Excitatory synaptic transmission in mammalian CNS is mostly mediated by ionotropic glutamate receptors. NMDA receptors, one of three subclasses of this ligand-activated ion channels family, are involved in memory formation and learning and also play a role in the pathogenesis of various neurodegenerative diseases. Current knowledge about NMDA receptors function is predominantly based upon results of in vitro experiments conducted at room temperature, far from physiological. The aim of this PhD thesis was to describe the temperature dependence of NMDA receptors. We determined the rate constants that characterise each step in the mechanism of recombinant NR1/NR2B receptors activation in the temperature range 25-45°C. The receptor desensitization, resensitization and glutamate unbinding turned out to be the most temperature sensitive of these processes. In addition to that, we described the temperature dependence of deactivation kinetics in various experimental models of NMDA receptors (both recombinant and native).

The second part of the thesis focused on the modulation of NMDA receptors function by steroid compounds derived from pregnanolone sulfate, an endogenously occuring neurosteroid. We tested 21 steroids that showed various degree of ability to inhibit (or, in one case, potentiate) the current responses of NMDA receptors.