

**P017** Simulations of positive and negative cooperativity based on model of tandemly arranged ligand binding sites in receptor dimer. Case of melanocortin 4 receptor subtype.

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Two alternative approaches has been commonly accepted to describe the cooperative behaviours in allosterical models of ligand binding. One of them describes process as sequential multistep reactions, where bimolecular binding steps follow each other without other limitations. The alternative approach accounts also conformational transitions of the receptor and/or its dimer/oligomer, before the subsequent ligand binding. The comparative analysis of the binding of the peptide analogue [<sup>125</sup>I]NDP-MSH, and the low molecular weight radionucleid [<sup>125</sup>I]THIQ to melanocortin 4 receptor (MC<sub>4</sub>R) revealed that the binding is a sequential multistep reaction in which the bimolecular binding step is followed by first-order steps and the next bimolecular binding step. Herewith we present a minimal mathematical model for the describing obtained data, where MC<sub>4</sub>Rs exist as preformed dimmers and the first bound ligand has to be locked before the binding of the second ligand. Mathematical analysis of the dependences “global dissociation quotient” according to the proposed model opened possibilities to determine the nature and degree of cooperativity of ligand binding.