GRAL PhD PROJECT 2020-2023

Title of the PhD project: Structural insight into bacterial chromatin assembly by cryo-electron tomography

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Summary of the project: In all cells, DNA has to be tightly packaged into a restricted volume and yet remain accessible for DNA-related processes such as replication or transcription. How this is achieved is a question that has fascinated researchers for decades. In bacteria, DNA compaction is largely achieved by DNA supercoiling, macromolecular crowding and DNA compaction by nucleoid associated proteins (NAPs), but the molecular mechanisms underlying these processes remain largely unexplored. This is mainly due to the small size of bacterial cells, making conventional methods of sample preparation and imaging by optical and electron microscopy poorly suitable. Moreover, the number and nature of NAPs are not conserved across bacterial species. In E. coli, for example, a dozen partly functionally redundant NAPs have been identified, which complicates in vivo investigations. In contrast, the radiation-resistant bacterium *Deinococcus radiodurans*, possesses only two essential NAPs, the abundant HU protein and a versatile DNA Gyrase. Our goal is thus to investigate how bacteria package their genomes into highly compact structures by making use of the remarkably simple chromatin of *D. radiodurans*. Here we will combine biochemical and structural studies of the chromatin building blocks HU and DNA Gyrase with cryo-electron tomography imaging of in vitro reconstituted chromatin.

Keywords: chromatin assembly, nucleoid-associated proteins, cryo-electron tomography, *D. radiodurans*, integrated structural biology

Applicant profile: The candidates should hold a Master's degree in Biology, Biochemistry, Chemistry, Biotechnology or Biophysics and should have excellent academic records. The candidates should be interested in structural biology, computing, 3D image analysis and visualisation. Experience in electron microscopy, recombinant protein expression and purification techniques would be an asset.

Three recent publications of the PhD supervisors

Burt A, Cassidy CK, Ames P, Bacia-Verloop M, Baulard M, Huard K, Luthey-Schulten Z, Desfosses A, Stansfeld PJ, Margolin W, Parkinson JS, Gutsche* I. Complete structure of the chemosensory array core signalling unit in an *E. coli* minicell strain. Nat Commun. 2020 Feb 6;11(1):743. doi: 10.1038/s41467-020-14350-9.

Floc'h K, Lacroix F, Servant P, Wong YS, Kleman JP, Bourgeois D and Timmins* J. Cell morphology and nucleoid dynamics in dividing *D. radiodurans*. Nat Comm. (2019) 10 (1). p.3815. doi: 10.1038/s41467-019-11725-5

Hognon C, Garaude S, Timmins J*, Chipot C, Dehez F and Monari A. Molecular basis of DNA packaging in bacteria revealed by all-atoms molecular dynamic simulations: The case of histone-like proteins in *Borrelia burgdorferi*. J. Phys. Chem. Lett. (2019). doi: 10.1021/acs.jpclett.9b02978