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Interrogating the biophysics of protein cage nanoreactors

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Living cells use compartments to organise the vast and seemingly incompatible plethora of biochemical reactions required for metabolism. In my lab, we aim to emulate Nature's organisation principles by using biological cage-like compartments as macromolecular nanoreactors for controlling catalysis.

Recently, our laboratory has studied a family of self-assembling bacterial protein cages known as encapsulins (Figure 1).[1] These nanosized protein cages can non-covalently encapsulate any given cargo protein of interest when that cargo is fused to a short peptide that acts as a tag for encapsulation. Despite significant bioengineering efforts, our fundamental understanding of such nanoreactor systems is still remarkably limited, especially in terms of the biophysical parameters that govern their stability and molecular flux through their pores.

I will outline our systematic analysis of 24 designed cage variants based on the *T. maritima* encapsulin protein organelle, each featuring pores of different size and charge.[2] Of the twelve variants that formed stable assemblies, we determined the structure and porosity of seven variants by single particle cryo-EM. We then combined molecular dynamics and stopped flow kinetics, to uncover the complex interplay of factors that determines the kinetics of such nanoreactor systems, finding evidence for a balance between influx rates and caged reaction kinetics.

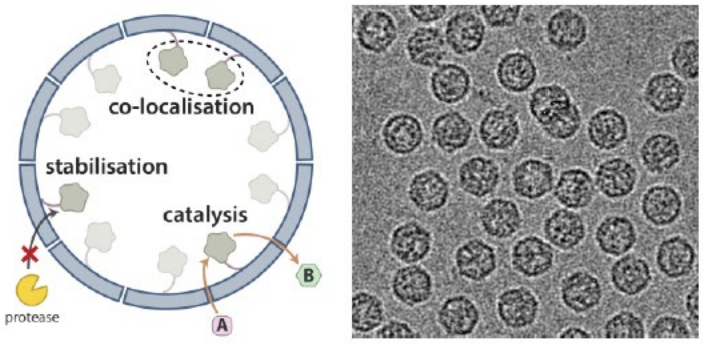

Figure 1. Encapsulins are nanosized protein cages that can house enzyme catalysis.

1. Y.H. Lau, T.W. Giessen, W.J. Altenburg, P.A. Silver, Nat. Commun. (2018), 9, 1311.

2. L.S.R Adamson, N. Tasneem, M.P. Andreas, W. Close, E.N. Jenner, T.N. Szyszka, R. Young, L.C. Cheah, A. Norman, H.I. MacDermott-Opeskin, M.L. O'Mara, F. Sainsbury, T.W. Giessen, Y.H. Lau, Sci. Adv. (2022), 8, eabl7346.