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Molecular Dynamics simulations of magnetic field acting on Superoxide dismutase (SOD)

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The superoxide dismutase (SOD) is one of the enzymes that controls the levels of ROS and reactive nitrogen species, thus both limiting the potential toxicity of these molecules and controlling broad aspects of cellular life that are regulated by their signaling functions. Chemically, the activity of SOD accelerates the reaction of the superoxide anion (O_2^-) with itself to form hydrogen peroxide and oxygen, therefore by controlling the superoxide anion the enzyme also controls the concentrations of these species [1].
Altered SOD expression or activity changes are observed in various pathological conditions such as, for example, cancer and amyotropic lateral sclerosis [2, 3]. These changes may not only perturb protection from potential ROS toxicity but also misregulate many redox-sensitive pathways that contribute to disease outcome.
Here, we investigate the action of magnetic fields on SOD enzyme starting from in silico molecular modeling with the aim of evaluating if the external magnetic field could influence the conformation of the active site of the enzyme. Therefore, a rigorous and fully atomistic approach based on molecular dynamics simulations is proposed for the Cu/Zn-SOD enzyme whose active site is responsible for the binding of the superoxide anion.
We then used the structure as reported in [4], where an available structure of bovine Cu/Zn-SOD complexed with an azido group (PDB code: 1SXZ) has been equilibrated and minimized replacing the azido group with O_2^- in one of the two monomers (see Figure 1a). Simulation parameters can be found in [5]. 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 static magnetic field is applied [6]. After a 200 ns of equilibration, molecular simulations have been performed both with no field applied and with an intensity of the B field equal to 5 T, for a total duration of 200 ns.
The core of our analysis was to find possible modulations of SOD active sites as a consequence of the magnetic field application. As an example, Getzoff [7] focused on the SOD active site region, finding that changing in the residues forming the sides of the active site channel (THR 56, GLU 131, THR 135 and ARG 141), could modulate the interaction of Cu ion with the electron exchange partner. To this end, we calculated the mean active site area between the four cited residues and compared results in both unexposed and exposed conditions.
Looking at the normalized distributions of mean active site areas for both unexposed (200 ns) and exposed (5 T, 200 ns) simulations, data suggest that magnetic field seems to exert a force sufficient to modify the active site geometry of the enzyme. Interestingly, when comparing the behavior of the complexed (with the radical ion included) active site and the not complexed one, the geometrical modulation seems opposite in the two cases, pointing out that a radical-free active site could enhance (the area increases) its reactivity in presence of a strong enough magnetic perturbation.

References

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