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Title: LIGAND-PROTEIN INTERACTION STUDIED BY COMPUTER SIMULATION AND TIME-RESOLVED X-RAY CRYSTALLOGRAPHY.

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Recently, high resolution x-ray crystallography demonstrated breathing motion of internal cavities in concert with ligand migration in myoglobin(Mb) [1].Continuous pulsed illumination of carbomonoxy-Mb crystals at low temperatures has illustrated structural changes around each cavity in response to ligand migration. In the present study, we examined the effect of the breathing motion on the potential of mean force(PMF) for ligand- protein interactions by using molecular dynamics simulation and experimental derived from the x-ray study[1]. Conformational sampling of Mb was performed by NPT molecular dynamics simulation for 92 ns. We introduced three-dimensional lattice of regularly spaced grid points, and evaluated PMF at each point by the implicit ligand sampling method [2]. The effect of the breathing motion of Mb on the ligand-protein interaction was illustrated by the difference map of PMFs for Mb structures before and after light illumination. Our results show ligand escaping mechanism via Xe1 pocket and gate opening between Xe2 pocket and Xe3 pocket.

References

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