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An asymptotic maximum principle for essentially linear evolution models

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Abstract. Recent work on mutation-selection models has revealed that, under specific assumptions on the fitness function and the mutation rates, asymptotic estimates for the leading eigenvalue of the mutation-reproduction matrix may be obtained through a low-dimensional variational principle in the limit $N \to \infty$ (where N is the number of types). In order to generalize these results, we consider here a large family of reversible $N \times N$ matrices and identify conditions under which the high-dimensional Rayleigh-Ritz variational problem may be reduced to a low-dimensional one that yields the leading eigenvalue up to an error term of order $1/N$. For a large class of mutation-selection models, this implies estimates for the mean fitness, as well as a concentration result for the ancestral distribution of types.

1. Introduction

Many systems of population biology, or reaction kinetics, may be cast into a form where individuals (or particles) of different types reproduce and change type independently of each other in continuous time. If the types come from a finite set S and the population is so large that random fluctuations may be neglected, one is led to a linear system of differential equations of the form

$$\dot{y} = yH \tag{1}$$

with initial condition $y(0)$. Here, $y = (y_i)_{i\in S} \in \mathbb{R}^{|S|}_{\geqslant 0}$ holds the abundance of the various types. $H = (H_{ij})_{i,j\in S}$ is an $|S| \times |S|$ matrix, which represents a linear operator on $\mathbb{R}^{|S|}$. Important examples include models of age-structured populations, which are often referred to as matrix population models, see Caswell's monograph [10]. The main application we have in mind here is in population genetics, where types are alleles, so that Equation (1) is a haploid mutation-reproduction model; but one may also think of a compartment model, where types are locations of a certain chemical. In line with large parts of the population genetics, and most of the stochastics, literature, we will use the convention that y is a row vector to which H is applied from the right, so that H_{ij} $(i \neq j)$ is the coefficient for the change from i to j.

We will assume throughout that the linear operator H generates a positive semigroup, $\{\exp(tH) \mid t \geqslant 0\}$. Since S is finite, this is equivalent to $H_{ij} \geqslant 0$ for $i \neq j$. The flow so generated leaves $\mathbb{R}^{|S|}_{\geqslant 0}$ invariant. We will further assume that H is irreducible (i.e., if $G(H)$ is the directed graph with an edge from i to j if $i \neq j$ and $H_{ij} > 0$, then there is a directed path from any vertex to any other vertex).

We will often use the decomposition

$$H = M + R \tag{2}$$

into a Markov generator M and a diagonal matrix R. More precisely, we have $M = (M_{ij})_{i,j\in S}$ with $M_{ij} := H_{ij}$ for $i \neq j$, $M_{ii} := -\sum_{j\in S\setminus\{i\}} M_{ij}$ (so that $\sum_{j\in S} M_{ij} = 0$), and $R = \mathrm{diag}\{R_i \mid i \in S\}$ with $R_i := H_{ii} - M_{ii}$. Clearly, the decomposition in (2) is unique, and M is irreducible iff H is, because $G(M) = G(H)$. M_{ij} is the rate at which an i-individual produces j-offspring $(j \neq i)$, and R_i is the net rate at which individuals of type i reproduce themselves; this may also include death terms and thus be negative.

Solutions of (1) cannot vanish altogether (unless $y(0) = 0$), since $\mathrm{tr}(H)$ is finite, hence $\det\big(\exp(tH)\big) = \exp(t\,\mathrm{tr}(H)) > 0$ and $\ker\big(\exp(tH)\big) = \{0\}$, for all $t \geqslant 0$. Therefore, we may also consider the corresponding normalized equation for the proportions $p_i := y_i/(\sum_{j\in S} y_j)$, which is sometimes more relevant. Clearly,

$$\dot{p}_i = \sum_{j\in S} p_j M_{ji} + \big(R_i - \sum_{j\in S} R_j p_j\big) p_i \,. \tag{3}$$

In the population genetics context, this is the mutation-selection equation for a haploid population, or a diploid one without dominance; for a comprehensive review of this class of models, see [8]. It is well known, and easy to verify, that the way back from (3) to (1) is achieved through 'Thompson's trick' [36]:

$$y(t) := p(t) \exp\Big(\sum_{j\in S} R_j \int_0^t p_j(\tau) d\tau\Big)\,.$$

This substitution can thus be viewed as a global linearization transformation and explains why (3) is an 'essentially linear' equation.

Clearly, the solution of (3) is obtained from that of (1) through normalization:

$$y(t) = y(0)\exp(tH), \quad p(t) = \frac{y(t)}{\sum_i y_i(t)}\,.$$

Of course, proportions of types in a population that grows without restriction (which is biologically reasonable only over short time scales) is not the only way in which (3) may arise. Actually, the same equation for p results if (1) is replaced by

$$\dot{y} = y\bigl(H - \gamma(t)\bigr) ,$$

where $\gamma(t)$ is some scalar (possibly nonlinear) function which describes the elimination of individuals by population regulation. This is obvious from the invariance of (3) under $R_i \to R_i + \gamma(t)$ if performed simultaneously for all i. The function $\gamma(t)$ may, for example, describe the flow out of a chemostat, or an additional death term caused by crowding, which may depend on t through y, but acts on all types in the same way.

Eq. (3) may be read in two ways (cf. [23]). If mutation and reproduction go on independently of each other, the parallel (or decoupled) version is adequate. Here, every i-individual gives birth to offspring of its own type at rate B_i, dies at rate D_i, and mutates to j at rate M_{ij} ($j \neq i$). $R_i := B_i - D_i$ then is the net reproduction rate or Malthusian fitness [11, Ch. 5.3], and Eq. (3) is immediate. If, however, mutation is a side effect of reproduction (through copying errors of the replication process, for example), the coupled version [1,20] is more relevant. When an i-individual reproduces (which it does, as before, at rate B_i, while it dies at rate D_i), the offspring is of type j with probability V_{ij} ($\sum_j V_{ij} = 1$). This leads to

$$\dot{p}_i = \Bigl(\sum_{j \in S} p_j B_j V_{ji}\Bigr) - \Bigl(D_i + \sum_{j \in S} R_j p_j\Bigr) p_i \, , \tag{4}$$

where, again, $R_i = B_i - D_i$. But if we set $M_{ij} := B_i(V_{ij} - \delta_{ij})$, we arrive again at Eq. (3). In both cases, $\sum_j R_j p_j$ is the mean fitness of the population. Obviously, a mixture of both the parallel and the coupled mutation mechanisms can be tackled in the same way, but we omit further details.

The model (4) also arises in the infinite population limit of the well-known Moran model with selection and mutation, see [15, Ch. 3] or [12, p. 126]. This is a *stochastic* model where, in a population of m individuals, every individual of type i reproduces at rate B_i, and the offspring, which is of type j with probability V_{ij}, replaces a randomly chosen individual in the population (possibly its own parent). To describe the entire population, let $Z_i(t)$ be the random variable that gives the number of i-individuals at time t, and $Z(t) = \bigl(Z_i(t)\bigr)_{i \in S}$. Hence, if $Z(t) = z$, and $j \neq k$, we can have transitions from z to $z + e_j - e_k$, where e_j denotes the unit vector corresponding to j. Such a transition occurs at rate $\sum_i B_i V_{ij} z_i z_k / m$. Let us look at the influence of increasing m, whence we write $Z^{(m)}(t)$ to indicate dependence on system size. As $m \to \infty$, the sequence of random processes $Z^{(m)}(t)/m$ converges almost surely, and uniformly for every finite interval $[0, t]$, to the solution of the differential equation (4) with $D_i \equiv 0$, and initial condition $Z^{(m)}(0)/m$ (resp. its limit as $m \to \infty$), compare [14, Thm. 11.2.1].

The linear equation (1) has a more direct stochastic interpretation in terms of a continuous-time multitype branching process. After an exponential waiting time with expectation τ_i, an individual of type i produces a random offspring with a finite expectation of b_{ij} children of type j (we will not specify the distribution explicitly since we will not fully develop the stochastic picture here). The matrix H with $H_{ij} = b_{ij}/\tau_i$ then is the generator of the first-moment matrix. That is, if $Z_j(t)$ is again the (random) number of individuals of type j at time t, and $\mathbb{E}^i$ the associated expectation in a population started by a single i individual at time 0, then

$$\mathbb{E}^i(Z_j(t)) = \bigl(\exp(tH)\bigr)_{ij}. \tag{5}$$

Further, with the identification $y_i(t) = \mathbb{E}\bigl(Z_i(t)\bigr)$, Equation (1) then simply is the forward equation for the expectations. (See [2] or [27] for the general context of multitype branching processes, and [21] for the application to mutation-selection models.)

Important first questions concern the asymptotic properties of the systems discussed. A key to these properties is the leading eigenvalue, $\lambda_{\max}$, of H (i.e., the real eigenvalue exceeding the real parts of all other eigenvalues), for various reasons. If, on short time scales, unrestricted growth according to (1) is relevant, then $\lambda_{\max}$ is the asymptotic growth rate of the population. The stationary distribution of types in (3) is given by the left eigenvector of H corresponding to $\lambda_{\max}$. The knowledge of $\lambda_{\max}$ is a prerequisite for the calculation of this eigenvector. In the population genetics context, the stationary state is often referred to as mutation-selection balance, with $\lambda_{\max}$ as the mean fitness. Finally, and perhaps most importantly, the dependence of $\lambda_{\max}$ on certain model parameters is of great interest. For example, a lot of research has been directed towards the question of how the mean fitness changes when the mutation rate increases (i.e., when

M is varied by some nonnegative scalar factor), and interesting effects have been observed, for example error thresholds (for reviews, see [8, Ch. III] and [13]).

In general, exact expressions for eigenvalues are hard to obtain if $|S|$ is large but fixed. In recent work on mutation-selection models, however, scalar or low-dimensional maximum principles for the leading eigenvalue have been identified for certain examples [21,17] in a suitable continuous limit as $|S| \nearrow \infty$. It is the purpose of this paper to generalize these results to a large class of operators. We will do so under the general assumption that the Markov generator M is reversible, which covers a large class of mutation models; in particular, reversibility is a standard assumption in molecular population genetics, cf. [34] or [16, Ch. 13].

The paper is organized as follows. In Section 2, we will apply the Rayleigh-Ritz maximum principle to our class of matrices. This leads to a high-dimensional problem, which is hard to solve in practice. An example of how the problem may be reduced to a scalar one is given in Section 3. The main results are given in Section 4. Here, we identify fairly general conditions under which the high-dimensional problem may be reduced to a low-dimensional variational problem that yields the leading eigenvalue up to an error term of order $1/N$, in the limit $N = |S| \to \infty$. Sections 5 and 6 are devoted to the lumping procedure. They show that a large class of models on a type space S arises, in a natural way, from models defined on a 'larger' space $\mathfrak{S}$, by combining several types in $\mathfrak{S}$ into a single one in S. The general framework is set out in Section 5, and in Section 6, we apply it to the important case where $\mathfrak{S}$ is the space of all sequences over a given alphabet, and of fixed length. Section 7 makes the connection back to the maximum principle and shows how the lumping procedure may lead to 'effective' models (on S) to which our asymptotic results may then be applied. The Hopfield fitness function, along with sequence space mutation, emerges as an example.

2. The general maximum principle for reversible generators

Let us first fix our assumptions and notation. Since we assume M to be an irreducible Markov generator, Perron-Frobenius theory, cf. [26, Appendix], tells us that it has a leading eigenvalue 0 which exceeds the real parts of all other eigenvalues, and an associated strictly positive left eigenvector π. It will be normalized s.t. $\sum_i \pi_i = 1$; then, π is the stationary distribution of the Markov semigroup generated by M.

We will assume throughout that M is reversible, i.e.,

$$\pi_i M_{ij} = \pi_j M_{ji} \tag{6}$$

for all i and j, which also entails $\pi_i H_{ij} = \pi_j H_{ji}$ since R is diagonal. Likewise, due to irreducibility, the leading eigenvalue, $\lambda_{\max}$, of H is simple; we will meet the corresponding eigenvectors in due course.

Let us note in passing that, due to reversibility, the equilibrium distribution π of M is available explicitly. To see this, let $(k_1, k_2, \ldots, k_{|S|})$ be the vertices of a Hamiltonian path of length $|S| - 1$ in our graph $G(M)$, i.e., $k_i \neq k_j$ for $i \neq j$; such a path exists due to irreducibility. Set $\tilde{\pi}_{k_1} = 1$ and, for $2 \leqslant i \leqslant |S|$,

$$\tilde{\pi}_{k_i} = \frac{M_{k_{i-1},k_i}}{M_{k_i,k_{i-1}}} \tilde{\pi}_{k_{i-1}} = \prod_{j=2}^{i} \frac{M_{k_{j-1},k_j}}{M_{k_j,k_{j-1}}} > 0 \, .$$

Then, as an immediate consequence of (6), $\pi_i = \tilde{\pi}_i / \big(\sum_{j \in S} \tilde{\pi}_j\big)$ is the stationary probability distribution of the Markov generator M; in particular, the choice of the path is arbitrary, which reflects the path independence of reversible Markov chains.

For $i \neq j$, we now define

$$F_{ij} \;:=\; \sqrt{\pi_i}\, M_{ij} \, \frac{1}{\sqrt{\pi_j}} \;=\; F_{ji} \, , \tag{7}$$

where the symmetry follows from the reversibility of M. Clearly, $F_{ij} \geqslant 0$ and $F_{ij} = (F_{ij} F_{ji})^{1/2} = (M_{ij} M_{ji})^{1/2}$. As a consequence, the matrix

$$\tilde{H} := \Pi^{1/2} H \Pi^{-1/2} \tag{8}$$

with $\Pi := \mathrm{diag}\{\pi_i \,|\, i \in S\}$ has off-diagonal entries F_{ij}, is symmetric and has the same spectrum as H, with correspondingly transformed eigenvectors. We now decompose $\tilde{H}$ in the same way as we did with H in (2), namely into a Markov generator F plus a diagonal matrix E. To this end, let $F = (F_{ij})_{i,j \in S}$ with

F_{ij} as in (7) for $i \neq j$, and complete this by $F_{ii} := -\sum_{j\in S\setminus\{i\}} F_{ij}$. With $E_i := R_i + M_{ii} - F_{ii}$, one now has $\tilde{H}_{ij} = F_{ij} + E_i\delta_{ij}$ for all $i, j \in S$, i.e.,

$$\tilde{H} = F + E \tag{9}$$

with F a Markov generator and $E = \mathrm{diag}\{E_i \mid i \in S\}$.

This now allows us to formulate a suitable variant of the Rayleigh-Ritz (or Courant-Fisher) maximum principle for the leading eigenvalue of $\tilde{H}$, compare [32, Thm. 19.4]. Clearly,

$$\begin{aligned} \lambda_{\max} &= \sup_{v:\sum_{\ell\in S} v_\ell^2=1} \sum_{i,j\in S} v_i \tilde{H}_{ij} v_j \\ &= \sup_{v:\sum_{\ell\in S} v_\ell^2=1} \Big(\sum_{i,j\in S} v_i F_{ij} v_j + \sum_{k\in S} E_k v_k^2 \Big) , \end{aligned} \tag{10}$$

where we have used the decomposition (9) in the second step. Note that the supremum is, indeed, assumed, since the space of probability measures on S is compact. The maximizer, i.e., the normalized principal eigenvector of $\tilde{H}$, is unique and strictly positive (since the same holds for the corresponding eigenvector of H), so that the above may also be read as an L^1 variant through the substitution $\nu_i := v_i^2$.

Note that, since F is a Markov generator, the quadratic form $\sum_{i,j\in S} v_i F_{ij} v_j$ is negative semidefinite with maximum 0, which is assumed for the stationary distribution of F (since F is symmetric and irreducible, this is the equidistribution, and unique). We thus have a simple upper bound on $\lambda_{\max}$:

$$\lambda_{\max} \leqslant \sup_{v:\sum_{\ell\in S} v_\ell^2=1} \sum_{k\in S} E_k v_k^2 = \max_{k\in S} E_k , \tag{11}$$

while we can obtain a lower bound for any $v \geqslant 0$ with $\sum_i v_i^2 = 1$ via

$$\sum_{i,j\in S} v_i F_{ij} v_j + \sum_{k\in S} E_k v_k^2 \leqslant \lambda_{\max} . \tag{12}$$

Even though each step of the above derivation is elementary, it is worthwhile to summarize the findings as follows.

Proposition 1. *Let S be a finite set, and let H be an $|S|\times|S|$-matrix with decomposition $H = M + R$ into an irreducible and reversible Markov generator M and a diagonal matrix R. If π is the stationary distribution of M, H can be symmetrized to $\tilde{H} = \Pi^{1/2} H \Pi^{-1/2}$ with $\Pi = \mathrm{diag}\{\pi_i \mid i \in S\}$. The matrices H and $\tilde{H}$ are isospectral, and their leading eigenvalue $\lambda_{\max}$ is given by the maximum principle* (10)*. Furthermore, simple upper and lower bounds for $\lambda_{\max}$ are provided by Eqns.* (11) *and* (12).

It is our aim to identify conditions under which the inequality (11) becomes an equality, at least asymptotically as $|S| \to \infty$.

As a first step, consider the maximizer of (10), i.e., the principal eigenvector w of $\tilde{H}$, normalized via $\sum_{i\in S} w_i^2 = 1$. Since $\tilde{H}$ is symmetric, we have $w\tilde{H} = \lambda_{\max} w$ and, simultaneously, $\tilde{H}w^T = \lambda_{\max} w^T$. Hence,

$$z^T := c_z \Pi^{-1/2} w^T \quad \text{and} \quad h := c_h w \Pi^{1/2} \tag{13}$$

are the principal right and left eigenvectors of $H = \Pi^{-1/2}\tilde{H}\Pi^{1/2}$. We will adjust the constants c_h and c_z s.t. $\sum_i h_i = \sum_i h_i z_i = 1$; clearly, this implies $c_z \cdot c_h = 1$.

The vector h gives the stationary distribution of types in Equation (3). Further, it is well-known that, for irreducible H and $t \to \infty$, the matrix $\exp(tH - \lambda_{\max}\mathbf{1})$ becomes a projector onto h, with matrix elements $z_i h_j$ (compare [26, Appendix]). Therefore,

$$\lim_{t\to\infty} \frac{\sum_{j\in S} \big(\exp(tH)\big)_{ij}}{\sum_{k,\ell\in S} h_k \big(\exp(tH)\big)_{k\ell}} = \frac{\sum_{j\in S} z_i h_j}{\sum_{\ell\in S} h_\ell} = z_i . \tag{14}$$

With (5) in mind, z_i may therefore be understood as the asymptotic offspring expectation of an i individual, relative to the mean offspring expectation of an equilibrium population. If $R = C\mathbf{1}$ for some constant C, we have $z_i \equiv 1$, in line with the fact that $H - C\mathbf{1}$ is then a Markov generator.

¿From (13) along with the normalization of h and z, the relations

$$h_i = \frac{\pi_i z_i}{\sum_{j \in S} \pi_j z_j} \quad \text{and} \quad w_i^2 = h_i z_i \tag{15}$$

are obvious. In particular, with

$$a_i := w_i^2 = h_i z_i > 0\,, \tag{16}$$

we obtain the corresponding L^1-maximizer of (10).

To arrive at another interpretation of a, consider the Markov generator Q with elements

$$Q_{ij} = z_i^{-1}(H_{ij} - \lambda_{\max}\delta_{ij})z_j\,. \tag{17}$$

It is easily confirmed that Q is indeed a Markov generator (i.e., $Q_{ij} \geqslant 0$ for $i \neq j$, and $\sum_j Q_{ij} = 0$). Using (15) and reversibility, one observes that Q may also be rewritten as

$$Q_{ij} = h_i^{-1}(H_{ji} - \lambda_{\max}\delta_{ij})h_j\,. \tag{18}$$

In the form (18), Q is the generator of the backward process on the stationary distribution as described in [25, Corollary 1] for general multitype branching processes, and used in [21] in the context of mutation-selection models. Loosely speaking, Q describes the Markov chain which results from picking individuals randomly from the stationary distribution h and following their lines of descent backward in time. Eq. (17) is the corresponding forward version as used in [24] and [19]. It is immediately verified that Q has principal left eigenvector (i.e., stationary distribution) a. This is known as the *ancestral distribution* of types; its properties are analyzed in [19]. Let us summarize as follows.

Proposition 2. *Let the assumptions be as in Proposition* 1. *Then, the principal eigenvector w of $\tilde{H}$ gives the principal left and right eigenvectors of H and their mutual relations through Eqns.* (13) *and* (15). *The L^1-maximizer $a = (a_i)_{i \in S}$ of* (10) *admits the interpretation of an ancestral distribution as the stationary state of the backward Markov generator Q of* (17) *and* (18).

3. A scalar maximum principle: An example

The maximum principle (10) is not very useful in practice if $|S|$ is large but fixed, since maximization is then over a large space. In [21], this high-dimensional maximization could be reduced to a scalar one for special choices of M and R. We will re-derive this result here in a simplified way, which will also lead the way towards the more general methods and results we are aiming at. Let $S = \{0, 1, \ldots, N\}$ with the following mutation scheme:

$$\boxed{0} \underset{U_1^-}{\overset{U_0^+}{\rightleftarrows}} \boxed{1} \underset{U_2^-}{\overset{U_1^+}{\rightleftarrows}} \boxed{2} \;\cdots\; \underset{U_{k+1}^-}{\overset{U_k^+}{\rightleftarrows}} \;\cdots\; \boxed{N{-}1} \underset{U_N^-}{\overset{U_{N-1}^+}{\rightleftarrows}} \boxed{N}$$

Suppressing the (relevant!) dependence on N in the notation, we then have

$$M_{i,i+1} = U_i^+, \quad M_{i,i-1} = U_i^- \tag{19}$$

for $i \in S$, where we set $U_N^+ = U_0^- = 0$. This is a variant of the so-called single-step mutation model of population genetics [8, Ch. III.4]. It emerges if sequences of sites (nuceotide sites or loci) are considered, and the 'type' is identified with the number of sites at which the sequence differs from a given reference sequence or wildtype; see [33] for a recent application. If fitness is a function of this number only, and if mutations occur independently of each other in continuous time, we are in the setting of the single-step mutation model.

Hence, for all $i \in S$, we have

$$F_{i,i+1} = (M_{i,i+1}M_{i+1,i})^{1/2} = (U_i^+ U_{i+1}^-)^{1/2} = F_{i+1,i} \tag{20}$$

with the obvious meaning for $i = 0$ and $i = N$; also, $F_{ij} := 0$ whenever either i or j is not in S, or if $|i - j| > 1$. In order to evaluate the lower bound in (12), let N be large, $1 \leqslant L \ll N$, and $\ell \in S$. We will use the simple test function $\nu := (\nu_0, \nu_1, \ldots, \nu_N)$ defined through

$$\nu_i = c_\ell \cdot \begin{cases} 0, & i \notin \big(\ell + [-L, L]\big) \cap S \\ 1, & i \in \big(\ell + [-L, L]\big) \cap S \end{cases}$$

with $[-L, L] := \{-L, -L+1, \ldots, L-1, L\}$, and the constant c_ℓ chosen so that $\sum_i \nu_i = 1$. That is, ν is a normalized step function around ℓ, which does not extend beyond 0 or N. If $\ell + [-L, L] \subset S$, one always has $c_\ell = 1/(2L+1)$; a short calculation shows that, in any case,

$$\frac{1}{2L+1} \leqslant c_\ell \leqslant \frac{1}{L+1},$$

due to $L \ll N$. With $\nu_i = v_i^2$, the quadratic form in (10) and (12) reduces to

$$\sum_{i,j \in S} v_i F_{ij} v_j = c_\ell \sum_{i,j \in \ell + [-L,L]} F_{ij} = -c_\ell (F_{\ell-L,\ell-L-1} + F_{\ell+L,\ell+L+1}),$$

due to the tridiagonal nature of the Markov generator F. Since $\frac{1}{2}(F_{\ell-L,\ell-L-1} + F_{\ell+L,\ell+L+1}) \leqslant \max_i F_{i,i+1} = \max_{i,j \in S} F_{ij} =: F_{\max}$, one has

$$\Big| \sum_{i,j \in S} v_i F_{ij} v_j \Big| \leqslant \frac{2F_{\max}}{L+1}. \tag{21}$$

On the other hand, the second term in (10) resp. (12) (to be called the 'diagonal part' in what follows) becomes

$$\sum_{i \in S} E_i v_i^2 = c_\ell \sum_{i=\ell-L}^{\ell+L} \Big(R_i - U_i^+ - U_i^- + \sqrt{U_i^+ U_{i+1}^-} + \sqrt{U_i^- U_{i-1}^+} \Big), \tag{22}$$

where $U_i^\pm := 0$ is implied whenever $i \notin S$.

We now assume that

$$U_i^\pm = u^\pm(x_i) + \mathcal{O}(1/N) \quad \text{and} \quad R_i = r(x_i) + \mathcal{O}(1/N) \tag{23}$$

with continuous functions u^+, u^-, and r on [0,1], and the new 'type variable' $x_i = i/N$; it is further implied that the constant in the $\mathcal{O}(1/N)$ bound is uniform for all i. (Eq. (23) differs from the scaling in [21] by a global factor of N, which means nothing but a change of the time scale.)

Define $g(x) := u^+(x) + u^-(x) - 2\sqrt{u^+(x)u^-(x)}$, let x^* be a position at which $r(x) - g(x)$ assumes its supremum, and choose $\ell := \lfloor Nx^* \rfloor$. With an appropriate scaling of L (such as $L \sim \sqrt{N}$, to be specific), the right-hand side of (21) is $\mathcal{O}(1/\sqrt{N})$. In (22), the sum has $\mathcal{O}(\sqrt{N})$ terms, which is balanced by $c_\ell = \mathcal{O}(1/\sqrt{N})$; together with (23), this turns the right-hand side of (22) into $r(x^*) - g(x^*) + \mathcal{O}(1/N)$. At the same time, the upper bound in (11) also behaves like $r(x^*) - g(x^*) + \mathcal{O}(1/N)$. Taking everything together, we obtain the asymptotic maximum principle for $N \to \infty$:

$$\lambda_{\max} = \sup_{x \in [0,1]} \big(r(x) - g(x) \big) \tag{24}$$

up to $\mathcal{O}(1/\sqrt{N})$.

Finally, recall from Section 2 that, for finite N, the maximizer of (10) is unique and given by the ancestral distribution $a = (h_i z_i)_{i \in S}$. However, in the limit as $N \to \infty$, uniqueness may be lost, which is also reflected by the fact that the supremum in (24) may be assumed at more than one point. In these degenerate situations, error thresholds may occur [21].

Remark 1. The maximum principle derived in [21] also holds for functions r and $u^\pm$ with a finite number of jumps. This can be dealt with in the current framework with slightly more effort, but we avoid this here to keep the example as transparent as possible.

Remark 2. With a more careful choice for the scaling of L, one gets the quadratic form (defined by the matrix F) down to $\mathcal{O}(1/N^{1-\varepsilon})$ for arbitrary $\varepsilon > 0$, but $\mathcal{O}(1/N)$ is only obtained with the help of better (smooth) test functions. This will now be done.

4. Asymptotics for the leading eigenvalue

The maximum principle allows for an asymptotic estimation of the leading eigenvalue when the Markov generator F can be considered as 'small' in a suitable sense, in comparison to the derived effective 'diagonal' part. Before stating precise conditions and results, let us briefly discuss the heuristics behind this. Due to the symmetry of F, we can rewrite Eq. (10) as

$$\lambda_{\max} = \sup_{v: \sum_{\ell \in S} v_\ell^2 = 1} \Big(-\frac{1}{2} \sum_{i,j \in S} F_{ij} (v_i - v_j)^2 + \sum_{k \in S} E_k v_k^2 \Big) . \tag{25}$$

Thus, it is obvious that the F-term favours constant v while the diagonal E-part favours v that are concentrated on the points k where E_k is maximal. Clearly, the outcome of this competition depends on some concentration and smoothness properties of the matrices involved.

For simplicity, let us now assume that our set S consists of integers or, more generally, d-tuples of integers. So, $S \subset \mathbb{Z}^d$, with $|S| < \infty$. We will now look more closely into the situation where $|S| \nearrow \infty$. Consider a family of sets

$$S = S(N), \quad S \subset \mathbb{Z}^d, \quad \text{so that} \quad |S| \sim N^d \quad \text{as } N \to \infty, \tag{26}$$

where we suppress once again the dependence of S on N. A reasonable setup is then obtained if $\frac{1}{N} \cdot S \subset D$, where D is a compact domain in $\mathbb{R}^d$, $\frac{1}{N} \cdot S$ becomes dense in D for $N \to \infty$, and there exist functions E and f_k from $C_b^2(D, \mathbb{R})$ with

$$E_i = E\Big(\frac{i}{N}\Big) + \mathcal{O}\Big(\frac{1}{N}\Big) \tag{27}$$

and

$$F_{ij} = f_k\Big(\frac{i}{N}\Big) + \mathcal{O}\Big(\frac{1}{N}\Big) , \tag{28}$$

where $k = j - i$, and the constant in the $\mathcal{O}(1/N)$ bound is uniform for all i and j. More generally, one can replace $\mathcal{O}(1/N)$ in (27) and (28) by $\mathcal{O}(1/\eta(N))$ for some function $\eta(N)$ that grows with N, if that better suits the individual situation.

Our main result will be the following theorem. For $S \subset \mathbb{Z}^d$, we will use throughout the slightly abusive notation $S - j := \{i - j \mid i \in S\}$.

Theorem 1. *Assume that E_i and F_{ij} are as in Eqns.* (27) *and* (28) *. Assume further that the $C_b^2(D, \mathbb{R})$ function E assumes its absolute maximum in int(D), and that f satisfies*

$$\sum_{k \in S - i} f_k\Big(\frac{i}{N}\Big) |k_\ell| k_m^2 \leqslant C \tag{29}$$

for some constant C, uniformly for all $i \in S$, and $1 \leqslant \ell, m \leqslant d$. Then, there exist constants $0 \leqslant C', C'' < \infty$ such that

$$E(x^*) - \frac{C'}{N} \leqslant \lambda_{\max} \leqslant E(x^*) + \frac{C''}{N}, \tag{30}$$

where x^* is a point where $E(x)$ assumes its maximum.

Remark 3. It will become clear when we proceed that the condition on the derivatives of $E(x)$ and the $f_k(x)$ may be relaxed; it is indeed sufficient that these functions be C_b^2 *locally*, in a neighbourhood of x^*.

Note that the upper bound is clear in view of Eqns. (27) and (11) (recall that the quadratic form defined by F is negative semidefinite); it can be made sharper if the order of the approximation in (27) and (28) is improved. It remains to prove the lower bound (which cannot be improved by sharpening the $\mathcal{O}(1/N)$ in (27) and (28)). We will do so by evaluating the quadratic form in (25) for a sequence of test functions of Gaussian type centred around x^* in the interior of D (and approaching a Dirac measure located at x^* with increasing N). Specifically, we will use throughout

$$v_i := c e^{-\alpha N |i/N - x^*|^2} \quad \text{with } c = c(N) \quad \text{s.t.} \quad \sum_{i \in S} v_i^2 = 1, \tag{31}$$

where $\alpha > 0$ is a positive real number independent of N.

We will first consider the diagonal part and show

Proposition 3. *Let E_i be as in* (27) *and x^* be a point in the interior of D where $E(x)$ assumes its maximum. Let the v_i be as in Eq.* (31). *Then,*

$$\sum_{i\in S} E_i v_i^2 = E(x^*) + \mathcal{O}\Big(\frac{1}{N}\Big)\,.$$

The upper bound in the proposition being immediate, we only need to prove the lower bound. We will use the following fact.

Lemma 1. *Let $g:\ \mathbb{R}^d \longrightarrow \mathbb{R}_{\geqslant 0}$ be a non-negative, continuous, integrable function with $g(x) \leqslant C/(1+|x|)^{d+\varepsilon}$ for all x, and (fixed) positive constants C and ε. Then, for any $x^* \in \mathbb{R}^d$,*

$$\lim_{n\to\infty} \frac{1}{n^d} \sum_{i\in\mathbb{Z}^d} g\Big(\frac{i}{N} - nx^*\Big) = \int_{\mathbb{R}^d} g(x)\,\mathrm{d}x\,. \tag{32}$$

Proof. Note first that the sum in (32) exists for arbitrary, but fixed n due to the assumed decay condition for g. Let $b_n := \times_{k=1}^{d}(-1/2n, 1/2n]$. Then, one has $\mathbb{R}^d = \dot{\bigcup}_{i\in\mathbb{Z}^d}(i/n + b_n)$, and, for all x, there is a (unique) element γ of $\mathbb{Z}^d/n$ with $x \in \gamma + b_n$; this will be called $\gamma_n(x)$. We now define

$$g_n^+(x) := \sup_{z\in(\gamma_n(x)+b_n)} g(z), \quad g_n^-(x) := \inf_{z\in(\gamma_n(x)+b_n)} g(z)\,. \tag{33}$$

Since integration over $\mathbb{R}^d$ is invariant under a shift of argument, and $g_n^\pm$ are step functions, we have

$$\begin{aligned}\int_{\mathbb{R}^d} g_n^-(x)\,\mathrm{d}x &= \int_{\mathbb{R}^d} g_n^-(x - nx^*)\,\mathrm{d}x = \frac{1}{n^d}\sum_{i\in\mathbb{Z}^d} g_n^-(i/n - nx^*)\\ &\leqslant \frac{1}{n^d}\sum_{i\in\mathbb{Z}^d} g(i/n - nx^*) \leqslant \frac{1}{n^d}\sum_{i\in\mathbb{Z}^d} g_n^+(i/n - nx^*)\\ &= \int_{\mathbb{R}^d} g_n^+(x - nx^*)\,\mathrm{d}x = \int_{\mathbb{R}^d} g_n^+(x)\,\mathrm{d}x\,.\end{aligned} \tag{34}$$

Both g_n^+ and g_n^- converge to g pointwise (since g is continuous). Further, $g_n^\pm(x)$ are both bounded from above due to the properties of the assumed majorizing function, and hence $\int_{\mathbb{R}^d} g_n^-(x)\,\mathrm{d}x$ and $\int_{\mathbb{R}^d} g_n^+(x)\,\mathrm{d}x$ both converge to $\int_{\mathbb{R}^d} g(x)\,\mathrm{d}x$ as $n\to\infty$ by the dominated convergence theorem. But then, the same must be true of the sum in (34), which proves the assertion.

We will use the following immediate corollary.

Corollary 1. *For any non-negative integer k, and any $\alpha > 0$*

$$\lim_{N\to\infty} N^{(k-d)/2} \sum_{i\in\mathbb{Z}^d} \Big|\frac{i}{N} - x^*\Big|^k e^{-\alpha N|i/N - x^*|^2} = \int_{\mathbb{R}^d} |x|^k e^{-\alpha|x|^2}\,\mathrm{d}x\,. \tag{35}$$

Proof. Use Lemma 1 with $n = \sqrt{N}$ and $g(x) = |x|^k e^{-\alpha|x|^2}$.

The following is a simple consequence of the preceding corollary.

Lemma 2. *For any $A \subset \mathbb{Z}^d$, $\delta > 0$ and $k \in \mathbb{N}$,*

$$N^{(k-d)/2} \sum_{\substack{i\in A:\\ |i/N - x^*|\geqslant\delta}} \Big|\frac{i}{N} - x^*\Big|^k e^{-2\alpha N|i/N - x^*|^2} = \mathcal{O}\big(e^{-\alpha N\delta^2}\big)\,. \tag{36}$$

Proof. Just note that

$$\begin{aligned}&N^{(k-d)/2} \sum_{\substack{i\in A:\\ |i/N - x^*|\geqslant\delta}} \Big|\frac{i}{N} - x^*\Big|^k e^{-2\alpha N|i/N - x^*|^2}\\ &\qquad\qquad \leqslant e^{-\alpha N\delta^2} N^{(k-d)/2} \sum_{i\in\mathbb{Z}^d} \Big|\frac{i}{N} - x^*\Big|^k e^{-\alpha N|i/N - x^*|^2}\end{aligned} \tag{37}$$

and apply Corollary 1 to the last expression to get the assertion.

This yields a variant of Corollary 1:

Corollary 2. *Corollary* 1 *holds true with* $\mathbb{Z}^d$ *replaced by* $S(N)$ *of* (26).

Proof. Since $x^* \in \mathrm{int}(D)$, we may choose a $\delta > 0$ so that $\mathbb{Z}^d \setminus S(N) \subset \{i \in \mathbb{Z}^d : |i/N - x^*| \geqslant \delta\}$. Then, the difference in the sum in (35) is $\mathcal{O}(e^{-\alpha N \delta^2})$, according to Lemma 2, with $A = S(N)$.

We are now ready to prove Proposition 3.

Proof. Since we may write

$$\Big|\frac{i}{N} - x^*\Big|^k v_i^2 = \frac{1}{N^{k/2}} \frac{N^{(k-d)/2}|i/N - x^*|^k e^{-2\alpha N|i/N-x^*|^2}}{N^{d/2}\sum_{j\in S} e^{-2\alpha N|i/N-x^*|^2}} \,,$$

Lemma 2 and Corollary 2 entail that, for $k > 0$,

$$\sum_{\substack{i\in S(N):\\ |i/N-x^*|\geqslant\delta}} \Big|\frac{i}{N} - x^*\Big|^k v_i^2 = \mathcal{O}(e^{-\alpha N\delta^2}) \tag{38}$$

and

$$\sum_{\substack{i\in S(N):\\ |i/N-x^*|<\delta}} \Big|\frac{i}{N} - x^*\Big|^k v_i^2 = \mathcal{O}\Big(\frac{1}{N^{k/2}}\Big)\,. \tag{39}$$

So far, we have only used that x^* is in $\mathrm{int}(D)$. But x^* is also a point where $E(x)$ assumes its maximum, and $E(x)$ is twice differentiable in a neighbourhood of x^*. Hence, there exist $\delta > 0$ and $0 \leqslant C < \infty$, such that for all $|x - x^*| < \delta$, $E(x) \geqslant E(x^*) - C|x - x^*|^2$. Therefore,

$$\begin{aligned}
\sum_{i\in S} v_i^2 E_i &= \mathcal{O}\Big(\frac{1}{N}\Big) + \sum_{\substack{i\in S:\\ |i/N-x^*|<\delta}} E\Big(\frac{i}{N}\Big)v_i^2 + \sum_{\substack{i\in S:\\ |i/N-x^*|\geqslant\delta}} E\Big(\frac{i}{N}\Big)v_i^2 \\
&\geqslant E(x^*)\big(1 + \mathcal{O}(e^{-\alpha N\delta^2})\big) - C \sum_{\substack{i\in S:\\ |i/N-x^*|<\delta}} \Big|\frac{i}{N} - x^*\Big|^2 v_i^2 \\
&\quad + \mathcal{O}\Big(\frac{1}{N}\Big) + \inf_{x\in D}\big(E(x)\big) \sum_{\substack{i\in S:\\ |i/N-x^*|\geqslant\delta}} v_i^2 \\
&= E(x^*) + \mathcal{O}\Big(\frac{1}{N}\Big),
\end{aligned}$$

where we have used (27) along with normalization in the first, (38) in the second, and (38) and (39) in the last step. This proves the assertion of Proposition 3.

After dealing with the diagonal part, we are now ready to embark on the quadratic form.

Proposition 4. *Let* F_{ij} *be as in* (28)*, and assume that* f *satisfies condition* (29) *of Theorem* 1*. Then,*

$$\sum_{i,j\in S} v_i F_{ij} v_j = \mathcal{O}\Big(\frac{1}{N}\Big)\,.$$

Proof. Evaluating the difference between $|i/N - x^*|^2 = \langle i/N - x^*, i/N - x^*\rangle$ and $|j/N - x^*|^2 = \langle j/N - x^*, j/N - x^*\rangle$, we first note that $|j/N - x^*|^2 - |i/N - x^*|^2 = \langle (i+j)/N - 2x^*, (j-i)/N\rangle$ (here, $\langle .\,,.\rangle$ denotes the scalar product). In view of $v_i = ce^{-\alpha N\langle i/N-x^*, i/N-x^*\rangle}$, and with $j = i + k$,

$$v_i > v_{i+k} \iff \eta(i,k) := \Big\langle \frac{2i+k}{N} - 2x^*, \frac{k}{N}\Big\rangle > 0$$

(note that $\eta(i,0)=0$). Using $F_{ij}=F_{ji}$ (see (7)), $(v_i-v_j)^2=(v_j-v_i)^2$, and $F_{i,i+k}=f_k(i/N)+\mathcal{O}(1/N)$ (see (28)), we can rewrite the quadratic form as

$$\begin{aligned}\sum_{i,j\in S} v_i F_{ij} v_j &= -\frac{1}{2}\sum_{i\in S}\sum_{k\in S-i} F_{i,i+k}(v_i-v_{i+k})^2 \\ &= -\sum_{i\in S}\sum_{\substack{k\in S-i\\ \eta(i,k)>0}} F_{i,i+k}(v_i-v_{i+k})^2 \\ &= -\sum_{i\in S}\sum_{\substack{k\in S-i:\\ \eta(i,k)>0}} \Big(f_k\Big(\frac{i}{N}\Big)+\mathcal{O}\Big(\frac{1}{N}\Big)\Big)(v_i-v_{i+k})^2 \,.\end{aligned}$$

We have thus achieved that the summation includes only terms where $v_i>v_{i+k}$, which entails that

$$v_i-v_{i+k}=ce^{-\alpha N|i/N-x^*|^2}(1-e^{-\alpha N\eta(i,k)})\leqslant c\alpha Ne^{-\alpha N|i/N-x^*|^2}\eta(i,k)\,,$$

since $1-e^{-x}\leqslant\min(x,1)\leqslant x$ for $x\geqslant 0$ (of which we only use the latter inequality). Together with the fact that the quadratic form is negative semidefinite, this gives

$$\begin{aligned}0 &\geqslant -\frac{1}{2}\sum_{i\in S}\sum_{k\in S-i} F_{i,i+k}(v_i-v_{i+k})^2 \\ &\geqslant -\alpha^2N^2\sum_{i\in S} v_i^2 \sum_{\substack{k\in S-i:\\ \eta(i,k)>0}} \Big(f_k\Big(\frac{i}{N}\Big)+\mathcal{O}\Big(\frac{1}{N}\Big)\Big)\big(\eta(i,k)\big)^2 \\ &\geqslant -\alpha^2N^2\sum_{i\in S} v_i^2 \sum_{k\in S-i} \Big(f_k\Big(\frac{i}{N}\Big)+\mathcal{O}\Big(\frac{1}{N}\Big)\Big)\big(\eta(i,k)\big)^2\,. \end{aligned}\tag{40}$$

In the last step, the constraint on the sum could be removed since we added to the sum nonnegative terms only: $f_k(i/N)\geqslant 0$ for $k\neq 0$, and $\big(\eta(i,k)\big)^2\geqslant 0$ with equality for $k=0$.

We now note that (29) entails that, for $1\leqslant \ell,m\leqslant d$,

$$\sum_{k\in S-i} f_k\Big(\frac{i}{N}\Big)k_\ell k_m,\qquad \sum_{k\in S-i} f_k\Big(\frac{i}{N}\Big)k_\ell k_m^2,\qquad\text{and}\qquad \sum_{k\in S-i} f_k\Big(\frac{i}{N}\Big)k_\ell^2k_m^2/N \tag{41}$$

are all bounded from above by a positive constant C (the latter case relies on $S/N\subset D$ with compact D). Writing

$$\begin{aligned}\big(\eta(i,k)\big)^2 &= \Big\langle 2\Big(\frac{i}{N}-x^*\Big)+\frac{k}{N},\frac{k}{N}\Big\rangle^2 \\ &= \frac{1}{N^2}\sum_{\ell,m=1}^{d} k_\ell k_m\Big[4\Big(\frac{i_\ell}{N}-x_\ell^*\Big)\Big(\frac{i_m}{N}-x_m^*\Big)+4\Big(\frac{i_\ell}{N}-x_\ell^*\Big)\frac{k_m}{N}+\frac{k_mk_\ell}{N^2}\Big]\end{aligned}$$

allows us to bound the various parts of the sum in (40) as follows:

$$\begin{aligned}&-4\sum_{i\in S}v_i^2\sum_{k\in S-i}f_k\Big(\frac{i}{N}\Big)\sum_{\ell,m=1}^{d}k_\ell k_m\Big(\frac{i_\ell}{N}-x_\ell^*\Big)\Big(\frac{i_m}{N}-x_m^*\Big) \\ &\qquad\qquad \geqslant -4Cd\sum_{m=1}^{d}\sum_{i\in S}\Big(\frac{i_m}{N}-x_m^*\Big)^2v_i^2=\mathcal{O}\Big(\frac{1}{N}\Big)\,,\end{aligned}\tag{42}$$

where we used the Cauchy-Schwarz inequality for

$$\sum_{\ell,m=1}^{d}k_\ell k_m\Big(\frac{i_\ell}{N}-x_\ell^*\Big)\Big(\frac{i_m}{N}-x_m^*\Big)\leqslant\sum_{\ell=1}^{d}k_\ell^2\sum_{m=1}^{d}\Big(\frac{i_m}{N}-x_m^*\Big)^2,$$

(41) in the first, and (38) and (39) in the last step.

Again, with (41), (38), and (39), we obtain

$$-4\sum_{i\in S} v_i^2 \sum_{\ell,m=1}^{d} \sum_{k\in S-i} f_k\Big(\frac{i}{N}\Big)\frac{k_\ell k_m^2}{N}\Big(\frac{i_\ell}{N}-x_\ell^*\Big)$$
$$\geqslant -4\frac{Cd}{N}\sum_{i\in S} v_i^2 \sum_{l=1}^{d}\Big|\frac{i_\ell}{N}-x_\ell^*\Big| = \mathcal{O}\Big(\frac{1}{N^{3/2}}\Big), \quad (43)$$

where we further used that $\sum_{\ell=1}^d |i_\ell/N - x_\ell^*| \leqslant c|i/N - x^*|$ for some positive constant c. Finally, (41) also gives that

$$\sum_{i\in S} v_i^2 \sum_{\ell,m=1}^{d} \sum_{k\in S-i} f_k\Big(\frac{i}{N}\Big)\frac{k_\ell^2 k_m^2}{N^2} = \mathcal{O}\Big(\frac{1}{N}\Big). \quad (44)$$

Combining (42), (43), and (44), we arrive at the assertion.

Remark 4. Eq. (44) is the reason that the lower bound in (30) cannot be improved by better approximations in (27) and (28).

Remark 5. We have, so far, assumed that x^* is in the interior of D. If x^* is on the boundary of D, a similar approach may be taken with a one-sided, exponentially decaying test function. The error in the approximation will, however, be larger than in the case tackled here.

In both cases, much finer results can be obtained using more advanced methods of perturbation theory [28], which, however, require much more work.

So far, we have used the Rayleigh-Ritz variational principle (10) to obtain results on the leading eigenvalue of H, but said nothing about the maximizer (note that this need *not* coincide with the test function v). Recall from Section 2 that, for finite N, the maximizer is unique and – in its L^1 version – given by the ancestral distribution $a = (h_i z_i)_{i\in S}$. Actually, from the bounds above, we can also conclude that a is concentrated in a neighbourhood of x^*, where the size of the neighbourhood depends on the behaviour of E near its maximum. In the generic case of a quadratic maximum, a is concentrated in a region with a width of order $1/\sqrt{N}$.

More precisely, we have:

Theorem 2. *Let E_i and F_{ij} satisfy the hypotheses of Theorem 1. Assume that E assumes its maximum at a unique point $x^* \in int(D)$, and that the Hessian of E at x^* is positive definite. Then, for every $0 < \beta \leqslant 1$, there is a $\rho > 0$, independent of N, so that, for N large enough:*

$$\sum_{\substack{i\in S:\\ |i/N - x^*|\geqslant\sqrt{\rho/\beta N}}} a_i \leqslant \beta\,,$$

where a is the ancestral distribution (of (16) and Prop. 2).

Proof. Recall first that the (L^2) maximizer of (10) is given by $w = (\sqrt{a_i})_{i\in S}$ (cf. (16)). Hence, by Theorem 1, the negative semidefiniteness of F, and (27), we have

$$\begin{aligned} E(x^*) - \frac{C'}{N} \leqslant \lambda_{\max} &= \sum_{i,j\in S} w_i F_{ij} w_j + \sum_{i\in S} E_i w_i^2 \\ &\leqslant \sum_{i\in S} E_i w_i^2 \leqslant \max_{i\in S} E_i = E(x^*) + \mathcal{O}\Big(\frac{1}{N}\Big)\,. \end{aligned} \quad (45)$$

Now, consider $E(x)$ in a neighbourhood of x^*. Since the Hessian at x^* is positive definite, we have $E(x) \leqslant E(x^*) - C|x - x^*|^2$ for some $C > 0$ in a neighbourhood of x^*. For ε small enough and $\delta(\varepsilon) := \sqrt{\varepsilon/C}$, therefore,

$$E(x) \leqslant \begin{cases} E(x^*), & |x - x^*| < \delta(\varepsilon) \\ E(x^*) - \varepsilon, & |x - x^*| \geqslant \delta(\varepsilon). \end{cases}$$

Together with (27) and (45), this implies

$$E(x^*) + \mathcal{O}\Big(\frac{1}{N}\Big) = \sum_{i\in S} E_i w_i^2 \leqslant E(x^*) - \varepsilon \sum_{\substack{i\in S:\\ |i/N - x^*| \geqslant \delta(\varepsilon)}} w_i^2 + \mathcal{O}\Big(\frac{1}{N}\Big)$$
$$\leqslant E(x^*) + \mathcal{O}\Big(\frac{1}{N}\Big)\,.$$

Hence, for some positive constant γ, $0 \leqslant \varepsilon \sum_{i:|i/N-x^*|\geqslant\delta(\varepsilon)} w_i^2 \leqslant \gamma/N$. Choosing $\varepsilon = \gamma/\beta N$ gives the assertion.

Remark 6. For notational simplicity, we have assumed above that $E(x)$ assumes its (absolute) maximum at a unique point x^*, which is the generic case. It is obvious from the proof, however, that an analogous result holds if the maximum is assumed at a finite number of points (each with a positive definite Hessian). Then, the ancestral distribution is concentrated on the union of the corresponding neighbourhoods of these points (or a subset thereof), again with widths of order $1/\sqrt{N}$.

Let us return to the case where $E(x)$ assumes its (absolute) maximum at a unique point x^*. We have seen that the ancestral distribution concentrates around x^* for $N \to \infty$, in the sense that any given fixed fraction β (or even more) of the distribution's mass is contained in a region whose width decreases with $1/\sqrt{N}$. Since this is true for arbitrary β, it is clear that the ancestral distribution must approach a point measure located at x^*. As a consequence, the *mean ancestral type*, $\sum_i x_i a_i$, converges to x^*, which adds some interpretation to the scalar maximum principle in Theorem 1; for further details, see [21].

5. Lumping

So far, we have not specified the type space S. In the example of Section 3, the types were defined in terms of some intermediate genetic level that could be derived from a more detailed picture. In this Section, we will show that a large class of models on a type space S can be derived, in a natural way, from models defined on a 'larger' space $\mathfrak{S}$ (to be called genotype space) if the branching and mutation rates fulfill certain symmetry or compatibility conditions. The idea rests on the common assumption that fitness depends on the genotype through an intermediate level of 'effective' parameters (which may, for example, be 'phenotypes', or 'genetic values' in quantitative genetics), and the mapping from the genotype to this intermediate level is multiple-to-one. One will therefore try and combine several of the genotypes into a single one; if this is also compatible with the mutation scheme, a reduction of the number of dimensions is possible. In the theory of Markov chains, this approach is known as *lumping* [29, Ch. VI]. We will proceed in two steps: First, the lumping procedure will be described in an abstract setting, with arbitrary genotype and type spaces $\mathfrak{S}$ and S, respectively. In a second step, we will specialize to the concrete sequence (or multi-locus) picture.

For the first step, let $\mathfrak{S}$ be a possibly large, but finite set. In analogy with (1), consider the dynamics

$$\dot{\rho} = \rho(\mathcal{M} + \mathcal{R}) \tag{46}$$

on $\mathbb{R}^{|\mathfrak{S}|}$, with $\mathcal{M}$ a Markov generator and $\mathcal{R} = \mathrm{diag}\{\mathcal{R}_\sigma \mid \sigma \in \mathfrak{S}\}$. Consider a mapping

$$\varphi:\ \mathfrak{S} \longrightarrow S = \mathrm{im}(\varphi) \tag{47}$$

so that $\mathfrak{S}$ may be understood as the disjoint union of fibres Φ_m:

$$\mathfrak{S} = \dot{\bigcup}_{m\in S} \Phi_m\,, \quad \text{with} \quad \Phi_m := \{\sigma \in \mathfrak{S} \mid \varphi(\sigma) = m\} = \varphi^{-1}(m)\,.$$

We will now give conditions under which the dynamics (46) may be reduced to a dynamics on S. The following result is a variant of a theorem by Burke and Rosenblatt [9], see also [29, Chapter VI].

Theorem 3. *Let $\mathfrak{S}$ and S be finite, let φ be the mapping of* (47)*, and assume that there are matrices $M = (M_{nm})_{n,m\in S}$ and $R = \mathrm{diag}\{R_i \mid i \in S\}$ with*

$$\mathcal{R}_\sigma = R_{\varphi(\sigma)} \qquad \textit{for all } \sigma \in \mathfrak{S}, \tag{48}$$

$$\sum_{\tau \in \Phi_m} \mathcal{M}_{\sigma,\tau} = M_{\varphi(\sigma),m} \quad \textit{for all } \sigma \in \mathfrak{S},\ m \in S\,, \tag{49}$$

where $\mathcal{M}$ is the Markov generator of Eq. (46). *Then, M is a Markov generator on $\mathbb{R}^{|S|}$. If ρ solves* (46)*, then*

$$y_m := \sum_{\sigma \in \Phi_m} \rho_\sigma \tag{50}$$

satisfies the differential equation (1)*, i.e., $\dot{y}_m = \sum_n y_n(M_{nm} + R_n \delta_{nm})$. If $\mathcal{M}$ is reversible with respect to $\tilde{\pi} = (\tilde{\pi}_\sigma)_{\sigma \in \mathfrak{S}}$, M is reversible with respect to $\pi = (\pi_m)_{m \in S}$, where $\pi_m = \sum_{\sigma \in \Phi_m} \tilde{\pi}_\sigma$. If $\mathcal{M} + \mathcal{R}$ has principal left eigenvector $\tilde{h}$, then $M + R$ has principal left eigenvector h with $h_m = \sum_{\sigma \in \Phi_m} \tilde{h}_\sigma$.*

Proof. The proof is a straightforward verification. Note first that M is a Markov generator (on $\mathbb{R}^{|S|}$), because, for any $\sigma \in \Phi_m$,

$$\sum_{n \in S} M_{mn} = \sum_{n \in S} \sum_{\tau \in \Phi_n} \mathcal{M}_{\sigma\tau} = \sum_{\tau \in \mathfrak{S}} \mathcal{M}_{\sigma\tau} \;=\; 0\,,$$

since $\mathcal{M}$ is a Markov generator.

Starting now from (50) and (46), we find

$$\begin{aligned} \dot{y}_m &= \sum_{\sigma \in \Phi_m} \dot{\rho}_\sigma = \sum_{\sigma \in \Phi_m} \sum_{\tau \in \mathfrak{S}} \rho_\tau (\mathcal{M}_{\tau\sigma} + \mathcal{R}_\tau \delta_{\tau\sigma}) \\ &= \sum_{n \in S} \sum_{\tau \in \Phi_n} \rho_\tau \big(M_{\varphi(\tau),m} + R_{\varphi(\tau)} \delta_{\varphi(\tau),m} \big) \\ &= \sum_{n \in S} y_n (M_{nm} + R_n \delta_{nm})\,, \end{aligned}$$

where we have used (48) and (49) in the second step, and (50) in the last, together with the fact that both $M_{\varphi(\tau),m}$ and $R_{\varphi(\tau)} \delta_{\varphi(\tau),m}$ are constant on every fibre Φ_m.

Finally, the assertions on stationary distributions and reversibility are direct verifications in the same spirit.

6. From sequence space to type space

In this Section, we will be more explicit and start from sequence space. The natural scheme that will emerge involves the grouping of sequence positions together with a 'coarse-grained' dependence on some 'genetic distance'. Many of the frequently-used models fall into this scheme. Related results appear in statistical physics, cf. [7,6], from where we will borrow some techniques.

Let us begin with the general setup for a mutation-reproduction model on sequence space. We will assume that the type σ of an individual is characterized by a (DNA, RNA) sequence which we take to be an element of the space $\mathfrak{S} := \Sigma^N$ with $\Sigma = \{1, \ldots, q\}$; we write $\sigma = (\sigma_1, \ldots, \sigma_N)$. For generality, we let q be an integer $\geqslant 2$; if $q = 2$, the alternative choice $\Sigma = \{-1, 1\}$ is often more convenient. Consider now the partition of the index set $\Lambda = \{1, \ldots, N\}$ into d disjoint subsets Λ_i, i.e.,

$$\Lambda = \dot{\bigcup}_{1 \leqslant i \leqslant d} \Lambda_i. \tag{51}$$

Let $\mathcal{P}(\Sigma) = \{(\mu_1, \ldots, \mu_q) \mid \mu_\ell \geqslant 0, \sum_\ell \mu_\ell = 1\}$ denote the set of probability measures on Σ. Set, with obvious meaning,

$$\mathcal{P}_{\Lambda_i}(\Sigma) := \mathcal{P}(\Sigma) \cap \Big\{0, \frac{1}{|\Lambda_i|}, \frac{2}{|\Lambda_i|}, \ldots, 1 - \frac{1}{|\Lambda_i|}, 1\Big\}^q$$

and

$$\mathcal{P}_{(\Lambda_1, \ldots, \Lambda_d)}(\Sigma) = \bigotimes_{i=1}^{d} \mathcal{P}_{\Lambda_i}(\Sigma)\,. \tag{52}$$

That is, $\mathcal{P}_{(\Lambda_1, \ldots, \Lambda_d)}(\Sigma)$ is the set of product measures with values restricted to certain rationals induced by the partition.

Consider now the mapping (which will take the role of φ from the previous Section)

$$\mathfrak{m}:\ \Sigma^N \longrightarrow \mathbb{Q}^{dq}, \quad \sigma \mapsto \mathfrak{m}(\sigma) \tag{53}$$

with $\mathfrak{m}(\sigma) = \big(\mathfrak{m}_i^\ell(\sigma)\big)_{1\leqslant i\leqslant d}^{1\leqslant \ell\leqslant q}$ and

$$\mathfrak{m}_i^\ell(\sigma) := \frac{1}{|\Lambda_i|}\sum_{j\in\Lambda_i}\delta_{\ell,\sigma_j} = \frac{1}{|\Lambda_i|}\big|\{j \mid j\in\Lambda_i, \sigma_j=\ell\}\big|. \tag{54}$$

So, $\mathfrak{m}_i^\ell(\sigma)$ is the fraction of the sites at positions in Λ_i which are in state ℓ. Note that these quantities satisfy $\sum_{\ell=1}^q \mathfrak{m}_i^\ell(\sigma) = 1$, i.e., for each i, $\mathfrak{m}_i(\sigma) := \big(\mathfrak{m}_i^1(\sigma),\dots,\mathfrak{m}_i^q(\sigma)\big)$ defines a probability measure on Σ, with $\mathfrak{m}_i \in \mathcal{P}_{\Lambda_i}(\Sigma)$.

Describing the system in terms of these lumped quantities will only lead to a simplification in connection with a suitable symmetry. In our case, this is given by those permutations of the sites that are compatible with the chosen partition.

Let Γ_Λ be the permutation group on $\Lambda = \{1,\dots,N\}$, i.e.,

$$\Gamma_\Lambda := \{\gamma \mid \gamma:\ \Lambda\to\Lambda \text{ is a bijection}\},$$

and $\Gamma_{(\Lambda_1,\dots,\Lambda_d)}$ the subgroup compatible with the partition (51), i.e.,

$$\Gamma_{(\Lambda_1,\dots,\Lambda_d)} = \big\{\gamma\in\Gamma_\Lambda \mid \gamma(\Lambda_i)=\Lambda_i, 1\leqslant i\leqslant d\big\} \simeq \Gamma_{\Lambda_1}\times\cdots\times\Gamma_{\Lambda_d}.$$

We introduce the canonical action of the permutation group on Σ^N through the inverse permutation of sites, i.e., $(\gamma\sigma)_i = \sigma_{\gamma^{-1}(i)}$. We are now ready for

Theorem 4. *Let $\Sigma^N = \{1,\dots,q\}^N$, and matrices $\mathcal{M} = (\mathcal{M}_{\sigma,\tau})_{\sigma,\tau\in\Sigma^N}$ and $\mathcal{R} = \operatorname{diag}\{\mathcal{R}_\sigma \mid \sigma\in\Sigma^N\}$ be given, with $\mathcal{M}$ a Markov generator. Let ρ solve $\dot\rho = \rho(\mathcal{M}+\mathcal{R})$. Further, let $\mathfrak{m}$ be as in (53), and $S = \mathfrak{m}(\Sigma^N) \subset \mathbb{Q}^{dq}$. Assume now that there exist a function $g:\ \Sigma^N\times\Sigma^N \longrightarrow \mathbb{R}_{\geqslant 0}$, and matrices $\hat M = (\hat M_{mn})_{m,n\in S}$ and $R = \operatorname{diag}\{R_n \mid n\in S\}$, so that the following conditions are satisfied:*

(a) $g(\gamma\tau,\gamma\sigma) = g(\tau,\sigma)$ *for all* $\gamma\in\Gamma_{(\Lambda_1,\dots,\Lambda_d)}$;
(b) $\mathcal{M}_{\sigma\tau} = \hat M_{\mathfrak{m}(\sigma),\mathfrak{m}(\tau)}\, g(\sigma,\tau)$ *for all* $\sigma,\tau\in\Sigma^N$;
(c) $\mathcal{R}_\sigma = R_{\mathfrak{m}(\sigma)}$ *for all* $\sigma\in\Sigma^N$.

Then, $y_m := \sum_{\sigma\in\Phi_m}\rho_\sigma$ solves the differential equation $\dot y = y(M+R)$, where

$$M_{nm} = \hat M_{nm}\sum_{\tau\in\Phi_m} g(\sigma,\tau)$$

independently of the choice of $\sigma\in\Phi_n$. M is a Markov generator. If $\mathcal{M}$ is reversible with respect to $\tilde\pi = (\tilde\pi_\sigma)_{\sigma\in\mathfrak{S}}$, then M is reversible with respect to $\pi = (\pi_m)_{m\in S}$, where $\pi_m = \sum_{\sigma\in\Phi_m}\tilde\pi_\sigma$. If $\mathcal{M}+\mathcal{R}$ has principal left eigenvector $\tilde h = (\tilde h_\sigma)_{\sigma\in\mathfrak{S}}$, then $M+R$ has stationary distribution $h = (h_m)_{m\in S}$ with $h_m = \sum_{\sigma\in\Phi_m}\tilde h_\sigma$.

Proof. For $\gamma\in\Gamma_{(\Lambda_1,\dots,\Lambda_d)}$, we have

$$\mathfrak{m}(\gamma\sigma) = \mathfrak{m}(\sigma) \quad\text{and}\quad \gamma(\Sigma^N) = \Sigma^N, \tag{55}$$

where the first identity is obvious from (54). Equation (55) entails that

$$\gamma(\Phi_m) = \Phi_m, \tag{56}$$

i.e., $\Gamma_{(\Lambda_1,\dots,\Lambda_d)}$ acts transitively on Φ_m.

In order to apply Theorem 1, we have to check assumption (49). Consider therefore $\sum_{\tau\in\Phi_m}\mathcal{M}_{\sigma\tau} = \hat M_{\mathfrak{m}(\sigma),m}\sum_{\tau\in\Phi_m} g(\sigma,\tau)$. For arbitrary $\gamma\in\Gamma_{(\Lambda_1,\dots,\Lambda_d)}$, assumption (a) and Eq. (56) give

$$\psi(\sigma) := \sum_{\tau\in\Phi_m} g(\sigma,\tau) = \sum_{\tau\in\Phi_m} g(\gamma\sigma,\gamma\tau)$$

$$= \sum_{\tau' \in \gamma(\Phi_m)} g(\gamma\sigma, \tau') = \sum_{\tau' \in \Phi_m} g(\gamma\sigma, \tau') = \psi(\gamma\sigma) .$$

Due to the transitivity of $\Gamma_{(\Lambda_1,\ldots,\Lambda_d)}$ on Φ_m, $\psi(\sigma)$ is constant on the fibres $\Phi_{\mathfrak{m}(\sigma)}$. Assumption (49) is therefore valid, and an application of Theorem 1 then gives the desired result.

Examples of particular relevance emerge if g is a $\Gamma_{(\Lambda_1,\ldots,\Lambda_d)}$-invariant *distance*, such as the Hamming distance (i.e., the number of sites at which two sequences differ). A very simple case was implicit in our example in Section 3, where the single-step mutation model on $S = \{0, 1, \ldots, N\}$ was interpreted in terms of a model on $\{0, 1\}^N$. Here, a site in state 0 or 1 corresponds to a site whose state does or does not coincide with the respective state of a reference sequence (sometimes called the 'wildtype'). If the reproduction and mutation rates only depend on the Hamming distance from the reference sequence, we are in a setting with $d = 1$. In such a simple case, the reduced model is immediate. More elaborate examples will be discussed in the next Section.

7. Applications and examples

In many examples of sequence space models, the lumping construction as described in the previous Sections leads to an effective model to which the maximum principle of Section Section 4 may then be applied. In particular, the following conditions are necessary for Theorem 1 to apply:

(C1) The partition $\{\Lambda_i\}_{i=1}^d$ in (51) is relatively uniform, in the sense that there exist constants $0 < c \leqslant C < 1$ such that

$$c \leqslant \inf_{1 \leqslant i \leqslant d} \frac{|\Lambda_i|}{N} \leqslant \sup_{1 \leqslant i \leqslant d} \frac{|\Lambda_i|}{N} < C$$

uniformly in N. (Alternatively, this may be replaced by the single, and slightly weaker, condition $\liminf_{N\to\infty} \inf_{1\leqslant i \leqslant d} \frac{|\Lambda_i|}{N} > 0$; note that $\sum_i |\Lambda_i| = N$ by construction.) This condition ensures that $x = i/N$ will become a meaningful continuous type variable for $N \to \infty$.

For the following two conditions, a suitable enumeration of the elements of S is required to ensure an appropriate representation of the matrices M and R.

(C2) The function g that occurs in the sequence space mutation matrix and is required in the lumping procedure (see Theorem 4) decreases sufficiently fast away from the diagonal. Note that under condition (C1), for any σ, τ we have that

$$d_{\mathrm{H}}(\sigma, \tau) \geqslant \frac{N}{C} \, \|\mathfrak{m}(\sigma) - \mathfrak{m}(\tau)\|_1 ,$$

where d_{H} is the Hamming distance. Thus, if g has compact support independent of N (as in the example in Section 3), or if it decays sufficiently fast (e.g., exponentially) with d_{H}, this entails the decay condition on f in Theorem 1.

(C3) After lumping, the effective reproduction and mutation matrices R and M must lend themselves to a continuous approximation. That is, $R_m = r(m/N) + \mathcal{O}(1/N)$ and $M_{mn} = s\big(m/N, n/N\big) + \mathcal{O}(1/N)$ with functions r and s that are $C_2^b(D, \mathbb{R})$, where the implied constant in the $\mathcal{O}(1/N)$ bound is uniform for all m and n. This entails the approximation condition on E and F in (27) and (28) that is also required for Theorem 1.

Clearly, (C2) and (C3) stipulate that the enumeration of the types is adapted to the problem. Often the right choice is intuitively clear, as in the examples in Section 3, and in [17]. But sometimes more thought is required, as will be illustrated by means of a few examples and special cases below.

1. Some simplifications arise in the case $q = 2$, where we now use $\Sigma = \{-1, 1\}$ rather than $\{0, 1\}$. Here, the constraint $\mathfrak{m}_i^1 + \mathfrak{m}_i^2 = 1$ can be used to reduce the number of variables per subset to one. It is convenient to set $b_i \equiv \mathfrak{m}_i^1 - \mathfrak{m}_i^2$. Eq. (52) is then replaced by

$$\mathcal{P}_{(\Lambda_1,\ldots,\Lambda_d)}(\Sigma) = \bigotimes_{i=1}^{d} \{-1, -1 + \frac{2}{|\Lambda_i|}, \ldots, 1 - \frac{2}{|\Lambda_i|}, 1\} ,$$

and we obtain the simple formula

$$b_i(\sigma) = \frac{1}{|\Lambda_i|} \sum_{j \in \Lambda_i} \sigma_j .$$

2. The case $d = 1$ corresponds to so-called 'mean field models'. They have been studied in the case where $g(\sigma, \tau) = 0$ for $d_{\mathrm{H}}(\sigma, \tau) \geqslant 1$, i.e., mutation is restricted to neighbours in sequence space (see [3,4,37, 5,21] for $q = 2$, and [22,17] for $q = 4$).
3. A special type of models that falls into the above class is related to fitness landscapes based on Hopfield Hamiltonians. These are special cases of spin-glass models [31] that were originally motivated by neural networks, then became prototype models for random interactions in statistical physics, and were later also used as tunably rugged fitness landscapes in biology [30,35]. We adopt from [6] the lumping procedure for the case $q = 2$ (the general setting $q > 2$ can be found in [18]). We consider the sequence space $\mathfrak{S} = \Sigma^N = \{-1, 1\}^N$. A Hopfield Hamiltonian is constructed by choosing at random M independent elements $\xi^1, \ldots, \xi^M$ from Σ^N. Given such a choice, one defines
$$\mathcal{H}_N(\sigma, \xi) := \frac{1}{N} \sum_{\mu=1}^{M} \sum_{i,j=1}^{N} \sigma_i \sigma_j \xi_i^\mu \xi_j^\mu = N \sum_{\mu=1}^{M} \big(\omega_\mu(\sigma)\big)^2,$$
where
$$\omega_\mu(\sigma) := \frac{1}{N} \sum_{i=1}^{N} \sigma_i \xi_i^\mu = \frac{1}{N} \langle \sigma, \xi^\mu \rangle \,.$$
It is convenient to associate with the collection of row vectors ξ^μ the $M \times N$ matrix $\xi = (\xi_i^\mu)_{1 \leqslant i \leqslant N}^{1 \leqslant \mu \leqslant M}$. We denote by ξ^μ the rows and by ξ_i the columns of this matrix. A partition $\Lambda_1, \ldots, \Lambda_d$ with $d = 2^M$ is now obtained as follows. Let $e_1, \ldots, e_d$ $\big(e_k = (e_k^\mu)^{1 \leq \mu \leqslant M}\big)$ denote an enumeration of all M-dimensional column vectors with entries ± 1. Then we set
$$\Lambda_k := \{ i \in \Lambda \mid \xi_i = e_k \} \,.$$
This results in
$$\omega_\mu(\sigma) = \frac{1}{N} \sum_{k=1}^{d} e_k^\mu \sum_{i \in \Lambda_k} \sigma_i = \frac{1}{N} \sum_{k=1}^{d} |\Lambda_k| e_k^\mu b_k(\sigma) \,,$$
and so
$$\mathcal{H}_N(\sigma, \xi) = N \sum_{\mu=1}^{N} \sum_{k,\ell=1}^{d} e_k^\mu e_\ell^\mu |\Lambda_k| |\Lambda_\ell| b_k(\sigma) b_\ell(\sigma)$$
is a function of $b_i(\sigma)$. Thus, if we consider reproduction and mutation rates of the form
$$\begin{aligned} \mathcal{M}_{\sigma\tau} &= \alpha\big(H_N(\sigma, \xi), H_N(\tau, \xi)\big)\, g(\sigma, \tau) \,, \\ \mathcal{R}_\sigma &= \beta\big(\mathcal{H}_N(\sigma, \xi)\big) \,, \end{aligned}$$
with a nonnegative function α and any real function β, we may apply Theorem 4 to derive the effective dynamics with lumping according to the values of $b_i(\sigma)$. In particular, the choice $\beta(x) = x$ gives the familiar Hopfield fitness landscape, and $\alpha(x) \equiv 1$ along with $g(\sigma, \tau) = \mu$ for $d_H(\sigma, \tau) = 1$, $g(\sigma, \tau) = 0$ for $d_H(\sigma, \tau) > 1$, and $g(\sigma, \sigma) = -2N\mu$ yields the well-known sequence space mutation model where every site mutates independently and at the same rate μ (e.g., [5]).

8. Concluding remarks

The motivation for this work came from continuous-time mutation-selection models, cf. (3) and (4). However, it should have become clear that our results are not tied to these specific models. They also hold for the corresponding discrete-time dynamical systems, or if there is no underlying dynamics at all. Our main result (Theorem 1) simply yields asymptotic estimates for the leading eigenvalues of large matrices that possess a certain continuous approximation, and whose elements decay sufficiently fast away from the diagonal. These properties are shared by many systems, in particular, by many spatially extended systems, where interactions between distant components are weak.

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