

Exercise Sheet #12

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Problem 1 (*Error Catastrophe for Epistatic Interactions, 20 pts*)

Epistatic interactions in a genome are characterized by the fact that the overall fitness of the genome is not given by a simple superposition of contributions of individual genes. An extreme case is discussed in the lecture under Section 8.3.3: for some genome \mathbf{s} , the fitness $W(\mathbf{s})$ is given by

$$W(\mathbf{s}) = \begin{cases} 1 & \text{if } \mathbf{s} = \mathbf{s}_0 \\ 1 - \sigma & \text{else} \end{cases} \quad (1)$$

where $\sigma \in [0, 1]$ and \mathbf{s}_0 denotes the optimal genome. It was shown that this model shows a phase transition from a state where the hamming distance from the optimal genome in the population stays finite towards a state where the population spreads evenly across the space of possible genomes (the "error catastrophe").

We would like to compare this result with a particular case of the quasispecies model introduced in section 8.5.1: Here, the dynamics of a population of information carrying macromolecules, described by their respective concentrations x_i is given by

$$\dot{x}_i = W_{ii}x_i + \sum_{j \neq i} W_{ij}x_j - x_i\phi(t) \quad (2)$$

where the diagonal entries of the matrix W denote the self-replication rates, the off-diagonal elements are the mutation rates and $\phi(t)$ is some external time dependent factor that modulates the self-replication rates of all molecules. In our case, we simply choose a competition factor $\phi(t) = \sum_{ij} W_{ij}x_j(t)$, thereby preventing runaway growth.

To compare this model with the previously discussed epistatic model, we choose

$$W_{ii} = \begin{cases} 1 & i = 1 \\ 1 - \sigma & i > 1 \end{cases}, \quad W_{ij} = \begin{cases} u_+ & \text{if } i = j + 1 \\ u_- & \text{if } i = j - 1 \\ 0 & \text{if } i \neq j \text{ otherwise} \end{cases} \quad (3)$$

where $\sigma, u_{\pm} \in [0, 1]$. This matrix essentially describes a chain-like mutation structure.

- a) Analyze the dynamics and determine the error catastrophe for two cases: $u_+ = u_i \equiv u$ (that is, "forward" and "backward" mutations are equally likely) and $u_+ = u, u_i = 0$ (only "forward" mutations).

Hint: Look for the stationary solution, giving you an eigenvalue equation. Then, for $i > 1$, you can write x_{i+1} as a two-step recursive relation leading to a 2×2 matrix. Find the eigenvalues and eigenvectors of this matrix and use it to solve the initial eigenvalue problem. The criterion for the error catastrophe is then whether or not $\sum_i x_i$ stays finite.

- b) Compare the results to the tower landscape in Sect. 8.3.3.