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The effect of protein structure on optical absorption spectra of oxyhemoglobin: QM/MM study

Afanasieva T.V.[1], Prokhorets V.A.[1,2], Mamilov S.O.[3]

[1] Institute of Physics of the NAS of Ukraine, e-mail: tetiana.v.afanasieva@gmail.com
[2] Taras Shevchenko University of Kyiv, Ukraine
[3] Institute of Magnetism NAS of Ukraine and MES of Ukraine. Kyiv, Ukraine

Motivation

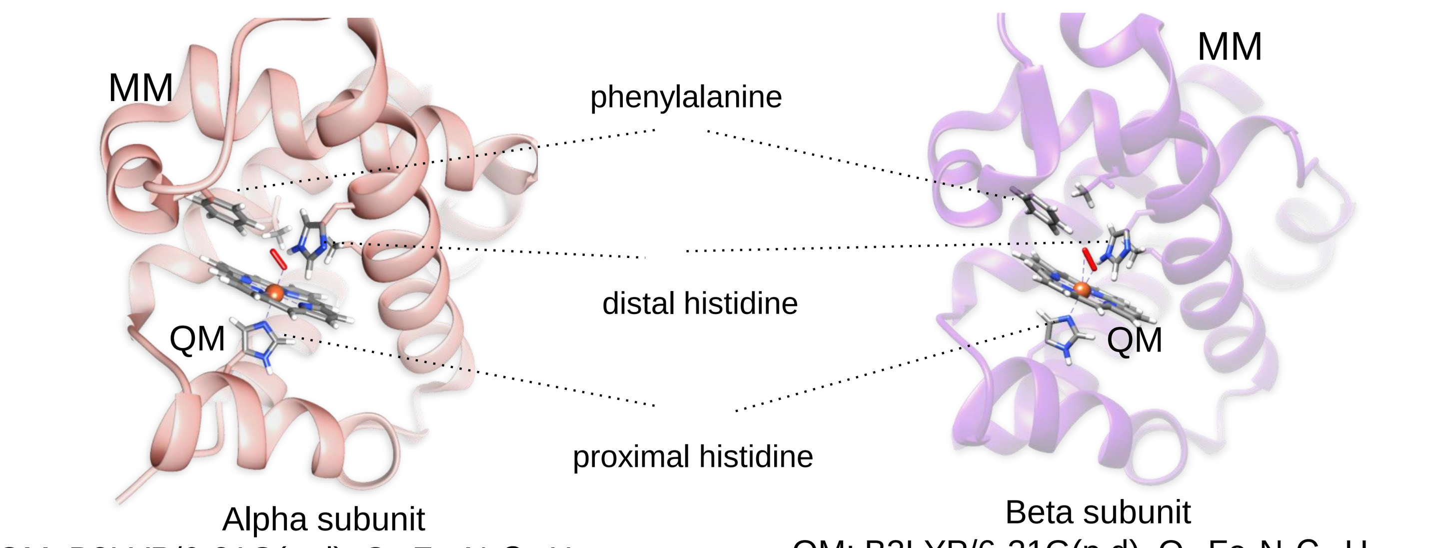
We present the results of the detailed study of the optical absorption spectra of oxyhemoglobin in R (relaxed) and T (tense) states.

The optical properties of oxyhemoglobin are explored because of its use in biomedical applications such as photodynamic phototherapy. UV-VIS spectroscopy and ab initio calculations are widely used to clarify the mechanisms of laser-induced photodissociation. It is known that the photodissociation of oxyhemoglobin involves structural changes in the protein. However, the difference between the α and β subunits of R and T states has been neglected in the theoretical models.

This work mainly aimed to compare the optical absorption spectra of α and β subunits of the oxyhemoglobin in R and T states.

Methodology

We explore the effect of protein structure as well as solvation effect on optical absorption spectra of oxyhemoglobin using a hybrid quantum mechanical-molecular mechanical (QM/MM) method and embedded clusters - SIMOMM (Surface Integrated Molecular Orbital Molecular Mechanics) with GAMESS/TINKER software [1,2]. Density functional theory method and all-electron 6-31G(p,d) basis set with p, d polarization functions were used for the QM region. The MM region was described using the MM3 force field for the protein atoms. Solvent effects are included using the polarizable continuum model (PCM) in a water solvent. The initial coordinates for the hemoglobin in R and T forms were taken from the Protein Data Bank codes: 2dn1 [3] and 2dn2 [4], respectively.



Alpha subunit
QM: B3LYP/6-31G(p,d), O_2-$Fe_1N_8C_{34}H_{34}$
MM: MM3 Force Field, 2201 atoms of the alpha chain, from 2dn1.pdb (RCSB PDB)

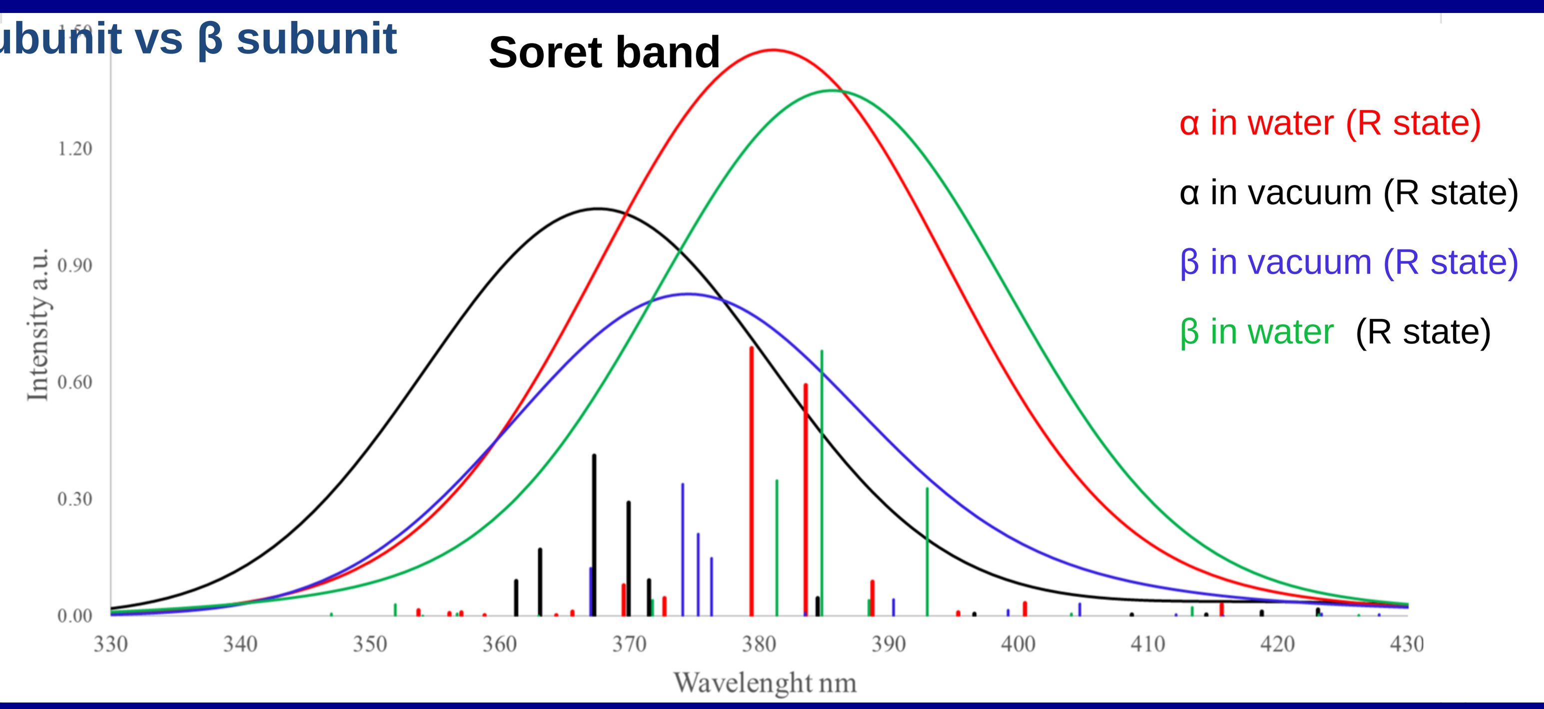
Beta subunit
QM: B3LYP/6-31G(p,d), O_2-$Fe_1N_8C_{32}H_{26}$
MM: MM3 Force Field, 2290 atoms of the beta chain, from 2dn1.pdb (RCSB PDB)

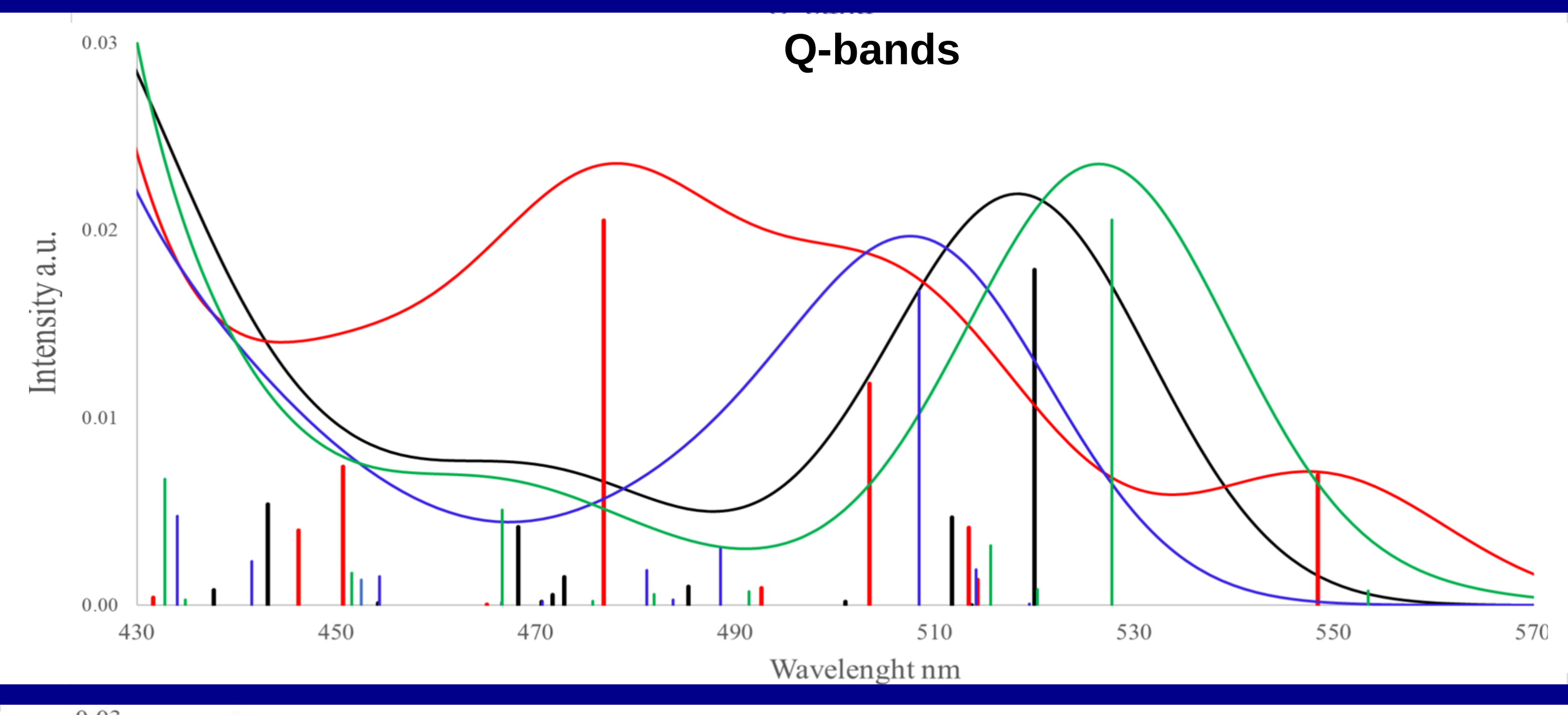
First, we obtained optimized structures for α and β subunits of the hemoglobin in T and R states in vacuum and solvent. Then, we calculated electronic excitation spectra for α and β subunits of oxyhemoglobin in R and T states using TD-DFT approach. Optical absorption spectra were obtained from the first 30 vertical singlet-singlet $S_0 \rightarrow S_n$ transitions with Gaussian broadening with a width at half peak of 20 nm. The first 30 singlet-triplet excitations $S_0 \rightarrow T_n$ are also considered. Singlet-triplet transitions are not shown on the graphs.

References
[1] M. W. Schmidt et al. // *J. Comput. Chem.*, **1993**, 14, pp.1347-1358.
[2] J. R. Shoemaker et al. // *J. Phys. Chem. A*, **1999**, 103, pp.3245-3251.
[3] S. Y. Park et al. //J. Mol. Biol., **2006**, 360, pp. 690-701. https://www.rcsb.org/structure/2DN1.
[4] S. Y. Park et al. //J. Mol. Biol., **2006**, 360, pp. 690-701. https://www.rcsb.org/structure/2DN2.

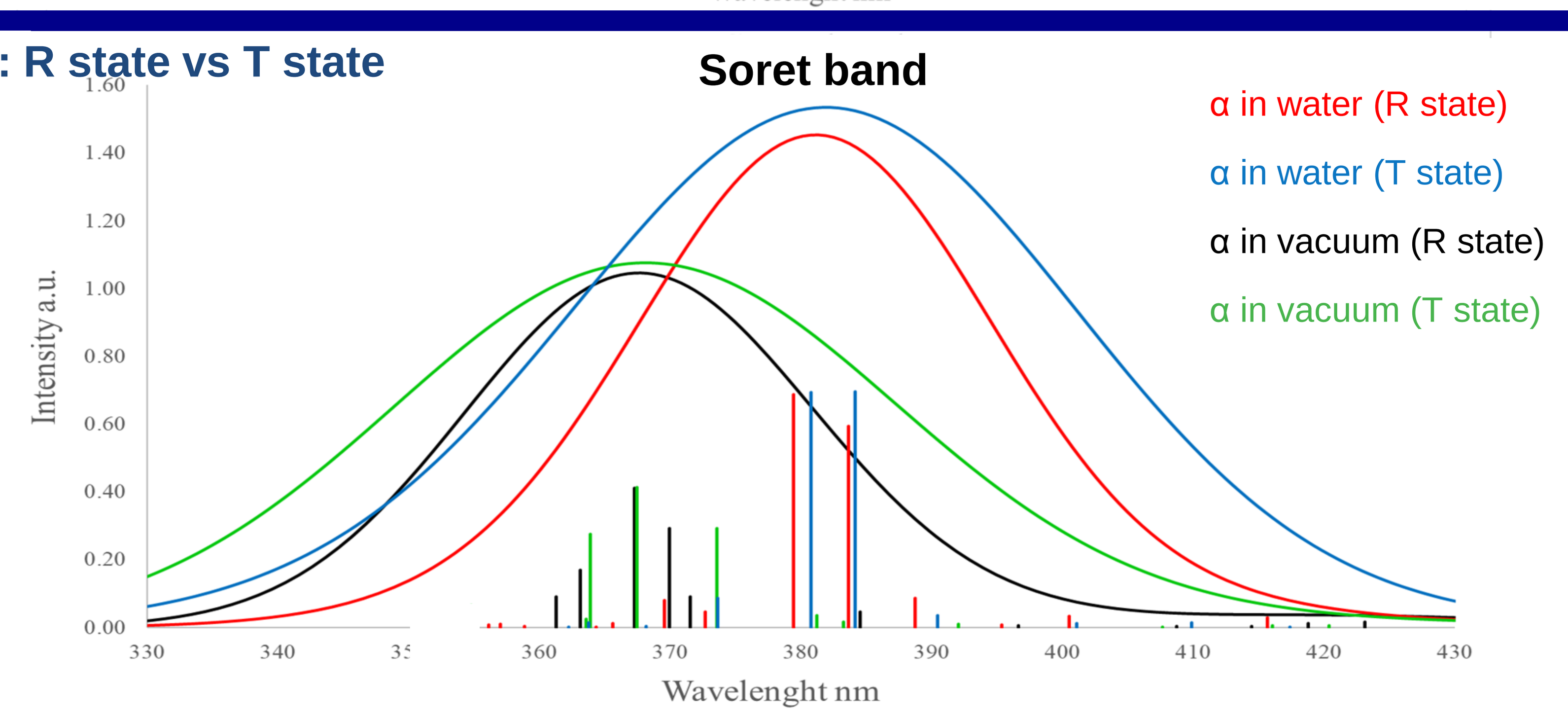
Optical absorption spectra of the oxyhemoglobin

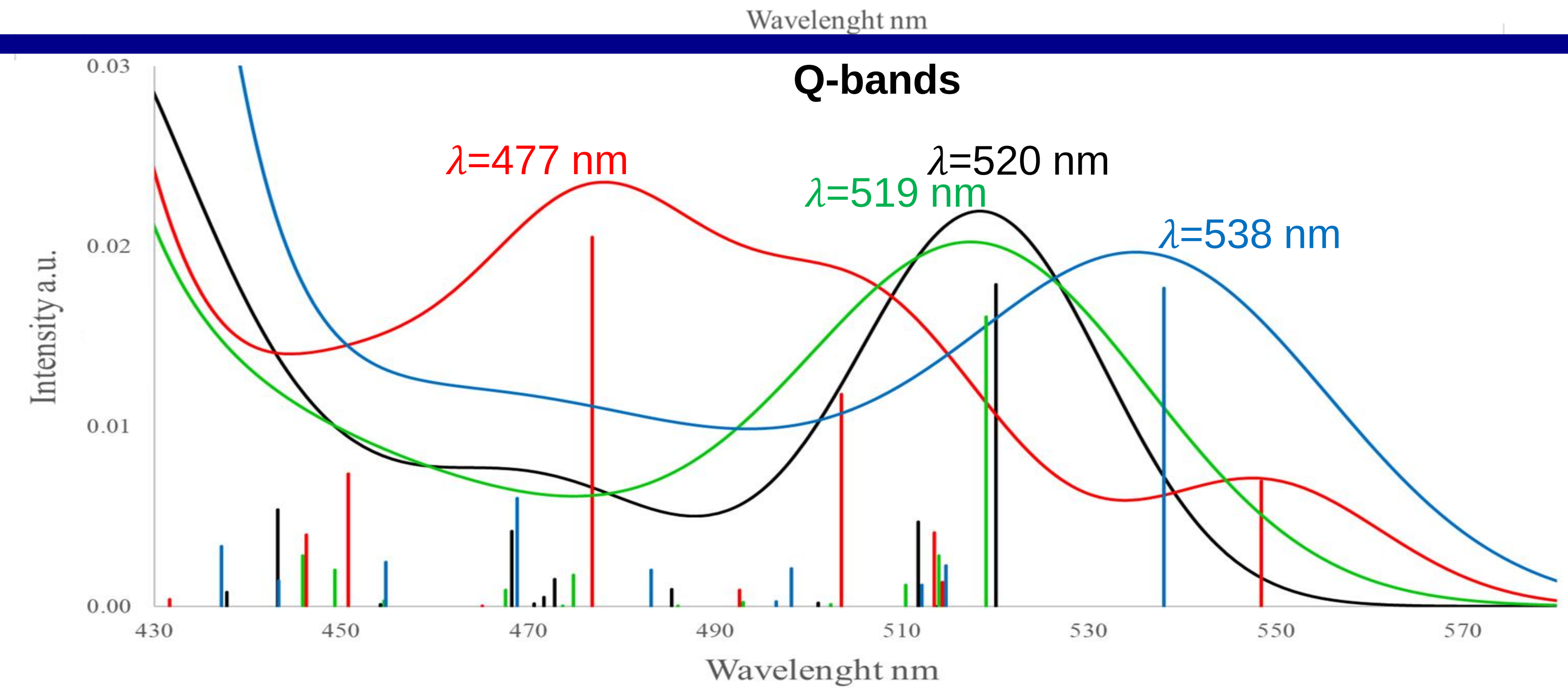
R state: α subunit vs β subunit





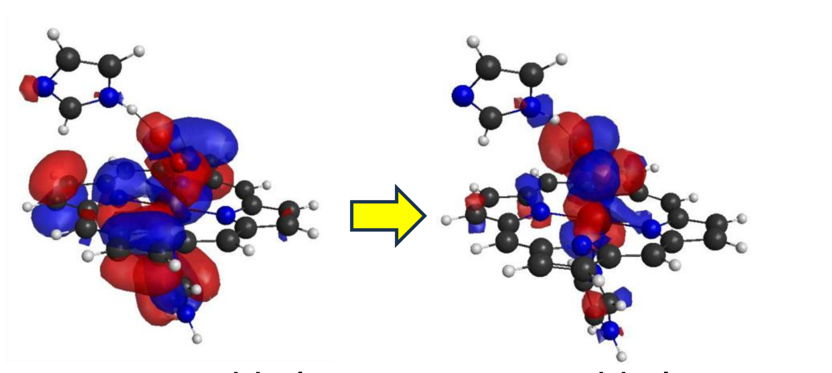
α subunit: R state vs T state





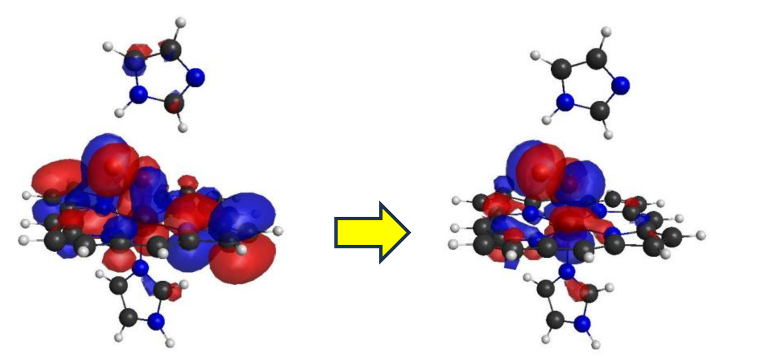
Distribution of the electron density corresponding to the electronic transition with the largest oscillator strength in spectrum Q-bands of the α subunit of oxyhemoglobin in R and T states:

R state wavelength (λ=477 nm)
water



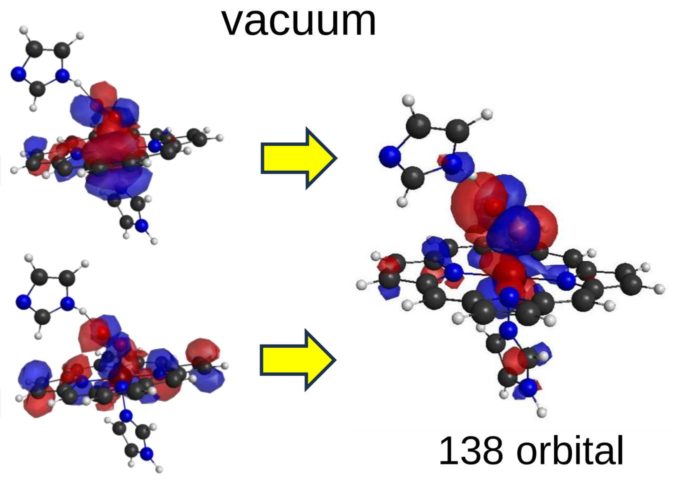
130 orbital   138 orbital

T state wavelength (λ=538 nm)
water



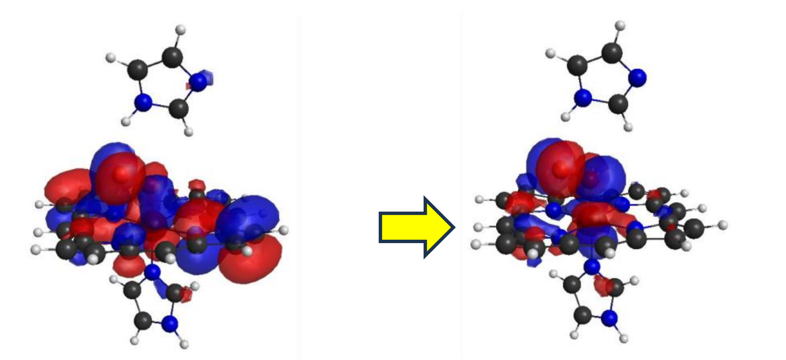
133 orbital   138 orbital

R state wavelength (λ=520 nm)
vacuum



138 orbital

T state wavelength (λ=519 nm)
vacuum



133 orbital   138 orbital

Conclusions

The protein environment induces a larger redshift of the Soret band in the β subunit than in the α subunit. Additionally, the Soret band of the isolated oxyheme is blue-shifted relative to those of both the α and β subunits. Solvation significantly redshifts the Soret band for the α and β subunits and the Q-bands for the β subunit.
In contrast, solvation significantly blueshifts the Q-bands for the α subunits in the R state. The main maximum in the spectrum Q-bands of the oxyhemoglobin in the R state is the blueshifted relatively main maximum of the oxyhemoglobin in the T state. In a vacuum, the positions of the main maxima of the oxyhemoglobin in R and T states are the same.
Furthermore, we have examined singlet-triplet excited states up to 1300 nm. No significant spectral features were observed between 900 and 1200 nm in the singlet-singlet spectra. Nevertheless, singlet-triplet transitions can be responsible for spectral features within the 800-1000 nm range.