Ecole Doctorale COMPLEXITE DU VIVANT – Fiche Projet CONCOURS

Fiche à nommer selon le format Nom_Prenom (sans accents ni cédilles), à enregistrer en format PDF et à renvoyer à l'adresse : edcdv@sorbonne-universite.fr

Nom et prénom du directeur de thèse (et si besoin du co-directeur) : SALECKER, Iris
Le directeur de thèse et le co-directeur doivent impérativement avoir l'HDR ou équivalent
Coordonnées Tel : ++33 (0) 1 44 32 39 80 e-mail : iris.salecker@bio.ens.psl.eu

Nom et prénom du co-encadrant (*non HdR*) (s'il y a lieu) :
Coordonnées Tel :
e-mail :

Y-a-t-il un candidat déjà identifié pour le projet: ~~OUI~~ NON

Nom et prénom du responsable de l'équipe : SALECKER, Iris

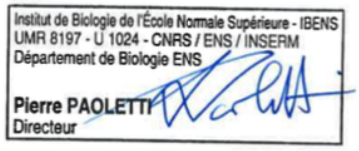
Intitulé de l'équipe : Assemblage de Circuits Visuels
Nombre de chercheurs et enseignants-chercheurs statutaires de l'équipe titulaires d'une HDR (ou équivalent) : 1

Nom et prénom du responsable d'UMR ou de département: PAOLETTI, Pierre

Intitulé et N° d'UMR ou de département : Institut de Biologie de l'École Normale Supérieure (IBENS), UMR 8197

Titre du projet de thèse *: Neurite remodeling during visual topographic map assembly*

Signature du directeur d'UMR ou de département (vaut avis favorable pour le dépôt du projet) :

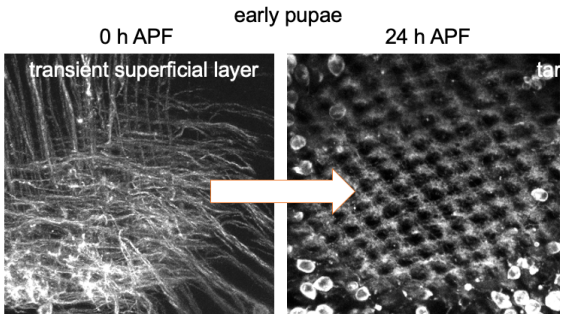


Spécialité : Biologie du Développement, Neurobiologie

Résumé du projet de thèse *(1 page maximum, en anglais)*
Pour les thèses avec 2 co-directeurs, ou en partenariat entre 2 laboratoires ou structures, indiquer la participation de chaque co-directeur et structure dans la gestion du projet.

Neurite remodeling during visual topographic map assembly

During neural circuit formation progressive events, such as branch outgrowth, pathfinding, targeting and synaptogenesis establish basic wiring patterns. However, in some developmental contexts, neuron subtypes form initially excessive branches and synaptic contacts. Regressive events then lead to the selective elimination of their branches or synapses to refine circuits by developmental neurite remodeling. In the *Drosophila* visual system, photoreceptors in the retina extend axons into the optic lobe, consisting of the lamina, medulla, lobula and lobula plate. These ganglia are structured into an array of columnar units. The medulla, lobula and lobula plate neuropils are additionally organized into parallel synaptic layers. The correct targeting of each neuron subtype to specific antero-posterior and dorso-ventral coordinates within the ganglionic neuropils is essential for retinotopic map formation. Targeting steps to columns and layers are thought to be direct, economical, and largely stereotyped. However, based on work in progress, we propose that these developmental processes coexist with more fluid programs. These rely on a distinct form of developmental neurite remodeling during columnar topographic mapping that involves the intricate dialog with two glial cell classes.



Medulla neuron subtypes undergoing neurite remodeling in the *Drosophila* visual system during early metamorphosis.

In the medulla, neural stem cells generate lineages of neuron subtypes which differ in their composition depending on their spatial position. Yet, each of the synaptic columns is innervated by the branches of a similar repertoire of neuron subtypes, requiring a plastic distribution mechanism at the level of the neuropil. While photoreceptor axons R8 and R7 axons project to a temporary layer deep within the medulla neuropil, we had observed that many medulla neuron subtypes transiently establish a neurite layer above R8 and R7 growth cones, that remarkably disappears after 24 hours of pupal development. Focusing initially on amacrine-like Dm3 neurons, single cell analysis revealed that these and many other subtypes undergo neurite remodeling during early metamorphosis that does not involve large-scale fragmentation. Moreover, following genetic manipulations of glia this superficial layer persisted, further supporting the notion that a distinct form of neurite modeling occurs. To elucidate the underlying cellular and molecular mechanisms, the thesis project will have the following objectives.

Aim 1: Dynamics of columnar topographic map formation. Using a comprehensive binary expression and intersectional toolset, involving *Gal4*/*Gal80-UAS*, *split-Gal4* and *LexA/lexAop* lines, the project will characterize the behavior of selected neuron subtypes with high resolution. It will implement a live multiphoton imaging approach in early pupae to image and quantify the dynamic aspects of the column selection process. Furthermore, it will use a conditional cell-killing strategy to test whether early-born non-remodeling medulla neurons establish a protomap for later born remodeling neurons.

Aim 2: Dialog of glia with neurons during neurite remodeling. To gain insights into the relative contributions of responsible glial cell types –medulla cortex glia, ensheathing individual neuronal somata and astrocyte-like glia, extending branches into the neuropil– the project will use correlative light and electron microscopy (TEM) in connection with membrane-bound GFP-coupled Apex2 to determine the mutual interactions between glia, and glia and neurons. Furthermore, it aims at defining the nature of neurite remodeling exploring small-scale events, including local pruning, neurite retraction via cytoskeletal alterations, axon thinning or shedding.

Aim 3: Identification of the underlying molecular mechanisms. Finally, to identify the cell-intrinsic mechanisms within neurons and extrinsic mechanisms mediating the interactions with glia, the project will test candidate genes obtained by our earlier TRAPseq analysis, using expression, as well as loss- and gain-of-function genetic manipulations.

Together, these findings will contribute to establishing the visual system as a model for studying a distinct form of neurite remodeling. This developmental process is highly disease-relevant as defects have been linked to neuropsychiatric disorders.

Faisabilité du projet de thèse (*1/2 page maximum, en anglais)*

Expliciter la faisabilité du projet en terme d'expertise de l'équipe d'accueil, des collaborations potentielles qui pourront être mises en place pour certains aspects du projet, de la disponibilité des appareils nécessaires au bon déroulement du projet...

The proposed project will be part of the longstanding efforts in our laboratory to dissect the mechanisms that control neuron-glial interactions during visual circuit assembly in *Drosophila*. Our current team, established at the IBENS in December 2019, consists currently of one PhD student, two postdoctoral fellows and the PI. It has extensive expertise in neurodevelopmental topics, including visual circuit assembly, neurogenesis, axon guidance and glial biology. The team is part of our highly interactive Section of Developmental Biology at the IBENS with a focus on neurobiology, providing contextual and technical feedback for our studies. The project is based on our earlier characterization of neurite remodeling in the visual system at the Francis Crick Institute, London, UK, facilitating the start of this project. It will provide training in advanced molecular biology and genetics approaches, including Crispr/Cas9 technology, as well as microdissections, immunolabeling and imaging of fixed and live tissue using confocal and multiphoton microscopy imaging. All basic technologies have been implemented in our laboratory at the IBENS, which includes a fly room with three fly stations, a stock room, and a food kitchen set-up. The laboratory is furthermore equipped with all instruments to conduct molecular biology and biochemistry experiments, an injection set-up to generate transgenic lines, and dissection and fluorescence microscopes for sample preparation and imaging. Finally, the team has access to an independent Leica SP5 laser confocal microscope and, within the imaging platforms of the IBENS, to a multiphoton microscope and electron microscope for high resolution imaging studies. The Fablab platform will provide invaluable support for building devices that enable live imaging of *Drosophila* pupal brains.

Thèses actuellement en cours dans l'équipe

Tous les encadrements doivent être indiqués (y compris les co-directions avec un autre HDR pour des doctorants d'une autre ED, et les encadrements dans le cadre de programmes doctoraux tels qu'IPV, FDV...)

Nom et Prénom du doctorant	Directeur(s) de thèse	Année de 1ère inscription	ED	Financement
BOSCOLO, Erica	SALECKER, Iris	2021	CdV	Labex startup/UK transition funding

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Trois publications récentes du directeur de thèse (du co-directeur ou du co-encadrant s'il y a lieu). Mettre en gras le nom du directeur de thèse.

1. Apitz, H., and **Salecker, I.** (2016) Retinal determination genes coordinate neuroepithelial specification and neurogenesis modes in the *Drosophila* optic lobe. Development *143*, 2431-2442.
   ISSN: 1477-9129; doi: 10.1242/dev.135004
2. Richier, B., de Miguel Vijandi, C., Mackenzen, S., and **Salecker, I.** (2017) Lapsyn controls branch extension and positioning of astrocyte-like glia in the *Drosophila* optic lobe. Nature Communications *8,* 317
   ISSN: 2041-1723; doi: 10.1038/s41467-017-00384-z
3. Apitz, H., and **Salecker, I.** (2018) Spatio-temporal relays control layer identity of direction-selective neuron subtypes in *Drosophila*. Nature Communications *9*, 2295
   ISSN: 2041-1723; doi: 10.1038/s41467-018-04592-z

Docteurs encadrés par le directeur de thèse ayant soutenu entre la date de dépôt de ce dossier et il y a 5 ans et publications relatives à leur sujet de thèse. Mettre en gras le nom du directeur de thèse et celui du docteur.

1. Nom Prénom : POWELL, Emma — Date de soutenance : 25/10/2019
   Durée de thèse (en mois) : 48 mois (soumission)
   Ecole Doctorale : Francis Crick Institute/KCL, London

Publications :
- **Powell, E.L.** and **Salecker, I.** (2020) Flybow to dissect circuit assembly in the *Drosophila* brain – an update. Methods Mol. Biol. *2047,* 137-152.
- Manuscrit sur le projet de thèse est en train d'être préparé

2. Nom Prénom : DOLAN, Kathleen — Date de soutenance : 15/02/2018
   Durée de thèse (en mois) : 51 mois (soumission, 3 mois extension à cause du déménagement de l'équipe du MRC-NIMR au Francis Crick Institute à Londres)
   Ecole Doctorale : NIMR/Crick/UCL

Publications :
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