Structural investigation of the *E. coli* proteins HdeA and YmgD by MD simulations

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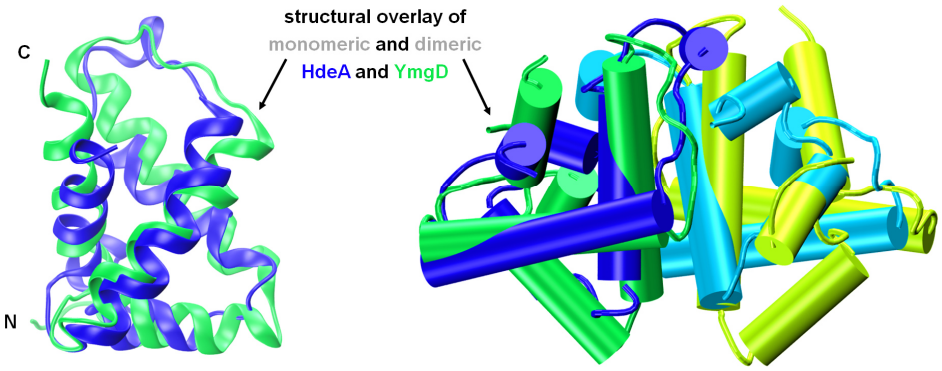
Enteropathogenic bacteria, which are for instance swallowed with food or water, need to survive the acid conditions in the host stomach before they can infect the intestine. For fulfilling this challenging task, different strategies have emerged: One mechanism for acid resistance in *Escherichia coli* is the expression of the periplasmic protein HdeA. HdeA has been shown to represent an acid-activated chaperone, which helps *E. coli* to tolerate very acidic environments, such as the mammalian stomach where the pH varies between 1 and 3.

YmgD is a structurally homologous protein to HdeA and it is also expressed in the periplasm of *E. coli*. In contrast to the function of HdeA, the function of YmgD has not yet been characterized. We performed pH-titrating molecular dynamics (pHtMD) simulations [1] to investigate the structural changes of both proteins and to assess whether YmgD may also exhibit an unfolding behavior similar to that of HdeA.



The unfolding pathway of HdeA includes partially unfolded dimer structures, which represent a prerequisite for subsequent dissociation. In contrast to the coupled unfolding and dissociation of HdeA, YmgD displays dissociation of the folded subunits, and the subunits do not undergo significant unfolding even at low pH values. The differences in subunit stability between HdeA and YmgD may be explained by the structural features of helix D, which represents the starting point of unfolding in HdeA. In summary, the present study suggests that YmgD either is not an acid-activated chaperone or, at least, does not require unfolding for activation. [2]

[1] E. Socher, H. Sticht, *Sci. Rep.*, **2016**, *6*, 22523.
[2] E. Socher, H. Sticht, *J. Phys. Chem. B*, **2016**, *120*, 11845-11855.