

Is chromosome segregation robust under mechanical pressure?

Context

Errors in chromosome segregation during mitosis lead to aneuploidy (an abnormal number of chromosomes), which has deleterious or even lethal consequences for eukaryotic cells. In the yeast *S. cerevisiae*, aneuploidy is very often synonymous with growth defects¹; in humans, it contributes to cancer progression by promoting the emergence of advantageous or resistant clones². The fidelity of chromosomal segregation is therefore crucial for cells; however, the mitotic process is sensitive to the forces experienced by cells³.

Most cells proliferate in a confined environment, in both physiological and pathological conditions⁴. Confined proliferation leads to the development of a mechanical, growth-induced, compressive stress, which is relevant to many pathologies such as cancer. How mitosis fares under mechanical pressure is still unknown, in particular when it comes to chromosome segregation and potential mechanically-driven aneuploidy.

We propose to study the fidelity of chromosomal segregation under mechanical pressure in the fission yeast *Schizosaccharomyces pombe*. This unicellular eukaryote is an excellent model for studying mitosis: it is easy to culture, has only three chromosomes in the haploid state, and divides symmetrically along the cell axis. Thanks to a strain carrying a minichromosome whose loss results in a red pigmentation detectable at the colony scale⁵, we have already shown that a hyperosmotic shock does not impair the fidelity of chromosomal segregation in *S. pombe*.

Objectives of this internship

The objective of this internship is to carry out this same investigation on yeast mechanically confined. To do this, we have a microfluidic chip that allows confinement of the yeast while maintaining a circulation of fresh nutrient medium. The student will participate in developing the experimental strategy (testing the device, refining the protocol, defining controls) within a quantitative exploratory rather than mechanistic approach to mitotic robustness. They will conduct the experiments and interpret the results.

How to postulate

For this essentially experimental internship, we are primarily looking for a candidate with knowledge in cell biology and/or microfluidic, imaging. The candidate must have a strong will to work at the interface between physics and biology. The student will be trained in microbe cell culture and imaging, as well as microfabrication principles.

For more information or to apply, please send your motivation letter and a CV to nnguyen@laas.fr and morgan.delarue@laas.fr.

1. Pavelka, N. *et al.* Aneuploidy confers quantitative proteome changes and phenotypic variation in budding yeast. (2010). doi:10.1038/nature09529
2. Li, R. & Zhu, J. Effects of aneuploidy on cell behaviour and function. *Nat. Rev. Mol. Cell Biol.* 2022 234 **23**, 250–265 (2022).
3. Fink, J. *et al.* External forces control mitotic spindle positioning. *Nat. Cell Biol.* 2011 137 **13**, 771–778 (2011).
4. M. Delarue. Spatial confinement and life under pressure: From Physiology to Pathology *Nature Biological Physics and Mechanics* (2025).
5. Niwa, O. Determination of the frequency of minichromosome loss to assess chromosome stability in fission yeast. *Cold Spring Harb. Protoc.* **2018**, 216–219 (2018).