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Design principles for robust oscillatory behavior

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Abstract

Oscillatory responses are ubiquitous in regulatory networks of living organisms, a fact that has led to extensive efforts to study and replicate the circuits involved. However, to date, design principles that underlie the robustness of natural oscillators are not completely known. Here we study a three-component enzymatic network model in order to determine the topological requirements for robust oscillation. First, by simulating every possible topological arrangement and varying their parameter values, we demonstrate that robust oscillators can be obtained by augmenting the number of both negative feedback loops and positive autoregulations while maintaining an appropriate balance of positive and negative interactions. We then identify network motifs, whose presence in more complex topologies is a necessary condition for obtaining oscillatory responses. Finally, we pinpoint a series of simple architectural patterns that progressively render more robust oscillators. Together, these findings can help in the design of more reliable synthetic biomolecular networks and may also have implications in the understanding of other oscillatory systems.

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