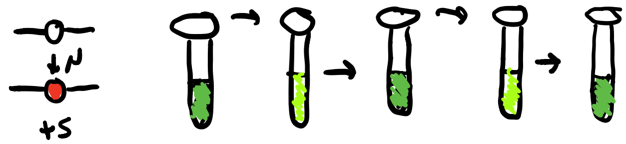
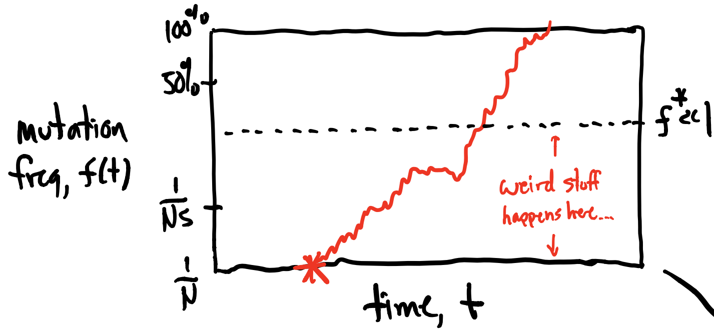
Announcements: PSET 2 DUE TUES [Anita problem session – see Slack]

Last time: Quick review – how did we get here?



$$\Rightarrow \quad \frac{\partial f}{\partial t} = \underbrace{sf(1-f)}_{\text{selection}} + \underbrace{\sqrt{\frac{f(1-f)}{N}}\,\eta(t)}_{\text{genetic drift}} + \underbrace{\left[\mu(1-f) - \nu f\right]}_{\text{mutation}}$$

$$\Downarrow$$



"Linear Branching Process"

$$\frac{\partial f}{\partial t} = sf + \sqrt{\frac{f}{N}}\,\eta(t) + \left[\mu - \nu f\right]$$

w/ no mutations ($\mu = \nu = 0$)

$\Rightarrow$ Generating function

$$H(z,t) \equiv \left\langle e^{-z f(t)} \right\rangle = \exp\left[-\frac{z\langle f(t)\rangle}{1 + \frac{z}{2}\langle f(t)\rangle \sigma_v^2(t)}\right]$$

$$\langle f(t)\rangle = f_0 e^{st}$$

$$\sigma_v^2(t) = \frac{1-e^{-st}}{2Nsf_0}$$

Time-dependent extinction probability:

$$p_{ext}(t) \equiv \lim_{z\to\infty} H(z,t) = \exp\left[-\frac{2}{\sigma_v^2(t)}\right] \equiv 1 - p_s(t) \leftarrow \text{"survival probability"}$$

Today: ① what can we learn from these formal results?

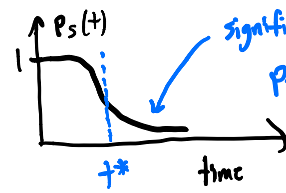
② can we do the same thing by cheating ("heuristics")

Basic behavior follows from $C_v^2(t) = \dfrac{1-e^{-st}}{Nsf_0} \approx \begin{cases} \ll 1 & \text{when } t \ll t^* \\ \gg 1 & \text{when } t \gg t^* \end{cases}$

w/ $C_v^2(t^*) \sim 1 \Rightarrow t^*(N,s,f_0) \approx \begin{cases} \infty & \text{if } s>0;\ f_0 \gg 1/Ns \quad [C_v^2(t) \text{ always} \ll 1] \\ Nf_0 & \text{if } f_0 \ll 1/N|s| \\ \frac{1}{s}\log(N|s|f_0) & \text{if } s<0;\ f_0 \gg 1/N|s| \end{cases}$

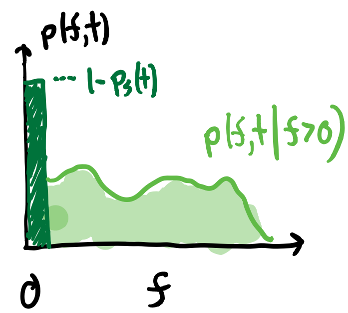
$\Rightarrow$ for survival probability,

$$p_s(t) = 1 - \exp\left[-\frac{2}{C_v^2(t)}\right] \approx \begin{cases} 1 & \text{if } s>0;\ f_0 \gg 1/Ns \quad \text{(always alive)} \\ \text{or:} & \end{cases}$$



significant chance of going extinct
$p_s(t) \approx 2/C_v^2(t) \quad [\ll 1]$

$\Rightarrow$ can anticipate that distribution, $p(f,t)$ will be ~case 2 dist'n that is a mixture of 2 different kinds of paths:



$$p(f,t) \approx \underbrace{[1-p_s(t)]\,\delta(f)}_{\text{extinct paths}} + \underbrace{p_s(t)\cdot p(f,t|f>0)}_{\text{non-extinct paths}}$$

distribution of $f(t)$
* conditioned on survival *

$\Rightarrow$ what can we say about $p(f,t|f>0)$?

easy to calculate <u>mean</u> by decomposing:

$$\langle f(t)\rangle = 0\cdot(1-\cancel{p_s(t)}^{\,0}) + p_s(t)\cdot\langle f(t)\,|\,f>0\rangle$$

$$\Rightarrow \langle f(t)\,|\,f>0\rangle = \frac{\langle f(t)\rangle}{p_s(t)} = \begin{cases} f_0 e^{st} & \text{if } t \ll t^* \\ \frac{e^{st}-1}{2Ns} & \text{if } t \gg t^* \end{cases}$$

← independent of f_0!

Depending on selection coefficient, $t \gg t^*$ limit looks like:

$$\langle f(t)\,|\,f>0\rangle \xrightarrow{t\gg t^*} \begin{cases} \frac{e^{st}}{2Ns} & \text{if } s>0;\ t\gg 1/s \\ \frac{t}{2N} & \text{if } t \ll 1/|s| \\ \frac{1}{2N|s|} & \text{if } s<0;\ t\gg 1/|s| \end{cases}$$

← looks like deterministic case, w/ different $f_0 \approx \frac{1}{2Ns}$

← grows <u>linearly</u> in time.

← saturates @ const value.

corresponding survival probabilities are:

$$p_s(t) \xrightarrow{t\gg t^*} \begin{cases} 2Ns f_0 & \text{if } s>0;\ t\gg 1/s \\ 2Nf_0/t & \text{if } t\ll 1/|s| \\ 2N|s| f_0 e^{-|s|t} & \text{if } s<0;\ t\gg 1/|s| \end{cases}$$

← saturates @ constant value.

$$\boxed{\text{perfectly set up so that } \langle f(t)|f>0\rangle\cdot p_s(t) = \langle f(t)\rangle}$$

$\Rightarrow$ can use same argument for full distribution, $p(f,t|f>0)$ via the generating function:

$$H(z,t) \equiv \langle e^{-z\cdot f(t)} \rangle = [1-p_s(t)]\cdot \cancelto{1}{e^{-z\cdot 0}} + p_s(t)\, H(z,t|f>0) \quad ?$$

$\Downarrow$ rearrange to obtain:

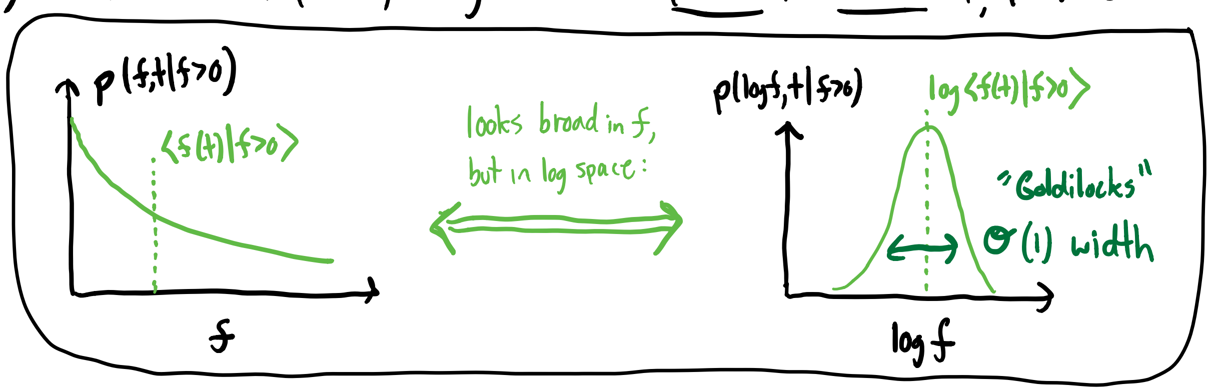
$$H(z,t|f>0) = \frac{H(z,t)-[1-p_s(t)]}{p_s(t)} = \frac{e^{-\frac{z\langle f(t)\rangle}{1+\frac{z}{2}\langle f(t)\rangle \omega_v^2(t)}} - e^{-\frac{2}{\omega_v^2(t)}}}{1-e^{-2/\omega_v^2(t)}}$$

$\Rightarrow$ when $t \gg t^*$ $\left(\omega_v^2(t) \gg 1\right)$, can Taylor expand exponentials

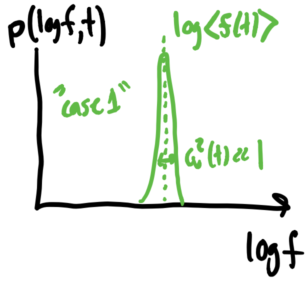
(p11. in notes)

$$\Rightarrow \quad H(z,t|f>0) \xrightarrow{t \gg t^*} \Big(1+z\cdot \underbrace{\frac{\langle f(t)\rangle\, \omega_v^2(t)}{2}}_{\langle f(t)|f>0\rangle \text{ from before}}\Big)^{-1} \sim \frac{1}{1+az}$$

By "method of wikipedia", recognize as exponential distribution, $p(u) \propto e^{-u/\langle u \rangle}$

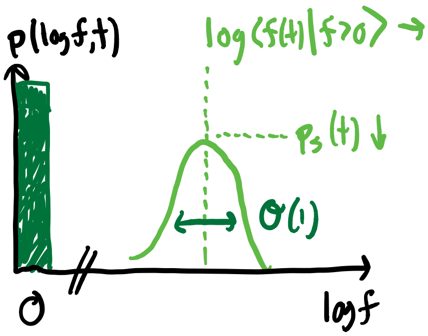


Putting everything together, we have:

① 

when $t \ll t^* \approx \begin{cases} \infty & \text{if } s>0;\ f_0 \gg 1/Ns \\ Nf_0 & \text{if } f_0 \ll 1/N|s| \\ \frac{1}{s}\log(N|s|f_0) & \text{if } s<0;\ f_0 \gg 1/N|s| \end{cases}$

② when $t \gg t^*$



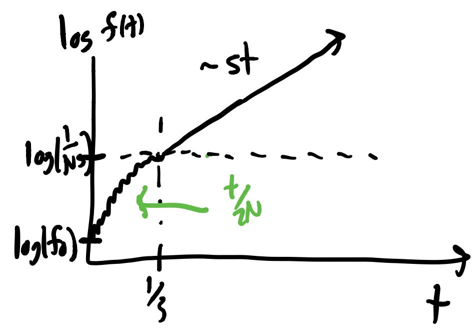
$\langle f(t) | f>0 \rangle \approx \begin{cases} \frac{e^{st}}{2Ns} & \text{if } s>0,\ t \gg 1/s \\ \frac{t}{2N} & \text{if } t \ll 1/|s| \\ \frac{1}{2N|s|} & \text{if } s<0;\ t \gg 1/|s| \end{cases}$

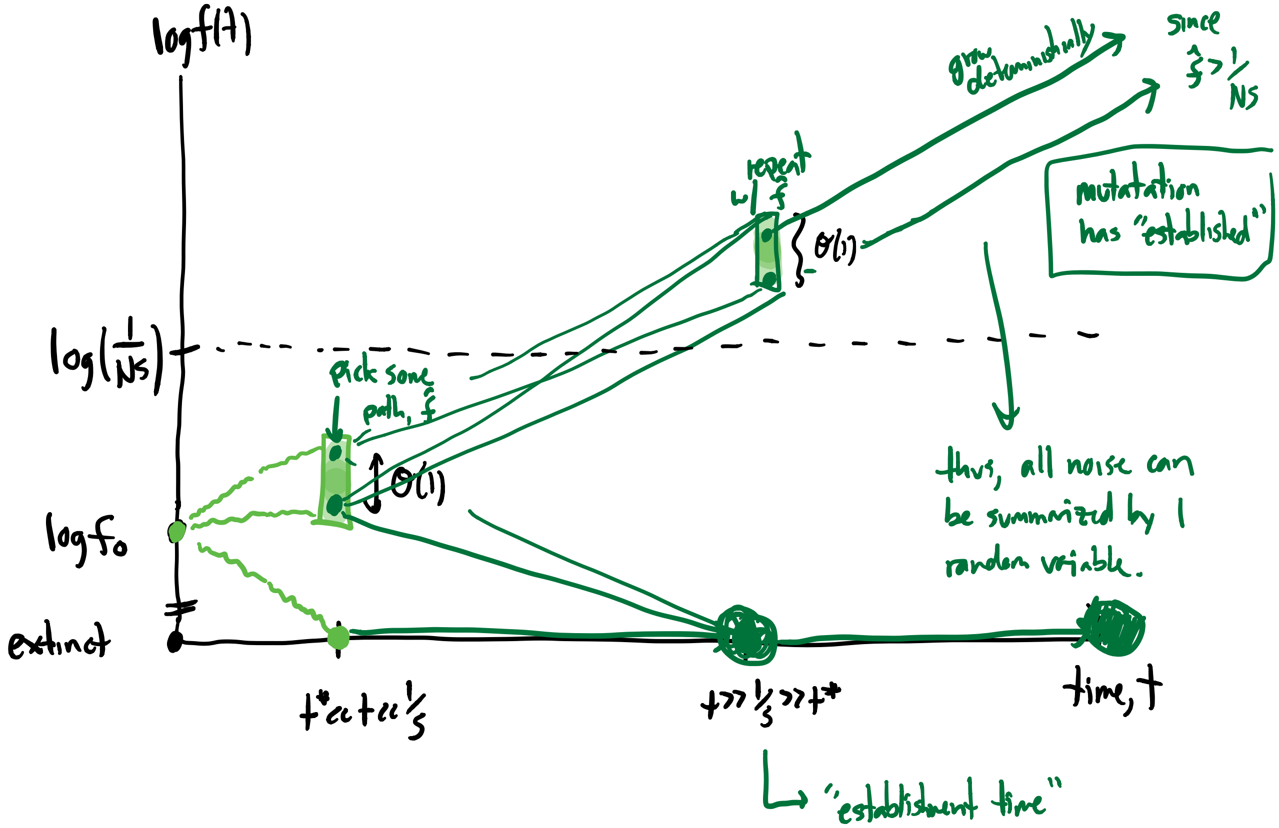
$\Rightarrow$ if $t^* \ll t \ll 1/|s|$, then

$\Rightarrow$ mutations look neutral ($s=0$) even when $N|s| \gg 1$!

$\Rightarrow$ need $t \sim Nf$ generations to go from $f_0 \to f$

For beneficial mutation ($s>0$):
faster than deterministic @
early times ($t \ll 1/s$, $f(t) \ll 1/Ns$)





$\Rightarrow$ for $s>0$, $t \gg \frac{1}{s}$, $\quad f(t) = \nu e^{st}$

↳ "random variable" (but const in time)

$$\Rightarrow H_\nu(z) = \langle e^{-z\cdot\nu} \rangle = \langle e^{-z\cdot e^{-st}\cdot f(t)} \rangle$$

$$= H_f(z_{eff} = z e^{-st}, t) \xrightarrow{t \gg \frac{1}{s}} \left(1 + \frac{z}{2Ns}\right)^{-1}$$

$$\Rightarrow \nu \sim \text{Exponential}\left(\frac{1}{2Ns}\right) \Rightarrow \nu \sim \frac{1}{2Ns}\cdot \underbrace{\text{Exponential}(1)}_{\text{"c"}}$$

Get full picture w/ "asymptotic matching"

<u>Step 1</u>: pick some time t_i s.t. $t_i \gg \frac{1}{s}$

but $f(t_i) \ll \frac{1}{2}$

$\Rightarrow$ need s: $\left[\frac{1}{s} \ll t_i \ll \frac{1}{s}\log(Ns) \right]$

$\Rightarrow$ @ time t_i, $f(t_i) = \nu e^{st_i}$

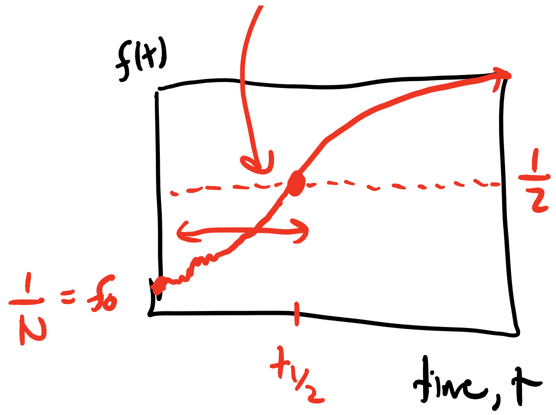
<u>Step 2</u>: use t_i as starting point for deterministic model:

$(\partial_t f = sf(1-f))$

$$\Rightarrow f(t) = \frac{f(t_i)e^{s(t-t_i)}}{f(t_i)\, e^{s(t-t_i)} + 1 - f(t_i)} \approx \frac{f(t_i)e^{s(t-t_i)}}{f(t_i)e^{s(t-t_i)} + 1}$$

<u>Step 3</u>: plug in for $f(t_i) = \nu e^{st_i}$

$$\Rightarrow \boxed{f(t) = \frac{\nu e^{st}}{\nu e^{st} + 1}} \Rightarrow \boxed{\text{independent of time } t_i! \checkmark}$$



How long to go from $f_0 = \frac{1}{N}$ (new mutation) to $f = \frac{1}{2}$?

$$\Rightarrow \quad f(t_{1/2}) = \frac{v e^{s t_{1/2}}}{v e^{s t_{1/2}} + 1} = \frac{1}{2}$$

$$\Rightarrow \quad t_{1/2} = \frac{1}{s} \log\left(\frac{1}{v}\right) = \frac{1}{s}\left[\underbrace{\log(Ns)}_{\text{deterministic part.}} + \underbrace{\log\left(\frac{2}{c}\right)}_{\text{stochastic part}}\right]$$

$$\simeq \frac{1}{s}\log(Ns) \pm \mathcal{O}\left(\frac{1}{s}\right)$$

$$\Rightarrow \quad \text{fixation time, } T_{fix} = 2 t_{1/2} = \frac{2}{s}\log(Ns) \pm \mathcal{O}\left(\frac{1}{s}\right)$$