Evolutionary genetics

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Goals of evolutionary genetics

- Basis of genetic and phenotypic variation
  - # and effects of genes
  - gene interactions
  - pleiotropic effects of genes
  - genotype-phenotype relationship
- Origin of variation
  - Distribution of mutational effects
  - Recombination
- Maintenance of variation
  - Drift
  - Selection
- Distribution of variation
  - within and among populations (metapop. structure)
  - within and among species
  - clinal variation

Major questions

- Molecular evolution
  - rate of neutral and selected sequence changes
  - gene and genome structure
- Character evolution
  - rate of evolution
  - predicted or reconstructed direction of Δ
  - evolutionary constraints
  - genotype-phenotype relationship (development)
- Process of population differentiation
  - outbreeding depression and hybrid inviability
- Process of speciation
  - genetic differentiation
  - reproductive isolation

Approaches

- Traditionally two major approaches have been used
  - Mendelian population genetics
    - examine dynamics of a limited # of alleles at a limited # of loci
  - quantitative genetics
    - assume a large # of genes of small effect
    - continuous variation
    - statistical description of genetics and evolution

Population genetic example

- Example captures basic approach to evolutionary models
  - evolution proceeds by changes in the frequencies of alleles
  - basic processes underlie almost all other approaches to modeling
- Conclusions from simple pop-gen models can be a useful first approach

A population genetic model

- Assumptions
  - a single locus with two alleles (*A* and *a*)
  - diploid population
  - random mating
  - discrete generations
  - large population size

The population

- With random mating the frequencies of the three genotypes are the product of the individual allele frequencies
- This is the "Hardy-Weinberg equilibrium"
- $F(A) = p$ $F(a) = q$

AA	Aa	aa
p^2	$2pq$	q^2

Selection

	Genotype			Total
	AA	*Aa*	*aa*	
Freq. before selection	p^2	$2pq$	q^2	$1 = p^2 + 2pq + q^2$
Relative fitness	w_{AA}	w_{Aa}	w_{aa}	$\bar{w} = p^2 w_{AA} + 2pq w_{Aa} + q^2 w_{aa}$
After selection	$p^2 w_{AA}$	$2pq\, w_{Aa}$	$q^2 w_{aa}$	
Normalized	$\frac{p^2 w_{AA}}{\bar{w}}$	$\frac{2pq\, w_{Aa}}{\bar{w}}$	$\frac{q^2 w_{aa}}{\bar{w}}$	

Evolution

Allele frequencies in the next generation

$$p' = \frac{p^2 w_{AA} + pq w_{Aa}}{\bar{w}}$$

$$q' = \frac{pq w_{Aa} + q^2 w_{aa}}{\bar{w}}$$

- Selection biases probability of sampling the two alleles when constructing the next generation
- Genotype frequencies are still in H-W equilibrium at the frequencies defined by p' and q'

Selection can change population genetic structure

Selection – nonrandom survival or reproductive success (RS) of different phenotypes

– **differential reproductive success** of different phenotypes

When can selection lead to evolution?

When different **phenotypes** represent different **genotypes**

$R = S \times h^2$ (i.e., when **phenotypic** differences are **heritable**).

IF:

genotypes differ in average fitness

THEN:

some genotypes will contribute more alleles to future generations

How does **selection** cause change in allele frequencies?

Parental allele freq:
0.5 A 0.5 a

	sperm: 0.5 A	sperm: 0.5 a
eggs: 0.5 A	0.25 AA	0.25 Aa
eggs: 0.5 a	0.25 Aa	0.25 aa

1000 zygotes:
250 AA
500 Aa
250 aa

Survival to repro:
100% for AA
75% for Aa
50% for aa

Survivors:
250 AA
375 Aa
125 aa
750 indv's

Offspring allele freq:
250 x 2 + 375 = 875 / 1500 = 0.58 A
125 x 2 + 375 = 625 / 1500 = 0.42 a

Did allele frequencies change?

Why?

Case study: Sickle cell disease

aa – abnormal ß hemoglobin
sickle-cell disease

very low fitness

AA – normal ß hemoglobin

Aa – both ß hemoglobins

Case study: Sickle cell disease

aa – abnormal ß hemoglobin
sickle-cell disease

very low fitness

AA – normal ß hemoglobin
vulnerable to malaria

intermed. fitness

Aa – both ß hemoglobins
resistant to malaria

high fitness

Heterozygote advantage in populations with malaria.

Mutation can change population genetic structure

Mutation rates are low

typically <1/10,000 per generation ($\mu \leq 0.0001$)

Loss-of-function mutations are much more common than back mutations that restore function

WHY?

How does **mutation** cause change in allele frequencies?

Allele freq. before mutation:

0.5 A **0.5 a**

Mutation rate:

0.0001 A → a

Allele freq. after mutation:

0.5000 A **0.5000 a**

- 0.0001 **+ 0.0001**

0.4999 A **0.5001 a**

Did allele frequencies change?

What if mutation continued over many generations?

How does **mutation** cause change in allele frequencies?

Most mutations are <u>deleterious</u>

should be eliminated by selection ($\mu \leq 0.0001$)

<u>Mutation-selection balance</u>

removal by selection offsets recurrent mutations

more mutations per generation → **higher frequency of mutant allele at equilibrium**

stronger selection against mutant allele → **lower frequency of mutant allele at equilibrium**

Genetic drift can change population genetic structure

Genetic drift – **random change** in allele frequencies
due to **sampling error**

random difference between **expectation** and **actual results**

count all alleles in the gene pool	sample only some alleles from the gene pool

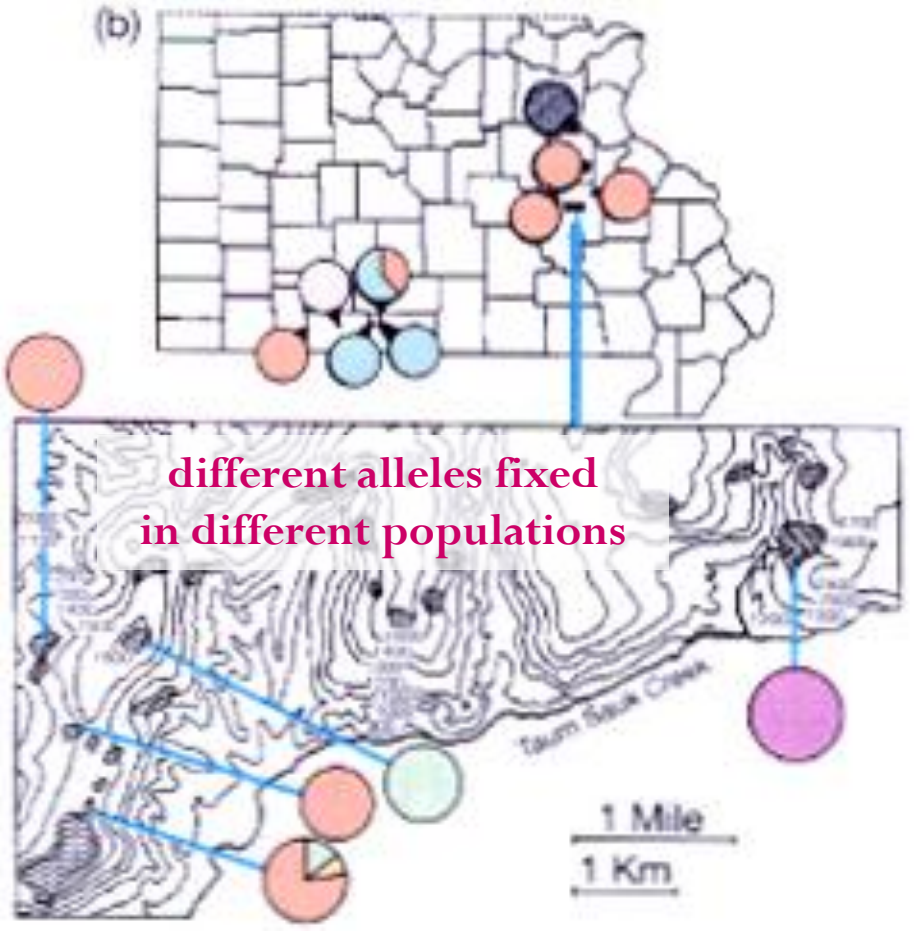
Genetic drift – **does not lead to adaptation**, because it is purely **random**

alleles get passed on
based on luck or chance

– most pronounced in **small populations**

Key points about **genetic drift**

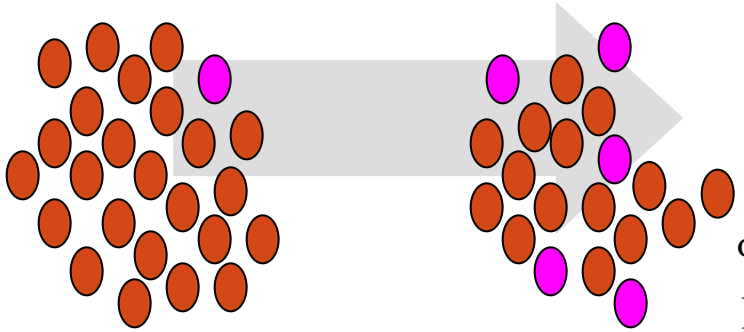
1. Each population has a unique trajectory.
2. Drift has greater influence in small populations.
3. Drift can lead to large changes in allele frequencies over time.
4. Over time, alleles can be lost.



Forms of **genetic drift**

Founder effect

– a small group leaves a large population and starts a new population



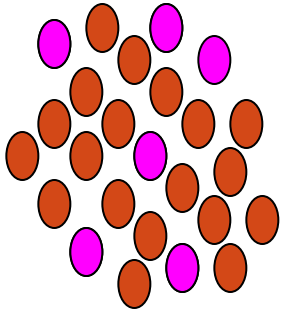
ancestral population

descendent population

allele frequencies may differ due to sampling error

Population bottleneck

– large population shrinks to a small number of individuals,
which reproduce to repopulate



ancestral population

descendent population

allele frequencies may differ due to sampling error

Migration can change population genetic structure

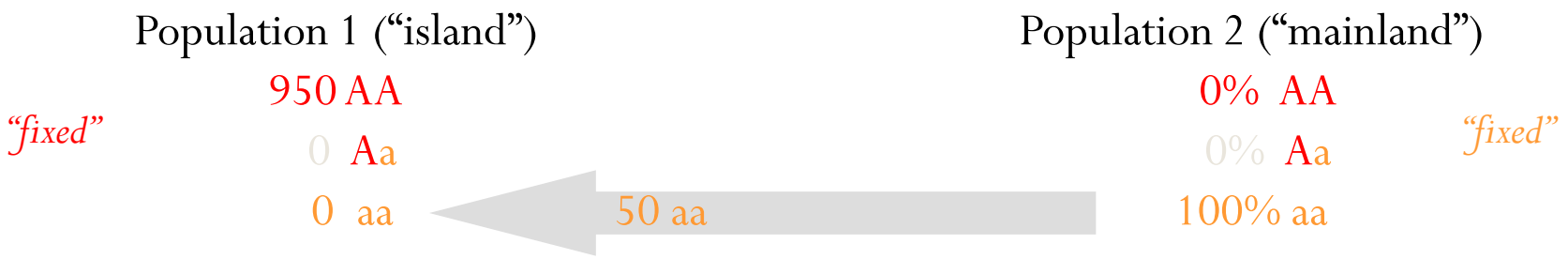
Migration – movement of **alleles** between populations

– movement of individuals will result in evolution only if it results in **gene flow**

*(must move and **reproduce** in new population)*

WHY?

How does migration cause change in allele frequencies?



Allele freq. before migration:

Did allele frequencies change?

Allele freq. after migration:

Is the population in Hardy-Weinberg equilibrium?

$p^2 = (0.95)^2 = 0.9025$

$2pq = 2(0.95)(0.05) = 0.0950$

$q^2 = (0.05)^2 = 0.0025$

What if migration continued over many generations?

Migration makes population more similar

AlleleA1 simulation – one-way migration (gene flow)

Population 1 ("island")

Population 2 ("mainland")

Migration makes population more similar

AlleleA1 simulation – one-way migration (gene flow)

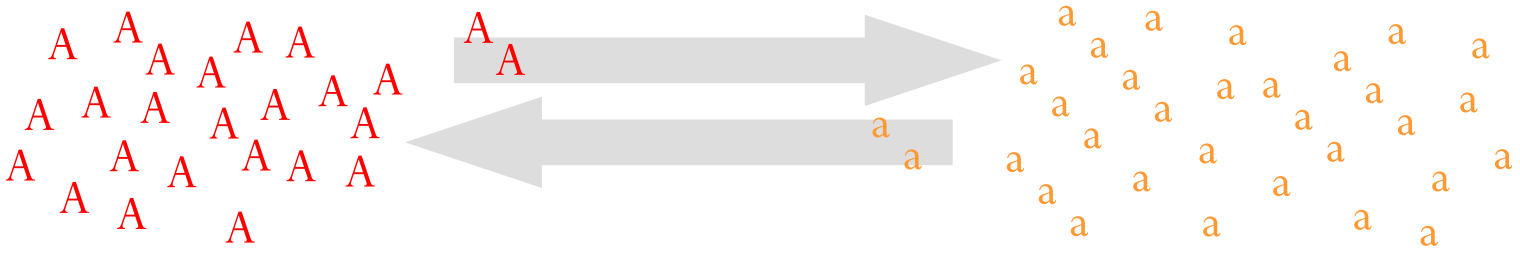
Population 1 ("island")

Population 2 ("mainland")

Real life – gene flow can be one-way or two-way

Population 1

Population 2

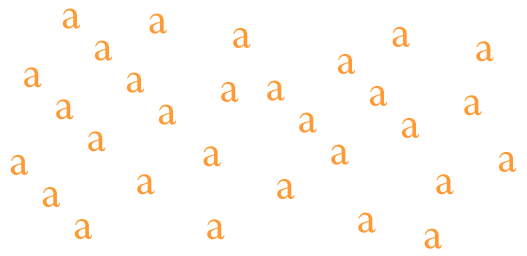


Migration makes population more similar

AlleleA1 simulation – one-way migration (gene flow)

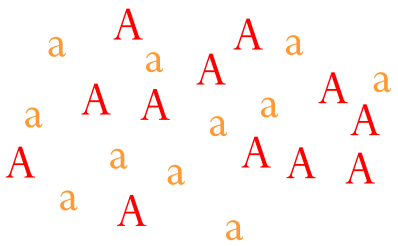
Population 1 ("island")

Population 2 ("mainland")

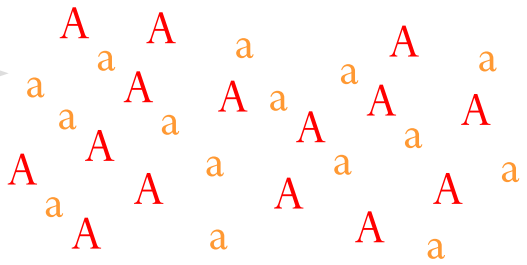


Real life – gene flow can be one-way or two-way

Population 1



Population 2



What can change population genetic structure?

change in p & q

genotype freq's aren't p^2, $2pq$, q^2

- **mutation**
  - introduces new alleles
  - ↑ *diversity within populations*
- **migration**
  - introduces new alleles
  - ↑ *diversity within populations*
  - ↓ *diversity between populations*
- **genetic drift**
  - loss of alleles
  - ↓ *diversity within populations*
  - ↑ *diversity between populations*
- **selection**
  - removes harmful alleles
  - usually ↓ *diversity within populations*
  - can ↑ or ↓ *diversity between populations*
- non-random mating

Population genetic forces can interact

- mutation

introduces new alleles

diversity within populations

- migration
- genetic drift
- selection

removes harmful alleles

usually  *diversity within populations*

can  *diversity between populations*

- non-random mating

Population genetic forces can interact

mutation vs. selection

introduces new alleles

↑ *diversity within populations*

removes harmful alleles

↓ *diversity within populations*

Mutation-selection balance

recurrent mutations offset removal by selection

more mutations per generation → higher frequency of mutant allele at equilibrium

stronger selection against mutant allele → lower frequency of mutant allele at equilibrium

Population genetic forces can interact

- mutation
- migration
- genetic drift
- selection
- non-random mating

introduces new alleles

↑ *diversity within populations*

↓ *diversity between populations*

removes harmful alleles

↓ *diversity within populations*

usually ↓ *diversity between populations*

can ↑

Population genetic forces can interact

migration vs. selection

introduces new alleles

↑ *diversity within populations*

↓ *diversity between populations*

removes harmful alleles

usually ↓ *diversity within populations*

can ↑ or ↓ *diversity between populations*

Balance between migration and selection

- input from migration offsets removal by selection
- homogenizing force of migration offset by diversifying force of selection

more migration per generation → higher frequency of migrant allele at equilibrium; populations become similar

stronger selection against migrant allele → lower frequency of migrant allele at equilibrium; populations remain distinct

Population genetic forces can interact

- mutation
- migration
  - introduces new alleles
  - ↑ *diversity within populations*
  - ↓ *diversity between populations*
- genetic drift
  - loss of alleles
  - ↓ *diversity within populations*
  - ↑ *diversity between populations*
- selection
- non-random mating

Population genetic forces can interact

migration vs. drift

migration	drift
introduces new alleles	loss of alleles
↑ *diversity within populations*	↓ *diversity within populations*
↓ *diversity between populations*	↑ *diversity between populations*

Balance between migration and drift

- input from migration offsets removal by drift
- homogenizing force of migration offset by diversifying force of drift

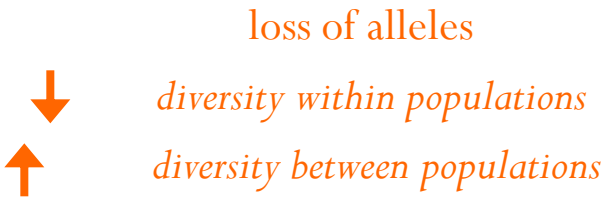
more migration per generation → higher frequency of migrant allele at equilibrium; populations become similar

smaller population size → drift affects frequency of migrant allele (usually lost); populations remain distinct

Balance depends on population size

Population genetic forces can interact

- mutation
- migration
- genetic drift



- selection

- non-random mating

Population genetic forces can interact

selection vs. drift

removes harmful alleles

↓ *diversity within populations*

↑ can ↓ *diversity between populations*

loss of alleles

↓ *diversity within populations*

↑ *diversity between populations*

Balance between selection and drift

- random force of drift can oppose selection against deleterious allele
- drift opposes adaptation

stronger selection against deleterious allele → lower frequency of deleterious allele at equilibrium; populations become adapted

smaller population size → drift affects frequency of deleterious allele (may be kept); populations drift

Balance depends on population size

What can change population genetic structure?

change in p & q

- mutation
- migration
- genetic drift
- selection

genotype freq's aren't p^2, $2pq$, q^2

- non-random mating

How can evolutionary biology help fight disease?

How do pathogens evolve to be harmful?

Can we stop pathogens from evolving harmful traits?

- **Evolution of drug resistance**

  mutation – rare mutations for resistance genes

  natural selection – resistant individuals have higher fitness in environments with the drug

  → *changing the **selective environment** can slow the evolution of resistance*
  (presence of drug)

- **Evolution of virulence**

  virulence – how harmful a pathogen is to its host

  depends on **natural selection** and **migration**

  → *decreasing opportunities for **migration** can make virulence less adaptive*
  (spread to new host)

When should pathogens evolve high virulence?

Pathogen populations that grow quickly are more harmful (virulent)

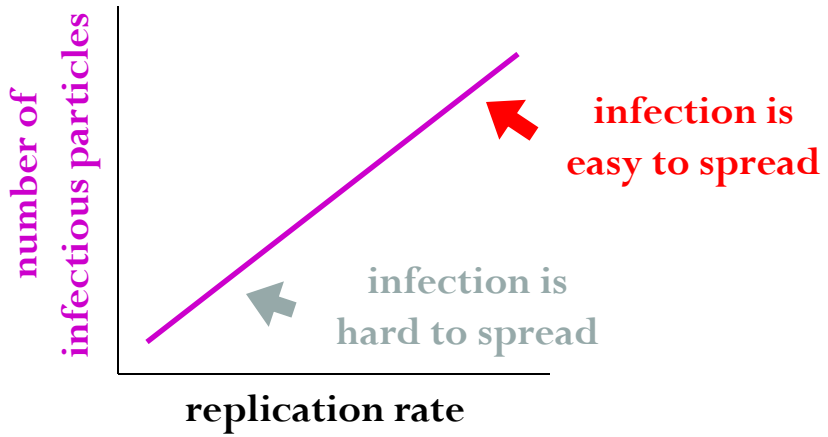
Should natural selection favor alleles that promote high replication rates?

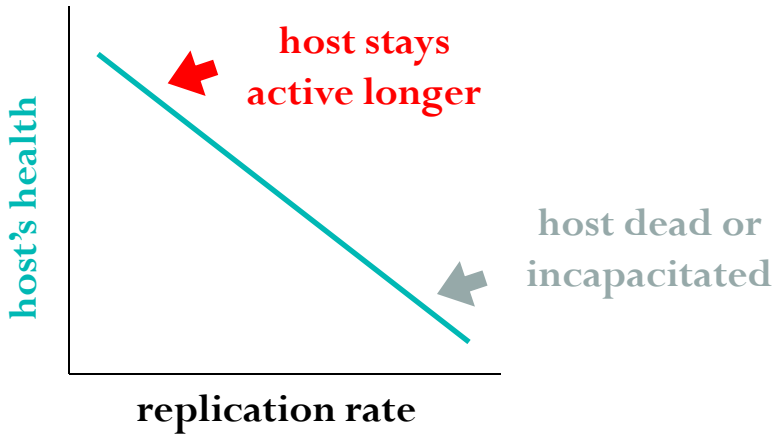
Pathogen fitness depends on spread to new hosts *(migration)*

high replication → **more infectious particles produced**

→ **more likely to kill the host**

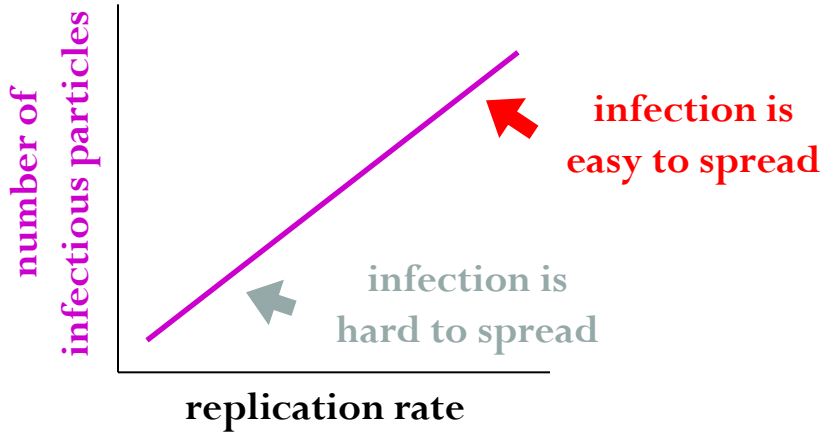
trade-off

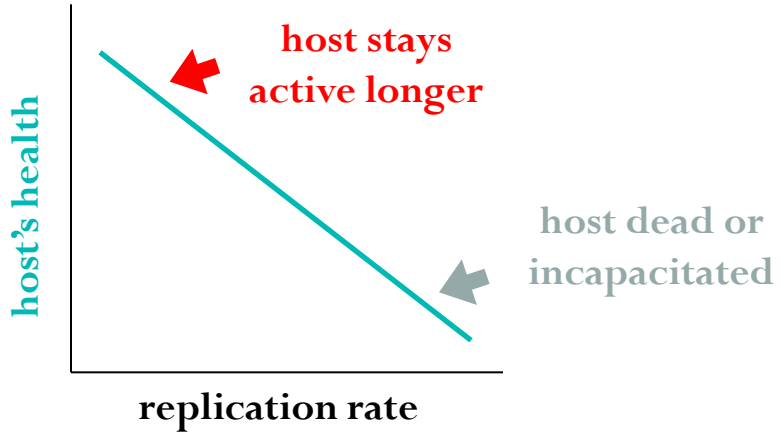




When should pathogens evolve high virulence?

Should natural selection favor alleles that promote high replication rates?





Virulent pathogens → many infectious particles in host → **easy to spread** → **host very sick**

Avirulent pathogens → few infectious particles in host → **hard to spread** → **host not very sick**

trade-off

When should pathogens evolve high virulence?

Virulent pathogens → many infectious particles in host **→ easy to spread → host very sick**

Avirulent pathogens → few infectious particles in host **→ hard to spread → host not very sick**

trade-off

transmission rate (trade-off) hypothesis: transmission requires opportunities for pathogen to spread to new hosts

many transmission opportunities

→ contact with many potential hosts

→ if infectious, can transmit to many new hosts in short time

→ **favors high virulence**

few transmission opportunities

→ contact with few potential hosts

→ must live a long time to have transmission opportunities

→ **favors low virulence**

When should pathogens evolve high virulence?

transmission rate (trade-off) hypothesis: **transmission requires opportunities for pathogen to spread to new hosts**

many transmission opportunities favor high virulence

→ contact with many potential hosts

→ if infectious, can transmit to many new hosts in short time

few transmission opportunities favor low virulence

→ contact with few potential hosts

→ must live a long time to have transmission opportunities

***Example 1*:**

virulent HIV strains

→ high risk of spread to sexual partner(s)

→ low life expectancy of patient

→ **favored when sex is promiscuous**

less virulent HIV strains

→ low risk of spread to sexual partner(s)

→ high life expectancy of patient

→ **favored when sex is monogamous**

When should pathogens evolve high virulence?

transmission rate (trade-off) hypothesis: **transmission requires opportunities for pathogen to spread to new hosts**

many transmission opportunities favor high virulence

→ contact with many potential hosts

→ if infectious, can transmit to many new hosts in short time

few transmission opportunities favor low virulence

→ contact with few potential hosts

→ must live a long time to have transmission opportunities

Example 2:

vertically-transmitted pathogens

(e.g., hepatitis, some STD's)

→ parent-to-offspring spread

→ host must live to reproduce

→ **favors low virulence**

horizontally-transmitted pathogens

(e.g., malaria, influenza)

→ spread to any other individual

→ can spread rapidly

→ **favors high virulence**

When should pathogens evolve high virulence?

transmission rate (trade-off) hypothesis: **transmission requires opportunities for pathogen to spread to new hosts**

many transmission opportunities favor high virulence

→ contact with many potential hosts

→ if infectious, can transmit to many new hosts in short time

few transmission opportunities favor low virulence

→ contact with few potential hosts

→ must live a long time to have transmission opportunities

***Example 3*:**

water-borne or vector-borne pathogens
(e.g., cholera, malaria)

→ can spread without contact between hosts
→ can spread rapidly
→ **favors high virulence**

directly transmitted pathogens
(e.g., common cold, mononucleosis)

→ require direct contact between hosts
→ hosts must remain active
→ **favors low virulence**

When should pathogens evolve high virulence?

transmission rate (trade-off) hypothesis: **transmission requires opportunities for pathogen to spread to new hosts**

many transmission opportunities favor high virulence

→ contact with many potential hosts

→ if infectious, can transmit to many new hosts in short time

few transmission opportunities favor low virulence

→ contact with few potential hosts

→ must live a long time to have transmission opportunities

***In general*:**

if pathogen can quickly spread to other hosts

→ can afford to have negative effects on host

→ **favors high virulence**

if pathogens cannot spread quickly

→ needs to keep host around for a while

→ **favors low virulence**

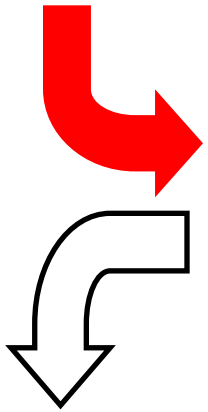
When should pathogens evolve high virulence?

transmission rate (trade-off) hypothesis:
evolution of virulence depends on **rate of pathogen spread**

rate of pathogen spread depends on →

- pathogen ecology – mode of transmission
- host behavior – contact with others
  - sanitation
  - control of disease vectors

→ ***decreasing disease spread*** *(migration) can make virulence a less adaptive trait*



- controlling mosquito outbreaks
- providing clean water for drinking
- washing hands
- preventing spread of STD's

(1) less disease spread
(2) transmission rate hyp. predicts that pathogens should evolve lower virulence