Workshop on Molecular Evolution

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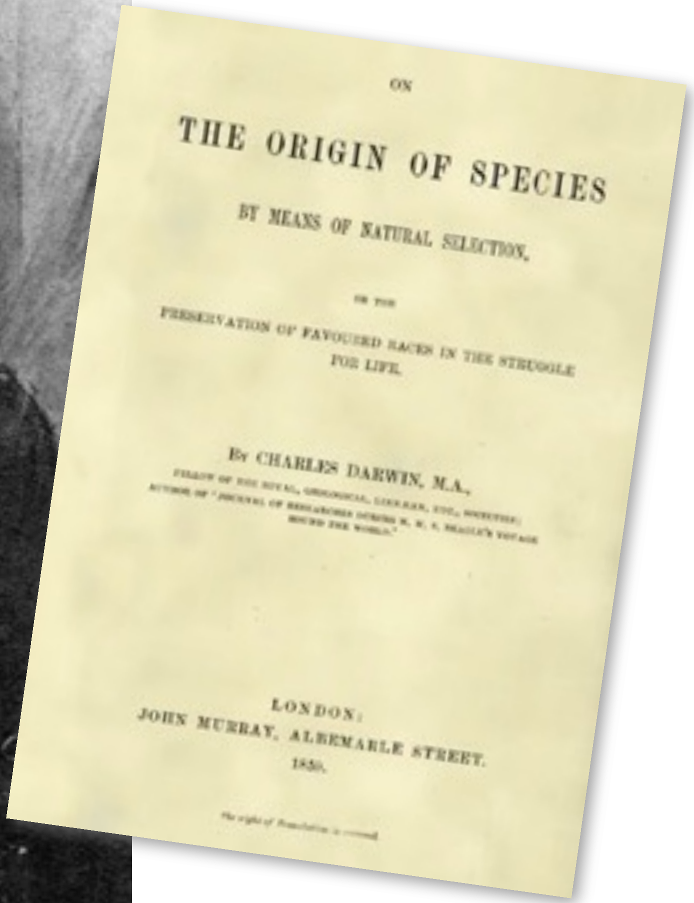
UNI
BASEL

Molecular evolution deals with the process of evolution at the scale of DNA, RNA and proteins

1859

Charles R. Darwin publishes "*On the origin of species by means of natural selection*" and establishes the theory of evolution



ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE
FOR LIFE.

By CHARLES DARWIN, M.A.,

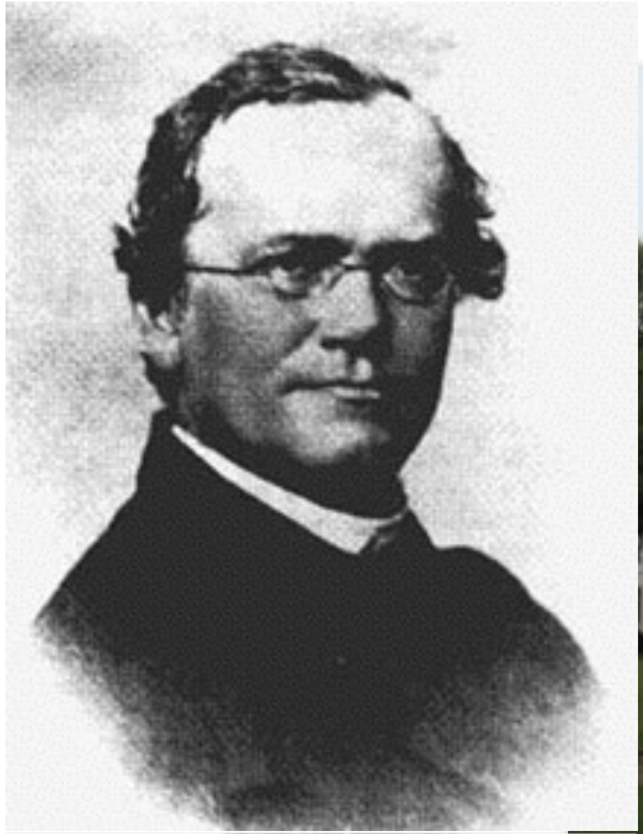
LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

Charles R. Darwin (1809-1882)

A brief history

1866

Gregor Mendel publishes "*Experiments in plant hybridization*". This paper established what eventually became formalized as the Mendelian laws of inheritance.



Gregor Mendel
(1822-1884)

1866

Gregor Mendel publishes "*Experiments in plant hybridization*". This paper established what eventually became formalized as the Mendelian laws of inheritance.

"Brother Mendel! We grow tired of peas!"

Cartoon by J. Chase

1869

Johann Friedrich Miescher extracts what comes to be known as DNA from the nuclei of white blood cells.

Johann F. Miescher (1844-1895)

1900

Independently of one another, **Hugo de Vries** (1848-1935), **Erich von Tschermak-Seysenegg** (1871-1962) and **Carl Correns** (1864-1933) rediscover Mendel’s published, but long neglected, paper outlining the basic laws of inheritance.

Hugo de Vries

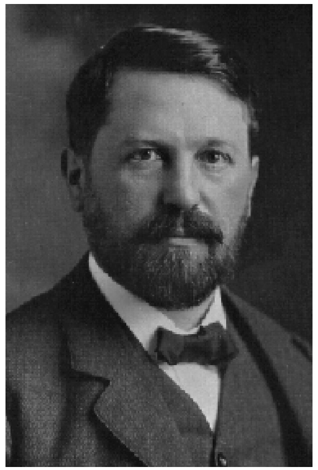
Erich v. Tschermack

Carl Correns

1902

Theodor Boveri and **Walter Sutton** propose that chromosomes bear heritary factors in accordance with Mendelian laws.

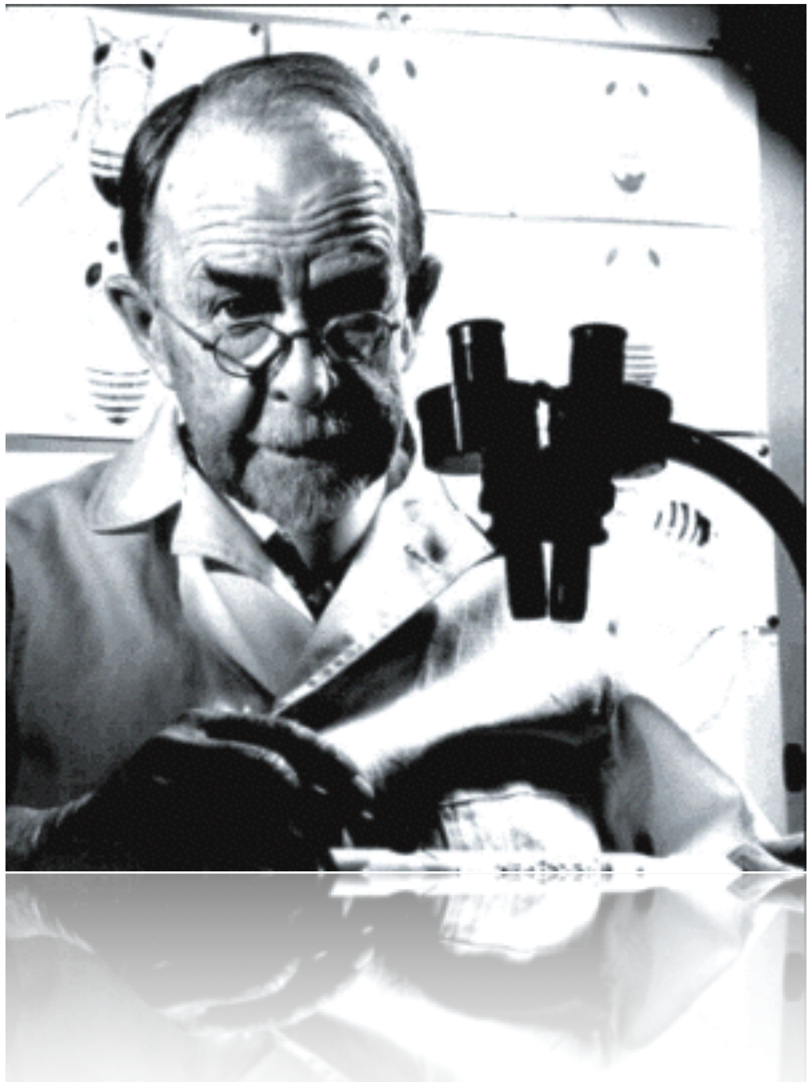
Walter Sutton
(1877-1916)



Theodor Boveri
(1862-1915)

1910

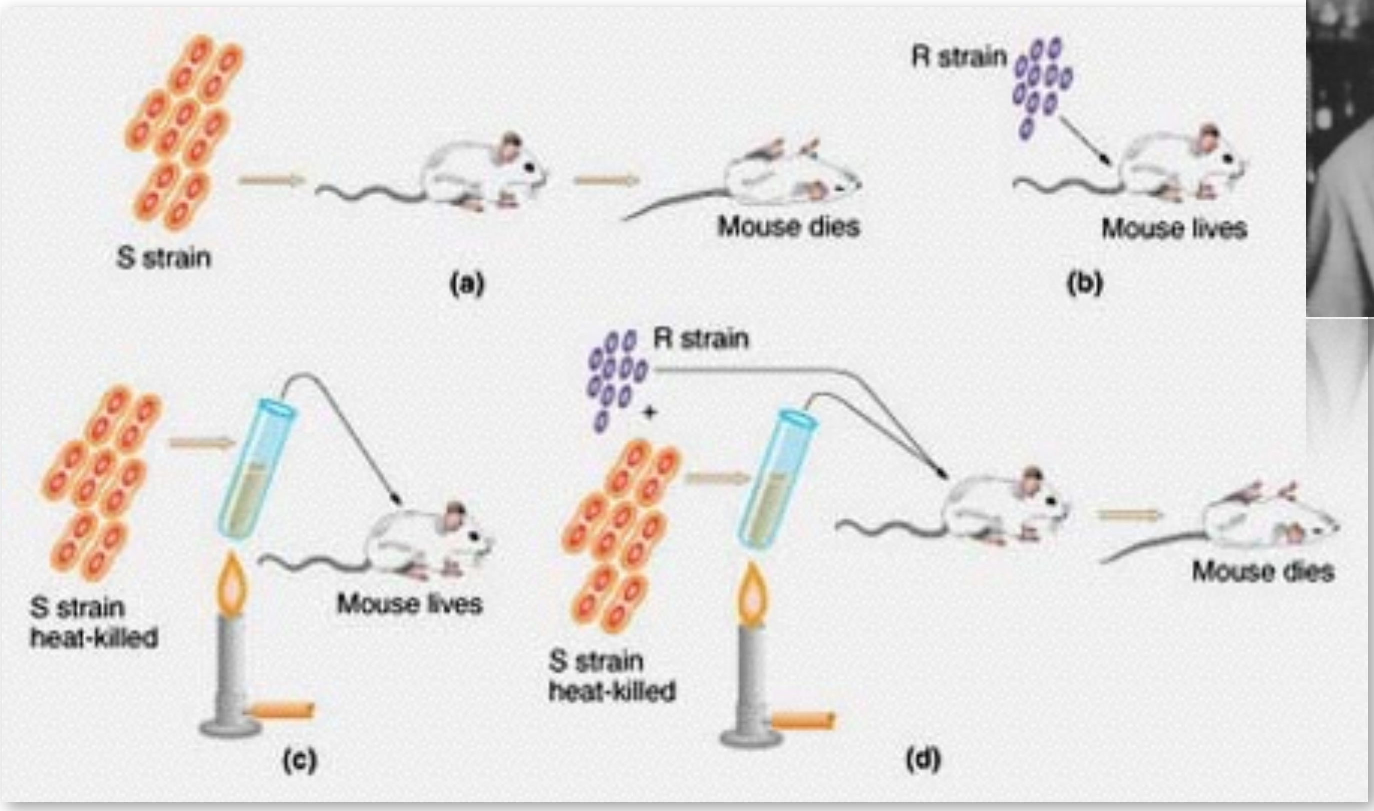
Thomas H. Morgan establishes the chromosomal theory of inheritance. He also discovered the recombination of homologous chromosomes during meiosis.



Thomas Hunt Morgan (1866-1945)

1944

Oswald T. Avery (1877-1955), **Maclyn McCarty** (1911-2005) and **Colin MacLeod** (1909-1972) identify deoxyribonucleic acid (DNA) as the “transforming principle”.



Oswald T. Avery
(1877-1955)

1950

Erwin Chargaff discovers regularity in proportions of DNA bases. In all organisms he studied, the amount of adenine (A) equaled that of thymine (T), and guanine (G) equaled cytosine (C).

Erwin Chargaff (1905-2002)

A brief history

1953

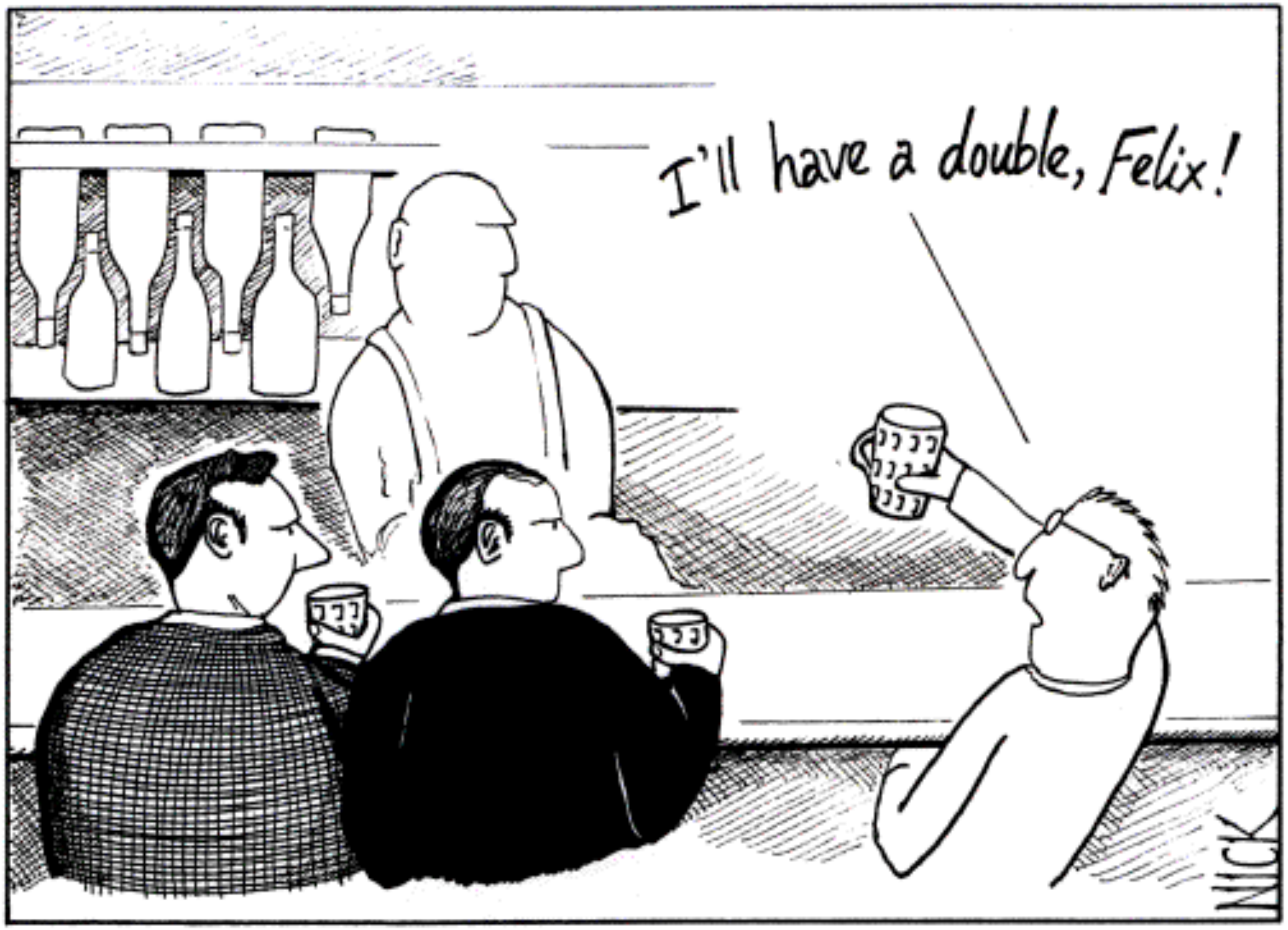
James Watson and **Francis Crick** discover the double helical structure of the DNA and that this structure meets the unique requirements for a substance that encodes genetic information.

James D. Watson (1928-)
Francis H. C. Crick (1916-2004)

April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

1953



Cambridge, 1953. Shortly before discovering the structure of DNA, Watson and Crick, depressed by their lack of progress, visit the local pub.

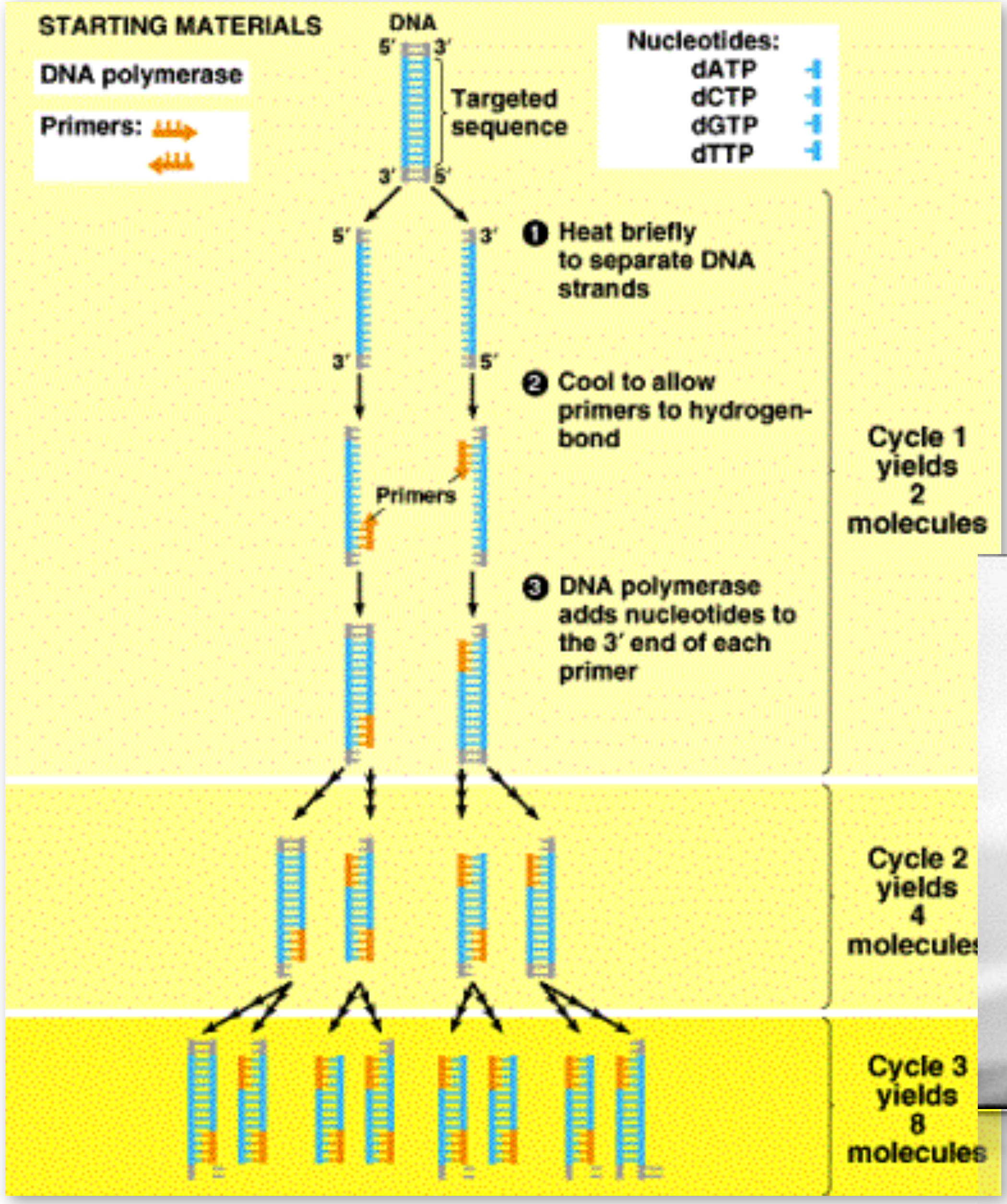
1977

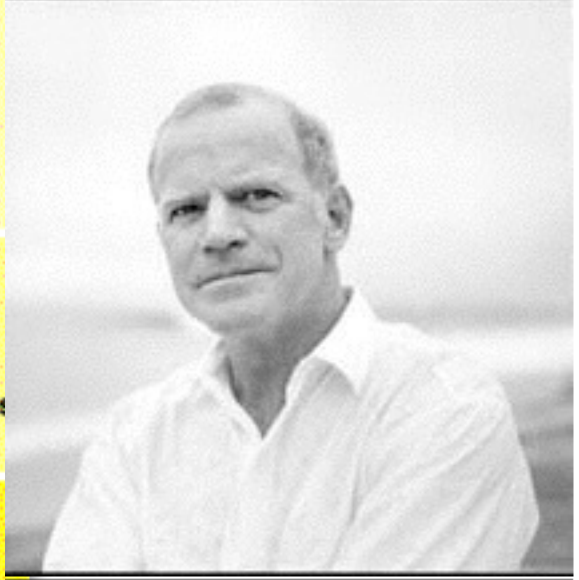
Frederick Sanger (1918-) and **Walter Gilbert** (1932) develop techniques for DNA sequencing

Walter Gilbert Frederick Sanger

1983

Kary B. Mullis (1944-) invents and helps to develop the polymerase chain reaction (PCR)



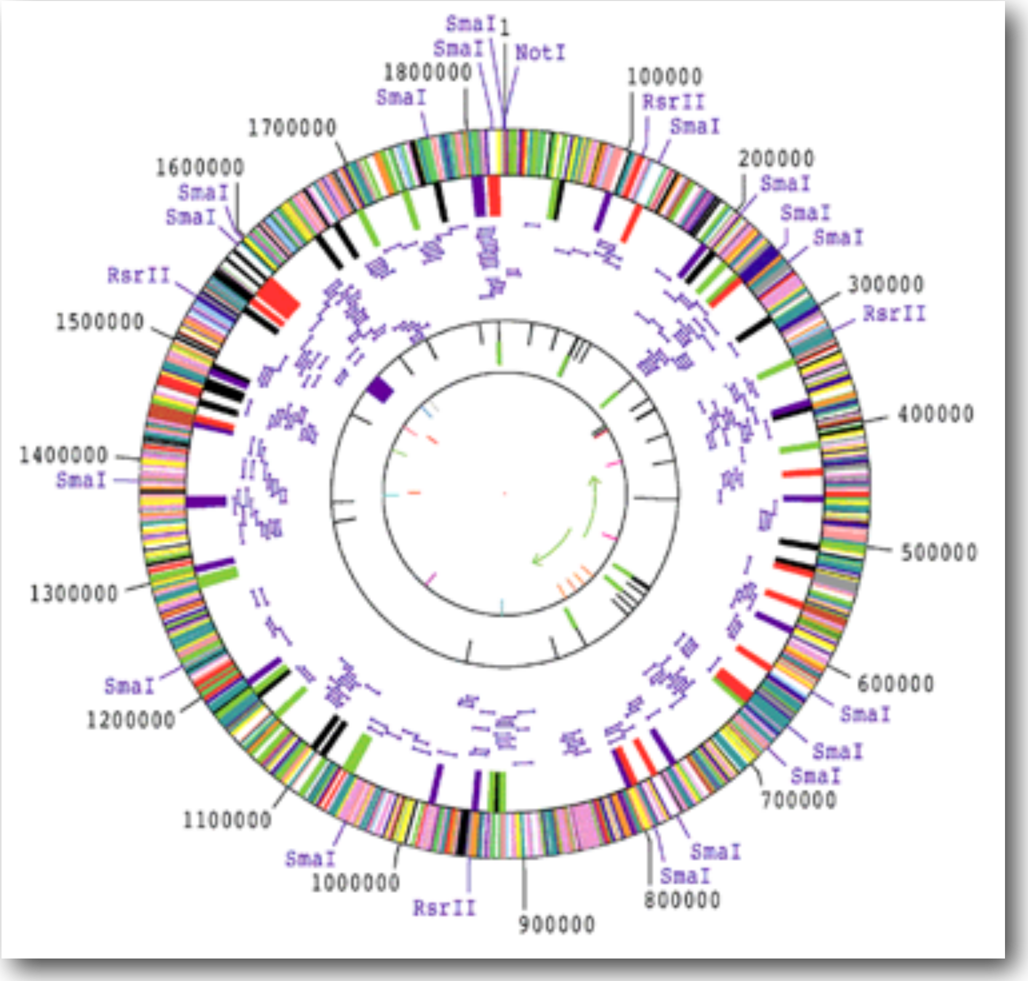


Kary B. Mullis

A brief history

1995

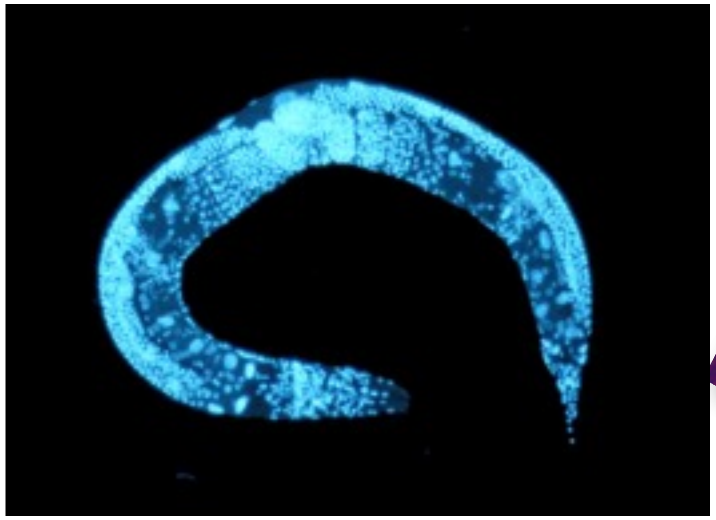
1,830,137 bp of *Hamophilus influenzae* sequenced: the first genome of a free living organisms determined



A brief history

1998

Caenorhabditis elegans sequenced

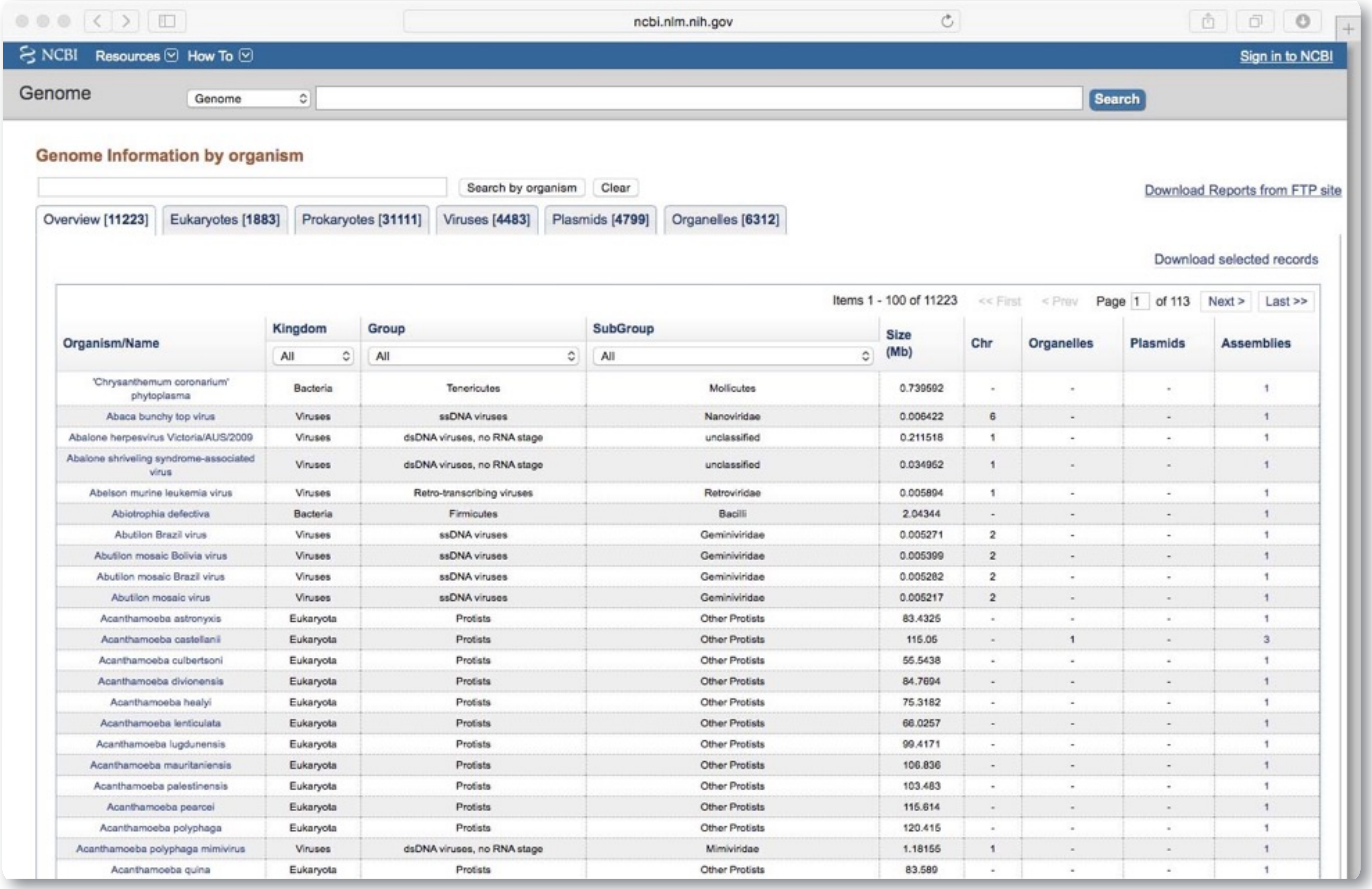


2000

Drosophila melanogaster sequenced

GenBank, January 2015

A brief history



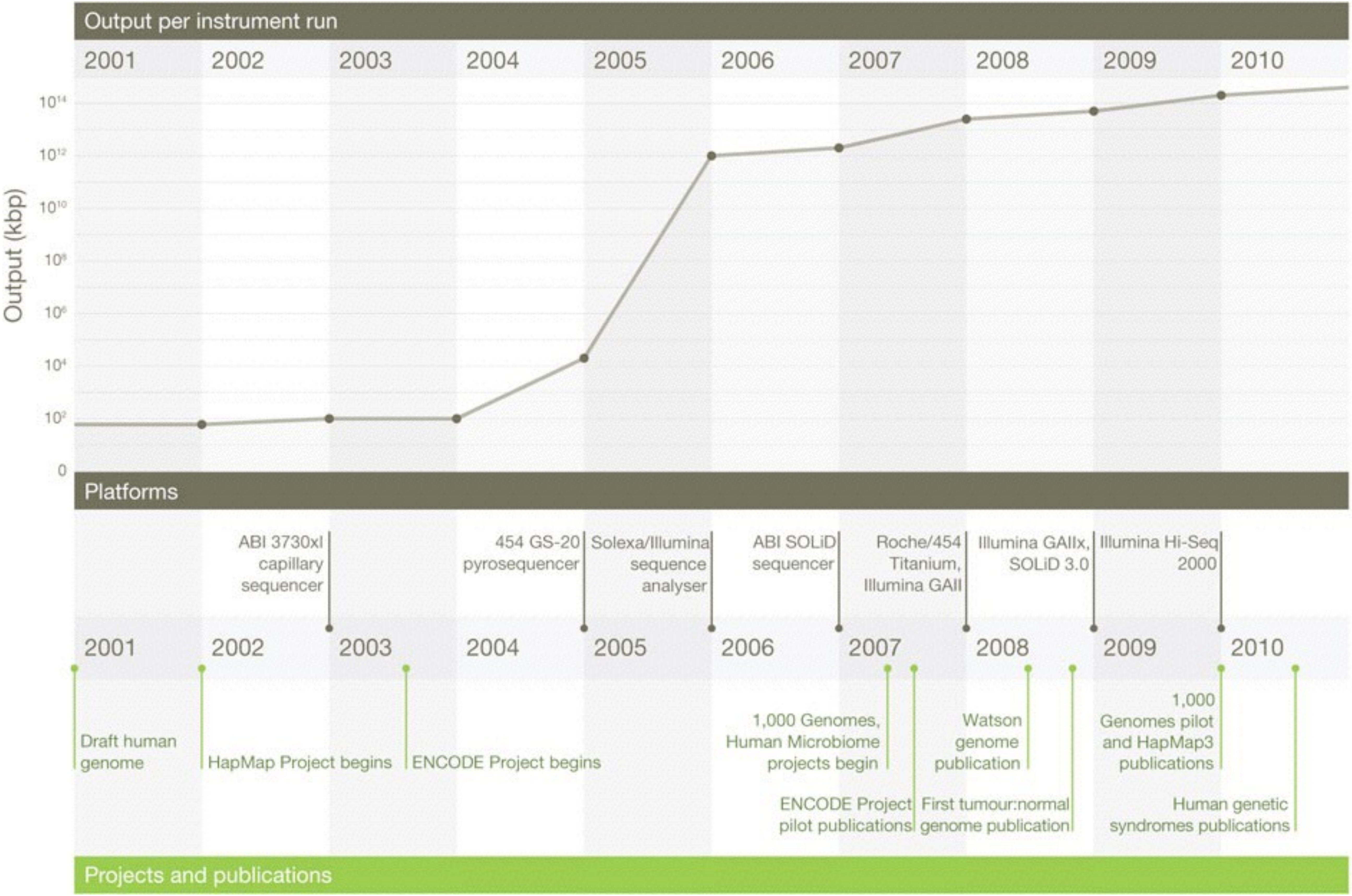
Genome Information by organism

Overview [11223] | Eukaryotes [1883] | Prokaryotes [31111] | Viruses [4483] | Plasmids [4799] | Organelles [6312]

Items 1 - 100 of 11223 << First < Prev Page 1 of 113 Next > Last >>

Organism/Name	Kingdom All	Group All	SubGroup All	Size (Mb)	Chr	Organelles	Plasmids	Assemblies
'Chrysanthemum coronarium' phytoplasma	Bacteria	Tenericutes	Mollicutes	0.739592	-	-	-	1
Abaca bunchy top virus	Viruses	ssDNA viruses	Nanoviridae	0.006422	6	-	-	1
Abalone herpesvirus Victoria/AUS/2009	Viruses	dsDNA viruses, no RNA stage	unclassified	0.211518	1	-	-	1
Abalone shriveling syndrome-associated virus	Viruses	dsDNA viruses, no RNA stage	unclassified	0.034952	1	-	-	1
Abelson murine leukemia virus	Viruses	Retro-transcribing viruses	Retroviridae	0.005894	1	-	-	1
Abiotrophia defectiva	Bacteria	Firmicutes	Bacilli	2.04344	-	-	-	1
Abutilon Brazil virus	Viruses	ssDNA viruses	Geminiviridae	0.005271	2	-	-	1
Abutilon mosaic Bolivia virus	Viruses	ssDNA viruses	Geminiviridae	0.005399	2	-	-	1
Abutilon mosaic Brazil virus	Viruses	ssDNA viruses	Geminiviridae	0.005282	2	-	-	1
Abutilon mosaic virus	Viruses	ssDNA viruses	Geminiviridae	0.005217	2	-	-	1
Acanthamoeba astronyxis	Eukaryota	Protists	Other Protists	83.4325	-	-	-	1
Acanthamoeba castellanii	Eukaryota	Protists	Other Protists	115.05	-	1	-	3
Acanthamoeba culbertsoni	Eukaryota	Protists	Other Protists	55.5438	-	-	-	1
Acanthamoeba divionensis	Eukaryota	Protists	Other Protists	84.7694	-	-	-	1
Acanthamoeba healyi	Eukaryota	Protists	Other Protists	75.3182	-	-	-	1
Acanthamoeba lenticulata	Eukaryota	Protists	Other Protists	68.0257	-	-	-	1
Acanthamoeba lugdunensis	Eukaryota	Protists	Other Protists	99.4171	-	-	-	1
Acanthamoeba mauritaniensis	Eukaryota	Protists	Other Protists	106.836	-	-	-	1
Acanthamoeba palestinensis	Eukaryota	Protists	Other Protists	103.483	-	-	-	1
Acanthamoeba pearcei	Eukaryota	Protists	Other Protists	115.614	-	-	-	1
Acanthamoeba polyphaga	Eukaryota	Protists	Other Protists	120.415	-	-	-	1
Acanthamoeba polyphaga mimivirus	Viruses	dsDNA viruses, no RNA stage	Mimiviridae	1.18155	1	-	-	1
Acanthamoeba quina	Eukaryota	Protists	Other Protists	83.589	-	-	-	1

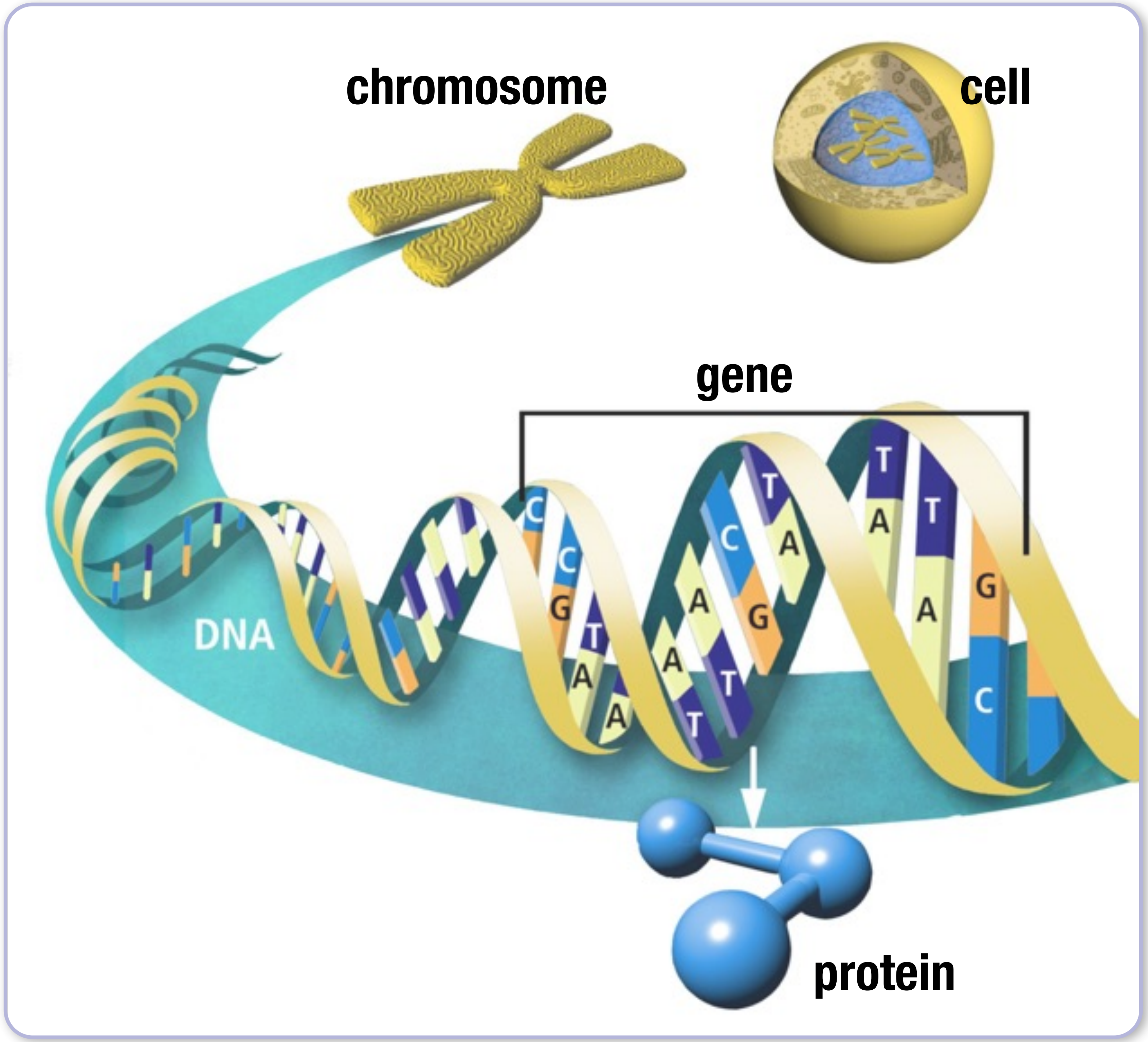
A brief history



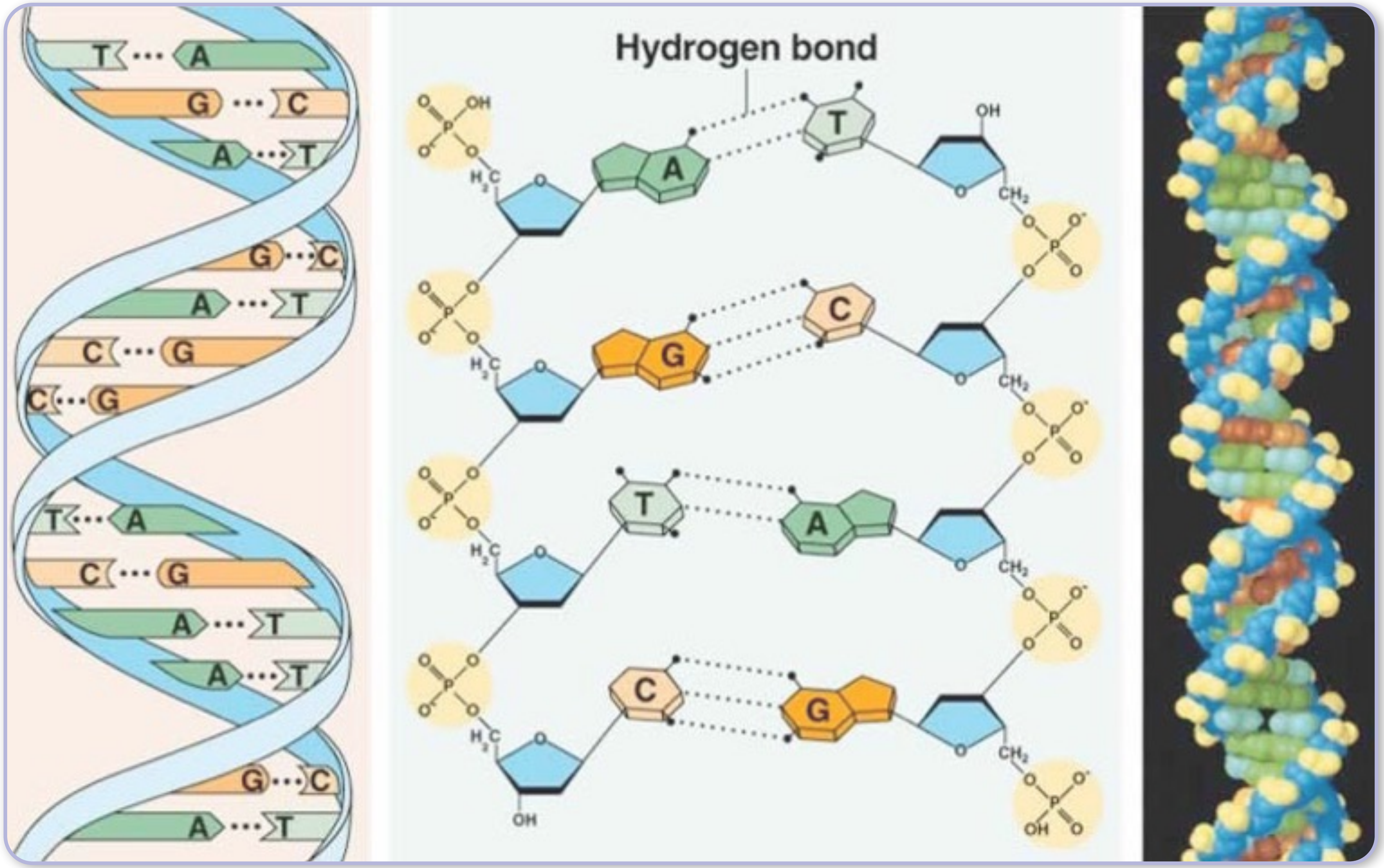
ER Mardis. *Nature* **470**, 198-203 (2011)

Genetic Organization

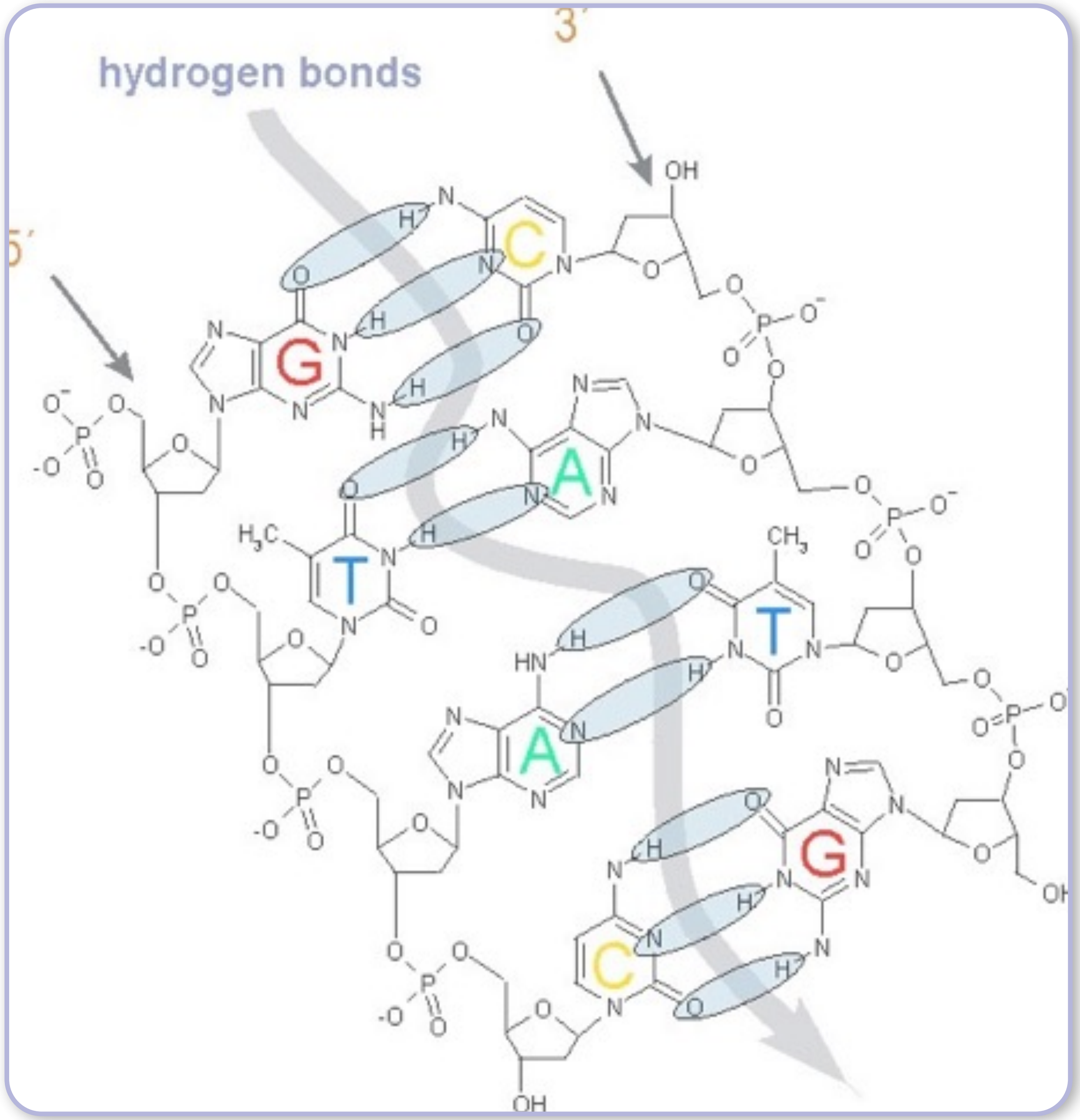
Genetic Organization



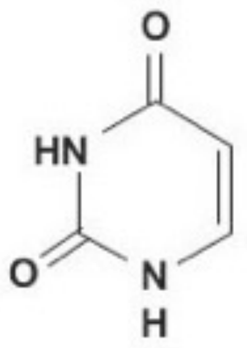
desoxyribonucleic acid (DNA)

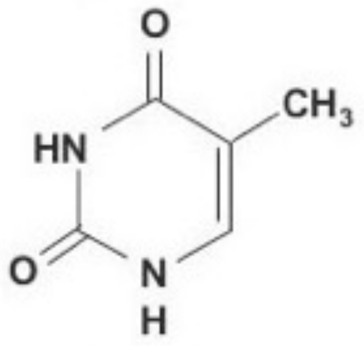


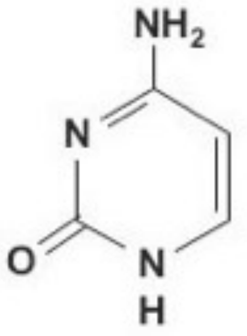
DNA double helix



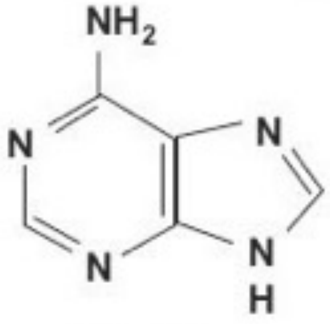
pyrimidines

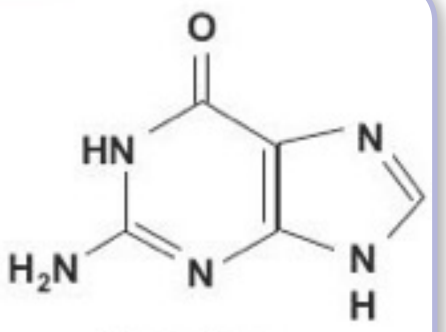

Uracyl


Thymine

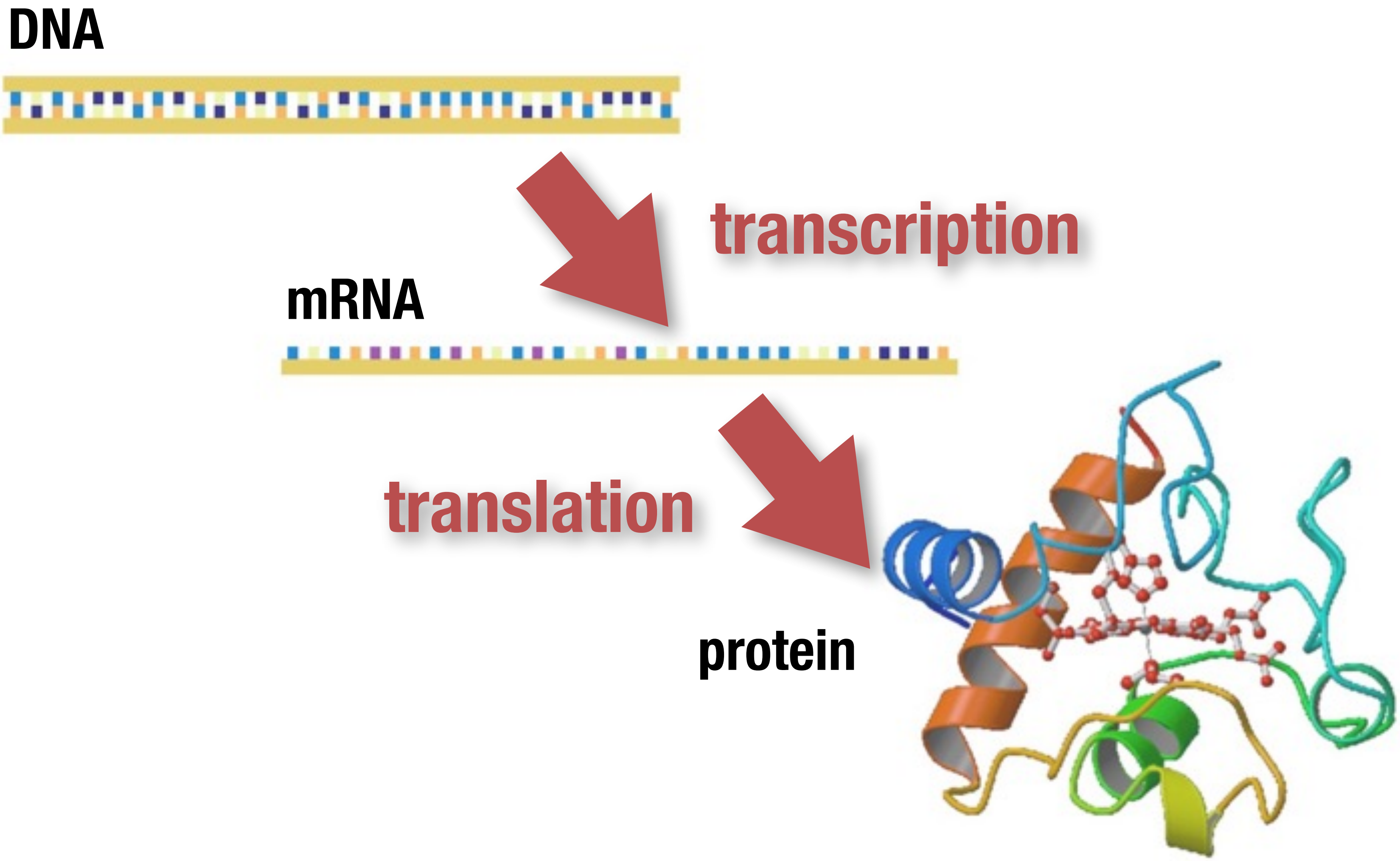

Cytosine

purines


Adenine


Guanine

Genetic Organization



DNA

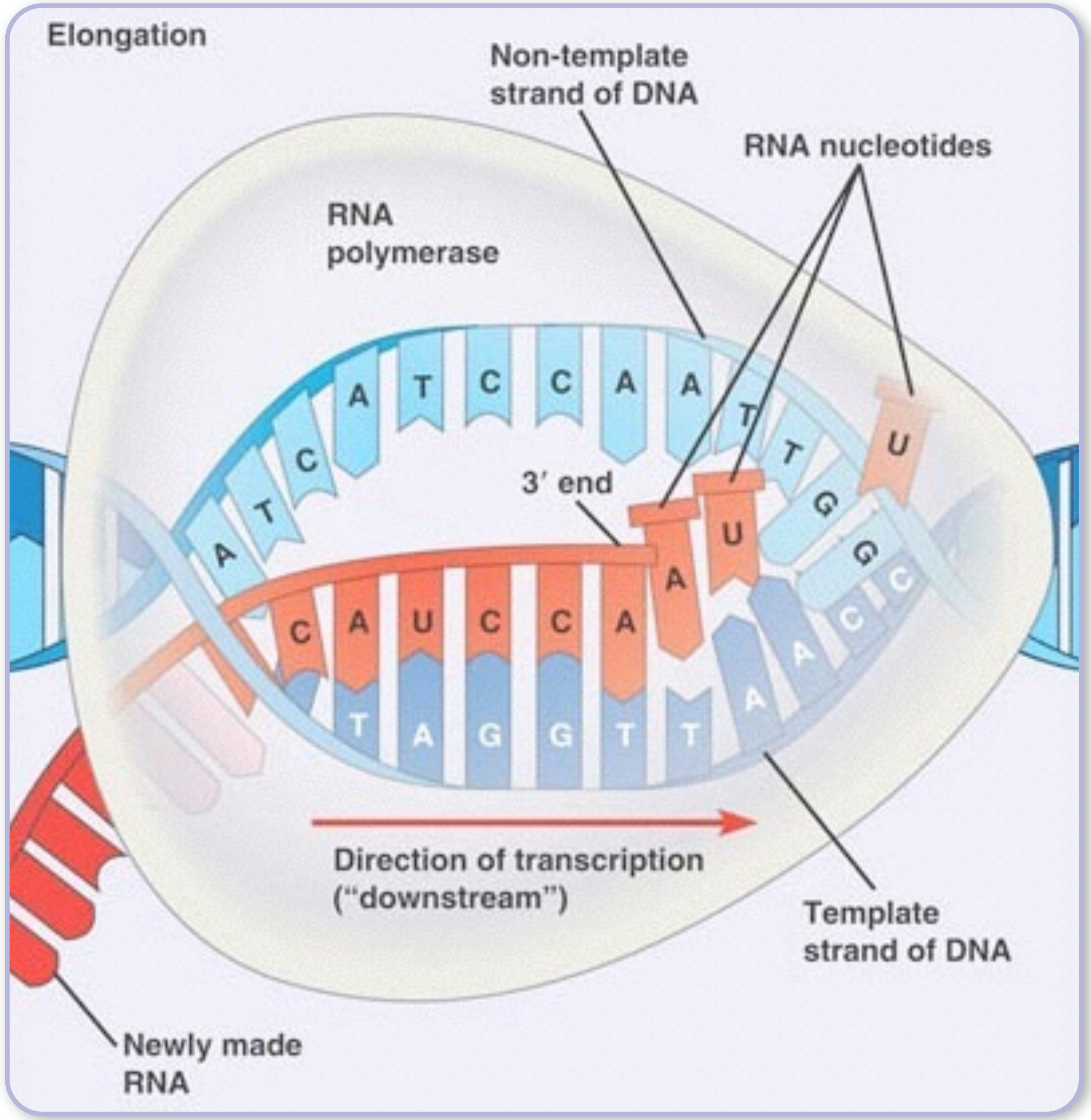
transcription

mRNA

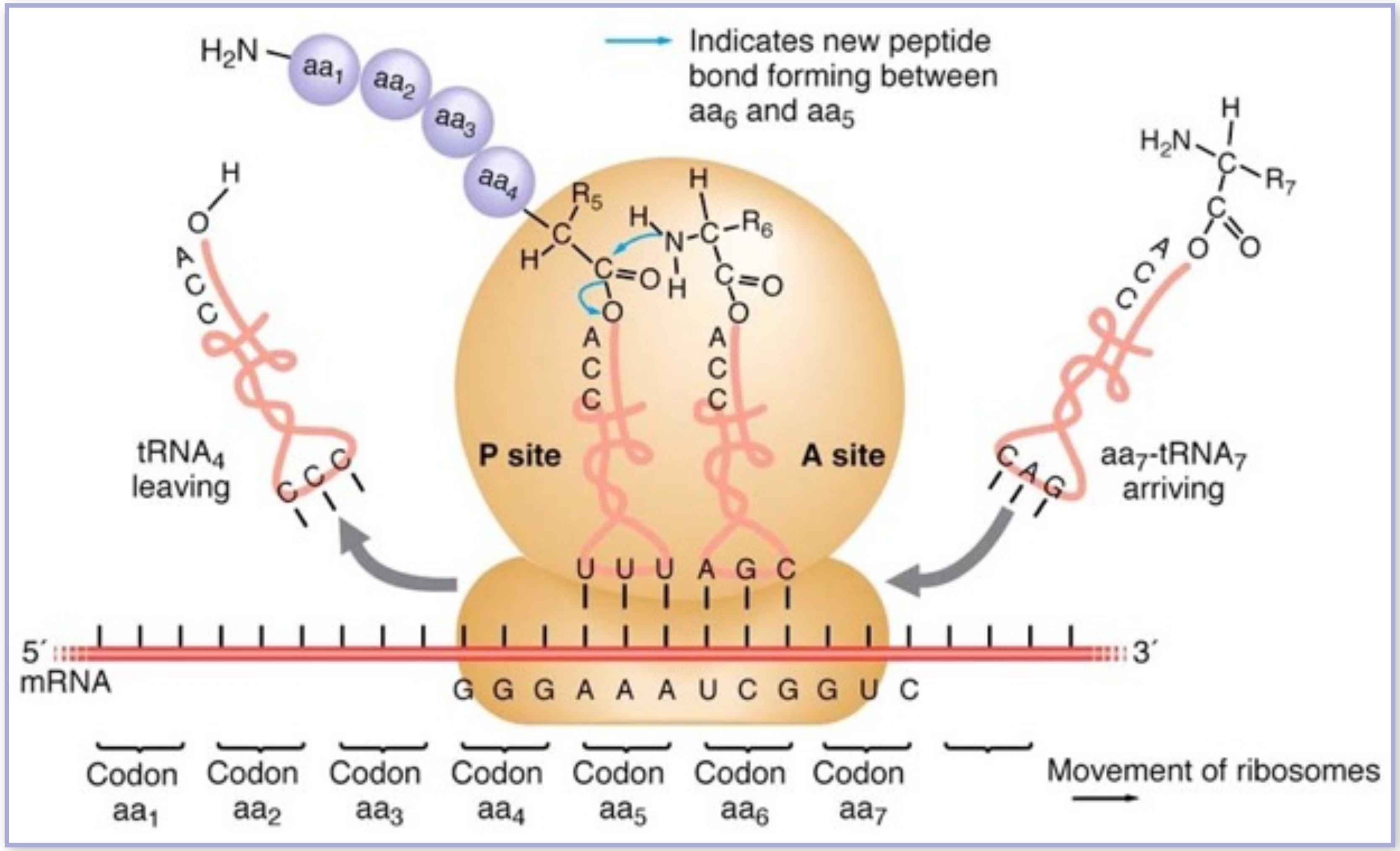
translation

protein

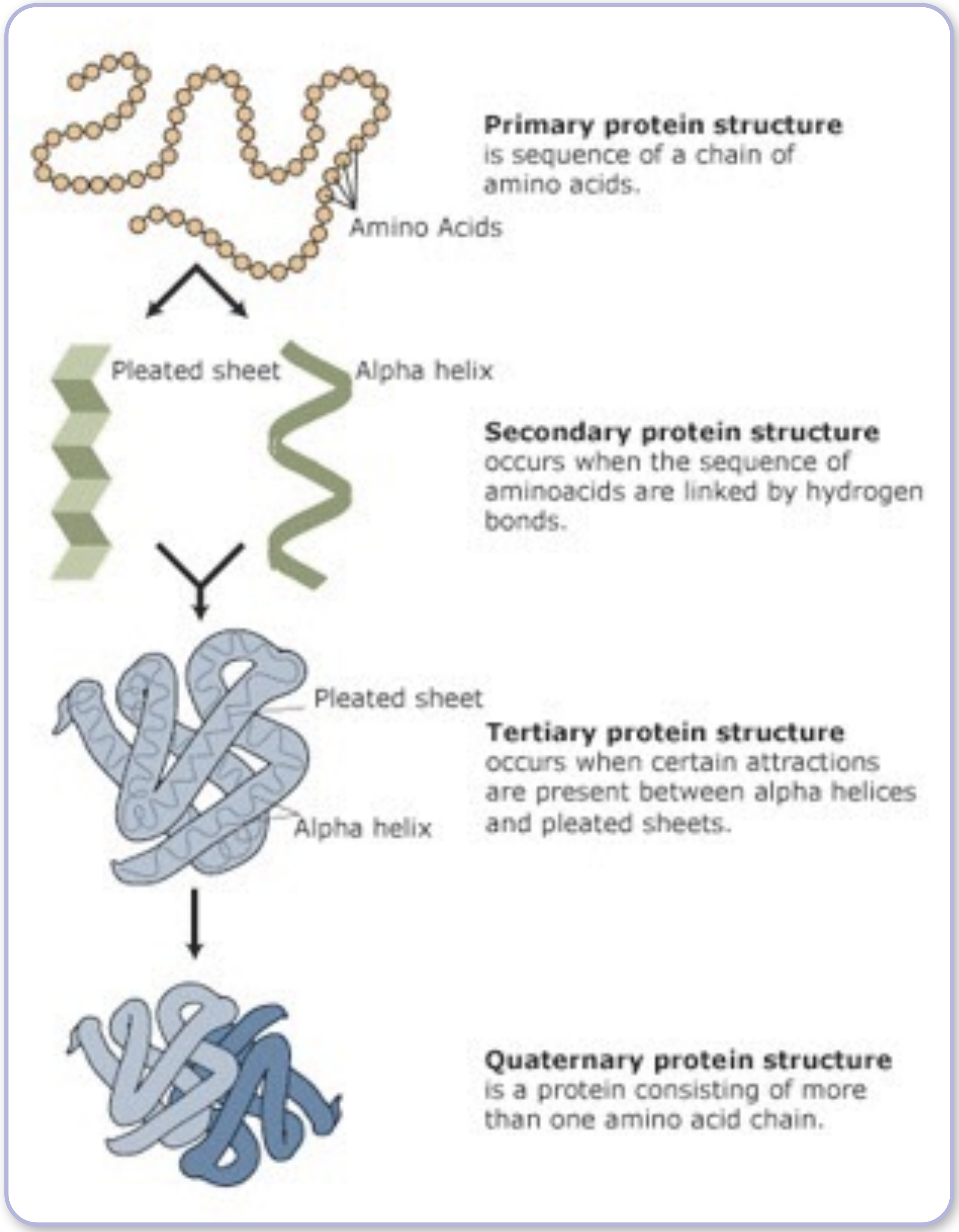
transcription



translation



protein structure



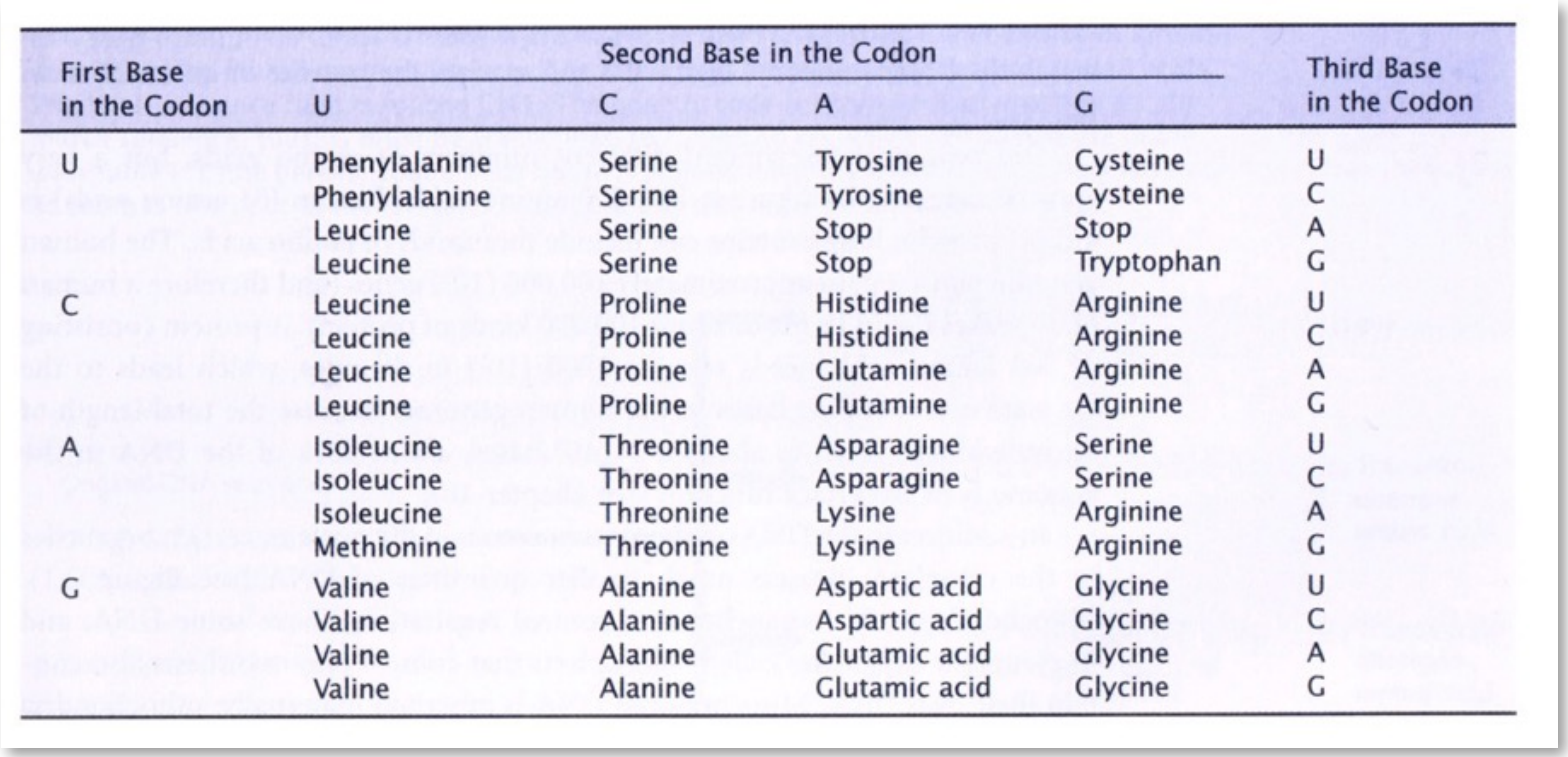
Primary protein structure is sequence of a chain of amino acids.

Secondary protein structure occurs when the sequence of aminoacids are linked by hydrogen bonds.

Tertiary protein structure occurs when certain attractions are present between alpha helices and pleated sheets.

Quaternary protein structure is a protein consisting of more than one amino acid chain.

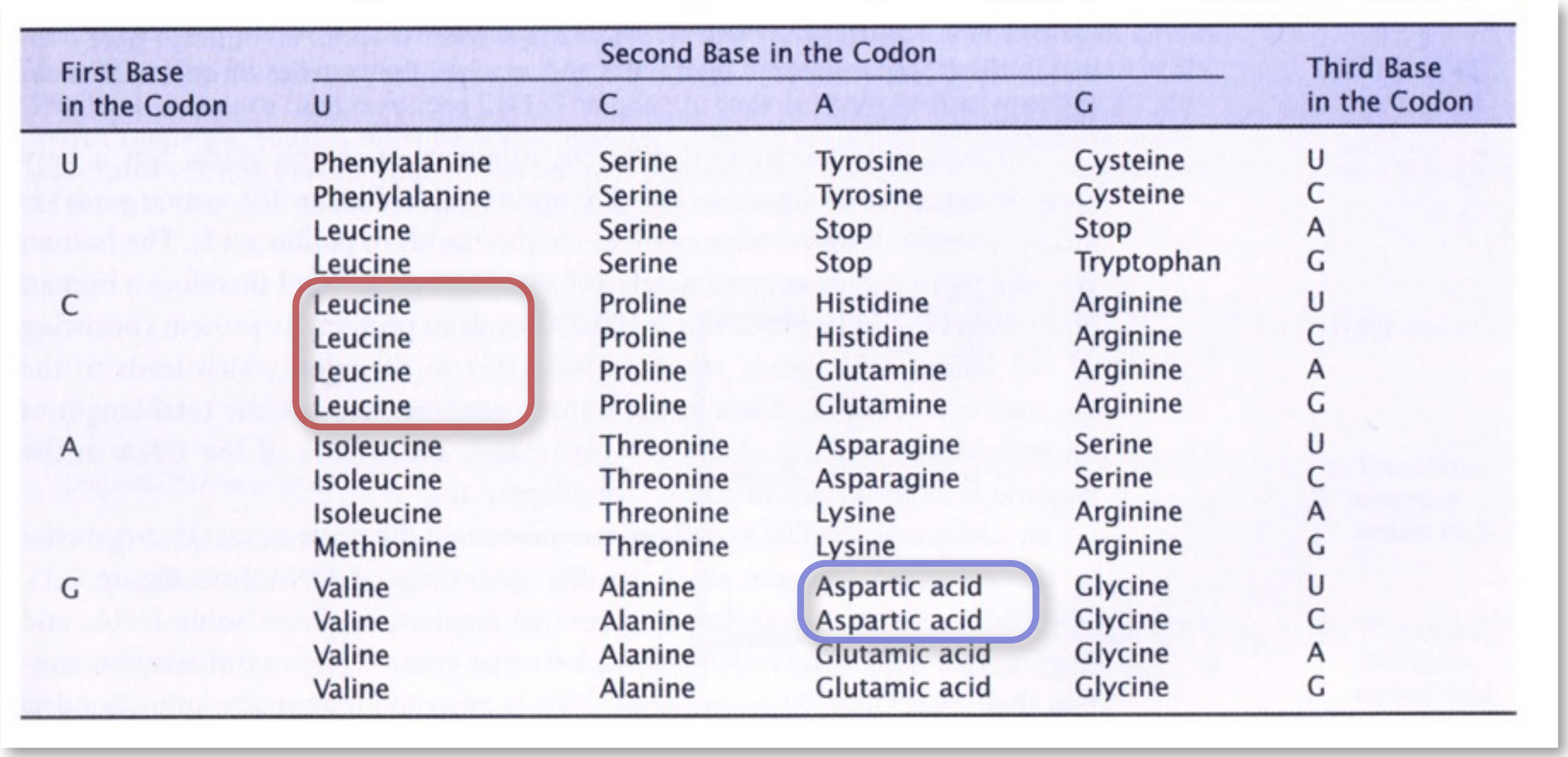
The genetic code*



First Base in the Codon	Second Base in the Codon				Third Base in the Codon
	U	C	A	G	
U	Phenylalanine	Serine	Tyrosine	Cysteine	U
	Phenylalanine	Serine	Tyrosine	Cysteine	C
	Leucine	Serine	Stop	Stop	A
	Leucine	Serine	Stop	Tryptophan	G
C	Leucine	Proline	Histidine	Arginine	U
	Leucine	Proline	Histidine	Arginine	C
	Leucine	Proline	Glutamine	Arginine	A
	Leucine	Proline	Glutamine	Arginine	G
A	Isoleucine	Threonine	Asparagine	Serine	U
	Isoleucine	Threonine	Asparagine	Serine	C
	Isoleucine	Threonine	Lysine	Arginine	A
	Methionine	Threonine	Lysine	Arginine	G
G	Valine	Alanine	Aspartic acid	Glycine	U
	Valine	Alanine	Aspartic acid	Glycine	C
	Valine	Alanine	Glutamic acid	Glycine	A
	Valine	Alanine	Glutamic acid	Glycine	G

*Note that there is not just one ‘universal’ genetic code!

The degenerated genetic code



First Base in the Codon	Second Base in the Codon				Third Base in the Codon
	U	C	A	G	
U	Phenylalanine	Serine	Tyrosine	Cysteine	U
	Phenylalanine	Serine	Tyrosine	Cysteine	C
	Leucine	Serine	Stop	Stop	A
	Leucine	Serine	Stop	Tryptophan	G
C	Leucine	Proline	Histidine	Arginine	U
	Leucine	Proline	Histidine	Arginine	C
	Leucine	Proline	Glutamine	Arginine	A
	Leucine	Proline	Glutamine	Arginine	G
A	Isoleucine	Threonine	Asparagine	Serine	U
	Isoleucine	Threonine	Asparagine	Serine	C
	Isoleucine	Threonine	Lysine	Arginine	A
	Methionine	Threonine	Lysine	Arginine	G
G	Valine	Alanine	Aspartic acid	Glycine	U
	Valine	Alanine	Aspartic acid	Glycine	C
	Valine	Alanine	Glutamic acid	Glycine	A
	Valine	Alanine	Glutamic acid	Glycine	G

4-fold degenerated

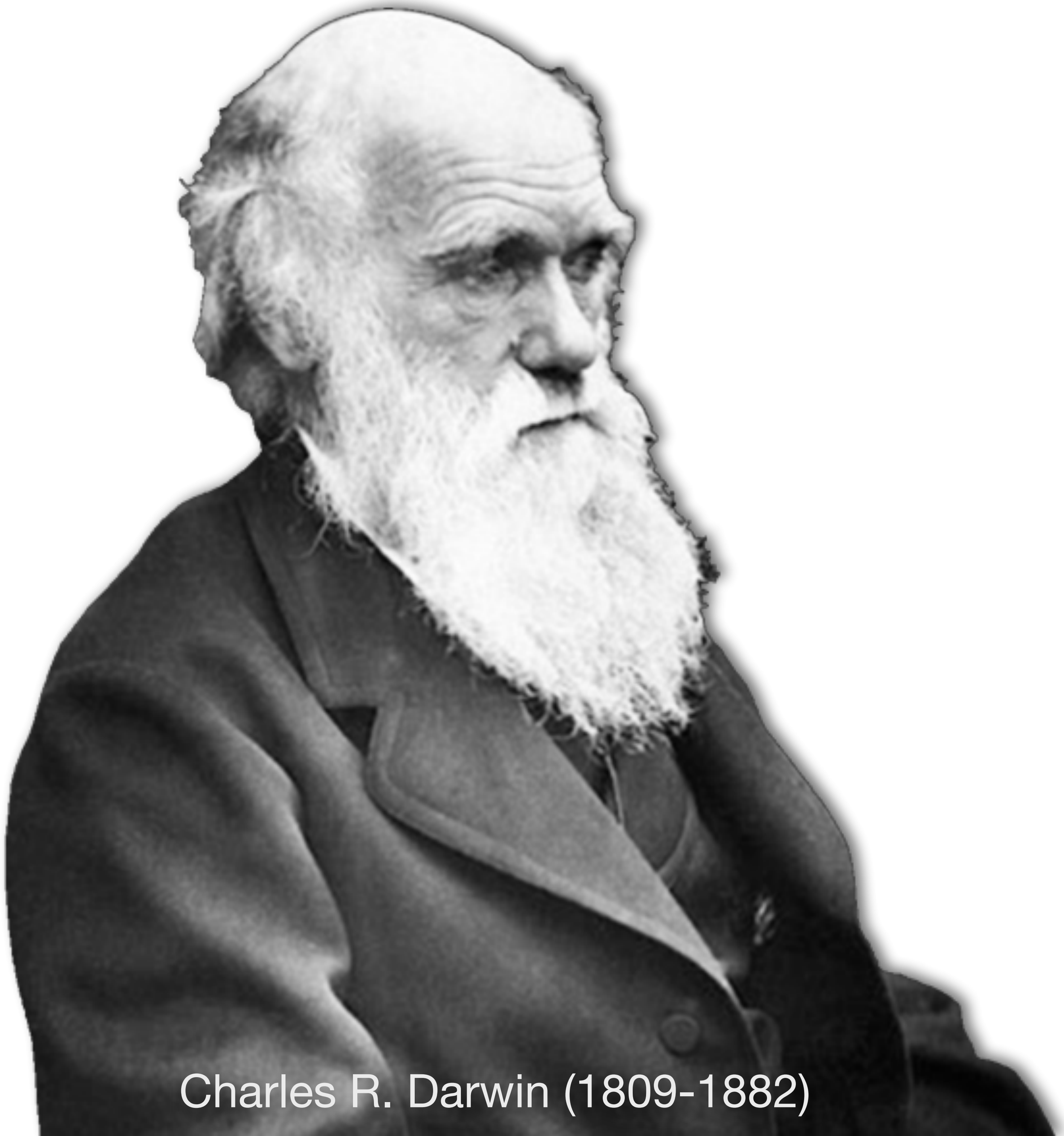
2-fold degenerated

Molecular Evolution & Phenotypic Diversity

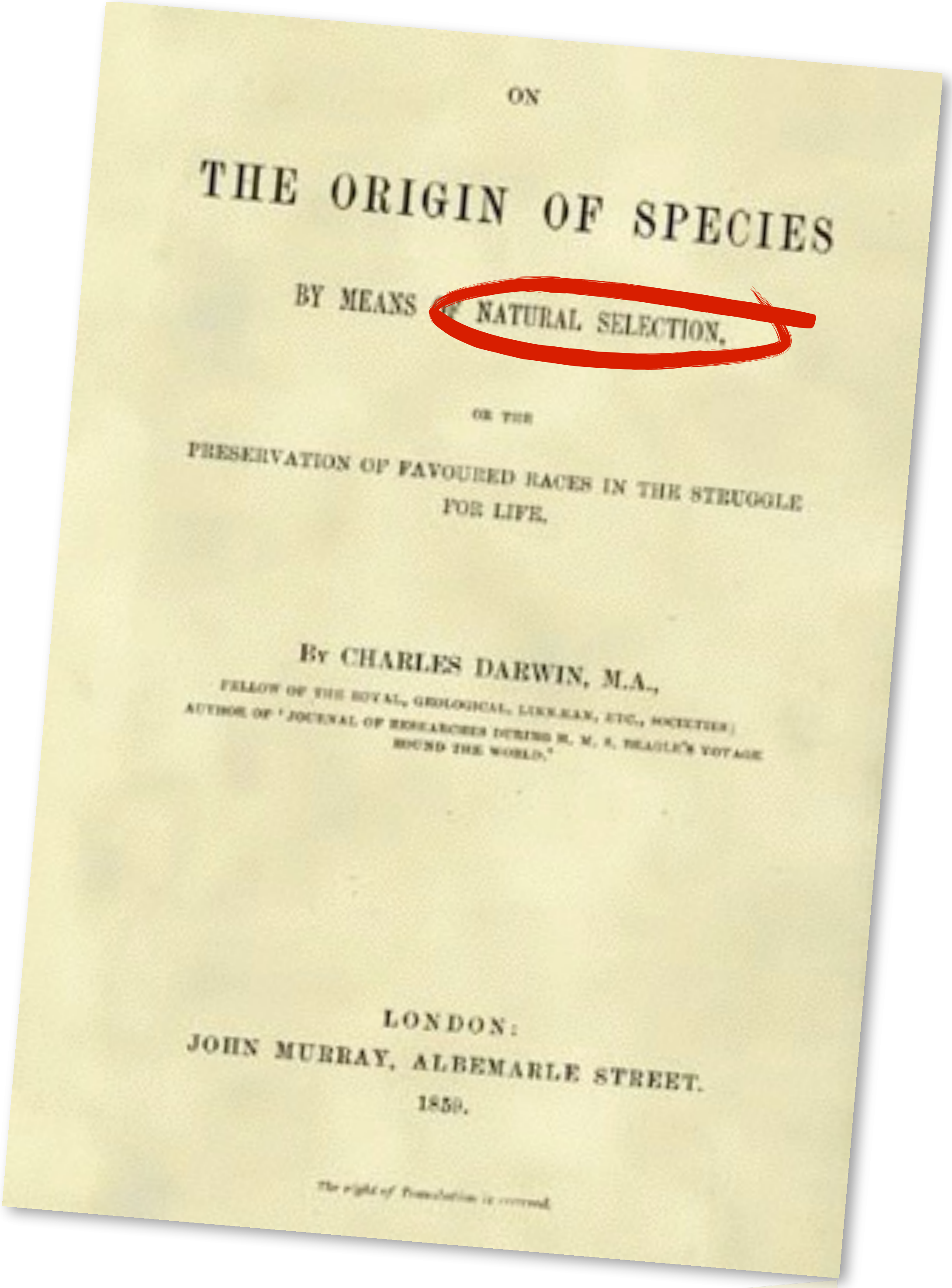
Walter Salzburger

Zoological Institute
University of Basel, Switzerland

Natural Selection...



Charles R. Darwin (1809-1882)



ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

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PRESERVATION OF FAVOURED RACES IN THE STRUGGLE
FOR LIFE.

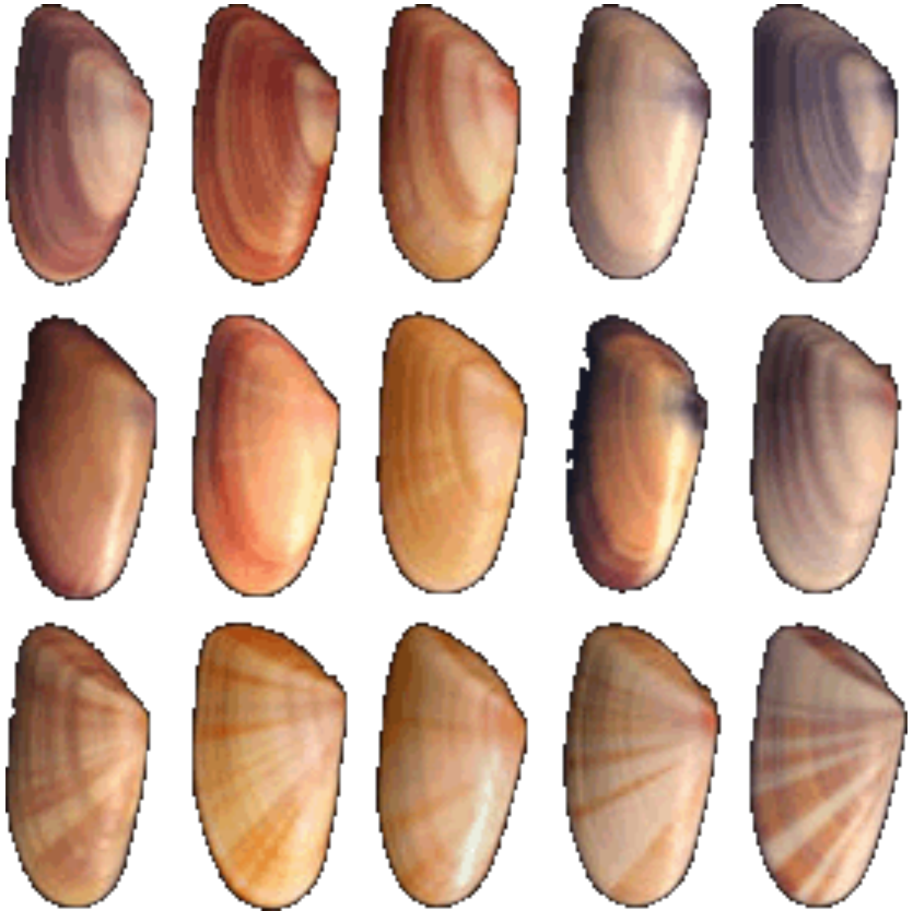
BY CHARLES DARWIN, M.A.,
FELLOW OF THE ROYAL, GEOLOGICAL, LINNÆAN, ETC., SOCIETIES;
AUTHOR OF 'JOURNAL OF RESEARCHES DURING H. M. S. BEAGLE'S VOYAGE
ROUND THE WORLD.'

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

The right of Translation is reserved.

Natural Selection...

- **...** "is the process by which the forms of organisms in a population that are **best adapted** to the environment **increase in frequency** relative to less well-adapted forms over a **number of generations**" (Ridley 1996)



images: www.idscaro.net, www.wikipedia.com

Sexual Selection...

- ...“is the selection on mating behavior, either through **competition among members of one sex** (usually males) for access to members of the other sex or through **choice by members of one sex** (usually females) for certain members of the other sex” (Ridley 1996)

images: www.crbs.umd.edu, www.smh.com.au

Natural Selection... ...Sexual Selection

	fitness	**competitors**
sexual selection	individual fitness	other members of the same sex
natural selection	fitness of the genotype	other individuals in the same population

Natural Selection... ...Sexual Selection

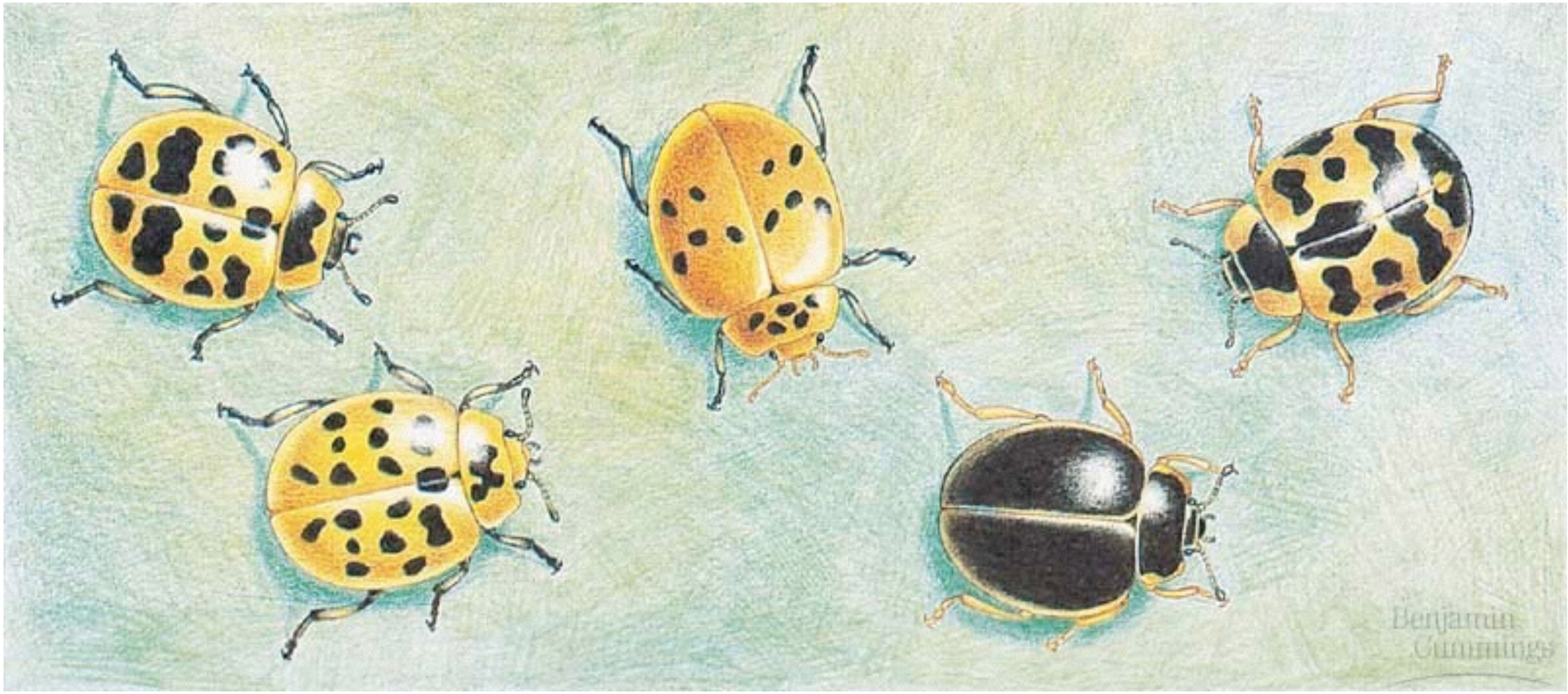
- **...operates** if the following **conditions** are met:

reproduction	organisms must reproduce to form new generations
heredity	offspring resemble parents (“**like must produce like**”)
trait variation	individuals in natural populations vary in (adaptive) traits
variation in fitness	individuals in natural populations vary in the number of their offspring that survive to reproduce (‘**lifetime reproductive success**’)

(Ridley 2004; Stearns & Hoekstra 2005)

Natural Variation

- **Natural populations** show **variation** at all levels, from gross morphology to DNA sequences. Selection can only operate, if heritable variation exists.



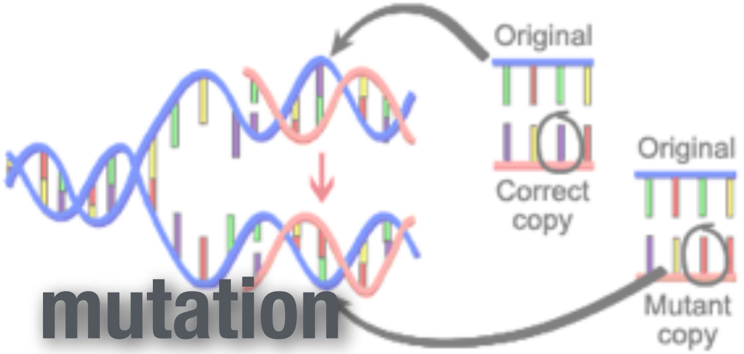
Benjamin Cummings

Natural Variation

- **Natural populations** show **variation** at all levels, from gross morphology to DNA sequences. Selection can only operate, if heritable variation exists.
- Natural variation is generated by two processes:

recombination

“reshuffling” of genetic material by introducing or breaking up physical linkage

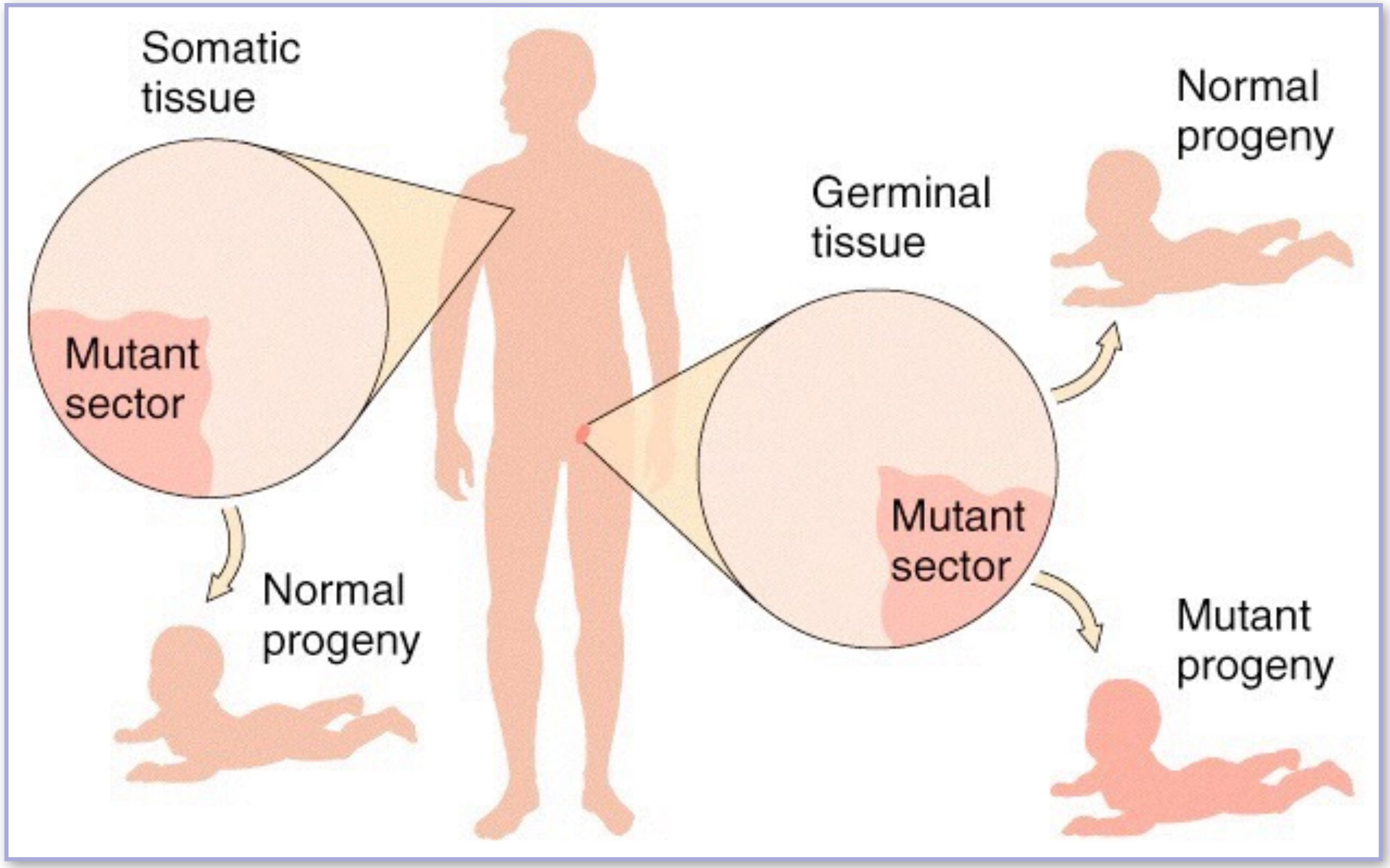


mutation

generation of new genetic variation by “mistakes” during the copying of a DNA strand

Natural Variation

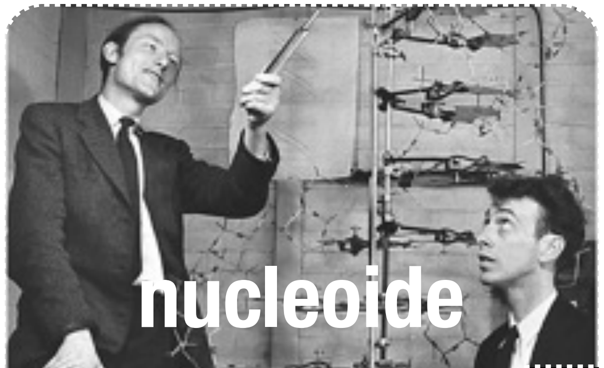
- New mutations are only transmitted to the next generation, if they occur in **germinal tissue**!



Phenotypic Evolution

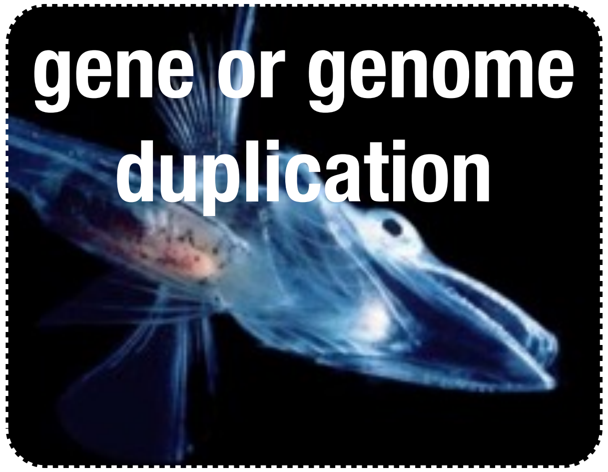
“The primary cause of evolution is the mutational change of genes”

Nei and Kumar (2000)



nucleoide substitution

insertion/ deletion

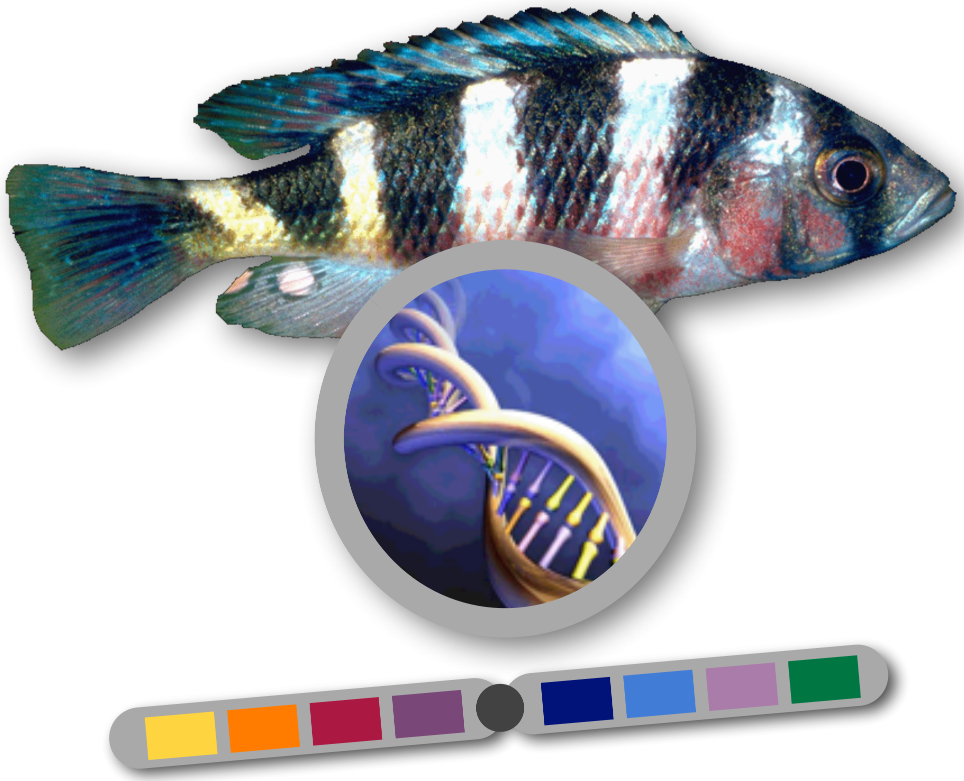


gene or genome duplication

chromosome rearrangements

Phenotypic Evolution

phenome



morphology
ecology
behavior

genome

genome structure

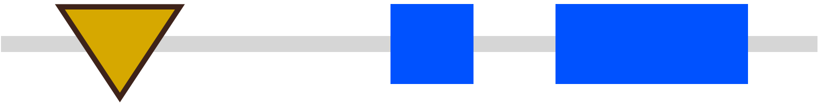
and/or

```
ATG AAC GTA TGG AGG...
Met Asn Val Trp Arg
```

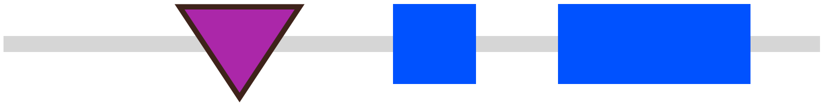
coding sequence

```
ATG AAC GCA TGG AGG...
Met Asn Ala Trp Arg
```

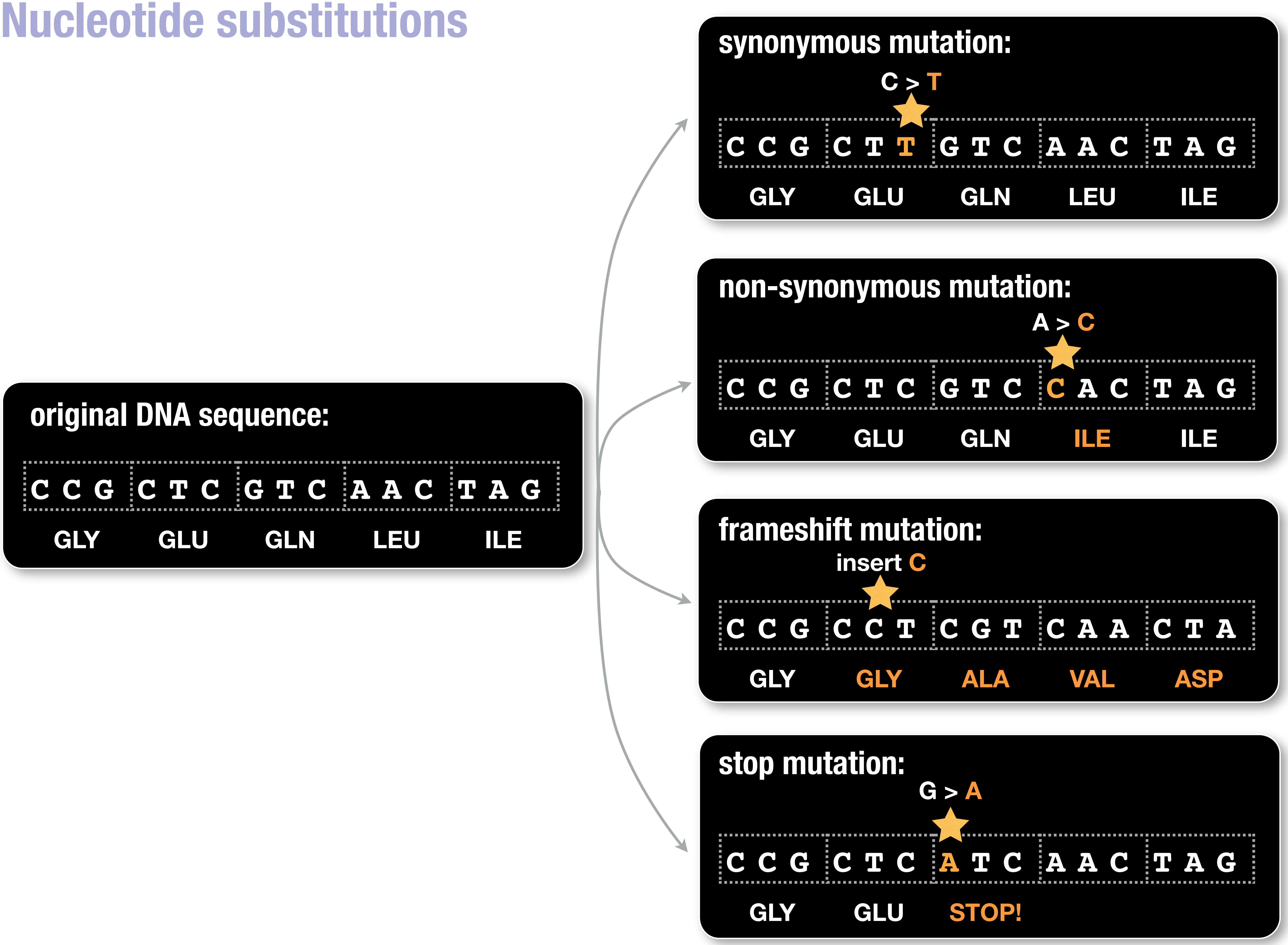
and/or



regulatory regions



Nucleotide substitutions



original DNA sequence:

C C G	C T C	G T C	A A C	T A G
GLY	GLU	GLN	LEU	ILE

synonymous mutation:

C > T

C C G	C T T	G T C	A A C	T A G
GLY	GLU	GLN	LEU	ILE

non-synonymous mutation:

A > C

C C G	C T C	G T C	C A C	T A G
GLY	GLU	GLN	ILE	ILE

frameshift mutation:

insert C

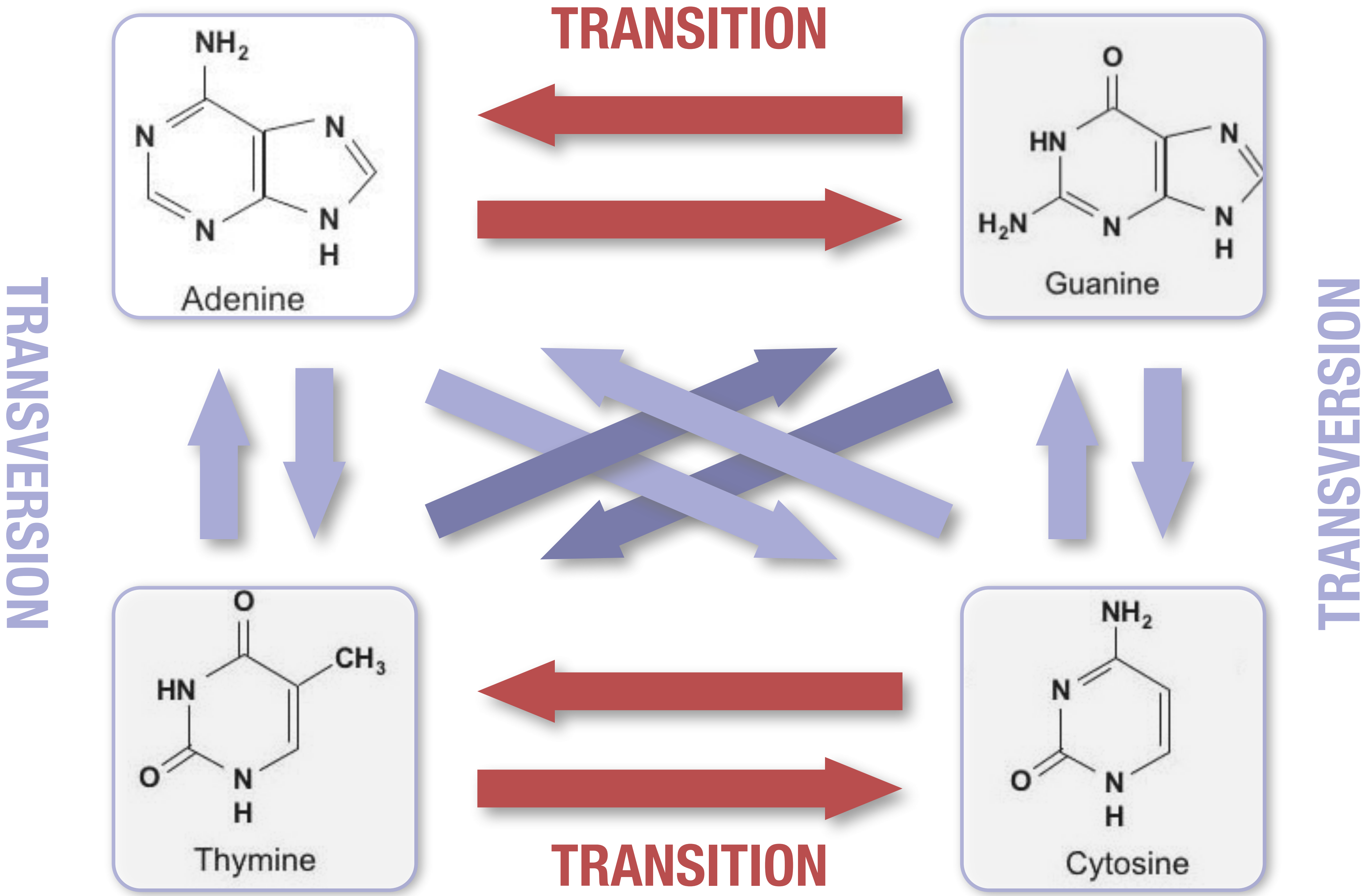
C C G	C C T	C G T	C A A	C T A
GLY	GLY	ALA	VAL	ASP

stop mutation:

G > A

C C G	C T C	A T C	A A C	T A G
GLY	GLU	STOP!		

Nucleotide substitutions



TRANSITION

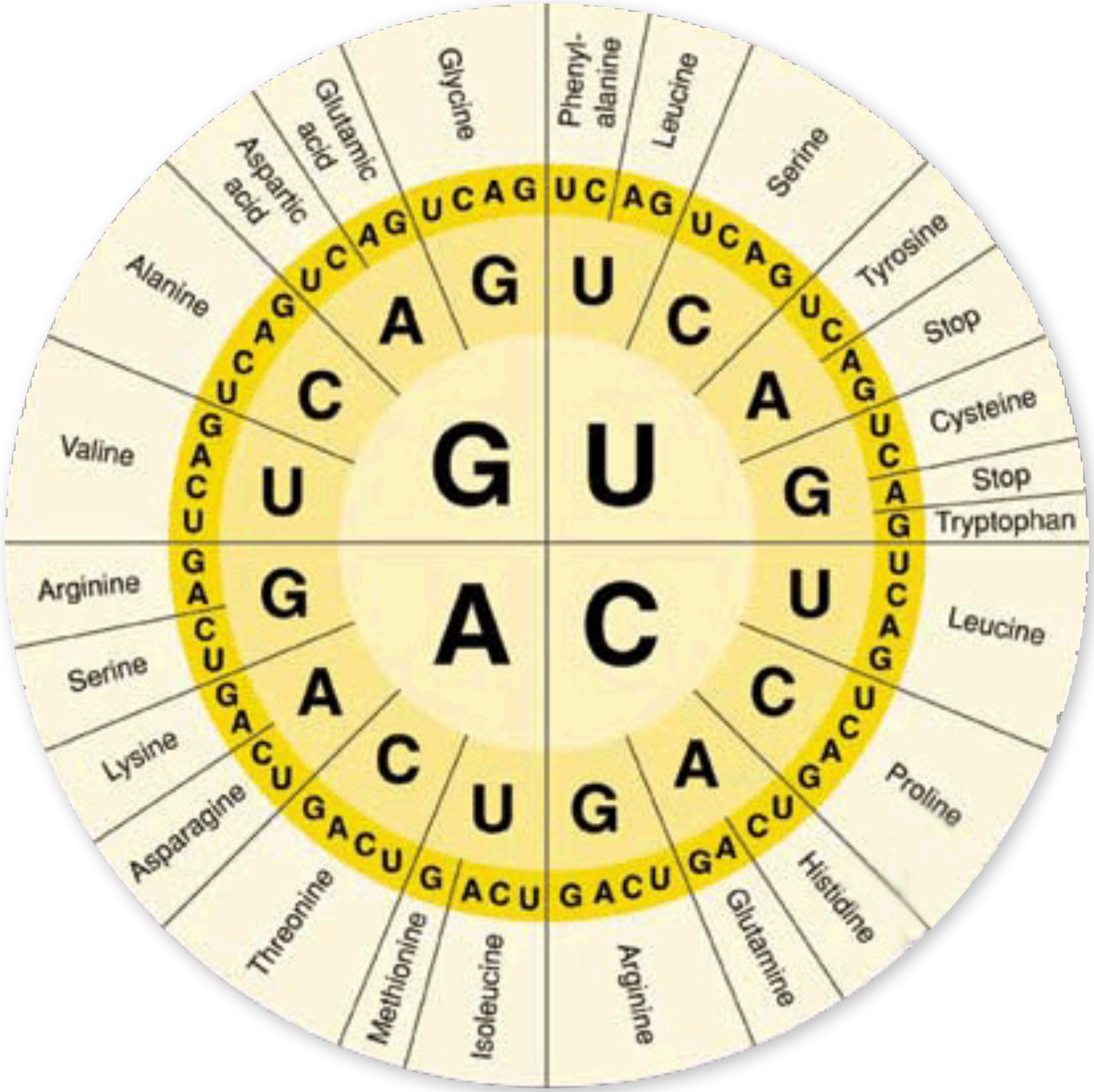
TRANSVERSION

TRANSVERSION

TRANSITION

Transition mutations outnumber transversions!

Adaptive Sequence Evolution



Adaptive Sequence Evolution

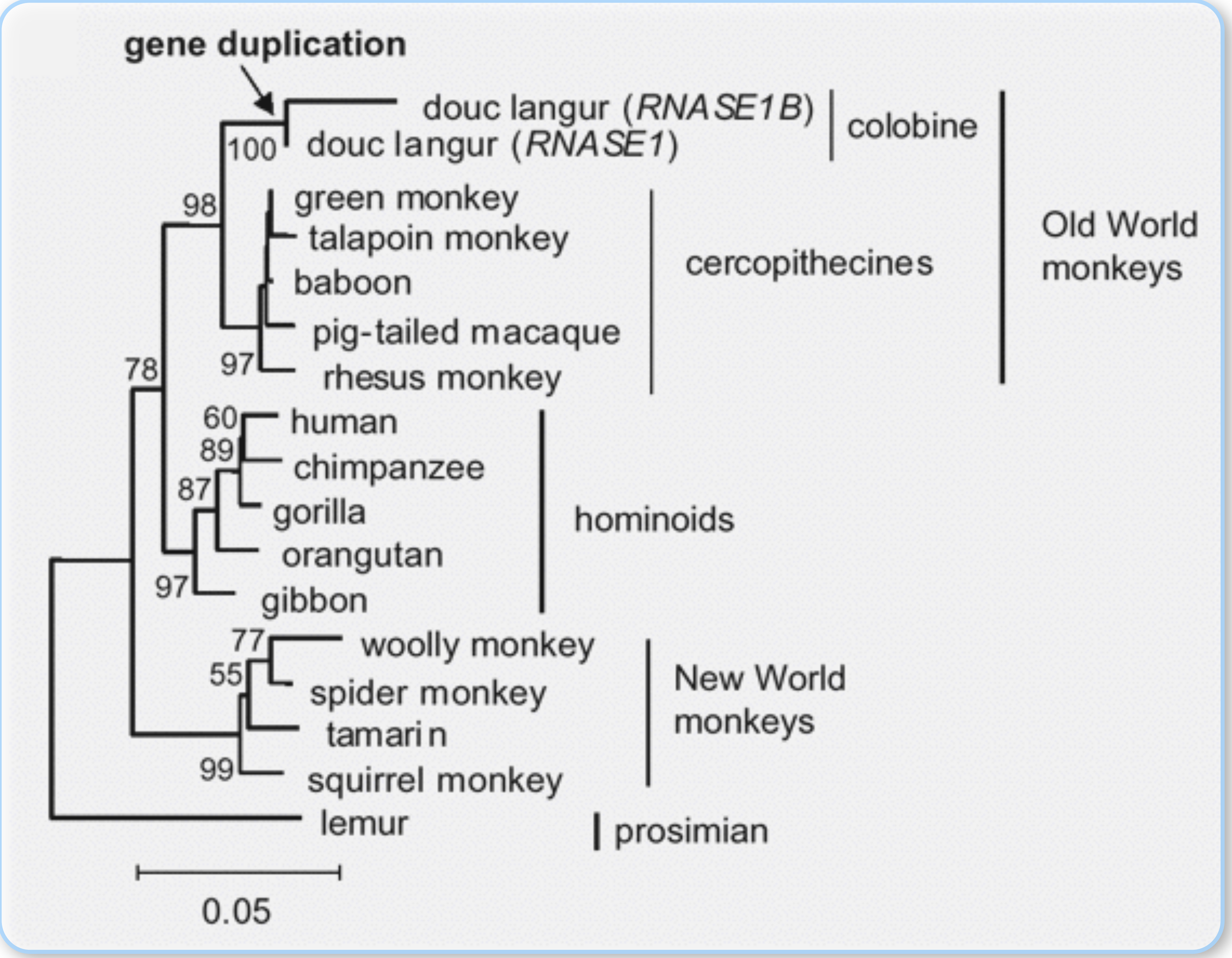
dN/dS ratio

- *dN/dS* (*Ka/Ks*) provides information about the form of sequence evolution in a gene*:
  - **dN/dS < 1: purifying selection** (non-synonymous sites are evolving slower than synonymous sites)
  - **dN/dS = 1: neutrality** (non-synonymous and synonymous sites are evolving at equal rates)
  - **dN/dS > 1: positive selection** (non-synonymous sites are evolving faster than synonymous sites; natural selection has acted to change the amino acid sequence)

**dS* is used as proxy for the neutral rate of molecular evolution

Adaptive Sequence Evolution

Pancreatic ribonuclease in colobine monkeys



Zhang et al. (2002)

douc langur

Adaptive Sequence Evolution

Pancreatic ribonuclease in colobine monkeys

douc langur

Ka = 0.0310

substitutions per non-synonymous sites

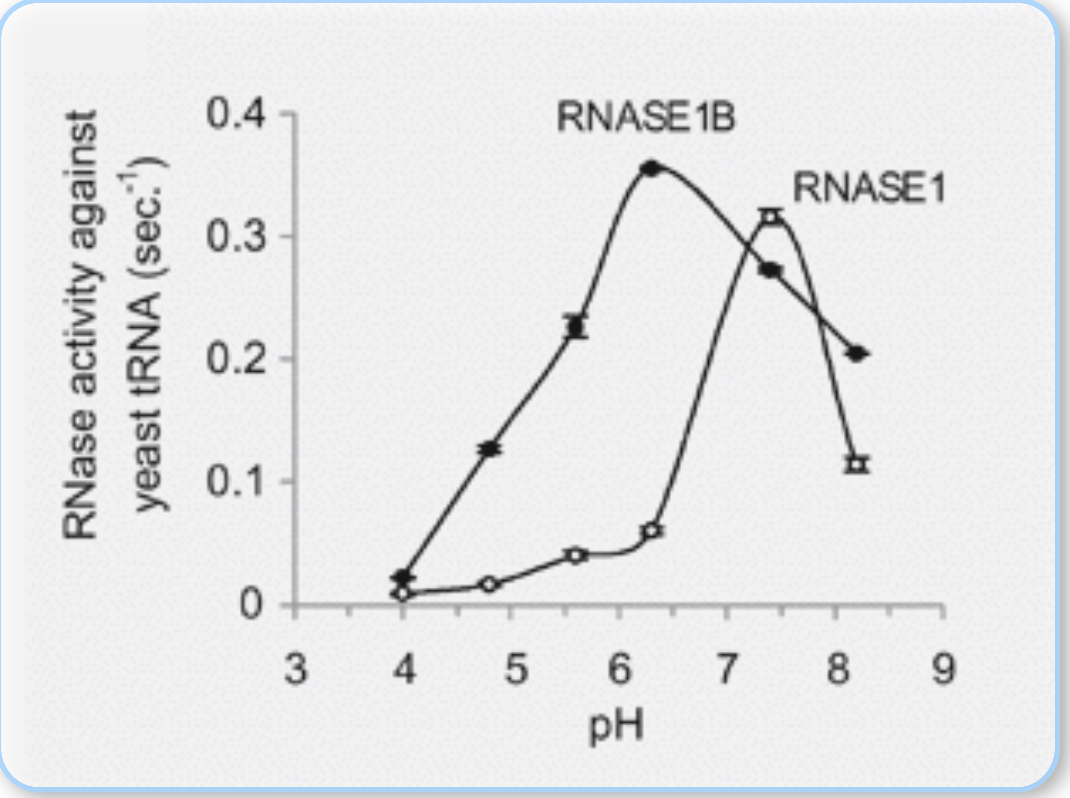
Ks = 0.0077

substitutions per synonymous sites
(and non-coding sites)

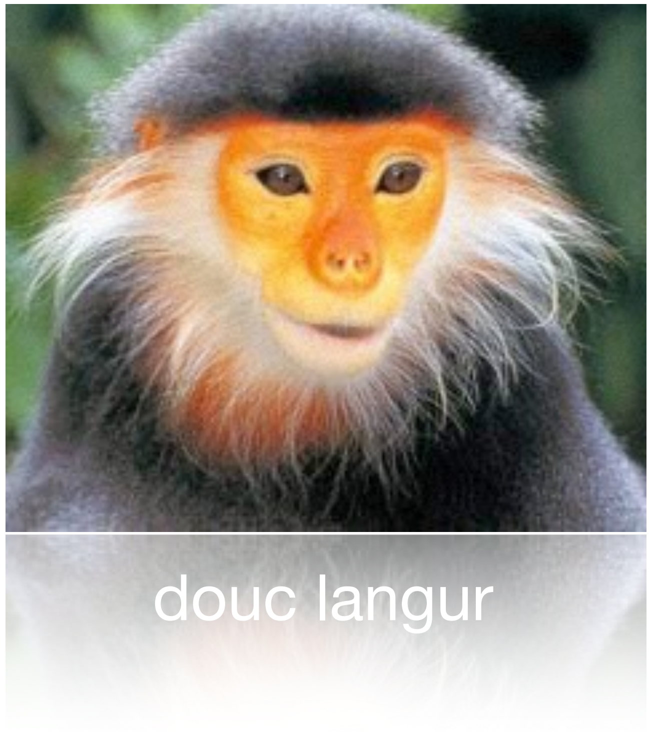
Ka/Ks = 4.026

Adaptive Sequence Evolution

Pancreatic ribonuclease in colobine monkeys



Zhang et al. (2002)

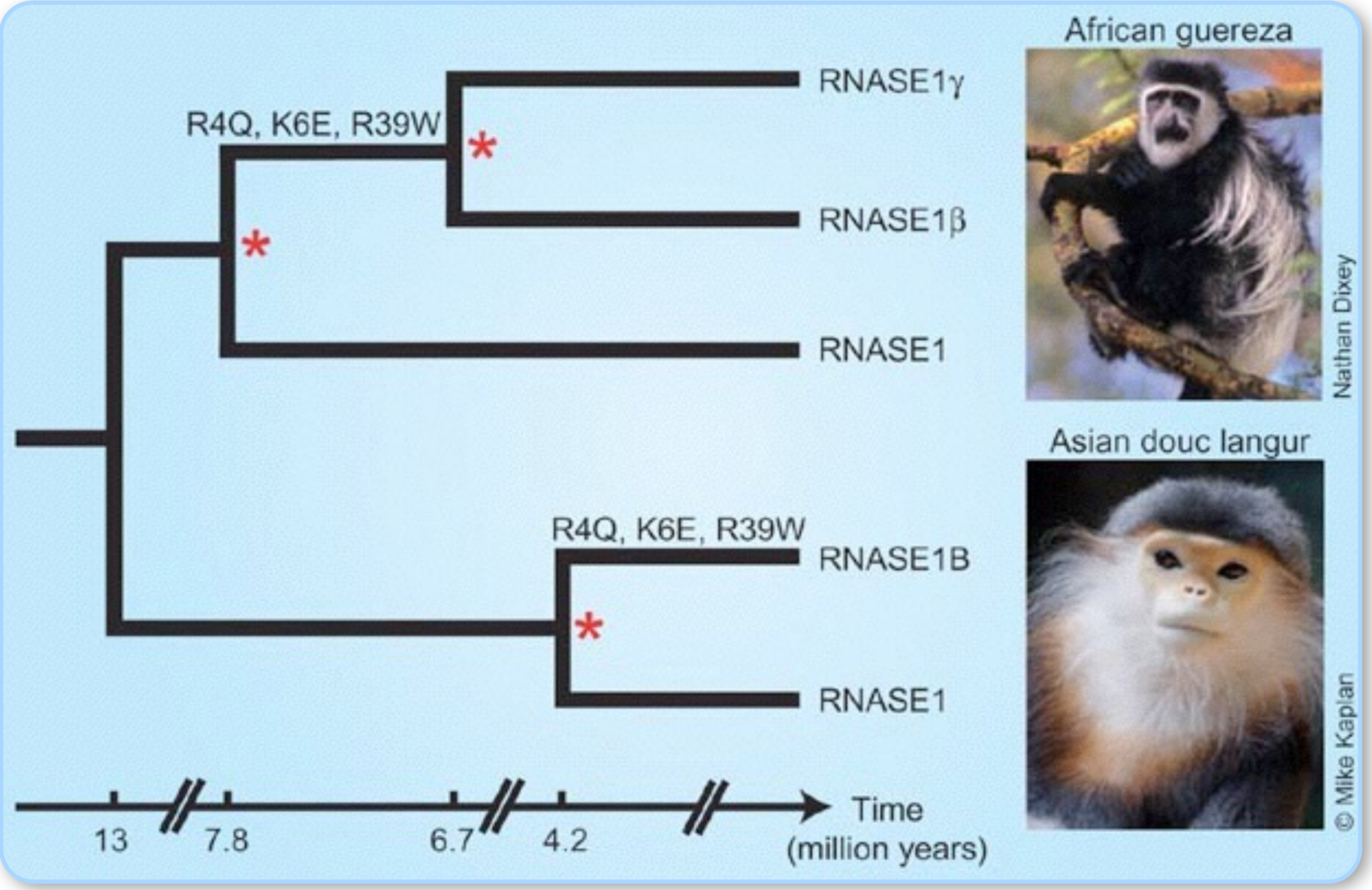


douc langur

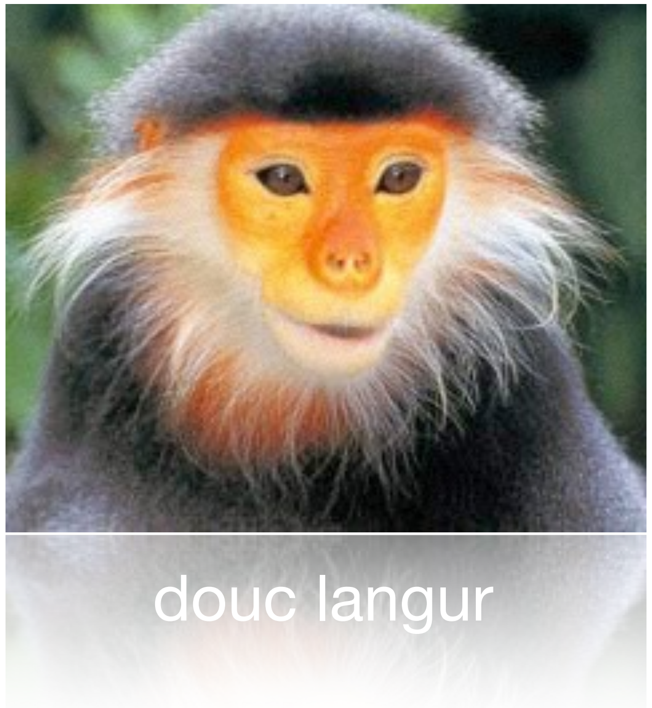
adaptation to different pH in the colobine small intestine

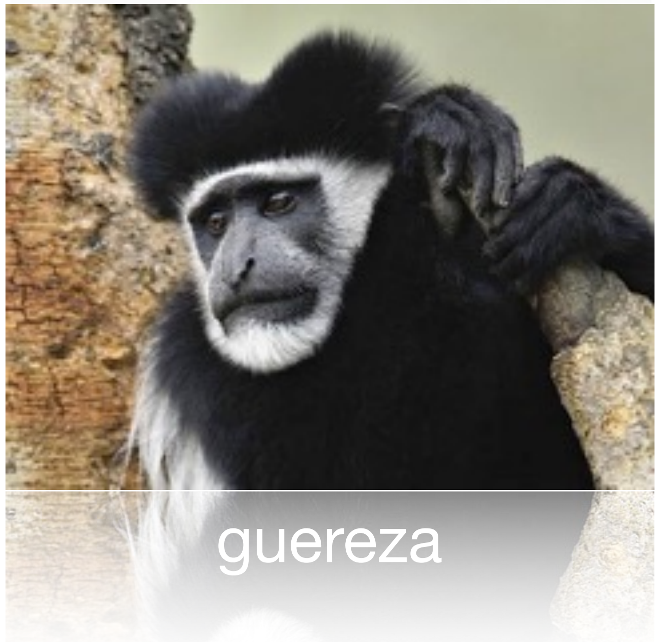
Adaptive Sequence Evolution

Pancreatic ribonuclease in leaf-eating monkeys



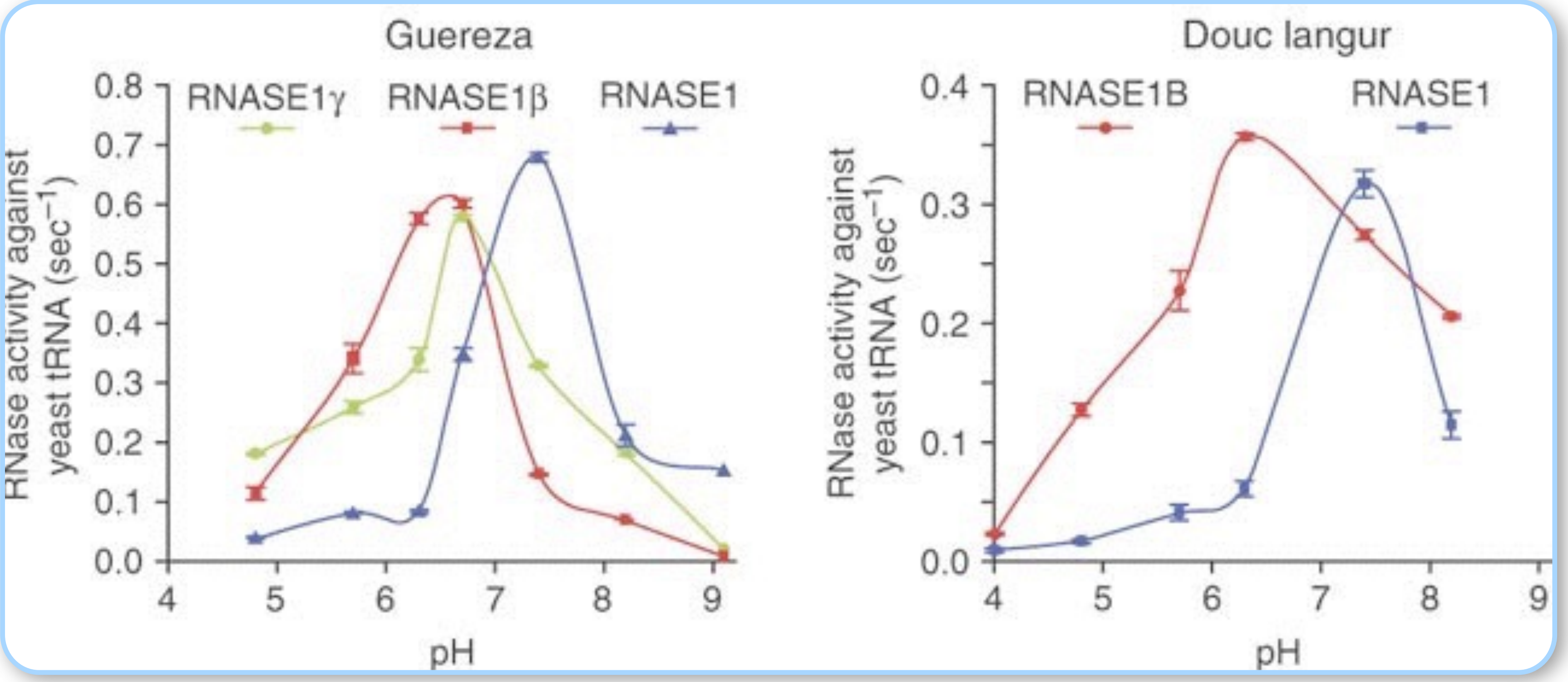
Prud'homme & Carroll (2006)



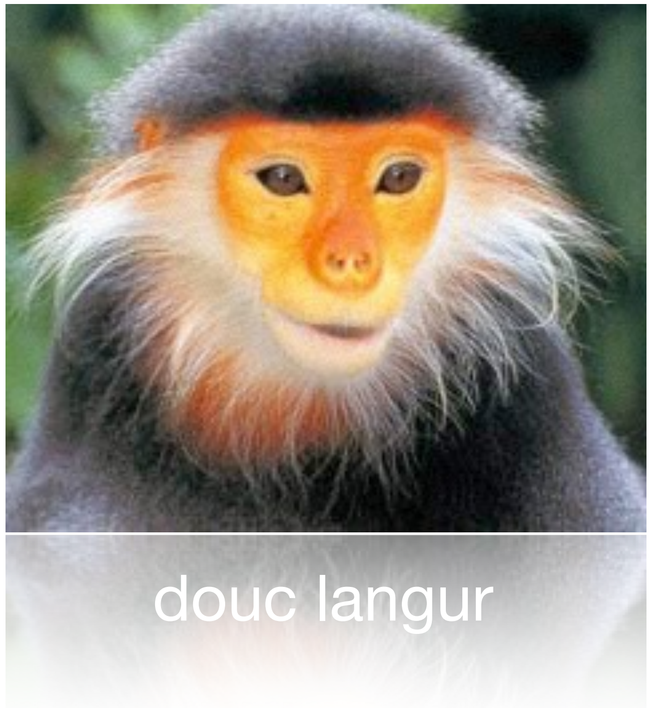


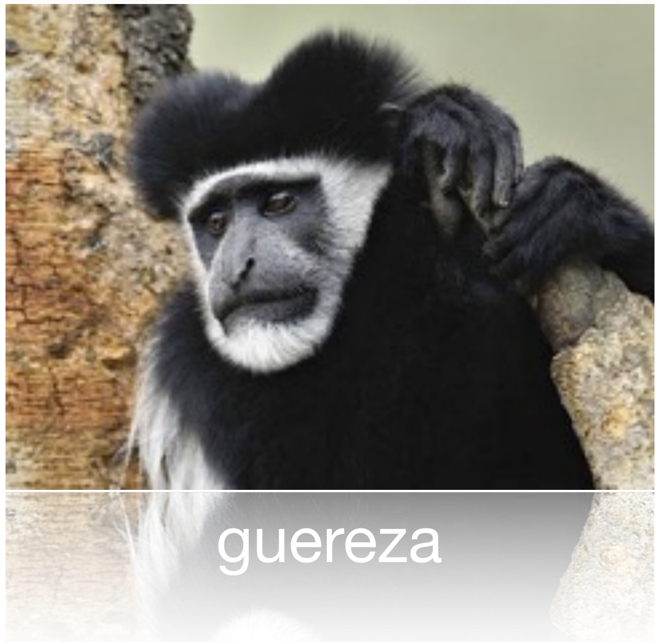
Adaptive Sequence Evolution

Pancreatic ribonuclease in leaf-eating monkeys



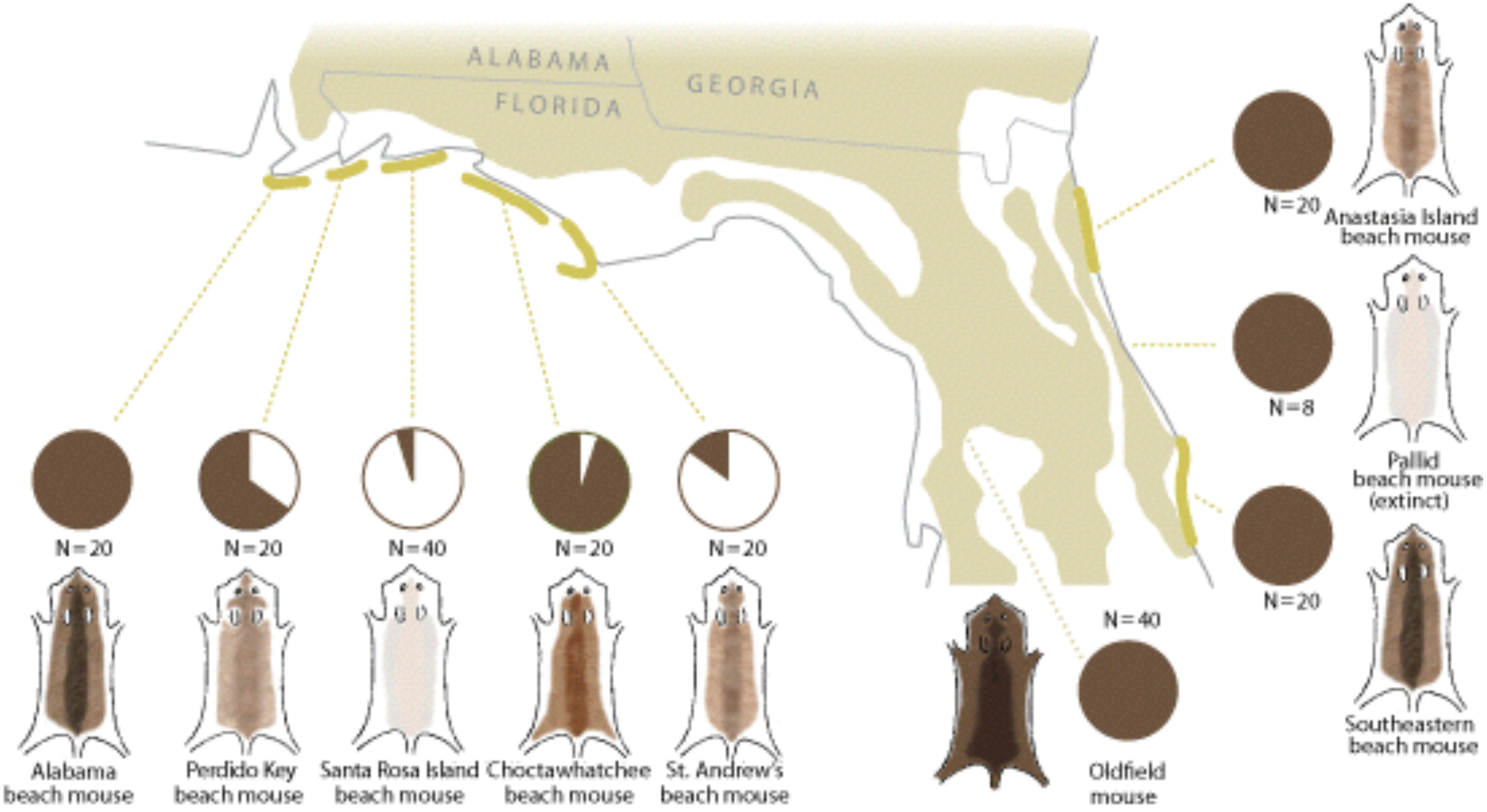
Zhang (2006)





Coding Sequence Evolution

beach mice



Hoekstra et al. (2006)

Coding Sequence Evolution

beach mice

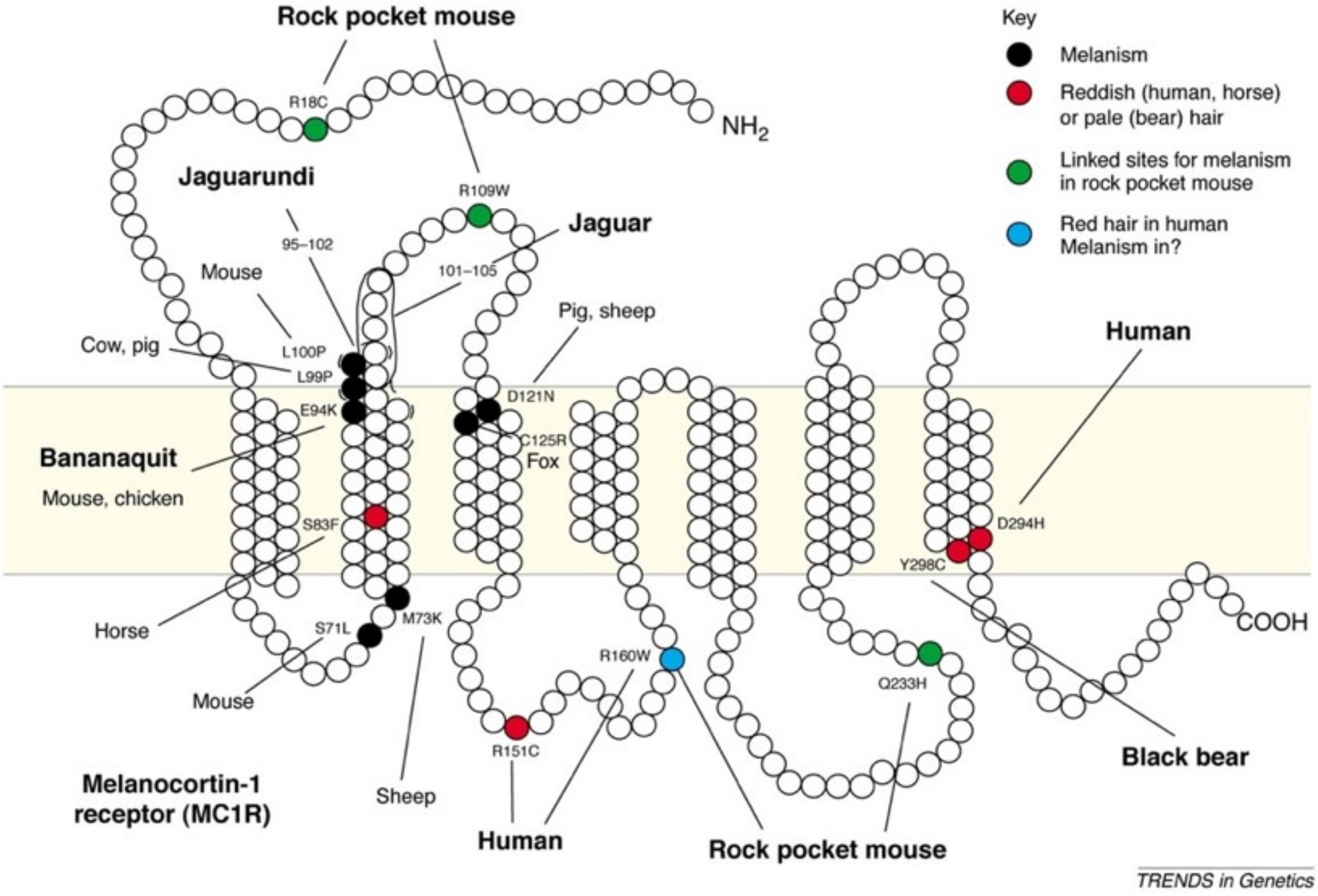
Nachman et al. (2003)

Coding Sequence Evolution

phenotype	***mc1r* alignment position**								
	52	**205**	**313**	**325**	**478**	**633**	**699**	**720**	**819**
dark (1371)	T	C	G	T	T	C	C	T	C
	.	.	.	.	.	.	.	.	.
dark (1373)	.	.	T	.	.	.	.	.	.
	.	.	.	.	.	.	.	.	.
dark (1384)	.	.	T	.	.	.	.	.	.
	C	.	.	C	C	T	A	.	.
dark (1412)	.	.	.	.	.	.	.	.	.
	C	T	.	C	C	T	A	.	.
light (1387)	C	.	.	C	C	T	A	G	T
	C	.	.	C	C	T	A	G	T
light (1403)	C	.	.	C	C	T	A	.	.
	C	.	.	C	C	T	A	.	.
AS change	R<>C			R<>W	R<>W		Q<>H		
AS position	18			109	160		233		

Nachman et al. (2003)

Coding Sequence Evolution



Majerus & Mundy (2003)

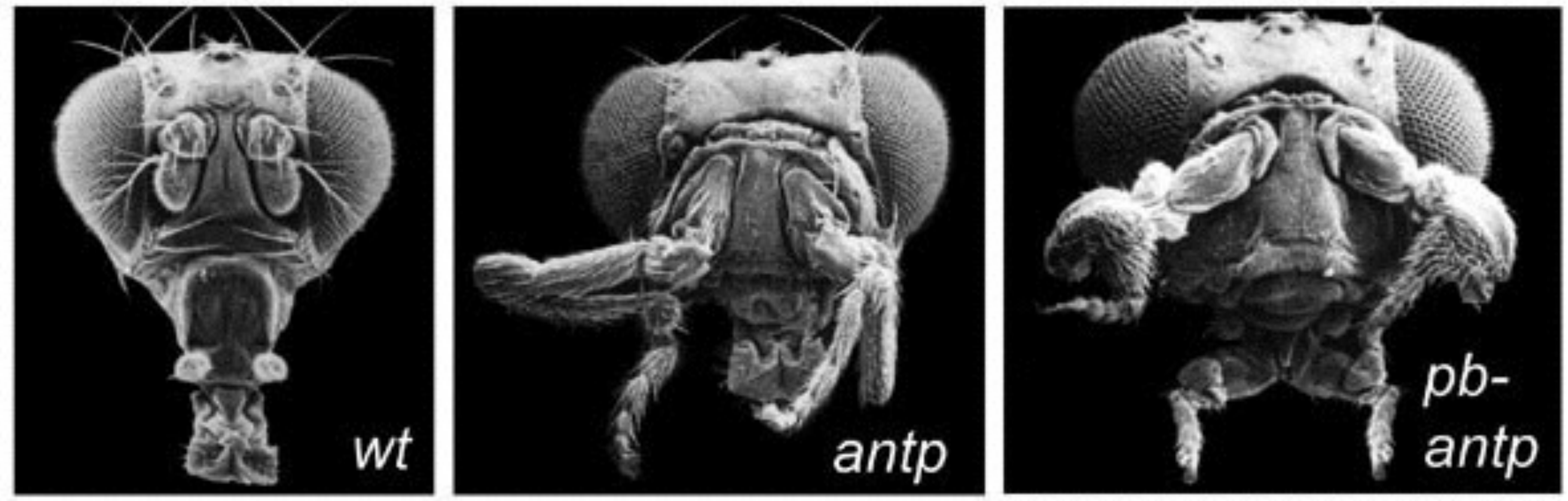
Regulatory Evolution

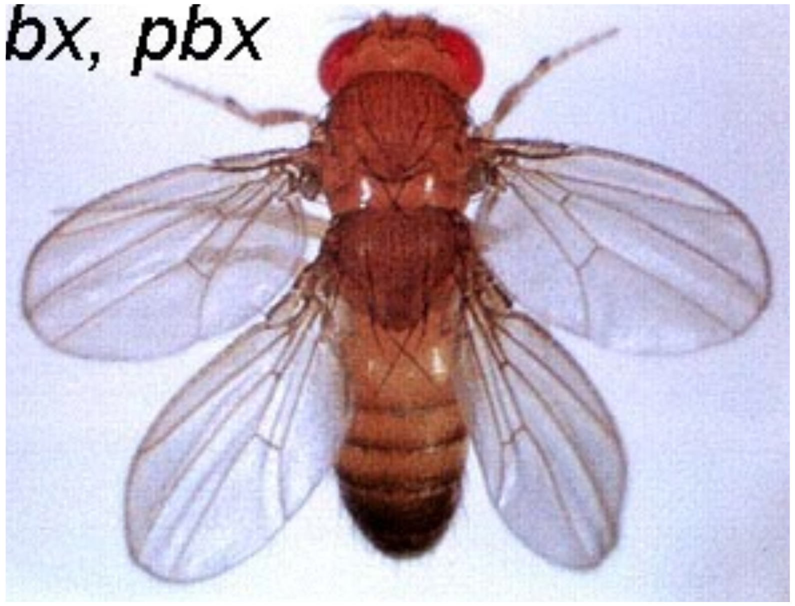
Hox genes

- **=homeotic genes:** genes that regulate the identity of body regions
- Hox genes contain a **homeobox**, a 180 bp region of DNA encoding a particular class of DNA-binding domains. Approximately 20 families of homeobox-containing genes exist.
- The homeobox encodes the **homeodomain**
- Mutations in homeotic genes cause the transformation of one body region or part into the likeness of another

Regulatory Evolution

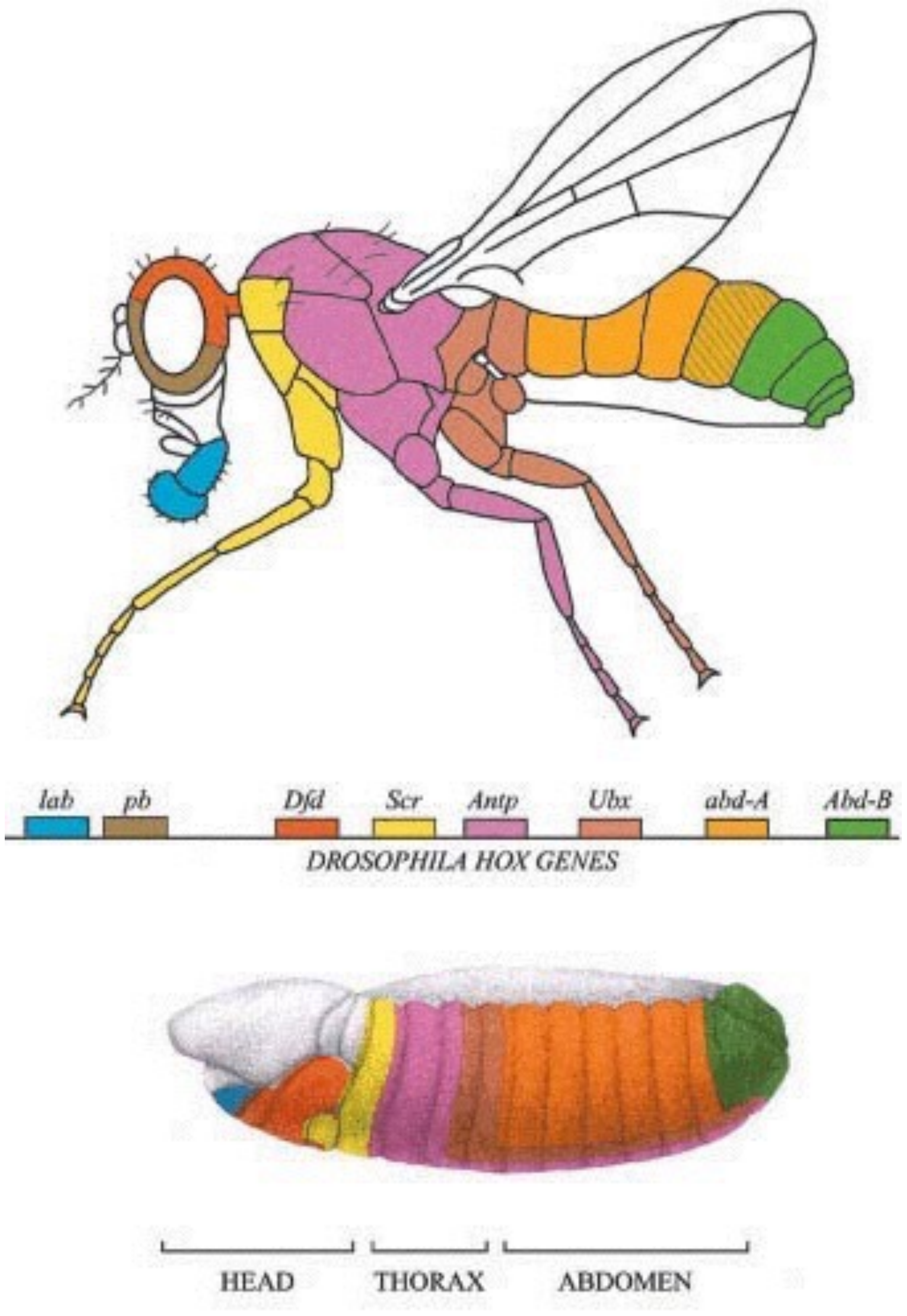
Hox genes, Drosophila





Regulatory Evolution

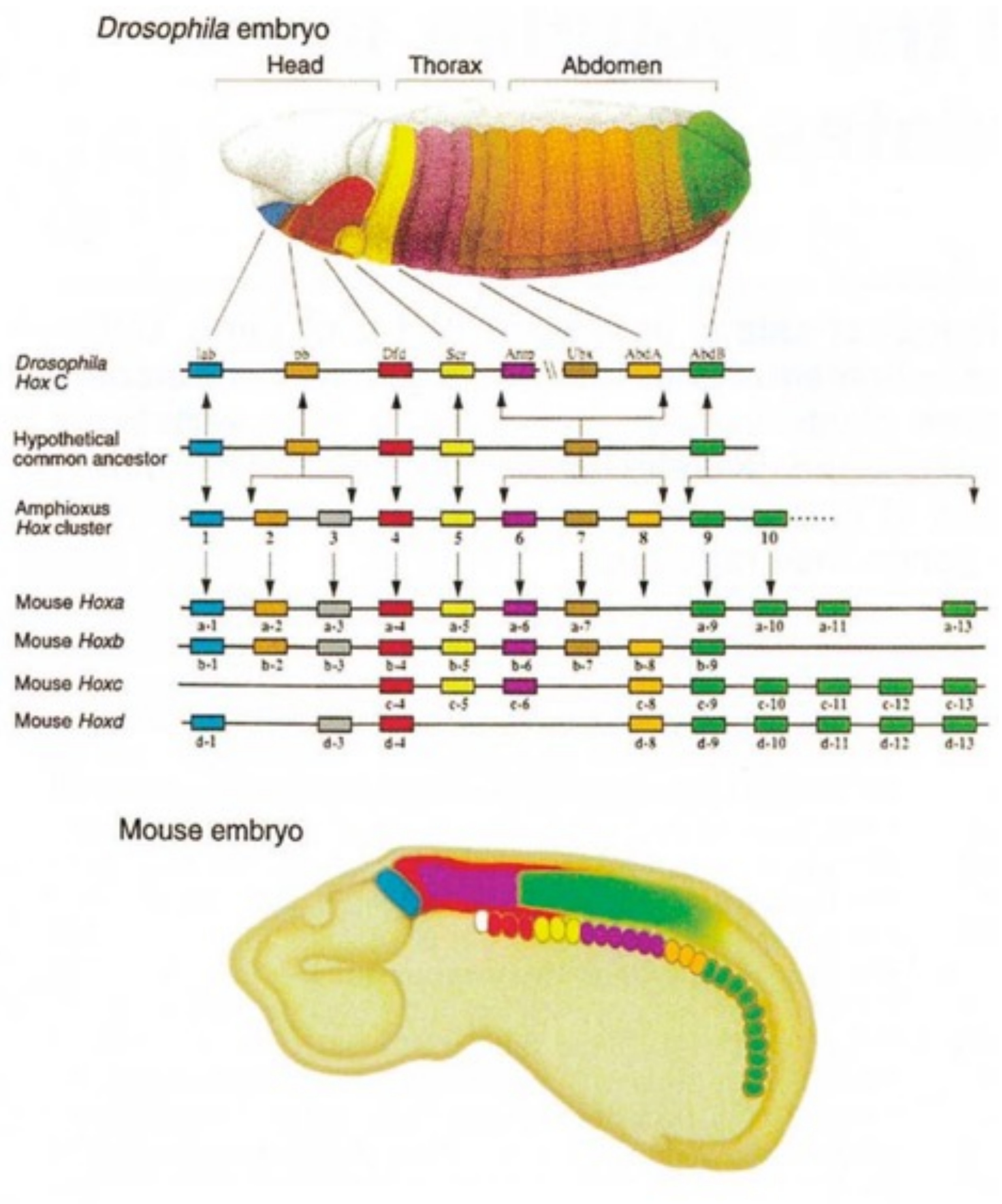
Hox genes and animal body plan



Carroll et al. (2001)

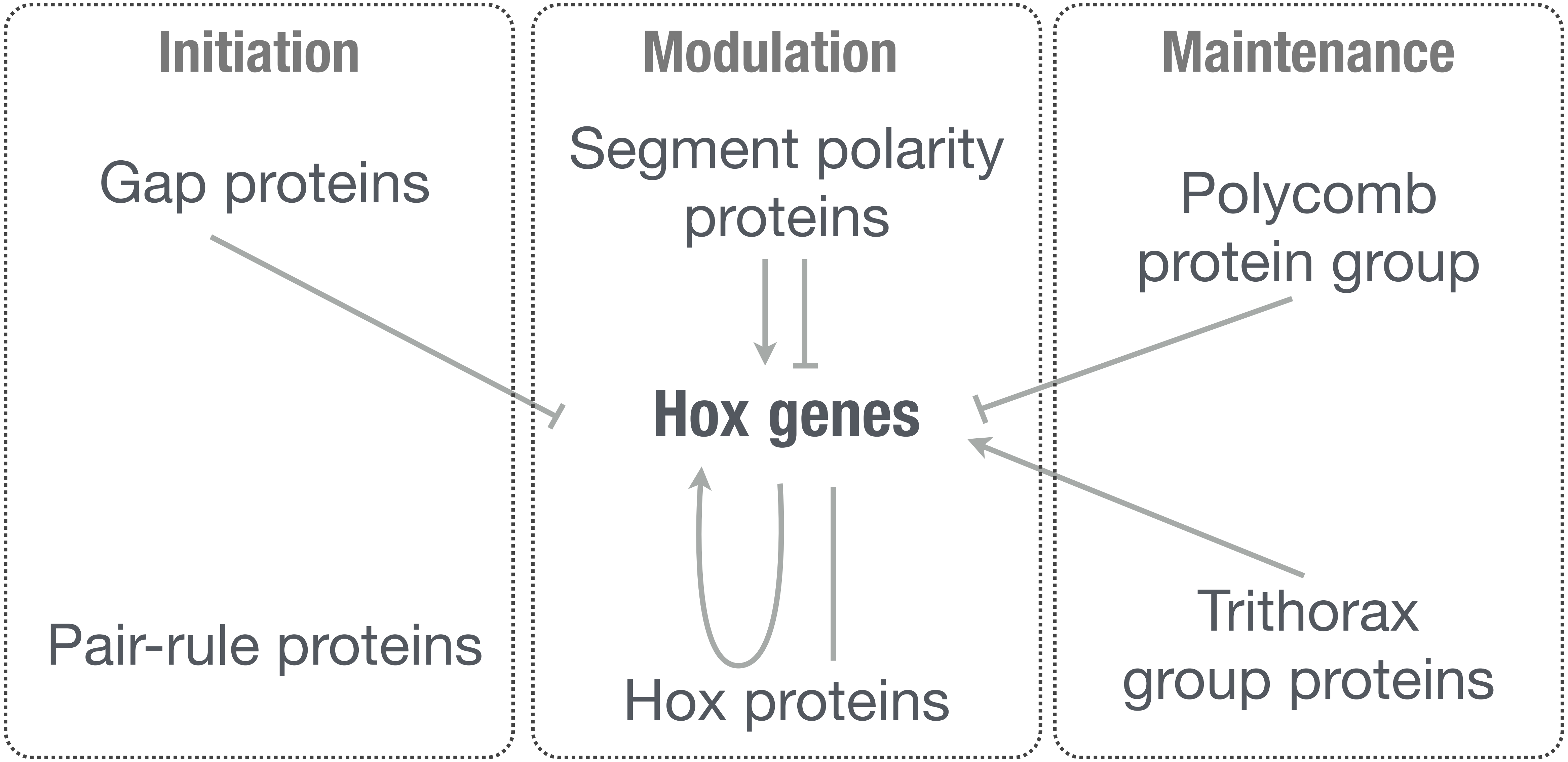
Regulatory Evolution

Hox genes and animal body plan



Carroll et al. (2001)

Hox gene regulation



Initiation

Gap proteins

Pair-rule proteins

Modulation

Segment polarity proteins

Hox genes

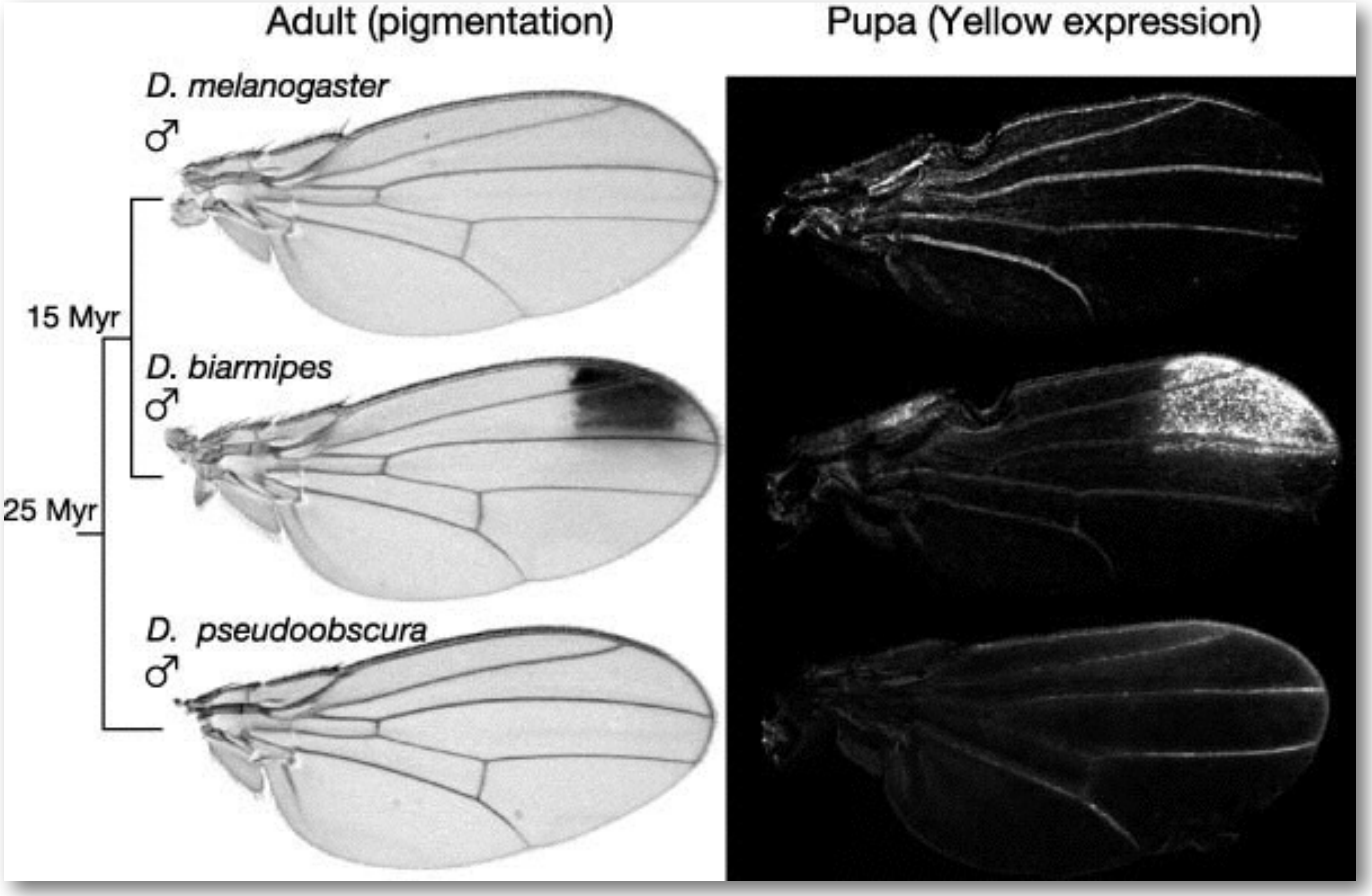
Hox proteins

Maintenance

Polycomb protein group

Trithorax group proteins

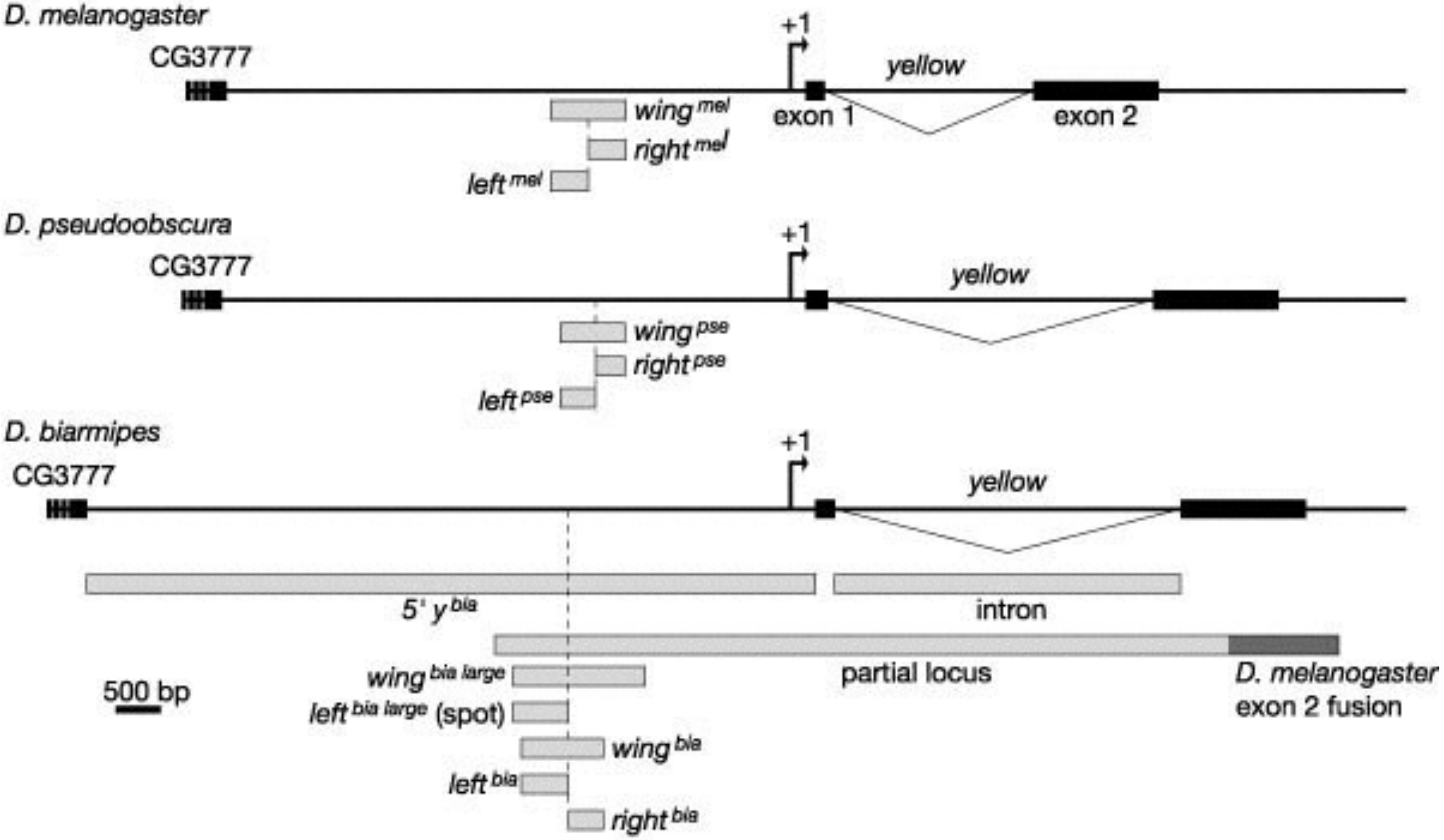
cis-regulatory evolution, Drosophila



Gompel et al. 2005

Regulatory Evolution

cis-regulatory evolution, Drosophila

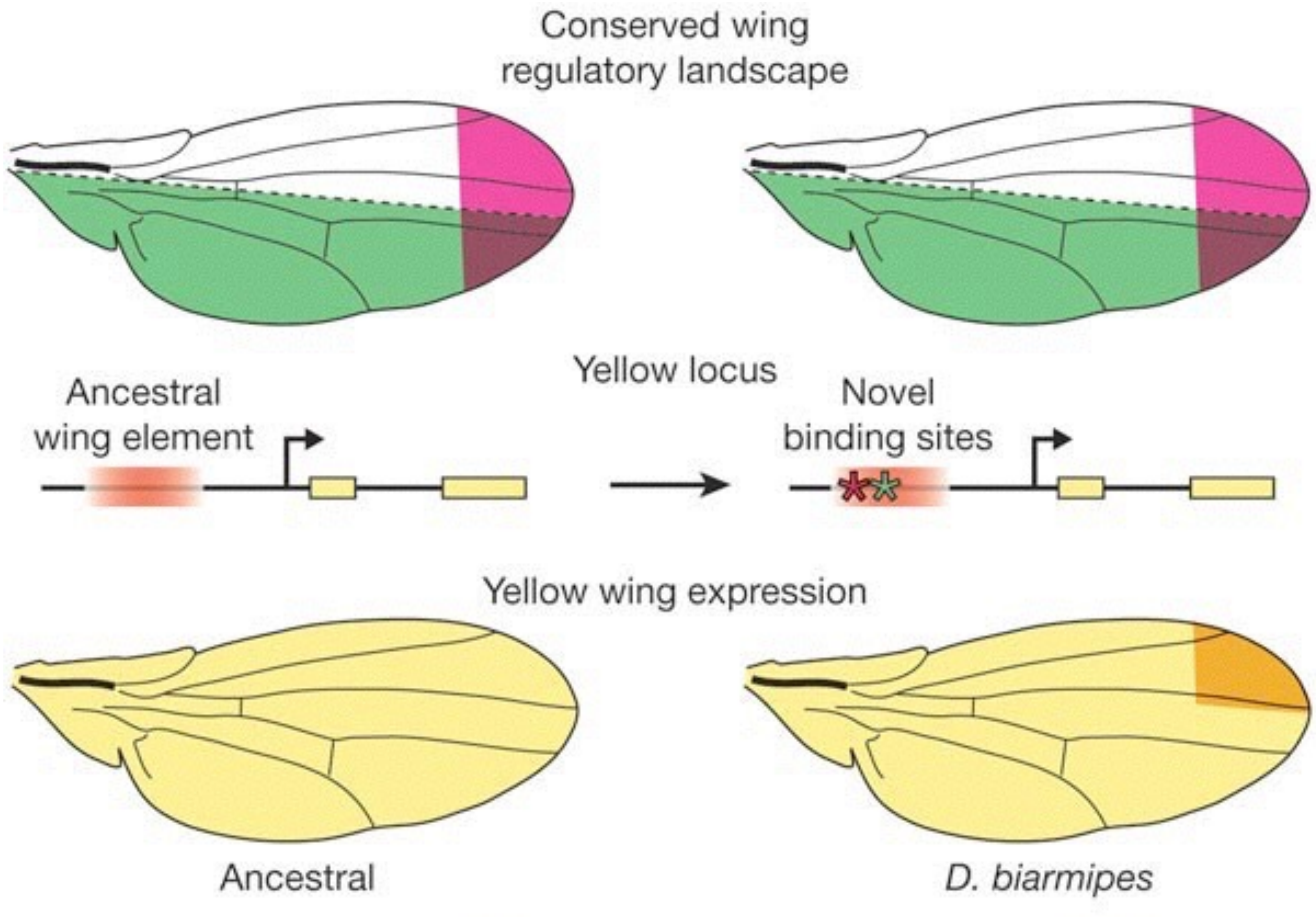


Gompel et al. 2005

yellow locus

Regulatory Evolution

cis-regulatory evolution, Drosophila



Gompel et al. 2005

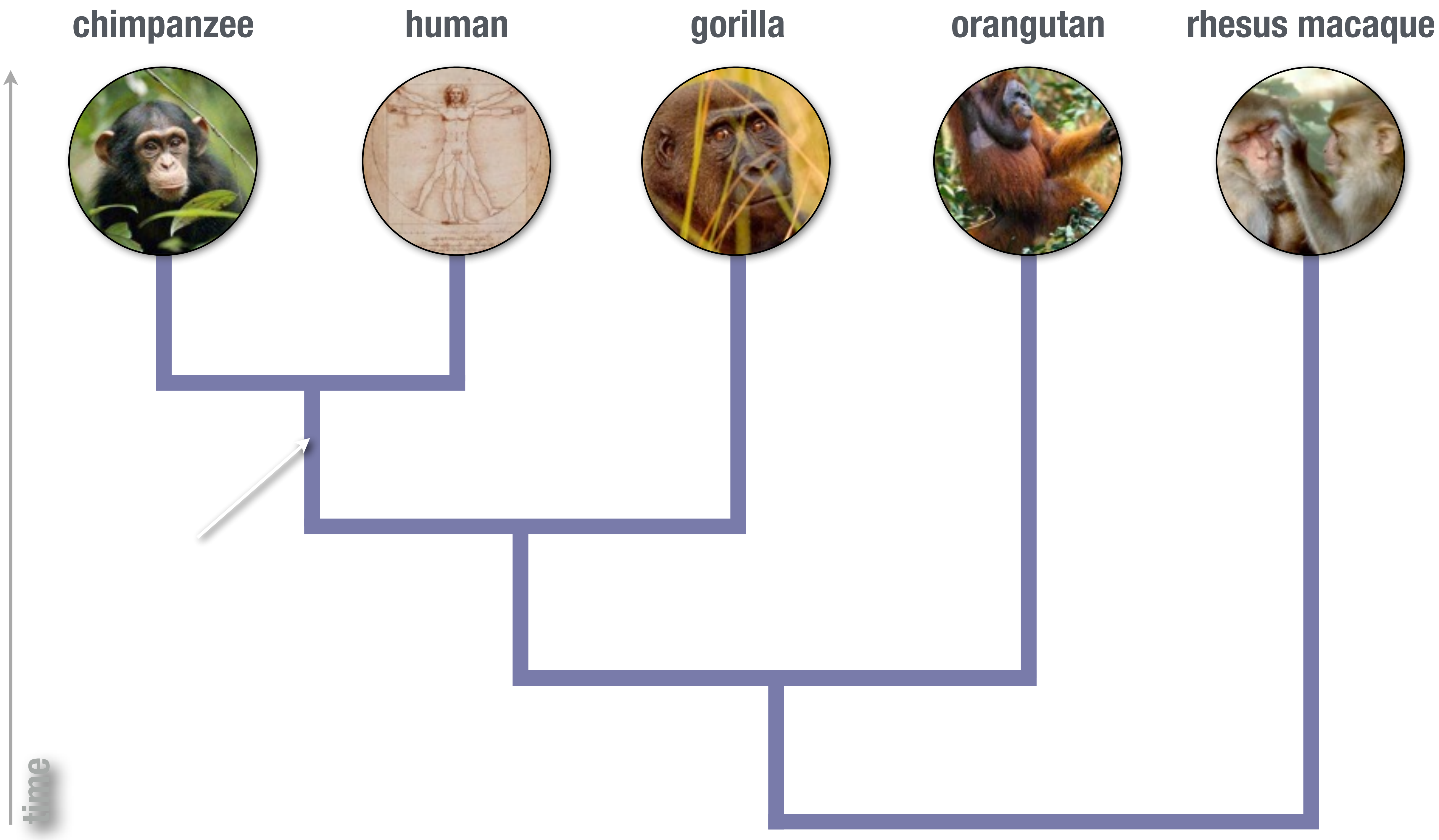
Phylogeny

“The tree of life”, Gustav Klimt (1907)

What is a phylogeny?

- A **phylogney=phylogenetic tree=evolutionary tree=tree** is a **branching diagram...**
- **...**that shows the evolutionary relationships between taxa.
- A **taxon** is a named taxonomic group, *e.g.*:
  - a family (*Felidae*)
  - a genus (*Felis*)
  - a species (*Felis catus*)
  - a single individual (‘Nufta’)

What is a phylogeny?



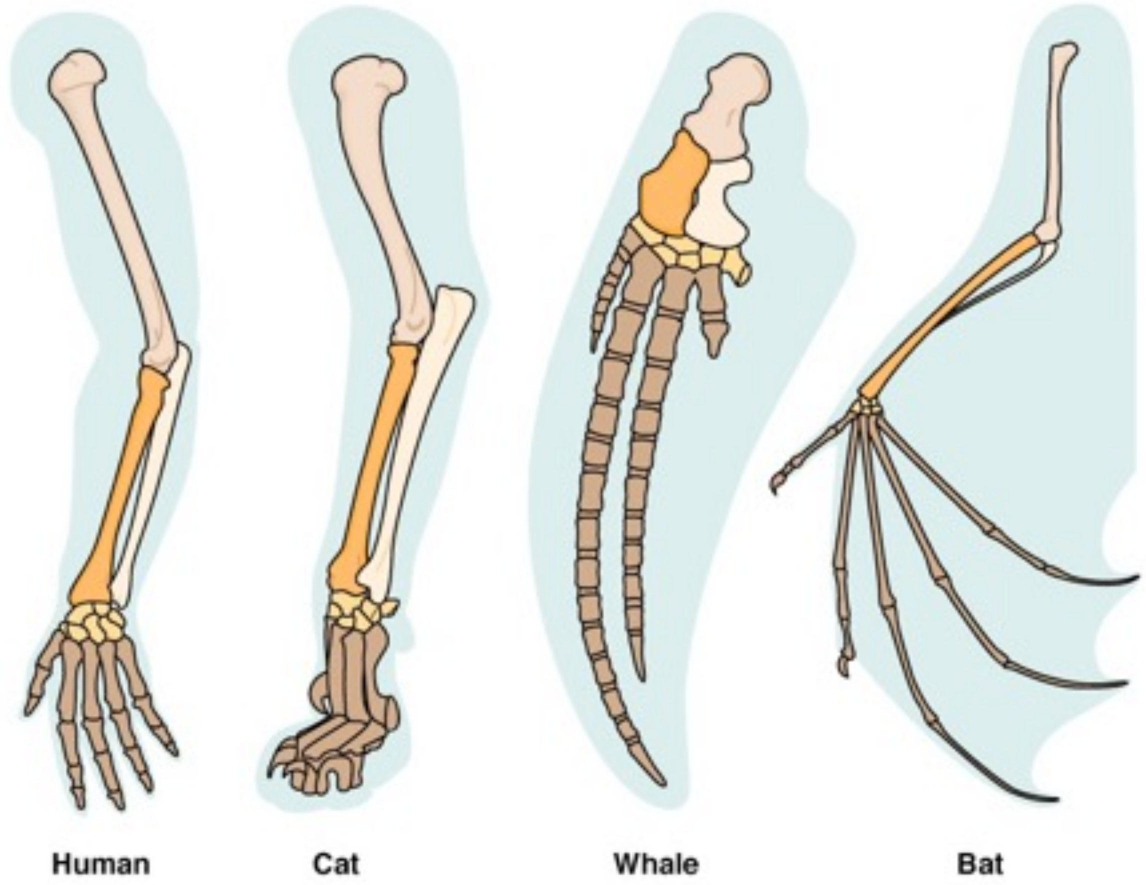
images: National Geographic, Leonardo da Vinci

Phylogeny reconstruction

- **Phylogenies** are inferred from **homologous characters**

Homology:

A homology is a character that is shared between two or more species and that was already present in their common ancestor. Hence, (morphological) similarity between homologous characters is due to common ancestry.



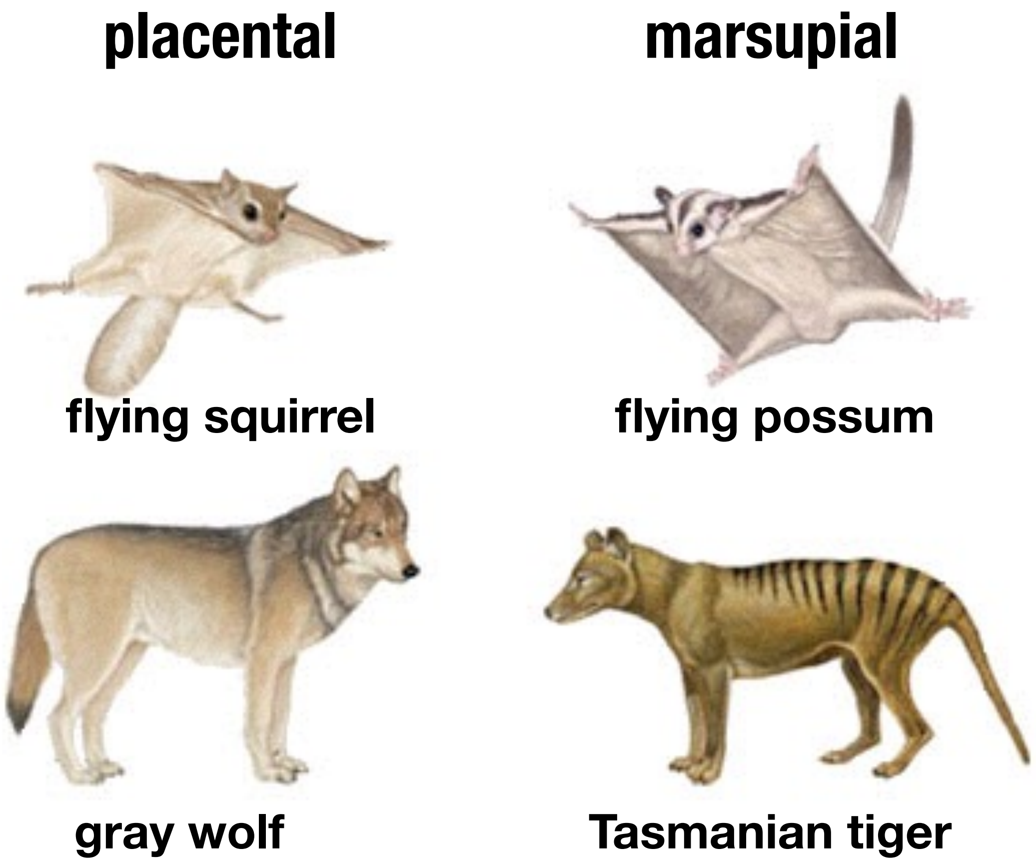
©1999 Addison Wesley Longman, Inc.

Phylogeny reconstruction

- **Phylogenies cannot** be inferred from **homoplasious characters**

Homoplasy:

A homoplasy is a character that is shared between two or more species and that was **not** present in their common ancestor. Similarity between homoplasious characters is **not** due to shared ancestry (but due to *e.g.*, chance or similar selection regimes).



images: Encyclopaedia Britannica

Phylogeny reconstruction

- **Homology** can be inferred by several **criteria**

structural similarity	Homologous characters are likely to have the **same fundamental structure**.
relations between parts	Homologous characters usually have the **same relations to surrounding characters** (*e.g.*, homologous bones are connected in a similar way with their neighboring bones).
embryonic development	Homologous characters are likely to have the **same embryonic development.** A character that looks similar in adult forms but has a different developmental history, is unlikely to be homologous.
intermediate forms	Characters are likely to be homologous, if they can be **linked through intermediate forms** (*e.g.*, homology between swim bladder of fishes and tetrapod lungs).

Phylogeny reconstruction

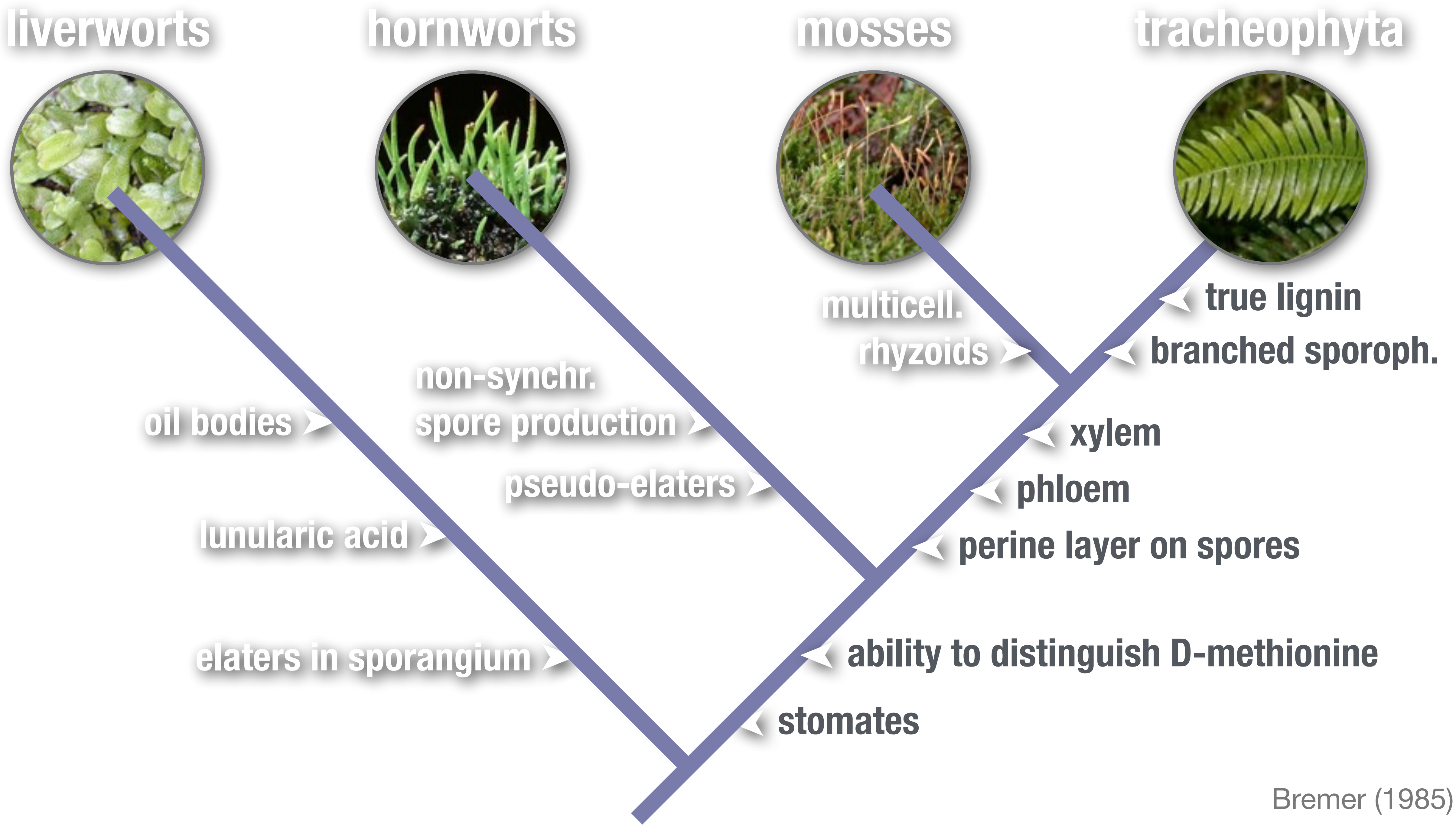
- Phylogenies can be inferred from **morphological characters** using **cladistic techniques***:
  - “morphological” refers to all observable characters in an organism: meristic and morphometric measurements; physiological, reproductive, behavioral characteristics, etc.
  - cladistic techniques are (usually) the only way to analyze fossil data

- Nowadays, phylogenies are inferred from **genetic data** using **phylogenetic techniques***:
  - genetic data are homologous by nature (“the ultimate homologous data”)
  - “Molecular phylogenetics” uses sophisticated statistical techniques based on discrete models of DNA sequence evolution

*Some of the analyses used are the same for morphological and genetic data

Phylogeny reconstruction

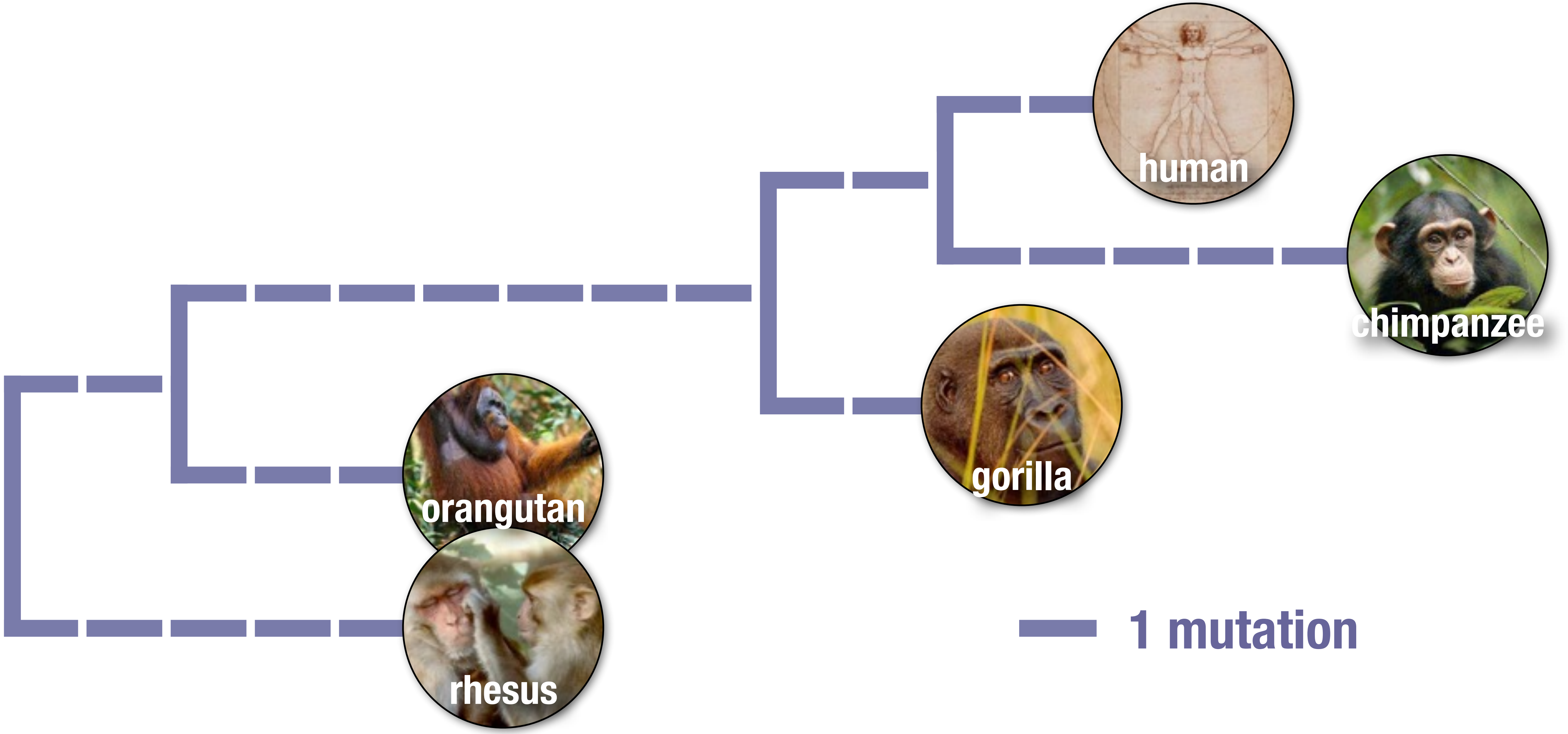
- Phylogeny of plants based on **morphological characters**



Bremer (1985)

Phylogeny reconstruction

- Phylogeny of higher primates based on **genetic characters**



phylogeny based on DNA sequences of the *foxp2* gene (Enard et al. 2002)