

Calculating redox potential of flavoproteins with the AMOEBA force field

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Electron transfers are at the heart of many key biological processes such as photosynthesis and respiration. Such transfers rely on protein cofactors, either inorganic hemes or organic prosthetic groups like flavins, the redox properties of which are tailored to their proteic environment. Understanding redox properties of those cofactors is thus necessary to fully comprehend the chemical and biological processes involving electron transfers.

Redox potential of flavoproteins can be predicted with molecular simulations combining quantum chemistry calculations and molecular dynamics simulations using force fields to extensively sample the potential energy surface¹. In the case of systems involving proteins, an accurate representation of electrostatic interactions is crucial hence the use of polarizable force fields, going beyond the monopolar approximation.

In this context, we aim at validating the use of the polarizable force field AMOEBA² for the prediction of the redox potential of flavoproteins. As there are no-preexisting set of parameters to describe flavins in the AMOEBA force field, a calibration step is carried out to generate such parameters for the different types of flavins (lumiflavin, flavin mononucleotide FMN, flavin adenine dinucleotide FAD) based on a process already used to calibrate a heme cofactor³. This method consists in performing QM calculations and calculations using the AMOEBA force field with Tinker⁴ on different redox states of flavins to generate the parameters which then undergo a validation step. We will present here the first results obtained for the calibration procedure of the AMOEBA parameters for flavins and their validation.

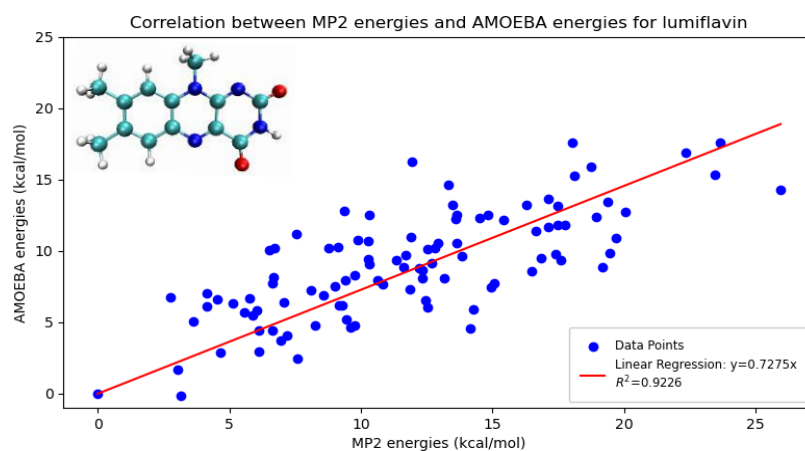


Figure 1. Comparison of MP2 energies and AMOEBA energies for the lumiflavin.

Keywords: polarizable forcefield, redox potential, molecular simulation, flavins, proteins

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