Time resolved X-ray scattering studies at ID09 of structural changes in integral membrane proteins

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Time-resolved X-ray solution scattering (TR-XSS) has become a powerful method for elucidating the nature and number of conformational states of proteins. The key advantage of time-resolved solution scattering is that there is no need for protein crystals and therefore protein crystal contacts do not constrain the motions of the protein studied. Conversely, since data is only one dimensional, TR-XSS does not yield three-dimensional protein structures and conformational changes must be modelled using additional structural and chemical knowledge. Proof-of-principle TR-XSS studies of structural changes in haemoglobin were reported more than a decade ago [1] and our first TR-XSS studies of bacteriorhodopsin [2] followed a year later. We have also observed ultrafast motions in photosynthetic reaction centres under conditions of extreme multiphoton excitation [3].

In this presentation I wish to give an update of the status of our more recent TR-XSS studies at ID09 of the ESRF on three other integral membrane proteins: sensory rhodopsin II (an archaeal photoreceptor) in isolation and in complex with its transducer protein; channel rhodopsin (a light-gated channel); and cytochrome *c* oxidase (the enzyme which reduces oxygen to water in mitochondria). We have excellent quality TR-XSS data for all three integral membrane proteins but have delayed publication due to issues of modelling structural changes within integral membrane proteins embedded within a detergent micelle. I will therefore also update our progress in modelling conformational changes and my reason for believing that this bottleneck will soon be solved. Finally, I will report on time resolved serial millisecond crystallography (TR-SMX) studies of light-driven structural changes in sensory rhodopsin II performed at the protein crystallography station of the Swiss Light Source. All methods appear very promising in future time-resolved studies at the ESRF.

References

[1] Cammarata, M., *et al.* "Tracking the structural dynamics of proteins in solution using time-resolved wide-angle X-ray scattering." *Nature Methods* **5**, 881-886 (2008).
[2] Andersson, M., *et al.* "Structural dynamics of light-driven proton pumps." *Structure* **17**, 1265-1275 (2009).
[3] Arnlund, D., et al. "Visualizing a protein quake with time-resolved X-ray scattering at a free-electron laser." *Nature Methods* **11**, 923-926 (2014).