



Faculty of Science and Engineering

Profile report: Structural Biology – Electron Microscopy

- Disciplines: Chemistry, Biology, (Bio)Physics
- Level: Assistant to Associate Professor
- Fte: Full time (1.0)

1. Scientific discipline

Structural biology is a flourishing scientific field, which not only has provided groundbreaking fundamental insight in the mechanisms of action of biological macromolecules over the past 70 years, but also is integrated in the work-flow of drug discovery in pharmaceutical companies, and more generally allows for optimization of processes in the biotechnological industry.

Over the last decade the technical developments of modern cryo-Electron Microscopes have led to an unprecedented advance in the determination of structures of proteins and complex molecular assemblies by single particle analysis, at a resolution band that in the past was almost exclusively reserved for X-ray crystallography. Particularly, this advance in cryo-EM has impacted our insight in membrane proteins or complex assemblies, for which it has been difficult to obtain structural information by other techniques. At the same time, developments in electron tomography now make it possible to directly observe protein structures in their (near) native environment, albeit at slightly lower resolution, and not as generally applicable as single particle cryo-EM analysis. Structural biology will further develop by integrating advanced approaches for single-molecule biophysics, machine learning and molecular dynamics simulation.

2. Vacancy

A position for an Assistant – Associate Professor in Structural Biology – Electron Microscopy is opened at the Faculty of Science and Engineering (FSE) of the University of Groningen (FSE reference PT/gl/22/0451) and will be embedded in the Groningen Biomolecular Sciences and Biotechnology Institute (GBB). The position will be open to applicants with a (potentially) world-leading research line in any subfield of Structural Biology and who will lead fundamental work into academic and societal applications, has a strong academic teaching experience, and has demonstrable capability in leading fundamental discoveries. The position fits well with the Faculty's strategic research themes (e.g. Molecular Life and Health) and Impact, and will strengthen the structural focus of the research institute GBB and the faculty's discipline Chemistry. The position falls within the framework of 'Career Paths in Science 4' ('Bèta's in Banen 4').

3. Selection committee

- Prof. Dirk Slotboom (Scientific Director, GBB), chair
- Prof. Dirk-Jan Scheffers (Director of Education, GBB)
- Prof. Albert Guskov (Professor in Protein X-ray Crystallography, GBB)
- Prof. Siewert-Jan Marrink (Professor in Molecular Dynamics, GBB)



- Prof. Tessa Quax (Professor in Molecular Biology Archaea and Viruses, GBB)
- Prof. Ariane Briegel (Professor in Ultrastructural Biology, University of Leiden)
- Prof. Patrick van der Wel (Professor in Solid-State NMR Spectroscopy, Zernike Institute)
- Student member (to be assigned)

Additional (external) advisors (proposed):

- Prof. Bert Poolman (GBB)
- Prof. Giovanni Maglia (Professor in Chemical Biology)
- Prof. Christine Ziegler (University of Regensburg)
- Prof. Vera Moiseenkova-Bell (University of Pennsylvania)
- Prof. Susan Lea (National Cancer Institute, US)
- Prof. Stefan Raunser (MPI Dortmund)
- Prof. Cristina Paulino (University of Heidelberg; Electron Microscopy, GBB)
- Ms. Mariska Laning (Human Resources, FSE)
- Dr. Engel G. Vrieling (Managing Director of GBB), secretary

4. Research area

In the field of structural biology, single particle cryo-electron microscopy has complemented X-ray crystallography in the structural analysis of increasingly complex molecular systems. Electron microscopy (EM) is a technique to study macromolecules, and cellular- and subcellular structures. Electron microscopy has developed enormously because of instrumental and computational innovations. The advent of direct electron detection cameras, together with ultrahigh stability of the modern microscopes, allows single-particle biomolecular complexes to be resolved at atomic resolution. Furthermore, powerful algorithms to correct for radiation-induced motion of particles and methods for image processing and classification have been developed. The attractiveness of cryo-EM for structure determination compared to X-ray crystallography is that crystals, the formation of which is a bottleneck in the structure determination of membrane proteins and complex multi-domain proteins, are no longer necessary. The method of single-particle cryo-EM has become the main tool in the determination of large complexes and membrane proteins, which are especially difficult to approach by X-ray protein crystallography. Next to single particle cryo-EM, cryo-electron tomography (cryo-ET) is a complementary electron microscopy method for structural biology application. This method allows for resolving structures in their (near) native cellular context. Although there are limitations in the applicability of cryo-ET, rapid technological advances will make the use of this technique more widespread in the near future

5. Embedding: institute (and base unit)

The position will be embedded in the institute GBB and the candidate will lead the independent research unit Electron Microscopy. The envisaged expertise of the new GBB member will make it possible to cover the teaching activities currently carried out by the group (currently coordinated by Dr. Cristina Paulino). The GBB institute



has 13 creative research units, targeting challenging biological questions in the focal areas 'Molecular Mechanisms of Biological Processes' and 'Physiology and Systems Biology'. Depending on the research focus, the newly appointed staff member will be able to connect to ongoing studies in structural biology (Profs. Siewert Jan Marrink, Dirk Slotboom, Albert Guskov), molecular enzymology and biotechnology (Prof. Marco Fraaije and Dr. Max Fürst), chemical biology (Profs. Giovanni Maglia, Bert Poolman, Gerard Roelfes, Geert van den Bogaart, Arjan Kortholt), synthetic biology (Profs. Arnold Driessen, Roel Bovenberg, Oscar Kuipers, Gert Moll, Tessa Quax and Dr. Sonja Billerbeck) and systems biology (Prof. Matthias Heinemann, Dr. Andreas Millias, Dr. Kamenz). Furthermore, the work may connect to research in the areas of chemistry, biophysics and drug development at the Stratingh Institute for Chemistry, the Zernike Institute for Advanced Materials and the Groningen Research Institute for Pharmacy, respectively. The envisioned research also directly contributes to the actions in the FSE theme Molecular Life & Health.

6. Local and (inter)national position

The Faculty of Science and Engineering, together with the research institutes GBB, Stratingh and Zernike, have established an Electron Microscopy Facility that is connected to NanoLabNL and the Netherlands Electron Microscopy Infrastructure (NEMI). These frameworks aim at boosting the Dutch electron microscopy infrastructure to the latest state of the art and to guarantee first-rate research on the structural analysis of (bio)molecules, macromolecular complexes and (soft-)materials at the highest resolution. Since the establishment of the research institute GBB in 1993, structural biology has played a central role in understanding the structure-function relationships of (membrane) proteins and complex subcellular structures at the molecular level, making use of advanced analytical approaches from single-molecule biophysics and molecular dynamics to protein crystallography and high-resolution electron microscopy (i.e. single particle analysis, electron tomography). This exciting field remains multifaceted at GBB, allowing strong internal interactions as well as those between academia and industry.

(Inter)nationally, the use of single-particle EM for structure determination is becoming more and more widespread, with leading groups in the Netherlands (incl. GBB in Groningen), Austria, Germany, Denmark, United Kingdom, Spain, Sweden and Switzerland. Some of these groups also study cellular structures by cryo-EM tomography. High-resolution structural analysis by EM requires expensive hardware. The only place in the Netherlands that currently meets the optimal hardware requirements for extensive and high-quality data acquisition is the Netherlands Centre for Electron Nanoscopy (NeCEN). The University of Groningen (via GBB) is an active partner of NeCEN and has ample access to this facility. To meet in-house capacity for electron microscopy research, a high-end electron microscope (Thermo Fisher - FEI Europe Talos Artica) equipped with a K2 direct electron detector has been acquired in 2017. This instrument operates perfectly to solve structures of protein to a resolution of ~ 2.5 Å and will provide the new staff member a workhorse to establish his/her own research in Groningen.



The fundamental biomolecular and microbial research in Groningen is very strong and links to SMEs and industry (e.g. DSM, EnzyPep, Genentech, Corbion, Avebe, Gecco Biotech, Portal Biotech) are excellent. For example, the work on biocatalysts, membrane proteins and transporters, host-microbe interactions as well as antimicrobials was boosted through public-private partnerships. Also, honorary professors R.A.L. Bovenberg (DSM) and G.N. Moll (Lanthiopharma) and spin-off companies (e.g. Lanthiopharma, Gecco Biotech, Portal Biotech, Omnicin Therapeutics) provide successful examples of bringing fundamental knowledge to application.

7. Expected contribution to research

The new staff member will conduct fundamental research resulting in publications appearing in influential internationally leading scientific journals. The research activities will contribute to the strengthening of the international position of GBB' research in structural biology as well as the research institute's activities in biomolecular sciences and biotechnology. Furthermore, the research will lead to collaborations with private parties in the life and/or biomedical sciences. Acquiring substantial external funding is vital, and it is encouraged that funding will partially come from industrial partners or investors. Supervision of PhD students is a crucial part of the research activities.

8. Expected contribution to teaching

The new staff member will contribute to the relevant teaching programs of the bachelor, master and PhD programs of the Faculty of Science and Engineering, predominantly in Biology, Life Science & Technology and Biomedical Sciences, appropriate to the career stage. The requirements for the University Teaching Qualification will have to be fulfilled.

9. Expected contribution to the organization

An active input is anticipated in order to provide a valuable contribution to the management and organizational tasks of the institute GBB and the Faculty of Science and Engineering, appropriate to the career stage. At the level of the faculty, the staff member may participate in working groups and committees in the fields of teaching, research and management. The candidate is also encouraged to participate in relevant national and international science forums.