Organic solvent effects on protein tertiary structure and enzyme stability: A computational study

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Enzymes never exist *in vacuum*, but either in crystalline, glass-transition, or solvated state, with the solvated state being the "functional" one and the primary solvent being a water/salt mixture. However, already in the 1970s the stabilizing effect of various organic solvents on a protein was described experimentally (1). Nevertheless, to date computational simulations focused mainly on modeling enzyme reactivity in water. Little computational work has been done with the aim to study the molecular reasons for the stabilizing or destabilizing effect of organic solvents and gain a fundamental understanding of its influence on protein structure-function relationships. In this study we have chosen two enzymes, DhaA from *Rhodococcus rhodochrous* NCIMB13064 and DbjA from *Bradyrhizobium japonicum* USDA110, belonging to the haloalkane dehalogenase family that are able to cleave carbon-halogen bonds (2). As the enzymes come from bacteria that use halogenated organic compounds as their growth substrate, their interaction with organic solvents is not an artifical *in vitro* situation, but physiologically relevant. These two enzymes are structural and functional homologs with a primary sequence identity of 50%, and a homology of 63%. Despite this fact, they exhibit a very different behavior in various organic solvents. While an isopropanol/water mixture dampens vibrational and rotational modes in the DbjA structure, the structure of DhaA gets destabilized. For formamide/water mixtures the result is opposite. Therefore a detailed analysis of the molecular interactions on the protein surface and in the solvent shell around the protein leads to a fundamental understanding and a generalization of the organic solvent effects on protein structure-dynamics-function.

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References

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