

RESEARCH ARTICLE

Limits on amplifiers of natural selection under death-Birth updating

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Abstract

The fixation probability of a single mutant invading a population of residents is among the most widely-studied quantities in evolutionary dynamics. Amplifiers of natural selection are population structures that increase the fixation probability of advantageous mutants, compared to well-mixed populations. Extensive studies have shown that many amplifiers exist for the Birth-death Moran process, some of them substantially increasing the fixation probability or even guaranteeing fixation in the limit of large population size. On the other hand, no amplifiers are known for the death-Birth Moran process, and computer-assisted exhaustive searches have failed to discover amplification. In this work we resolve this disparity, by showing that any amplification under death-Birth updating is necessarily *bounded* and *transient*. Our boundedness result states that even if a population structure does amplify selection, the resulting fixation probability is close to that of the well-mixed population. Our transience result states that for any population structure there exists a threshold r^* such that the population structure ceases to amplify selection if the mutant fitness advantage r is larger than r^* . Finally, we also extend the above results to δ -death-Birth updating, which is a combination of Birth-death and death-Birth updating. On the positive side, we identify population structures that maintain amplification for a wide range of values r and δ . These results demonstrate that amplification of natural selection depends on the specific mechanisms of the evolutionary process.

Author summary

Extensive literature exists on amplifiers of natural selection for the Birth-death Moran process, but no amplifiers are known for the death-Birth Moran process. Here we show that if amplifiers exist under death-Birth updating, they must be bounded and transient. Boundedness implies weak amplification, and transience implies amplification for only a limited range of the mutant fitness advantage. These results demonstrate that amplification depends on the specific mechanisms of the evolutionary process.

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Introduction

The evolutionary rate of populations is determined by their ability to accumulate advantageous mutations [1–5]. Once a new mutant has been randomly generated in a population, its fate is governed by the dynamics of natural selection and random drift. The most important quantity in this process is the *fixation probability* which is the probability that the invading mutant fixates in the population as opposed to being swept away. A classical mathematical framework for rigorous study of the mutant spread is the discrete-time Moran process [6]. Given a population of N individuals, at each time step, (1) an individual is chosen randomly for reproduction proportionally to its fitness and (2) an individual dies uniformly at random; then the offspring of the reproducing individual replaces the dead individual, and the population size remains constant.

Many evolutionary properties are affected by the spatial arrangement of the population [7–15]. Evolutionary graph theory represents population structure of size N by a graph (network) G_N [16–22]: each individual occupies a vertex, and neighboring vertices mark sites of spatial proximity (see Fig 1a). Mutant spread must respect the structure, in that the offspring of a reproducing individual in one vertex can only move to a neighboring vertex. The Moran process on graphs has two distinct variants:

- In the *Birth-death* Moran process, the death event is conditioned on the Birth event. That is, first an individual is chosen for reproduction and then its offspring replaces a random neighbor (see Fig 1b).
- In the *death-Birth* Moran process, the Birth event is conditioned on the death event. That is, first an individual is chosen for death and then its neighbors compete to fill the vacancy with their offspring (see Fig 1c).

The fixation probability of the invading mutant is a function of its fitness r , as well as the graph G_N . In alignment with most of the literature, we focus on advantageous mutants, where $r > 1$.

The well-mixed population of size N is represented by a complete graph K_N . In the Birth-death Moran process, the fixation probability in the well-mixed population is $\rho^{Bd}(K_N, r) = (1 - 1/r)/(1 - 1/r^N)$ [3]. Under death-Birth updating, the fixation probability is $\rho^{dB}(K_N, r) = (1 - 1/N) \cdot (1 - 1/r)/(1 - 1/r^{N-1})$ [23]. Specifically, as $N \rightarrow \infty$, both the expressions converge to $1 - 1/r$.

Amplifiers of natural selection are graphs that increase the fixation probability of the advantageous mutants compared to the well-mixed population [16, 24]. Under Birth-death updating, many amplifying families of graphs have been constructed, such as the Star graph [25–27], the

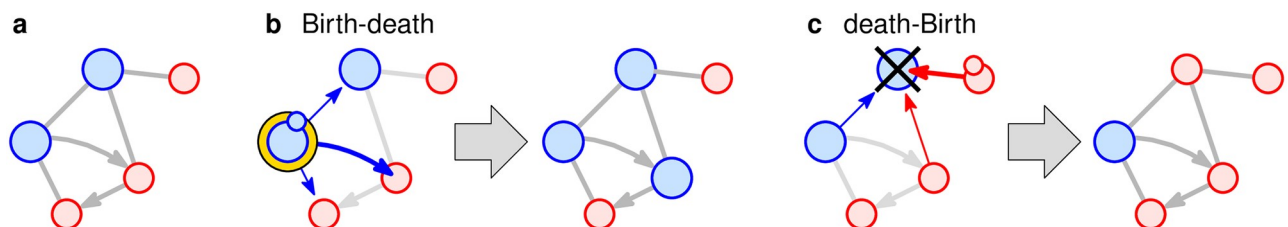


Fig 1. Moran process on graphs. a, The spatial structure is represented by a graph. Each vertex represents a site and is occupied either by a resident (red) with fitness 1 or by a mutant (blue) with relative fitness $r > 1$. Each edge can be one-way (arrow) or two-way. b, In each step of the Birth-death process, one individual is sampled for reproduction proportionally to fitness, and then its offspring replaces a random neighbor. c, In each step of the death-Birth process, a random individual dies and then it is replaced by a neighbor sampled proportionally to fitness.

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Complete Bipartite graph [28] and the Comet graph [29], as well as families that guarantee fixation in the limit of large population size [16, 30–33]. Extensive computer simulations on small populations have also shown that many graphs have amplifying properties [34–37]. While the above results hold for the Birth-death Moran process, no amplifiers are known for the death-Birth Moran process, and computer-assisted search has found that, under death-Birth updating, most small graphs suppress the fixation probability rather than amplifying it [35].

Here we prove two negative results on the existence of amplifiers under death-Birth updating. Our first result states that the fixation probability in any graph is bounded by $1 - 1/(r + 1)$. Hence, even if amplifiers do exist, they can provide only limited amplification. In particular, there are no families of graphs that would guarantee fixation in the limit of large population size. Our second result states that for any graph G_N , there exists a threshold r^* such that for all $r \geq r^*$, the fixation probability is bounded by $\rho^{dB}(r, K_N)$. Hence, even if some graphs amplify for certain values of r , their amplifying property is necessarily transient, and lost when the mutant fitness advantage r becomes large enough. We note that a companion work [38] identifies transient amplifiers among graphs that have weighted edges. Finally, we also study the mixed δ -death-Birth Moran process, for $\delta \in [0, 1]$, under which death-Birth and Birth-death updates happen with rate δ and $1 - \delta$, respectively [39]. We establish analogous negative results for mixed δ -updating, for any fixed $\delta > 0$. Note that as δ vanishes ($\delta \rightarrow 0$), we approach (pure) Birth-death Moran process for which both universal and super amplifiers exist. We find that some of those amplifiers are less sensitive to variations in δ than others. In particular, certain bipartite structures achieve transient amplification for δ as big as 0.5.

Model

The Moran process on graphs

In evolutionary graph theory, a population structure has traditionally been represented by a graph $G_N = (V, E)$, where V is the set of N vertices representing sites and $E \subseteq V \times V$ is the set of edges representing neighborships between the sites. We say that G_N is *undirected* when all edges are two-way, that is, (v, u) is an edge whenever (u, v) is. Since the focus of this work is on death-Birth updating, we require that there are no self-loops in G_N (that is, (u, u) is never an edge). More generally, a population structure can be represented by a *weighted* graph. In that case, every edge (u, v) is assigned a weight $w_{u,v} \in [0, 1]$ which indicates the strength of interaction from site u to site v . In full generality, we allow for non-symmetric weights (that is, possibly $w_{u,v} \neq w_{v,u}$). The family of *unweighted* graphs is recovered when we insist that all edges have weight 1. Even though our primary focus is on unweighted graphs, our results apply to weighted graphs too. A population of N residents inhabits the graph G_N with a single individual occupying each of the vertices of G_N .

In the beginning of the Moran process, one vertex is chosen uniformly at random to host the initial mutant. The mutant has a fitness advantage $r > 1$, whereas each of the residents has fitness normalized to 1. We denote by $f(u)$ the fitness of the individual occupying the vertex u . From that point on, the process proceeds in discrete time steps, according to one of the two variants of updating:

1. Under *death-Birth* (*dB*) updating, first an individual is selected to die uniformly at random. This leaves a vacancy in the corresponding vertex v of G_N and one neighbor of v is randomly chosen to fill it. The probability of choosing a particular neighbor depends on their fitnesses. Specifically, a neighbor u of v is chosen for reproduction with probability proportional to $f(u) \cdot w_{u,v}$, and the selected individual places a copy of itself on v .

- Under *Birth-death (Bd)* updating, first an individual is selected to reproduce with probability proportional to its fitness, that is, with probability proportional to $f(u)$ for the individual occupying the vertex u . The offspring of u then replaces a random neighbor v of u with probability proportional to $w_{u,v}$.

We also consider a combination of dB and Bd updating, which yields the mixed δ -death-Birth Moran process.

- Under δ -death-Birth (δ -dB) updating, for $\delta \in [0, 1]$, in each step, the Moran process follows a dB update with probability δ , and a Bd update with probability $1 - \delta$. In this notation, $\delta = 1$ corresponds to pure dB updating, and $\delta = 0$ corresponds to pure Bd updating.

We only consider strongly connected graphs for which, with probability 1 in the long run, the Moran process leads either to the fixation of the mutant in the population (all vertices are eventually occupied by mutants) or to the extinction of the mutant (all vertices are eventually occupied by residents). We denote by $\rho^{dB}(G_N, r)$, $\rho^{Bd}(G_N, r)$ and $\rho^\delta(G_N, r)$ the fixation probability under dB, Bd and δ -dB updating, respectively.

Amplifiers

The well-mixed population is modelled by the undirected complete graph K_N . When $r \neq 1$, the fixation probability on K_N under Bd updating is [3]

$$\rho^{Bd}(K_N, r) = \frac{1 - 1/r}{1 - 1/r^N}. \tag{1}$$

Similarly, the fixation probability on K_N under dB updating is [23]

$$\rho^{dB}(K_N, r) = \left(1 - \frac{1}{N}\right) \cdot \frac{1 - 1/r}{1 - 1/r^{N-1}}. \tag{2}$$

Specifically, as $N \rightarrow \infty$, both the expressions converge to $1 - 1/r$ when $r > 1$ and to 0 when $r < 1$.

Population structure can affect the fixation probability of invading mutants. Amplifiers are population structures that exaggerate the effect of selection—they increase the fixation probability of advantageous mutants and decrease the fixation probability of disadvantageous mutants. Formally, for fixed $r > 1$ we say that a graph G_N is a Bd (resp., dB) r -amplifier if $\rho^{Bd}(G_N, r) > \rho^{Bd}(K_N, r)$ (resp., $\rho^{dB}(G_N, r) > \rho^{dB}(K_N, r)$). Conversely, for fixed $r \in (0, 1)$ we say that a graph G_N is a Bd (resp., dB) r -amplifier if $\rho^{Bd}(G_N, r) < \rho^{Bd}(K_N, r)$ (resp., $\rho^{dB}(G_N, r) < \rho^{dB}(K_N, r)$). If G_N is an r -amplifier for all $r > 0$, then we say that G_N is a *universal amplifier*. (In the earlier literature, the word “amplifier” had typically been used to mean “universal amplifier”.) If G_N is an r -amplifier for only a limited range of r -values, that is, there exists a threshold value r^* such that G_N does not increase the fixation probability for any $r > r^*$, we say that G_N is a *transient amplifier*. (Note that, in principle, an amplifier could be neither universal nor transient—it could indefinitely alternate between amplifying and suppressing as r grows larger.) In this work, we study advantageous mutants ($r > 1$) and provide upper bounds on their fixation probability. Our results thus delimit possible behavior of amplifiers and generally of any other graphs, regardless of how they behave when $r < 1$.

A renowned example of a universal Bd amplifier is a Star graph S_N (of any fixed size $N \geq 3$) which consists of one central vertex connected to each of the $N - 1$ surrounding leaf vertices. The fixation probability of an invading mutant with fitness advantage r depends on its initial placement. When a mutant appears at a leaf, its fixation probability converges to $1 - 1/r^2$ as $N \rightarrow \infty$, whereas when a mutant appears at the center, its fixation probability converges to 0.

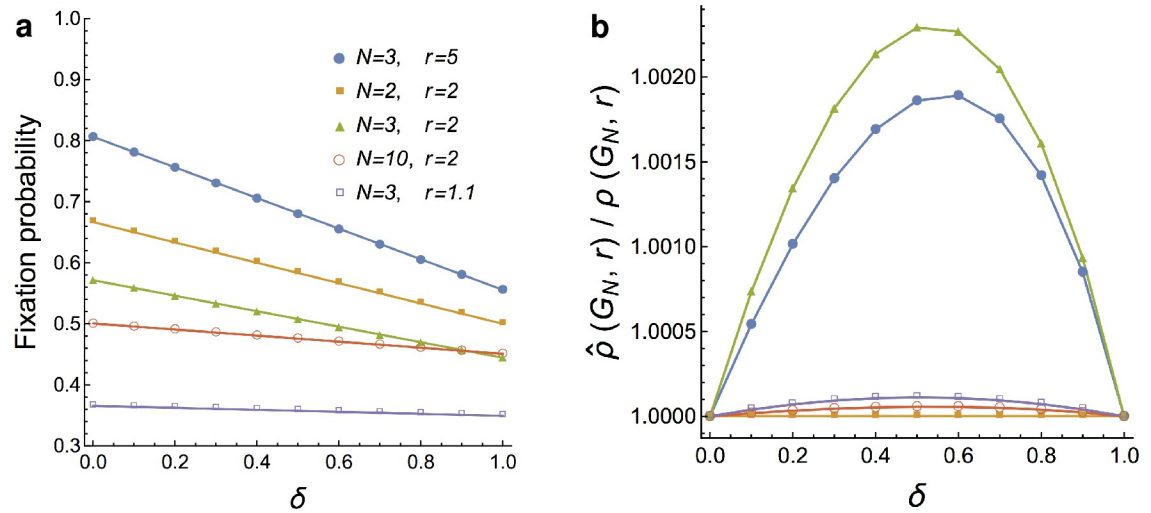


Fig 2. Linear interpolation for δ -dB updating. On a complete graph K_N , the fixation probability $\rho^\delta(K_N, r)$ under δ -dB updating is essentially indistinguishable from the linear interpolation $\hat{\rho}^\delta(K_N, r)$ between fixation probability under pure dB and pure Bd updating. **a**, The x -axis shows $\delta \in [0, 1]$, the y -axis shows the fixation probability $\rho^\delta(K_N, r)$ (marks) and the linear interpolation $\hat{\rho}^\delta(K_N, r)$ (lines) for several pairs (N, r) . The marks lie almost exactly on the lines. **b**, The ratio $\hat{\rho}^\delta(K_N, r) / \rho^\delta(K_N, r)$ is well within 1%, typically even within 0.1% of 1. The interpolation is exact for $N = 2$.

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Averaging over all N possible starting positions we get $\rho^{Bd}(S_N, r) \rightarrow_{N \rightarrow \infty} 1 - 1/r^2$. Effectively, the Star population structure rescales the fitness of the mutant from r to r^2 . Under Bd updating, there also exist population structures that amplify for only some values of $r > 1$ [40].

Although there are simple formulas for fixation probability on K_N under both dB and Bd updating, there seems to be no similarly simple formula for $\rho^\delta(K_N, r)$. One can still use the standard method [3, 41] to write

$$\rho^\delta(K_N, r) = \frac{1}{1 + \sum_{k=1}^{N-1} \prod_{i=1}^k \gamma_i},$$

where γ_i is the bias towards decreasing the number of mutants as opposed to increasing it in one step, but the right-hand side does not simplify. We have computed $\rho^\delta(K_N, r)$ numerically for various values of N and r and we observed that $\rho^\delta(K_N, r)$ is essentially indistinguishable from the linear interpolation

$$\hat{\rho}^\delta(K_N, r) = \delta \cdot \rho^{dB}(K_N, r) + (1 - \delta) \cdot \rho^{Bd}(K_N, r) \tag{3}$$

between $\rho^{Bd}(K_N, r)$ and $\rho^{dB}(K_N, r)$ (see Fig 2a). In fact, the ratio $\hat{\rho}^\delta(K_N, r) / \rho^\delta(K_N, r)$ appears to be well within 1% of 1, and most of the time even within 0.1% of 1 (see Fig 2b). Therefore, in δ -dB updating we use $\hat{\rho}^\delta(K_N, r)$ as the baseline comparison, and say that for $r > 1$ a graph G_N is a δ -dB r -amplifier if $\rho^\delta(G_N, r) > \hat{\rho}^\delta(K_N, r)$.

Implied scale of fitness

Here we are interested in the fixation probability when the population size is large. This leads us to the study of families of graphs $\{G_N\}_{N=1}^\infty$ of increasing population size, the fixation probability of which is taken in the limit of $N \rightarrow \infty$. Graph families can be classified by amplification strength. Given such a family, the implied scale of fitness for that family [24] is a function $\text{isf}(r)$

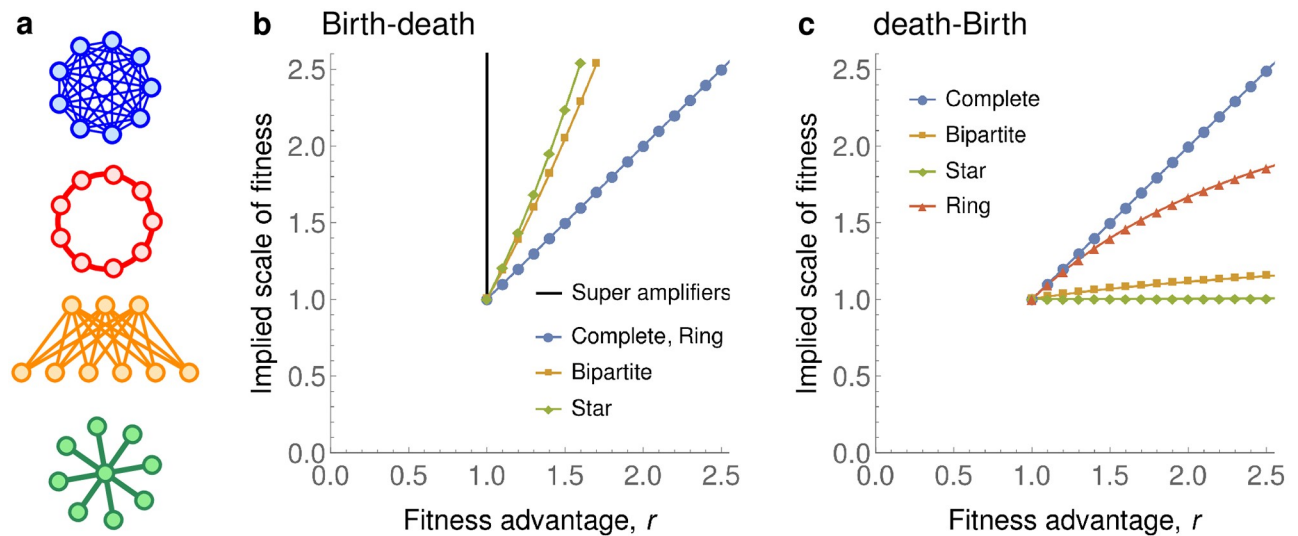


Fig 3. Implied scale of fitness. The implied scale of fitness for several graph families. **a**, Complete graphs K_N , Ring graphs R_N , complete Bipartite graphs $B_{\sqrt{N}, N-\sqrt{N}}$ and Star graphs S_N . **b**, Under Birth-death updating, the Star graphs and the Bipartite graphs are quadratic amplifiers, whereas the Ring graphs are equivalent to Complete graphs. There also exist super amplifiers that guarantee fixation with probability 1 for any $r > 1$. (To model the limit $N \rightarrow \infty$ we show values for $N = 400$.) **c**, Under death-Birth updating, none of Bipartite graphs, Star graphs or Ring graphs amplify selection.

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such that

$$\liminf_{N \rightarrow \infty} \rho^{dB}(G_N, r) = 1 - 1/\text{isf}(r)$$

Specifically, for the family of complete graphs K_N we have $\text{isf}(r) = r$, under both dB updating and Bd updating. We say that the family is (at most) a bounded amplifier if $\text{isf}(r) \leq r + c_0$ for some constant c_0 . We say that the family is (at least) a linear amplifier if $\text{isf}(r) \geq c_1 r + c_0$ for some constants $c_1 > 1, c_0$. We say that the family is (at least) a quadratic amplifier if $\text{isf}(r) \geq c_2 r^2 + c_1 r + c_0$ for some constants $c_2 > 0, c_1, c_0$. For instance, Star graphs are quadratic amplifiers under Bd updating [3], however they do not amplify under dB updating [23]. Finally, the family is a super amplifier if $\text{isf}(r) = \infty$ for any $r > 1$. That is, for any $r > 1$ we have $\rho^{dB}(G_N, r) \rightarrow 1$ as $N \rightarrow \infty$ and hence fixation is guaranteed in the limit of large population size (see Fig 3). The above definitions carry naturally to the δ -dB Moran process, where the implied scale of fitness is defined such that

$$\liminf_{N \rightarrow \infty} \rho^\delta(G_N, r) = 1 - 1/\text{isf}(r)$$

Questions

For the Bd Moran process, various results on amplifiers exist. The Star graph is a prominent example of a graph that is a quadratic amplifier for any $r > 1$ [25–29] and there exist super amplifiers, that is, families of graphs that guarantee fixation in the limit of large population size, for any fixed $r > 1$ [16, 30–33]. Furthermore, computer simulations on small populations have shown that many small graphs are amplifiers [34–37]. Given the vast literature on results under Bd updating, the following questions arise naturally.

Q1: Do there exist universal amplifiers for the dB Moran process?

Q2: Do there exist families that are amplifying for the dB Moran process? More specifically, do there exist linear, quadratic, or even super amplifiers?

The first question is concerned with small populations, and asks for a graph that amplifies for all $r > 1$. The second question asks for amplification in the limit of large populations.

Results

Here we establish some useful observations about the dB Moran process, and then answer questions Q1 and Q2.

First, consider the dB Moran process on any (fixed) graph G_N . The fixation probability can be bounded from above in terms of the number of neighbors of the vertex where the initial mutant has appeared. As a simple example, consider that G_N is unweighted and undirected, and each vertex has precisely d neighbors (e.g. a square lattice where $d = 4$). Denote by v the vertex that hosts the initial mutant. We observe that if v is selected for death before any of its d neighbors then the mutants have just gone extinct. Since this event has probability $1/(d + 1)$, the fixation probability is at most $1 - 1/(d + 1) = d/(d + 1)$, regardless of r . A more refined version of this argument, which also accounts for arbitrary graphs, yields the following stronger bound.

Lemma 1. Fix $r > 1$ and let G_N be a graph (possibly with directed and/or weighted edges) with average out-degree d . Then

$$\rho^{dB}(G_N, r) \leq \frac{d \cdot r}{d \cdot r + d + r - 1}.$$

For large enough r and small (fixed) d , the bound of Lemma 1 coincides with the bound we obtained with our intuitive argument above. Observe that even when $r \rightarrow \infty$, the lemma yields an upper-bound on the fixation probability that is strictly less than 1. On the other hand, under Bd updating, the fixation probability tends to 1 as $r \rightarrow \infty$, regardless of the graph. Hence we have the following corollary, which states that for all population structures, Bd updating favors fixation more than dB updating, provided that the fitness advantage is large enough.

Corollary 1. For any graph G_N , there exists some r^* , such that for all $r > r^*$, we have $\rho^{Bd}(G_N, r) > \rho^{dB}(G_N, r)$.

Amplifiers of the dB Moran process

Here we answer the two questions Q1, Q2. We start with Q1 which asks for the existence of universal amplifiers under dB updating. We show the following theorem.

Theorem 1 (All dB amplifiers are transient). Fix a non-complete graph G_N (possibly with directed and/or weighted edges). Then there exists $r^* > 1$ such that for all $r > r^*$ we have $\rho^{dB}(G_N, r) < \rho^{dB}(K_N, r)$, where K_N is the complete graph on N vertices. In particular, we can take $r^* = 2N^2$.

Since our baseline for amplifiers is the complete graph K_N , Theorem 1 implies that, under dB updating, every (unweighted) graph is, at best, a transient amplifier. Moreover, the only graph that may be a universal (that is, non-transient) amplifier is a weighted version of the complete graph K_N . This is in sharp contrast to Bd updating, for which universal amplifiers exist (e.g., the Star graph [28]).

To sketch the intuition behind Theorem 1, consider again our toy example of an unweighted undirected graph G_N where each vertex has precisely d neighbors. Then the fixation probability is at most $d/(d + 1)$, regardless of r . On the other hand, Eq 2 implies that the fixation probability on a complete graph tends to $1 - 1/N$ as $r \rightarrow \infty$. If $d < N - 1$, then $1 - 1/N$ is strictly more than $d/(d + 1)$, hence the graph G_N ceases to amplify in the limit $r \rightarrow \infty$. In the proof, we use Lemma 1 which applies to possibly weighted, directed, and/or non-regular graphs and which yields an explicit bound on the threshold r -value $r^* \leq 2N^2$.

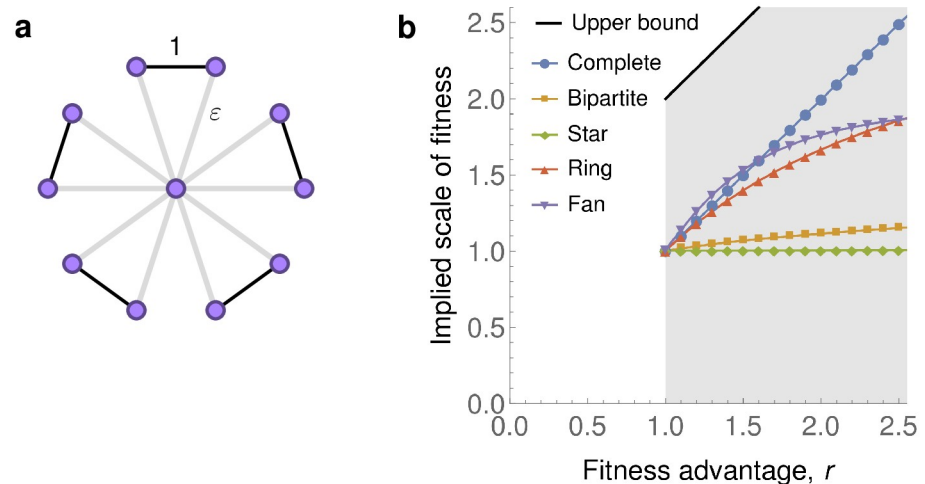


Fig 4. Transient amplifiers under death-Birth updating. A companion work [38] identified certain weighted graphs that are transient dB-amplifiers. **a**, The Fan graph $F_{N,\epsilon}$ with N blades is a weighted graph obtained from a Star graph S_{2N+1} by pairing up the $2N$ leaves and rescaling the weight of each edge coming from the center to $\epsilon < 1$. **b**, The implied scale of fitness of a large Fan (here $N = 101$ and $\epsilon = 10^{-5}$, values computed by numerically solving the underlying Markov chain). If r is small enough then the Fan amplifies selection under dB updating. The level of amplification is well within the scope allowed by Theorem 2 (shaded region). For comparison, we again show the implied scale of fitness for the Complete, Bipartite, Star, and Ring graphs ($N = 400$).

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Second, we turn our attention to question Q2, which asks for the existence of strong amplifying families. We establish the following theorem, which answers Q2 in negative.

Theorem 2 (All dB amplifiers are bounded). *Fix $r > 1$. Then for any graph G_N (possibly with directed and/or weighted edges) we have $\rho^{dB}(G_N, r) \leq 1 - \frac{1}{r+1}$.*

In particular, Theorem 2 implies that, under dB updating, the implied scale of fitness of any graph is at most $r + 1$. Thus every graph is, at best, a bounded amplifier (see Fig 3b). In particular, there exist no linear amplifiers, and thus no quadratic amplifiers or super amplifiers. Again, this is in sharp contrast to Bd updating for which super amplifiers exist [16, 30, 31] and, in fact, are abundant [32].

The proof again follows from Lemma 1: for any $r > 1$, the fraction on the right-hand side of Lemma 1 is at most the desired $1 - 1/(r + 1)$, with equality when $d \rightarrow \infty$.

We remark that even though universal amplification is impossible by Theorem 1, some population structures might achieve a certain level of amplification for a certain range of r -values. In fact, a companion work [38] presents weighted population structures called *Fans* that, in the appropriate limit, amplify selection in a range $1 < r < (1 + \sqrt{5})/2$. The extent to which these structures amplify is well within the bounds provided by Theorem 2 (see Fig 4). It is not known whether there exist unweighted graphs that provide transient amplification.

Extensions to δ -dB amplifiers

Given the negative answers to questions Q1 and Q2 above, we proceed with studying the δ -dB Moran process, in which the death-Birth updates are interleaved with the Birth-death updates. The insight of Corollary 1 is that mutants have a higher fixation probability under Bd updating, compared to dB updating (given a large enough fitness advantage r). Qualitatively, we expect that given a fixed population structure under δ -dB updating, the fixation probability increases as δ decreases. Fig 5 confirms this intuition numerically, for Complete graphs, Ring graphs and Star graphs.

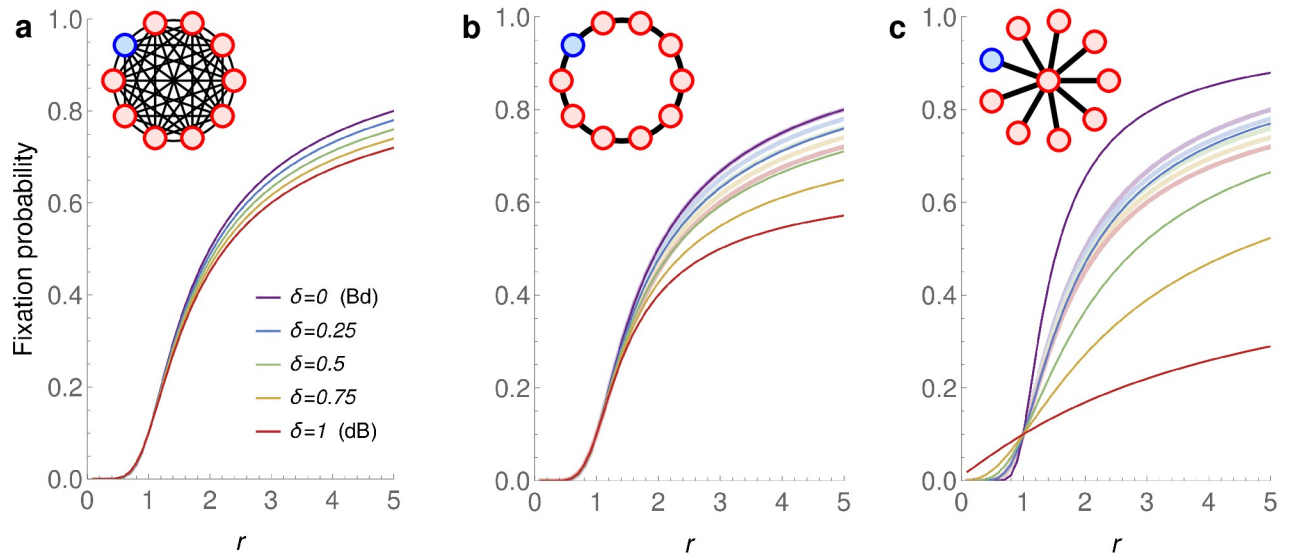


Fig 5. Fixation probability under δ -dB updating. Three different graphs on $N = 10$ vertices: **a** Complete graph, **b** Ring graph, **c** Star graph. For each $\delta \in \{0, 0.25, 0.5, 0.75, 1\}$ we show the fixation probability under δ -dB updating as a function of r . For reference, we show the Complete graph again in panels **b**, **c** (thick faint lines). On the latter two graphs, the dependence of the fixation probability on δ is more pronounced and not roughly linear as is the case for the Complete graph. Due to the isothermal theorem [16], the Complete graph and the Ring have the same fixation probability under Bd updating ($\delta = 0$). The Star graph is an amplifier under Bd updating and also a δ -dB r -amplifier for small δ and $r > 1$ (e.g. for $\delta = 0.2$ and $r = 2$ we have $\rho^\delta(S_{10}, r) > 0.494 > 0.491 > \hat{\rho}^\delta(K_{10}, r)$) but ceases to be an amplifier for large δ (e.g. for $\delta = 0.5$ and $r = 2$ we have $\rho^\delta(S_{10}, r) < 0.37 < 0.47 < \hat{\rho}^\delta(K_{10}, r)$).

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The two extremes of the δ -dB Moran process are the pure Bd ($\delta = 0$) and pure dB ($\delta = 1$) Moran processes. It is known that under Bd updating, both universal amplifiers and super amplifiers exist. On the other hand, we have shown here that under pure dB updating, any amplification is inevitably transient and bounded. The next two natural questions are to investigate whether universal or strong amplifiers exist for small values of $\delta \in (0, 1)$, for which the process is heavily biased towards Bd updating. Perhaps surprisingly, we answer both questions in negative. Concerning universality, we show the following theorem.

Theorem 3 (All δ -dB amplifiers are transient). *Fix a non-complete graph G_N on N vertices (possibly with directed and/or weighted edges) and $\delta \in (0, 1)$. Then there exists $r^* > 1$ such that for all $r > r^*$ we have $\rho^\delta(G_N, r) < \hat{\rho}^\delta(K_N, r)$, where K_N is the complete graph on N vertices.*

Theorem 3 is a δ -dB analogue of Theorem 1. It implies that, compared to the baseline given by a weighted average $\hat{\rho}^\delta(K_N, r)$ between $\rho^{dB}(K_N, r)$ and $\rho^{Bd}(K_N, r)$, every unweighted graph is at best a transient amplifier, and a weighted graph can only be a universal amplifier if it is a weighted version of the complete graph K_N . Hence for any positive $\delta > 0$, no matter how small, universal amplification is impossible among unweighted graphs.

Next, we turn our attention to the limit of large N , and ask whether strong amplification is possible for the δ -dB Moran process. We show the following theorem.

Theorem 4 (All δ -dB amplifiers are at most linear). *Fix $r > 1$ and $\delta \in (0, 1)$. Then for any graph G_N (possibly with directed and/or weighted edges) we have $\rho^\delta(G_N, r) \leq 1 - \frac{1}{(r/\delta)+1}$.*

Theorem 4 implies that for fixed $\delta > 0$, no matter how small, no better than linear amplifiers exist. In particular, there are no quadratic amplifiers and no super amplifiers. For $\delta \rightarrow 1$ (pure dB updating), the bound coincides with the one given in Theorem 2. For $\delta \rightarrow 0$ (pure Bd updating), the bound becomes vacuous (it simplifies to $\rho^{Bd}(G, r) \leq 1$) which is in alignment

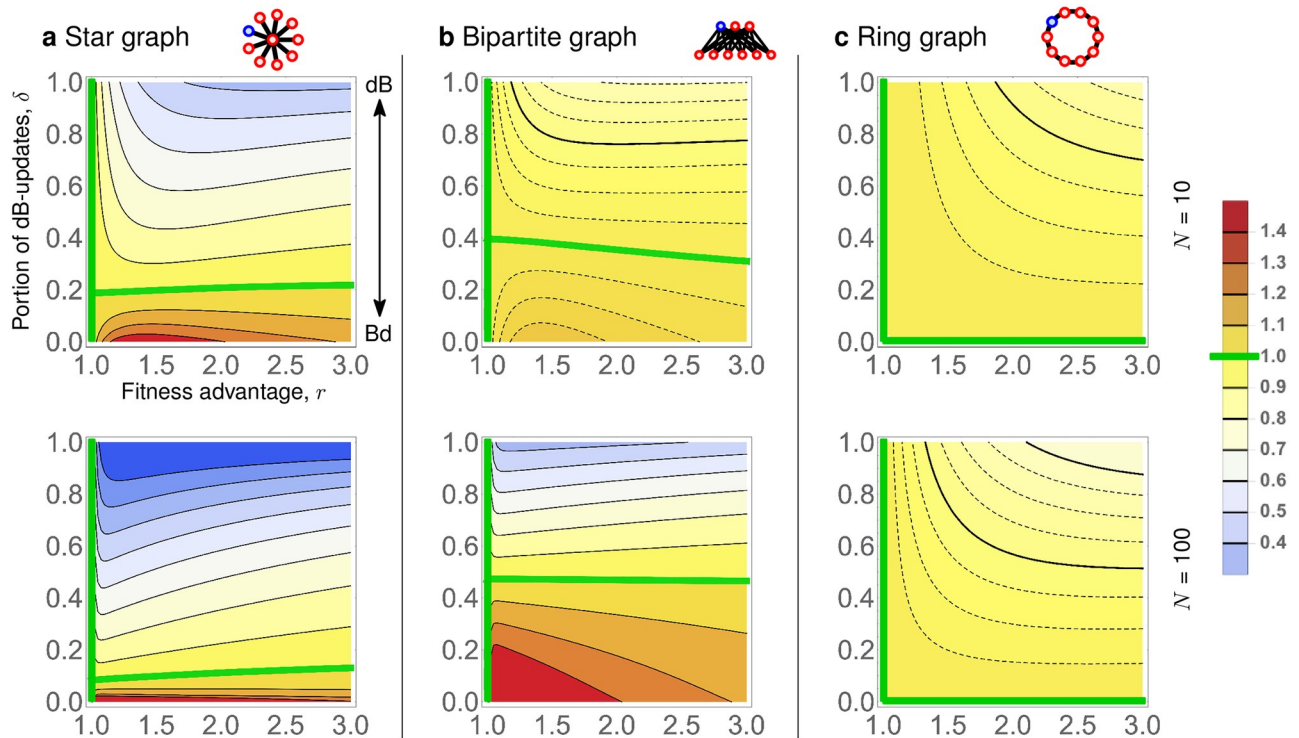


Fig 6. Strength of amplification in terms of r and δ . a, Star graphs, b, complete Bipartite graphs with smaller part of size \sqrt{N} , and c, Ring graphs, of size either $N = 10$ (top row) or $N = 100$ (bottom row). For each of the six graphs, we plot the ratio $\rho^\delta(G_N, r) / \rho^\delta(K_N, r)$ as a function of the fitness advantage r (x -axis) and the portion of dB-updates δ (y -axis). Red (blue) color signifies that the population structure amplifies (suppresses) selection for the given regime (r, δ) . Green curves denote regimes where the ratio equals 1. When $r = 1$, the fixation probability equals $1/N$ regardless of δ and the population structure. By Theorem 3, all δ -amplifiers are transient, hence the “horizontal” green curves eventually hit the x -axis for r large enough. Plotted values were obtained by numerically solving the underlying Markov chain for every $r \in \{1, 1.025, \dots, 3\}$ and $\delta \in \{0, 0.025, \dots, 1\}$.

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with the existence of quadratic and super amplifiers under (pure) Bd updating. The proofs of Theorems 3 and 4 rely on a δ -analogue of Lemma 1.

Even though universal amplification and super amplification are impossible for any $\delta > 0$ due to Theorems 3 and 4, some population structures do achieve reasonable levels of amplification for various combinations of r and δ . Specifically, we consider Star graphs, Bipartite graphs, and Ring graphs of fixed size $N = 10$ and $N = 100$ and show how strongly they amplify, depending on the fitness advantage r of the initial mutant and on the portion δ of dB updates (see Fig 6). We make several observations. First, when δ is small enough, both Star graphs and Bipartite graphs do amplify selection, for a certain range of $r > 1$. Interestingly, large Bipartite graphs are less sensitive to variations in δ than Star graphs, and for small $r > 1$ they maintain amplification even for δ almost as big as 0.5. On the other hand, if δ is small enough, Star graphs tend to achieve stronger amplification than Bipartite graphs. Second, for any of the six population structures and any fixed r , increasing δ diminishes any benefit that the population structure provides to advantageous mutants. Specifically, there appears to be no regime (r, δ) where a ring graph would amplify selection. This observation is consistent with Corollary 1.

Discussion

In this work, we have investigated the existence of amplifiers for the death-Birth (dB) Moran process. We have shown that such amplifiers, if they exist, must be both transient and bounded. Transience means that any population structure can amplify selection only in a

limited range $r \in (1, r^*)$ of relative fitness values r of the mutant. Boundedness means that even when a population structure does amplify selection for a fixed $r > 1$, it can do so only to a limited extent. In particular, quadratic amplification which is achieved by the Star graphs under Birth-death (Bd) updating is impossible to achieve under dB updating. As a consequence, there are no super amplifiers under dB updating. These results are in sharp contrast to the Bd Moran process, for which amplifiers and super amplifiers have been constructed repeatedly [16, 28, 31, 33], and, in fact, can be abundant [35]. Our findings suggest that the existence of amplifiers is sensitive to specific mechanisms of the evolutionary process, and hence their biological realization depends on which process captures actual population dynamics more faithfully.

Note that the situation is more favorable in the broader family of weighted population structures. Under Bd updating, super amplifiers are abundant [32], and under dB updating, transient amplifiers have recently been constructed in a companion work [38]. It remains to be seen whether transient amplification can be achieved by unweighted structures.

To reconcile the apparent discrepancy in the results of the two processes, we have also investigated the mixed δ -dB Moran process, which combines dB and Bd updating. On one hand, we have extended our boundedness and transience results to δ -dB updating. Specifically, our results imply that for any fixed $\delta > 0$, any amplification is necessarily transient and that there are no quadratic amplifiers or super amplifiers under δ -dB updating. In this sense, the case of the (pure) Bd updating is singular. On the other hand, when δ is small, some population structures that amplify for the pure Bd updating ($\delta = 0$) maintain reasonable level of amplification under δ -dB updating, for a wide range of fitness advantages r . Specifically, we find that suitable Bipartite graphs are less sensitive to variations in δ than the Star graphs, and maintain amplification for δ as big as 0.5, when r is close to 1.

There is an interesting connection to the situation of evolutionary games on graphs. There, the desirable population structures are those that promote cooperation. It is known that under any δ -dB updating for $\delta > 0$, population structures can promote cooperation [39], whereas for pure Bd updating, no regular structure that promotes cooperation exists [42]. Therefore, in the setting of games, the desirable structures exist for all $\delta > 0$, whereas in our setting of constant selection, the desirable structures (strong and/or universal amplifiers) exist only in the regime $\delta = 0$. In both settings, the case of pure Birth-death updating appears to be a singular one.

Supporting information

S1 Appendix. Supplementary information for “Limits on amplifiers of natural selection under death-Birth updating”.

(PDF)

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