Molecular modelling of photoreceptor systems for light-inducible gene networks

Supervisors / institute:

Main supervisor: Birgit Strodel, Structural Biochemistry (ICS-6), Forschungszentrum Jülich
Co-supervisor: Karl-Erich Jaeger, Institut für Molekulare Enzymtechnologie, HHU Düsseldorf

Project background and description:

Biological signal-transducing receptors are modular proteins which enable organisms to perceive environmental information and to convert them into cellular signals that elicit specific physiological responses. Many of the light-induced signal transduction complexes consist of a light-oxygen-voltage (LOV) sensing input domain that harbours a flavin chromophore and C-terminally located histidine kinase, and an interacting response regulator protein. For the rational design of synthetic photoreceptors, an improved molecular understanding of structure, function and signaling mechanism is indispensable.

Using molecular modelling, this project will investigate a LOV-type photoreceptor, which in the group of K.-E. Jaeger was fused to a lipase. It could be biochemically shown that a blue-light signal gets transmitted to the lipase, increasing its activity. To unravel the molecular mechanism of the underlying signal transduction pathway, molecular simulations will be performed in the group of B. Strodel. The photophysical response of the LOV domain will be tested by nonequilibrium MD simulations, which allow us to follow the flow of the excess energy through the proteins and into the solvent, revealing the intra-peptide and inter-domain signalling pathways. Important amino acid residues along these pathways will be identified as candidates for subsequent mutation studies – *in silico*, *in vitro* and *in vivo*. The ultimate goal is to propose mutations and make predictions about their effect on the signal transduction, leading to novel light-sensing regulatory modules.

The *in vitro* and *in vivo* studies will be performed in collaborating iGRASP*seed* groups. The production and biochemical analysis of photo-switchable fusion proteins (e.g., LOV+lipase) will be accomplished in the group of K.-E. Jaeger. Structural information about the fusion proteins will be provided by the group of D. Willbold using X-ray crystallography and NMR spectroscopy.

Aims of the project:

- Establishing non-equilibrium MD simulations in the Strodel group.
- Understanding the signal flow in the LOV-lipase system.
- Identification of important amino acids along the signal transduction pathway.
- Proposing mutations, which will be tested *in silico*, *in vitro* and *in vivo*
- Cooperations with D. Willbold (Structural Biology) and K.-E. Jaeger (Biotechnology)

Requirements:

- Master degree in biochemistry; chemistry; physics; or computer science with a minor in chemistry, physics or biology
- Experience in molecular modeling and programming (C/C++, Perl, Python or FORTRAN)

Additional information:

http://www.fz-juelich.de/ics/ics-6/DE/strodel
http://www.iet.uni-duesseldorf.de/