Dimensional reduction in evolving spin-glass model: correlation of phenotypic responses to environmental and mutational changes

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The evolution of high-dimensional phenotypes is investigated using a statistical physics model of spins, whose stochastic change is governed by a Hamiltonian that includes the two-body spin-spin interaction $J_{i,j}$ under thermal noise, specified by the temperature $T$ [5]. In the model, the following correspondences are taken: phenotypes $\rightarrow$ spin configurations $\{S_i\}$; rule to shape the phenotype $\rightarrow$ Hamiltonian for spin-spin interaction $H = -\sum J_{i,j} S_i S_j$; environmental condition $\rightarrow$ external field $h_i$ to each spin in the Hamiltonian. The evolution process is introduced by the “mutation” in $J_{i,j}$ and a selection according to the fitness defined from the spin configuration. By evolving the Hamiltonian under a certain temperature, we have previously demonstrated the evolution of Hamiltionians to shape phenotypes to be robust to perturbations at an intermediate temperature, whereas replica symmetry breaking (RSB) was demonstrated to lead to a non-robust phenotype at a lower temperature.

By taking advantage of this spin model and evolving it under a certain temperature, one can investigate if the dimension reduction in phenotypic changes, as observed in biological systems, is formulated and understood in terms of statistical physics. Specifically, we focus on the following questions: (i) Are high-dimensional phenotypic changes against various environmental changes correlated? (ii) Are the changes induced by environmental and genetic changes correlated? (iii) If the above two correlations are observed, are they a result of dimension reduction from a high-dimensional phenotypic space, shaped by evolution? (iv) Finally, within what range of temperature are the above questions answered affirmatively? In other words, is the appropriate noise relevant to the evolution of dimension reduction? By answering these questions, we will elucidate the origin of dimension reduction in terms of statistical physics, in possible relationship with replica symmetry (breaking).

Now, we define a spin-statistical physics model for phenotypic evolution, in which the phenotype is denoted by...
spins $S = [S_1, \cdots, S_N] \in \{-1, +1\}^N$. The dynamics of the spins are given by the stochastic dynamics, prescribed by the Hamiltonian $H$ as

$$H(S|J) = -\frac{1}{2} S^T J S,$$

(1)

where superscript $T$ denotes the transpose, and $J \in \mathbb{R}^{N \times N}$ is a symmetric matrix whose diagonal components are zero. With this Hamiltonian, the spin dynamics with discrete time $t$ is given by the transition probability

$$\text{Pr}[S^{(t)} \rightarrow S^{(t+1)}|J] = \min\{e^{-\beta \Delta H(S^{(t)}, S^{(t+1)}|J)}, 1\},$$

(2)

where $S^{(t)}$ is the phenotype at step $t$, and $\Delta H(S, S'|J) \equiv H(S'|J) - H(S|J)$. The inverse temperature $\beta = T^{-1}$ describes the stochasticity of the phenotype expression process. The elements of the interaction matrix are chosen as $J_{ij} \in \Omega_j (i \neq j)$ with $\Omega_j = \{-1/\sqrt{N}, 0, 1/\sqrt{N}\}$, and $J_{ii} = 0$ ($i = 1, \cdots, N$). This matrix represents the genotype, which evolves over generations, as will be described later.

The fitness is generally given as a function of phenotypes, i.e., the spin configuration. Here, we assume that a part of the spins, named targets $i \in \mathcal{T}$, contributes to the fitness, such as the active site residues of protein. As more of the target spins have the same value $+1$ or $-1$, the fitness $\psi(J)$ is higher, as defined as

$$\psi(J) = m_T, \quad m_T = \frac{1}{N_T} \sum_{i \in \mathcal{T}} S_i$$

(3)

where $N_T$ is the size of $\mathcal{T}$, and $\bar{\bar{\cdots}}$ denotes the average over the trajectories of the phenotype expression dynamics, which depend on genotype $J$.

The evolution to select genotypes with higher fitness is represented by the following stochastic update rule with discrete time,

$$\text{Pr}[J^{(g)} \rightarrow J^{(g+1)}] = \min\{e^{\beta J \Delta \psi(J^{(g)}, J^{(g+1)})}, 1\},$$

(4)

where $\Delta \psi(J', J) = \psi(J') - \psi(J)$. The parameter $\beta_j = T_j^{-1}$ represents the selection pressure; as $T_j$ decreases, only the genotypes with sufficient fitness survive to the next generation.

We mainly describe the results for $N = 100$ and $\rho = N_T/N = 0.05$, unless otherwise mentioned. For the phenotype dynamics eq. [2], we adopt the Markov Chain Monte Carlo (MCMC) method with detailed balance condition. After a sufficient number of updates, the distribution of $S$ is expected to converge to the equilibrium distribution, $P(S) \propto \exp(-\beta H(S|J))$, for a given genotype. We numerically calculated the thermal average over $t_\lambda = 2 \times 10^4$ MC steps, after discarding the initial $t_i = 10^4$ steps.

At each generation $g$, the candidates of genotype $J^{(g+1)}$ are generated by introducing the mutations with probability $p_\mu = 0.05$. The values of $J_{ij}$ ($i \neq j$) change into one of the components in $\Omega_j \setminus J_{ij}$ with equal probability, where $A \setminus a$ denotes the members of $A$, excluding $a$. We numerically update genotypes over generation $g_{\text{max}}$ at $T_j = 0.05$. [20]. Without a loss of generality, hereafter, we set the target sites as $\mathcal{T} = \{1, \cdots, N_T\}$. We numerically obtain 100 genotypes evolved at $\rho$ and $T$ with different initial conditions, and the set is denoted as $\mathcal{J}(T)$.

First, we present the existence of three phases that depend on $T$. [19]. Fig.1(a) shows the temperature dependence of the averaged fitness over $\mathcal{J}(T)$. At $T > T_{c_1}$, the fitness value is at the level expected by the random spin configuration, which indicates that the target spins do not show any order, and we define the phase $T > T_{c_1}$ as paramagnetic phase. The high-fitness phase is separated into two phases at $T = T_{c_2}$. This phase boundary is characterized by the convergence of the belief propagation (BP) algorithm [21]. From the correspondence between the replica analysis and BP algorithm, it is expected that the convergence limit of the BP algorithm corresponds to the replica-symmetry-breaking transition [22]. As shown in Fig.1(b), the fraction of $J \in \mathcal{J}(T)$, in which the BP algorithm does not converge within $10^5$ steps, increases from zero at $T_{c_2}$. Hence, the phases $T_{c_1} \leq T \leq T_{c_2}$ and $T > T_{c_2}$ correspond to the replica symmetric (RS) and RSB phases, respectively.
Now, we discuss if the response to different environmental conditions is correlated or not, depending on the phase. Hereafter, we study the symmetry breaking local magnetization $\mu_i = \text{sign}(mT)S_i$, considering the $\mathbb{Z}_2$ symmetry. Under the infinitesimal external fields, the difference between expression patterns $\delta \mu^{(h)}(h, J; \delta h) \equiv \mu_i(h + \delta h, J) - \mu_i(h, J)$ is expanded as
\[
\delta \mu^{(h)}_i(h, J; \delta h) \sim \sum_j \chi_{ij}(h, J) \delta h_j,
\]
where $\chi_{ij}(h, J) = \partial \mu_i(h, J)/\partial h_j$ is the susceptibility.

We regard eq. (5) as the response of the $i$-th component to the additional external field, for a system with genotype $J$ subject to external field $h$. For simplicity, we consider the case that an external field $\delta h_i$, whose $i$-th component is $\delta h_i(\neq 0)$, otherwise 0, is applied to the system at $h = 0$. The first-order response of the $j$-th component to $\delta h_i$ is $\chi_{ij}(0, J)$. At the equilibrium, $\chi_{ij}(h, J) = \beta((S_iS_j)_h - (S_i)_h(S)_h)$ holds, where $\langle \cdot \rangle_h$ means the average according to the equilibrium distribution under the external field $h$: $P(S) \propto \exp(-\beta H(S, J) + h^T S)$. We numerically compute $\chi_{ij}$ by MCMC simulation as $\chi_{ij} = \langle S_iS_j \rangle - \mu_i \mu_j$. Fig. 1 shows the scatter plots of $\chi_{11}$ and $\chi_{12}$ under one realized genotype for $i \geq 3$ at (c) $T = 1$ (RS) and (c) $T = 0.4$ (RSB). Their correlation coefficients are (b) 0.59, and (d) -0.035, respectively. Here, we ignore the responses of $\mu_1$ and $\mu_2$ to remove the trivial strong response directly to $\delta h_1$ and $\delta h_2$ itself.

In Fig. 2, the correlation between the responses to external fields $\delta h_i$ ($i \in T$) is discernible in the RS phase.

Next, we study the correlation between responses to the environment, $\delta \mu^{(h)}_i$, and those to genetic changes, $\delta \mu^{(J)}_i(J; \delta J) \equiv \mu_i(0, J + \delta J) - \mu_i(0, J)$, expanded as
\[
\delta \mu^{(J)}_i(J; \delta J) \sim \sum_{j,k} \mathcal{M}_{i,j,k}(J) \delta J_{jk},
\]
where $\mathcal{M}_{i,j,k} = \partial \mu_i(J)/\partial J_{jk}$, which corresponds to $\beta((S_iS_jS_k)_h - (S_i)_h(S_j)_h)$ at the equilibrium. For the comparison between $\delta \mu^{(h)}_i$ and $\delta \mu^{(J)}_i(J)$, we assume that the components of $\delta h$ and $\delta J$ independently follow a Gaussian distribution with mean 0 and variance $\epsilon$ for $\delta h$, and variance $\epsilon^2\sqrt{N}$ for $\delta J$, respectively. The expected squared responses are given by
\[
E_{\delta h} \left[ \delta \mu^{(h)}_i(h, J; \delta h) \right]^2 \simeq \epsilon^2 \chi_i(h, J),
\]
\[
E_{\delta J} \left[ \delta \mu^{(J)}_i(J; \delta J) \right]^2 \simeq \epsilon^2 \mathcal{M}_i(J),
\]
where $E_{\delta h}[]$ and $E_{\delta J}[]$ denote the average over $\delta h$ and $\delta J$, respectively, and $\chi_i = \sum_{j \neq i} \chi_{ij}$, and $\mathcal{M}_i = N^{-1} \sum_{j,k,j \neq k} \mathcal{M}_{i,j,k}$. The quantities $\chi_i(h, J)$ and $\mathcal{M}_i(J)$ correspond to the spin-glass susceptibility and

"susceptibility to interaction matrix," and indicate the sensitivity of the $i$-th component to the external field and mutation, respectively. Fig. 2 shows the scatter plot between $\mathcal{M}_i(J)$ and $\chi_{ij}(0, J)$ for genotype $J \in J(T)$ at (b) $T = 1$ (RS) and (b) $T = 0.2$ (RSB). A linear relationship between $\chi_i$ and $\mathcal{M}_i$ arises in the RS phase.

These numerical simulations indicate that the evolution under thermal fluctuation that leads to the RS phase induces the correlations between the responses. To understand the emergence of the correlation, we decompose the evolved genotypes into eigenvalues and eigenvectors as $J = \Xi \Lambda \Xi^T$, where $\Lambda \in \mathbb{R}^{N \times N}$ is a diagonal matrix consisting of eigenvalues $\lambda_i = \lambda_1 \geq \lambda_2 \geq \cdots \geq \lambda_N$, and $\Xi = [\xi^1, \cdots, \xi^N] \in \mathbb{R}^{N \times N}$ is the set of corresponding eigenvectors. Fig. 3(a) shows the averaged values of the first and second eigenvalues over $J \in J(T)$. The first eigenvalue is much larger in the RS phase than those in the other phases. The evolutionary change of the second eigenvalue is vanishingly small for any $T$. This tendency is common for any $\lambda_i$ ($i \geq 2$). Hence, the dominance of the first eigenmode is enforced as a result of the evolution at $T_{c2} \leq T \leq T_{c1}$.

On the basis of the large contribution of the first eigenvalue in the RS phase, we apply a 1-rank approximation of genotype $J \sim \eta \xi^1 \xi^T$. By a straightforward calcula-
Hence, the proportionality between in Fig. 2. We quantify the deviation of the observed evolved in the RS phase, i.e., the evolutionary dimension reduction. If the temperature is reduced, robustness in the phenotype is lost by caused by the dominance of the first eigenmode. From eq. (10), the leading term of susceptibility is \( \chi_{ij} = \eta_i \xi^i_j \xi^j_i v_j + \gamma \), hence, \( \chi_{ij} = \xi^i_j v_j / (\xi^j_i v_k) \). In the RS phase, both \( v_j \) and \( \xi^i_j \) are functions of \( \mu_i \); hence, \( \chi_{ij} / \xi_{ik} \approx 1 \) holds when \( \mu_i \gg \mu_k \). This is the origin of the linear relationship between \( \chi_{ij} \) and \( \chi_{ik} \).

In summary, we applied an evolving spin-statistical physics model, representing phenotypes, genotypes, and the environment by spin configuration, interaction matrix, and the external field, respectively, and have answered the questions addressed at the beginning of this paper. (i) Correlated responses across different environmental changes are demonstrated by the correlation in susceptibilities \( \chi_{ij} \) and \( \chi_{ik} \) in the evolved genotypes at the RS phase. (ii) Proportional responses to mutation and environmental changes are demonstrated by the proportionality between the “susceptibility to interaction matrix” \( M_{ij} \) and spin-glass susceptibility \( \xi_i \). (iii) These proportional responses originate in the reduction of rank in the interaction matrix. (iv) Such dimension reduction and proportional changes are observed for the evolved genotypes at the RS phase, i.e., at an intermediate level of thermal noise.

Hence, robustness of phenotypes to noise is essential to the evolutionary dimension reduction, leading to the correlated responses in the high-dimensional phenotypes to different types of perturbations. Although the present statistical physics model is highly simplified, it gives a theoretical basis for dimension reduction in biological systems, in which robustness to noise is also essential. For example, recent reports on protein dynamics suggest the existence of large collective motion, which may be a manifestation of dimension reduction. Although dynamics at the cellular level are not represented by a Hamiltonian, the similarity between spin-glass dynamics and gene expression dynamics with mutual activation and inhibition is now well recognized.

In terms of statistical physics, the evolution to the RS phase under appropriate levels of noise should be considered, in which both higher fitness and robustness to noise are achieved with the dimension reduction. If the temperature is reduced, robustness in the phenotype is lost by...
RSB, even though a higher fitness state is reached after sufficient time steps of expression. Here, we have studied the simplest fitness condition. For higher biological functions, the response to diverse environmental conditions, say, different target spin configurations upon the application of different external fields, may be required. The extension to such problems would be straightforward, in which the need for both robustness and plasticity may lead to dimension reduction with higher ranks.

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[27] -Evolved genotypes in RS phase do not perfectly agree with this Mattis-type model in the sense that eigenmodes other than the first mode remain. These modes induce frustration between non-target spins [15], which is considered to be hamper the correlations between responses of non-target spins [30].
[28] See Fig.1 of supplements for $\rho$-dependence of the embedded pattern.
[29] If $\chi_{ij}$ for every $i \neq j$ were exactly zero, the proportional-ity between $\chi_i$ and $M_i$ would not be observed, because $\chi_i$ in our definition turns to be zero.
[30] See Supplement Fig.2, for $\epsilon$-dependence of $d$ over different values of target ratio $\rho$ at $T = 1$. Although a strong correlation at $\epsilon = 0$ is observed for any $\rho$, the relationship is not robust to noise $\epsilon$ as $\rho$ increases. The existence of redundant spins other than targets is relevant to robustness and dimension reduction.
[31] Approximations eq.[9] and eq.[10] are relatively inaccurate for components with small local magnetization, in the sense that they are sensitive to the correction of first eigenmodes by taking higher modes into account. Therefore, the correlations between $\{\chi_{ij}\}$ and $\{\chi_{ik}\}$ are observed for components whose local magnetizations are sufficiently large, including target components.
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