Project title: Decipher the nanoscopic muscle organization with Expansion Microscopy
Type of rotation: M2 (6 months)
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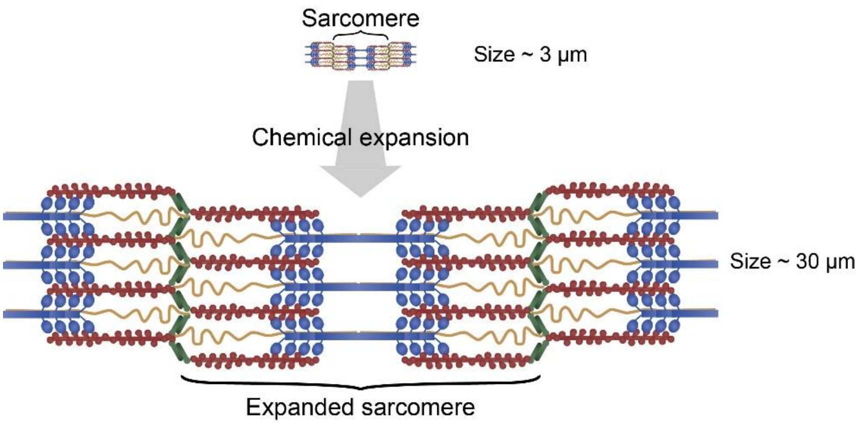

Background: Sarcomeres are the contractile units of **muscles**: tens of thousands of sarcomeres are arranged in series spanning the entire muscle length. During muscle contraction, actin and myosin filaments, the main sarcomeric components, slide along each other, producing contractile forces and shortening each sarcomere and hence the entire muscle. Tens of different proteins associate with these filaments, resulting in a very well-ordered structure that can sustain millions of contraction cycles. Even though the contraction mechanism is well characterized, the assembly of sarcomeres remains a mystery.

The main question: How do the key **sarcomeric proteins assemble highly regular sarcomeres during muscle development?**

What you will do: You will use a novel method called **Expansion Microscopy** to investigate the structure of ***Drosophila*** **muscles**. This innovative method allows super-resolution imaging down to the nanometer scale by enlarging the sample and observing it with an optical microscope. You will improve our Expansion Microscopy pipeline for *Drosophila* samples and observe filaments and key sarcomeric proteins in enlarged samples with a confocal microscope and novel nanobody labels that we are developing in our team. At a later stage of the internship, super-resolution microscopes such as Airyscan, STED, and DNA-PAINT, available in our team or our institute, will be combined with expansion to reveal intimate molecular details of the muscles.

The team: We are a multidisciplinary and multinational team, located on the Luminy campus, surrounded by the Calanques National Park on Marseille outskirts. We are experts in *Drosophila* development and genetics (Luis & Schnorrer, 2021), microscopy, image analysis, and biophysics. We have recently investigated the organization of sarcomeric proteins in *Drosophila* using the super-resolution method DNA-PAINT (Schueder et al., 2023). Several labs of our institute use Expansion Microscopy daily and we have collaborations with leading groups in the field. On top of DNA-PAINT, we have expertise in Airyscan and STED microscopy in our lab (Mangeol et al., 2024).

References

Luis, N. M., & Schnorrer, F. (2021). Mechanobiology of muscle and myofibril morphogenesis. *Cells & Development*, *168*, 203760. https://doi.org/10.1016/j.cdev.2021.203760

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Schueder, F., Mangeol, P., Chan, E. H., Rees, R., Schünemann, J., Jungmann, R., Görlich, D., & Schnorrer, F. (2023). Nanobodies combined with DNA-PAINT super-resolution reveal a staggered titin nanoarchitecture in flight muscles. *eLife*, *12*, e79344. https://doi.org/10.7554/eLife.79344