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On the intrinsic flexibility of the opioid receptor through multiscale modeling approaches DANIEL VERCAUTEREN, MATHIEU FOSSPR, LAURENCE LEHERTE, Univ Namur, AATTO LAAKSONEN, Stockholm Univ — Numerous releases of 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 opioid receptor OR. First, one performed classical all-atom (AA) Molecular Dynamics (MD) simulations of OR in its apo-form. We highlighted that the various degrees of bendability of the α-helices present important consequences on the plasticity of the binding site. Hence, this latter adopts a wide diversity of shape and volume, explaining why 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). The CG ENMs reproduced in a high accurate way the flexibility properties of OR versus the AA simulations. At last, one 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 constitute hierarchical and multiscale approach for tackling the flexibility of OR.

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