Simulating signaling pathways: the motile photoresponse of H. salinarum as a case study

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Motivation

The simulation of signaling pathways is an important current challenge in Systems Biology, since it shows some characteristics that are difficult to manage by means of the simulation approaches usually adopted for constitutive metabolic pathways. In particular, it is multi-scale with respect both to metabolite concentrations (because of the amplification) and reaction kinetics. We focused our interest on the simulation of a specific signaling pathway: the photoperception in Halobacterium salinarum, which belongs to Archæa and possesses four different rhodopsins, two of which have a sensory role (SR1 and SR2). These two pigments allow H. salinarum to react to light stimuli by altering its motile behavior. This photoresponse is very complex and depends on the duration, intensity and spectral composition of the stimulus; several models have been proposed in the literature to explain this puzzling behavior. Recently H. salinarum, independently of our work , has been suggested as a model system for Systems Biology in a international congress (CMSB 2008).

Methods

We developed a stochastic simulator that provides an optimized implementation of the Gillespie's direct-method. The input file is an ASCII list where each chemical species, its initial concentration, each reaction with kinetic coefficient is declared. This input can also contain user-specified dynamic parameters, whose values can change during the simulation: this allows to represent the time course of experimental stimuli in the simulation. Three output files contain the time course of the concentration of each metabolite, the time course of the effective rate of each reaction, the time course of the propensity coefficient of each reaction, respectively. These three files allow us to monitor the simulation and check for possible artifacts. We have selected from the literature the two most representative qualitative models proposed to explain the molecular basis of the photomotile responses of such archæon: that by Marwan et al., and that by Hoff et al. (here called M1 and M2, respectively, for short). By harvesting the literature, we collected any available data on the kinetic coefficients of the reactions involved in M1 and M2.

Results

We simulated the behavior in the dark (absence of light stimulation) and we tested the response of both M1 and M2 to several experimentally described responses to different irradiation regimes: orange flash; long-lasting orange illumination; blue flash; long-lasting blue illumination; blue flash during a long lasting orange illumination. In all these cases, both M1 and M2 have shown a similar behavior, qualitatively in agreement with that reported in the literature. We can then conclude that the simulation approach is efficient to describe this signaling pathway and that M1 and M2 are equivalent in describing the experimentally known responses of H. salinarum. Further work is in progress to exploit the simulation of M1 and M2 in order to infer which experimental conditions would behaviorally distinguish the two models.

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