4.1) Drift - mutation : two alleles

H_t : prob. that two randomly chosen alleles are $\neq$
G_t : prob. that ________ are the same !

1) Même ancêtre ; allèles $\neq$ si un mute et pas l'autre
$\rightarrow 2\mu(1-\mu) \simeq 2\mu$

2) Ancêtres $\neq$:
$$\begin{cases} \text{si } H_t : \text{ aucune ou deux muts} : \mu^2 + (1-\mu)^2 \sim 1 - 2\mu \\ \text{si } (1-H_t) : \text{ un mute et pas l'autre} : 2\mu \end{cases}$$

3)
$$H_{t+1} = \frac{1}{N} \cdot 2\mu + \left(1 - \frac{1}{N}\right) \left\{ H_t (1 - 2\mu) + (1 - H_t) 2\mu \right\}$$
$$\simeq \frac{2\mu}{N} + \left(1 - \frac{1}{N}\right) \cdot 2\mu + \left(1 - \frac{1}{N}\right)(1 - 4\mu) H_t$$
$$= 2\mu + \left(1 - \frac{1}{N} - 4\mu\right) H_t \quad , \quad \frac{\mu}{N} \ll \mu, N$$

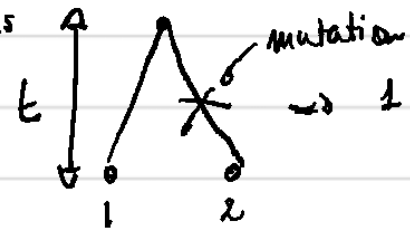
Donc $\boxed{H_{eq} = \dfrac{2\mu N}{1 + 4\mu N}}$

4.2) Drift - mutation with the coalescent

1) From coalescent theory, we have $p(t) = \left(1 - \frac{1}{N}\right)^{t-1} \cdot \frac{1}{N}$

since $n = 2 \to \binom{n}{2} = 1$

2) For the two to share the same allele, we need <u>no</u> mutations on either two lineages



$\to$ 1 and 2 will differ !

Prob. of no mutations in <u>2t</u> generations : $(1-\mu)^{2t}$

2t because the total branch length is 2t!

3) Prob. that the two alleles are the same: $G = \sum_{t=1}^{\infty} p(t) \cdot (1-\mu)^{2t}$

$$G = \frac{1}{N} \sum_{t=1}^{\infty} \left(1 - \frac{1}{N}\right)^{t-1} \left((1-\mu)^2\right)^t = \frac{(1-\mu)^2}{N} \sum_{t=1}^{\infty} \left[\left(1-\frac{1}{N}\right)(1-\mu)^2\right]^{t-1}$$

Neglecting order 2 terms: $\left(1-\frac{1}{N}\right)(1-\mu)^2 \simeq 1 - \frac{1}{N} - 2\mu$ and $(1-\mu)^2 \simeq 1-2\mu$

$$\to G = \frac{(1-2\mu)}{N} \cdot \frac{1}{1-\left(1-\frac{1}{N}-2\mu\right)} = \frac{1-2\mu}{1+2\mu N}$$

Prob. that alleles are $\neq$: $1 - G = H = \frac{2\mu(N+1)}{1+2\mu N} \simeq \frac{2\mu N}{1+2\mu N}$ for $N \to \infty$

A bit easier with the continuous time version

Continuous coalescent
t measured in units of N

Prob. of coalescence at time t : $e^{-t}\,dt$

Prob. of no mutations in time $2t$: $e^{-2\mu N t}$

μN because one unit of continuous time = N units of discrete!

Prob. that the two alleles are $\neq$: $G = \int_0^t e^{-2\mu N t} e^{-t}\,dt$

$$\rightsquigarrow G = \int_0^\infty e^{-(1+2\mu N)t}\,dt = \frac{1}{1+2\mu N}$$

And finally $H = 1 - G = \dfrac{2\mu N}{1+2\mu N}$

Poisson from the binomial

Remember that k is fixed!

1) $$\mathbb{P}(k) = \binom{n}{k} p^k (1-p)^{n-k} = \binom{n}{k}\left(\frac{\lambda}{n}\right)^k \left(1-\frac{\lambda}{n}\right)^{n-k}$$

2) $$\left(1-\frac{\lambda}{n}\right)^n = \exp\left(n \cdot \log\left(1-\frac{\lambda}{n}\right)\right) \xrightarrow[n\to\infty]{} e^{-\lambda}$$

$$\left(1-\frac{\lambda}{n}\right)^{-k} \xrightarrow[n\to\infty]{} 1 \quad \text{since } \left(1-\frac{\lambda}{n}\right) \xrightarrow[n\,\infty]{} 1$$

$$\frac{n!}{(n-k)!} = \frac{1\times 2 \cdot \ldots \times n}{1\times 2\times \cdots \times (n-k)} = (n-k+1)\times \cdots \times n = \prod_{i=0}^{k-1}(n-i)$$

$$= n^k \underbrace{\prod_{i=0}^{k-1}\left(1-\frac{i}{n}\right)}_{\xrightarrow[n\to\infty]{} 1} \quad \text{since } \left(1-\frac{i}{n}\right) \xrightarrow[n\to\infty]{} 1$$

Now the main calculation:

$$\mathbb{P}(k) = \frac{n!}{k!(n-k)!}\left(\frac{\lambda}{n}\right)^k \left(1-\frac{\lambda}{n}\right)^{n-k}$$

$$= \frac{\lambda^k}{k!}\left(1-\frac{\lambda}{n}\right)^n \cdot \underbrace{\frac{n!}{(n-k)!}}_{\to n^k} \cdot \left(\frac{1}{n}\right)^k \underbrace{\left(1-\frac{\lambda}{n}\right)^{-k}}_{\to 1}$$

$$\boxed{\mathbb{P}(k) \xrightarrow[n\to\infty]{} \frac{\lambda^k}{k!} e^{-\lambda}}$$

Number of offsprings in WF (clonal)

Given by a binomial : $\mathbb{P}(k) = \binom{N}{k}\left(\frac{1}{N}\right)^{k}\left(1-\frac{1}{N}\right)^{N-k}$

$\sim \text{Binomial}(n,p)$ with $\begin{cases} n = N \\ p = \frac{1}{N} \end{cases}$

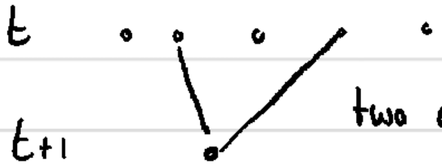
if $N \to \infty$, we have (with notations of the previous problem)

- $n \to \infty$
- $p \to 0$
- $\lambda = n \cdot p = \frac{N}{N} = 1$ constant

↳ this goes to a Poisson distribution with $\lambda = 1$!

Diploid/sexual case?

Prob. of not being picked as an ancestor is now $\left(1-\frac{1}{N}\right)^2 \simeq \left(1-\frac{2}{N}\right)$ if $N \gg 1$



two ancestors picked by each offspring!

$\to \mathbb{P}(k) = \binom{N}{k}\left(\frac{2}{N}\right)^{k}\left(1-\frac{2}{N}\right)^{N-k} \sim \text{Binomial}\left(N, \frac{2}{N}\right)$

↳ still Poisson with $N \to \infty$, but $\lambda = \frac{2}{N} \cdot N = 2$!