

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 uppercase 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 (typically 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, strategy, 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 particular 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
- $M \rightarrow 0$ is *extinction*, $M \rightarrow N$ 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())
```

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

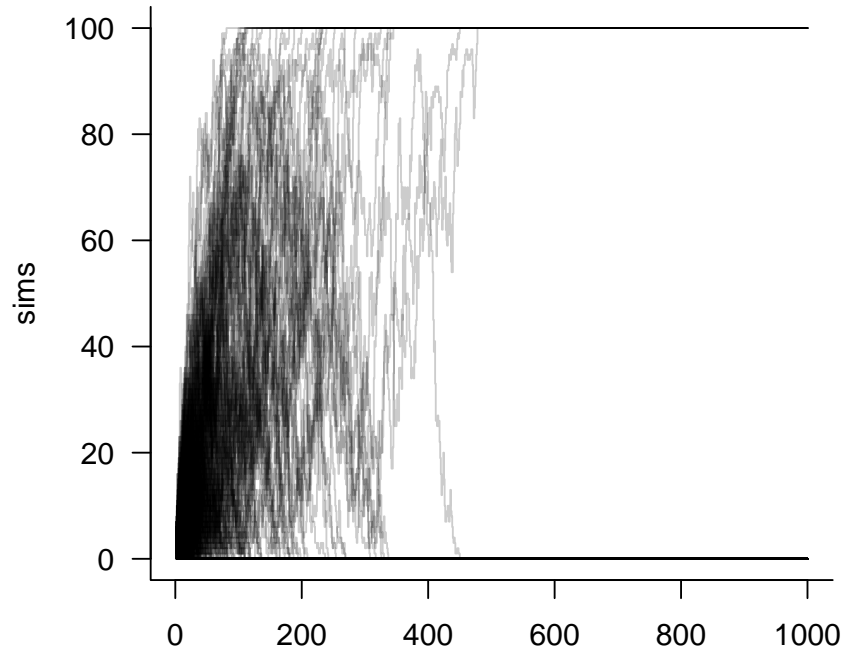


Figure 1: Neutral simulation 1

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

```
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?

```
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))
```

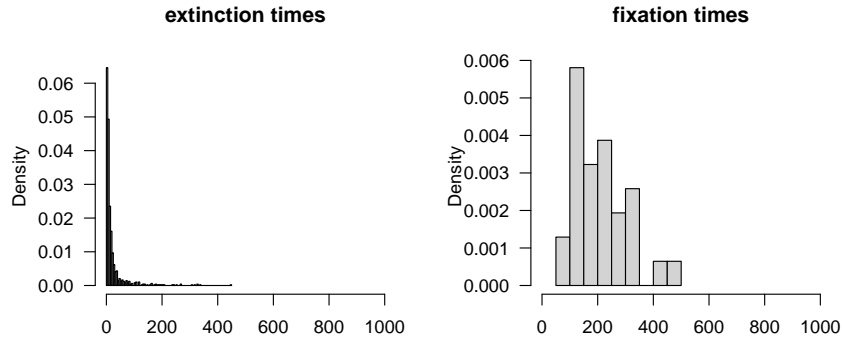


Figure 2: extinction and fixation times

Non-neutral dynamics

- assume *relative fitness* of mutant is w_m
- 1 advantageous, <1 deleterious
- if wild-type have C offspring each, mutants have $w_m C$, then probability of an offspring being mutant is $Mw_m C / (Mw_m C + WC) = Mw_m / (Mw_m + W)$ 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*

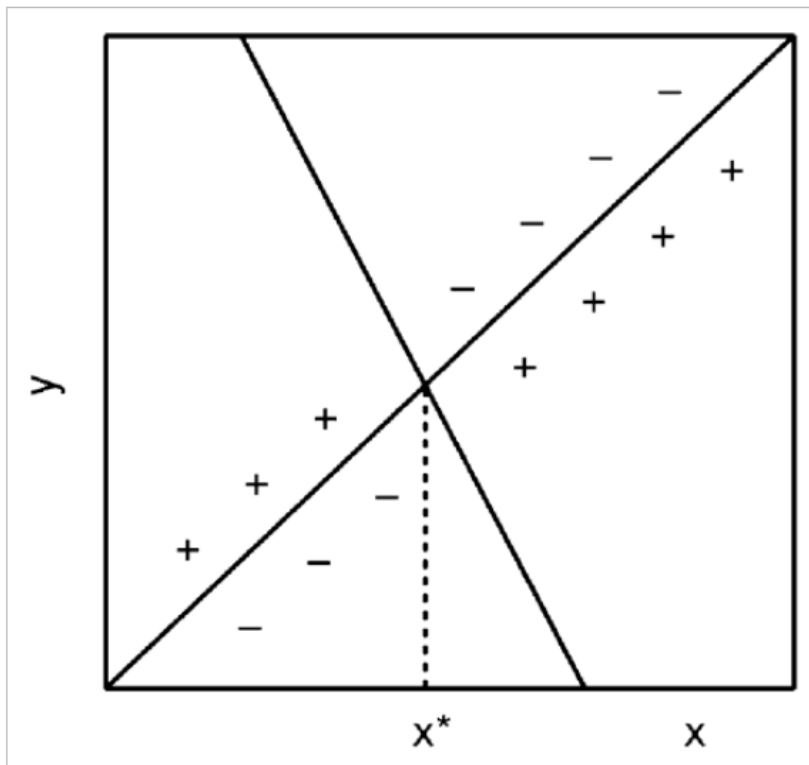


Figure 3: pairwise invasion plot

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 virulence

- Very broadly, maximizing \mathcal{R}_0 is an ESS
- 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 ?
- $\rightarrow \beta' = \beta/(\alpha + \mu)$

Invasion of VOCs

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

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

References

- Apaloo, Joseph, Joel S. Brown, and Thomas L. Vincent. 2009. "Evolutionary Game Theory: ESS, Convergence Stability, and NIS." *Evolutionary Ecology Research* 11 (4): 489–515. <http://www.evolutionary-ecology.com/abstracts/v11/2445.html>.
- Day, Troy, and Stephen R. Proulx. 2004. "A General Theory for the Evolutionary Dynamics of Virulence." *The American Naturalist* 163 (4): E40–E63. <http://www.jstor.org/stable/10.1086/382548>.
- Hamilton, W. D. 1998. *Narrow Roads of Gene Land: The Collected Papers of W. D. Hamilton Volume 1: Evolution of Social Behaviour*. Oxford ; New York: Oxford University Press, USA.
- Hardy, G. H. 1908. "Mendelian Proportions in a Mixed Population." *Science* 28 (706): 49–50. <http://www.jstor.org/stable/1636004>.
- Rice, Sean H. 2004. *Evolutionary Theory: Mathematical and Conceptual Foundations*. 1st edition. Sunderland, Mass., USA: Sinauer Associates/Oxford University Press.
- Smith, John Maynard. 1982. *Evolution and the Theory of Games*. 1 edition. Cambridge ; New York: Cambridge University Press.

