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Mechanism of disaccharide-induced protein stabilization from neutron scattering and modeling

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Proteins are an important component in many medical and food products, and the long-time properties of these products are directly dependent on the stability of their proteins. To enhance this stability it has become common to add disaccharides in general, and trehalose in particular. However, the mechanisms by which disaccharides stabilize proteins and other biological materials are still not fully understood, and therefore we have used neutron diffraction and quasielastic neutron scattering (QENS) in combination of molecular modeling to investigate the stabilizing role of the disaccharides trehalose and sucrose on myoglobin. Our aim was to enhance the general understanding of the role of disaccharides and to obtain specific insights into why trehalose exhibits extraordinary stabilizing properties. The diffraction results show that both disaccharides are preferentially excluded from the protein surface, but that this effect is more pronounced for trehalose than sucrose. Hence, the disaccharide molecules are generally not affecting the protein by direct interactions. Instead, the QENS and modeling results show that the protein dynamics is slowed down by a slowing down of the protein hydration water, as a result of the “slaving mechanism”. Since the water dynamics and protein motions are slower in the trehalose solution, the results explain the more efficient stabilizing effect of trehalose on proteins.

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