Some mathematical models from population genetics

2: Recombination

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joint work with Stuart Baird (Montpellier) and Nick Barton (Edinburgh)

What is recombination?

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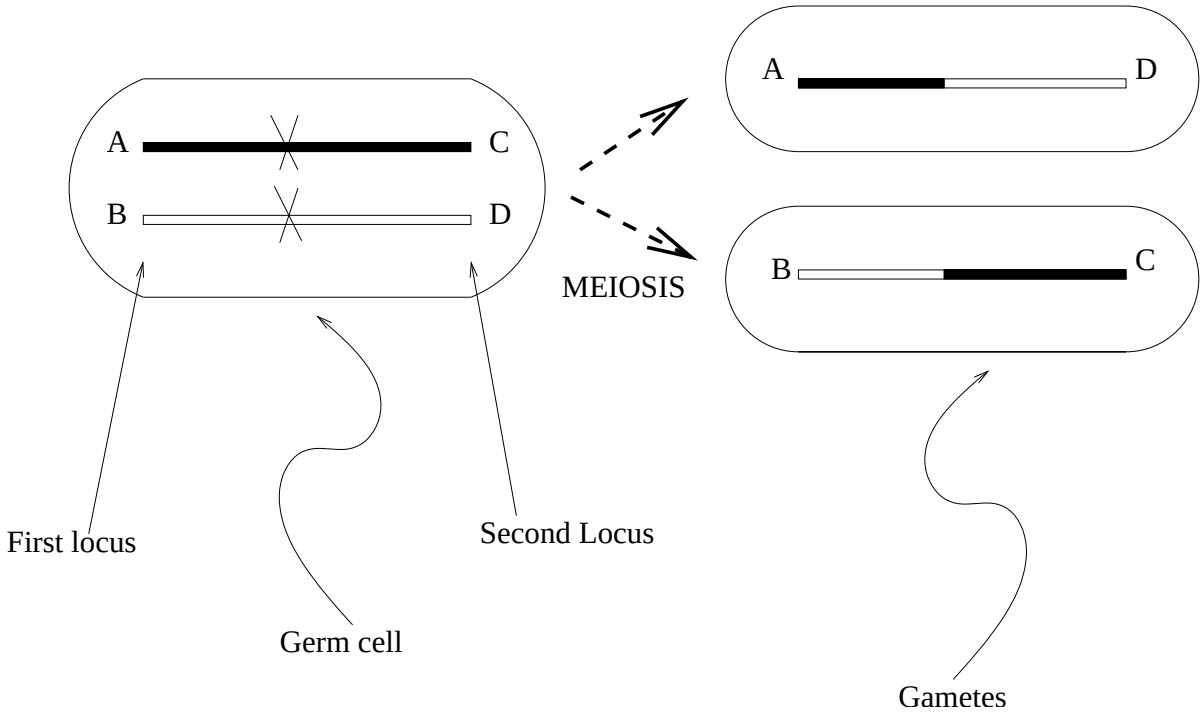
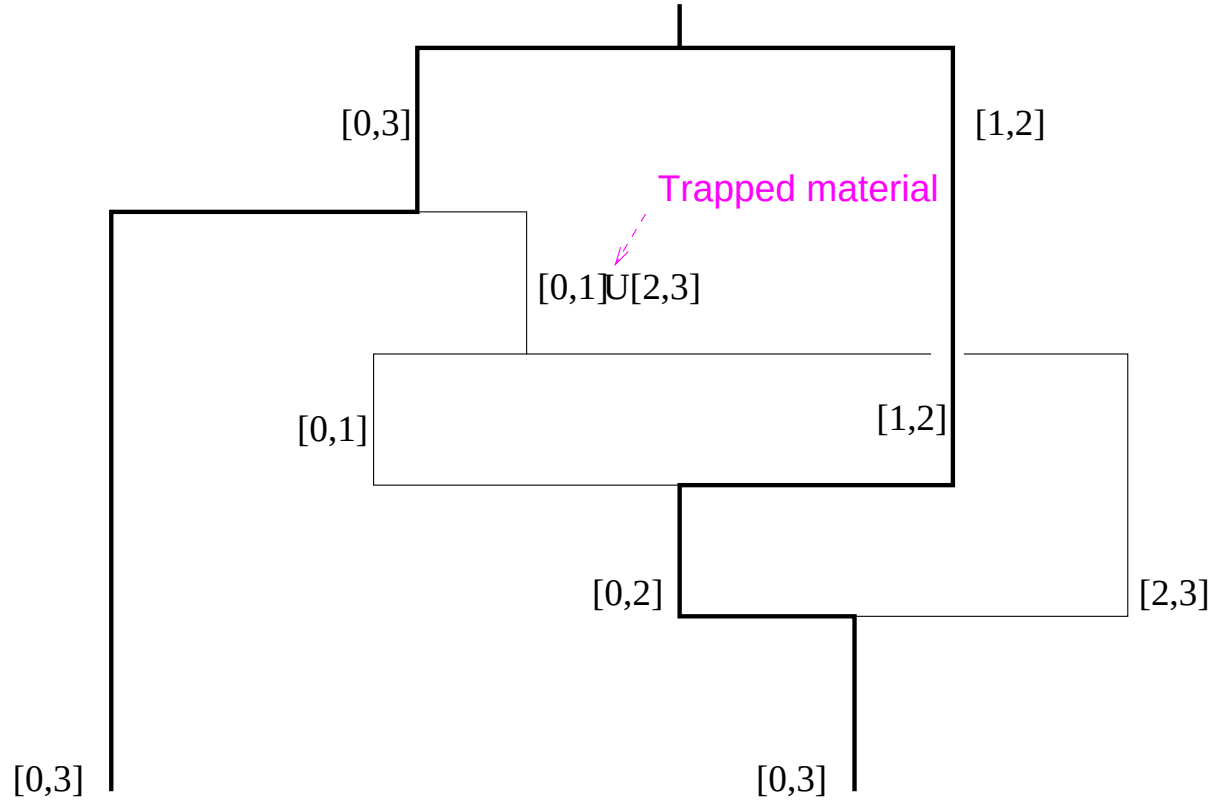


The ancestral recombination graph

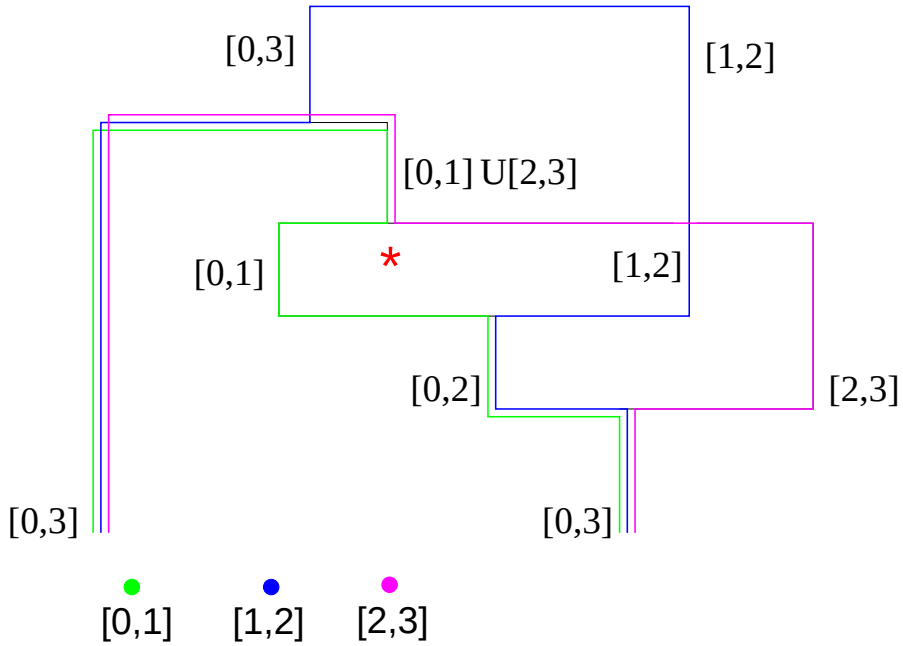
At a recombination event, we must trace *two* ancestral lineages: we see branches as well as coalescences in the genealogy.



Ancestry of the block denoted $[0, 3]$ for a sample of size two.

Local trees

Wiuf and Hein scan along the genome and study the process of ‘local trees’.



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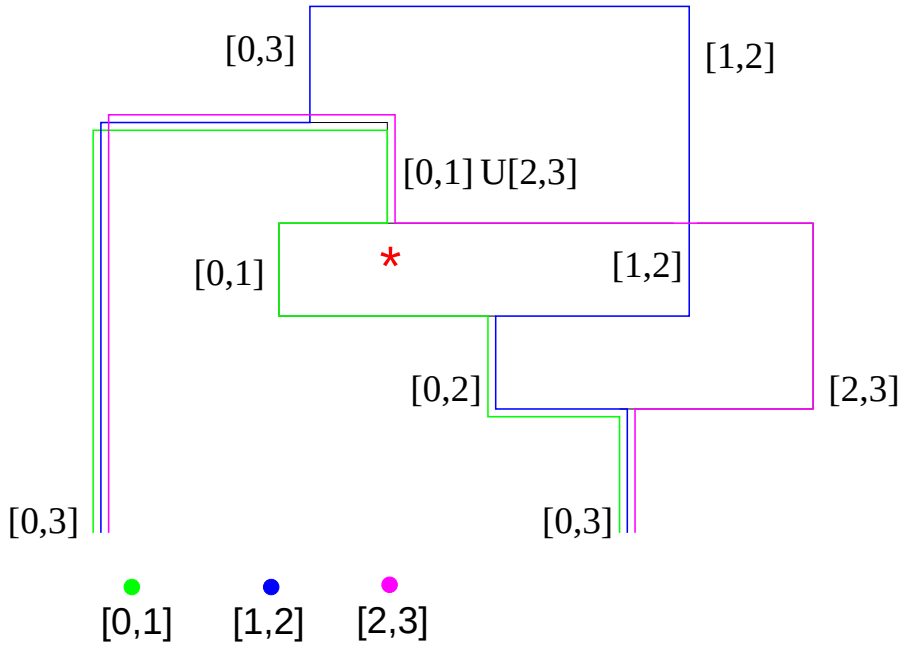

Knowing only the local tree for $[1,2]$, would not see the coalescence $*$.

Local trees do not form a Markov process.

A diversion

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Analytic results are hard to find. We consider a simpler process: the descent of a block of genome *forwards* in time.

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Note: If $s = 0$, the expected total block length is conserved.

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Notation: $Q_t(y) =$ probability total loss by time t of ancestral block of length y. $P_t(y) = 1 - Q_t(y)$.

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$$Q_{t+1}(y) = \Phi\left[\frac{1-y}{2} + \frac{1-y}{2}Q_t(y) + \int_0^y Q_t(z)dz\right], \quad Q_0(y) = 0.$$

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Substituting for Φ,

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or, in differential form,

$$\frac{d}{dy}P_{t+1}(y) = (1+s)\,(1-P_{t+1}(y))\left(P_t(y) + (1-y)\frac{d}{dy}P_t(y)\right).$$

Probability of survival for ever

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General solution

$$\tilde{P}_C = \frac{y^*}{y^* + \pi\left(Cy^* e^{-y^*}\right)}, \quad y^* = y - s(1-y),$$

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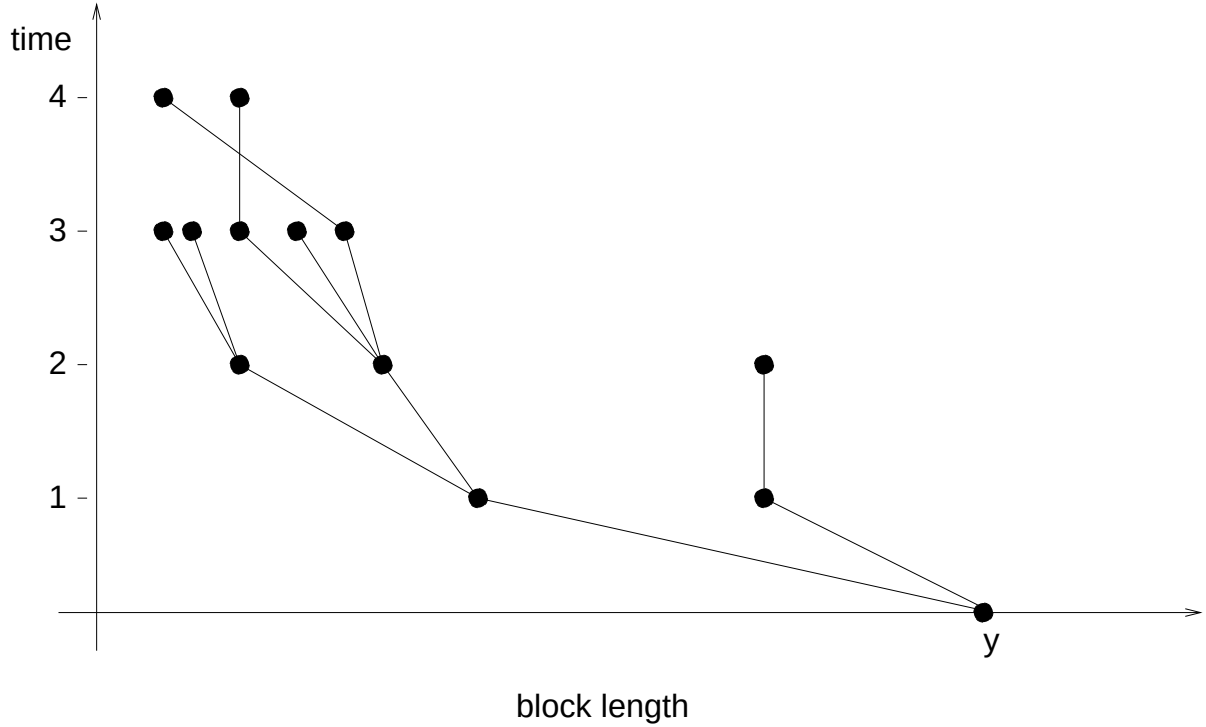

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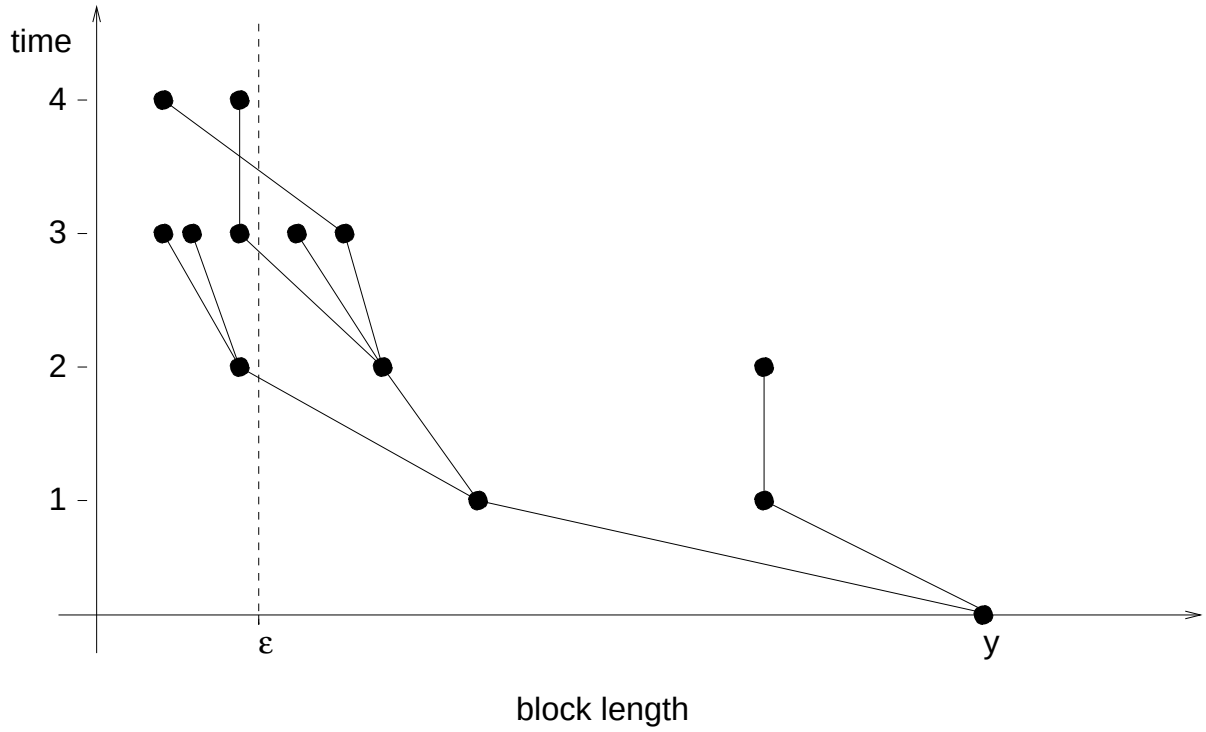

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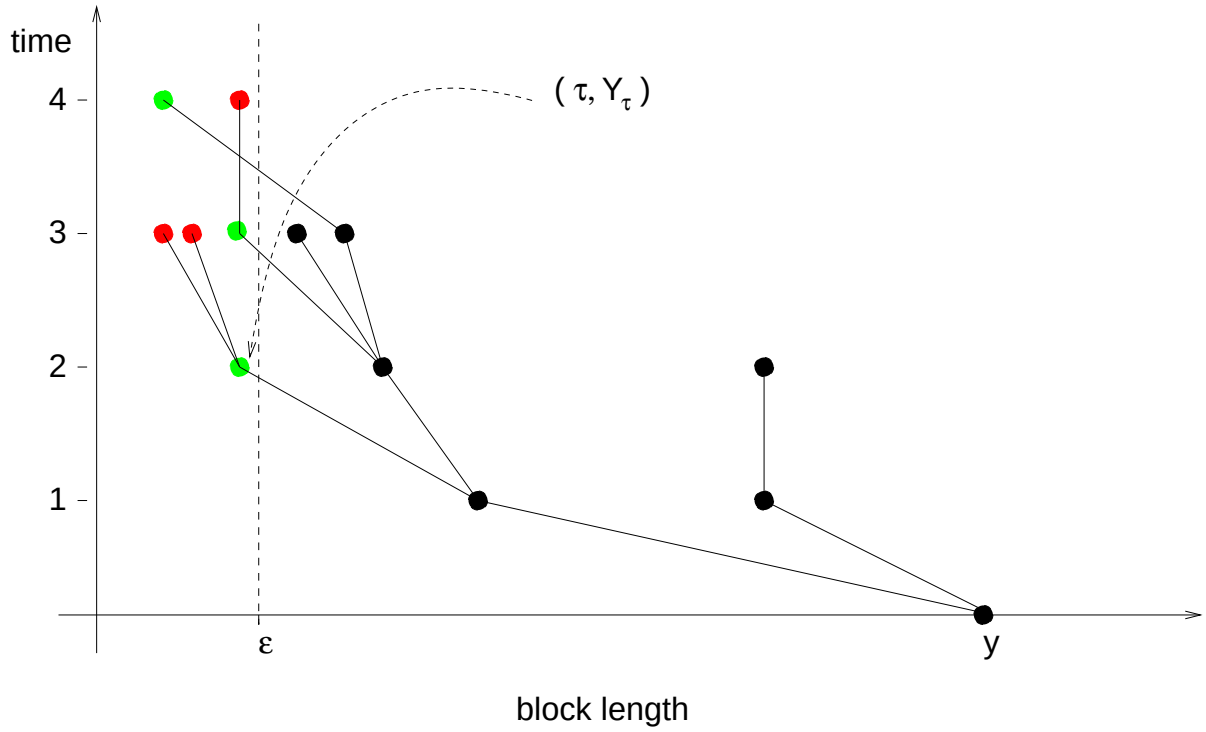

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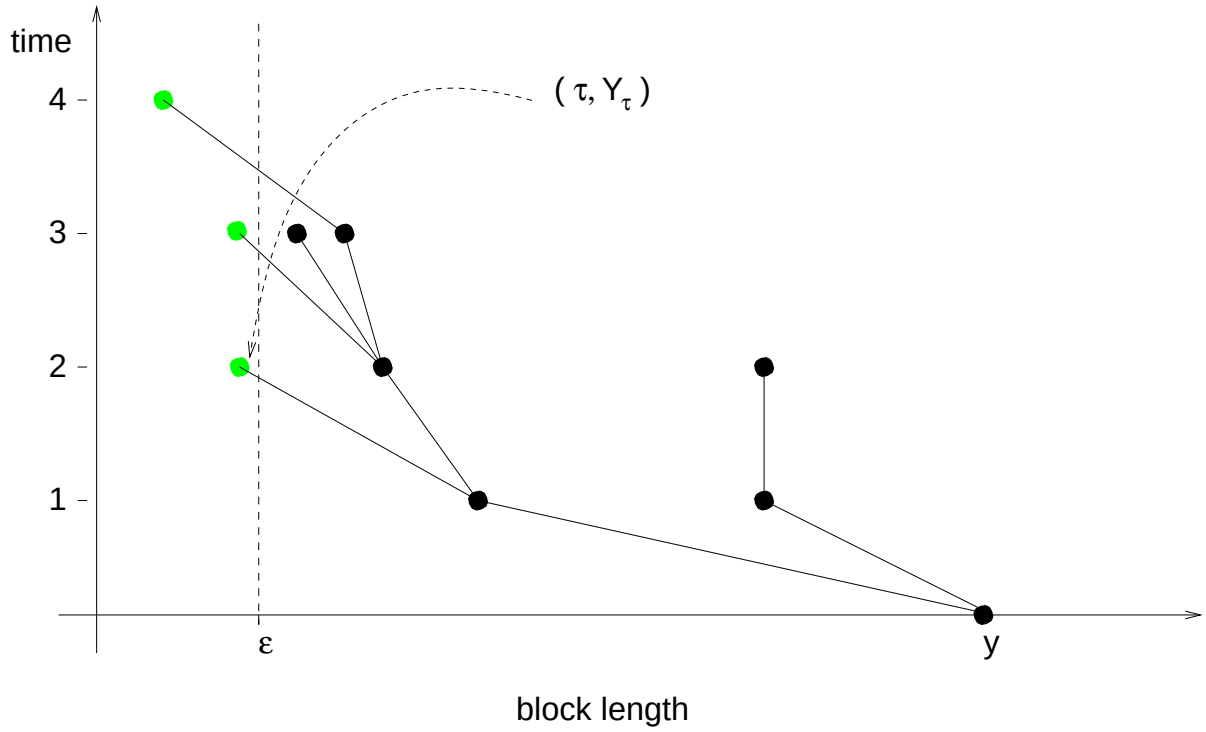
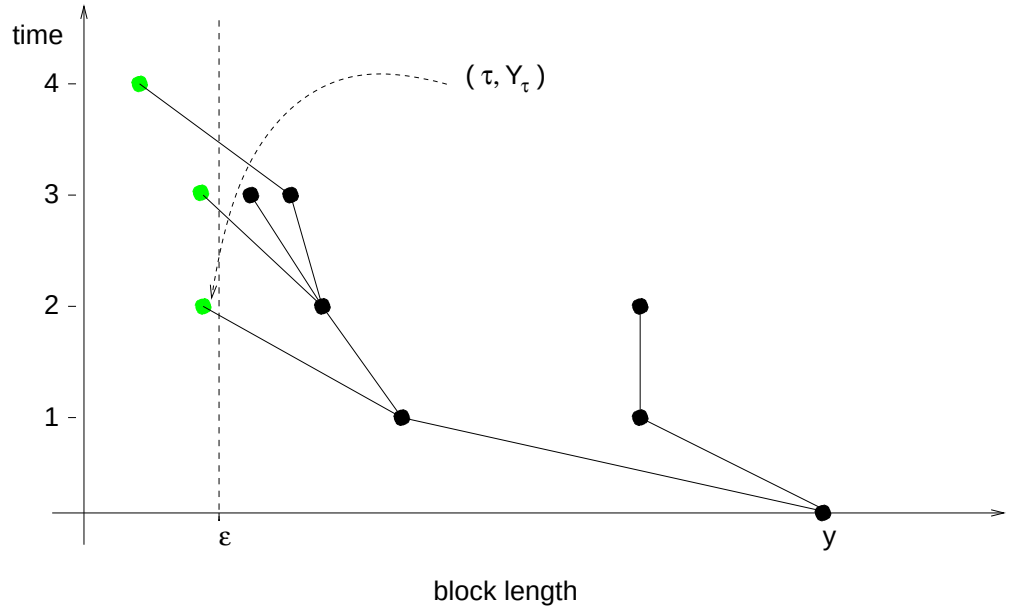


A Special Markov property

Notation: $N_\tau =$ number of individuals in new process at time t. $\tau_i =$ time of freezing of ith particle. $Y_{\tau_i} =$ corresponding block length.



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To estimate the right-hand side we superimpose recombinations on a *pedigree*.

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The *pedigree* is the tree of *all* descendants of the ancestor.

Take initial block length $y = 1$*.*

Consider one line of descent through the pedigree:

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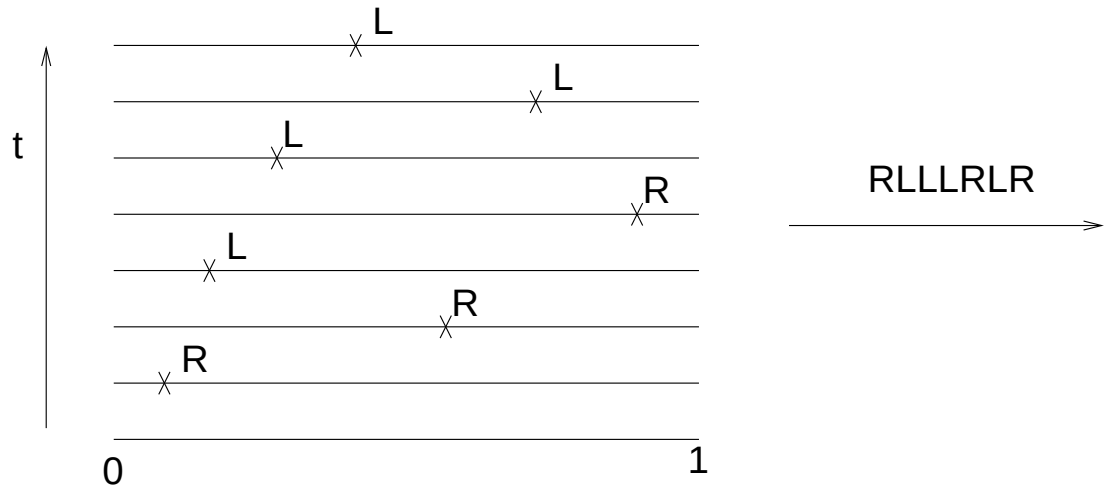

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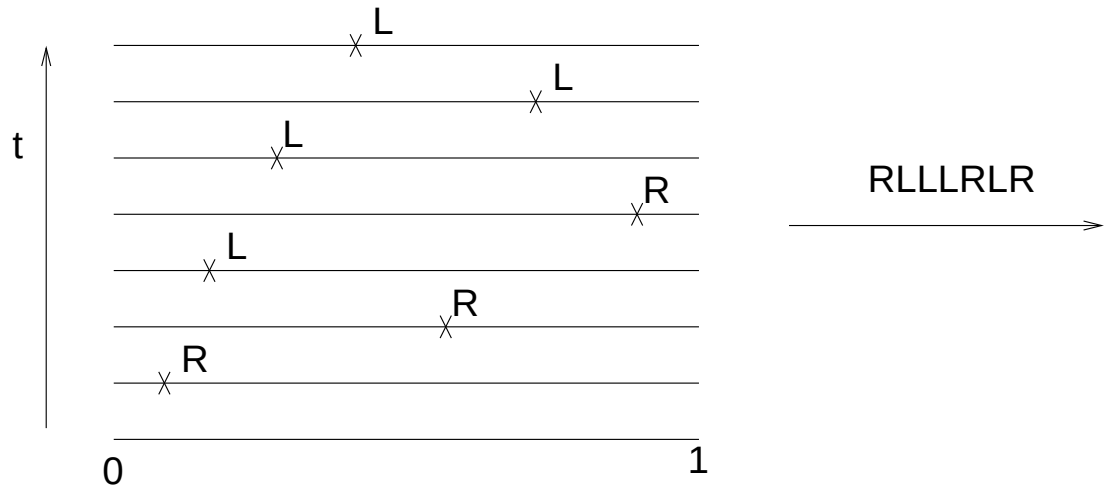

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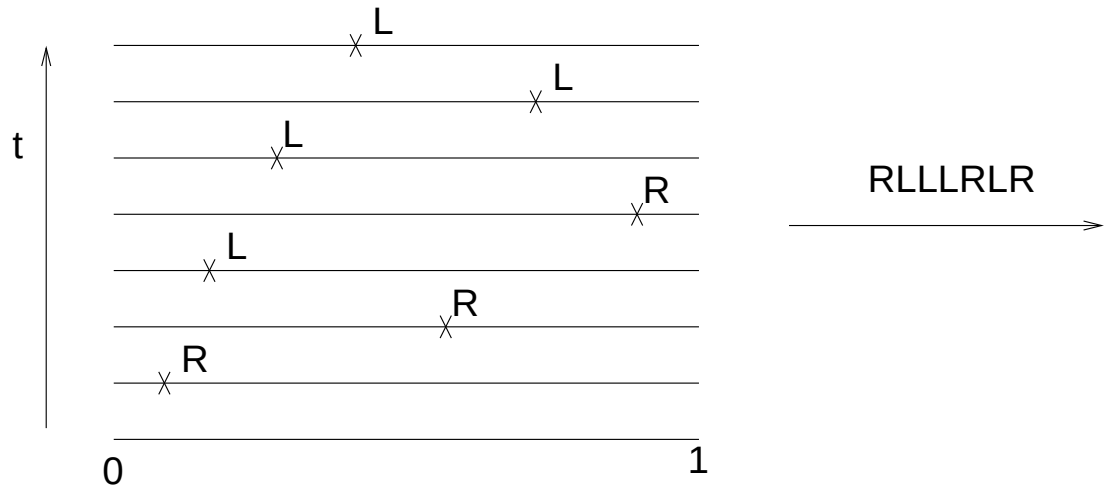

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Survival requires $\underbrace{RR\ldots R}_{m \text{ times}}\ \underbrace{LL\ldots L}_{t_0-m \text{ times}}$ for some $m \in \{0, 1, \ldots, t_0\}$.

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Approximate $P_t(0)$ e.g. via Feller's diffusion.

An example

Suppose $s = 0$ (so $y^* = y$) and $yt \gg 1$, since $\pi(z) \sim \log z$ as $z \to \infty$,

$$P_t(y) \sim \frac{y}{\log(yt/2)}.$$

Survival until time t declines like $1/\log t$.

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Recombination rapidly breaks the ancestral genome into small blocks, but these can persist for a very long time.

Long genomes

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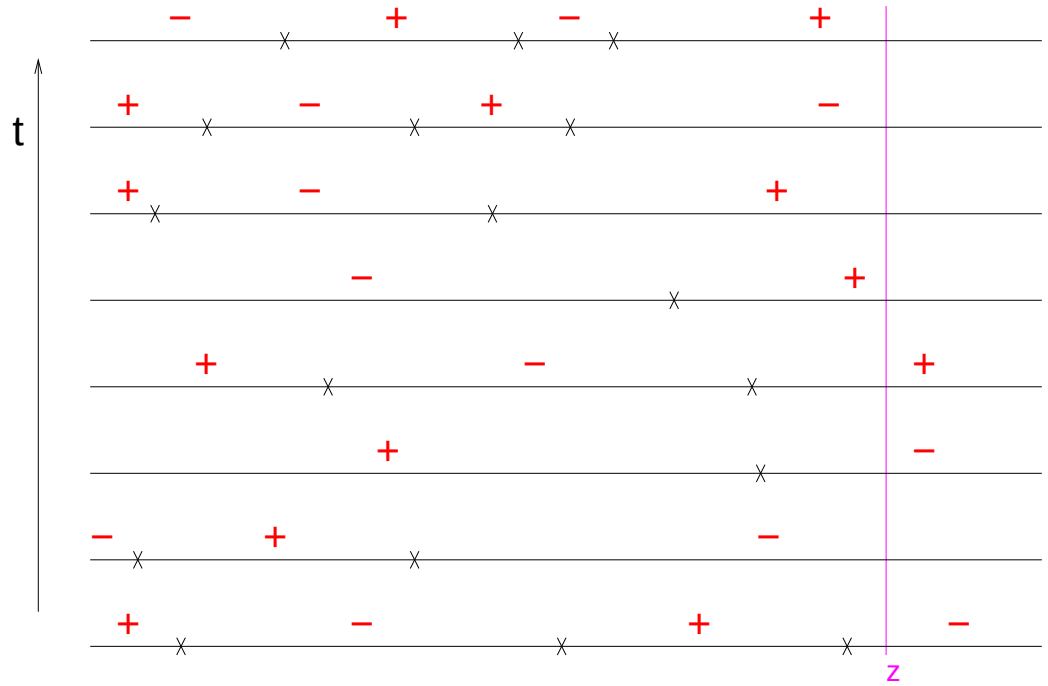
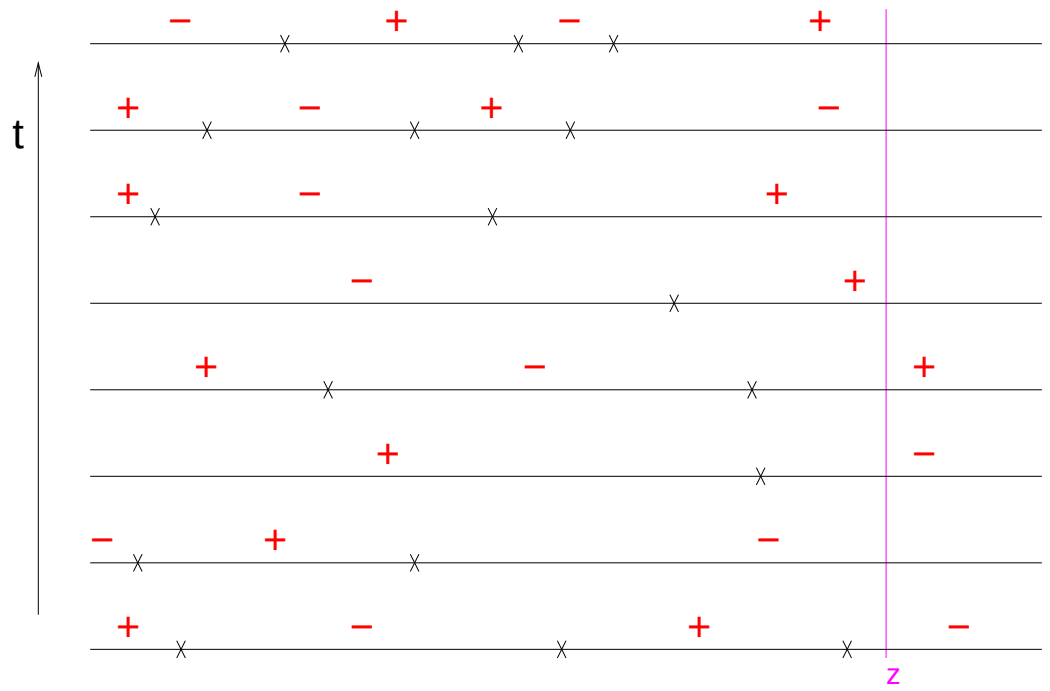
Again consider a single line of descent



Label $z \in [0, y]$ by $\underline{a}(z) = (a_1(z), a_2(z), \ldots, a_t(z)) \in \{-, +\}^t$.



a(z)=− − − + + + − +

Label $z \in [0, y]$ by $\underline{a}(z) = (a_1(z), a_2(z), \ldots, a_t(z)) \in \{-, +\}^t$. A point z is in a block that is passed down iff $\underline{a}(z) = (+, +, \ldots, +)$.

A change of perspective

Define continuous time Markov chain $\{X_z\}_{z\in[0,y]}$ by

$$X_z = \#\{i \in \{1, 2, \ldots, t\} : a_i(z) = -\}.$$

We seek $\mathbb{P}\left[X_z = 0, \text{for some } z \in [0, y]\right]$.

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Transitions of X_z occur at rate t.

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Continuous time version of the *Ehrenfest model*. P & T Ehrenfest (1907).

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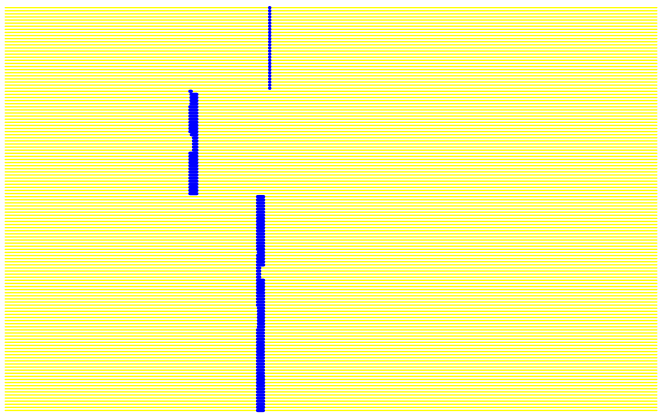
- The length of an inherited block is distributed approx as Exp(t).
- For a single line of descent, the probability of inheriting multiple blocks is at most

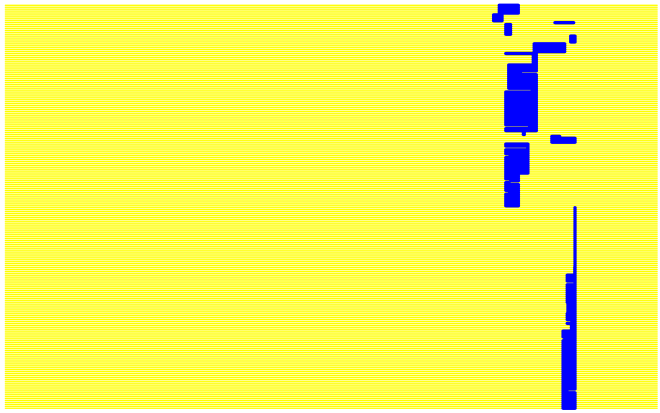
$$\mathbb{P}[\text{A single block survives}] \times \mathbb{P}[X_z = 0 \text{ for some } z \in [0, y] | X_0 = 1]$$

$$\approx \frac{(ty + 1)}{2^t} \frac{ty}{2^t}$$

For example, if $s = 0$, $y = 1$ and $t = 10$, this suggests that there is a $< 1\%$ chance of seeing multiple blocks.

We expect some portion of introgressed genome to persist for a long time, but the effect will be highly variable along the genome.





50 generations, $y = 1$.