A Computational Study of Ionotropic Glutamate Receptors

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Ionotropic glutamate receptors, a family of ligand gated ion channels, are located in the post-synaptic neural membrane and play important roles in the majority of fast excitatory neurotransmissions in the central nervous system. This family is comprised of different members who each serve distinct roles at glutamatergic synapses. AMPA receptors mediate fast depolarization while NMDA receptors mediate the slower component of the excitatory postsynaptic potential. Binding of the neurotransmitter glutamate to an extracellular binding site on these receptors causes a conformational change which opens a pore, thus allowing cations to flow into the post-synaptic neural cell. Since glutamate is the major excitatory neurotransmitter in the central nervous system, the level of activity of iGluRs is tightly controlled. Mis-regulation has been implicated in schizophrenia, and Alzheimer's, Huntington's, and Parkinson's diseases. Computational tools can be utilized in cooperation with experimental techniques to understand the atomistic nature and structural behavior of glutamate receptors. We will utilize homology and RMSD comparison methods to develop, test, and refine a three dimensional model for our experimental structure. Energy minimization will prepare the generated model structures for testing using molecular dynamics to evaluate the structure and dynamics of NMDA receptors which have binding sites in their S1S2 ligand-binding core and amino-terminal domains. The information gained will be used to further our examination of the structure and function of glutamate receptors.