Introduction to Markov genealogy processes

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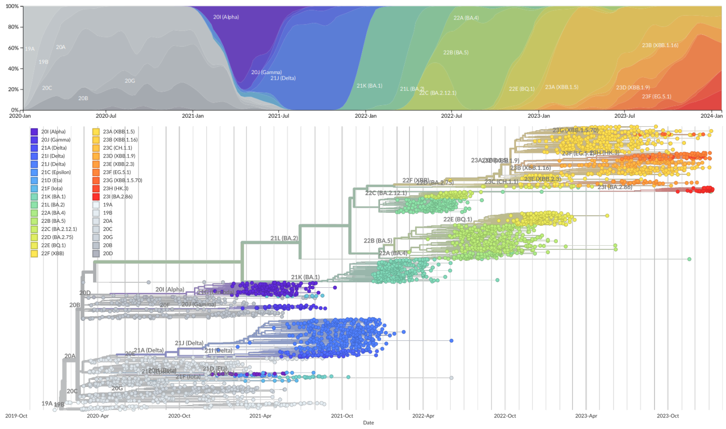
Contents

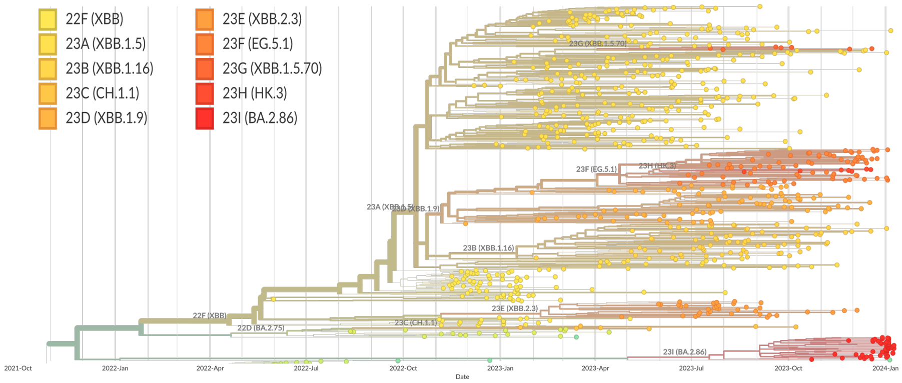
1 Context

1.1 Example: emerging variants

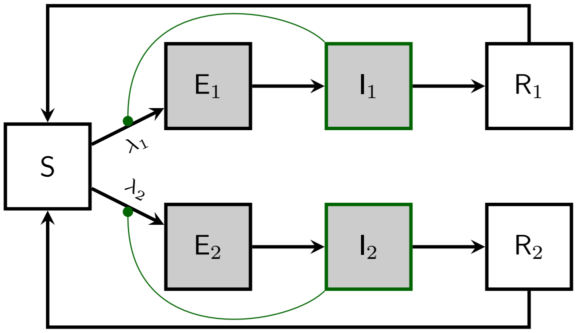
Example: surveillance for emerging SARS-CoV-2 variants



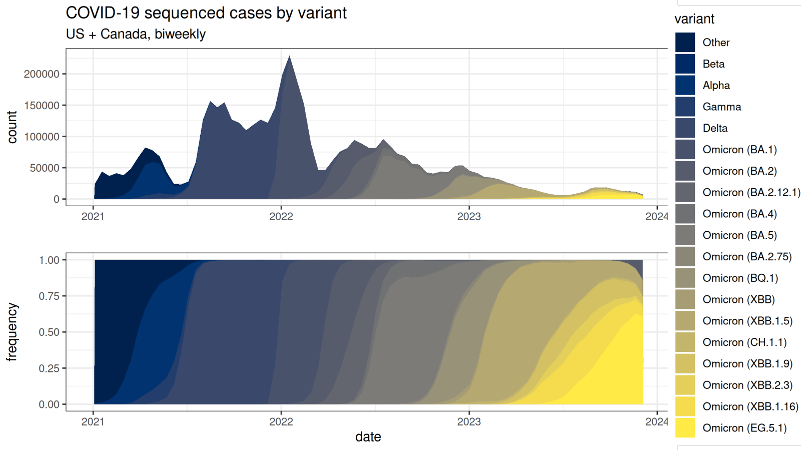
nextstrain.org (Hadfield *et al.*, 2018)



nextstrain.org (Hadfield *et al.*, 2018)



$$\lambda_1 = \beta_1 \frac{I_1}{N} \qquad \lambda_2 = \beta_2 \frac{I_2}{N}$$



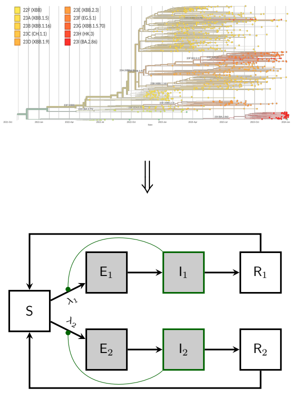
(Mathieu *et al.*, 2020)

1.2 Phylodynamics

What is phylodynamics?

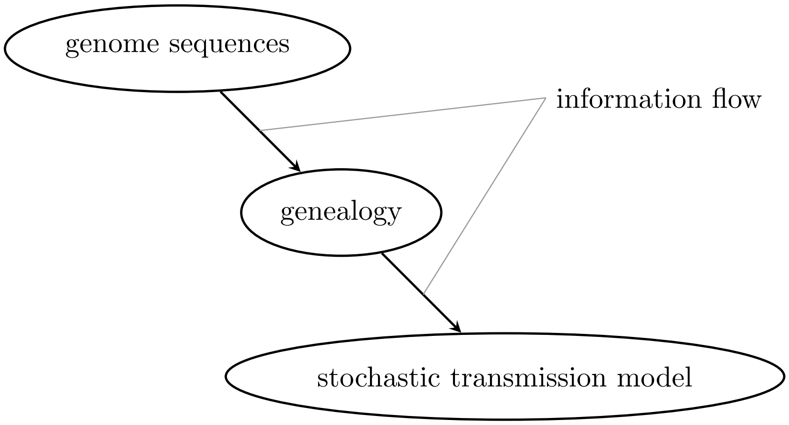
Broadly: Phylodynamics is the project of inferring *determinants of epidemic spread* using *genomic data from pathogen samples.*

In this talk: Phylodynamics means using *genomic data* to infer *stochastic dynamic transmission models.*



1.3 Problems of phylodynamics

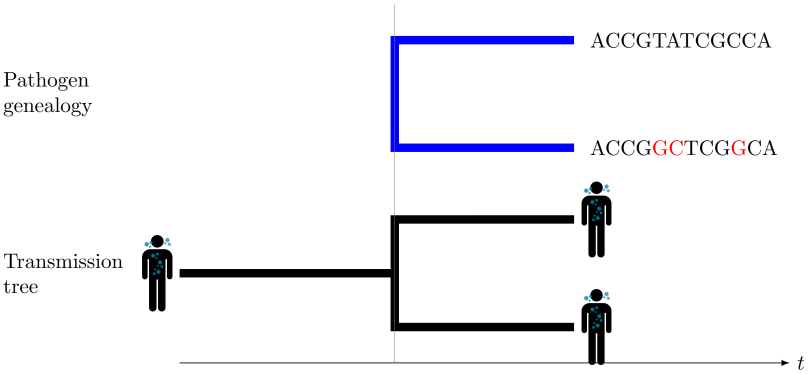
Core problems of phylodynamics

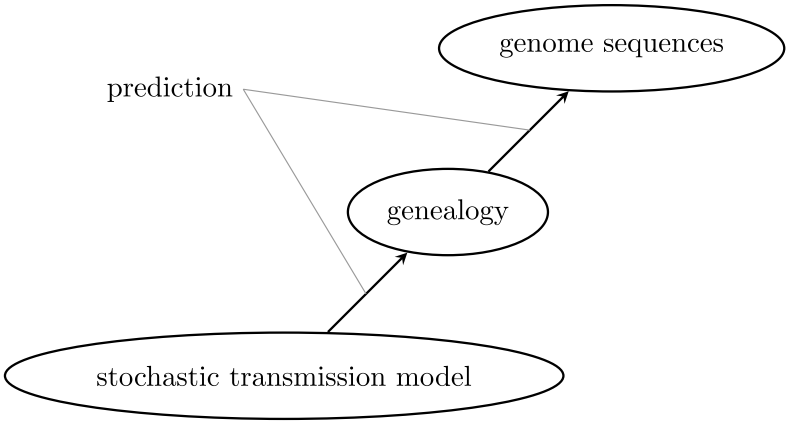

genome sequences

information flow

genealogy

stochastic transmission model





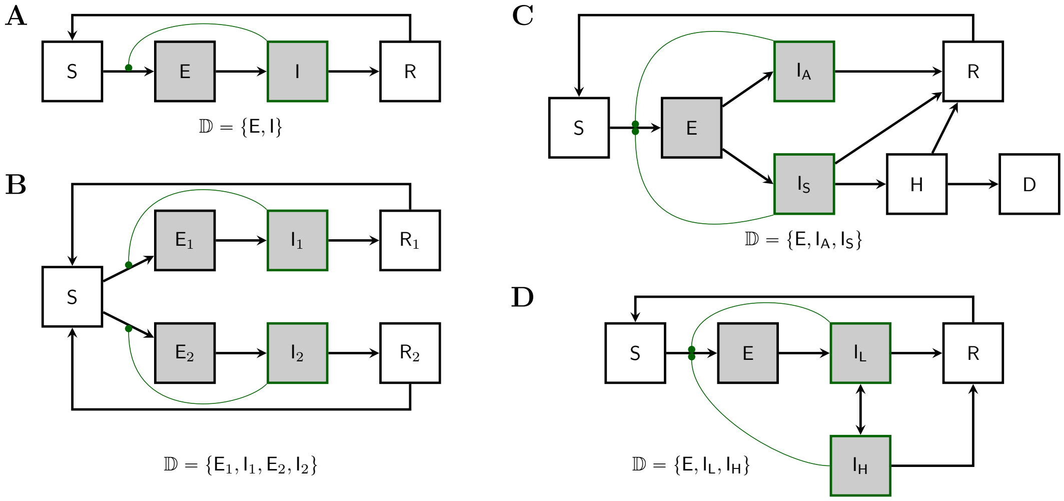
Overview

- We show how a given population process induces a unique genealogy process.
- *Pruning* and *obscuration* project a genealogy onto observable data.

2 Population process

2.1 Examples

Population process


A
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$\mathbb{D} = \{\mathsf{E}, \mathsf{I}\}$
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$\mathbb{D} = \{\mathsf{E}_1, \mathsf{I}_1, \mathsf{E}_2, \mathsf{I}_2\}$
C
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D
$\mathbb{D} = \{\mathsf{E}, \mathsf{I}_\mathsf{A}, \mathsf{I}_\mathsf{S}\}$
D
S
E
I_L
R
I_H
$\mathbb{D} = \{\mathsf{E}, \mathsf{I}_\mathsf{L}, \mathsf{I}_\mathsf{H}\}$

2.2 Formalization

Population process

- Non-explosive Markov jump process, $\mathbf{X}_t \in \mathbb{X}$, $t \in \mathbb{R}_+$: the *population process*.
- Initial-state distribution, p_0:

$$\mathsf{Prob}\left[\mathbf{X}_0 \in \mathcal{E}\right] = \int_{\mathcal{E}} p_0(x)\,\mathrm{d}x$$

- Jump rates: $\alpha(t,x,x')$ = rate of jump $x \to x'$

$$\alpha(t,x,x') \geqslant 0, \qquad \int_{\mathbb{X}} \alpha(t,x,x')\,\mathrm{d}x' < \infty$$

- Multiple events at each jump are allowed.

Kolmogorov forward equation (KFE): If

$$\frac{\partial w}{\partial t}(t,x) = \int w(t,x')\,\alpha(t,x',x)\,\mathrm{d}x' - \int w(t,x)\,\alpha(t,x,x')\,\mathrm{d}x'$$

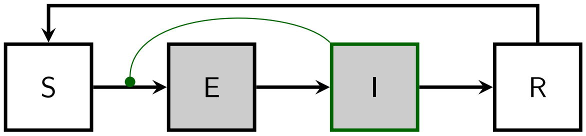
and

$$w(0,x) = p_0(x)$$

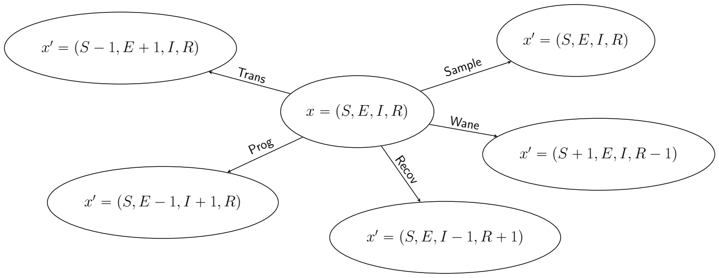
then

$$\int_{\mathcal{E}} w(t,x)\,\mathrm{d}x = \mathsf{Prob}\left[\mathbf{X}_t \in \mathcal{E}\right].$$

KFE is sometimes called the *master equation* for $\mathbf{X}_t$.



$$\frac{\partial w}{\partial t}(t,x) = \int w(t,x')\,\alpha(t,x',x)\,\mathrm{d}x' - \int w(t,x)\,\alpha(t,x,x')\,\mathrm{d}x'$$



$\mathbb{U} = \{\text{Trans}, \text{Prog}, \text{Recov}, \text{Wane}, \text{Sample}\}$

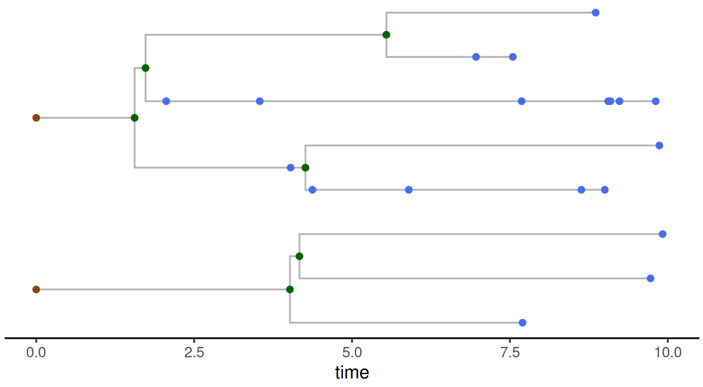
$$\frac{\partial w}{\partial t}(t,x) = \sum_{u\in\mathbb{U}} \left\{ \int w(t,x')\,\alpha_u(t,x',x)\,\mathrm{d}x' - \int w(t,x)\,\alpha_u(t,x,x')\,\mathrm{d}x' \right\}$$

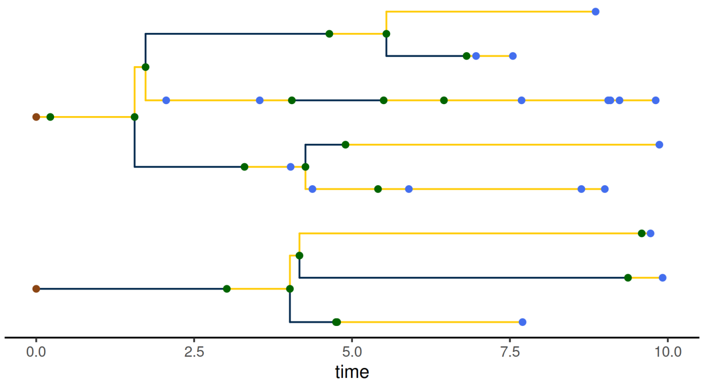
$$\begin{aligned}\frac{\partial w}{\partial t}(t,S,E,I,R) = {} & \frac{\beta(t)\,(S+1)\,I}{N}\,w(t,S+1,E-1,I,R) - \frac{\beta(t)\,S\,I}{N}\,w(t,S,E,I,R)\\ &+ \sigma\,(E+1)\,w(t,S,E+1,I-1,R) - \sigma\,E\,w(t,S,E,I,R)\\ &+ \gamma\,(I+1)\,w(t,S,E,I+1,R-1) - \gamma\,I\,w(t,S,E,I,R)\\ &+ \omega\,(R+1)\,w(t,S-1,E,I,R+1) - \omega\,R\,w(t,S,E,I,R)\end{aligned}$$

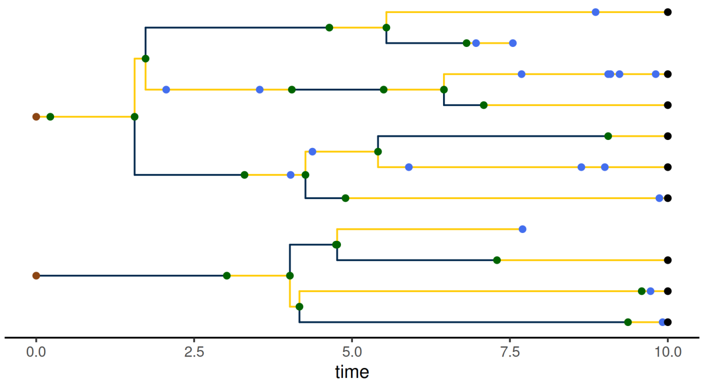
3 Genealogy process

3.1 Genealogies

What is a genealogy?

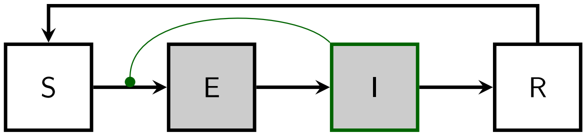




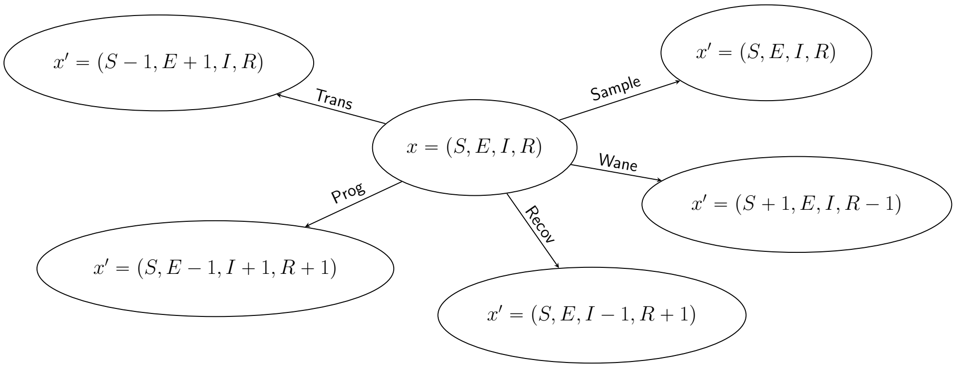


3.2 Induced genealogy process

Event types



$$\mathbb{D} = \{\mathsf{E}, \mathsf{I}\}$$



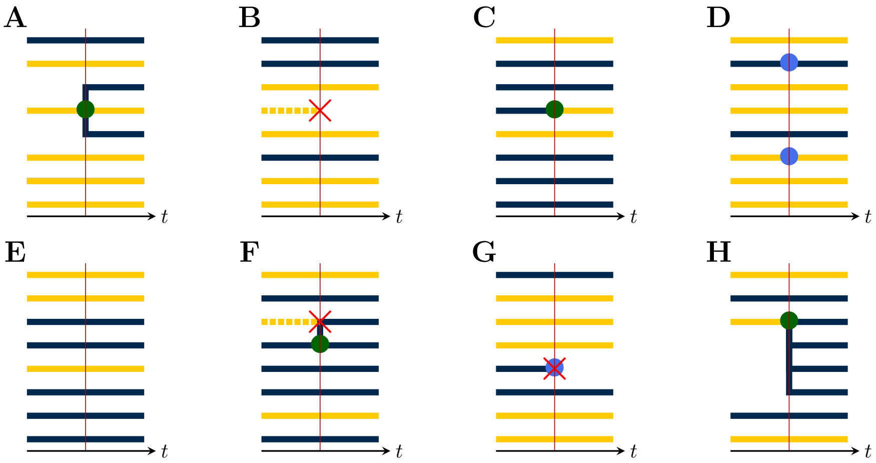
$\mathbb{U} = \{\mathsf{Trans}, \mathsf{Prog}, \mathsf{Recov}, \mathsf{Wane}, \mathsf{Sample}\}$

If we write

$$\alpha(t, x, x') = \sum_{u \in \mathbb{U}} \alpha_u(t, x, x'),$$

the KFE becomes

$$\frac{\partial w}{\partial t}(t, x) = \sum_u \int w(t, x')\, \alpha_u(t, x', x)\, \mathrm{d}x' - \sum_u \int w(t, x)\, \alpha_u(t, x, x')\, \mathrm{d}x'$$



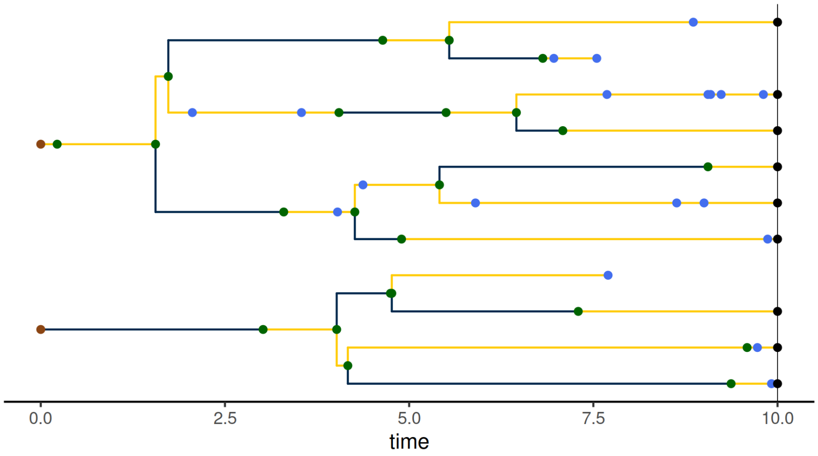
A population process induces a genealogy process

- $\mathbf{G}_t$ is a stochastic process on the space of genealogies.
- The map $\mathbf{X} \mapsto \mathbf{G}$ is random.
- **Key assumption:** Lineages within a deme are *exchangeable*. There is no more structure than is implied by the population process.

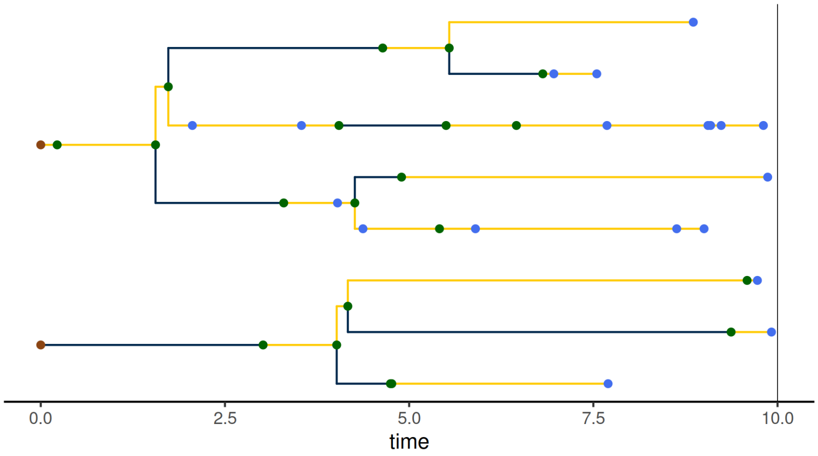
- Simulation code on github.com/kingaa/phylopomp
- Animations at https://kingaa.github.io/manuals/phylopomp/vignettes/

4 Pruned and obscured genealogies

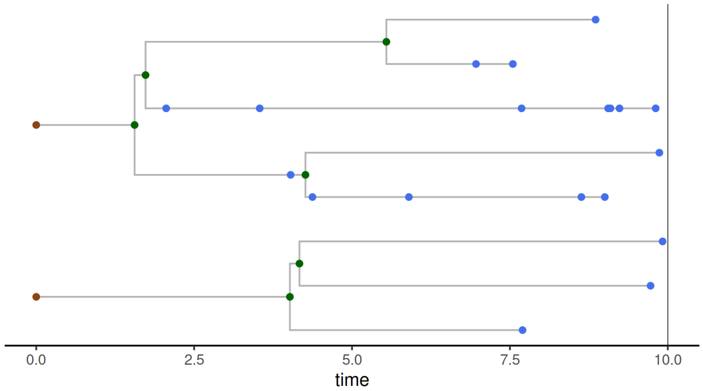
Full genealogy



Pruned genealogy



Obscured genealogy



An obscured genealogy is specified by (T, Z).

Summary and outstanding challenges

Summary

- A discretely structured Markov population process uniquely induces a genealogy-valued Markov process.
- The likelihood of an observed genealogy satisfies a nonlinear filtering equation, which can be efficiently computed via Feynman-Kaç (sequential Monte Carlo) algorithms.
- In principle, these results liberate us to entertain models that more closely match our biological questions, without less hindrance from inference methodology.

References

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License, acknowledgments, and links

- The materials build on previous versions of this course and related courses.
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- Produced with R version 4.3.2 and **pomp** version 5.6.

- Compiled on March 4, 2024.

Back to Lesson
R codes for this lesson