

Mathematical modelling of the Platelet-Derived Growth Factor (PDGF) signalling pathway

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Constructing a mathematical/computational model for a biological system consists of two main steps: first, of specifying the model structure and, second, of determining the numerical values for the parameters of the model. Usually, the structure of the model is represented in the form of a biochemical reaction network and the parameters are the reaction rate constants. The values of the reaction rates can either be measured directly in experiments or determined by fitting the model to experimental data by performing parameter estimation. Since the former approach is often impeded by technical limitations or high costs of experimental practice, parameter fitting is a fundamental problem in systems biology research.

In this study we consider issues related to parameter estimation for a model of the Platelet-Derived Growth Factor (PDGF) signalling pathway with use of steady-state data and so called knock-down mutant models, i.e., variants of the original model obtained by suppressing one or more interactions in the model. Since the knock-down mutants of the real biological system can be obtained and investigated in experimental practice as well as the physical/chemical properties are usually common for all variants, the measurements of the mutants can enrich the set of data available for parameter estimation. We consider parameter estimation both in the deterministic (system of ordinary differential equations) and stochastic (continuous-time Markov chain) modelling frameworks. We discuss certain difficulties related to parameter estimation we encountered while modelling the PDGF signalling pathway and present our solutions.