Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

Laboratory/Institute: IBS
Director: W. Weissenhorn
Team: PG and GSY
Head of the team: C. Morlot & A. Royant

Name and status of the scientist in charge of the project: Dr Pauline Macheboeuf and Dr Sylvain Engilberge

HDR: yes X (PM)
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Program of the Master's degree in Biology:

X Biochemistry & Structure

Title of the project: Tackling antibiotic resistance using time-resolved functional rotation crystallography

Objectives (up to 3 lines):

In order to better understand the mechanism of antibiotics recognition by their protein targets, we will use a combination of X-ray crystallography at room temperature on single crystal with antibiotics nanodroplets injection. We will record molecular movies depicting enzymatic activities and allow for atomic-scale visualization of substrates binding and processing.

Abstract (up to 10 lines):

The antibiotic resistance against bacterial infections is of major concern and could lead to over 10 million annual deaths by 2050. Thus, this unprecedent crisis constantly demands new therapeutic molecules. The major target for antibiotics is the bacterial peptidoglycan (PG), a giant macromolecular network wrapping the bacterial cell that is essential for its survival. The β-lactam antibiotics such as penicillins, cephalosporins and carbapenems have been widely used for decades and target enzymes involved in the PG biosynthesis, i.e., the Penicillin-Binding Proteins (PBPs). In order to envisage the biosynthesis of new therapeutic molecules, we will need to decipher, at a molecular level, the catalytic reaction involved in antibiotics recognition by the PBP active site. We will use time-resolved functional rotation crystallography at room temperature using a nanodispenser that can dispense droplets of 2 to 70 nL of substrate onto a single crystal. The BM07 beamline will allow us to record low-dose room temperature datasets on single crystals to monitor the conformational changes associated with the direct injection of antibiotics in a time-resolved manner. These data will inform on ligand and protein dynamics, aiding drug discovery efforts to develop new antimicrobial molecules.

Methods (up to 3 lines):

We will use biochemistry and X-ray crystallography techniques in order to decipher the mechanism of antibiotics recognition and acylation by PBPs.

Up to 3 relevant publications of the team:

- P.L. Flanders, J.R Gillingham, C. Contreras-Martel, A. Dessen, E.E. Carlson, E.A. Ambrose. doi: 10.1021/acschembio.5c00788. 2026.

- J.M.J. Martel, N. Caramello, S. Coquille, E. Mathieu, L. Petit, P. Jacquet, A. Appolaire, F. Leonarski, V. Olieric, M. Wang, D. Madern, A. Royant, S. Engilberge. doi: https://doi.org/10.64898/2026.04.24.718481. 2025
- P. Macheboeuf, C. Contreras-Martel, V. Job, O. dideberg, A. Dessen. doi: 10.1111/j.1574-6976.2006.00024.x. 2006.

Requested domains of expertise (up to 5 keywords): Protein purification, Biochemistry, crystallography