An individual-based model for the Lenski experiment, and the deceleration of the relative fitness

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Joint work with Noemi Kurt, Anton Wakolbinger and Linglong Yuan

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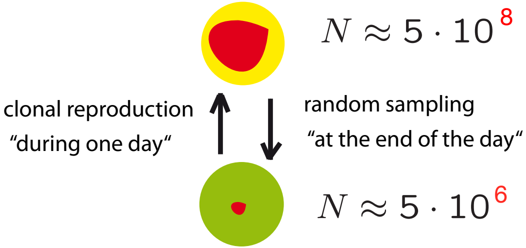
The Lenski experiment (one day cycle)



Relative fitness

Measuring adaptation

- A population of size A_0 of the unevolved strain and a population of size B_0 of the evolved strain perform a direct competition.
- The respective population sizes at the end of the day are denoted by A_1 and B_1.
- The (empirical) *relative fitness* $F(B|A)$ of strain B with respect to strain A is

$$F(B|A) = \frac{\log(B_1/B_0)}{\log(A_1/A_0)}.$$

Lenski, Travisano, PNAS, 1994

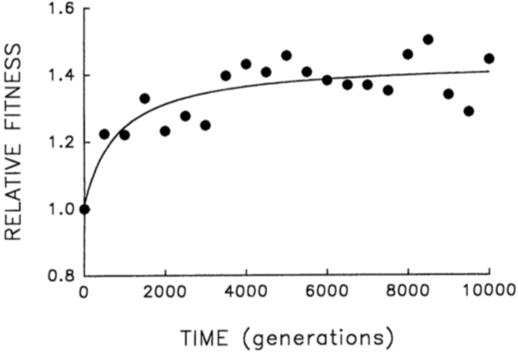
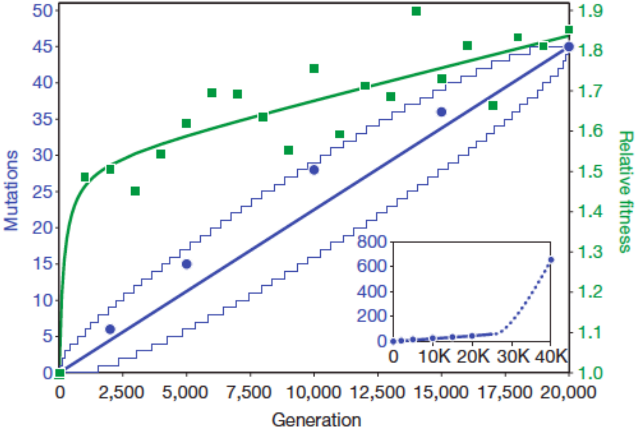


FIG. 4. Trajectory for mean fitness relative to the ancestor in one population of *E. coli* during 10,000 generations of experimental evolution. Each point is the mean of three assays. Curve is the best fit of a hyperbolic model.

Barrick, Yu, Yoon, Jeong, Oh, Schneider, Lenski, Kim, Nature 2009

$$\omega(t) = 1 + at/(t + b)$$



Wiser, Ribeck, Lenski, Science express 13-11-12

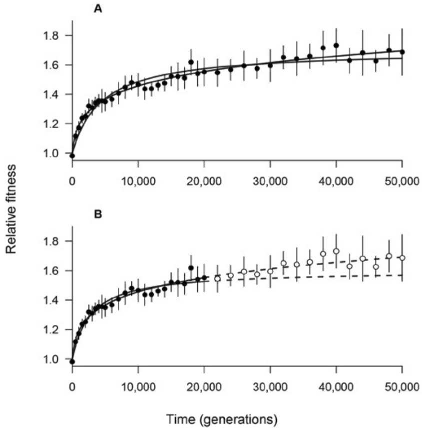


Fig. 2. Comparison of hyperbolic and power-law models. (**A**) Hyperbolic (red) and power-law (blue) models fit to the set of mean fitness values (black symbols) from all 12 populations. (**B**) Fit of hyperbolic (solid red) and power-law (solid blue) models to data from first 20,000 generations only (filled symbols), with model predictions (dashed lines) and later data (open symbols). Error bars are 95% confidence limits based on the replicate populations.

$$w(t) = (1 + ct)^{1/2g}$$

Questions

- Which curve describes better the trajectory of the relative fitness?
- Why is the relative fitness decelerating?

Possible explanations

- Clonal interference
- Epistasis
- The design of the experiment

The daily cycle model[1]

Information about the experiment

- At the beginning of each day there are N individuals.
- Within each day individuals split at constant rate.
- The reproduction process will stop when the glucose has been consumed. (This happens when there are around $100N$ individuals).
- N individuals out of the $\sim 100N$ are uniformly sampled without replacement, to be starting individuals at the next day.

[1] An individual-based model for the Lenski experiment, and the deceleration of the relative fitness. Adrian Gonzalez Casanova, Noemi Kurt, Anton Wakolbinger and Linglong Yuan. (2015) arXiv 1505.0175

Pruned Yule trees

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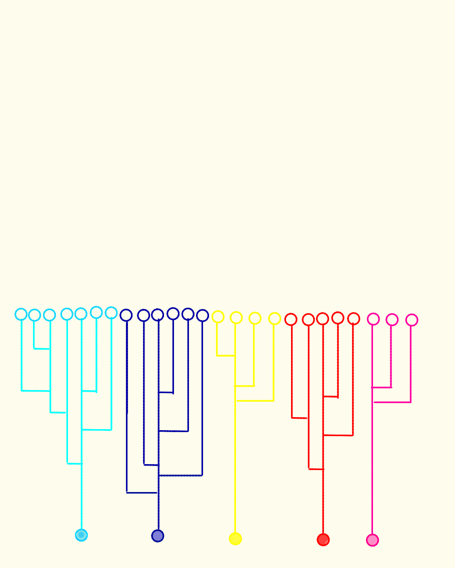
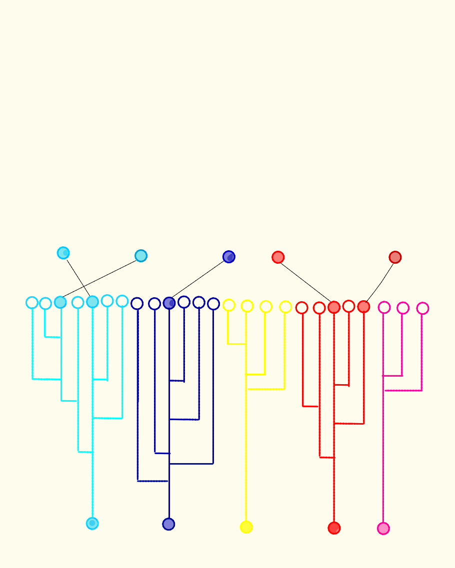


Pruned Yule trees



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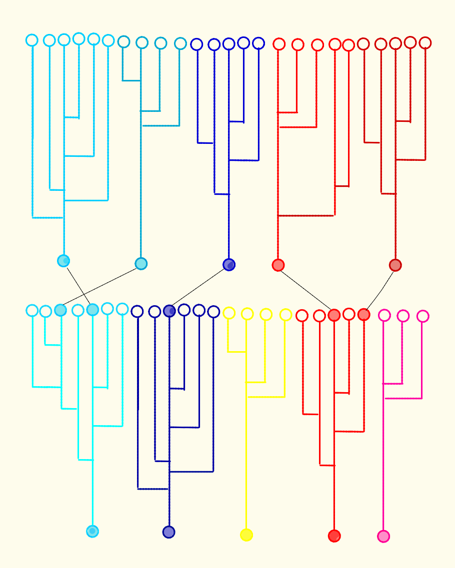

Inside a day

Let $Y_{i,j}(t)$ be a pure birth process with rate $r \in \mathbb{R}^+$, for every $i \in \mathbb{N}$ and $j \in \{1, 2, ..., N\}$. (Yule Processes with parameter r).
The total population size at time t of day i is

$$\sum_{j=1}^{N} Y_{i,j}(t)$$

Stopping rule

Each day, the reproduction stops at time σ , where

$$\sigma = \inf\{t : E[\sum_{j=1}^{N} Y_{i,j}(t)] = \gamma N\}.$$

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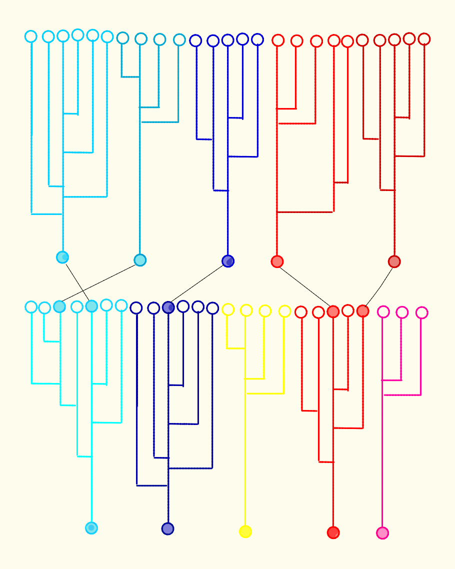
The total population size at the end of the day is

$$\sum_{j=1}^{N} Y_{i,j}(\sigma) \sim \gamma N.$$

Sampling rule

To go from one day to the next, we sample uniformly at random N individuals (out of $\sim \gamma N$), and we say that each sampled individual is a root of a Yule tree in the next day.

We are dealing with a Cannings process.



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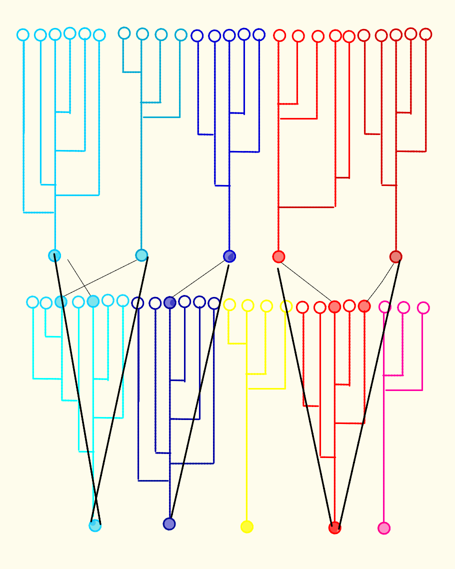

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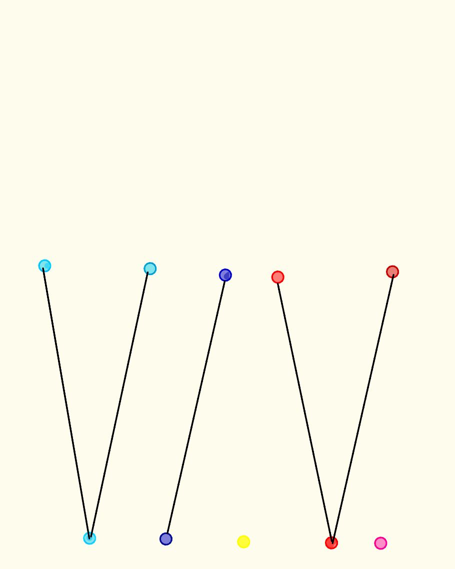

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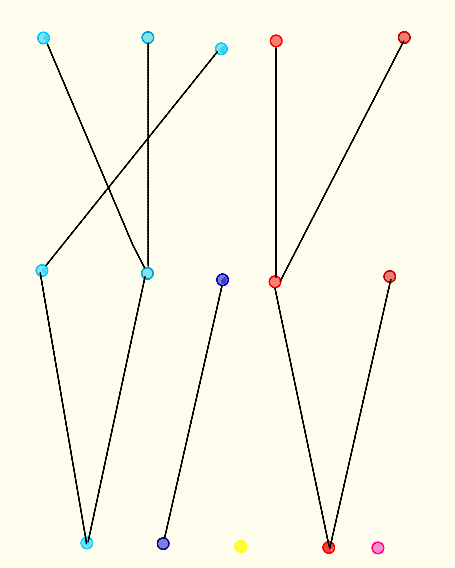


Convergence to Kingman's coalescent

Let $\big(B_i^{(N,n)}\big)_{i\in\mathbb{N}}$ be the ancestral process of a sample of n individuals, when the population at the beginning of each day is N.

Theorem

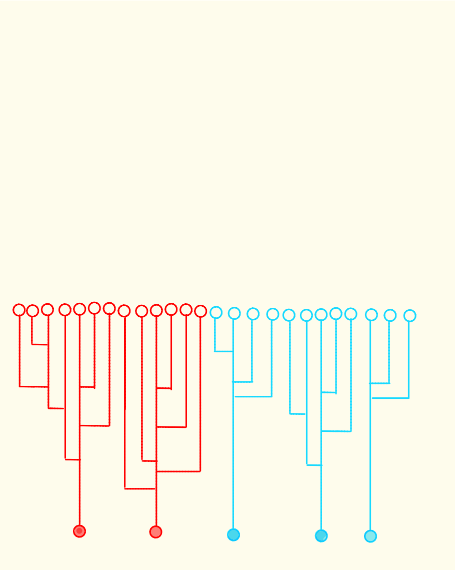
For all $n \in \mathbb{N}$, the sequence of ancestral processes $\big(B^{(N,n)}_{\lfloor Nt/2(1-\frac{1}{\gamma})\rfloor}\big)_{t\geq 0}$ converges weakly on the space of càdlàg paths as $N \to \infty$ to Kingman's n-coalescent.

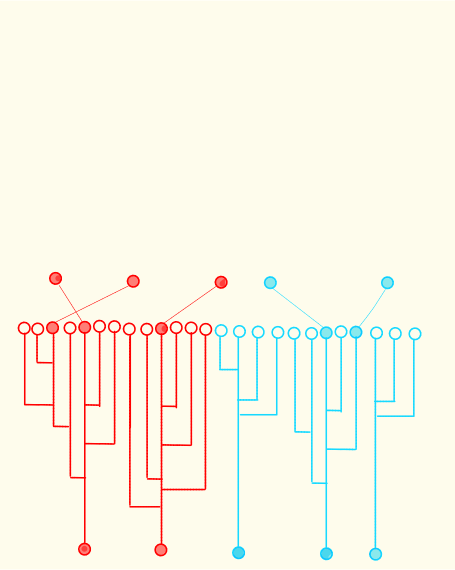
Introducing selective advantage

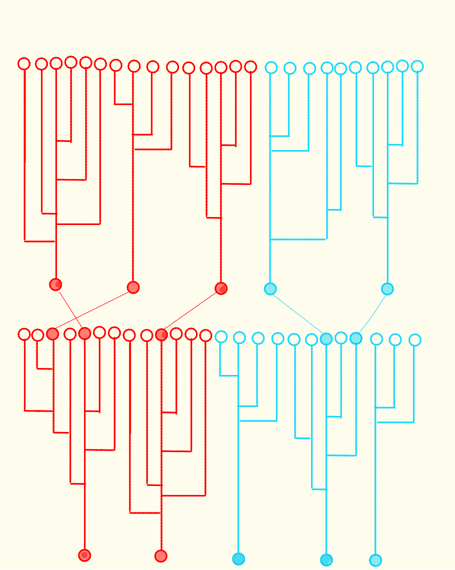
- Assume that some individuals reproduce at rate $r + \varrho_N$ (mutants), while other reproduce at rate r (basis population).
- Stopping rule: the reproduction stops when the expectation of the total population is γN.
- Let $M_i(t)$ be the number of mutants at time t of day i.
- We are interested in the process

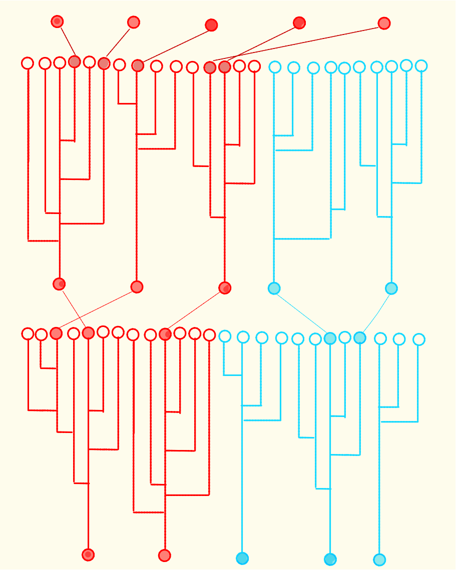
$$\{K_i\}_{i\in\mathbb{N}} := \{M_i(0)\}_{i\in\mathbb{N}},$$

which is constructed recursively using uniform sampling.







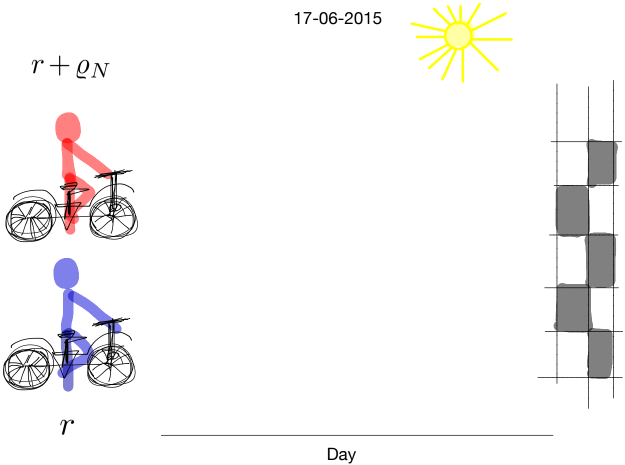


Selective advantage

Basic population reproduces at rate r.
Mutants reproduce at rate $r + \varrho_N$.

$$\mathbb{E}[K_1 | K_0 = 1] = 1 + \varrho_N \frac{\log \gamma}{r} + o(\varrho_N).$$

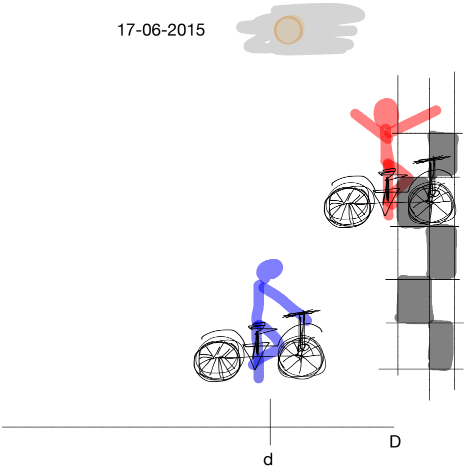
Race until the sun is gone



Race until the sun is gone

17-06-2015

$r + \varrho_N$



r

Race until the sun is gone

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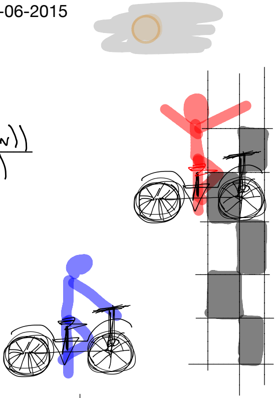
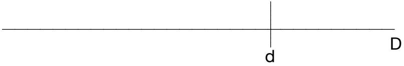


$r + \varrho_N$

$$\frac{\exp(D)}{\exp(d)} = \frac{\exp(|Day|(r+e_N))}{\exp(|Day|(r))}$$

$$\sim 1 + |Day| e_N$$

r



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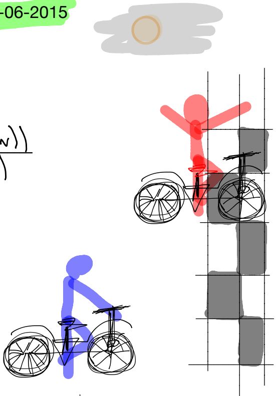
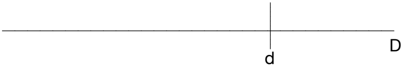


$r + \varrho_N$

$$\frac{\exp(D)}{\exp(d)} = \frac{\exp(|Day|(r+e_N))}{\exp(|Day|(r))}$$

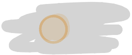
$$\sim 1 + 23 e_N$$

r

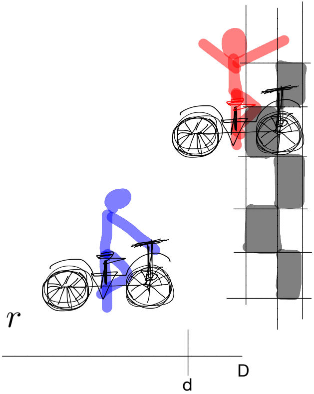


Race until the sun is gone

17-12-2015



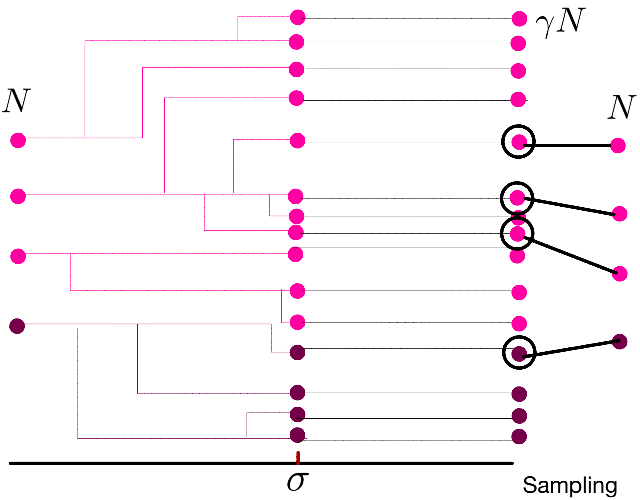
$r + \varrho_N$



$$\frac{\exp(D)}{\exp(d)} = \frac{\exp(|Day|(r+e_N))}{\exp(|Day|(r))}$$

$$\sim 1 + 1\, e_N$$

The *effective competition time*, and its dependence on r



Let $\pi_N := \mathbb{P}\big(\exists i \in \mathbb{N} : K_i = N \,|\, K_0 = 1\big)$, and $\tau^N := \tau^N_{\mathrm{fix}} \wedge \tau^N_{\mathrm{ext}}$.

Theorem (Probability and speed of fixation)

Under the assumptions of our model, as $N \to \infty$,

$$\pi_N \sim \frac{\gamma}{\gamma - 1} \frac{\varrho_N \log \gamma}{r}.$$

Moreover, for any $\delta > 0$ *there exists* $N_\delta \in \mathbb{N}$ *such that for all* $N \geq N_\delta$

$$\mathbb{P}(\tau^N > \varrho_N^{-1-3\delta}) \leq (7/8)^{\varrho_N^{-\delta}}.$$

The weak mutation - moderate selection model (Assumption A)

i) Beneficial mutations add ϱ_N to the reproduction rate of the individual that suffers the mutation.

ii) In each generation, with probability μ_N there occurs a beneficial mutation. The mutation affects only one (uniformly chosen) individual, and every offspring of this individual also carries the mutation.

iii) There exists $0 < b < 1/2$, and $a > 3b$, such that $\mu_N \sim N^{-a}$ and $\varrho_N \sim N^{-b}$ as $N \to \infty$.

$$\mu_N << \varrho_N$$

We define the fitness of the population at the beginning of day i with respect to that at the beginning of day 0 as

$$F_i := \frac{\log \frac{1}{N} \sum_{j=1}^{N} e^{R_{i,j} t}}{\log e^{r_0 t}}$$

where $R_{i,j}, j = 1, \dots, N$ are the reproduction rates of the individuals present at the beginning of day i, and t is a given time for which the two populations are allowed to grow together.

If the whole population reproduces at the same rate (R_i), then

$$F_i = \frac{R_i}{r_0}$$

where $r_0 := R_0$.

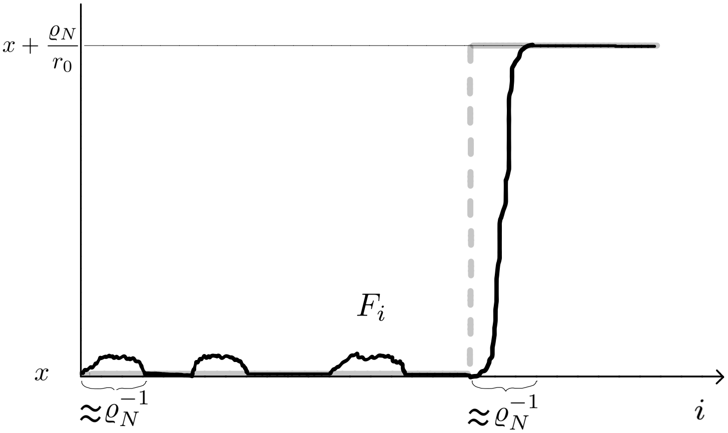


Figure: The number of attempts to go to fixation, when the reproduction rate of the basic population is x, is distributed Geometric with parameter $\pi_N \sim \varrho_N \frac{C(\gamma)}{x}$.

Theorem (Convergence of the relative fitness process)

Assume $R_{0,j} = r_0$ for $j = 1, ..., N$, and let $(F_i)_{i\in\mathbb{N}_0}$ be the process of relative fitness. Then under Assumption A, the sequence of processes $(F_{\lfloor(\varrho_N^2\mu_N)^{-1}t\rfloor})_{t\geq 0}$ converges in distribution as $N \to \infty$ locally uniformly to the deterministic function

$$f(t) = \sqrt{1 + \frac{\gamma\log\gamma}{\gamma - 1}\frac{2t}{r_0^2}},\ \ t \geq 0\,.$$

Table: Our model compared with Wiser et al.

	Our model	Wiser et al
Clonal interference	No	Yes
Epistasis	No	Yes
Design of the experiment	Yes	No
	$f(t) = (1 + \frac{2C(\gamma)t}{r_0^2})^{1/2}$	$w(t) = (1 + ct)^{1/2g}$

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If we include Epistasis in our model, by assuming that the selective advantage provided by a single mutation to an individual that reproduce at rate x is $\varrho_N^{(x)} = x^q \varrho_N$, for some $q > -1$, then

$$h(t) = \left(1 + \frac{2(1+q)C(\gamma)}{r_0^2} t\right)^{\frac{1}{2(1+q)}}$$

Final remarks

- How to measure the fitness? (See Chevin, Biology Letters, 2011.)

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- Beyond measuring the fitness.
- Indirect evidence.
- Are there further consequences of the days getting shorter? (See Wahl, Dai Zhu, Genetics 2015)

Bibliography

A. González Casanova, N. Kurt, A. Wakolbinger and L. Yuan,
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to appear in Stoch. Processes Appl.

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Thank you

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$$N = 4$$

$$\sigma_k$$

$$\sigma_{\lfloor \epsilon N \rfloor}$$

$$\mu_N^{-1} \varrho_N^{-1}$$

$$\mu_N^{-1} \varrho_N^{-2}$$

$$\frac{1}{\gamma} - N^{-\alpha}$$

$$\alpha \in (0, 1/2)$$

Day $i + 1$

$$(A^N_{\lfloor Nt \rfloor}) \Rightarrow (|K_t|),$$

$$(X^N_{\lfloor Nt \rfloor}) \Rightarrow (X_t),$$

where (X_t) is the solution to the SDE

$$dX_t = \sqrt{X_t(1 - X_t)}dB_t, \; X_0 = x \in [0, 1]$$

$$\frac{N}{\gamma N}$$