***Our s***

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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
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Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

- 20 replicates of equilibrium simulations were run for each system. Figure 2-Figure Supplement 1

- 800 replicates of non-equilibrium simulations were run for each system. Figure 2-Figure Supplement 1

- The students T-test was used to assess statistical significance (Figure 2 & 3)

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
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**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
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(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

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* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

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Not applicable

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* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
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The script files can be downloaded from the doi [10.6084/m9.figshare.13583384](https://doi.org/10.6084/m9.figshare.13583384%22%20%5Ct%20%22_blank)