Micro-evo-devo: Genotype-phenotype relationships, convergences, environmental factors

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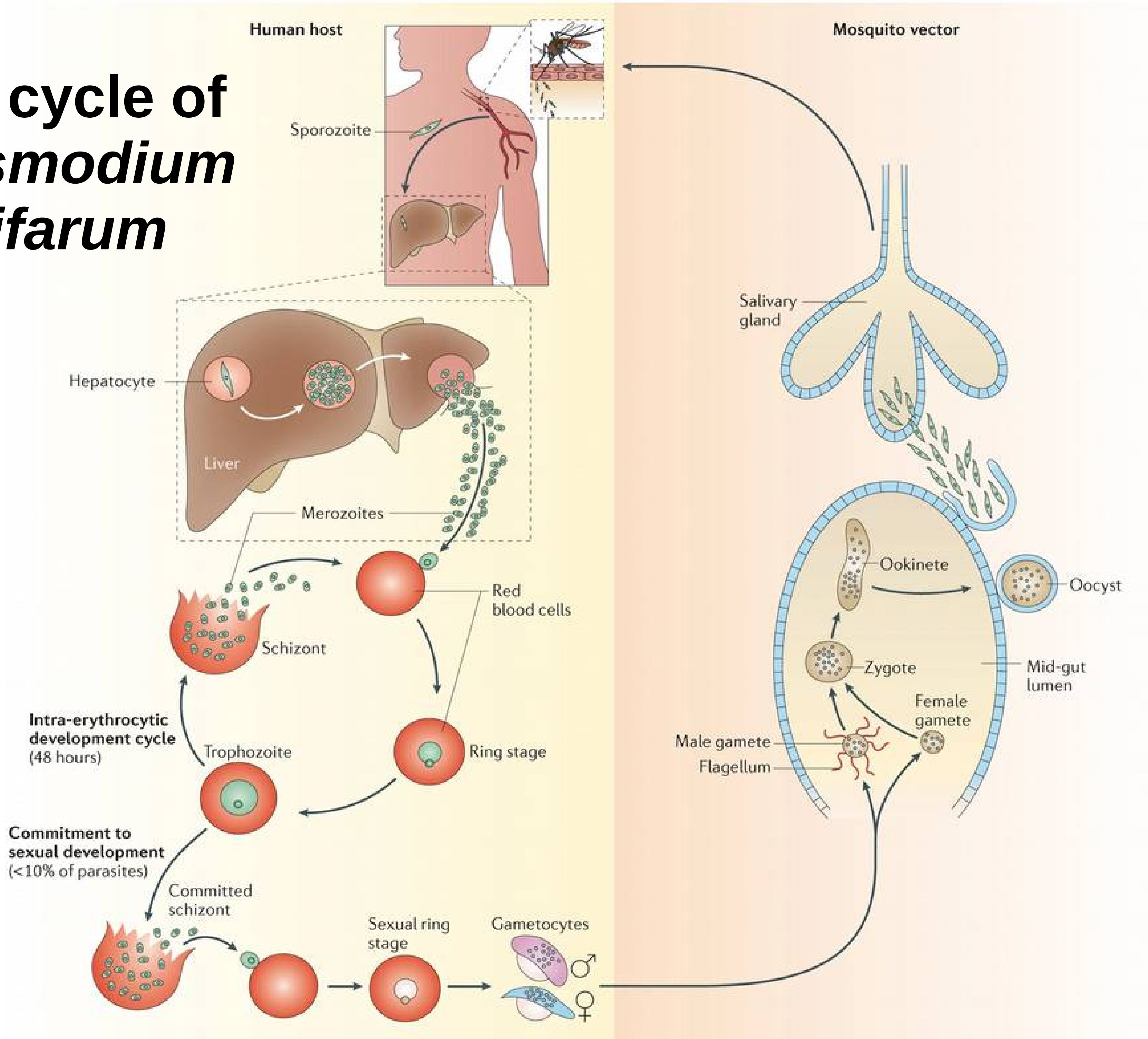
What is evo-devo?

- Development
- Evolution
- Evo-devo

Life cycle of *Plasmodium falciparum*



https://www.nature.com/articles/nrmicro3519/figures/1

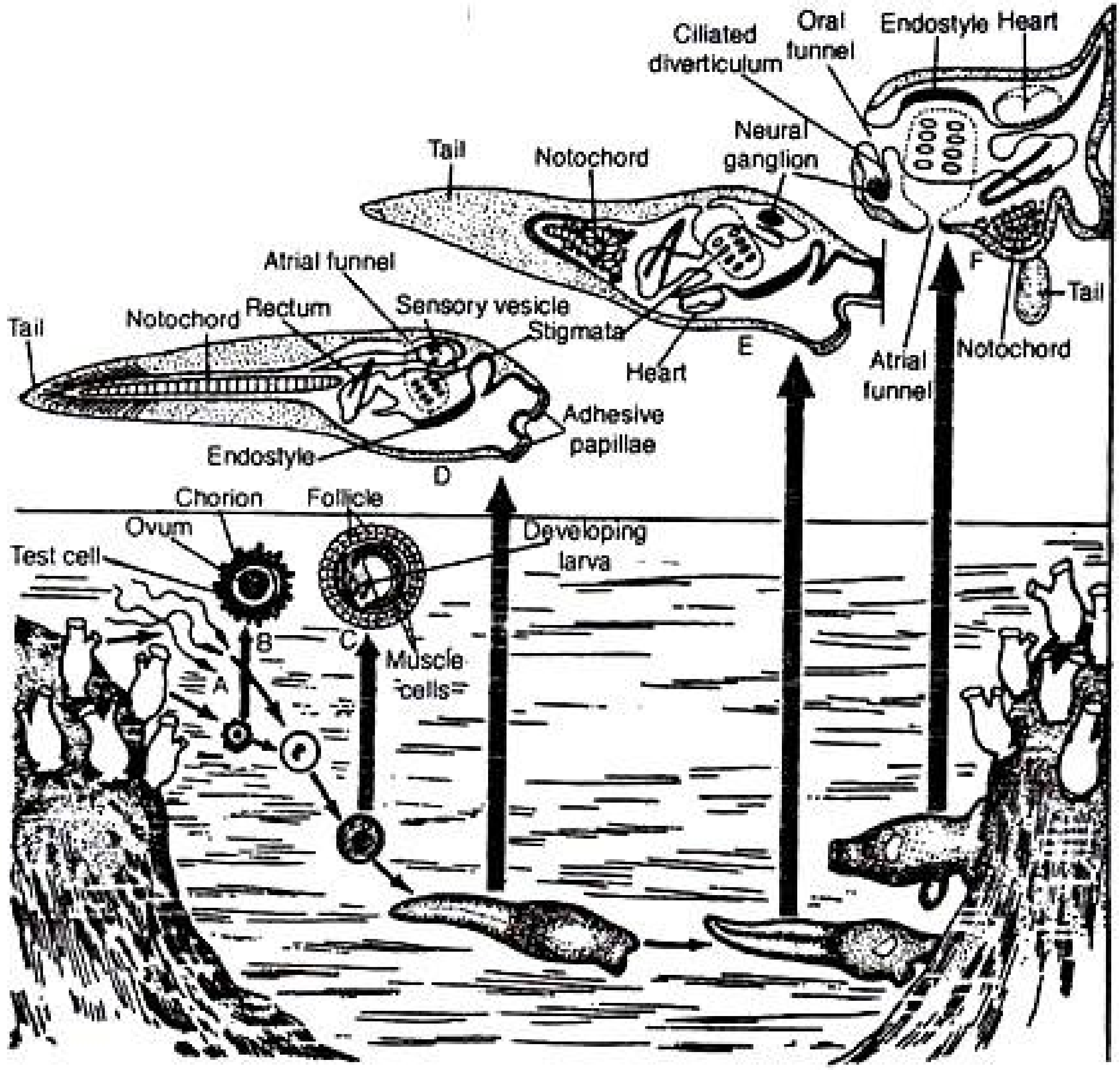


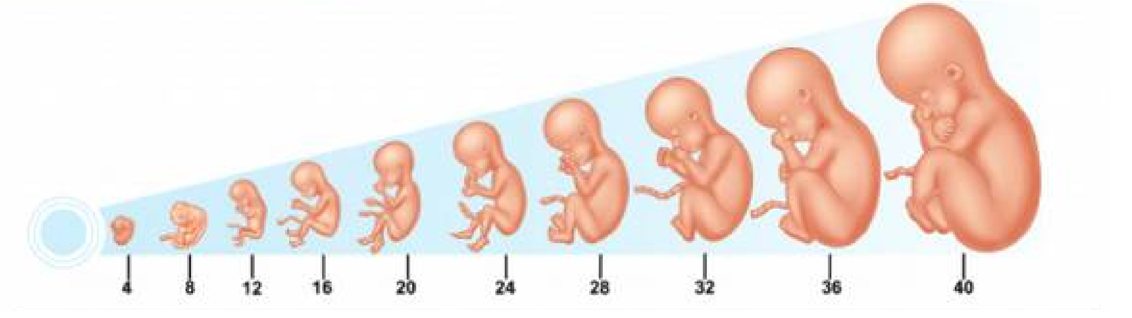
Fig. 1.10 : Developmental sequences of *Ascidia*. A. Spermatozoa. B. Fertilised egg. C. Developing larva prior to hatching. D-F. Sectional view showing the metamorphosis of the free-swimming tadpole into the fixed adult stage. (D. A full-grown free-swimming tadpole larva. E. The tadpole immediately after fixation. Note the reduction of the length of the tail. F. Advanced fixed tadpole)

https://www.notesonzoology.com/phylum-chordata/ascidia-habit-locomotion-and-life-history-zoology/3974

Development

process through which a single cell (often a fertilized egg)
gives rise to a complex multicellular organism

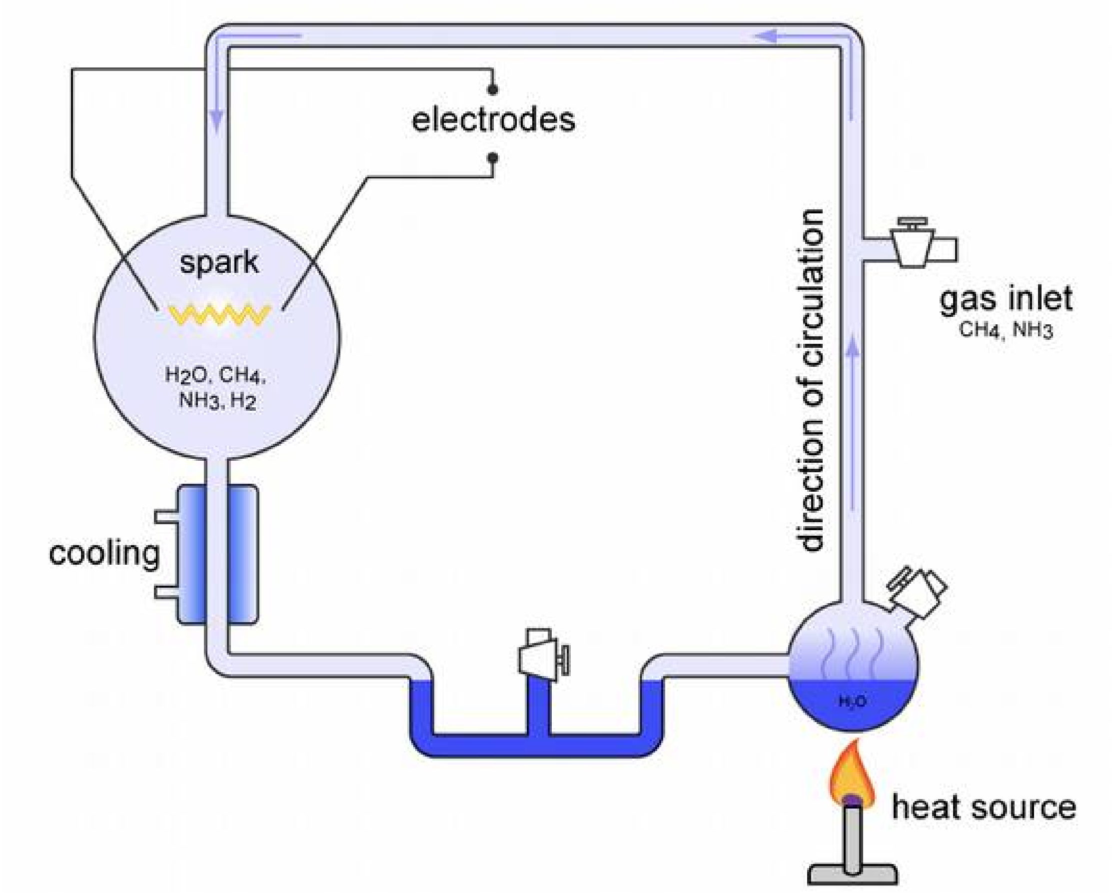
Frontiers:
Regeneration
Unicellular organisms
Asexual reproduction
Aging
Cell death



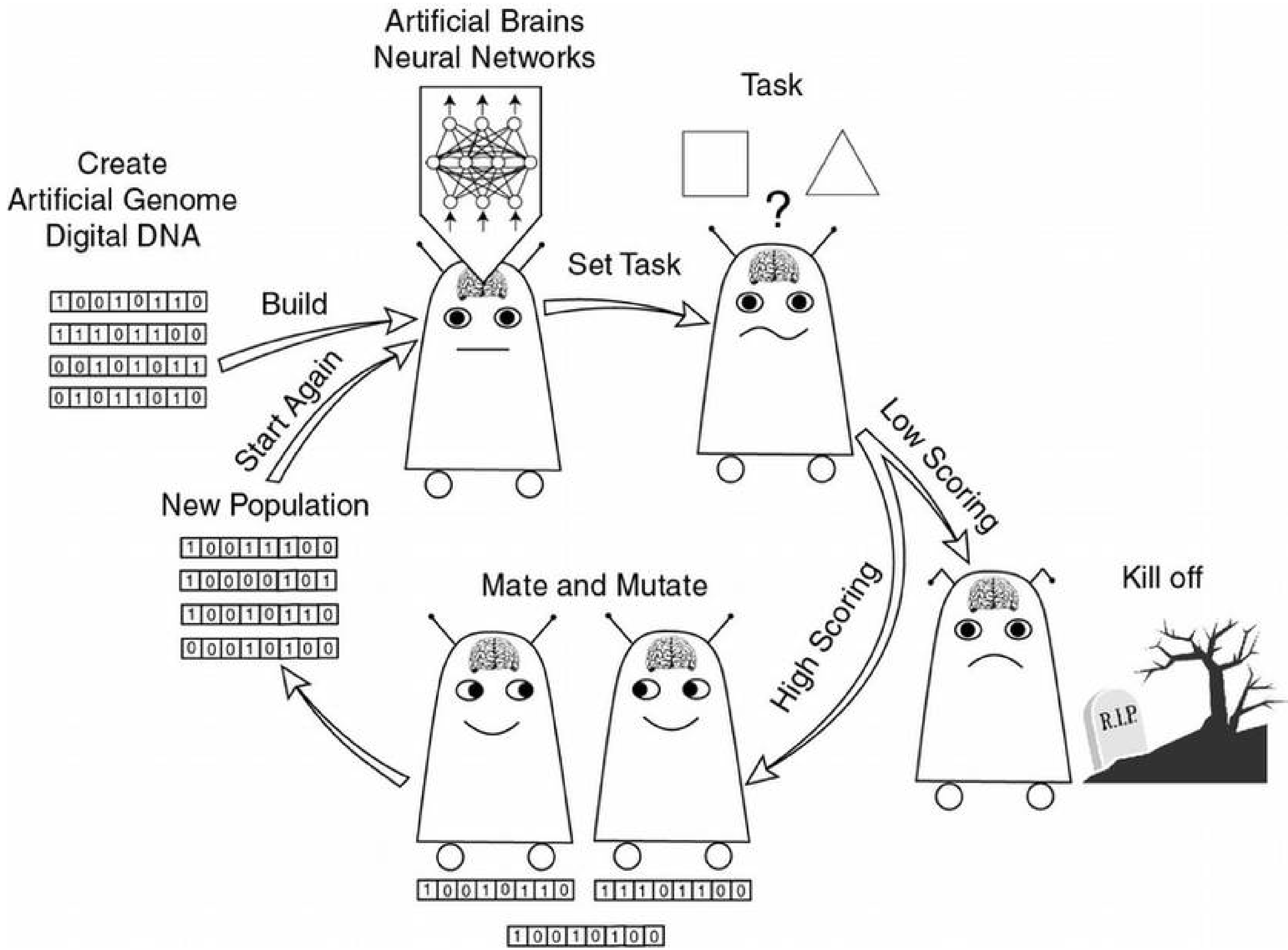
Examples of subfields:
Morphogenesis
Organogenesis
Cell differentiation

Pradeu, T., Laplane, L., Prévot, K., Hoquet, T., Reynaud, V., Fusco, G., ... & Vervoort, M. (2016). Defining “development”. In Current topics in developmental biology (Vol. 117, pp. 171-183). Academic Press.

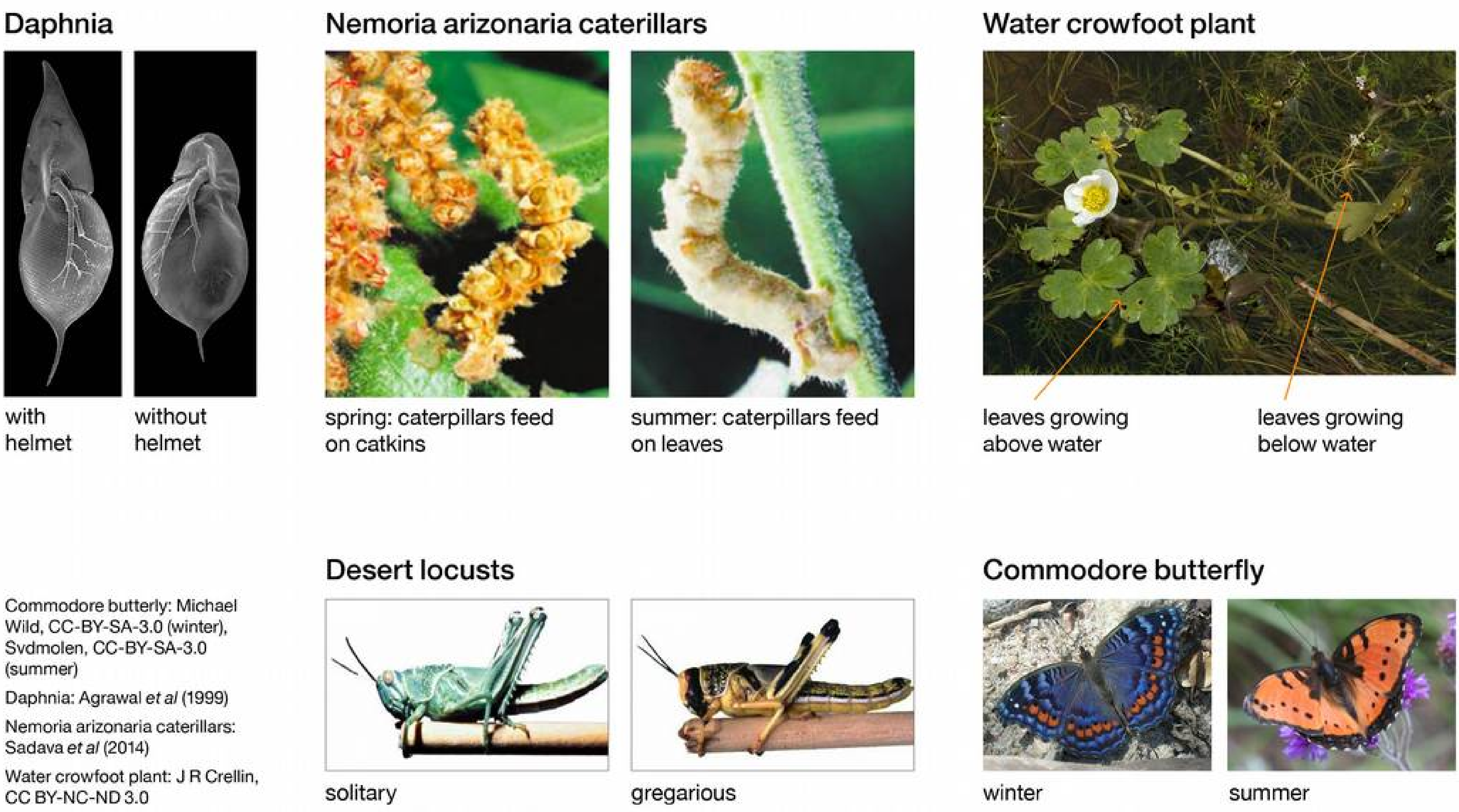
What is Evolution?



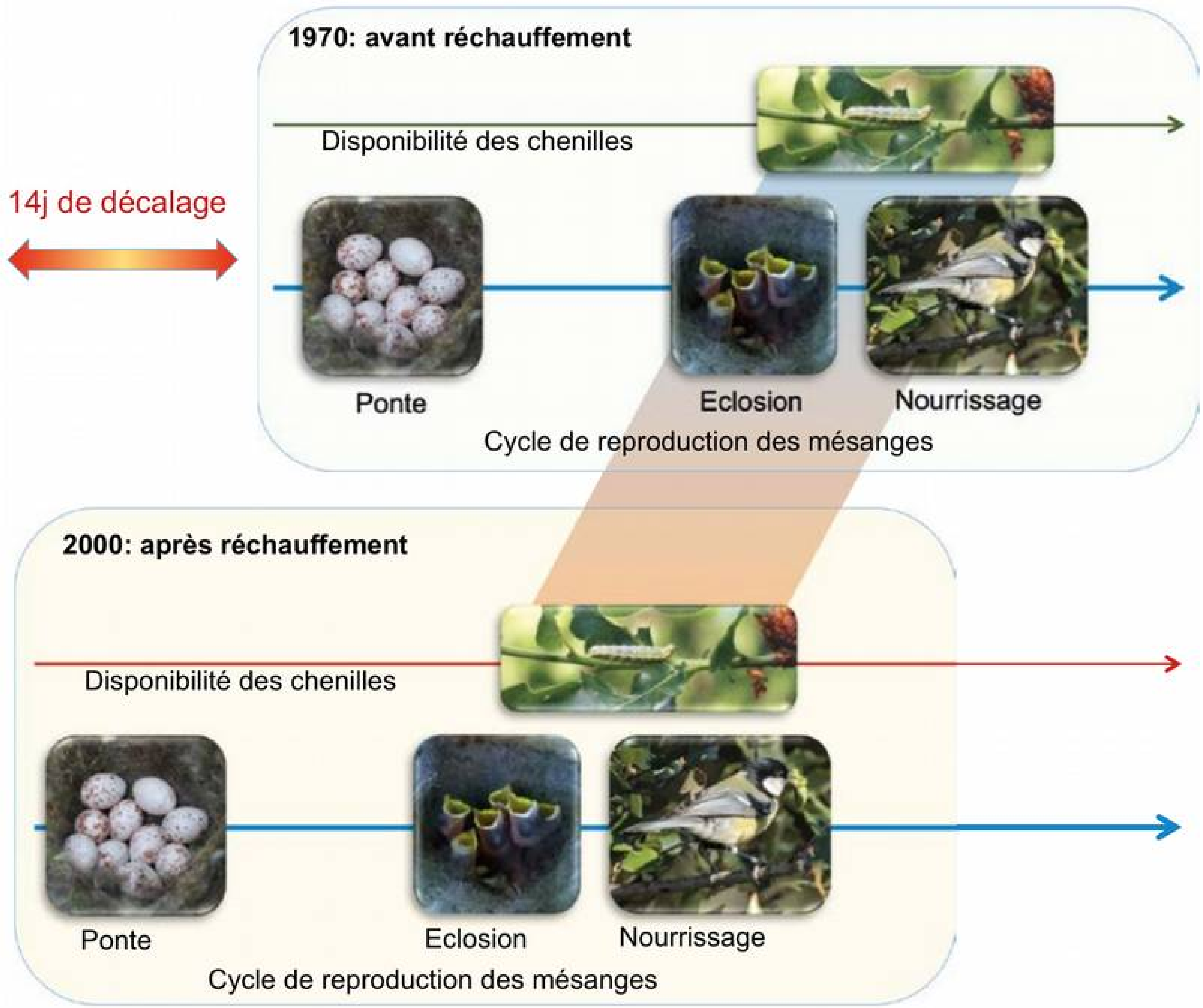
https://en.wikipedia.org/wiki/Miller%E2%80%93Urey_experiment


Create
Artificial Genome
Digital DNA
100101110
111011100
001010111
010111010
Build
Artificial Brains
Neural Networks
Set Task
Task
?
Start Again
New Population
100111100
100000101
100101110
000101100
Low Scoring
High Scoring
Kill off
R.I.P.
Mate and Mutate
100101110
111011100
100101100

Plasticity: one genotype → several phenotypes



Rapid evolution of great tits



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

Evolution

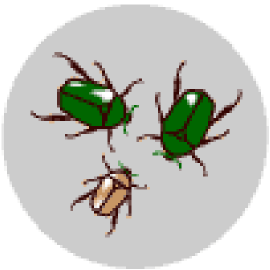
process through which the characteristics of populations or species change over successive generations

Frontiers:
Origin of Life
Evolutionary robotics
Plasticity

Examples of subfields:
Paleontology
Experimental evolution
Modelling of Evolution

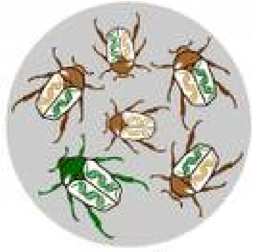
Classical Darwinian Evolution

Variation

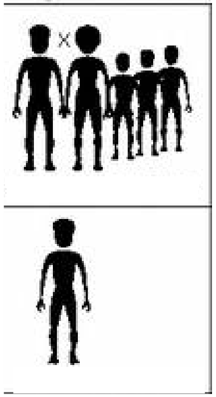


Mutations in DNA

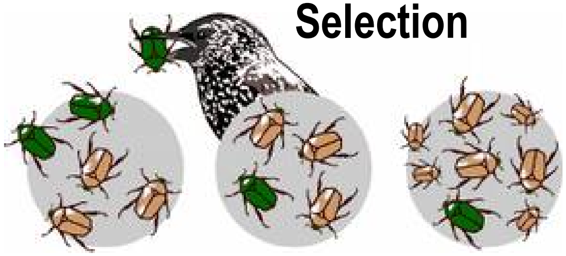
Transmission



Differential reproduction



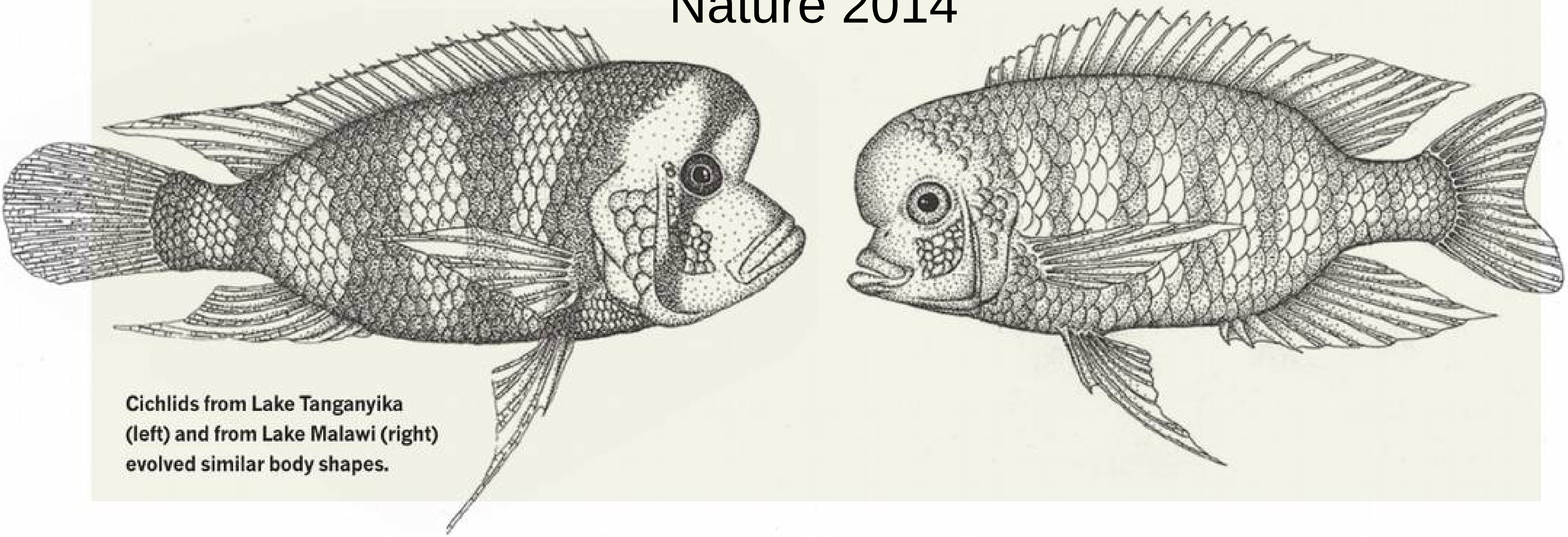
Selection



Genetic Drift

http://evolution.berkeley.edu

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

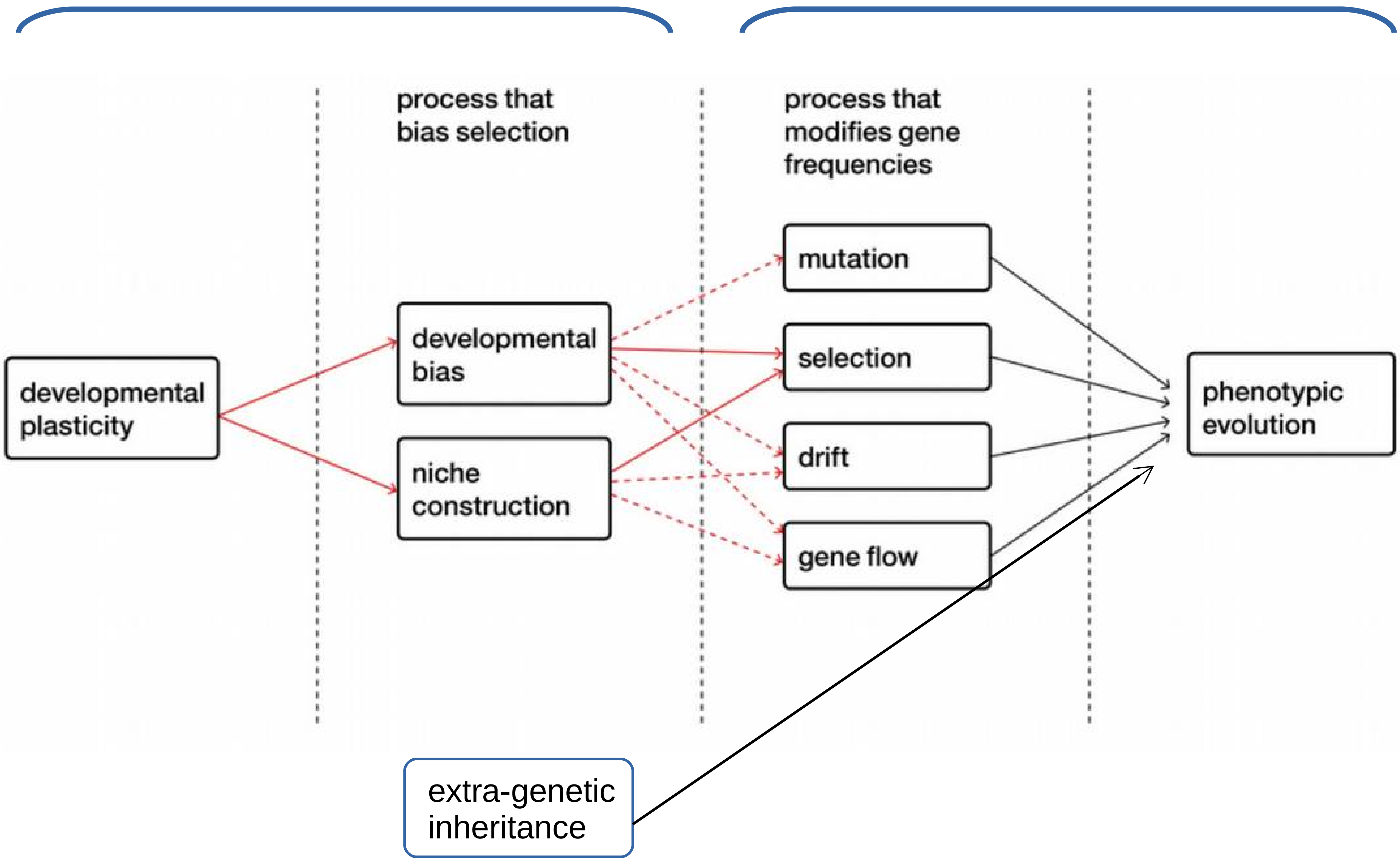
No, all is well

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

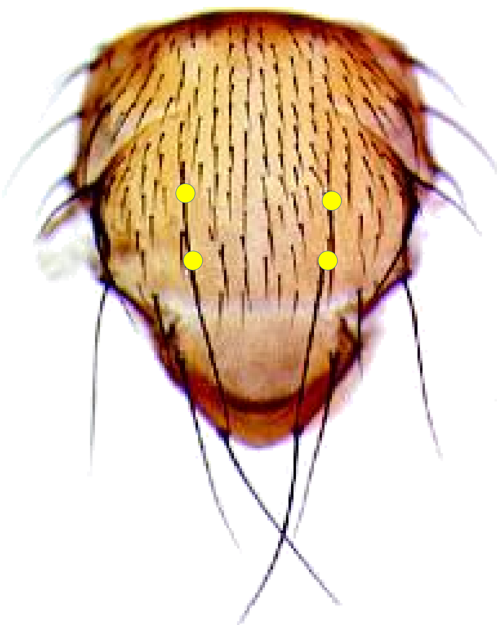
Extended evolutionary synthesis

Additions

Classical view

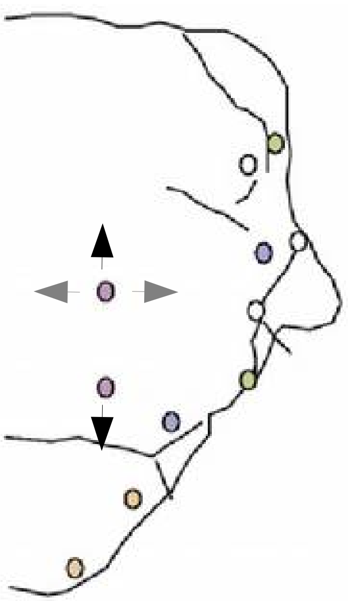


Developmental Bias



Standing variation

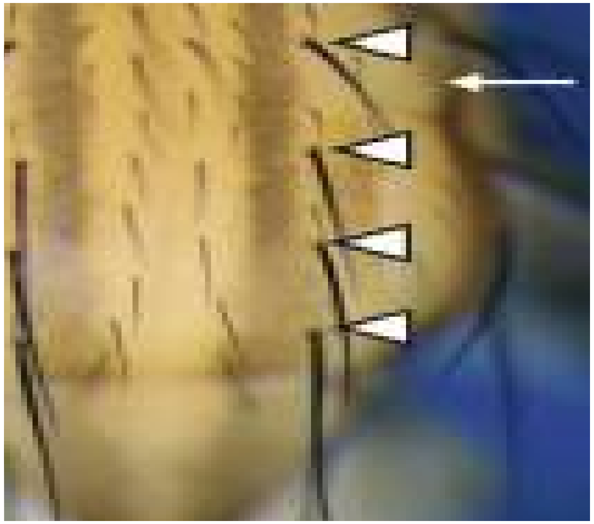
D. melanogaster



variation
no variation

Natural evolution

D. quadrilineata

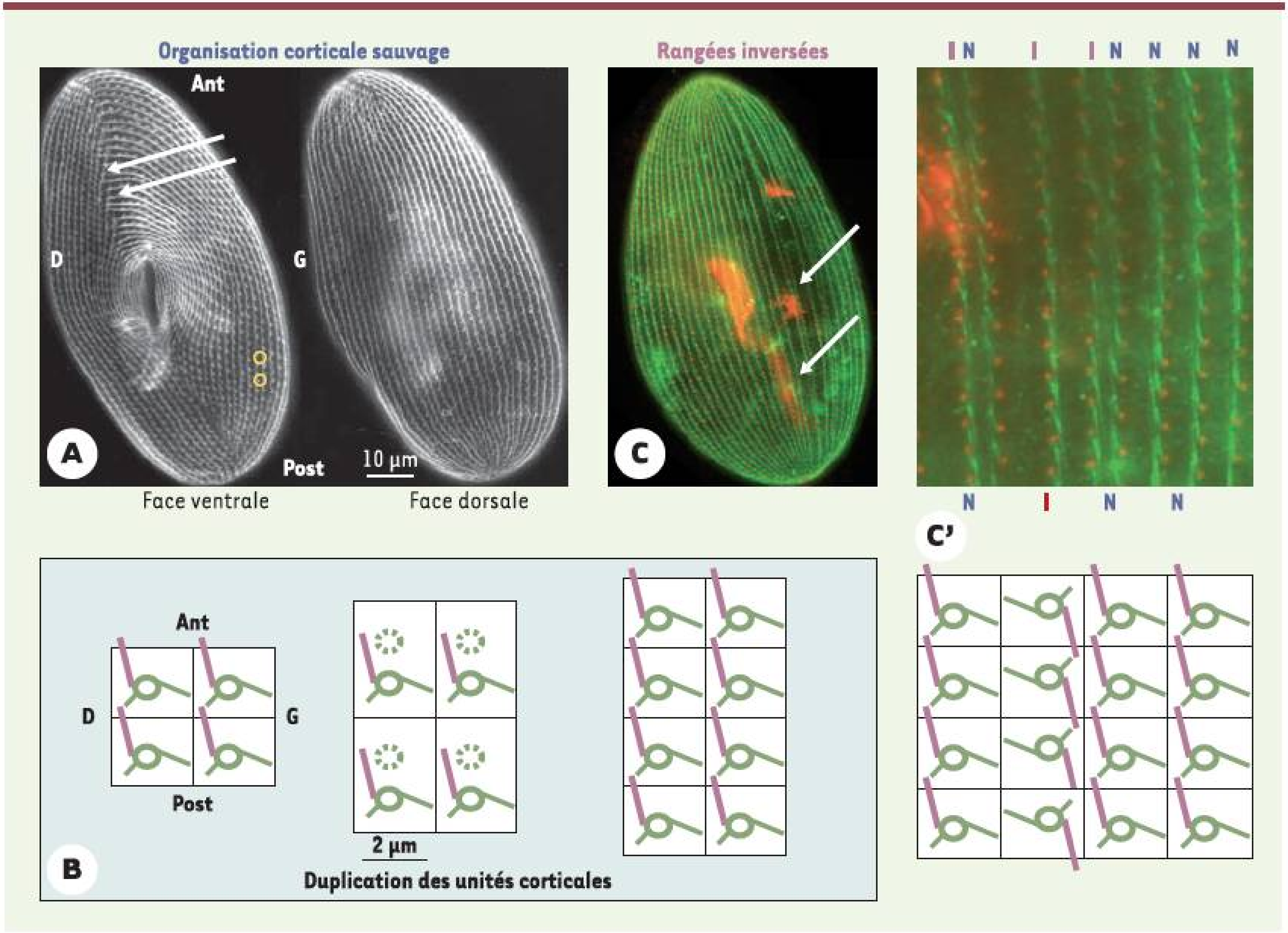


Marcellini et al 2006 PloS Biol

Garcia-Vázquez 1988 J. Heredity

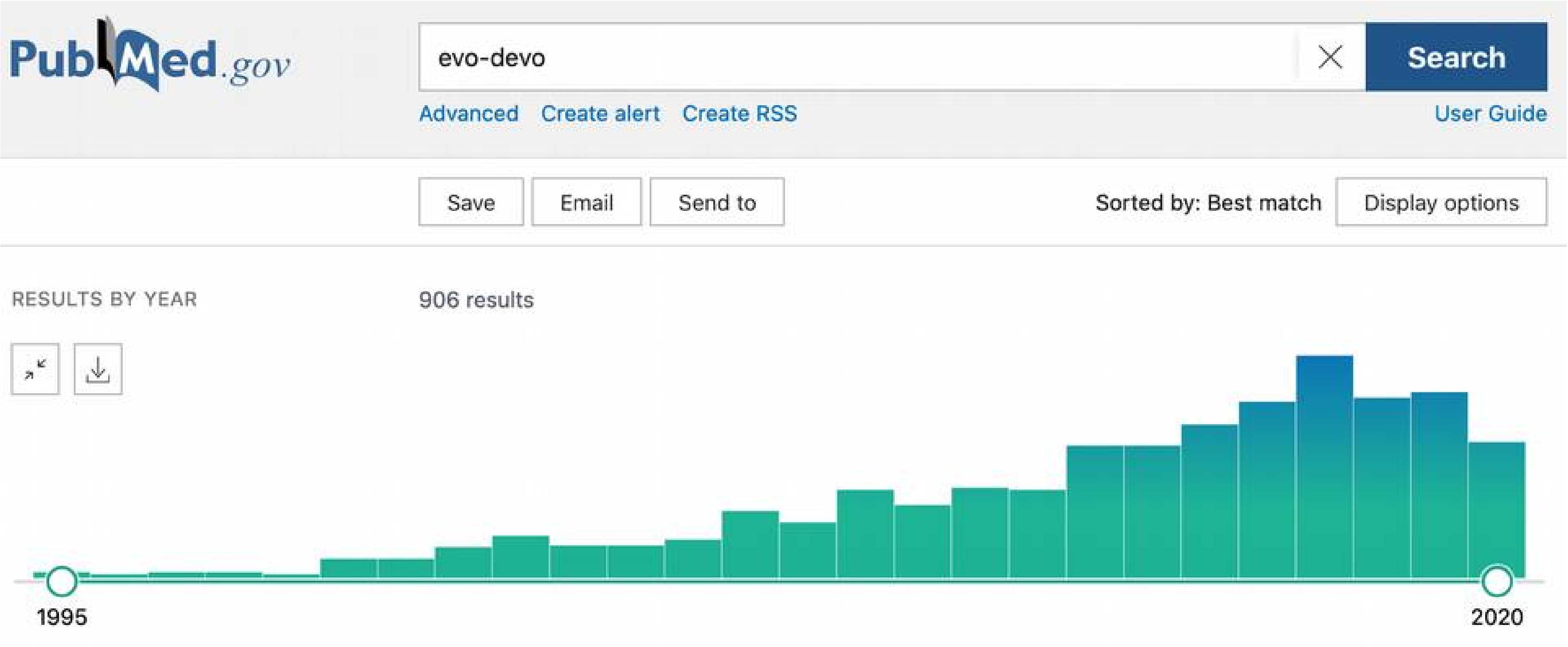
Niche construction

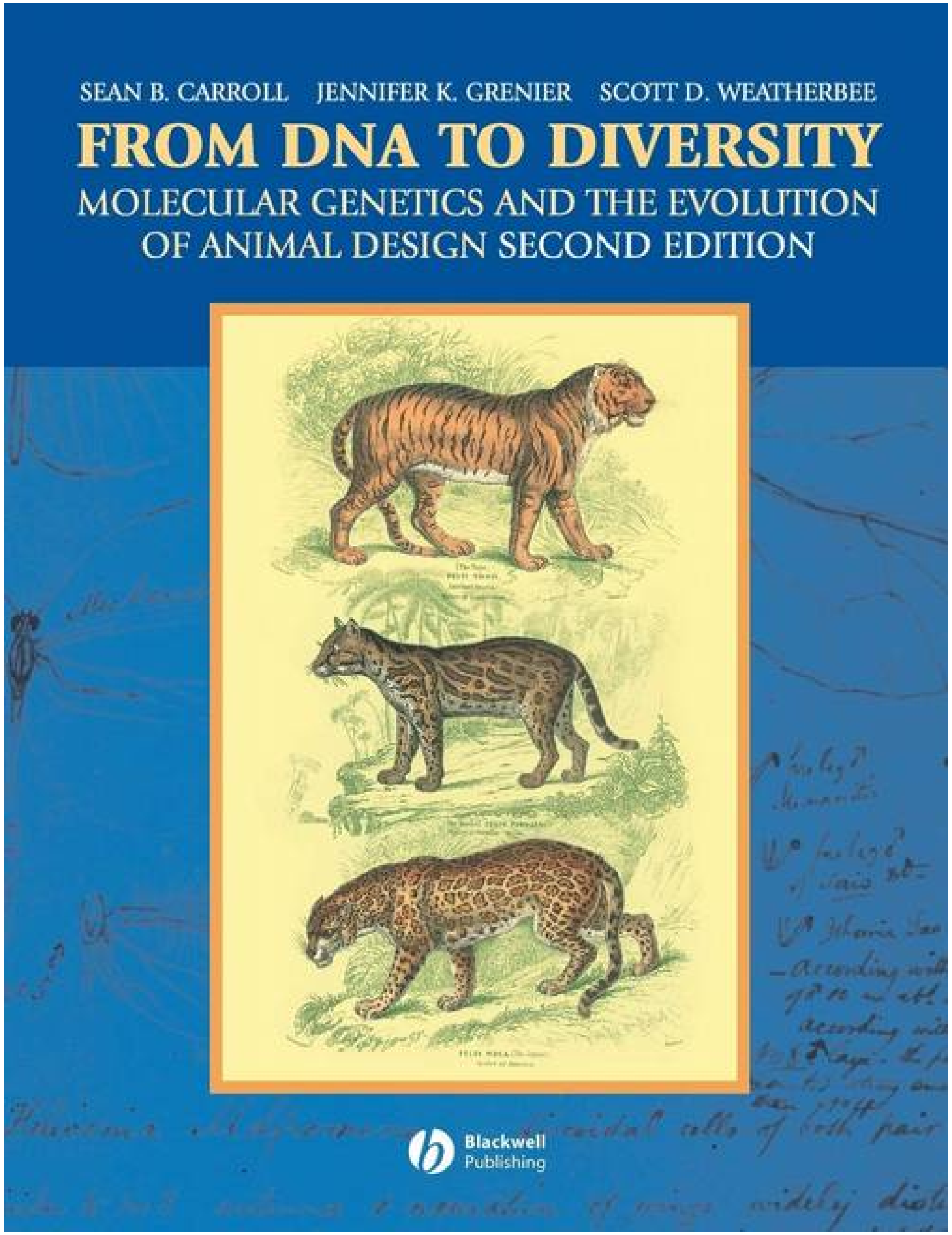
Cortical heredity in *Paramecium*

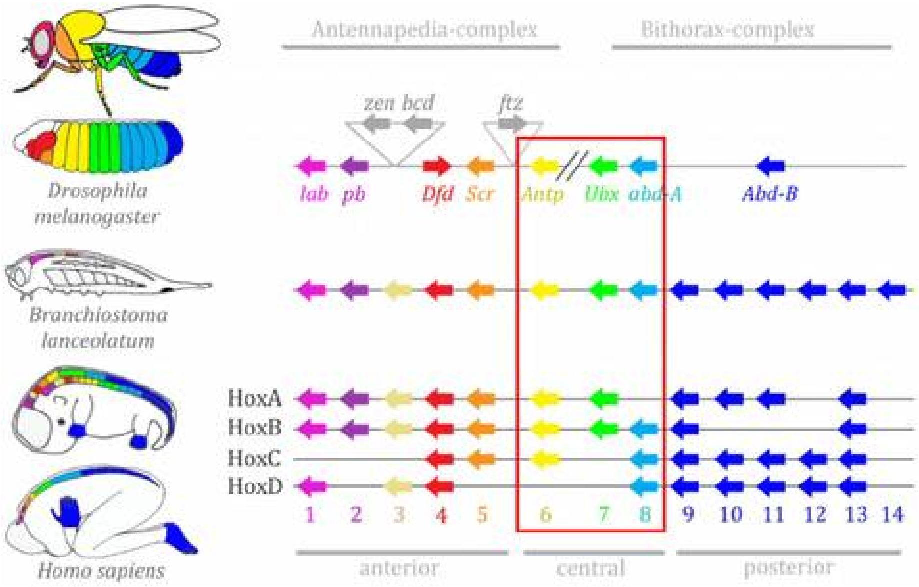


Meyer & Beisson M/S 2005

What is Evo-Devo?




SEAN B. CARROLL JENNIFER K. GRENIER SCOTT D. WEATHERBEE
FROM DNA TO DIVERSITY
MOLECULAR GENETICS AND THE EVOLUTION OF ANIMAL DESIGN SECOND EDITION
Blackwell Publishing

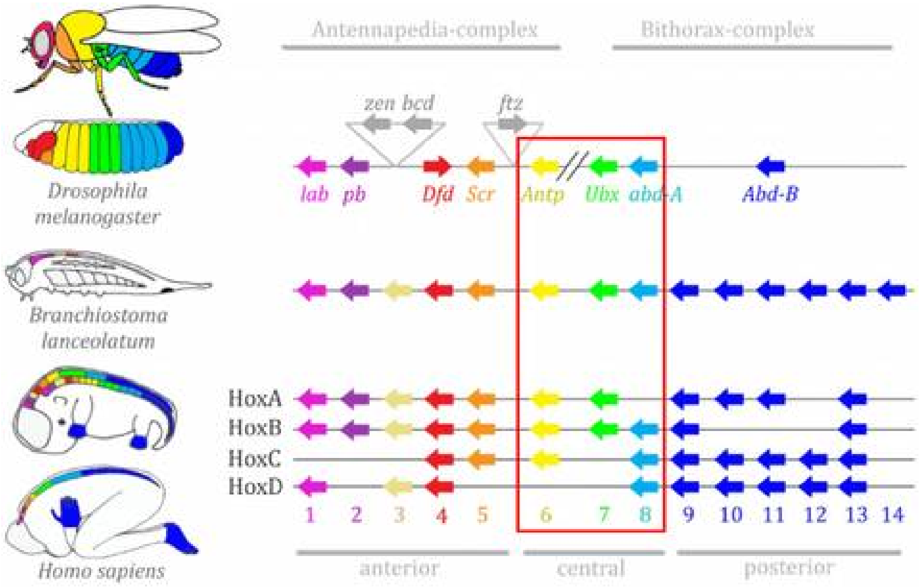

Antennapedia-complex
Bithorax-complex
zen bcd
ftz
lab pb Dfd Scr Antp Ubx abd-A Abd-B
Drosophila melanogaster
Branchiostoma lanceolatum
HoxA
HoxB
HoxC
HoxD
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Homo sapiens
anterior
central
posterior

2001

Evo-devo

field of biological research that compares development between species to understand how they evolved

Frontiers:
Same as development and evolution
Ecology
Physiology, Behavior



subfields:
Macro-evo-devo (distantly related species)
Micro-evo-devo (closely related species or populations)

The distinction between genotype and phenotype is the basis of genetics

“The view of natural inheritance as realized by an act of transmission, viz., the transmission of the parent's (or ancestor's) personal qualities to the progeny, is the most naive and oldest conception of heredity.”

“All "types" of organisms, distinguishable by direct inspection or only by finer methods of measuring or description, may be characterized as "**phenotypes**.”

“ A "**genotype**" is the sum of all the "genes" in a gamete or in a zygote.”

Johansen 1911

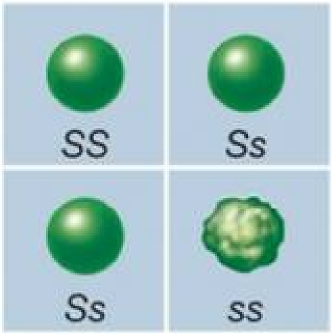
Phenotype = observable attributes of an individual

Genotype = inheritable genetic material
= DNA or RNA

How do genotypes map onto phenotypes ?

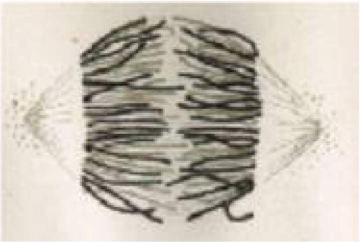
A very brief history of genetics

Transmission + *Phenotypic expression*



- **Mendel 1860s**

Controlled breeding, use of probabilities
Dominant/recessive/intermediate expression of traits
Random transmission of "factors"



- **Cytology from 1880-90s** Flemming, Boveri, Sutton

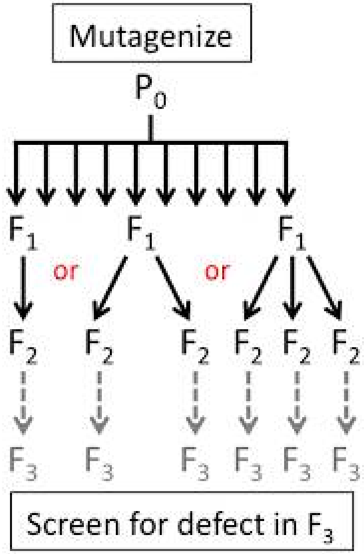
chromosomes as support of heredity, meiosis

- **Classical genetics 1900-1950**

distinction genotype-phenotype
segregation of characters & genes
genetic map, sex chromosomes
penetrance - expressivity

"Rediscovery" of Mendel's law
Extension to animals

- **Foundation of molecular biology 1940-1970**
  in part using bacteria and phage genetics
  DNA as the material support of heredity



- Deciphering the role of the genes: 1970-
Cellular, developmental, behavioral genetics: Screens
"High-throughput" versions 2000- (e.g. deletion libraries)
Reverse genetics

- Association mapping on natural populations: 2000-

Divergences and syntheses

Mendelian genetics
"Mendelians"

Statistical genetics
"Biometricians"

1900

agriculture

"Neodarwinian
synthesis"

1930

Laboratory
genetics

Population genetics
evolution
genotype

Quantitative
genetics
phenotype

1950 Molecular biology

1975

Molecular genetics
cell biology,
development
physiology, etc.

Molecular evolution

Molecular
markers

1990

Functional
genomics

Evo-
Devo

Evolutionary
genomics

Quantitative
genetics
molecular basis

How do genotypes map onto phenotypes ?

DEVELOPMENTAL BIOLOGY

EVO-DEVO

Both are direct descendants of Morgan's school. Emphasis on genes.

How does an organism form from a single cell?

What makes one organism different from another one?

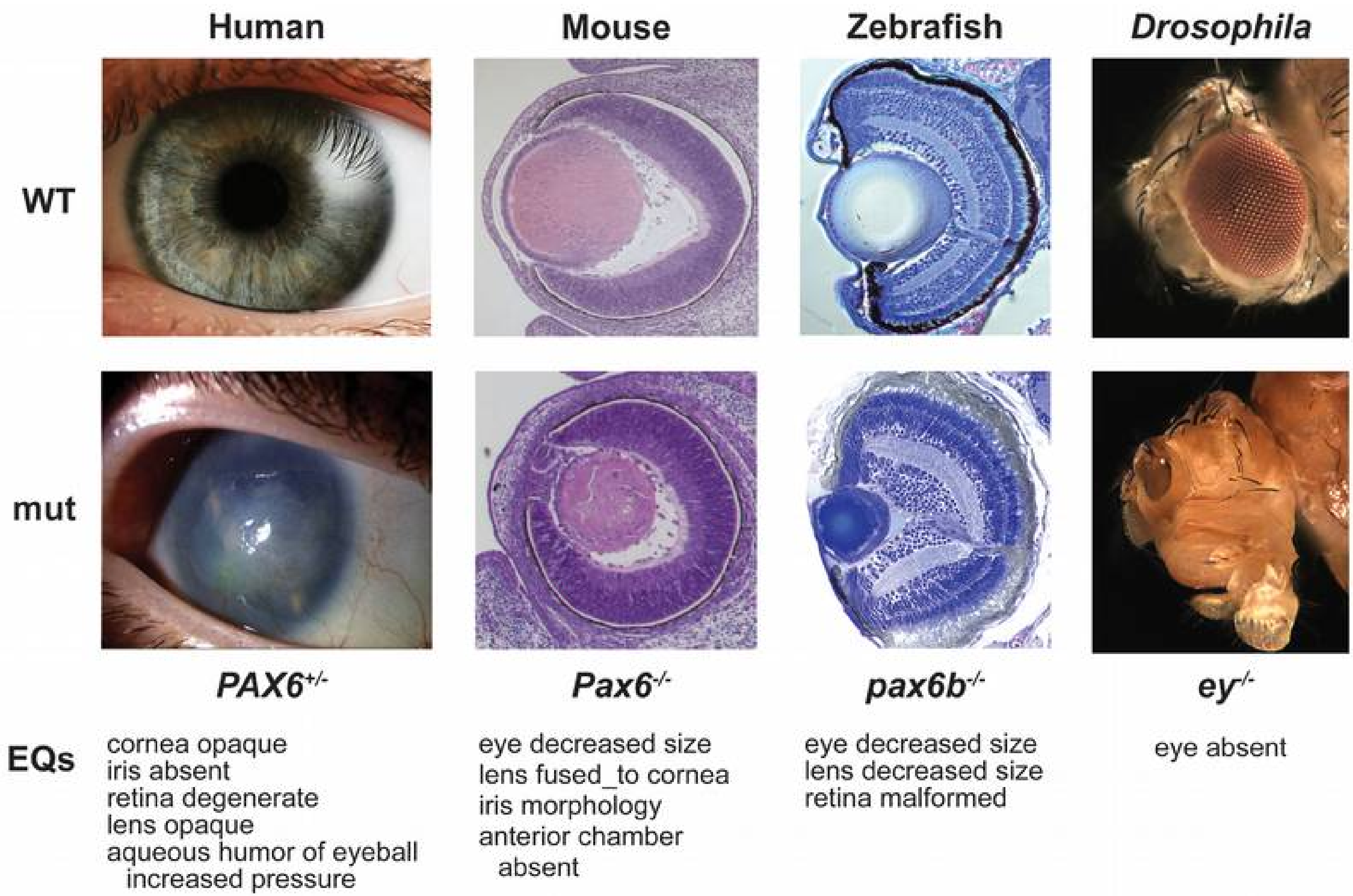
One of the central problems of biology is that of differentiation - how does an egg develop into a complex many-celled organism? That is, of course, the traditional major problem of embryology; but it also appears in genetics in the form of the question,
“How do genes produce their effects?

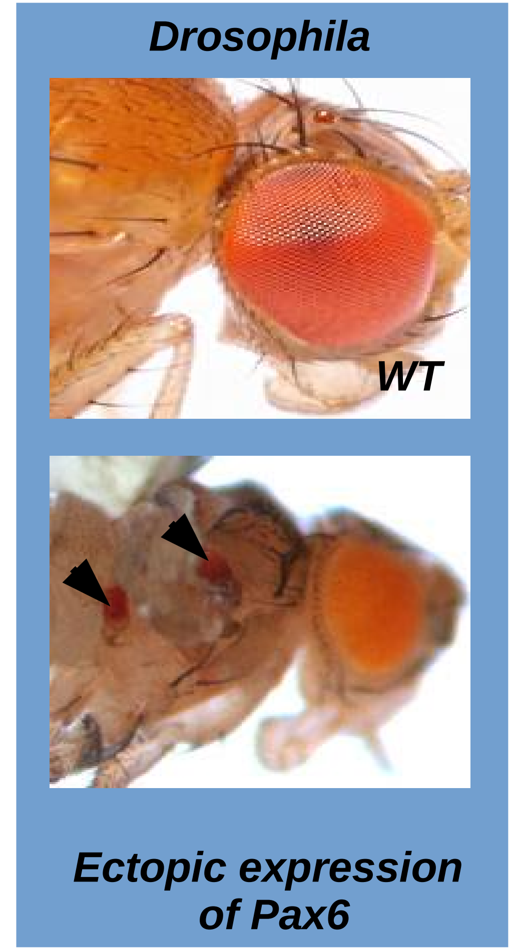
Sturtevant, 1932

How do genes produce observable traits?

Gene → Observable character

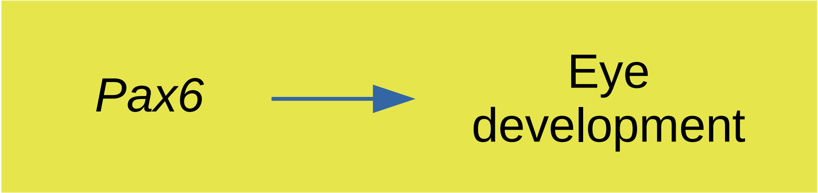
Pax6 : an eye gene ?



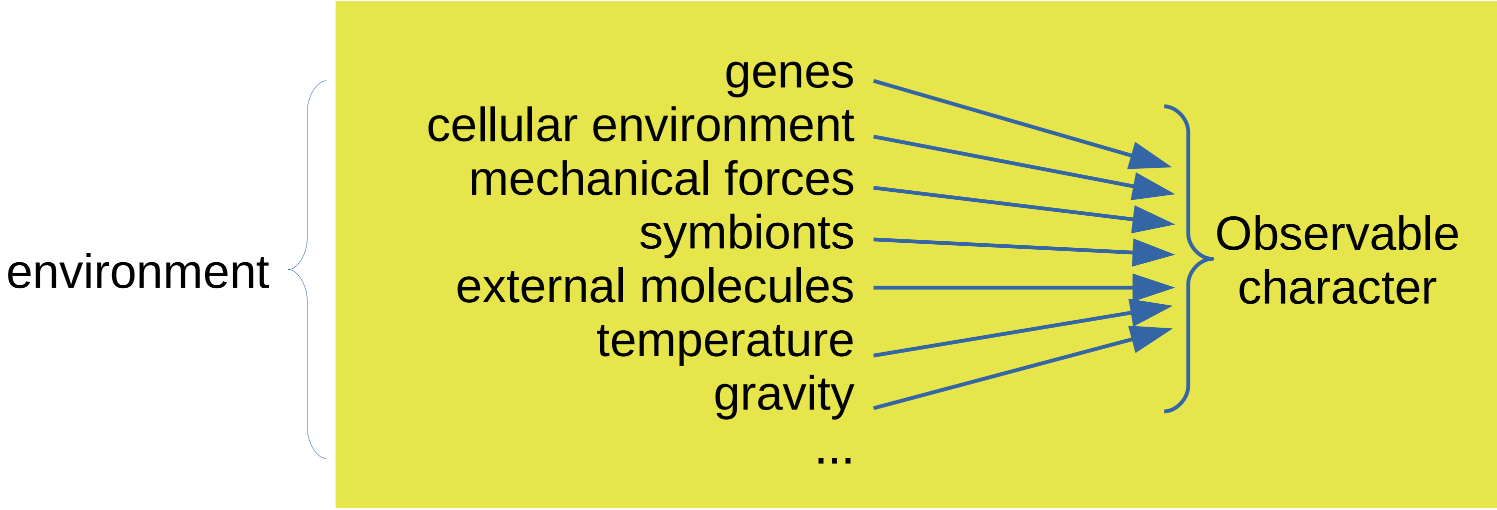


Gene → Observable character

Pax6 → Eye development

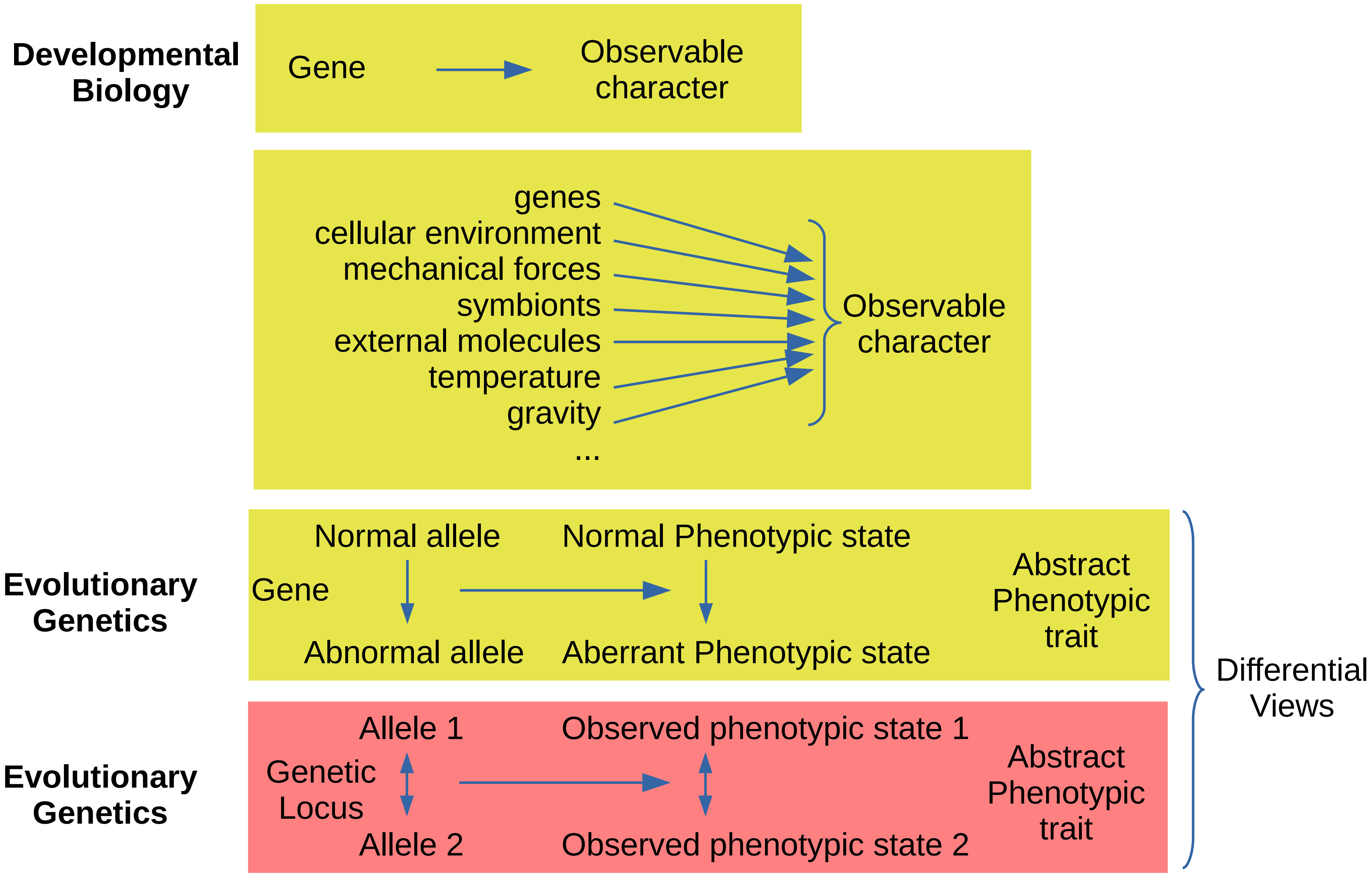


Too simplistic



Better, but difficult to disentangle the effects

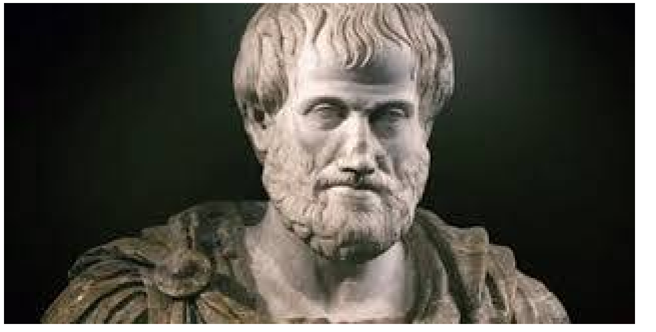
A Cause/Mechanism relates to a Difference



Different kinds of phenotypes

Morphology

- Color
- Size and shape
- Presence/ absence
- Position



Aristote, Historia animalium, book I, 2, 300BC

Physiology

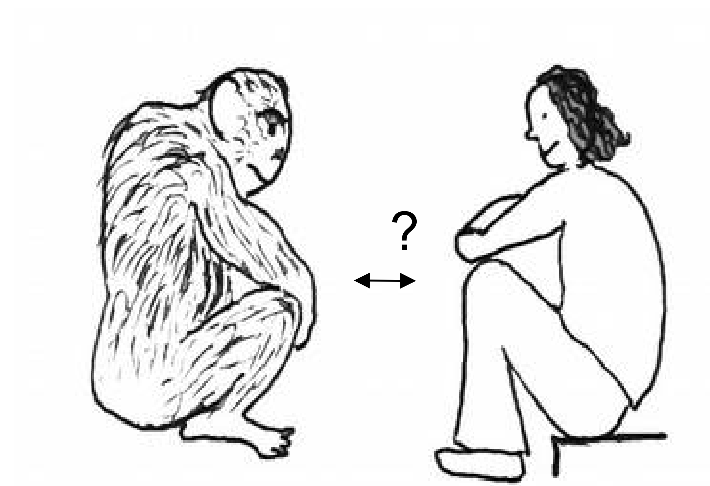
Behavior

Micro-evo-devo

What makes us different?

between individuals

between species



Where do we come from?

What are the mutations responsible for phenotypic differences?

Genomic approach

identifies rapidly-evolving genomic regions, new genes, deleted genes

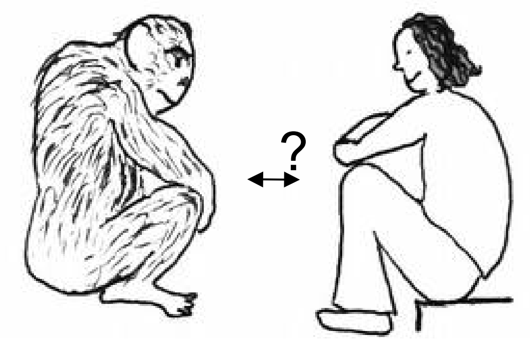
?

Genomes

```
CCTCCTCCATACCCAAATGGATGGTACGGCATTCTTGAATCATCAAAGCT
TAGAGCGGGGGAATCGAAGCATATATCATGTCTAGGCGAGCAACTTATAG
TGTTCCGTTCCCAAGCTGGTGAAGTTTATATCTTGGATGCGTATTGCCCG
CACTTGGGCGCTAATTTGAGTAAGGGAGGTCGAGTTATAGGAGATAATAT
TGAATGTCCCTTTCACCACTGGAGCTTTAGAGGCAGTGATGGCATGTGTA
CCAATATTCCCTACAGCAGCAATATACACTCATCTACAAAAACTAAAAAA
TGGACCTCCACCGAAGTGAATGGATTCATATTTCTTTGGTACAATGTCGA
AGAATCTGAAGTTCCGTGGAATATACCAAAATCAGTTGGTGTTGCAAAAA

CCTCCTCCATACCCAAATGGATGGTACGGCATTCTCGAATCATCAAAGCT
TAGAGCGGGGGAATCGAAGCATATATCATGTCTAGGCGAGCAACTTATAG
TGTTCCGTTCCCAAGCTCGTGAAGTTTATATCTTGGATTCGTATTGCCCG
CACTTGGGCGCTAATTNGAGTAAGGGAGGTCGAGTTATAGGAGATAATAT
TGAATGTCCCTTTCACCACTGGAGCTTTAGAGGCAGTGATGGCATGTGTA
CCAATATTCCCTACAGCAGCAATATACACTCATCTACAAAAACTAAAAAA
TGGACTTCCACCTAAGTGAATGGATTCATATTTCTCTGGTACAATGTCGA
AGAATCTGAAGTTCCGTGGAATATACCAAAATCAGTTGGTGTTGCAAAAA
```

Phenotypic differences



Phenotypic approach

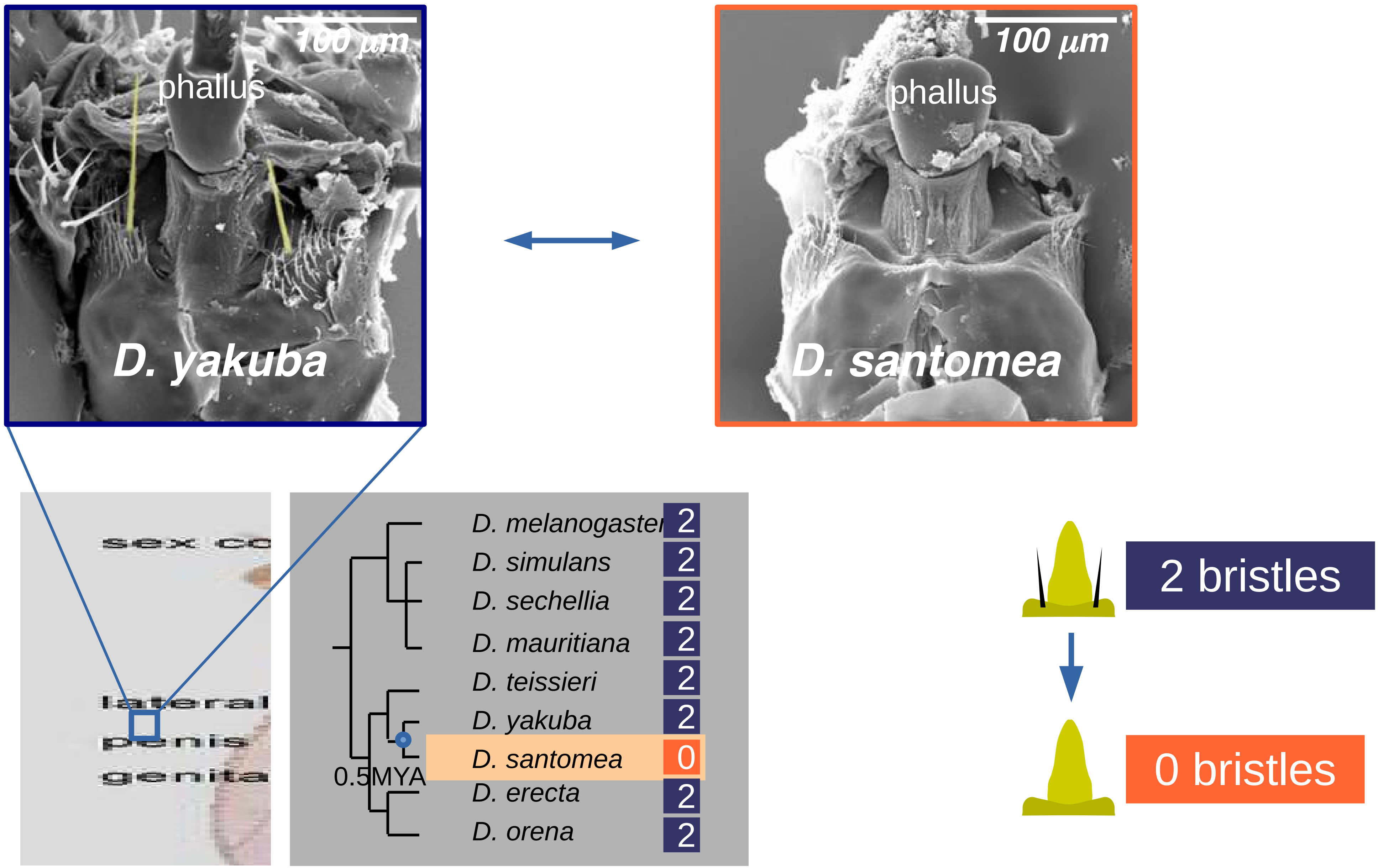
identifies the gene(s) and the mutation(s) responsible for a phenotypic change

A case study

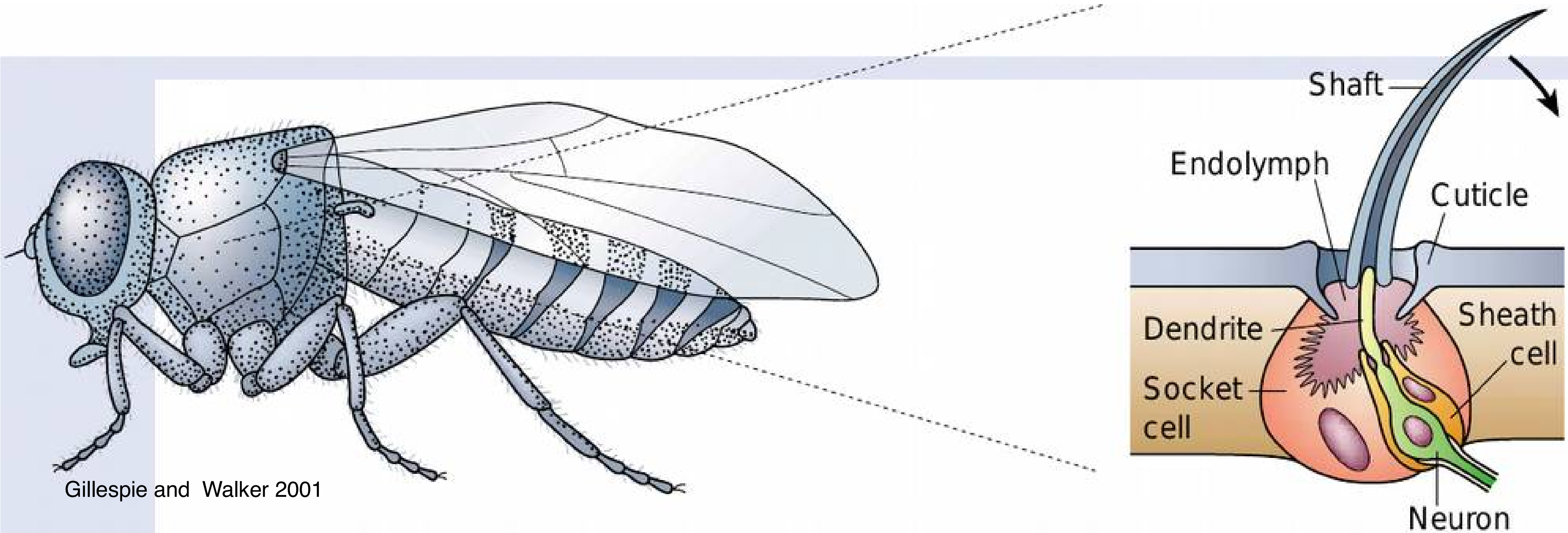
Evolutionary loss of bristles in *D. santomea*

Nagy et al Current Biology 2018

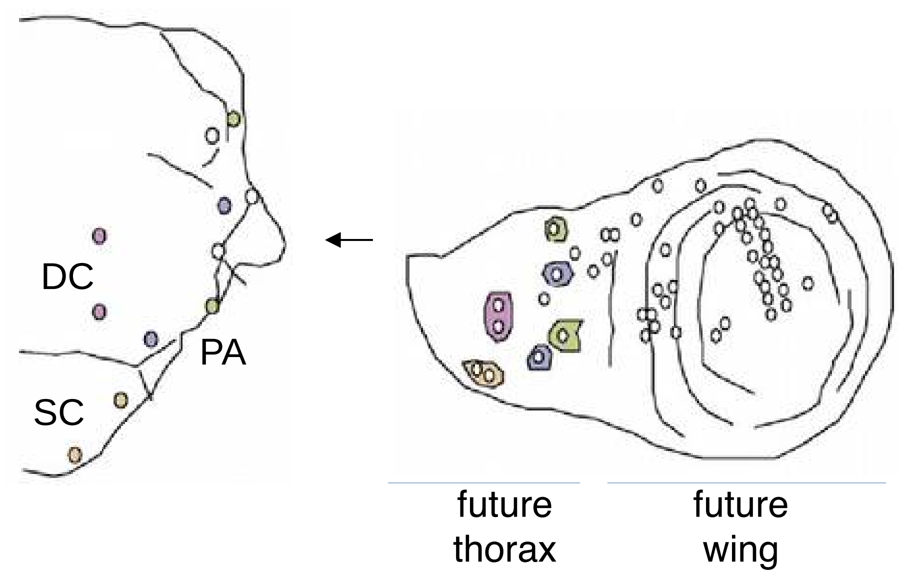
D. santomea has lost sex bristles



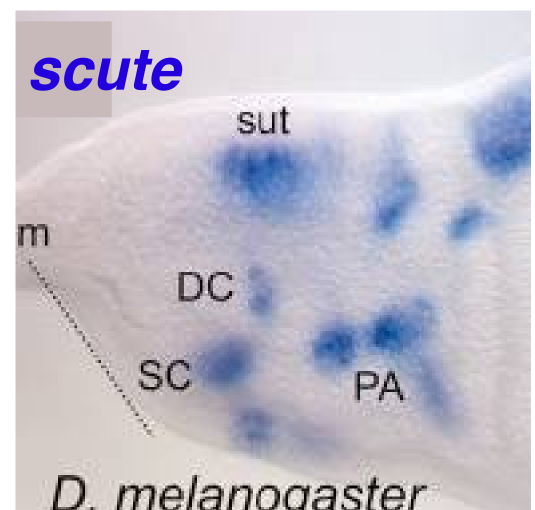
Bristle development



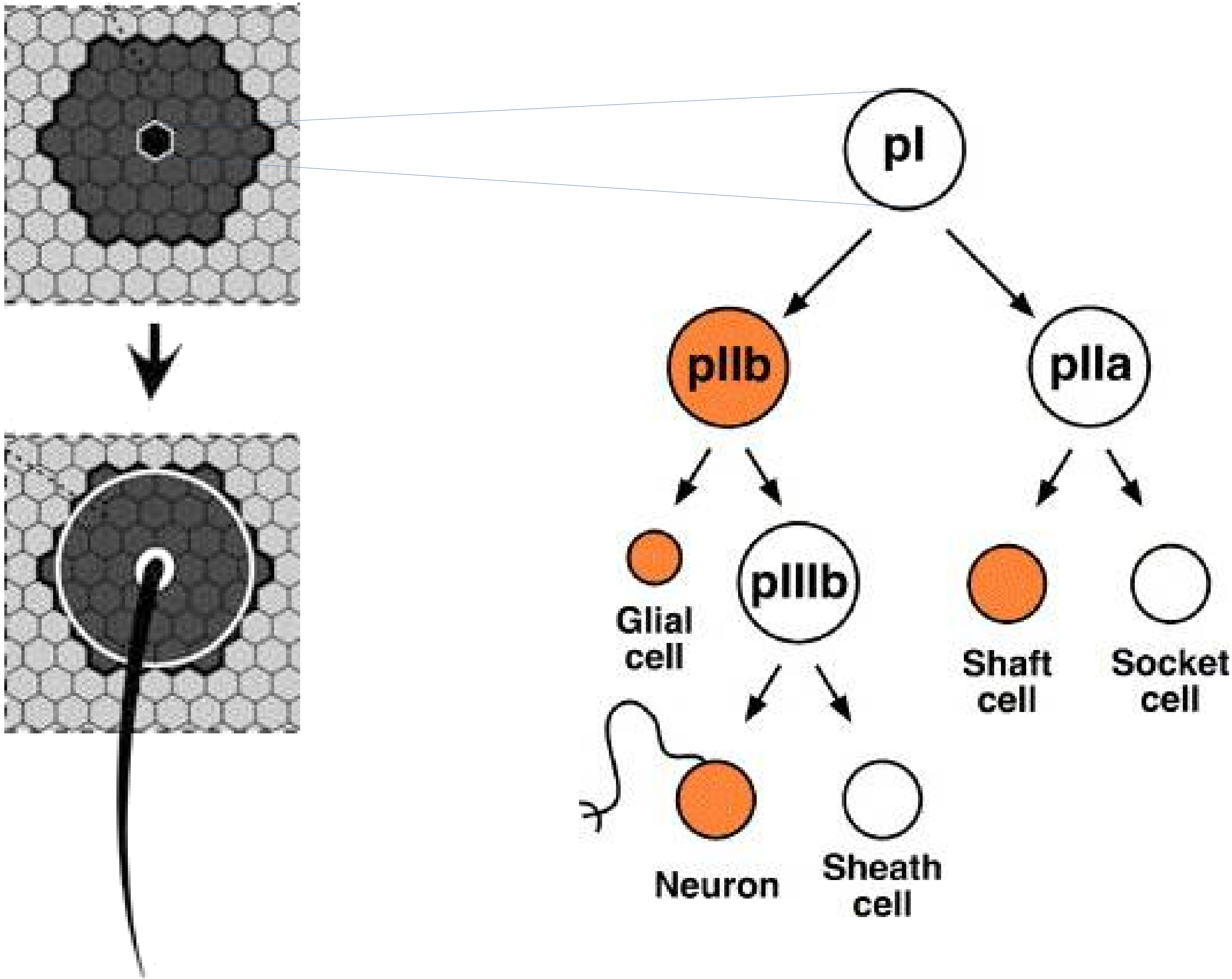
Gillespie and Walker 2001



Simpson 2007

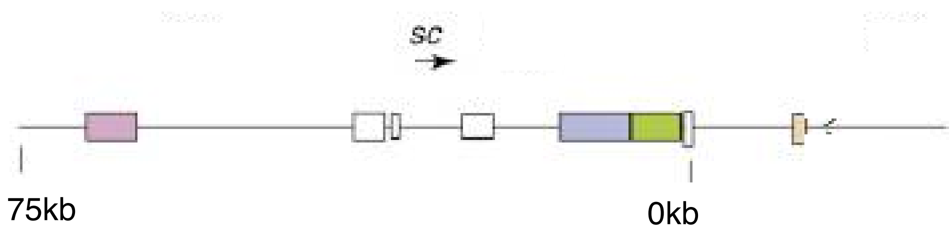


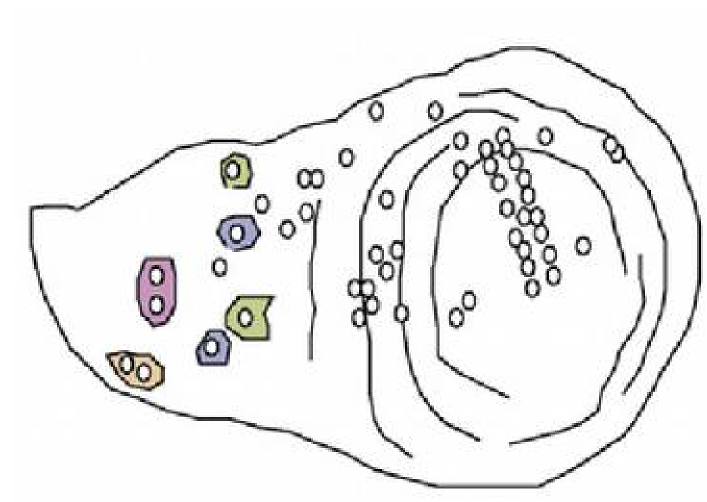
Marcellini 2006 - PloS Biology



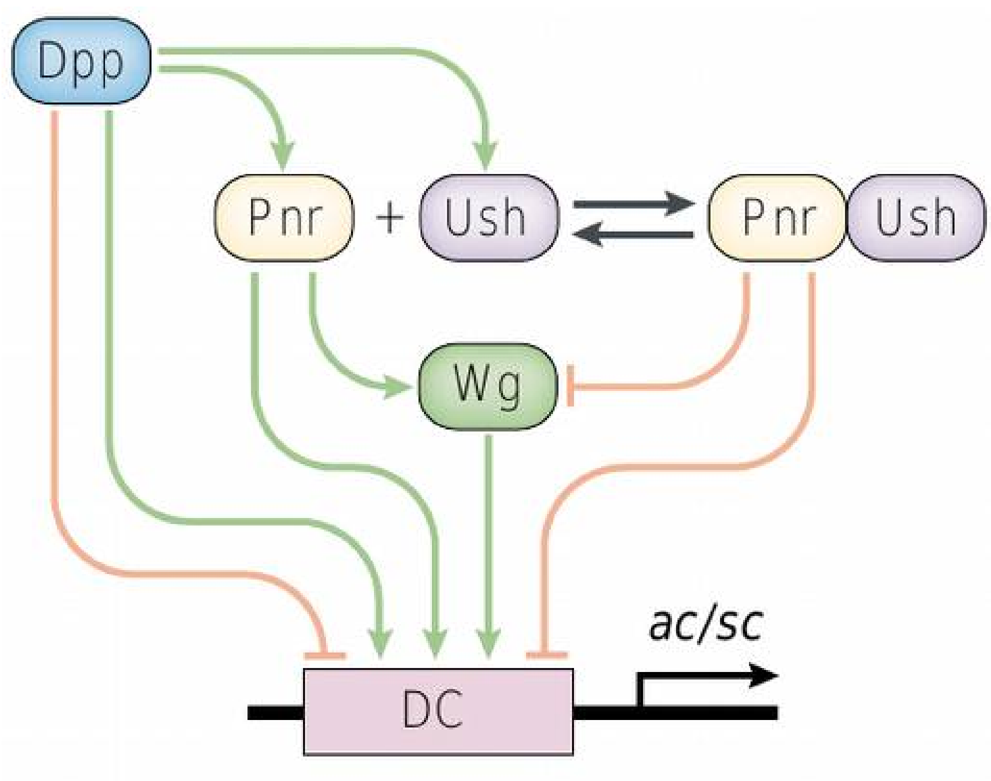
Lewis - Imaginal discs

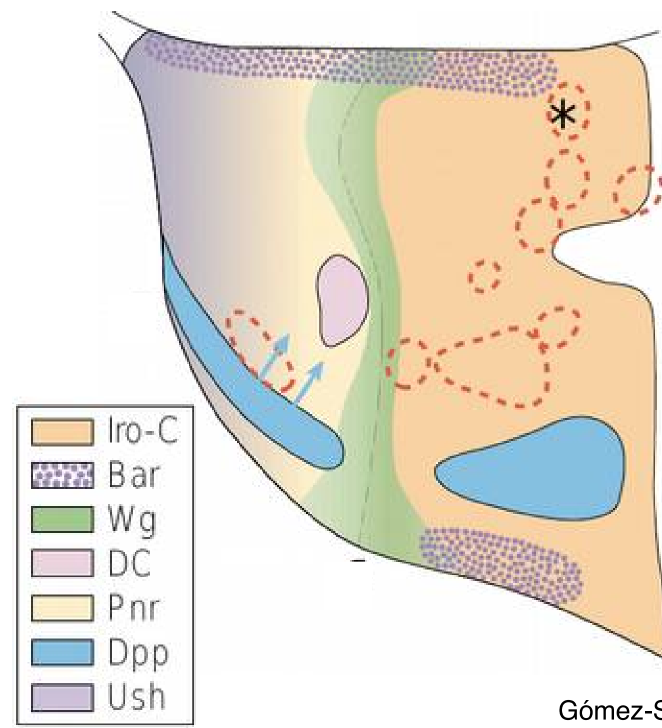
scute cis-regulatory elements are “master switches”





Simpson 2007

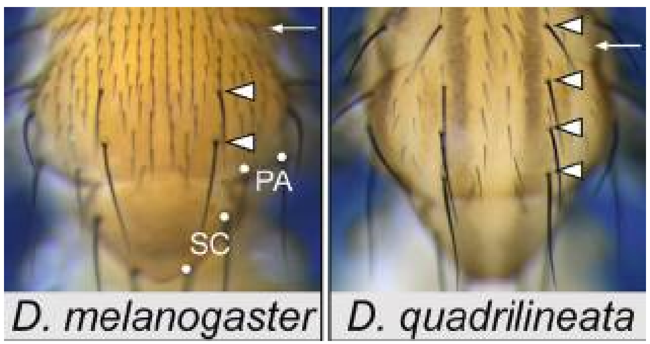


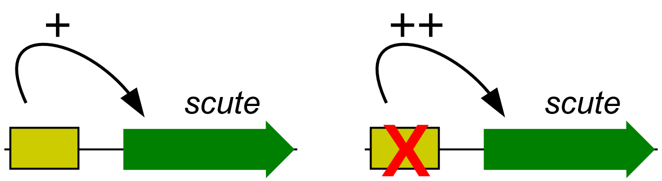


Gómez-Skarmeta 2003

Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*



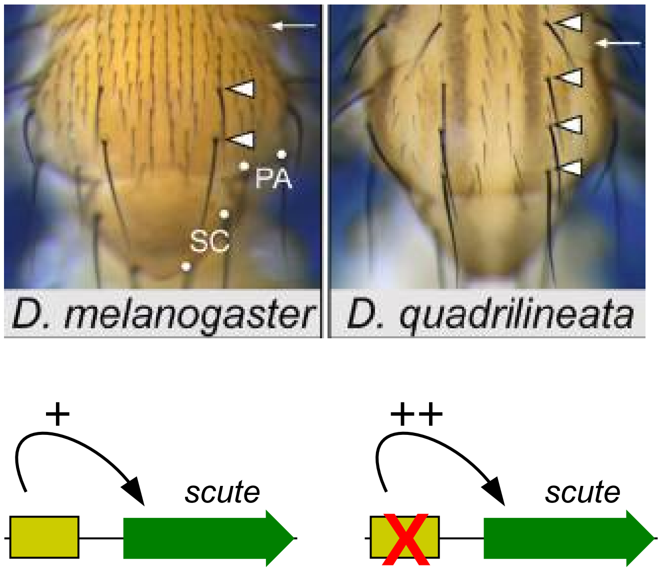


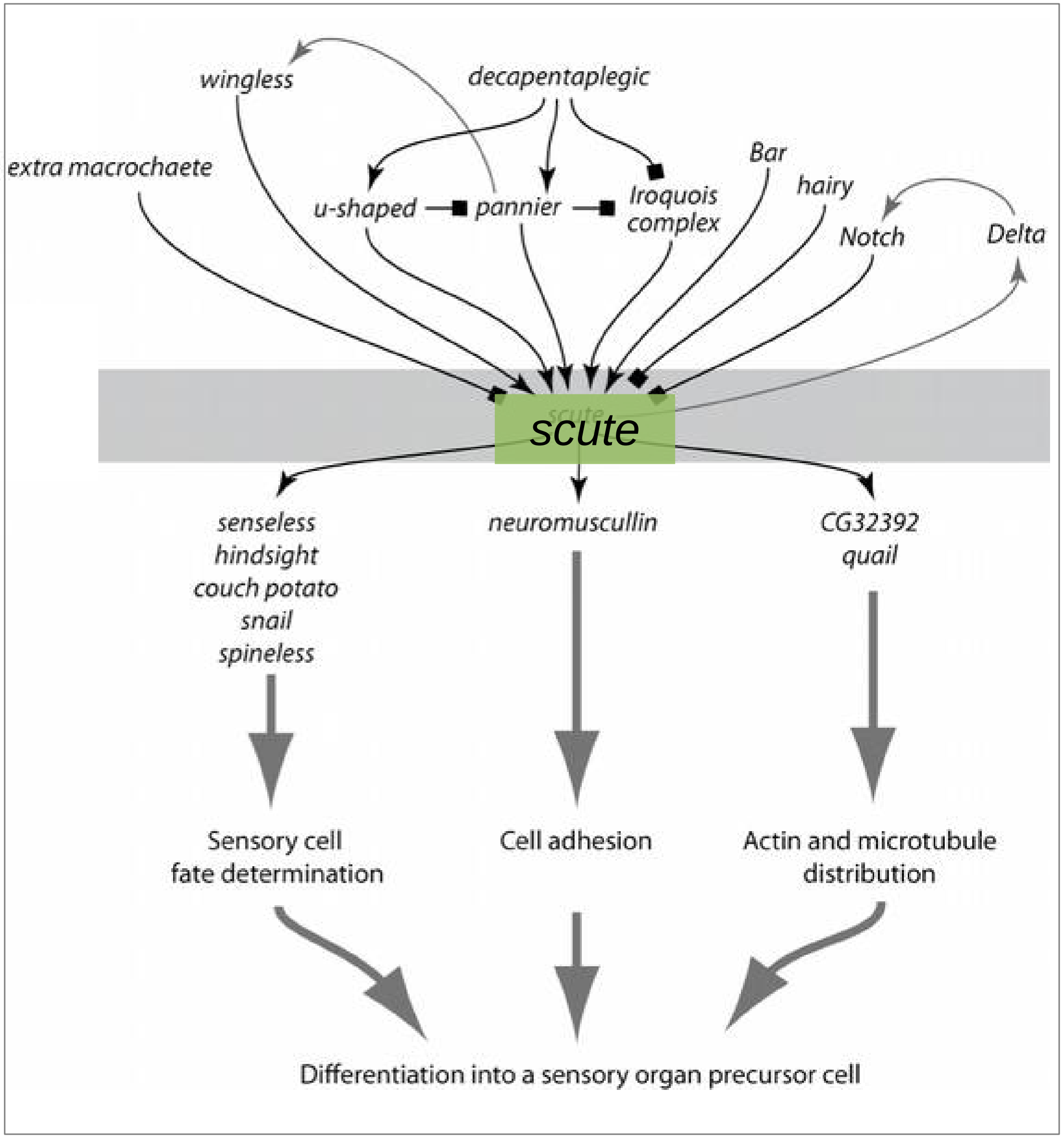
Marcelini and Simpson 2006 PloS Biology

Genetic evolution is predictable

Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*

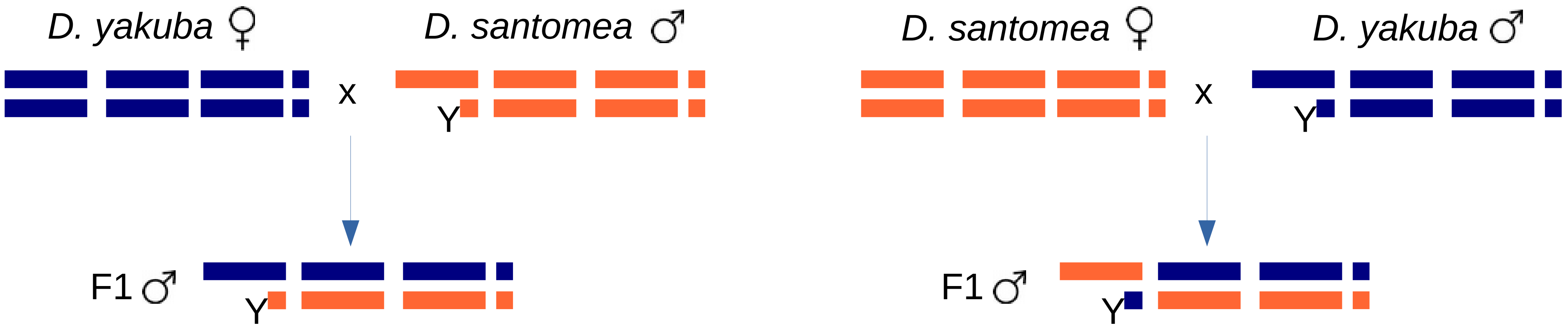




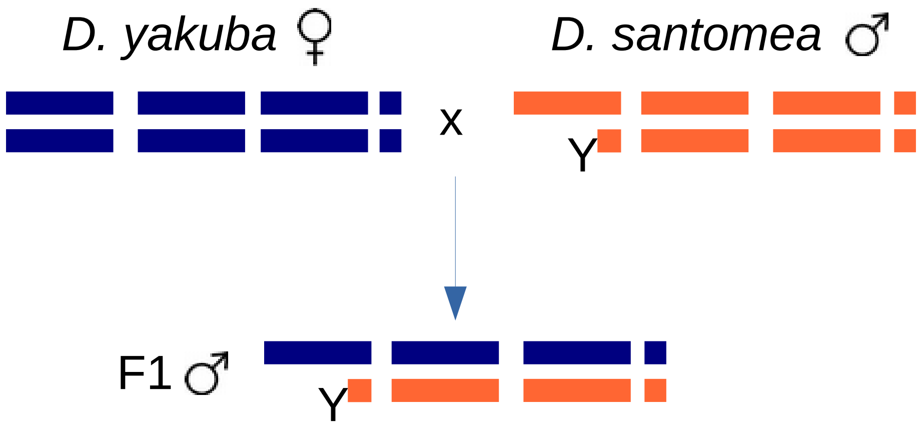
Marcelini and Simpson 2006 PloS Biology

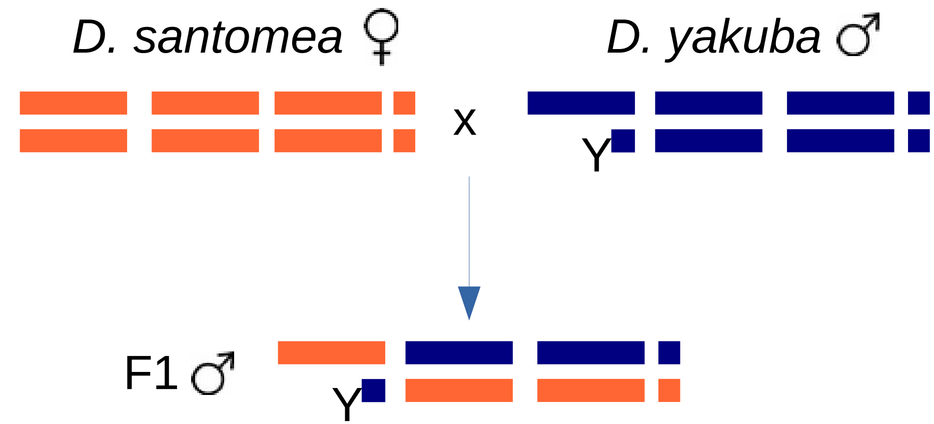
Stern and Orgogozo 2009 Science

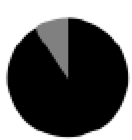
Is the causing mutation X-linked?



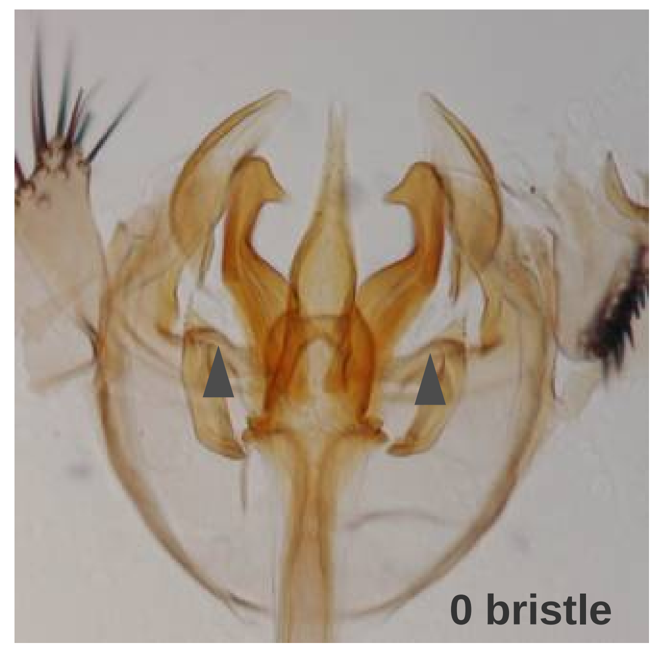
Is the causing mutation X-linked ?

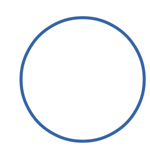






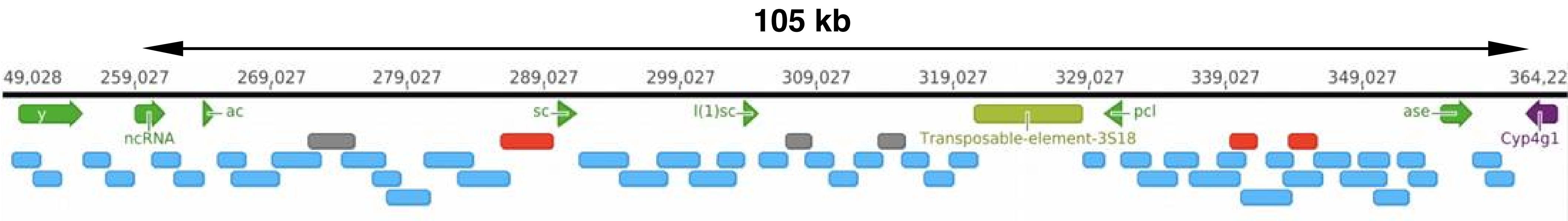
The causing mutation is X-linked





- ■ 2 bristles
- ▣ 1 bristle
- □ 0 bristle

Screening a 100-kb region

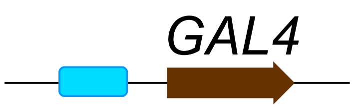


drives expression in developing genital bristles

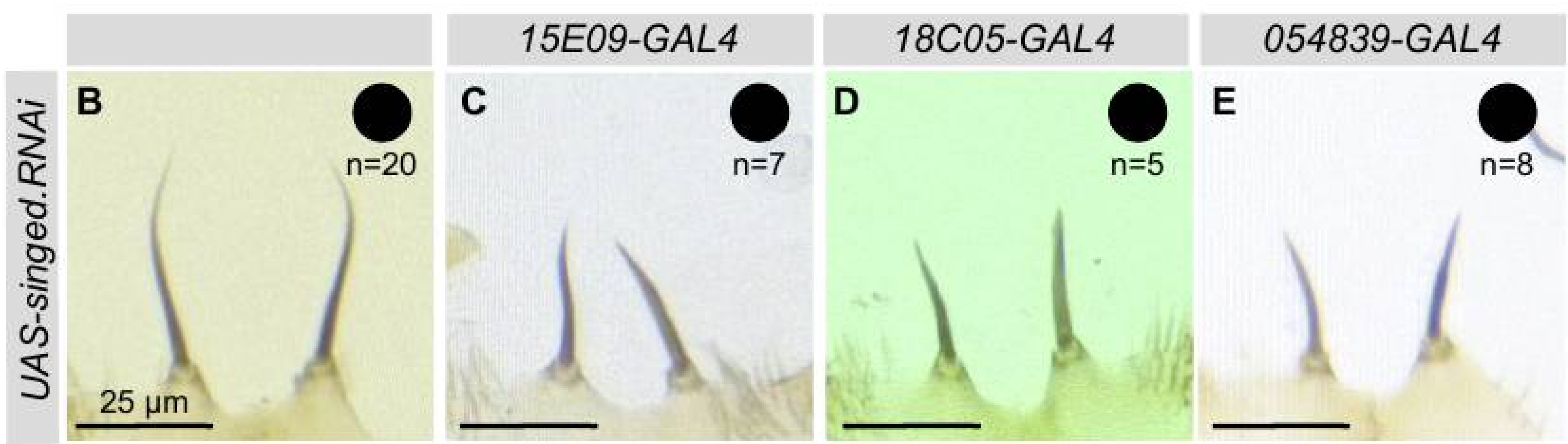
drives no expression

not tested yet

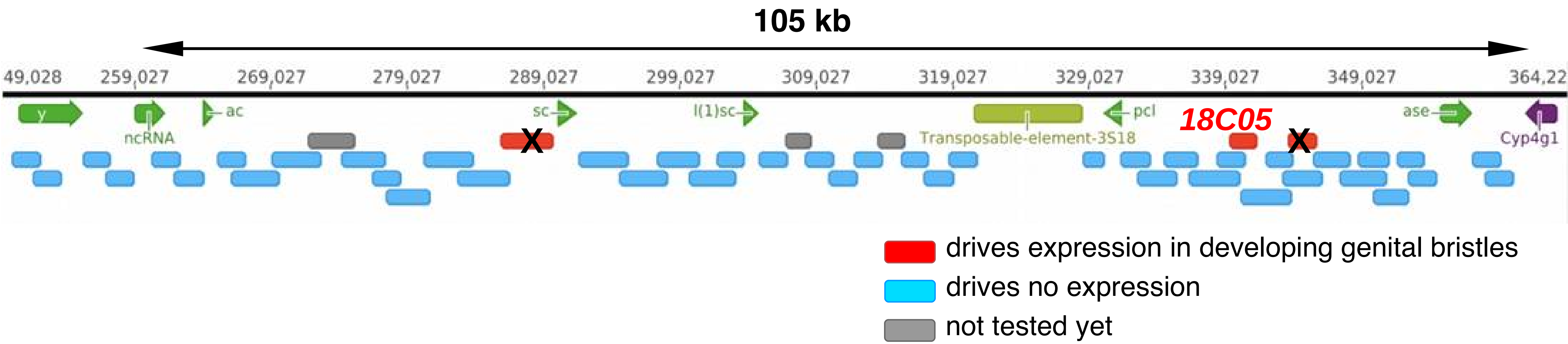
screen of
D. melanogaster
***GAL4* lines**

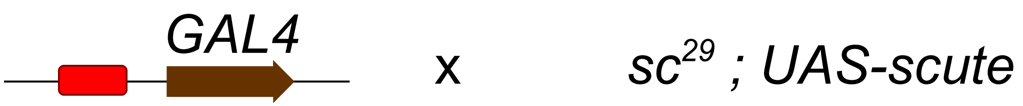


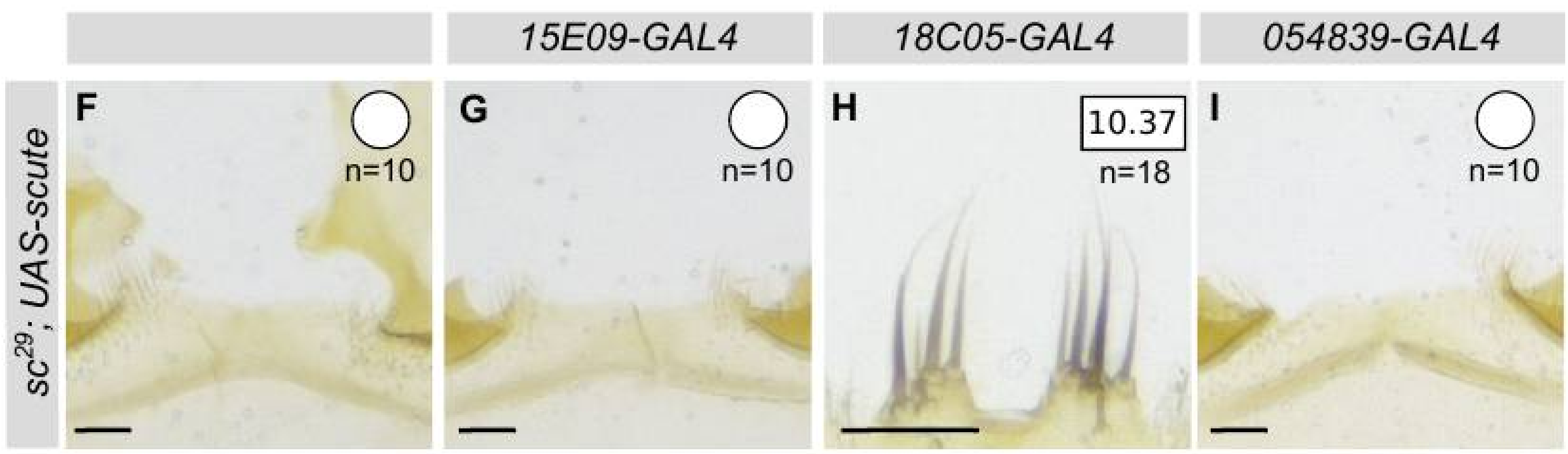
x *UAS-RNAi-singed , UAS-Dicer2*



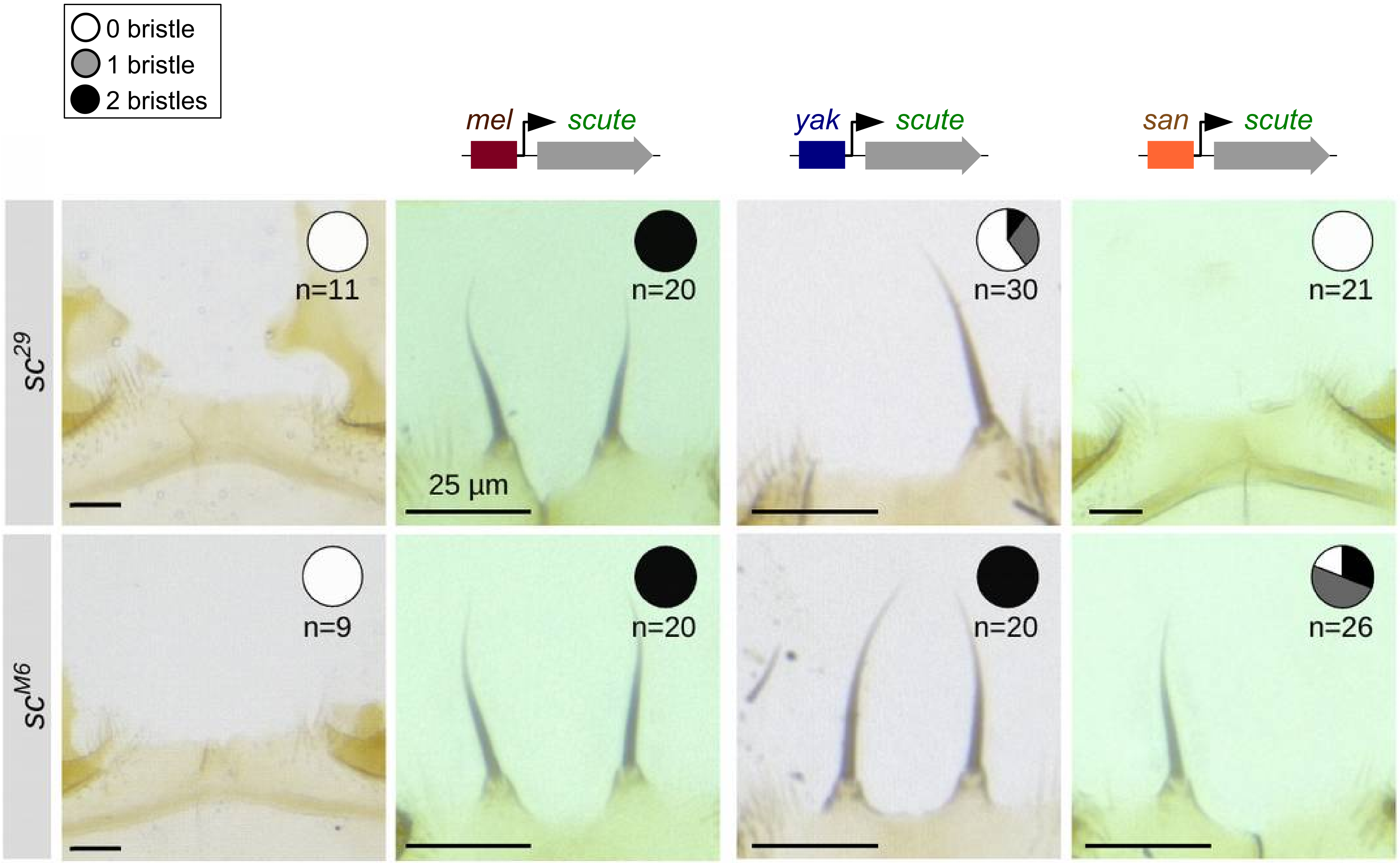
18C05 drives expression independently of *scute*







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

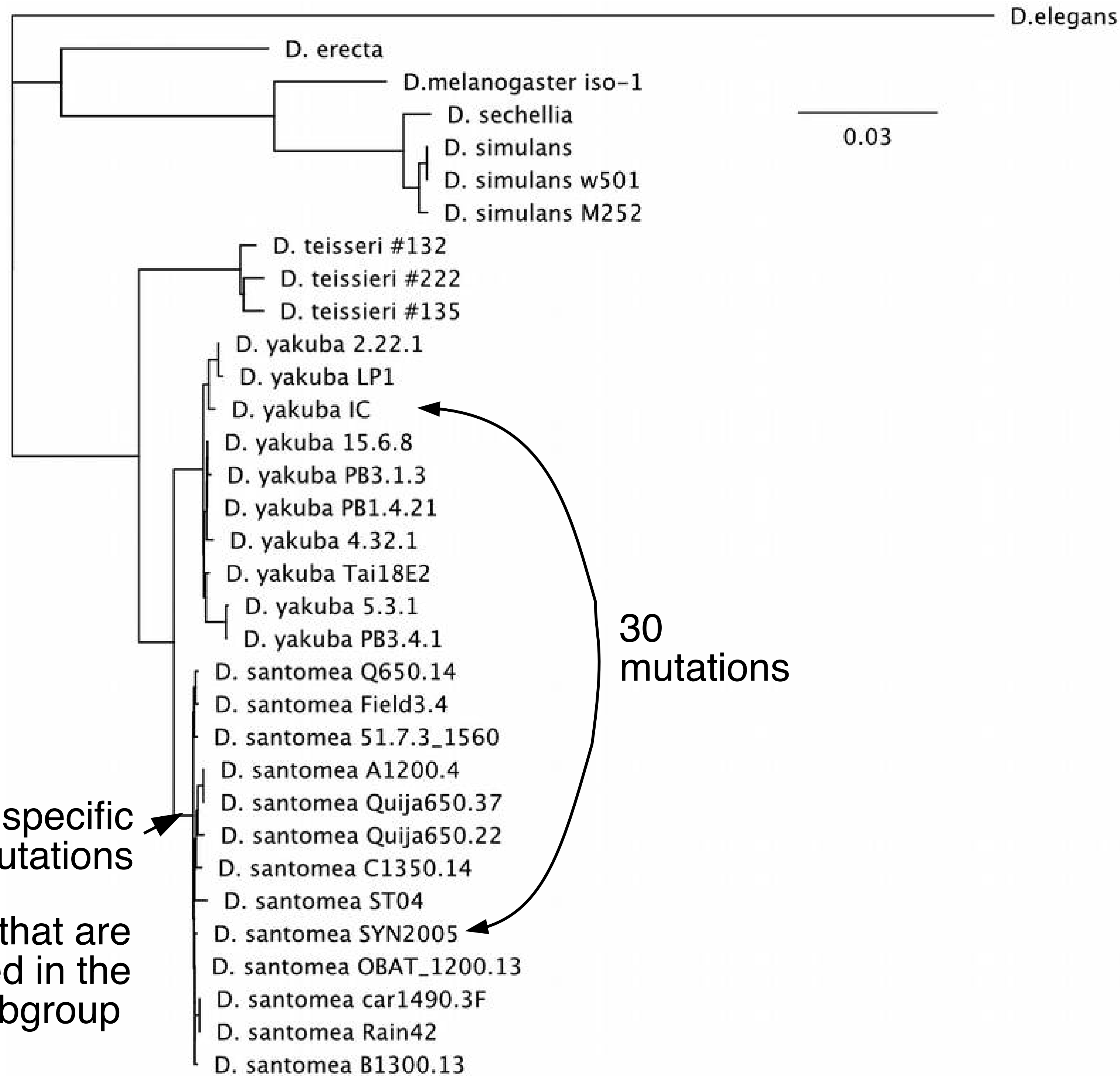


D. melanogaster transgenics

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

```
    1        10        20        30        40        50        60        70        80        90        100       110
san GAGTGAGTGGACCGCTATTTGTACACCGAAAAAATACATGTCATATAACAACTTAACCCCCTTTTCATTATAACGTCTTTAATTCAATACGTTAAATGCTCTATGTATCAGCCATT
yak GAGTGAGTGGACCGCTATTTGTACACCGAAAAAATACATGTCATATAACAACTTAACCCCCTTTTCATTATAACGTCTTTAATTCAATGCGTTCAATGCTCTATGTATCAGCCATT
    120       130       140       150       160       170       180       190       200       210       220       230
san TAAAACGTTGATTGAATTGCAACTTGAAAATTAGAAGAACATTTAAATGTCCTGCCTTTTTAAATTAGATATTATGCAGAGTTTTTATCTGTGCATTTAATGGCACATTATTATCT
yak TAAAACGTTGATTGAATTGCAACTTGAAAATTAGAAGAACATTTAAATGTCCTGCTTTTTTAAATTAGATATTATGCAGAGTTTTTATCTGTGCATTTAATGGCACATTATTATCT
    240       250       260       270       280       290       300       310       320       330       340
san CTGATGAGCGAGCGAACACATCAGGGAAGATTGCAGGATGGGCTGCAATATGAAGCCACTTCCTTCGCAACACGTGCATCGCCAGCAAATCGCGTCCAAATCAAACACACTACCTG
yak CTGATGAGCGAGCGAACACATCAGGGAAGATTGCAGGATGGGCTGCAATATGAAGCCACTTCCTTCGCAACACGTGCATCGCCAGCAAATCGCGTCCAAATCAAACACACTACCTG
    350       360       370       380       390       400       410       420       430       440       450       460
san GCCAAAATTGTGTTTAATGAGTGACTTTTGAAGGGGAAGATGGGAAGATCGGAAGATCCCATCCCAAATGAGAGATCCCAAAGGAAAGGTGAGGGATAAGAGTTGGTATGCTGCTG
yak GCCAAAATTGTGTTTAATAAGTGACTTTTGAAGGGGAAGATGGGAAGATTCGAAGATCCCATCCCAAATGAGAGATCCCAAAGGAAAGGTGAGGGATAAGAGTTGGTATGCTGCTG
    470       480       490       500       510       520       530       540       550       560       570       580
san CTGAGCTGCTGAGGTAGCTTAGCCCATTATTCAGGCTTTATTTATTTTGCGGACTCAGATCGCGCAGGTCCACGGGGCCCAAATTAAAAGTCCGGTGCGCCCAAGTCAAAAGTGCA
yak CTGAGCTGCTGAGGTAGCTTAGCCCATTATTCAGGCTTTATTTATTTTGCGGACTCAGATCGCGCAGGTCCACGGGGCCCAAATTAAAAGTCCGGTGCGCCCAAGTCAAAAGTGCA
    590       600       610       620       630       640       650       660       670       680       690
san AATTTTCGCAGCCGCATCAGACGTCATATTAGCGAATCAACTGACAAAGCATATGAATATCAACAGCGTTTGAACAAGTGGATTAAAGAGCGATCTGAAAACGGATCGAAACGGCG
yak AATTTTCGCAGCCGCATCAGACGTCATATTAGCGAATCAACTGACAAAGCATATGAATATCAACAGCGTTTGAACAAGTGGATTAAAGAGCGATCTGAAAACGGATCGAAACGGCG
    700       710       720       730       740       750       760       770       780       790       800       810
san AGTGCAGACACACAGACAGGTCTTTCGGCTCTCGTTCCTTATAATTAAAACAGGAATCGGGCATTCGCA---------GCCTTCACAGCCTTCACAGCGGCCAAGGGGAACTCAAT
yak AGTGCAGACACACAGACAGGTCTTTCGGCTCTCGTTCCTTATAATTAAAACAGGAATCGGGCATTCGCAGCCTTCACAGCCTTCACAGCCTTCACAGCGGCCAAGGGGAACTCAAT
    820       830       840       850       860       870       880       890       900       910       920
san TTACTCTACTTTACAATCATTTTTACGTAACGGCATTCTAGGCTAGGCTGCTCTTTAAAGTCGGCTTAACAAGCTCTTGACGATGGTGGACATGTCTATTTTCTATTTTCACGTGA
yak TTACTCTACTTTACAATCCTTTTTACGTAACGGCATTCTAGGCTAGGCTGCTCTTTGAAGTCGGCTTAACAAGCTCTTGACGATGGTGGACATGTCTATTTTCTATTTTCATGTGA
    930       940       950       960       970       980       990       1,000     1,010     1,020     1,030     1,040
san GCTTTCTATAAATAGAAAGTGTTCGGGGCAGCGATTTAGTTAAGAGCCAGGTACGCGCTACTTTCCACCAAGTTAAAGCCGTTCAAGGTGTTAAAGGAATTGTACGCAGCCAAGAT
yak GCTTTCTATAAATAGAAAGTGTTCGGGGCAGCAATTTAGTTTAGAGCCAGGTACGCGCTACTTTCCACCAAGTTAAAGCTGTTCAAGGTGTAAAAGGAATTGTACGCAGCCAAGAT
    1,050     1,060     1,070     1,080     1,090     1,100     1,110     1,120     1,130     1,140     1,150     1,160
san CACGTGGTGAATGGACTTCTTGGACAGTTGGCAATCGGGTCTCCATGCTGAGCTGCGATACCAGTTTCAGTTGGCAATCGGGTTTCGGTGGGATTCATTCATGGAGTTCGCGGACC
yak CACGTGGTGAATGGACTTCTTGGACAGTTGGCAATCGGGTCTCCATGCTGAGCTGCGATACCAGTTTCAGTTGGCAATCGGGTTTCGGTGGGATTCATTCATGGAGTTCGCGGACC
    1,170     1,180     1,190     1,200     1,210     1,220     1,230     1,240     1,250     1,260     1,270
san TAAGCCGCTTAAGTTCTCTCTTTCATTTCCTTCTTTTTTTCCCGCACATTTCGAGGACCTGTTTATTTTTTTATCGGGTGCTTTTTGTATTTGTTTGTATTTTTCCCTCTTTTTGA
yak TAAGCCGCTTAAGTTCTCTCTTTCATTTCCTTCTTTTTTTCCCGCACATTTCGAGGACCTGTT--TTTTTTTATCGGGTGCTTTTTGTATTTGTTTGTATTTTTCCCTCTTTTTGA
    1,280     1,290     1,300     1,310     1,320     1,330     1,340     1,350     1,360     1,370     1,380     1,390
san CTAATGTGCAACTTACACTTGACTGGCGCACAATCAACACCATCAACGGGAGCAGCAGATTCCGCGGGTTTTGTCTGGTTTTTTAGGGTTCTTGGCTGCTTCATGGGATCCTCATG
yak CTAATGTGCAACTTACACTTGACTGGCGCACAATCAACACCATCAACGGGAGCAGCAGATTCCGCGGGTTTCGTCTGGTTTTTTAGGGTTCTTGGCTGCTTCATGGGATCCTCATG
    1,400     1,410     1,420     1,430     1,440     1,450     1,460     1,470     1,480     1,490     1,500
san GGTCTCATCAGCTCCAGCTGTATCACGGAAATAAATGTTGCCTTCTTTGGAAATAGTAGTGAAGCATCTTATATATATTTTGTTTTGGGCAAACAACTGCAATGTGACTTGATTGC
yak GGTCTCATCAGCTTTAGTTGTATCACGGAAATAAATTCTGCCTTCTTTGGAAATAGTAGTGAAGCATCTTATATATATTTTGTTTTGGGTAAACAACTGCAATGTGACTTGATTAC
    1,510     1,520     1,530     1,540     1,550     1,560     1,570     1,580     1,590     1,600     1,610     1,620
san CTCATTTAATTGAATGTTTAACTCATCATCGAGCACCTAAATATGTGTGAGAAAATACTAGTTGTGGCATTTGTTGTTCTCTGTGCGGCGCTCATCAATTTTTGGCCGAAAGGAGG
yak CTCATTTAATTGAATGTTTAACTCATCATCGAGCACCTAAATTTGTGTGAGAAAATACTAGTTGTGGCATTTGTTGTTCTCTGTGCGGCGCTCATCAATTTTTGGCCGAAAGGAGG
    1,630     1,640     1,650     1,660     1,670     1,680     1,690     1,700     1,710     1,720     1,730     1,740
san GATTTGATCCCGATTGCTCATATTAAAGCCAACGCGTGCTGCCAACGTACTGATTCCGCTGTGGATAGCTCATCTTGATGCCCGTCATTTACTTACGCCAAGAAGAGGGCCTTCCT
yak GATTTGATCCCGATTGCTCATATTAAAGCCAACGCGTGCTGCCAACGTACTGAATCCGCTGTGGATAGCTCATCTTGATGCCGGTCATTTACTTACGCCAAGAAGAGGGCTTTCCT
    1,750     1,760     1,770     1,780     1,790     1,800     1,810     1,820     1,830     1,840     1,850
san CTGAAGCTCCTTGGCCACCAATGTACCGTTTCTTGTATTTGACTTTGTTACGCCCACCTCGGAATAATAACCAAGATACCAATAACCACGACGCAGGAAGGCAAGAGAAAAGGGTG
yak CTGAAGCTCCTTGGCCACCAATGTACCGTTTCTTTTATTTGACTTTGTTACGCCCACCTCGGAATAATAACCAAGATACCAATAACCACGACGCAGGAAGGCAAGAGAAAAGGGTG
    1,860     1,870     1,880     1,890     1,900     1,910     1,920     1,930     1,940     1,950     1,960     1,970
san GCGGCCCTGGTCATCAAGTTTTCGGATTGCCTAACGGCGCTTCAGATTAGCCATCTTGCTACATCCTCTTATTTTTTTTTATTATTTTTCTCTGAAAAGCCCTGGTTACTCATTAC
yak GCGGCCCTGGTCATCAAGTTTTCGGATTGCCTAACGGCGCTTCAGATTAGCCATCTCGCTACATCCTCTTA-TTTTTTTTATTATTTTTCTCTGAAAAGCCCTGGTTACTCATTAC
    1,980     1,990     2,000     2,010     2,020     2,030     2,040     2,050     2,060     2,070     2,080     2,088
san CAACAGAAGATCTAAATTGAAACGGTAGCTTCAATTGACGGCATCTTGATGGAAAGGTGATGTAAGAGGCAGCCTTTTGCAGAGAGACATCATCGCACCCCGATAGCAAACAGCTC
yak CAACAGAAGATCTAAATTGAAACGGTAGCTTCAATTGACGGCATCTTGATGGAAAGGTGATGTAAGAGGCAGCCTTTTGCAGAGAGACATCATCGCACCCCGATAGCAAACAGCTC
```

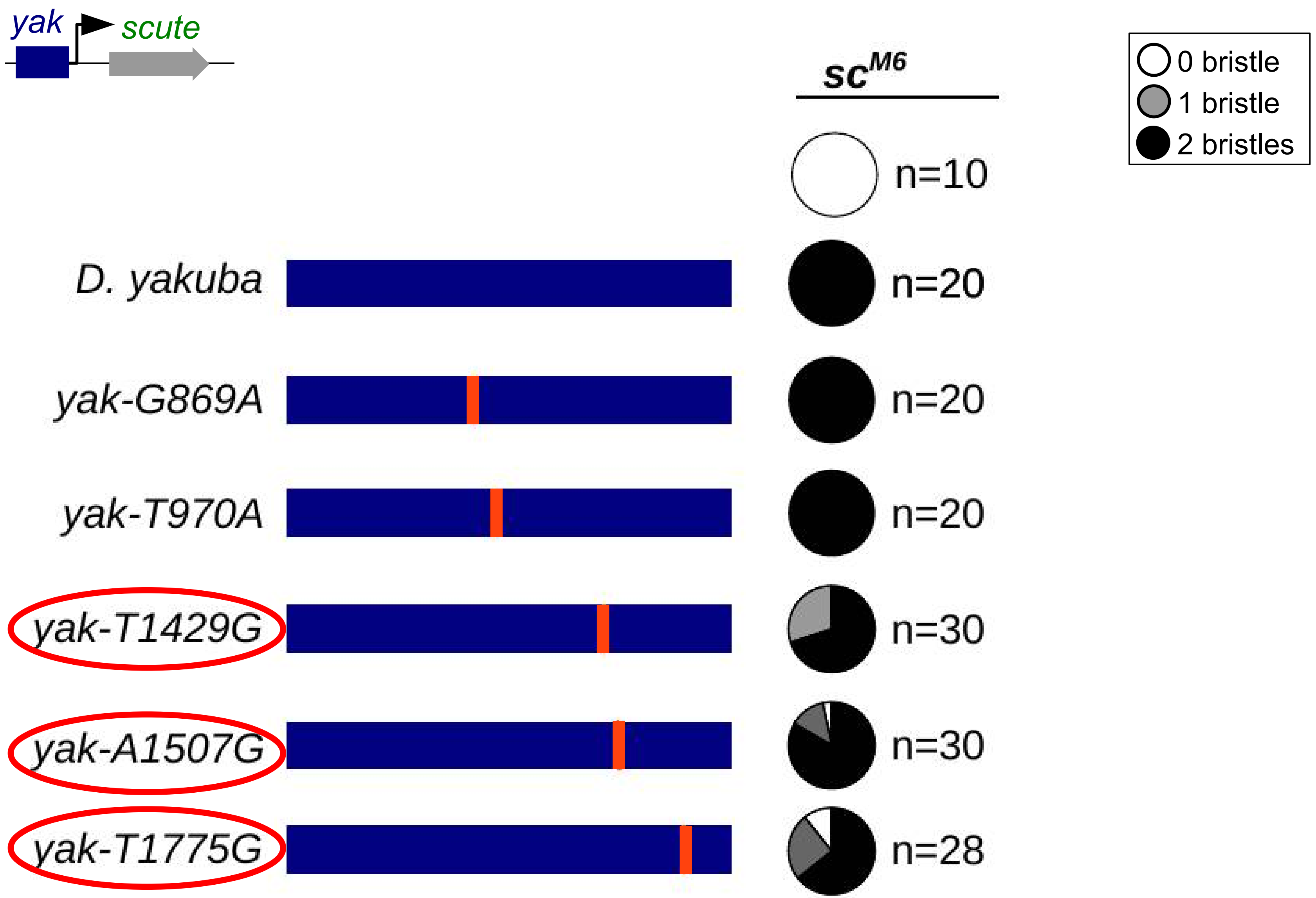
18C05 alignment



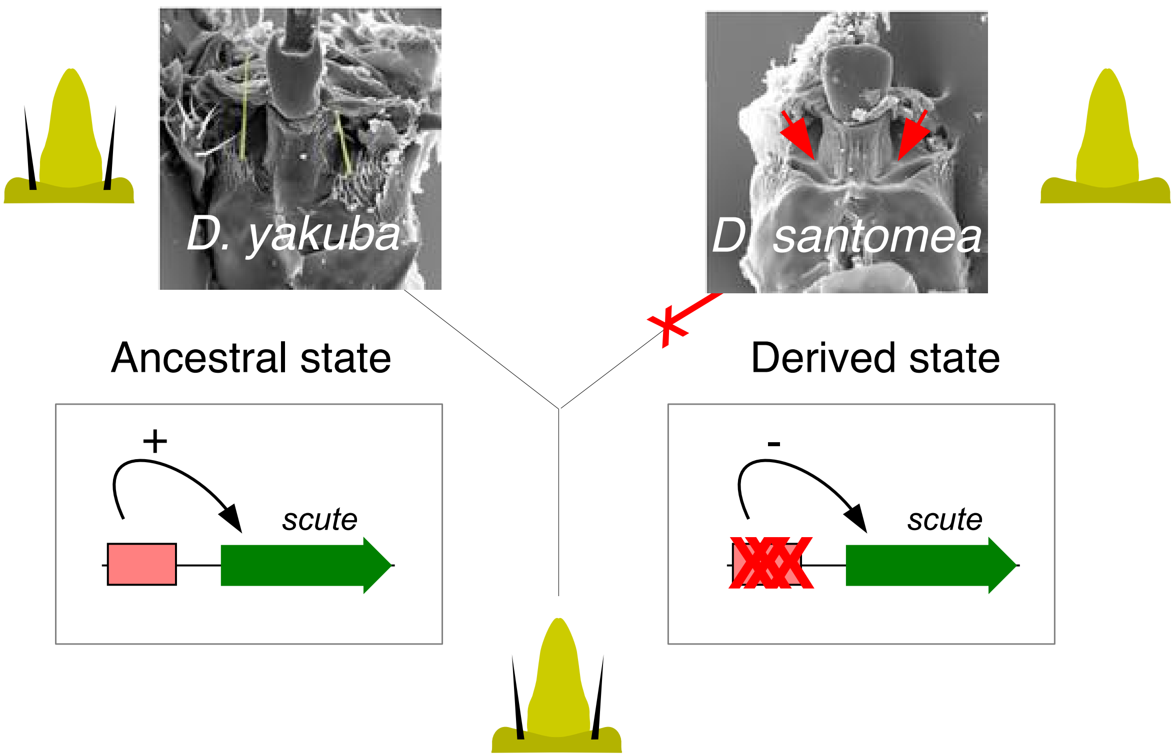
12 *D. santomea*-specific mutations

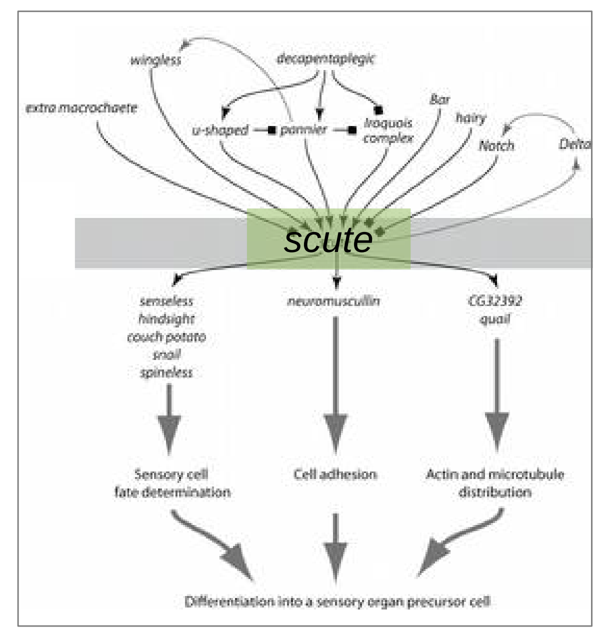
7 affect sites that are conserved in the *melanogaster* subgroup

3 mutations affect genital bristle number



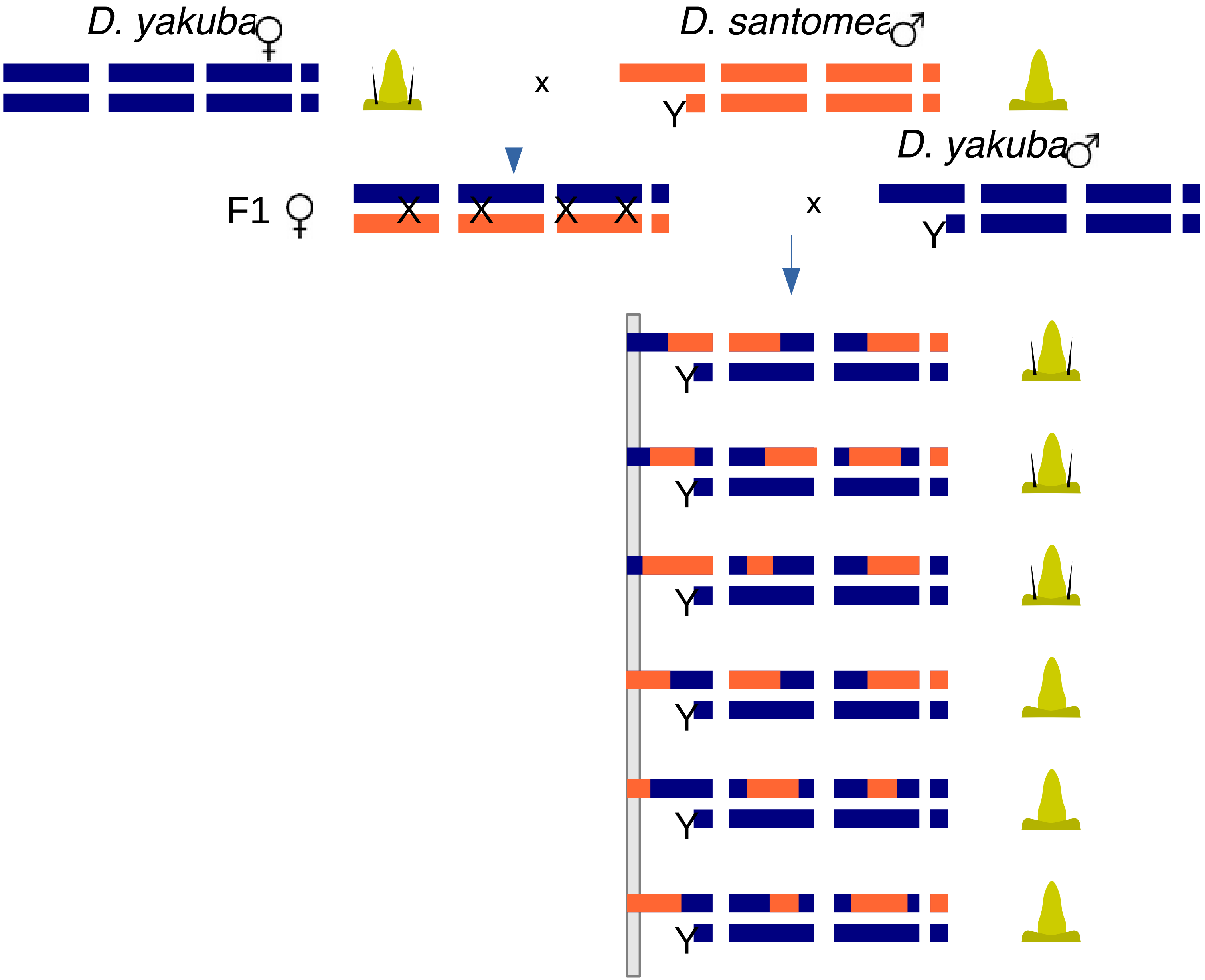
D. santomea lost genital bristles via 3 mutations in *scute*





QTL mapping

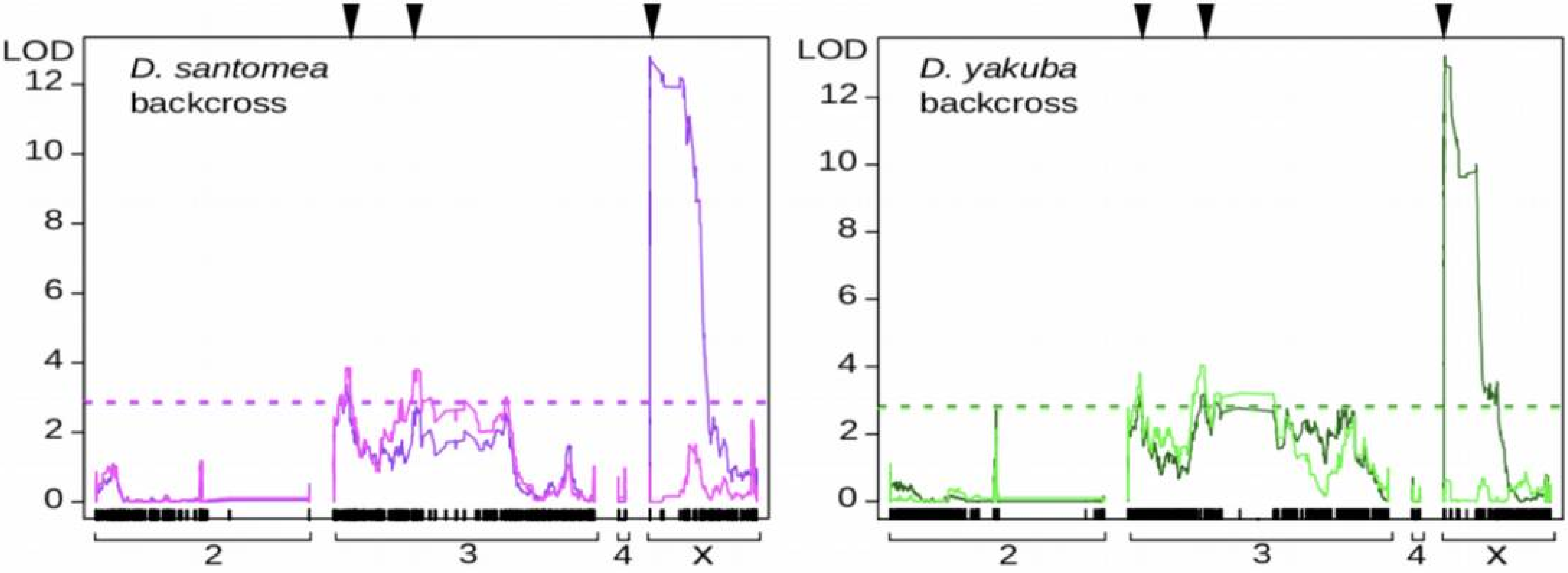
***D. yakuba* backcross**



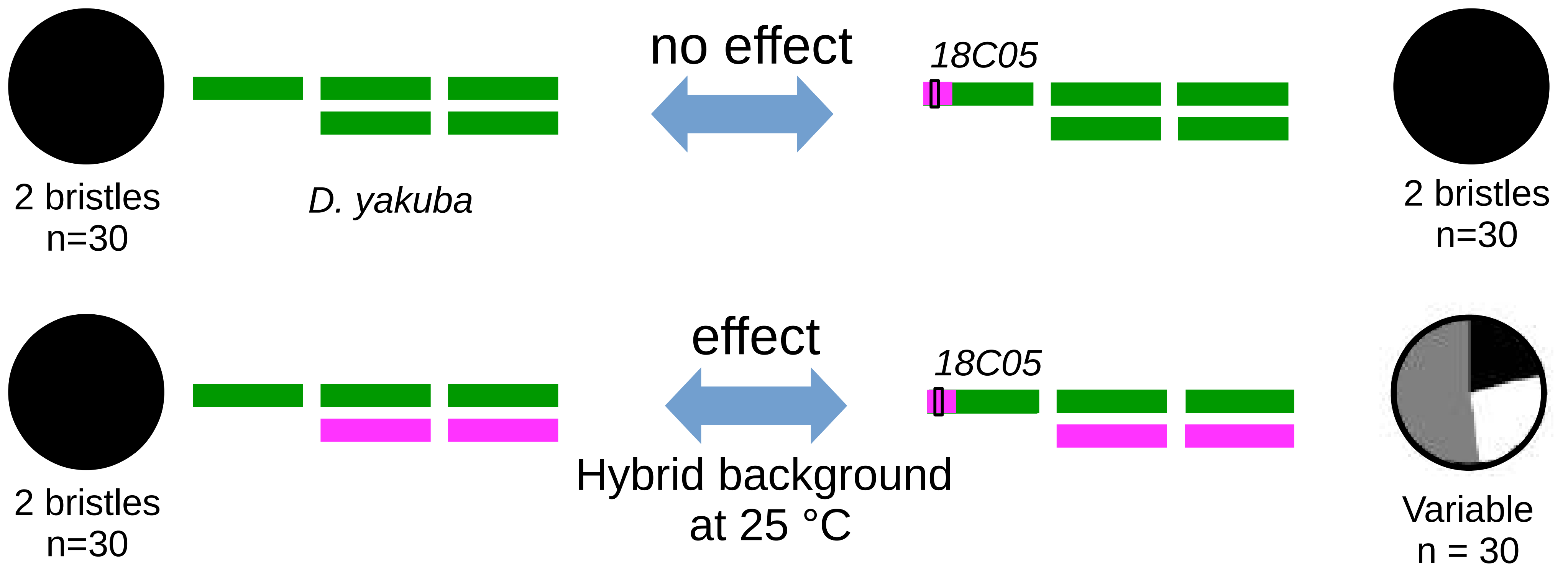
Genomic region associated with the phenotype

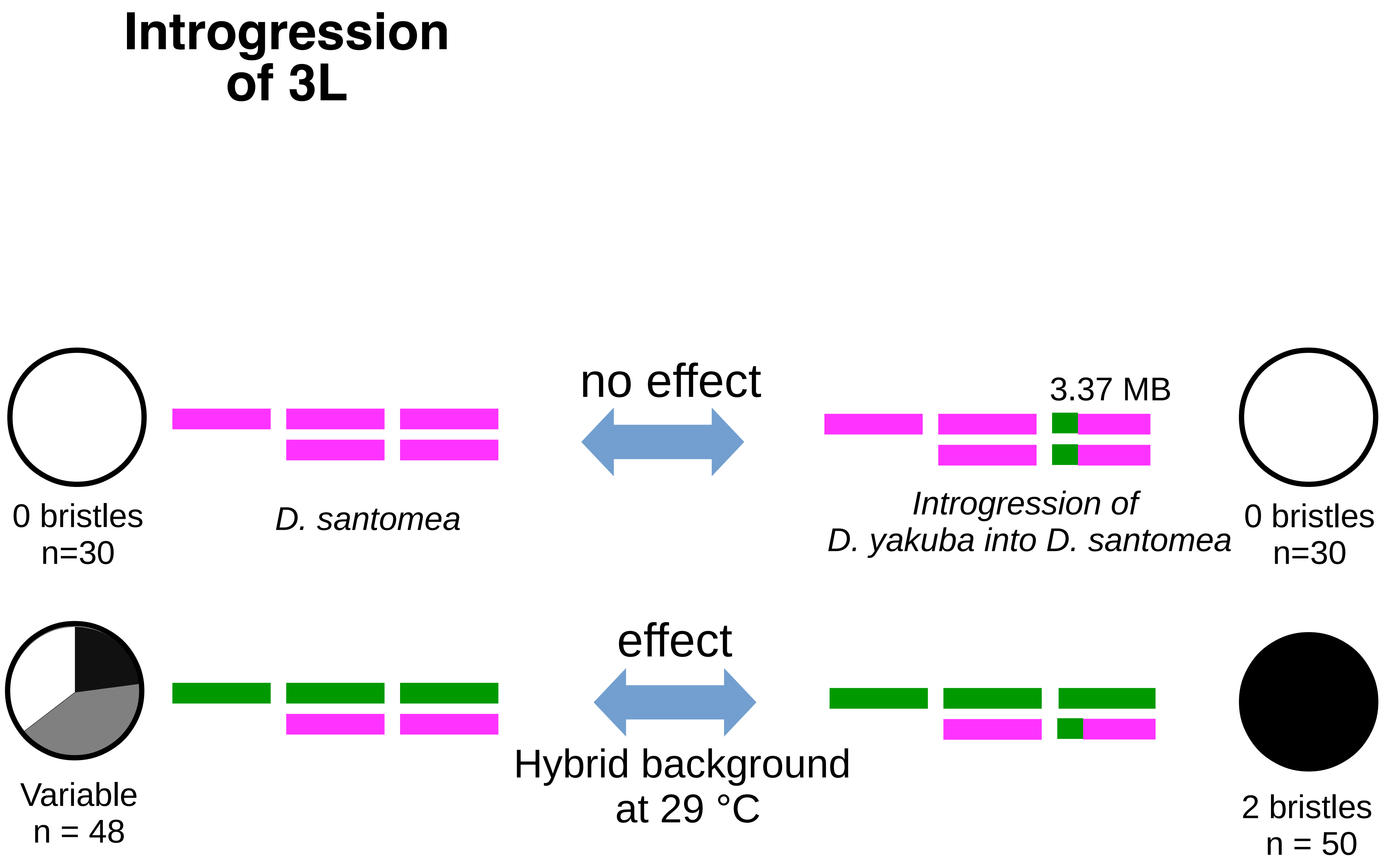
QTL mapping

One major QTL at the tip of the X chromosome
Two minor QTL on the 3rd chromosome

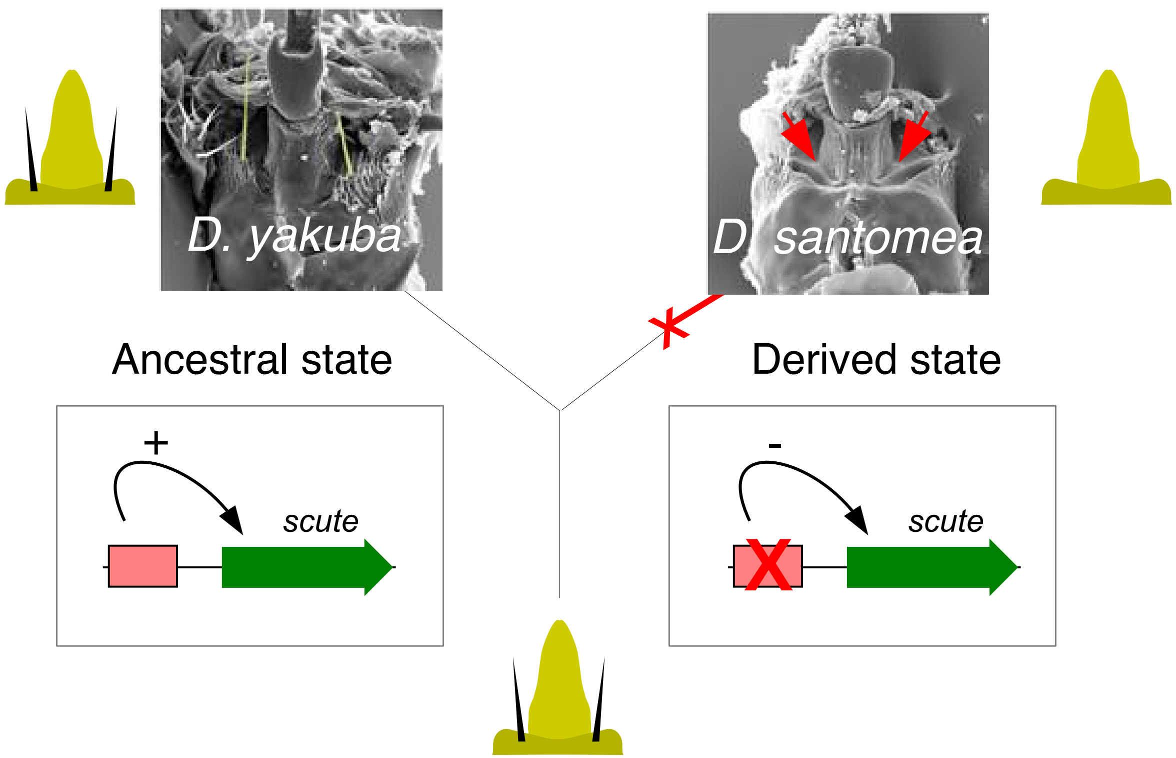


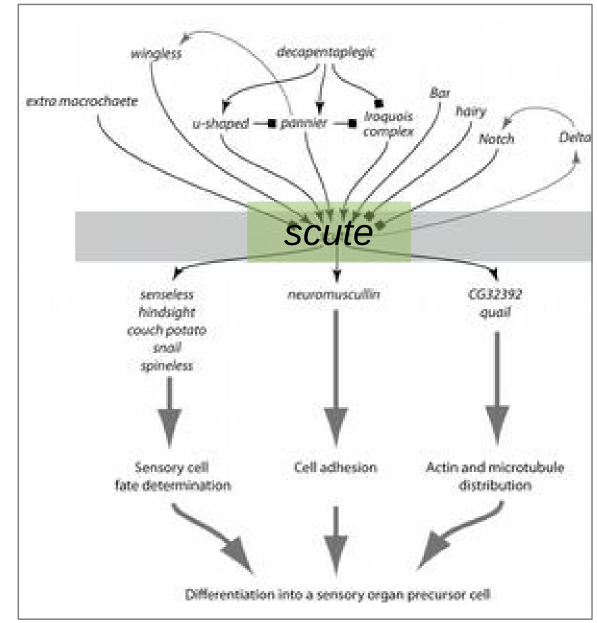
Introgression of *18C05* (*scute*)




Introgression
of 3L
no effect
3.37 MB
0 bristles
n=30
D. santomea
Introgression of
D. yakuba into D. santomea
0 bristles
n=30
effect
Variable
n = 48
Hybrid background
at 29 °C
2 bristles
n = 50

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





.. and in at least 2 other genes on 3L.

The *scute* locus has no effect alone.

Sensitive genetic and environment backgrounds help to magnify the QTL effects.

The genotype-phenotype relationship

Genotype & Phenotype

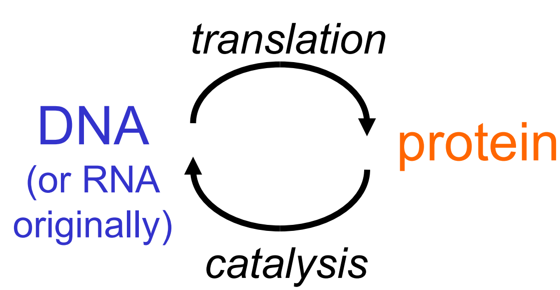
= what engenders = what is apparent

DNA/RNA

- **Regulation of gene expression**
- **Biochemical reactions**
- **Subcellular architecture**
- **Assembly of cells**
- **Organism morphology and behavior**

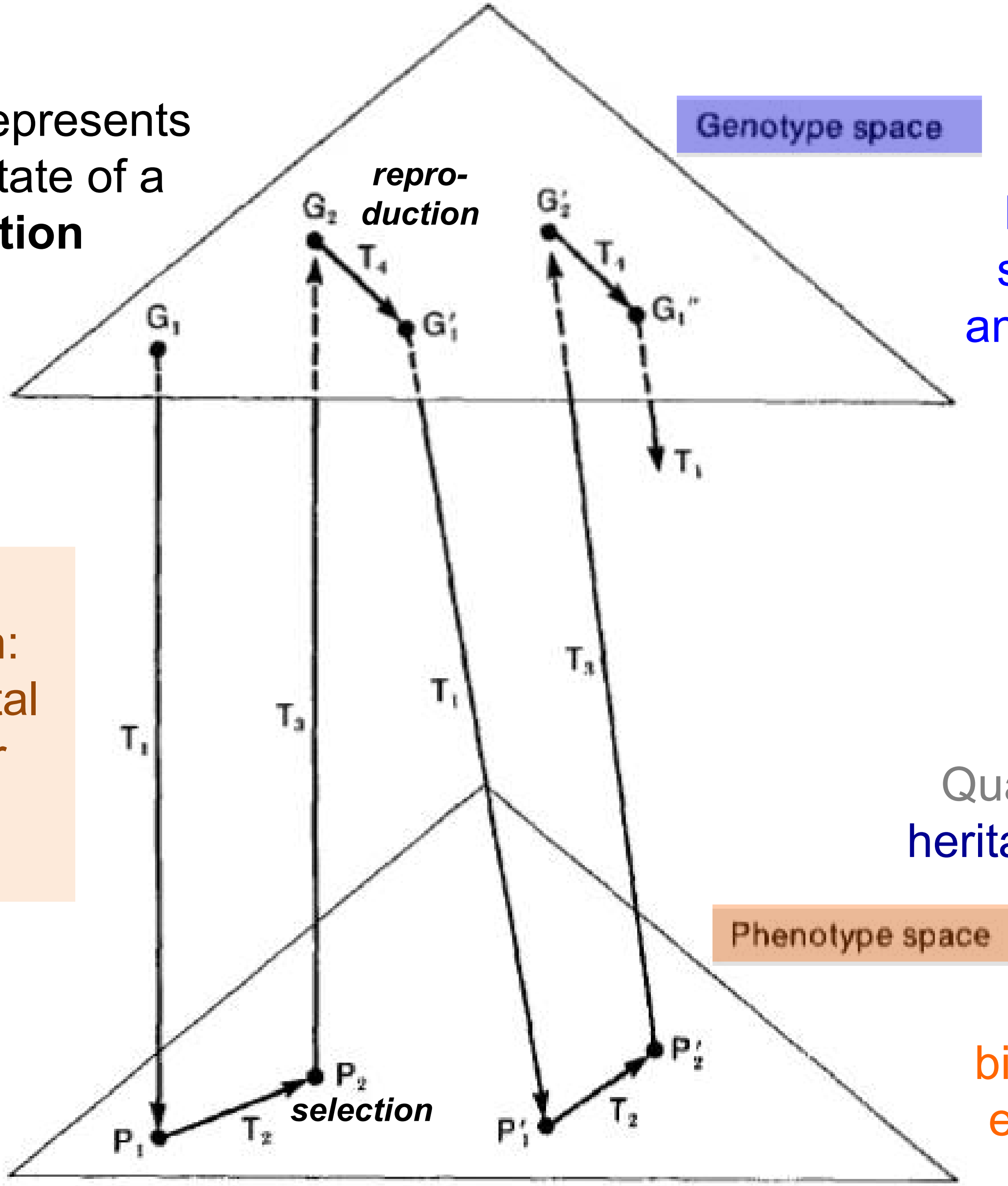
etc.

distinction appeared at the origin of life:



The first genotype-phenotype map

Here a dot represents the mean state of a **population**



Phenotype construction: developmental and cellular biology physiology

Population genetics: stochastic processes and selection coefficient

Quantitative genetics: heritability of phenotypes

Evolutionary biology of phenotypes, evolutionary ecology

Lewontin 1974

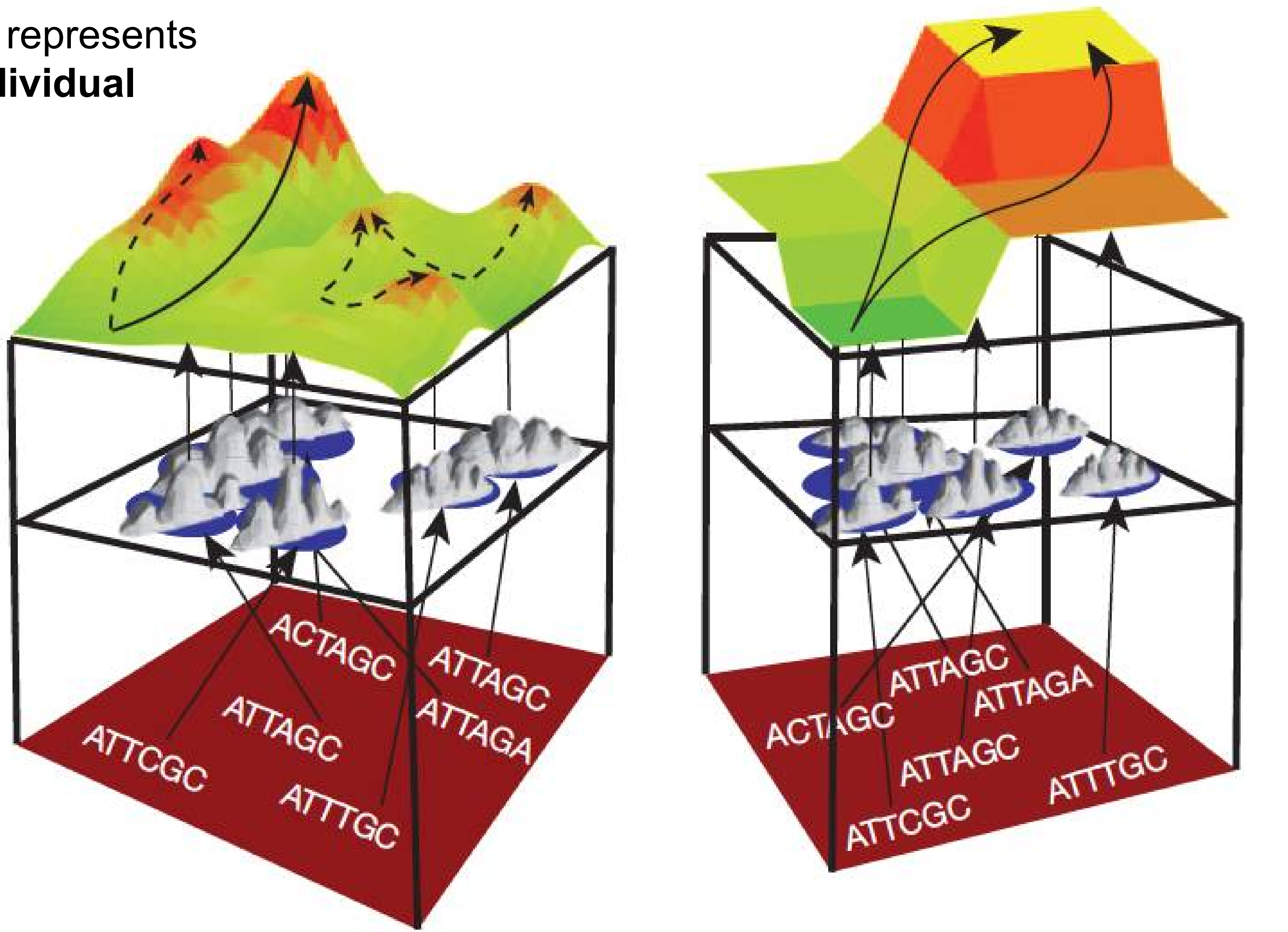
The genotype-phenotype-fitness map

Here a dot represents one **individual**

Fitness

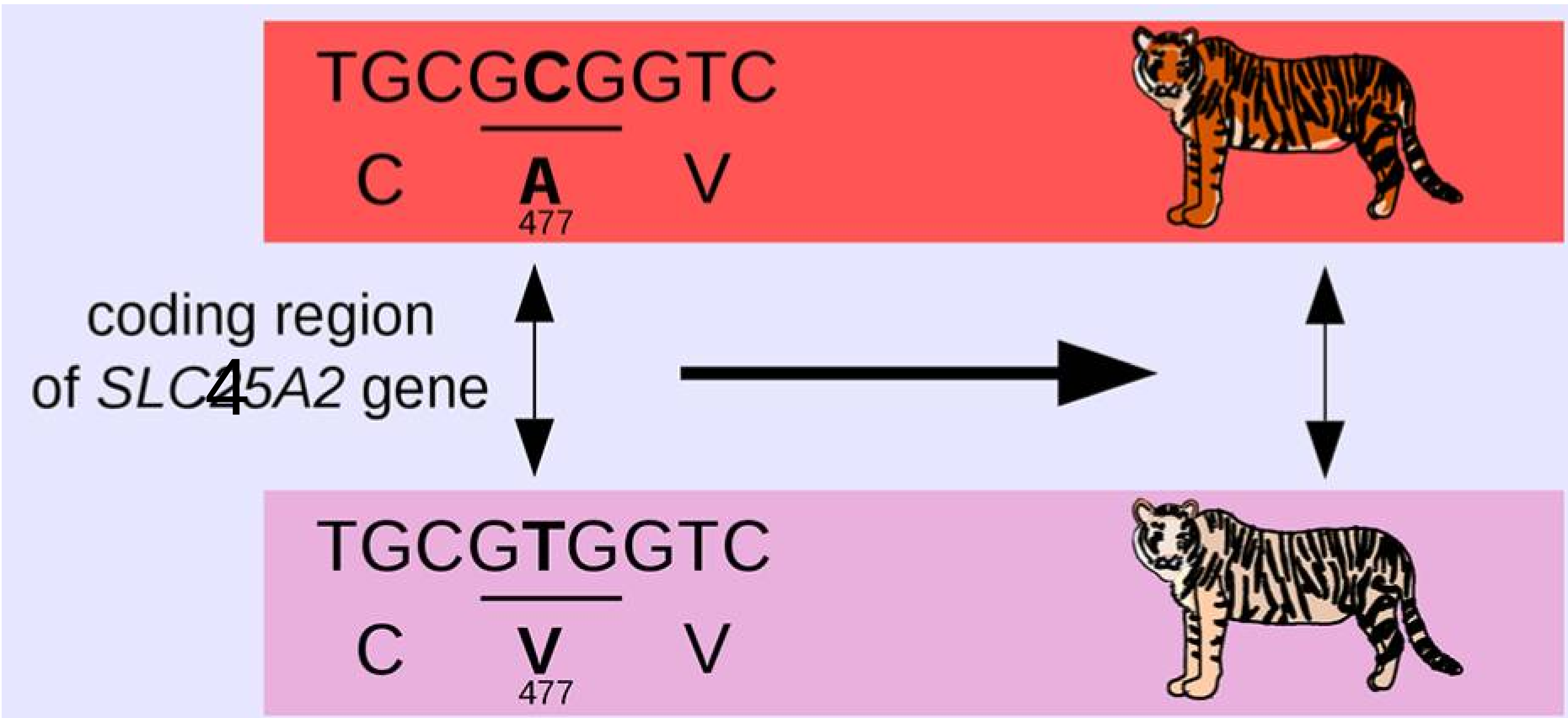
Phenotype
Tooth
morphology

Genotype



Salazar-Cuidad & Martin-Riera 2013

The genotype-phenotype connection



Xu et al 2013 Current Biology

Orgogozo et al 2015 Frontiers Genetics

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

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

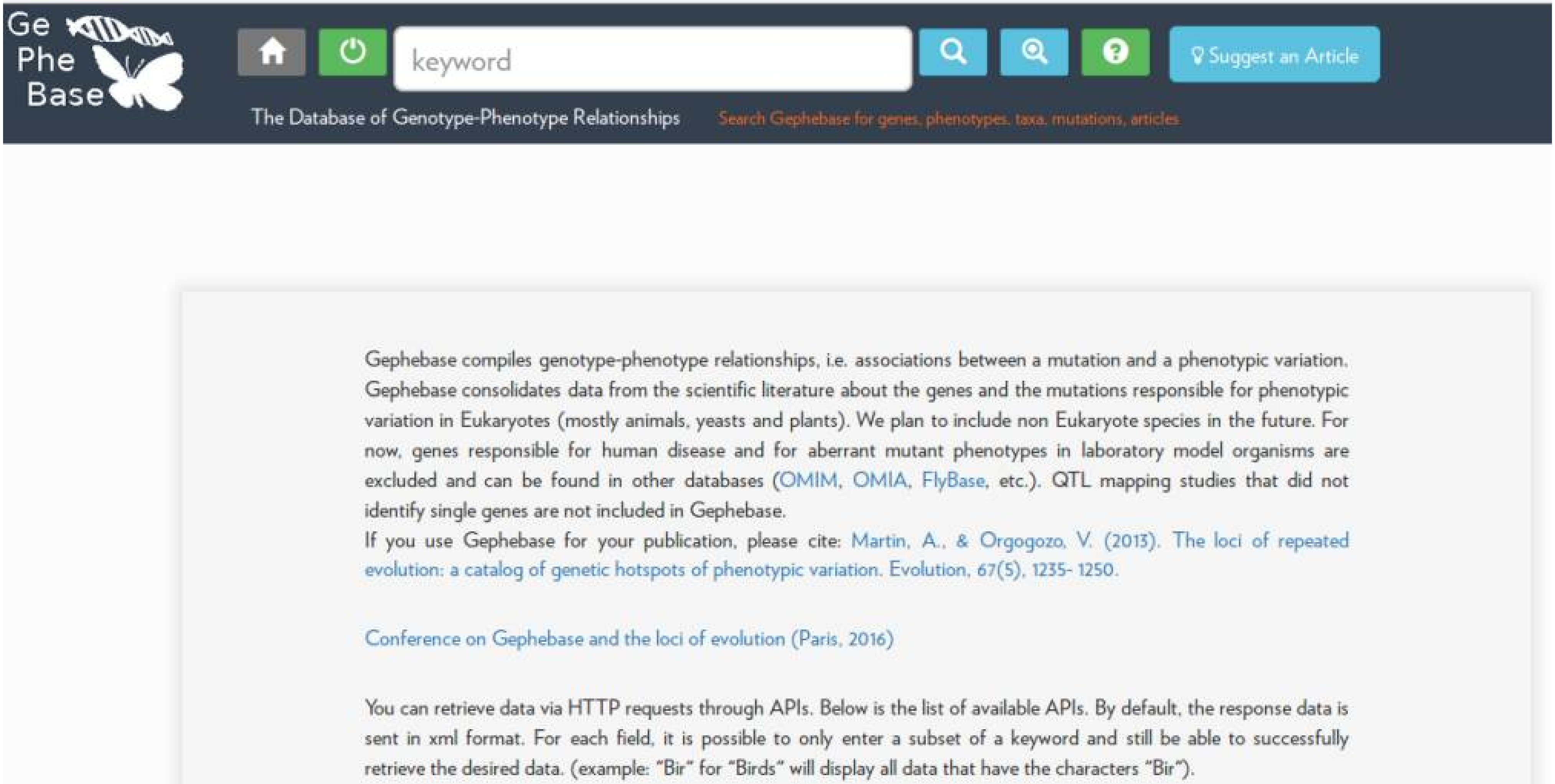
NO!

The genotype-phenotype connection is about differences

The genes contributing to evolution

www.Gephebase.org
>2000 entries

@gephebase



Orgogozo et al Nucleic Acid Research 2019

oca2 in cavefish

Ge Phe Base

The Database of Genotype-Phenotype Relationships

keyword

Suggest an Article

Search Gephebase for genes, phenotypes, taxa, mutations, articles

GEPHE SUMMARY

Gephebase Gene	Oca2	GepheID	GP00000745
Entry Status	Published	Main curator	Courtier

PHENOTYPIC CHANGE

Show All Details

Trait Category	Morphology
Trait	Coloration (albinism)
Trait State in Taxon A	Astyanax mexicanus surface
Trait State in Taxon B	Astyanax mexicanus Molino
Ancestral State	Taxon A
Taxonomic Status	Intraspecific

Taxon A

Latin Name	*Astyanax mexicanus*
Common Name	Mexican tetra
Synonyms	Mexican tetra; blind cave fish; Astyanax mexicanus (De Filippi, 1853)
Rank	species
Lineage	Show more ... eopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Otomorpha; Ostariophysi; Otophysi; Characiphysae; Characiformes; Characoidei; Characidae; Characidae incertae sedis; Astyanax clade; Astyanax
Parent	Astyanax () - (Rank: genus)
NCBI Taxonomy ID	7994
is Taxon A an Infraspecies?	No

Taxon B

Latin Name	*Astyanax mexicanus*
Common Name	Mexican tetra
Synonyms	Mexican tetra; blind cave fish; Astyanax mexicanus (De Filippi, 1853)
Rank	species
Lineage	Show more ... eopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Otomorpha; Ostariophysi; Otophysi; Characiphysae; Characiformes; Characoidei; Characidae; Characidae incertae sedis; Astyanax clade; Astyanax
Parent	Astyanax () - (Rank: genus)
NCBI Taxonomy ID	7994
is Taxon B an Infraspecies?	Yes
Taxon B Description	Astyanax mexicanus Molino

Trait Category	Morphology
Trait	Coloration (albinism)
Trait State in Taxon A	Astyanax mexicanus surface
Trait State in Taxon B	Astyanax mexicanus Molino
Ancestral State	Taxon A
Taxonomic Status	Intraspecific

Taxon A

Latin Name	*Astyanax mexicanus*
Common Name	Mexican tetra
Synonyms	Mexican tetra; blind cave fish; Astyanax mexicanus (De Filippi, 1853)
Rank	species
Lineage	Show more ... eopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Otomorpha; Ostariophysi; Otophysi; Characiphysae; Characiformes; Characoidei; Characidae; Characidae incertae sedis; Astyanax clade; Astyanax
Parent	Astyanax () - (Rank: genus)
NCBI Taxonomy ID	7994
is Taxon A an Infraspecies?	No

Taxon B

Latin Name	*Astyanax mexicanus*
Common Name	Mexican tetra
Synonyms	Mexican tetra; blind cave fish; Astyanax mexicanus (De Filippi, 1853)
Rank	species
Lineage	Show more ... eopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Otomorpha; Ostariophysi; Otophysi; Characiphysae; Characiformes; Characoidei; Characidae; Characidae incertae sedis; Astyanax clade; Astyanax
Parent	Astyanax () - (Rank: genus)
NCBI Taxonomy ID	7994
is Taxon B an Infraspecies?	Yes
Taxon B Description	Astyanax mexicanus Molino

GENOTYPIC CHANGE

Show All Details

Generic Gene Name	**Oca2**	**UniProtKB**	**Q62052**
Synonyms	p; D7Nic1; p<cas>; D7H15S12; D7Icr28RN; P	Mus musculus	
String	10090.ENSMUSP00000032633	**GenebankID or UniProtKB**	**ABB29299**
Sequence Similarities	Belongs to the CitM (TC 2.A.11) transporter family.		
GO - Molecular Function	-		
GO - Biological Process	GO:0055085 : transmembrane transport ... **show more**		
GO - Cellular Component	GO:0016021 : integral component of membrane ... **show more**		

Presumptive Null	**Yes**
Molecular Type	**Coding**
Aberration Type	**Deletion**
Deletion Size	-
Molecular Details of the Mutation	**Deletion of exon 21**
Experimental Evidence	**Linkage Mapping**
Main Reference	Genetic analysis of cavefish reveals molecular convergence in the evolution of albinism. (2006)
Authors	Protas ME; Hersey C; Kochanek D; Zhou Y; Wilkens H; Jeffery WR; Zon LI; Borowsky R; et al. ... **show more**
Abstract	The genetic basis of vertebrate morphological evolution has traditionally been very difficult to examine in naturally occurring populations. Here we describe the generation of a genome-wide linkage map to allow quantitative trait analysis of evolutionarily derived morphologies in the Mexican cave tetra, a species that has, in a series of independent caves, repeatedly evolved specialized characteristics adapted to a unique and well-studied ecological environment. We focused on the trait of albinism and discovered

Additional References

RELATED GEPHE

Related Genes 1 (MC1R)

Related Haplotypes 1

COMMENTS

YOUR FEEDBACK is welcome!

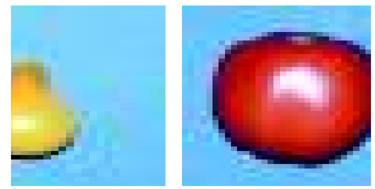
Feedback

Your E-mail

Optional and remains confidential (not displayed online). Only used to contact you if

Wrinkled seed: TE insertion
(Bhattacharyya 1990)

OVATE coding region
(Liu 2002)



FRI coding region
(Johanson 2000)

myostatin coding region
(Grobet 1997)

luciferase coding region
(Stolz 2003)

anthocyanin-2 coding region
(Quattrocchio 1999)

Mc1r coding region
(Eizirik 2003)

THREE APPROACHES to FIND the GOLDEN LOCI of EVOLUTION

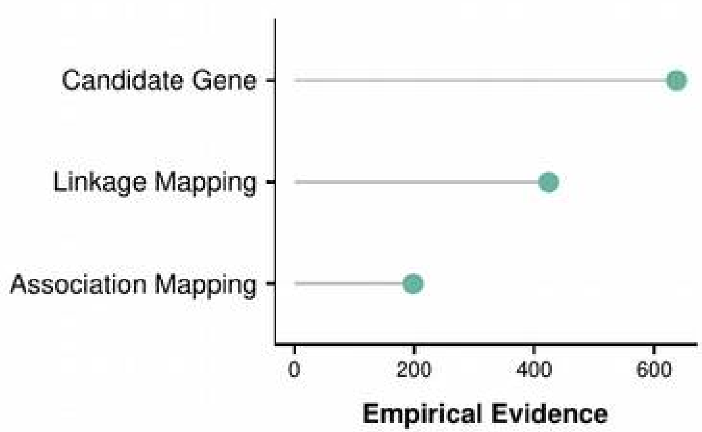
REVERSE GENETICS

From genes to traits

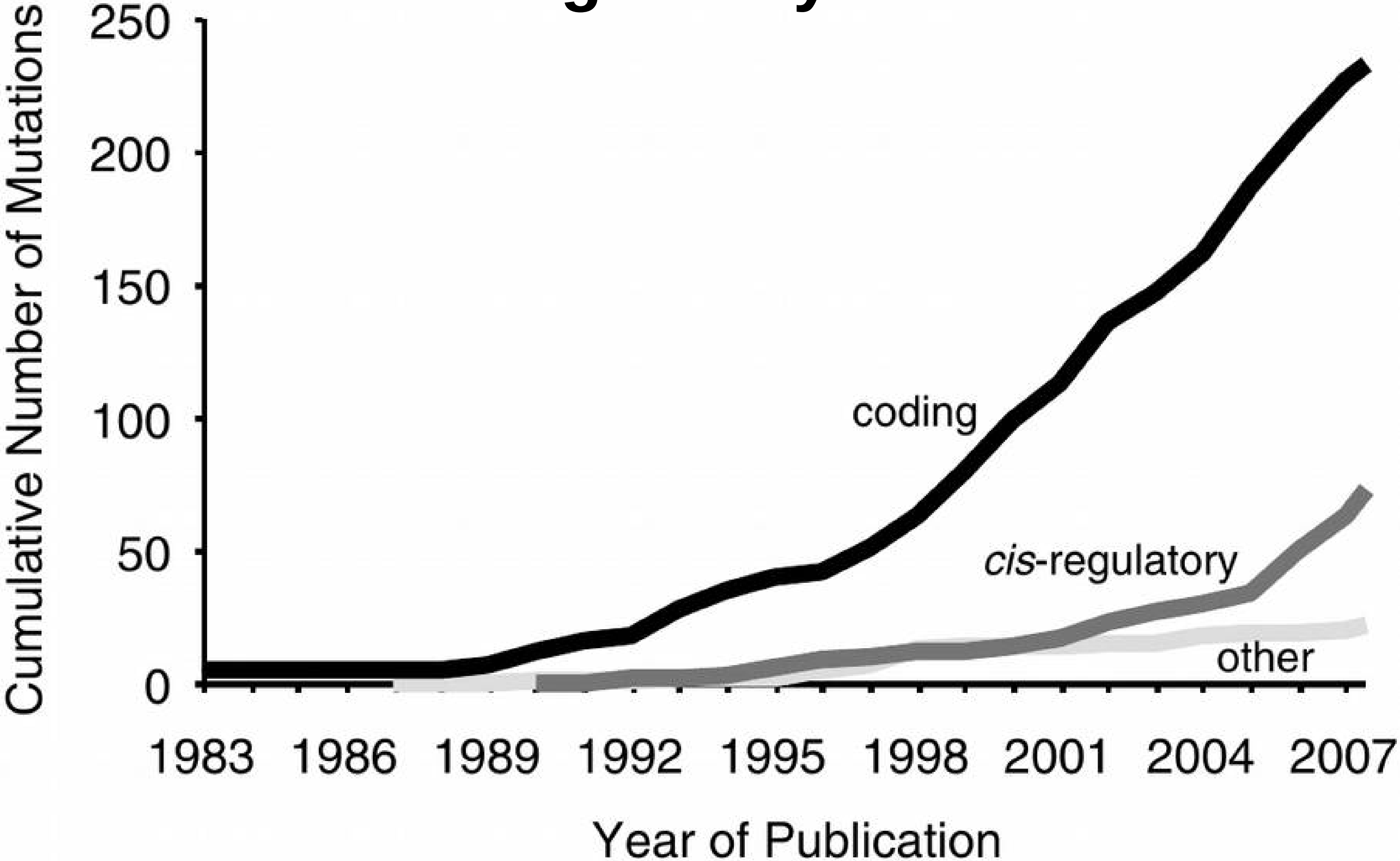
FORWARD GENETICS

From traits to genes

Little Ascertainment Bias, but Micro-Evolution only

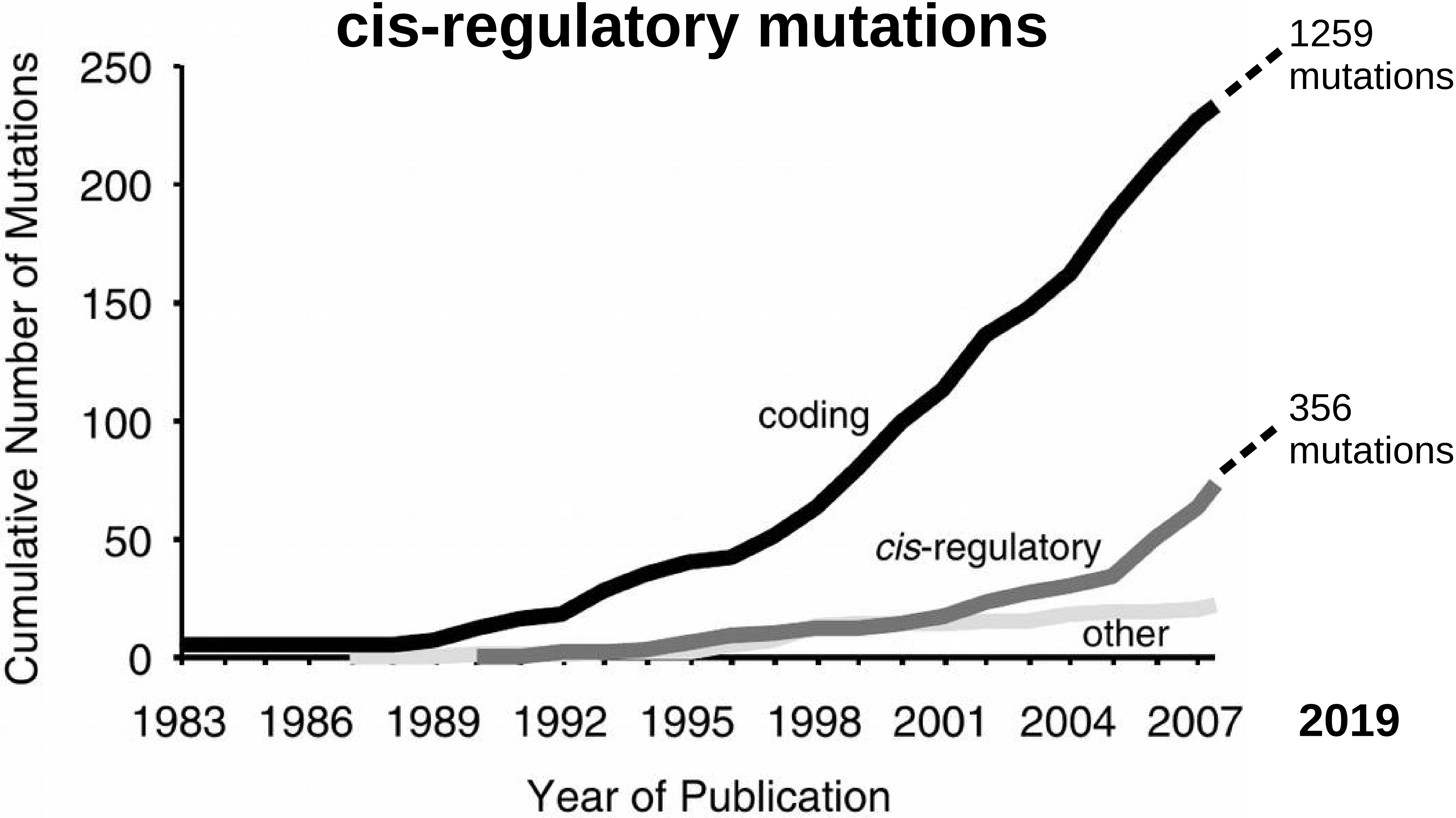


More cases of coding than cis-regulatory mutations



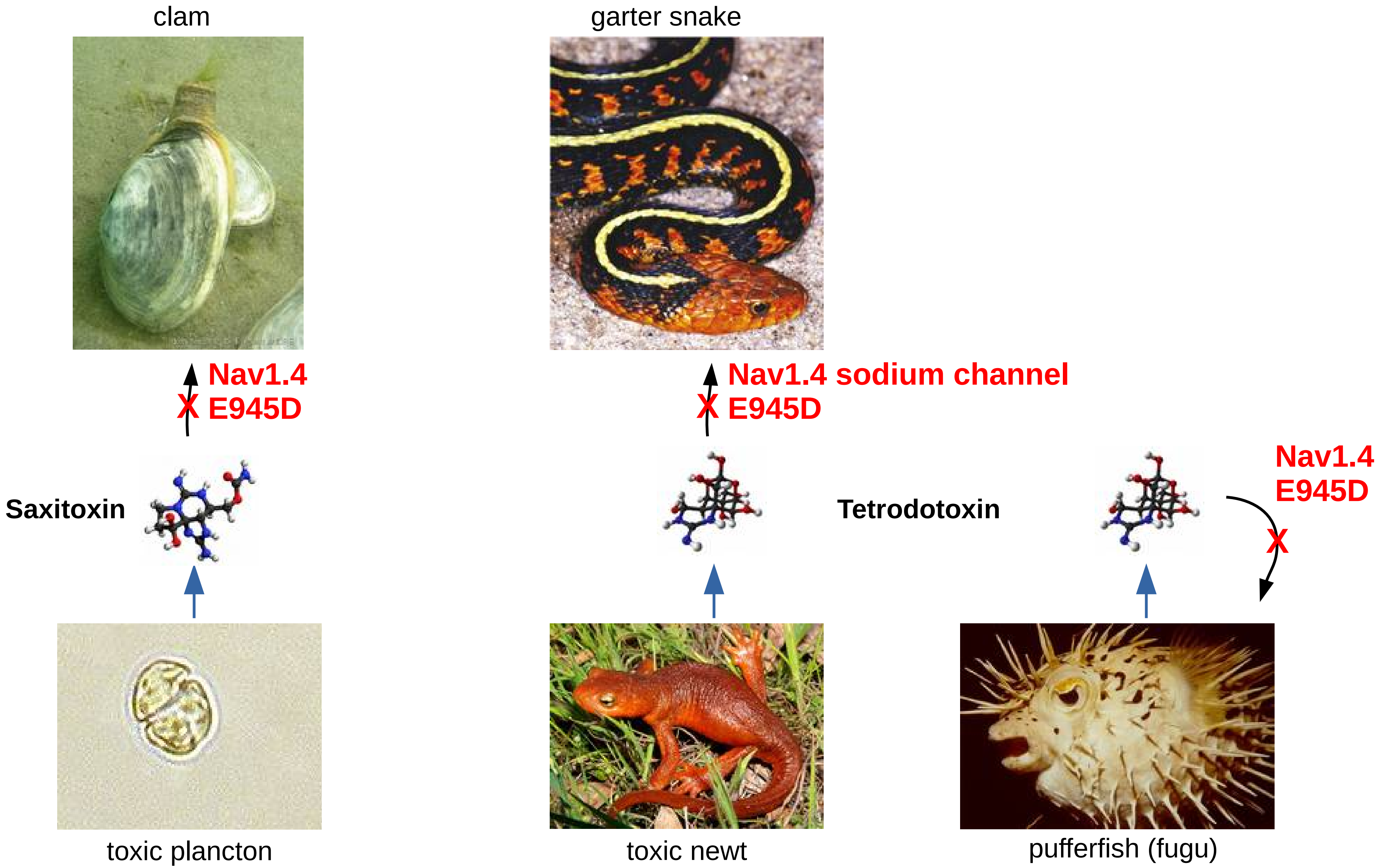
survey of ~300 articles
Stern and Orgogozo 2008 Evolution

More cases of coding than cis-regulatory mutations



Evolution repeats itself

Repeated evolution via the same amino acid change



Bricelj 2005
Geffeney 2005
Venkatesh 2005

Repeats in..

.. the genes responsible for natural evolution

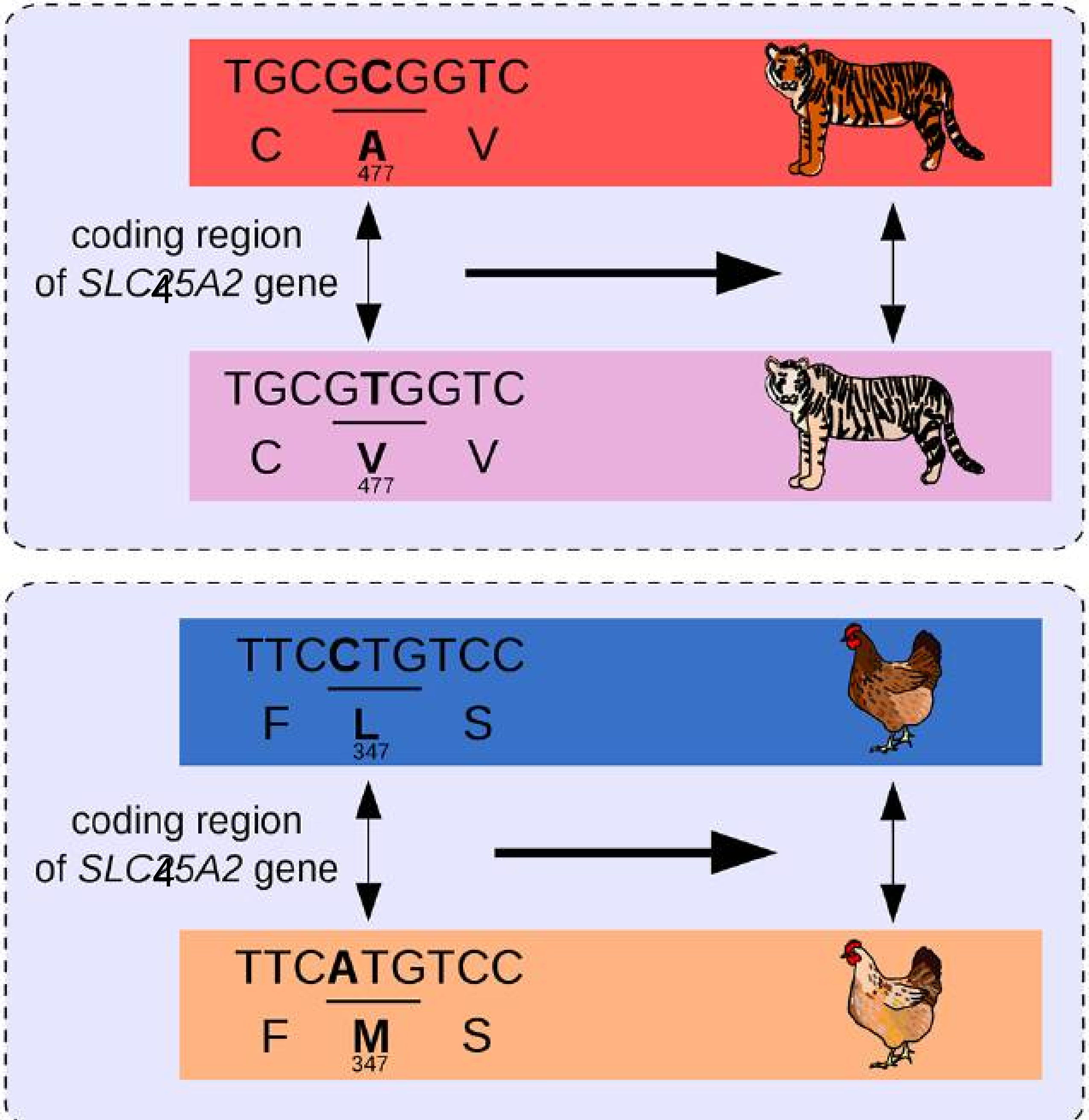
Ex : *hemoglobin* in dogs and humans in Tibet
(Wang et al 2014 GBE)

.. the genes responsible for experimental evolution

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

Orgogozo 2014 Interface Focus

Repeated evolution



Also in:
Humans
Horses
Quails
Chickens
Mice
Pigeons

Orgogozo et al 2015 Frontiers Genetics

TOP HOTSPOT GENES

- MC1R (86)
- para (kdr) (54)
- Na/K-ATPase alpha-subunit (45)
- beta-tubulin (33)
- beta-tubulin (ben-1) (27)
- SCN4A (Nav1.4) (26)
- AtGA20ox1 (=GA5=Sd1) (23)
- alcohol dehydrogenase (Adh) (23)
- Agouti (22)
- opsin - rhodopsin1 (RH1) (20)
- kelch 13 (20)
- opsin - (SWS1) (20)

Specialized loci in the genome

Proteins that interact with external molecules

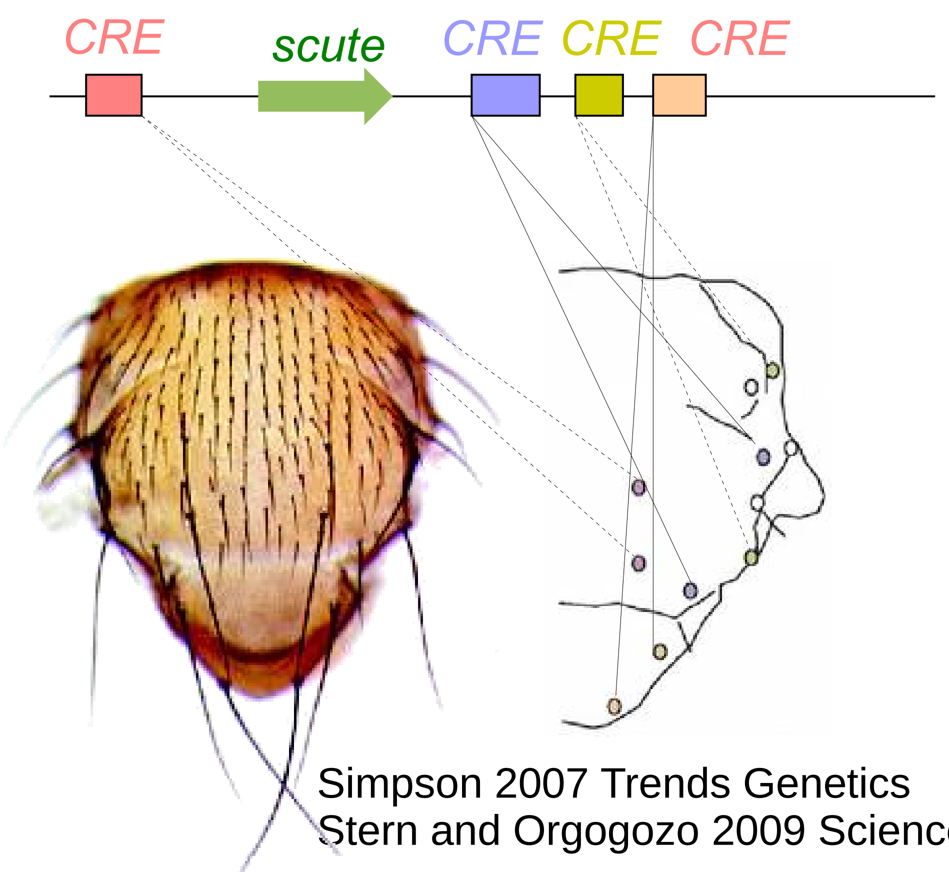
oxygen, photons, insecticide, cholesterol...

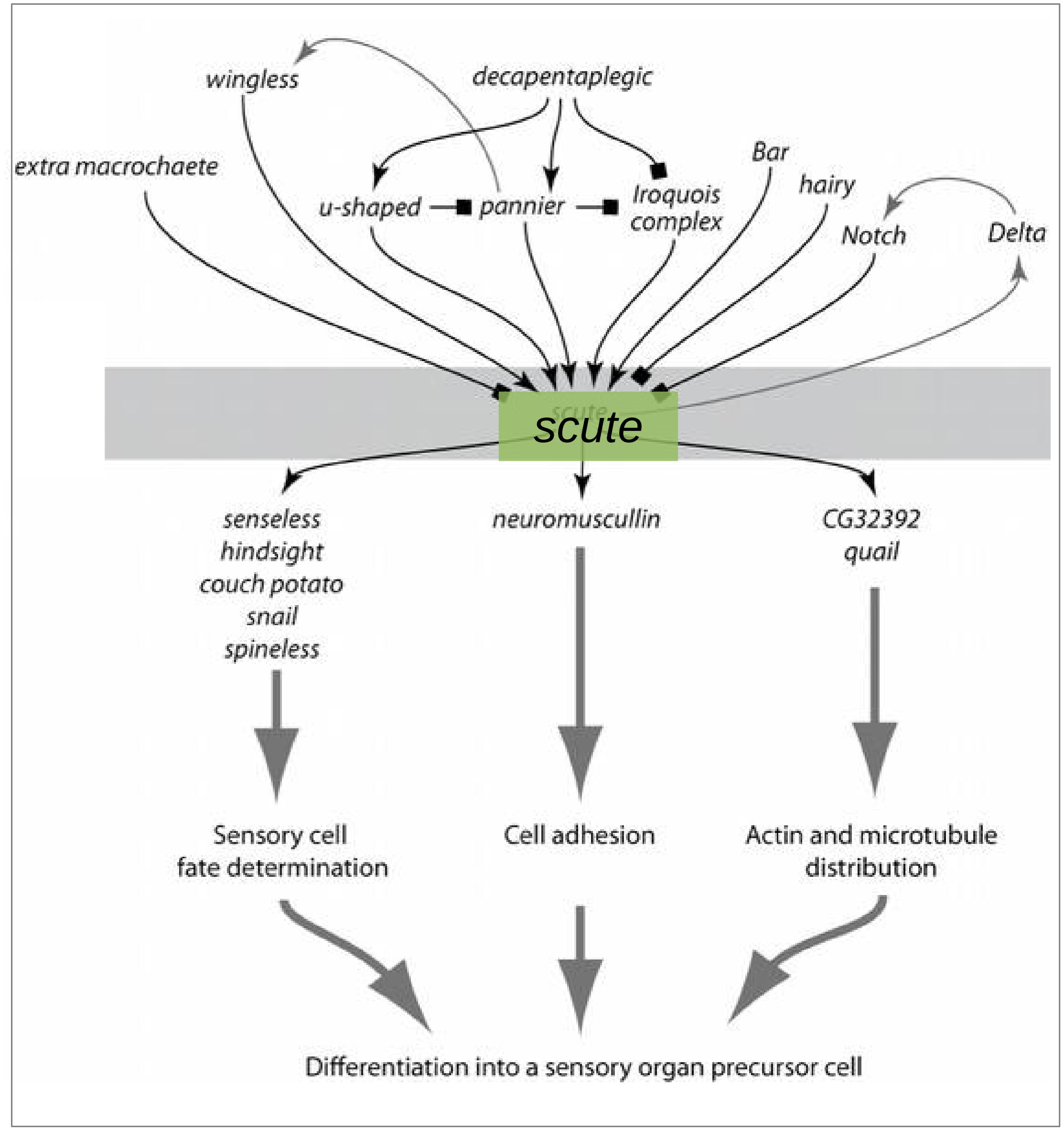
Specialized loci in the genome

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

From random processes can emerge predictability

Many unpredictable processes
at a low level

→

Predictable Evolution
at the genetic level

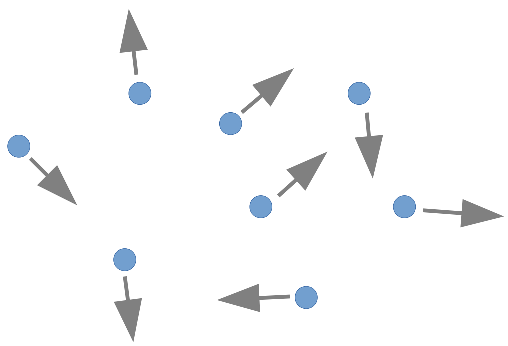
Mutations in DNA
Chromosome segregation during meiosis
Assortative mating
Gamete competition during fecondation
Life history traits
Genetic linkage
Environmental changes (meteorite, etc.)
...

coding mutation in
VKORC1 gene

Orgogozo 2014 Interface Focus

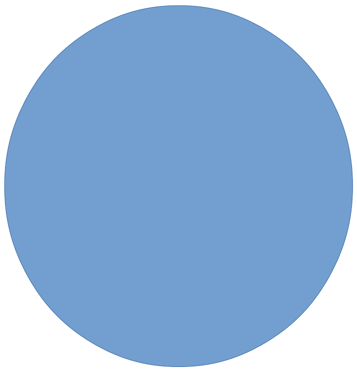
From random processes can emerge predictability

Microscopic world

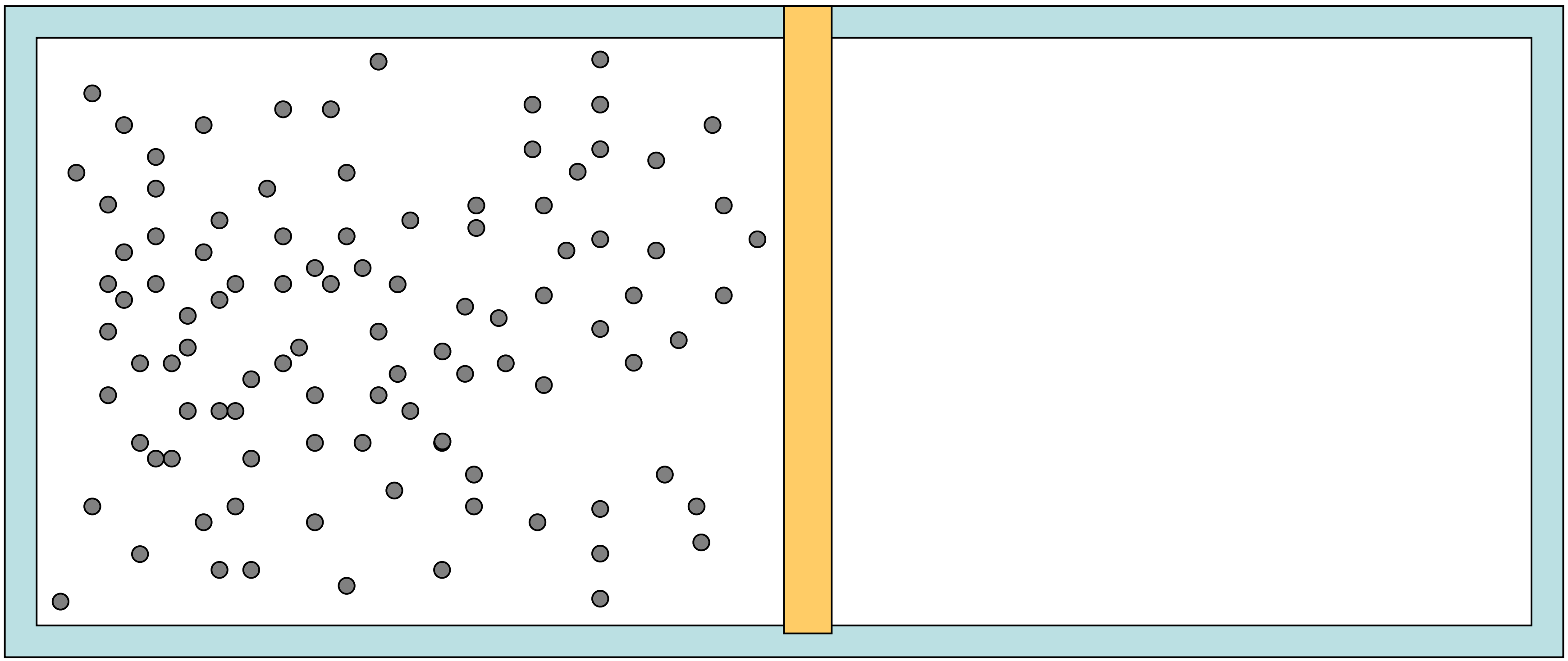


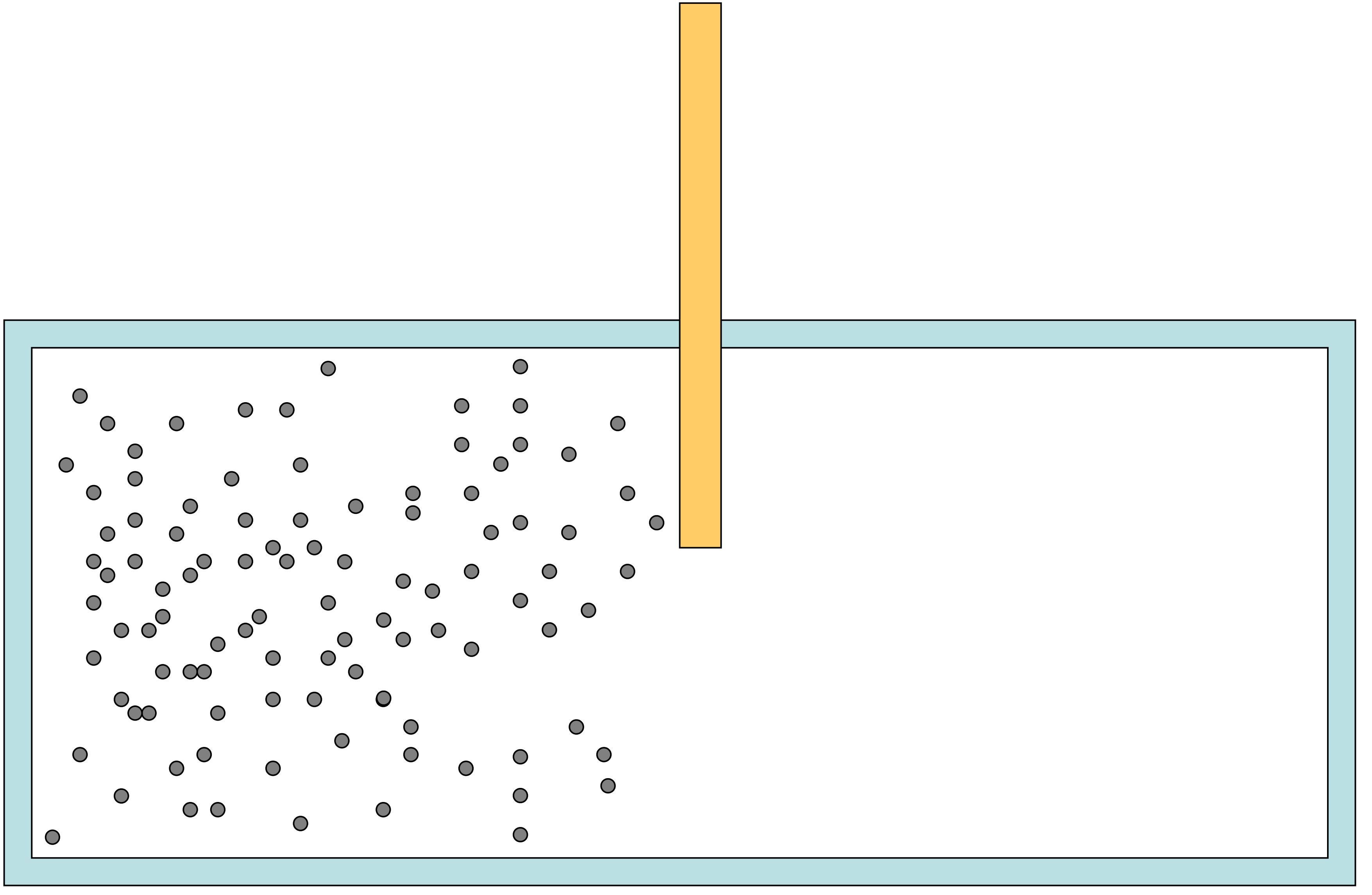
Position, mass, velocity of each particle

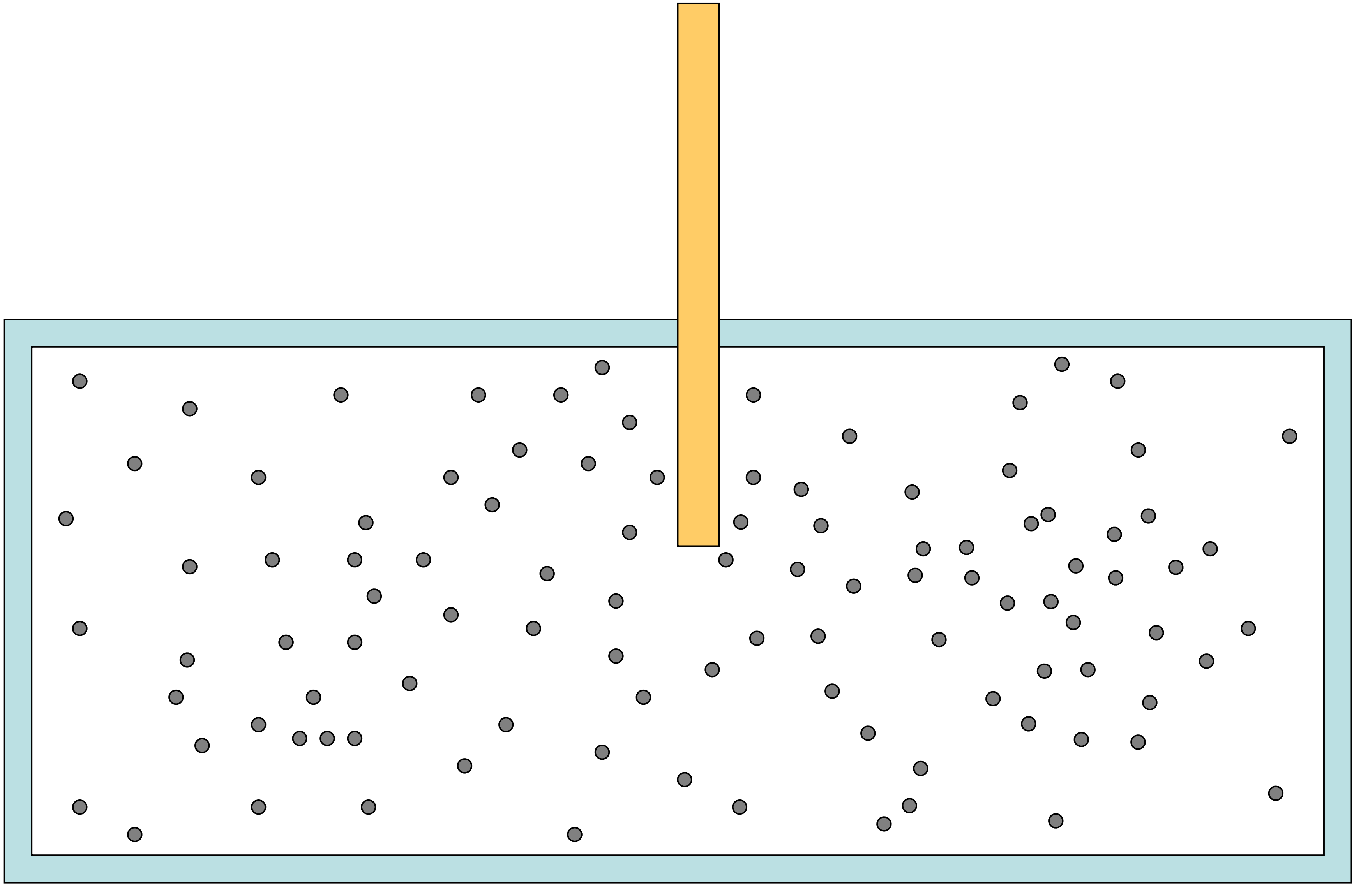
Macroscopic world



Pressure, Volume, Temperature,
Number of moles

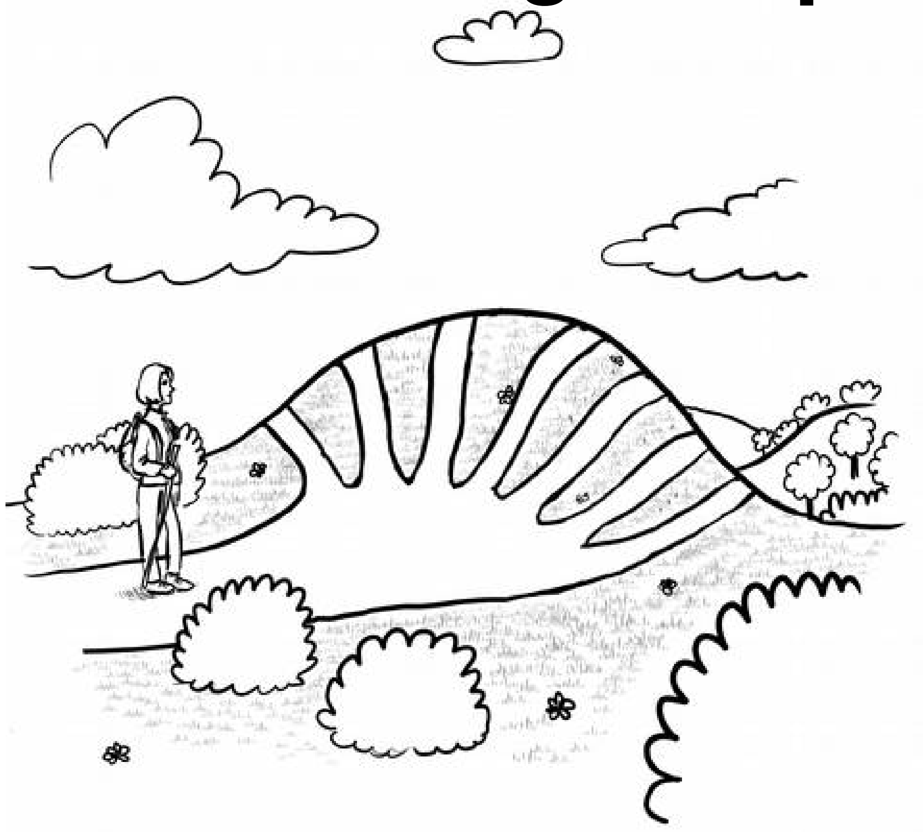


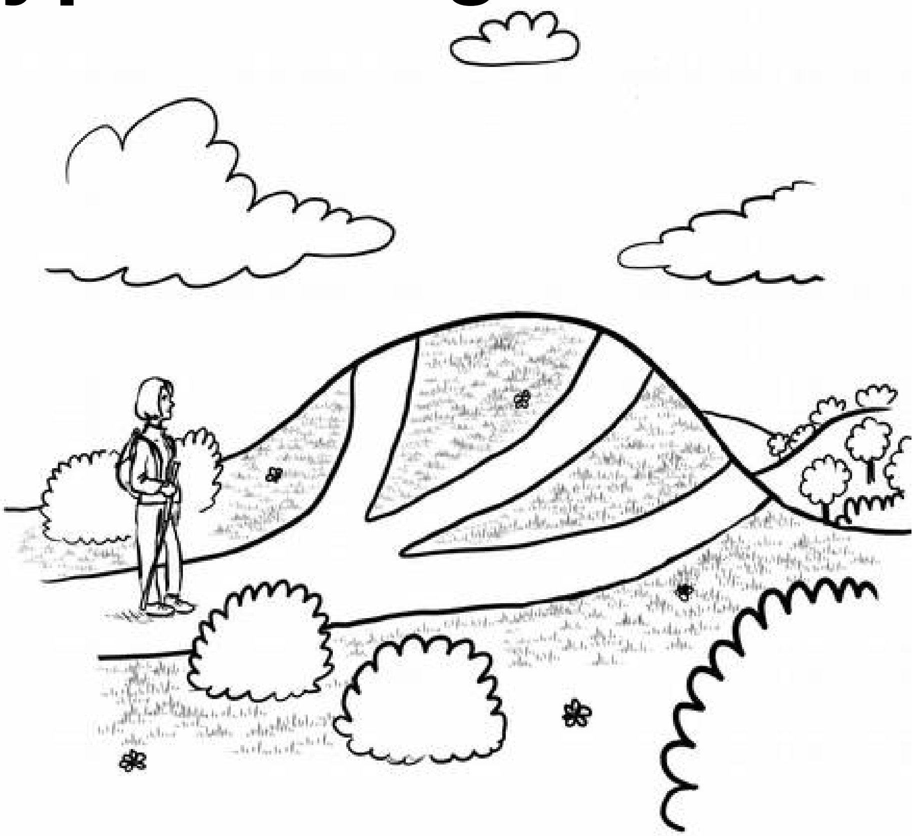




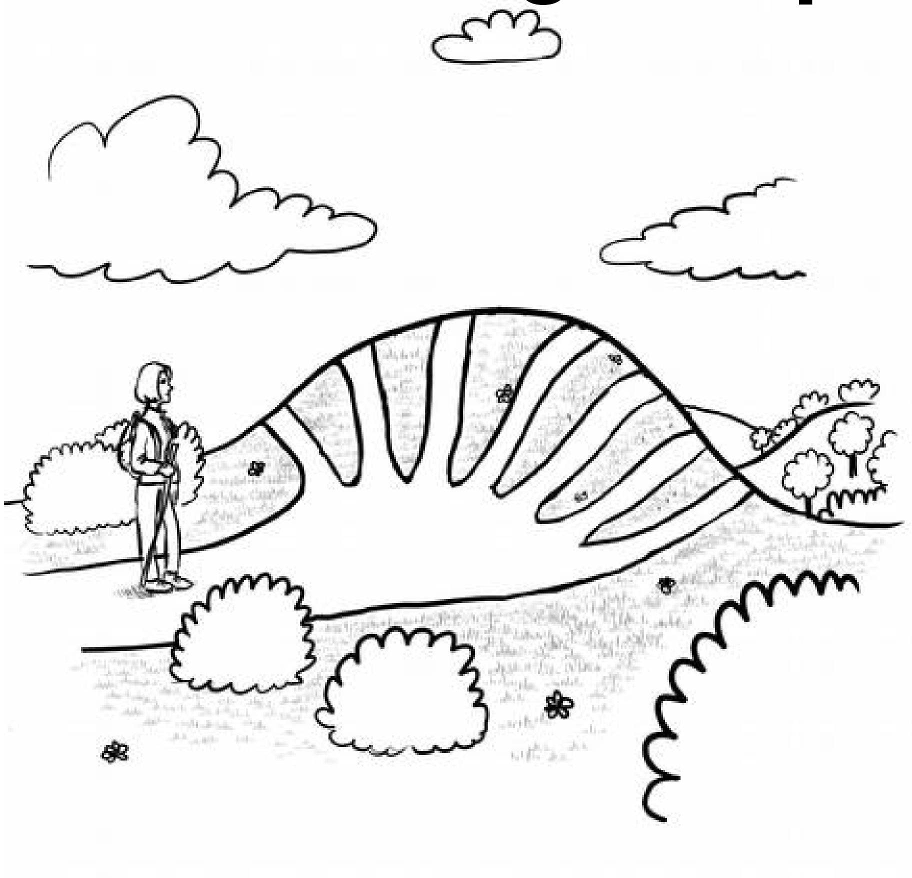
After a few seconds

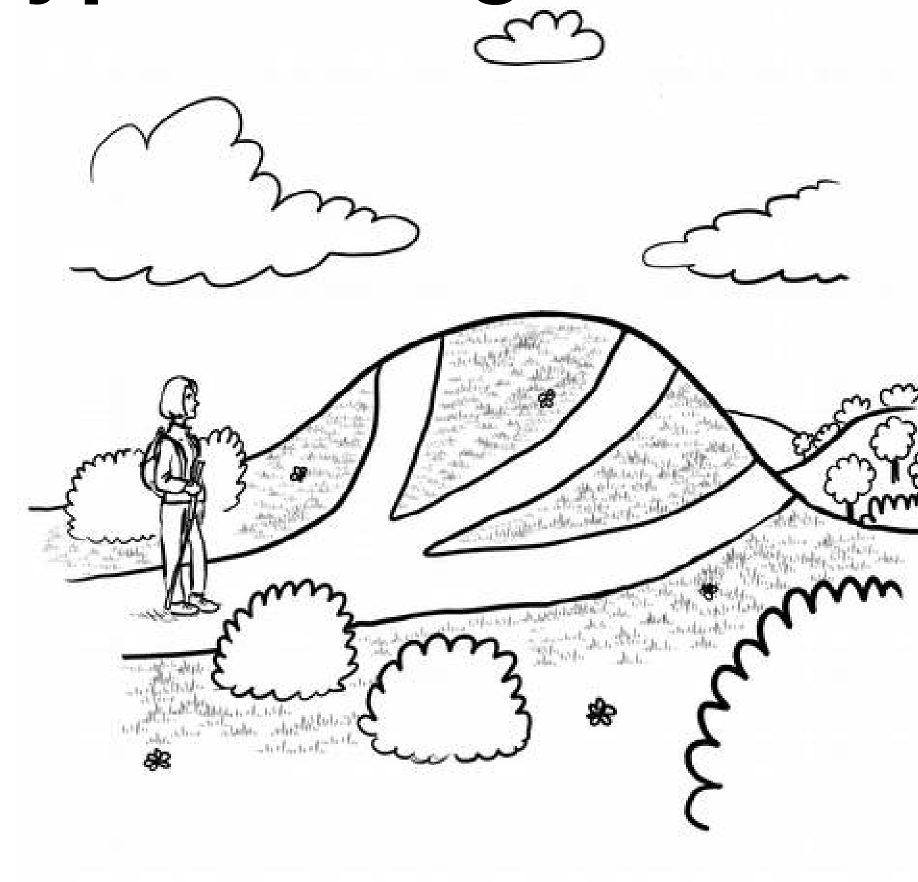
A small number of genetic solutions for a given phenotypic change





A small number of genetic solutions for a given phenotypic change



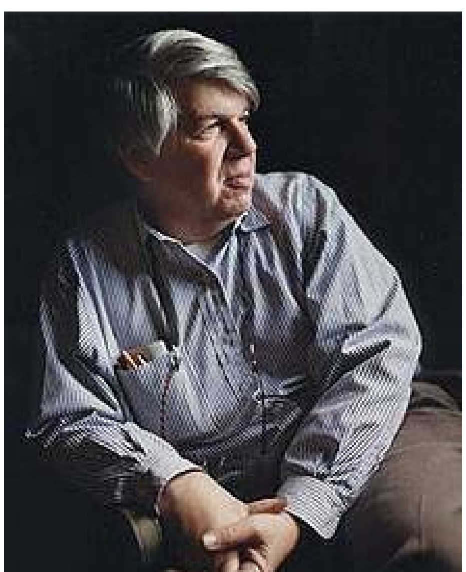


We sometimes seem to have forgotten that the original question in genetics was not what makes a protein but rather 'what makes a dog a dog, a man a man'.
(D. Noble – The Music of Life)

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



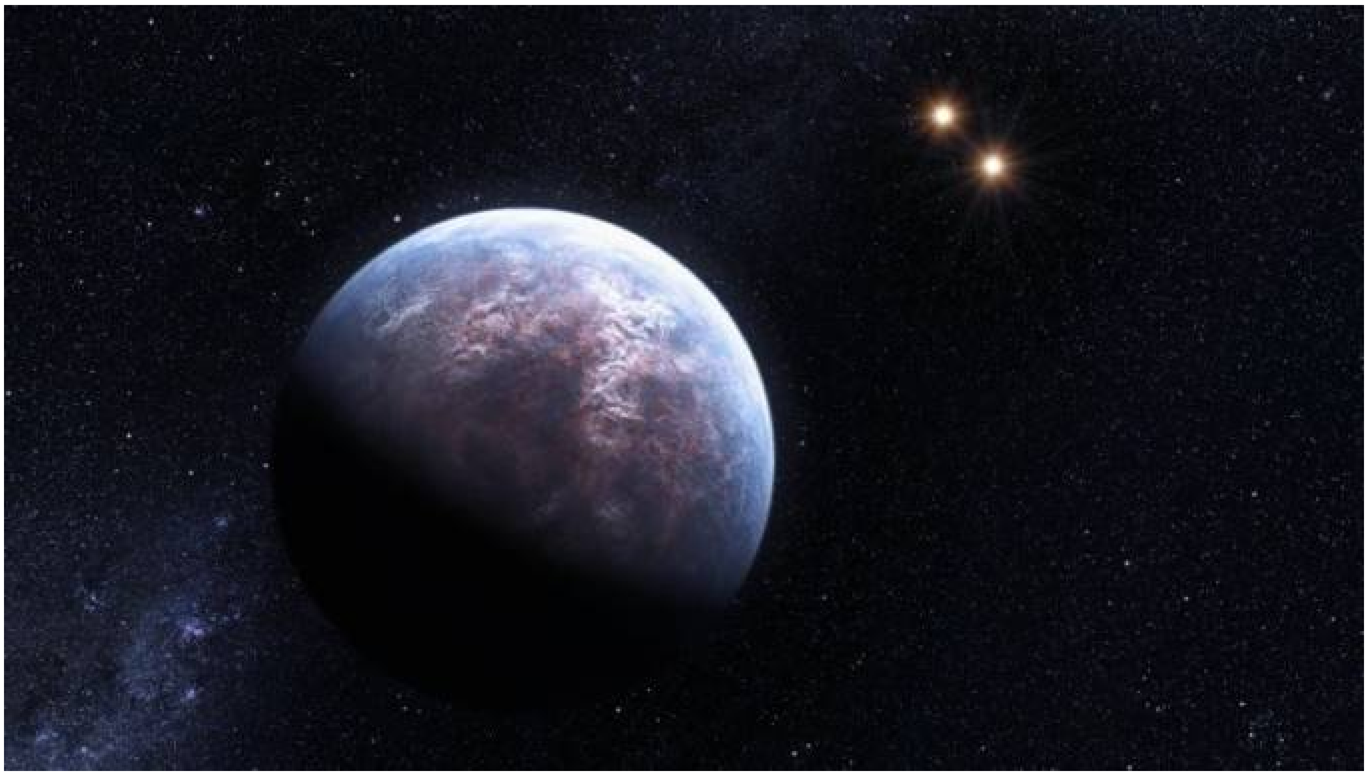
It is hard to realize that the living world as we know it is just one among many possibilities; that its actual structure results from the history of the earth.

1977

Evolution and Tinkering

François Jacob

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



How?

evolution

Why? (1) rather than nothing

Why? (2) rather than another change

Lab
Olga Nagy (past member)
Isabelle Nuez (IE)

Michael Lang (CR)
Alexis Lalouette (MCU)

Bénédicte Lefèvre (PhD)
Flora Borne (PhD)
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Genotyping
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Fly crosses
Daniel Matute (UNC, USA)

Gephebase
Arnaud Martin (Berkeley, USA)

The differential view of genotype–phenotype relationships

frontiers in Genetics

Virginie Orgogozo[1*], Baptiste Morizot[2] and Arnaud Martin[3]

The "Mendelian Gene" and the "Molecular Gene": Two Relevant Concepts of Genetic Units

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THE LOCI OF REPEATED EVOLUTION: A CATALOG OF GENETIC HOTSPOTS OF PHENOTYPIC VARIATION

Arnaud Martin[1,2] and Virginie Orgogozo[3]

Nucleic Acids Research, 2019 1
doi: 10.1093/nar/gkz796

Gephebase, a database of genotype–phenotype relationships for natural and domesticated variation in Eukaryotes

Virginie Courtier-Orgogozo[1,*], Laurent Arnoult[1], Stéphane R. Prigent[1], Séverine Wiltgen[2] and Arnaud Martin[3,*]

INTERFACE FOCUS

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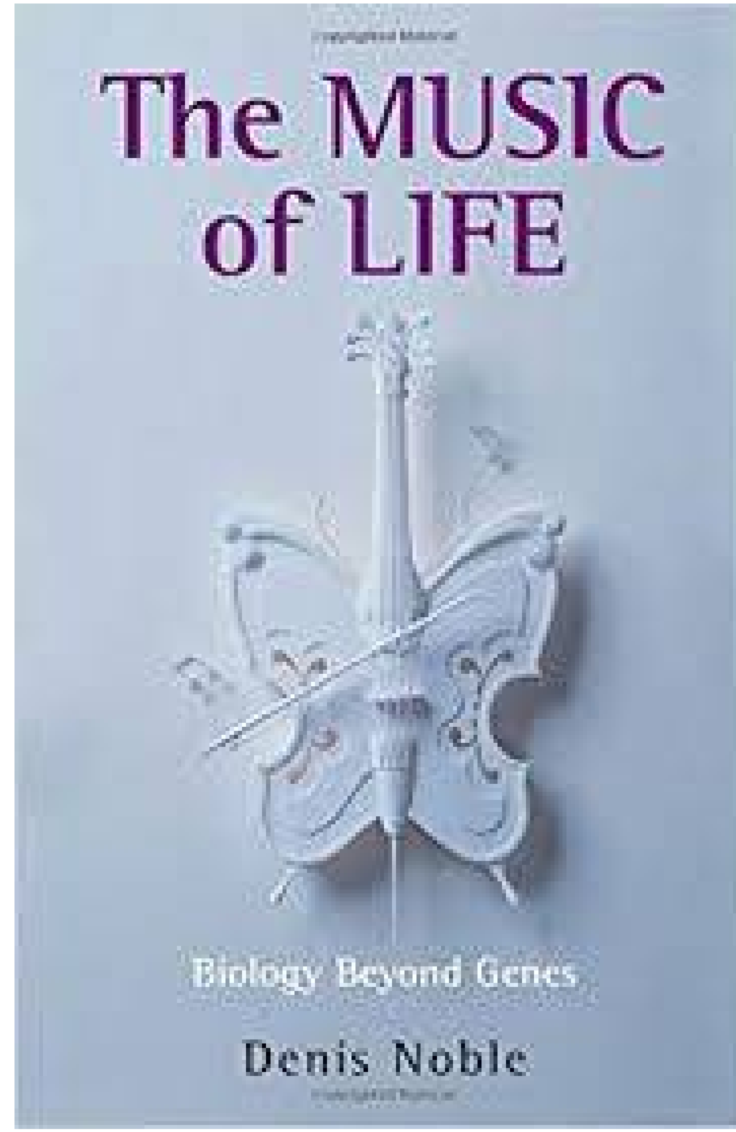
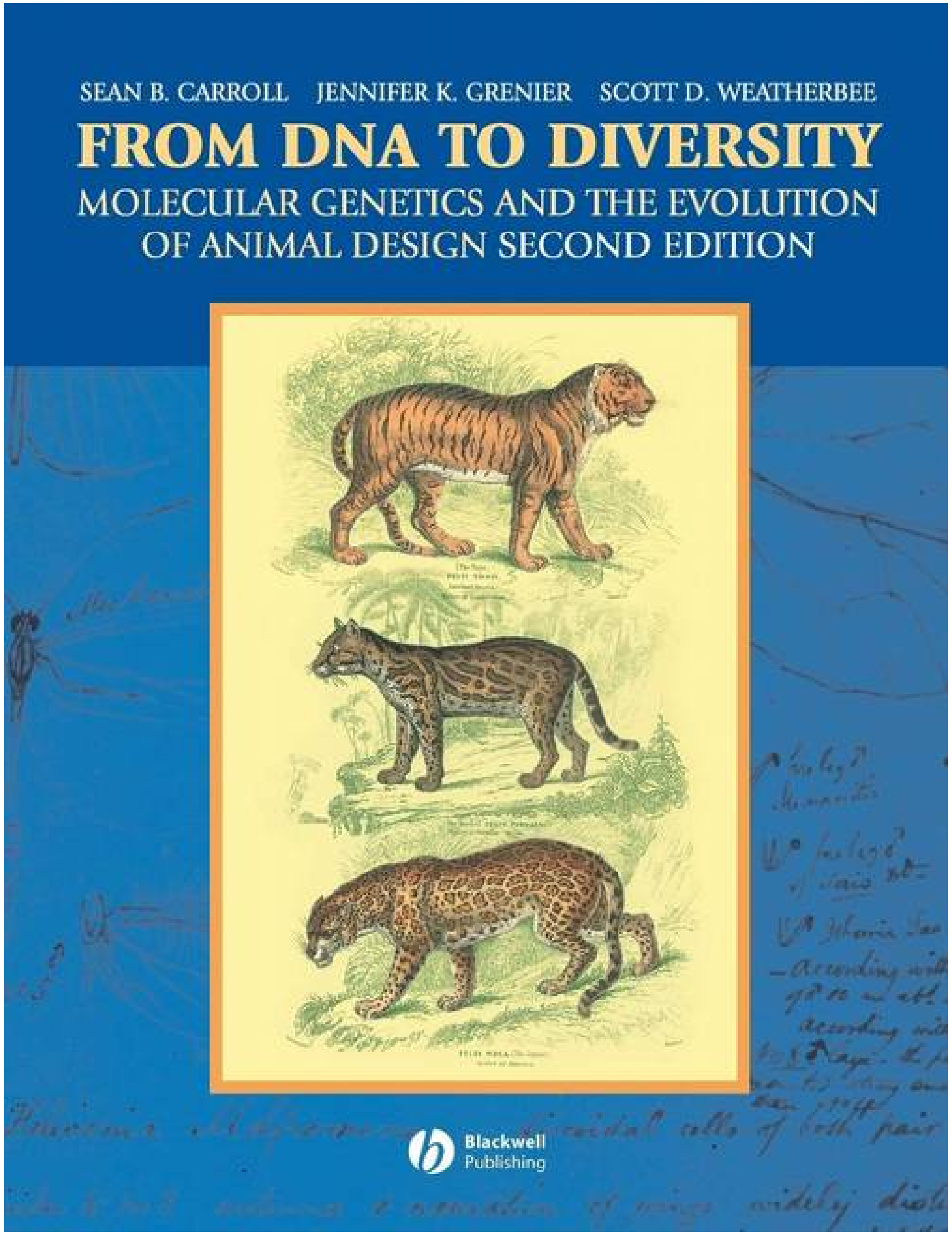
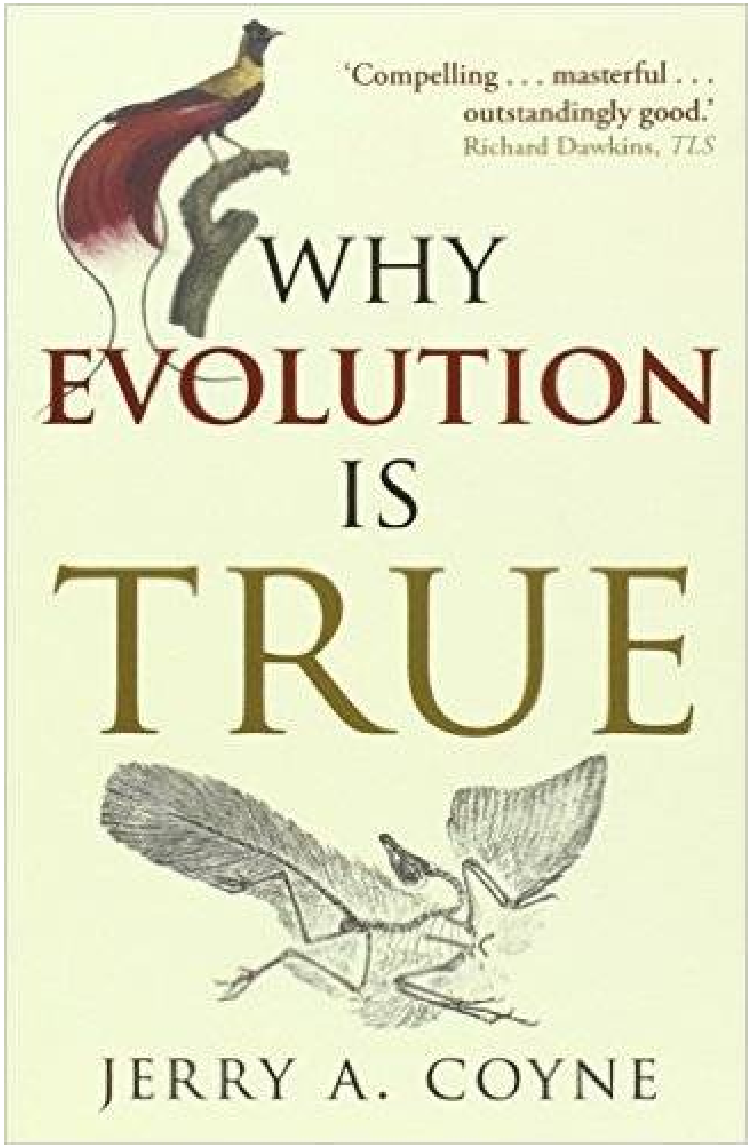
Replaying the tape of life in the twenty-first century

Virginie Orgogozo





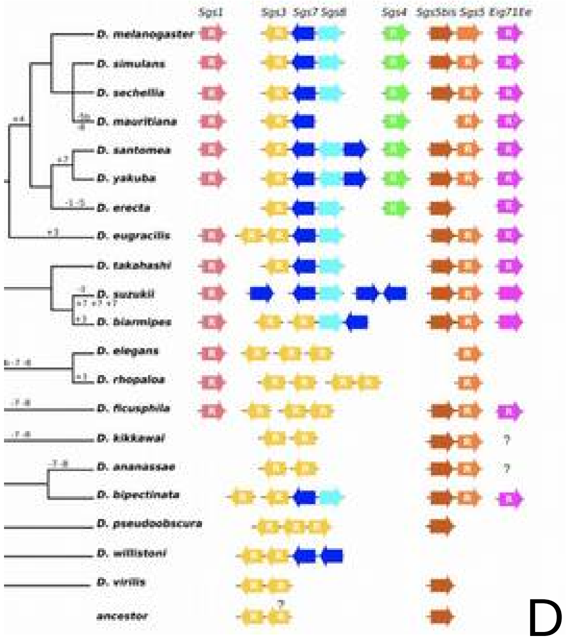


https://www.youtube.com/watch?v=Ov30-7rXZCY
Une brève histoire de l'évo-dévo (Denis Duboule)

Evolution of Drosophila glue

soil rotten strawberry grape potato

. grimshawi D. suzukii D. melanogaster D. repleta D. carcinophila



Da Lage et al. 2019 BMC Evol Biol

Evolution of left-right asymmetry in *D. pachea*