

SL14 Atomic Structure and Molecular Mechanism of Receptors and Transporters at Chemical Synapses

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Most of the signaling between nerve cells in the central and peripheral nervous system occurs at neuron-neuron junctions called chemical synapses. Communication across the canonical chemical synapse occurs by the calcium-stimulated release of chemical neurotransmitter from the presynaptic nerve cell, the ensuing rise in transmitter concentration within the synaptic cleft, and the subsequent activation of receptors localized primarily to the postsynaptic cell. Fast signaling, on the millisecond time scale, occurs upon activation of postsynaptic ligand-gated ion channels of which ionotropic glutamate receptors represent a paradigm. To enable repeated and rapid trains of signaling, the neurotransmitter must be cleared from the synapse to allow for receptor deactivation and recovery from desensitization. In the central nervous system, sodium coupled transporters typically accomplish this task, driving the chemical neurotransmitter up a thermodynamic hill, into surrounding glial cells and neurons, thereby reducing the transmitter concentration below that required for receptor activation, and thus allowing for another cycle of transmitter release, receptor activation, and signaling. In my presentation I will focus on our current understanding of the relationships between atomic structure and molecular mechanism of key ligand-gated ion channels and sodium coupled transporters, endeavoring to describe the function of these biologically crucial molecules in detailed, three-dimensional terms.