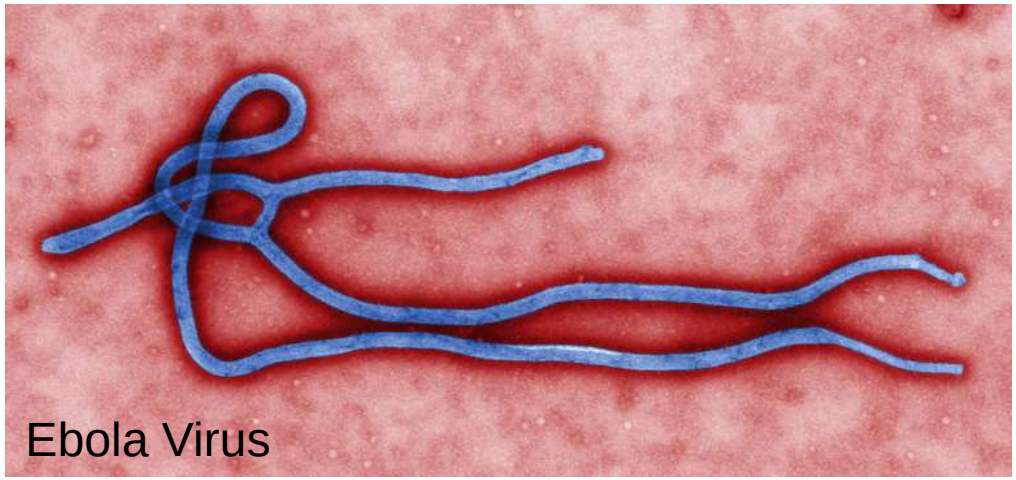

Ebola Virus

Emerging Diseases

Biosciences in the 21st Century

Dr. Amber Rice

October 25, 2019

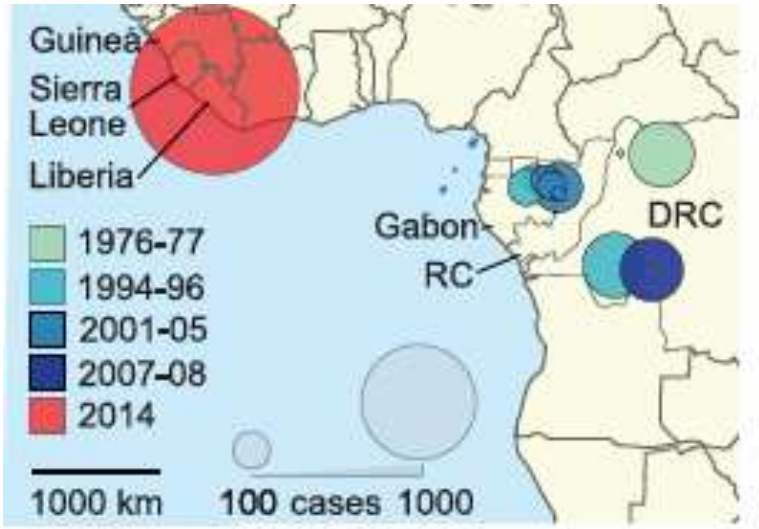
Outline

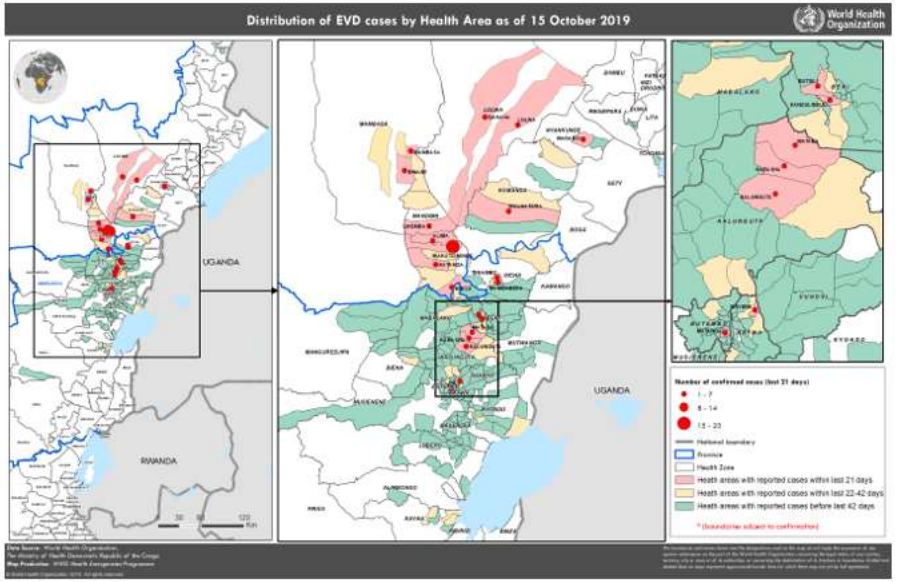
- Disease emergence: a case study
- How do pathogens shift hosts?
- Evolution within hosts: The evolution of virulence
- Treatments: the evolution of drug resistance

Disease emergence: a case study

Ebola Virus

- First identified in Zaire, 1976
- Outbreaks in mid-90s, early 2000s, mid 2000s, **2014-2016 (West Africa), 2018-2019 (DRC)**
- Average 50% fatality rate





Gire et al. 2014, *Science;* WHO

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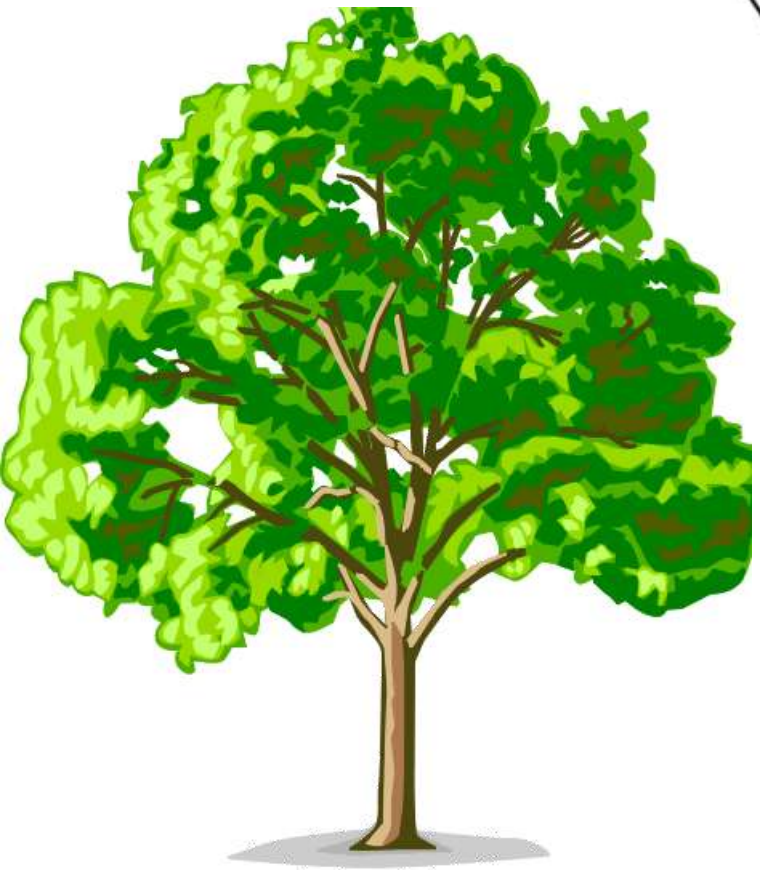
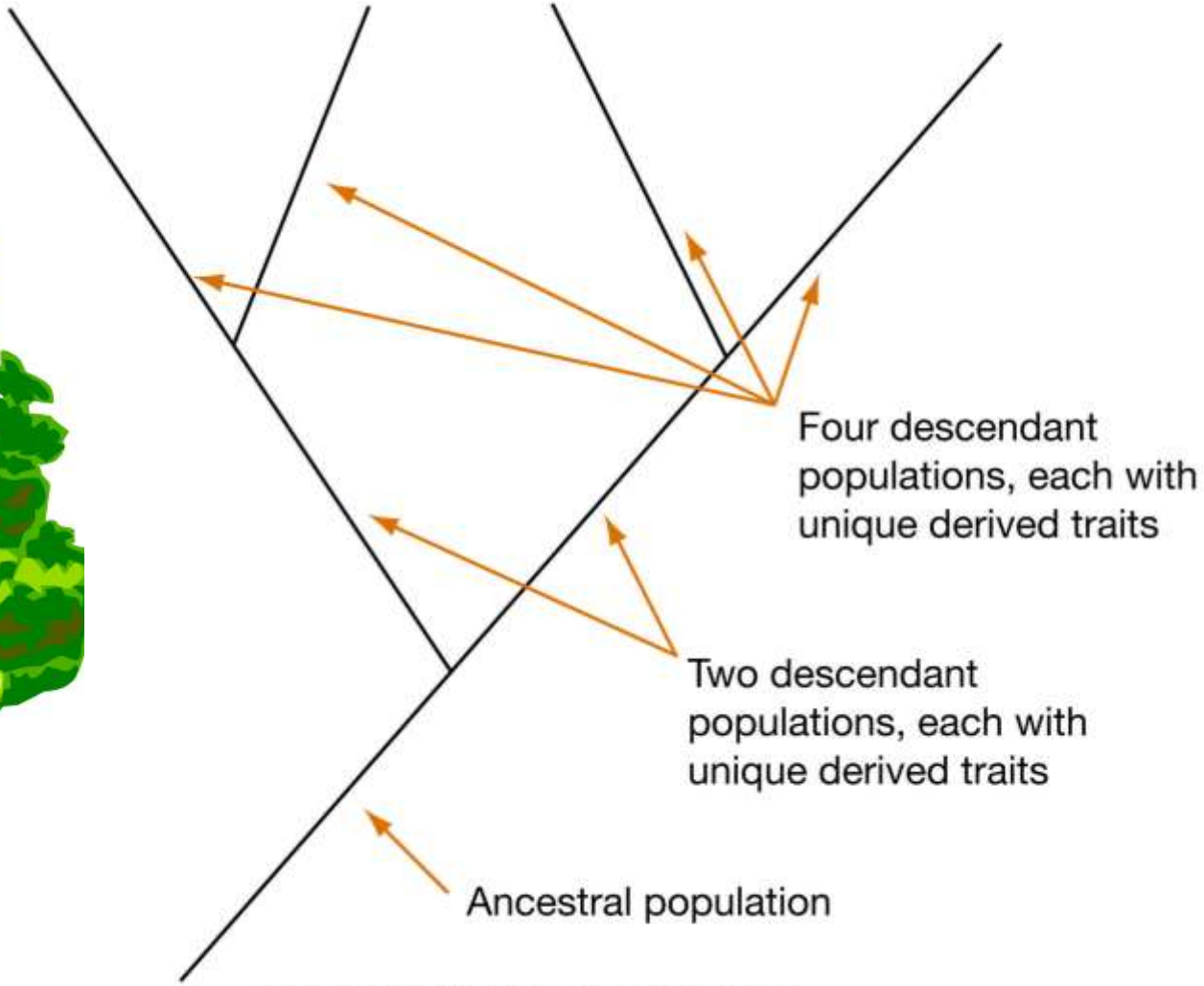
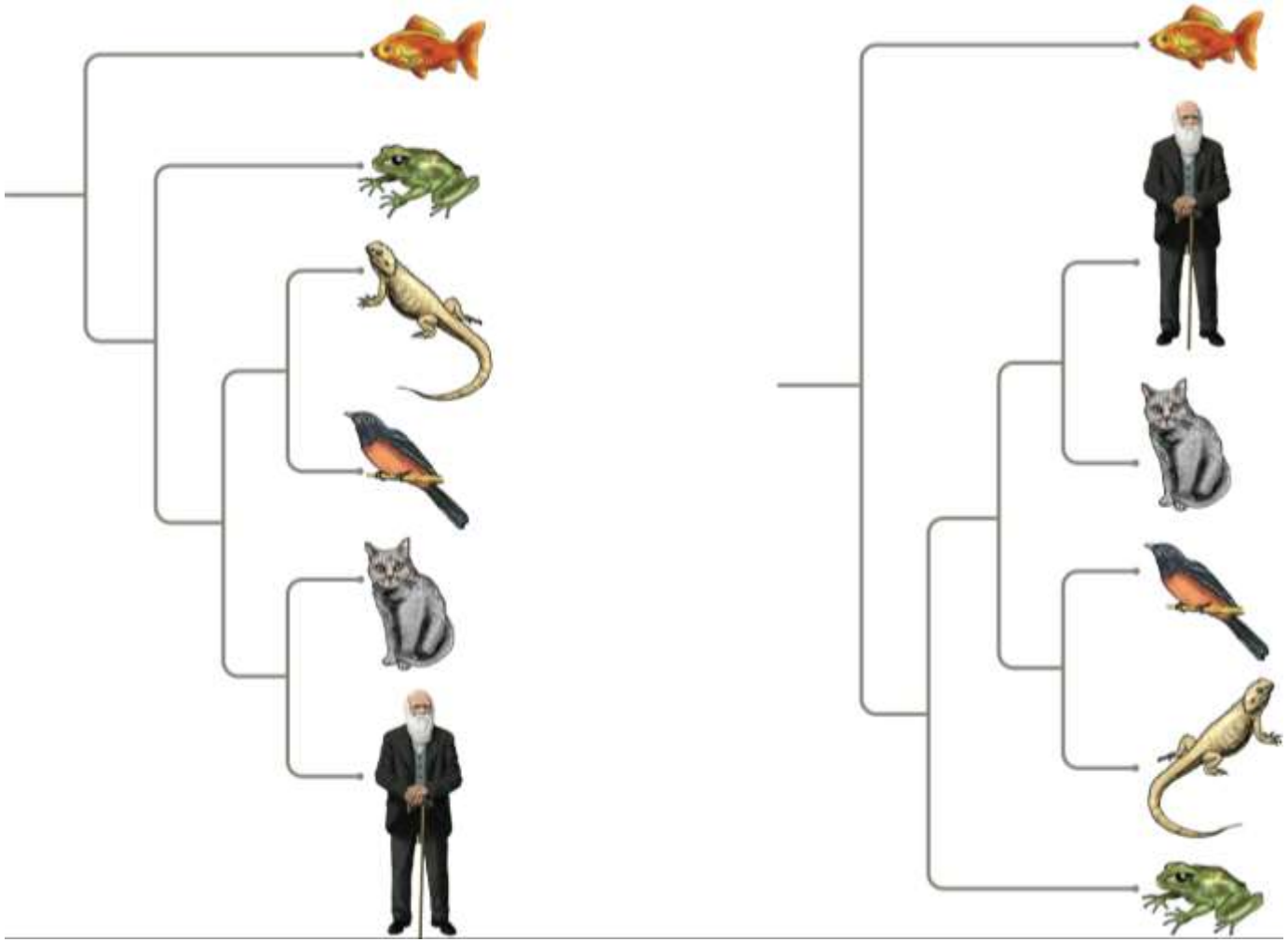
Reading a phylogenetic tree



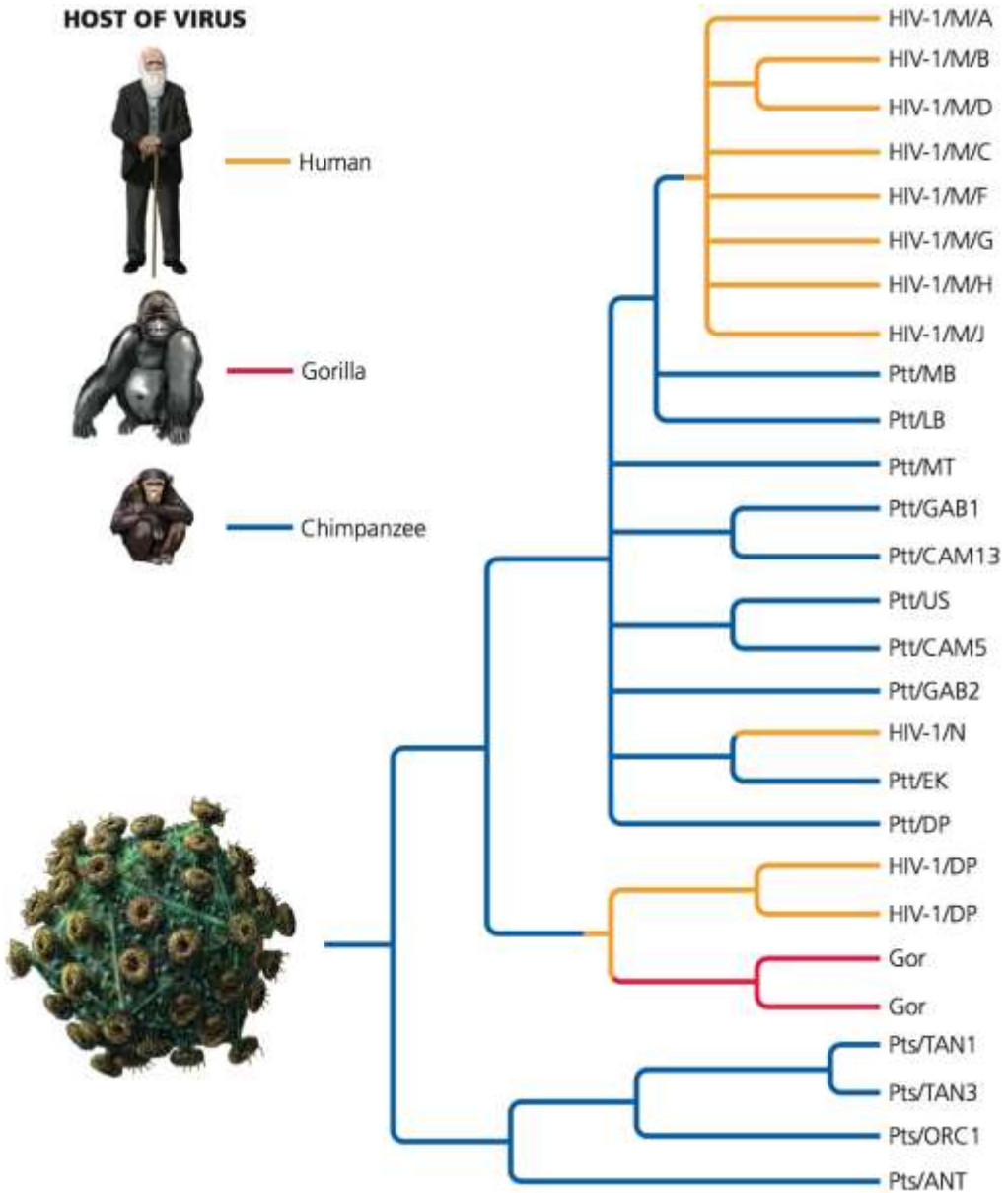


No currently existing species is ancestral to any other



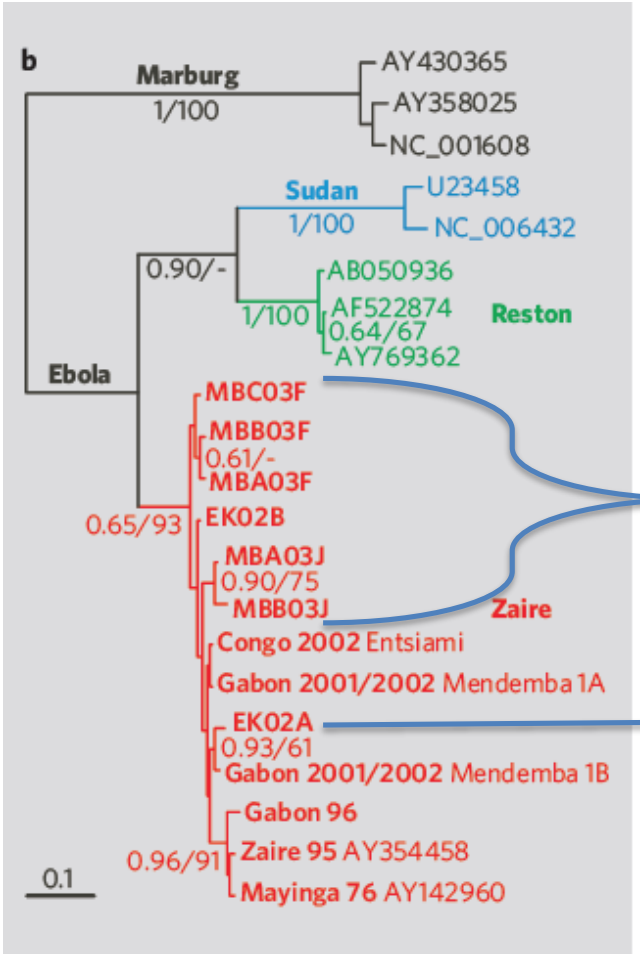
There is no linear ancestor-descendent relationship! Humans did not evolve from cats or fish!

Phylogeny of HIV



Three separate introductions from chimpanzees

Back to our case study: Ebola's natural reservoir



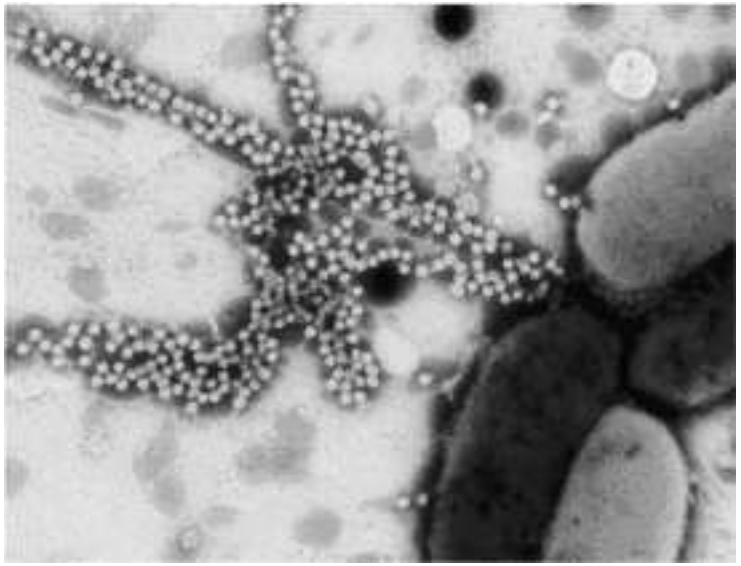
Ebola isolates from fruit bats

Ebola isolate from fruit bats

Leroy et al. 2005, *Nature*

Shifting to another host species

- phi 6: virus that infects bacteria (bacteriophage)
- phi 6 only infects *Pseudomonas syringae*



Shifting to another host species

- Could phi 6 switch hosts?
- Plated on 14 different *Pseudomonas* species
- A few viruses infected and survived
- All had mutation in protein for attaching to host

Duffy et al. 2007

Shifting to another host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction

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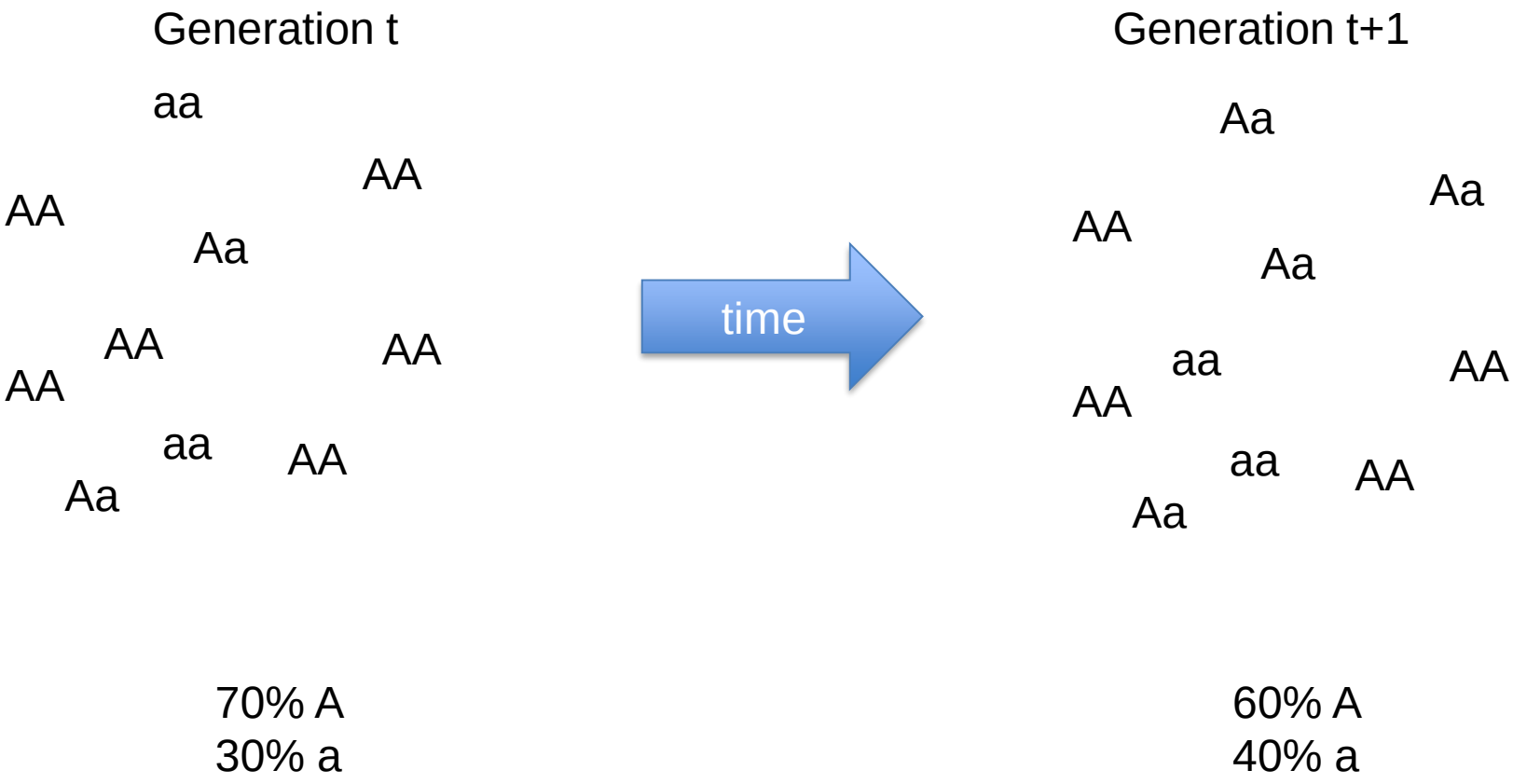
What is evolution?

Evolution is a change in a population's allele frequencies over time.



Mechanisms of evolution: sources of variation

Mutation: a change in DNA sequence, gene order, or chromosome number

- Random
- Increases genetic variation within populations
- Types of mutations:
  - Point mutations
  - Insertions
  - Deletions
  - Gene duplications
  - Chromosomal inversions
  - Polyploidy

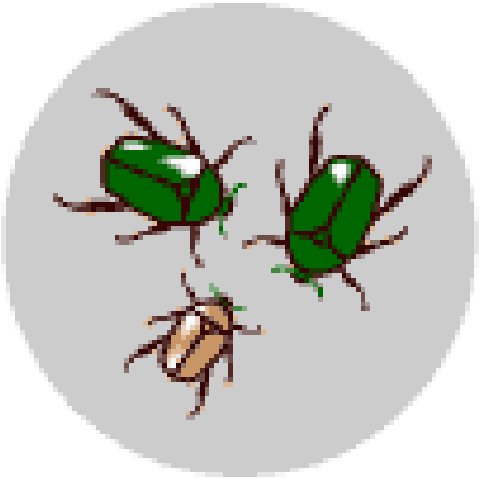


Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site

Mechanisms of evolution: sources of variation

Gene flow (or migration): movement of genes between populations

- Increases genetic variation within populations
- Makes populations more similar to each other

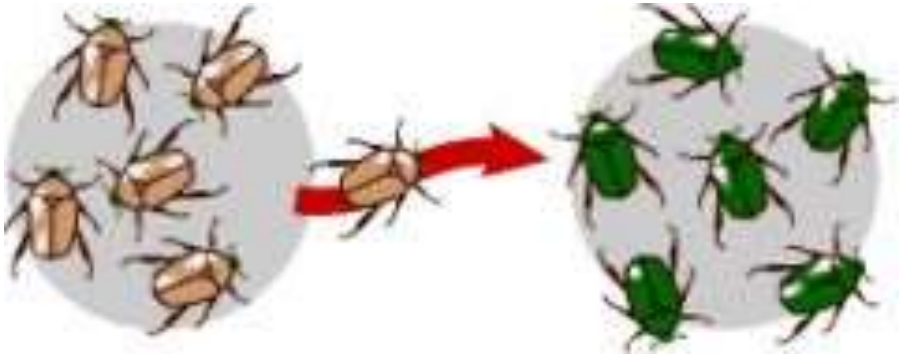


Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site

Mechanisms of evolution

Natural selection: differential reproductive success

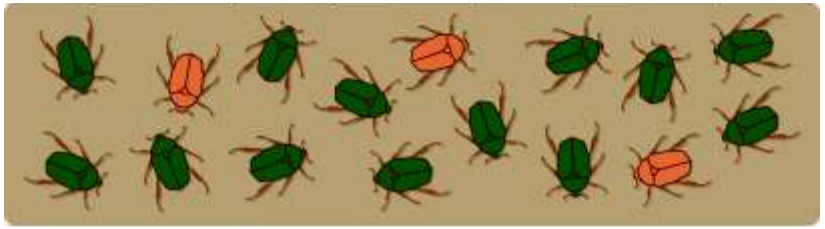
- Non-random
- Not forward-looking, can only work with existing variation
- Only adaptive mechanism of evolution

Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site

Evolution by natural selection

<u>Ingredients needed for evolution by natural selection</u>

- Variation in traits
- Inheritance
- Differential reproduction (natural selection)



End result: Traits that increase reproductive success increase in frequency in a population.

Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site

Evolution within the host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction
- Host switching leads to strong selection:
  - Infection
  - Evade immune system and replicate
- **What factors allow pathogens to evolve quickly?**

Evolution of virulence: a trade-off

Selection **within host** favors
rapid replication (increased virulence).

Competition
within host

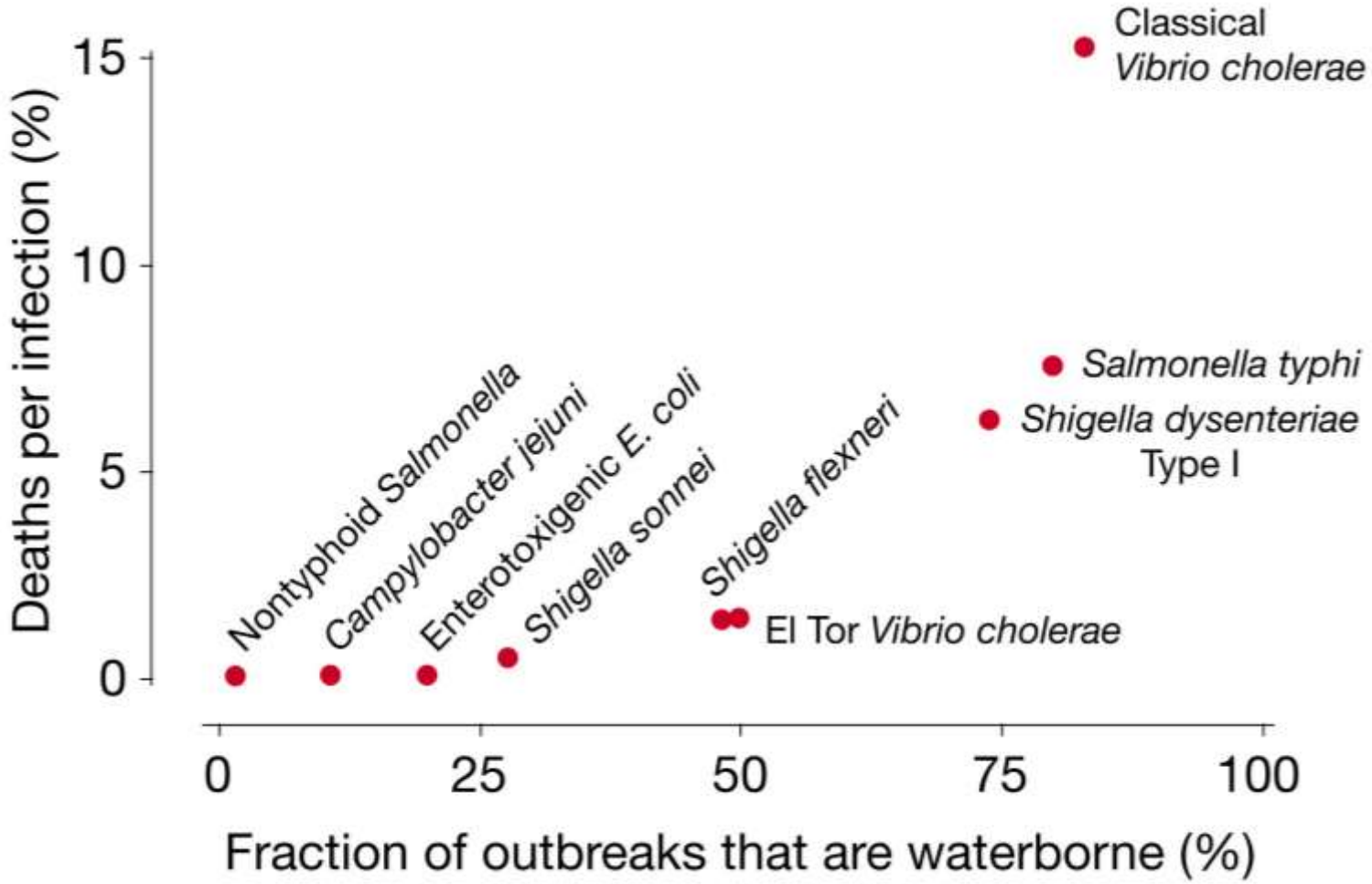
Transmission to
new hosts

Selection **across hosts** favors
reduced virulence.

Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne

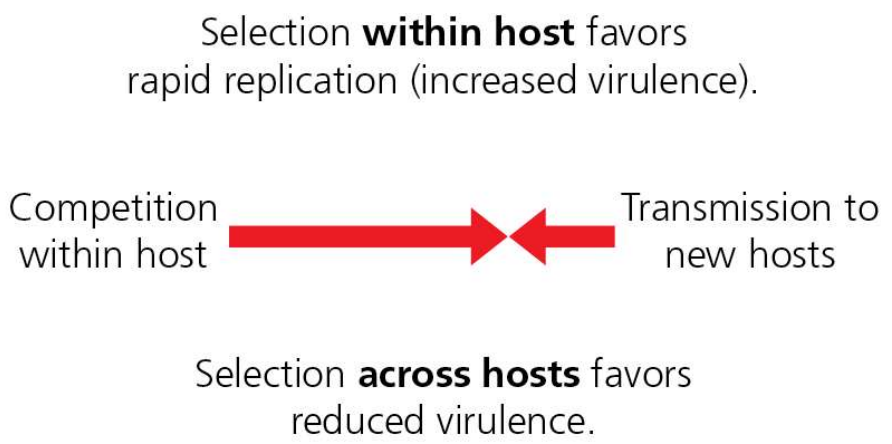
Mode of transmission affects virulence



Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission

- Improve hygiene
- Wear masks
- Provide clean water
- Widespread vaccination



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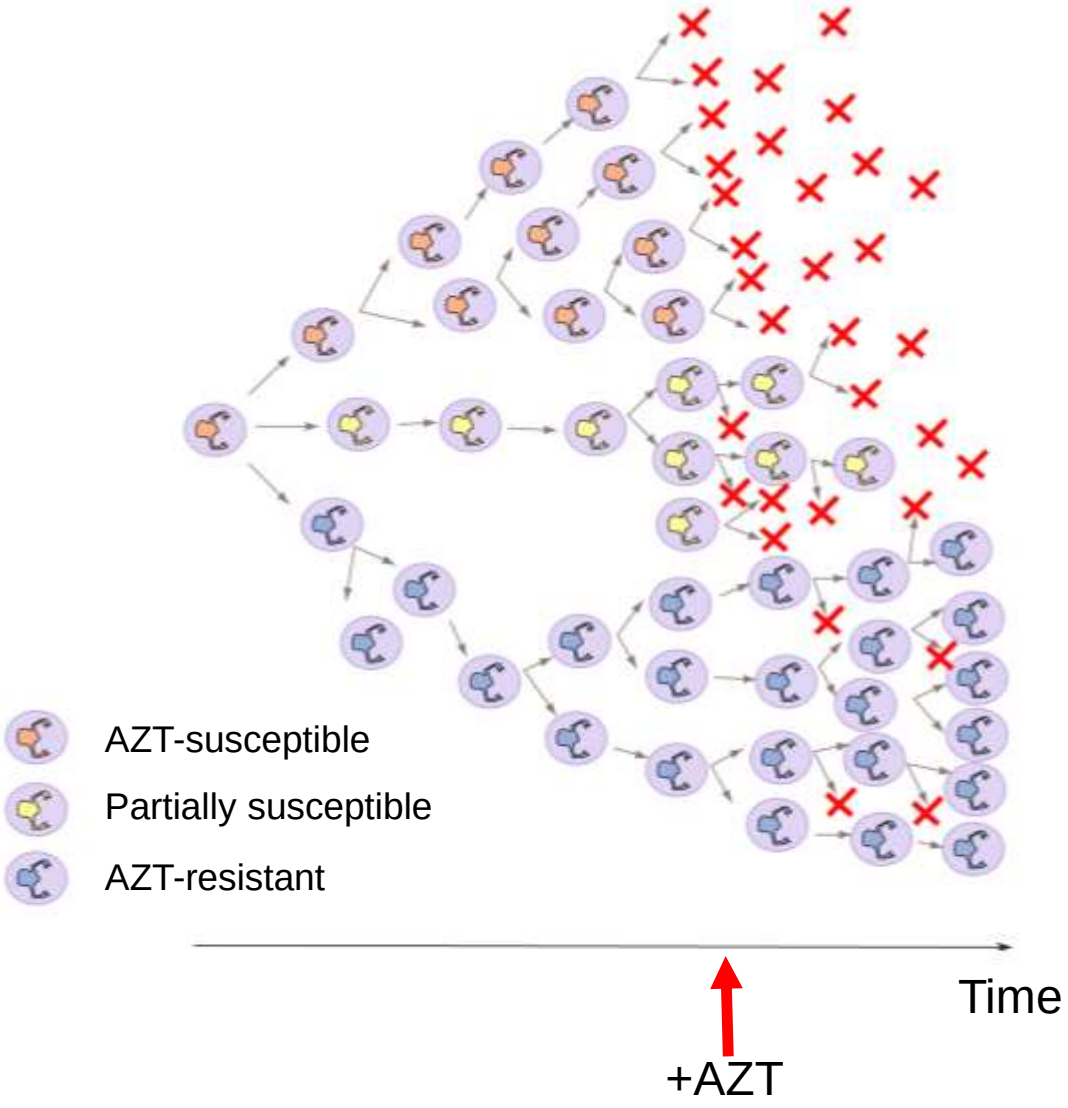
Evolution within the host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction
- Host switching leads to strong selection:
  - Infection
  - Evade immune system and replicate
- **What's another source of strong selection?**

The evolution of drug resistance by natural selection



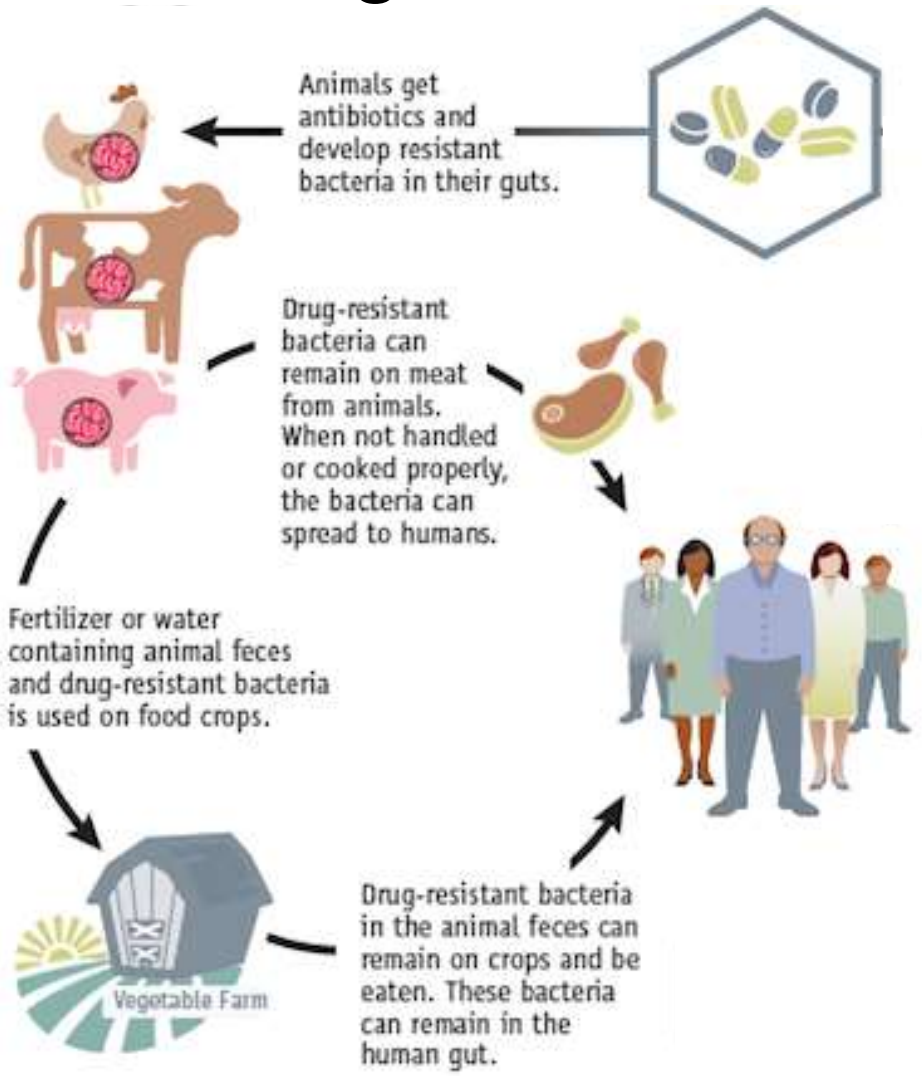
The evolution of antibiotic resistance before your eyes

- https://youtu.be/plVk4NVIUh8
- 11 day time-lapse video

Avoiding more widespread resistance

1. Avoid contracting infections
2. Minimize transmission of resistant microbes
3. Improve use of antimicrobial drugs
   - Take only when appropriate (i.e., don't take an antibiotic for the flu!)
   - Use antibacterial soaps/cleaners ONLY around people with weakened immune systems
   - Avoid broad-spectrum antibiotics if possible.
   - Take ALL of the medication
   - Reduce agricultural use of antibiotics

Why can reducing inappropriate use of antimicrobial drugs combat resistance?



- Resistant bacteria escape livestock, spread to humans

Current research aims

- Can we predict which pathogens are more likely to shift to humans?
- What makes some strains so much more deadly than others?
- How can we develop effective new vaccines and drugs?
- What is the mechanism of resistance?
- How can we develop better and faster diagnostic tools?