Studying the role of mechanical cues in biological pattern formation and regeneration

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Level : M2/PhD

Scientific context

Regeneration is a fascinating biological phenomenon by which some organisms spontaneously reform missing tissues or organs. From a physics point of view, regeneration can be seen as a self-organized morphogenetic process relying on the *de novo* apparition of patterns and large scale cell migration in which forces felt by the cells play important roles.

In recent years, our understanding of biological pattern formation has been transformed. It has been demonstrated that mechanical properties can directly influence the differentiation of stem cells[1] or the patterning of whole organisms[2]. A modern investigation of regeneration thus requires an interdisciplinary approach taking into account both mechanical aspects and genetic pathways[3].

In this project, **we will use *Hydra vulgaris* as a model organism to study this question of the mechanical regulation of biological patterning**. Hydras are freshwater polyps with unique regenerative capacities. Any tissue piece excised from an organism regrows into a functional adult. Furthermore, a suspension of dissociated Hydra cells is also capable of self-organizing back to a normal morphology[4] (Fig 1). To decipher mechano-genetic interactions, we will develop microfluidics tools to constrain regenerating Hydras, observe possible defects in regeneration and study how the mechanical perturbations affected the expression of key patterning genes.

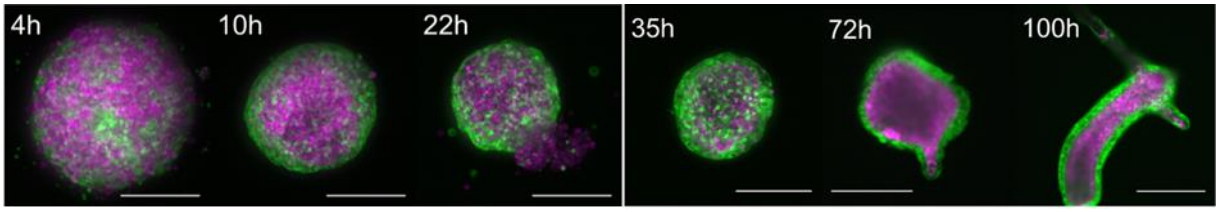

Fig 1. ***Timelapse of Hydra regeneration*** *from a cellular aggregate. The two main tissues are shown in green and magenta. Scale: 200μm up to 72h, 500μm at 100h.*

Missions

Hydra care: The student will learn how to maintain, grow and use *Hydra* populations for experiments.

Microfluidics: The student will use micro-milling and microfabrication techniques to develop new constriction chambers (Fig 2) to streamline the experiments. This work will be done in the clean room of the Institut des Nanotechnologies de Lyon (INL) and in collaboration with the LAAS, Toulouse.

Microscopy: Fluorescence, brightfield and spinning disk microscopy will be used to image the reaction of the sample to mechanical perturbations on time scales of 1-2 days.

Molecular biology: The student will be exposed to molecular biology techniques (cloning, RNA interference, in situ hybridization, gene editing) allowing to observe the response of the organism at the molecular scale to understand patterning defects.

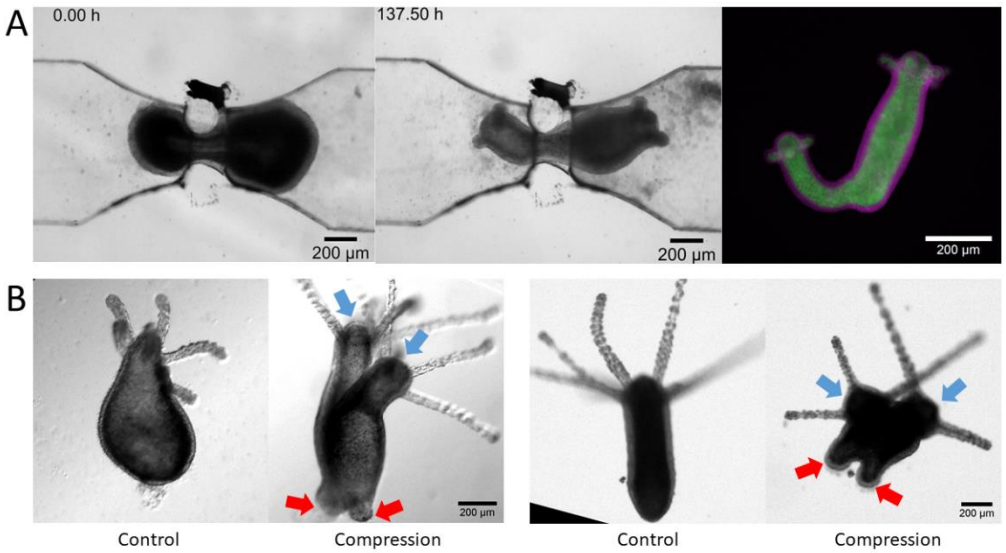

Fig 2. ***Preliminary experiments on microfluidics****. A: Microsystem for mechanical perturbations of regenerating Hydras. Final state is shown on the right and displays patterning defects. B: Example of patterning defects obtained after mechanical compressions, red/blue arrows show ectopic feet/heads being regenerated after compression, bars: 200µm.*

Outlook

Possibility to apply for PhD funding through doctoral schools and foundations.

Bibliography

1. Discher, D. E., Janmey, P. & Wang, Y.-L. Tissue cells feel and respond to the stiffness of their substrate. *Science* **310**, 1139–43 (2005).

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3. Chiou, K. & Collins, E.-M. S. Why we need mechanics to understand animal regeneration. *Dev. Biol.* **433**, 155–165 (2018).

4. Cochet-Escartin, O., Locke, T. T., Shi, W. H., Steele, R. E. & Collins, E.-M. S. Physical Mechanisms Driving Cell Sorting in Hydra. *Biophys. J.* **113**, 2827–2841 (2017).