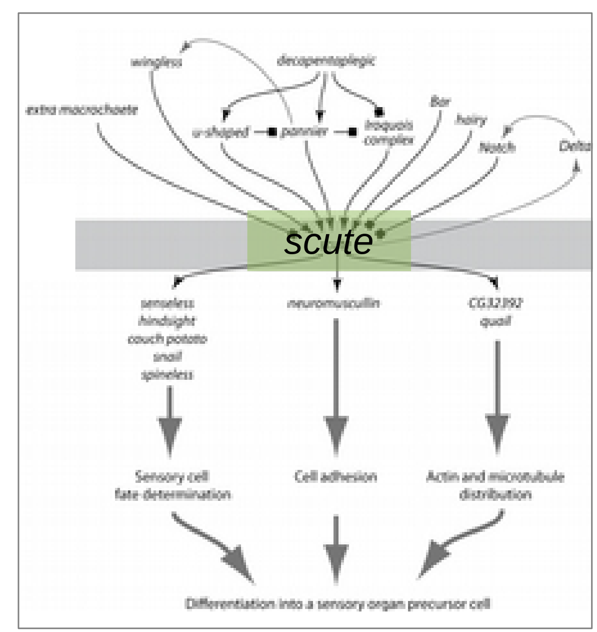
25ºC

At least 3 mutations affect bristle number



D. santomea lost genital bristles via mutations in *scute*

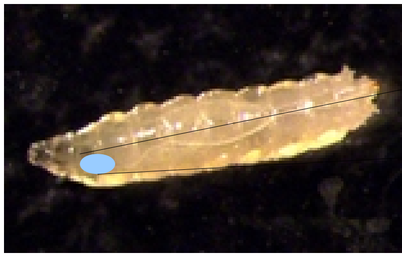




Why is the set of genes causing evolution limited?

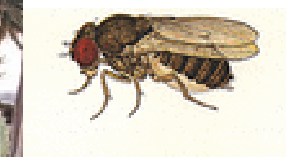
There are specialized genes in a genome

Steroid hormone biosynthesis

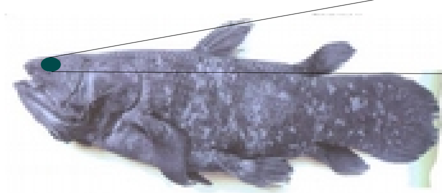


a specialized tissue
specialized enzymes

2-4 mutations in *nvd*



Color vision



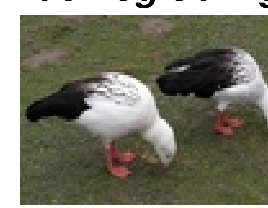
a specialized tissue
specialized molecules

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

Specialized loci in the genome

Proteins that interact with external molecules

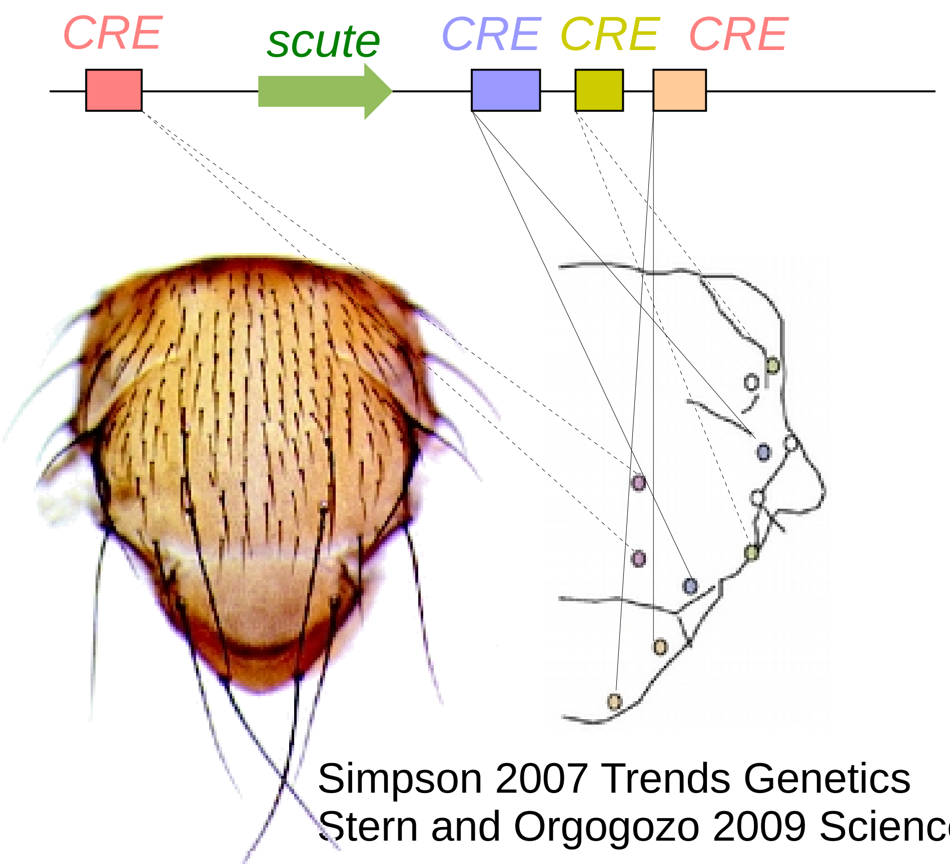
oxygen, photons, insecticide, cholesterol...

Specialized loci in the genome

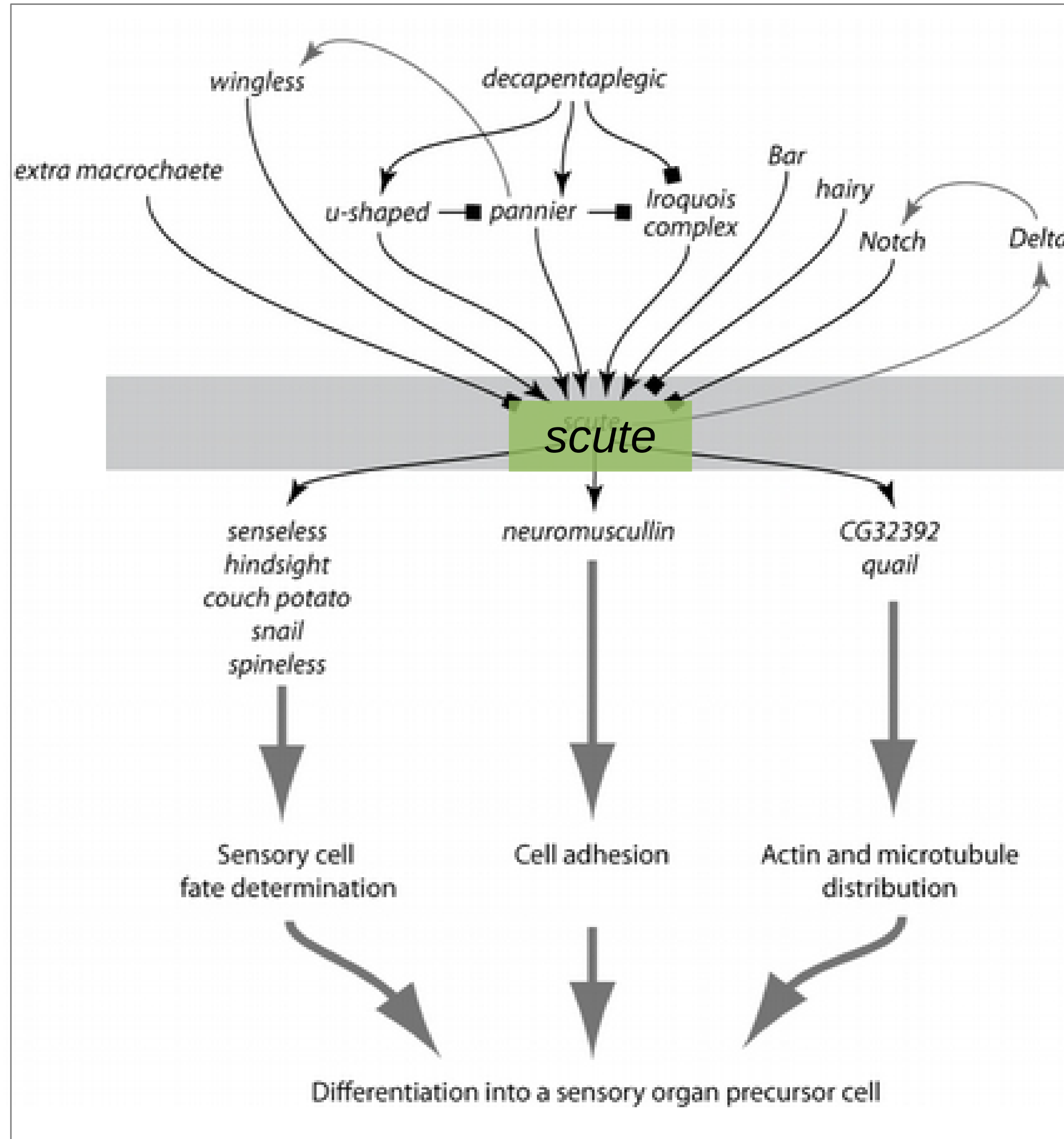
Proteins that interact with external molecules

oxygen, photons, insecticide, cholesterol...

Cis-regulatory elements of “developmental switch genes”



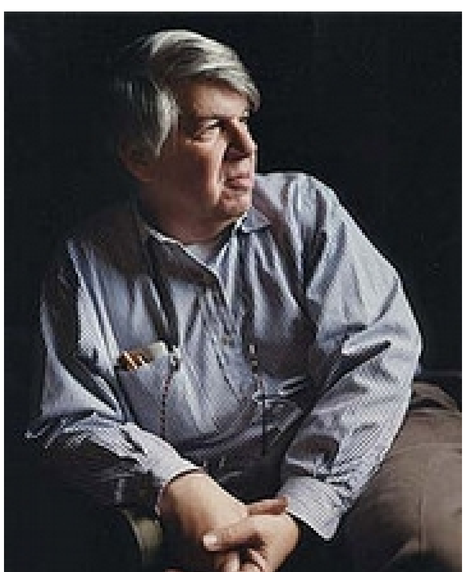
Simpson 2007 Trends Genetics
Stern and Orgogozo 2009 Science



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

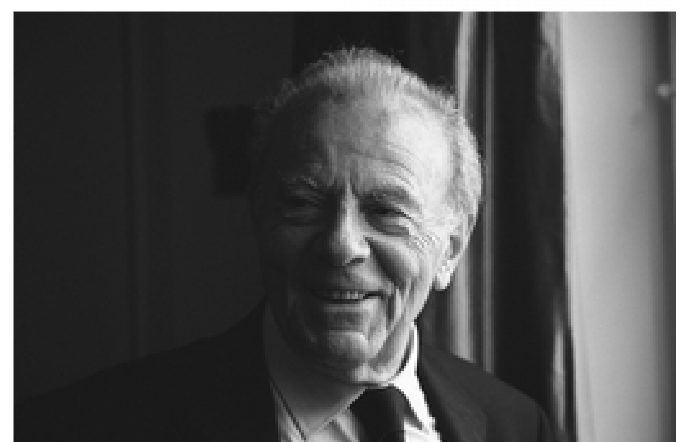


It is hard to realize that the living world as we know it is just one among many possibilities; that its actual structure results from the history of the earth.

1977

Evolution and Tinkering

François Jacob



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

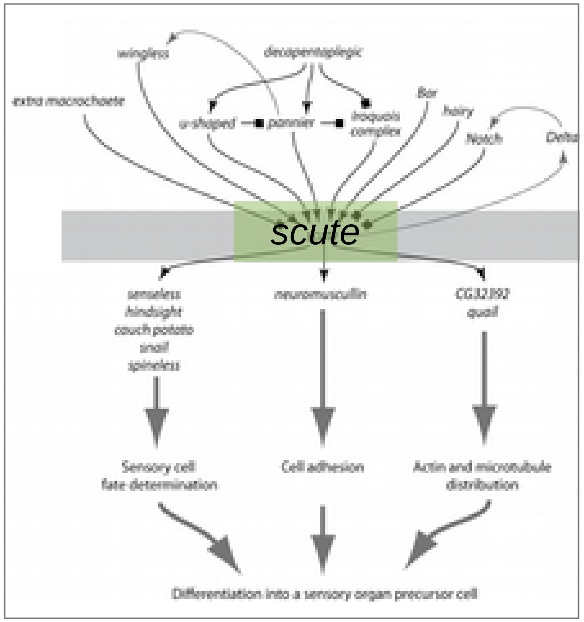
evolution
- **How?**
- **Why?** (1) rather than nothing
- **Why?** (2) rather than another change

From random processes can emerge predictability

Many unpredictable processes
at a low level

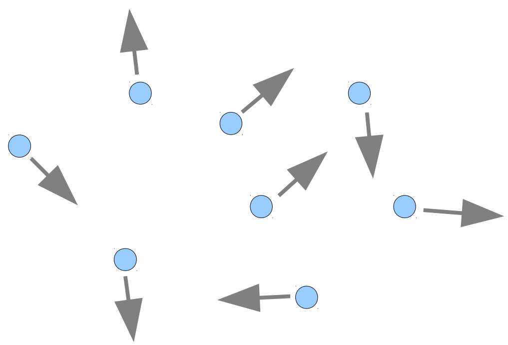
Predictable Evolution
at the genetic level

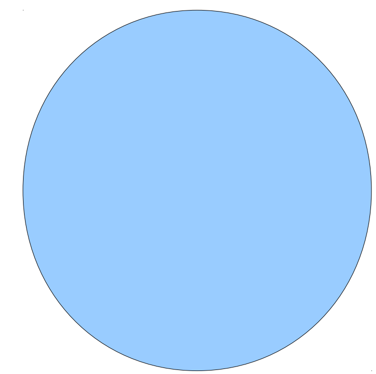
Mutations in DNA
Chromosome segregation during meiosis
Assortative mating
Gamete competition during fecondation
Life history traits
Genetic linkage
Environmental changes (meteorite, etc.)
...



From random processes can emerge predictability

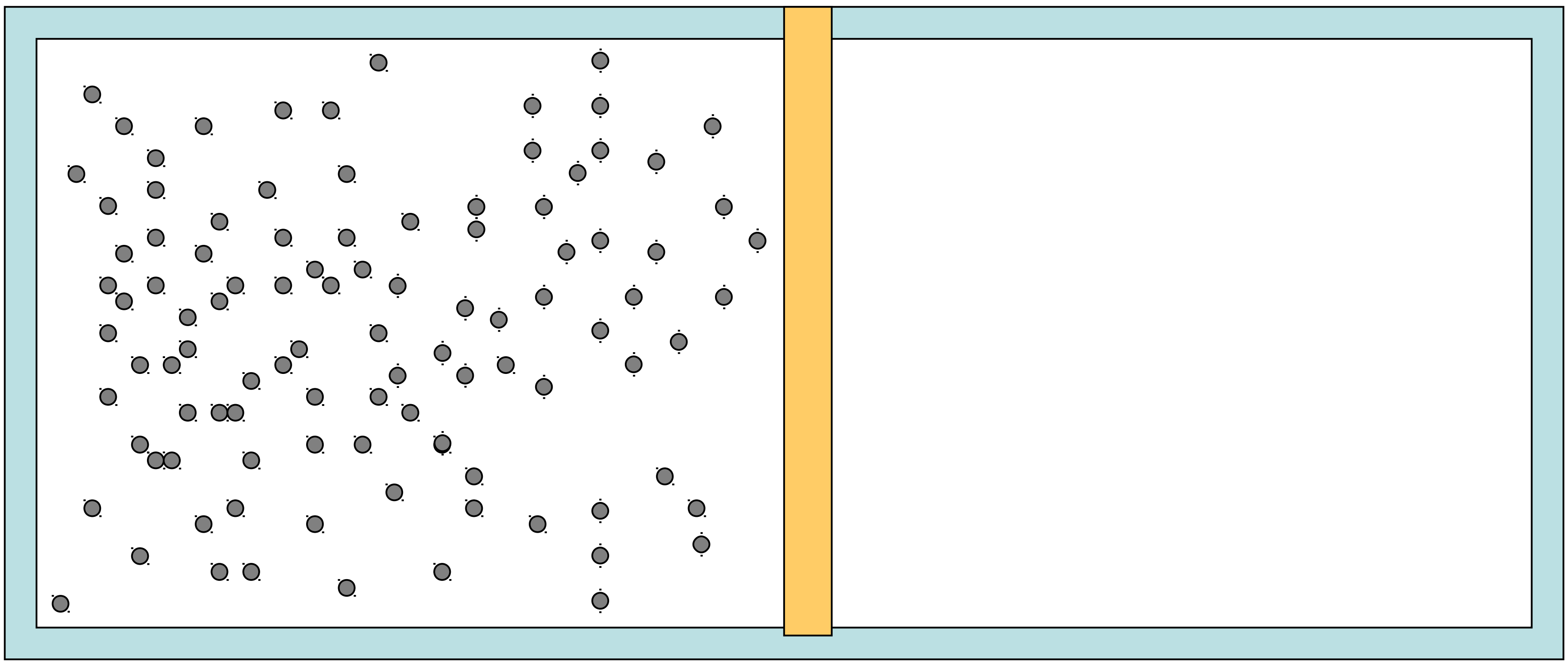
Microscopic world → Macroscopic world

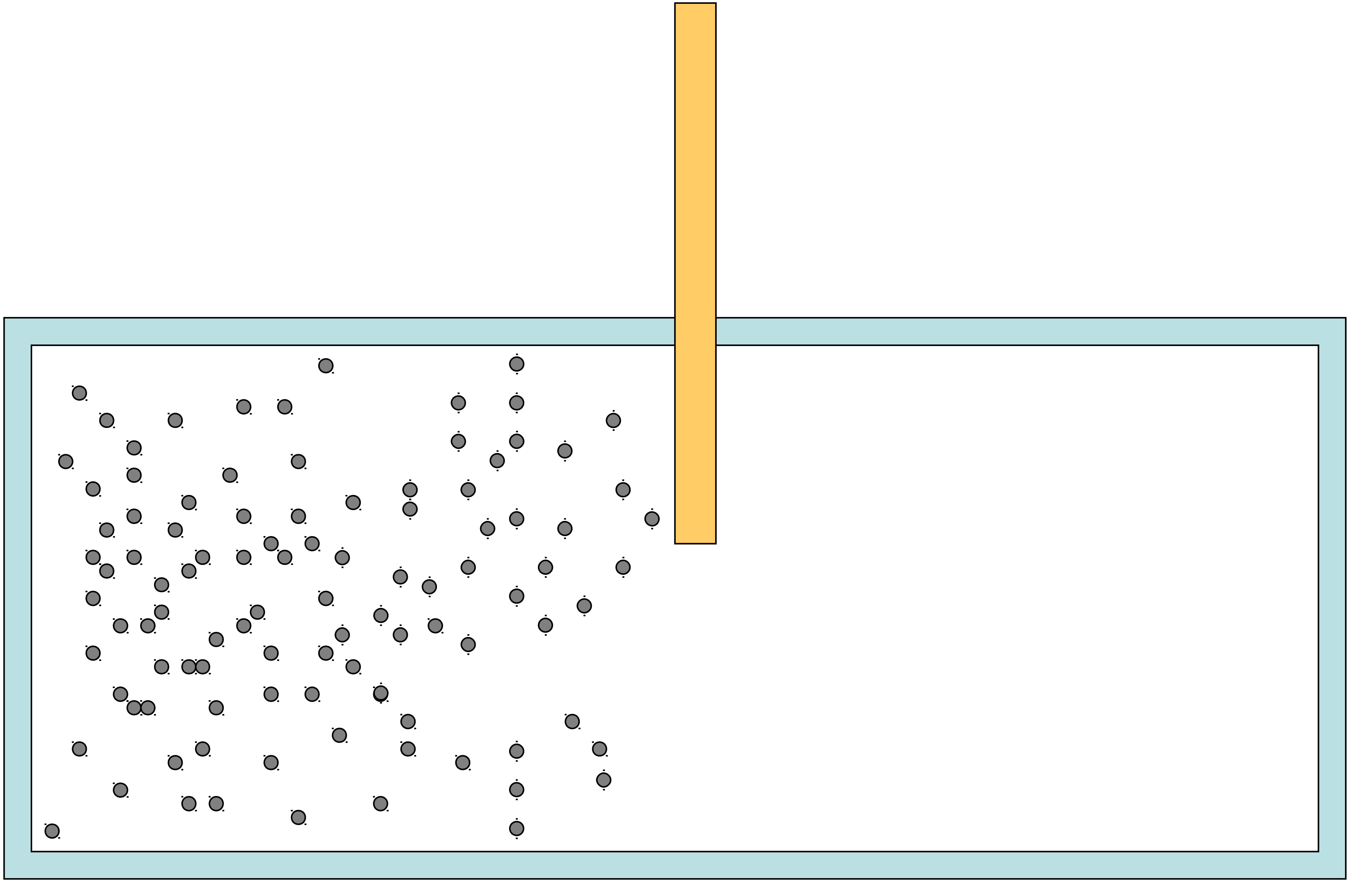


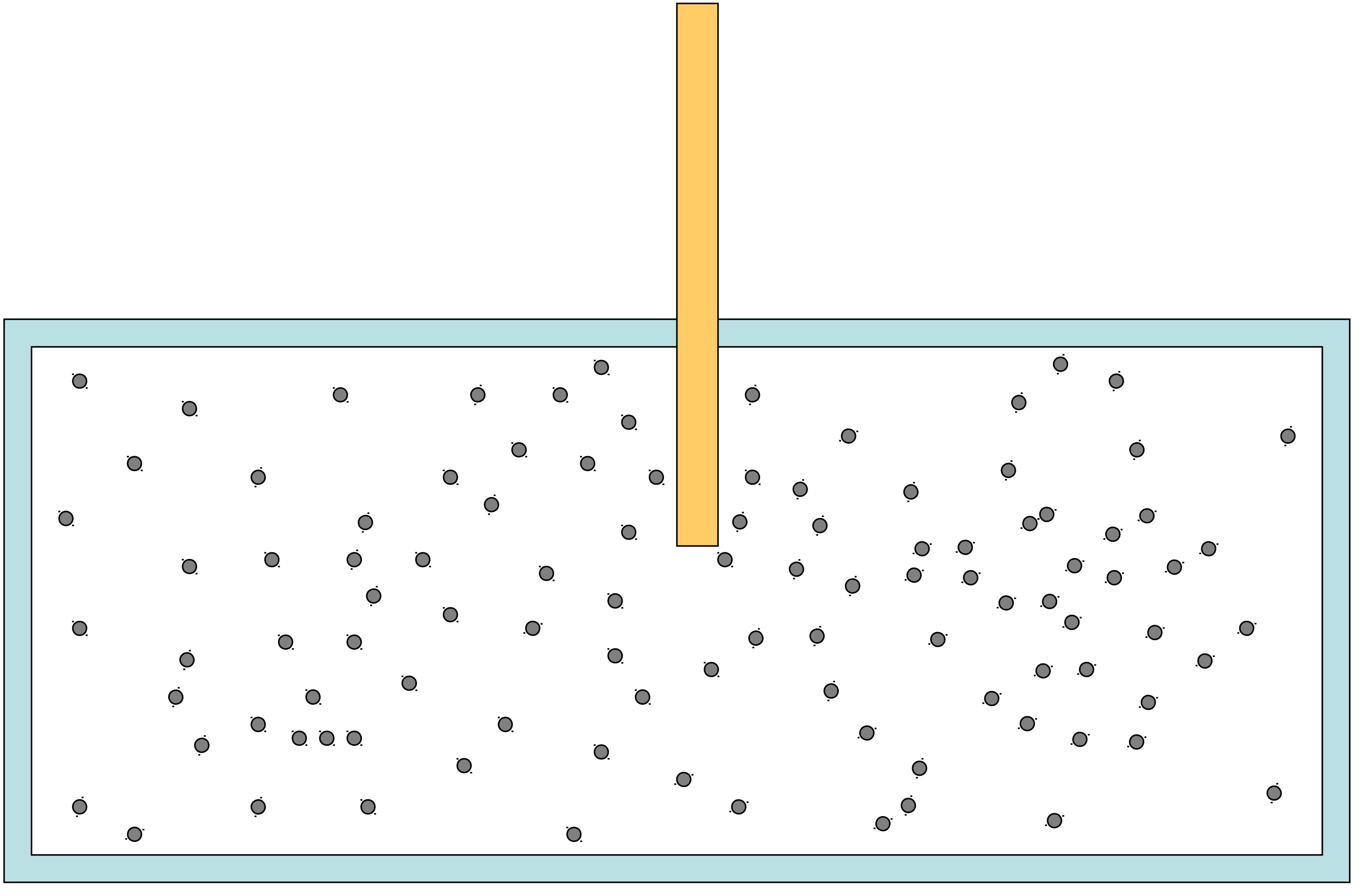


Position, mass, velocity of each particle

Pressure, Volume, Temperature, Number of moles





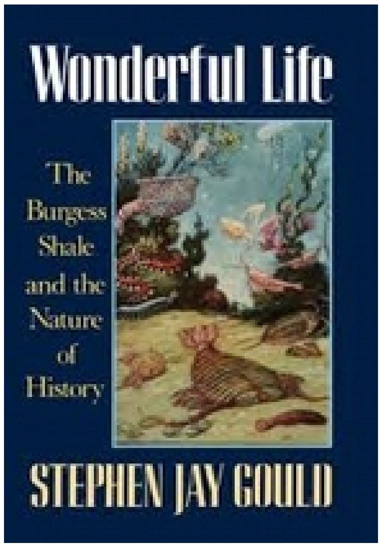


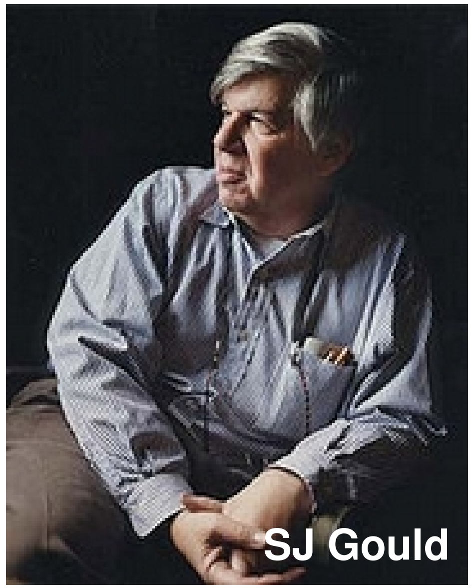
After a few seconds

UNPREDICTABLE ?

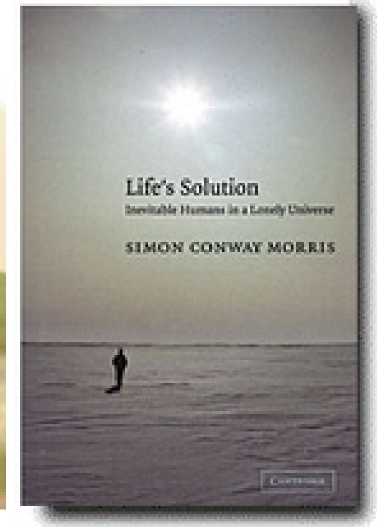
Evolution

PREDICTABLE ?

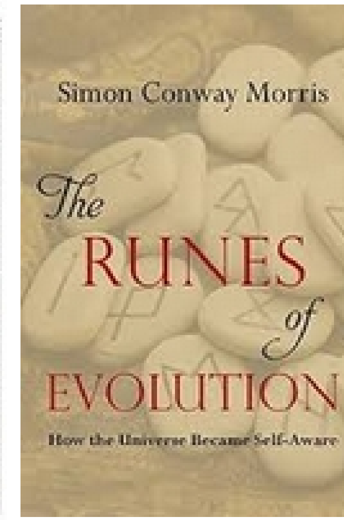




1989



2003



2015

Rare events with important consequences

Evolutionary mechanisms are random

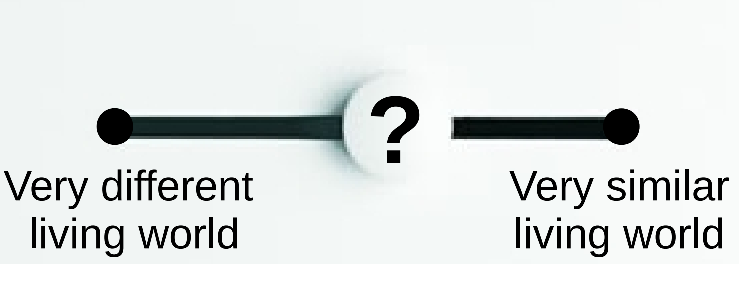
Many possibilities unexplored

Multiple convergences

Not that many possibilities

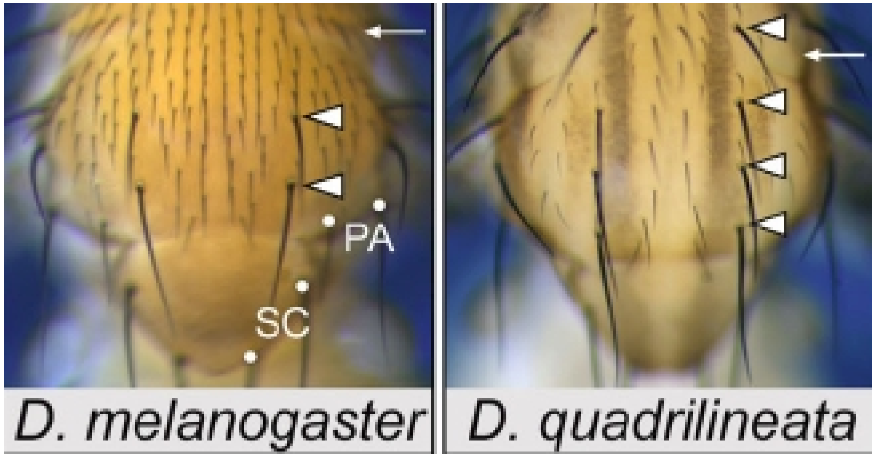
All possibilities explored

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



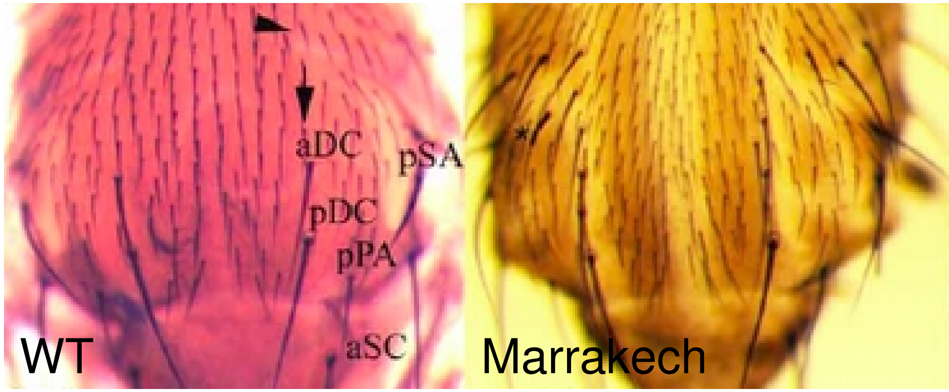
Bristle evolution:
always *scute* cis-regulatory elements?

1) extra bristles in *D. quadrilineata*



Marcelini and Simpson 2006

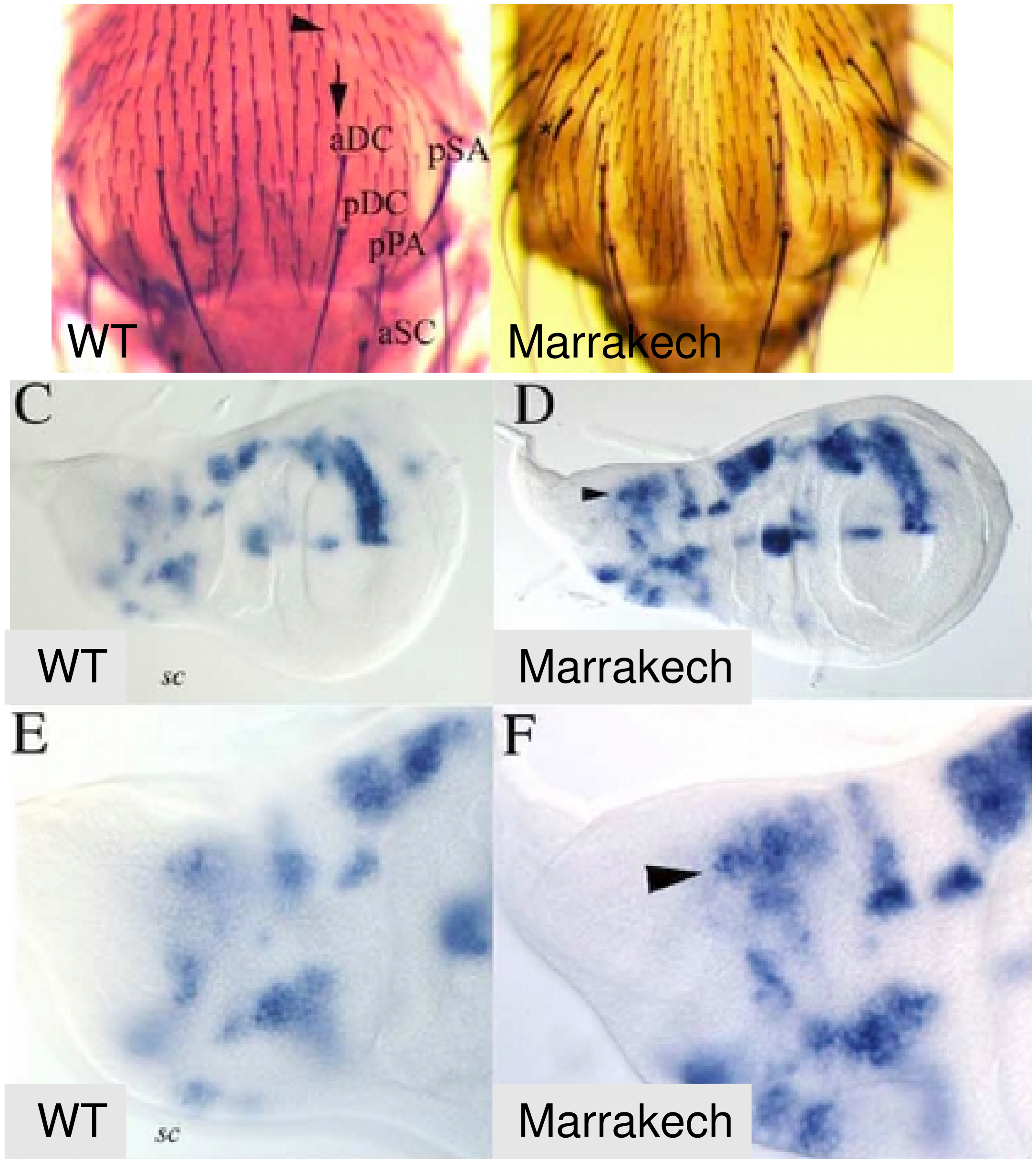
2) extra bristles in a *D. melanogaster* subpopulation



Gibert et al 2005

3) bristle loss in *D. santomea*

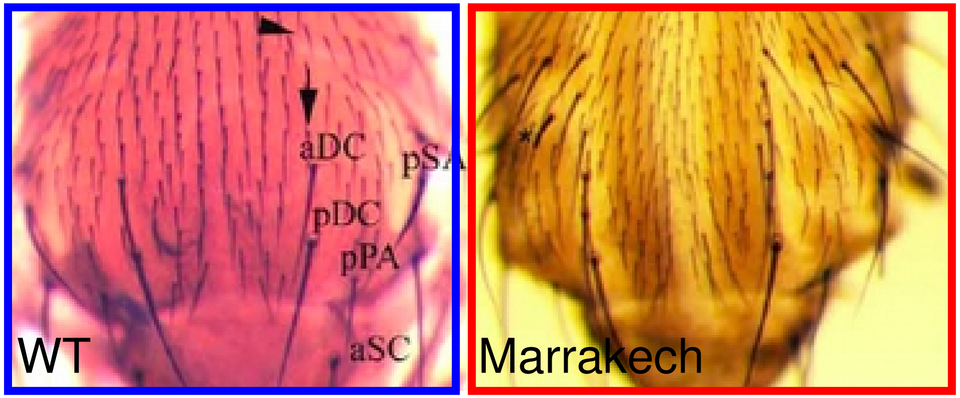
Extra bristles in *D. melanogaster*-Marrakech correlate with larger *scute* expression domain

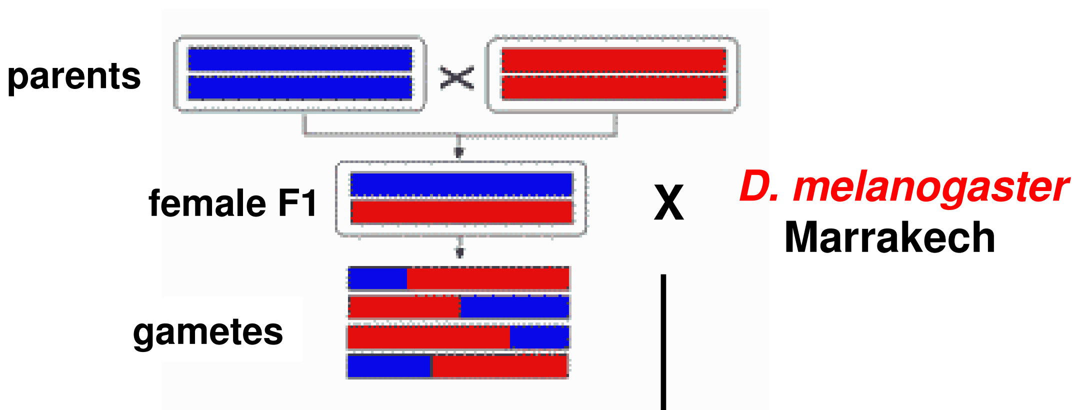


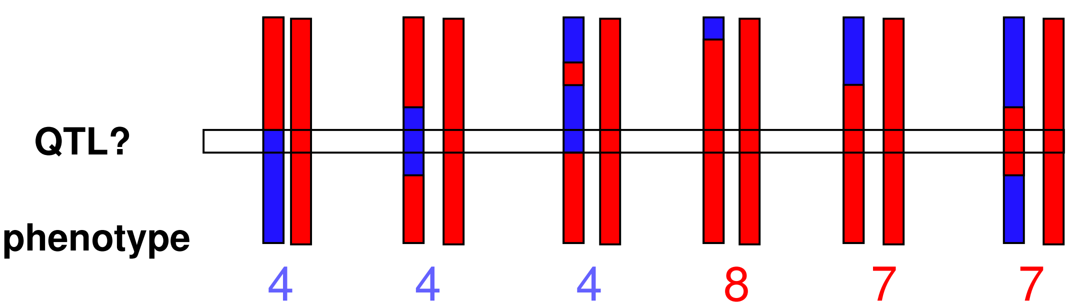
scute

Gibert et al 2005

Extra bristles in *D. melanogaster*-Marrakech due to mutation(s) in *poils-au-dos*

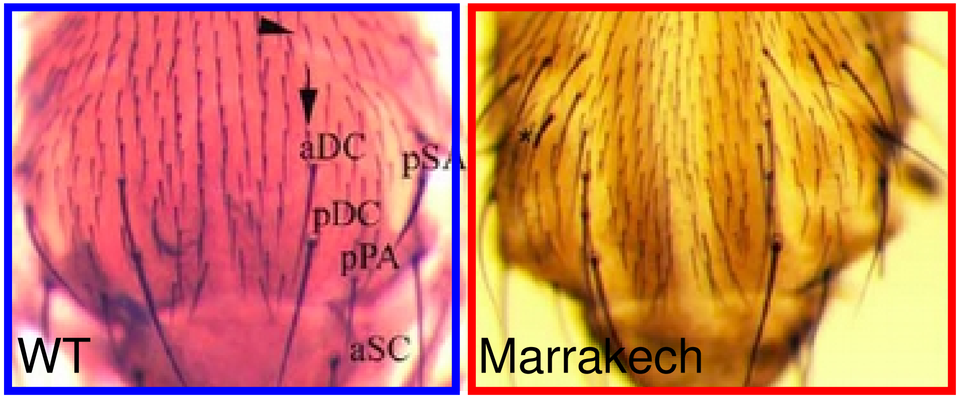


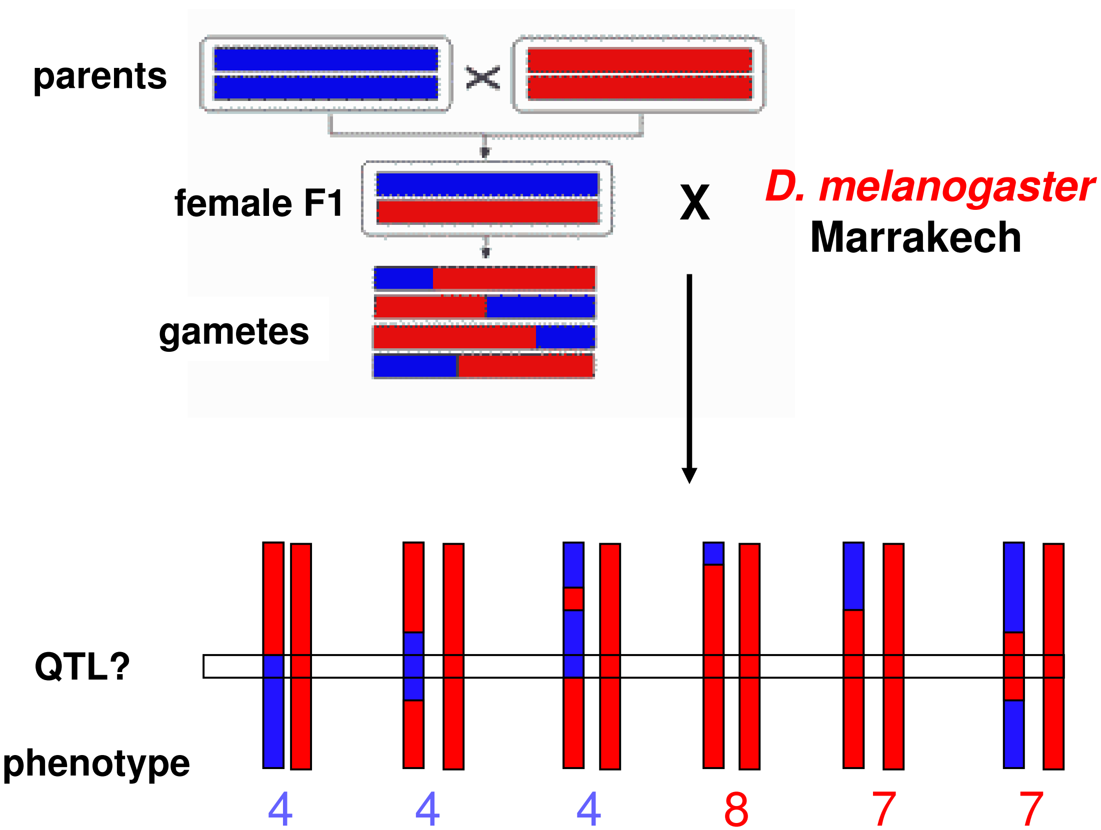


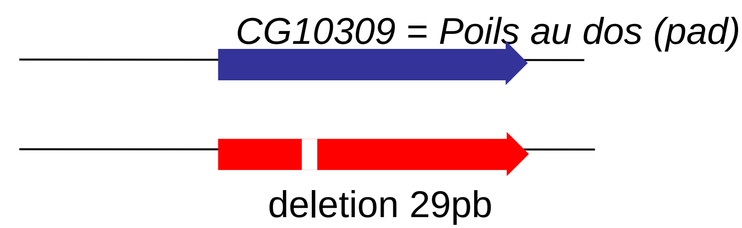


Gibert et al 2005

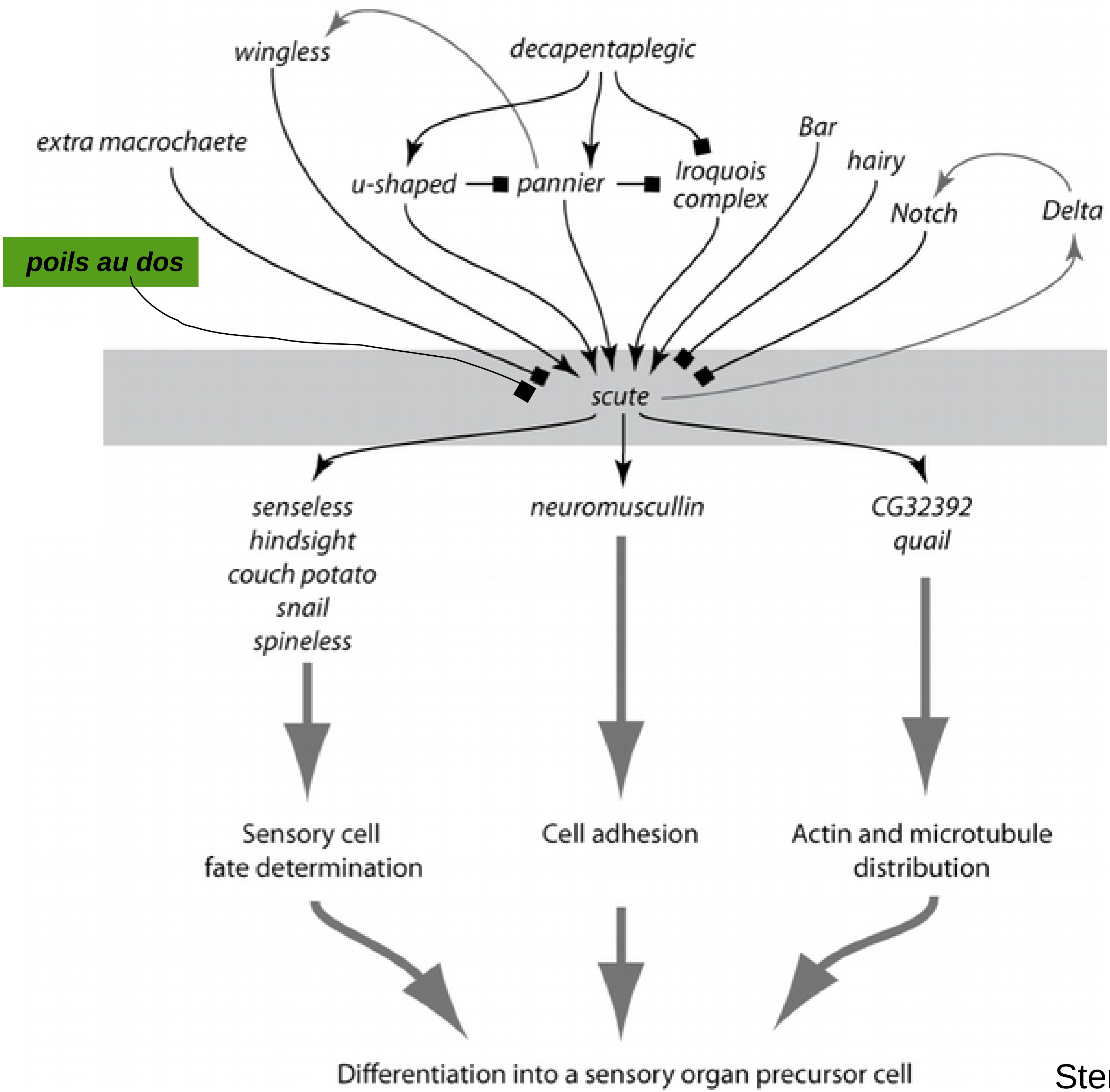
Extra bristles in *D. melanogaster*-Marrakech due to mutation(s) in *poils-au-dos*





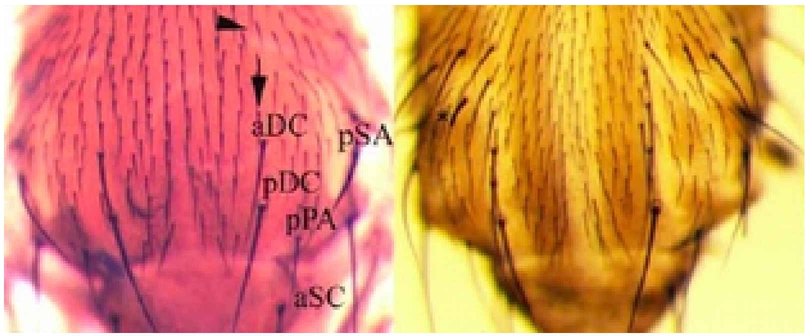


Gibert et al 2005

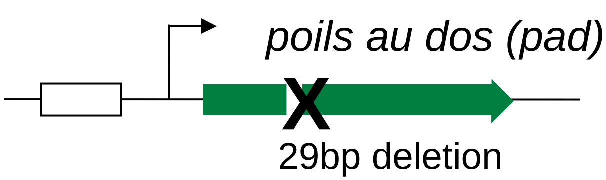


Stern 2009 Science

Short-term evolution…



D. melanogaster ***D. melanogaster* variant**

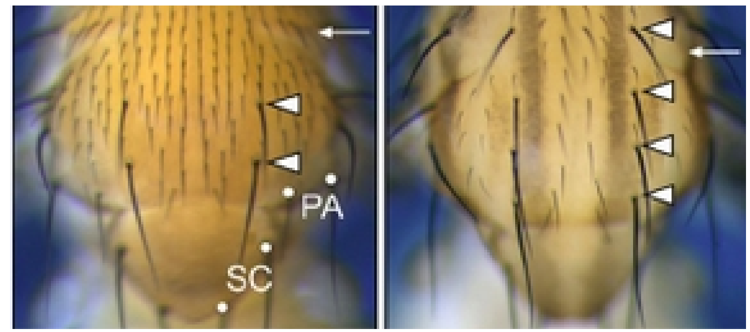


null mutation in coding region

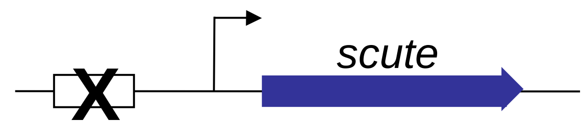
change in thorax and wing

(Gibert et al., 2005)

…versus long-term evolution



D. melanogaster ***D. quadrilineata***



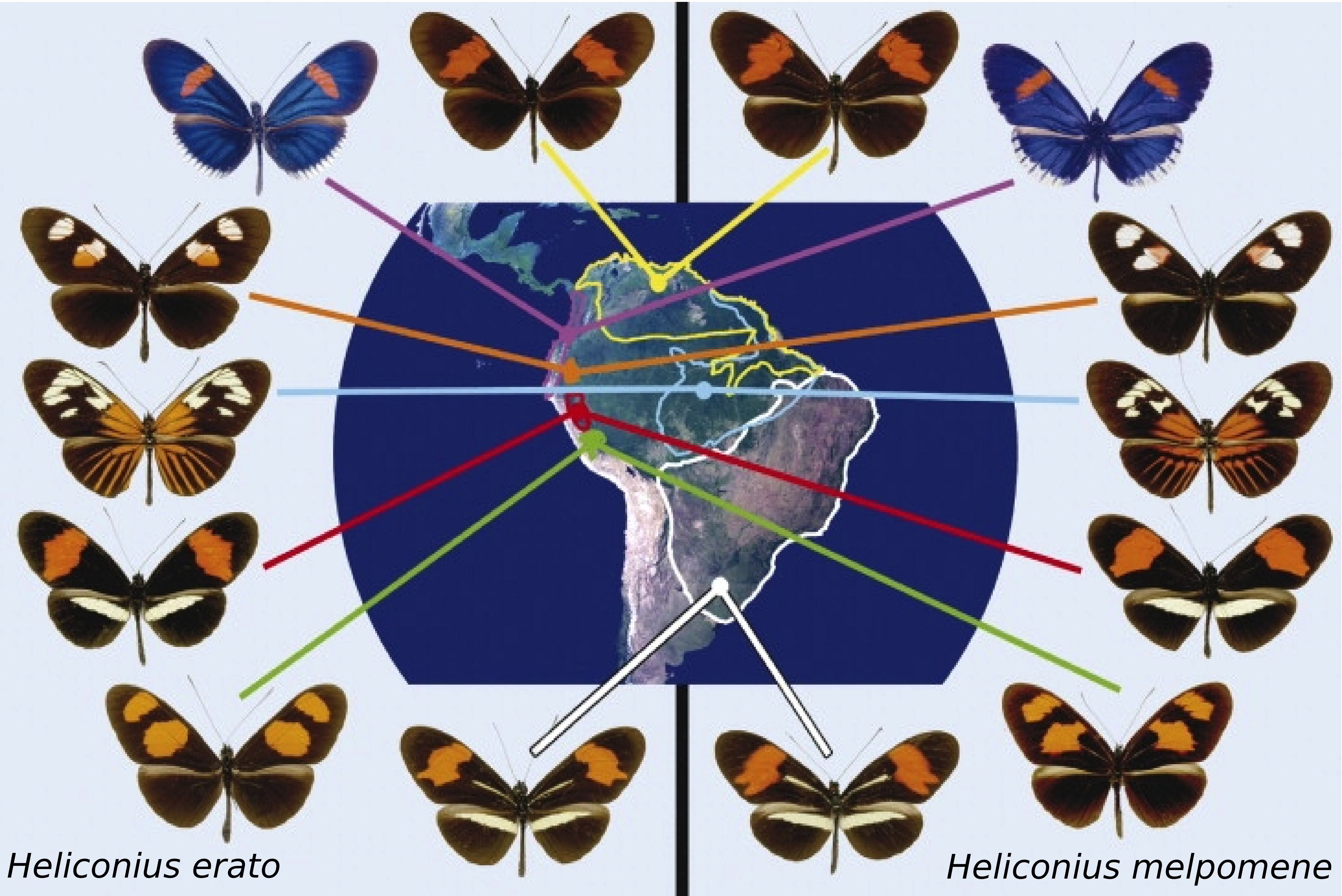
cis-regulatory mutation

change in the thorax only

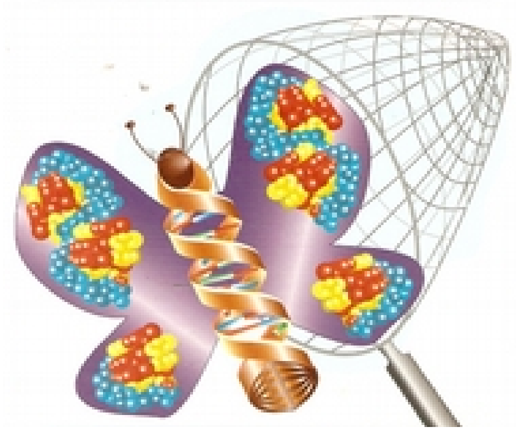
(Marcellini et al. 2006)

The tree of life is not a tree

Natural replicates of evolution



This drawer = SIBLINGS from a hybrid cross

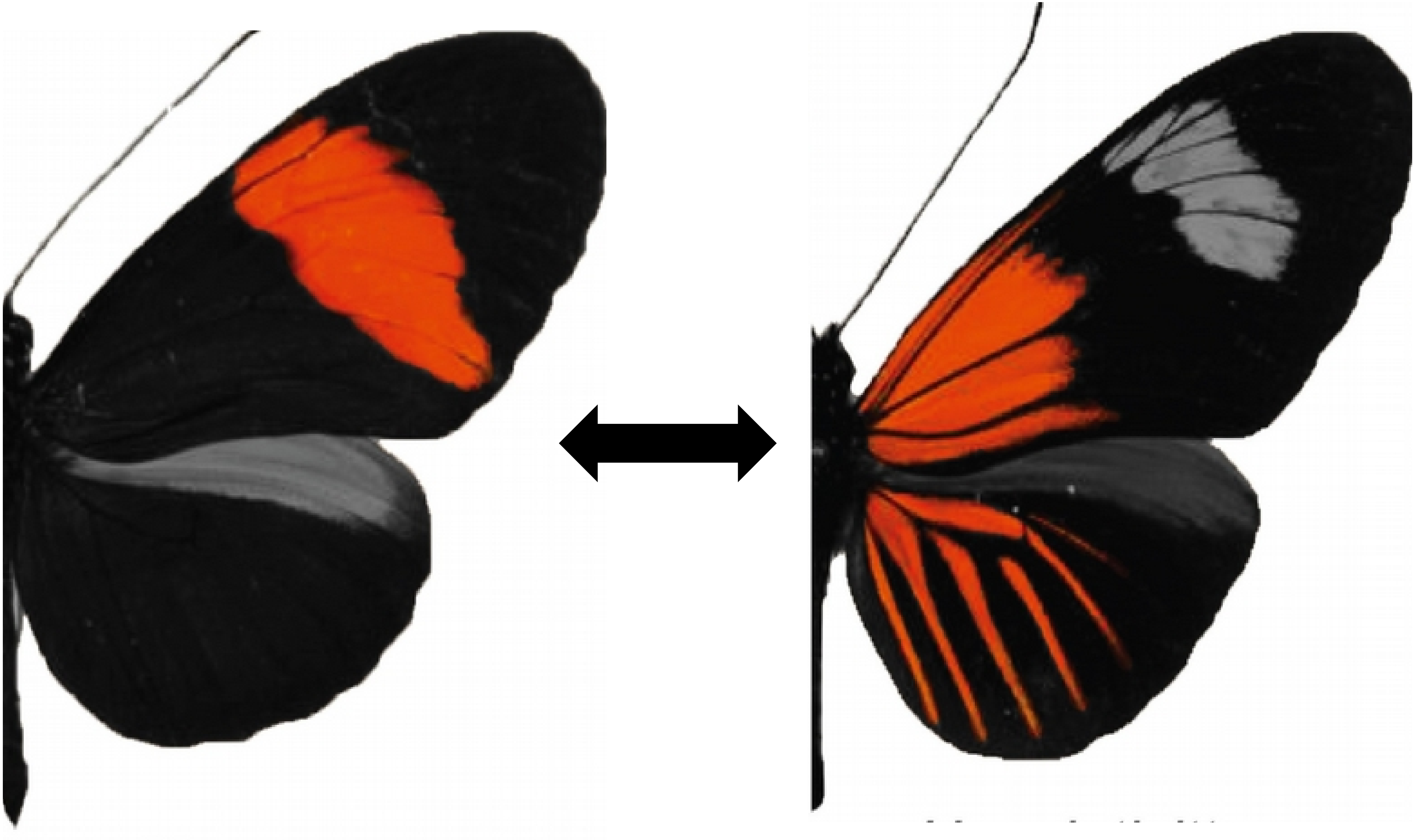


GENE HUNT

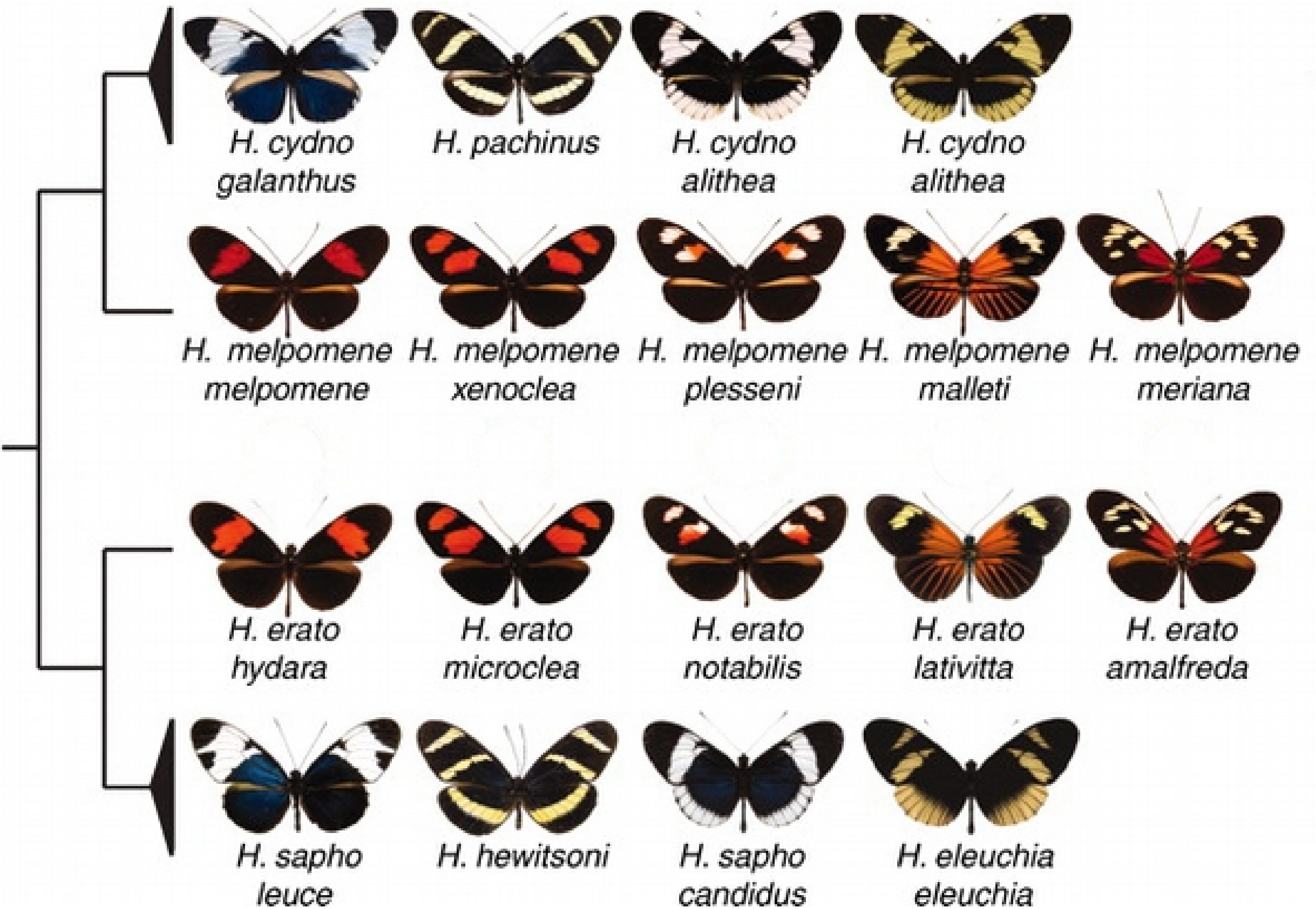
Heliconius melpomene

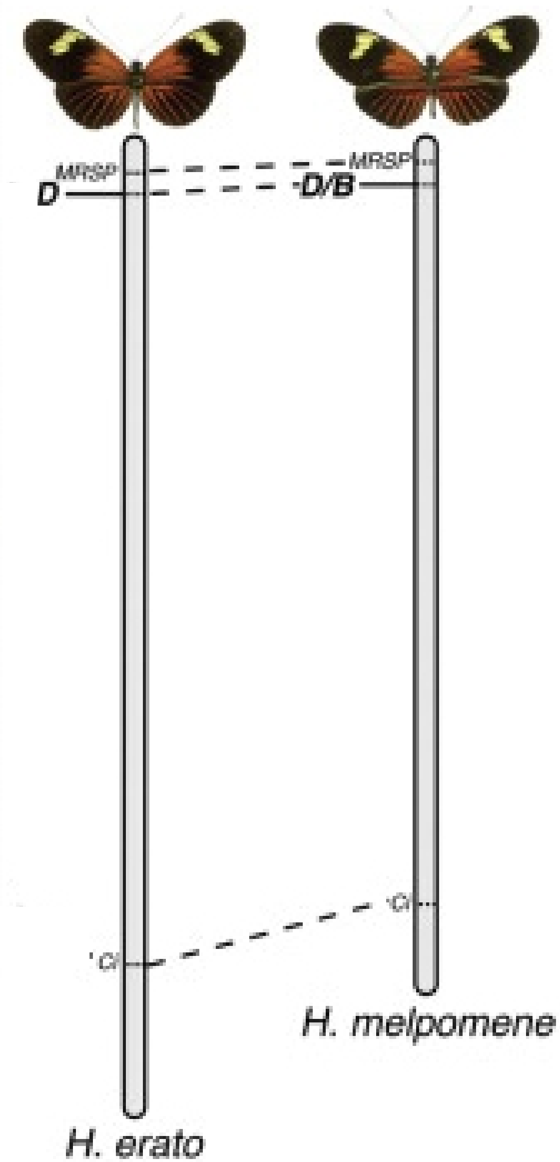
Heliconius erato

Which genes?
Same genes in co-mimics?



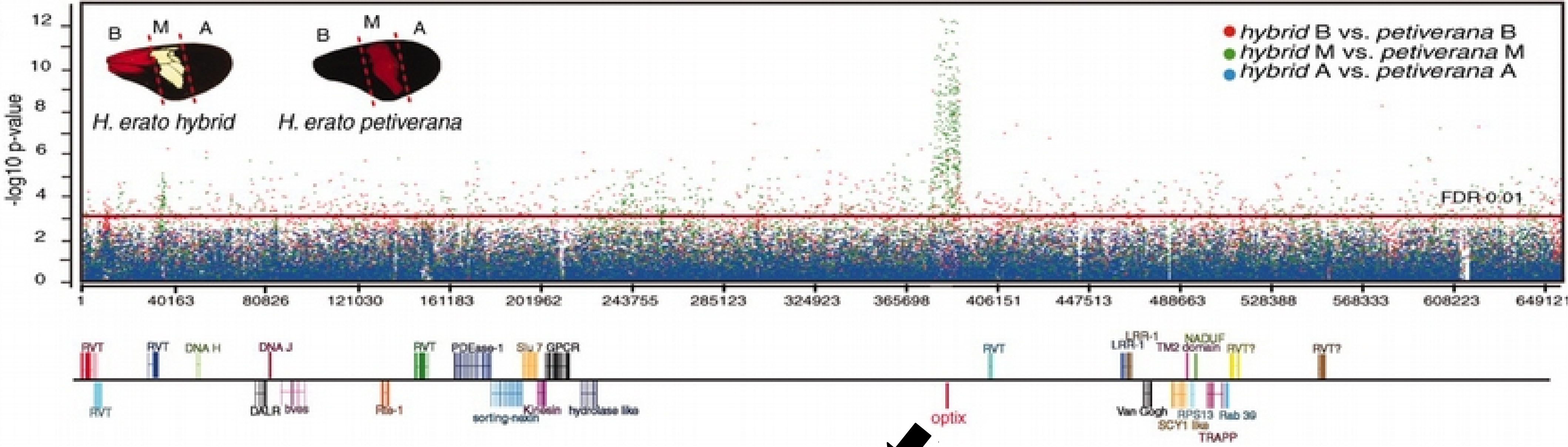
Genetic parallelism in co-mimics



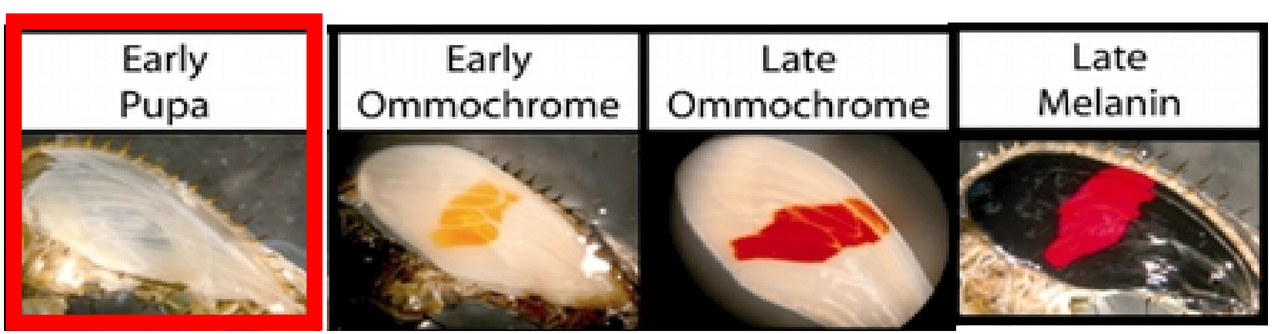


"Same locus" for variation of "same trait"

Fine mapping done by the labs of Chris Jiggins and Owen McMillan
Baxter *Genetics* 2008

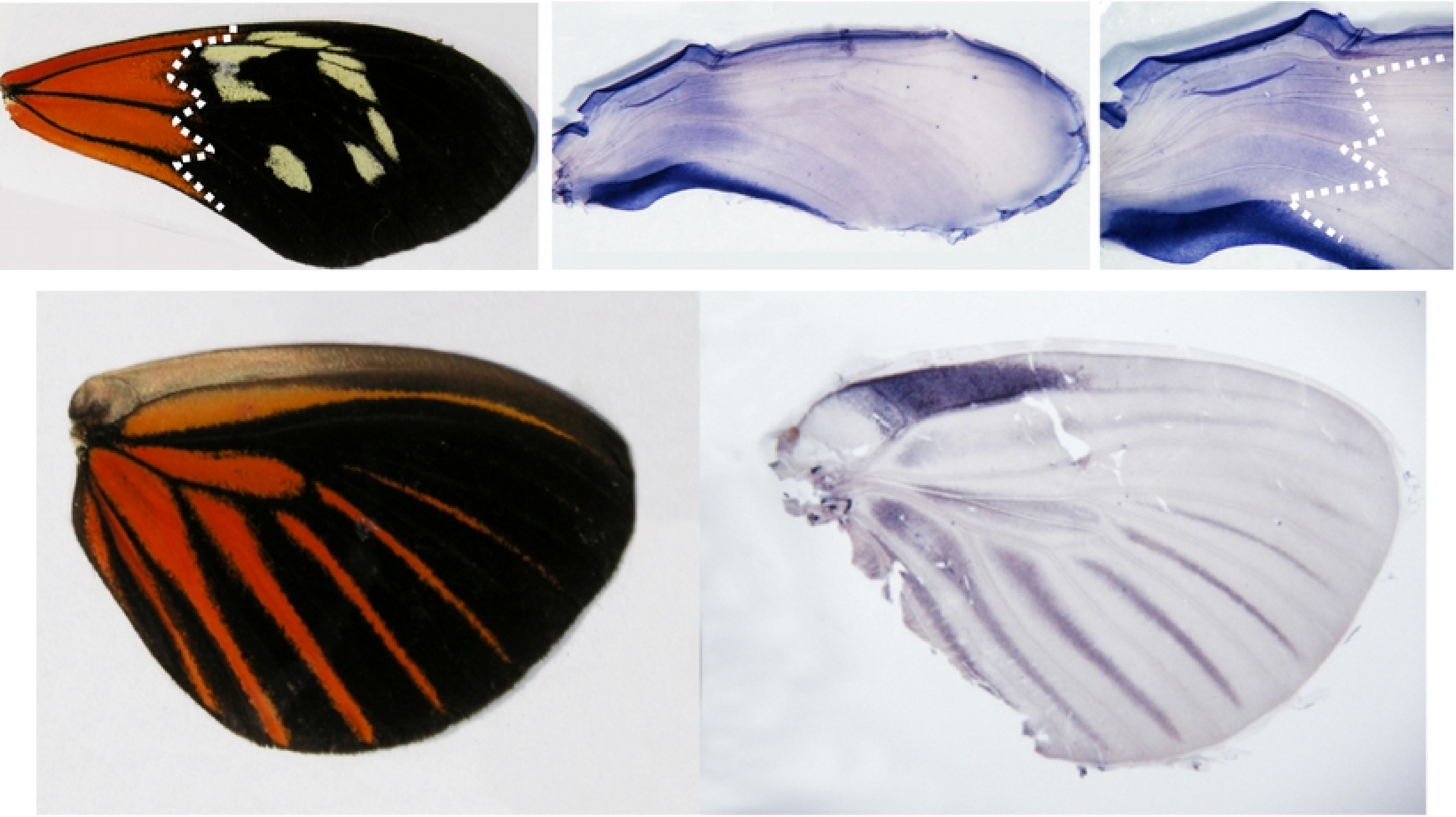


Microarray signal:
optix



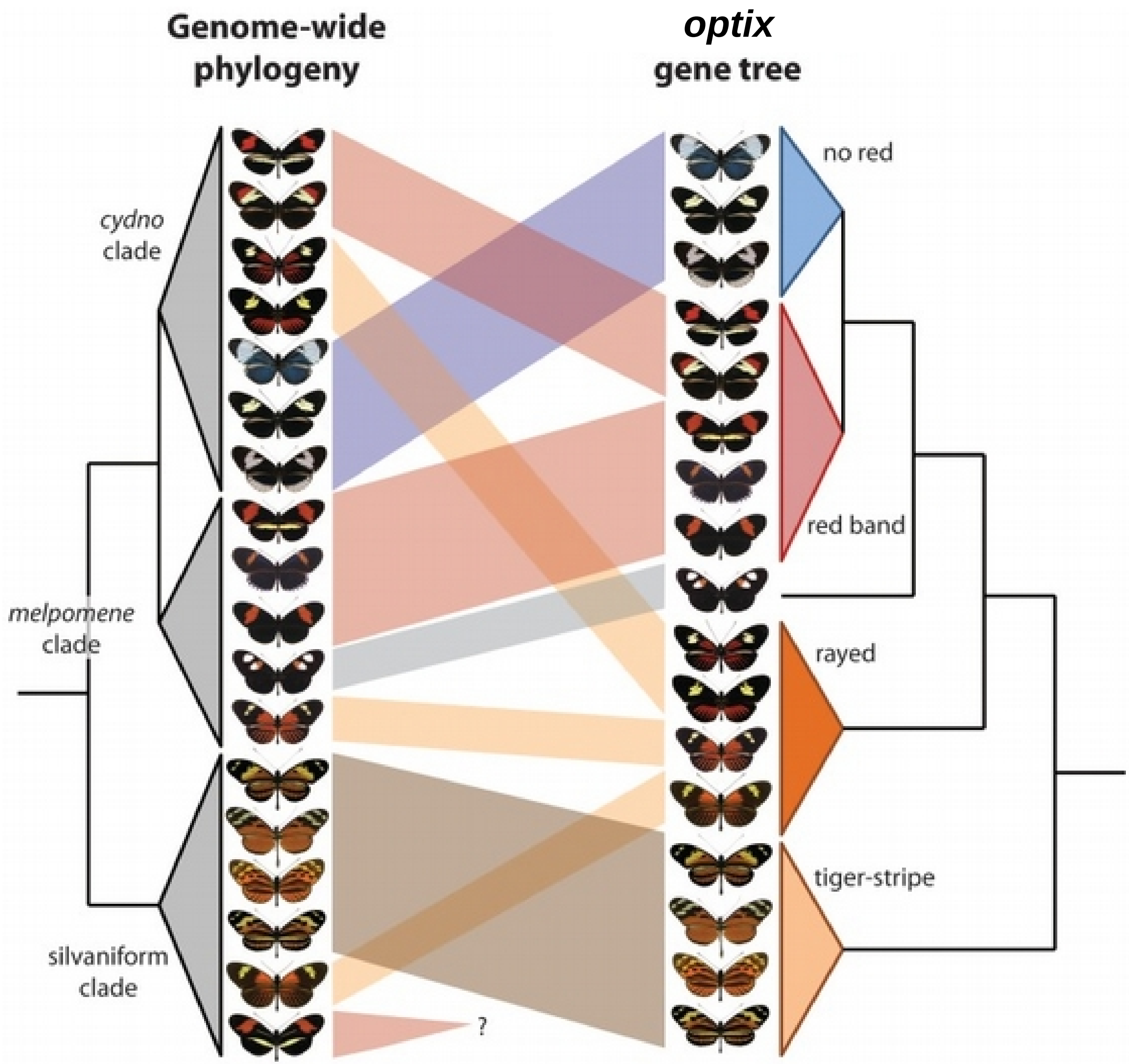
Reed et al. Science 2011

Optix marks red scale precursors



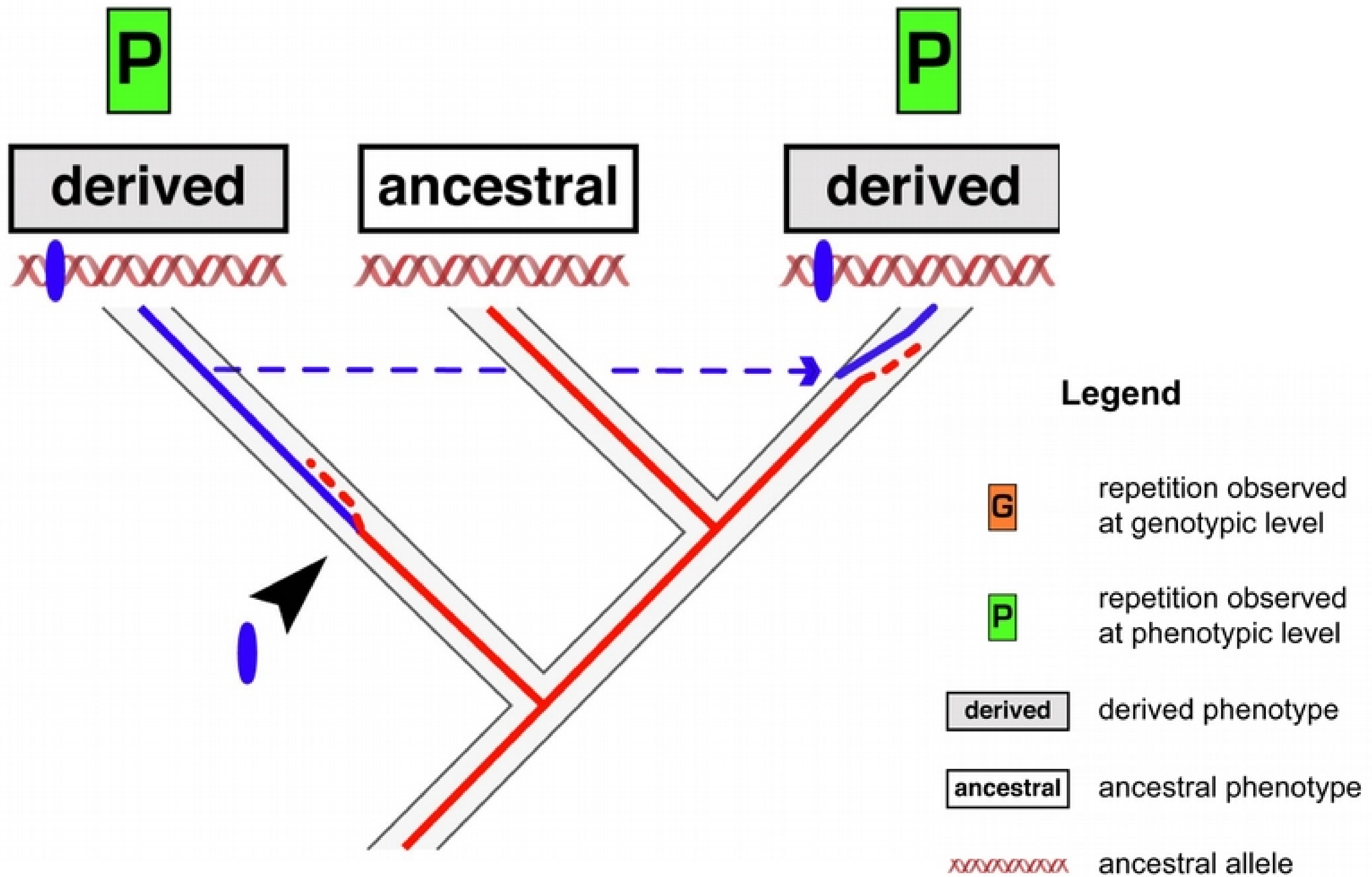
Reed Science 2011

Genetic plagiarism of the red wing color pattern

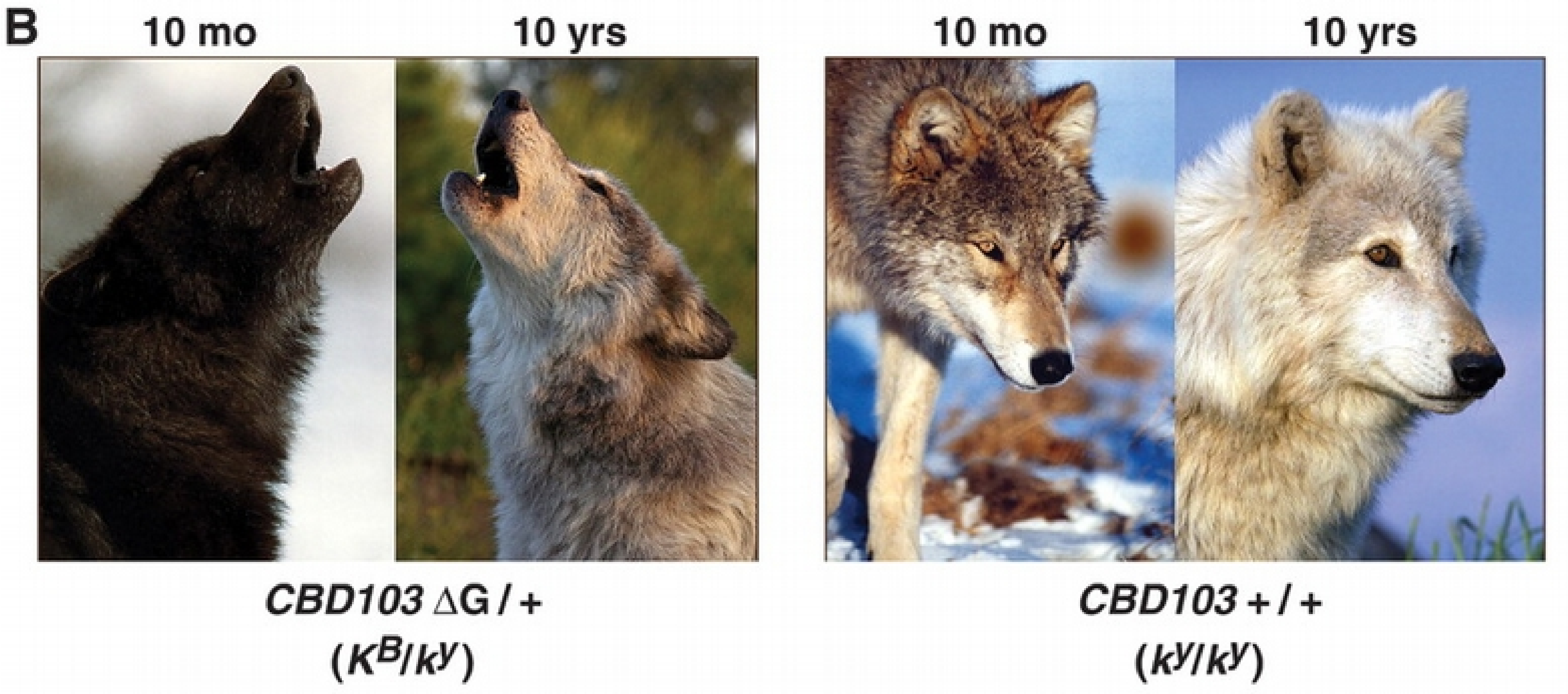


(Reed 2011, Pardo-Diaz 2012, Heliconius Consortium 2012)

Lateral transfer

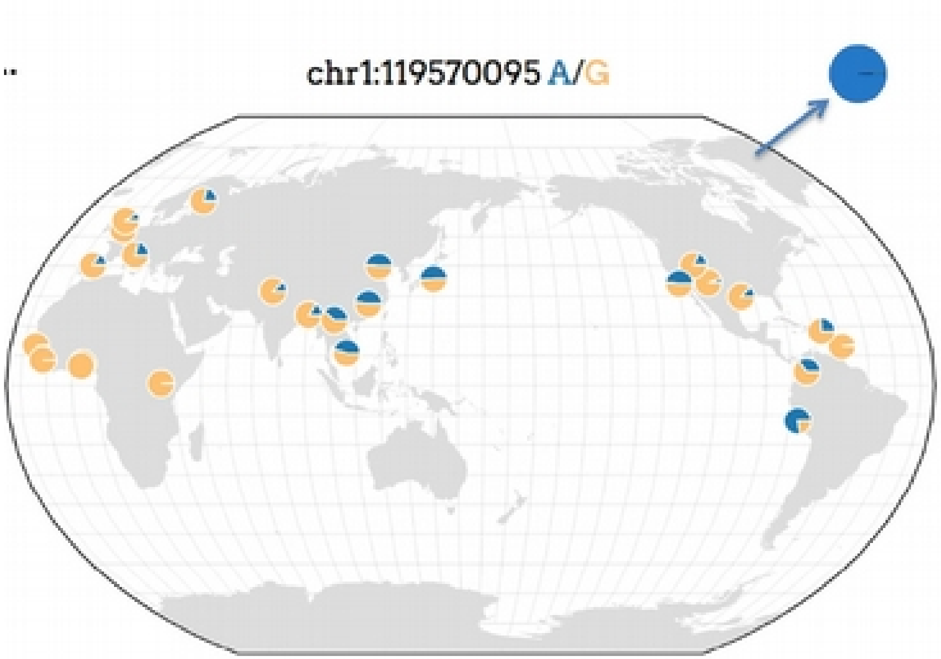


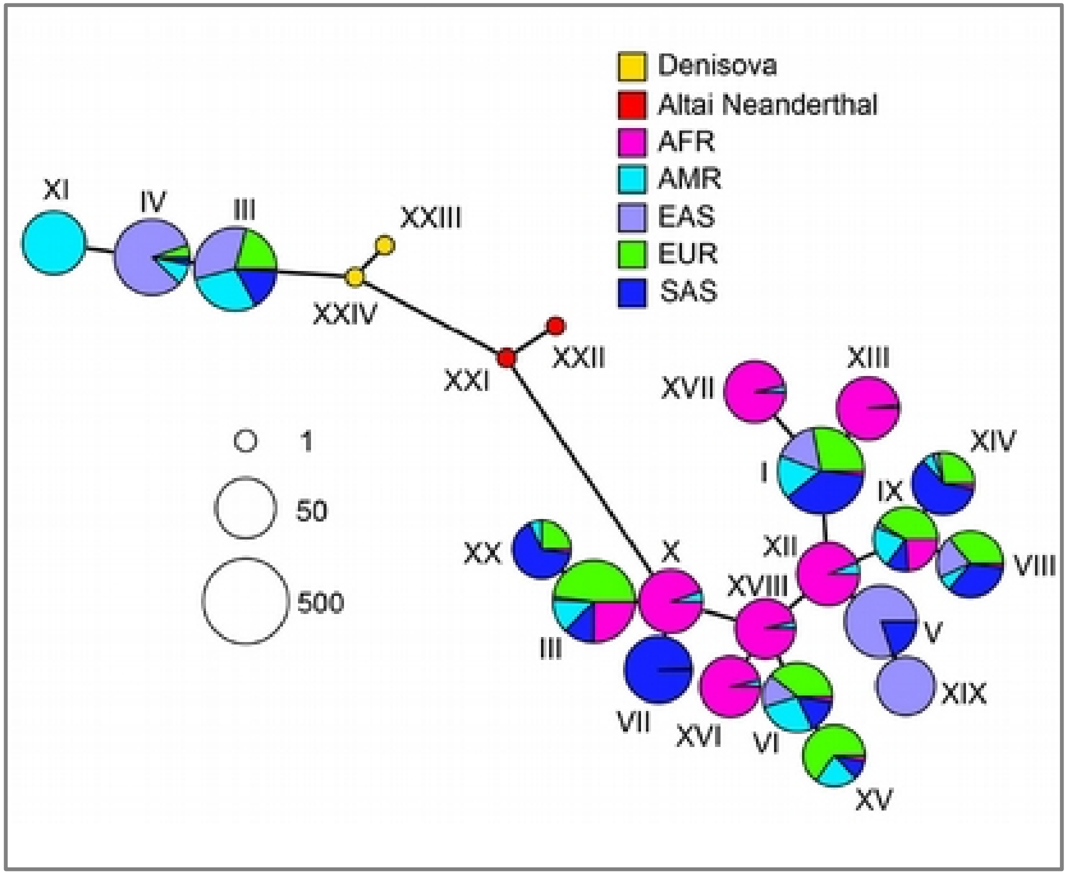
Black color in wolves comes from a dog gene



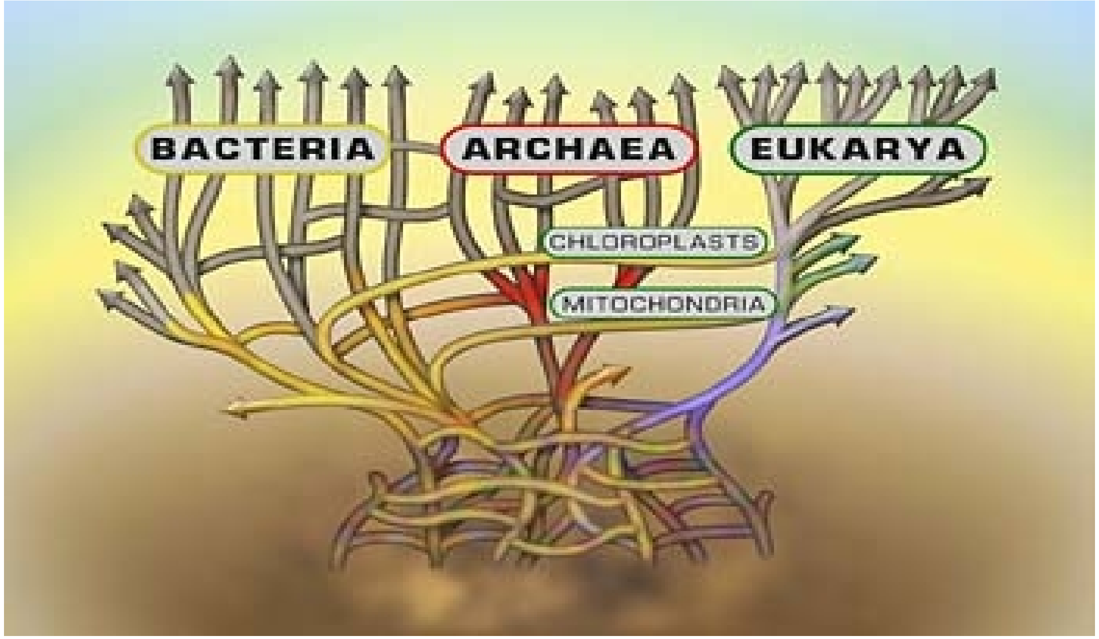
Anderson 2009 Nature

Cold Tolerance in Inuits
may come from Archaic Denisovan DNA





Racimo 2016 MBE


BACTERIA
ARCHAEA
EUKARYA
CHLOROPLASTS
MITOCHONDRIA

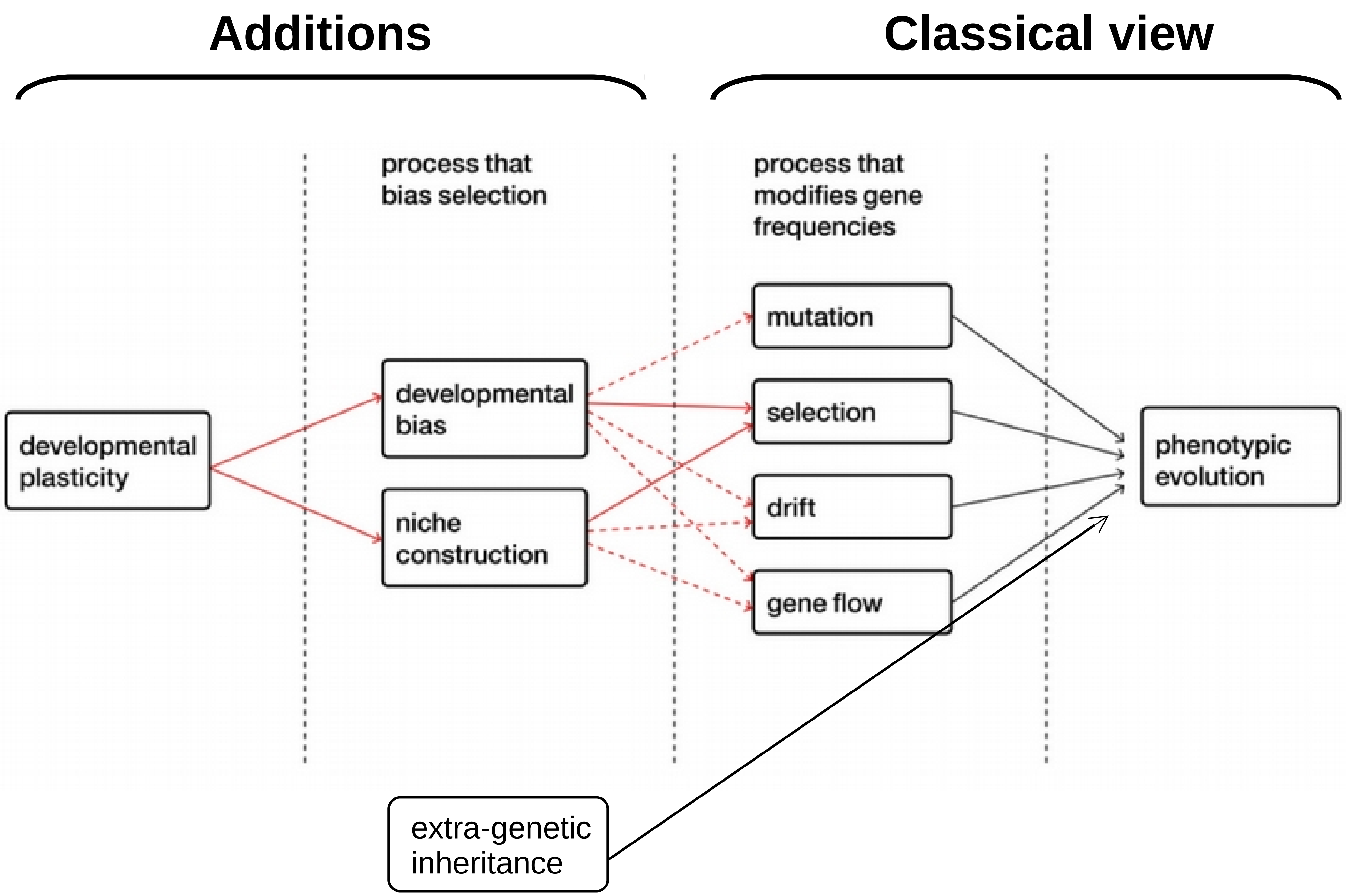
Conclusion

Our research approach: finding the mutations causing evolution

The genetic program is dead

Evolution is not as random as previously thought

The tree of life is not a tree



Additions
Classical view
process that
bias selection
process that
modifies gene
frequencies
mutation
developmental
bias
selection
developmental
plasticity
phenotypic
evolution
niche
construction
drift
gene flow
extra-genetic
inheritance