

(Document edited the 29th of May 2020)

These two internship offers are for Master students (or equivalent), who have trainings in cellular and molecular biology and ideally some basic knowledge in microscopy.

The two complementary projects aim to **understand the function of the mitotic spindle**, in particular in chromosome segregation, and **how the cell adapts to chromosomal defects** using the nematode *Caenorhabditis elegans* as a model organism.

One project will study the contribution of external forces of the mitotic spindle (subject # 1), and the other that of its internal mechanics (subject # 2).

The 2 internships will be carried out within the Rennes Institute of Genetics and Development (IGDR, Univ. Rennes 1, UMR-CNRS 6290), and more specifically in the CeDRE team "Reverse Engineering of the Cell Division".

Host team research project:

Our team – which has the peculiarity of being an interdisciplinary team made up of specialists in biology, physics, image analysis and statistics – **studies cell division using a biophysical approach**. For this, we use the first division of the *C. elegans* one-cell embryo, which is an asymmetric, very dynamic and reproducible division. We aim to **understand the robustness of cell division** by studying and modeling the biophysical and mechanical interactions between the molecular actors of mitosis, which are microtubules and their regulators, as well as the molecular motors.

Context of the studies :

Our previous work allows us to have **readouts of the forces positioning the mitotic spindle, which are resolved in time and space**. These external forces are generated by the astral microtubules, which in contact with the periphery of the cell (called cortex) can continue to grow and generate pushing forces, or else be captured by cortical force generators and generate pulling forces. This tool will be **used to question the role of external forces in the proper functioning of the mitotic spindle (subject # 1)**.

In addition, we are able to have the **mechanical signature of the mitotic spindle** by studying its small variations in length, and have highlighted a spindle drifting over time. The forces it undergoes are not balanced. This could explain its adaptability to internal disturbances (eg chromosome attachment errors). This tool will be used **to identify whether changes in the spindle mechanics take place during genetic disturbances targeting the robustness of the division (subject # 2)**.

Thus, these two tools allow us to study cell division from two points of view: external and internal to the mitotic spindle. We also have the capacity to study the functioning of the mitotic spindle **in two situations of chromosomal aberrations**.

Indeed, we have the **possibility of generating chromosome attachment defects** of the merotelic type (approach by RNAi or by thermosensitive AurB mutant) and of looking at their possible resolution. We also have a **tetraploid strain** (with double number of chromosomes). These defects have been identified as intermediates towards aneuploidy, a recognized marker of cancer cells.

Goals of the internships :

We aim to **highlight (subject # 1) the role of the external forces of the mitotic spindle and (subject # 2) the contribution of the internal mechanics of the mitotic spindle, to its proper functioning**, in particular the correct partitioning of the sister chromatids. We will also **investigate a**

possible adaptation (subject # 1) of the forces external to the mitotic spindle and (subject # 2) of its mechanics in these perturbed conditions (merotely and tetraploidy).

Tasks to be carried out:

During his/her internship, the student will perform three major tasks:

- (1) **acquisition of movies** of embryos during cell division by fluorescence microscopy (subject # 1: acquisitions to visualize microtubule contacts at the cortex; subjects # 1 & 2: acquisitions at the median plane to visualize the poles of the mitotic spindle, or with double fluorescent labellings the spindle poles and the chromosomes; and subject # 2: acquisitions using the airyscan to visualize the distribution of the chromosomes with high spatial resolution),
- (2) **depletion by a targeted approach** (RNAi or mutant) of actors regulating the forces external to the mitotic spindle, or its mechanics,
- (3) **the analysis of images and data** generating by microscopy acquisitions using tools developed within the host team to characterize the forces external to the spindle and its mechanical behavior.

This internship will allow the student to acquire skills in breeding, dissection and image acquisition on living samples (*C. elegans* nematode), in fluorescence microscopy (spinning disc microscopy, large-field microscopy and superresolution microscopy), in cell biology, and in image and data analysis. It will also contribute to **improving his/her English and teamwork skills**.

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Website of the team and institute: <http://pecreaux.openwetware.org/> and <https://igdr.univ-rennes1.fr/en/cedre-lab>

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