Modeling electromagnetic field effects in a biochemical reaction: understanding reactivity inhibition due to the magnetic field

Andrea Amadei[1], Laura Zanetti[2], Francesca Apollonio[3] and Guglielmo d'Inzeo[3]

[1]Dept. of Chemistry,University of Rome Tor Vergata, ITALY, andrea.amadei@uniroma2.it
[2]Dept. of Chemistry,University of Rome La Sapienza, ITALY, l.zanettipolzi@caspur.it
[3]ICEmB@DIET, University of Rome La Sapienza, ITALY, dinzeo@die.uniroma1.it

1. Introduction

The understanding of electromagnetic effects on biochemical systems is a long standing problem which, in the last decades, raised an increasing interest in the biochemical-biophysical and engineering communities. Possible relevant outcomes of a detailed theoretical comprehension of electromagnetic field-biomolecular systems interaction might be important for biomedical studies, as well as for new technological approaches. The electric field perturbation of a biochemical system is well understood from an atomistic point of view, allowing the development of sophisticated models to describe and predict the biochemical-biophysical transitions induced by the electric field on molecules. On the contrary the magnetic field effects on biomolecular systems are still elusive as a consequence of the extremely limited perturbation energy associated. Although experimental evidences of the magnetic field effects on biochemical reactions have been reported [1] the understanding of the physical-chemical mechanism involved is still a challenge. In this context, we have extended and optimized a theoretical approach based on molecular dynamics (MD) simulations and mixed quantum-classical calculation, the Perturbed Matrix Method (PMM) [2, 3] introduced in the last decade, to explicitly model at atomistic level the effects of the magnetic field on a chemical reaction. In this work we present the results obtained for a prototypical biochemical reaction, i.e. the triplet to singlet relaxation following the electron transfer reaction in the flavin-indole complex, compared to those investigated experimentally [1].

Methods

The simulated system consisted of a dodecahedric box in which we placed flavin and indole molecules surrounded by Single Point Charge (SPC) [4] water molecules resulting in a typical density of 55.32 mol/l. Following an energy minimization and subsequent solvent relaxation, the system was gradually heated from 50 K to 300 K using short MD simulations. An extended trajectory was propagated up to several ns in the NVT ensemble using an integration step of 2 fs with no constraints on flavin and indole movements (rotational and translational). The temperature was kept constant at 300 K by with the isokinetic temperature coupling [5]. All bond lengths were constrained using LINCS algorithm [6] while long range electrostatics were computed by the Particle Mesh Ewald method [7]. The chemical process we consider in this work is the flavin-indole electron transfer process (see Eq. 1), which involves as a second reaction step (step II) a triplet to singlet spin state relaxation of the ionic complex, just after the electron transfer reaction (step I).

$$ {}^3Fl+In \underset{\text{I}}{\rightleftharpoons} {}^3[Fl^-\ In^+] \underset{\text{II}}{\rightleftharpoons} {}^1[Fl^-\ In^+] \qquad (1) $$

By calculating at each MD frame of the simulation of the ionic complex the energy change (transition energy) for the singlet to triplet transition, we can obtain a direct measure for the spin state transition as occurring each time the energy difference becomes zero (i.e. each time the triplet and singlet energies are equal). In fact the true spin state (adiabatic state) is virtually identical to either the triplet or singlet spin state except at each crossing, where it becomes a triplet-singlet combination. Therefore, the true spin relaxation process is given by the spin transition provided along the adiabatic energy surface that we approximate via the triplet-singlet energy surfaces. In this conceptual scheme each crossing then becomes a signature for the spin transition within the adiabatic state.

978-1-4244-6051-9/11/$26.00 ©2011 IEEE

Discussion

In Figure 1 we show the singlet to triplet transition energy as a function of time as obtained by the atomistic MD simulation of the ionic complex [Fl^- In^+] in water at 300K. In the upper panel we provide the transition energy for the ±1 triplet states and in the lower panel the transition energy corresponding to the 0 triplet state. Such transition energy profiles, obtained in absence of an exogenous magnetic field, clearly show the presence of several abscissa crossings corresponding to singlet to triplet and triplet to singlet transitions. The application of a static magnetic field (a +0.2 T field oriented along the z-axis) provides constant energy shifts for the ±1 triplet states, as shown in Figure 2 (note that, given its null z-component of the magnetic moment, for the 0 triplet state, no perturbation energy due to the applied magnetic field is present). From this last figure it is evident that the applied magnetic field shifts the transition energy curves in such a way no crossings are present, hence completely inhibiting the spin transition reaction for the ±1 triplet states. Therefore in such a condition only the 0 triplet to singlet reaction channel remains active thus considerably reducing the relaxation kinetics of the overall reaction.

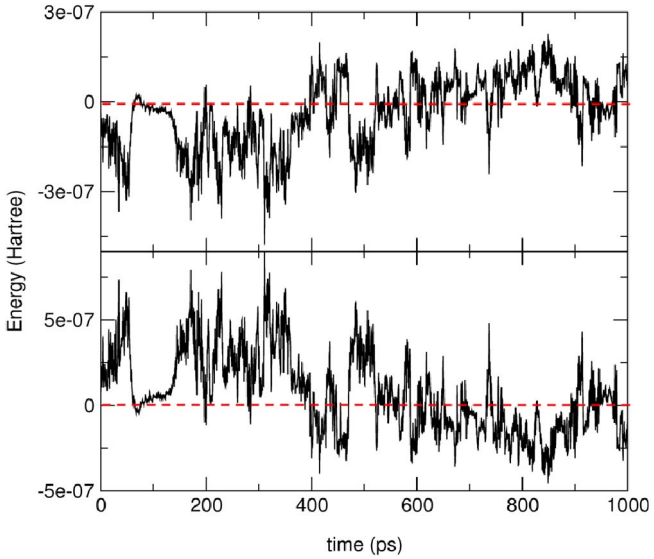

Figure 1. Upper panel: singlet to triplet transition energy vs simulation time at null magnetic field for the ±1 triplet states. Lower panel: singlet to triplet transition energy vs simulation time at null magnetic field for the 0 triplet state.

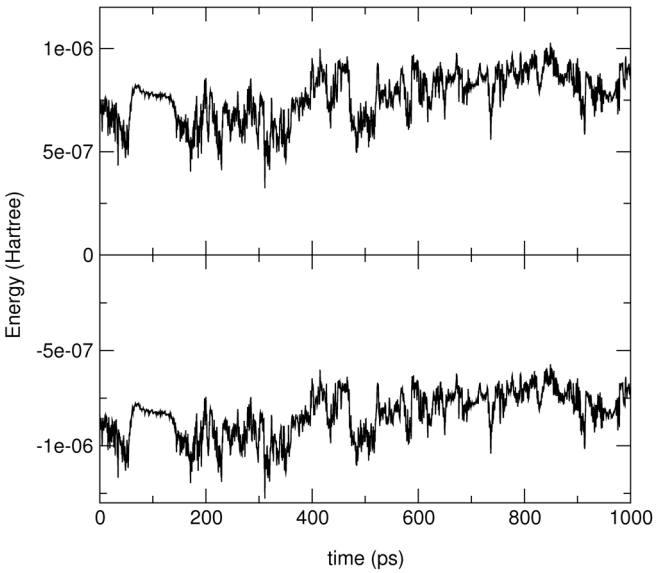

Figure 2. Upper panel: singlet to triplet transition energy vs simulation time at +0.2 T magnetic field for the -1 triplet state. Lower panel: singlet to triplet transition energy vs simulation time at +0.2 T magnetic field for the +1 triplet state.

Conclusions

In this work we have used atomistic MD simulations combined with basic quantum mechanical calculations to explicitly model the spin state relaxation of a common biochemical reaction utilized for an experimental study on the magnetic field effects [1]. Our theoretical-computational results clearly show that a 0.2 T static magnetic field strongly inhibits the spin relaxation process avoiding the ±1 triplet to singlet state transitions. Such a result, in agreement with the experimentally observed inhibition of the reaction at 0.2 T, sheds light on the atomistic mechanism of the magnetic field effects and opens the way to further investigations possibly leading to a detailed description of the complex biochemical-biophysical processes involved in the interaction between the electromagnetic fields and a biomolecular system.

References

[1] M. Horiuchi, K. Maeda, T. Arai, "Magnetic fields effect on electron transfer reactions of flavin derivatives associated with micelle", *Appl. Magn. Reson*., 2003, vol. 23, pp. 309-318

[2] M. Aschi, R. Spezia, A. Di Nola and A. Amadei, "A first principle method to model perturbed electronic wavefunctions: the effect of an external homogeneous field", *Chem. Phys. Lett*., 2001, vol. 244, pp. 374-380

[3] A. Amadei, M. d'Alessandro, M. d'Abramo and M. Aschi, "Theoretical characterization of electronic states in interacting chemical systems", *J. Chem. Phys*, 2009, vol. 130, pp. 08410

[4] Berendsen, H. J. C.; Postma, J. P. M.; Gunsteren, W. F. V.;Hermans, J. In *Intermolecular Forces*, Pullman, B. Ed.: Reidel Publishing Company: Dordrecht, 1981

[5] A Evans, D. J. and Morriss, G. P., "Statistical Mechanics of Nonequilibrium Liquids", *Academic Press, London*, 1990

[6] Hess, B.; Bekker, H.; Berendsen, H. J. C.; Frajie, J. G. E. M. *J. Comput. Chem*., 1997, vol. *18*, pp. 1463-1472

[7] Darden, T. A.; York, D. M.; Pedersen, L. G., *J. Chem. Phys*., 1993, vol. *98*, pp. 10089