# Trading off stability against activity in extremophilic aldolases

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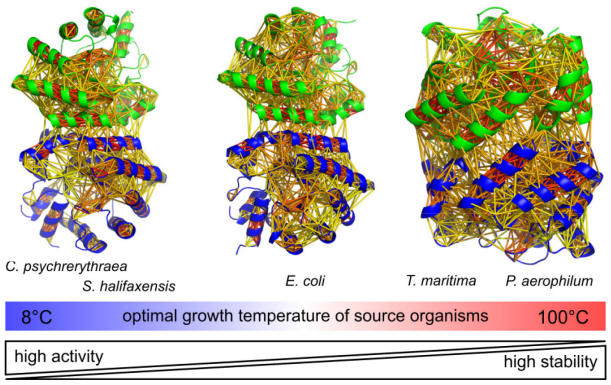
Understanding what determines thermostability and activity of enzymes has always been an important issue. To investigate factors that describe the relationship between stability and flexibility, we performed comparative studies with variants from psychrophilic (cold loving), mesophilic and hyperthermophilic organisms. As model enzymes we are investigating acetaldehyde dependent aldolases, specifically 2-deoxy-D-ribose-5-phosphate aldolases (DERAs), which have a high potential as biocatalysts: they form chiral building blocks for organic synthesis *via* a highly selective aldol reaction.[1]

Using X-ray crystallography and rational enzyme design, supported by computational methods in terms of contraint network analysis (CNA),[2] we were able to identify hot spot positions in the dimeric interface responsible for the high heat tolerance in hyperthermophilic DERAs.[3] With this knowledge at hand, we have successfully implemented these stabilisation factors into psychrophilic DERAs, resulting in increased thermostability. Furthermore, CNA revealed particularly sparse interactions between the substrate pocket and its surrounding α-helices in psychrophilic DERAs, which indicates that a more flexible active centre underlies their high turnover numbers. [3]




[1] P. Clapés, W.-D. Fessner, G. A. Sprenger, A. K. Samland, *Curr. Opin. Chem. Biol.*, **2010**, *14*, 154-167.

[2] C. Pfleger, P. C. Rathi, D. Klein, S. Radestock, H. Gohlke, *J. Chem. Inf. Model.*, **2013**, *53*, 1007-1015.

[3] M. Dick, O. H. Weiergräber, T. Classen, C. Bisterfeld, J. Bramski, H. Gohlke, J. Pietruszka, *Sci. Rep.*, **2016**, *6,* 17908.