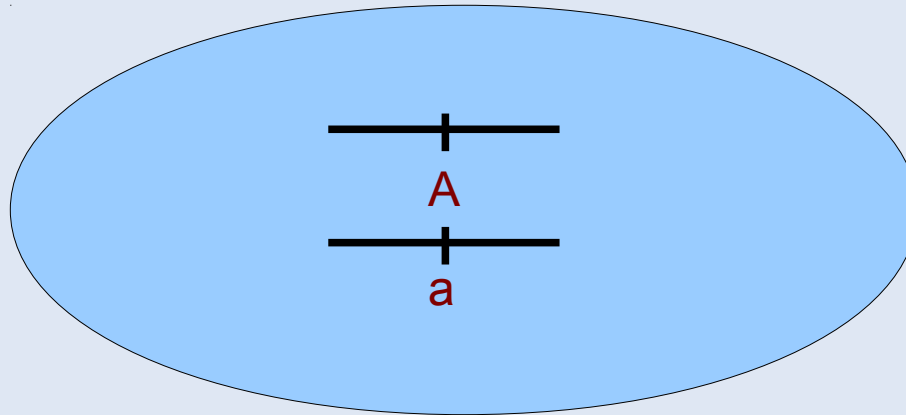


Selection at a single diploid locus



Evolution at a single diploid locus

- Today, let's look at a diploid system with 1 locus and 2 alleles.
- Because of diploidy, we have to think about genotype frequencies in addition to allele frequencies.
- There are three genotypes: AA , Aa , and aa .
- Let p and $q = 1 - p$ denote the allele frequencies for A and a .
- Let P_{AA} , P_{Aa} and P_{aa} denote the genotype frequencies.
- Before considering selection, let's see how the genotype frequencies change over time in the absence of anything interesting (no selection, no migration, no drift, random mating).

Random mating

Mating	Mating probability	Probability of progeny		
		AA	Aa	aa
AA x AA	$(P_{AA})^2$	1	0	0
AA x Aa	$2 P_{AA} P_{Aa}$	1/2	1/2	0
AA x aa	$P_{AA} P_{aa}$	0	1	0
Aa x Aa	$(P_{Aa})^2$	1/4	1/2	1/4
Aa x aa	$P_{Aa} P_{aa}$	0	1/2	1/2
aa x aa	$(P_{aa})^2$	0	0	1

- After one round of reproduction, the genotype frequencies are given by the **Hardy-Weinberg proportions**

$$P_{AA} = p^2, P_{Aa} = 2pq, P_{aa} = q^2$$

- Random mating does not change the allele frequencies.
- That is, alleles assort independently.

Remarks on the HW equilibrium

- The result generalizes to more than two alleles. The frequency of genotype A_1A_2 at HW equals $p(A_1)p(A_2)$, where the latter terms are the respective allele frequencies.
- Reaching HW takes 2 generations if the initial genotype frequencies differ between sexes.
- In continuous time, HW is approached gradually.
- For sex-linked genes, HW proportions apply only to the homogametic sex. The equilibrium is approached gradually.
- Assuming HW proportions following reproduction (where appropriate) greatly facilitates modeling.

Dominance

- Assume the following fitness values for the three genotypes:

$$w_{aa} = 1, w_{Aa} = 1 + hs, w_{AA} = 1 + s$$

- If $h = 1$ (0), allele A (a) is **dominant** and allele a (A) is **recessive**.
- If $h = 0.5$, the two alleles are **codominant** or additive.
- If $0.5 < h < 1$, allele A is **partially dominant**.
- If $h > 1$, we have a situation of **overdominance** (heterozygote advantage, heterosis).
- If $h < 0$, we have a situation of **underdominance** (heterozygote disadvantage).
- Note that dominance can also be defined with respect to phenotype instead of fitness.

Marginal fitnesses

- Assuming Hardy-Weinberg proportions, the **mean fitness** of the population is

$$\bar{W} = p^2 W_{AA} + 2p(1-p) W_{Aa} + (1-p)^2 W_{aa}.$$

- The **marginal fitnesses** (induced fitnesses) of the two alleles are

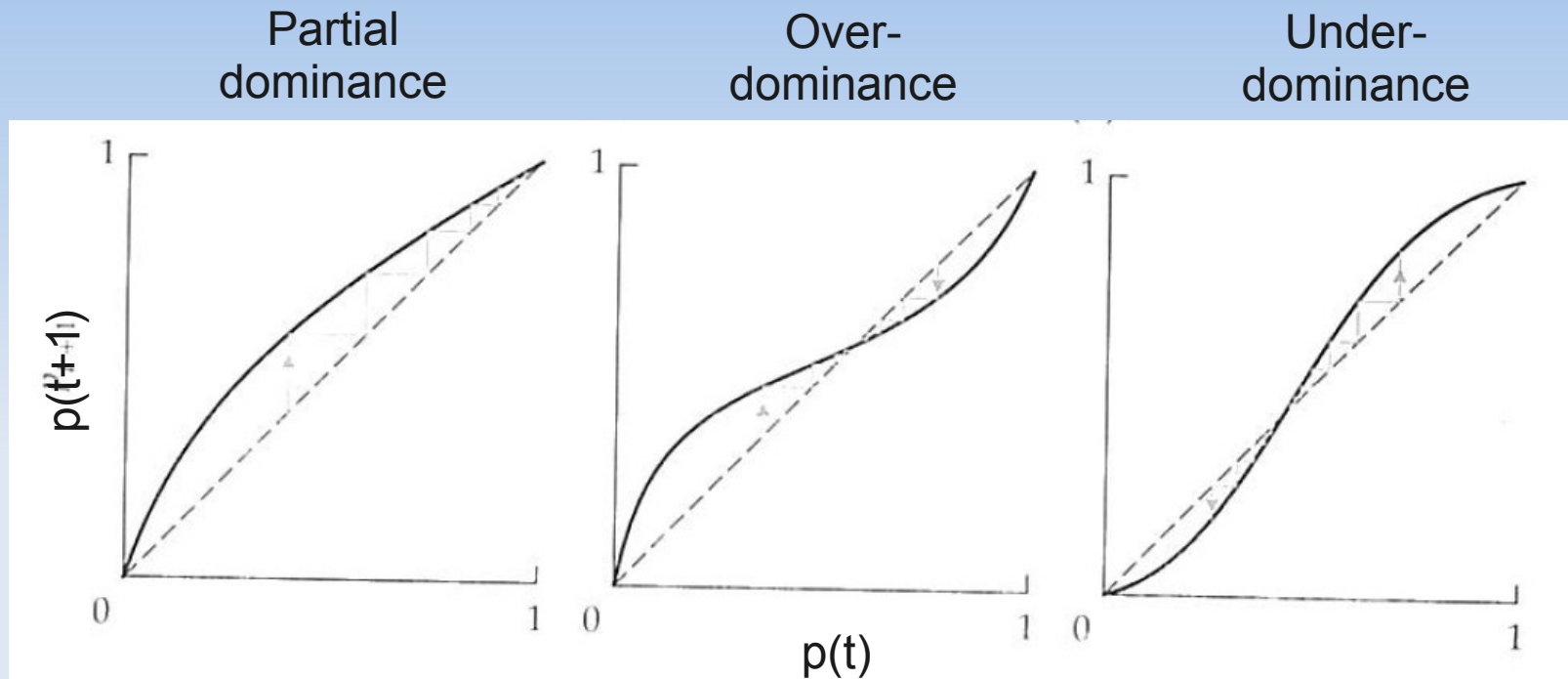
$$W_A^* = p W_{AA} + (1-p) W_{Aa}$$

$$W_a^* = p W_{Aa} + (1-p) W_{aa}$$

- The basic selection equation then is

$$p' = \frac{W_A^*}{\bar{W}} p$$

Equilibria



- With (partial) dominance, the fitter allele goes to **fixation**.
- Overdominance leads to a **stable polymorphism**.
- With underdominance, the system is **bistable**.
- The results from over- and underdominance can be explained by noting that the rarer allele is more likely to find itself in a heterozygote.

The selection gradient

- The previous result can be rewritten as

$$\Delta p = \frac{p(W_A^* - \bar{W})}{\bar{W}} = \frac{p(1-p)(W_A^* - W_a^*)}{\bar{W}}$$

- Now, it happens that

$$2(W_A^* - W_a^*) = \frac{d\bar{W}}{dp}$$

- Using this, we can write

$$\Delta p = \frac{p(1-p)}{2\bar{W}} \frac{d\bar{W}}{dp} = \frac{p(1-p)}{2} \frac{d \ln(\bar{W})}{dp}.$$

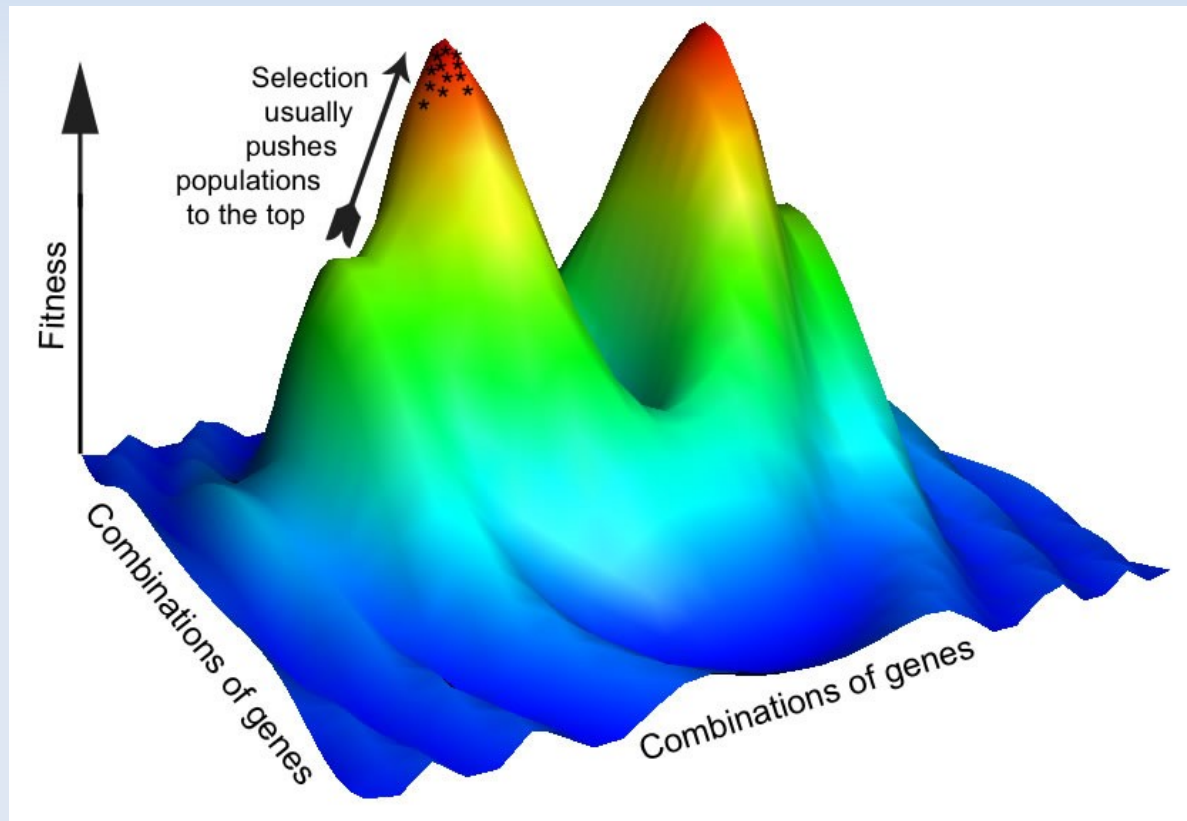
A closer look

$$\Delta p = \frac{p(1-p)}{2} \frac{d \ln(\bar{W})}{dp}.$$

- Here the term $p(1-p)/2$ is the **genetic variance** (the variance in the proportion of A alleles in one individual). Without genetic variance ($p = 0$ or $p = 1$), there is no evolution.
- $\ln(\bar{w}) = \bar{m}$ is the mean **Malthusian fitness** (the continuous-time version of **Wrightian fitness** w).
- The derivative is the **selection gradient** (or fitness gradient).
- Thus, the rate of change in allele frequency is equal to the genetic variance times the selection gradient.
- This is a very general result that will re-appear multiple times in more complex situations.

Adaptive landscapes

The gradient dynamics motivate the metaphor of an **adaptive landscape** (fitness landscape), in which evolution is visualized as hill-climbing.



A caveat

- The above equation seems to suggest that selection always increases mean fitness.
- However, this is only true if selection is **frequency-independent**.
- Often, however, the fitness of an individual depends not only on its own genotype, but also on the genotypes of the other individuals it is interacting with.
- With **frequency-dependent selection**, mean fitness is no longer maximized. Indeed, it may even be minimized.
- This reflects the fact that individuals generally do not act in order to increase the common good.
- Frequency-dependent selection underlies many of the big problems in evolution, such as cooperation and diversity.

Frequency-dependent selection

- Formally, if fitnesses w depend on allele frequency p , the fitness gradient can be shown to be

$$\frac{d\bar{w}}{dp} = 2(w_A^* - w_a^*) + E\left(\frac{dw}{dp}\right)$$

where E denotes the expectation.

- This leads to

$$\Delta p = \frac{p(1-p)}{2\bar{W}} \left[\frac{d\bar{W}}{dp} - E\left(\frac{dw}{dp}\right) \right]$$

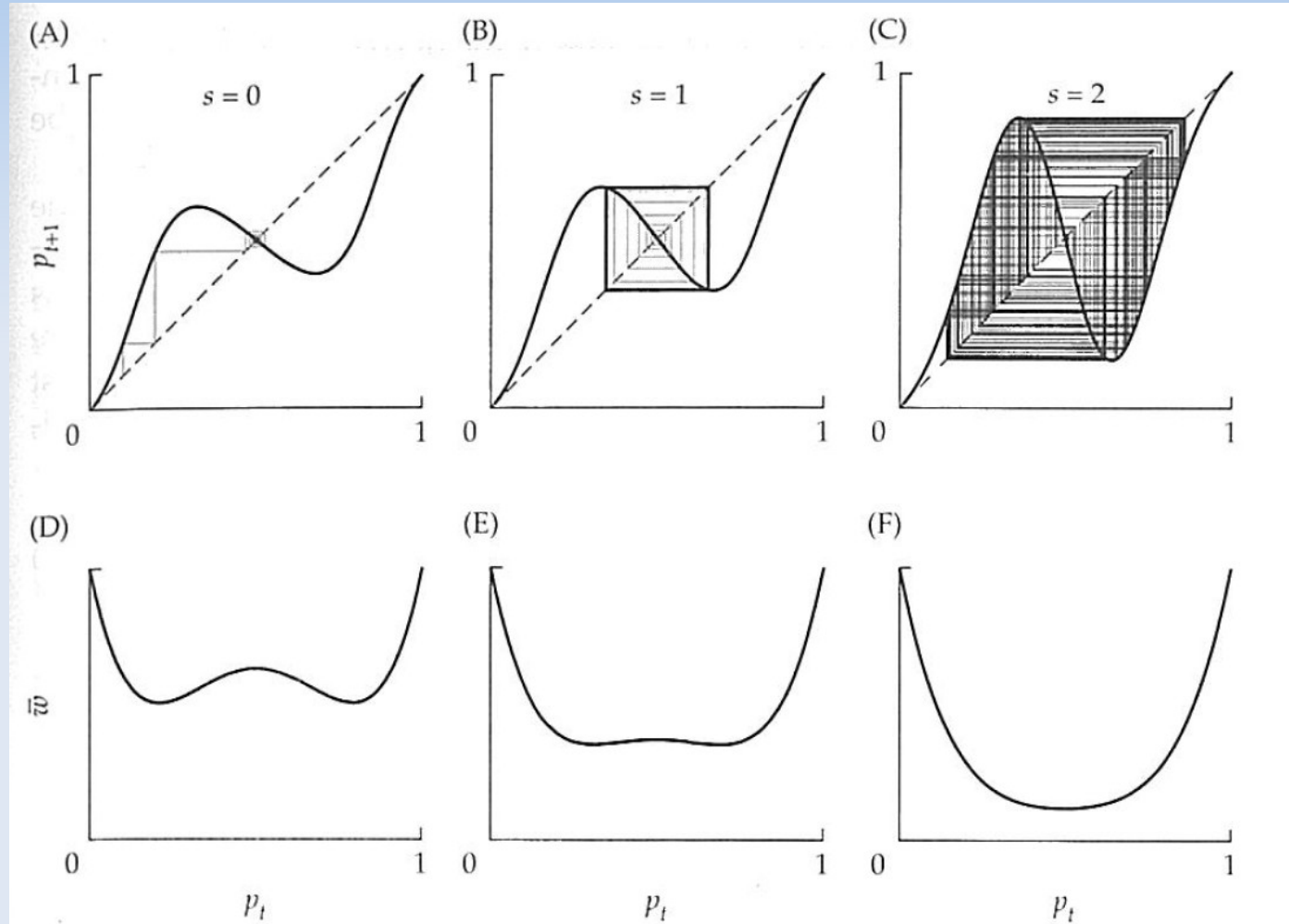
showing that simple maximization of mean fitness no longer applies.

Example for frequency-dependent selection

$$w_{AA} = 1 - 3P_{Aa} + 3P_{aa}$$

$$w_{Aa} = 1 - sP_{Aa}$$

$$w_{aa} = 1 - 3P_{Aa} + 3P_{AA}$$



Kinds of frequency-dependence

- **Negative frequency-dependence** arises if rare genotypes have an advantage (e.g. resource competition). It favors maintenance of polymorphism (balancing selection).
- **Positive frequency-dependence** arises if common genotypes have an advantage (e.g. under some models of sexual selection, where females favor the most common type of males). It often induces bistability (i.e. dependence on initial conditions).

Mutation

- Ultimately, evolution depends on the input of new mutations.
- Most mutations are **deleterious**.
- What is the frequency of deleterious mutations in a population?
- Let's change our notation for fitness:

$$\begin{aligned}w_{aa} &= 1 \\w_{Aa} &= 1 - hs \\w_{AA} &= 1 - s\end{aligned}$$

- That is, a is the **wild-type** allele, and A a deleterious mutation.
- a mutates to A at rate μ per generation. Back mutations are neglected.

Mutation-selection balance

- The change in allele frequency (of the mutant) becomes

$$p_{t+1} = \frac{W_A^*}{\bar{W}} p + \mu(1-p)$$

with $W_A^* = (1-p)(1-hs) + p(1-s) = 1 - sp - hs + hsp$

- We can simplify by setting $\bar{W} \approx 1$, leading to the equilibrium condition

$$\mu(1-\hat{p}) \approx s\hat{p}^2 + hs\hat{p}(1-\hat{p})$$

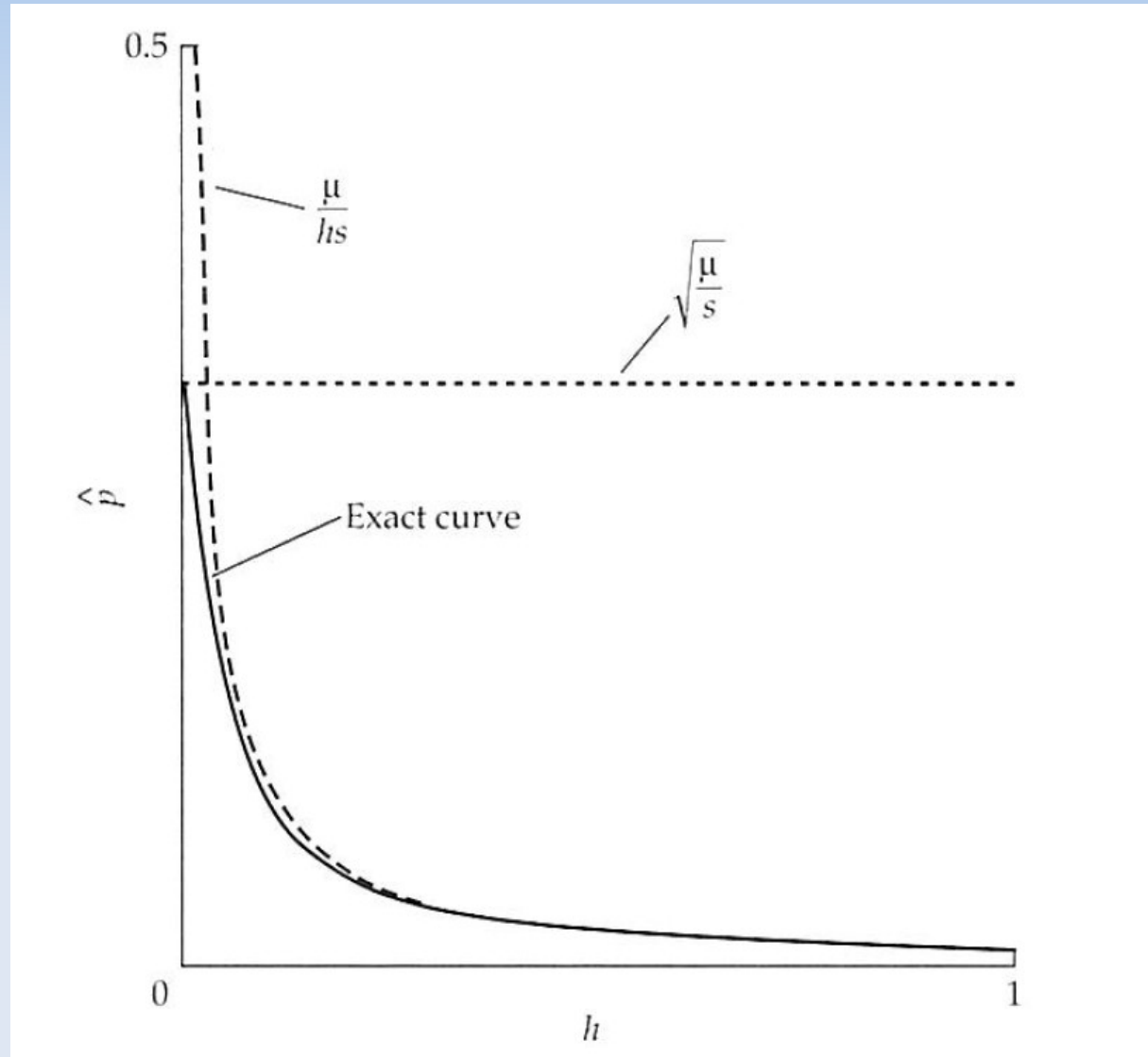
- p will be small, so for $h > 0$, we set $s\hat{p}^2 \approx 0$ and get

$$\hat{p} \approx \frac{\mu}{hs}$$

For $h = 0$ (recessive mutant), we instead set $1 - \hat{p} \approx 1$, yielding

$$\hat{p} \approx \sqrt{\mu/s}$$

Mutation-selection balance (cont.)



Maintenance of genetic variation

- Evolution by natural selection requires genetic variation, but at the same time destroys it.
- In practice, we observe abundant variation for most traits.
- So, the problem of what maintains this variation is mainly a theoretical one.
- Mutation-selection balance is one possible explanation, but it is unclear whether it can account for all variation.
- Obvious alternatives are balancing selection, temporarily fluctuating or spatially heterogeneous selection.
- Despite its fundamental nature, the question is still open.