Laboratoire de Physico-Chimie Curie,
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M2 thesis internship proposal

Desynchronizing Cellular Oscillators Through Microfluidics-based Steep Temperature Gradients in a living animal

Start Date: January 2026, **Duration:** 6 months, Follow-up PhD thesis possible

Internship project description

Temperature impacts all biochemical reactions inside a cell. For developing multicellular organisms, temperature fluctuations pose challenges because morphogenetic events depend on both, spatially and temporally coordinated cellular decisions. Despite this, most multicellular systems show a surprising degree of robustness with respect to temperature changes within certain temperature limits. With climate change pushing organisms more and more often towards those limits, it is important to understand how those limits are set, what molecular mechanisms coordinate overall development of an organism and whether there are ways to control these mechanisms.

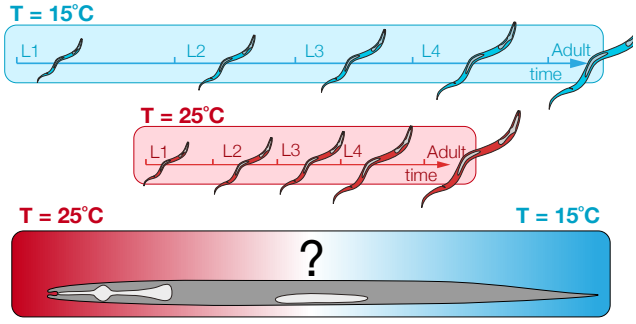

Figure 1. Graphical illustration of the main project idea. The *C. elegans* larva robustly develops through the four larval stages (L1-L4), almost twice as fast at 25°C compared to 15°C. The goal of the project is to uncover mechanisms that enable this adaptivity of development, by challenging *C. elegans* with a linear temperature gradient and observing gene expression dynamics in the hypodermis before, during, and after perturbation.

To address this question, our team has developed a new experimental setup, that allows us to place a small (1mm long) multicellular model organism (the nematode roundworm *C. elegans*) in a **linear temperature gradient during its larval development** (Fig. 1). In our setup, the anterior part (head) of the animal can be maintained at either warmer or colder temperatures compared to the posterior part of the animal while high-resolution live-imaging is performed for several days. Surprisingly, animals develop normally in these extreme conditions, suggesting intercellular and interorgan signaling to achieve and maintain developmental coordination (Schlang et al., in preparation). Similar temperature gradient experiments have been performed with embryos of fruitflies (Lucchetta et al., *Nature* 2005) and frogs (Anderson et al, *Cell Reports* 2017), but gave strikingly different results, implying novel molecular mechanism underlying developmental synchrony during the post-embryonic phase of animal development.

The goal of this internship is to better understand how individual gene expression programs in animals respond to temperature gradients. The student will focus on genes in *C. elegans* whose expression has been shown to oscillate during larval development (Fig. 2). The dynamics of these genes provides ideal readouts (amplitude change, phase shift etc.) to quantify the response of individual cells across the organism.

The student will perform spinning-disc confocal live-microscopy of animals kept in microfluidics device, and analyze various gene expression and cell division synchrony with and without the temperature gradient and how this may be changing in various genetic backgrounds. Additionally, our team has recently developed technologies that allow us to visualize and analyze transcription dynamics in developing larva in real-time using the MS2-MCP-GFP tethering system (Kinney & Sahu et al. 2023). The

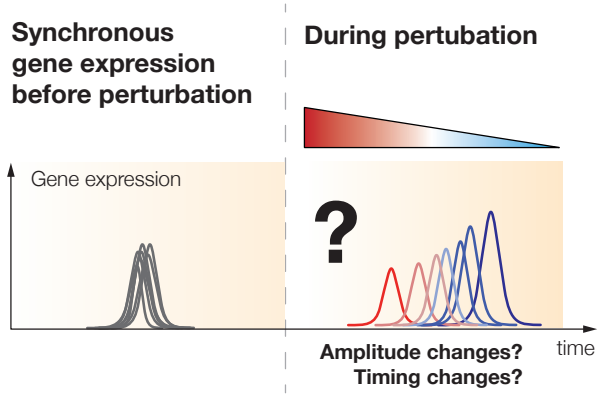

Figure 2. Potential scenarios for the impact of temperature gradients on synchronous oscillatory gene expression during *C. elegans* larval development.

student will use this system to ask whether and how transcriptional kinetics of developmental genes are affected at different temperatures and how the temperature gradient condition impacts these kinetics.

Requirements

Candidates for this internship should have a strong motivation for interdisciplinary research at the interface between bioengineering, microfluidics, physics, and developmental biology. Experience in live-microscopy or microfluidics with biological systems is a plus. Most importantly, the student should demonstrate a passion to see and study life in action. For details, please contact wolfgang.keil@curie.fr.

Environment

The Keil lab at Institut Curie in Paris uses an interdisciplinary strategy to study transcriptional regulation, cell-fate patterning and morphogenesis in the model organism *C. elegans*. We are particularly interested in how developing system achieve robustness and precision in the face of environmental variability and molecular noise. To tackle this question, we develop and apply novel techniques for obtaining quantitative high-resolution dynamic gene expression data. We also develop theoretical approaches to conceptualize mechanisms of development and uncover general principles of developmental patterning.

Our lab is located at the Institut Pierre-Gille de Genes (IPGG), an institute in the heart of Paris dedicated to microfluidics and its applications. The institute hosts a cutting-edge cleanroom facility allowing for *in-house* micro- and nano-fabrication. Check out https://curie.fr/equipe/keil for more information and feel free to contact us directly.

The Research Center at Institut Curie is a major player in the field of cancer research. It comprises a Hospital and a Research Center with over 1000 employees covering a wide range of nationalities. The Curie Institute Research Center aims to develop opened-ended science to progress in knowledge while exploiting arising possibilities to improve cancer care by stimulating synergies between research, training and innovation to support patients and serve our society.

Project references

Dynamics of Drosophila embryonic patterning network perturbed in space and time using microfluidics. Nature (2005) Lucchetta et al. https://doi.org/10.1038/nature03509

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