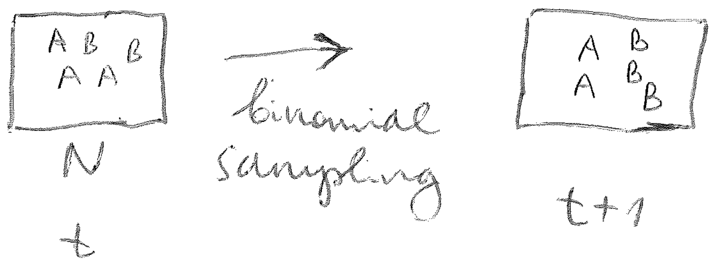
Kimura, 1962 | Lecture 8

Fixation of mutant genes in a population



Consider a population of N genes in which the freq. of the allele A is p $(0 \le p \le 1)$. The freq. of allele B is then $q = 1-p$

Define $u(p,t)$ = prob. that A is fixed (i.e. its freq. $= 1$) in $\le t$ generations (continuous time approx'n)

$$u(p, t+\delta t) = \int d(\delta p)\, \underbrace{f(p, p+\delta p\,;\, \delta t)}_{\substack{\text{prob. density} \\ p \to p+\delta p \text{ in } \delta t}} \times u(p+\delta p, t)$$

Introduce

$$\begin{cases} \lim\limits_{\delta t \to 0} \dfrac{1}{\delta t} \int (\delta p)\, f(p, p+\delta p\,;\, \delta t)\, d(\delta p) \equiv M, \\ \lim\limits_{\delta t \to 0} \dfrac{1}{\delta t} \int (\delta p)^2\, f(p, p+\delta p\,;\, \delta t)\, d(\delta p) \equiv V \end{cases}$$

Just as before, we obtain:

$$\frac{\partial u(p,t)}{\partial t} = \frac{V}{2}\frac{\partial^2 u}{\partial p^2} + M\frac{\partial u}{\partial p}$$

BCs: $u(0,t) = 0, \quad u(1,t) = 1$

Measure time in generations →

→ M, V are the mean & variance of the change of p ~~per~~ generation.

Consider $u(p) = \lim_{t\to+\infty} u(p,t)$:

$$\frac{\partial u}{\partial t} = 0 \implies \frac{V}{2}\frac{d^2u}{dp^2} + M\frac{du}{dp} = 0. \quad (*)$$

"steady state" $\qquad u(0) = 0, \quad u(1) = 1$

(*) can be solved: $\qquad u(p) = \dfrac{\int_0^p G(x)\,dx}{\underbrace{\int_0^1 G(x)\,dx}_{=C_1}}$

Indeed, $\frac{du}{dp} = \frac{G(p)}{C_1}$; $\frac{d^2u}{dp^2} = G(p)\left[-\frac{2M(p)}{V(p)}\right]\frac{1}{C_1}$

$-G(p)M(p)\frac{1}{C_1} + \frac{M(p)G(p)}{C_1} = 0$, as expected!

$$G(x) = e^{-\int_0^x \frac{2M(y)}{V(y)}\,dy}$$

Note that $u(\frac{1}{N})$ is a chance of fixation of a "novel" mutant gene.

Now, for the binomial distr'n we have:

$$\begin{cases} \mu = \underset{\#\text{ trials}}{n}\,\underset{\text{prob. of success}}{p}, \\ \sigma^2 = npq \end{cases}$$

Prob. (i alleles of type A) =

$$= \frac{N!}{i!(N-i)!} \underset{\substack{\uparrow \\ \text{freq. of} \\ \text{allele A}}}{p^i} (1-p)^{N-i} .$$

No selection:

$$E(\Delta p | p) = \underbrace{\frac{E(i)}{N}}_{\substack{\text{new} \\ \text{freq,} \\ \text{on average}}} - \underbrace{p}_{\substack{\text{old} \\ \text{freq}}} = \frac{Np}{N} - p = 0$$

$$Var(\Delta p | p) = Var\left(\frac{i}{N} - p \,|\, p\right) = \frac{Var(i)}{N^2} = \frac{Np(1-p)}{N^2} =$$

$$= \frac{p(1-p)}{N} .$$

With selection,

	A	B	
	$1+s$	1	← prob. of survival
before selection ⇒	p	q	

after selection ⇒ $p' = \dfrac{p(1+s)}{p(1+s)+q}$ $\qquad \dfrac{q}{p(1+s)+q} = q'$

$p'+q'=1$

$$p'-p \equiv \Delta_s p = \frac{p(1+s) - p^2(1+s) - pq}{p(1+s)+q} =$$

$$= \frac{pqs}{\underbrace{p(1+s)+q}_{1+ps \approx 1 \text{ if } s \text{ is small}}} \approx pqs .$$

So, $E(\Delta p | p) = s p(1-p)$.

In our notation, $\frac{2M(y)}{V(y)} = 2NS$ & $G(x) = e^{-2NSx}$

$$" \frac{2[Spq]}{pq/N}$$

Finally, $u(p) = \frac{1-e^{-2NSp}}{1-e^{-2NS}}$. Kimura's formula

$$u\left(\tfrac{1}{N}\right) = \frac{1-e^{-2S}}{1-e^{-2NS}} \approx \frac{2S}{1-e^{-2NS}}.$$

$\lim_{S\to 0} u\left(\tfrac{1}{N}\right) = \frac{2S}{2NS} = \frac{1}{N}$, as expected.

$u(p) = p$ is a well-known neutral result.