A Simulation for the G-Protein Coupled Receptor Signaling Model

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Abstract. G-protein-coupled receptors (GPCRs) comprise the largest superfamily of signal-transducing receptors with almost 2,000 members identified, including more than 800 members in human. Although GPCRs have a conserved 7-transmembrane domain structure, they recognize a vast array of extracellular signals, ranging from light to huge glycoproteins. Various responses for each signal are triggered by coupling with a specific effect molecule through G-protein. Especially, the desensitization of receptors induced by agonist affects affinity between receptor and G-protein. The internalization of receptors also contributes to functional desensitization and drug tolerance. In this paper, we propose a new computational model. The proposed model provides insights into a specific mechanism that controls the endocytosis of receptor from plasma membrane and regulates the proteolytic degradation of receptors for understanding desensitization and internalization processes for GPCRs. This model shows that the signal transduction efficacy is controlled with a slow negative feedback which is leaded from the extracellular signals.

Keywords: GPCR, Computational Model, Simulation, Desensitization, Internalization

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