How does spatial structure interact with natural selection?

Alison Etheridge

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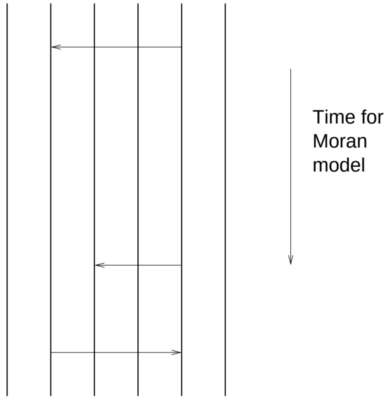
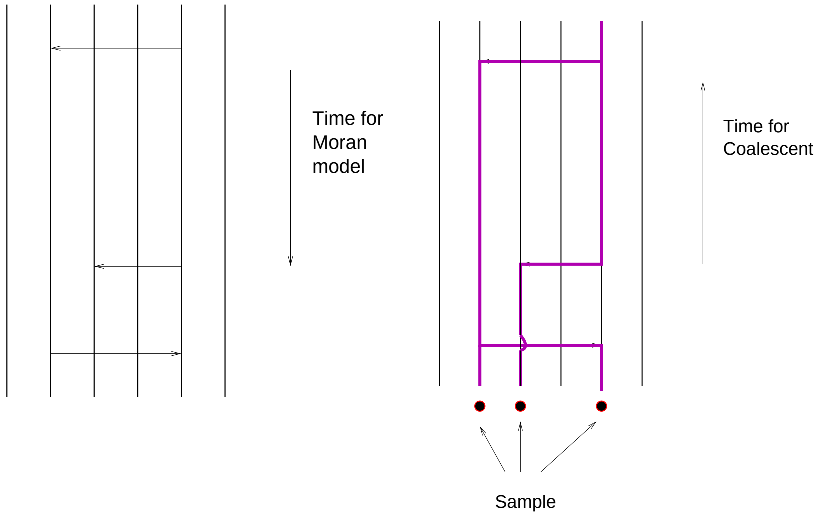
Engineering and Physical Sciences Research Council

Genetic drift



- Events determined by Poisson Process intensity $\binom{N}{2}dt$;
- Parent chosen at random;
- Individual chosen at random to die

Genetic drift



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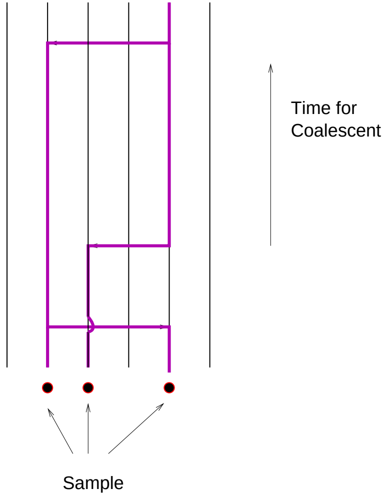
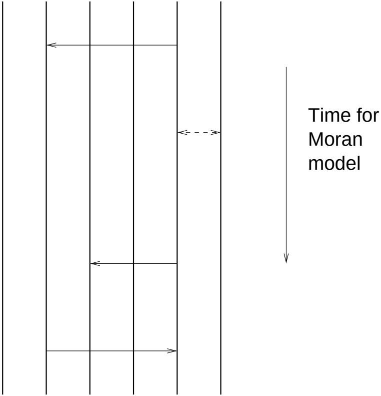


Two types, a, A.

$$dp_t = \sqrt{p_t(1-p_t)}dW_t,$$

$$\mathbb{E}[p(t)^{n(0)}] = \mathbb{E}[p(0)^{n(t)}].$$

Adding selection



Relative fitnesses:

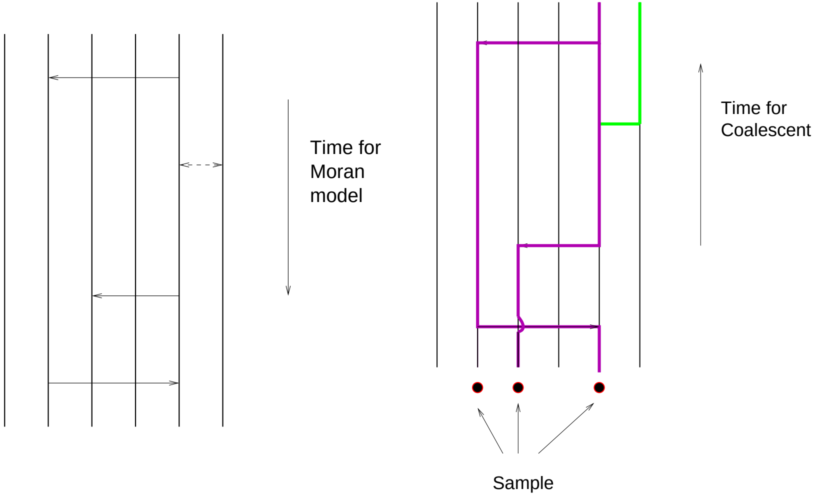
a	A
$1 - s_N$	1

- Events fall at rate $\binom{N}{2}$;
- Parent chosen in *weighted* way;
- Individual chosen at random to die

Probability parent of type a:

$$\frac{(1-s_N)p}{1-s_N p} = (1-s_N)p + s_N p^2 + \mathcal{O}(s_N^2)$$

Adding selection



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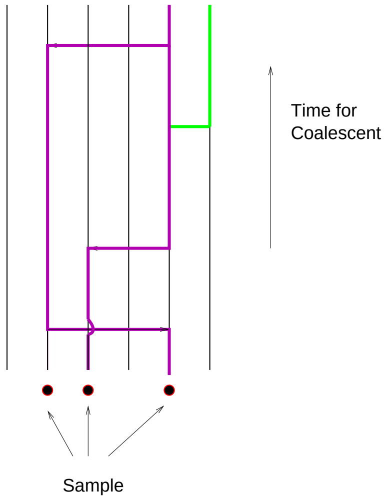


Neutral events at rate $(1 - s_N)\binom{N}{2}$;

Selective events at rate $s_N\binom{N}{2}$:
if aA chosen, A reproduces.

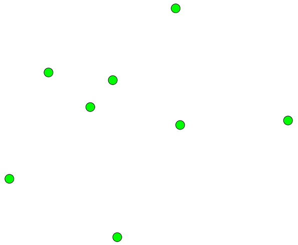
$$Ns_N \to \sigma,$$

$$dp_t = -\sigma p_t(1 - p_t)dt + \sqrt{p_t(1 - p_t)}dW_t$$

$$\mathbb{E}[p(t)^{n(0)}] = \mathbb{E}[p(0)^{n(t)}].$$

Introducing Space: An individual based model

- Start with Poisson point process intensity λdx;



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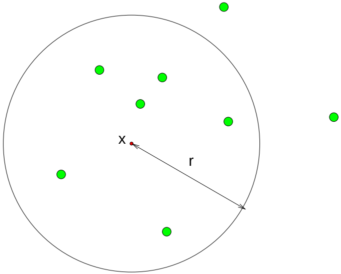
- Start with Poisson point process intensity λdx;
- At rate $\mu(dr) \otimes dx \otimes dt$ throw down ball centre x, radius r;



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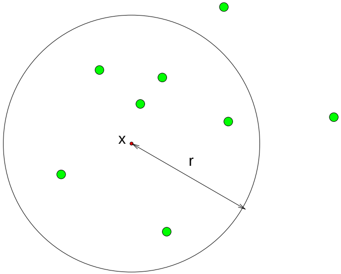

If ball empty, do nothing

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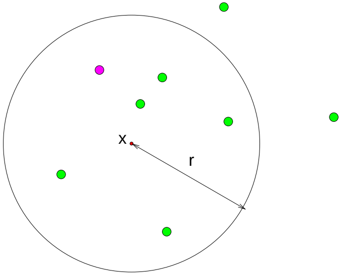

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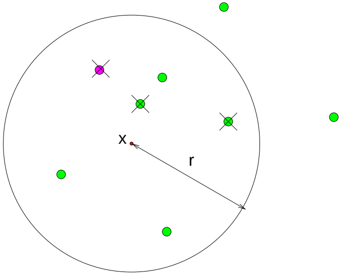

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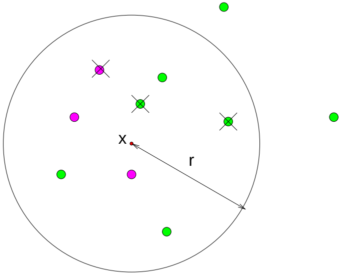

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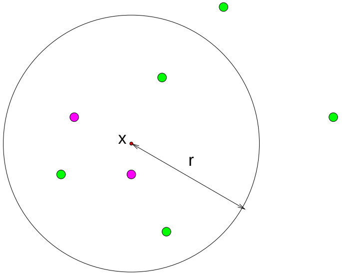


If ball empty, do nothing

$\lambda \to \infty$ limit (no space)

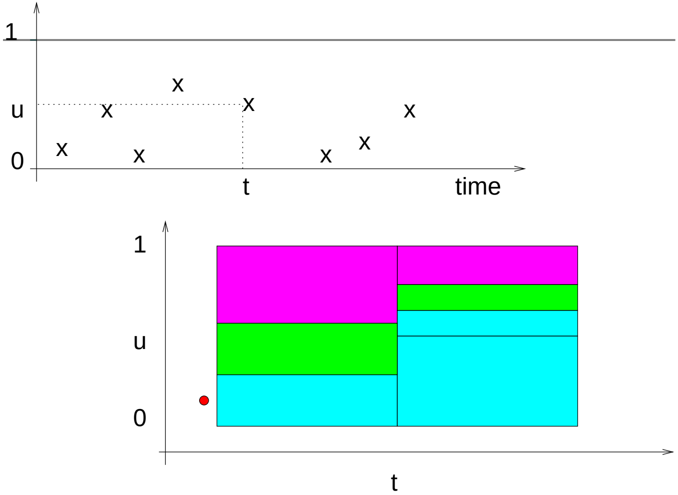
Distribution of types. State $\{\rho(t,\cdot) \in \mathcal{M}_1(K), t \geq 0\}$.

- Poisson point process intensity $dt \otimes F(du)$
- individual sampled at random from population
- proportion u of population replaced by offspring of chosen individual

$$\rho(t,\cdot) = (1-u)\rho(t-,\cdot) + u\delta_k.$$

Generalised Fleming-Viot process Bertoin & Le Gall (2003)
$F(du) = \frac{\Lambda(du)}{u^2}$, Λ finite measure on $[0,1]$.

The Λ-Fleming-Viot process



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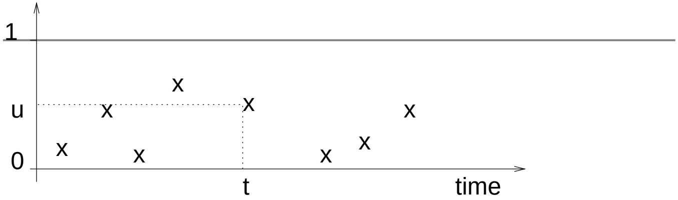
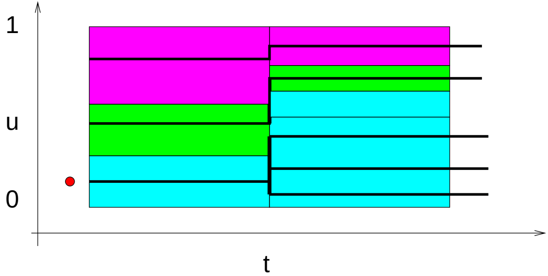




Λ-coalescent dual

Donnelly & Kurtz (1999), Pitman (1999), Sagitov (1999)

If there are currently n ancestral lineages, each transition involving j of them merging happens at rate

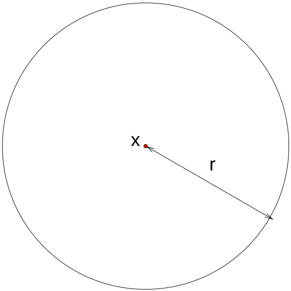
$$\beta_{n,j} = \int_0^1 u^j (1-u)^{n-j} \frac{\Lambda(du)}{u^2}$$

- Λ a finite measure on $[0,1]$
- Kingman's coalescent, $\Lambda = \delta_0$

The spatial Λ-Fleming-Viot process

State $\{\rho(t,x,\cdot) \in \mathcal{M}_1(K), x \in \mathbb{R}^d, t \geq 0\}$.
Π Poisson point process rate $dt \otimes dx \otimes \xi(dr, du)$ on $[0,\infty) \times \mathbb{R}^d \times [0,\infty) \times [0,1]$.

Dynamics: for each $(t,x,r,u) \in \Pi$,



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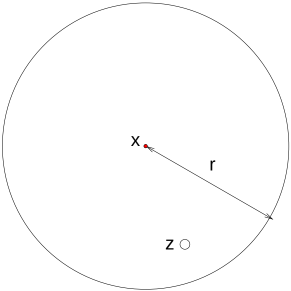
- $z \sim U(B_r(x))$



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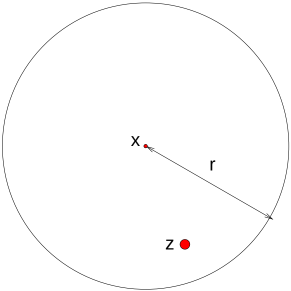

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- $z \sim U(B_r(x))$
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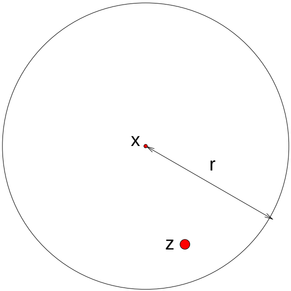
For all $y \in B_r(x)$,

$$\rho(t,y,\cdot) = (1-u)\rho(t-,y,\cdot) + u\delta_k.$$

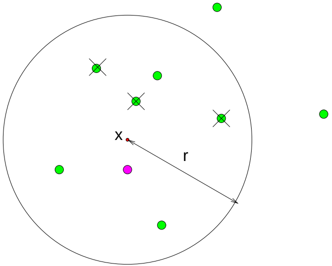


Backwards in time

- A *single* ancestral lineage evolves in series of jumps with intensity

$$dt \otimes \int_{(|x|/2,\infty)} \int_{[0,1]} \frac{L_r(x)}{\pi r^2}\, u\, \xi(dr, du)dx$$

on $\mathbb{R}_+ \times \mathbb{R}^2$ where $L_r(x) = |B_r(0) \cap B_r(x)|$.



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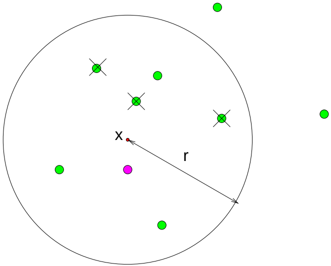
- Lineages can coalesce when hit by same 'event'.



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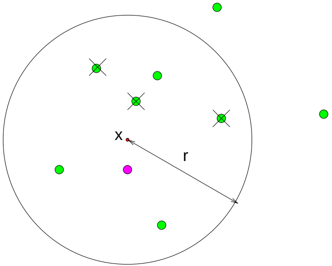

Note: If $\xi(dr, du) = \mu(dr) \otimes \delta_u$, rate of jumps $\propto u$.

Introducing selection to the SLFV

Warning: There are lots of different ways to do this.

- Easy to cook up examples where allele frequencies the same, but genealogies different

. . . but that's another talk

Introducing selection to the SLFV

Here we mimic what we did for the Moran model

Introducing selection to the SLFV

$K = \{a, A\}$, $w(t,x) = \rho(t,x,a)$ proportion of type a

- (i) Two types, a, A. Weight type a by $(1-s)$. If a reproduction event affects a region $B(x,r)$ in which current proportion of a-alleles is $\overline{w}$, then probability offspring are type a is

$$\frac{(1-s)\overline{w}}{1-s\overline{w}}$$

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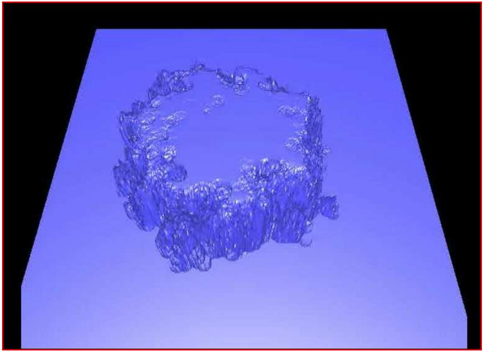
$$\frac{(1-s)\overline{w}}{1-s\overline{w}} = \overline{w}(1-s) + s\overline{w}^2 + \mathcal{O}(s^2).$$
- (ii) Neutral events rate $\propto (1-s)$, selective events rate $\propto s$. At selective reproduction events, sample two potential parents. If types aa, then an a reproduces, otherwise an A does.

Spread of a favoured allele

- Two types, a, A. If a reproduction event affects a region $B(x,r)$ in which current proportion of a-alleles is $\overline{w}$, then probability offspring are type a is $\frac{(1-s)\overline{w}}{1-s\overline{w}}$.



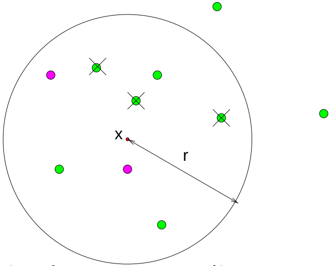
(Spatial) Ancestral selection graph

Evolution of ancestry due to neutral events as before:

- lineages evolve in a series of jumps;
- they can coalesce when covered by same event.

At *selective* events

- *Two 'potential' parents must be traced;*
- Lineages can coalesce when hit by same 'event'.



A sampled individual is type a *iff* all lineages in the corresponding ASG are type a at any previous time.

Why rescale?

Neutral mutation rate, μ, sets timescale

- Mutation rates are low;
- Scaling limits are ‘robust’.

Natural question:
Over what spatial scales can we expect to observe the signature of natural selection?

Scaling limits I: Small neighbourhood size:

Fix $u \in (0, 1)$.

Consider only 'small' events.

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Set $n = 1/\mu$ and rescale: $w(nt, \sqrt{n}x)$.

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Heuristics:

- At a 'branching' event in ASG, two lineages born at separation $\mathcal{O}(1/\sqrt{n})$.
- Probability they separate to $\mathcal{O}(1)$ before coalescing is
  - $d = 1$: $\mathcal{O}(1/\sqrt{n})$,
  - $d = 2$: $\mathcal{O}(1/\log n)$,
  - $d \geq 3$: $\mathcal{O}(1)$.
- Selection will only be visible if expect to see at least one pair 'separate' by time 1.

Scaling limits I: Small neighbourhood size:

Fix $u \in (0,1)$. Consider only 'small' events.

Set $n = 1/\mu$ and rescale: $w(nt, \sqrt{n}x)$.

Ability to detect selection depends on dimension:

- $d = 1$, selection only visible if $s = \mathcal{O}(1/\sqrt{n})$, *limiting ASG embedded in Brownian net*;
- $d = 2$, selection only visible if $s = \mathcal{O}(\log n/n)$, *limiting ASG 'Branching BM'*;
- $d \geq 3$, selection only visible if $s = \mathcal{O}(1/n)$, *limiting ASG Branching BM*.

Technical challenges because $ns_n \to \infty$.

Straulino (2015), E., Freeman, Straulino (2015)

Scaling limits II: High neighbourhood size (small events)

Set $u_n = u/n^\gamma$, $s_n = s/n^\delta$, $w^{(n)}(t,x) = w(nt, n^\beta x)$,
Jump rate nu_n, jump size $1/n^\beta$. Diffusive scaling: $2\beta = 1 - \gamma$

- At 'branching' event, two lineages at separation $\mathcal{O}(1/n^\beta)$.
- Probability separate to $\mathcal{O}(1)$ is $\mathcal{O}(1/n^\beta)$, $(d = 1)$; $\mathcal{O}(1/\log n)$, $(d = 2)$; $\mathcal{O}(1)$. $(d \geq 3)$.
- If two lineages hit by same event, given one jumps, they coalesce with probability $\mathcal{O}(1/n^\gamma)$.

$d \geq 2$: Probability 'long' excursion before coalesce $\mathcal{O}(1)$;

$d = 1$: Number attempts to reach separation $\mathcal{O}(1)$
$\sim$ number of attempts to coalesce: $\beta = \gamma$;

Selection events rate $nu_n s_n$ $\mathcal{O}(1)$: $1 - \gamma - \delta = 0$.
$\rightsquigarrow \beta = \gamma = 1/3, \quad \delta = 2/3.$

Scaling limits II: High neighbourhood size (small events)

- Choose $\xi(dr, du) = \mu(dr) \otimes \delta_u$ with $\mu(dr) = \delta_r$
- Set $u_n = u/n^{1/3}$, $s_n = s/n^{2/3}$, $w^{(n)}(t,x) = w(nt, n^{1/3}x)$,

$$dw = \frac{1}{2}\Delta w dt + sw(1-w)dt + \mathbf{1}_{d=1}\epsilon\sqrt{w(1-w)}W(dt, dx)$$

E. Véber, Yu.

Hybrid zones

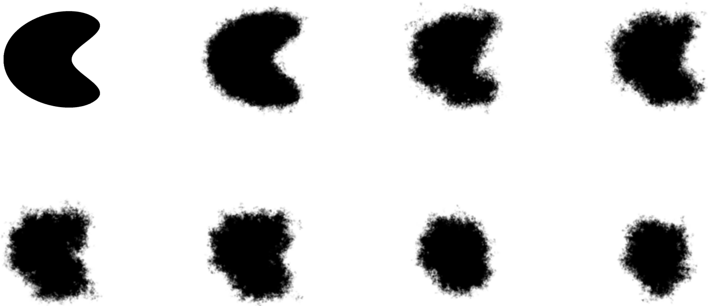
Hybrid zones develop when have selection against heterozygosity.

Two spatial dimensions; only small events

During selective events:

- sample *three* individuals;
- the type of the parent is chosen by 'majority voting'.

Scaling limits III



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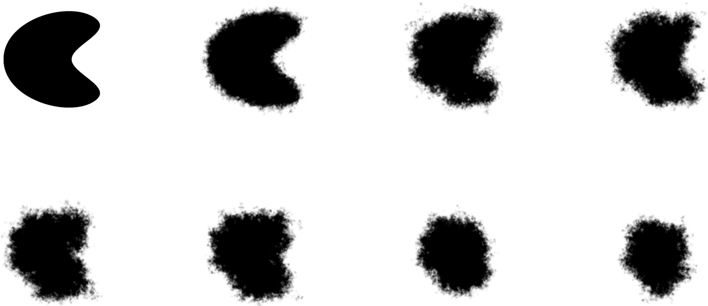

Under suitable rescaling, interface becomes sharp and evolves (deterministically) according to motion by mean curvature.

(E. Freeman, Penington)