Notes on (pathogen) evolution

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Evolution

Definition: change in allele or genotype frequencies across multiple generations

- Rice (2004) (fundamentals)
- Smith (1982) (evolutionary game theory)
- Hamilton (1998) (evolution of behaviour, dispersal . . .)

  (ask me about other topics!)

Terminology

- locus: a "location" in the genome (e.g. a particular base pair)
- allele: a possible value at a locus (e.g. A or a; by convention upper-case is dominant, lowercase is recessive)
- homozygous (AA, aa) vs heterozygous (Aa)
- dominance: if A is dominant, phenotypes of (AA, Aa) are the same (e.g. brown eyes), homozygous recessive (aa) phenotype is different (e.g. blue eyes)
- diploid: two alleles at each locus (one from each parent)
- haploid: only one allele per locus
- assortative mating: individuals with similar genotypes more likely to mate (disassortative is the opposite)
- linkage: non-independent inheritance of alleles at two loci (typi-cally because the loci are close together on a chromosome)
- genotype: complete information about both alleles at every locus (e.g. aaBbCC)
- phenotype: the physical body (determines fitness, behaviour, strat-egy, virulence, etc.) generated by a particular genotype

population genetics models

- generally discrete-time, often stochastic
- Mendelian or **infinite alleles model** (continuous traits)

  - Punnett squares: what genotype mixture do we get when we cross genotypes (e.g. Aa x aa) ?
  - this only tells us what happens over one mating of one particu-lar cross . . .
  - want to track dynamics of allele/genotype frequencies through time

- usual simplifying assumptions:

  - non-overlapping generations
  - fixed population size
  - unconditional fitness

Neutral haploid genetics

- with only two alleles competing, the state space is just the number (or proportion) of individuals with "wild type" vs "mutant" allele
- expected number of offspring identical for W and M

  - expect *on average* number of M to stay constant over time

- stochastic, discrete-time, non-overlapping generations model: pick N offspring at random in next generation
- number of M will be **binomial**: $M_{t+1} \sim \text{Binom}(N, M_t/N)$
- could have any outcome between 0 and N - but some outcomes are very unlikely
- e.g. if $M_1 = 3, N = 100, \text{Prob}(M_2 = 100) = (0.03)^{100} \approx 10^{-153}$ (dbinom(x=100, size=100, prob=0.03))

More details

- Markov chain (memoryless)
- system has **absorbing boundaries** at 0 and N
- $M \to 0$ is *extinction*, $M \to N$ is *fixation* (extinction of wild type)
- we want to think about what will happen with an *ensemble* of Markov chains

code

```
simfun <- function(nt=1000, N=100, init=3, mfit=1) {
    M <- numeric(nt)
    M[1] <- init
    for (i in 2:nt) {
        ## prob of M offspring: reduces to M[i-1]/N for mfit=1
        ## (neutral model)
        prob <- M[i-1]*mfit/(M[i-1]*mfit + (N-M[i-1]))
        M[i] <- rbinom(1, size=N, prob=prob)
    }
    return(M)
}
set.seed(101)
sims <- replicate(1000, simfun())
```

```r
par(las=1,bty="l")
black_trans <- adjustcolor("black",alpha.f=0.2)
matplot(sims, type="s", lty=1, col=black_trans)
```
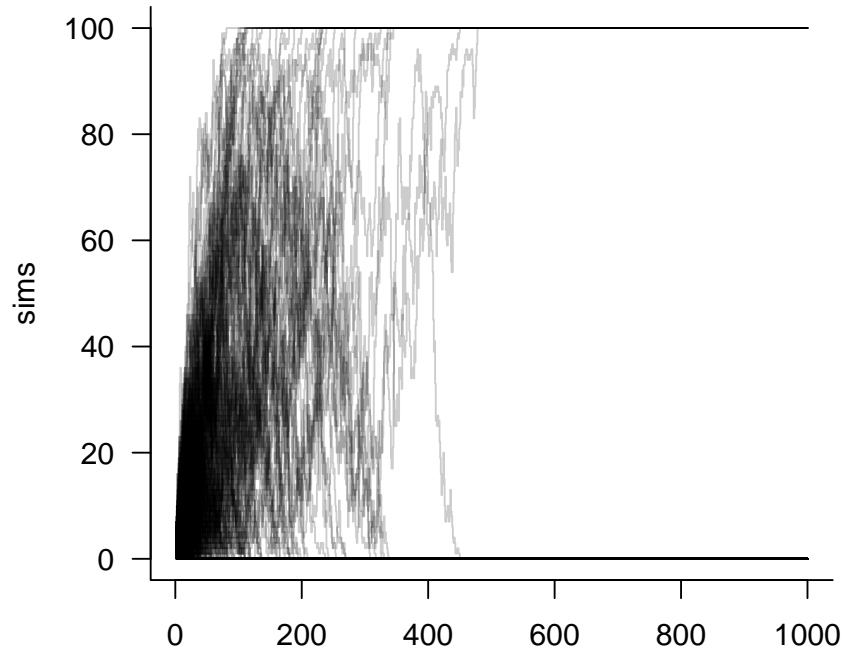

Figure 1: Neutral simulation 1

- basic result: for neutral model, $P(\text{fix}) = M_1/N$

```r
table(sims[nrow(sims),])
```

```
##
##   0 100
## 969  31
```

- Other questions, e.g. what is the expected time (or distribution of times) to extinction or fixation?

```r
par(mfrow=c(1,2),las=1,bty="l")
extinct <- sims[nrow(sims),]==0
etimes <- apply(sims[,extinct],2, function(m) which(m==0)[1])
hist(etimes,breaks=100, freq=FALSE, main="extinction times",xlab="",
     xlim=c(0,1000))
fixed <- sims[nrow(sims),]==100
ftimes <- apply(sims[,fixed],2, function(m) which(m==100)[1])
hist(ftimes,breaks=10, freq=FALSE, main="fixation times",xlab="",
     xlim=c(0,1000))
```
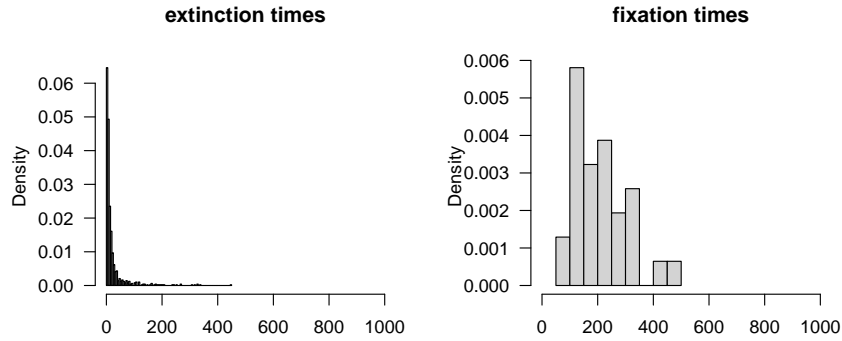
Figure 2: extinction and fixation times

Non-neutral dynamics

- assume *relative fitness* of mutant is w_m

-    1 advantageous, <1 deleterious

- if wild-type have C offspring each, mutants have w_mC, then probability of an offspring being mutant is $Mw_mC/(Mw_mC + WC) = Mw_m/(Mw_m + W)$ as above

- Hardy-Weinberg equilibrium/story (Hardy 1908)

invasion analysis

- can species/type A *invade* a *monomorphic* equilibrium of type B? (evaluate Jacobian at $\{0, B^*\}$)
- can measure in terms of *fitness r* (eigenvalue) or R (fitness scaled by generation time)

evolutionary game theory

- competing strategies; "payoff" (fitness) dependent on coexisting strategies
- evolutionary stable state/strategy (non-invadable) (vs. convergent stable strategy: Apaloo, Brown, and Vincent (2009))

adaptive dynamics

- *pairwise invasibility plots*
- separation of time scales: mutation $\ll$ population dynamics

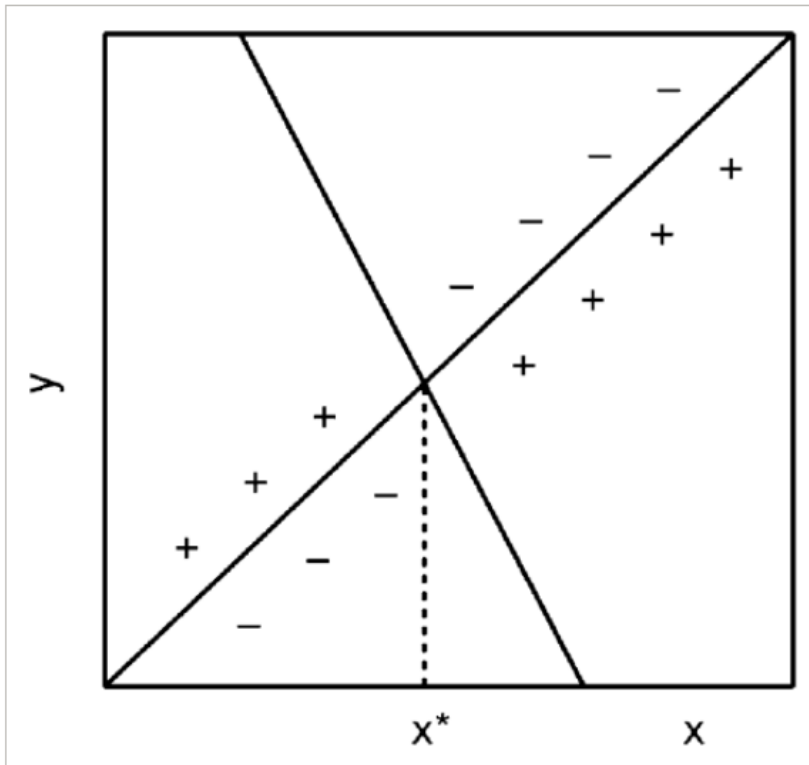- typically looking for *evolutionary branching points*

Figure 3: pairwise invasion plot

eco-evolutionary dynamics

- keep track of population dynamics *and* trait distribution
- full model: PDEs (distribution), *or* mean and variance, *or* just mean
- *Price equation* (Day and Proulx 2004)

evolution of pathogens ($\mathcal{R}_0$)

- maximizing $\mathcal{R}_0$ is *sometimes* an ESS (Lion and Metz 2018; Abrams 2001)
- $\approx$ strain that *minimizes* susceptible population ($S^* = 1/\mathcal{R}_0$)

evolution of virulence

- What is ESS if transmission rate β is a *decelerating* function of disease-induced mortality (α)?

  - $d\beta/d\alpha > 0, d^2\beta/d\alpha^2 < 0$
  - $\rightarrow \mathcal{R}_0 = \beta(\alpha)/(\alpha + \mu)$

- more generally *clearance rate* $\alpha + \gamma$ (recovery plus virulence)
- what value of β maximizes $\mathcal{R}_0$?
- $\rightarrow \beta' = \beta/(\alpha + \mu)$

Models of a continuum of virulence (or some other trait)

- from distribution model (integral equation)
- to advection-diffusion equation
- to equation for the mean (Price equation)

Transient virulence evolution (Bolker, Nanda, and Shah 2010)

$$\frac{dS}{dt} = m(N - S) - \beta(\bar{\alpha})SI$$

$$\frac{dI}{dt} = \qquad\quad \beta(\bar{\alpha})SI - (m + \alpha)I$$

$$\frac{d\bar{\alpha}}{dt} = V_g(Sd\beta/d\alpha - 1)$$

Invasion of VOCs

$$I_1 = \exp(r_1 t)$$

$$I_2 = \exp(r_2 t)$$

Figure 4: tradeoff curves
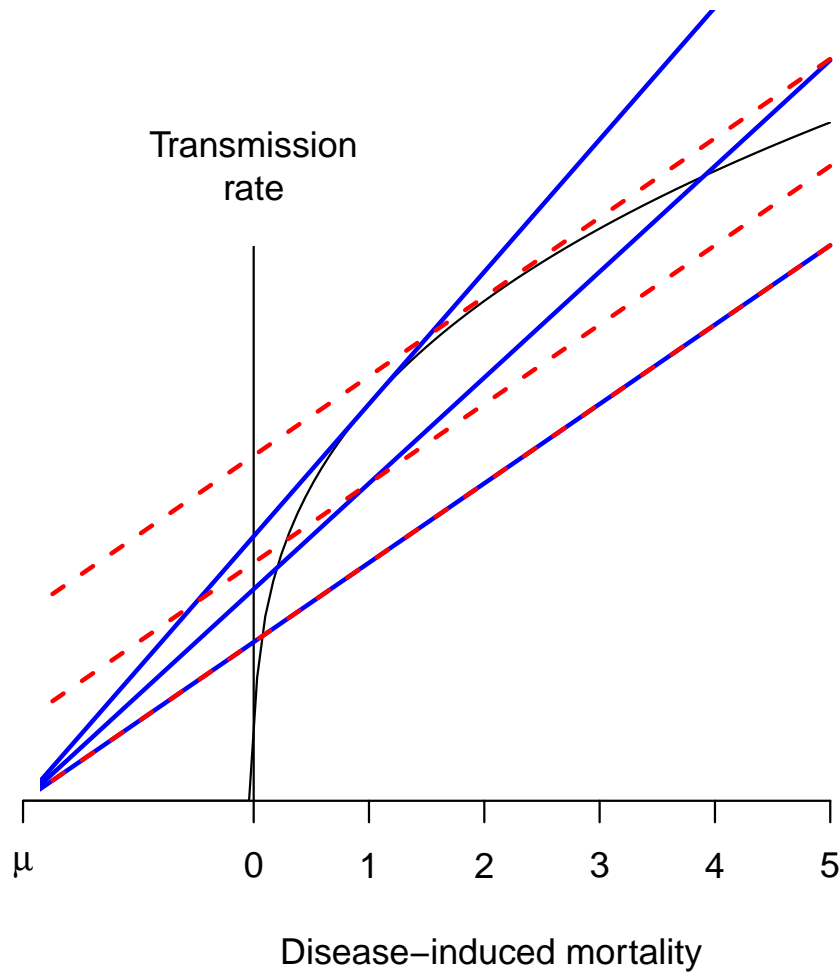
Transmission rate

Disease−induced mortality

μ   0   1   2   3   4   5

References

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