Combining super-resolution polarized imaging with deep-learning to reveal the 3D orientation of individual molecules during sarcomere assembly

Host laboratories : Institut Fresnel and IBDM (Marseille, France)

Duration : 2 years

Application : https://centuri-livingsystems.org/recruitment/

Deadline for application : April 13, 2022

Supervisors :

Sophie Brasselet, Institut Fresnel : sophie.brasselet@fresnel.fr /

https://www.fresnel.fr/perso/brasselet/

Brasselet's team develops optical microscopy methods to investigate biological processes in cells and tissues, in particular how molecular organization occurs at the nanoscale.

Frank Schnorrer, IBDM : frank.schnorrer@univ-amu.fr

http://www.ibdm.univ-mrs.fr/equipe/muscle-dynamics/

Schnorrer's team investigates the biomechanics of muscle morphogenesis, particularly focusing on how the contractile apparatus develops its quasi crystalline regularity across the muscle.

The topic :

Understanding muscle development requires insight into how individual sarcomeric proteins come together to construct a sarcomere. Accessing their 3D position and orientation in muscles is however challenging. In this project, we will combine recent super resolution Single Molecule Orientation and Localization Microscopy (SMOLM) developed at I. Fresnel with novel nanobody labelling strategies and deep learning, established at IBDM, to analyse the 3D spatio-temporal conformational dynamics of key sarcomeric proteins during sarcomere assembly in Drosophila flight muscle : actin, the Z-disc protein α-actinin, muscle myosin and the gigantic titin spring. This approach will reveal when and how the different proteins acquire their high molecular order, which will provide a molecular-scale readout of conformational changes required for sarcomere assembly.

The candidate :

The candidate should be a physicist with a strong experience in optical microscopy and data analysis applied to biology. As he/she will work together with biologists and physicists in the Brasselet and Schnorrer groups, previous experience with biological samples is recommended. The candidate will be guided to label sarcomeric proteins for polarized super resolution imaging of fly muscles, and will profit from the complementary expertise of both teams. The candidate will bring his/her knowledge on data processing, data analysis and will get support to develop deep learning analysis tools.

References

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- Curcio V. et al. (2020). Nature Comm. 11 (1). doi: 10.1038/s41467-020-19064-6
- Avellaneda J. et al. (2021). MNature Comm. 12(1):2091. doi: 10.1038/s41467-021-22058-7
- Lemke S.B. et al. (2019). PLoS Biology. 17(3):e3000057. doi: 10.1371/journal.pbio.3000057