ANR-funded PhD position

Forward and inverse modeling of cleavage patterning in early embryos

Deadline: February 1st 2024

Application: CV, letter of motivation & 2 letters of recommendation to herve.turlier@college-de-france.fr

Place: Collège de France
Center for Interdisciplinary Research in Biology
11, place Marcelin Berthelot, 75005 Paris

Team: *Multiscale Physics of Morphogenesis* www.turlierlab.com

Supervision: Hervé Turlier, team leader herve.turlier@college-de-france.fr

Duration: 36 months, from Mar/Apr 2024

Salary: between € 2,100 gross monthly

Activities: The project will consist in exploring how cell divisions spatiotemporally sculpt embryo's shape from a biophysical and computational perspective. The research will combine biophysical and computational modeling, inverse modeling and deep-learning. It will therefore leverage methods from various fields and will develop highly transversal skills. It will be conducted in tight collaborations with developmental biologists specialists of mouse [**1**] and ascidian embryos [**2**]. The work will rely on powerful models of multicellular mechanics [**1**] as well as convolutional neural networks recently developed in the team. It will involve both forward modeling and data-driven approaches, including the development of novel approaches to infer biophysical model parameters from images using neural networks. The research activities will be funded by an ANR grant and are part of a larger ERC DeepEmbryo project led by Hervé Turlier, whose goal is to reverse-engineer the development of embryos by combining biophysical and machine learning methods.

Missions: The successful candidate will design a generic and differentiable biophysical model of cell division patterning in early embryos and tissues [**3**] (**Fig.1a**). The model will be used both to explore how combinations of polarity cues, geometric constraints and mechanical stress may spatiotemporally control cleavage patterning in a cell assembly (**Fig.1b**). The differentiable model will be coded in Python and C++ and will be used to explore self-organisation and shape emergence upon specified division rules but also to infer known or new division rules from time-lapse imaging data of embryo development (**Fig.1c**). The combination of forward & inverse modeling approaches will allow us training neural networks on realistic simulated data before extending our methodology to real data. The selected candidate will have to work in collaboration with biologists and with the team's software engineer. She/he will have to present her/his results at scientific conferences, write scientific articles and actively participate in the scientific and social life of the team and of the host Institute.

Expected profile: The candidate must hold a Master in physics, computer science or applied mathematics and should demonstrate excellent computer science skills (python, C++). Prior experience with deep learning or optimisation methods will be a strong asset. No prior knowledge of biology is expected, but a genuine interest in biological systems and morphogenesis is necessary. Prior experience of collaboration with biologists or biophysicists will be considered very positively. Genuine work autonomy, initiative and scientific curiosity are key assets for this position. Fluency in English, good communication skills and motivation for research are naturally expected.

Working environment: The successful candidate will be welcomed into the interdisciplinary team "Multiscale physics of morphogenesis" led by Hervé Turlier and composed of ~10 researchers. We are committed to establishing a welcoming place for all and fostering inclusion and diversity. The team is located at the Collège de France, in the heart of the Latin Quarter in Paris. Integrated within the PSL University, and close to other major institutions such as the Ecole Normale Supérieure and the Institut Curie, the Collège de France constitutes an exceptional scientific environment unique in the world. The successful candidate will have access at an individual workstation in renovated premises, to a powerful laptop and to a high performance computing cluster fully dedicated to the team (12 GPUs, 396CPUs). The position does not pose any particular constraints or risks and 1 day of teleworking is possible per week.

For enquiries please contact Dr. Hervé Turlier - herve.turlier@college-de-france.fr

[**1**] Maître, Turlier et al. ***Nature*** 2016
[**2**] Ichbiah et al. ***Nature Methods*** 2023
[**3**] Rosfelter et al. **bioRxiv**, 2023-03.
[**4**] Ichbiah, Delbary & Turlier ***arXiv*** 2023

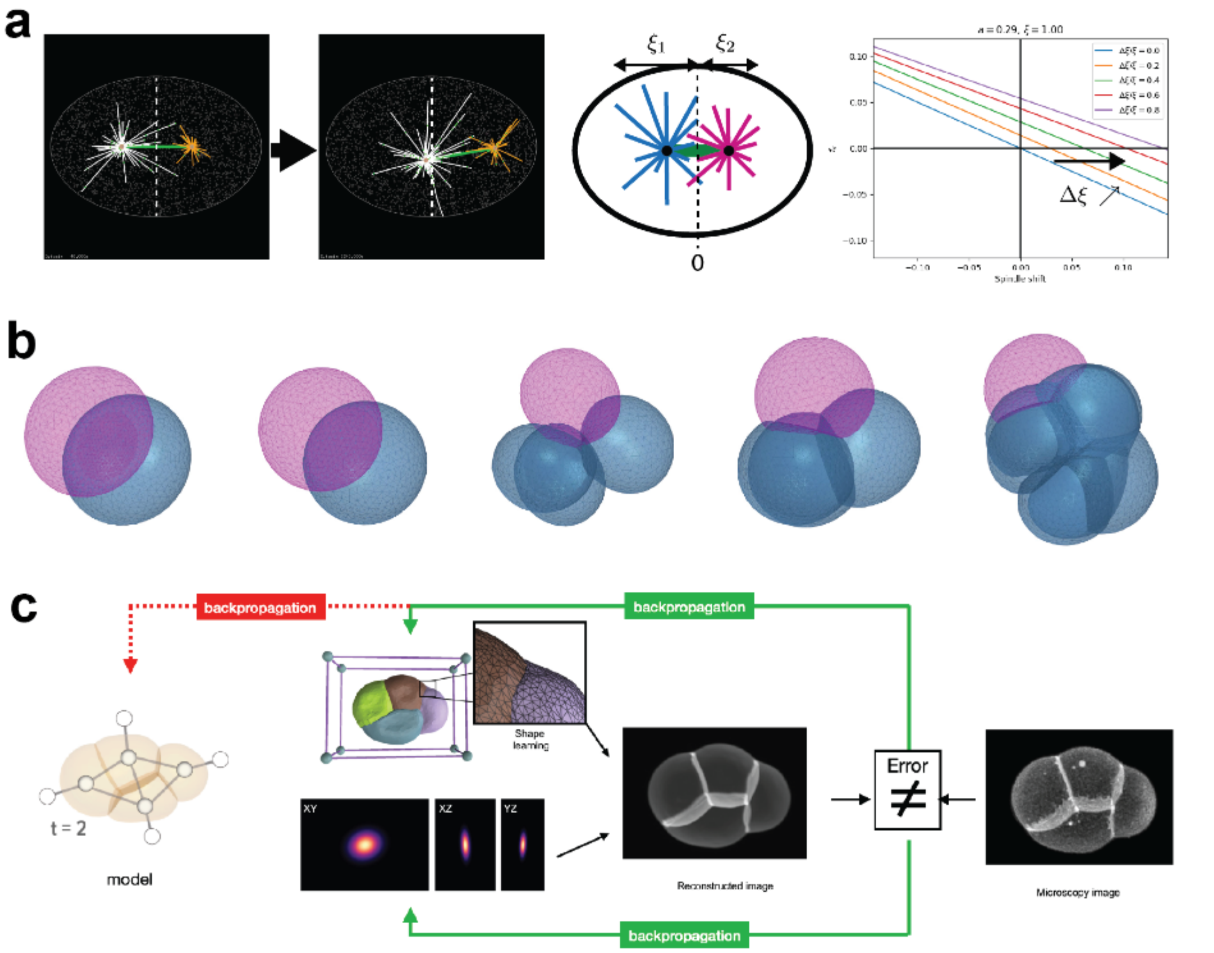

Figure 1: **a**) Computational (agent-based) and analytical models of the positioning in a single cell of the mitotic spindle, that defines the future division plane. The two models consistently predict an off-centering upon asymmetry of aster sizes in the spindle. **b**) 3D computational mechanical model of a multicellular aggregate with dividing cells. Here the division planes are randomly chosen, but one goal is to implement models such as in **a**) in this multicellular context and to account for cells geometry, surface stresses and polarity domains as various cues to control division patterning and, as a consequence, the emergence of a given structure. **c**) Differentiable fluorescence microscopy image generation pipeline allowing to optimise directly the shape of individual cells given a true microscopy image, and that may be extended to optimise a mechanical model including a parameterised model for cell divisions.