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Sensitivity Analysis of Bacterial Chemotaxis Models

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Abstract

Chemotaxis is the process, by which cells sense changes in their chemical environment and move towards more favorable conditions. This process is controlled by signaling pathways, which are relatively simple, but bear several important features of the ones of higher organisms. Sensitivity analysis of mathematical chemotaxis models of bacteria *Escherichia coli* and *Bacillus subtilis* was carried out and the most important parameters of the signal transduction cascades were determined. Global and local similarities of the sensitivity−time functions were found. Groups of parameters were identified in both models and changes of parameters within the same group can compensate each other to produce exactly the same response of the cell. This means that the parameter values in these models are not unique. On the other hand, this feature indicates a novel type of robustness of the signaling pathways.

Keywords: signaling pathways; systems biology; chemotaxis; computer modeling; model identification

1. Introduction

Synergy of disciplines biology, medicine, chemistry and mathematics is an expected way to obtain scientific results of novel type. One example for such a transdisciplinary approach is the creation of detailed mathematical models of molecular biological processes and the analysis of these models using new algorithms. It is expected that this cross-disciplinary approach will result in a new paradigm for the quest of human medical drugs.

Flagellated bacteria detect the change of the gradients of chemicals with specific receptors and move accordingly by changing the rotation of the flagella [1]. The signaling pathways of chemotaxis are among the most studied systems in biology. The models of chemotaxis are very important at the investigation of the signaling networks of more complex organisms. In this work a computational study of mathematical models of the chemical reactions of bacterial chemotaxis was carried out. In a longer term, similar investigations may lead to the understanding of the signaling pathways in the human body, resulting in a new family of anti-cancer drugs.

2. Bacterial chemotaxis and models

The process of chemotaxis is controlled by an intracellular signal transduction pathway between the receptors and the flagellar motor. In *E. coli* and *B. subtilis* the counter-clockwise rotation of the flagella results in straight runs, while clockwise rotation is responsible for tumbling and reorientation of the cell. The models of chemotaxis developed

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by Rao *et al.* [2] were investigated. Their *E. coli* chemotaxis model is based on experimental results, while the *B. subtilis* model is a version of the *E. coli* model, modified according to theoretical considerations. The models were encoded in SBML using software COPASI Version 4.6 (Build 32) [3]. These models were then investigated in a series of simulations and sensitivity−time functions were calculated by COPASI [3].

3. Results

Based on the sensitivity−time functions, the most important reactions of the cascades were determined. There are significant differences between the two chemotaxis models, even if these are based on similar sets of reactions. In both models the first step of the cascade is very important and small changes of these reaction rate coefficients cause large response. Other important reactions are the feedback reactions of the pathways, but the important feedback reactions are different in the two models.

Local and global similarities of the sensitivity functions [4,5] are unusual feature of some chemical kinetic models. We identified both type of similarity of the calculated sensitivity functions. Parameters belonging to the same group of globally similar sensitivity functions can compensate each other. If these parameters are changed simultaneously, the calculated concentrations can be identical to the originals. This means that in both models infinite set of parameters may provide identical results. Also, this feature of the systems is a sign of robustness and refers to a potential failure correcting method.

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