Influence of parameter values on the oscillation sensitivities of two p53–Mdm2 models

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Abstract

Biomolecular networks that present oscillatory behavior are ubiquitous in nature. While some design principles for robust oscillations have been identified, it is not well understood how these oscillations are affected when the kinetic parameters are constantly changing or are not precisely known, as often occurs in cellular environments. Many models of diverse complexity level, for systems such as circadian rhythms, cell cycle or the p53 network, have been proposed. Here we assess the influence of hundreds of different parameter sets on the sensitivities of two configurations of a well-known oscillatory system, the p53 core network. We show that, for both models and all parameter sets, the parameter related to the p53 positive feedback, i.e. self-promotion, is the only one that presents sizeable sensitivities on extrema, periods and delay. Moreover, varying the parameter set values to change the dynamical characteristics of the response is more restricted in the simple model, whereas the complex model shows greater tunability. These results highlight the importance of the presence of specific network patterns, in addition to the role of parameter values, when we want to characterize oscillatory biochemical systems.

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