Solvable biological evolution models with general fitness functions and multiple mutations in parallel mutation-selection scheme

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In a recent paper [Phys. Rev. E **69**, 046121 (2004)], we used the Suzuki-Trottere formalism to study a quasispecies biological evolution model in a parallel mutation-selection scheme with a single-peak fitness function and a point mutation. In the present paper, we extend such a study to evolution models with more general fitness functions or multiple mutations in the parallel mutation-selection scheme. We give some analytical equations to define the error thresholds for some general cases of mean-field-like or symmetric mutation schemes and fitness functions. We derive some equations for the dynamics in the case of a point mutation and polynomial fitness functions. We derive exact dynamics for two-point mutations, asymmetric mutations, and the four-value spin model with a single-peak fitness function. The same method is applied for the model with a royal road fitness function. We derive the steady-state distribution for the single-peak fitness function.

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I. INTRODUCTION

An important application of statistical physics outside its traditional area is the investigation of simple microscopic biological evolution models [1–14]. Two famous models in this direction which have wide applications [5] are the Eigen model [1,2] and the Crow-Kimura model [3,4]. In the Eigen model [1,2], the species are subjected to mutation during the process of giving offsprings, so mutation is connected with the selection and the Eigen model is called a connected mutation-selection scheme. In the Crow-Kimura model [3,4], mutations and selections are two independent processes and the Crow-Kimura model is called a parallel mutation-selection scheme. Both schemes of mutation selection are relevant for biology [5]. Some interesting results have been derived for both discrete time versions [8–10] and the original continuous time version [5–7] of the Eigen and the Crow-Kimura model.

In 1997 Baake *et al.* [4] proved that for the parallel mutation-selection scheme [3] the evolution equations for the frequencies of different species are equivalent to the Schrödinger equation (in imaginary time) for quantum spins in a transverse magnetic field. Both the static [4] and dynamics [7] of the model have been solved exactly with a ferromagnetic two-spin interaction fitness function. In 2001 Hermission *et al.* proved that the four-state biological evolution model can also be related to a quantum spin model [11].

In a recent paper [12], we mapped the Eigen model onto a quantum spin model with non-Hermitian Hamiltonian. Using the Suzuki-Trottere formalism [15–17], we studied the statics and dynamics of the Eigen model and the Crow-Kimura model with the single-peak fitness function [13] and found that the relaxation in the parallel model is faster than that in the connected model [13]. It is of interest to know whether such an approach can be extended to more general and realistic cases. Following our recent works [12,13], in the present paper we will solve exactly the dynamics of several more complicated models in the parallel scheme [3,4,6] and derive some exact results in statics: an error threshold expression for the model with general fitness functions and steady-state distribution for the single peak fitness landscape. We are going to solve models with both binary and (more realistic) four-value spins. Besides the simplest single-point mutation, we will investigate also the case of multiple and asymmetric mutations, which are realistic sometimes [18,19]. In another paper [14], we will study similar problems for the evolution model with the connected mutation-selection scheme [8–10].

Here we first briefly introduce the Crow-Kimura model [3] and its quantum spin version [4] so that it is easier to understand its generalizations to be studied in the present paper. In the simple Crow-Kimura model, any genotype configuration i is specified by the values of N two-values spins $s_k=\pm 1$, $1\leqslant k\leqslant N$. We will denote such a configuration i by $S_i\equiv(s_i^1,\ldots,s_i^N)$. The difference between two configurations S_i and $S_i\equiv(s_i^1,\ldots,s_i^N)$ can be quantitatively represented by the Hamming distance $d_{ij}=(N-\Sigma_k s_i^k s_j^k)/2$, which represents the number of different spins between S_i and S_j. The relative frequencies p_i of different configurations for $1\leqslant i\leqslant 2^N$ satisfy the equations

$$\frac{dp_i}{dt}=p_i\Big(r_i-\sum\nolimits_{j=1}^{2^N}r_jp_j\Big)+\sum\nolimits_{j=1}^{2^N}m_{ij}p_j. \tag{1}$$

Here r_i are the fitness (the efficient number of offsprings per unit period of time) and m_{ij} is the mutation rate to move from the original configuration state S_j to the new genome state S_i per unit period of time and is given by

$$m_{ij}=\gamma,\quad \text{when}\quad d_{ij}=1;-N\gamma,\quad \text{when}\quad i=j;0,\quad \text{when}\quad d_{ij}>1. \tag{2}$$

This choice of mutation matrix corresponds to the case of a

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point mutation. Equation (1) with mutation rates of Eq. (2) makes sure that the condition

$$\sum_{i=1}^{2^N} p_i = 1$$

will be satisfied during the time evolution of p_i.

The choice of different fitness corresponds to the choice of different functions $r_i = f(S_i)$. It has been observed in [4] that system (1) with $r_i \equiv f(s_i^1, \ldots, s_i^N)$ evolves according to the Schrödinger equation at imaginary time

$$\frac{d}{dt}\sum_i p_i(t)|S\rangle = -H\sum_i p_i(t)|S\rangle, \tag{3}$$

with the Hamiltonian

$$-H = \gamma\sum_{i=1}^{N}(\sigma_i^x - 1) + f(\sigma_1^z \cdots \sigma_N^z). \tag{4}$$

Here S means the spin configuration of the N spins $s_i = \pm 1$, $|S\rangle$ is a product of N spinors, and σ^x and σ^z are Pauli matrices

$$\sigma^x = \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}, \quad \sigma^z = \begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}$$

which operate on the column vectors

$$\begin{bmatrix} 1 \\ 0 \end{bmatrix} \text{ and } \begin{bmatrix} 0 \\ 1 \end{bmatrix}$$

representing spin up and spin down, respectively.

If one originally has some distribution of frequencies p_j^0, then after a period of time t the new distribution should be

$$p_i(t) = \frac{\sum_j p_j^0 \langle S_i|e^{-Ht}|S_j\rangle}{Z},$$

$$Z = \sum_{ij} p_j(0)Z_{ij}, \quad Z_{ij} = \langle S_i|e^{-Ht}|S_j\rangle. \tag{5}$$

For the single-peak fitness function, without lost of generality we choose

$$f(S_1) = J_0 N, \quad \text{when} \quad S_1 \equiv (1,1,\ldots,1),$$

$$f(S_i) = 0, \quad \text{when} \quad S_i \neq S_1. \tag{6}$$

To study the dynamics of the system, we should calculate the matrix elements of the operator $T(t) \equiv e^{-Ht}$. It can be done in the Suzuki-Trottere formalism [15–17].

For the mutation scheme of Eq. (4) and the fitness function Eq. (6), the dynamics has been solved in [13]. In following sections, we will extend the methods of [13] to study dynamics for other fitness functions and/or mutation schemes. We will also calculate the error thresholds for the multiple-site mutations [instead of a single-site mutation in Eq. (4)].

The following sections are organized as follows. In the Sec. II, we use the Suzuki-Trottere formalism to derive error thresholds for very general fitness and mutation schemes. In Sec. III, we derive a complicated field-theoretical-like equation for the dynamics with a point mutation and a general fitness function. In Sec. IV, we derive exact steady-state distribution for the single-peak fitness function. Using the simple ansatz from [13], we derive in Sec. V exact relaxation periods for the royal road fitness function [20] and in Sec. IV for the realistic case of the four-value spin model. In Appendix A, we give the dynamics for the asymmetric mutations (mutation from $S_i \to S_j$ and from $S_j \to S_i$ have different rates), and in Appendix B for the two-point mutations.

II. ERROR THRESHOLDS FOR GENERAL FITNESS AND MUTATION SCHEMES

A. Error threshold for quadratics fitness and mutation schemes

Let us consider a more general Hamiltonian

$$-H = g(\sigma_1^x \cdots \sigma_N^x) + f(\sigma_1^z \cdots \sigma_N^z),$$

$$g(\sigma_1^x \cdots \sigma_N^x) = \sum_{l=1}^{N} \sum_{1 \leqslant k_1 \neq k_2 \neq \cdots \neq k_l \leqslant N} \frac{\gamma_l}{lN^{l-1}}(\sigma_{k_1}^x \sigma_{k_2}^x \cdots \sigma_{k_l}^x - 1),$$

$$f(\sigma_1^z \cdots \sigma_N^z) = \sum_{l=1}^{N} \sum_{1 \leqslant k_1 \neq k_2 \neq \cdots \neq k_l \leqslant N} \frac{\alpha_l}{lN^{l-1}} \sigma_{k_1}^z \sigma_{k_2}^z \cdots \sigma_{k_l}^z. \tag{7}$$

Here f describes the fitness and g describes the mutation (the rate of l-point mutations is γ_l / l). With the accuracy of $1/N$, we can write

$$g(\sigma_1^x \cdots \sigma_N^x) = N\sum_{l=1}^{N} \frac{\gamma_l}{l}\left(\frac{1}{N}\sum_{k=1}^{N}\sigma_k^x\right)^l - N\sum_{l=1}^{N}\frac{\gamma_l}{l}$$

$$\equiv Ng_0\left(\frac{1}{N}\sum_{k=1}^{N}\sigma_k^x\right) - N\sum_{l=1}^{N}\frac{\gamma_l}{l},$$

$$f(\sigma_1^z \cdots \sigma_N^z) = N\sum_{l=1}^{N}\frac{\alpha_l}{l}\left(\frac{1}{N}\sum_{k=1}^{N}\sigma_k^z\right)^l \equiv Nf_0\left(\frac{1}{N}\sum_{k=1}^{N}\sigma_k^z\right). \tag{8}$$

One can calculate the dynamics by means of Eq. (5). In the future we can neglect the constant term in g of Eq. (8), due to symmetry of Eqs. (3)–(5); see also Ref. [13].

To define the phase structure of the model (error threshold), we need only to consider a simpler partition

$$Z_0 = \mathrm{Tr}e^{-H\beta}; \tag{9}$$

i.e., the dynamical problem of Eq. (1) becomes a simple problem of statistical mechanics.

One can interchange σ^x and σ^z in H and Eq. (9) will be invariant. Therefore, it is possible to get the same phase structure, replacing the functions of mutation and selection.

Let us consider a quadratic form for both fitness and mutation:

$$-H = \gamma_1 \sum_{k=1}^{N} \sigma_k^x + \frac{\gamma_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^x \sigma_{k_2}^x + \alpha_1 \sum_{k=1}^{N} \sigma_k^z + \frac{\alpha_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^z \sigma_{k_2}^z. \tag{10}$$

To transform the quantum statistical mechanical problem into a problem in classical mechanics, instead of quantum spins σ^x, σ^z, we introduce $N(L+1)$ classical spins s_k^l, $1 \leqslant k \leqslant N$, $1 \leqslant l \leqslant L+1$ (corresponds to introducing the identity $\hat{I} = \Sigma_\alpha |\alpha\rangle\langle\alpha|$ between any brackets $|\rangle\langle|$), and use an identity $\mathrm{Tr} e^{A+B} = \mathrm{Tr}[e^{A/L} e^{B/L}]^L$ for a large L [15]. Using the Stratanovich transformation

$$\exp\left[\frac{\gamma_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^x \sigma_{k_2}^x \frac{\beta}{L} \right] = \sqrt{\frac{N\beta\gamma_2}{2\pi L}} \int_{-\infty}^{\infty} dz_l \exp\left[-N\beta\gamma_2 \frac{z_l^2}{2L} + \frac{\beta}{L} z_l \gamma_2 \sum_{k=1}^{N} \sigma_k^x \right] \tag{11}$$

for $Z_{ij} = \langle S_i | e^{-H\beta} | S_j \rangle$, we have

$$\begin{aligned} Z_{ij} &= \mathrm{Tr}\left\{ \exp\left[\left(\gamma_1 \sum_{k=1}^{N} \sigma_k^x + \frac{\gamma_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^x \sigma_{k_2}^x \right) \frac{\beta}{L} \right] \times \exp\left[\left(\alpha_1 \sum_{k=1}^{N} \sigma_k^z + \frac{\alpha_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^z \sigma_{k_2}^z \right) \frac{\beta}{L} \right] \right\}^L \\ &= \prod_{l=0}^{L} \sqrt{\frac{N\beta\gamma_2}{2\pi L}} \int_{-\infty}^{\infty} dz_l \mathrm{Tr}_s \exp\left[-N\beta\ \gamma_2 \sum_l \frac{z_l^2}{2L} + \frac{\beta}{L} \sum_l \times (\gamma_1 + z_l \gamma_2) \sum_{k=1}^{N} \sigma_k^x + \left(\alpha_1 \sum_{k=1}^{N} \sigma_k^z + \frac{\alpha_2}{2N} \sum_{k_1 \neq k_2 = 1}^{N} \sigma_{k_1}^z \sigma_{k_2}^z \right) \frac{\beta}{L} \right]. \end{aligned} \tag{12}$$

Here Tr_s means a summation over all spin configurations $\Sigma_{s_k^l = \pm 1}$. We take for the boundary configurations the following: s_k^1 is the kth component of S_j and s_k^{L+1} is the kth component of S_i. We then use a representation of the σ^x in the basis of $|s\rangle$, $s = \pm 1$ and for small x:

$$\langle s_1 | e^{\sigma_x x} | s_2 \rangle = e^{B(s_1 s_2 - 1)}, \quad e^{-2B} = x. \tag{13}$$

For the partition Z_0 at the limit $L \to \infty$, in this way it is possible to derive [12,16,17]

$$Z_0 = \prod_{l=0}^{L} \sqrt{\frac{N\beta\gamma_2}{2\pi L}} \int_{-\infty}^{\infty} dz_l \mathrm{Tr}_s \exp\left[-N\beta \sum_l \frac{\gamma_2 z_l^2}{2L} + \sum_{l=1}^{L} \sum_{k=1}^{N} B_l (s_k^l s_k^{l+1} - 1) + \frac{\beta N}{L} \sum_{l=1}^{L} \alpha_1 \left(\frac{\sum_{k=1}^{N} s_k^l}{N} \right) + \frac{\alpha_2}{2} \left(\frac{\sum_{k=1}^{N} s_k^l}{N} \right)^2 \right],$$

$$B_l = \frac{1}{2} ln \frac{L}{\beta(\gamma_1 + z_l \gamma_2)}. \tag{14}$$

While considering the Z_0 (instead of Z_{ij}) we sum boundary spins, which are symmetric ($s_k^1 = s_k^{L+1}$). In the last expression the interaction is only via magnetization $m_l \equiv \Sigma_{k=1}^{N} s_k^l / N$. We introduce magnetization variable m_l and corresponding Lagrange coefficient βh_l. Using the identity $\Pi_l\ N \int dm_l \delta(N m_l - \Sigma_k\ s_k^l) = 1$ and an integral representation for a δ function: $(\beta / 2\pi i L) \int_{-i\infty}^{i\infty} dh_l \exp\left[-(N\beta/L) h_l m_l + \frac{\beta}{L} h_l \Sigma_k\ s_k^l \right] = \delta(N m_l - \Sigma_k\ s_k^l)$, we derive

$$Z_0 = \prod_{l=1}^{L} \frac{\sqrt{\gamma_2}}{i} \left(\frac{\bar{\beta}}{2\pi} \right)^{3/2} \int_{-i\infty}^{i\infty} dh_l \int_{-\infty}^{\infty} dz_l dm_l \mathrm{Tr}_s \times \exp\left\{ \sum_l \left[\bar{\beta} \left(\alpha_1 m_l + \frac{\alpha_2 m_l^2}{2} \right) - \frac{\bar{\beta}\gamma_2}{2} z_l^2 - \bar{\beta} h_l m_l \right] + \sum_l \left(\frac{\beta}{L} h_l \sum_{k=1}^{N} s_k^l + B_l \sum_{k=1}^{N} (s_k^l s_k^{l+1} - 1) \right) \right\}. \tag{15}$$

Here $\bar{\beta} = N\beta / L$. In the last expression spins s_k^l with different k decouple and we can perform calculations, considering the saddle point via m_l and h_l. We take $h_l = h$, $m_l = m$, $z_l = M$, $B = \frac{1}{2} \ln [L / \beta(\gamma_1 + \gamma_2 z)]$ and missing the preexponent terms to derive

$$Z_0 \sim \int_{-i\infty}^{i\infty} dh \int_{-\infty}^{\infty} dM dm \exp\left[-\frac{N\beta\gamma_2}{2} M^2 - N\beta h m + N\beta \left(\alpha_1 m + \alpha_2 \frac{m^2}{2} \right) + N \ln z(B, h/L, L) - NBL \right], \tag{16}$$

where $z[B, h/L, L]$ is the partition function of the one-dimensional (1D) Ising model with inverse temperature B and magnetic field h/L. We should consider different saddle point solutions for m and h and choose the one with maximal value in the exponent.

We have an expression for the 1D Ising L spin partition in a magnetic field h/L [21] at an inverse temperature B:

$$z\left(B,\frac{h}{L},L\right) = \sum_{s_l} \exp\left[B\sum_{l=1}^{L} s_l s_{l+1} + \frac{\beta h}{L}\sum_{l=1}^{L} s_l\right] = z_+^L + z_-^L.$$

Here $z_\pm=\{e^B\cosh(\beta h/L)\pm\sqrt{e^{2B}\sinh^2(\beta h/L)+e^{-2B}}\}$. For a small $\beta h/L$, we have

$$z\left(B,\frac{h}{L},L\right) \approx e^{BL}\left[\left(1+\frac{\beta}{L}\sqrt{h^2+(\gamma_1+M\gamma_2)^2}\right)^L + \left(1-\frac{\beta}{L}\sqrt{h^2+(\gamma_1+M\gamma_2)^2}\right)^L\right] \approx 2e^{BL}\cosh[\beta\sqrt{h^2+(\gamma_1+M\gamma_2)^2}]. \quad (17)$$

Combing all the formulas and missing the preexponent, we have

$$Z_0 \sim \int_{-\infty}^{\infty} dmdM \int_{-i\infty}^{i\infty} dh \exp\left\{N\left[-\beta\gamma_2\frac{M^2}{2} - \beta hm + \beta\left(\alpha_1 m + \alpha_2\frac{m^2}{2}\right) + \ln 2\cosh[\beta\sqrt{h^2+(\gamma_1+\gamma_2 M)^2}]\right]\right\}. \quad (18)$$

If we put the saddle point condition via m, $h=\alpha_1+\alpha_2 m$, the last equation transforms into

$$Z_0 \sim \int_{-\infty}^{\infty} dmdM \exp\left[N\left(-\beta\gamma_2\frac{M^2}{2} - \beta\alpha_2\frac{m^2}{2} + \ln 2\cosh[\beta\sqrt{(\alpha_1+\alpha_2 m)^2+(\gamma_1+\gamma_2 M)^2}]\right)\right]. \quad (19)$$

Here m is a longitudinal magnetization and M is a transverse one. We see a symmetry under the transformation

$$\alpha_1 \to \gamma_1,\ \alpha_2 \to \gamma_2,\ m \to M.$$

The self-duality point corresponds to the case $\alpha_1=\gamma_1$ and $\alpha_2=\gamma_2$.

Let us consider the interesting case $\alpha_1=0$. At the $\beta\to\infty$ and large-N limits, the equations are simplified, and we have

$$\frac{1}{N}\ln Z_0 \to \left[-\beta\gamma_2\frac{M^2}{2} - \beta\alpha_2\frac{m^2}{2} + \beta\sqrt{(\alpha_2 m)^2+(\gamma_1+\gamma_2 M)^2}\right]. \quad (20)$$

There is a paramagnetic (no selection) phase with $m=0$ and $M=1$, and

$$\frac{1}{N}\ln Z_0 = \beta(\gamma_1+\gamma_2/2). \quad (21)$$

In the ferromagnetic phase (successful selection), we should consider the saddle point of Eq. (20) with nonzero m:

$$M = \frac{\gamma_1}{\alpha_2-\gamma_2},$$

$$m = \sqrt{1-\frac{\gamma_1^2}{(\alpha_2-\gamma_2)^2}}. \quad (22)$$

At the phase transition point, we have $m=0$. Therefore, error threshold corresponds to

$$\alpha_2 > \gamma_1 + \gamma_2. \quad (23)$$

Equations (22) and (23) at the $\gamma_2=0$ coincide with the result of [4].

B. Error threshold for the general mean-field-like mutation and fitness schemes

Now we consider any mean-field-like symmetric mutation schemes. Besides the single-site mutation at any site k with rate γ_1, there are multiple mutations with a change of 2^n spins per generation. In this case it is possible to repeat our derivations. Let us take one point, two-point and four-point mutations:

$$g(\sigma^x) = \gamma_1\sum_{k=1}^{N}\sigma_k^x + \frac{\gamma_2}{2N}\sum_{k_1\neq k_2=1}^{N}\sigma_{k_1}^x\sigma_{k_2}^x + \frac{\gamma_4}{4N^3}\sum_{k_1\neq k_2\neq k_3\neq k_4=1}^{N}\sigma_{k_1}^x\sigma_{k_2}^x\sigma_{k_3}^x\sigma_{k_4}^x. \quad (24)$$

For the four-point mutation, we use the formula

$$e^{c/4(a)^4} = \sqrt{\frac{c}{\pi}}\int_{-\infty}^{\infty} dx \exp[-cx^2 + xa^2 c] = \frac{c}{\pi}\int_{-\infty}^{\infty} dxdy \exp[-cx^2 - cy^2 + 2cy\sqrt{x}a]. \quad (25)$$

Let us take $a=\Sigma_k\sigma_k^x/N$ and $c=N\beta\gamma_4/L$. In the Suzuki-Trottere formalism we should introduce at any site l the integration via dx_l, dy_l, dz_l [similar to dz_l integration in Eq. (12)]. Repeating the calculation of the previous section, for the mutation scheme of Eq. (24) and fitness function f_0 we derive an expression

$$Z \sim \int_{-\infty}^{\infty} dmdzdxdy \int_{-i\infty}^{i\infty} dh \exp[-N\beta\gamma_2\frac{z^2}{2} - N\beta\gamma_4 x^2 - N\beta\gamma_4 y^2 + N\{\ln 2\cosh[\beta\sqrt{(\gamma_1+\gamma_2 z+2y\sqrt{x})^2+h^2}] - \beta hm + \beta f_0(m)\}. \quad (26)$$

Let us introduce an identity

$$1 = \int_{-\infty}^{\infty} db\,\delta(b-\gamma_1+\gamma_2 z+2y\sqrt{x}) = \frac{1}{2\pi i}\int_{-\infty}^{\infty}\int_{-i\infty}^{i\infty} dMdb \exp[M(b-\gamma_1+\gamma_2 z+2y\sqrt{x})].$$

The integration of the auxiliary variables dx_l, dy_l and dz_l gives

$$Z \sim \int dhdmdMdb \exp\{N[\ln 2\cosh(\beta\sqrt{b^2+h^2}) - \beta hm - \beta Mb + \beta g_0(M) + \beta f_0(m)]\}. \tag{27}$$

We should consider the saddle point of the last integral. At the limit $\beta \to \infty$, the equations become very simple:

$$\ln Z = N\beta[\sqrt{b^2+h^2} - hm - Mb + g_0(M) + f_0(m)],$$

$$b = g_0'(M), \quad h = f_0'(m),$$

$$m = \frac{h}{\sqrt{b^2+h^2}}, \quad M = \frac{b}{\sqrt{b^2+h^2}}. \tag{28}$$

According to the last two equations $\sqrt{b^2+h^2} - hm - Mb = 0$, $M^2 + m^2 = 1$; therefore we should look for a maximum of $\ln Z/\beta$, equivalent to the mean fitness

$$\frac{\ln Z}{\beta} = N[g_0(M) + f_0(m)], \tag{29}$$

at $m^2 + M^2 = 1$, $-1 \leqslant m \leqslant 1$, and $-1 \leqslant M \leqslant 1$. Here m describes the longitudinal magnetization, $m \sim \leqslant \sigma^z \leqslant$ and M the transverse one, $M \sim \leqslant \sigma^x \leqslant$. To find the error threshold, we should find parameters of functions f_0 and g_0 such that the ferromagnetic-phase solution [saddle point of Eq. (29) with $m > 0$] coincides with the paramagnetic solution [$M = 1$, $m = 0$, $f_0(0) = 0$]:

$$f_0'(m) = g_0'(\sqrt{1-m^2})\frac{m}{\sqrt{1-m^2}},$$

$$g_0(\sqrt{1-m^2}) + f_0(m) > g_0(1). \tag{30}$$

We derived Eq. (27) for the one-point, two-point and four-point mutations. It can be derived also if there are any $l = 2^k$ multiple mutations. For $\exp[N\beta \Sigma_l \gamma_l (\Sigma_k \sigma_k^x / N)^l / l]$ one should perform several Stratanovich transformations (k_l variables z for $l = 2^{k_l}$; the total number of different z is $K = \Sigma_l k_l$), eventually having only first degree of σ_k^x:

$$\exp\left[\sum_l N\beta \frac{\gamma_l}{l}\left(\frac{\sum_k \sigma_k^x}{N}\right)^l\right] = \int_{-\infty}^{\infty} D(z) \exp\left[\frac{\sum_k \sigma_k^x}{N}\phi(z_1 \ldots z_K)\right], \tag{31}$$

where $D\hat{z}$ is some integration measure with a Gaussian distribution for a vector $\hat{z} \equiv \{z_1 \cdots z_K\}$ and $\phi(z_1 \cdots z_K)$ is some function. The situation is similar to one in Eq. (26), and $(\gamma_1 + \gamma_2 z + 2y\sqrt{x})$ should be replaced by $\phi(z_1 \cdots z_K)$. Performing integration via $D\hat{z}$, we will return to the expression in Eq. (27). We guess that Eqs. (27)–(30) are correct for any mean-field-like mutation scheme in Eq. (7) and (8), but we could not prove this conjecture yet. Perhaps it can be proved in the general case by means of a high-temperature expansion.

It has been shown in [6] that for the fitness as a quadratic function of magnetization m, the mean fitness f_{mean} defines also the surplus of the distribution, $s = \Sigma_{i=1}^{2^N} p_i \Sigma_{l=1}^N s_i^l / N$:

$$f_0(s) = f_{mean}. \tag{32}$$

Arguments of [6] actually can be applied for any mean-field fitness. Let us give their qualitative derivation. We assume that in the steady state the majority of the population is at some Hamming distance d. Then we have immediately for the surplus $s = 1 - 2d/N$ and mean fitness $f_{mean} = f_0(1 - 2d/N)$. Therefore we derive an equation

$$f_0(s) = g_0(\sqrt{1-m^2}) + f_0(m), \tag{33}$$

where m is given by Eq. (29). Let us consider a simple site mutation with $g_0(M) = M\gamma$ and a flat peak with a fitness

$$f_0(m) = J_0 N, \quad m_0 \leqslant m \leqslant 1,$$

$$f_0(m) = 0, \quad 0 \leqslant m \leqslant m_0, \tag{34}$$

where m is the overlap of the configuration with the peak one and the Hamming distance is $d = (1-m)N/2$. When $m_0 \to 1$, we recover the single-peak landscape. At the paramagnetic phase we have $\ln Z = N\beta\gamma$ and at the ferromagnetic phase we take $m = m_0$ and $M = \sqrt{1-m_0^2}$. We immediately derive the error threshold condition

$$J_0 > \gamma(1 - \sqrt{1-m_0^2}). \tag{35}$$

Therefore flatness shifts the error threshold. The role of flatness has been investigated in Refs. [22–24]. The idea of "the survival of the flattest" at high mutation rates has been proposed in [23]. We guess that the role of fitness is more crucial in the stable environment while flatness (neutrality) may become a main factor in dynamic environments.

C. Error threshold for a single-peak fitness and any symmetric mutation schemes

Our results from the previous subsections concern only mean-field-like mutations when two spins are chosen arbitrary from all sites. A more realistic case in nature is the existence of some geometry, when, for example, two neighboring spins are flipped simultaneously. We cannot solve such a situation for the general case of fitness, but the picture for the single-peak fitness function is very simple. In the Suzuki-Trottere approach, the classical Hamiltonian is a sum of two terms: without interaction terms (free diffusion) and with an interaction term, when all the intermediate configurations S_l coincide with the peak one S_1. In thermodynamic limit, one should keep either interaction term or only mutation term.

For the case of a single-point mutation with a rate γ_1, double- and triple- (neighbor) site mutations with a rate γ_2 and γ_3, we have an expression for Z in Suzuki-Trottere approach:

$$Z = \left\{\exp\sum_k\left[(\gamma_1\sigma_k^x + \gamma_2\sigma_k^x\sigma_{k+1}^x + \gamma_3\sigma_k^x\sigma_{k+1}^x\sigma_{k+2}^x)\frac{\beta}{L}\right] \times \exp\left[\frac{\beta J_0 N}{L}\left(\frac{\sum_k \sigma_k^z}{N}\right)^p\right]\right\}^L \tag{36}$$

at $p \to \infty$. When we ignore the diffusion, we have an expression $\ln Z = NJ_0\beta$. The diffusion term at the limit $\beta \to \infty$ gives that $\ln Z = \beta N(\gamma_1 + \gamma_2 + \gamma_3)$. Therefore we have for the error threshold

$$J_0 > \gamma, \tag{37}$$

where $\gamma = \gamma_1 + \gamma_2 + \gamma_3$ is a total rate of all mutations in the system. This result could be generalized for any other symmetric mutation scheme, with γ as a total mutation rate.

III. DYNAMIC EQUATION FOR THE POLYNOMIAL FITNESS

Let us consider the dynamics for the Hamiltonian with a single-point mutation:

$$-H = \gamma \sum_{k=1}^{N} (\sigma_k^x - 1) + f_0\left(\frac{\sum_{i=1}^{N} \sigma_i^z}{N}\right). \tag{38}$$

For the partition $Z_{ij} \equiv Z(S_i, S_j) = \langle S_i | e^{-H\beta} | S_j \rangle$ at the limit $L \to \infty$, simple derivations similar those in Sec. II A give

$$Z(S_i,S_j) = \left[\frac{\sinh(2\beta\gamma/L)}{2}\right]^{LN/2} \prod_{l=1}^{L} \frac{\beta N}{2\pi i L} \int_{-i\infty}^{i\infty} dh_l \int_{-\infty}^{\infty} dm_l \times \exp\left[-\frac{N\beta}{L}\sum_l h_l m_l + \frac{N\beta}{L}\sum_l f_0(m_l) - \gamma\beta N + N \ln z[B,\{h_l/L\},L]\right], \tag{39}$$

where $z[B,\{h_l/L\},L]$ is the partition of the 1D Ising model with inverse temperature B and magnetic field h_l/L at position l. If we consider $Z_0 = \mathrm{Tr}\, e^{-\beta H}$, then the saddle point equations for the ferromagnetic phase are

$$\ln Z_0 = N \ln 2\cosh[\beta\sqrt{h^2+\gamma^2}] + N\beta f_0(m) - Nh\beta m - \gamma\beta N,$$

$$h = f_0'(m),$$

$$m = \frac{h}{\sqrt{h^2+\gamma^2}} \tanh[\beta\sqrt{h^2+\gamma^2}]. \tag{40}$$

To calculate $Z_{i,j}$ we consider a continuous function $h(x), 0 \leqslant x \leqslant 1$. Then h_l in Eq. (39) are given by a function $h(l/L) = h_l$.

We define the functional $z(B,h(x),\beta) \equiv z[B,\{h_l/L\},L]\exp[-NBL]$ as

$$z(B,h(x),\beta) = \sum_{s_l} \exp\left[B\sum_l (s_l s_{l+1} - 1) + \frac{\beta h(l/L)}{L}\sum_l s_l\right] \equiv \mathrm{Tr}(1+\sigma^x)\prod_l \hat{g}_l,$$

$$\hat{g}_{11} = \exp\left[1 + \beta\frac{h(x)}{L}\right],$$

$$\hat{g}_{22} = \exp\left[1 - \beta\frac{h(x)}{L}\right],$$

$$\hat{g}_{12} = g_{21} = \exp[-2B] = \frac{\gamma\beta}{L}. \tag{41}$$

Therefore, we have a representation for the $z(B,h(x),\beta)$:

$$z(B,h(x),\beta) = \mathrm{Tr}(1+\sigma^x)\,\hat{G}(\beta)$$

$$\hat{G}(\beta) = \hat{T}\exp\left[\int_0^\beta dx(h(x)\sigma_z + \gamma\sigma_x)\right], \tag{42}$$

where in the right part of the equation the exponent is time ordered. The last expression is a solution of the equation $d\hat{G}/dx = \hat{G}[h(x)\sigma_z + \gamma\sigma_x]$.

Then instead of Eq. (40) one should consider the saddle point of

$$\ln\langle S_i|T(t)|S_j\rangle = N \ln \mathrm{Tr}(1+\sigma^x)\,\hat{G}(\beta) + N\int_0^\beta dx[f_0(m(x)) - h(x)m(x)]dx - \gamma N\beta,$$

$$h(x) = f_0'[m(x)]. \tag{43}$$

Using the last equation we reformulate the variation problem: to find the maximum of

$$\ln\langle S_i|T(t)|S_j\rangle = N \ln \mathrm{Tr}(1+\sigma^x)\,\hat{G}(\beta) + N\int_0^\beta dx\{f_0[m(x)] - m(x)f_0'[m(x)]\} - \gamma\beta N \tag{44}$$

over all distributions of $m(x)$, $0 < x < \beta$, where

$$\hat{G}(\beta) = \hat{T}\exp\left\{\int_0^\beta dx \exp[f_0'[m(x)]\sigma_z + \gamma\sigma_x]\right\},$$

$$m(0) = m_i,$$

$$m(\beta) = m_f. \tag{45}$$

The maximum condition of Eq. (43) gives

$$m(x) = \frac{\mathrm{Tr}(1+\sigma^x)\,\hat{G}(x)\sigma_z\hat{G}(x)^{-1}\hat{G}(\beta)}{\mathrm{Tr}(1+\sigma^x)\,\hat{G}(\beta)},$$

$$\hat{G}(\beta) = \hat{T}\exp\left\{\int_0^\beta dy\{f_0'[m(y)]\sigma_z + \gamma\sigma_x\}\right\}. \tag{46}$$

One can check that at $\beta \to \infty$, Eq. (46) transforms to the last equation of Eqs. (40) with $m(x) = m$ outside the boundaries 0 and β. We can compare our equation (46) with Eq. (61) in [7]. Actually they suggested an ansatz

$$\hat{G}(x) = \exp\{x[f_0'(\phi(m(x)))\sigma_z + \gamma\sigma_x]\}, \tag{47}$$

where $\phi(s)$ is some function. In principle it is possible to solve Eq. (46) numerically to define the relaxation to the steady state. Having an expression of $\hat{G}(\beta)$ one can calculate the dynamics of distributions $p_i(t)$ using Eqs. (5) and (44).

IV. SINGLE-PEAK FITNESS LANDSCAPE

A. Relaxation in a single-peak fitness landscape

Let us briefly give the results of our work [13] for the relaxation in a single peak fitness landscape of Eq. (6).

In the Hamiltonian there are transverse terms (functions of σ^x), longitudinal terms (function of σ^z), and diagonal terms (constant terms). While calculating matrix elements of evolution operator $\langle S_i|e^{-tH}|S_j\rangle$, one can miss either transverse or longitudinal terms. This is an exact result at the thermodynamical limit. Let us consider an evolution from some original configuration S_i, having an overlap Nm with the peak configuration S_i: $\langle S_1|S_i\rangle=\Sigma_{k=1}^N s_k^i s_k^1=Nm$. First there is a random diffusion phase until the moment t_0. When $t>t_0$, one has

$$\langle S_1|\exp[-Ht]|S_i\rangle = \langle S_1|e^{-H_{int}(t-t_0)}|S_1\rangle\langle S_1|\exp[-H_{int}t]|S_i\rangle, \tag{48}$$

where t_0 is defined from the maximum condition of Eq. (48). For other configuration we take

$$\langle S_j|\exp[-Ht]|S_i\rangle = \langle S_j|\exp[-H_{diff}t]|S_i\rangle. \tag{49}$$

We miss the transverse part of the Hamiltonian and take $H_{int}=(J_0-\gamma)|S_1\rangle\langle S_1|$. In H_{diff}, the interaction term is missed.

When the partition of the peak configuration $\langle S_1|e^{-Ht}|S_i\rangle$ is becoming larger than the sum of partitions by other configurations $\Sigma_{j\neq 1}\langle S_j|e^{-Ht}|S_i\rangle$, system relaxes to the steady-state configuration.

There is an equation for t_0:

$$\tanh[\gamma t_0] = \frac{1-m_0}{k+\sqrt{k^2-1+m_0^2}}, \tag{50}$$

where $k=J_0/\gamma$.

For the relaxation period t_1 we derive

$$t_1(J_0,\gamma,m) = \frac{\left[J_0t_0 - \dfrac{1+m}{2}\ln\cosh(\gamma t_0) - \dfrac{1-m}{2}\ln\sinh(\gamma t_0)\right]}{J_0-\gamma}. \tag{51}$$

The error threshold condition is given by Eq. (37).

B. Steady-state distribution

Let us consider directly the steady-state distribution of Eq. (1) with the single-peak fitness of Eq. (6). We assume below the error threshold

$$p_1 \sim 1,$$

$$p_{(i+1)} \sim 1/N^{d(i,1)}, \tag{52}$$

where $d(i,1)$ is the Hamming distance between S_1 and S_i. Then it is easy to find the steady-state solution. We can group different configurations with the same distance from S_1 into the classes. The first class contains only the peak configuration. For the p_i from the class k the total probability of the class is

$$\sim \frac{N^{k-1}}{(k-1)!}\Big/ N^{k-1} \sim 1.$$

While considering the evolution of p_1,

$$\frac{dp_1}{dt} = (J_0-\gamma)Np_1 + \gamma\sum_{i,d(i,1)=1} p_i - p_1^2J_0N,$$

we can miss the second term on the right-hand side, as the sum is over configurations of the second class, there are N ones with a value $\sim 1/N$. At the statics we have, for the probability of a peak configuration and mean fitness

$$p_1 = \frac{J_0-\gamma}{J_0},$$

$$\sum_j p_jr_j = (J_0-\gamma)N. \tag{53}$$

For the p_2 we again ignore the influence of the kth classes with $k>2$ classes and take into account the flux from the first class. Putting the solution of Eq. (53) into the equation for the p_2, we derive

$$\frac{dp_2}{dt} = -\gamma Np_2 + \gamma p_1 - p_2J_0Np_1,$$

$$p_2 = p_1\frac{\gamma}{J_0N}. \tag{54}$$

In the same way we have for the class $k>1$

$$p_{k+1} = p_1k!\left(\frac{\gamma}{J_0N}\right)^k. \tag{55}$$

It is easy to check that the total probability is equal to 1:

$$p_1\left[1+\sum_{i>1}\frac{i!}{N^i}\frac{N!}{i!(N-i)!}\left(\frac{\gamma}{J_0}\right)^i\right] \approx \frac{J_0-\gamma}{J_0}\frac{1}{1-\dfrac{\gamma}{J_0}} = 1. \tag{56}$$

Equations (53) and (55) define a microscopic distribution of probabilities in a steady state of quasispecies.

C. Single-peak landscape with asymmetric mutations

Asymmetric mutations recently have been investigated in [26], and several results have been derived for simplified versions of the parallel mutation-selection scheme. Now besides symmetric mutations with rate x there are also asymmetric ones with the rate y, and the Hamiltonian H is given by [26]

$$H = \left[x\sum_i(\sigma_i^x - I) - y\sum_i(i\sigma_i^y+\sigma_i^z)\right] + f(\sigma_1^z\cdots\sigma_N^z), \tag{57}$$

where the rate $+1\to-1$ is $x+y$ and the rate $-1\to+1$ is $x-y$. We take again a single-peak landscape $f(S_1)=J_0N$ and

$f(S_i)=0$, $i>1$. In this subsection we derive the expression for the steady-state distribution and error threshold in Appendix A we will solve the dynamics.

Let us consider directly the nonlinear differential equation version of the model with mutation scheme of Eq. (57). We assume that in the peak configurations there is a k fracture of $s_i=1$ and $1-k$ fracture of $s_i=-1$. Now we have an equation

$$\frac{dp_1}{dt}=[J_0-x+(1-2k)y]Np_1-p_1^2J_0N. \qquad (58)$$

Therefore we have for the p_1 and mean fitness

$$p_1=\frac{J_0-x-(2k-1)y}{J_0},$$

$$\sum_j p_jr_j=J_0[x-(2k-1)y]N. \qquad (59)$$

As p_1 should be nonzero, we have an error threshold condition

$$J_0>x+(2k-1)y. \qquad (60)$$

V. ROYAL-ROAD-LIKE FITNESS FUNCTION

The results of the single-peak landscape are meaningful for the infinite-population limit. Let us consider a construction for the fitness that can work for smaller populations. Before we specified the indices of 2^N configurations via the collection of N spins s_j^i, $S_j\sim\{s_j^1\cdots s_j^N\}$. Let us group those $\pm$ spins into K subgroups of n spins, $S_j\sim\{(s_j^1\cdots s_j^n),(s_j^{n+1}\cdots s_j^{2n})\cdots(s_j^{N-n}\cdots s_j^N)\}$. There is a hierarchy structure of configurations with a branching $Q=2^n$. At the first step we consider just different collections of $s_j^1\cdots s_j^n$. There are 2^n points at this level. At the second level we involve also the second group of spins and consider $S_j\sim\{(s_j^1\cdots s_j^n),(s_j^{n+1}\cdots s_j^{2n})\}$. There are 2^{2n} points at this level. At the lth level we have 2^{ln} points and at the last Kth level there are 2^N spin configurations. The peak configuration has a spin specification $s_1^i=1$ for all $1\leqslant i\leqslant N$. Such problem is exactly solvable in dynamics. We write a royal-road-like [20] fitness function

$$\frac{f(S)}{n}=j_1\left[\frac{s_1+\cdots+s_n}{n}\right]^p\left[\frac{s_{n+1}+\cdots+s_{2n}}{n}\right]^p\cdots\left[\frac{s_{N-n+1}+\cdots+s_N}{n}\right]^p+j_2\left[\frac{s_{n+1}+\cdots+s_{2n}}{n}\right]^p\cdots\left[\frac{s_{N-n+1}+\cdots+s_N}{n}\right]^p+\cdots+j_K\left[\frac{s_{N-n}+\cdots+s_N}{n}\right]^p. \qquad (61)$$

We take a mutation scheme as in Eq. (2). For the full concentration in the vicinity of the peak configuration we have a condition

$$\gamma<j_l \qquad (62)$$

similar to Eq. (37). Let us now consider the dynamics. Due to our construction, the last group of n spins would first relax. Assume that have an overlap m_K with the peak configuration: $\sum_{j=1}^n s_{N-n+j}=nm_K$. At the first stage only the last term in Eq. (61) is relevant. Therefore, the system will relax to the configuration with the last subchain equal to $\{1,1,\ldots,1\}$ after period $t_K=t_1(m_K,j_K,\gamma)$. Next we consider the step relaxation at the $K-1$ level. Now the term

$$j_{K-1}\left[\frac{s_{N-2n}+\cdots+s_{N-n}}{n}\right]^p\left[\frac{s_{N-n+1}+\cdots+s_N}{n}\right]^p$$

is relevant. The last multiplier is equal to 1, as $s_{N-n+i}=1$, for $i=1$, n. Again we have a situation of fitness function in Eq. (6).

After K steps we have

$$t=\sum_{l=1}^K t_1(j_l,\gamma_l,m), \qquad (63)$$

where t_1 is defined by Eq. (51). We used spin model representation with integer n for the simplicity of derivation and our results could be generalized to a large class of hierarchic fitness functions which are realistic in biology. When is such a deterministic dynamics valid? A minimal number of molecules is $\sim 2^{N/K}$, less than 2^N, necessary for the single-peak fitness function. Perhaps there are collective driven random walks; then, when the number of individuals is becoming more than $2^{N/K}$, quasispecies equations begin to work.

In principle we can give another version of the block spin interaction, like the original version of the royal road fitness [20]:

$$\frac{f(S)}{n}=j_1\left[\frac{s_1+\cdots+s_n}{n}\right]^p+j_2\left[\frac{s_{n+1}+\cdots+s_{2n}}{n}\right]^p+\cdots+j_K\left[\frac{s_{N-n}+\cdots+s_N}{n}\right]^p. \qquad (64)$$

Now different blocks of spins relax in a parallel way; therefore the total relaxation period should be the maximal among all $t_1(j_l,\gamma_l,m)$. The error threshold condition is again given by Eq. (62).

VI. RELAXATION IN THE FOUR-VALUE SPIN MODEL

Let us consider a model [11], where at every site i there are two spins s_i^1, s_i^2; for the DNA case one can take the following identification: $++\sim A$, $+-\sim G$, $-+\sim C$, $--\sim T$.

There are $A-G$, $C-T$ transitions with rate μ_2; $A-T$, $G-C$ transitions with rate μ_3; and $A-C$, $T-G$ transitions with rate μ_1. According to Kimura one takes $\mu_2 > \mu_1 > \mu_3$. It has been proposed in [11] that the evolution dynamics again can be described by an equation like Eq. (4) with the Hamiltonian

$$-H = \sum_{i=1}^{N} [\mu_1(\sigma_{i,1}^x - 1) + \mu_2(\sigma_{i,2}^x - 1) + \mu_3(\sigma_{i,1}^x \sigma_{i,2}^x - 1)] + f(\sigma_{1,1}^z, \sigma_{1,2}^z \cdots \sigma_{N,1}^z, \sigma_{N,2}^z). \tag{65}$$

Here operators $\sigma_{i,1}^z$, $\sigma_{i,1}^x$ act in the Hilbert space of the first spin in the site i and $\sigma_{i,2}^z$, $\sigma_{i,2}^x$ in the Hilbert space of the second spin in the site i. One again has

$$\langle S_1|T(t)|S_i\rangle \to \langle S_1|T_{int}(t-t_0)|S_1\rangle\langle S_1|T_{diff}(t_0)|S_i\rangle = e^{N\phi(t_0)-N(\mu_1+\mu_2+\mu_3)t+NJ_0(t-t_0)}, \tag{66}$$

where the function $\phi(t_0)$ is defined via amplitudes of transition with flips: Nx_1 like μ_1, Nx_2 like μ_1, Nx_3 like μ_3 and $N(1-x_1-x_2-x_3)$ diagonal one:

$$\begin{aligned}\phi(\mu_1,\mu_2,\mu_3,x_1,x_2,x_3,t) &= x_1 \ln\langle + + |e^{H_0 t}| - + \rangle + x_2 \ln\langle + + |e^{H_0 t}| + - \rangle \\ &\quad + x_3 \ln\langle + + |e^{H_0} t| - - \rangle + (1 - x_1 - x_2 - x_3) \\ &\quad \times \ln\langle + + |e^{H_0 t}| + + \rangle,\end{aligned}$$

$$H_0 = (\mu_1\sigma_1^x + \mu_2\sigma_2^x + \mu_3\sigma_1^x\sigma_2^x). \tag{67}$$

In the last system one calculates the matrix element of the two-spin system. It is easy to derive

$$\begin{aligned}\phi(\mu_1,\mu_2,\mu_3,x_1,x_2,x_3,t_0) &= (2 - x_1 - x_2 - x_3)\ln[\cosh(\mu_1 t_0)\cosh(\mu_2 t_0)\cosh(\mu_3 t_0) + \sinh(\mu_1 t_0)\sinh(\mu_2 t_0)\sinh(\mu_3 t_0)] \\ &\quad + x_3 \ln[\sinh(\mu_1 t_0)\sinh(\mu_2 t_0)\cosh(\mu_3 t_0) + \cosh(\mu_1 t_0)\cosh(\mu_2 t_0)\sinh(\mu_3 t_0)] \\ &\quad + x_1 \ln[\sinh(\mu_1 t_0)\cosh(\mu_2 t_0)\cosh(\mu_3 t_0)] + x_2 \ln[\sinh(\mu_2 t_0)\cosh(\mu_1 t_0)\cosh(\mu_3 t_0)].\end{aligned} \tag{68}$$

One should take value of t_1 from the optimum condition of Eq. (66):

$$J_0 = \frac{d\phi(\mu_1,\mu_2,\mu_3,x_1,x_2,x_3,t_0)}{dt_0}. \tag{69}$$

Having t_0, it is possible to define the relaxation period

$$t_1 = \frac{J_0 t_0 - \phi(\mu_1,\mu_2,\mu_3,x_1,x_2,x_3,t_0)}{J_0 - (\mu_1 + \mu_2 + \mu_3)}. \tag{70}$$

At the limit of small distance between the original and fit configurations $x_1 \ll 1$, $x_2 \ll 1$, $x_3 \ll 1$

$$t_0 \approx \frac{1}{J_0}(x_1 + x_2 + x_3),$$

$$t_1 \approx \frac{1}{J_0}\left[(x_1 + x_2 + x_3)\ln\frac{e}{(x_1 + x_2 + x_3)}\right] + \frac{1}{J_0}\left[x_1 \ln\frac{J_0}{\mu_1} + x_2 \ln\frac{J_0}{\mu_2} + x_3 \ln\frac{J_0}{\mu_3}\right]. \tag{71}$$

This expression coincides with the corresponding one in [13] in the main approximation (after the redefinition $J_0 \to J_0/2$).

For the Kimura two-parameter model, we have $\mu_1 = \mu_3$ and

$$t_1 \approx \frac{1}{J_0}\left[(x_1 + x_2 + x_3)\ln\frac{e}{(x_1 + x_2 + x_3)}\right] + \frac{1}{J_0}\left[(x_1 + x_3)\ln\frac{J_0}{\mu_1} + x_2 \ln\frac{J_0}{\mu_2}\right]. \tag{72}$$

We can repeat the derivation of Sec. IV B for the steady-state distribution. Equation (37) is still correct, but γ should be replaced by the total rate of mutations. Thus we have the error threshold condition

$$J_0 > (\mu_1 + \mu_2 + \mu_3). \tag{73}$$

For the peak configuration probability p_1 and mean fitness, we have

$$p_1 = \frac{J_0 - (\mu_1 + \mu_2 + \mu_3)}{J_0},$$

$$\sum_j p_j r_j = [J_0 - (\mu_1 + \mu_2 + \mu_3)]N. \tag{74}$$

VII. CONCLUSION

To conclude, in the present paper we give a comprehensive investigation of quasispecies models in a parallel mutation-selection scheme. We extend our earlier results about the dynamics of the model with a single-peak fitness function and a single mutation per generation [13] to more complicated cases: two-point mutations, single-point asymmetric mutations, and four-value spin models with a single-peak fitness function, as well as for the royal road fitness function. We derive a field-theoretical-like equation, Eq. (46), for the dynamics of any mean-field-like fitness function. We derive the error threshold for the parallel scheme with any mean-field-like fitness function and rather general multiple-point mutation schemes, Eq. (30), which can be formulated as a simple maximum problem for Eq. (29). It should be noted that in [26], the authors considered the mean-field fitness for a simplified parallel scheme model: the maximum principle considered in [26] qualitatively resembles Eq. (29) of the present paper.

The quasispecies concept is becoming more and more popular [25]. In the present paper, we show that many problems for parallel models [3,4,6] can be solved exactly; therefore there is no need for a further simplification of the evolution models, which is the usual practice in biological research. Some principal aspects of evolution could be missed due to too much simplification [13].

We hope that our exact results for parallel models (error thresholds, surplus, steady-state distributions) could be useful for practical applications, as parallel scheme sometimes are related to real systems [5,6] and sometimes one is using them as a methodologically simpler (compared with Eigen model) way to investigate complex biological problems [22]. The methods developed in this work for the complicated mutation scheme could be applied to solve exactly the mutation landscape introduced in [27]. The mutation landscape could be quite realistic for retro-viruses [28].

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APPENDIX A: ASYMMETRIC MUTATIONS FOR TWO-VALUE SPINS

To solve the dynamics of the system defined by the Hamiltonian of Eq. (57), we need to calculate $\langle\pm|\exp[At]|\pm\rangle$ with $A=x\sigma^x-iy\sigma^y-y\sigma^z$. First we should make diagonal the matrix A with elements $-y$, $x-y$; $x+y$, y. We have for the eigenstates

$$\lambda_{1,2}=\pm x,$$

$$|1\rangle=\{(x-y),(x+y)\},$$

$$|2\rangle=\{1,-1\},$$

$$\langle 1|1\rangle=2(x^2+y^2),\quad \langle 2|2\rangle=2,\quad \langle 1|2\rangle=-2y. \tag{A1}$$

Thus there is a representation

$$|-\rangle=\frac{1}{2x}|1\rangle-\frac{(x-y)}{2x}|2\rangle,$$

$$|+\rangle=\frac{1}{2x}|1\rangle+\frac{(x+y)}{2x}|2\rangle. \tag{A2}$$

A is not a symmetric matrix; thus two eigenvectors are not orthogonal. Let us expand $|+\rangle=a_1|1\rangle+a_2|2\rangle$, $|-\rangle=b_1|1\rangle+b_2|2\rangle$. Then we have

$$\begin{aligned}\langle+|T(t)|+\rangle&=e^{\lambda_1 t}[\langle 1|1\rangle a_1^2+\langle 2|1\rangle a_1a_2]\\&\quad+e^{\lambda_2 t}[\langle 2|2\rangle a_2^2+\langle 1|2\rangle a_1a_2],\\&=e^{xt}\left[(x^2+y^2)\frac{1}{2x^2}-y\frac{(x+y)}{2x^2}\right]\\&\quad+e^{-xt}\left[\frac{(x+y)^2}{2x^2}-y\frac{(x+y)}{2x^2}\right],\end{aligned} \tag{A3}$$

$$\begin{aligned}\langle-|T(t)|-\rangle&=e^{\lambda_1 t}[\langle 1|1\rangle b_1^2+\langle 2|1\rangle b_1b_2]\\&\quad+e^{\lambda_2 t}[\langle 2|2\rangle b_2b_2+\langle 1|2\rangle b_1b_2]\\&=e^{xt}\left[(x^2+y^2)\frac{1}{2x^2}+y\frac{x-y}{2x^2}\right]\\&\quad+e^{-xt}\left[\frac{(x-y)^2}{2x^2}+y\frac{(x-y)}{2x^2}\right],\end{aligned} \tag{A4}$$

$$\begin{aligned}\langle-|T(t)|+\rangle&=e^{\lambda_1 t}[\langle 1|1\rangle a_1b_1+\langle 2|1\rangle a_1b_2]\\&\quad+e^{\lambda_2 t}[\langle 2|2\rangle a_2b_2+\langle 1|2\rangle b_1a_2]\\&=e^{xt}\left[(x^2+y^2)\frac{1}{2x^2}+y\frac{x-y}{2x^2}\right]\\&\quad+e^{-xt}\left[(y^2-x^2)\frac{1}{2x^2}-y\frac{x+y}{2x^2}\right],\end{aligned} \tag{A5}$$

$$\begin{aligned}\langle+|T(t)|-\rangle&=e^{\lambda_1 t}[\langle 1|1\rangle a_1b_1+\langle 2|1\rangle b_1a_2]\\&\quad+e^{\lambda_2 t}[\langle 2|2\rangle a_2b_2+\langle 1|2\rangle b_1a_2]\\&=e^{xt}\left[(x^2+y^2)\frac{1}{2x^2}-y\frac{x+y}{2x^2}\right]\\&\quad+e^{-xt}\left[\frac{y^2-x^2}{2x^2}-y\frac{x+y}{2x^2}\right].\end{aligned} \tag{A6}$$

For given initial and fit configurations one should calculate the number of different mutations $n_{++}\sim\langle+|T|+\rangle$, $n_{--}\sim\langle-|T|-\rangle$, $n_{+-}\sim\langle+|T|-\rangle$, and $n_{-+}\sim\langle-|T|+\rangle$.

We take

$$\begin{aligned}\phi(x,y,t)=&\ \ln[\langle+|T(t)|+\rangle^{n_{++}}\langle-|T(t)|-\rangle^{n_{--}}\\&\times\langle+|T(t)|-\rangle^{n_{+-}}\langle-|T(t)|+\rangle^{n_{-+}}]\end{aligned} \tag{A7}$$

and derive relaxation periods t_0, t_1:

$$J_0=\frac{d\phi(x,y,t_0)}{dt_0},$$

$$t_1=\frac{J_0t_0-\phi(x,y,t_0)}{J_0-x-y(2k-1)}. \tag{A8}$$

We used the fact that

$$\langle S_1|\exp[-Ht]|S_1\rangle=\exp[J_0Nt-Ny(2k-1)t].$$

APPENDIX B: DYNAMICS FOR TWO-POINT MUTATIONS

Let us consider the dynamics of the system defined by the Hamiltonian

$$-H=\gamma_1\sum_{i=1}^{N}(\sigma_i^x-1)+\frac{\gamma_2}{N}\sum_{1\leq i<j}^{N}(\sigma_i^x\sigma_j^x-1)+f(\sigma_1^z\cdots\sigma_N^z). \tag{B1}$$

In the Suzuki-Trottere scheme one needs to calculate

$$\langle S_i|\exp\left(\gamma_1 t\sum_{i=1}^{N}(\sigma_i^x-1)+\frac{\gamma_2 t}{N}\sum_{1\leq i<j=1}^{N}(\sigma_i^x\sigma_j^x-1)\right)|S_j\rangle.$$

Let us perform Stratanovich transformation

$$\exp\left[\frac{\gamma_2 t}{N}\sum_{1\leq i<j\leq N}\sigma_i^x\sigma_j^x\right]=\exp\left[\frac{\gamma_2 t}{2N}\left(\sum_{i=1}^{N}\sigma_i^x\right)^2-N\frac{\gamma_2 t}{2}\right]=\sqrt{\frac{N}{2\pi}}\int_{-\infty}^{\infty}dz\exp\left[-\frac{Nz^2}{2}+z\sqrt{\gamma_2 t}\sum_{1\leq i\leq N}\sigma_i^x-N\frac{\gamma_2 t}{2}\right]. \tag{B2}$$

Similar to the derivations in the Sec. II, we take for $\langle S_1|T(t)|S_i\rangle$,

$$\langle S_1|T_{int}(t-t_0)|S_1\rangle\langle S_1|T_{diff}(t_0)|S_i\rangle=\sqrt{\frac{N}{2\pi}}\int_{-\infty}^{\infty}dz\exp[N\phi(m,z,t_0)-N(\gamma_1+\gamma_2/2)t_0+NJ_0(t-t_0)]. \tag{B3}$$

The saddle point condition by z gives

$$z=\sqrt{\gamma_2 t_0}\left[\frac{1+m}{2}\tanh(\gamma_1 t_0+\sqrt{\gamma_2 t_0}z)+\frac{1-m}{2\tanh(\gamma_1 t_0+\sqrt{\gamma_2 t_0}z)}\right]. \tag{B4}$$

The function $\phi(m,z,t_0)$ in Eq. (B3) is defined as

$$\phi(m,z,t_0)=-\frac{z^2}{2}+\frac{1+m}{2}\ln\cosh[\gamma_1 t_0+z\sqrt{\gamma_2 t_0}]+\frac{1-m}{2}\ln\sinh[\gamma_1 t_0+z\sqrt{\gamma_2 t_0}],$$

$$\langle S_1|T_{int}(t-t_0)|S_1\rangle\langle S_i|T_{diff}(t_0)|S_1\rangle=e^{N\phi(m,z,t_0)-N(\gamma_1+\gamma_2/2)t_0+NJ_0(t-t_0)}. \tag{B5}$$

To find the relaxation period t_1 one should consider an additional constraint that the contribution of Eq. (B3) to partition $Z=\Sigma_j\langle S_j|e^{-Ht}|S_i\rangle$ is larger compared with the contribution of other configurations, $\Sigma_{j\neq i}\langle S_j|e^{-Ht}|S_i\rangle=1$:

$$\exp[N\phi(m,z,t_0)-N(\gamma_1+\gamma_2/2)t_1+NJ_0(t_1-t_0)]\geq 1,$$

$$t_1=\frac{J_0 t_0-\phi(m,t_0)}{J_0-(\gamma_1+\gamma_2/2)}. \tag{B6}$$

Let us consider first the case $m=0$. Now we have a simpler expression for the ϕ:

$$\phi(m,z,t_0)=-\frac{z^2}{2}+\frac{1}{2}\ln\frac{1}{2}\sinh[2(\gamma_1 t_0+z\sqrt{\gamma_2 t_0}].$$

The saddle point condition via z and t_0 gives a system of equations

$$\frac{\sqrt{t_0\gamma_2}}{z}=\tanh[2(\gamma_1 t_0+\sqrt{\gamma_2 t_0}z)],$$

$$\frac{\gamma_1+\frac{z}{2}\sqrt{\frac{\gamma_2}{t_0}}}{J_0}=\tanh[2(\gamma_1 t_0+\sqrt{\gamma_2 t_0}z)],$$

$$\phi(t_0)=-\frac{z^2}{2}+\frac{\ln\{\sinh[2(\gamma_1 t_0+z\sqrt{\gamma_2 t_0})]/2\}}{2}. \tag{B7}$$

We can simplify this system. Let us put $J_0=1$; later we can recover J_0 using a rescaling $\gamma_0\to\gamma_0/J_0$, $\gamma_1\to\gamma_1/J_0$. First, z can be expressed by t_0 from the first and second equations of a system (B7):

$$z=\sqrt{t_0}\frac{-\gamma_1+\sqrt{\gamma_1^2+2\gamma_2}}{\sqrt{\gamma_2}}. \tag{B8}$$

Then we can derive the t_0:

$$\frac{\gamma_1+\sqrt{\gamma_1^2+2\gamma_2}}{2}=\tanh[2(\sqrt{\gamma_1^2+2\gamma_2})t_0]. \tag{B9}$$

Therefore we have

$$t_0=\frac{\ln\frac{2+(\gamma_1+\sqrt{\gamma_1^2+2\gamma_2})}{2-(\gamma_1+\sqrt{\gamma_1^2+2\gamma_2})}}{4\sqrt{\gamma_1^2+2\gamma_2}}. \tag{B10}$$

Thus for the relaxation period t_1, from the original configuration at the Hamming distance $N/2$ from S_1, we have

$$\frac{J_0-\left(\gamma_1+\frac{\gamma_2}{2}\right)}{J_0}t_1=\frac{\ln\frac{2J_0+(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})}{2J_0-(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})}}{4\sqrt{\gamma_1^2+2J_0\gamma_2}}\times\left(1+\frac{2\gamma_2}{(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})^2}\right)-\frac{1}{2}\ln\frac{(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})}{2\sqrt{4J_0^2-(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})^2}}. \tag{B11}$$

Let us derive the equations for the general m case. For the z, we again have the expression in Eq. (B8). We derive for t_0

$$\frac{2J_0}{\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2}}=\left[\frac{1+m}{2}\tanh(t_0\sqrt{\gamma_1^2+2J_0\gamma_2})+\frac{1-m}{2\tanh(t_0\sqrt{\gamma_1^2+2J_0\gamma_2})}\right]. \quad \text{(B12)}$$

Then for the relaxation period t_1, we derive

$$t_1\frac{J_0-\left(\gamma_1+\frac{\gamma_2}{2}\right)}{J_0}=t_0\left(1+\frac{2\gamma_2}{(\gamma_1^2+\sqrt{\gamma_1^2+2J_0\gamma_2})^2}\right)-\frac{1+m}{2}\ln\cosh[t_0\sqrt{\gamma_1^2+2J_0\gamma_2}]-\frac{1-m}{2}\ln\sinh[t_0\sqrt{\gamma_1^2+2J_0\gamma_2}]. \quad \text{(B13)}$$

The biological situation corresponds to the limit of small $1-m=\delta\ll 1$:

$$t_0\approx\delta\frac{\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2}}{4J_0\sqrt{\gamma_1^2+2J_0\gamma_2}},$$

$$t_1\approx\frac{\delta\ln\frac{4eJ_0}{\delta(\gamma_1+\sqrt{\gamma_1^2+2J_0\gamma_2})}}{2[J_0-(\gamma_1+\gamma_2/2)]}. \quad \text{(B14)}$$

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