Selective sweeps in structured populations

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We are interested in populations living on one island or being distributed equally on two islands with symmetric migration.

Assume a beneficial allele is introduced once to the population and eventually goes fixed under strong constant selection and the population is evolving according to the diffusion setting, i.e.

- Selection strength α
- Migration rate μ
- frequency path $(Y_1(t), Y_2(t))_{t\geq 0}$ of the beneficial allele conditioned on fixation solves the SDE

$$dY_1 = (\alpha Y_1(1-Y_1)\coth(\alpha(Y_1+Y_2)) + \mu(Y_2-Y_1))dt + \sqrt{Y_1(1-Y_1)}dW_1$$

$$dY_2 = (\alpha Y_2(1-Y_2)\coth(\alpha(Y_1+Y_2)) + \mu(Y_1-Y_2))dt + \sqrt{Y_2(1-Y_2)}dW_2,$$

started with $Y_1(0) = Y_2(0) = 0$ for two independent standard Brownian motions W_1, W_2.

Define the fixation time

$$T_{\text{fix}} := \inf\{t | Y_1(t) = Y_2(t) = 1\}.$$

Analogously define the fixation time for a panmictic population.

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Theorem:

One island

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha\to\infty} 2 \text{ in probability, i.e. for large } \alpha$$

$$T_{\text{fix}} \approx 2\frac{\log(\alpha)}{\alpha}.$$

Two islands

- If $\mu \in \Omega(\alpha)$,

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha\to\infty} 2 \text{ in probability.}$$

- If $\mu \in \Theta(\alpha^p)$ for $p \in [0,1)$,

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha\to\infty} (3-p) \text{ in probability, i.e. for large } \alpha$$

$$T_{\text{fix}} \approx (1-p+2)\frac{\log(\alpha)}{\alpha} = (3-p)\frac{\log(\alpha)}{\alpha}.$$

- If $\mu = c/\log(\alpha)$, for some $c \in \mathbb{R}_+$

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha\to\infty} 3+X \text{ in distribution, where } X \sim \text{Exp}(2c).$$

  That is for large α

$$T_{\text{fix}} \approx (1+X+2)\frac{\log(\alpha)}{\alpha} = (3+X)\frac{\log(\alpha)}{\alpha}.$$

Heuristic explanation: One island

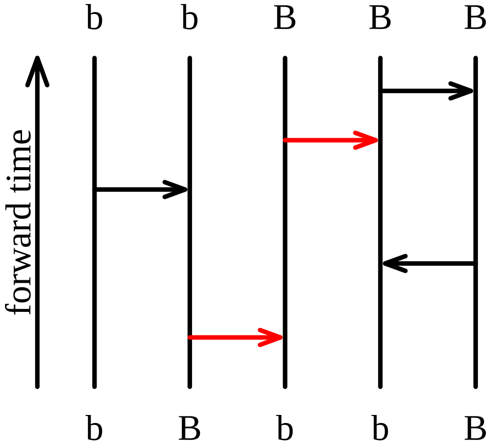
Main tool:

Ancestral selection graph (Krone and Neuhauser, 1997)

- analog to Kingman coalescent in setting with selection:
- gives potential genealogies of a sample of a large population evolving under constant selection.

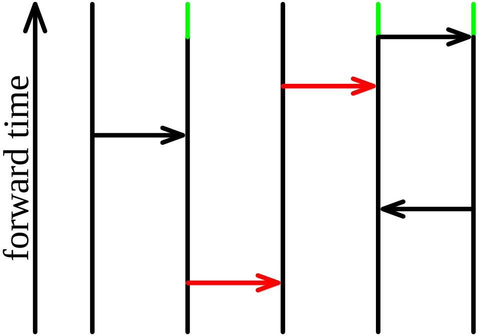
Motivation ASG

Moran model with selection



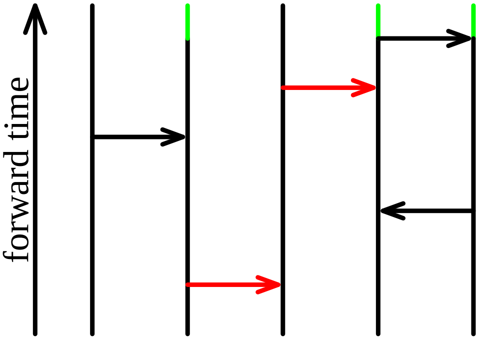
- Alleles are b and B
- Each pair resamples at rate 1
- Each line creates red arrows at rate α
- Black arrows can be used by any allele
- Only B alleles can use red arrows

Motivation ASG



- Consider a sample of the population
- Forget types of individuals

Motivation ASG



- If two lines meet a common black arrow, they coalesce

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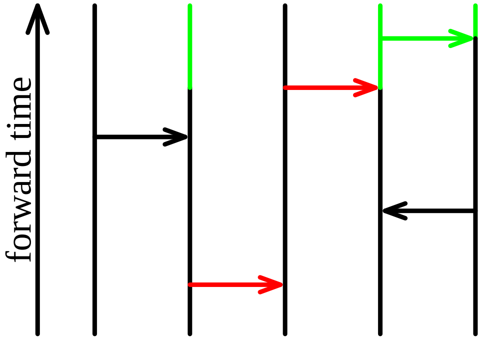

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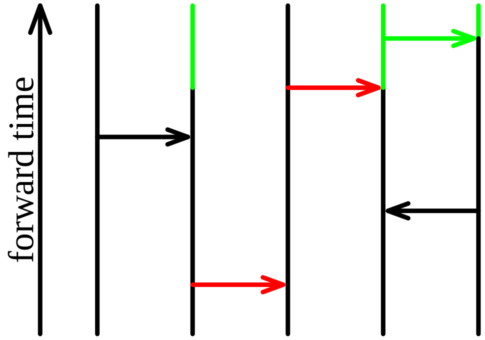

- If two lines meet a common black arrow, they coalesce
- If a line meets a red arrow, the line splits

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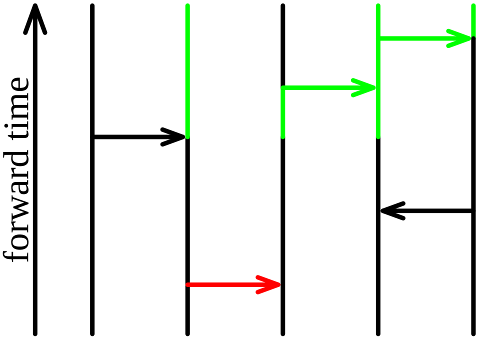

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Definition: Ancestral selection graph (ASG)

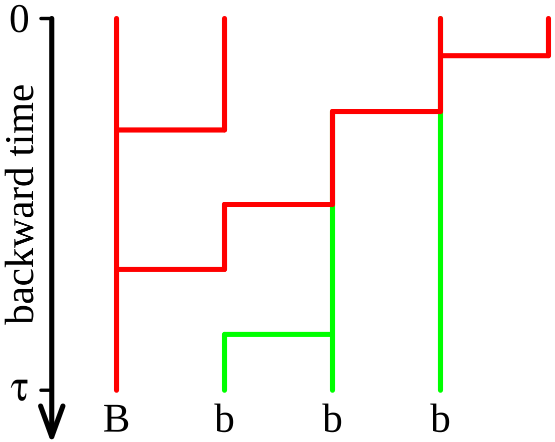
- each pair of lines coalesces at rate 1
- each line splits at rate α

Fixation in the ASG:

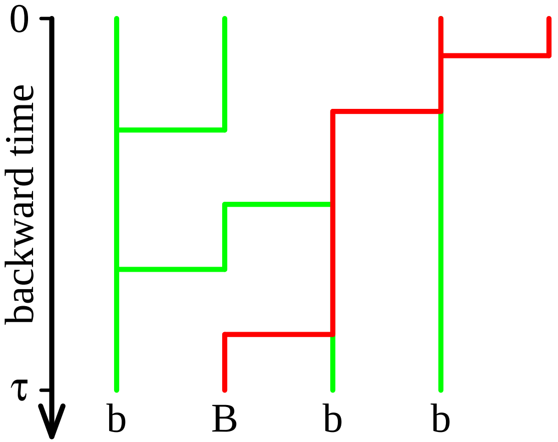
Mark one random individual i_0 with good type B, others with wild type b at time τ in the past.

The beneficial allele is fixed at time 0 (the present), if there exist directed paths between the individual (τ, i_0) and all individuals $(0, k)$.

Fixed



Not fixed



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Write $(0, k) \leftrightarrow (\tau, i_0)$.

Proposition:
"Fixation time in ASG is distributed as fixation time in diffusion:"

$$\mathbf{P}(T_{\text{fix}} \leq \tau) = \mathbf{P}\Big(\text{for all } k = 1, 2, \ldots \text{ it holds } (0, k) \leftrightarrow (\tau, 1) \text{ in ASG}\Big)$$

Important property: Reversibility of ASG

- Line counting process of ASG has reversible equilibrium.
  In equilibrium have $\approx n = 2\alpha$ lines
  (splitting rate $n \cdot \alpha = 2\alpha \cdot \alpha \approx \frac{2\alpha(2\alpha-1)}{2} = \binom{2\alpha}{2} = \binom{n}{2}$ coalescing rate)
- Reversibility can be conferred to ASG $\rightarrow$ in equilibrium the reversed ASG is also an ASG

Sketch of the proof

Step 1: Start ASG in equilibrium instead of with ∞-ly many individuals. Have at most 2α ancestors within time of order $1/\alpha$

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- Step 4: Approximately deterministic growth according to differential equation $dQ = Q(1 - Q/2)dt$ from $\varepsilon\alpha$ lines to $2\alpha - \varepsilon\alpha$ lines within time frame $\mathcal{O}(1/\alpha)$.

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- Step 4: Approximately deterministic growth according to differential equation $dQ = Q(1 - Q/2)dt$ from $\varepsilon\alpha$ lines to $2\alpha - \varepsilon\alpha$ lines within time frame $\mathcal{O}(1/\alpha)$.
- Step 5: Backward ASG of typical individual $(0, k)$ reaches $\varepsilon\alpha$ lines after time $t = \log(\varepsilon\alpha)/\alpha$
  Size of underlying ASG $\approx 2\alpha \Rightarrow$ Forward ASG of (τ, i_0) meets with backward ASG of typical individual $(0, k)$.

Two islands

Definition: Ancestral selection graph (ASG)

- each pair of lines coalesces within islands at rate 1
- each line splits at rate α within its island
- each line migrates to the neighboring island at rate μ

Note:

- ASG on two islands has also a reversible equilibrium
- to compute fixation time can again start ASG in equilibrium

Migration rate $\mu \gtrsim \alpha$

First migrant to island 2: immediate migrant, i.e. within time of order $\mathcal{O}(1/\alpha)$.

Show: Other migrants do not speed up the sweep on island 2 and do not slow down the sweep on island 1.

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha \to \infty} 2 \text{ in probability.}$$

Migration rate $\mu \approx \alpha^p$ for $p \in [0, 1)$

First migrant to island 2:
Size of (τ, i_0)-ASG $\approx e^{\alpha \cdot \log(\alpha)(1-p)/\alpha} = \alpha^{1-p}$ at time $\log(\alpha)(1-p)/\alpha$
$\Rightarrow$ first migrant approximately at time $\log(\alpha)(1-p)/\alpha$

$$\frac{\alpha}{\log(\alpha)} T_{\text{fix}} \xrightarrow{\alpha \to \infty} 1 - p + 2 = 3 - p \text{ in probability.}$$

Migration rate $\mu = c/\log(\alpha)$

First migrant to island 2:

- no migrant until time $\log(\alpha)/\alpha$
- after time $\log(\alpha)/\alpha$: Size of (τ, i_0)-ASG $\approx 2\alpha$

$\Rightarrow$ At ("constant") rate $2\alpha \cdot c/\log(\alpha)$ individuals migrate to island 2
$\Rightarrow$ waiting time scaled by $\log(\alpha)/\alpha$ is exponentially distributed with rate $2c$.

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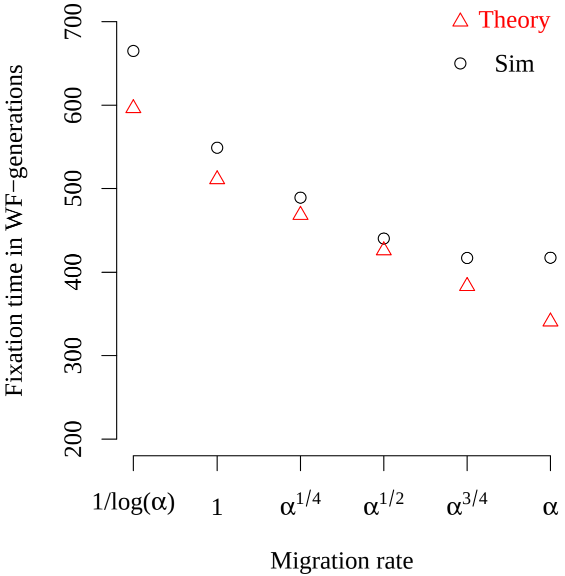

$N = 10^5$,
$s = 0.05$, i.e.
$\alpha = N \cdot s = 5000$
simulations based on 1000 draws