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To the Editors,

Please find enclosed our submission of ‘Self-organization can guide natural selection’ to be considered for publication in *Science*.

Self-organization and natural selection are fundamental forces that work together to shape all biological systems, but the nature of this interaction is not yet fully understood. Here we show how self-organizing attractor dynamics in gene networks can accelerate natural selection to facilitate the discovery of networks that map patterns of early gene expression to specific target patterns in later development.

For example, we show that for a simple Boolean network model of five interacting genes, for which there are more than 1048 possible configurations, less than a thousand generations of an evolutionary algorithm are required to discover dynamics matching those recently described for a network that regulates neocortical development.

The key insight is to measure the fitness of a network by comparing target levels of gene expression to the average levels produced as the dynamics transition between the states comprising limit cycles.

Our results reveal a fundamental relationship between the ‘genome space’ in which network dynamics evolve, and the ‘phenotype space’ in which network dynamics self-organize, which can be exploited in a way that is entirely consistent with conventional descriptions of natural selection.

We suggest that this new and fundamental result, which we have taken care to explain clearly and in its simplest terms in the manuscript, make this paper highly suitable for the broad readership of *Science*.

In line with online guidance, please note the following: None of the material has been published or is under consideration for publication elsewhere; We include in the submission a minimal standalone c++ implementation of the model algorithm as an auxiliary file, and a script for re-creating the main figure; The paper has not been reviewed by any colleagues except for those mentioned in the acknowledgements (Hannes Saal, Jim Stone, and Drew Halley).

We look forward to receiving your comments about the suitability of ‘Self-organization can guide natural selection’ for publication in *Science*.

Sincerely,

Stuart Wilson

Sebastian James

Daniel Whiteley

Leah Krubitzer