GÖTEBORGS UNIVERSITET

Conformational Dynamics of Rhodopsins Visualized by Time-resolved Wide Angle X-ray Scattering

ERIK MALMERBERG
Institutionen för kemi
Naturvetenskapliga fakulteten

Akademisk avhandling för filosofie doktorsexamen i Naturvetenskap, som med tillstånd från Naturvetenskapliga fakulteten kommer att offentligt försvaras fredagen den 18:e november 2011 kl. 09.00 i KB-salen, Institutionen för kemi, Kemigården 4, Göteborg.

ISBN: 978-91-628-8371-3
Online: http://hdl.handle.net/2077/27026

GÖTEBORGS UNIVERSITET

Conformational Dynamics of Rhodopsins Visualized by Time-resolved Wide Angle X-ray Scattering

ERIK MALMERBERG
Institutionen för kemi
Naturvetenskapliga fakulteten

ABSTRACT

Rhodopsins are a family of light-sensitive proteins found in the cellular membranes of a wide range of living organisms. These membrane proteins share a common molecular architecture and are able to use light energy to perform a variety of different biological functions. Mapping the conformational changes required for these proteins to function is important for understanding how light energy is used for energy transduction and sensory perception in biological systems.

In order to visualize these conformational changes over time, the emerging technique of time-resolved wide angle X-ray scattering (TR-WAXS) was employed. Several technical and analytical developments of this solution based method were made during the course of this work, including the development of a new data collection strategy based on a rapid readout X-ray detector.

The light-driven proton pumps bacteriorhodopsin and proteorhodopsin were the first membrane proteins to be characterized using TR-WAXS. The results from these studies indicated that significant α-helical rearrangements precede the primary proton transfer event in bacteriorhodopsin. Comparison with the evolutionary related proteorhodopsin provided important insights into shared conformational dynamics between the two proton-pumps.

Proteorhodopsin was further investigated by probing the conformational changes occurring within its chromophore binding pocket, where the chromophore of proteorhodopsin was substituted with a chemically modified retinal analogue. Comparison between the native and modified form of proteorhodopsin indicated significant chromophore dependant differences in their conformational kinetics. These differences provided new insights into the coupling between retinal isomerisation and protein conformational changes.

The conformational dynamics within visual rhodopsin, the primary light sensor of vertebrate vision, were also investigated using TR-WAXS. By using the rapid readout X-ray detector we were able to follow the activation of this G-protein coupled receptor in real-time. Structural analysis further indicated that dramatic conformational changes are associated with the activation of this receptor.