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Max-Planck-Institut für
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DNA *in vivo* imaging

The research group of R.J. Dwayne Miller at the Max Planck Institute for the Structure and Dynamics of Matter has an opening for **1 PhD and 1 Postdoc position** to work on the *in vivo* imaging of nucleic acids with newly developed liquid phase electron microscopy. The position will be co-funded by the Canadian Institute for Advanced Research (CIFAR) and the candidate will be awarded the prestigious *CIFAR-junior fellowship*. The CIFAR Molecular Architecture of Life program connects some of the most renowned scientists in Canada and Germany in the field of structural biophysics including 2 Nobel-laureates. Regular access to the CIFAR meetings provides a unique networking opportunity to the candidates. We are looking for highly motivated individuals with a strong interest in interdisciplinary research bridging the fields of physics and biology. It is our aim to further develop liquid phase electron microscopy to resolve the structural dynamics of biological systems under *in vivo* conditions.

Ever since the invention of the electron microscope it has been a dream to record images from liquid samples similar to light microscopes. This would allow for high resolution, and structure determination over a wide range of scales without the sacrifice of dynamic information. The major obstacle to achieving this goal is the requirement that the thickness of the sample must be on the 100 nm scale to enable electron transmission with low enough scatter to maintain the required spatial resolution. Recent advances in nanofluidics have enabled control over liquid pathlengths to the prerequisite pathlengths with stability of better than 1 nm changes in pathlength for stable imaging. Liquid phase transmission electron microscopy (liquid TEM or *in situ* TEM) finally combines all these requirements: a spatial resolution up to 1 nm and a temporal resolution in the millisecond to microsecond domain are perfectly aimed at biological systems.
Thus, liquid TEM could be a game-changing development in structural biology with the ability to move beyond the limitations of traditional methods and capture dynamics of living system at the molecular level. In liquid TEM the sample species are not dried or frozen but retained in solution and are protected from the vacuum of the microscope by placing them between two thin (30-50 nm) silicon nitride (SiN) windows. The liquid films that are generated are thin enough to allow electron microscopic imaging and still keep the sample under physiological conditions. This is a major breakthrough in imaging technology for biological systems and will have tremendous impact in structural biology. We will exploit this new technology to to directly observe the dynamics of nucleic acid compaction under *in vivo* conditions. We aim to understand to what degree DNA compaction is a driven process, requiring complex molecular machinery with associated energy consumption, and to what degree does the system rely solely on entropic driving forces? Put in another way, to what extent does DNA behave as a frustrated poly-electrolyte polymer in its compaction and to what extend is net energy input needed to drive compaction and other DNA roles?

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I) A PhD-student position in structural biophysics

We aim to understand the process of viral DNA release mechanism using bacteriophages and Herpes viruses as model systems. To understand how exactly DNA is ejected into the host cells, we will record a full "molecular movie" providing insight into the causal relationship between DNA structure and its dynamical sampling leading to function.

Applicants should hold a Master's degree in structural biology, biochemistry or equivalent. Previous experience in electron microscopy or X-ray crystallography would be advantageous. The candidate will initially be guided by his/her supervisor(s) but should soon be able to plan and organize his/her daily work independently. The candidate will have the opportunity to join the International Max Planck Research School (IMPRS). Excellent verbal and written communication skills and good proficiency of English are essential.

II) A Postdoctoral Researcher with experience in single particle EM:

Chromosomes adopt a remarkably complex three-dimensional architecture. This architecture is neither random nor static but well organized and highly dynamic. Chromosomes are organized in distinct regions termed territories, which bring functional elements into spatial proximity and lead to the formation of nuclear sub-compartments. This organization is directly linked to epigenetic modifications of the chromatin fiber, which influence its structural plasticity and regulate gene activity. A long standing view of chromatin organization suggested that the 11-nm fiber is subsequently further folded up into a 30-nm fiber, which again is wound up to higher order structures in condensed mitotic chromosomes. However, the transition between the two structures, or structural intermediates, have never been observed in molecular detail and the physiological relevance of the 30-nm fiber remains controversial. Using in-liquid electron microscopy under physiological conditions, we aim to understand the dynamic structural transitions these compaction processes.

Applicants should hold a PhD in biochemistry, structural biology or related fields with experience in protein and nucleic acid biochemistry. Experience in single particle electron microscopy is essential for this position. A background in structural biology of chromatin would be advantageous. Experience in X-ray crystallography and / or molecular biology would be a bonus. The candidate should be able to plan and organize his/her research independently, and be able to interact with colleagues in an interdisciplinary research environment. Excellent verbal and written communication skills are essential. The post is available for 2 years.

Further information:

For further information about the **Miller group** please refer to:

- http://www.mpsd.mpg.de/en/research/ard/ard
- http://www.mpsd.mpg.de/62107/People
- http://www.mpsd.mpg.de/publication-search/62107?person=persons136024

For further information about the **CIFAR MAL** program please refer to:

- https://www.cifar.ca/research/molecular-architecture-of-life/

For further information about the **institute** please refer to:

- http://www.mpsd.mpg.de/en
- https://www.cfel.de/
- http://www.desy.de/

Group publications about liquid phase electron microscopy:

1. Mueller, C., Harb, M., Dwyer, J. R. & Miller, R. J. D. Nanofluidic Cells with Controlled Pathlength and Liquid Flow for Rapid, High-Resolution In Situ Imaging with Electrons. *J. Phys. Chem. Lett.* 4, 2339–2347 (2013).
2. Keskin, S. *et al.* Visualization of Multimerization and Self-Assembly of DNA-Functionalized Gold Nanoparticles Using In-Liquid Transmission Electron Microscopy. *J. Phys. Chem. Lett.* **6,** 4487–4492 (2015).

Contact information:

Interested candidates should provide a CV with publication record and arrange that 2 letters of recommendation are sent to us.

Please contact *either*:

- Prof. Dr. R.J. Dwayne Miller –dwayne.miller@mpsd.mpg.de
- Dr. Eike C. Schulz – eike.schulz@mpsd.mpg.de