Evolutionary Dynamics on Graphs

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Evolutionary dynamics have been traditionally studied in the context of homogeneous or spatially-extended populations[1–3]. Here we generalize population structure by arranging individuals on a graph. Each vertex represents an individual. The weighted edges denote reproductive rates which govern how often individuals place offspring into adjacent vertices. The homogeneous population, described by the Moran process[4], is the special case of a fully connected graph with evenly-weighted edges. Spatial structures are described by graphs where vertices are connected with their nearest neighbors. We also explore evolution on random and scale-free networks[5–6]. We determine the fixation probability of mutants, and characterize those graphs whose fixation behavior is identical to that of a homogeneous population[7]. Furthermore, some graphs act as suppressors and others as amplifiers of selection. It is even possible to find graphs that guarantee the fixation of any advantageous mutant. We also study frequency dependent selection and show that the outcome of evolutionary games can depend entirely on the structure of the underlying graph. Evolutionary graph theory has many fascinating applications ranging from ecology to multi-cellular organization, and economics.

Evolutionary dynamics act on populations. Neither genes, nor cells, nor individuals but populations evolve. In small populations, random drift dominates, whereas large populations are sensitive to subtle differences in selective values. The tension between selection and drift lies at the heart of the famous dispute between Fisher and Wright[8–10]. There is evidence that population structure affects the interplay of these forces[11–15]. But the celebrated results of Maruyama[16] and Slatkin[17] indicate that spatial structures are irrelevant for evolution under constant selection.

Here we introduce evolutionary graph theory, which suggests a promising new lead in the effort to provide a general account of how population structure affects evolutionary dynamics. We study the simplest possible question: what is the probability that a newly introduced mutant generates a lineage that takes over the whole population? This fixation probability determines the rate of evolution, which is the product of population size, mutation rate, and fixation probability. The higher the correlation between the mutant's fitness and its probability of fixation, ρ, the stronger the effect of natural selection; if fixation is largely independent of fitness, drift dominates. We will show that some graphs are governed entirely by random drift, whereas others are immune to drift and are guided exclusively by natural selection.

Consider a homogeneous population of size N. At each time step an individual is chosen for reproduction with a probability proportional to its fitness. The offspring replaces a randomly chosen individual. In this so-called Moran process (Fig 1a), the population size remains constant. Suppose all the resident individuals are identical and one new mutant is introduced. The new mutant has relative fitness r, as compared to the residents, whose fitness is 1. The fixation probability of the new mutant is

$$\rho_1 = \frac{1 - 1/r}{1 - 1/r^N}. \tag{1}$$

This represents a specific balance between selection and drift: advantageous mutations have a certain chance - but no guarantee - of fixation; disadvantageous mutants are likely - but again, no guarantee - to become extinct.

We introduce population structure as follows. Individuals are labelled $i = 1, 2, ...N$. The probability that individual i places its offspring into position j is given by w_{ij}.

Thus the individuals can be thought of as occupying the vertices of a graph. The matrix $W = [w_{ij}]$ determines the structure of the graph (Fig 1b). If $w_{ij} = 0$ and $w_{ji} = 0$ then the vertices i and j are not connected. In each iteration, an individual i is chosen for reproduction with a probability proportional to its fitness. The resulting offspring will occupy vertex j with probability w_{ij}. Note that W is a stochastic matrix, which means that all its rows sum to 1. We want to calculate the fixation probability ρ of a randomly placed mutant.

Imagine that the individuals are arranged on a spatial lattice that can be triangular, square, hexagonal, or any similar tiling. For all such lattices ρ remains unchanged: it is equal to the ρ_1 obtained for the homogeneous population. In fact, it can be shown that if W is symmetric, $w_{ij} = w_{ji}$, then the fixation probability is always ρ_1. The graphs in Fig 2a-c, and all other symmetric, spatially extended models, have the same fixation probability as a homogeneous population[17,18].

There is an even wider class of graphs whose fixation probability is ρ_1. Let $T_i = \sum_j w_{ij}$ be the temperature of vertex i. A vertex is *hot* if it is replaced often and *cold* if it is replaced rarely. The 'isothermal theorem' states that an evolutionary graph has fixation probability ρ_1 if and only if all vertices have the same temperature. Fig 2d gives an example of an isothermal graph where W is not symmetric. Isothermality is equivalent to the requirement that W is doubly stochastic, which means that each row and each column sums to one.

If a graph is not isothermal, the fixation probability is not given by ρ_1. Instead, the balance between selection and drift tilts; now to one side, now to the other.

Suppose N individuals are arranged in a linear array. Each individual places its offspring into the position immediately to its right. The leftmost individual is never replaced. What is the fixation probability of a randomly placed mutant with fitness r? Clearly it is $1/N$ irrespective of r. The mutant can only reach fixation if it arises in the leftmost position, which happens with probability $1/N$. This array is an example of a simple population structure whose behavior is dominated by random drift.

More generally, an evolutionary graph has fixation probability $1/N$ for all r if and

only if it is one-rooted (Fig 2f,g). A one-rooted graph has a unique global source without incoming edges. If a graph has more than one root, then the probability of fixation is always zero: a mutant originating in one of the roots will generate a lineage which will never die out, but also never fixate (Fig 2i). Small upstream populations feeding into large downstream populations are also suppressors of selection (Fig 2h). Thus, it is easy to construct graphs that foster drift and suppress selection. Is it possible to suppress drift and amplify selection? Can we find structures where the fixation probability of advantageous mutants exceeds ρ_1?

The star structure (Fig 3a) consists of a center that is connected with each vertex on the periphery. All the peripheral vertices are connected only with the center. For large N, the fixation probability of a randomly placed mutant on the star is $\rho_2 = (1 - 1/r^2)/(1 - 1/r^{2N})$. Thus, any selective difference r is amplified to r^2. The star acts as evolutionary amplifier, favoring advantageous mutants and inhibiting disadvantageous mutants. The balance tilts towards selection, and against drift.

The super-star, funnel, and metafunnel (Fig 3) have the amazing property that for large N, the fixation probability of any advantageous mutant converges to one, while the fixation probability of any disadvantageous mutant converges to zero. Hence, these population structures guarantee fixation of advantageous mutants however small their selective advantage. In general, we can prove that for sufficiently large population size N, a super-star of parameter K satisfies

$$\rho_K = \frac{1 - 1/r^K}{1 - 1/r^{KN}}. \tag{2}$$

Numerical simulations illustrating eq (2) are shown in Fig 4a. Similar results hold for the funnel and metafunnel. Just as one-rooted structures entirely suppress the effects of selection, super-star structures function as arbitrarily strong amplifiers of selection and suppressors of random drift.

Scale-free networks, like the amplifier structures in Fig 3, have most of their connectivity clustered in a few vertices. Such networks are potent selection amplifiers for mildly advantageous mutants (r close to 1), and relax to ρ_1 for very advantageous

mutants ($r \gg 1$) (Fig 4b).

Further generalizations of evolutionary graphs are possible. Suppose in each iteration an edge ij is chosen with a probability proportional to the product of its weight, w_{ij}, and the fitness of the individual i at its tail. In this case, the matrix W need not be stochastic; the weights can be any collection of non-negative real numbers.

Here the results have a particularly elegant form. In the absence of upstream populations, if the sum of the weights of all edges leaving the vertex is the same for all vertices - meaning the fertility is independent of position - then the graph never suppresses selection. If the sum of the weights of all edges entering a vertex is the same for all vertices - meaning the mortality is independent of position - then the graph never suppresses drift. If both these conditions hold then the graph is called a circulation, and the structure favors neither selection nor drift. An evolutionary graph has fixation probability ρ_1 if and only if it is a circulation (See Fig 2e). It is striking that the notion of a circulation, so common in deterministic contexts like the study of flows, arises naturally in this stochastic evolutionary setting. The circulation criterion completely classifies all graph structures whose fixation behavior is identical to that of the homogeneous population, and includes the subset of isothermal graphs. (The mathematical details of these results are discussed in the supplemental online materials.)

Let us now turn to evolutionary games on graphs[18–19]. Consider, as before, two types A and B, but instead of having constant fitness, their relative fitness depends on the outcome of a game with payoff matrix

$$\begin{array}{cc} & \begin{array}{cc} A & B \end{array} \\ \begin{array}{c} A \\ B \end{array} & \begin{pmatrix} a & b \\ c & d \end{pmatrix} \end{array} \tag{3}$$

In traditional evolutionary game dynamics, a mutant strategy A can invade a resident B if $b > d$. For games on graphs, the crucial condition for A invading B, and hence the very notion of evolutionary stability, can be quite different.

As an illustration, imagine N players arranged on a directed cycle (Fig 5) with player i

placing its offspring into $i+1$. In the simplest case, the payoff of any individual comes from an interaction with one of its neighbors. There are four natural orientations. We discuss the fixation probability of a single A mutant for large N.

(i) Positive Symmetric: i interacts with $i+1$. The fixation probability is given by eq (1) with $r = b/c$. Selection favors the mutant if $b > c$.

(ii) Negative Symmetric: i interacts with $i-1$. Selection favors the mutant if $a > d$. In the classical Prisoner's Dilemma, these dynamics favor unconditional cooperators invading defectors.

(iii) Positive Anti-symmetric: mutants at i interact with $i-1$, but residents with $i+1$. The mutant is favored if $a > c$, behaving like a resident in the classical setting.

(iv) Negative Anti-symmetric: Mutants at i interact with $i+1$, but residents with $i-1$. The mutant is favored if $b > d$, recovering the traditional invasion criterion.

Remarkably, games on directed cycles yield the complete range of pairwise conditions in determining whether selection favors the mutant or the resident.

Circulations no longer behave identically with respect to games. Outcomes depend on the graph, the game, and the orientation. The vast array of cases constitutes a rich field for future study. Furthermore, we can prove that the general question of whether a population on a graph is vulnerable to invasion under frequency-dependent selection is NP-hard.

The super-star possesses powerful amplifying properties in the case of games as well. For instance, in the positive symmetric orientation, the fixation probability for large N of a single A mutant is given by eq (1) with $r = (b/d)(b/c)^{K-1}$. For a super-star with large K, this r value diverges as long as $b > c$. Thus, even a dominated strategy ($a < c$ and $b < d$) satisfying $b > c$ will expand from a single mutant to conquer the entire super-star with a probability that can be made arbitrarily close to 1. The guaranteed fixation of this broad class of dominated strategies is a unique feature of evolutionary game theory on graphs: without structure, all dominated strategies die out. Similar results hold for the super-star in other orientations.

Evolutionary graph theory has many fascinating applications. Ecological habitats

of species are neither regular spatial lattices nor simple 2-dimensional surfaces, as is usually assumed[20−21], but contain locations that differ in their connectivity. In this respect, our results for scalefree graphs are very suggestive. Source and sink populations have the effect of suppressing selection like 1-rooted graphs[22−23].

Another application is somatic evolution within multi-cellular organisms. For example, the hematopoietic system constitutes an evolutionary graph with a suppressive hierarchical organization; stem cells produce precursors which generate differentiated cells[24]. We expect tissues of long-lived multicellular organisms to be organized so as to suppress the somatic evolution that leads to cancer. Star structures can also be instantiated by populations of differentiating cells. For example, a stem cell in the center generates differentiated cells, whose offspring either differentiate further, or revert back to stem cells. Such amplifiers of selection could be used in various developmental processes like affinity maturation of immune response.

Human organizations have complicated network structures[25−27]. Evolutionary graph theory offers an appropriate tool to study selection on such networks. We can ask, for example, which networks are well suited to ensure the spread of favorable concepts. If a company is strictly one-rooted, then only those ideas will prevail that originate from the root (the CEO). A selection amplifier, like a star structure or a scalefree network, will enhance the spread of favorable ideas arising from any one individual. Notably, scientific collaboration graphs tend to be scalefree[28].

We have sketched the very beginnings of evolutionary graph theory by studying the fixation probability of newly arising mutants. For constant selection, graphs can dramatically affect the balance between drift and selection. For frequency dependent selection, graphs can redirect the process of selection itself.

Many more questions lie ahead. What is the maximum mutation rate compatible with adaptation on graphs? How does sexual reproduction affect evolution on graphs? What are the timescales associated with fixation, and how do they lead to coexistence in ecological settings[29]? Furthermore, how does the graph itself change as a consequence of evolutionary dynamics[30]? Coupled with the present work, such studies will

make increasingly clear the extent to which population structure affects the dynamics of evolution.

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Acknowledgments

The Program for Evolutionary Dynamics is supported by Jeffrey Epstein. E.L. is supported by a National Defense Science and Engineering Graduate Fellowship. C.H. is supported in part by the Swiss National Science Foundation 8220-064682. We are deeply indebted to M. Brenner for many helpful discussions.

Competing interests statement The authors declare that they have no competing financial interests.

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Figure legends

Figure 1: Models of evolution. **a**, The Moran process describes stochastic evolution of a finite population of constant size. In each time step, an individual is chosen for reproduction with a probability proportional to its fitness; a second individual is chosen for death. The offspring of the first individual replaces the second. **b**, In the setting of evolutionary graph theory, individuals occupy the vertices of a graph. In each time step, an individual is selected with a probability proportional to its fitness; the weights of the outgoing edges determine the probabilities that the corresponding neighbor will be replaced by the resulting offspring. The process is described by a stochastic matrix W, where w_{ij} denotes the probability that an offspring of individual i will replace individual j. In a more general setting, at each time step, an edge ij is selected with a probability proportional to its weight and the fitness of the individual at its tail. The Moran process is the special case of a complete graph with identical weights.

Figure 2: Isothermal graphs, and, more generally, circulations, have fixation behavior identical to the Moran process. Examples of such graphs include **a**, the square lattice, **b**, hexagonal lattice, **c**, complete graph, **d**, directed cycle, and **e**, a more irregular circulation. Whenever the weights of edges are not shown, a weight of one is distributed evenly across all those edges emerging from a given vertex. Graphs like **f**, the 'burst' and **g**, the 'path' suppress natural selection. The 'cold' upstream vertex is represented in blue. The 'hot' downstream vertices, which change often, are colored in orange. The type of the upstream root determines the fate of the entire graph. **h**, Small upstream populations with large downstream populations yield suppressors. **i**, In multirooted graphs, the roots compete indefinitely for the population. If a mutant arises in a root then neither fixation nor extinction is possible.

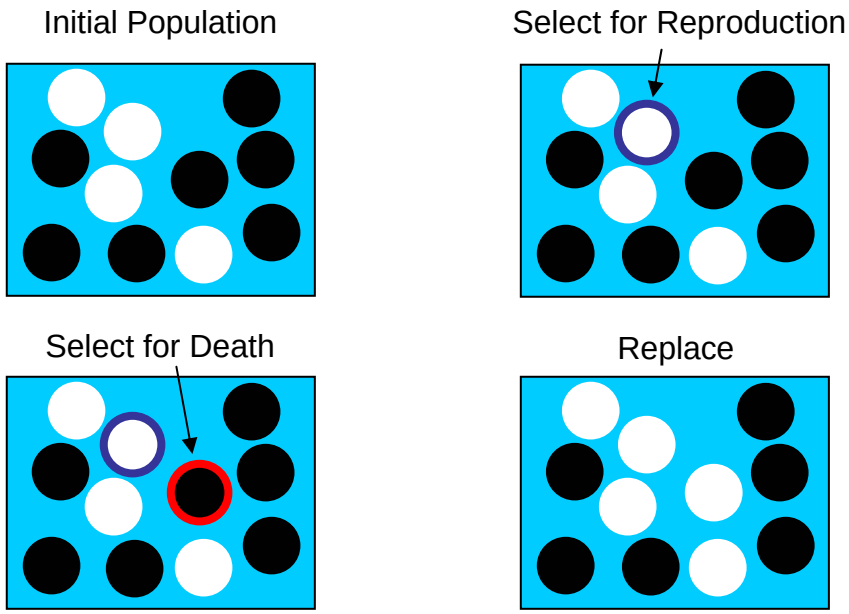
Figure 3: Selection amplifiers have remarkable symmetry properties. As the number of leaves and the number of vertices in each leaf grows large, these amplifiers dramatically increase the apparent fitness of advantageous mutants: a mutant with fitness r on an amplifier of parameter K will fare as well as a mutant of fitness r^K in the Moran process. **a**, The star structure is a $K = 2$ amplifier. **b**, The super-star, **c**, the funnel, and **d**, the metafunnel can all be extended to arbitrarily large K thereby guaranteeing the fixation of any advantageous mutant. The latter three structures are shown here for $K = 3$. The funnel has edges wrapping around from bottom to top. The metafunnel has outermost edges arising from the central vertex (only partially shown). The colors red, orange, and blue indicate hot, warm, and cold vertices.

Figure 4: Simulation results showing the likelihood of mutant fixation. **a**, Fixation probabilities for an r=1.1 mutant on a circulation (black), a star (blue), a $K = 3$ super-star (red), and a $K = 4$ super-star (yellow) for varying population sizes N. Simulation results are indicated by points. As expected, for large population sizes, the simulation results converge to the theoretical predictions (broken lines) obtained using eq (2). **b**, The amplification factor K of scalefree graphs with 100 vertices and an average connectivity of $2m$ with $m = 1$ (violet), $m = 2$ (purple), or $m = 3$ (navy) is compared to that for the star (blue line) and for circulations (black line). Increasing m increases the number of highly connected hubs. Scalefree graphs do not behave uniformly across the mutant spectrum: as the fitness r increases, the amplification factor relaxes from nearly 2 (the value for the star) to circulation-like values of unity. All simulations are based on 10^4 - 10^6 runs. Simulations can be explored online at http://www.univie.ac.at/virtuallabs/

Figure 5: Evolutionary games on directed cycles for four different orientations. **a**, Positive symmetric. The invading mutant (red) is favored over the resident (blue) if $b > c$. **b**, Negative symmetric. Invasion is favored if $a > d$. For the Prisoner's Dilemma, the implication is that unconditional cooperators can invade and replace

defectors starting from a single individual. **c**, Positive anti-symmetric. Invasion is favored if $b > d$. We recover the traditional invasion condition of evolutionary game theory. **d**, Negative anti-symmetric. Invasion is favored if $a > c$. The tables are turned: the invader behaves like a resident in a traditional setting.

a



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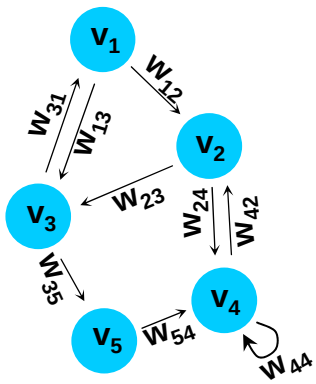
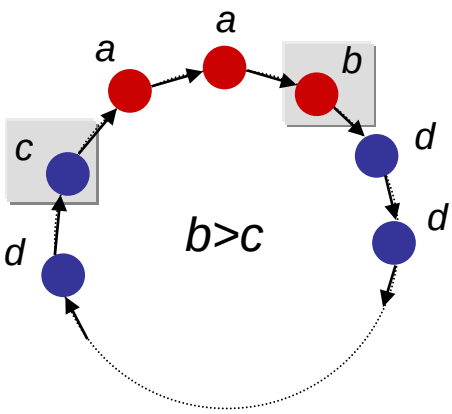
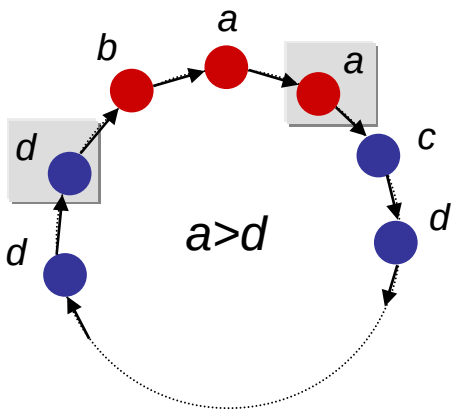


$$W=\begin{bmatrix} 0 & w_{12} & w_{13} & 0 & 0 \\ 0 & 0 & w_{23} & w_{24} & 0 \\ w_{31} & 0 & 0 & 0 & w_{35} \\ 0 & w_{42} & 0 & w_{44} & 0 \\ 0 & 0 & 0 & w_{54} & 0 \end{bmatrix}$$

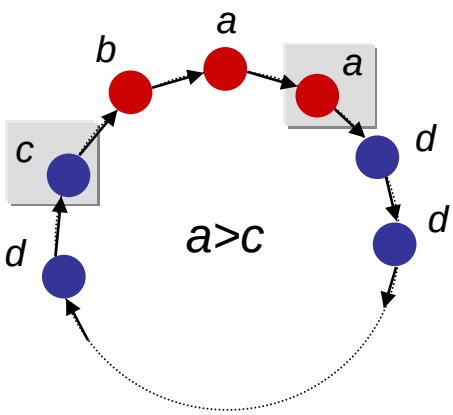
a positive, symmetric



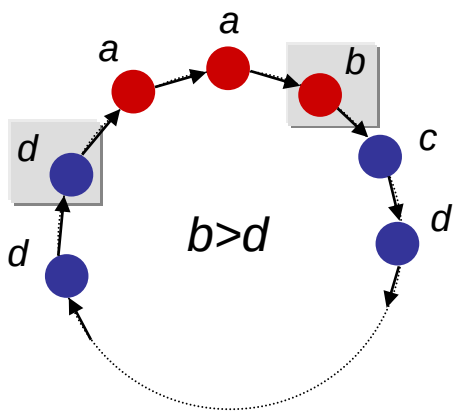
b negative, anti-symmetric

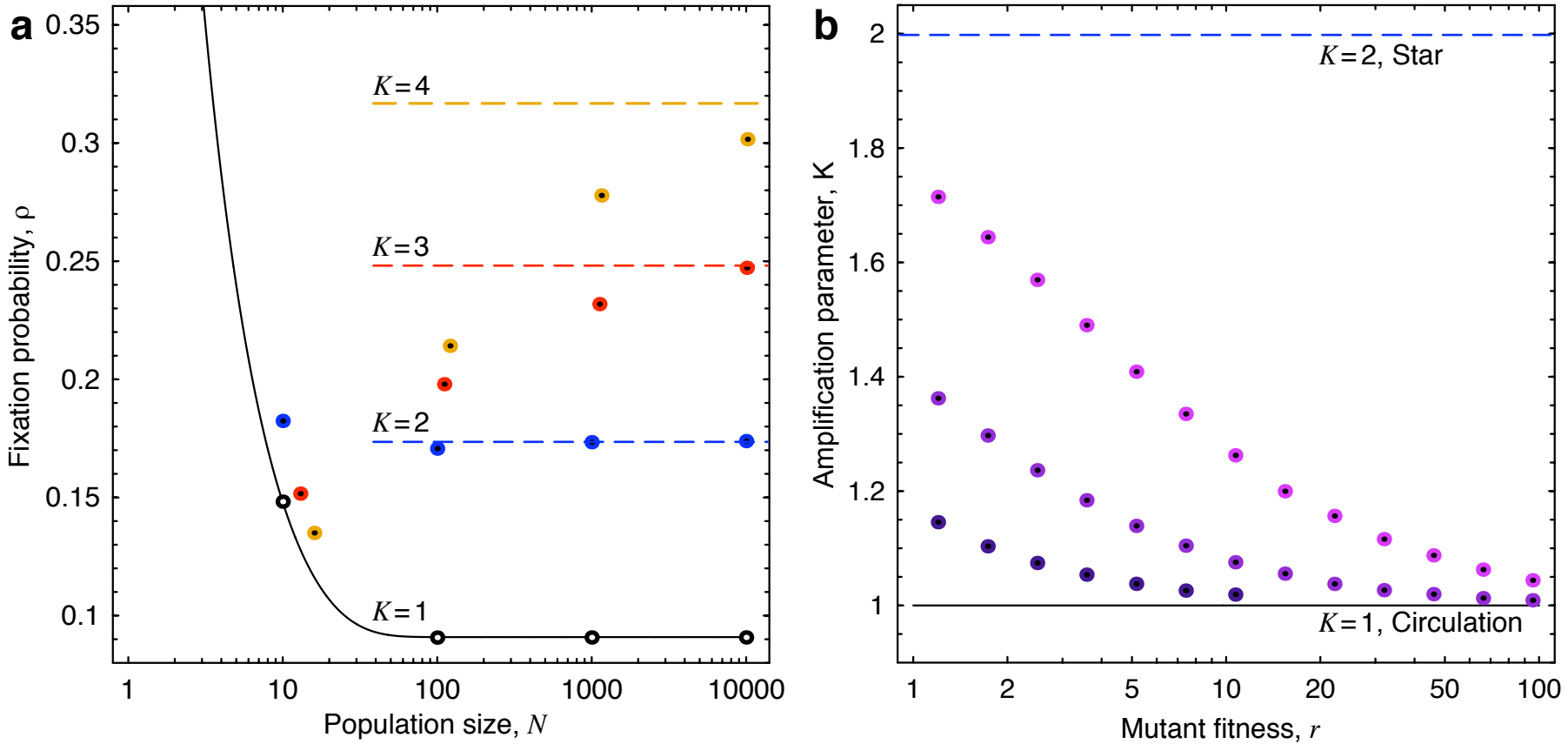


c positive, anti-symmetric



d negative, anti-symmetric

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K=3
K=2
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10
100
1000
10000
Population size, N
b
2
1.8
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Amplification parameter, K
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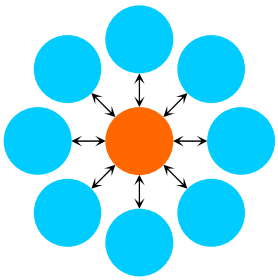

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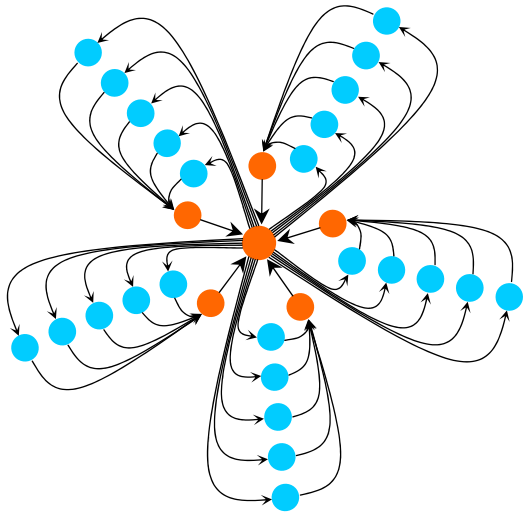

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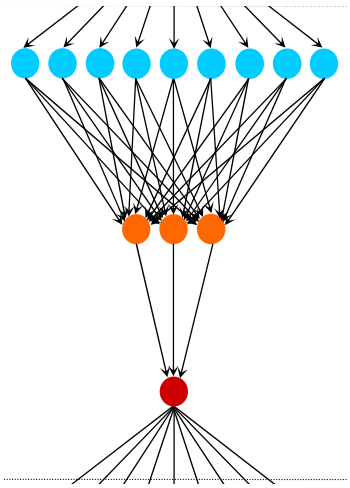

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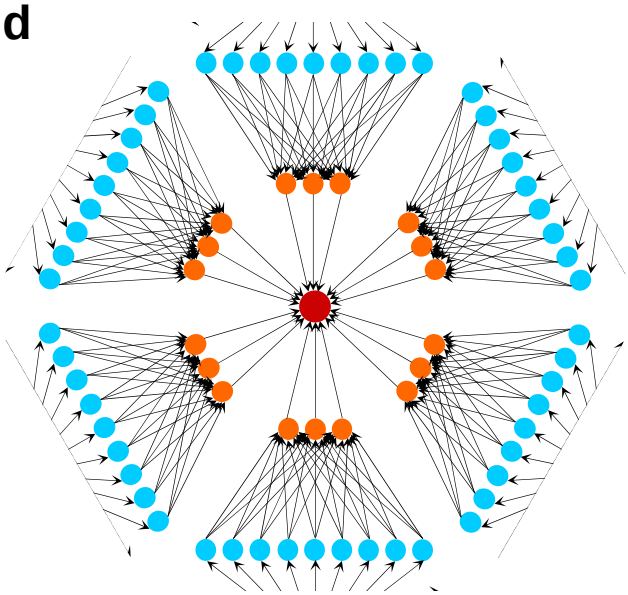

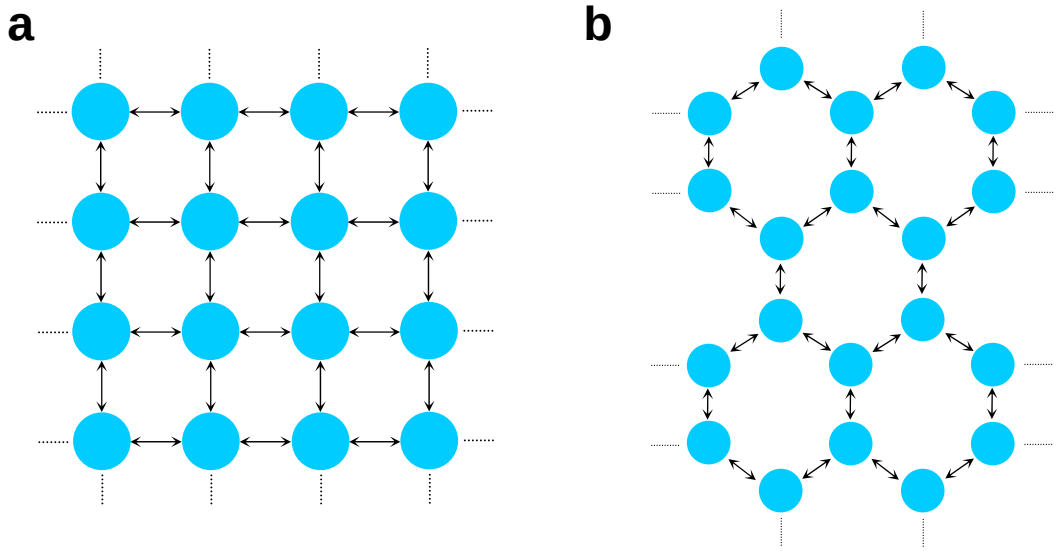
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Supplementary Notes

Here we sketch the derivations of eq (1) for circulations and eq (2) for superstars. We give a brief discussion of complexity results for frequency-dependent selection and the computation underlying our results for directed cycles. We close with a discussion of our assumptions about mutation rate and the interpretations of fitness which these results can accommodate.

Evolution on graphs is a Markov process.

If W is an adjacency matrix, then let G_W be the corresponding graph. Let $\mathbf{P} \subset \mathbf{V}$ be the set of vertices occupied by a mutant at some iteration. $\mathbf{P}$ represents a state of the typical Markov chain E_G which arises on an evolutionary graph. Analogously, the states $P = \{1, 2, ...N\}$ are the typical states of the Moran process M.

(For two types of individuals, the states of the explicit Markov chain E_G are the 2^n possible arrangements of mutants on the graph. The transition probability between two states P, P' is 0 unless $\mid \mathbf{P} \backslash \mathbf{P'} \mid = 1$ or vice versa. Otherwise, if $\mathbf{P} \backslash \mathbf{P'} = v^*$, then the probability of a transition from $\mathbf{P}$ to $\mathbf{P'}$ is

$$\frac{\sum_{v \in G \backslash \mathbf{P}} w(v, v^*)}{N + \mid \mathbf{P} \mid (r-1)}$$

where the numerator is the sum of the weights of edges entering v* from vertices in $\mathbf{P}$. Similarly, the probability of a transition from $\mathbf{P'}$ to $\mathbf{P}$ is

$$\frac{\sum_{v \in \mathbf{P'}} w(v, v^*)}{N + \mid \mathbf{P'} \mid (r-1)}$$

In practice, the resulting matrix is too large and not very sparse. Consequently, it is rarely appealed to directly, and we will not revisit it in the course of these notes.)

We now define the notion of ρ-equivalency.

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Supplementary Notes

Here we sketch the derivations of eq (1) for circulations and eq (2) for superstars. We give a brief discussion of complexity results for frequency-dependent selection and the computation underlying our results for directed cycles. We close with a discussion of our assumptions about mutation rate and the interpretations of fitness which these results can accommodate.

Evolution on graphs is a Markov process.

If W is an adjacency matrix, then let G_W be the corresponding graph. Let $\mathbf{P} \subset \mathbf{V}$ be the set of vertices occupied by a mutant at some iteration. $\mathbf{P}$ represents a state of the typical Markov chain E_G which arises on an evolutionary graph. Analogously, the states $P = \{1, 2, ...N\}$ are the typical states of the Moran process M.

(For two types of individuals, the states of the explicit Markov chain E_G are the 2^n possible arrangements of mutants on the graph. The transition probability between two states P, P' is 0 unless $\mid \mathbf{P} \backslash \mathbf{P'} \mid = 1$ or vice versa. Otherwise, if $\mathbf{P} \backslash \mathbf{P'} = v^*$, then the probability of a transition from $\mathbf{P}$ to $\mathbf{P'}$ is

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where the numerator is the sum of the weights of edges entering v* from vertices in $\mathbf{P}$. Similarly, the probability of a transition from $\mathbf{P'}$ to $\mathbf{P}$ is

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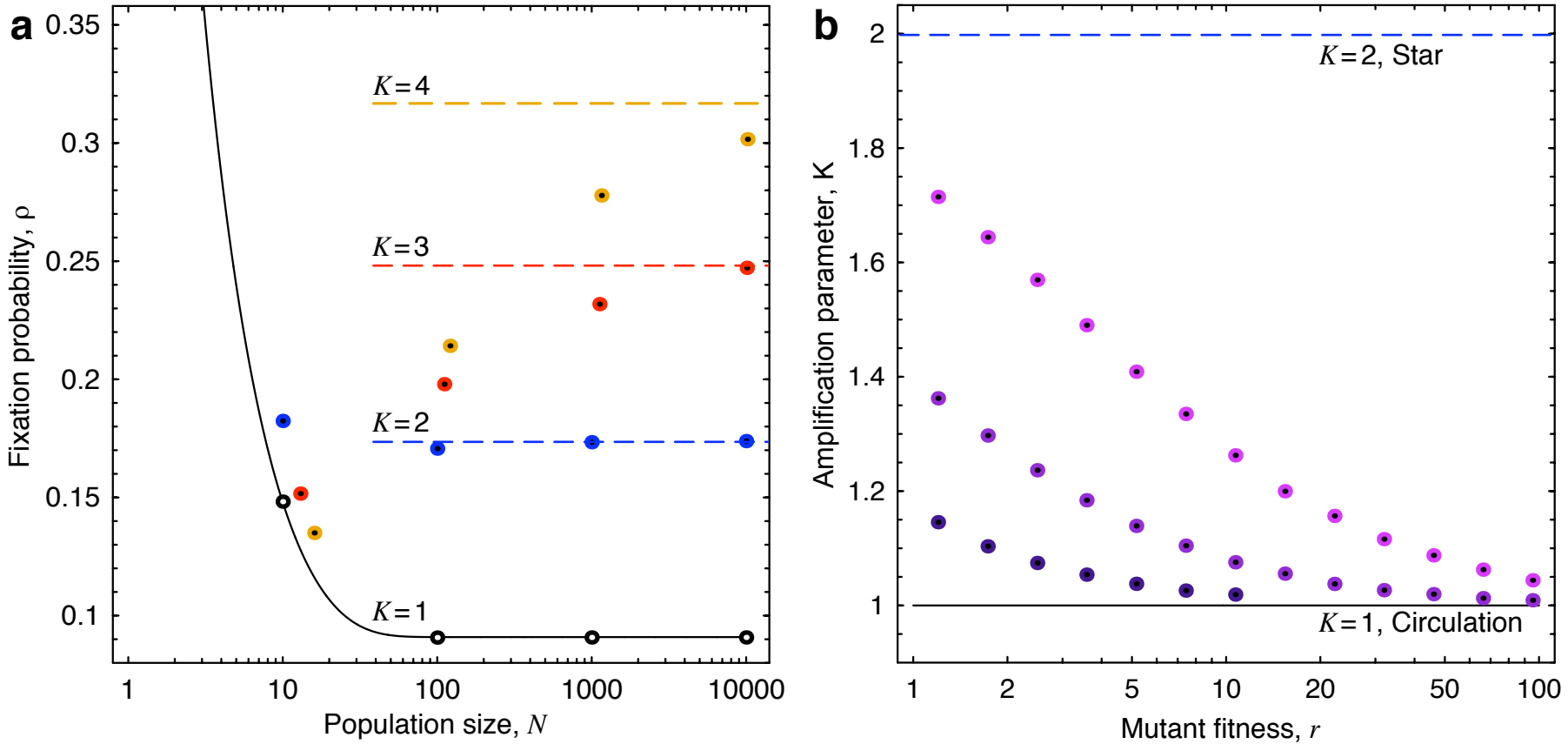
a
0.35
0.3
0.25
0.2
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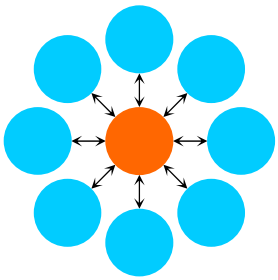
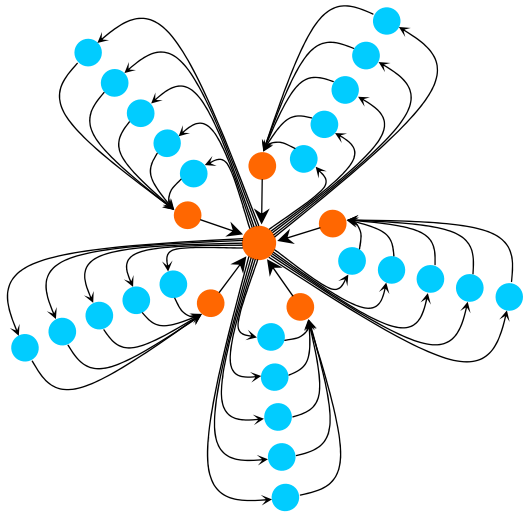
0.1
Fixation probability, ρ
K=4
K=3
K=2
K=1
1
10
100
1000
10000
Population size, N
b
2
1.8
1.6
1.4
1.2
1
Amplification parameter, K
K=2, Star
K=1, Circulation
1
2
5
10
20
50
100
Mutant fitness, r

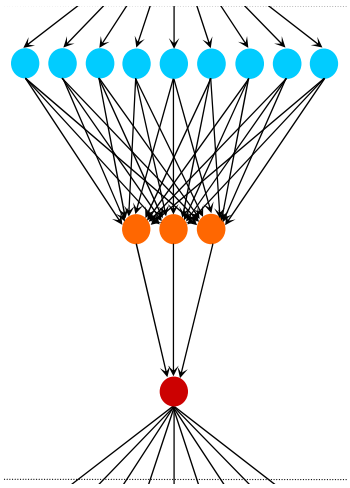
a



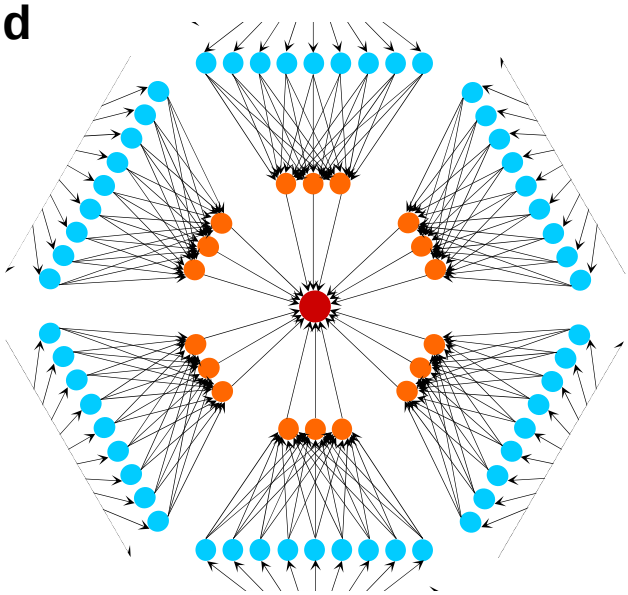
b

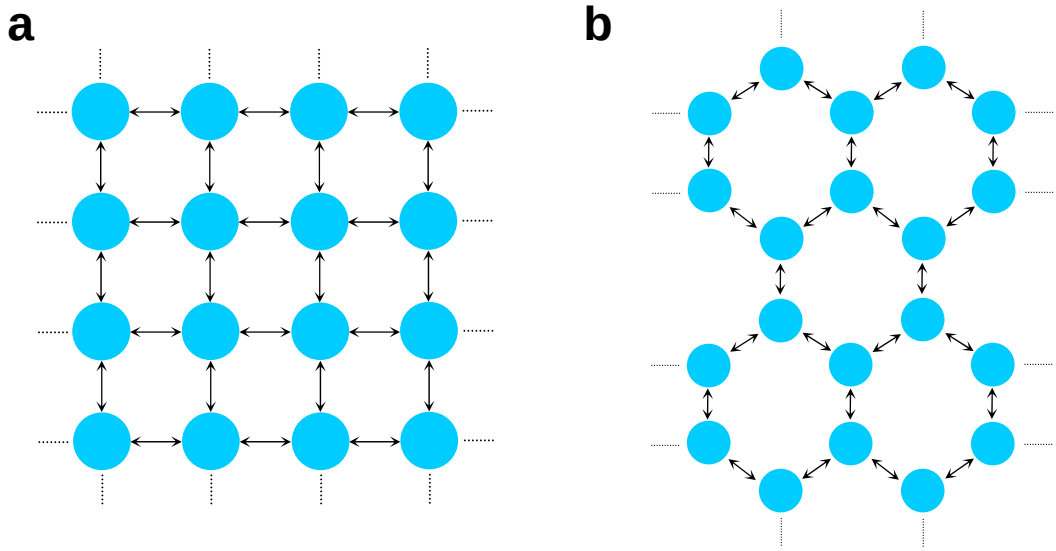


c

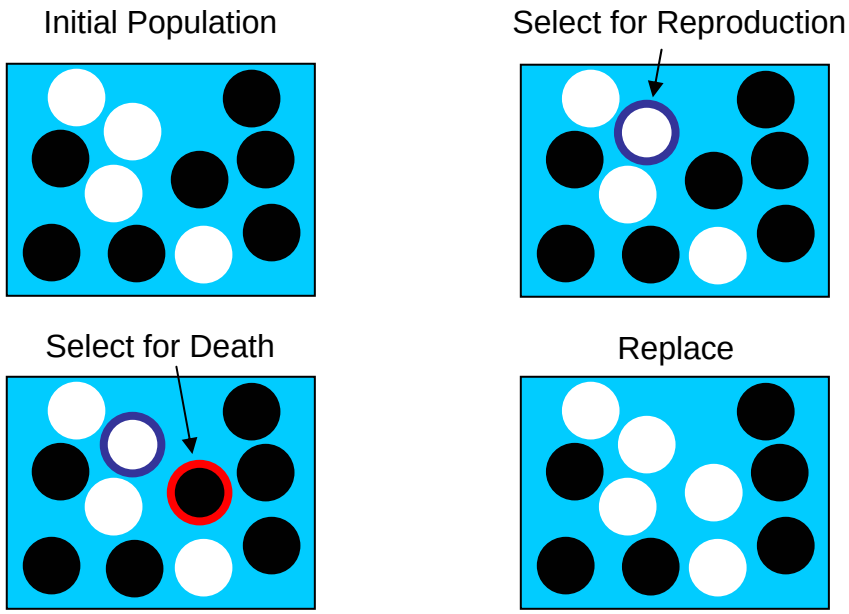


d

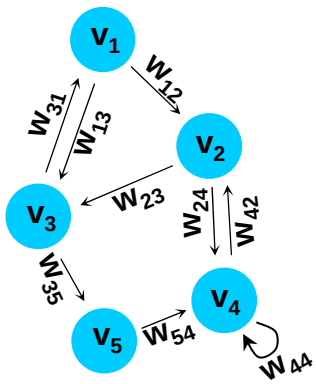



a
b
c
d
e
1/2
1/2
1/2
1/2
1
1/2
1
1/2
2
1/2
3/2
1
1
1
1
f
g
h
i

a

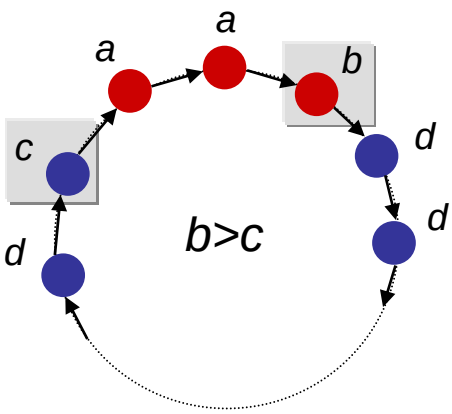


b

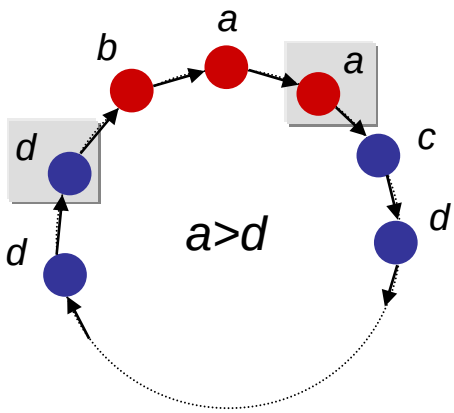


$$W=\begin{bmatrix} 0 & w_{12} & w_{13} & 0 & 0 \\ 0 & 0 & w_{23} & w_{24} & 0 \\ w_{31} & 0 & 0 & 0 & w_{35} \\ 0 & w_{42} & 0 & w_{44} & 0 \\ 0 & 0 & 0 & w_{54} & 0 \end{bmatrix}$$

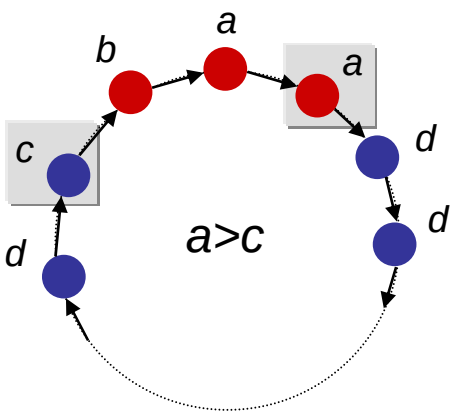
a positive, symmetric



b negative, anti-symmetric



c positive, anti-symmetric



d negative, anti-symmetric