Modeling TRP receptors exposure to RF EM fields

Laura Caramazza [1,2], Carmen Pisano [1], Paolo Marracino [3], Federico Del Signore [1], Micaela Liberti [1,2], and Francesca Apollonio [1,2]
(1) DIET@Sapienza University of Rome, Italy, 00184; e-mail:
(2) CLNS@Sapienza, Istituto Italiano di Tecnologia, Rome, Italy, 00161
(3) Rise Technology S.r.l., L.re Paolo Toscanelli 170, Rome, Italy, 00121

In recent decades much research has taken place concerning the exposure to radiofrequency electromagnetic fields (RF-EMF) and the assessment of its potential effects on health [1]. The number of RF-EMF sources and their use in our general environment continues to grow even thanks to the introduction of new generation communication technologies, fueling the ongoing research (with several international projects, also funded by the EU) into potential biological effects across different scales that remain still uncleared [2]. Prior *in vitro* and *in vivo* experiments exposing to low levels of 900 and 1800 MHz RF signals, suggest potential alterations in the functioning of thermo-sensitive receptors [3], [4]. These are transient receptor potential (TRP) channels, which are non-selective calcium channels, playing a crucial role in numerous cellular mechanisms such as anti-inflammatory pathways [5] and being responsive to various stimuli such as temperature changes. However, a direct observation of the physical conformational changes of TRP channels would require sophisticated and expensive equipment. In this context, Molecular dynamics (MD) simulations offer a potent and supplementary technique to support biological outcomes. In fact, these simulations allow for the exploration of conformational changes in biomolecules, such as proteins interacting with their environment or external physical stimuli like EM fields [6]. The challenges of studying the effect of an EM field on TRPs channels in MD simulations are given by the need to build accurate receptors' models, which should include both primary and secondary protein structures but also specific sites of interactions [7]. In the present work, for the first time, authors investigate the effects of an RF stimulus on two different receptors TRPV4 and TRPM8 identified as potential targets for exploring molecular-level interaction mechanisms. Specifically, a procedure made of five steps has been adopted to obtain the molecular model for both receptors; a scheme of the procedure is reported in Fig. 1-A. Such complete models, (see Fig. 1-B, C as an example) are used for MD simulations without (control) and with the application of an external RF source (a golden standard RF signal of 900 MHz) for 100 ns. Simulation outcomes reveal that the external RF field affect protein's secondary structures that are in direct contact with the aqueous solution. These data provide predictive insights into potential cellular-scale outcomes and represent a starting point for further analyses with 5G signals.

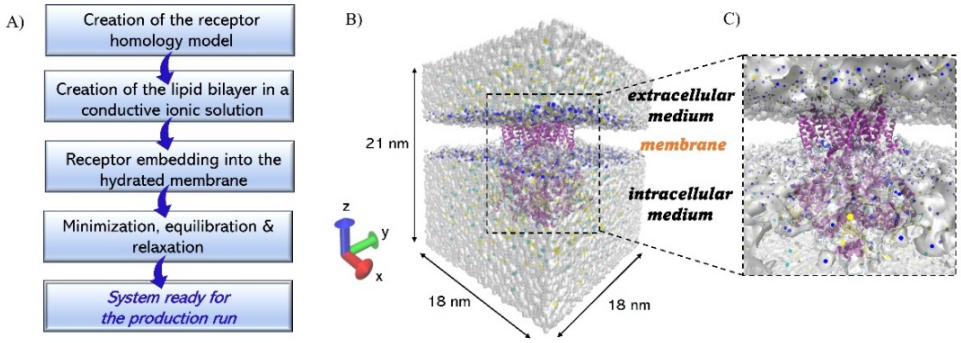

Figure 1. A) Scheme of the procedure used to prepare the TRP-based system. B) TRMP8 model embedded in the hydrated membrane environment (atoms ~700000). C) 3D details of the TRPM8 secondary structures.

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