Supplementary Information - Selective Phenome Growth adapted NK model: a novel landscape to represent aptamer ligand binding

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1 SUPPLEMENTARY FIGURES

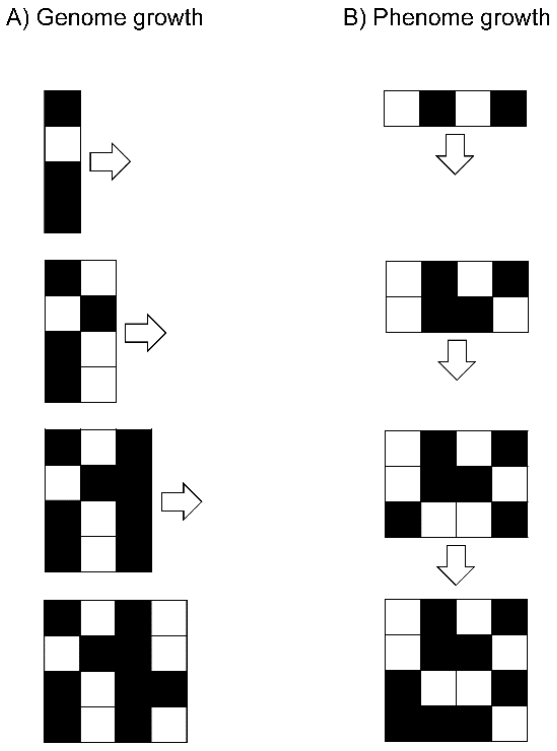

Figure S1: Constructional selection of interaction maps. A) Selective genome growth of an interaction map. Genes (columns) with many phenotypic contributors are added sequentially. B) Selective phenome growth of an interaction map. Phenotypic contributors (rows) with any gene interactions are added sequentially.

2 SUPPLEMENTARY METHODS

Visual Basic .NET (Microsoft Corporation) was used to code the three programs EpiMapSelection, NKLandscapeTester and MonotonicTrajectoryCalculator which were used in this manuscript. For all three programs base interaction value tables were generated for *K* values from 1 to 16 from a random distribution between 0 and 1.

2.1 EpiMapSelection

The program EpiMapSelection uses constructional selection, similar to that used by Altenberg (1) to create both genome selected and phenome selected interaction maps.

For selective genome growth interaction maps, the program randomly selects a lead sequence of size *N* before iterative cycles of constructional selection to build the interaction map. The selective genome growth constructional selection cycle consists of adding a new gene with *1* to $K + 1$ randomly selected interactions. The new fitness of the selected lead sequence is calculated and if the new addition increases the fitness it is kept, if the new addition decreases fitness it is removed. The selected lead sequence is then adapted by point mutations in a monotonic, uphill direction until it reaches an optimum. This process is repeated until the number of desired genes is reached.

For selective phenome growth interaction maps, the program randomly selects a lead sequence of size *N* before iterative cycles of constructional selection to build the interaction map. The selective phenome growth constructional selection cycle consists of adding a new phenotypic contributor with *1* to $K + 1$ randomly selected interactions. The new fitness of the selected lead sequence is calculated and if the new addition increases the fitness it is kept, if the new addition decreases fitness it is removed. The selected lead sequence is then adapted by point mutations in a monotonic, uphill direction until it reaches an optimum. This process is repeated until the number of desired phenotypic contributors is reached.

2.2 NKLandscapeTester

The program NKLandscaeTester measures the basins of attraction for NK landscapes similarly to Kauffman (2). 100,000 adaptive walks are performed from random points on the landscape in a monotonic, uphill direction until an optimum is reached. These optimums are recorded and analysed to characterise basins of attraction and to calculate hamming distance from fittest optima. Both uphill and downhill basins of attraction are measured by reversing the direction of the adaptive walker.

2.3 MonotonicTrajectoryCalculator

The program MonotonicTrajectoryCalculator measures the mean path divergence (MPD) of a given landscape similarly to Lobkovsky *et al*. (3). Briefly, the program measures the path divergence of each individual point on the landscape and bins this data by hamming distance. For a detailed description of MPD calculation please refer to Lobkovsky *et al*. (3).

3 REFERENCES

1. Altenberg L (1994) Evolving better representations through selective genome growth. in *Evolutionary Computation, 1994. IEEE World Congress on Computational Intelligence., Proceedings of the First IEEE Conference on* (IEEE), pp 182-187.
2. Kauffman SA (1993) *The origins of order: Self organization and selection in evolution* (Oxford University Press).
3. Lobkovsky AE, Wolf YI, & Koonin EV (2013) Quantifying the similarity of monotonic trajectories in rough and smooth fitness landscapes. *Molecular BioSystems* 9(7):1627-1631.