

Variation

- Selection acts on variation
- Where does variation come from?
- How it is maintained?
- What processes affect this variation?

Mechanisms that affect variation

- Mutation
 - Generates new variation directly
- Recombination
 - Generates variation by shuffling of genes
- Genetic drift
 - Decreases variation within a population
 - Increases variation between populations
- Migration
 - Tends to decrease variation between populations

Variation: Mutation

Many kinds of mutation

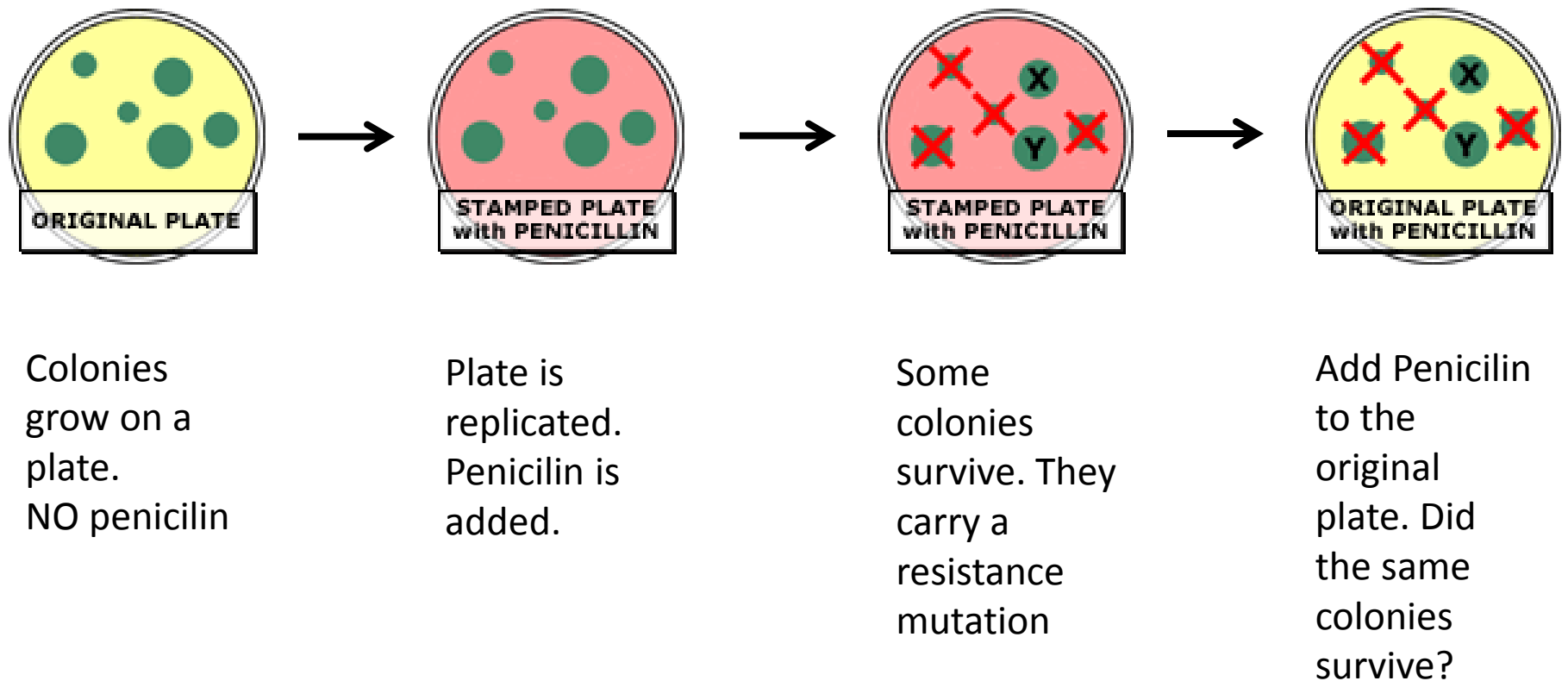
- Single Point Mutations
- Insertions / deletions
- Inversions
- Duplications
- Chromosome abnormalities

Category	Wild type	Missense	Frameshift by insertion
DNA	5' AAA-GCT-ACC-TAT-CGG-TTA 3' 3' TTT-CGA-TGG-ATA-GCC-AAT 5'	5' AAT-GCT-ACC-TAT-CGG-TTA 3' 3' TTA-CGA-TGG-ATA-GCC-AAT 5'	5' AAA-GCT-ACC-ATA-TCG-GTT 3' 3' TTT-CGA-TGG-TAT-AGC-CAA 5'
mRNA	5' UUU-CGA-UGG-AUA-GCC-AAU 3'	5' UUA-CGA-UGG-AUA-GCC-AAU 3'	5' UUU-CGA-UGG-TAU-AGC-CAA 3'
Protein	N PHE-ARG-TRP-ILE-ALA-ASN C / Amino Carboxyl	N LEU-ARG-TRP-ILE-ALA-ASN C / Amino Carboxyl	N PHE-ARG-TRP-TYR-SER-GLY C / Amino Carboxyl

Many sources of mutations

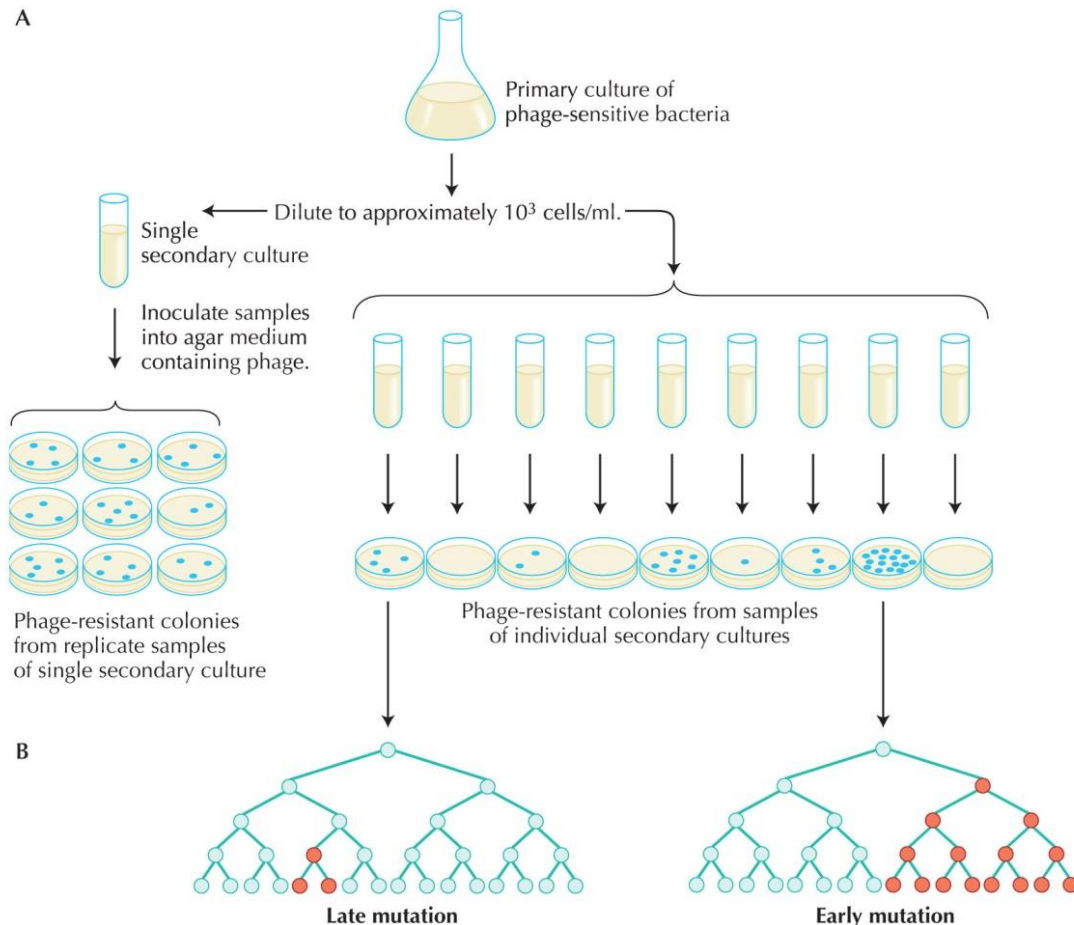
- DNA replication
- Missegregation of chromosomes
- Physical Damage
 - UV light

Mutations occur before selection: The Lederberg experiment

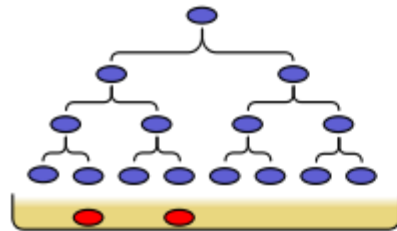
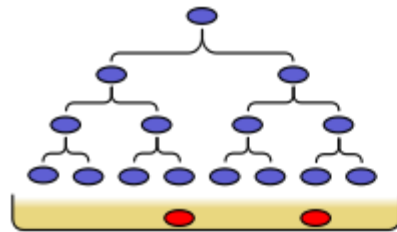
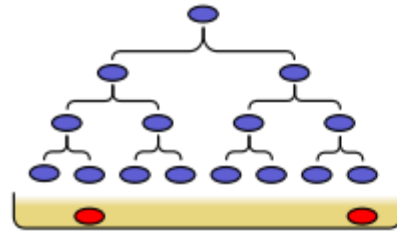
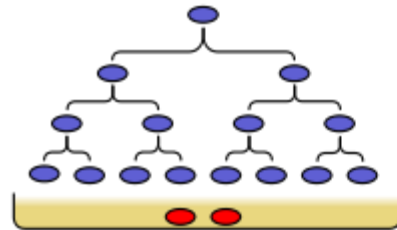


Mutations are random with respect to selection

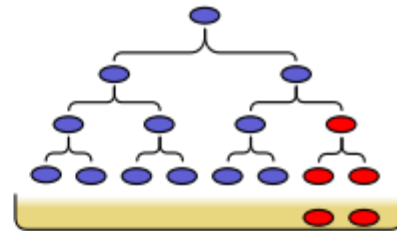
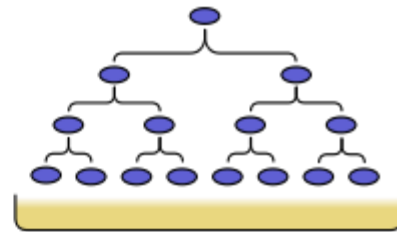
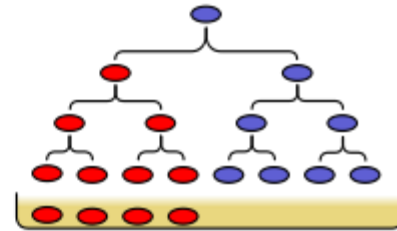
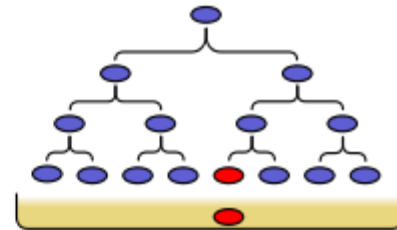
- Mutations do not happen in a directed fashion



Luria-Delbrück Experiment



(A) Induced
mutation

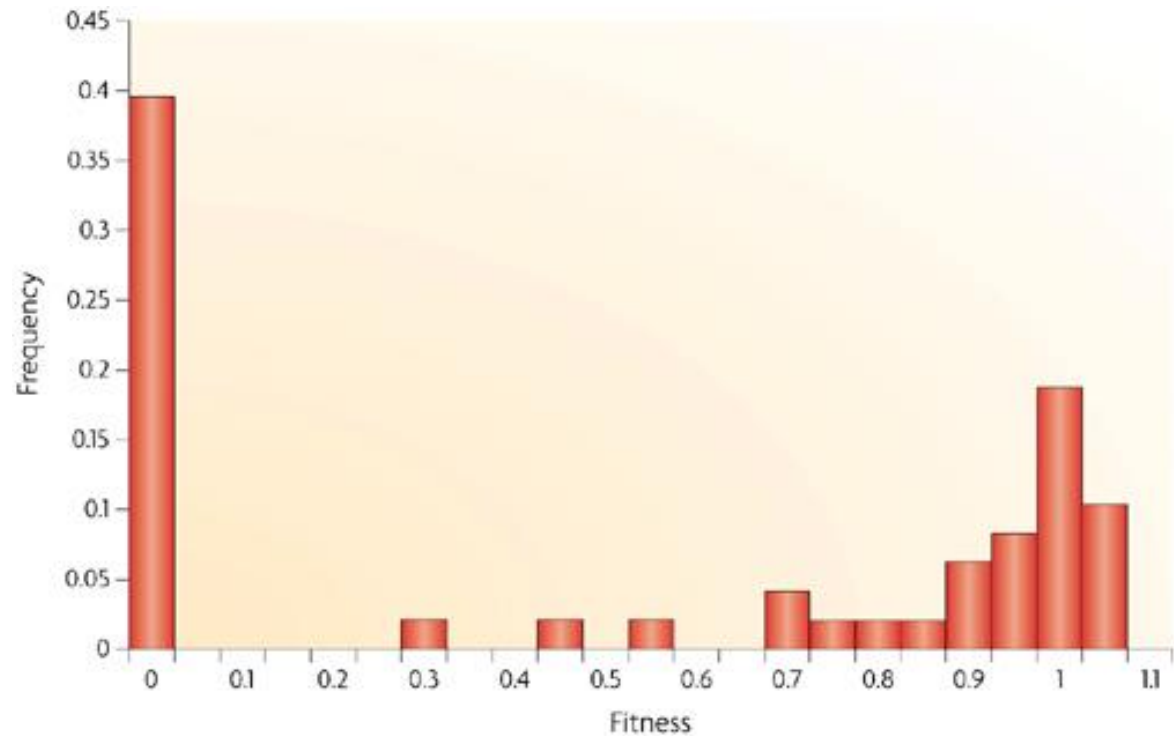


(B) Spontaneous
mutation

The effects of mutations

- The effects of new mutations:
 - No effect (neutral)
 - Beneficial
 - Deleterious (bad)
- The relative frequency and magnitude of each of these classes is an open question in evolutionary biology

The effects of mutations

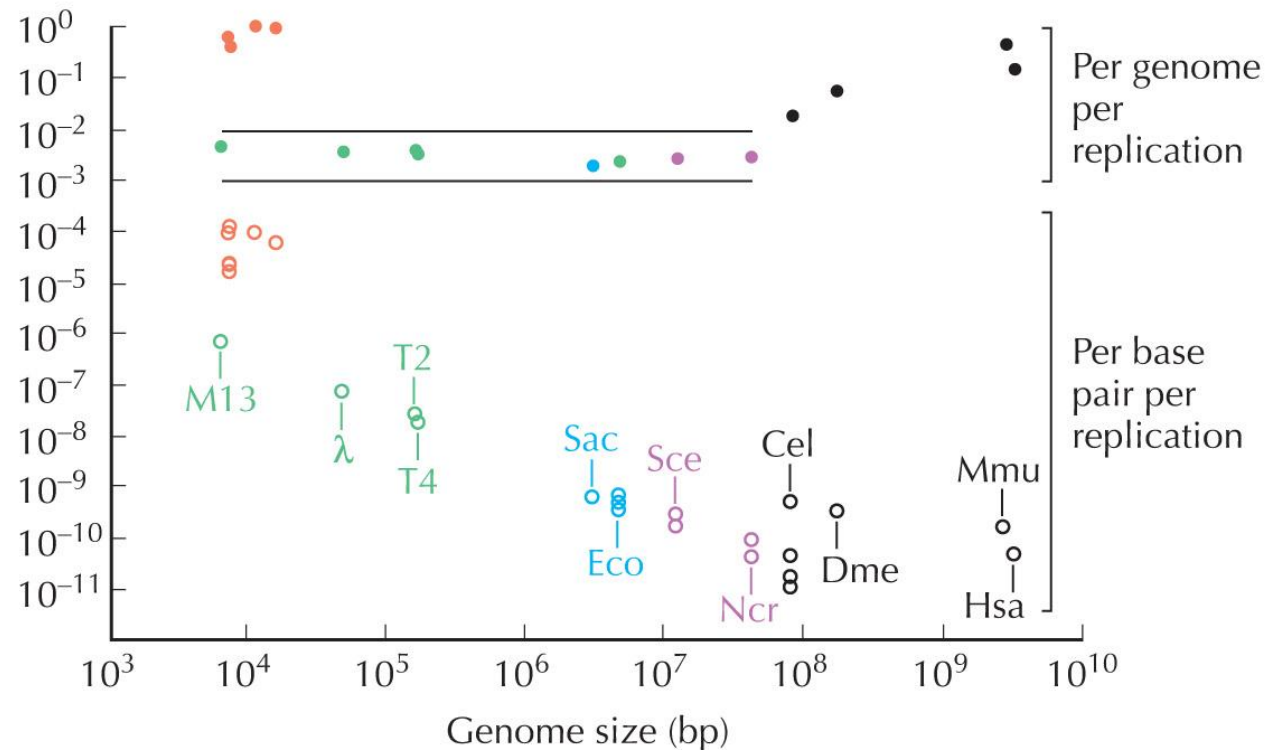


Nature Reviews | Genetics

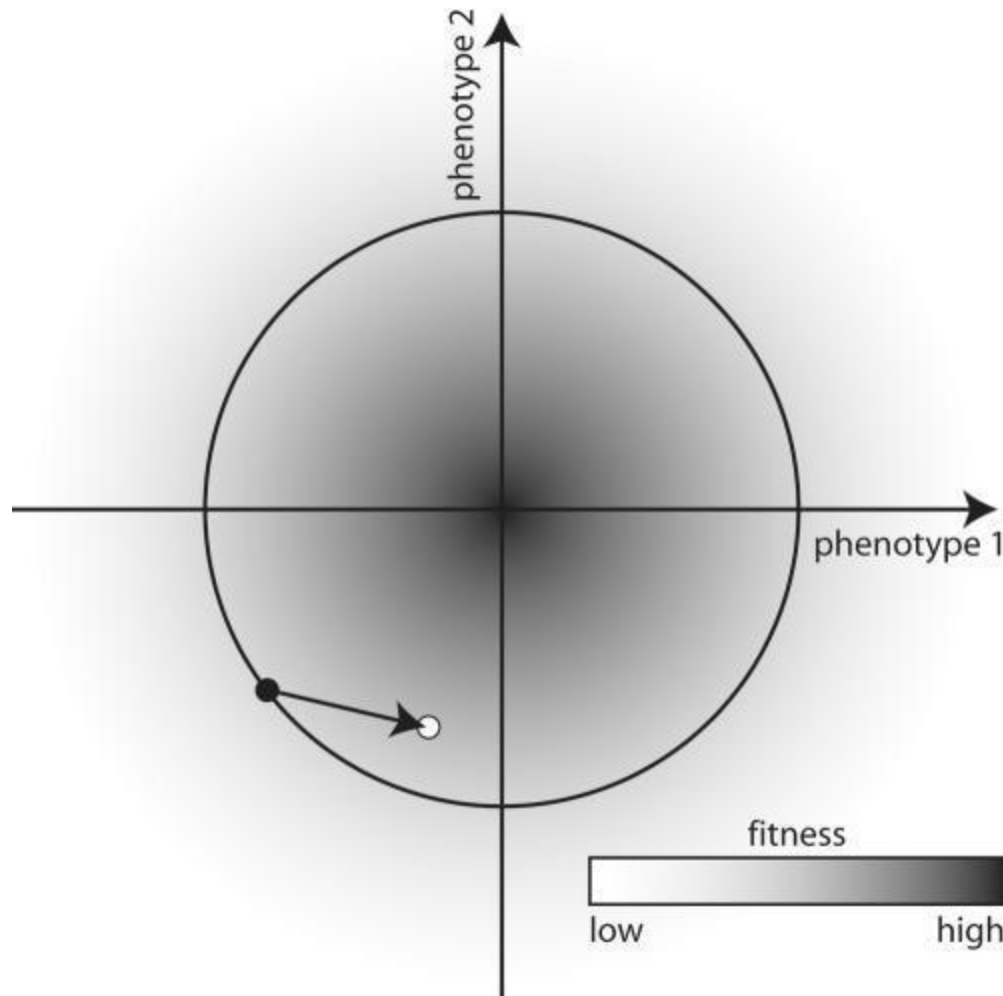
Most people believe that most mutations are deleterious

Mutation Rates

Mutation rates per base pair are small.
Mutation rate per genome are roughly constant



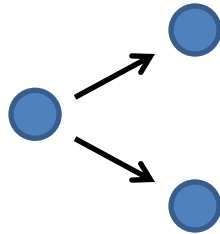
An argument for small effect beneficial mutations: Fisher's geometric model



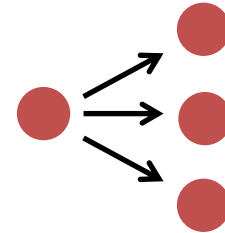
Deleterious Mutations can be maintained under mutation selection balance

- Deleterious mutations are eliminated by selection
- But are generated by mutation

The replicator equation: introducing mutations

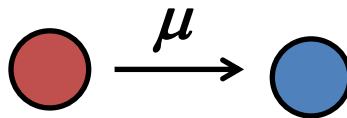


$$W_a = 1$$

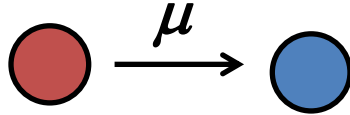


$$W_A = 1 + s$$

$$\Delta p_{t+1} = \frac{\Delta W}{\overline{W}} p_t (1 - p_t)$$



The replicator equation: introducing mutations

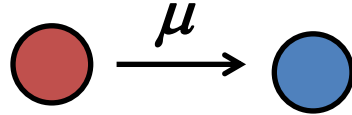


$$\Delta p_{t+1} = \frac{\Delta W}{\overline{W}} p_t (1 - p_t) \quad \text{Change due to selection}$$

Change due to mutation:

$$\begin{aligned} p_A(t+1) &= p_A(t) - \mu p_A(t) \\ p_a(t+1) &= p_a(t) + \mu(1 - p_a(t)) \end{aligned}$$

The replicator equation: introducing mutations



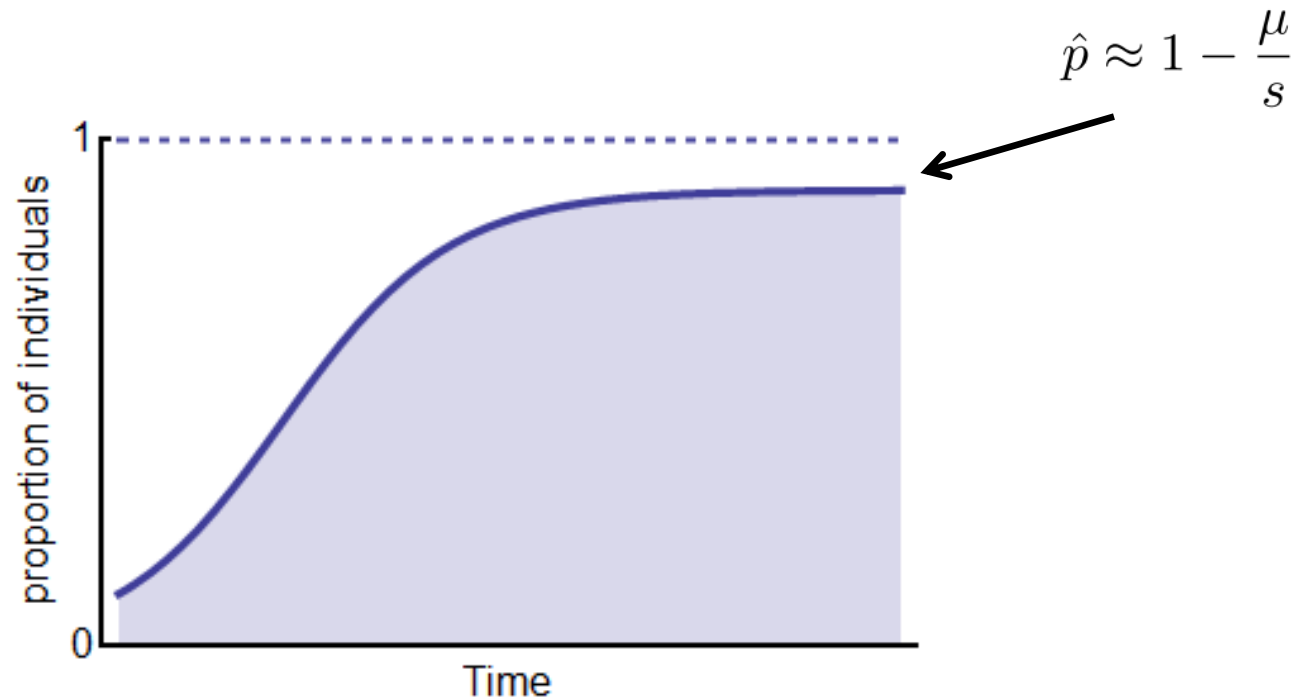
$$\Delta p_t^m = -\mu p_t$$

$$\Delta p_t = \frac{\Delta W}{\overline{W}} p_t (1 - p_t) - \mu p_t$$

$$\Delta p_t = 0 \Rightarrow \hat{p}_t \approx 1 - \frac{\mu}{s}$$

The replicator equation: introducing mutations

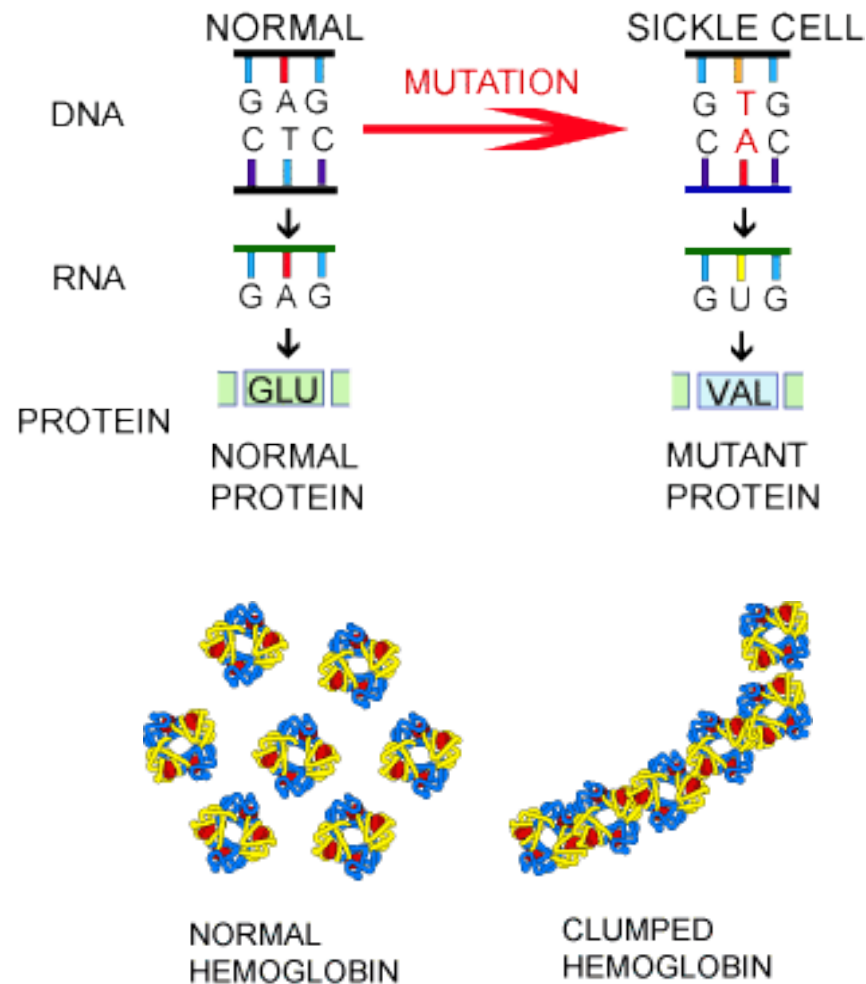
$$\Delta p_t = \frac{\Delta W}{\overline{W}} p_t (1 - p_t) - \mu p_t$$



Mutation Selection Balance

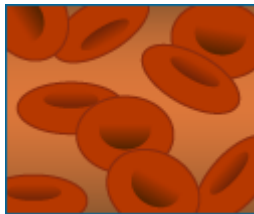
- Deleterious (“bad”) mutations can be maintained by mutation
- Mutational Load
- Maintains genetic variation

Example: sickle cell anemia



Sickle cell anemia

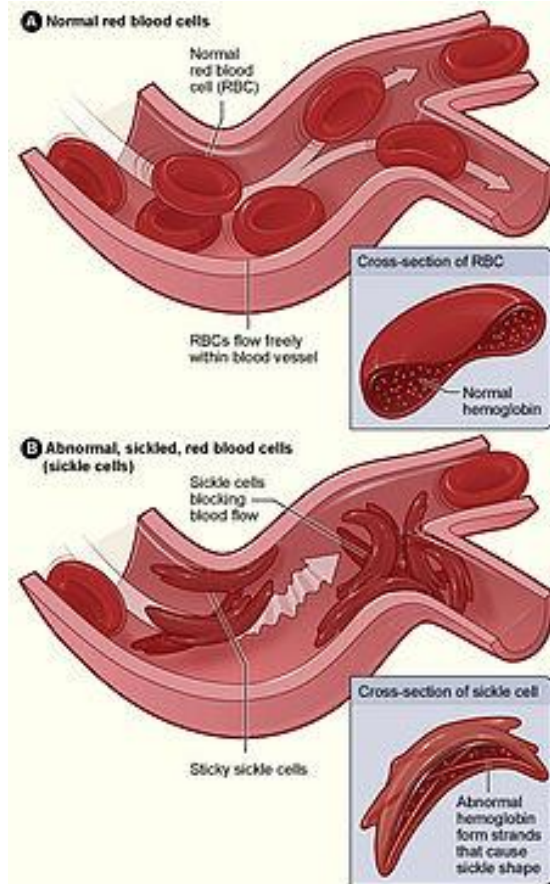
Consequences from the molecular, to the cellular and to the organismal level



Normal red
Blood Cells

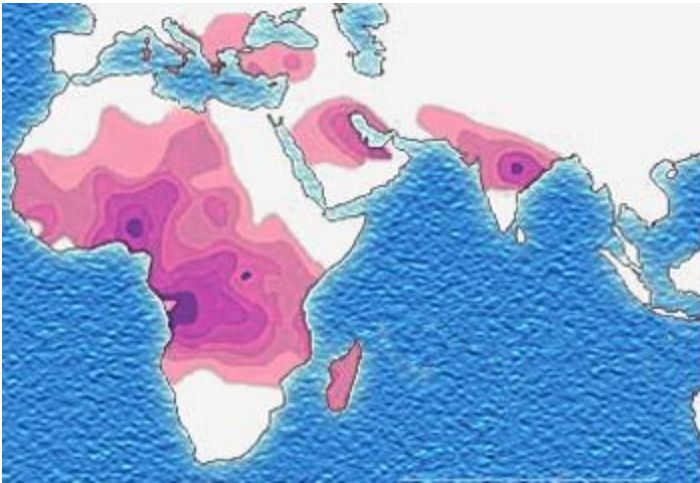


Sickle cells



Sickle cell anemia

Confers protection from Malaria.



Distribution of the sickle cell trait



Distribution malaria

Summary

- Mutations are the basis for variation
- Mutations are mostly deleterious
- Deleterious mutations can be maintained by mutation-selection balance
- Beneficial mutations are expected to be of small effect