2021-11-30

EuReCa International PhD Program

PhD thesis project

2022 Call for application

Control of two antagonistic cellular phenotypes with a single molecule

General information

Call	2022
Reference	2022-05-COPPEY
Keyword(s)	Optogenetics; Cell migration; Polariy; RhoA; Modeling

Director(s) and team

Thesis director(s)	Mathieu Coppey
Research team	Light-based Observation and Control of Cellular Organization
Research department	UMR168 - Physico-Chimie Curie Lab

Description of the PhD thesis project

The LOCCO (Light-based Observation and Control of Cellular Organization) Team is composed of physicists and biologists tackling biological questions. We use quantitative live cell imaging together with precise spatiotemporal optogenetic perturbations to understand how protein dynamics - such as transport and reaction - ensure cellular order and functions. We are covering multiple scales, from transient molecular assemblies to cell migration and polarity, and even up to multicellular systems.

In the context of the EuReCa 2022 call, we propose a PhD subject on 'paradoxical signaling' in cell migration. The ability of cells to migrate is a fundamental biological process, implied in numerous situation such as cancer. Cells move thank to a balance between contraction and extension of their body which is finely orchestrated by a set of small proteins, the RhoGTPases. Among these, RhoA has a mysterious role: it has been shown that this protein is active both in contracting regions of the cell and in extending ones. How can the same protein be involved in two opposite processes? To answer this question, we propose to use optogenetics to activate RhoA with a spatial and temporal control in single cells. We know from preliminary experiments that we can indeed induce the two phenotypes with the same protein, but we are looking for the quantitative rules that dictate the choice.

Understanding how such signals can encode two distinct decisions would be transformative to explain how cells compute and answer to spatiotemporal signals, how they coordinate their molecular activities to migrate and how we can prevent cancer cells migration when RhoA is deregulated.

International, interdisciplinary & intersectoral aspects of the project

The project is at the interface between physics and biology: it combines cutting-edge experimental tools to manipulate protein activities and live cell microscopy with advanced quantitative analysis and modeling. The student will be integrated to the very active international community of 'quantitative optogenetics' and will benefits from short lab exchanges with foreign collaborators in Switzerland and USA. The development of the experimental setup will lead to innovative solutions in the field of active microscopy, where the setup is engineered to respond specifically to predefined biological events in real time thanks to image-based feedback routines. We expect that these solutions, such as cell active tracking and local activation, will be of interest for a large community of users.

Recent publications

1. "Persistent cell migration emerges from a coupling between protrusion dynamics and polarized trafficking", Vaidžiulytė K, Macé AM, Battistella A, Beng W, Schauer K, **Coppey M**; bioRxiv, 2021.

2. "Parallelized manipulation of adherent living cells by magnetic nanoparticles-mediated forces", Bongaerts M, Aizel K, Secret E, Jan A, Nahar T, Raudzus F, Neumann S, Telling N, Heumann R, Siaugue JM, Ménager C, Fresnais J, Villard C, El Haj A, Piehler J, Gates MA, **Coppey M**; International Journal of Molecular Sciences, 2020.

3. "Optogenetic dissection of Rac1 and Cdc42 gradient shaping", de Beco S, Vaidžiulytė K, Manzi J, Dalier F, di Federico F, Cornilleau G, Dahan M, **Coppey M**; Nature Communications, 2018.

4. "Non-specific interactions govern cytosolic diffusion of nanosized objects in mammalian cells", Etoc F, Balloul E, Vicario C, Normanno D, Liße D, Sittner A, Piehler J, Dahan M, **Coppey M**; Nature Materials, 2018.

5. Gradients of Rac1 nanoclusters support spatial patterns of Rac1 signaling, Remorino A, De Beco S, Cayrac F, Di Federico F, Cornilleau G, Gautreau A, Parrini MC, Masson JB, Dahan M, **Coppey M**; Cell Reports, 2017.

Expected profile of the candidate

Applicants should have a background in physics or math and be highly motivated to work in biology. We expect a solid knowledge of a computing language such as Matlab or Python for image analysis, modeling, and microscope control. The applicant should know some basics about fluorescence microscopy, molecular and cell biology, cell signaling, or be strongly motivated to learn them. Given the diversity of tasks (cell culture, transfection, microscopy, computer routines, mathematical modeling), we are looking for a resourceful applicant willing to learn.