OVER- AND UNDERDOMINANCE IN FITNESS; STABILITY

• Introduction

– What if an allele is favored most or least when present with its alternative?

  • Situations called, respectively, **overdominance** and **underdominance** in fitness.

– Over-/underdominance in nature

  • Overdominance: Sickle cell anemia

  • Underdominance: chromosomal rearrangements; *Rh* locus

– NOTE: Absence of over- or under-dominance in phenotype $\not\Rightarrow$ Over-/underdominance in *fitness*

• Evolutionary dynamics of over- and underdominance

• Fitnesses: $\overset{w_{AA}}{1-s} : \overset{w_{Aa}}{1} : \overset{w_{aa}}{1-t}$

  – If $s, t > 0$, overdominance in fitness: $w_{AA} < w_{Aa} > w_{aa}$.
  – If $s, t < 0$, underdominance in fitness: $w_{AA} > w_{Aa} < w_{aa}$.

• Plugging these fitnesses into general formula $\Delta p = pq\frac{\overline{w}_A - \overline{w}_a}{\overline{w}}$ get:

$$\Delta p = pq\frac{qt - ps}{1 - p^2 s - q^2 t}$$

• Ways to study this equation:

  – Iterate equation for different values of t and s and initial p (e.g., using EXCEL).

  – Other approach: ***Analysis***

    • Step 1: **Find equilibria**.

      – I.e., find values of p for which $\Delta p = 0$ or $p' = p$.

      – Three possibilities: (a) $p = 0$; (b) $p = 1$; (c) $p = \frac{t}{s+t}$

      – (c) is biologically feasible ($0 \le p \le 1$) only if $t, s > 0$ or $t, s < 0$.

- In this case, have **polymorphic** equilibrium.

- Step 2: **Determine stability**

- **Digression: analyzing evolutionary (dynamical) systems**

– Computational approaches are limited to exploring relatively small number of scenarios.

– Alternatively, can incompletely analyze an *infinite* number of scenarios: "mathematical **analysis**"

- General Approach: answer the following two questions

(1) Q: "What are the eventual outcomes of evolution?
– Evolution ceases if equilibrium is reached, i.e., if $\Delta p = 0 \Leftrightarrow p' = p$.
– An allele frequency at which evolution stops is called an **equilibrium** value.
- denoted $\hat{p}$

– Can be more than one equilibrium value.

(2) Q: Are these equilibria ever approach in the course of evolution?
A: Depends on **stability** of the equilibria, $\hat{p}$.

– Stability

- A taxonomy of equilibrium stabilities:

1) **Unstable** equilibrium: perturbed system actively moves away

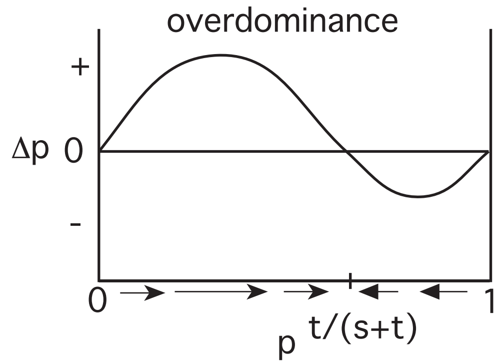
2) **Stable** equilibrium
a) **Neutrally** stable: perturbed system neither moves away or returns

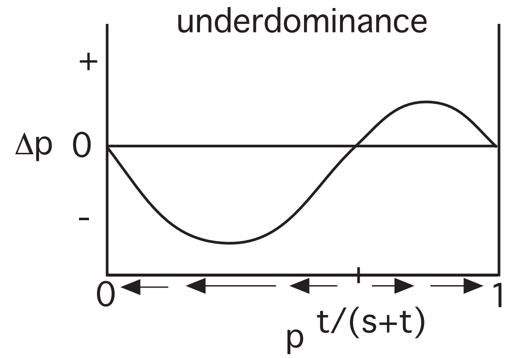
b) **Locally** stable: perturb system slightly & it returns to equilibrium

c) **Globally** stable: any perturbation returns to equilibrium

- Back to over-/underdominance...**STABILITY OF** $\hat{p} = 0, 1, \frac{t}{s+t}$

• Qualitative Approach





– Populations near "boundary" equilibria ($\hat{p} = 0, 1$):
  - driven away with overdominance
  - return with underdominance

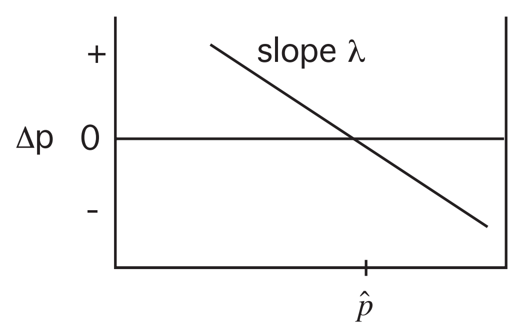
– Populations near polymorphic equilibrium [$\hat{p} = t/(s+t)$]:
  - move towards polymorphic equilibrium with **over**dominance
  - move away with **under**dominance
    - – NOTE: which direction depends on which side of $t/(s+t)$ population lies initially.

• Mathematical Approach

– Blow up graph of Δp near $\hat{p}$;

- λ = slope of Δp at $\hat{p}$ = $\left.\frac{d}{dp}(\Delta p)\right|_{p=\hat{p}}$

- λ is called an **eigenvalue**.



– Look at frequencies starting slightly <u>above</u> $\hat{p}$: $p = \hat{p} + \varepsilon$:

- $\varepsilon > 0$ = initial distance from $\hat{p}$

- $p' = p + \Delta p \approx (\hat{p} + \varepsilon) + \lambda\varepsilon = \hat{p} + (1+\lambda)\varepsilon$ or $p' - \hat{p} \approx (1+\lambda)\varepsilon$

– Look at frequencies starting slightly <u>below</u> $\hat{p}$: $p = \hat{p} - \varepsilon$ ($\varepsilon > 0$):

- $p' = p + \Delta p \approx (\hat{p} - \varepsilon) + \lambda(-\varepsilon) = \hat{p} + (1+\lambda)(-\varepsilon)$ or $p' - \hat{p} \approx (1+\lambda)(-\varepsilon)$

– Both cases: Initial distance of p from $\hat{p}$ (ε or $-\varepsilon$) multiplied by factor $(1+\lambda)$.
  - T generations later, initial distance from $\hat{p}$ multiplied by $(1+\lambda)^T$

- Possibilities:
  1) If $\lambda > 0$, $(1+\lambda)^T$ increases with *T*; <u>Unstable</u>

  2) If $\lambda < 0$, have three cases
     a) $-1 < \lambda < 0$: $(1+\lambda)^T$ decreases steadily to 0. <u>Stable</u>
     b) $-2 < \lambda < -1$: $(1+\lambda)^T$ oscillates + and - but decreases in size to 0. <u>Stable</u>
     c) $\lambda < -2$: $(1+\lambda)^T$ oscillates but increases in size. <u>Unstable</u>

– Technique ("a two-step recipe for performing a local stability analysis"):

1) Locate Equilibria: I.e., Determine values of *p* at which $\Delta p = 0$.

2) Find the eigenvalues. I.e., for each $\hat{p}$, compute: $\lambda = \left.\frac{d}{dp}(\Delta p)\right|_{p=\hat{p}}$

- **Math Approach Applied to over-/underdominance**

– Recall:

- $\begin{matrix} w_{AA} & & w_{Aa} & & w_{aa} \\ 1-s & : & 1 & : & 1-t \end{matrix}$
- *s, t* > 0 overdominance; *s, t* < 0 underdominance
- $\Delta p = pq\frac{qt - ps}{1 - p^2 s - q^2 t}$

1) Know $\hat{p} = 0,\ 1,\ \text{or}\ \frac{t}{s+t}$ (3 equilibria)

2) $\hat{p} = 0$: $\lambda = t/(1-t)$
   - Unstable for overdominance; Stable for underdominance.

   $\hat{p} = 1$: $\lambda = s/(1-s)$
   - Unstable for overdominance; Stable for underdominance.

   $\hat{p} = \frac{t}{s+t}$: $\lambda = 1/(1 - 1/t - 1/s)$
   - Stable for overdominance; Unstable (non-oscillatory) for underdominance.
   - Turns out: overdominance case is also globally stable.

- **More than 2 alleles (highlights)**

  - Like diallelic case:

  - If a locally stable polymorphic equilibrium with all alleles is present, it's also globally stable.
  - mean fitness at equilibrium > any homozygote fitness

- In contrast to diallelic case:
  - can have $w_{ii} < w_{ij} > w_{jj}$ for all pairs of alleles but polymorphic equilibrium with all alleles present is impossible
  - can have polymorphic equilibrium with all alleles present without all heterozygotes being superior in fitness to homozygotes (e.g., e.g., could have $w_{11} > w_{34}$)

Biological Significance of over-/underdominance

- Overdominance maintains genetic variation

- Role in "heterosis": superiority of hybrid crosses between different populations (strains)

- Underdominance leads to unstable polymorphic equilibrium

  - Underdominance won't maintain genetic variability within a population

  - With 2 alleles, there are 2 stable equilibria. Which one is approached depends on history (initial state) of the population.