Intrinsic Flexibility of the Opioid Receptor through Multiscale Modelling Approaches - COMP403

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403 - Intrinsic flexibility of the μ opioid receptor through multiscale modeling approaches

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Abstract

Recent releases of numerous G protein-coupled receptors crystalline structures created the opportunity for computational methods to widely explore their dynamics. Here, we study the biological implication of the intrinsic flexibility properties of μ opioid receptor (μOR). First, one performed classical all-atom (AA) Molecular Dynamics (MD) simulations of μOR in its apo-form. We highlighted that the various degrees of bendability of the α-helices present important consequences on the plasticity of the μOR binding site. Hence, this latter adopts a wide diversity of shape and volume, explaining why μOR interacts with very diverse ligands. Then, one introduces a new strategy for parameterizing purely mechanical but precise coarse-grained (CG) elastic network models (ENMs). Those CG ENMs reproduced in a high accurate way the flexibility properties of μOR as observed with the AA simulations. At last, ones uses network modularization to design multi-grained (MG) models. They represent a novel type of low resolution models, different in nature *versus* CG models as being true multi-resolution models, *i.e.*, each MG grouping a different number of residues. The three parts of our work constitute an integrated hierarchical and multiscale approach for tackling the flexibility of μOR.

Time	**Wednesday, March 21, 2018 4:15 PM**
Session	COMP: Structure-Based Drug Design for GPCRs: PM session (1:30 PM - 4:50 PM)
Location	**New Orleans Marriott Convention Center**
Room	**Blaine Kern F**