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On the Existence and Uniqueness of Biological Clock Models Matching Experimental Data

The development of luciferase markers and other experiment techniques has allowed measurement of the timecourses of the expression of genes and proteins with remarkable accuracy. Since this data has been used to construct many mathematical models, it is important to ask if this problem of model building is well-posed. Here, we focus on a common form of ordinary differential equation (ODE) models for biological clocks, which consist of production and degradation terms, and assume we have an accurate measurement of their solution. Given these solutions, do ODE models exist? If they exist, are they unique? We show that timecourse data can sometimes, but not always determine the unique quantitative relationships (i.e. biochemical rates) of network species. In other cases, our techniques can rule out functional relationships between network components and show how timecourses can reveal the underlying network structure. We also show that another class of models is guaranteed to have existence and uniqueness, although its biological application is less clear. Our work shows how the mathematical analysis of the process of model building is an important part of the study of mathematical models of biological clocks.

Example 1. Timecourses data reveals the structure of a single Goodwin oscillator.
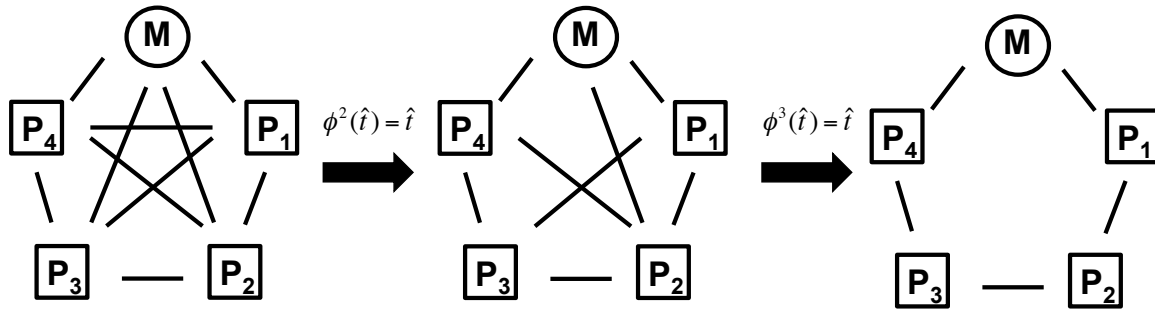
Example 2. Timecourses data reveals the most structure of two independent Goodwin oscillators.