BIO 4AE3 – Jan 9

PERRY 1997

integrity.

- how do we know?
- so what?

DEFINITIONS

infectious disease? parasite?

ECOLOGY

- abundance?

  malaria mapping project

  - INCIDENCE – new cases.
  - PREVALENCE – existing cases
    - ↳ serosurveys
  - proxies
- population genetics. *

EVOLUTION –

- mutation, selection, drift

BIO 4AE3 · 12 Jan 2023

DEFINITIONS.

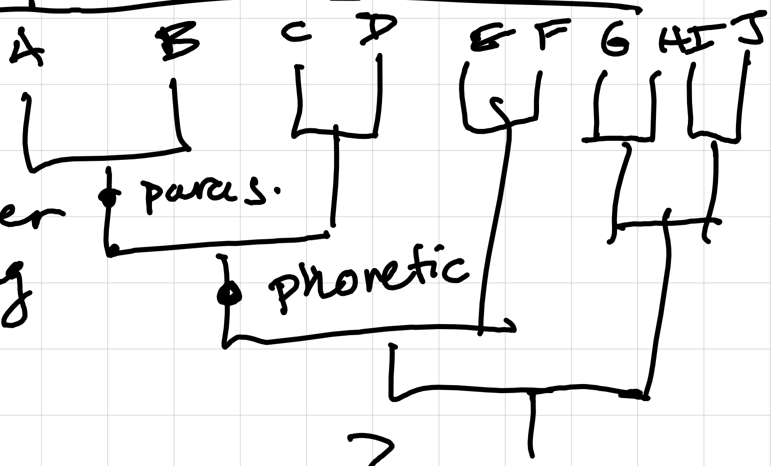
why be a parasite?

'natural enemy' interactions.
'(+/−)

- symbiosis?
  protection
- phoretic.

- comparative analysis.

character mapping



OBLIGATE
FACULTATIVE
LABILE / LABILITY

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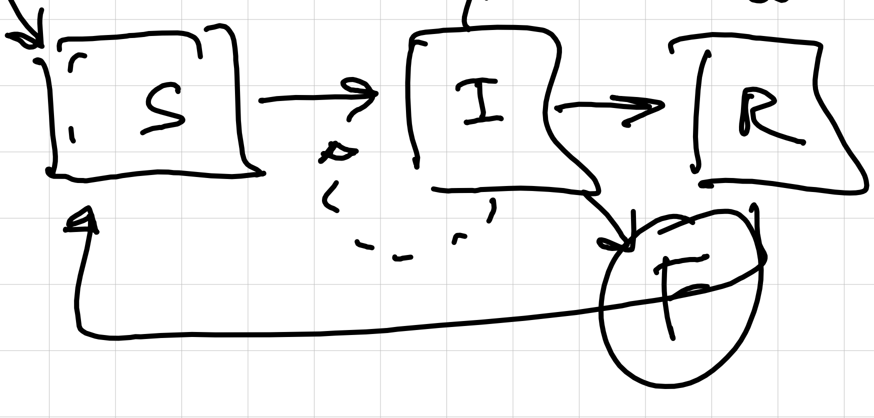
epidemic models.

- NATURAL HISTORY
- time scale –
  host demography?
  disease-induced mortality?

- BOX MODELS, compartmental models



BIO4AE3 · 12 Jan 2023

levels
· why doesn't?
char. loss
exploit

- not directed ·
- host counteracts
- CONSTRAINTS
  - physical / chemical limitation
  - tradeoffs
  - mutational spectrum
    - available genetic variation

generation time
mutation rate
fecundity ?

EPISTASIS

multiple loci interact

HAART

arms races ·

Red Queen

fitness landscapes

body size

DRIFT

LEVELS of SELECTION

BIO 4AE3 · 18 Jan

SIR model.

- special cases.
  - SI (tuberculosis)
  - SIS. gonorrhea.
  - SIRS. - COVID

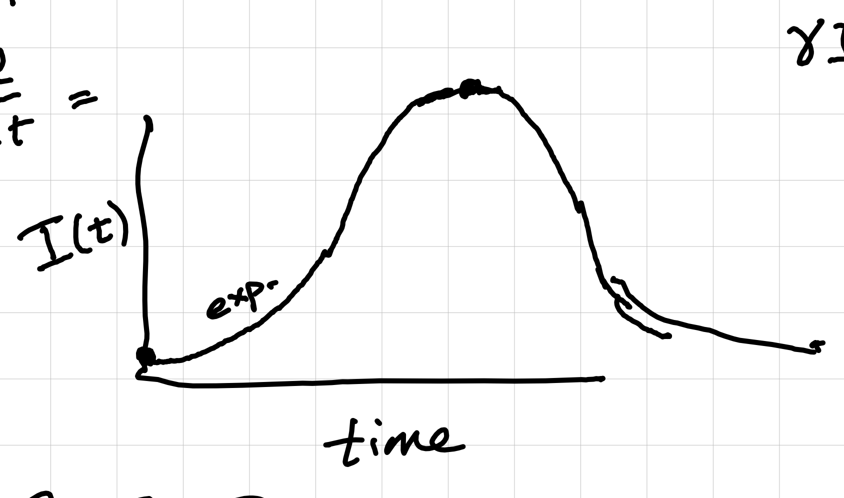
birth, death, disease-induced mortality, vaccination, treatment

PER CAPITA

$$\frac{dS}{dt} = b - \beta SI - \mu S$$

$$\frac{dI}{dt} \quad + \underline{\beta SI} - \mu I - \underline{\alpha I} - \gamma I$$

$$\frac{dR}{dt} = \quad \gamma I - \mu R$$



$R_0 = \frac{\beta N}{\gamma}$ INTRINSIC reprod number.

$\frac{1}{\gamma}$ = infectious period

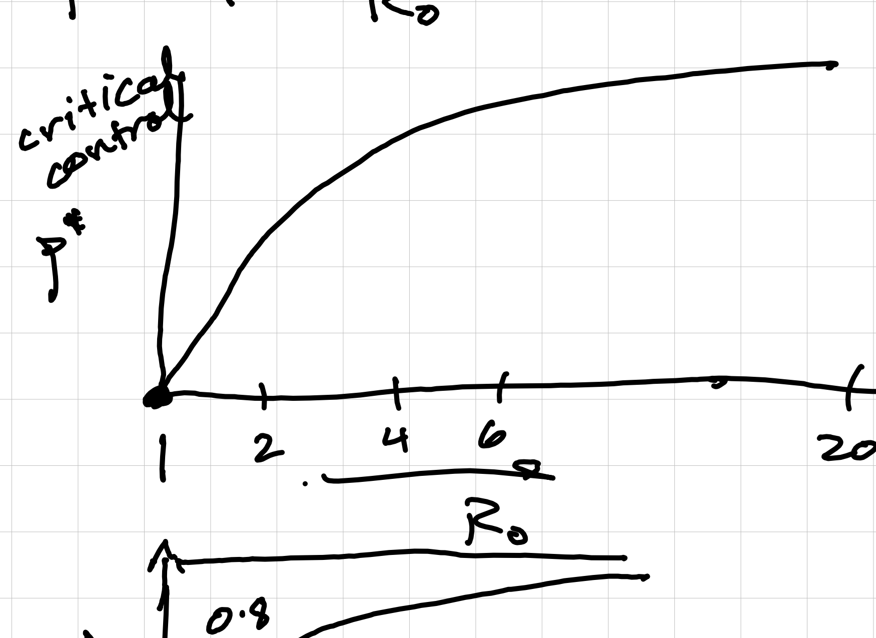
$\gamma = 0.2 \text{ day}^{-1}$

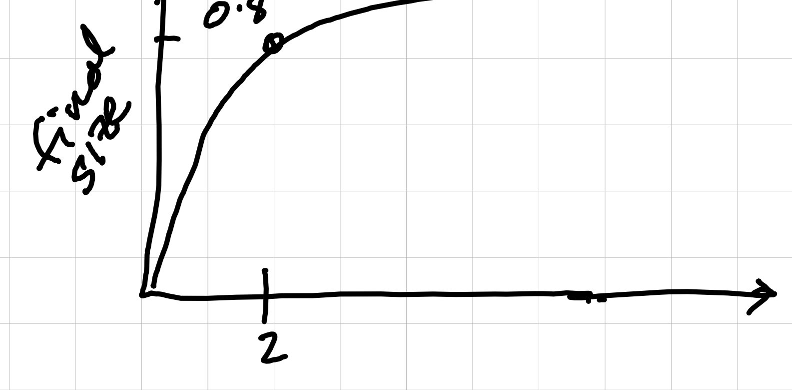
$\frac{1}{\gamma} = 5$ day

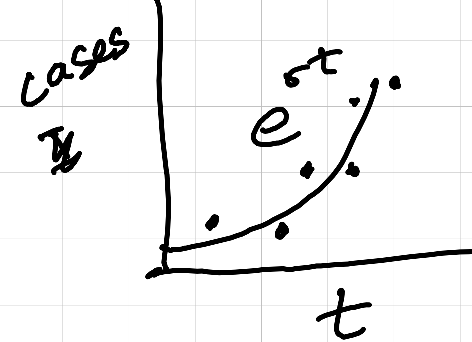
$R_0 > 1$; $r = \beta N - \gamma$ growth rate

CRITICAL CONTROL FRACTION

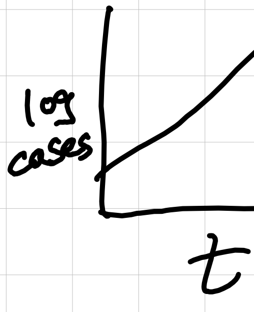
$p^* = 1 - \frac{1}{R_0}$







$\beta - \gamma$



$\gamma = ?$ $\frac{1}{\gamma}$ = infectious period

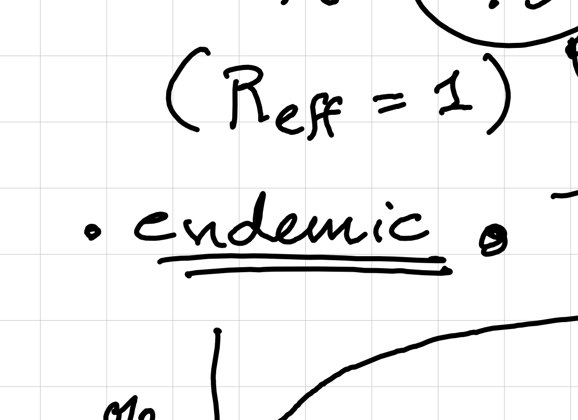
vector-borne diseases, STDs.

Contact tracing.

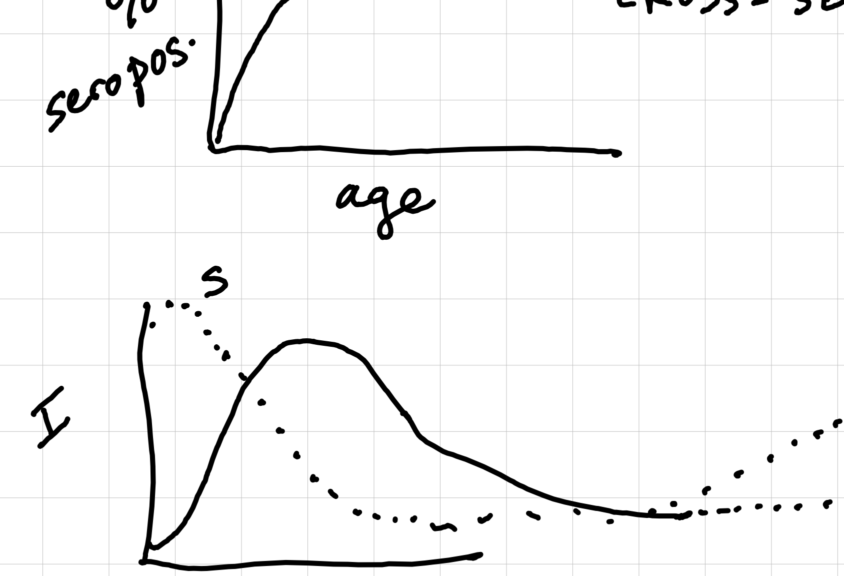
- $R_0 = \frac{N}{S^*}$ when disease is in equilibrium.

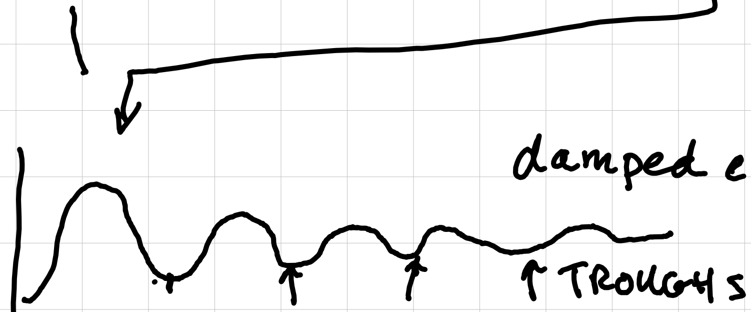
  ($R_{eff} = 1$)

- endemic



CROSS-SECTIONAL





- Stochastic fluctuations
- seasonal drivers

- genetic changes
- behavioural changes +

critical community size

≈250,000 - measles

Batrachochytrium dendrobatidis

Joyce Longcore

saprophytes

thallus → zoosporangia

→ zoospores

Central America

Australia

- SW US

novel pathogen hypothesis

tipping point hypothesis

'disease triangle' host-parasite-environment

{ RESISTANCE TOLERANCE

23 Jan — discussion, Vredenburg

- why doesn't pathogen evolve to not drive host extinct? George Williams ✓
- why noise/bounces in time series? environmental variation? (Fisher + Garner) 2020
- sexual reproduction
- why is epi theory 'stumped'? (DeCastro + Bolker) ✓
- one-time treatment? ✓
- conservation? captive breeding? ✓

enzootic endemic

deme

25 Jan BIO 4AE3

parasites + host population dynamics

SIR model / epidemics:
"populations": S, I, R -
no demography?

→ what if parasite affects host demography?

→ how do parasites affect the interactions among host species?

Do parasites control host population size?

high transmission rate, β
INTERMEDIATE virulence?
$\frac{1}{\gamma}$ ↑ short infectious period.

---

can parasites regulate a population?
↳ evolve towards commensality?

lab experiments:
H. polygyrus in mice
90% reduction (!)

BIOCONTROL.
• european RABBITS - in Australia
myxomatosis -
calicivirus

Opuntia cactus
Cactoblastis moths

---

humans demography + parasites

BIO 4AE3 - 26 Jan 2023

historical epidemiology

"Black Death" -

14th c. European - bubonic plague

Yersinia pestis

- symptoms.
- ancient DNA - Poinar!

↳ ? secondary infections.

- (1970s Colorado die-off - attributed bacterial outbreak)

↳ ? about the same genetically?

Plague of Athens. 430 - 429 BC
(25% of population)
measles? typhoid? plague?] -

'VIRGIN SOIL epidemics' -
invasion of the Americas.
pop of Mexico. 1518 ~20 million?
by 1568 ~ 3 million

genetics ~~X~~ Crosby 1976
→ epidemiological inexperience
→ societal breakdown

Guns, Germs, + Steel. Jared Diamond

HIV - demographic impact

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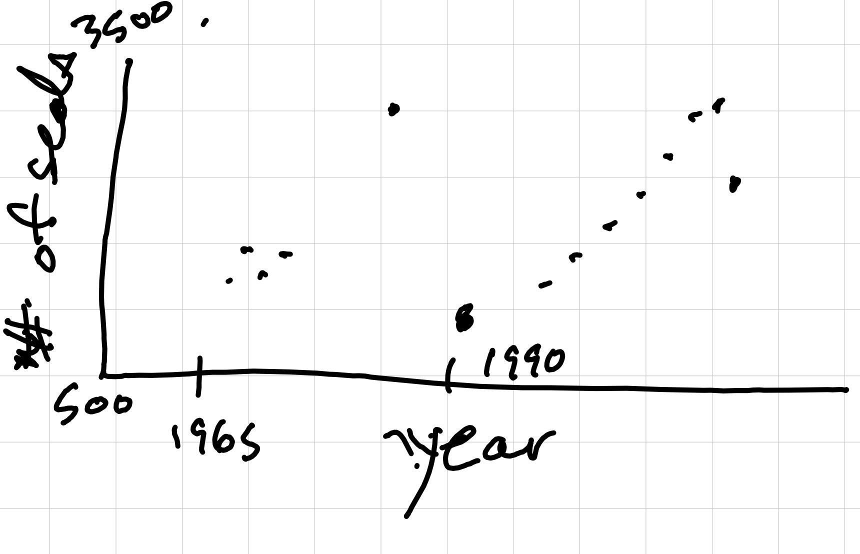
disease-induced population "cycles".

cycles in host population density



BIO 4AE3.

red grouse + *Trichostrongylus tenuis*

- herbivores. heather
- not many predators.

regular cycle (4 - 6 years in E, 7-10 in Scotland)

- behavioural changes?
- or host-parasite cycle?

→ individual grouse - survive better with antihelminthics.
→ higher fecundity
→ parasite densities also oscillate out of phase

- general consistency of patterns with models.

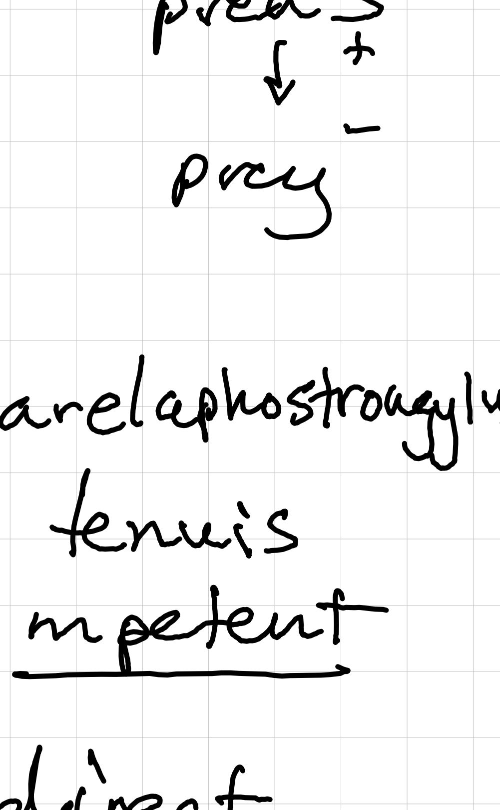
colder weather → worm development

---

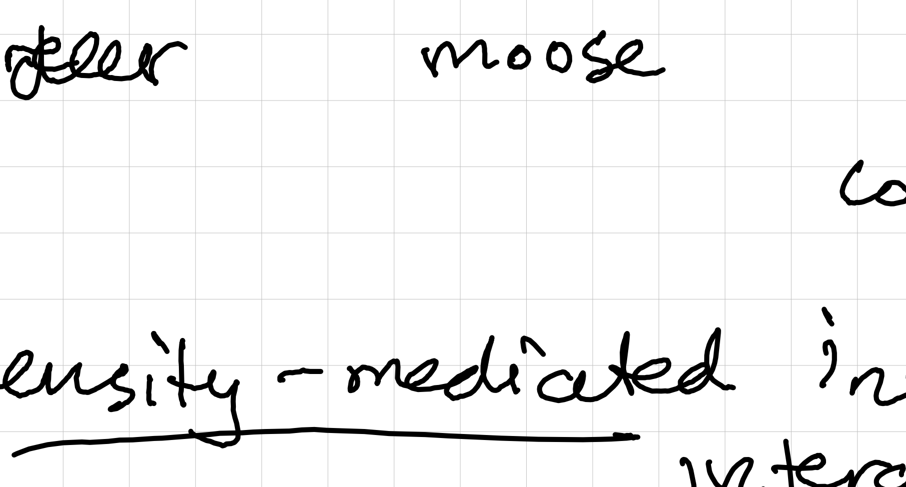
parasites + host communities

---

trophic cascades.



APPARENT competition



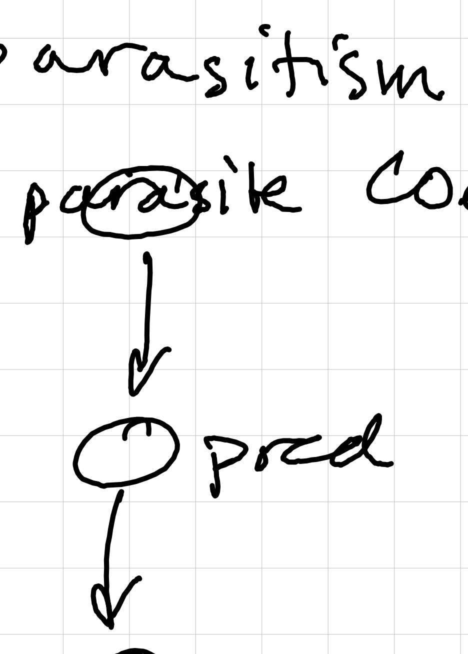
density-mediated indirect interactions

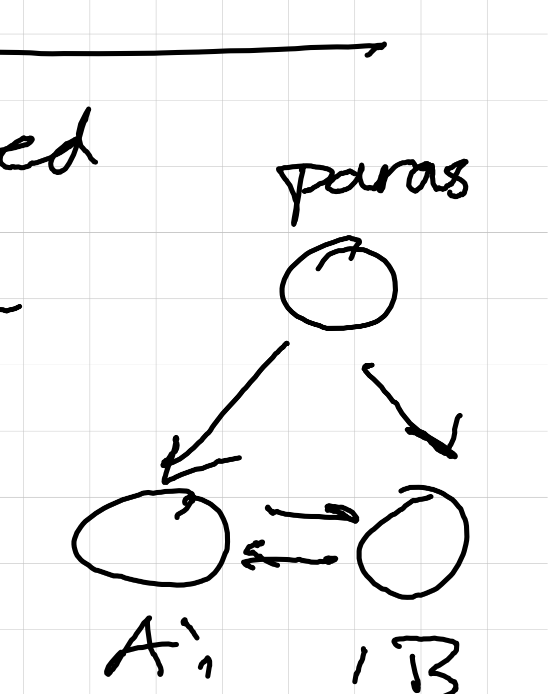
trait-mediated interactions

trophically transmitted parasites.

---

parasitism-mediated ~~parasite~~ coexistence





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experimental examples.

Drosophila melanogaster
simulans

L. boulardi (parasitoid wasp)

M > S

parasitoid. M = S

depends on temperature

Tribolium

---

prevention of hybridization

mouse subspecies

outbreeding depression

'breaks up coadapted gene complexes'

IMMUNE SYSTEM.

---

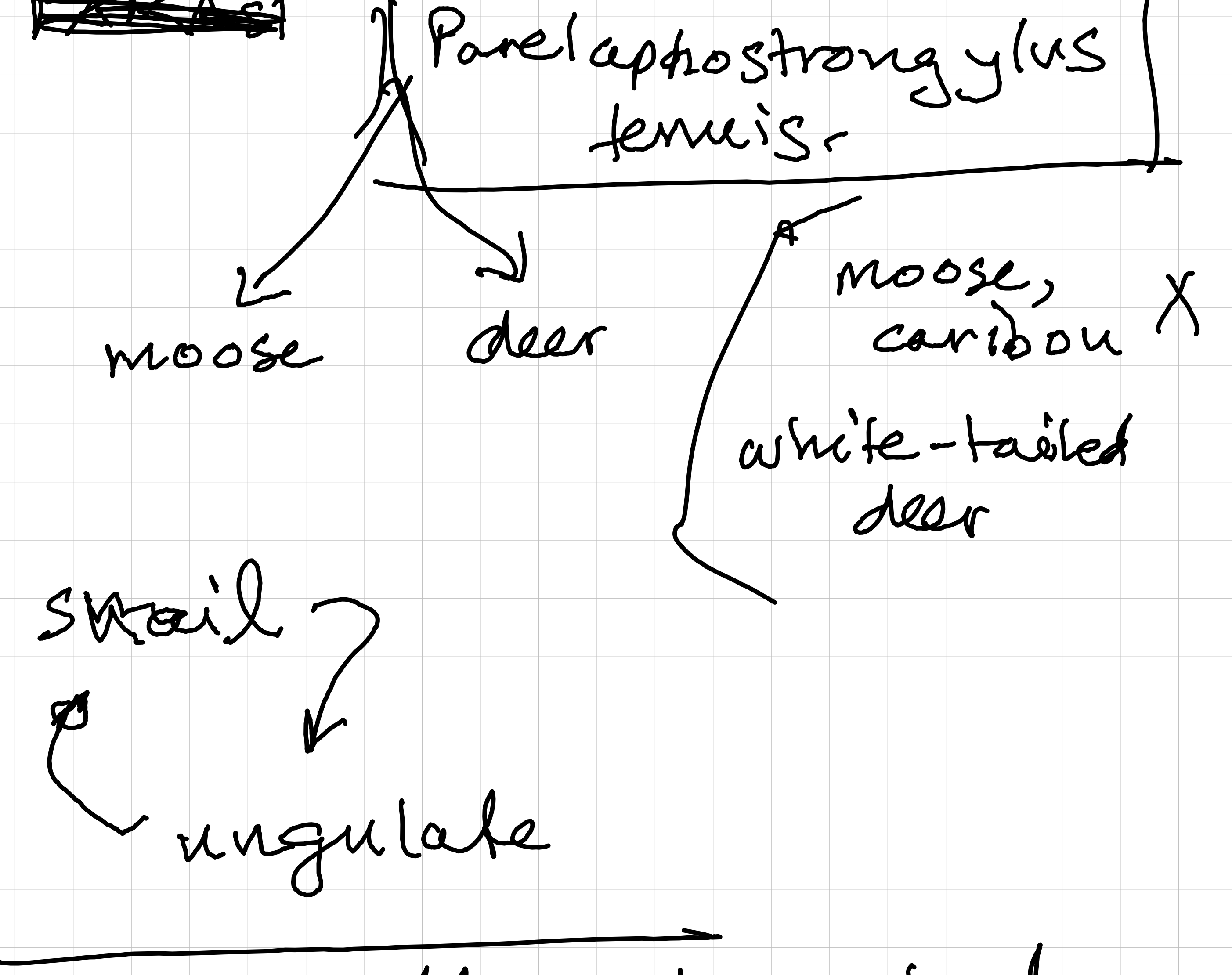
parasite-mediated invasion.

- NATURAL ENEMY hypothesis
- humans.

Europeans → New World.
Europeans → Africa

Acipenser stellatus (Caspian) → Aral.

Acipenser nudiventris



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moose usually outcompete deer (no parasite)

- Kluane project.

2 Feb, BIO 4AE3

trait-mediated indirect interaction

bird predators
↓
fish
↑
aquatic predator

moose/deer/ P. tenuis

- Pt kills moose, not deer
- life cycle
- moose typically outcompete deer
- deer now outcompeting moose

MODEL.

snails

moose deer

?
- growth rate of snails
- comp interaction moose/deer
- death rate of moose from parasites

→ avoid overconf.
→ tells us what to measure

trophic cascades

- is the parasite indirect mutualist of the predator?

pred seabird
parasite
prey fish

trophic pyramid.

ecosystem ecology
nutrients, energy, environment

stoats / rodents / tree seeds

EXCLUSION experiment.

toxoplasmosis ?

ecosystem engineering.

parasitized cockles

↳ changes surface of environment

RINDERPEST.

↓
ungulate
↓
brushy vegetation *
↓
tsetse flies
↓
trypanosomes (sleeping sickness)

rinderpest
− ↓
wildebeest
+ ↕
− grass
+ fire
− trees
rainfall

poaching
↓
elephants

CARBON STORAGE

BIO 4AE3 ~ discussion

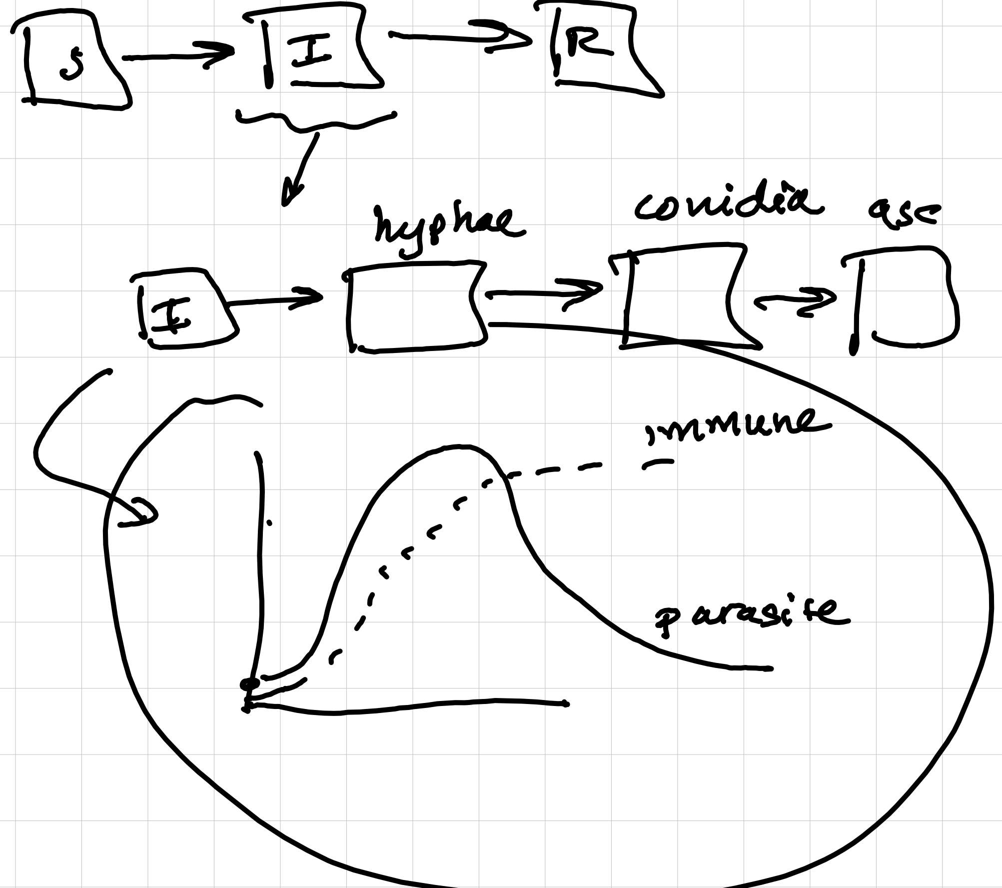
- death at last time step?
- between vs within —
  NESTED

@104. why does internal clearance get harder?

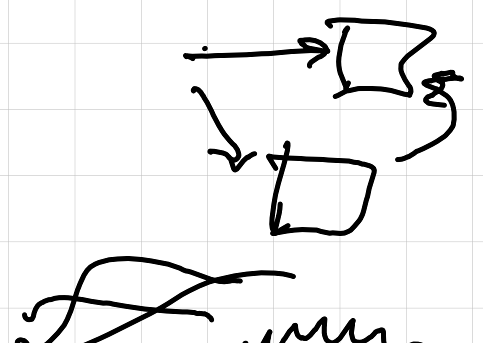
why is barrier resistance → improved clearance?

↓ budding

- applications to control?
- importance of variation
- why not...? / what if...?



Gillespie algorithm



$\frac{dS}{dt} =$

$\frac{dI}{dt} =$

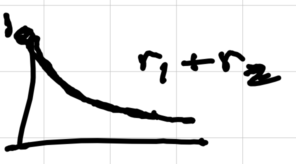
$\frac{dR}{dt} =$

Gillespie:
at time t,
we know the rates of
all of the transitions.

r_1: $S \to I$: 27.3 infections/day

r_2: $I \to R$: 10.5 recoveries/day

how long until the next event happens?



$\sim Exp(r_1 + r_2)$

Infection: $\frac{r_1}{r_1 + r_2}$, recovery: $\frac{r_2}{r_1 + r_2}$

1000 S, 10 I t = 0

999 S, 11 I t = 0.639

BIO 4AE3. 8 Feb 2023

within-host dynamics ~

- how does compatibility filter works?
- lot of mechanistic work — molecular genetics / immunology / biochemistry

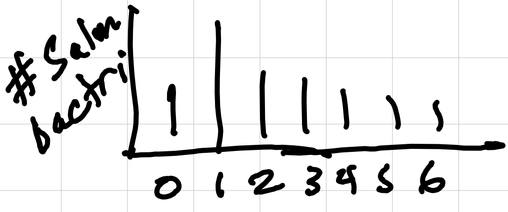
recognition + effector → antibodies → antigen.

→ macrophages — ~~T cells~~ NK cells CTL

model interaction?

longitudinal data ~

cross-sectional data (distributional)

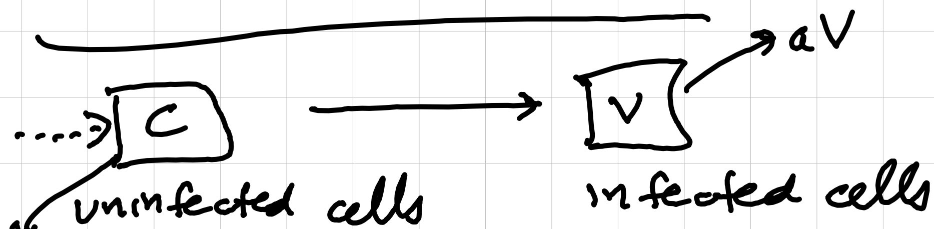


Bio 4ae3 - 9 Feb

- results are consistent with R_0 dropping from ~ 50 to JUST ABOVE 1 but never below 1 ...

$$\frac{dC}{dt} = \lambda - \mu C - \beta C V$$

$$\frac{dV}{dt} = \beta C V - a V$$

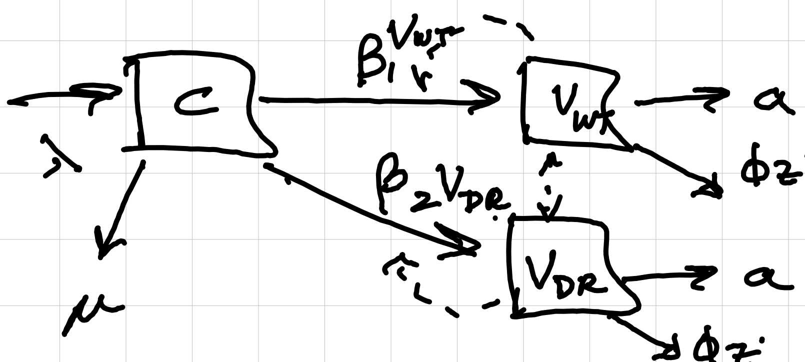


C^*, V^* $\qquad \dfrac{\beta\left(\frac{\lambda}{\mu}\right)}{a} \sim R_0$

V^*

---

add mutation and back-mutation

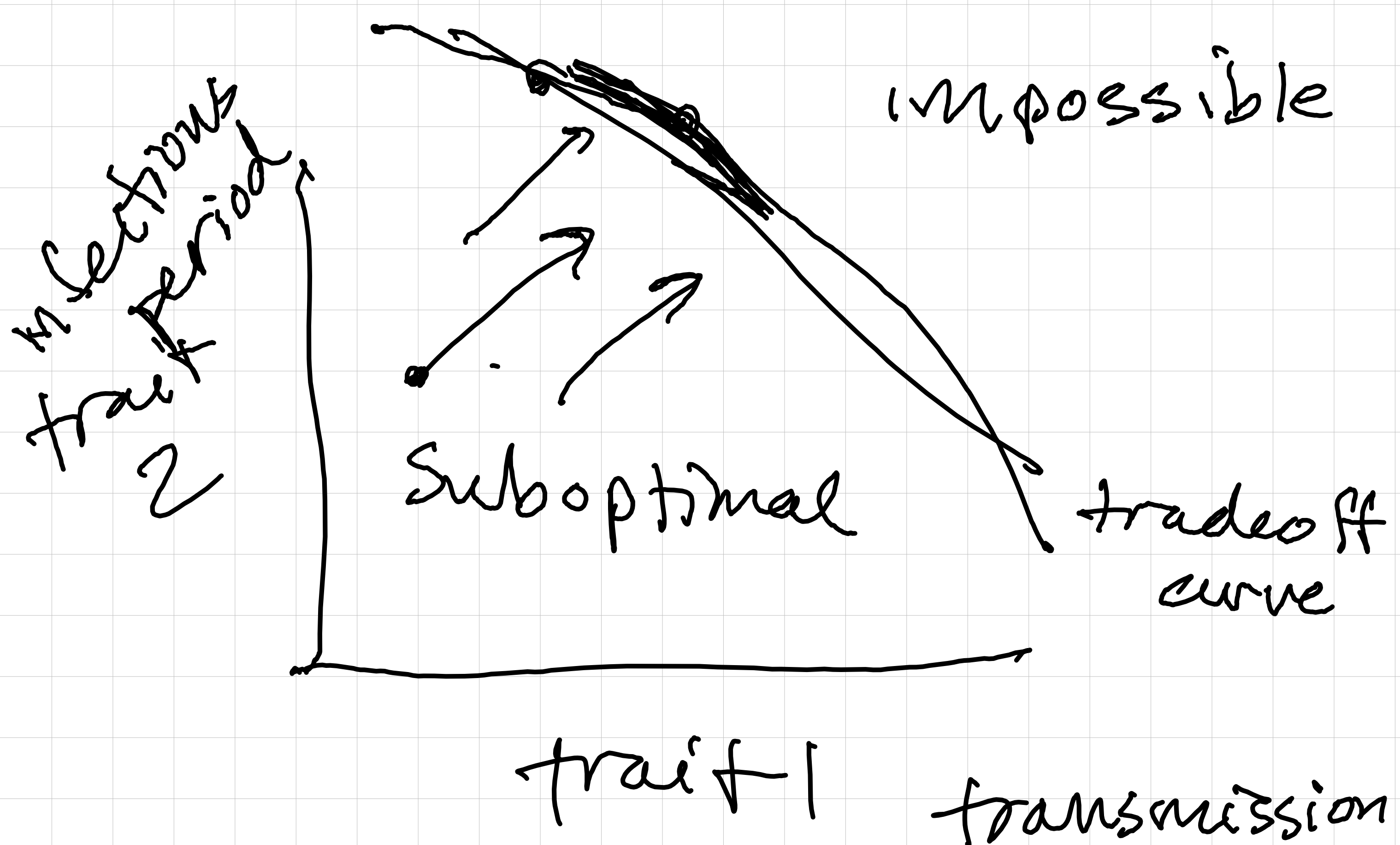


immune system $\boxed{Z}$ $\qquad \dfrac{dZ}{dt} = kV - \gamma Z$

~~DQ~~ BIO 4AE3

DQs

- time shift
  - mixing
- progressive change (vir, inf, paras fecundity) → frontiers
- outliers
- 'missing' values
- host age vs population age
- influence of other predators etc.
- sex vs asex
- reintroduce older populations



~~cuck~~ brood parasitism
cuckoos,
brown-headed cowbirds

overall rate of infection

$$S \xrightarrow{\beta I} I \xrightarrow{\gamma} R$$

βSI $\quad \frac{\beta SI}{N}$, ...

overall (absolute)

βI per capita (per-S)

absolute rate of recovery: γI

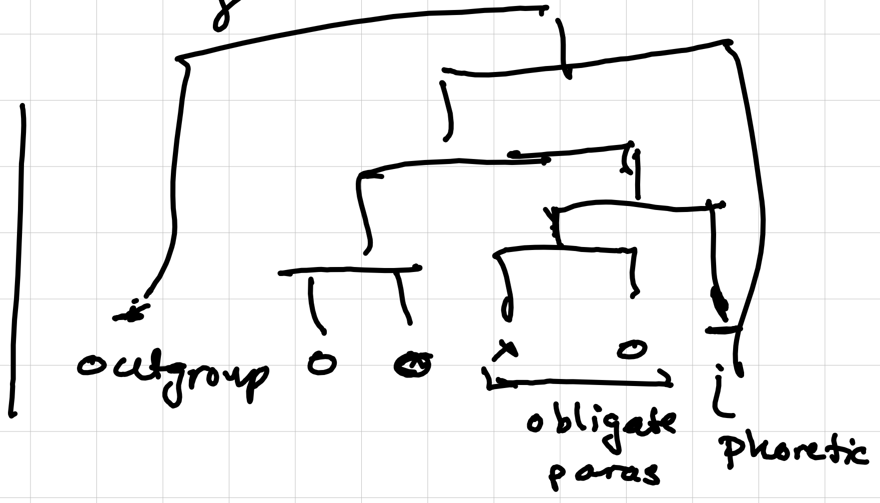
per capita: γ

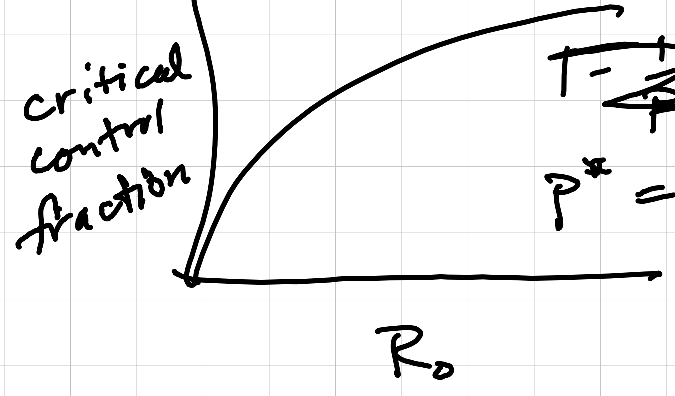
---

vs $\left\{\begin{matrix}\text{micro} \\ \text{macro}\end{matrix}\right\}$ intensity-independent / intensity-dependent

micro: viruses, bacteria, fungi

macro: nematodes, trematodes





$p^* = 1 - \frac{1}{R_0}$

---

chemicals –

- may have off-target effects
- have to be reapplied
- resistance is likely to evolve.

biocontrol.

- ↳ may be tailored to be host-specific
- persists in population (~~to~~ control pests to LOW levels
- ⇝ may coevolve
- ~ (less predictable?)

REDQUEEN .

antagonistic coevolution between hosts and parasites

"REDQUEEN" vs "ARMS RACE" "TRENCH WARFARE"

recognition + evasion

(self-nonself)

(specific antibodies)

+ effector

→ faster replication

suppressing immune system

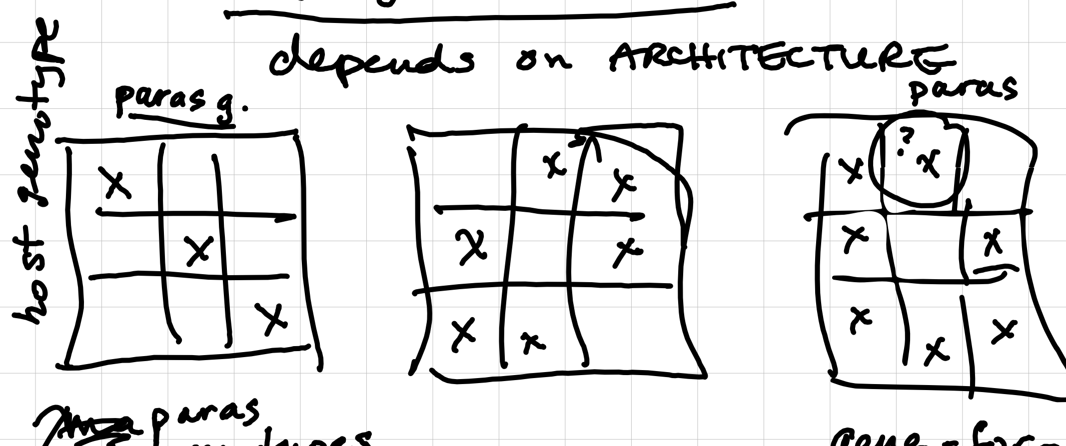
FREQUENCY-DEPENDENT selection

rare alleles have an advantage (parasite)

→ rare → common

~~RED~~ alleles involved in RQ dynamics tend to be polymorphic

depends on ARCHITECTURE



paras genotypes

BLANK = paras loses

X = paras succeeds

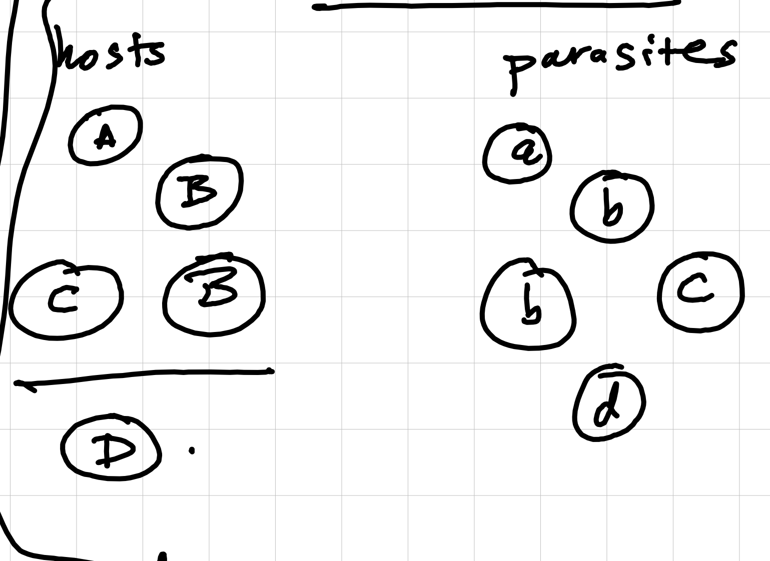
gene-for-gene model

MATCHING ALLELES

self-nonself recognition system

• DOES encourage cycling + local adaptation

dilution effects.



biodiversity – ecosystem function

DOES biodiversity lower levels of infectious disease? (does it lower chances of zoonosis?)

DILUTION EFFECT

Lyme disease.

human

deer ← tick

tick → white footed mice

host competence

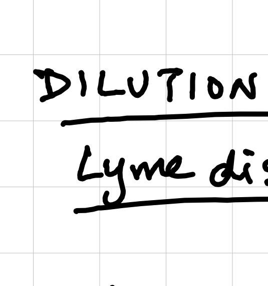
plant breeders –

R (resistance) plants

Avr (avirulence) fungi

• 'trench warfare'.

• suppose a 'resistance allele' (parasite recognition allele) exists in a population. what happens to it over time?



• FITNESS of resistant hosts

– LARGER the more parasites are around.

– intrinsic cost

Stahl et al. · Arabidopsis

→ resistance locus.

→ coalescent methods to determine the age of resistance alleles

→ 7000 · 9000. yrs?

old, time-varying

BIO 4AE3 - 1 March.

Interaction w/ sexual reproduction in hosts?

- how much can we explain the evolution and maintenance of sexual reproduction by invoking RQ?

Darwin, Fisher (1930s), 1970s

→ COST of MALES
of MEIOSIS

{ population genetics -
{ parasite - related

'maintain genetic variation'
eliminate deleterious alleles?

AB   ab

Ab aB

generating / maintaining variability in genotypes

→ recombination ←

gonochoric / dioecious
(separate male + female)

variability ≈ parasite resistance?

environmental changes

---

alternative hypotheses

- Muller's ratchet -

- requires small populations

Kondrashov's hatchet

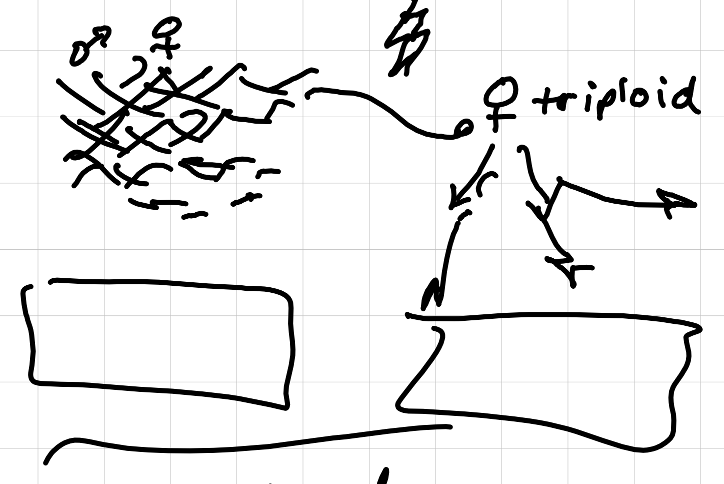
mutation purging.

ECOLOGICAL (not parasite-related)

hard habitat selection.
- if there are transient niches, genotypic variability is good.
- Soft 'tangled bank' -
- sexual lineages compete better because they can use more niches

?

SNAILS → asexual lineages



Curt Lively.

Potamopyrgus antipodarum

Microphallus. cestode

variability in hosts
variability in parasites

BIO 4AE3 - 2 March

Lively + ... mud snails

- hard selection/lottery
- tangled bank
- reproductive assurance
- RED QUEEN

(freq males)

- more and less disturbed habitats
- correlations betw paras density + freq of sexuals

- time lagged parasite resistance
- space / allopatric vs sympatric resistance

→ RQ is fairly well supported

formerly common clones.
more susceptible to current parasites
→ time lagged host matching

RQ ? only works if parasite have strong effects on host fitness

- what about competition between sexuals and a diverse set of clones?
- why obligate sex?

PLURALIST approach
'all of the above' - interactions.

Muller's ratchet + RQ

VIRULENCE.

→ decrease in host fitness due to infection
→ ? survival effects
RATE of parasite-induced mortality

- resistance → encounter/compatibility
- tolerance → ability to host parasite w/o losing fitness

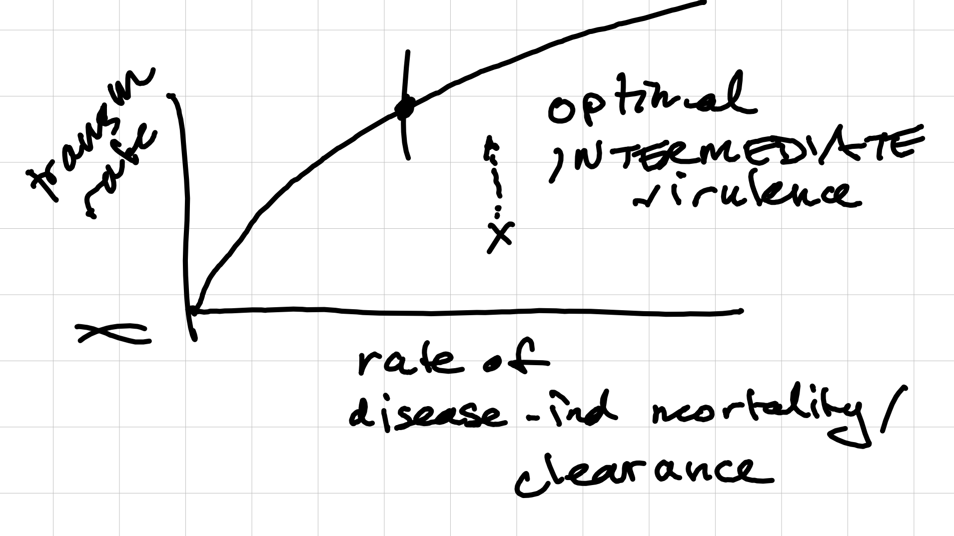
'classical dogma'
1970s.
"parasites evolve to become less virulent over time"
- GROUP selection?
→ syphilis - 1495
??
virulence decreased over 50 years
virgin soil epidemics. → previous exposure

- sampling bias.

tradeoff theory -
reprod rate of parasite → increases ability to spread between hosts
→ kills host faster
+/or (provokes immune response)

R_0 = (how fast can you infect) × (how long)

IF diminishing returns



& cytokine storm.

BIO4XE3

why not study tolerance?

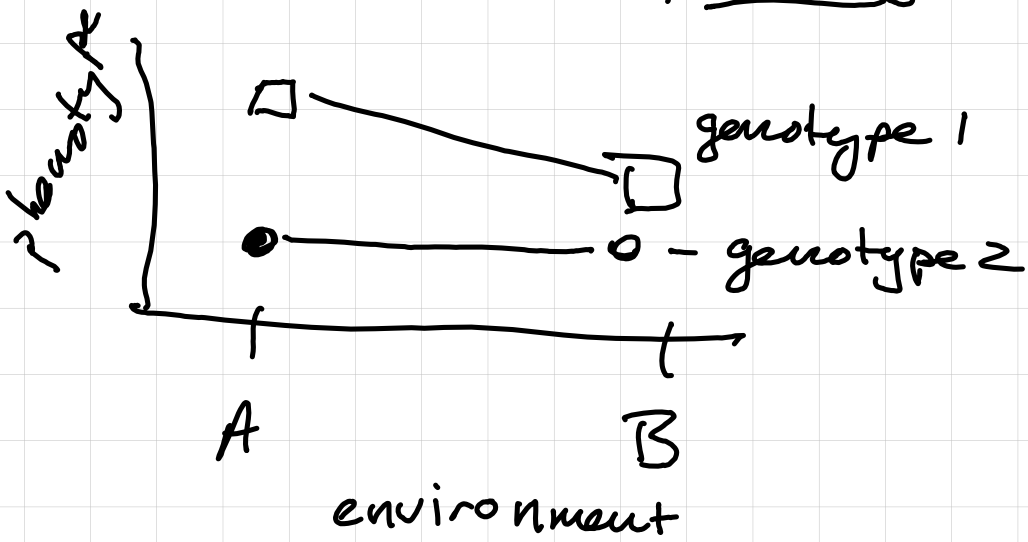
~~classes~~

behaviour as tolerance

~~reaction norms~~

evolvability

REACTION NORMS. plasticity.



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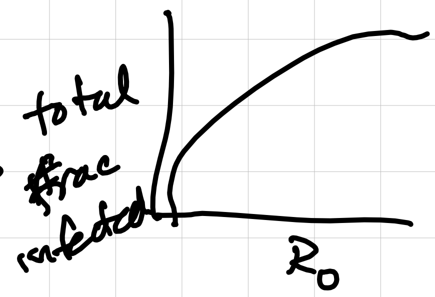
antipyretics → (increased viral load..)

increased mixing → increasing transmission → increased epidemic size

deaths ⟷



8 March 2023

- myxomatosis
- HIV
- transcient / eco-evolutionary dynamics

MYXOMATOSIS.

genetic / genomic analysis?

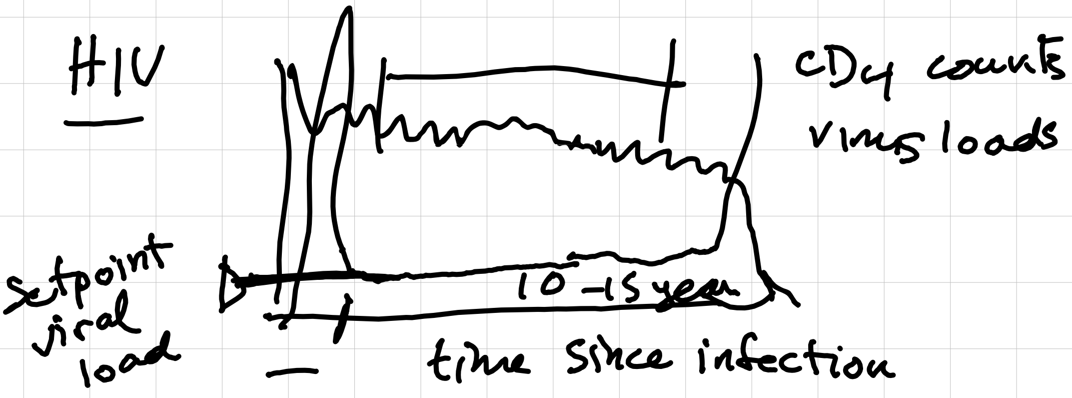
- virulence is decreasing because of 'deleterious' mutations.

insertion. - disrupting a reading frame - in cell cycle -

deletion: immuno suppressive pathway

Australia vs Britain

HIV



RAKAI. cohort study

- SERODISCORDANT couples
  - setpoint viral load
  - time to progression
  - infection of seroneg partner (time to)

- TRANSMISSION MODE.

MAY, ANDERSON.
EWALD.

vertical transmission

STDs direct transmission

vector borne

necro transmission

water borne

BIO 4AE3 7 Mar 2023

Evolution of virulence (final)

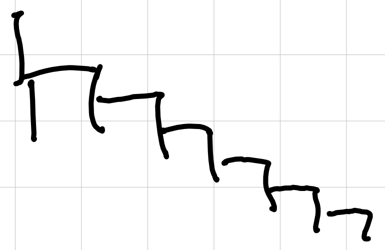
modes of transmission.

- Ewald - HTLV. / Anderson + May

do high transmission rates encourage high virulence?

1918 flu. antigenic drift / $\boxed{\text{shift}}$

ladder-like phylogeny



SHIFT

H1N1

H5N1

haemagluttinin

neuraminidase

EWALD

higher transmission rates

→ select for higher virulence

ANDERSON + MAY

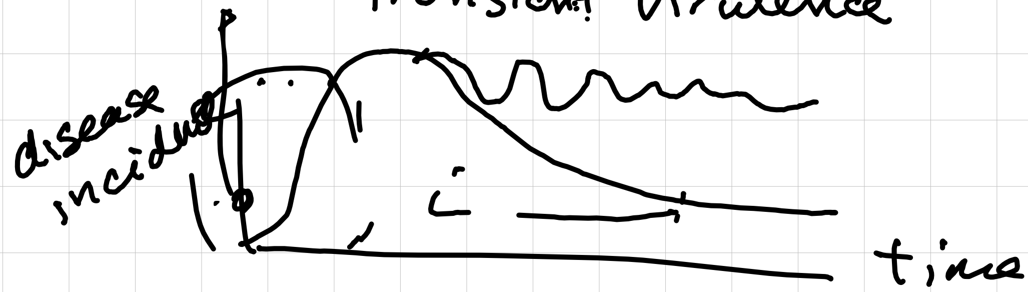
→ selection should be indep. of transm rate

↳ are we optimizing

$\frac{\beta}{\gamma}$ • R_0 (lifetime fitness) or (end.)

$\beta-\gamma$ r (growth rate/time)? (epi.)

transient virulence



could public health interventions select for higher virulence?

mouse malaria -

∟ anemia/weight loses

∟ gametocytes

BIO 4AE3
13 March 2023

resistance + tolerance.

- resistance
- tolerance
COMPETENCE. ability of a particular host to pass on/amplify disease.

tolerance + high infectivity
(≈ infectious period) (high parasite loads ≈ low resistance)

multi-host (generalist) parasites, esp. vector-borne w/ spillover.
(Lyme disease
West Nile Virus)

MECHANISMS

- recognition (resistance)
- effectors (resistance)

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constitutive. (always on)
: innate immune system.
[changes in cell surface proteins
- matching alleles model]
CCR5 Δ32,

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parasite countermeasures.

- immune evasion.
  PLASTIC.
  malaria ~60
  trypanosomes ~100s

[Schmid-Hempel 2009]

immune suppression.
myxomatosis
measles
anthrax

Population-level consequences.

- tolerance helps itself
  fitness of tolerance ∝ ~~incidence~~ prevalence of inf.
  tolerance increases prevalence of inf.
  → tolerance ~~alleles~~ alleles to fix in pop.

- resistance.
  fitness of resistance ∝ preval of inf.
  resistance decrease prevalence of inf.
  → polymorphism.

? what maintains genetic variability?

- why haven't deleterious alleles gone away?
  [genetic drift → pop size, age of allele, strength of sel.
  heterozygote advantage]
  freq. dependence

~~Aa~~ aa Aa AA

Tay-Sachs disease.
lethal recessive.
abnormality in lipid.
s = 1

1/300 ~ in US pop.

≈ 1/30 - Ashkenazi Jews,
French Canadians
Pennsylvania Dutch

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speculation: overdominance for Tb resistance, intelligence