

# Hybrid QM/MM studies of the UV-Vis absorption spectra of ThDP-dependent enzymes

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The identification of reaction intermediates in enzymatic systems is a continuing challenge, both for theoretical and experimental approaches. UV-Vis and circular dichroism (CD) spectra are commonly used to follow the progression and the appearance of such intermediates. However, the unequivocal assignment of a band to a particular compound can be a difficult task. Electronic structure methods can provide invaluable informations in this context, but only when an adequate description of the environment effects and the chromophore itself are available.

The thiamin diphosphate (ThDP) coenzyme participates in a multitude of enzymatic reactions and their progression is commonly followed by absorption spectra. [1] Even in the resting state of such enzymes, ThDP can be present in three different protonation states each having its own signature in the absorption spectra. [2] Therefore, a detailed knowledge about these native forms of ThDP is warranted to identify reaction intermediates by absorption spectroscopy. In order to better understand the signature of the different states, we have carried out time-dependent density functional theory (TDDFT) calculations for model systems, as well as for the pyruvate decarboxylase system in a QM/MM approach.

[1] H. Patel, N. S. Nemeria, F. H. Andrews, M. J. McLeish, F. Jordan, *Biochem.*, **2014**, 53, 2145-2152.

[2] D. Meyer, P. Neumann, C. Parthier, R. Friedemann, N. Nemeria, F. Jordan, K. Tittmann, *Biochem.*, **2010**, 49, 8197-8212.