MODELING OF THE EXOCYTOTIC PROCESS BY CHEMICAL KINETIC FORMALISM

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ABSTRACT

The exocytotic process in neurons and neuroendocrine cells consists of a consecutive reactions between well-defined proteins. Even that the partial reactions had been investigated by variety of methods, a comprehensive description, based on chemical kinetics had not been attempted. In the present study, we have, created, a comprehensive kinetic model that reconstructs the physiological process using a standard chemical kinetic formalism. the reactions between the synaptic proteins were transformed into a set of coupled, non-linear ordinary differential equations where the rate constants and some of the reactants concentrations are adjustable parameters. Upon integration over time the reactions equations, reconstructed the experimental signal. The model can perfectly reconstruct the kinetics of exocytosis, the calcium-dependent priming and fusion processes and the effects of genetic manipulation of synaptic proteins. The model suggests that fusion occurs from two parallel pathways and assigns precise, non-identical synaptic protein complexes to the two pathways. In addition, it provides a unique opportunity to study the dynamics of intermediate protein complexes during the fusion process, a possibility that is hidden in most experimental systems.

We have used the Genetic Algorithm analysis to achieve high level of accuracy and to find a single global minimum, over a multi dimensional parameter space. Our study demonstrates that complex biological processes can be mathematically modeled and gain high predictive power, up to the level of serving as research tools. It is our intention to expand the model from the level of a comprehensive description of the whole exocytotic process, to the level of cell physiology.