Relating structure, biomechanics and function of single membrane proteins

Sonia Antoranz Contera[1], *Kislon Voïtchovsky*[1], *Hayato Yamashita*[2], *Takayuki Uchihashi*[2], *Toshio Ando*[2], *J.F. Ryan*[1]

[1] Bionanotechnology IRC, Clarendon Laboratory, Physics Department, University of Oxford, Oxford OX4 3AP, UK
[2] Graduate School of Natural Science & Technology, Kanazawa University, Kakuma, Kanazawa, Ishikawa 920-1192, Japan

E-mail: s.antoranzcontera1@physics.ox.ac.uk

One of the greatest challenges of biophysics is to understand how membrane protein sequences relate to the local forces that dynamically control their structure and drive their function. AFM is one of the most powerful techniques to address this problem, however, most of the single membrane protein unfolding AFM studies available fail to relate the potential barriers observed to specific molecular interactions relevant for the protein function.
In some of our recent papers, we have combined membrane indentation with AFM[1], AC-force spectroscopy[2], AFM unfolding and extraction of model peptides inserted planar lipid bilayers at different speeds[3], unfolding and extraction of bacteriorhodopsin (bR) from purple membranes[4] and comparison of pulling experiments with molecular dynamics simulations[3] to relate structure, nano-biomechanics, local hydration, mechanical properties and function of membrane proteins.
In particular, retinal proteins convert the energy of a single photon into large structural changes subsequently used to carry out various tasks. This is achieved by a complex combination of local dynamical interactions controlling the protein biomechanics, allowing efficient amplification of the retinal isomerization. In the case of the retinal containing proton-pump bR we have shown that steric, specific interactions create a rigid scaffold in the protein extracellular region[4]. This scaffold, which encloses the retinal, controls bR local biomechanical properties and anchors the protein into the membrane. In contrast, the cytoplasmic side of bR is mainly governed by relatively weak non-specific electrostatic interactions which provide the flexibility necessary for large cytoplasmic structural rearrangements during the photocycle. Finally we show that bR mechanical properties are part of the strategy adopted by bR to efficiently function in extreme halophilic environments.

References

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