2 PhD positions in biophysics at the Institute of Structural Biology

IBS Grenoble, France

MECHANISTIC INVESTIGATIONS OF PHOTOSWITCHABLE FLUORESCENT PROTEINS BY NMR, SINGLE-MOLECULE IMAGING AND X-RAY CRYSTALLOGRAPHY

The recruited students will investigate the photophysical mechanisms of reversibly photoswitchable fluorescent proteins employing solution NMR spectroscopy coupled with in-situ laser illumination (PhD 1), and single-molecule fluorescence imaging / X-ray crystallography (PhD 2). The goal will be to contribute fundamental knowledge of these essential fluorescent markers and to engineer improved variants.

Advanced fluorescence imaging is essential to discover the secrets of life, and has largely benefited from the discovery of Fluorescent Proteins (FPs) and other protein-based fluorescent markers. Reversibly Switchable Fluorescent Proteins (RSFPs, Ref 1) are capable to switch between a fluorescent on-state and a nonfluorescent off-state under specific light illumination, and have fostered many types of imaging applications including super-resolution methods. Yet, RSFPs are still imperfect: e.g. their brightness is limited, their switching kinetics is perturbed by the involvement of multiple photophysical states, their resistance to irreversible photobleaching is lower than that of typical organic dyes. Moreover, whereas green RSFPs are performing relatively well, red RSFPs do not switch nicely and have been lagging behind. Non FP-based RSFPs also exist, such as FAST which is based on reversible fluorogenic chromophore binding to protein targets (Ref 2). The switching properties of green and red RSFPs and FAST systems, notably the intertwining with their intrinsic or light-activated protein dynamics can be studied by combining structural biology approaches such as NMR (Ref 3) and X-ray crystallography with optical spectroscopy and fluorescence imaging (Ref 4). In the proposed PhD projects, those techniques will be developed and used to better understand a variety of RSFPs and facilitate their rational engineering towards brighter and more photo-resistant variants.

Grenoble is situated in the middle of the beautiful French Alps, and the IBS provides a unique environment for state-of-the-art integrated cellular and structural biology (http://www.ibs.fr/).

Candidates should have a strong interest to work at the interface between physics, chemistry and biology. Basic knowledge of advanced fluorescence microscopy and/or NMR is required. Preliminary experience in image processing, protein crystallography, biochemistry, cell biology and/or molecular biology will be appreciated.

The project is financed by the French ANR (project: Photoswitch NMR), and the students will be employed by CEA (https://instn.cea.fr/en/theses-and-phds-at-the-cea/)

Applications are now open. Please send a CV, a detailed motivation letter, your transcripts, and at least one reference letter to Bernhard Brutscher (bernhard.brutscher@ibs.fr) (PhD 1) or Dominique Bourgeois (dominique.bourgeois@ibs.fr) (PhD 2). Selection will stop when suitable candidates have been identified.