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MD simulations of the A2A adenosine receptor in presence of magnetic field

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Several studies have shown how the use of low frequency magnetic fields may have biological effects on different cells functions. It has been reported that the use of pulsed magnetic fields increases the anti-inflammatory effect of different types of cells such as neutrophils, synoviocytes, chondrocytes and osteoblasts, with significant reduction in some of the most important inflammatory cytokines [1]-[2]. The mechanisms of interaction underlying such effects, pointed out an involvement of adenosine receptors (ARs), nevertheless it still remains to be elucidated which is the final endpoint of the exposure. To this regard, simulations based on Molecular Dynamics (MD) may become a strategic tool to study molecules behavior. Recently authors have implemented a procedure to introduce a static homogeneous magnetic field in the Gromacs software, one of the most used environments for MD [3].

In this work, using MD simulations, we want to show possible effects of magnetic fields on the behavior of A2A adenosine receptor comparing it with the physiological no-field condition.

MD simulations have been performed in NPT (number of particles, pressure and temperature constants) ensemble at a temperature of 300 K, in a box of 10x10x15 nm^3 of dimension (Fig. 1a). 272 lipids forming the membrane bilayer have been considered, moreover 60 and 70 ions of Na+ and Cl- respectively to neutralize the positive charge of the protein and 37.558 water molecules for a total number of atoms equal to 154.154. For the adenosine receptor A_{2A} molecular model, the P11617 structure has been chosen, in order to firstly analyze the protein behavior with no ligand (see Fig. 1a). To implement the magnetic field, we employed the Velocity Verlet (VV) algorithm, in which the Lorentz force acts on the charged particles, which perform Larmor oscillations at the Larmor frequency when an external magnetic field is applied [3].

After a 100 ns of equilibration, molecular simulations have been performed both with no field applied and with an intensity of the B field equal to 1T, for a total duration of 60 ns. No statistically significant variations have been observed for the secondary structure of the receptor meaning that the protein structures itself is not affected by the field. However, a finer analysis has been conducted selecting some specific residues especially those placed in the extracellular loop of the protein (see Fig. 1b); in particular the dipole vector of each residue has been projected on the direction of the field, as well as on the plane normal to it (Fig. 1c). These residues seems to play a fundamental role in ligand binding and receptor activation hence their conformation during exposure becomes a critical parameter.

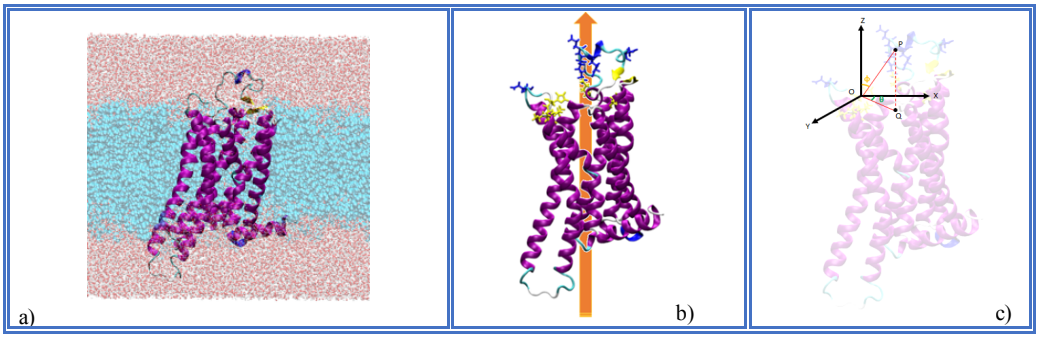

Fig. 1 Molecular model of the A_{2A} a) model embedded in the lipid bilayer; b) B field direction; c) spherical coordinates evidencing ϕ and θ angles.

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