Grenoble Alliance for Integrated Structural & Cell Biology

GRAL Research proposal for PhD projects

Institute and Group: IBS- PIXEL

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Title of the thesis project: **Manipulating fluorophore photophysics to boost single-particle tracking photo activated localization microscopy (spt-PALM).**

Keywords: super-resolution microscopy; single-particle tracking; fluorescent markers; protein dynamics; protein-DNA/lipid/sugar interactions

Summary of the project:

Fluorescence nanoscopy bridges cellular and structural biology. In particular, single-molecule localization techniques such as PALM and STORM provide nanoscale pictures of biological targets in cellulo, either static or dynamic. This project focuses on the dynamic picture, by introducing specific developments of single-particle-tracking approaches based on the use of photoactivatable fluorescent probes. Typically, these probes exhibit a highly complex photophysical behaviour: they “blink” and “bleach”, meaning that single-particle tracks are discontinuous and of limited length. The knowledge of fluorescent protein photophysics that we have developed in the IBS Pixel team offers new strategies to obtain longer and more continuous tracks, providing more information on the dynamic behaviour of the studied targets linked to e.g. binding, unbinding or changes in diffusion regimes. These developments form the basis of the proposed subject, which will contribute to establish spt-PALM/STORM as a state-of-the-art technique available to GRAL2 laboratories. The work will be carried out in the frame of well-defined biological projects with 4 collaborating teams. Dynamics of the peptidoglycan synthesis machinery (C. Morlot) and of nucleoid-associated proteins (J. Timmins) will be studied in bacterial cells while that of heparan sulfates (R. Sadir) and of the efferocytosis machinery (P. Frachet) will be investigated in mammalian cells.