Evolutionary dynamics on graphs

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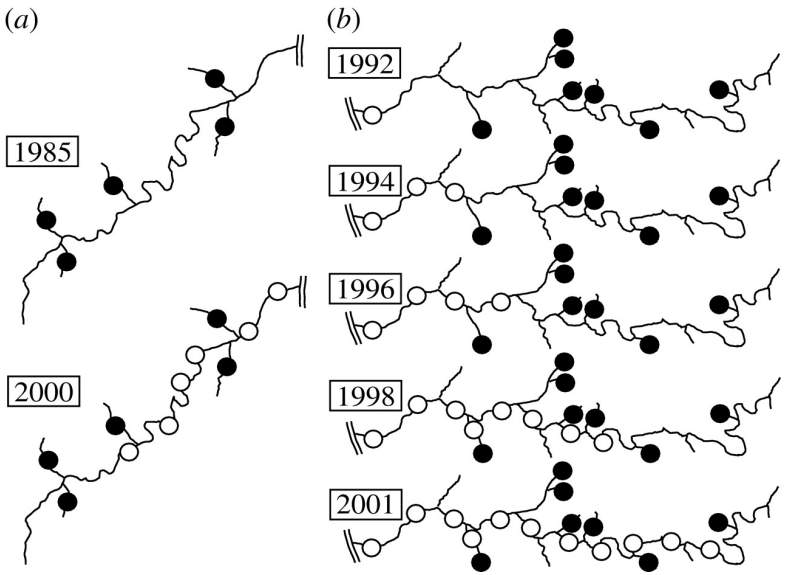
Evolutionary dynamics

Main ingredients:

- **Fitness:** The ability to survive and reproduce.
- **Selection** emerges when two or more individuals reproduce at different rates.
- **Mutation:** One type can change into another.
- **Neutral drift:** A finite population of two types will eventually consist of only one type.

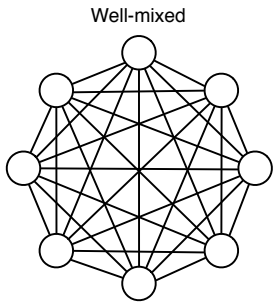
How does spatial population structure change the dynamics of evolution?

Empirical

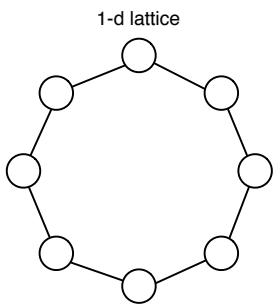


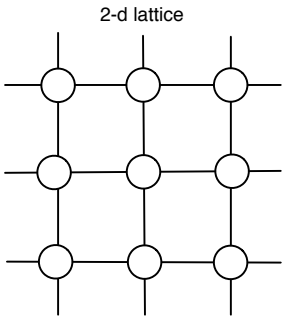
A. W. Nolte et al. Proc. R. Soc. B (2005)

Theoretical



$$\rho = \frac{1-\frac{1}{r}}{1-\frac{1}{r^N}}$$





The Moran Process

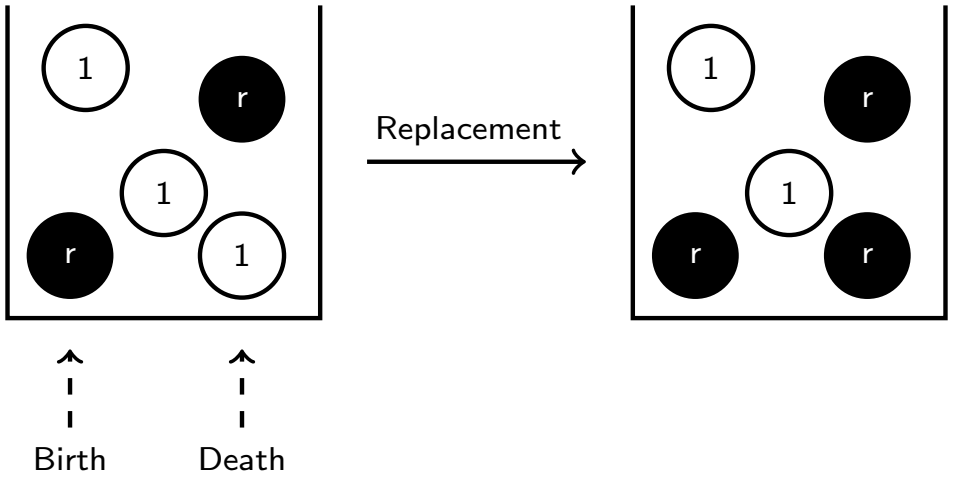
- Discrete time stochastic process $M := \{M_n\},\ n \in \mathbb{N}_0$.
- Birth-death process on a well-mixed population of N individuals.
- Here, the initial state of the population is:
  - $N - 1$ wild type individuals with fitness 1
  - 1 mutant with fitness $r > 0$

The Moran Process

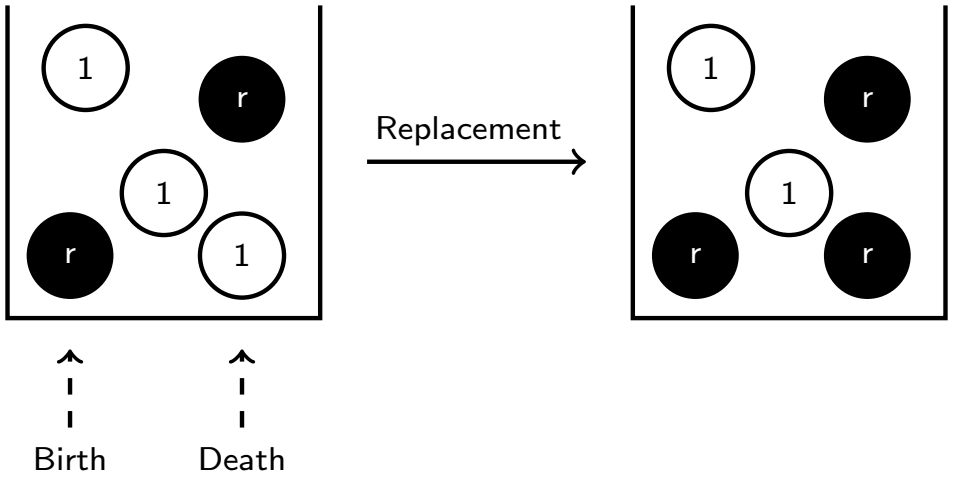
One reproductive event at each time step:

- Select one individual for birth at random, but with probability proportional to its fitness.
- This individual produces one clonal offspring.
- Randomly choose an individual to be replaced by the new offspring.

The Moran Process



The Moran Process



- Markov process on the number of mutants.
- State space $S = \{0, 1, 2, \ldots, N\}$ with initial state $M_0 = 1$.
- Assumption: no further mutations. Therefore, the states 0 and N are absorbing.

Transition Probabilities for the Moran Process

The probability to increase or decrease the number of mutants, or to stay with i mutants at the next time step are:

$$t_i^+ := P(M_{n+1} = i+1 \mid M_n = i) = \frac{ri}{ri+N-i} \cdot \frac{N-i}{N-1}$$

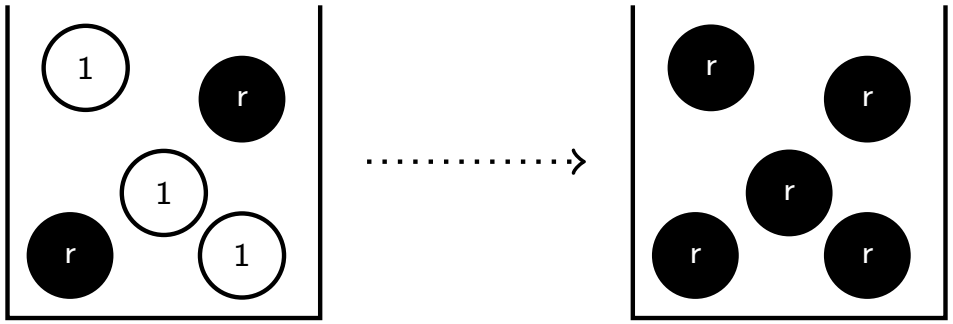
$$t_i^- := P(M_{n+1} = i-1 \mid M_n = i) = \frac{N-i}{ri+N-i} \cdot \frac{i}{N-1}$$

$$t_i^0 := P(M_{n+1} = i \mid M_n = i) = 1 - t_i^+ - t_i^-.$$

for $0 \leq i \leq N$.

Success Probability of the Mutants

Fixation probability:
Φ_i^N is the probability to reach state N from state i.



Success Probability of the Mutants

$$\Phi_i^N = t_i^- \Phi_{i-1}^N + t_i^+ \Phi_{i+1}^N + (1 - t_i^- - t_i^+)\Phi_i^N$$

where $\Phi_0^N = 0$; $\Phi_N^N = 1$.

Solving the recursion: $$\Phi_i^N = \frac{\sum_{n=0}^{i-1} \prod_{j=1}^{n} \frac{t_j^-}{t_j^+}}{\sum_{n=0}^{N-1} \prod_{j=1}^{n} \frac{t_j^-}{t_j^+}} .$$

For the Moran process in a well-mixed pop.: $$\Phi_i^N = \frac{1-\frac{1}{r^i}}{1-\frac{1}{r^N}}.$$

Conditional Fixation Time

The expected time until absorption into the state N starting from one single mutant, given that it will succeed:

$$\tau_1^N = \sum_{k=1}^{N-1} \sum_{l=1}^{k} \frac{\Phi_l^N}{t_l^+} \prod_{m=l+1}^{k} \frac{t_m^-}{t_m^+} \ .$$

Moran Process on Graphs

Let $G := (V, E)$ define a **graph**, consisting of a set of vertices V and edges E.
Individuals inhabit the nodes of a graph and reproduce into their adjacent nodes.

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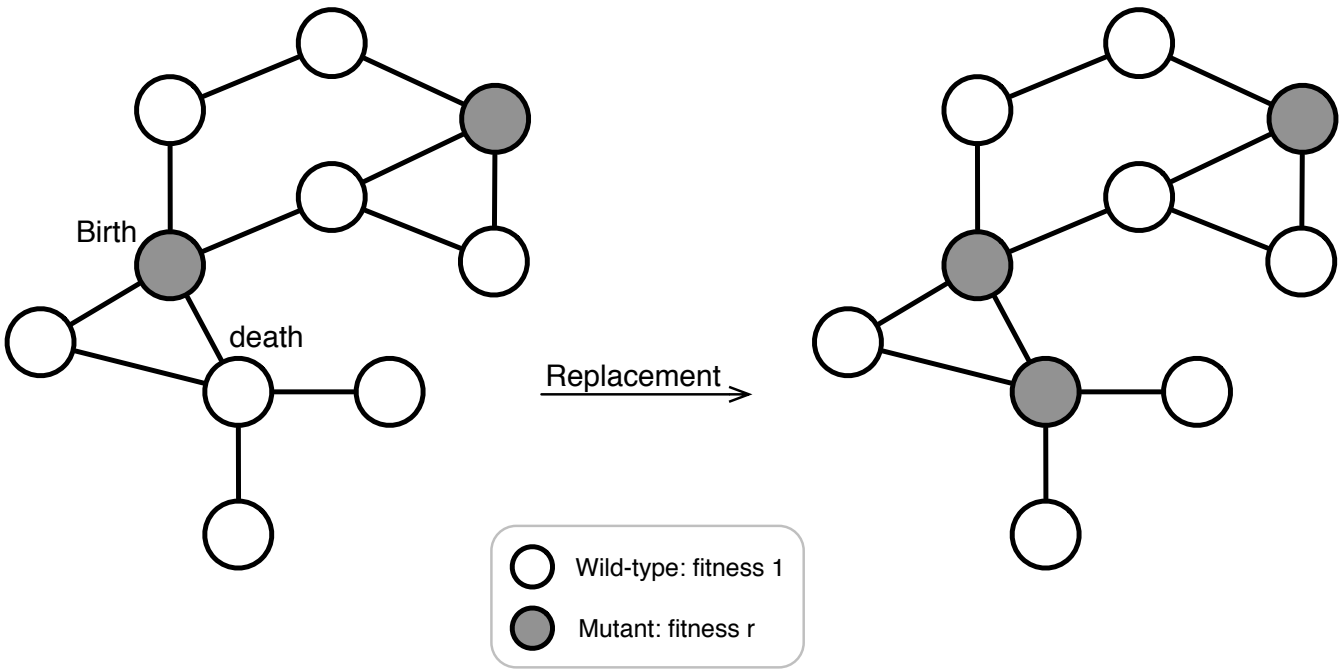
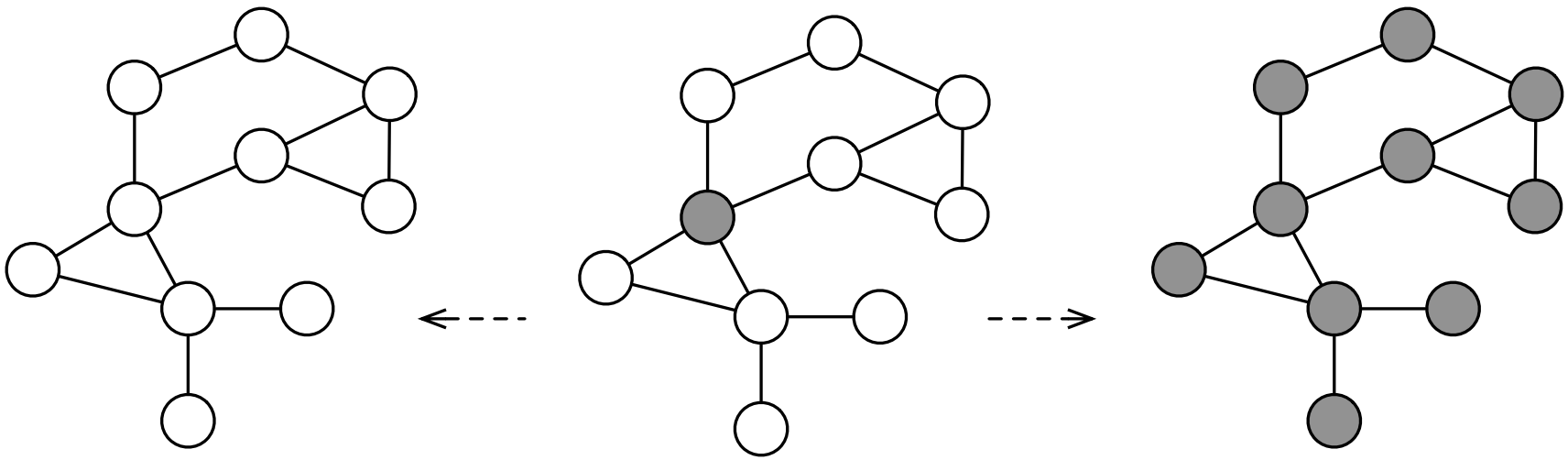
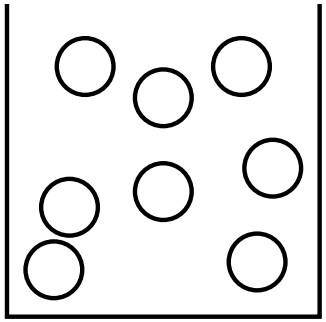


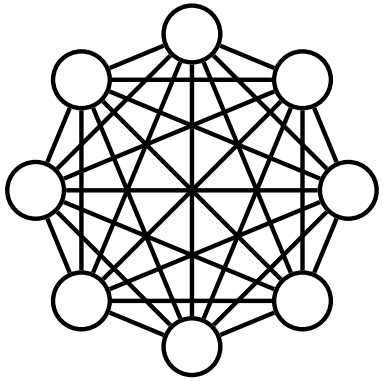
Moran Process on Graphs



Reference Case



Well-mixed population



Complete graph

Methods

Different approaches for calculating the fixation probability and time in graphs:

- Individual-based simulations
- Transition matrix for up to 2^N states.

Transition matrix

Renumber the $s = t + a$ states. The transition matrix now has the following canonical form:

$$\mathbf{T}_{s\times s} = \begin{pmatrix} \mathbf{Q}_{t\times t} & \mathbf{R}_{t\times a} \\ \mathbf{0}_{a\times t} & \mathbf{I}_{a\times a} \end{pmatrix} .$$

Call $\mathbf{F} = \sum_{n=0}^{\infty} \mathbf{Q}^n = (\mathbf{I} - \mathbf{Q})^{-1}$ the fundamental matrix of the Markov chain. The entry $F_{i,j}$ is the expected sojourn time in state j, given that the process starts in transient state i.

C.M. Grinstead & J.L. Snell *Introduction to Probability* (1997)

Transition matrix

Probability of absorption in state j after starting in state i:

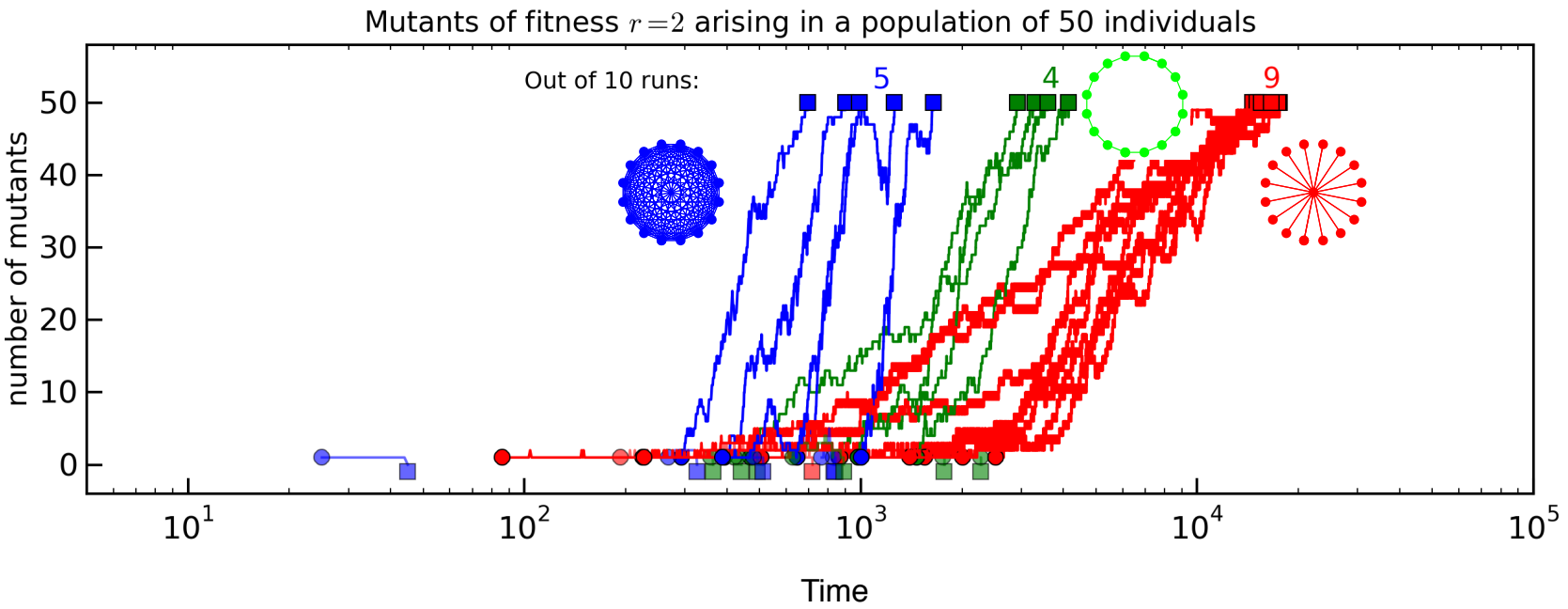
$$\Phi_i^j = (\mathbf{FR})_{i,j} \, . \tag{1}$$

Conditional fixation time[1]:

$$\tau_i^N = \sum_{j=1}^{N-1} \left(\frac{\Phi_j^N}{\Phi_i^N} \cdot F_{i,j} \right) \, .$$

[1] W.J. Ewens. Theoretical Population Biology (1973)

Popular Examples



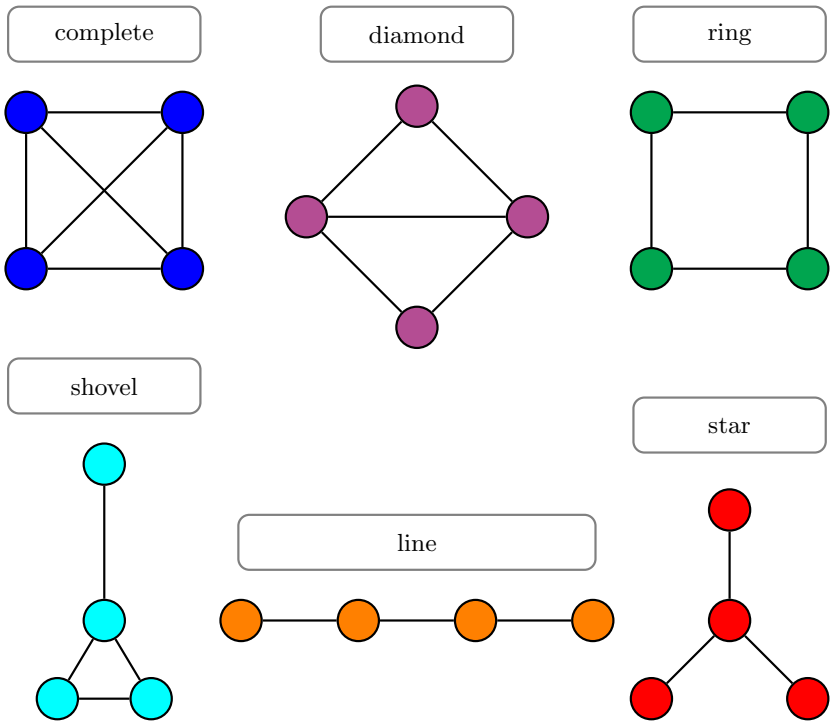
M. Frean et al. Proc. R. Soc. B (2013)

Questions

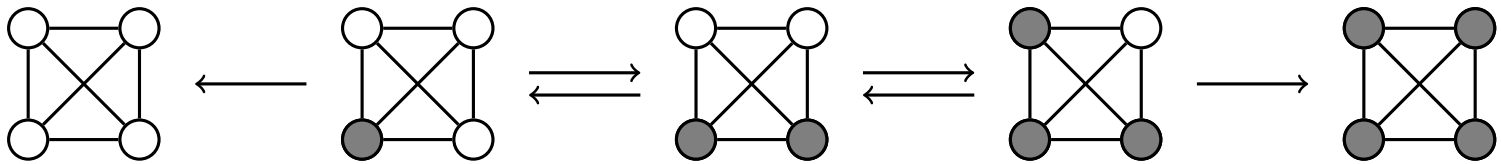
Question 1:
Does every undirected graph that differs from the well-mixed population increase the fixation time of advantageous mutants?

Question 2:
Given any population structure, does the removal of one link always lead to a higher fixation time?

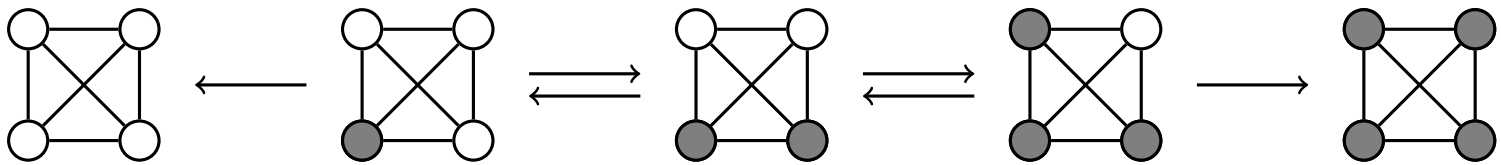
There are six different connected graphs of size four:



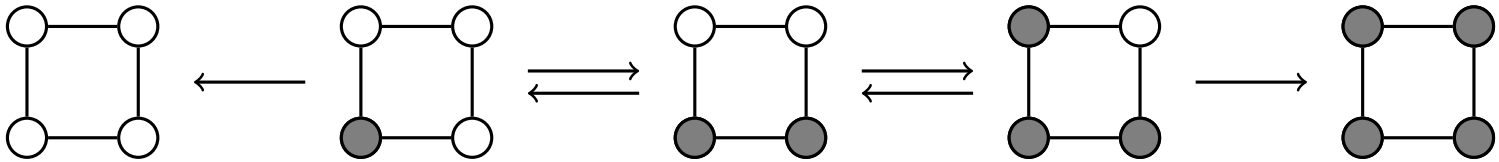
States of the Moran process on the complete graph:



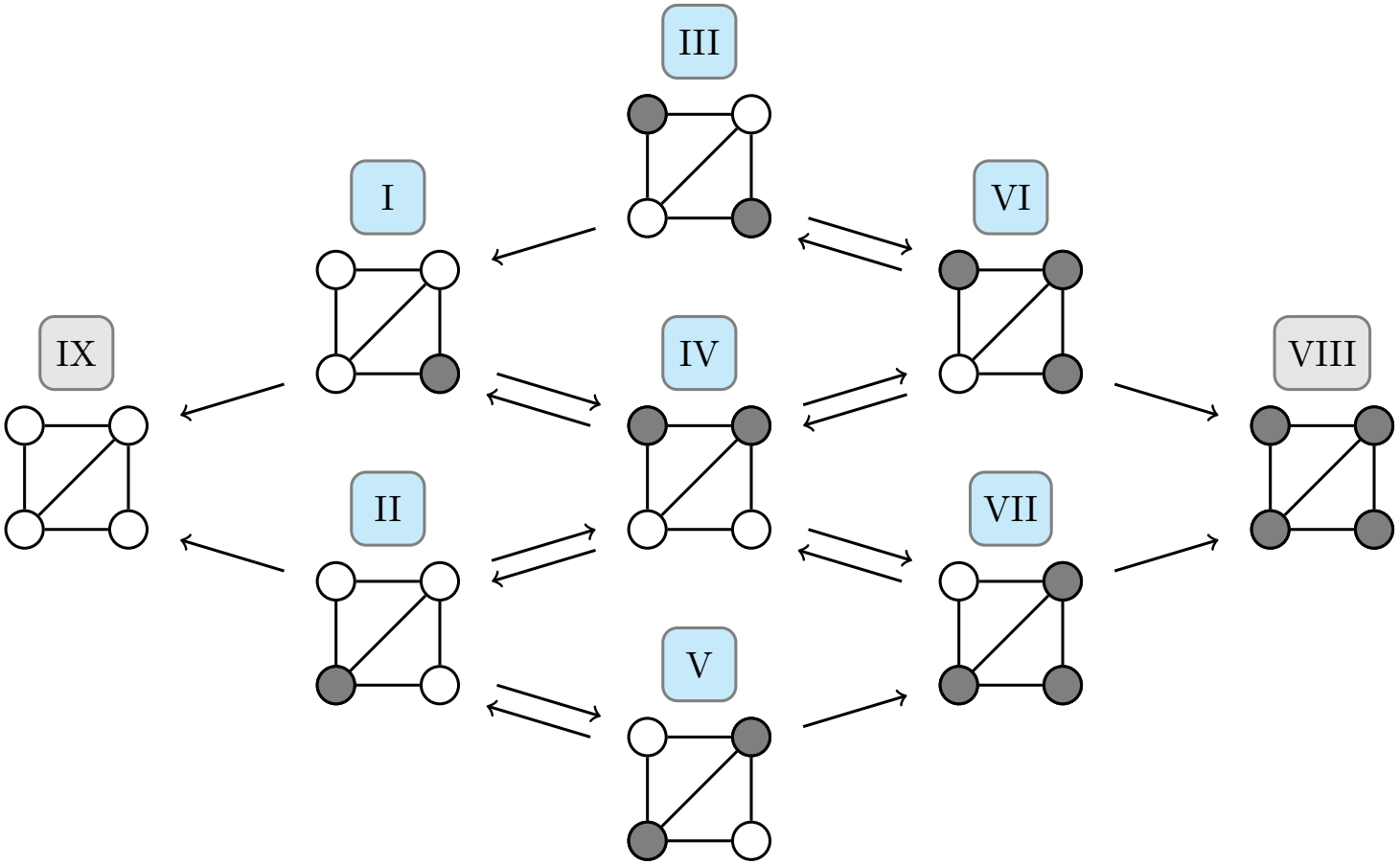
States of the Moran process on the complete graph:



And on the ring:

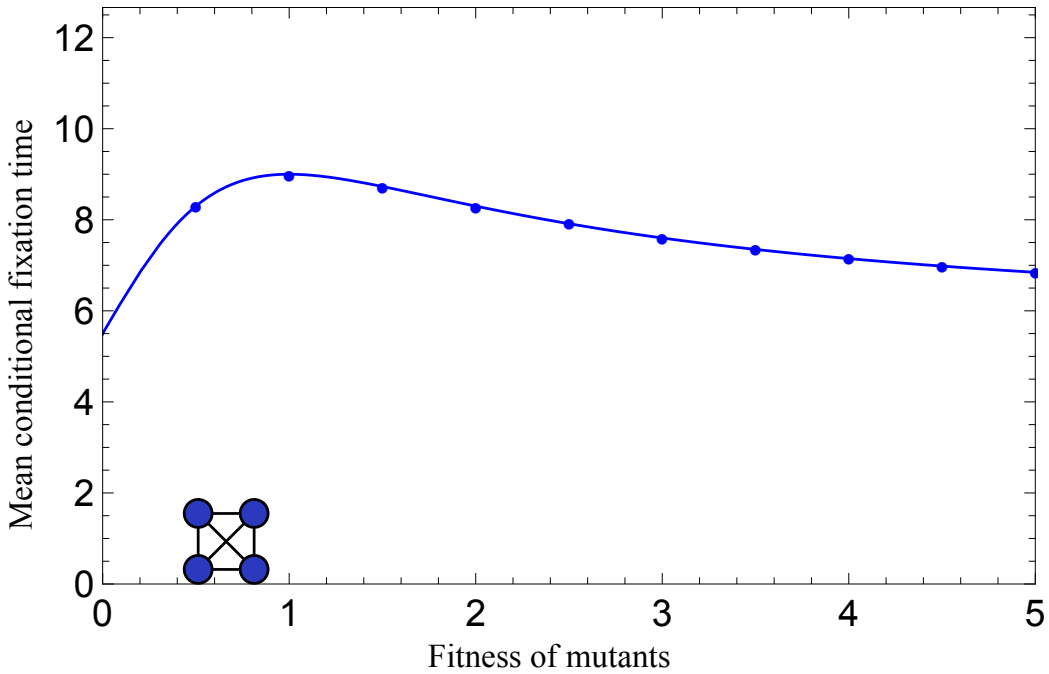


States of the Moran process on the diamond:



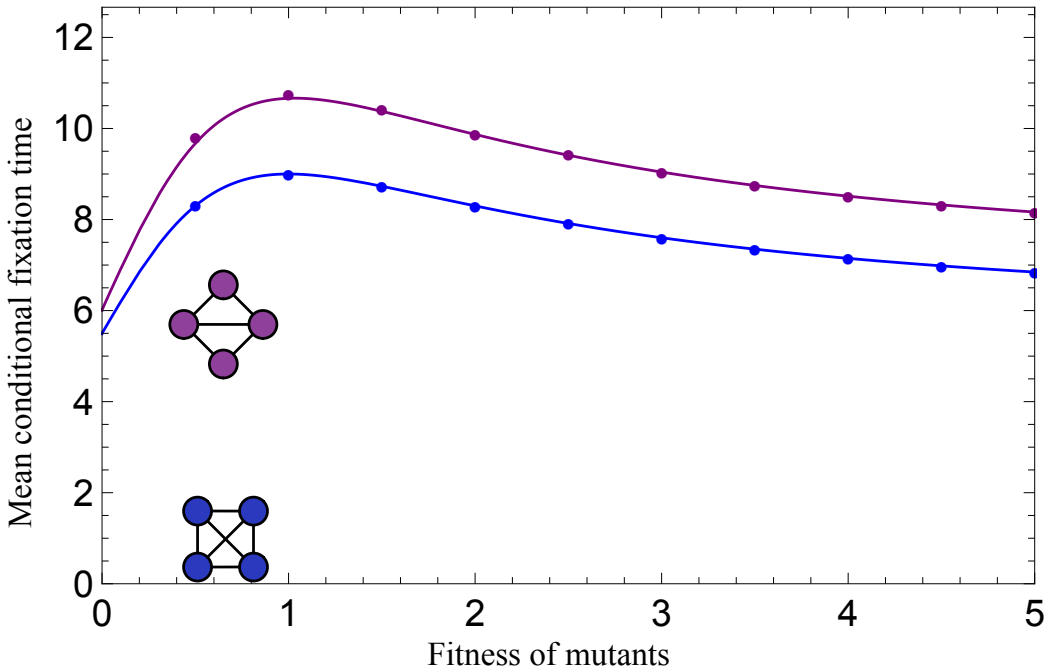
Fixation Time

Question 2: Does the removal of a link always lead to a higher fixation time?



Fixation Time

Question 2: Does the removal of a link always lead to a longer fixation time?



Fixation Time

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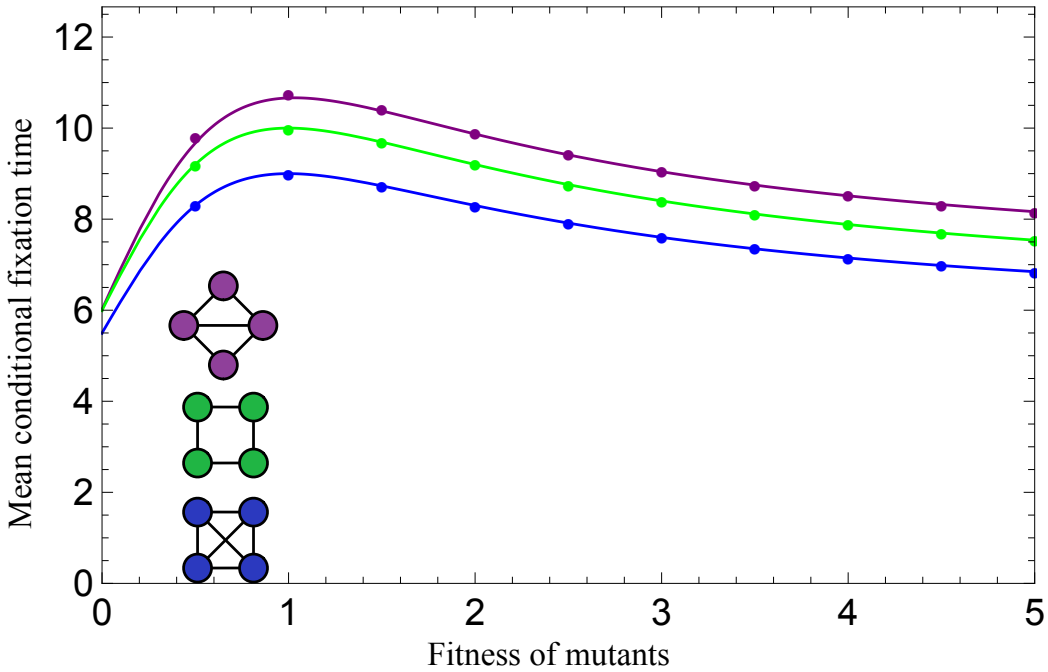


Answer: No!

Is this effect still present in larger networks?

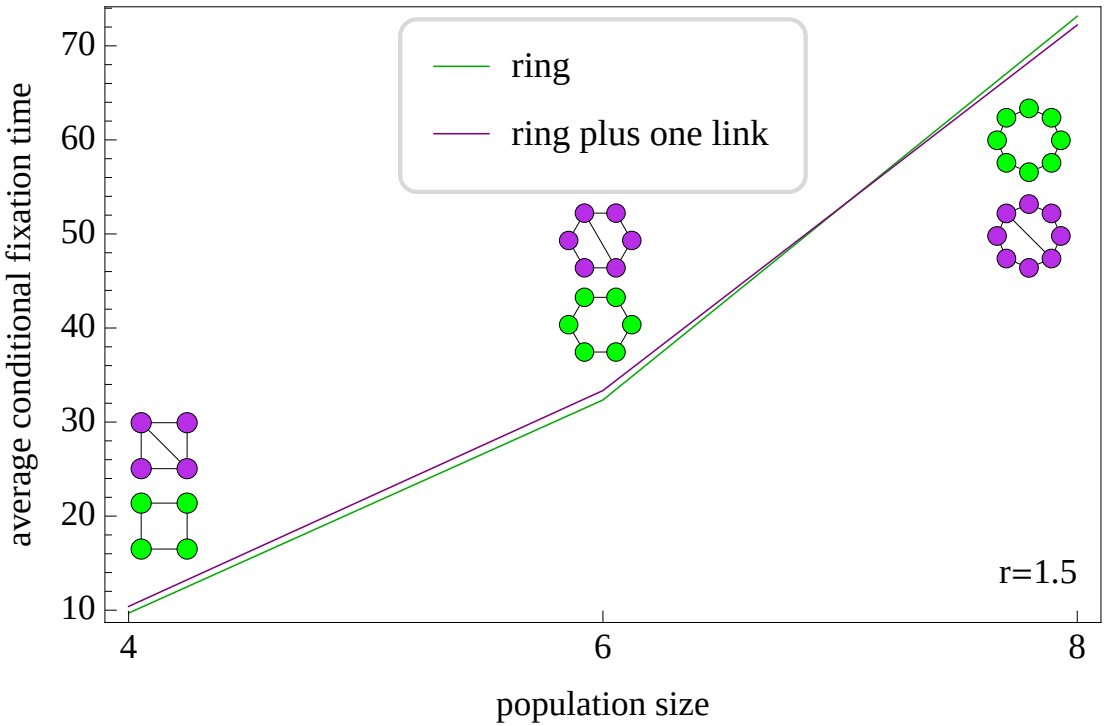
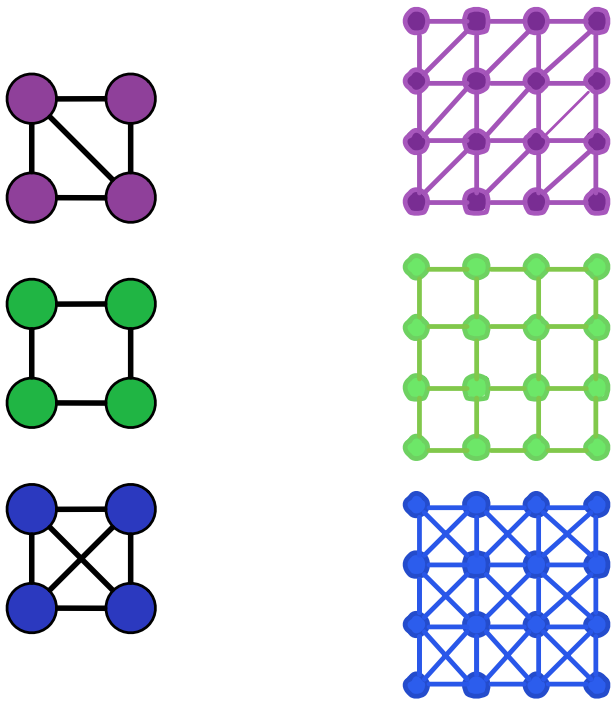
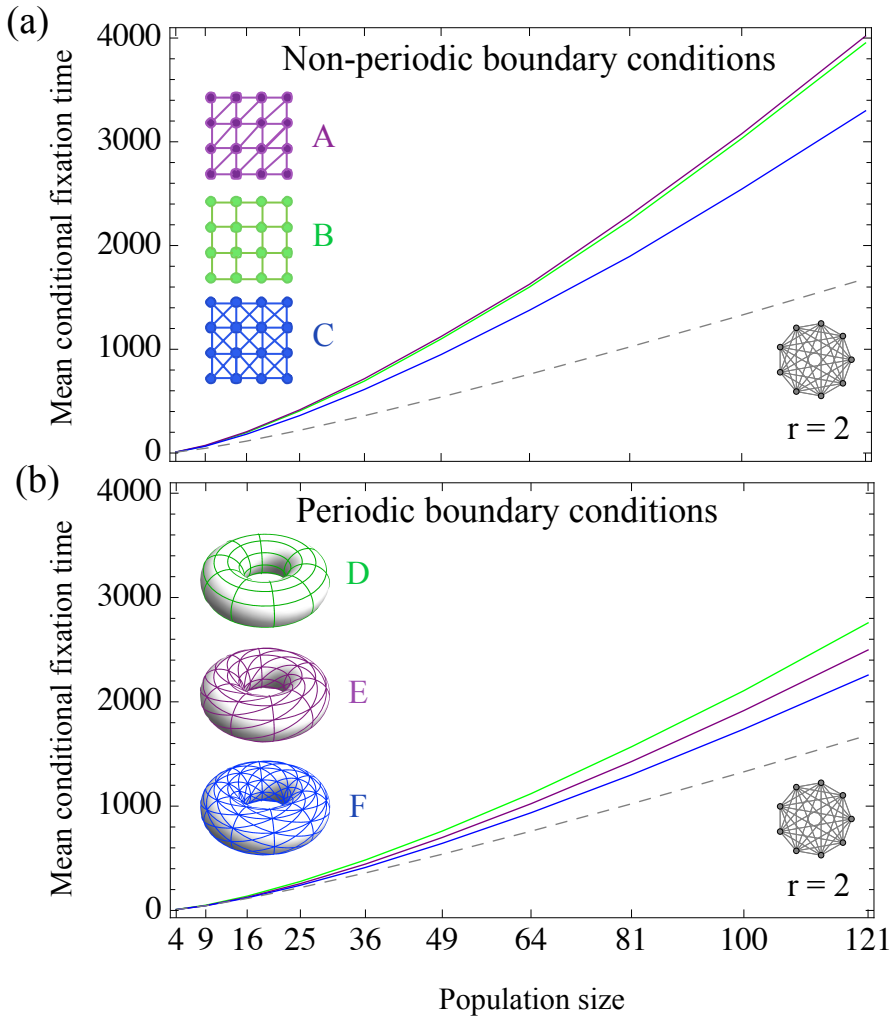


Figure : Influence of the extra link in rings of size four, six and eight. A mutant fitness $r = 1.5$ is used.

Is this effect still present in larger networks?





L. Hindersin & A. Traulsen. Proc. R. Soc. Interface (2014)

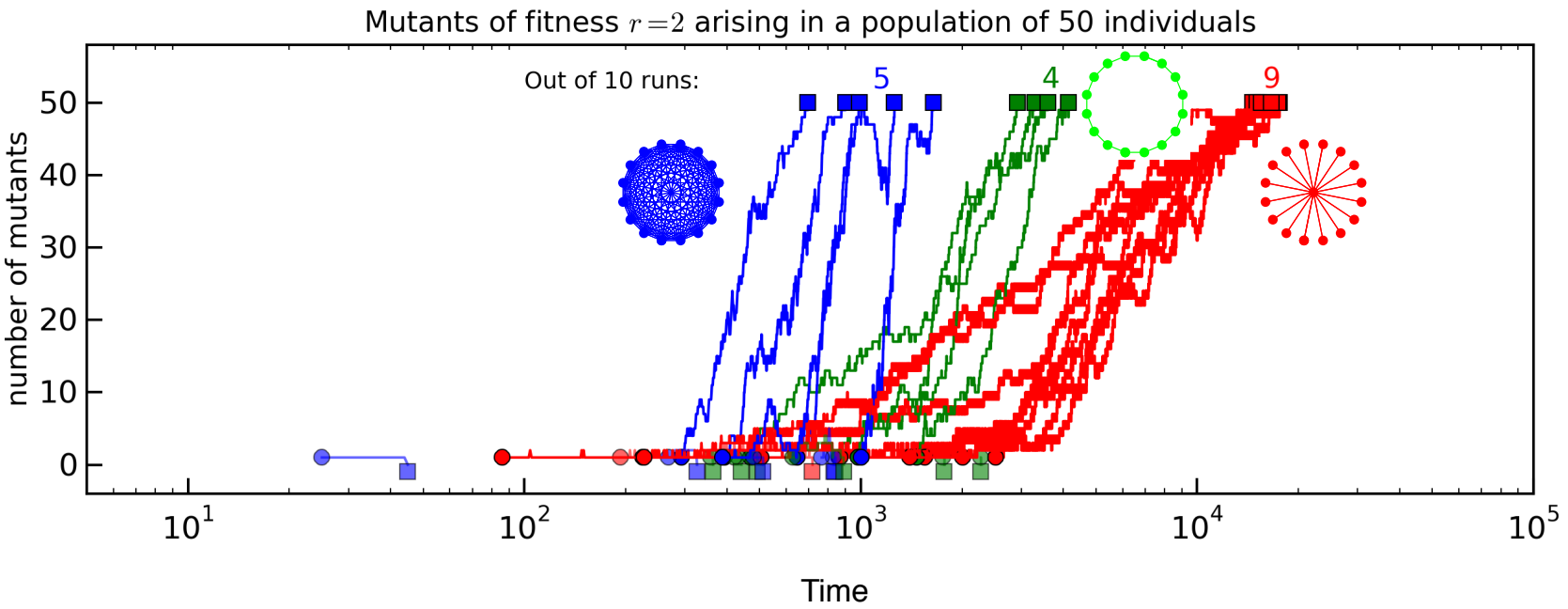
What makes it so hard to answer Question 1

Question 1:
Does every graph that differs from the well-mixed population increase the fixation time of advantageous mutants?

Problems:

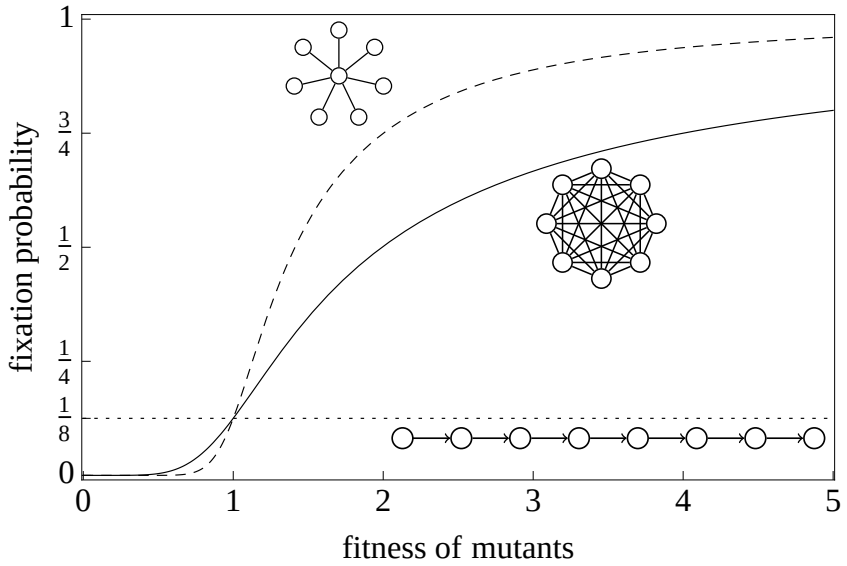
- Non-trivial relationship of the fixation probability and time, because the fixation time depends on the probability.
- For non-isothermal graphs, the transition matrix
  - does not have a tridiagonal shape, since it is generally not a simple birth-death process,
  - can be very large.

Popular Examples



M. Frean et al. Proc. R. Soc. B (2013)

Amplifier and Suppressor of Selection



Graph G is an **amplifier of selection** if

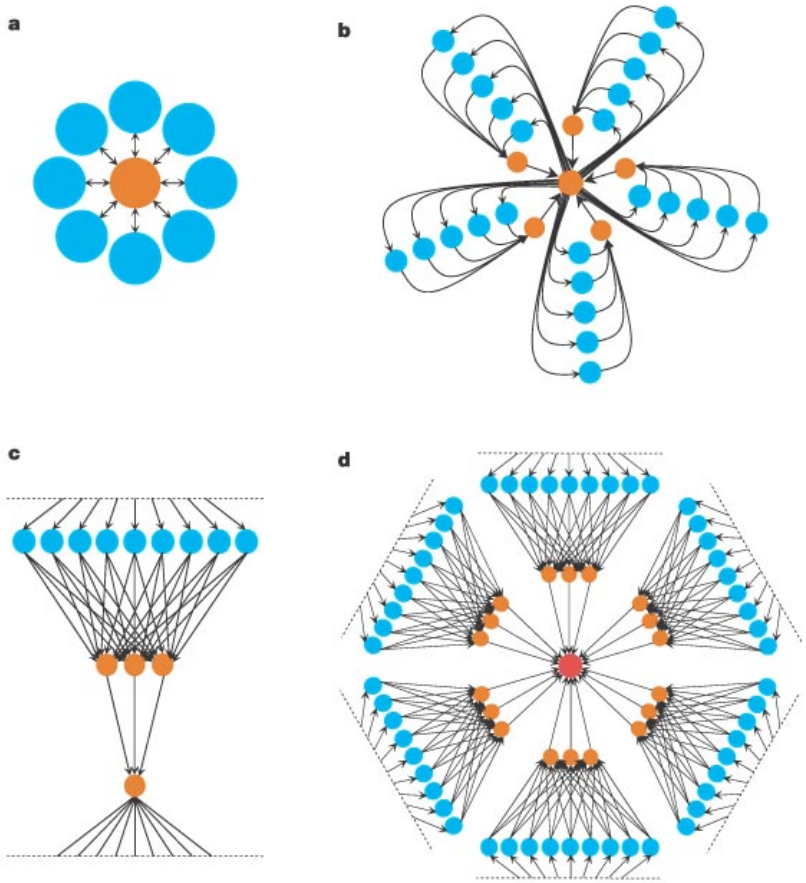
$$r > 1 \quad \Rightarrow \quad \rho_G > \rho_{\mathrm{mix}} \quad \text{and}$$
$$r < 1 \quad \Rightarrow \quad \rho_G < \rho_{\mathrm{mix}}.$$

G is a **suppressor of selection** if

$$r > 1 \quad \Rightarrow \quad \rho_G < \rho_{\mathrm{mix}} \quad \text{and}$$
$$r < 1 \quad \Rightarrow \quad \rho_G > \rho_{\mathrm{mix}}.$$

$$\rho_{\mathrm{star}} = \frac{1 - \frac{1}{r^2}}{1 - \frac{1}{r^{2N}}} \qquad \rho_{\mathrm{mix}} = \frac{1 - \frac{1}{r}}{1 - \frac{1}{r^{N}}} \qquad \rho_{\mathrm{directedLine}} = \frac{1}{N}$$

Amplifiers of Selection



E. Lieberman et al. Nature (2005)

Node Properties

Let $G = (V, E)$ be an undirected graph with N nodes.

The **degree** k_i of a node $i \in V$ is defined by the number of its neighbors:

$$k_i := |\{e_{i,j} : e_{i,j} \in E\}|.$$

The **temperature** $\mathcal{T}_i$ of a node $i \in V$ is defined by the sum over all incoming links, weighted by their degree:

$$\mathcal{T}_i := \sum_{j=1}^{N} \frac{e_{j,i}}{k_j}.$$

Graph Properties

A graph $G = (V, E)$ is called **isothermal** if $\mathcal{T}_i = \mathcal{T}_j$ for all $i, j \in V$.

Denote the fixation probability of a single mutant in a well-mixed population as $\rho_{\text{mix}} := \Phi_1^N$.
A population structure represented by a graph G, where one mutant has fixation probability

$$\rho_G = \rho_{\text{mix}}$$

is called ρ**-equivalent** to the well-mixed population.

Isothermal Theorem

Theorem

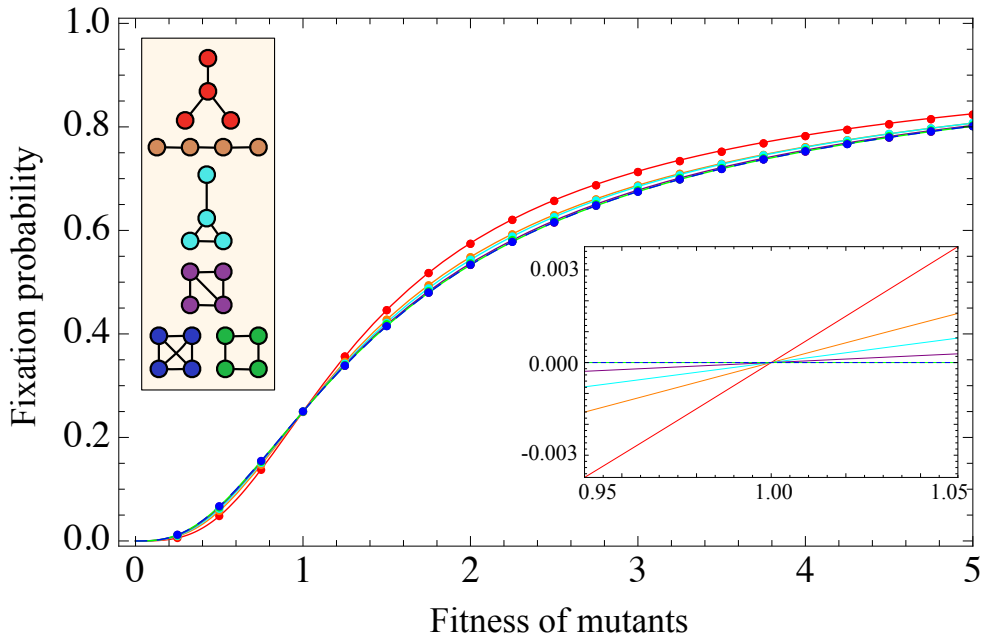
A graph G is ρ-equivalent iff it is isothermal.

A proof can be found in [2].

[2] Lieberman et al. [2005]: *Evolutionary dynamics on graphs.* Nature, 433, Pages 312-316, Supplementary Notes.

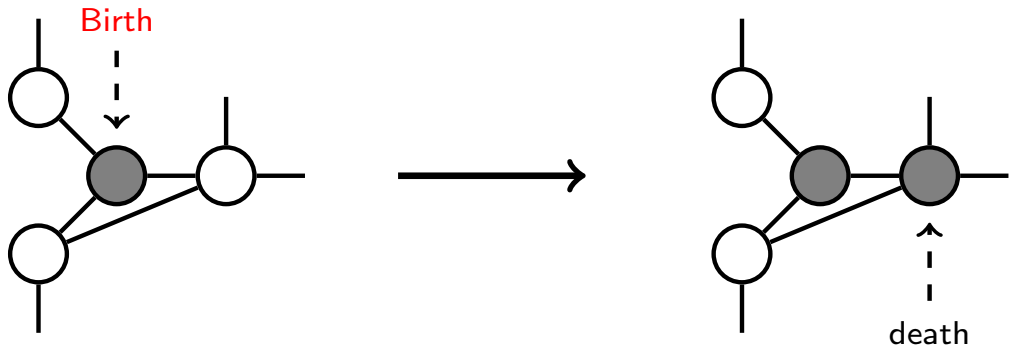
Observation

For size $N = 4$, all non-regular graphs are amplifiers of selection.



Underlying Update Mechanisms

Bd



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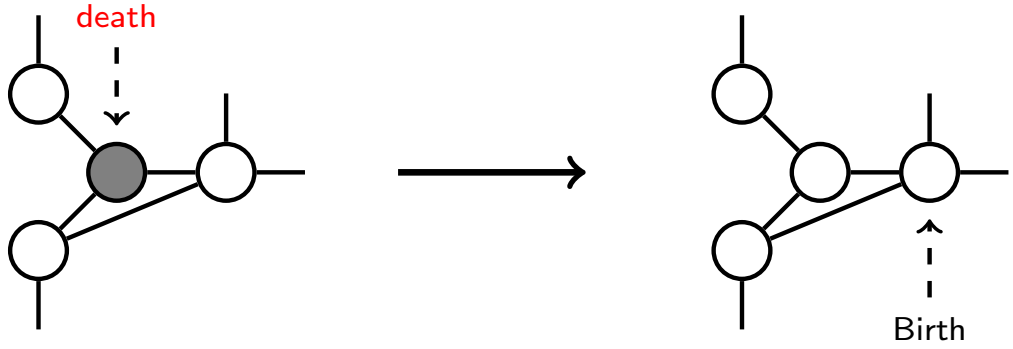
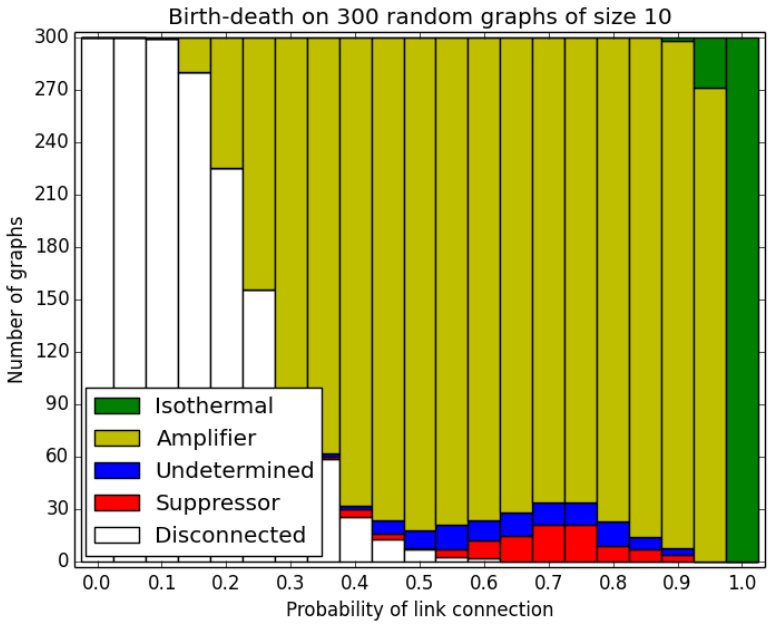


Procedure

- Generate an Erdős-Rényi random graph G for given N and p.
- Calculate the fixation probability ρ_G.
- Compare it to the fixation probability ρ_{mix}.
- Classify as amplifier or suppressor if possible.

Bd



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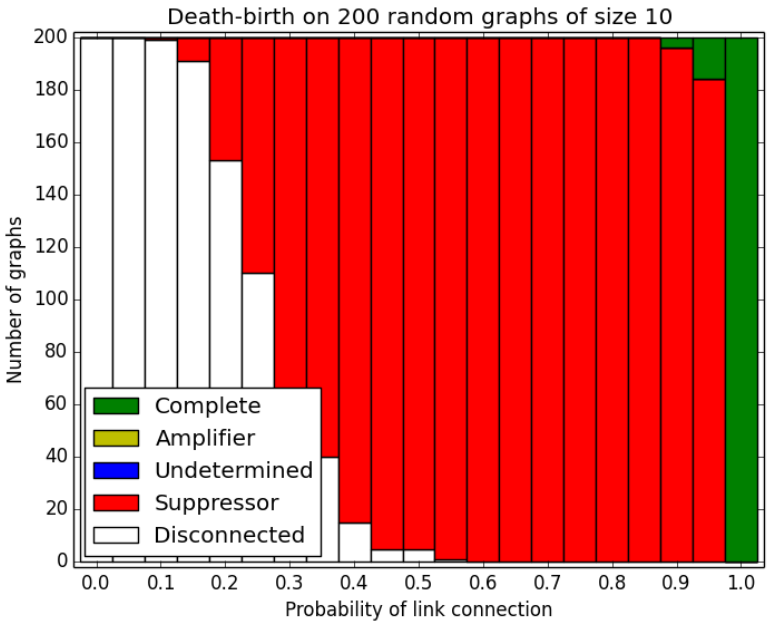


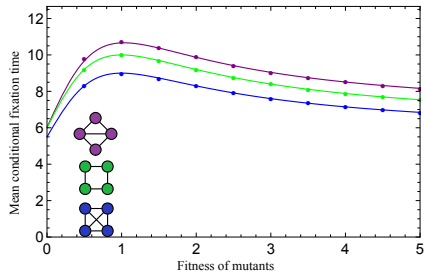
L. Hindersin & A. Traulsen. arXiv:1504.03832 (2015)

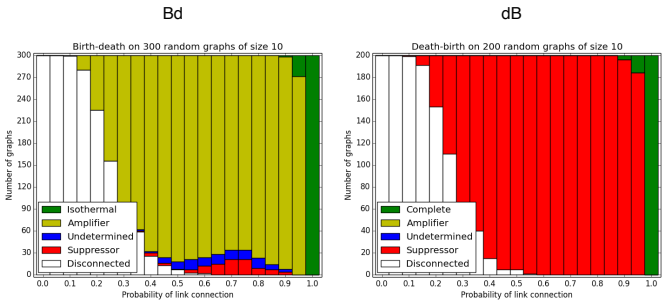
Summary

Changing the structure can have counterintuitive effects on the fixation time.

Bd: almost all random networks are amplifiers.

dB: almost all random networks are suppressors.





Applications

Biological:

- Experimental evolution: Using an amplifier graph increases fixation probability, but the time is increased as well.
- Biological networks, like protein or gene regulatory networks are often scale-free[3]. Scale-free networks can amplify selection.

Social:

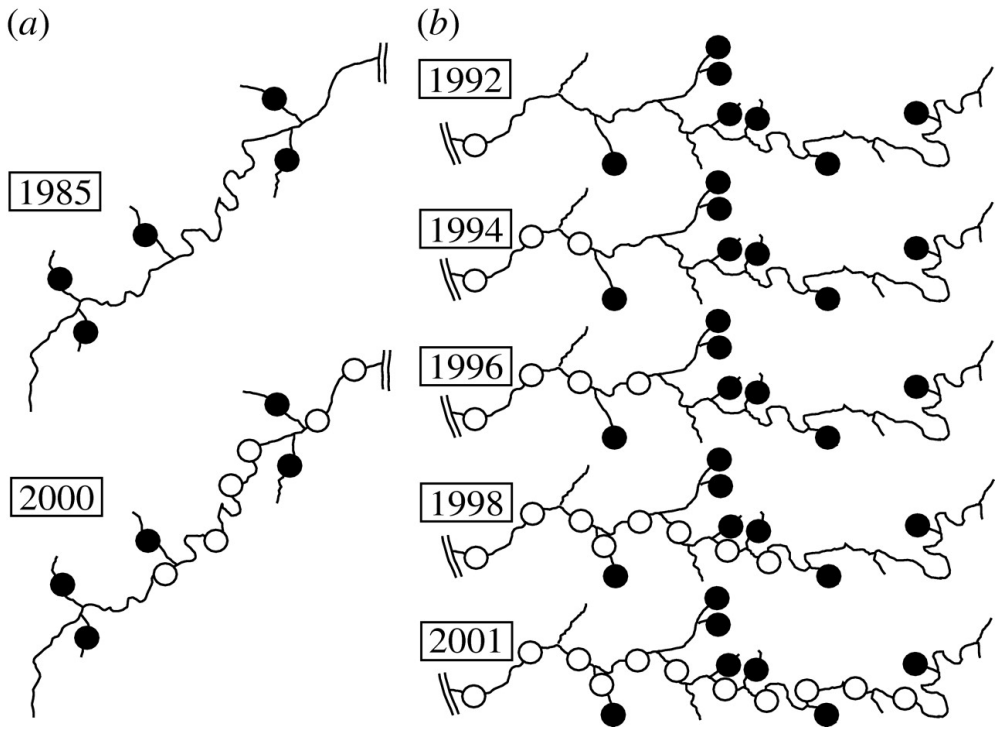
- Social networks: The spreading of ideas can be very likely, but may take a long time.
- Scientific collaborations networks are often scale-free.

[3] R. Albert & A.-L. Barabási, Review of Modern Physics (2002)

Next Step

Consider subpopulations at the nodes. The links determine the migration paths.

Next Step



A. W. Nolte et al. Proc. R. Soc. B (2005)

Acknowledgements

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