***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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- 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
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* 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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