

# Effect of heme binding in the dynamics of human serum albumin

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## The Goal

- Analyze the structural properties due to heme binding in HSA.
- Determine the residues responsible as molecular gate of heme.
- Quantify the effect of heme in the collective motions of the protein.

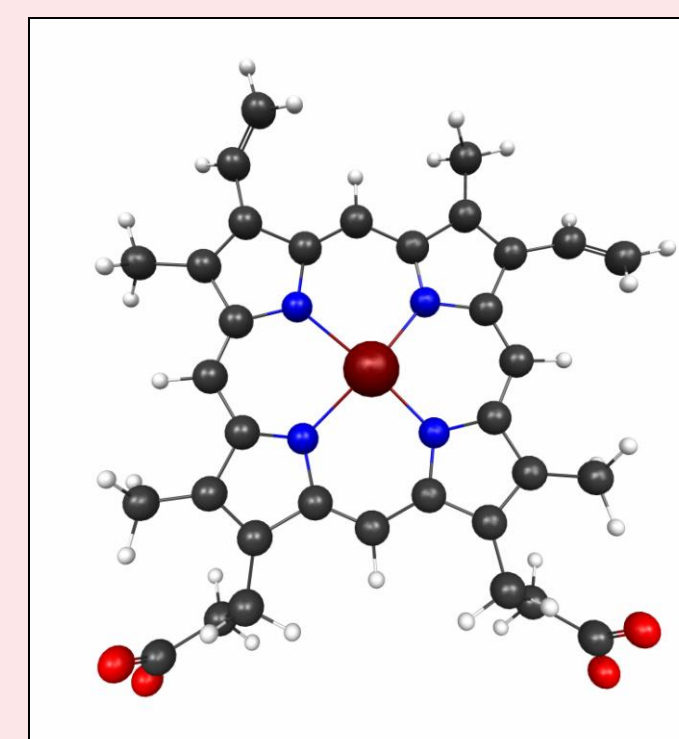
## Methodology

Mol. Quantum Mech./Gamess  
Molecular Docking/AutoDock  
Molecular Dynamics/Gromacs

## The protein and the heme

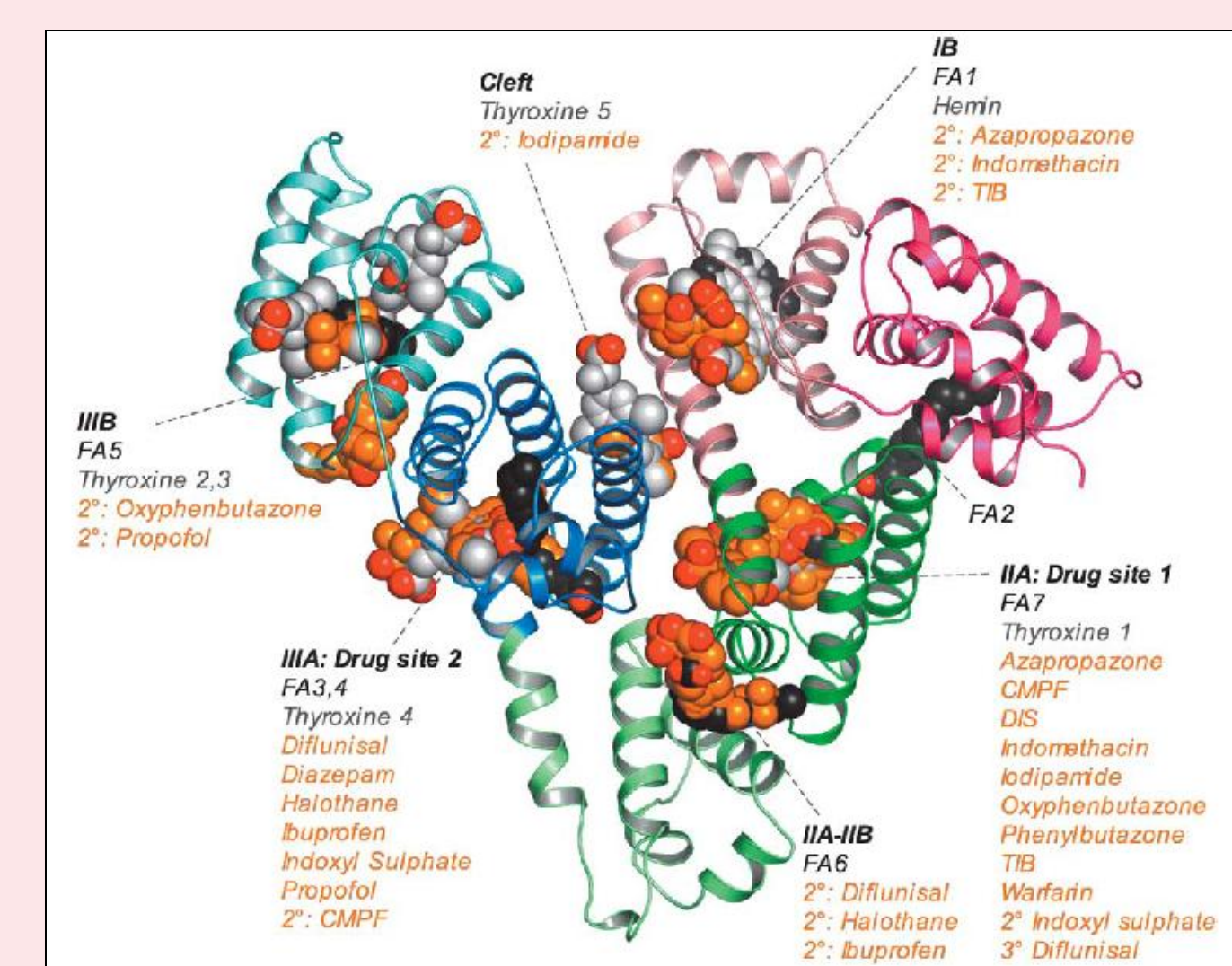
### Heme:

- Metalporphyrin, with Fe<sup>+2</sup> in its center.
- When complexed to myoglobin/hemoglobin it transports oxygen through the blood.

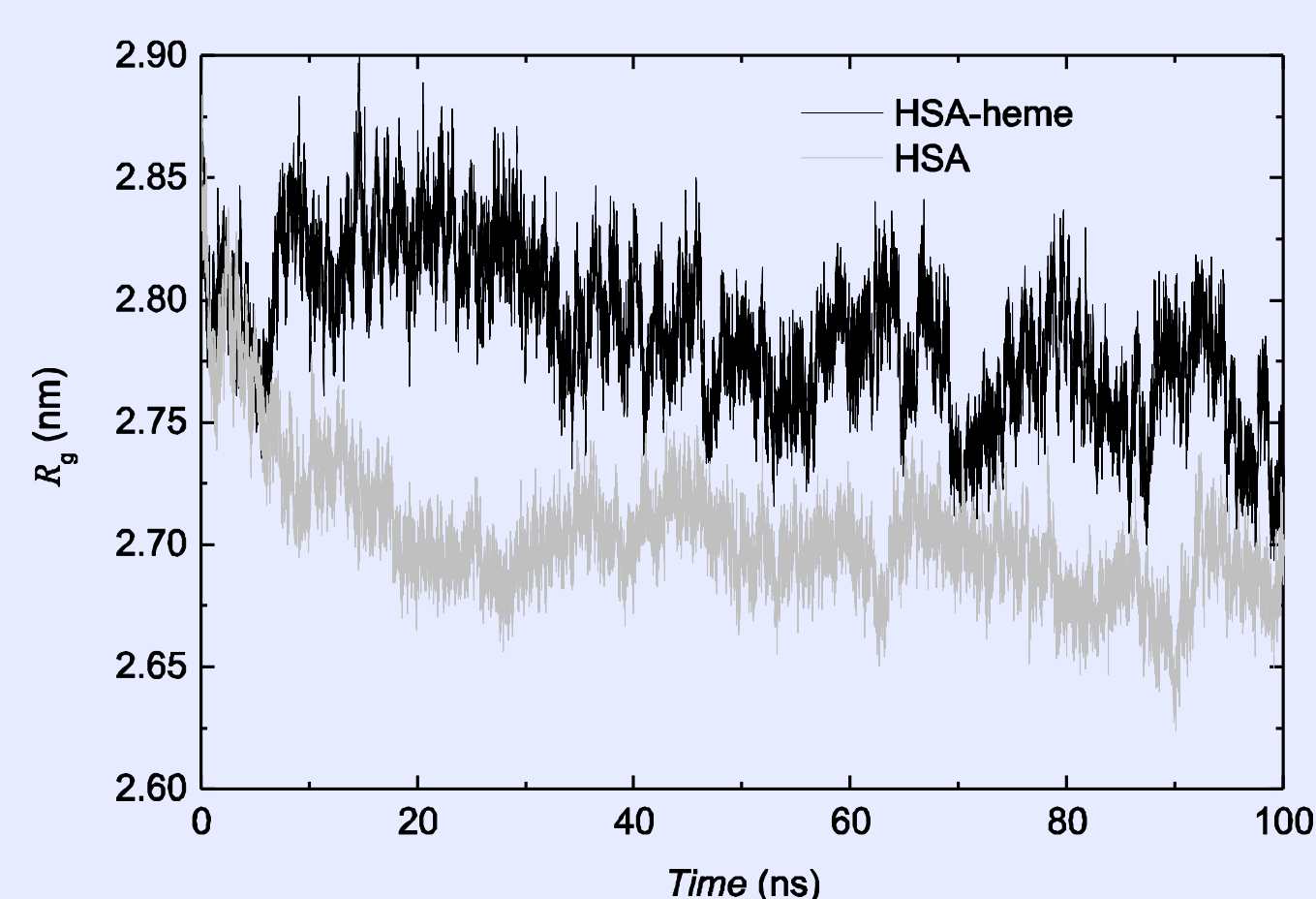


### Human Serum Albumin:

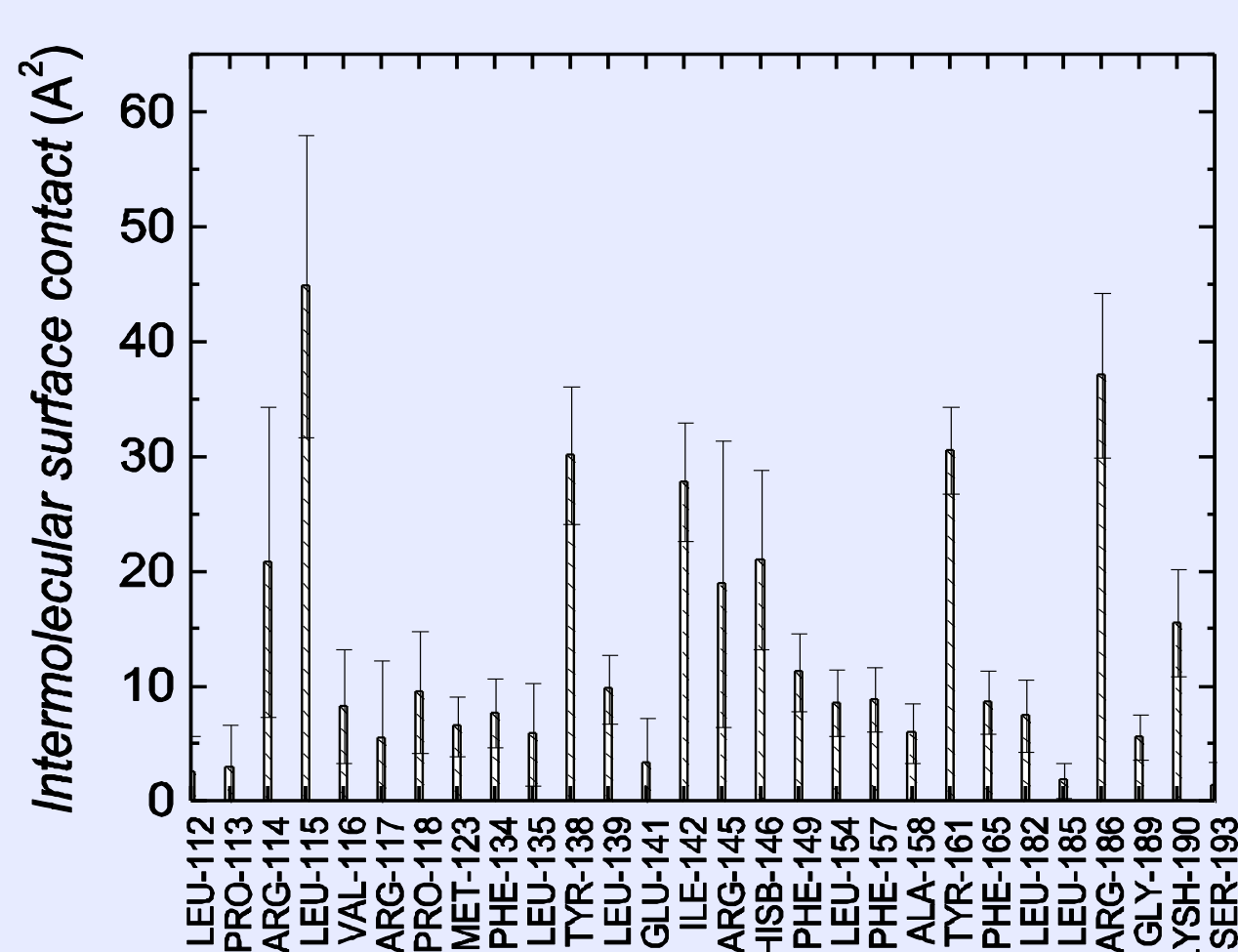
- The most abundant protein in blood plasma
- Molecular weight of 66 kDa.
- Binds several molecules, target in drug development.



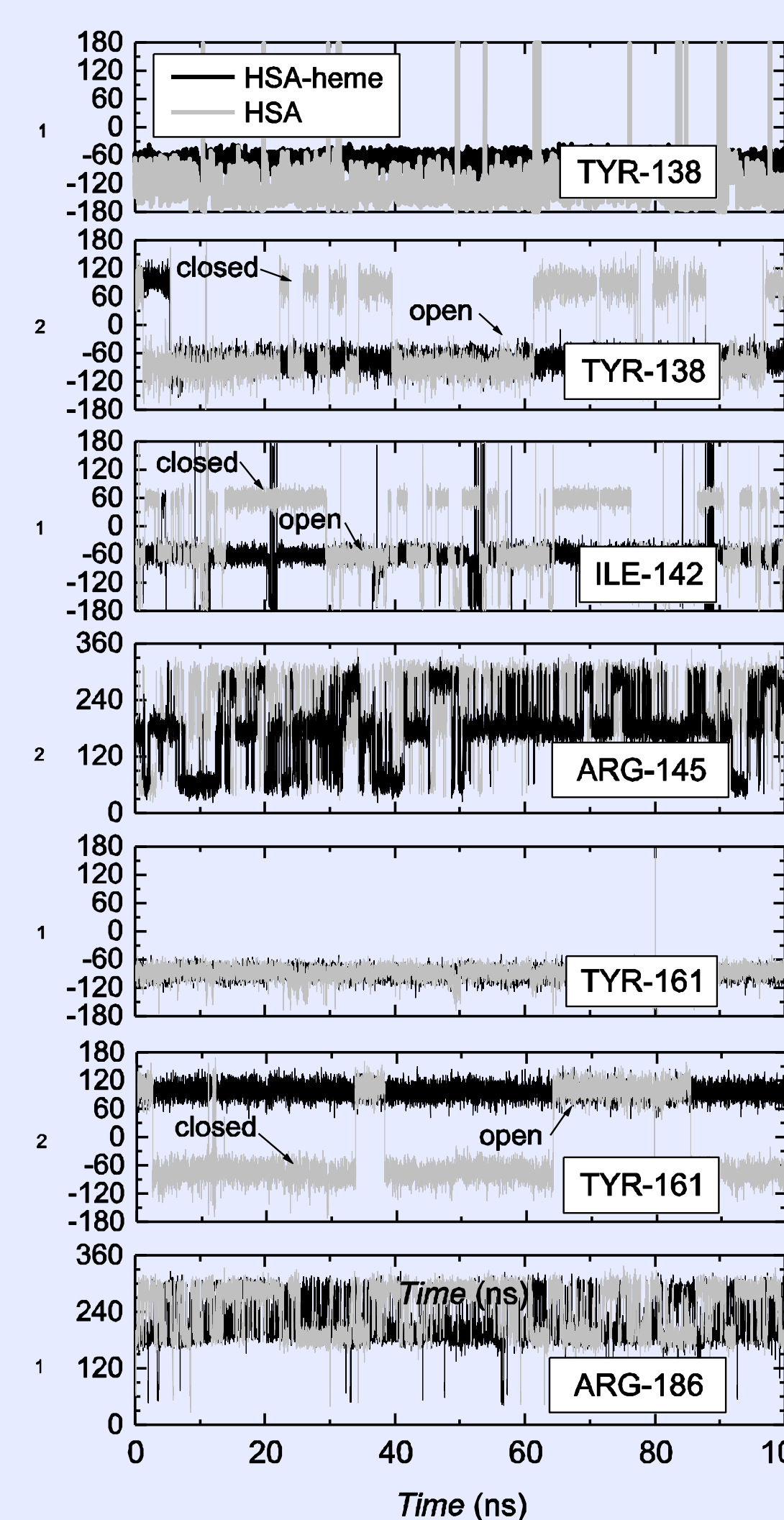
## Analysis of the molecular dynamics



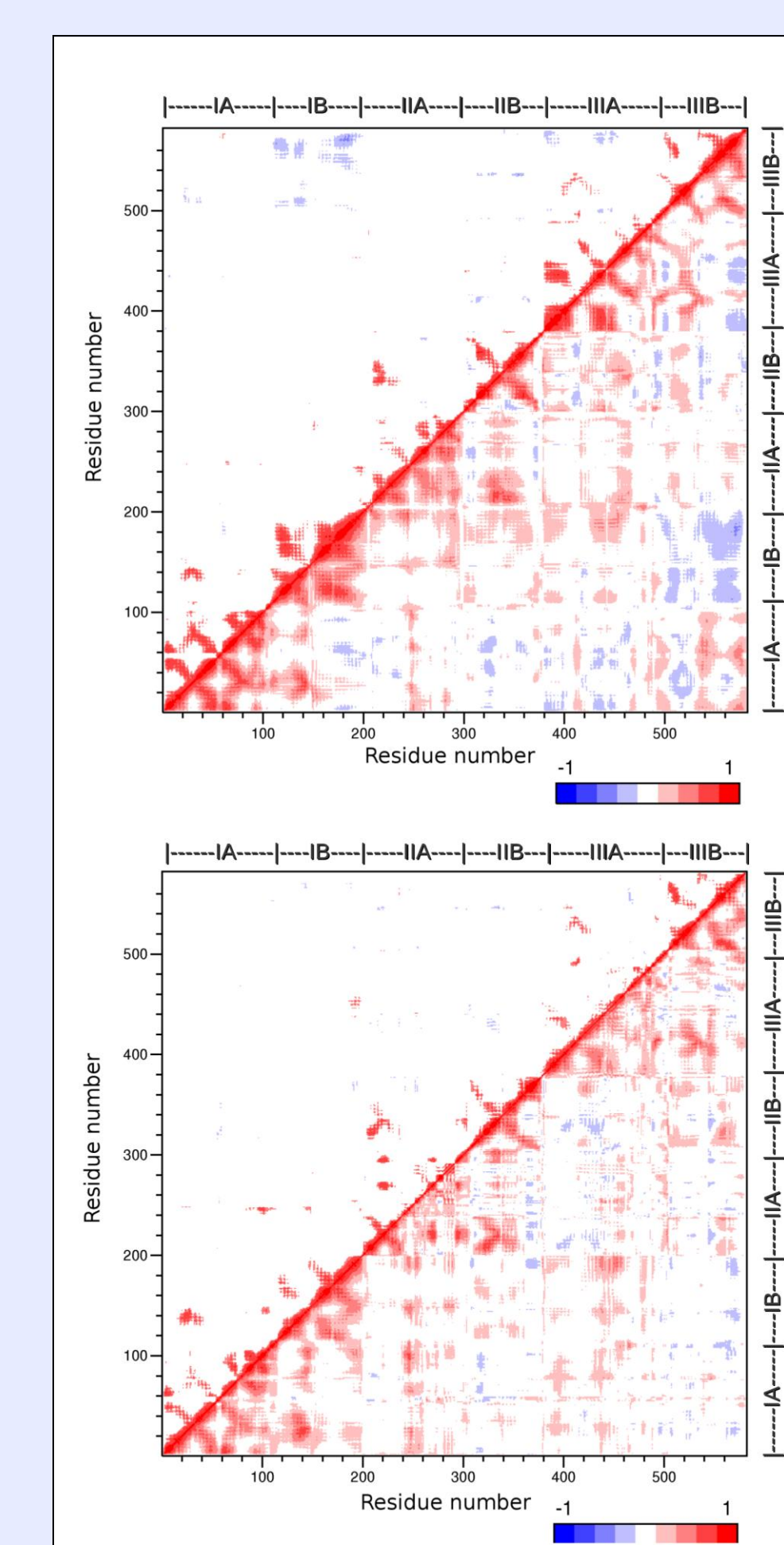
Rg (radius of gyration) of HSA achieved the experimental value in about 10-20ns.



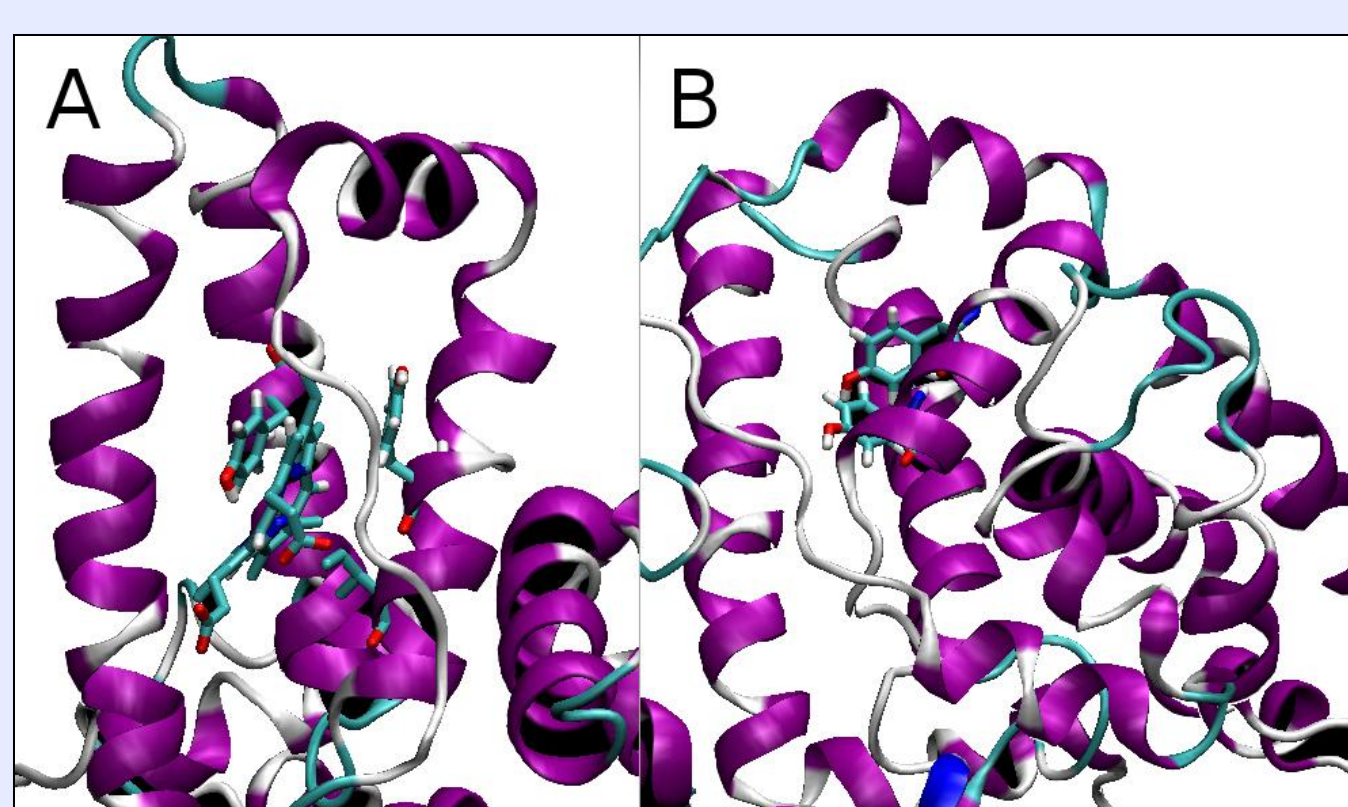
Residues with positive ISC (interact with heme)



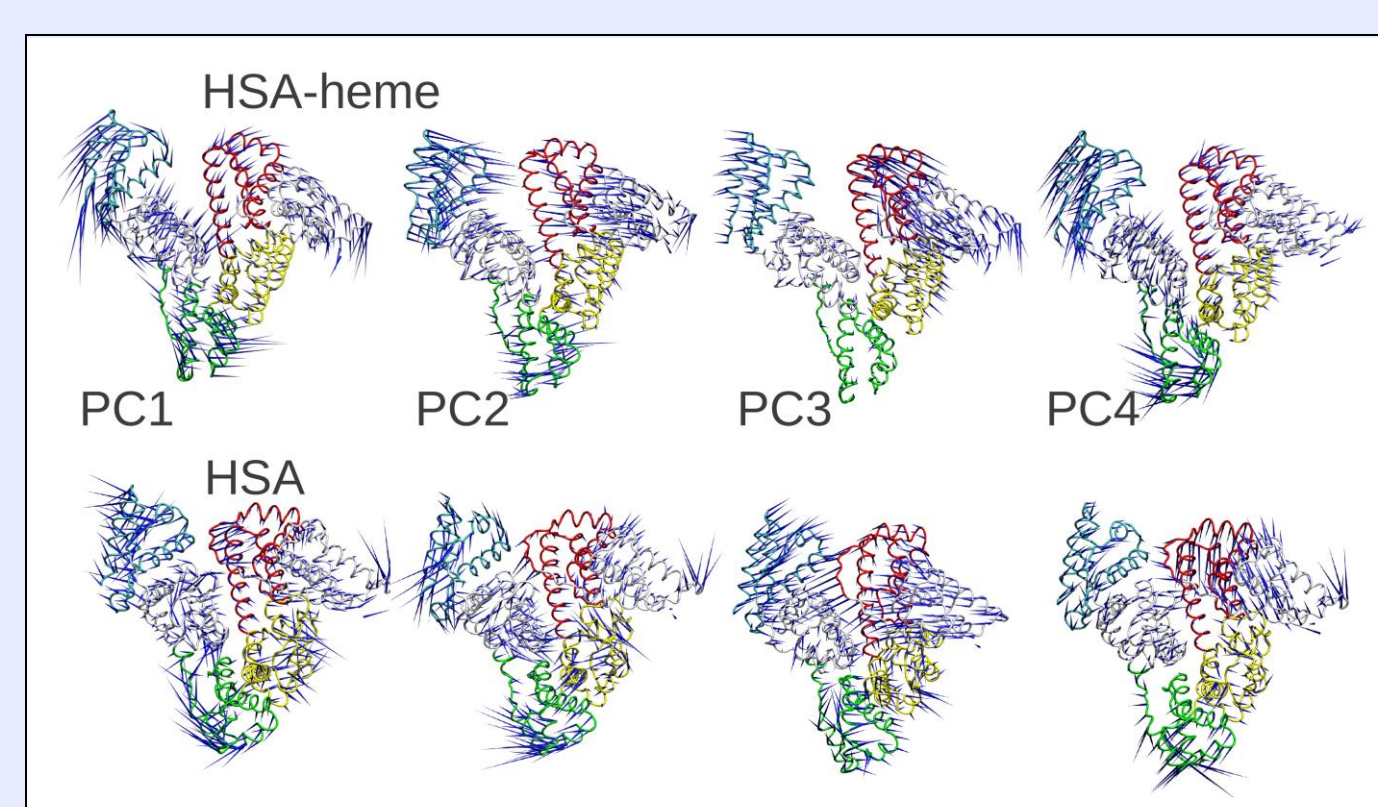
The  $\chi$  dihedrals vs time, show the molecular gate mechanism responsible for heme binding.



Heme binding affects the correlation profile of the protein



A: bounded B: unbounded conformation



The four predominant modes of movement

TRY-138, TRY-161 and ILE-142 are the residues responsible for the molecular gate that lets the heme enter into the hydrophobic pocket of HSA.  
LYS-19, HIS-146 and ARG-186 fix the heme in this entry.

## References

- [1] Cuya T, Pita S, Louro S, Pascutti P. Int. J. Quantum Chem. 108: 2603-2607 (2008)  
[2] Cuya Guizado T.R., S.R.W Louro and C. Anteneodo, J. Chem. Phys. 134, 055103 (2011).

## Conclusions and remarks

- Few internal motions are responsible for the total motion, both in HSA and HSA-heme.
- The heme induces an open state in the protein.
- TYR-138, TYR-161, ILE-142 act as molecular gates.
- Our results also suggest a inter-molecular correlation 100-200 and 200-300, 480-585.

## Acknowledgments

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