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Published in:

Abstracts of the 255th Annual Meeting and Exposition of the American Chemical Society

Publication date:

2018

Document Version

Publisher's PDF, also known as Version of record

[Link to publication](#)

Citation for published version (HARVARD):

Vercauteren, D, Fossepre, M, Leherte, L & Laaksonen, A 2018, Intrinsic Flexibility of the μ Opioid Receptor through Multiscale Modelling Approaches - COMP403. in *Abstracts of the 255th Annual Meeting and Exposition of the American Chemical Society*. ACS, 255th ACS National Meeting & Exposition, New Orleans, LA, United States, 18/03/18.

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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 (μ OR). First, one performed classical all-atom (AA) Molecular Dynamics (MD) simulations of μ OR in its apo-form. We highlighted that the various degrees of bendability of the σ -helices present important consequences on the plasticity of the μ OR binding site. Hence, this latter adopts a wide diversity of shape and volume, explaining why μ OR 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 μ OR 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 μ OR.

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