Moran dynamics in spatially heterogeneous environments with periodic fitness distribution

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Local environmental interactions are a major factor in determining the success of a new mutant in structured populations. Spatial variations of concentration of a resource change the fitness of competing strategies locally and thus can drastically change the outcome of evolutionary process in unintuitive ways. Environmental interactions can be asymmetric, i.e. the same local resource value affects the fitness of strategies differently. The question is how such local environmental variations in network population structures change the condition for selection and fixation probability of an advantageous (or deleterious) mutant. We consider linear graph structure and focus on the case where resources have a spatial periodic pattern. Our model covers several biologically relevant cases. We numerically calculate fixation probability and fixation time for a Moran birth-death process as fitness heterogeneity and period vary. The fixation probability is affected by not only the level of fitness heterogeneity, but also spatial scale of resource variations set by period of distribution $T$. For most (weak) asymmetric environmental interactions the chance of success of a mutant increases with heterogeneity. We identify conditions for which a previously deleterious mutant (in a uniform environment) becomes beneficial as fitness heterogeneity is increased. We observe cases where the fixation probability of both mutant and resident types are less than their neutral value, $1/N$, simultaneously. This corresponds to potential coexistence of resident and mutant types. Finally, we discuss the effect of ‘fitness shift’ where the fitness function of two types has a phase difference. This happens when there are more than one type of resources in the environment. We observe significant increase (or decrease) in the fixation probability of the mutant as a result of such phase shift.

I. INTRODUCTION

Evolutionary dynamics is the study of how strategies arise and compete with each other. Success of a new mutant strategy depends on several factors. In unstructured populations, the fate of a mutant is primarily determined by its relative fitness compared to that of the resident population. Success of a mutant is measured in its ability to establish a finite colony (fixation) [4, 8, 10, 11, 30, 39–41, 47].

Aside from the inherent fitness of competing strategies, other factors such as population structure can influence the outcome of the selection process. Population structure can represent spatial structure such as dispersal patterns in a population, a hierarchical phenotypic structure, or represents vicinity and neighborhood in social networks. There has been a significant amount of literature devoted to understanding the effect of population structure to evolutionary advantage and the fixation probability.

Evolutionary graphs, or network models are suggested as a powerful framework to study population structures [30]. In an evolutionary graph, population resides on nodes of a graph, $G$. Graph connections represent neighborhood topology and migration probability. Lieberman et al showed that a category of graphs known as isothermal graphs have the same fixation probability as that of an unstructured population (complete graph) [1, 30]. Regular undirected graphs are examples of isothermal structures. (A similar observation on regular island networks has been obtained by Maruyama [33–35]). Population structures that increase the fixation probability of a beneficial mutant - relative to that of unstructured populations are known as amplifier of selection [2, 42, 43]. Similarly, graph structures that reduce the fixation probability of an advantageous mutant, compared to that of an unstructured population, are known as suppressors of selection. Extensions to more general graph structures and/or update rules has been discussed in the literature [42, 44, 45, 22, 20, 27, 12, 10].

Fitness of each type or strategy is commonly assumed to be a function of the individual’s genotype or phenotype and decoupled from the population structure. Environmental interactions, however, can significantly contribute to the fitness of a type. Variations in environmental conditions couples the fitness of types with the population structure and makes the prediction of outcome an evolutionary process tediously more difficult.

Resource heterogeneity is a major example of local variations in environmental conditions. For example, in a population of E.coli bacteria, local con-
centration of nutrients (sugar) influences the fitness of E.coli. Higher concentration of nutrients lead to higher reproductive fitness. Competing E.coli strains metabolize different sugar types (glucose, lactose, etc). Variation in a nutrient type affects the fitness of the strain with the corresponding metabolism [27, 28, 35]. In the context of drug resistance, existence of a drug gradient increases the speed of evolution of resistant strains [6, 29, 44]. This is discussed in the context of viral evolution in [25, 38] and cancer evolution in [14, 48].

Environment is modeled as a scalar function denoting resource concentration distributed across the population. The distribution of resources can either be uniform spatially, or vary from location to location. Local interactions of each strategy with the local resources determines the fitness of that type at the given location. The change in fitness depends on the concentration of resource at that location. Environmental interactions can be asymmetric. This means that fitness of a mutant (type A) might not change the same amount as that of resident (type B) when encountered with the same concentration of resource.

Spatial variations in resources requires a unified model that incorporates spatial structure and environmental interactions in one framework. This has been the focus of recent works in literature [12, 13, 15, 23, 24, 31, 32, 36]. Maciejewski et al, and Kaveh et al, suggested to represent a population structure, represented by dispersal graph, G, and resource distribution, represented by a coloring map, C, affects the evolutionary advantage of a randomly placed mutant in a finite population setting. For any given coloring, with N colors, fitness sets of types are given by the vectors, $\mathbf{a} = (a_1, \cdots, a_N)$, $\mathbf{b} = (b_1, \cdots, b_N)$, where $a_i(b_i)$ is the fitness of type A(B) at location $\mathbf{G}$ respectively. We assume there are two resource levels, low-resource (poor) sites and high-resource (rich) sites (two-color scheme). The difference between fitnesses in poor and rich site denotes level of fitness heterogeneity in the system. Beside heterogeneity level, spatial distribution pattern of rich and poor sites, i.e. the coloring map, also affects the outcome of an evolutionary process.

In finite populations, condition for selection is defined as when the fixation probability of a type A (mutant) in a background of type B (resident), $\rho_A$, is larger than the fixation probability of a type B in a background of type A, $\rho_B$.

$$\rho_A(\mathbf{a, b, G}) > \rho_B(\mathbf{a, b, G}).$$

The question is how the changes in fitness heterogeneity from uniformly distributed resource case, changes the condition for selection. Especially, if the mean fitness of the two types is the same, can heterogeneity make one type advantageous relative to the other type? Furthermore, we can ask the same question when we re-distribute the fitnesses in a different spatial pattern.

For constant fitness evolutionary graph models, condition for selection of type A is $r_A > r_B$ where $r_A(r_B)$ is the constant fitness of the type A(B) respectively. Ref. [23] showed that for Complete graph with heterogeneous fitness distributions, similar condition holds in the strong selection limit, where $r_{A,B}$ is the (arithmetic) mean fitness of the corresponding types. We are interested to answer this question for other graph structures and colorings.

For constant fitness evolutionary graph models, the condition for selection coincides with the condition $\rho_A > 1/N > \rho_B$. Another important question is that whether this condition holds for non-uniform resource distributions and graph structures. Beside condition for selection we are interested on measures of evolutionary success as fixation probability and time-to-fixation of a mutant for a given fitness distribution and heterogeneity.

The answers to the above questions in the presence of an arbitrary fitness distribution are quite complex and depend on particular graph structure and colorings (i.e. fitness distributions $\mathbf{a, b}$). We focus on linear graph structure and spatially periodic distribution of resources (see figure 1). For periodically distributed fitness models, the heterogeneity is determined by two characteristic scales: 1) heterogeneity level, i.e. difference between fitness of poor and rich sites. 2) Period of distribution $T$. This is the length scale that fitness variation occurs.

The periodic fitness distribution has important biological and physical examples. When period is small, $T \sim 2$, rich and poor sites are well-mixed. This can be used as a periodic approximation of fine-grained (random) heterogeneities. When the system is divided into two geographically distinct environments, maximal period, $T = N$ is a good approximation. This is representative of two-island subdivided population models while unlike past works, the underlying population structure inside each island, a linear graph in this case, is taken into account.

For the current work we assume that the fitness contribution from environmental interaction is additive, i.e. it adds up to the inherent fitness of each type. Without loss of generality, we also shift the overall fitness of each type such that uniform resource distribution has no change in fitness of each
type. This underlines the effect of spatial environmental and resource variations.

We discuss how condition for selection and fixation probability of a beneficial mutant \( (r_A > r_B) \) (or neutral \( r_A = r_B \)) changes with heterogeneity and period. For condition for selection we consider a more general case that the heterogeneity, or inequality level, is different for each type \( (\sigma_A \text{ for type } A \text{ vs } \sigma_B \text{ for type } B) \). We determine for what range of values \( \sigma_A \) and \( \sigma_B \) a neutral mutant (neutral in uniform environment i.e. \( r_A = r_B \)) becomes advantageous or deleterious. We discuss similar conditions when \( r_A > r_B \) (inherently advantageous mutant) or \( r_A < r_B \) (inherently deleterious mutant).

Furthermore, we observe that for certain environmental interactions, i.e. maximally asymmetric, the condition for evolutionary advantage, \( \rho_A > 1/N > \rho_B \) is violated. We can now have a beneficial mutant, \( \rho_A > \rho_B \), while fixation probabilities of both types are less than the neutral case, i.e. \( 1/N \) or vice versa. This behavior is only seen for large periods, i.e. when fitness length scale is comparable to the system size.

Similarly, we discuss the fixation probability as the heterogeneity levels and period of fitnesses becomes varied. We consider \( r_A > r_B \), \( r_A < r_B \) as well as the neutral case \( r_A = r_B \). The increase or decrease of fixation probability depends on the period of fitness distribution. For background fitness heterogeneity, \( \sigma_A = \sigma_B \), in beneficial mutants the fixation probability is increased as heterogeneity is increased for low- and medium-periods. Similarly, for deleterious mutants the fixation probability is decreased for similar periods. For large periods, however, the behavior is reversed. This means that as length scale of fitness variations approaches the system size, the evolutionary dynamics changes in counter-intuitive ways.

In the last section, we investigate the scenarios where fitness distribution of both types are identical up to a phase-shift. We call this a fitness phase shift. This, for example, can be due to distribution of two different nutrients, periodically distributed, where each nutrient affects one type. We observe that in a neutral case, introducing a phase shift leads to significant change in fixation probability away from \( 1/N \).

II. MODEL

To model the selection dynamics we consider two competing types or strategies, A (mutant) and B (resident or Wild Type). Both types reside on a cycle graph, \( G \), that represents the spatial structure. Each node of the graph denotes a location. Each location, say node \( i \), is occupied by one strategy. We denote the occupancy by \( n_i \). If \( n_i = 1 \) node \( i \) is occupied by a mutant (strategy A) and if \( n_i = 0 \) there is a resident reside on that location. Total number of nodes is \( N \). Edges of the graph represents the neighborhood. Connectivity is manifested in the form of migration matrix \( m_{ij} = 1/(2)(\delta_{i,j+1} + \delta_{i,j-1}) \). \( \delta_{ij} \) is Kronecker \( \delta \)-function. If \( m_{ij} \neq 0 \) the two nodes \( i \) and \( j \) are connected \((i = j \pm 1)\). Furthermore, value of \( m_{ij} \) represents the probability that an offspring of an occupant of node \( i \) migrates to a neighboring node \( j \).

Local resource concentration at different locations can be relatively small (poor location) or large (rich location). We use coloring scheme to indicate the resource level at each location. Rich nodes are denoted with color green and poor nodes are colored red.

Fitness of either types A or B, depends on both their strategy and the resource concentration level at their corresponding location. If a type A is in rich node it has fitness \( a_G \). If a resident occupies the same node (say in a later time) the fitness is \( b_G \). Similarly fitness values at a red node are \( a_R \) and \( b_R \). This is a color-to-fitness map \([24]\) and can be summarized into a simple matrix form,

\[
\begin{pmatrix}
\text{red} & \text{green} \\
A & a_G \\
B & b_G \\
\end{pmatrix}
\]

We separate fitness values \( a_{R,G} \) (or \( b_{R,G} \)) into

\[
f = A \begin{pmatrix} a_R & a_G \\ b_R & b_G \end{pmatrix}.
\]
two additive parts, inherent fitness part and environment-dependent part,

\[
\begin{align*}
    a_{G,R} &= r_A + \sigma_A \\
    b_{G,R} &= r_B + \sigma_B
\end{align*}
\]  

(3)

where \( r_A (r_B) \) is the fitness of type A (B) in the absence of heterogeneity respectively. We have included the fitness gain/loss from a uniform resource distribution into the value of \( r_{A,B} \). \( \sigma_A \) and \( \sigma_B \) are heterogeneity levels (or inequality level) for each type \( A \) or \( B \). Therefore, \( 2\sigma_A \) \((2\sigma_B) \) is the fitness gap of a mutant (resident) in a rich location relative to a poor location respectively.

If the resource (at a given location) interacts with either types symmetrically, i.e. the fitness gain or loss due to the local resource is the same for each type, we have additive background fitness heterogeneity\([17]\). In this case \( \sigma_A = \sigma_B = \sigma \). The local resources affect the fitness of both types symmetrically additively: \( a_{G,R} = r_A + \sigma, b_{G,R} = r_B + \sigma \).

There can be different patterns of spatial distribution of resources. The specific pattern we are going to study, is the periodic distribution, having a square wave shape, which means that the fitness of each type oscillates spatially on the cyclic graph and has its own mean and an amplitude that are shown with \( r_A \) and \( r_B \), respectively. The schematic shape of such pattern is shown in figure 2. Throughout this study, we have considered the fitness patterns of the two types have the same period, \( T \). However, they can have some phase difference with each other. If we define the phase difference \( \delta \) between 0 and \( 2\pi \), the parameter pattern shift, \( m \), which we define as the number of nodes that one of the two patterns is shifted relative to the in phase waves, is calculated as:

\[
m = \frac{\delta}{2\pi} T.
\]  

(4)

Fitness shift could have relevant biological meaning, e.g. when each type feeds off from a separate nutrient or local resource. In the case of E.coli, we can have two competing strains which each metabolize a different sugar (say Glucose vs Lactose). (see [23] and references therein.) The distribution of each of these resources can be spatially independent. It is curious to consider identical spatial distributions for each sugar type while one is merely different from the other by a constant shift in spatial coordinates.

Except a short part at the end of the paper which we focused on the effect of phase shift, we are mainly going to study the case of \( m = 0 \) (in phase), which is equivalent to equation 3. This means that there are some green and red nodes periodically in the cyclic graph, and each type gets an amount of excess fitness on the green nodes and lose the same amount of fitness on the red ones.

A. Transition Matrix method

Every configuration \( n = (n_1, \ldots, n_j, \ldots, n_N) \) in which \( n_j \) for every \( j \in \{1, \ldots, N\} \) can be either 0 (occupied by B) or 1 (occupied by A), is a state in the state space of the problem. Since the stochastic dynamics of transition between states is a Moran process, we have a time-discrete finite Markov chain with two absorbing states, i.e. fixation and extinction of the mutant; all the other states are transient states. There is a standard method called transition matrix\([16]\) to solve such a Markov chain problem (see also [18]).

Suppose that there is \( t \) transient states and \( a \) absorbing ones and totally \( s = t + a \) states for the Markov chain. One can make up a stochastic matrix \( T_{s \times s} \) which contains the transition probabilities between any two states, i.e. \( T_{ij} \) is the transition probability from state \( i \) to state \( j \) (do not confuse the indexing of the states with the indexing of the nodes). If we label the states in such an order that the first \( t \) labels refer to the transient states and the last \( a \) ones refer to the absorbing states, the shape of \( T_{s \times s} \) is like this:

\[
T_{s \times s} = \begin{pmatrix} Q & R \\ 0 & I \end{pmatrix}
\]  

(5)

in which, blocks \( Q_{a \times t} \) and \( R_{a \times a} \) contain the transition probabilities between the transient states and from the transient to the absorbing states, respectively. The left bottom block \( Q_{a \times t} \) is a zero matrix, as there is no probability of transition from the absorbing states to the transient ones. The right bottom block \( I_{t \times a} \) is the identity matrix, because if the dynamics reaches an absorbing state, nothing will
change anymore. This form of the transition matrix is known as Canonical form. The procedure of obtaining $Q$ and $R$ matrices elements for a cycle graph is presented in [5].

For this transition matrix, the fundamental matrix of the Markov chain is defined as:

$$ F = \sum_{n=0}^{\infty} Q^n = (I - Q)^{-1}, \quad (6) $$

(see [16]).

The elements of this matrix have a special meaning. The element $F_{ij}$ is the average sojourn time in the state $j$ before the absorption, provided that the dynamics started from state $i$. The indices $i$ and $j$ refer to two transient states.

Having the matrices $F$ and $R$, we can have the matrix of absorption probabilities, which we call $\phi$ and its size is $t \times a$:

$$ \phi = FR \quad (7) $$

in which, the element $\phi_{ij}$ represents the probability of ultimate absorption to the $j$th absorbing state, provided that the dynamics is started from the $i$th transient state. As in the present problem there is just two absorbing states, we can calculate the fixation and extinction probabilities of the mutant, starting from any initial state.

As the elements of $F$ represent the mean sojourn times, we can also calculate the mean time to absorption, starting from any $i$th transient state, which we call $\tau_i$:

$$ \tau_i = \sum_{j=1}^{t} F_{ij}. \quad (8) $$

The conditional absorption time which means that the mean time to reach a specific absorbing state, say the state $k$, starting from the $i$th transient state is [11, Chapter 2] [5],

$$ \tau_{ik} = \sum_{j=1}^{t} \frac{\phi_{jk}}{\phi_{ik}} F_{ij}. \quad (9) $$

We labeled the states in such an order that the first $N$ labels refer to the configurations with a single mutant. In other words, by state $i$ ($1 \leq i \leq N$), we mean the specific configuration in which there is a mutant in the node $i$ and all the other nodes of the graph are occupied by the residents. In the canonical form we use here, the two absorbing states, totally resident and totally mutant configurations, are labeled as $s = 1$ and $s$, respectively. Thus, the fixation probability and average fixation time starting from a single mutant at the node $i$ are shown as $\phi_{is}$ and $\tau_{is}$. By definition, the fixation probability and fixation time are respectively:

$$ \rho = \frac{1}{N} \sum_{i=1}^{N} \phi_{is} \quad (10) $$

and

$$ \tau = \frac{1}{N} \sum_{i=1}^{N} \tau_{is}. \quad (11) $$

III. RESULTS

A. Effect of fitness heterogeneity in selection advantage

We write down the fixation probability $\rho_A(G, C)$ in terms of periodic fitness model parameters: $\rho_A = \rho_A(r_A, r_B, \sigma_A, \sigma_B, T)$. As before, $r_A, r_B$ are the mean fitnesses - or fitnesses in uniform model- $\sigma_A, \sigma_B$ are fitness heterogeneity levels, given by equation [3] and $T$ is the period of fitness distribution. Condition for selection of type $A$ against $B$ is defined as $\rho_A > \rho_B$ (equation [1]). In a uniform environment model, this is simply $r_A > r_B$. Condition for selection in variable environments is exactly known in two limits; i) Complete graph in strong selection limit. In this case the arithmetic mean fitness dictates the conditions for selection [23]. That is, $a_R + a_G > b_R + b_G$. ii) Properly two-colored regular graphs (two-chromatic graphs). In this case, the geometric mean fitnesses in the two environments determines the condition for selection, i.e. $a_{G,R} > b_{G,R}$ [23]. Substituting $a_{G,R} = r_A \pm \sigma_A, b_{G,R} = r_B \pm \sigma_B$, we have,

$$ r_A > r_B \quad \text{(Any-coloring complete graph)} \quad (12a) $$

$$ r_A^2 - r_B^2 > r_B^2 - r_B^2 \quad \text{(Two-chromatic regular graphs)} \quad (12b) $$

Eq. (12b) corresponds to the case of cycle with fitness period $T = 2$. If one type is inherently beneficial or advantageous compared to the other type, i.e., $r_A \neq r_B$, (say $r_A = 1.1$ and $r_B = 1$ which means the mutant is inherently advantageous) the curve of $\rho_A = \rho_B$ (for period of $T = 2$) is a hyperbola in $\sigma_A - \sigma_B$ plane, Eq. (12b). It is symmetric relative to the sign of $\sigma_A$ and $\sigma_B$. Notice that due to symmetry the condition for selection of a deleterious mutant with say $r_A = 1, r_B = 1.1$ can be obtained with swapping the indices $A \leftrightarrow B$, i.e. mirror reflecting the figure along line $\sigma_A = \sigma_B$.

We compare our results with the exact result for $T = 2$ case. The discrepancy between the curves
of $\rho_A = \rho_B$ and Eq. \cite{12b} becomes more significant as $T$ is increased. Figures 3 and 12 show the difference of the two fixation probabilities, $\rho_A - \rho_B$, for inherently advantageous and neutral mutants, respectively. The results are plotted for $N = 16$ and different fitness periods $T = 2, 4, 8, 16$. 

As can be seen from figure 3 for larger periods where the rich and poor sites are more segregated, the region in $\sigma_A - \sigma_B$ plane that signifies deleterious case shrinks. This means that increasing period of distribution can make a deleterious mutant into an advantageous one (area between dashed and solid lines). However, this is not true for intrinsically neutral mutations. As is seen from figure 13, no level of heterogeneity and period changes the neutrality line away from the diagonal lines $\sigma_A = \pm \sigma_B$.

We are also interested to see how changes in heterogeneity $\sigma_A$ and/or $\sigma_B$ affect the chance of success of a mutant in a heterogeneous environment compared to the case in a uniform environment. For brevity we only focus on the neutral case $r_A = r_B = 1$ and ask how introducing arbitrary values of heterogeneity levels, $\sigma_A$ and $\sigma_B$ changes the fixation probability away from its uniform environment value, $\rho_A = 1/N$.

Figure 4 shows the fixation probability of an inherently neutral mutant ($r_A = r_B = 1$ and type A as the mutant) in $\sigma_A - \sigma_B$ plane for different periods of fitness distribution ($T$). Panels a to d are plotted for periods $T = 2, 4, 8$ and 16, respectively. The dashed lines represent the condition in which the fixation probability equals to the value pertaining to neutral mutation in the uniform environment i.e. $\rho_A = 1/N$. For $T = 2$ (2-chromatic cycle) the above neutrality lines coincide with the lines $\sigma_A = \pm \sigma_B$. This can be readily observed by substituting $r_A = r_B$ in equation \cite{12b}.

Interestingly, as period is increased from minimum, $T = 2$, to medium values, $T = 4, 8$, the (uniform) neutrality lines are slightly different from the two diagonal lines $\sigma_A = \pm \sigma_B$. However, at maximal period $T = N$ the neutrality line is drastically different from the other cases (figure 4 panel d). This case represents a case when environmentally different habitats are furthest from each other. In this case, we can see how small random changes in a uniform fitness distribution, $\sigma_A = \sigma_B = 0$, affects the condition for selection. In the neighborhood of $\sigma_A = \sigma_B = 0$ (uniform environment) in the largest period, the fixation probability is mostly greater than $1/N$, except in a small angular interval below diagonals ($\sigma_A/\sigma_B = 1 - \epsilon$ ($0 \leq \epsilon \ll 1$)) that $\rho < 1/N$. Thus, for large periods, most often a weak heterogeneity leads to increase in the fixation probability of a neutral mutant away from $1/N$. Notice that along the diagonal line $\sigma_A = \sigma_B = \sigma$ (symmetric environmental interactions) the condition for selection is not changed. Fixation probability of type $B$, $\rho_B$, can be similarly read off from figure 4. To do so, one just have to change the axes $\sigma_A$ and $\sigma_B$, due to the symmetry of $r_A = r_B = 1$. Similar results are obtained for the case of advantageous mutant ($r_A = 1, r_B = 1$), and deleterious mutant ($r_A = 1, r_B = 1$). (See figures 14 and 15.)

Now we check the validity of the inequality $\rho_A > 1/N > \rho_B$ in a heterogeneous environment. In other words, we are interested to see if there are regions of heterogeneity plane ($\sigma_A - \sigma_B$ plane) for any value of period $T$ we can have $\rho_A$ and $\rho_B$ simultaneously lower or higher than $1/N$. To do so, we plot the quantity $\zeta = (\rho_A - 1/N)/(\rho_B - 1/N)$ as a function of $\sigma_A$ and $\sigma_B$. $\zeta$ is positive when both $\rho_{A,B} < 1/N$ or both $\rho_{A,B} > 1/N$ at the same time. Ref. \cite{22} showed that this does not happen for two-chromatic graphs ($T = 2$ in our case). This is confirmed from figure 4. a. However as period increases, some regions in the $\sigma$-plane appear that have $\zeta > 0$. For medium-$T$ values, $T = 4, 8$ ($N = 16$) this is around the diagonal line $\sigma_A = -\sigma_B$. At maximum period $T = N$, the $\zeta > 1$ area covers a large range of $\sigma$-plane. Most significantly, we observe that around the uniform environment point ($\sigma_A = 0, \sigma_B = 0$), we only have $\rho_A > 1/N > \rho_B$ (or $\rho_A < 1/N < \rho_B$) across the diagonal line $\sigma_A = \sigma_B$, corresponding to symmetric additive interactions. Otherwise, any other asym-
FIG. 4: Fixation probability of a neutral mutant vs. $\sigma_A$ and $\sigma_B$. Fixation probability of a mutant (type A) on a periodic cycle vs. $\sigma_A$ and $\sigma_B$ for small to large periods ($T$ denotes the period): (a)$T = 2$, (b)$T = 4$, (c)$T = 8$ and (d)$T = 16$. The size of the graph is $N = 16$ and the mutant is inherently neutral ($r_A = r_B = 1$). The dashed lines represent the fixation probability of neutral mutant in the uniform environment ($1/N$).

Asymmetry in environmental interactions causes $\zeta > 0$.

As mentioned before, the breakdown of inequality $\rho_A > 1/N > \rho_B$ has important potential implications. In large populations, commonly $\rho_A > 1/N$ means that the type A is an evolutionary stable strategy. This means that when a small number of type A is introduced into the population of type B they can take over eventually. In a corresponding deterministic model this means that eigenvalues for growth is positive near all-B fixed point. This condition for constant selection holds everywhere, i.e., type A is globally an evolutionary stable strategy. However, if $\rho_B > 1/N$, simultaneously with $\rho_A > 1/N$, it means that near an all-A fixed point the eigenvalue of the deterministic model can be negative now. This points to a coexistence interior equilibrium in infinite population case.

B. Background fitness heterogeneity

We now focus on the symmetric interactions, $\sigma_A = \sigma_B = \sigma$ (background fitness heterogeneity). Fitnnesses in the two environments are given by,

$$
\begin{align*}
\sigma_{G,R} &= r_A \pm \sigma \\
b_{G,R} &= r_B \pm \sigma
\end{align*}
$$

(13)

The fixation probability - and average fixation time - as functions of heterogeneity level $\sigma$ and the fitness period $T$ are studied in this scenario. In the case of $T = 2$ and $r_A = r_B = 1$, we know that the fixation probability does not depend on the heterogeneity parameters and equals to $1/N$. Interestingly, it turns out that this observation is true for any period. Figure [10] shows that the fixation probability of a neutral mutant ($r_A = r_B = 1$), neither depends on the heterogeneity level ($\sigma$), nor on its period; and equals to $1/N$, too. This is because in the case of inherently neutral mutant and symmetric interactions ($\sigma_A = \sigma_B$), we have effectively one type of fitness behavior, although labeled in two groups of A and B. Thus, the fixation probability of every individual of the population is the same and equal to $1/N$, as they feel exactly the same fitness from the environment, regardless of the distribution parameters.

More interesting observations are related to the case of intrinsically non-neutral mutants ($r_A \neq r_B$). The fixation probability of a mutant of type A among B residents is plotted for $N = 100$ in figure [9] for the inherent fitnesses $r_A = 1.1$, $r_B = 1$. Firstly in the panel a, it is shown that the fixation probability of an intrinsically advantageous mutant monotonically increases with $\sigma$ for all periods, but the rate
FIG. 6: Fixation probability of an advantageous mutant vs $\sigma$ and $T$. Fixation probability of an advantageous mutant (type A) plotted (a) vs. $\sigma$ for different periods and (b) vs. period for different values of $\sigma$. The graph size, $N$, is 100. The inherent fitnesses are $r_A = 1.1$, $r_B = 1$ and the fitness heterogeneity obeys the rule of equation 13. The lines between the data points in both panels are plotted merely to guide the eye.

of increment depends on the period $T$. Figure 6b is the same result as panel a but now the fixation probability is plotted vs. period for different values of $\sigma$. For each value of $\sigma$, the lowest and the highest periods (2 and 100) have approximately equal fixation probabilities (for the period 2 it is slightly higher). Moreover, for each $\sigma$ there is a middle $T$ value which has a minimum fixation probability among all the periods. The difference between the minimum and the maximum of fixation probability increases with the heterogeneity amplitude, $\sigma$.

Conversely, we consider the case of deleterious mutations. Figure 7 represents the fixation probability of type A with $r_A = 1$, $r_B = 1.1$. Other model parameters are just like figure 6. As shown in figure 7, for all the distribution periods except the largest one, the fixation probability decreases with $\sigma$, monotonically. For the largest period ($T = N$), it increases with $\sigma$ in small values, while decreases in large values. There is a certain value of $\sigma$ which shows a maximum fixation probability in the largest period. For all the periods, as $\sigma$ gets close to its upper limit, the fixation probability approaches zero. This happens because the fitness of the mutants in the poor nodes becomes close to zero and the graph becomes effectively disconnected in the pertaining edges. Figure 7b indicates that for a deleterious mutant and for all values of $\sigma$, the fixation probabilities never decrease with the period.

Thus, when the two types have the same rule of additive interaction with the local environment (equation 13), two inherently neutral types ($r_A = r_B$) remain neutral relative to each other, regardless of the environmental distribution parameters. For an inherently advantageous mutant, fixation probability increases with heterogeneity amplitude and for an inherently deleterious mutant, it decreases with it (except in the largest period).

C. Fixation Times

We numerically calculated conditional mean time to fixation $\tau$. (We call it Fixation time.) For the case of a neutral mutant ($r_A = r_B = 1$ and $A$ as the mutant) on a 100-node cyclic graph it is plotted vs. the $\sigma$ and $T$, for the symmetric environmental interaction 13 (figure 8). Panel a shows that fixation time increases with $\sigma$, but this variation is relatively small for the smallest and the largest periods. Figure 8b which represents the fixation time vs. the period for different heterogeneity levels, shows that
for every value of $\sigma$, the smallest and the largest period have approximately equal fixation times and it is the minimum among all the periods. On the other hand, there is a middle period which has the maximum fixation time for every value of $\sigma$. We call this specific period $T_{N=100}^*$. As it is obvious in figure 8, for $N = 100$, the mentioned period is $T_{100}^* = 20$.

Also, for inherently slightly deleterious and advantageous mutants the fixation time was studied. In the neighborhood of the neutral point ($r_A = r_B = 1$), the fixation time of the deleterious and advantageous mutants is almost behaviorally similar and considerably less than the fixation time of the neutral case. One can see an example in figure 17.

We investigated $N = 16, 32, 64, 80, 100$ and 128 for all of their even divisors as the period of fitness distribution. For each graph size $N$ and heterogeneity amplitude $\sigma$, we found a middle period in which the mutant has the highest fixation time among all values of $T$. If the mutant is inherently neutral ($r_A = r_B$), for each graph size, this period is independent of amount of $\sigma$, and we call it $T_{N}^*$. For different values of $N$, the list of periods studied as well as the period $T_{N}^*$ are presented in table 1.

For the special case of a neutral mutant, a scaling was observed between fixation time and graph size. Figure 9 shows this fact. In the panel a, the fixation time $\tau$ is plotted vs. the graph size $N$ for the period $T_{N}^*$ of each $N$ and selected values of $\sigma$ in the log-log scale for the case of an inherently neutral mutant. Also, the fitted lines using least square method are plotted and the slope of the lines and the coefficient of determination ($R^2$) for each fitting is reported.

The fittings have been done for the periods $T = 2$ and $T = N$ for comparison in figure 18. In figure 9b, the exponent of scaling which is the slope of fitting in log-log scale is plotted vs. $\sigma$, for the smallest and the highest period as well as the period $T_{N}^*$. Firstly, it is worth to declare that for all the fittings, $1 - R^2$ was less than $10^{-3}$ and for the majority of cases even less than $10^{-5}$. As shown in figure 9b, the exponent of scaling for the case of uniform environment effectively equals to 3, and with the heterogeneity level, it increases monotonically. The sensitivity of exponent to heterogeneity level is comparatively weak in the smallest period and is considerable in the two other periods $T = N$ and $T = T_{N}^*$, although in all of the studied cases, $\alpha \in [3, 3.2]$.

D. Phase shift effect

So far, the spatial fitness profiles of the two types are considered to be in-phase square wave distributions having different mean values ($\bar{r}_A, \bar{r}_B$) and amplitudes ($\sigma_A, \sigma_B$). But what happens to fixation probability if they have some phase difference as described in Model section?

The rule of symmetric interaction (equation 13) assumes that the rich and poor positions for the two types are the same. On the other hand, one can suppose that there is a pattern shift, $m$, between the two square wave distributions. This problem is a specific case of the general problem in which the types A and B have fitnesses ($a_i, b_i$) in the nodes $i = 1, 2, ..., N$ of the graph.

In this subsection, we have assessed the effect of phase difference in the fitness distributions of type A and B on fixation probability and fixation time. Figure 10 depicts the fixation probability of a 16-node cycle in two different periods of fitness distribution vs. the pattern shift $m$. The pattern shift varies between 0 and $N$. For the distribution period $T = 4$ (panel a), one can see that a non-zero (or equivalently non-zero) shift, decreases the fixation probability. Moreover, higher heterogeneity levels ($\sigma$) makes this reduction more significant. On the contrary, in the period $T = N$ (panel b) which is the largest possible length scale of fitness variations, adding a non-zero pattern shift, increases the fixation probability and the amount of this increment is more significant in higher $\sigma$’s. This means that de-
FIG. 9: Scaling of fixation time with \( N \). (a) Fixation time is plotted vs. \( N \) for the period \( T_N^* \) of each \( N \) in the case of \( r_A = r_B = 1 \) and equation \( 13 \) for some selected values of \( \sigma \). The slope of fitted lines and \( R^2 \) (coefficient of determination) of each fitting are presented in the legend. (b) The slope of log-log fittings of panel a, is plotted vs. \( \sigma \). This quantity is the exponent of scaling of \( T \propto N^\alpha \) and it is plotted for the periods \( T = 2 \), \( T = N \) and \( T = T_N^* \).

FIG. 10: Effect of fitness shift on fixation probability. Fixation probability of an inherently neutral mutant is plotted vs. \( m \) in the periods (a) \( T = 4 \) and (b) \( T = 16 \) for different values of \( \sigma \). A 16-node cyclic graph is considered and at \( m = 0 \), the rule of equation \( 13 \) is applied to the fitness pattern. The inherent fitnesses are considered to be \( r_A = r_B = 1 \).

Depending on the length scale of the distribution, the pattern shift can either increase or decrease the fixation probability. The observations in figure 10 are in agreement with figure 5. If \( m \) is an odd multiple of \( T/2 \), the heterogeneity pattern makes the environment be equivalent to the opposite fitness distribution \( (\sigma_A + \sigma_B = 0) \) in figure 5. One can see that on this line, for the middle distribution periods, the fixation probability of both types are smaller than uniform neutral case \( (\rho_A, \rho_B < 1/N) \) and for the largest period greater than it \( (\rho_A, \rho_B > 1/N) \). So, we have been expecting such behavioral difference between the two different coloring periods in figure 10. For the period \( T = 8 \), the behavior is like the period \( T = 4 \). For the smallest period, \( T = 2 \), there is just one distinct state other than no-phase shift case, i.e., \( m = 1 \) that this fitness shift is equivalent to opposite interaction distribution. For \( T = 2 \), there is no difference between the fixation probability of the two possible states as they are both 2-chromatic graphs according to [24]. This is in agreement with what is shown in the figure 4a on the lines \( \sigma_A - \sigma_B = 0 \) and \( \sigma_A + \sigma_B = 0 \).

In the same setup of figure 10, fixation time is studied when some pattern shift is imposed. In figure 11 the fixation time of a 16-node cyclic graph is plotted vs. pattern shift, \( m \), for two periods, panel a for \( T = 4 \) and panel b for \( T = 16 \). It can be seen that for \( T = 4 \), the fixation time decreases for every equivalently non-zero value of \( m \), while increases for \( T = 16 \). Like the fixation probability, the direction of changing is dependent on the distribution period. However, the variations in all periods get more drastic as the heterogeneity amplitude increases and the phase shift gets close to \( \pi/2 \). Besides, from figure 11b we learn that fixation time can increase several orders of magnitude in the case of \( \pi/2 \) phase shift (equivalent to opposite interaction fitness) compared to zero phase shift, if the heterogeneity period and amplitude are large enough.

We observed that the pattern shift in the fitness distribution can change fixation probability and time. The direction of changes depends on the het-
FIG. 11: Effect of fitness shift on fixation time. Fixation time of an inherently neutral mutant is plotted vs. $m$ in the periods (a) $T = 4$ and (b) $T = 16$ for different values of $\sigma$. A 16-node cyclic graph is considered and at $m = 0$, the rule of equation 13 is applied to the fitness pattern. The inherent fitnesses are considered to be $r_A = r_B = 1$.

heterogeneity length scale, but as the heterogeneity amplitude increases and the phase shift becomes closer to $\pi/2$, the changes become more significant.

IV. CONCLUDING REMARKS

We studied the evolution in linear spatial structures with spatial fitness distributions. We focused in periodic fitness distribution across a cycle graph. Environmental interaction is considered to be an additive factor to the inherent fitness of each type. Environmental variations are parametrized with heterogeneity level, i.e. standard deviation of fitnesses, as well as fitness length scale which is period of fitness distribution for the periodic resource distribution. We focused on changes to the fixation probability of a random mutant and condition for selection for various values of fitness heterogeneity $\sigma_A$ and $\sigma_B$ as well as period $T$.

We calculated the fixation probability of a random mutant using a transition matrix method for the Kolmogorov equation. Various population sizes ($N = 16, 32, \cdots, 100$) were considered. We observed that for the case of $r_A \neq r_B$, and certain environmental interactions, i.e. some ranges of $\sigma_A, \sigma_B$, the fixation probabilities of the two types change in such a way that the fixation probability of an inherently advantageous mutant ($\rho_A > \rho_B$ in a uniform graph) becomes less than the fixation probability of the inherently deleterious type. It can also happen in the opposite case, i.e., changing an inherently deleterious mutant into advantageous. This means that merely by changing the environmental fitness distribution, we can change a previously advantageous mutant into deleterious, and vice versa.

These are possible in every distribution periods, provided that $\sigma_A$ and $\sigma_B$ are chosen properly. On the other hand, for intrinsically neutral types ($r_A = r_B$) and symmetric environmental interaction ($\sigma_A = \sigma_B = 0$), the fixation probability is independent of the fitness distribution and regardless of the distribution, equals the value pertaining to the uniform distribution $(1/N)$.

While in unstructured populations, environmental fitness heterogeneity always decreases the fixation probability, we just learned that on a structured population, the effect of heterogeneity on the fixation probability depends on the type of heterogeneity, i.e., the interaction of the colors with the types.

For a cyclic graph with the fitness heterogeneity interaction rule of $\sigma_A = \sigma_B = 0$, the structure and distribution is determined knowing just the length scale of the fitness pattern (the period $T$) and the heterogeneity level $\sigma$. Having the distribution parameters in the symmetric environmental interaction ($\sigma$ and $T$) as well as $r_A$ and $r_B$, we can determine whether the fixation probability increases or decreases compared to the uniform graph.

In general, the condition $\rho_A = \rho_B$ is not equivalent to $\rho_{A,B} = 1/N$. The condition $\rho_A > \rho_B$ is not equivalent to $\rho_A > 1/N > \rho_B$, either. For certain environmental interactions, i.e., in the neighborhood of opposite interaction line ($\sigma_A + \sigma_B = 0$), the fixation probability of the two types can be larger or smaller than the neutral uniform case, simultaneously, while one of them is greater than the other one.

Increasing heterogeneity amplitude in symmetrically interaction ($\sigma_A = \sigma_B$), increases the fixation probability in all length scales (periods) for an inherently advantageous mutant ($r_A > r_B$) monotonically. For small heterogeneity periods as $T$ is increased, fixation probability is reduced for a fixed value of $\sigma$ while for very large $T$ the fixation probability is increased. There is a local minima for the fixation probability in medium values of distribution periods. Similarly, for an inherently deleterious mutant ($r_A < r_B$), fixation probability decreases with heterogeneity amplitude in almost all periods. However there is an exception about the largest period in
which, it increases for small heterogeneity levels and decreases for large ones in a non-monotonic manner. However, it monotonically increases with period for a deleterious mutant.

Average time to fixation, $\tau$, increases with heterogeneity in all periods. This increment can be in orders of magnitude as the heterogeneity increases to its upper limit in the symmetric interaction ($\sigma = 1$). For the case of neutral types ($r_A = r_B$), this increment is more significant than non-neutral case. Furthermore, fixation time shows a scaling with the graph size in the neutral types case ($\tau \propto N^\alpha$). $\alpha$ is around 3 (3 to 3.2) for different heterogeneity periods and amplitudes. For the uniform environment ($\sigma = 0$), $\alpha$ effectively equals 3.

If the fitness pattern of types A and B have some

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Appendix A: Elements of matrices $Q$ and $R$

If we calculate the elements of the matrices $Q$ and $R$, which are the transition probabilities between different states, there will be need to just some matrix manipulations to solve the problem. As an example, we show how to calculate the transition probabilities between some states. We are studying cyclic graphs. On a cyclic graph, when a mutant is put in a random node and the dynamics of Moran process begins, always the mutants form a connected subset of the graph. Thus, we can completely determine every possible configuration by denoting just the beginning and the end nodes of the mutant chain, like what is shown in figure 12. In this figure, the number written in each node, determines the number of mutants inside it. Nodes $i$ and $j$ are the begin and end nodes of the mutant chain. When referring every node label, we should be aware of periodicity. Thus, node 1 comes after node $N$.

![FIG. 12: Configuration of mutants and residents on a cycle. Every configuration of mutants and residents on a cyclic graph can be determined by mentioning the beginning ($i$th) and the end ($j$th) node of the mutants chain, which we have to go from beginning to the end node in a specific direction (say, CW) to cover the mutants. Green and red colors indicate rich and poor nodes (See text).](image)

Let’s suppose that the fitness of mutant and resident types in every node $k$ ($k \in \{1, ..., N\}$) is $a_k$ and $b_k$, respectively. If there are more than one element of each type in the graph, the current and the next states are both transient and all the possible transitions are between two transient states. Thus the probabilities of such transitions must be inserted into the matrix $Q$. In such a situation that is shown in figure 12, there is just 5 possible transitions in the next time step:

1. $n_{j+1} = 0 \to n_{j+1} = 1$:
   \[
P_1 = \frac{a_j/2}{\sum_{k=1}^{N} (a_k n_k + b_k (1 - n_k))}
   \]

2. $n_j = 1 \to n_j = 0$:
   \[
P_2 = \frac{b_j + 1/2}{\sum_{k=1}^{N} (a_k n_k + b_k (1 - n_k))}
   \]

3. $n_{i-1} = 0 \to n_{i-1} = 1$:
   \[
P_3 = \frac{a_i/2}{\sum_{k=1}^{N} (a_k n_k + b_k (1 - n_k))}
   \]

4. $n_i = 1 \to n_i = 0$:
   \[
P_4 = \frac{b_i - 1/2}{\sum_{k=1}^{N} (a_k n_k + b_k (1 - n_k))}
   \]

5. nothing changes (the birth and death happens inside the interior zone of either two types):
   \[
P_5 = 1 - \sum_{l=1}^{4} P_l
   \]

The transition probability to the other configurations is zero.

On the other hand, if any of the next time step probable states is either fully resident or fully mutant state, the pertinent transition probability must be inserted into the matrix $R$.

So, using this simple approach, we can find the transition probability between any two states and consequently, the matrix $T$ can be completely made up.

Appendix B: Supplementary figures and tables
FIG. 13: $\rho_A - \rho_B$ of neutral mutants vs. $\sigma_A$ and $\sigma_B$. $\rho_A - \rho_B$ on a periodic cycle vs. $\sigma_A$ and $\sigma_B$ for small to large periods ($T$ denotes the period): (a) $T = 2$, (b) $T = 4$, (c) $T = 8$ and (d) $T = 16$. The size of the graph is $N = 16$ and the mutant is inherently neutral ($r_A = r_B = 1$). The dashed lines represent $\rho_A - \rho_B = 0$ and the solid ones $\rho_A - \rho_B = 0$ for the case of 2-chromatic graph ($T = 2$).

FIG. 14: Fixation probability of an advantageous mutant vs. $\sigma_A$ and $\sigma_B$. Fixation probability of a mutant (type A) on a periodic cycle vs. $\sigma_A$ and $\sigma_B$ for small to large periods ($T$ denotes the period): (a) $T = 2$, (b) $T = 4$, (c) $T = 8$ and (d) $T = 16$. The size of the graph is $N = 16$ and the mutant is inherently neutral ($r_A = 1.1$, $r_B = 1$). The dashed lines represent the fixation probability of neutral mutant in the uniform environment ($1/N$).
FIG. 15: **Fixation probability of a deleterious mutant vs. $\sigma_A$ and $\sigma_B$.** Fixation probability of a deleterious mutant on a periodic cycle vs. $\sigma_A$ and $\sigma_B$ for small to large periods ($T$ denotes the period): (a)$T=2$, (b)$T=4$, (c)$T=8$ and (d)$T=16$. The size of the graph is $N=16$ and the mutant is inherently deleterious ($r_A = 1, r_B = 1.1$). The dashed lines represent the fixation probability of neutral mutant in the uniform environment ($1/N$).

FIG. 16: **Fixation probability of a neutral mutant.** Fixation probability of a neutral mutant (type A) plotted (a) vs. $\sigma$ for different periods and (b) vs. period for different values of $\sigma$. The graph size ($N$) is considered to be 100, the inherent fitnesses are $r_A = r_B = 1$ and the fitness heterogeneity obeys the rule of equation 13. The lines between the data points in both panels are plotted merely to guide the eye.
FIG. 17: **Fixation time of non-neutral mutants.** Fixation time of (a) a deleterious and (b) an advantageous mutant (type A) are plotted vs. $\sigma$ for different periods. The graph size ($N$) is considered to be 100 and the fitness heterogeneity obeys the rule of equation 13. The inherent fitnesses are considered $r_A = 0.9 = 0.9r_B$ and $r_A = 1.1 = 1.1r_B$ for the deleterious and advantageous mutants, respectively. The lines between the data points in both panels are plotted merely to guide the eye.

**TABLE I: Periods of heterogeneity studied for each graph size.** The values of the periods ($T$) studied for each graph size ($N$) as well as the specific period with the maximum fixation time ($T^*_N$) are presented. The heterogeneity is imposed based on the rule of equation 13 and in order to obtain $T^*_N$ for each graph size, the mutants are assumed to be inherently neutral ($r_A = r_B = 1$).

| $N$ | values of $T$ | $T^*_N$ |
|-----|--------------|--------|
| 16  | 2, 4, 8, 16  | 8      |
| 32  | 2, 4, 8, 16, 32 | 8      |
| 64  | 2, 4, 8, 16, 32, 64 | 16     |
| 80  | 2, 4, 8, 10, 16, 20, 40, 80 | 20     |
| 100 | 2, 4, 10, 20, 50, 100 | 20     |
| 128 | 2, 4, 8, 16, 32, 64, 128 | 32     |
FIG. 18: **Scaling of fixation time with $N$ for smallest and largest periods.** Fixation time is plotted vs. $N$ for the periods (a) $T = 2$ and (b) $T = N$ of each $N$ in the case of $r_A = r_B = 1$ and the rule of equation 13 for some selected values of $\sigma$. The slope of fitted lines and $R^2$ (coefficient of determination) of each fitting are presented in the legend.