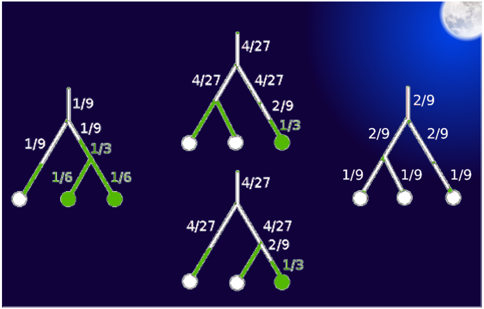
Time reversal of a Markov Chain on trees in a population-genetical context

PMSMA Montpellier 2023

Johannes Wirtz

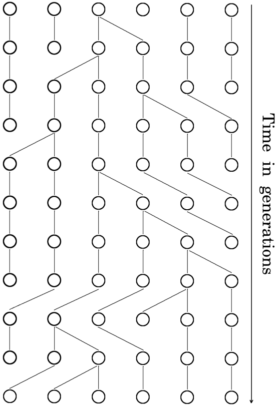


1. The Evolving Moran Genealogy

2. *EMG* time reversal

3. Transient Markov Chains

The basic population model



Moran Model (P. Moran, 1958) in discrete time:

- Constant population size n, one split and one death per generation

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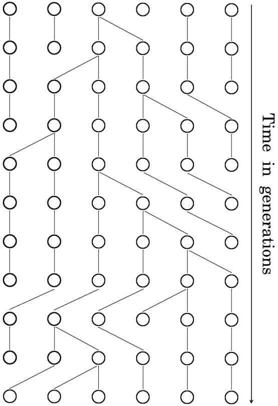


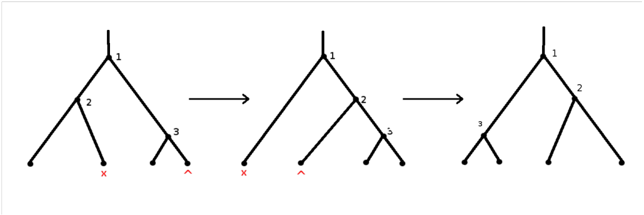
Moran Model (P. Moran, 1958) in discrete time:

- Constant population size n, one split and one death per generation
- The genealogy at any point $i > i^*$ can be interpreted as a Yule Tree T_i.

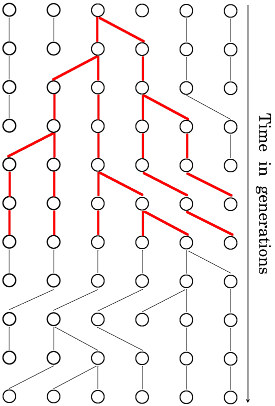
EMG definition and appearance

Definition

We call the process $(T_i)_{i\in\mathbb{N}}$, with $\Pr(T_{i+1} = T \in \mathcal{T}_n | T_i)$ dictated by the underlying Moran model, the *Evolving Moran Genealogy* (*EMG*).



Motivating example: *MRCA* jumps



Occasionally, the root of the tree (*MRCA*) changes

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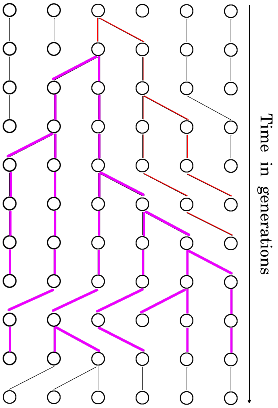

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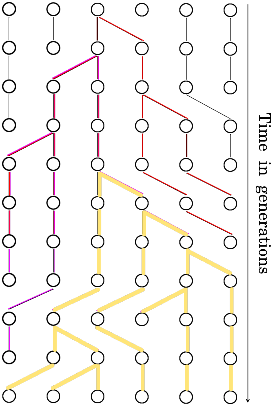

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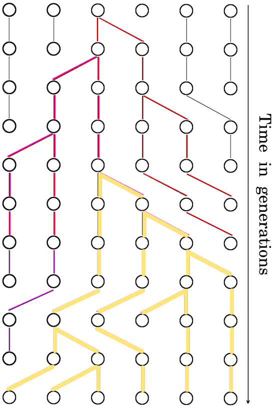

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Intervals in between changes are called *MRCA episodes*; changes are called *MRCA jumps* or *root jumps*.

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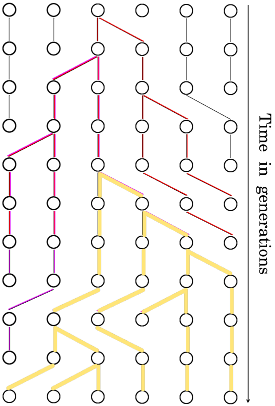

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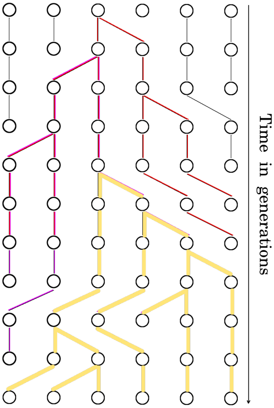

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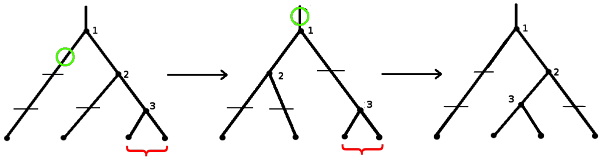
The derived process $(\mathcal{X}_i)_{i\in\mathbb{N}} \in \{0,1\}^{\mathbb{N}}$ with $\mathcal{X}_i = 1$ iff a root jump takes place from T_{i-1} to T_i is called *root jump process*.

Reversing the mechanics

Backward in time: "Merge" the most recent split and revive an individual by "regrafting" it into the tree at some branch segment *b*.



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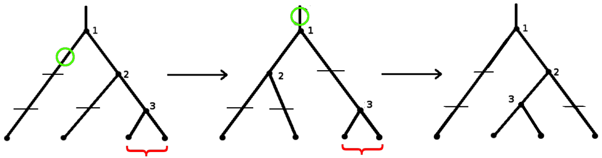
With what probability to choose the regrafting segment?



Kelly's Lemma

For a positive recurrent Markov Chain M on a state space S with transition matrix P, the matrix P' is the transition matrix of the reversed process iff

$$\forall s, t \in S : P^{\flat}_{st} = P_{ts} \cdot \frac{\pi_t}{\pi_s} \tag{1}$$

where π is the stationary distribution of M.

(Kolmogorov 1936, Kelly 1979, Lovasz & Winkler 1983)

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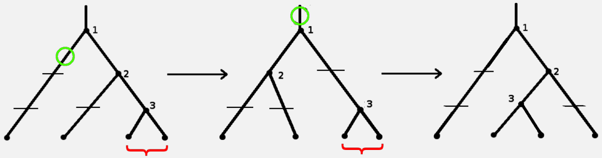
Corollary (Loop Property)

Closed loops have the same probability in forward and reversed process.

Lemma (Wiehe, W. 19)

The conditions of Kelly's Lemma are satisfied for the reversed process of the EMG iff the regrafting segment is chosen uniformly.



The $EMG^\flat$

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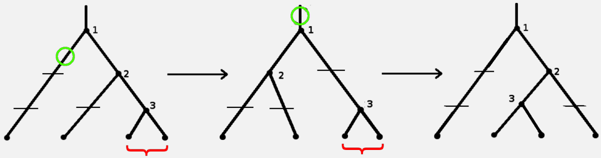
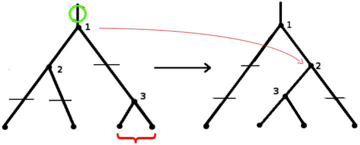
Definition

We call the reversed process *EMG backward in time*, for short $EMG^\flat$.



Analyzing jump times via $EMG^\flat$



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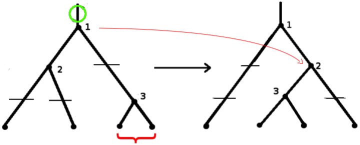

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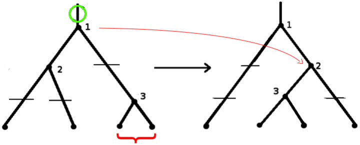
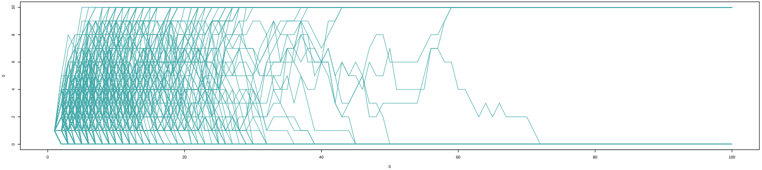


Only one possibility of making the root jump in $EMG^\flat$...

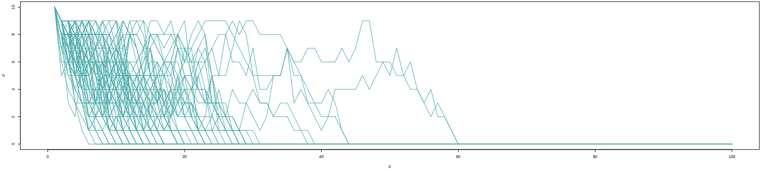
Under the $EMG^\flat$, the process of root jumps is geometric of intensity $2/n^2$.
Becomes a Poisson process of intensity 1 as $n \to \infty$ (Pfaffelhuber & Wakolbinger 2008).

Reversing a 2-allele Moran model

Assume one individual at time 0 has genotype *a*, all others have *b*.



Neutral 2-allele Moran, initial frequency $f(a) = 1/n$.



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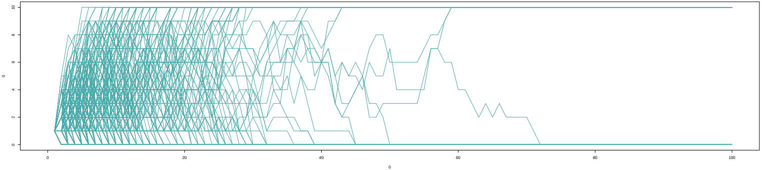

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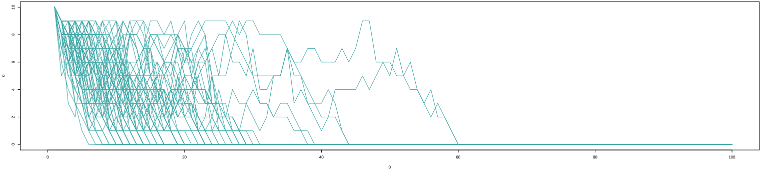

Fixation curves backward in time

The 2-allele Moran model is transient.

Let M be a Markov chain on a discrete state space $S \cup \{a, b\}$ such that for each path ω:

$$\forall i \leq \alpha(\omega) : \omega_i = a$$
$$\forall i \geq \beta(\omega) : \omega_i = b$$

where α, β are finite **a.s.**. Then

$$\forall s, t \in S : P^\flat_{st} = P_{st} \cdot \frac{\eta(t)}{\eta(s)} \qquad (2)$$

with $\eta(s)$ "average time" spent in state s

$$\eta(k) = \int_\omega \sum_{\alpha(\omega)<i<\beta(\omega)} \mathcal{X}_s(\omega_i) \mathrm{d}p(\omega)$$

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$$P_{f(a)} := \begin{array}{c} \begin{matrix} 0 & \qquad k/n \qquad & 1 \end{matrix} \\ \begin{pmatrix} 1 & 0 & & & \\ 0 & & \frac{k(n-k)}{n^2} & & \\ & & \frac{k^2+(n-k)^2}{n^2} & & \\ & & \frac{k(n-k)}{n^2} & & 0 \\ & & & 0 & 1 \end{pmatrix} \end{array} \begin{matrix} 0 \\ \\ k/n \\ \\ 1 \end{matrix}$$

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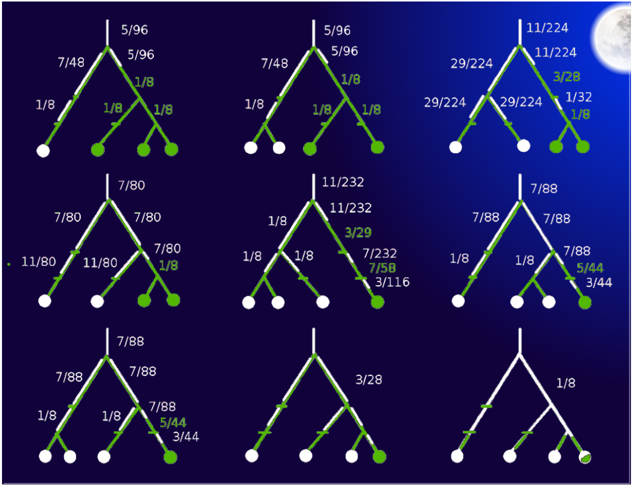
Associated tree-valued processes



Backward process on Yule Trees for $n = 4$.
Requires solving of a large nonlinear system (33 vars)

Birth-Death process with constant rate (MM1 queue)
Assume

$$
\begin{aligned}
&\Pr(X_{i+1} = X_i + 1)\\
=&\Pr(X_{i+1} = X_i - 1)\\
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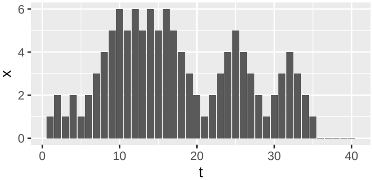
\end{aligned}
$$



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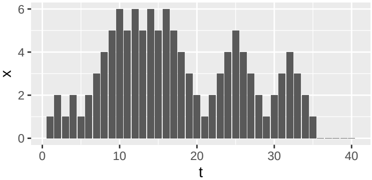

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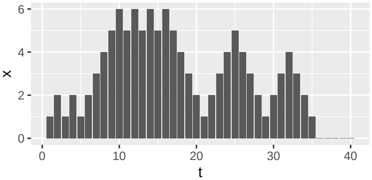

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$$P_{f(a)} := \begin{array}{c} \begin{array}{ccccc} 0 & 1 & \dots & n-1 & n \end{array} \\ \begin{pmatrix} 1 & 1/2 & & & \\ & 0 & \ddots & & \\ & 1/2 & \ddots & 1/2 & \\ & & \ddots & 0 & \\ & & & 1/2 & 1 \end{pmatrix} \end{array} \begin{array}{c} 0 \\ \\ \\ n-1 \\ n \end{array}$$

$$P^{\flat}_{f(a)} := \begin{array}{c} \begin{array}{ccccc} * & & & n-2 & n-1 \end{array} \\ \begin{pmatrix} 1 & & & & \\ & \ddots & & & \\ & \ddots & 2/3 & & \\ & \ddots & 0 & 3/4 & \\ & & 1/3 & 0 & 1 \\ & & & 1/4 & 0 \end{pmatrix} \end{array} \begin{array}{c} * \\ \\ \\ \\ n-2 \\ n-1 \end{array}$$

Time reversal of the genealogical process resulting from the standard population model

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Time reversal of Birth-Death processes

- Extendable to general birth and death probabilities and to continuous time
- Potential for application in phylogenetic/biostatistic simulation

Merci

Cher - *If I could turn back time*
written by Diane Warren
produced by Diane Warren and Guy Roche
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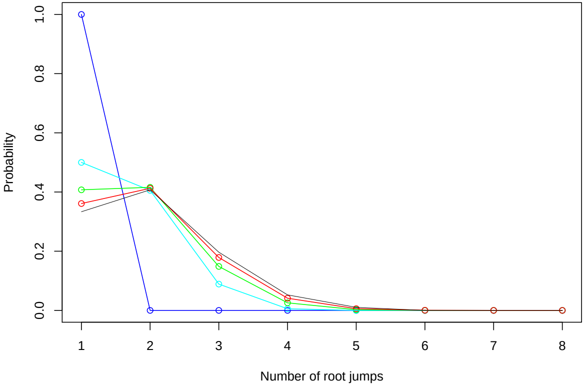
Lemma

In the time span between first occurrence and fixation of a mutant, the expected number of root jumps is $2 - \frac{2}{n}$.



Root jump distribution for $n = 2$ (blue), 5 (turquoise), 10 (green), 25 (red) and the