# PhD Research Proposal Form
# China Scholarship Council (CSC) - ENS Group

**FIELD:** Biology

Thesis subject title: **Deciphering the maintenance of muscle innervation by using nuclei sequencing and spatial transcriptomic technologies**

**Name of the French doctoral school : BMIC, BIOLOGIE MOLÉCULAIRE INTÉGRATIVE ET CELLULAIRE**

**Name of the Research team:** Development and function of the neuromuscular system

Website : http://igfl.ens-lyon.fr/equipes/j-enriquez-development-and-function-of-the-neuromuscular-system

**Name of the Supervisor :** : Jonathan Enriquez

Email : jonathan.enriquez@ens-lyon.fr

**Lab Language : English/French**

**Research Proposal Abstract :**

Life is constantly in motion, as the Renaissance philosopher Michel De Montaigne once said. One common behavior animals use to find food, mates, or evade predators is locomotion. In animal appendages, the morphology of muscles is key in ensuring precise movement. These muscles are innervated by a unique wiring of motoneuron axon terminals that control the timing and intensity of muscle contraction. However, how muscles and motoneurons coordinate their development to establish these unique axon-muscle connections and maintain them throughout adult life remains largely unknown.

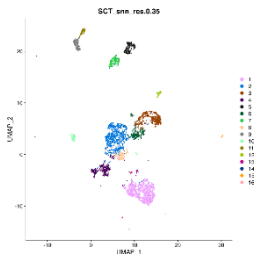
At our lab, we aim to define the genetic program controlling the development and maintenance of muscle morphologies and the axon-muscle connectome architecture in Drosophila legs at the single-cell level. To achieve our goals, we employ single-cell RNA profiling and a novel 3D spatial transcriptomic approach combined with genetic techniques to visualize and selectively modify the genotype of individual cells in a developing or adult organism. We use state-of-the-art microscopy (confocal and STED) and a unique behavioral technology (the Flywalker) to analyze the impact of these genetic manipulations on cell architecture and locomotion.

With these technologies, our research addresses three key questions:

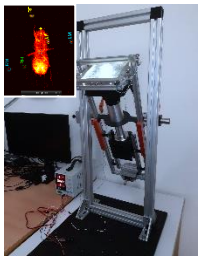
**Q1: Muscle Morphology Development** - Is there a muscle-specific program controlling the development of muscle morphology in parallel to the general program of myogenesis?

**Q2: Muscle Innervation Development** - What are the molecular and cellular mechanisms controlling the building of the axon-muscle connectome?

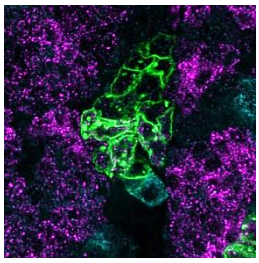
**Q3: Muscle Innervation Maintenance** - Is there a genetic program in adult motoneurons and muscles actively maintaining the architecture of the muscle innervation once it is established?



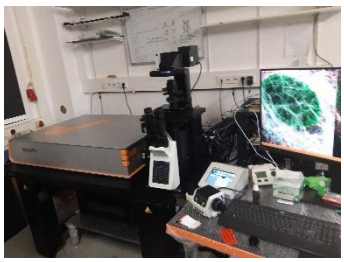
**Single cell Seq**



**Flywalker**



**smFISH/spatial transcriptomic**



**STED microscopy**

**References :**


1. Guan, W., Nie, Z., Laurençon, A., Bouchet, M., Godin, C., Kabir, C., Darnas, A., and **Enriquez, J.** (2023). The role of Imp and Syp RBPs in precise neuronal elimination by apoptosis through the regulation of TFs. eLife 12. 10.7554/eLife.91634.
2. Bouchet M., Urdy S., Guan W., Kabir C., Garvis S., **Enriquez J**. A simple smiFISH pipeline to quantify mRNA at the single-cell level in 3D. (2023). STAR Protocols. Volume 4, Issue 2, 2023, 102316.
3. Guan, W., Bellemin, S., Bouchet, M., Venkatasubramanian, L., Guillermin, C., Laurençon, A., Kabir, C., Darnas, A., Godin, C., Urdy, S., Mann, R.S., and **Enriquez, J**. (2022). Post-transcriptional regulation of transcription factor codes in immature neurons drives neuronal diversity. **Cell Rep**. *39*.

4. Babski, H., Jovanic, T., Surel. C., Yoshikawa, S., Zwart, MF., Valmier, J., Thomas, JB., **Enriquez, J.,** Carroll P, Garcès, A. (2019) A GABAergic Maf-expressing interneuron subset regulates the speed of locomotion in Drosophila. **Nat Commun**. 2019 Oct 22;10(1):4796.
5. Guan, W., Venkatasubramanian, L., Baek, M., Mann, R.S., and **Enriquez, J**. (2018). Visualize Drosophila Leg Motor Neuron Axons Through the Adult Cuticle. **corresponding author. J. Vis. Exp. JoVE**.
6. **Enriquez, J.,** Rio, L.Q., Blazeski, R., Bellemin, S., Godement, P., Mason, C., and Mann, R.S. (2018). Differing Strategies Despite Shared Lineages of Motor Neurons and Glia to Achieve Robust Development of an Adult Neuropil in Drosophila. **Co- corresponding author. Neuron** *97*, 538–554.e5. Cover article: https://www.cell.com/neuron/issue?pii=S0896-6273(17)X0004-4#fullCover
    - Hiesinger P: F1000Prime Recommendation 07 Aug 2018; 10.3410/f.732571328.793548920
    - CNRS press: https://insb.cnrs.fr/fr/cnrsinfo/construire-un-systeme-nerveux-fonctionnel
7. **Enriquez, J.,** Venkatasubramanian, L., Baek, M., Peterson, M., Aghayeva, U., and Mann, R.S. (2015). Specification of individual adult motor neuron morphologies by combinatorial transcription factor codes. **Co- corresponding author. Neuron** *86*, 955–970.
    - Drosophila image award: http://drosophila-images.org/2016
    - Highlight: Tuthill, J. (2015). A framework for fatalism in the fly. J. Exp. Biol. 218, 3349–3350.
    - Commented in a chapter book: Hobert, O. (2016). Chapter Twenty-Five - Terminal Selectors of Neuronal Identity. In Current Topics in Developmental Biology, P.M. Wassarman, ed. (Academic Press), pp. 455–475.

1.Full PhD

- Joint PhD/cotutelle (leading to a double diploma) : NO
- Regular PhD (leading to a single French diploma) : YES

2. Visiting PhD (for students enrolled at a Chinese institution who will be invited to a French institution to carry out a mobility period) : NO