Orienting cell division in the developing fly embryo: a joint mathematical-experimental approach

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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 is the fruit fly, *Drosophila melanogaster*. Its rapid life cycle makes 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 be made if 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 high resolution microscopy and image analysis, mathematical modelling and computer simulation. 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. Use state-of-the-art, light microscopes (including spinning disc and light sheet) to obtain time-lapse movies of cell division in the germ line stem cell precursors in the developing early *Drosophila* embryo.

2. Develop image analysis software to automatically extract the spindle orientation. This

will then inform both the mathematical modelling in part 1 and the experiments in part 3.

3. Design a 3D mathematical model of mitotic spindle orientation based on the famous

Ising model of interacting spins. This will be simulated using MATLAB and/or C++.

4. Test and apply the model to other oriented stem cell divisions in *Drosophila*, iterating the model where necessary.