Funnel Landscape and Mutational Robustness as a Result of Evolution under Thermal Noise

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Using a statistical-mechanical model of spins, the evolution of phenotype dynamics is studied. Configurations of spins and their interaction \(J\) represent the phenotype and genotype, respectively. The fitness for selection of \(J\) is given by the equilibrium spin configurations determined by a Hamiltonian with \(J\) under thermal noise. The genotype \(J\) evolves through mutational changes under selection pressure to raise its fitness value. From Monte Carlo simulations we find that the frustration around the target spins disappears for \(J\) evolved under temperature beyond a certain threshold. The evolved \(J\)s give the funnel-like dynamics, which is robust to noise and also to mutation.

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Under fixed conditions biological systems evolve to increase their fitness, determined by a biological state—phenotype—that is shaped by a dynamical process. This dynamics is generally stochastic as it is subject to thermal noise, and the rule for the dynamics is controlled by a gene that mutates through generations. Those genes that produce fitness for selection of \(J\) are transmitted to the next generation, whereas genotypes that produce a phenotype with a higher level of fitness are selected. We adopt the Glauber dynamics as an update rule, where the \(N\) spins are in contact with a heat bath of temperature \(T_S\). After the relaxation process, this dynamics yields an equilibrium distribution for a given \(J\),

\[
P(S|J,T_S) = e^{-\beta S H(S|J)}/Z_S(T_S), \quad \beta_S = 1/T_S \text{ and } Z_S(T_S) = \text{Tr}_S \exp\{-\beta_S H(S|J)\}.
\]

The genotype \(J\) is transmitted to the next generation with some variation, whereas genotypes that produce a phenotype with a higher level of fitness are selected. We assume that fitness is a function of the configuration of target spins \(t\), a given subset of \(S\), with size \(t\).

The probability of occurrence of a genotype \(S\) with fitness \(\Psi(J|T_S)\) is given by

\[
\Psi(J|T_S) = \left\langle \prod_{i<j \in t} \delta(S_i - S_j) \right\rangle.
\]

without losing generality, where \(\langle \cdot \cdot \cdot \rangle\) denotes the expectation value with respect to the equilibrium probability distribution. In other words, the expected fitness is given by the probability of the “target configuration” in which all target spins are aligned parallel under equilibrium condi-
conditions. Note that in our model only the target spins contribute to the fitness, and, as a result, the spin configuration for a given fitness value has redundancy.

The genotype $J$ evolves as a result of mutations, random flip-flop of the matrix element, and the process of selection according to the fitness function. We again adopt Glauber dynamics by using fitness instead of the Hamiltonian in the phenotype dynamics, where $J$ is in contact with a heat bath whose temperature $T_J$ is different from $T_S$. In particular, the dynamics is given by a stochastic Markov process with the stationary distribution $P(J, T_S, T_J) = e^{\beta J \Psi(J | T_S)} / Z(J | T_S, T_J)$, where $\beta_J = 1/T_J$ and $Z(J | T_S, T_J) = \exp[\beta J \Psi(J | T_S)]$. According to the dynamics, genotypes are selected somewhat uniformly at high temperatures $T_J$, whereas at low $T_J$, genotypes with higher fitness values are preferred. The temperature $T_J$ represents selection pressure.

Next, we study the dependence of the fitness and energy on $T_S$ and $T_J$, given by $\Psi(T_S, T_J) = \langle \Psi(J | T_S) \rangle_J$ and $E(T_S, T_J) = \langle \langle H(S(J)) \rangle \rangle_J$, respectively, where $\langle \cdots \rangle_J$ denotes the average with respect to the equilibrium probability distribution, $P(J, T_S, T_J)$. For the spin dynamics (unless otherwise mentioned), the exchange Monte Carlo (EMC) simulation [15] is used to accelerate the relaxation to equilibrium. Indeed, we have confirmed the equilibrium distribution for the simulations below. Two processes are carried out alternately: the equilibration of $S$ with the EMC simulation and the stochastic selection of $J$ according to the fitness value estimated through the first process.

Figures 1(a) and 1(b) show dependence of the fitness and energy on $T_S$ and $T_J$, respectively, for $N = 15$ and $t = 3$. For any $T_S$, the fitness value decreases monotonically with $T_J$. However, $T_S$ influences the slope of the decrease significantly. The fitness for sufficiently low $T_S$ remains at a high level and decreases only slightly with an increase in $T_J$, while for a medium value of $T_S$, the fitness gradually falls to a lower level as a function of $T_J$ and eventually, for a sufficiently high value of $T_S$, it never attains a high level. This implies that the structure of the fitness landscape depends on $T_S$, at which the system has evolved. The energy function, on the other hand, shows a significant dependence on $T_S$. Although the energy increases monotonically with $T_S$ for high $T_J$, it exhibits nonmonotonic behavior at a low $T_J$ and takes a minimum at an intermediate $T_S$. The $J$ configurations giving rise to the highest fitness value generally have a large redundancy. At around $T_S \approx 2.0$, using a fluctuation induced by $T_S$, a specific subset of adapted $J$'s giving rise to lower energy is selected from the redundant configurations with higher fitness.

In the medium-temperature range, such $J$'s that yield both lower energy and higher fitness are evolved. Now we study the characteristics of such $J$s. According to statistical physics of spin systems, triplets of interactions that satisfy $J_{il}J_{jk}J_{kl} < 0$ are known to yield frustration, which is an obstacle to attaining the unique global energy minimum [14]. In our model, however, the target spins play a distinct role. Hence, it becomes necessary to quantify the frustration by distinguishing target and nontarget spins. In accordance with the "ferromagnetic" fitness condition for target spins, we define $\Phi_1$ as the frequency of positive coupling among target spins, $\Phi_1(T_S, T_J) = \frac{2}{N^2 \pi^3} \times \langle \sum_{i < j \in T} J_{ij} \rangle_J$. Under ferromagnetic coupling, the target configurations are energetically favored, i.e., $\Phi_1 = 1$, for which no frustration exists among the target spins. Next, for a measure of the degrees of frustration between target and nontarget spins, and among nontarget spins themselves, we define $\Phi_2$ and $\Phi_3$ as

$$\Phi_2(T_S, T_J) = \frac{2}{t(t-1)(N-t)} \left\langle \sum_{i<j \in T} \sum_{i \in T} J_{ij} J_{kl} \right\rangle_J,$$

and

$$\Phi_3(T_S, T_J) = \frac{1}{C_2^{N-t}} \left\langle \sum_{k<l \in T} \left( \frac{1}{t} \sum_{i \in T} J_{ik} \right) \left( \frac{1}{t} \sum_{i \in T} J_{li} \right) \right\rangle_J,$$

where $C_2^{N-t}$ is the total number of possible pairs among the nontarget spins. Here, $\Phi_2$ is the fraction of the interaction pairs between target and nontarget spins that satisfy $J_{ik}J_{kl} = 1(i, j \in T, k \notin T)$. If $\Phi_2 = 1$, no frustration is introduced by the interaction between target and nontarget spins, so that the energy minimum of the target configuration is conserved by such interaction. If $\Phi_3 = 1$, the target configurations do not introduce frustration in $J_{kl}$ ($k, l \notin T$). If $\Phi_1 = \Phi_2 = \Phi_3 = 1$, there is no frustration at all over the interactions, as suggested by the Mattis model [16],

![FIG. 1 (color online). Contour maps on $T_S$ and $T_J$ of (a) fitness, (b) energy, and (c) $\Phi_2$, where $1 - \Phi_2$ is the frustration around the target spins, for evolved $J$ at a given $T_S$ and $T_J$ (see text for details). $N = 15$ and $t = 3$. For each generation of the genotype dynamics, the average in equilibrium is taken over 1500 MC steps after discarding the first 1500 MC steps, which are sufficient for equilibration. The data are averaged over the last $10^3$ generations.](148101-2)
which can be transformed into ferromagnetic interactions by gauge transformation [14].

For $J$ that is evolved under given $T_S$ and $T_J$, we have computed $\Phi_1$, $\Phi_2$ and $\Phi_3$. Figure 2 shows the dependence of $\Phi_1$, $\Phi_2$ and $\Phi_3$ on $T_S$ at a fixed $T_J = 0.5 \times 10^{-3}$. For $T_S \geq T_S^{c1}$, $\Phi_1$ takes the value $\sim 1$ [17], so that a target configuration is embedded as an energetically favorable state, while no specific patterns, apart from the target, are embedded in the spin configuration.

For $T_S^{c1} \leq T_S \leq T_S^{c2}$, $\Phi_2$ also takes the value around 1, implying that frustration is not introduced by means of interactions with a nontarget spin. In this temperature range, $\Phi_3$ is not equal to 1, except for $T_S \sim 2.0$ where the Mattis state is shaped. When $\Phi_2 \sim 1$ and $\Phi_3 \neq 1$, frustration is not completely eliminated from the nontarget spin interactions, in contrast to the Mattis state. Here, such a $J$ configuration without frustration around the target spins (but with frustration between nontarget spins) is referred to as “local Mattis state” (LMS), as characterized by $\Phi_1 = \Phi_2 \sim 1$ and $\Phi_3 \neq 1$. The interactions $J$ that form such LMSs arise as a result of the evolution at $T_S \leq T_S^{c1}$, where both a fitted target configuration and a lower energy level are achieved. As shown in Fig. 1(c), the $T_S$ range in which LMS is shaped becomes narrower with an increase in $T_J$ [18]. For sufficient low $T_J$, there are three phases: $T_S < T_S^{c1}(T_J)$, the phase in which frustration remains in spite of adaptation; $T_S^{c1}(T_J) \leq T_S \leq T_S^{c2}(T_J)$, the phase giving LMSs; $T_S > T_S^{c2}(T_J)$, the phase in which no adaptation and frustration is seen.

Let us consider the relaxation dynamics of spins for each $J$ adapted through evolution under a given $T_S$ and $T_J$, denoted as $J^{\text{adp}}_{T_S}$, where $T_J$ is fixed at $0.5 \times 10^{-3}$. To understand how the relaxation dynamics depends on $J^{\text{adp}}_{T_S}$, instead of using EMC simulations, we adopt standard MC simulations with the temperature $T_S^{*}$, fixed at $10^{-5}$, independently of $T_S$ used in obtaining $J^{\text{adp}}_{T_S}$. We compute the temporal change of the target magnetization $m_t = \sum_{i \in S} \hat{S}_i$. Relaxation dynamics of $\langle m_t \rangle_0$ for $J^{\text{adp}}_{T_S}$, $T_S = 10^{-3}(= T_S^{c1})$, and $T_S = 2.0(T_S^{c2} = T_S = T_S^{c3})$ are plotted in Fig. 3, where $\langle \cdot \rangle_0$ denotes the average over the randomly chosen initial conditions. As shown in Fig. 3, the relaxation process for $J^{\text{adp}}_{T_S}$ evolved at low temperatures is much slower. Furthermore, $\langle m_t \rangle_0$ converges to a value $m_t^*$ lower than 1 and remains at that value for a long time. Depending on the initial condition, the spins are often trapped at a local minimum, so that the target configuration is not realized over a long time span.

Such dependence on initial conditions is not observed for $J^{\text{adp}}_{T_S}$ for $T_S > T_S^{c1}$, where $\langle m_t \rangle_0$ approaches 1 somewhat quickly. From an estimate of the convergent value of the target magnetization $m_t^*$ within the above MC time scale, we obtain the relaxation time $\tau$ by fitting to the function $\langle m_t \rangle_0(s) = m_t^* + c \exp(-s/\tau)$, where $s$ is the MC step of the spin dynamics. The parameters $m_t^*$ and $\tau$ are plotted against $T_S$ in the inset of Fig. 3, which shows the increase of $\tau$ and the decrease of $m_t^*$ from 1 with the decrease of $T_S$ below $T_S^{c1}$. These results imply that the energy landscape for the interaction $J^{\text{adp}}_{T_S}$ is rugged for $T_S \leq T_S^{c1}$, as in a spin-glass phase, whereas it is smooth around the target for $T_S^{c1} \leq T_S \leq T_S^{c2}$. Thus, this landscape is interpreted as a typical funnel landscape. It demonstrates a transition from the spin-glass phase to the funnel at $T_S^{c1}$ (see also [7]).

Now, in the evolved genotypes, let us examine the robustness that represents the stability of $J$’s fitness with respect to changes in the $J$ configuration. From the adopted genotype $J^{\text{adp}}_{T_S}$, mutations are imposed by flip-flopping the sign of a certain fraction of randomly chosen matrix elements in $J^{\text{adp}}_{T_S}$. The value of the fraction represents the mutation rate $\mu$. We evaluate the fitness of the mutated
FIG. 4 (color online). Fitness of the mutated $J$ as a function of the mutation rate $\mu$ for $T_S = 10^{-4}$ (solid curve) and $T_S = 2.0$ (dotted curve). For each adapted genotype, the mutated genotypes $J$ are generated 150 times by flipping randomly chosen elements $J_{ij}$ with $J$ governed by the rate $\mu$, and the average is taken over 150 adapted genotypes.

$J_{T_S}^{adp}(\mu)$ at $T_S = 10^{-5}(\neq T_S)$, i.e., $\Psi(J_{T_S}^{adp}(\mu)|T_S' = 10^{-5})$, by taking an average over 150 samples of mutated $J_{T_S}^{adp}(\mu)$. Figure 4 shows $\mu$ dependence of the fitness for $T_S = 10^{-4}$ and $T_S = 2.0$. For low values of $T_S$, the fitness of mutated $J_{T_S}^{adp}(\mu)$ exhibits a rapid decrease with respect to the mutation rate, but for $T_S$ between $T_S^1$ and $T_S^2$, it does not decrease until the mutation rate reaches a specific value. We define $\mu_c(T_S)$ as the threshold point in the mutation rate beyond which the fitness $\Psi(J_{T_S}^{adp}(\mu)|T_S')$ begins to decrease from unity. Figure 2 shows the dependence of $\mu_c$ on $T_S$, which has a plateau at $T_S^1 \leq T_S \leq T_S^2$ where $\Phi_2$ is unity. This range of temperatures that exhibits mutational robustness agrees with the range that gives rise to the LMS. In other words, mutational robustness is realized for a genotype with no frustration around the target spins. Evolution in a mutationally robust genotype $J$ is possible only when the phenotype dynamics is subjected to noise within the range $T_S^1 \leq T_S \leq T_S^2$. This mutational robustness is interpreted as a consequence that the fitness landscape becomes non-neutral for $T_S \simeq T_S^1$ [18].

To check the generality of the transition to the LMS as well as the mutational robustness, we have examined the model by increasing the number of target spins $t$, and confirmed that the LMSs evolve at an intermediate range of $T_S$ (that depends on $t$), where both lower energy and higher fitness are realized together with mutational robustness, while the actual fitness value therein decreases with an increase in $t$. Simulations with larger $N$ (up to 30) have also confirmed the evolution of the LMSs at an intermediate range of $T_S$ [18].

In this study, in order to elucidate the evolutionary origin of robustness and funnel landscape, we have considered the evolution of a Hamiltonian system to generate a specific configuration for target spins. The findings can be summarized as follows. First, as a result of the formation of a funnel landscape through the evolution of the Hamiltonian, robustness to guard against noise is achieved in the dynamic process. Such shaping of dynamics is possible only under a certain level of thermal noise, given by temperatures $T_S^1 \leq T_S \leq T_S^2$. Second, under such a temperature range in the process, a funnel-like landscape that gives rise to a smooth relaxation dynamics toward the target phenotype is evolved to avoid the spin-glass phase. This may explain the ubiquity of such funnel-type dynamics observed in evolved biological systems such as protein folding and gene expression [6,12]. Third, this robustness to thermal noise induces robustness to mutation; this observation has also been discussed for gene transcription network models [12]. Relevance of thermal noise to robust evolutions is thus demonstrated.

The funnel-like landscape evolved at $T_S^1 \leq T_S \leq T_S^2$ is characterized by the local Mattis state without frustration around the target spins. This allows for a smooth and quick relaxation to the target configuration, which is in contrast with the relaxation on a rugged landscape in spin-glass evolved at $T_S < T_S^1$, where relaxation is often trapped into metastable states. Theoretical analysis of random spin systems such as replica symmetry breaking will be relevant to the local Mattis state and mutational robustness [18], as the model discussed in this Letter is a variant of spin systems with two temperatures [19].

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[17] For a finite system with finite $T_J$, $\Phi_j$ cannot be exactly 1. However, as long as $T_J$ is low, the deviation from 1 of $\Phi_j$ at the intermediate temperature is negligible.