

Principles of evolution (BIO 351)



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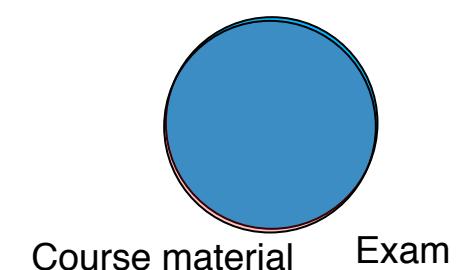
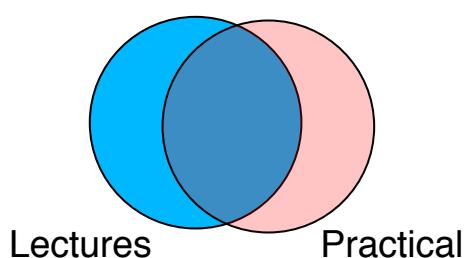
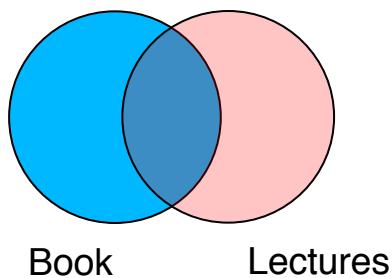
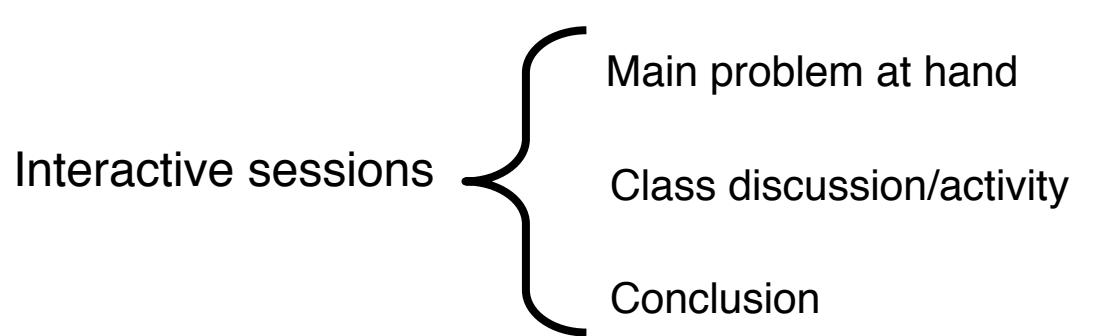
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General structure of the course



Theory + Practical Session

Variation among individuals

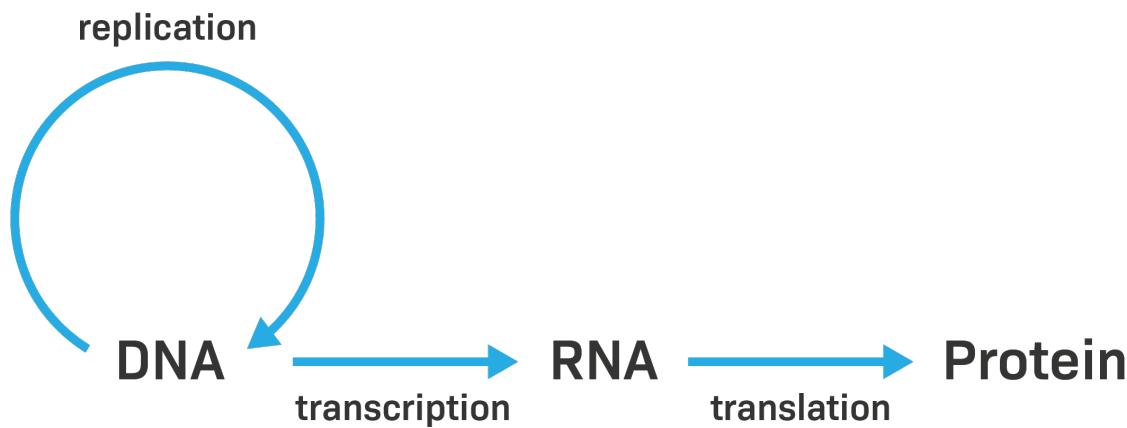


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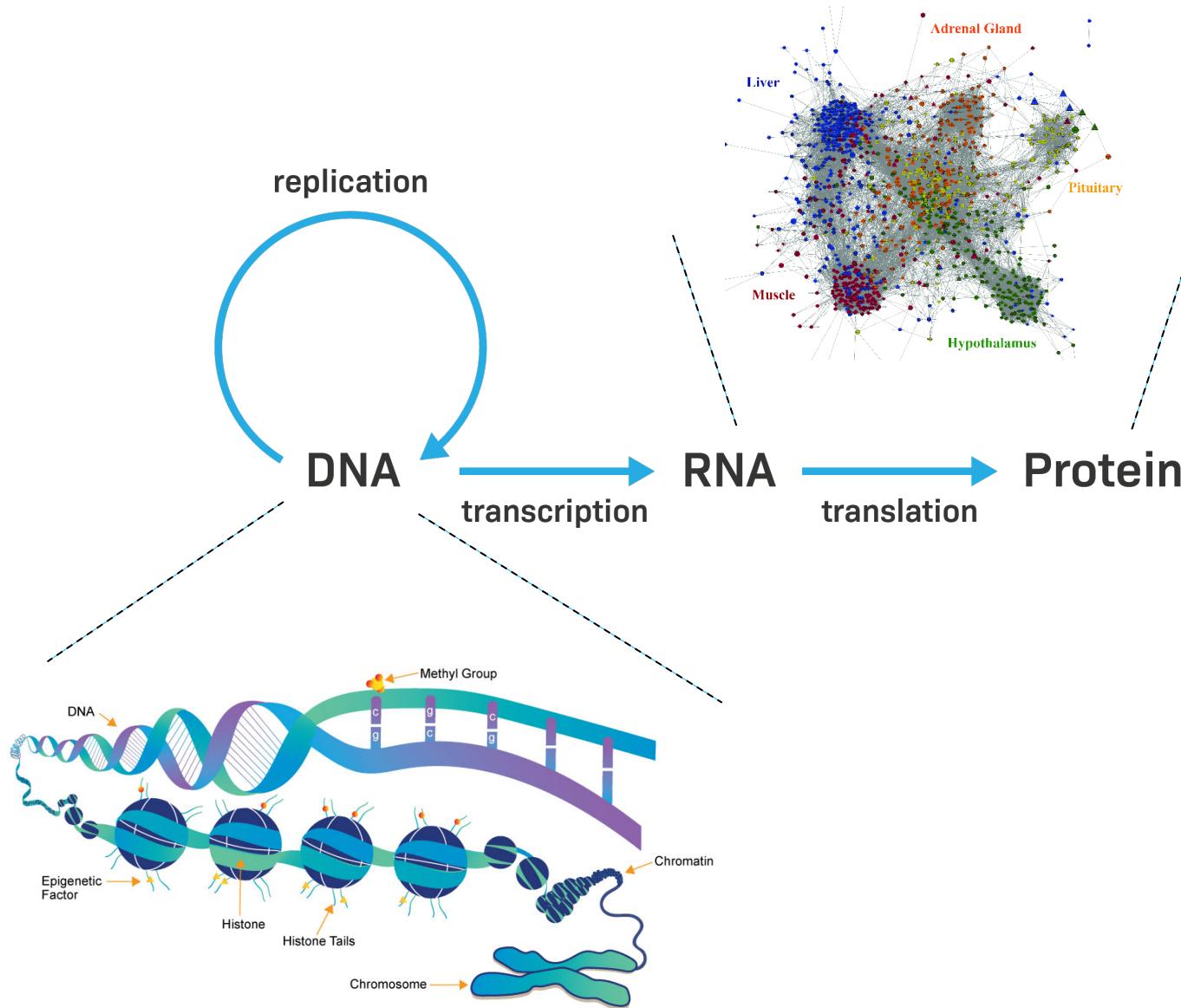
Figure 5.1 Variation among individuals Top, whiskerbrush (*Linanthus ciliatus*). Photo by Eric Knapp. Center, bat stars (*Asterina miniata*). Bottom, variable ground snakes (*Sonora semiannulata*). Photo by Alison Davis Rabosky and Christian Cox.

The sources of variation

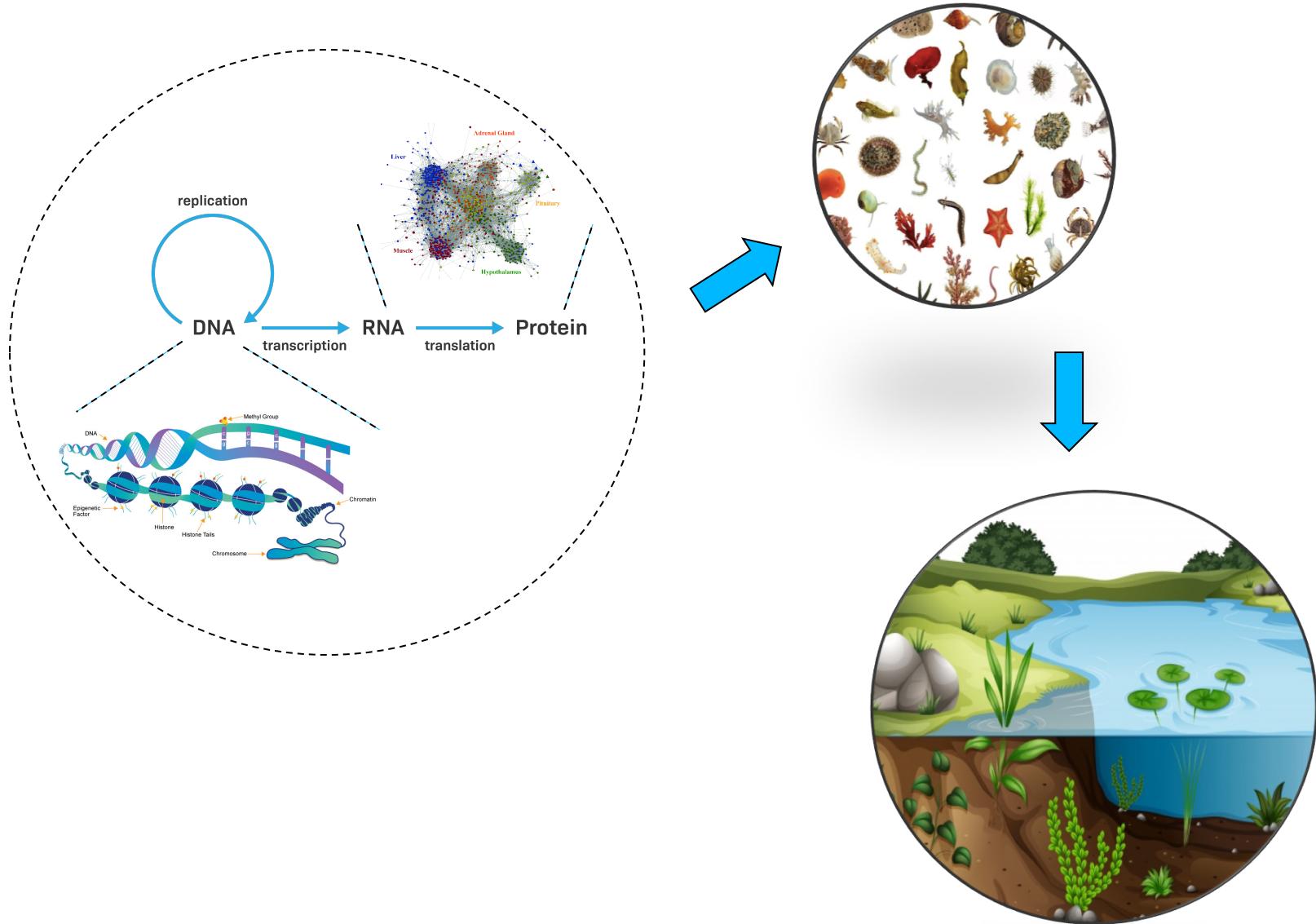


Central dogma of molecular biology

The sources of variation



Interaction with environment



Group projects (different types of variation)

Project 1: Genetic variation for bitter taste perception

Project 2: Inducible defenses in *Daphnia*

Project 3: Random variation in protein production

Project 4: A heritable epigenetic variant

Project 5: Sex determination in leopard geckos

If different kinds of variation exists,
why do we care “so much” about genetic variation?



Point mutations

Single base pair changes

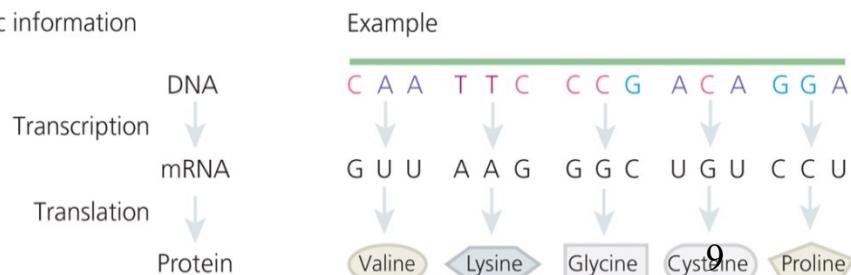
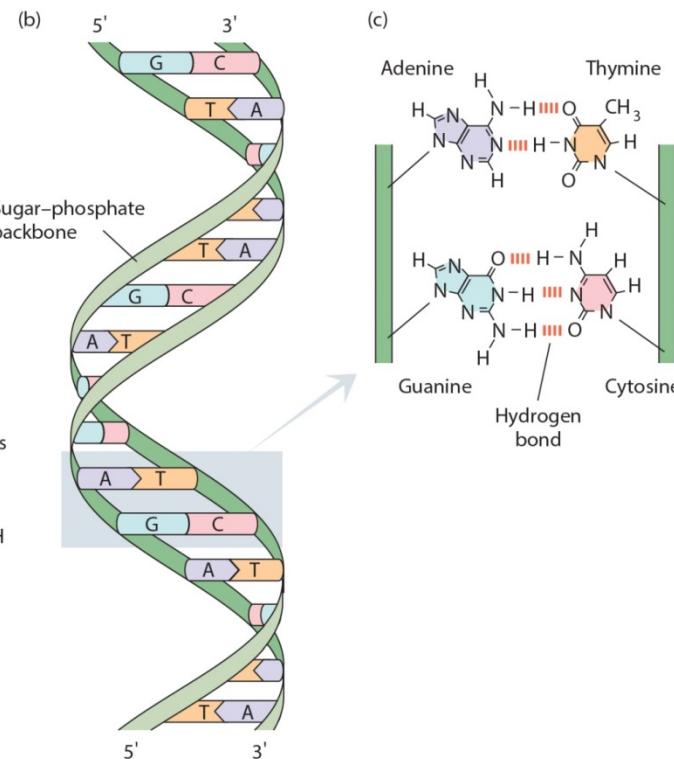
Historically the first characterized (1958): mutation causing sickle-cell anemia

GAG → GTG
glutamic acid → valine
at amino acid 6 of β-globin

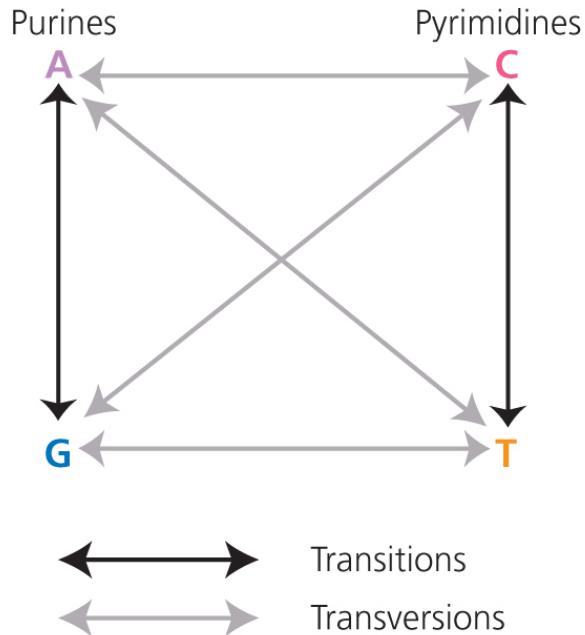
create new **alleles** (variants of a gene)

caused by
replication errors
chemical mutagens
radiation

related small changes: **indels**
(insertions or deletions)



Two main kinds of point mutations



Transitions are more frequent than transversions
e.g. 1.6:1 in the roundworm *C. elegans*

probably because transversions are more disruptive
and thus more likely to be detected and repaired

(The sickle-cell anemia mutation is a transversion.)

Redundancy of the genetic code

(b) The RNA genetic code

First base	Second base												Third base
	U			C			A			G			
U	UUU	Phenylalanine	UCU	Serine			UAU	Tyrosine		UGU	Cysteine		U C A G
	UUC	Phenylalanine	UCC	Serine			UAC	Tyrosine		UGC	Cysteine		
	UUA	Leucine	UCA	Serine			UAA	Stop		UGA	Stop		
	UUG	Leucine	UCG	Serine			UAG	Stop		UGG	Tryptophan		
C	CUU	Leucine	CCU	Proline			CAU	Histidine		CGU	Arginine		U C A G
	CUC	Leucine	CCC	Proline			CAC	Histidine		CGC	Arginine		
	CUA	Leucine	CCA	Proline			CAA	Glutamine		CGA	Arginine		
	CUG	Leucine	CCG	Proline			CAG	Glutamine		CGG	Arginine		
A	AUU	Isoleucine	ACU	Threonine			AAU	Asparagine		AGU	Serine		U C A G
	AUC	Isoleucine	ACC	Threonine			AAC	Asparagine		AGC	Serine		
	AUA	Isoleucine	ACA	Threonine			AAA	Lysine		AGA	Arginine		
	AUG	Start (Methionine)	ACG	Threonine			AAG	Lysine		AGG	Arginine		
G	GUU	Valine	GCU	Alanine			GAU	Aspartic acid		GGU	Glycine		U C A G
	GUC	Valine	GCC	Alanine			GAC	Aspartic acid		GGC	Glycine		
	GUA	Valine	GCA	Alanine			GAA	Glutamic acid		GGA	Glycine		
	GUG	Valine	GCG	Alanine			GAG	Glutamic acid		GGG	Glycine		

Codon Amino acid nonpolar polar basic acidic

Replacement (nonsynonymous) mutation: causes amino acid change
Silent (synonymous) mutation: causes no such change

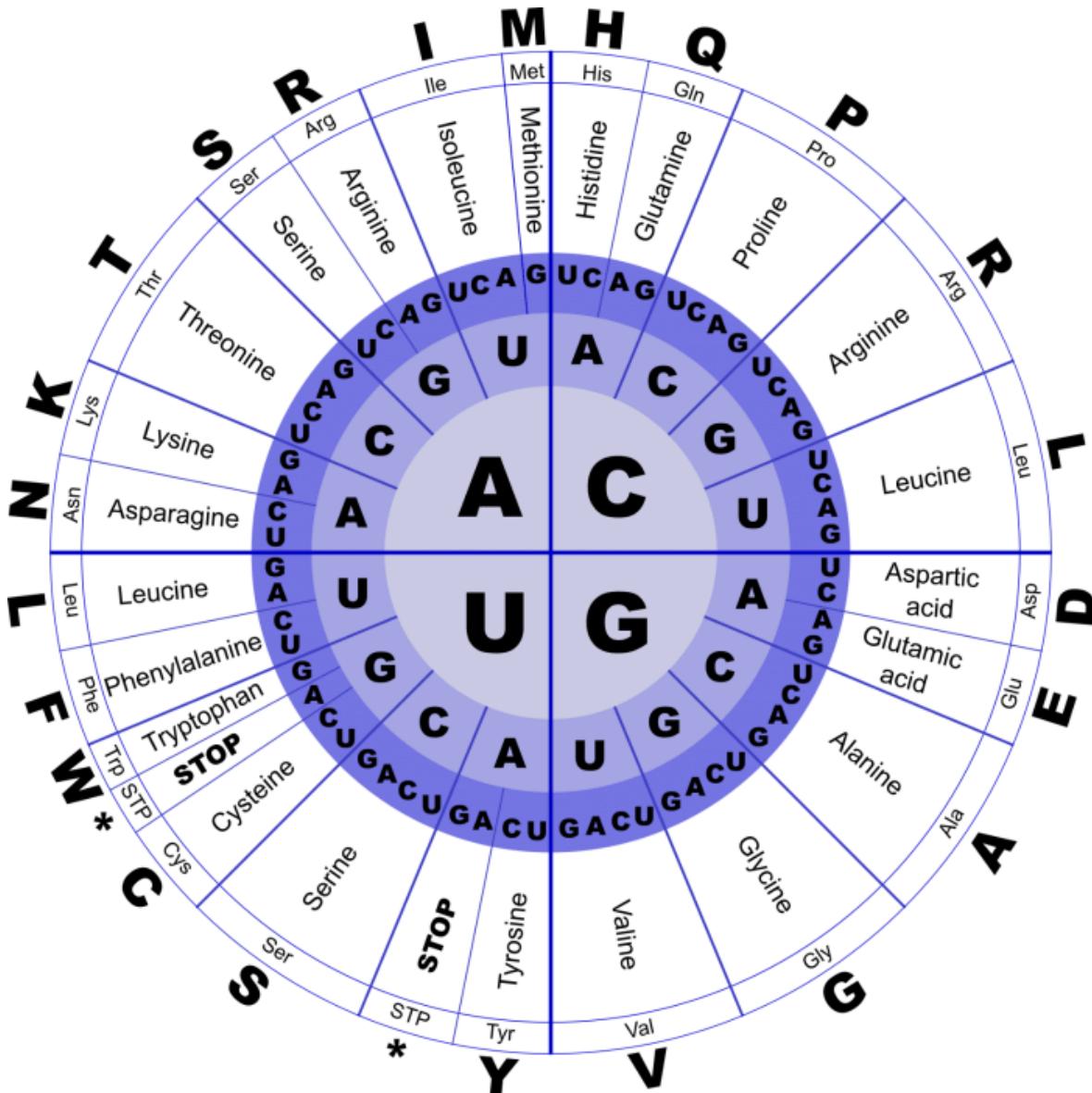
Most changes at 1st and 2nd codon positions are replacement changes

Many mutations at third positions are silent

Class activity

Amino acid
RNA base sequence
Mutation
Bases
A: adenine
C: cytosine
G: guanine
U: uracil

```
...CAGGAUGGUUAAC...
          ↓
...CAGGGUGGUUAAC...
```



Genetic code (RNA)

The case of D614G in SARS-CoV-2

nature

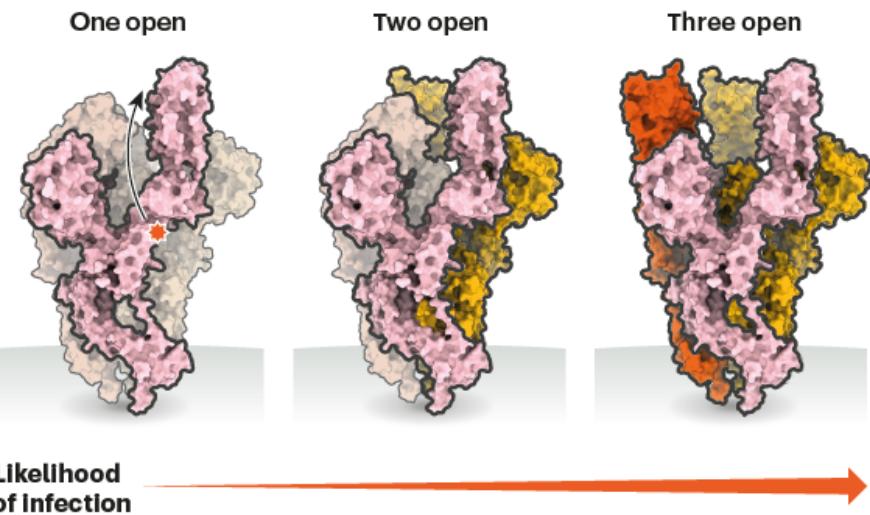
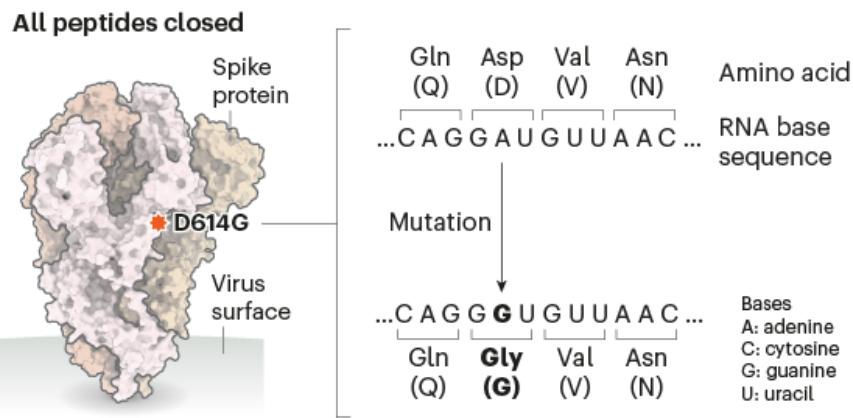
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NEWS FEATURE | 08 September 2020 | Correction [16 September 2020](#)

The coronavirus is mutating – does it matter?

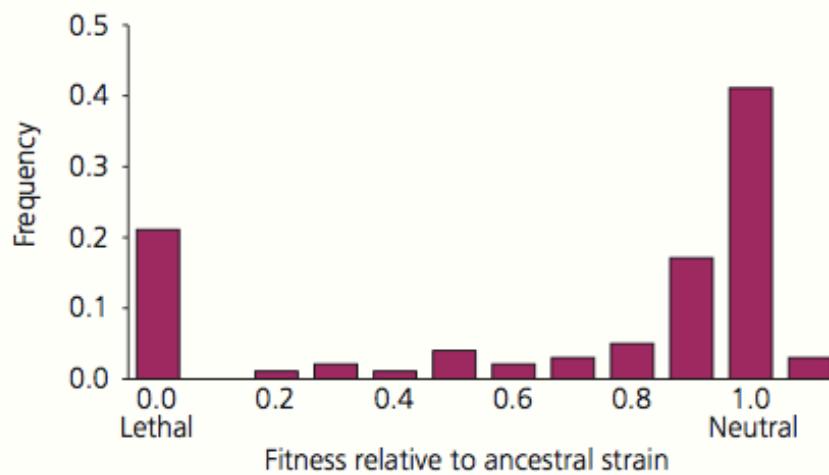
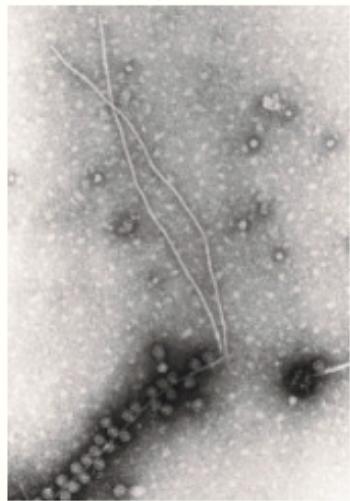
Different SARS-CoV-2 strains haven't yet had a major impact on the course of the pandemic, but they might in future.



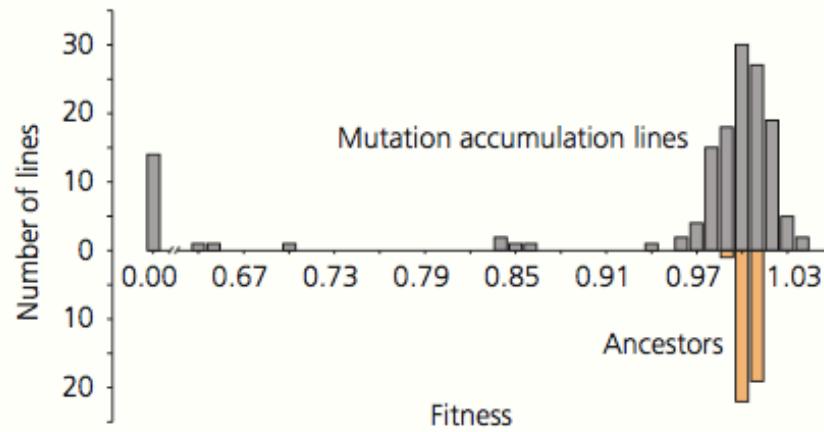
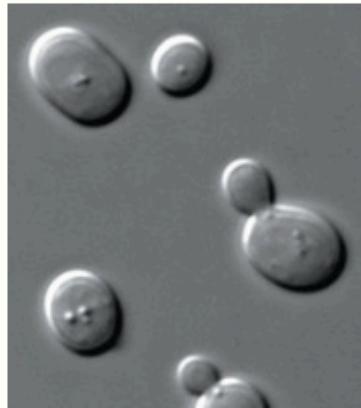
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Distribution of fitness effects (DFE)

(a) Bacteriophage f1



(b) Brewer's yeast



Mutation-accumulation experiments

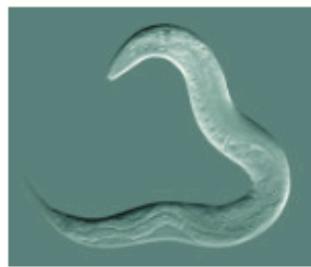
Direct estimation of mutation rates through mutation accumulation experiments

Principle: propagate an organism for many generations under conditions that minimize the effects of selection

ample food, little crowding, no predation
population bottlenecks (to maximize drift, see Ch. 7)

and then count the number of accumulated mutations by DNA sequencing

Mutation-accumulation experiments



Caenorhabditis elegans

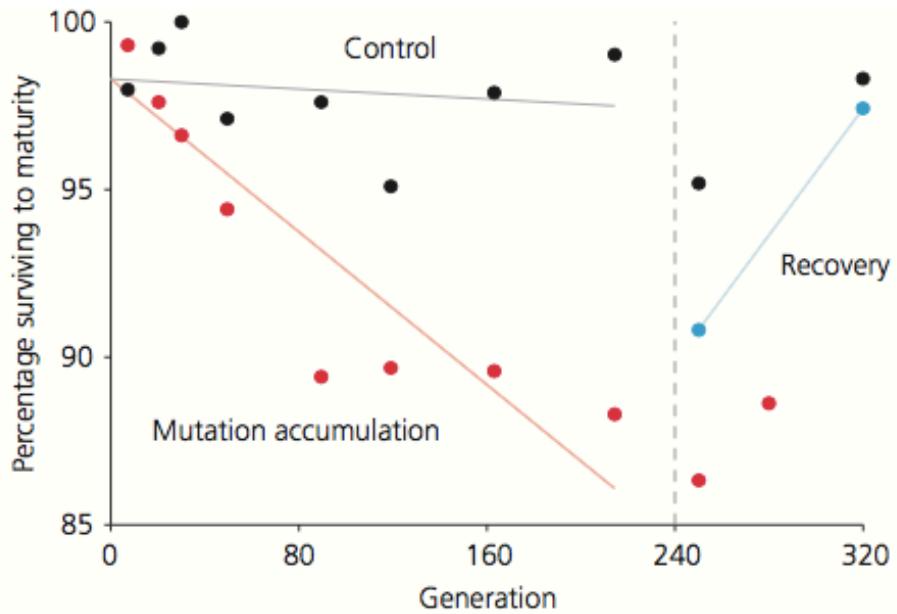


Figure 5.38 The balance between mutation and natural selection Nematode lineages insulated from natural selection declined in fitness relative to control lineages as they accumulated deleterious mutations. The lineages recovered upon exposure to natural selection due to the elimination of deleterious mutations and the preservation of favorable ones. Redrawn from Vassilieva et al. (2000), Estes and Lynch (2003). Photo by Bob Goldstein.

The importance of proofreading

LETTERS TO THE EDITOR

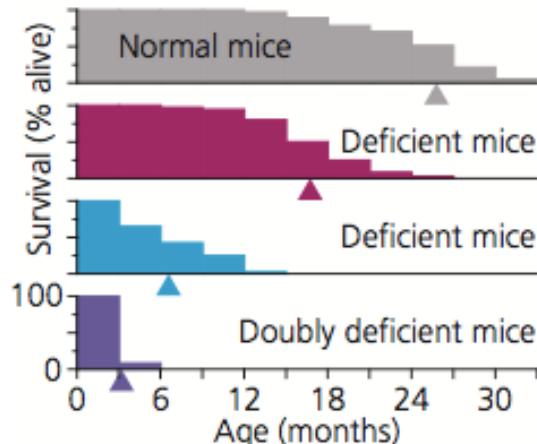
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Defective DNA polymerase- δ proofreading causes cancer susceptibility in mice

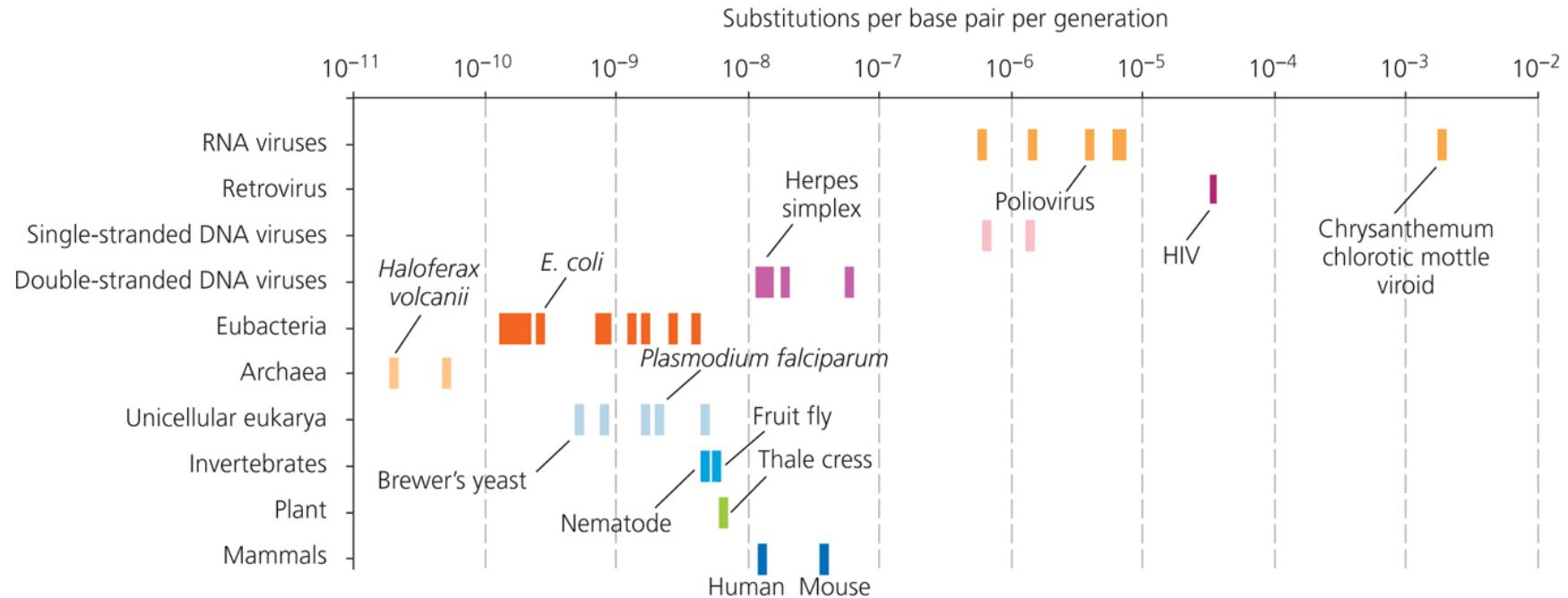
To the editor—Tumor development is a multistep process that requires an accumulation of mutations in genes regulating cell growth and metastasis¹. Spontaneous mutations occur rarely in normal cells, and thus it is argued that defects in pathways governing genetic

tant allele, we crossed a chimeric male with C57BL/6J females, and the resultant heterozygous F1 mice were interbred to generate a cohort of F2 animals. A total of 199 F2 mice were evaluated from 11 F1 breeding pairs (mean litter size, 6.8 pups). We obtained 53 wild-type, 97 *Pold1*^{+/-D400A}

23 tumors (Fig. 1b). The tumors were derived from two different cell lineages. Sixteen of the 23 tumors originated from mesenchymal tissue (12 thymic lymphomas, 2 diffuse lymphomas and 2 sarcomas) and 7 originated from epithelial tissue (6 tail-skin squamous-cell carcinomas and 1 mammary adenocarcinoma).



Mutation rates vary widely among different organisms



Class activity

Question 1: Estimate the number of mutations that can accumulate in E.coli and human in one generation.

The evolution of bacteria on a "mega-plate" Petri dish



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Different classes of mutations

point mutations and their rates

gene duplications and the origin of new genes

chromosome mutations

genome duplication (polyploidization)

Group projects (different classes of mutations)

Project 1: The lack of fingerprints

Project 2: A monkey with unusual diets

Project 3: Short leggedness in dogs

Project 4: Inversion in *Drosophila subobscura*

Project 5: The case of *Achillea borealis*

Gene duplications can create new genes

Two main causes of gene duplication

1. Retroposition

reverse transcription of
a mRNA into DNA by reverse transcriptase
integration of DNA into the genome

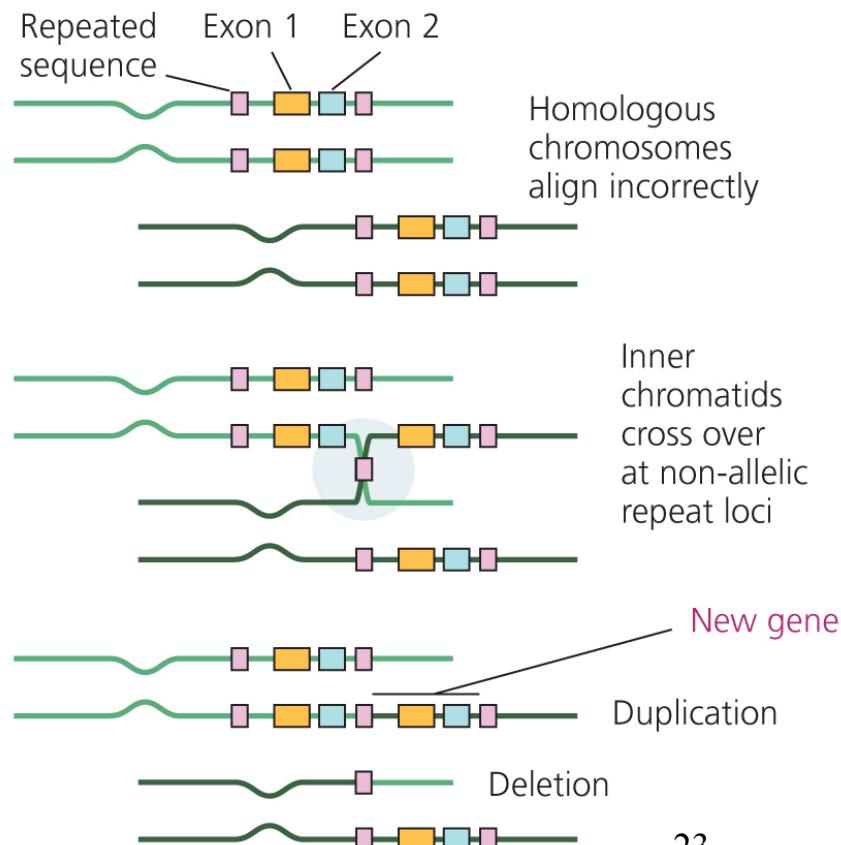
duplicates are often in new location,
lack introns, have poly A sequence

2. Unequal cross-over during meiosis

duplicates «in tandem»,

duplicates have introns,
lack poly A sequence

(a) Duplication by unequal crossing over



A retrotransposed duplicate gene is responsible for chondrodysplasia in dogs

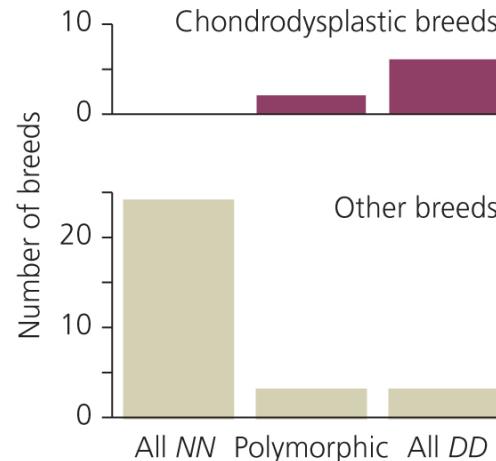
Chondrodysplasia is responsible for short-leggedness in some dog breeds

Fibroblast growth factor 4 (*fgf4*) is a protein important for bone development

In chondrodysplastic dogs the encoding gene is often duplicated

The second copy is intronless and occurs far from the original gene

(b) *Fgf4* retrogene genotypes in dogs of various breeds



NN... No known individual has two copies
DD... All known individuals have two copies

(a) Who's a good girl?



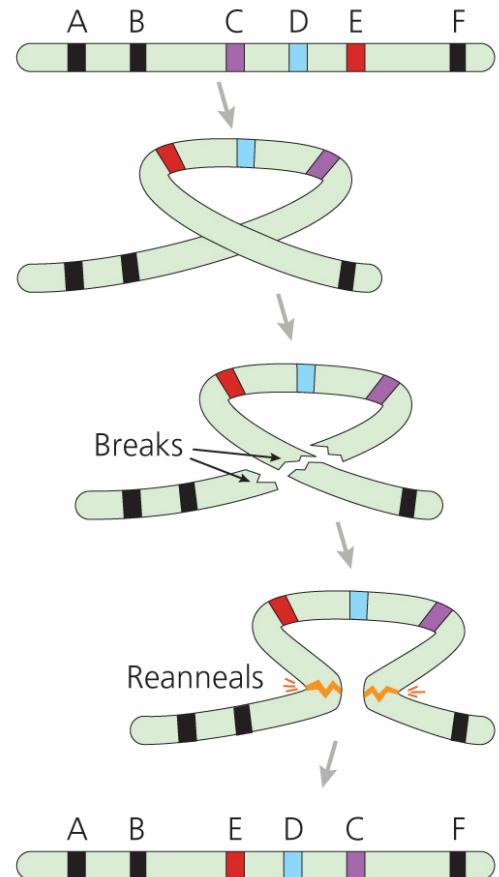
Chromosome mutations (inversions)

inversions affect **linkage**, the physical proximity of genes
e.g., they break up the linkage of B and C
and render C and F linked

inversion heterozygotes prevent alignment
of chromosomes during meiosis and thus
crossing over

alleles within an inversion are thus inherited
together

they form a **supergene**



Inversion polymorphisms and natural selection

Drosophila pseudoobscura is native to Europe, the Middle East, and North Africa

contains **inversion polymorphisms** on five of its six chromosomes

the incidence or **frequency** of these inversions varies with latitude and climate

such regular variation over a geographic area is also called a **cline**

is this variation a historical accident or caused by selection?

Inversion polymorphisms can be maintained by natural selection

in 1978, *D. pseudoobscura* invaded South America (Chile) and the US (Washington)
the invading populations contain the same inversion polymorphisms
they established the same clines, from wet/cold to desert/hot habitats

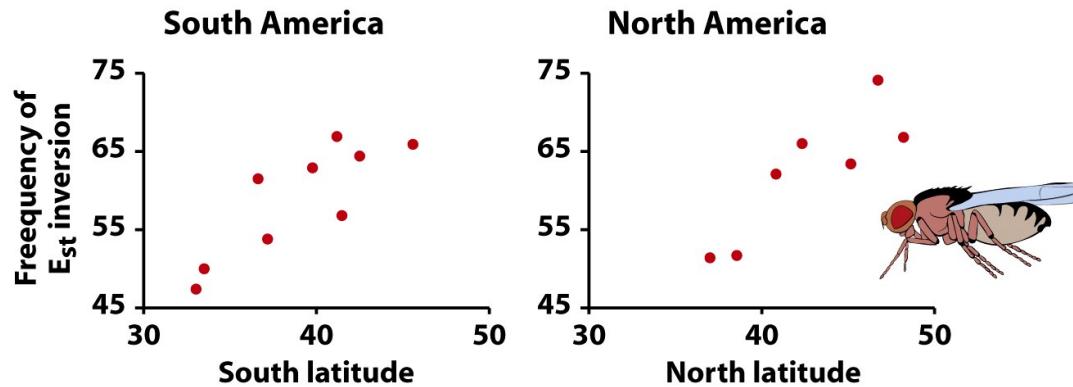


Figure 5-10 Evolutionary Analysis, 4/e
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Inversion polymorphisms can be maintained by natural selection

Small flies typically occur in dry, hot habitats

laboratory selection for small flies leads to inversion frequencies similar to those observed in dry, hot habitats in the wild

inversions likely contain genes affecting body size of *D.pseudoobscura*

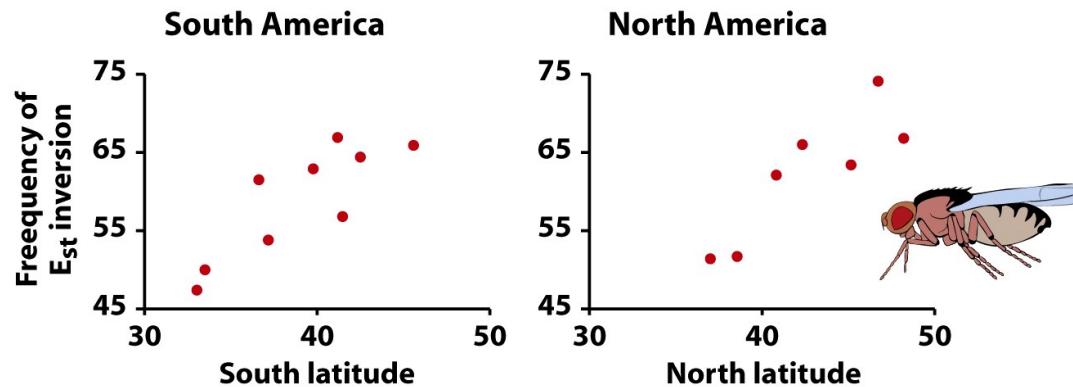


Figure 5-10 Evolutionary Analysis, 4/e
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Genome duplication (polyploidization)

polyploids are organisms with more than two chromosome sets
tetraploids ($4n$), hexaploids ($6n$), etc.

common in plants
many angiosperms (flowering plants)
estimated at 2 in every 100,000 offspring

less common in animals
but frequent in some groups, e.g., fish
facilitated by ability to self-fertilize and by
parthenogenesis, a form of asexual reproduction

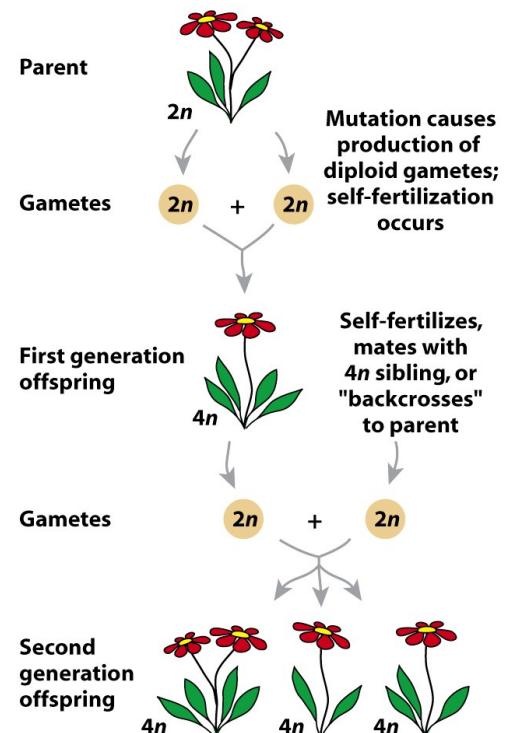


Figure 5-11 Evolutionary Analysis, 4/e
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Two evolutionary consequences of polyploidization

Reproductive isolation

e.g., offspring of tetraploid with diploid will be triploid, which will lead to meiotic problems

Evolutionary innovation and diversification

polyploidization creates many duplicate genes that can then diversify

it occurred early in the evolution of **ray-finned fish**, the most species-rich group of vertebrates

it also occurred in the evolution of **angiosperms**, which make up more than 80 percent of land plants

The connection between polyploidization and diversification is not proven

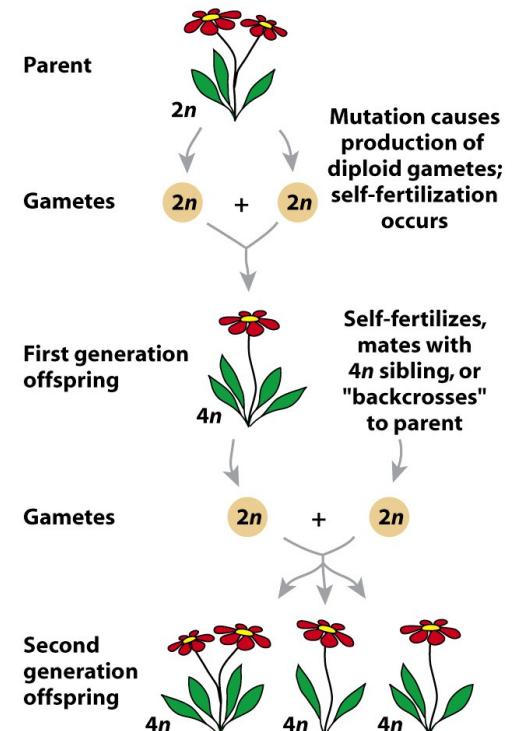


Figure 5-11 Evolutionary Analysis, 4/e
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Genome duplications can help organisms adapt to new environments

Populations of yarrow («Schafgarbe») in California vary in ploidy

Tetraploids live in wetter habitats (coastal grasslands and forests)

Hexaploids live in drier habitats (sand dunes and oak woodlands)

Tetraploids occasionally produce hexaploid offspring

(a)



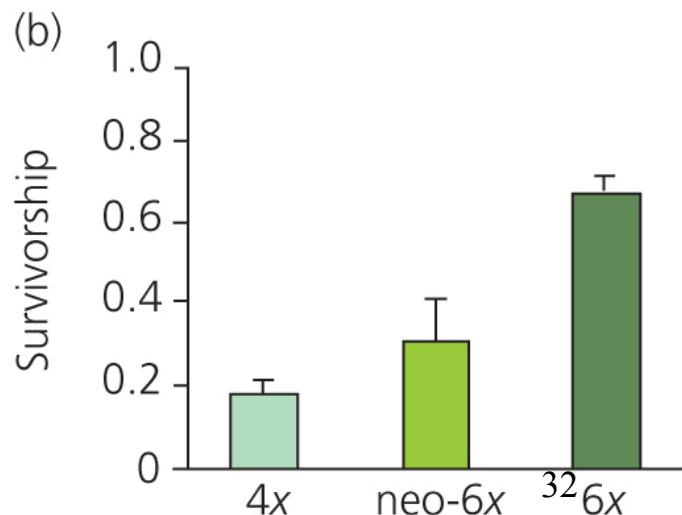
Genome duplications can help organisms adapt to new environments

Hypothesis: Hexaploids are better adapted to drier habitats

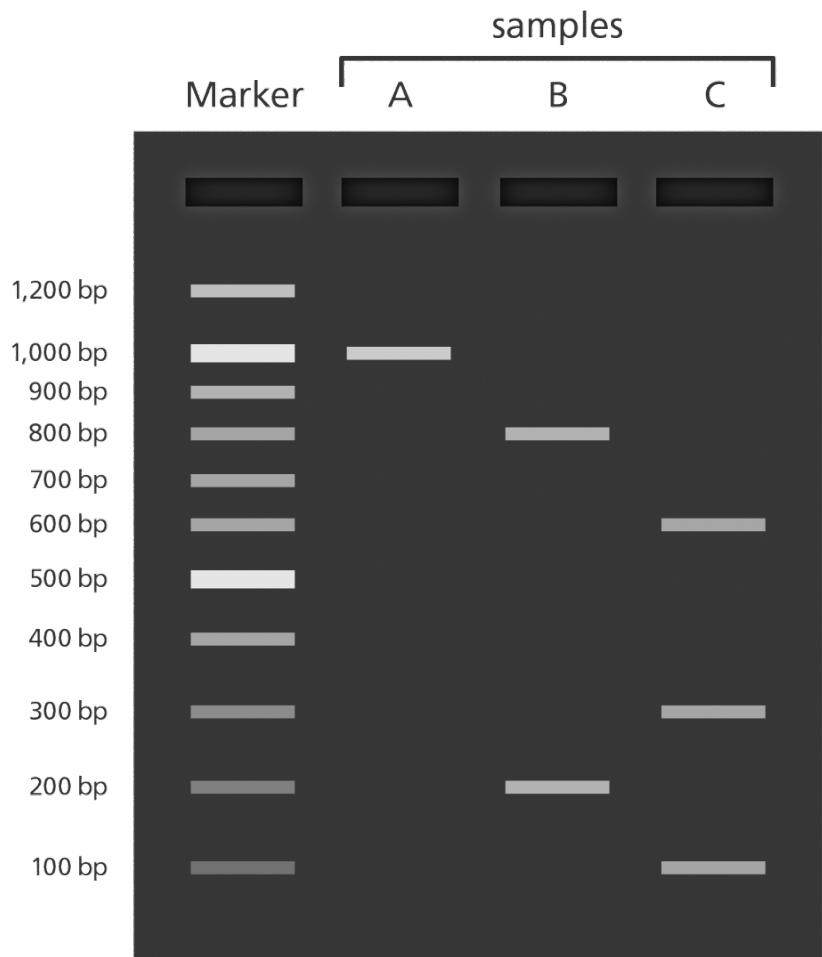
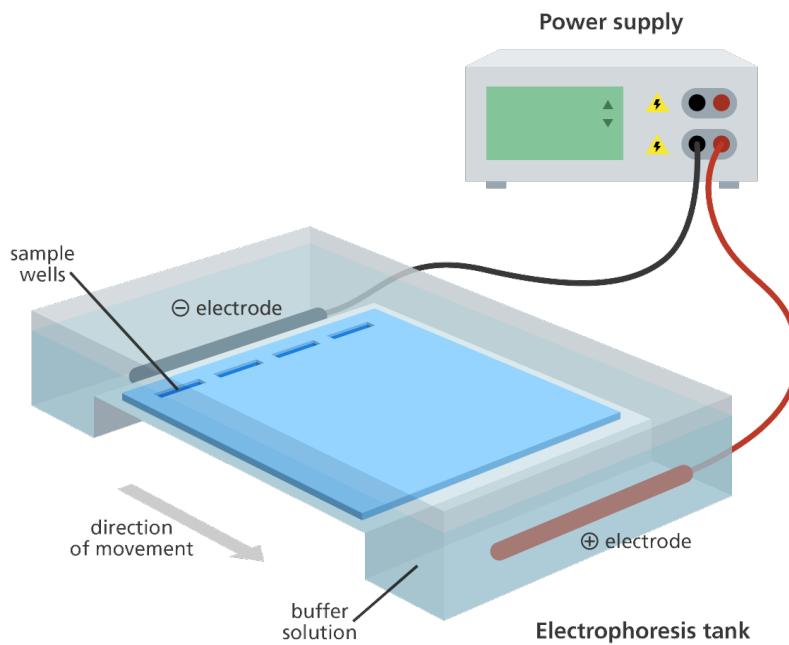
Test: Grow
tetraploids (4x)
first generation hexaploids (neo-6x)
hexaploids from wild populations (6x)
in sand-dunes (dry habitat)

Observation: Hexaploids are better adapted

Adaptation also occurs within hexaploids, because 6x plants do better than neo-6x plants



Detecting variations: Electrophoresis (review)



Early work revealed abundant genetic variation through protein electrophoresis

identified **allozymes**

different forms of an enzyme encoded by different alleles of the same gene

protein isolation followed by electrophoresis and visualization

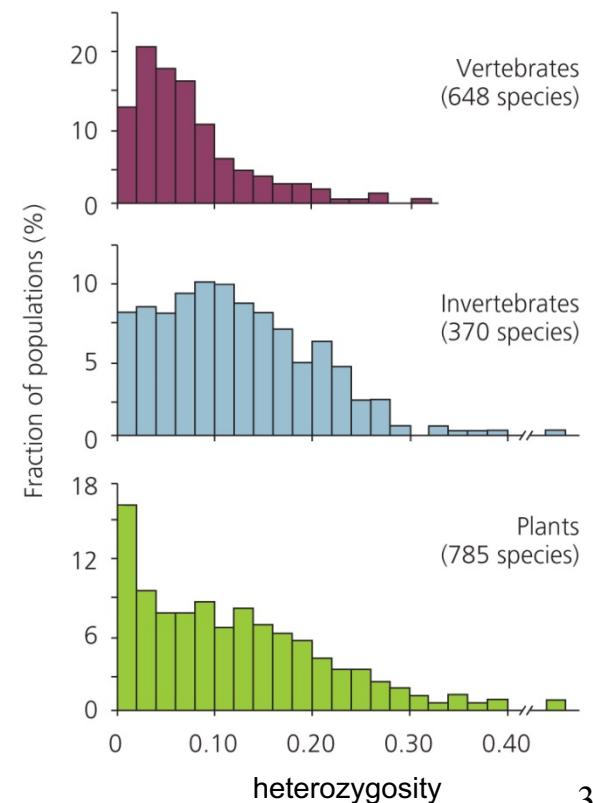
can identify protein enzymes that migrate at different velocities
and have different amino acid sequences

33-50% of genes encoding enzymes
are typically polymorphic

average individual is heterozygous at 4-15% of genes

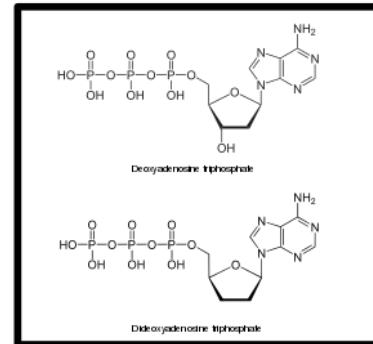
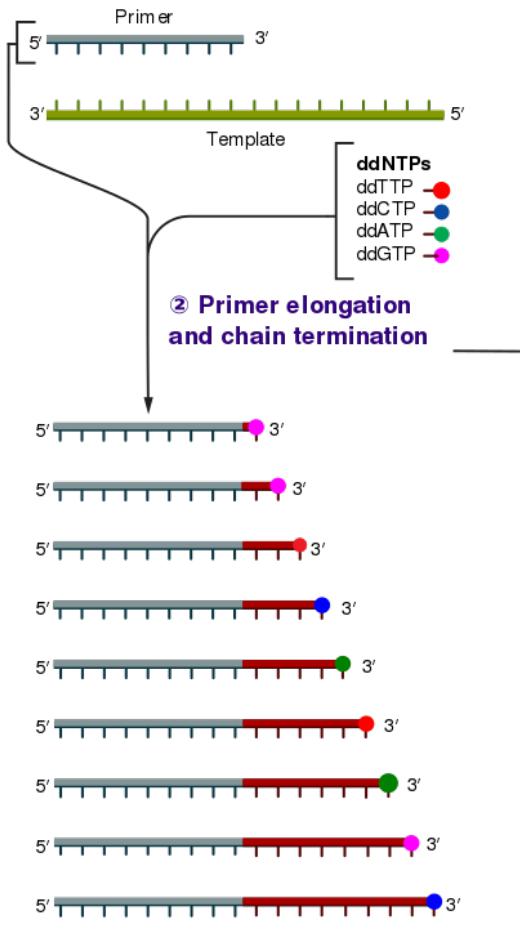
thousands of heterozygous genes per individual

Is most of this variation neutral or affected by selection?
leads to the **neutralist-selectionist** controversy

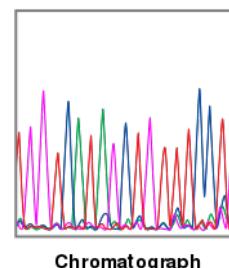
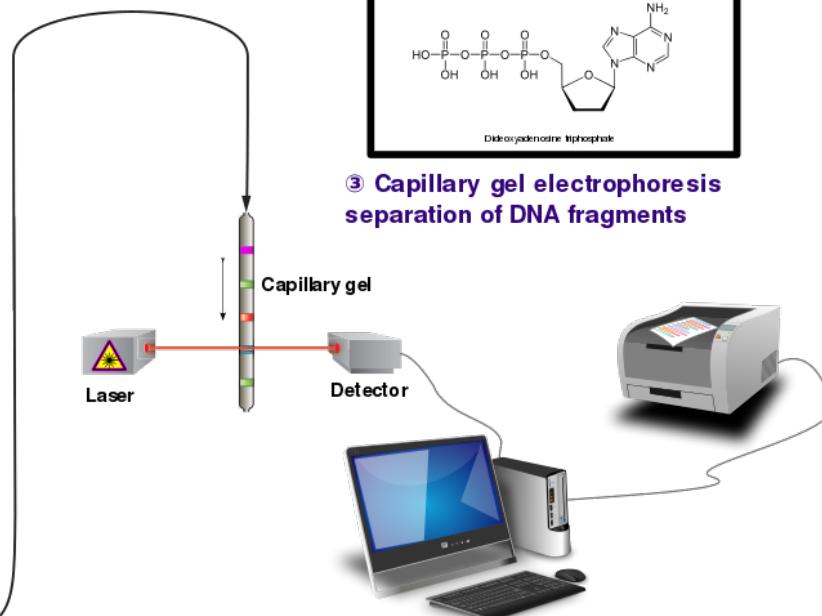


Detecting variations: DNA-sequencing (sanger sequencing)

- ① Reaction mixture
 - Primer and DNA template
 - DNA polymerase
 - ddNTPs with fluorochromes
 - dNTPs (dATP, dCTP, dGTP, and dTTP)

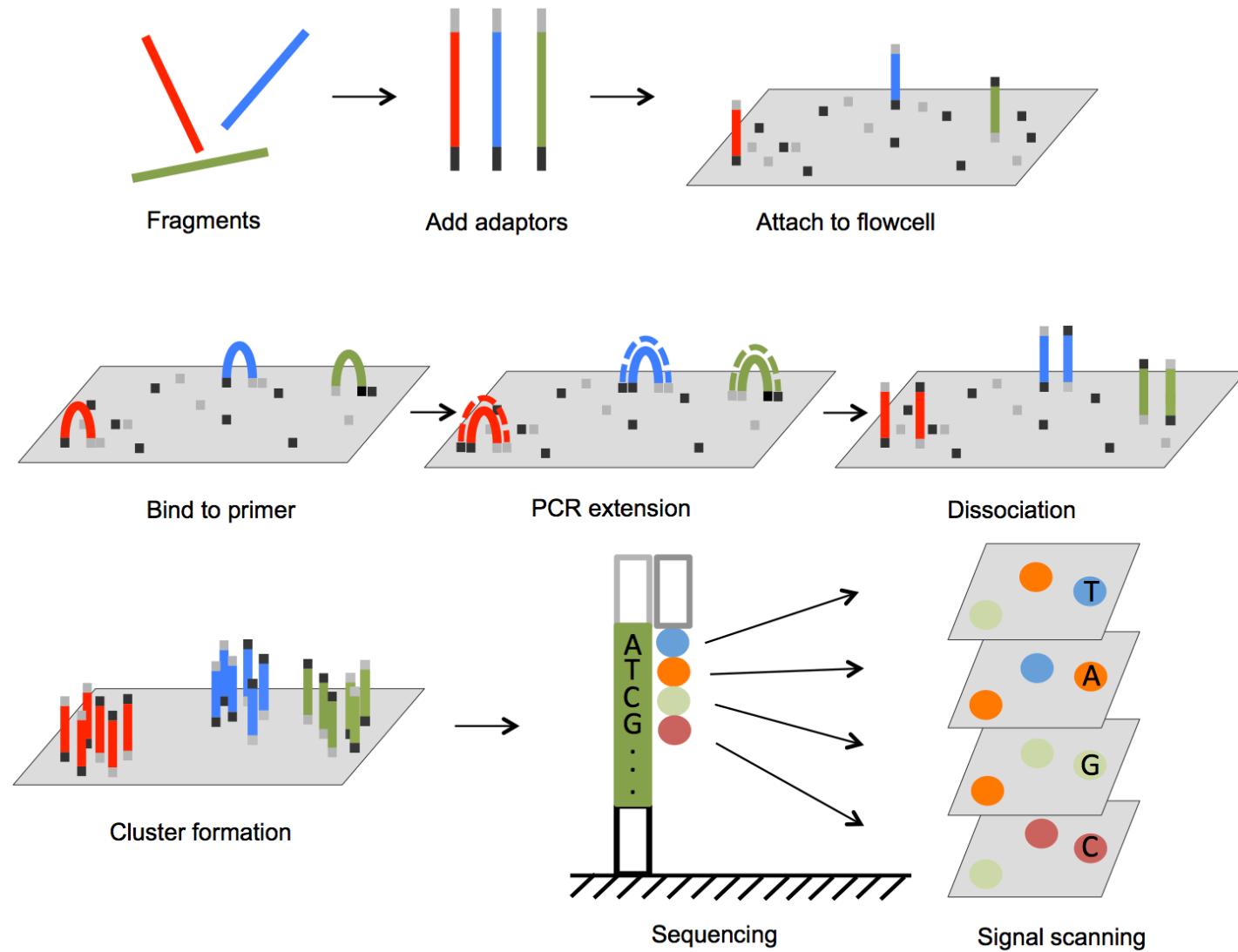


③ Capillary gel electrophoresis separation of DNA fragments

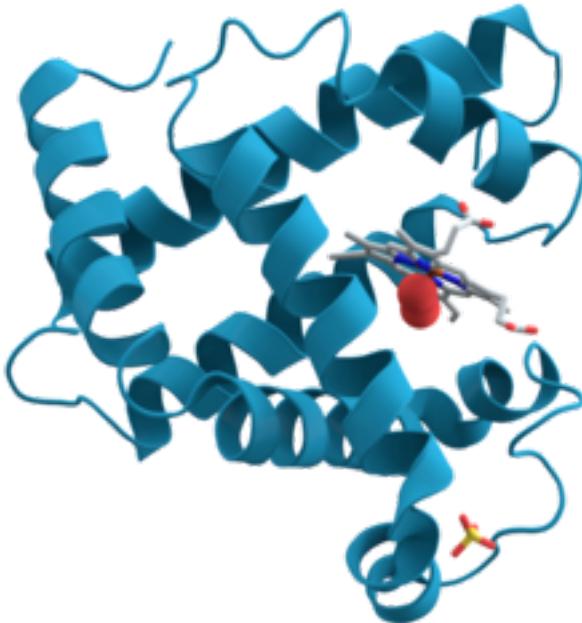
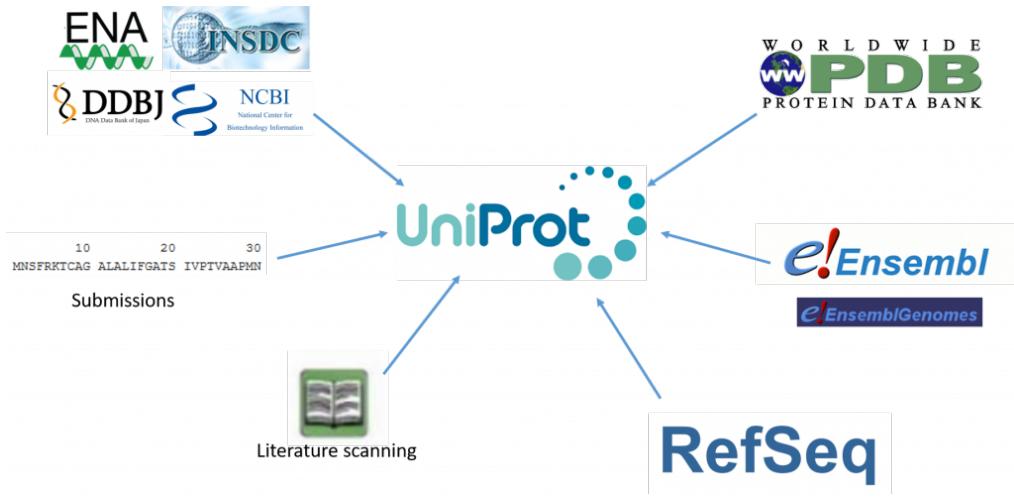


④ Laser detection of flurochromes and computational sequence analysis

Detecting variations: DNA-sequencing (Next generation sequencing)



Databases to find genetic variants (UniProt)



Class activity:
Find the natural variants of Myoglobin
in UniProt database

Databases to find genetic variants (NextStrain: SARS-CoV-2)

