Abstract:

A/Prof. Matthew Baker works on two systems of interest to biophysics and synthetic biology: A) the directed evolution and engineering of the bacterial flagellar motor, a rotary electric nanomachine which powers most bacterial swimming and B) using de novo DNA nanotechnology to control and shape lipid membranes.

The flagellar motor is one of the canonical molecular complexes, ~40 nm in diameter but capable of rotating at 1000 Hz, self-assembling in the membrane and changing rotational direction in milliseconds. Matt's team's recent work on the flagellar motor used directed evolution to monitor the adaptation of the stator units, the engine which drives rotation, to see how the motor evolves. The structure of the stator was recently solved, hinting that the stators themselves are an even tinier rotating nanomachine! Furthermore, strong structural homology with other ion powered rotary motors has opened new avenues for considering the common origin of these complexes. These new structures have revolutionised the study of motor biophysics, where many tiny 'wheels' in turn engage the larger rotor and ultimately the bacterial filament which enables cellular propulsion. Our most recent work consists of examining chimeric constructs of the separate components of the stator to examine what are the limits for what types of new proteins can power motility [1], as well as using rational design approaches such as stabilising the central stalk (the B-unit) to alter and impact motility [2].

Approaching synthetic biology from the other end, from the *in vitro* bottom-up perspective, we build multi-compartment interacting systems out of simple DNA and lipid components. Our work on DNA nanostructures has characterised the best way to connect DNA to lipids via cholesterol. We demonstrated that more cholesterols are not necessarily better and explored the most suitable linkage chemistry to allow strand displacement, the basis of all reaction and interaction in DNA nanotechnology [3]. We currently work on integrating light activatable DNA nanotechnology to direct and control the fusion of liposomes. We have also sought to make artificial bilayer technology more accessible and low-cost, with higher throughput, through the integration of droplet-printing and plate-reader technologies to assay membrane proteins in droplet-interface-bilayer arrays [4]

References:

[1] Ridone, P. and Baker, M.A.B. *bioRxiv*, 10.1101/2024.03.12.584617
[2] Ridone, P., et al. (2023). *Protein Science* 10.1002/pro.4811.
[3] Singh, J.K.D., et al. (2021). *Nucleic Acids Research* 10.1093/nar/gkab888.
[4] Mason, A.F., et al. *bioRxiv*, 10.1101/2024.01.26.577347.

Bio:

Matt grew up in Dunedin, New Zealand and finished a BSc (Honours) in Chemistry at the Australian National University studying Fluctuation Theorems before completing his DPhil in Physics at the University of Oxford as a John Monash Scholar looking at the molecular motor that makes many bacteria swim. He finished a postdoc on protein transport in the Department of Biochemistry in Oxford and then returned to Australia to study structural biology at the Victor Chang Cardiac Research Institute in Sydney, Australia. Matt started his group at the School of Biotechnology and Biomolecular Science (BABS) at the University of New South Wales in 2018 as a Scientia Fellow, was promoted to Scientia Senior Lecturer in 2019 and to Scientia Associate Professor in 2023. Matt's group focus primarily on how simple subunit interactions govern assembly and function of complex architectures, including the rotor and filament of the bacterial flagellar motor. Matt also loves radio: he was a Top 5 Under 40 Scientist in Residence at the Australian Broadcasting Corporation in 2015 and appears regularly on Radio National in Australia and Radio New Zealand with an audience of roughly 1 million.