Adaptation in structured populations

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LMU, July 2014

Population genetic models

Populations of constant size have been modelled by

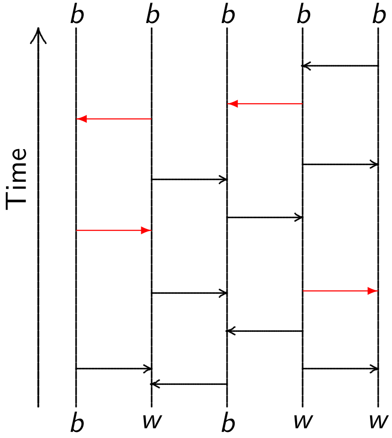
- **Markov Chains** (Wright-Fisher-model, Moran model)
- **Diffusion approximations** (Fisher-Wright diffusion)

$$dX = \alpha X(1-X)dt + \sqrt{X(1-X)}dW$$

or measure-valued diffusions (Fleming-Viot superprocess)

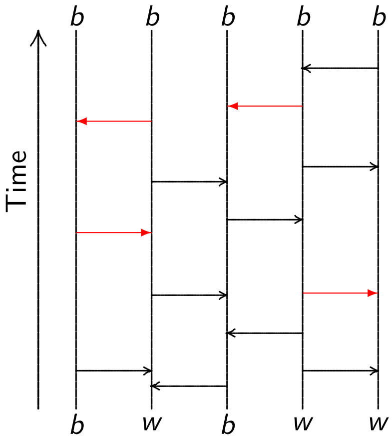
- **Keywords:** Superprocess, duality of Markov processes, random tree

The Moran model with selection



- Alleles are b and w ($b$eneficial, $w$ild-type)
- Each pair resamples with rate 1
- Each line creates red arrows with rate α

The Moran model with selection



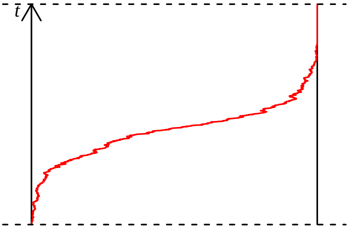
- Black arrows can be used by any allele
- Only b alleles can use red arrows
- The state at all times can be read from this graphical representation

The Wright-Fisher diffusion

- **Frequency path** of beneficial allele is

$$dX = \alpha X(1-X)dt + \sqrt{X(1-X)}dW, \qquad X_0 = x$$

N	population size
s	selective advantage
α	$:= sN$
dt	$\equiv Ndt$ generations

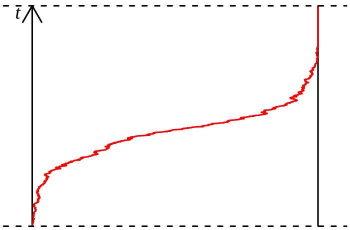


- **Conditioned on fixation**

$$dX = \alpha X \coth(\alpha X)(1-X)dt + \sqrt{X(1-X)}dW, \qquad X_0 \downarrow 0$$

Selective sweeps: Classical case

- A highly beneficial mutant eventually fixes in a panmictic population
- Fixation time $T := \inf\{t \geq 0 : X(t) = 1\}$



- Classical result: $\frac{\alpha}{\log \alpha} T \xrightarrow{\alpha \to \infty} 2.$

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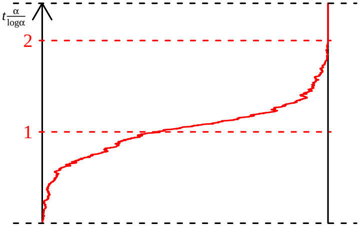
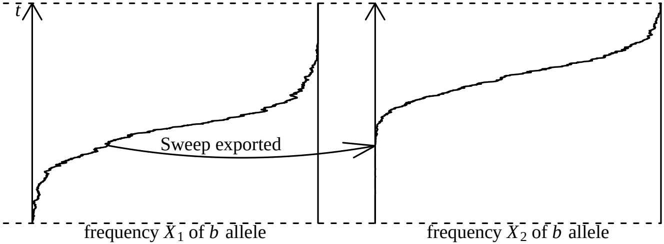


- Classical result: $\frac{\alpha}{\log \alpha} T \xrightarrow{\alpha\to\infty} 2.$

Selective sweeps: Case considered in this talk

- A highly beneficial mutant eventually fixes in a structured population
- Fixation time $T := \inf\{t \geq 0 : X_i(t) = 1, i = 1, ..., \nu\}$



- What is the distribution of T?

Selective sweeps: Case considered in this talk

- Conditioned on eventual fixation, on 2 islands

$$dX_1 = \big(\mu(X_2 - X_1) + \alpha X_1(1 - X_1)\coth\left(\alpha(X_1 + X_2)\right)\big)dt + \sqrt{X_1(1 - X_1)}dW_1$$
$$dX_2 = \big(\mu(X_1 - X_2) + \alpha X_2(1 - X_2)\coth\left(\alpha(X_1 + X_2)\right)\big)dt + \sqrt{X_2(1 - X_2)}dW_2$$

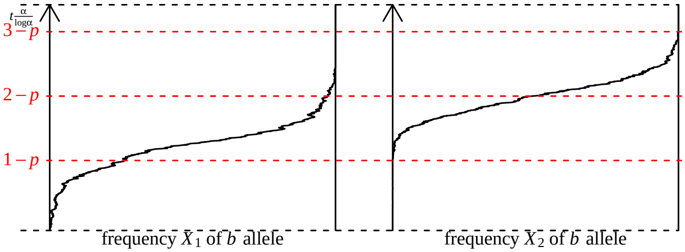
- Theorem: Let $T := \inf\{t \geq 0 : X_1(t)_t = X_2(t) = 1\}$.

$$\frac{\alpha}{\log \alpha} T \xRightarrow{\alpha \to \infty} \begin{cases} 3 - p, & \text{if } \mu \approx c\alpha^p \text{ for } p \in [0, 1], \\ 3 + X, & \text{if } \mu \approx \frac{c}{\log \alpha}, \end{cases}$$

where $X \sim \exp(2c)$.

Selective sweeps: Case considered in this talk

- Fixation time $T := \inf\{t \geq 0 : X_i(t) = 1, i = 1, ..., \nu\}$



$$\frac{\alpha}{\log \alpha} T \xrightarrow{\alpha\to\infty} 3 - p$$

Selective sweeps on ν islands

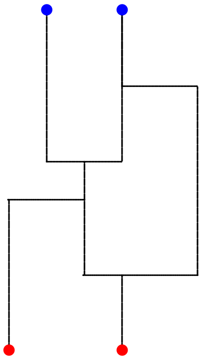
- Theorem: Condition on eventual fixation, on ν islands.
  Let $T := \inf\{t \geq 0 : X_i(t) = 1, i = 1, ..., \nu\}$. Then,

$$\frac{\alpha}{\log \alpha} T \xrightarrow[\alpha\to\infty]{} \begin{cases} 2 + (1-p)S_Y, & \text{if } \mu \approx c\alpha^p \text{ for } p \in [0,1], \\ 1 + S_Z, & \text{if } \mu \approx \frac{c}{\log \alpha}. \end{cases}$$

Take home

Even if the population is only weakly structured (i.e. μ is large), fixation can take a lot longer than under panmixia.

The Ancestral Selection Graph



- Two lines coalesce at rate 1
- At rate α each line is hit by a red arrow; thus it produces a new line in the ancestral graph

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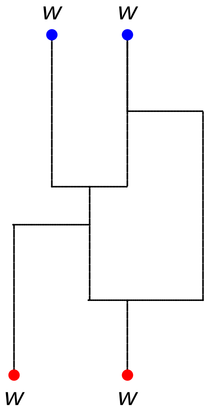

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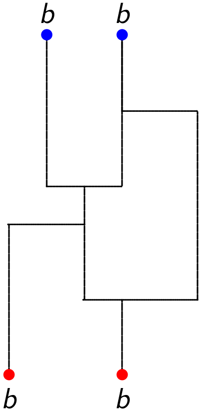

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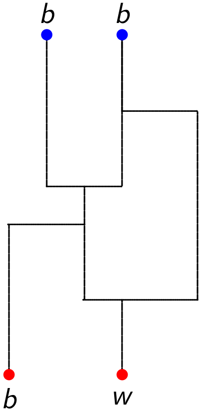

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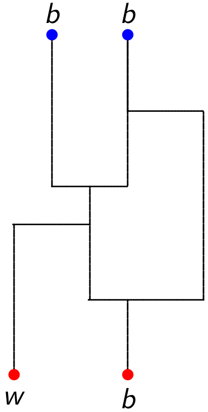

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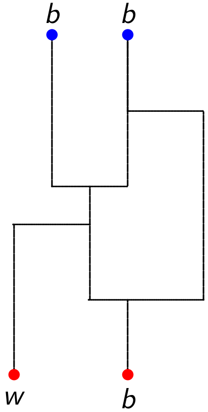
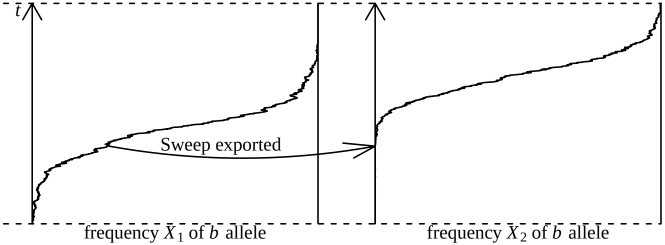


- An individual • has b iff there is an ancestor • which has b
- Reason: only b-alleles can use every branch

Fixation under strong selection in the ASG

- Consider 2 demes.
  Assume that deme 1 carries the immortal line at time 0.



Fixation under strong selection in the ASG

- **Lemma 1:** Start ASG with ∞ many lines in all demes. Wait until time t and mark a random line from deme 1 with b. Let

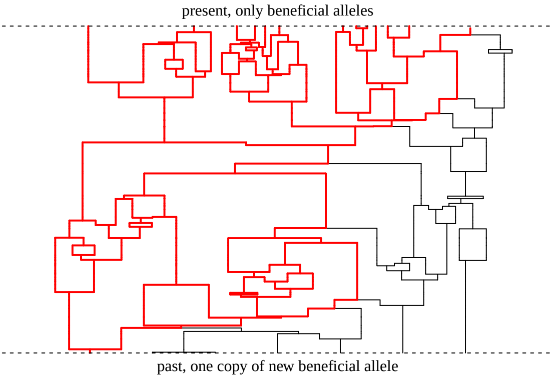
$$C_t := \{\text{marked line potential ancestor of all starting lines}\}.$$

Then,

$$\lim_{\varepsilon \to 0} \mathbf{P}_\varepsilon(T < t | \text{fixation}) = \mathbf{P}(C_t).$$

- Reason: Conditioning on eventual fixation means that at least one line is b at time 0.

Fixation under strong selection in the ASG



Fixation under strong selection in the ASG

- $\mathcal{K}$: line counting process of the ASG has the dynamics

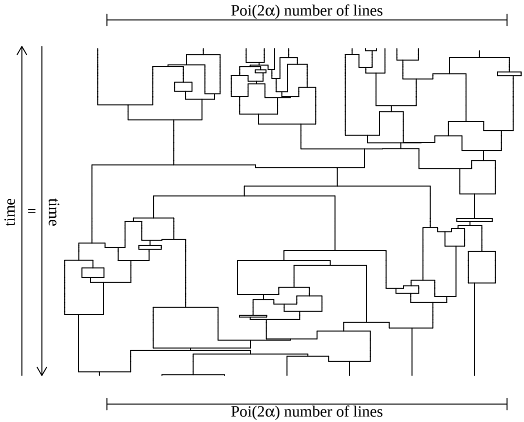
$$K_t \to \begin{cases} K_t + 1 & \text{at rate } \alpha K_t, \\ K_t - 1 & \text{at rate } \binom{K_t}{2} \end{cases}$$

  in each deme, and migration events.

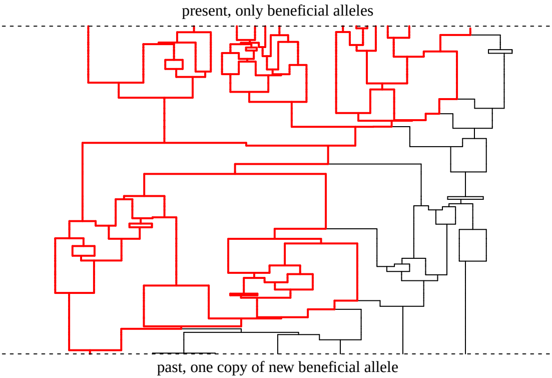
- **Lemma 2:** $K_\infty \sim \pi_{2\alpha}$, a vector of Poi$(2\alpha)$ distributions, conditioned on being positive.
  - $\pi_{2\alpha}$ is reversible for $\mathcal{K}$.
  - The full graph is reversible in its equilibrium.

- **Corollary:** Up to a small error, Lemma 1 still holds if ASG is started in equilibrium.

Fixation under strong selection in the ASG



Fixation under strong selection in the ASG



Some observations on a single deme

- Use reversibility of equilibrium in order to construct ASG from past to present.
- Start ASG in the past with equilibrium number of lines, one *b* allele in deme 1
- *b*-allele increases on deme 1 approximately according to a Yule process with rate α, up to having $\alpha^{1-\varepsilon}$ copies of *b*.
- If *w*-allele has $\sim \alpha^{1-\varepsilon}$ copies, *w*-allele decreases on deme 1 approximately according to a subcritical branching process.
- Fixation occurs iff all lines carry allele *b*.

Some observations for $\mu = c\alpha^p$

- Number of lines with allele b is about $e^{\alpha t}$ for $t < \frac{\log \alpha}{\alpha}$.
- Q: At what time $\tilde{T}$ does the first migrant (occurring at rate α^p) move from deme 1 to 2 in the ASG?

Some observations for $\mu = c\alpha^p$

- Number of lines with allele b is about $e^{\alpha t}$ for $t < \frac{\log \alpha}{\alpha}$.
- Q: At what time $\tilde{T}$ does the first migrant (occurring at rate α^p) move from deme 1 to 2 in the ASG?
- A: Not before $t' = (1 - p - \varepsilon)\frac{\log \alpha}{\alpha}$:
  Expected number of migration marks on Yule process before t' is

$$\mu \sum_{i=1}^{\alpha^{1-p-\varepsilon}} i \frac{1}{\alpha i} = \alpha^p \frac{\alpha^{1-p-\varepsilon}}{\alpha} = \alpha^{-\varepsilon} \xrightarrow{\alpha \to \infty} 0.$$

Some observations for $\mu = c\alpha^p$

- Number of lines with allele b is about $e^{\alpha t}$ for $t < \frac{\log \alpha}{\alpha}$.
- Q: At what time $\tilde{T}$ does the first migrant (occurring at rate α^p) move from deme 1 to 2 in the ASG?
- A: Not after time $t'' = (1 - p + \varepsilon)\frac{\log \alpha}{\alpha}$:
  Expected number of migration marks on rate-α Yule process up to time t'' is

$$\mu \sum_{i=1}^{\alpha^{1-p+\varepsilon}} i \frac{1}{\alpha i} = \cdots = \alpha^{\varepsilon} \xrightarrow{\alpha \to \infty} \infty.$$

Some observations for $\mu = c\alpha^p$

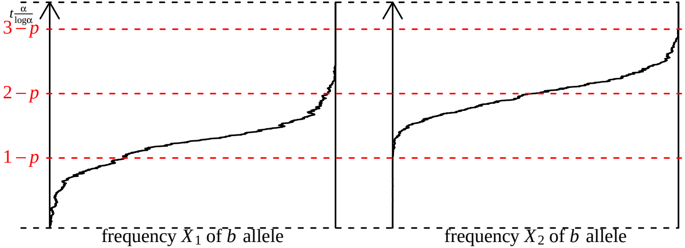
- Number of lines with allele b is about $e^{\alpha t}$ for $t < \frac{\log \alpha}{\alpha}$.
- Q: At what time $\tilde{T}$ does the first migrant (occurring at rate α^p) move from deme 1 to 2 in the ASG?
- A: Combining the arguments,

$$\frac{\alpha}{\log \alpha} \tilde{T} \xRightarrow{\alpha \to \infty} 1 - p.$$

Some observations for $\mu = c\alpha^p$

- b allele increases in frequency up to time $\tilde{T} \approx (1-p)\frac{\log \alpha}{\alpha}$.
- First migrants infects deme 2 at time $\tilde{T}$
- Fixation on island 2 after duration $2\frac{\log \alpha}{\alpha}$.

$$\implies \qquad \frac{\alpha}{\log \alpha} T \xrightarrow{\alpha\to\infty} 3 - p.$$



Summary and outlook

- If the migration rate is $\sim \alpha^p$, the fixation time of a beneficial mutant is $\frac{\log \alpha}{\alpha}(2 + (1-p)S_Y)$, where S_Y is maximal graph distance from the founder island.

- Ancestral selection graph can be extended to include recombination in order to compute other statistics.