National Technical University of Athens, School of Chemical Engineering

Department of Materials Science and Engineering

Computational Materials Science and Engineering Group (Co.M.S.E.)

"*Theoretical Investigation of the Interaction of Ligands with Heme Proteins*"

Post-doctoral Associate Polydefkis Diamantis, University of Basel

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Αίθουσα «Νίκος Κουμούτσος» Σχολής Χημικών Μηχανικών

Abstract

The binding and reaction of small ligands (O2, NO, CO) with heme proteins such as hemoglobin and myoglobin is involved in processes that are essential for the physiological function of living organisms. The active sites of many heme proteins are located in their interior, and a migration network ensures efficient ligand transport towards them. Given their biological relevance, various aspects of ligand migration and reaction with heme proteins have been extensively investigated. In the present work, (i) xenon (Xe) migration in truncated hemoglobin N (trHbN) of Mycobacterium Tuberculosis and (ii) NO rebinding to human wild-type/mutant myoglobins are investigated using molecular dynamics simulations.

Analysis of the trHbN-Xe simulations revealed that – in agreement to suggestions in the literature – Xe motion and the conformational dynamics of trHbN are strongly coupled. Xe migration in trHbN occurs in a 10-20 ps scale, and is a non-Markovian process, with memory effects arising due to the protein's conformational rearrangement as Xe moves through it.

Simulations of NO rebinding to myoglobin revealed that – in agreement to previous reports – NO rebinding to wild-type myoglobin can be divided into two sub-processes, occurring at time scales 20 ps and 200 ps respectively. Mutations were found to significantly affect the efficiency of the process, and the time scales to which it occurs. Finally, additional free energy simulations showed that the effect of a mutation on NO rebinding can be linked to thermodynamics i.e. the relative free energy difference of unfolding ($\Delta\Delta G$).