INTERNSHIP PROPOSAL

Laboratory name: Laboratoire Interdisciplinaire des Energies de Demain
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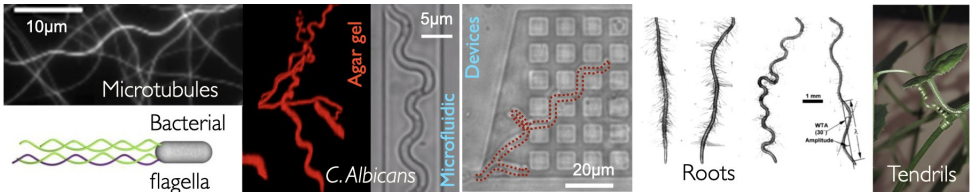
Internship location: LIED
Thesis possibility after internship: YES
Funding: YES - Type of funding: ANR



Title: Deciphering Decision Making and Path Finding in Helical Pathogens

Helical morphologies are found everywhere in nature. They are observed at different scales, from molecular to macroscopic structures, giving them great biological and ecological relevance. Described by Darwin in aerial and underground parts of plants as early as the 19th century, fundamental questions remain as to their roles and underlying mechanisms.

We have recently observed in the dimorphic yeast *Candida albicans*[1] - a benign member of the human microbiota which can turn into one of the most deadly opportunistic fungal pathogen - helical, coiled or wavy filamentous growth modalities as specific adaptative responses to environmental cues. *C. albicans* thus provides a relevant model system for the study of the oscillatory geometries of life from a fundamental standpoint with possible relevance for fungal pathologies. Overall, our observations are in line with the squeelix ("squeezed helix") concept developed by Kulic et al., based on an interplay between bending and twisting energies of filaments[2].

We are looking for an M2 student, with the possibility of continuing the work into a PhD thesis as part of the ANR-funded HELPATH (HELical PATHogen, 2024-2027) project, to uncover the mechanisms leading to oscillations. The internship project is interdisciplinary by nature and will be co-supervized by two biophysicists, Catherine Villard, (Laboratoire Interdisciplinaire des Energies de Demain, Paris) and Igor Kulić (Institut Charles Sadron, Strasbourg).

The M2 project will combine experimental and modeling approaches, with the emphasis on experiments. It will therefore be based in Paris, with eventually short stays in Strasbourg.
The experimental part includes cell biology, time-lapse experiments to follow the dynamics of hyphal growth, and microfluidics to constrain and probe hypha pathfinding through the use of controlled micro-environments. An exciting first step will be to explore the intriguing and biophysically still mysterious phenomenon of hypha directional memory, consisting of hypha remembering an initial growth direction over long distances within micro-mazes. In connection with medical issues brought in HELPATH by our collaborator at Institut Pasteur, we will use this tool to sort strains of different virulence according to their directional memory - reflected by transition probability matrices - with the idea that this score might eventually become a statistical predictor of virulence.
The modeling part will consist of helping in the development of imaging and analytic tools (ImageJ/Python/Matlab) for hyphal oscillatory time evolution and the critical testing of biophysical models that will be developed to explain the observed behavior.

[1] *C. albicans* displays two morphotypes, i.e. a budding yeast form and multicellular cylindrical filamentous morphology named hypha

[2] Nam, G. M., Lee, N. K., Mohrbach, H., Johner, A., and Kulić, I. M. (2012). Helices at interfaces. Europhysics Letters, 100(2), 28001.