Modeling of Glycine Transporters in Mammalian Using the Probability Approach

Authors : K. S. Zaytsev, Y. R. Nartsissov

Abstract : Glycine is one of the key inhibitory neurotransmitters in Central nervous system (CNS) meanwhile glycinergic transmission is highly dependable on its appropriate reuptake from synaptic cleft. Glycine transporters (GlyT) of types 1 and 2 are the enzymes providing glycine transport back to neuronal and glial cells along with Na^+ and Cl^- co-transport. The distribution and stoichiometry of GlyT1 and GlyT2 differ in details, and GlyT2 is more interesting for the research as it reuptakes glycine to neuron cells, whereas GlyT1 is located in glial cells. In the process of GlyT2 activity, the translocation of the amino acid is accompanied with binding of both one chloride and three sodium ions consequently (two sodium ions for GlyT1). In the present study, we developed a computer simulator of GlyT2 and GlyT1 activity based on known experimental data for quantitative estimation of membrane glycine transport. The trait of a single protein functioning was described using the probability approach where each enzyme state was considered separately. Created scheme of transporter functioning realized as a consequence of elemental steps allowed to take into account each event of substrate association and dissociation. Computer experiments using up-to-date kinetic parameters allowed receiving the number of translocated glycine molecules, Na^+ and Cl^- ions per time period. Flexibility of developed software makes it possible to evaluate glycine reuptake pattern in time under different internal characteristics of enzyme conformational transitions. We investigated the behavior of the system in a wide range of equilibrium constant (from 0.2 to 100), which is not determined experimentally. The significant influence of equilibrium constant in the range from 0.2 to 10 on the glycine transfer process is shown. The environmental conditions such as ion and glycine concentrations are decisive if the values of the constant are outside the specified range.

Keywords : glycine, inhibitory neurotransmitters, probability approach, single protein functioning
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