A null model for the observed transposition rate of transposons in the genome

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Null models and probability theory

Null models for processes with a stochastic component

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important question in biology and ecology

- Observations $\neq$ **intuition**
- Stochasticity **cannot be neglected**

EXAMPLE 1: Hubbell's "*unified neutral theory of biodiversity and biogeography*" [Hubbell (2001)] in community ecology

$\Longrightarrow$ **No need for selection/interaction between species to explain some of the diversity patterns observed in ecological communities**

Null models and probability theory

EXAMPLE 2: Genetic diversity in spatially expanding populations

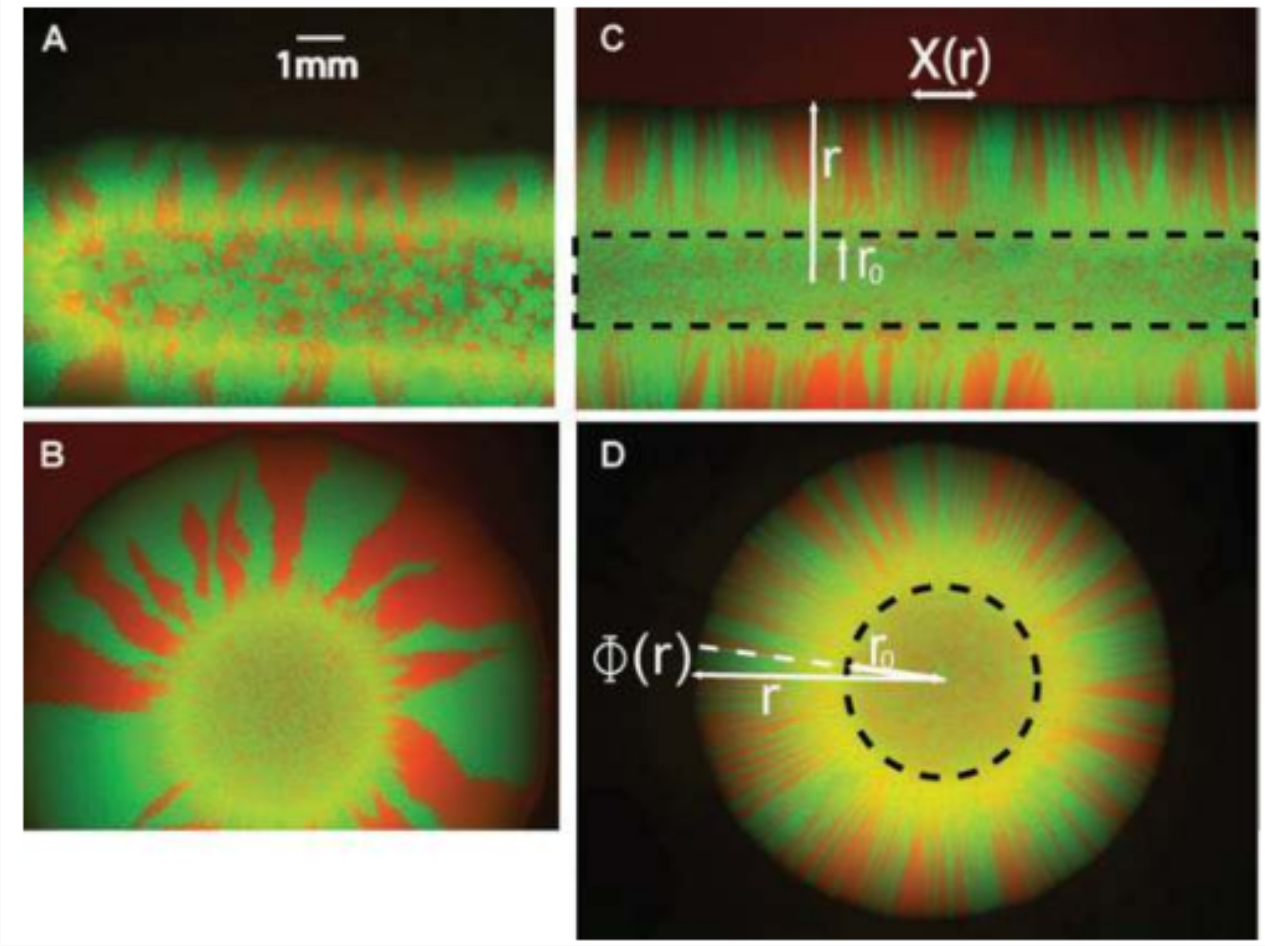


Image taken from [Hallatschek and Nelson (2010)].

Null models and probability theory

EXAMPLE 3: Ancestral reproductive bias in branching processes

- Consider a critical birth-death branching process, with birth rate = death rate = 1
- Let $T > 0$, assume that the process is still alive, and sample an individual uniformly at random
- [Cheek and Johnston (2023)]: Reproduction rate on the ancestral line ≈ 2 rather than 1

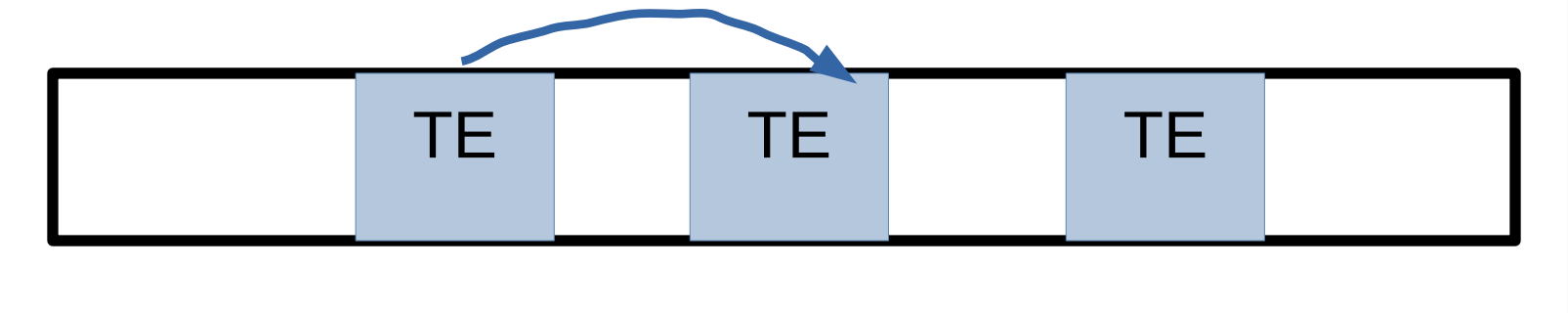
$\Longrightarrow$ **Observed** branching rate $\neq$ **actual** branching rate

What are transposons

transposons ≈ parasites of the genome

- Copied during cell division
- Can also self-duplicate (**"transpose"**) within the genome

What are transposons



Effect of transposition

- New TE in non-coding region ≈ neutral
- New TE in coding region = bad (generally)

Regulation of transposition rates

[Le Rouzic and Capy (2005)] : Optimal strategy for transposon dynamics :

- Initially, high transposition rate
- Reduce transposition rates when abundance increases

$\Longrightarrow$ Regulation of transposition rates (self or by external source)

- **Apparent regulation** of transposition rates observed experimentally
- Extensive literature on possible regulation mechanisms (see [Bourque et al. (2018)] for a review)

Regulation of transposition rates

How is apparent regulation observed

- Count TEs at time t, $2t$, $3t$,...
- Compute the difference in TE counts over time
- Deduce transposition rates

⚠Possible bias = only non-dead cells observed

Bias in observed transposition rates

ASSUMPTION

$$\text{Death rate of a cell} \sim \text{TE count}$$

- Cells with higher than average TE count = more likely to die
- Cells with lower than average TE count = less likely to die

$\Longrightarrow$ **We tend to only observe cells with lower than average TE count**

Is this sufficient to explain the temporal dynamics of the observed transposition rate ?

A first toy model

Model

"TE dynamics embedded in a neutral Wright-Fisher model"

- N haploid individuals
- Initially, each individual contains 1 TE

Step 1: "TE dynamics"

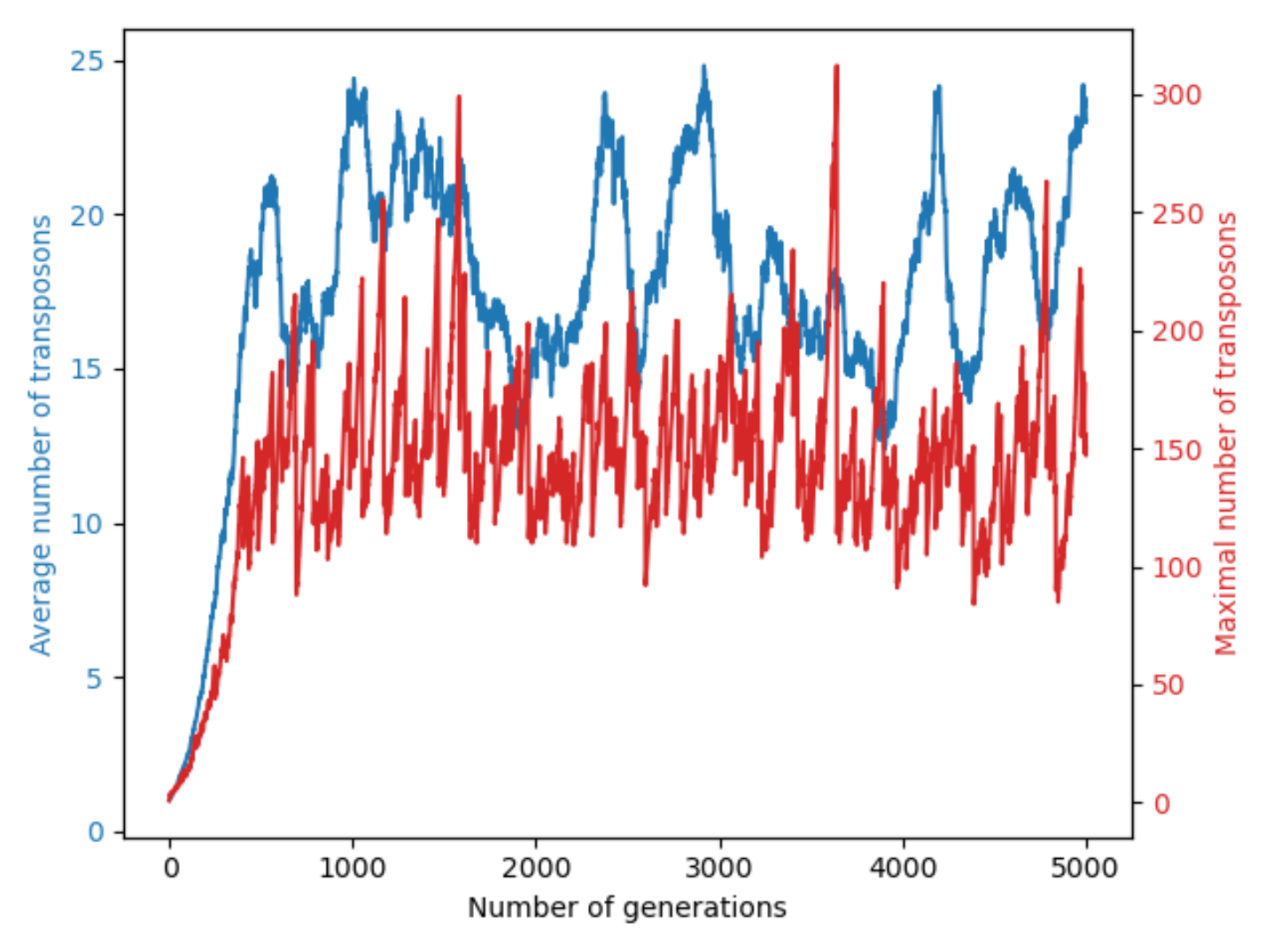
- Each TE attempts to transpose
- Three outcomes: no new TE, success, death of the cell

Step 2: "Neutral Wright-Fisher model"

- N new individuals produced from N' remaining individuals
- TE count conserved from parent to child

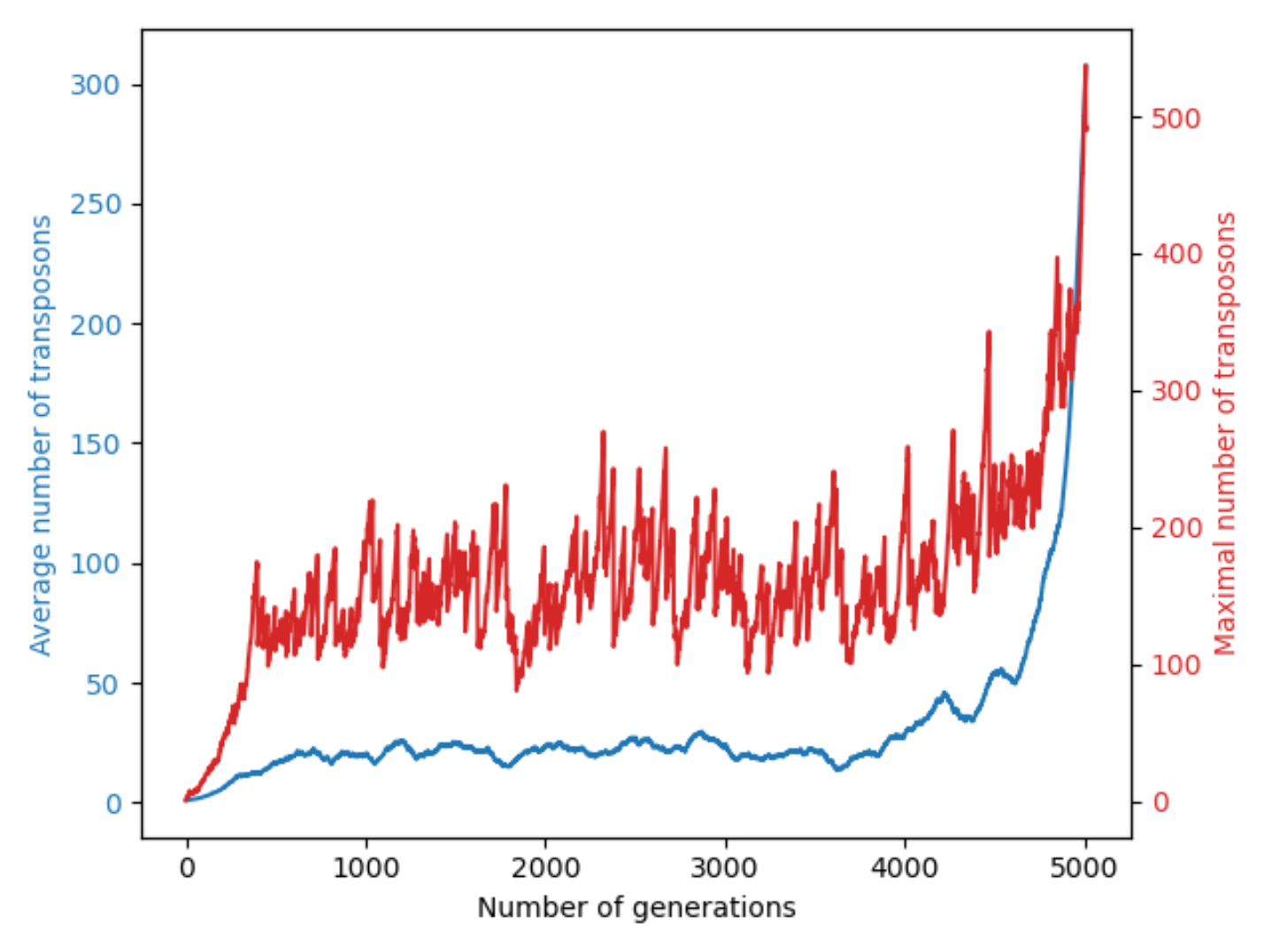
A first toy model

$\Longrightarrow$ **Possible to find parameter sets for which the TE count evolves as wanted for long durations**



A first toy model

$\Longrightarrow$ As no mechanism to reduce TE count in a cell, **eventual TE-driven population collapse** ($\approx$ Muller's ratchet)



A first toy model

Can we parametrize the model to generate biologically-relevant numbers of TEs ? Using biologically-relevant parameter values ?

- simulation study ($\Longrightarrow$ Quentin Cordeau)
- theoretical results on the probabilistic model

What are biologically-relevant values ? ($\Longrightarrow$ Luzie Wingen)

Ex: [Bourque et al. (2018)] LINE1 in humans = around 500.000 copies, but most are deactivated, only $\sim$ 100 active per individual

Towards a more complete model

In first model, **no mechanism** to reduce TE count in a cell

POSSIBLE WAYS

– "Soft reduction" by recombination (diploid individuals)

⚠**Need to take into account genome structure**

– Host-mediated deactivation

See LINE1 example

$\Longrightarrow$ "Dormant" and "active" TEs

Towards a more complete model

$\Longrightarrow$ More explicit model of transposition dynamics ?

⚠Huge variety of TEs

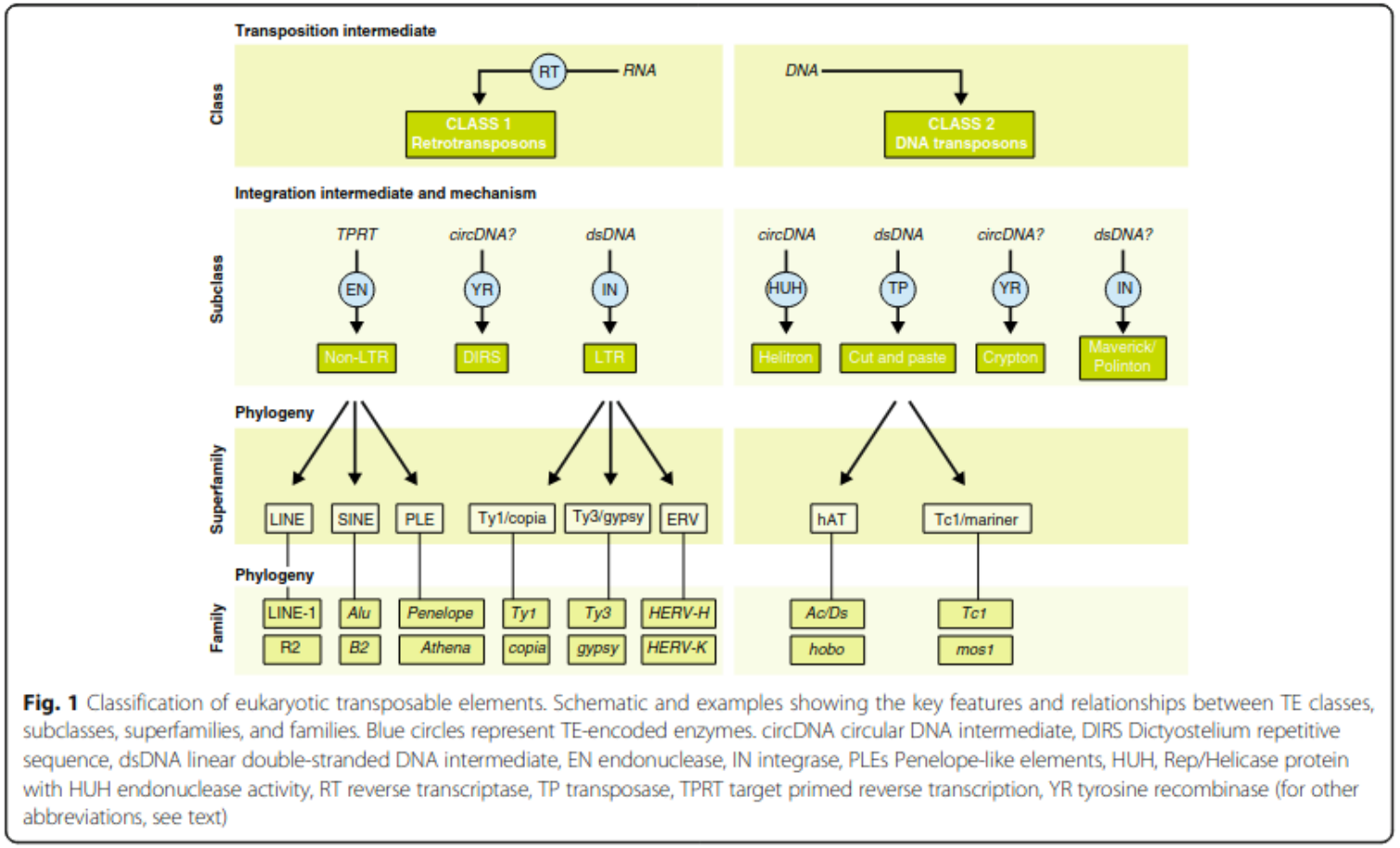


Fig. 1 Classification of eukaryotic transposable elements. Schematic and examples showing the key features and relationships between TE classes, subclasses, superfamilies, and families. Blue circles represent TE-encoded enzymes. circDNA circular DNA intermediate, DIRS Dictyostelium repetitive sequence, dsDNA linear double-stranded DNA intermediate, EN endonuclease, IN integrase, PLEs Penelope-like elements, HUH, Rep/Helicase protein with HUH endonuclease activity, RT reverse transcriptase, TP transposase, TPRT target primed reverse transcription, YR tyrosine recombinase (for other abbreviations, see text)

Image from [Bourque et al. (2018)]

Summary of the project

1. Construct a null model for TE dynamics without self-regulation
2. Parametrize it with biologically-relevant values
3. Study to what extent we can reproduce the documented observed transposition rate
    - Same overall shape, different values ?
    - Same overall shape AND values ?
    - None of the above ?

To learn more about transposons: [Bourque et al. (2018)]

References

Bourque, G., Burns, K., Gehring, M., Gorbunova, V., Seluanov, A., Hammell, M., ... others (2018). Ten things you should know about transposable elements. *Genome biology*, *19*, 1–12.

Cheek, D., & Johnston, S. (2023). Ancestral reproductive bias in branching processes. *Journal of Mathematical Biology*, *86*(5), 70.

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