Spindle orientation in the developing fly embryo: a joint mathematical-experimental approach

Supervisory team:
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Project description:
Despite decades of research, the very earliest stages of animal development are still not well understood. Some of the most fascinating unsolved questions are related to cellular symmetry breaking. How do cells formed from the first few divisions of the fertilised egg orientate themselves? How is cell orientation influenced by the neighbouring cells? And what happens when cell orientation goes wrong?

To answer such questions, it is important to first start with relatively simple cases. For this reason, the organism of choice for this field is the fruit fly, Drosophila. Its rapid life cycle and existence of transgenic flies expressing fluorescent proteins important in cell division make it possible to see exactly how cells are orientated and to follow this in real time.

Traditionally, problems like this have been tackled with a purely experimental approach. However, much quicker progress can often be made if instead mathematical modelling is intimately combined with experiments. This is the exciting program you will follow during this PhD.

You will use a multidisciplinary approach that combines mathematical modelling, computer simulations, light sheet microscopy and image analysis. This will allow you to learn a wide range of different skills and techniques, ideal for a future career in academia or elsewhere. You are not expected to already know both mathematical modelling and wet-lab techniques; full training will be provided in both areas during the PhD.

In particular, during this project, you will:

1. Design a three-dimensional mathematical model of mitotic spindle orientation. This will be based on the famous Ising model of interacting spins from physics. These models will be simulated and analysed using MATLAB and/or C++.
2. Use our brand new, state-of-the-art light sheet microscope to obtain images of the developing Drosophila embryo.
3. Develop image analysis software to automatically extract the spindle orientation. This will then be able to inform both the mathematical modelling in part 1 and the experiments in part 2.
4. Apply the model to the oriented cell divisions of the Drosophila larval testes niche.

This interplay between experiment and modelling is a key part of this project and will make for a truly exciting PhD.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.