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PhD Call – 2018
Turing Centre for Living Systems

Ref offer: PHD2018-11

Muscle building: bridging molecular order to macroscopic morphogenesis

Project abstract – The morphogenesis of muscles relies on the coordinated assembly of contractile stereotyped supramolecular structures, called sarcomeres, which are both force-generating and load-bearing devices. Each sarcomere contains a pseudo-crystalline order of bipolar actin and myosin filaments, which are linked by gigantic titin molecules. During development sarcomeres assemble into long periodic chains called myofibrils that span from one muscle fiber end to the other. How sarcomeres organize into molecularly ordered structures (**molecular order**) while assembling long myofibrils (**macroscopic order**) is an unsolved question.
Recently, F Schnorrer, P-F Lenne and S Brasselet have teamed up to analyze actin order during myofibrillogenesis using polarization resolved microscopy of phalloidin-labeled fixed *Drosophila* muscles at different stages. We found that as molecular actin order increases, mechanical tension builds up in the myotube, preceding the formation of a periodic actin pattern (Loison et al, in revision). The recruited PhD-student will extend these studies to implement a live imaging approach based on polarization resolved microscopy to probe the molecular order of sarcomeric constituents in developing *Drosophila* muscles and test the role of tension for order generation. The originality of the project relies on the integration of quantitative approaches to bridge the molecular to the macroscopic scale, thus to explain how large muscle fibers build their contractile machines.
Aim 1: The PhD student will probe the molecular order during sarcomerogenesis *in vivo*. He/she will develop live probes for measuring molecular ordering of actin, muscle myosin and titin and map the ordering process locally and across myofibrils. Applying tools developed in the Schnorrer lab, he/she will also quantify tension in myofibrils at different stages of development. This will be essential to relate protein assembly, order and mechanical tension.
Aim 2: Titin is the molecular linker between actin and myosin filaments. It itself contains an extensible force-bearing element and thus is our prime candidate to test for a putative role in tension-driven myofibril self-organization. Hence, the PhD student will investigate the role of titin for actin and myosin order generation during myofibrillogenesis with the established fixed probe and extend the studies to the live probes developed in Aim 1.

Expected profile – This will be a highly collaborative PhD project amongst three groups, biologists and physicists, at the interface between both disciplines. The ideal candidates are physicists with a strong interest in imaging and quantitative biology or cell biologists with a dedicated interest to consolidate their experience in quantitative imaging approaches. Most importantly, the candidates require to bring enthusiasm for curiosity-driven basic research in a highly collaborative environment.

Supervisors
Franck Schnorrer- IBDM, UMR 7288 - Muscle Dynamics
Sophie Brasselet- Institut Fresnel, UMR 7249 - Team Mosaic
Pierre-François Lenne - IBDM, UMR 7288 - Physical approaches to cell dynamics and tissue morphogenesis

Deadline for application: 15th April 2018