Fast and slow processes in honey bee population dynamics, bifurcation and population sustainability.

World-wide, bee keepers and scientists are concerned about the loss of honey bee hives. Colony-collapse disorder, where a hive becomes deserted by adult bees, leaving food behind, is the most widely publicized of these.

I have recently submitted a paper, together with colleagues at Macquarie University on the changing age of foragers in honeybee colonies and the impact that this has on the viability of the hive. The modelling in this paper shows that there are some variables (stored food, age of foragers) that change slowly but others (honey bee population) that can change rapidly once certain thresholds in the slow variables are reached.

This project will start from the complicated realistic models in the submitted manuscript, simplify them, non-dimensionalise them and then analyse them using perturbation theory and phase plane analysis to obtain a comprehensive understanding of the equations and the underlying processes in honey bee population dynamics.

This project will suit someone who enjoys working with systems of nonlinear ODE's, including stability analyses, sketching phase planes, bifurcation analyses, and generating numerical solutions.

Modelling the formation of necrotic cores in atherosclerotic plaques.

Atherosclerotic plaques form when low density lipoproteins, LDL ("bad cholesterol") permeates the artery wall. This sets up an immune reaction which leads to macrophages (a type of white blood cell) invading the blood vessel wall and engulfing the LDL. These macrophages become filled up with lipids and are then known as foam cells. The foam cells are eventually poisoned by the LDL that they consume and die. When they die, they rupture and release free lipids and release free lipids and cellular debris inside the blood vessel wall. This debris and lipid accummulation forms a fatty bubble in the artery wall that is called the necrotic core of the plaque. If the necrotic core ruptures, it releases its contents into the artery and this may cause blockages in the coronary arteries, leading to a heart attack.

This project will create and analyse an ODE model for necrotic core formation which includes the populations of macrophages, foam cells and the density of free lipids. The project has the potential to be expanded to look at other sorts of models, based on reaction-diffusion equations or McKendrick-von Foerster equations, for example.

This project will suit someone who likes untangling complicated biological processes with mathematical models and enjoys numerical computation, both with existing software and using their own code. This project has potential to lead into a PhD project which may attract a top-up scholarship.

Modelling the role of HDL (good cholesterol) in early atherosclerosis.

Atherosclerosis (the formation of fatty plaques inside the walls of major arteries) is a chronic inflammatory disease. It has similarities to other inflammatory diseases such as osteoarthritis, type 1 diabetes and chronic tendonitis, but it is silent and develops with few warning signs until an atherosclerotic plaque ruptures and causes a heart attack or stroke. In this project we focus on modelling events that occur in the early formation of atherosclerotic plaques.

In the blood vessel wall the endothelium separates the innermost layer, the intima, from the blood stream in the lumen. Beneath the intima lies the muscular media layer. LDL ("bad cholestrerol") penetrates the endothelium at places where there is low shear stress on the blood vessel wall, such as at artery junctions and bends. On entering the intima, the LDL becomes modified by oxidants and prompts the production of MCP-1, a chemoattractant for monocytes, a type of immune cell. The injured endothelium also produces adhesion molecules. Monocytes stick to the endothelium, are drawn into the intima by chemotaxis and differentiate into macrophages, which seek out and ingest modLDL. LDL-filled macrophages become immotile foam cells. High-density lipoproteins, or HDL ("good cholesterol") accept cholesterol from foam cells and carry it out of the intima.

We have already analysed a model for this process which has five PDEs with associated boundary conditions. (One of the major distinctive characteristics of the model is the way that the boundary

conditions drive what happens in the domain.) This model does not include HDL. We know that the system reaches a quasi-steady state where only foam cell population is changing and bifurcation analysis of this steady state using the software package AUTO shows that there are interesting and biologically relevant fold bifurcations. We would like to add HDL to the model and see how this will change the bifurcation behaviour and reduce plaque formation or encourage plaque regression.

In particular, there is scope to examine how endothelial permeability affects the effectiveness of HDL in plaque regression. This bit of work is inspired by experiments currently taking place at the heart research institute in Newtown on the effects of age on the action of HDL.

This project will suit someone who likes untangling complicated biological processes with mathematical models and enjoys numerical computation, both with existing software and using their own code. This project has potential to lead into a PhD project which may attract a top-up scholarship.

Differential equation models for symbiotically interacting clones in early carcinogenesis

The most common model of carcinogensis is *lineal evolution* where a single clone acquires a series of successive mutations to become malignant. In this model, the primary ecological interaction is *competition.* In this project we will model carcinogensis that is caused by *inter-clonal cooperativity*
where two mutated clones interact *symbiotically* with one another, either via the cells' microenvironment or via cell-autonomous effects. The resulting tumour contains both cell types and both are needed for the tumour to be malignant.

We currently have a detailed individual-oriented simulation of this system, but recently Hugh Ford, an undergraduate intern, devised an ODE model for two interacting clones and showed that it is possible for them to stably co-exist.

This project includes the complete analysis of the ODE system and then extending the model to include spatial movement which will produce a system of PDEs. These may be able to be analysed using travelling wave coordinates to describe the spread of the cancerous clones.

This project will suit someone who likes working with both nonlinear ODEs and parabolic PDEs, inlcuidng phase plane and bifurcation analysis, is happy to find numerical solutions and enjoys relating the results of modelling back to the underlying science.

Ordinary differential equations, honey bee hive loss and toxic forage.

World-wide, bee keepers and scientists are concerned about the loss of honey bee hives.
Colony-collapse disorder, where a hive becomes deserted by adult bees, leaving food behind, is the most widely publicized but there are more general problems with the health of hives, that can lead to colony death in other ways.

This project will create and examine mathematical models for the population dynamics of a hive that is foraging on a nectar source that contain honey bee toxins such as pesticides. The model will be based on similar ideas to the models for hive populations dynamics of Khoury et al, (2011, PLoS One, **6**: e18491; 2013, PLoS One, **8**: e59084) and the foraging models of Cox and Myerscough (2003, Journal of Theoretical Biology, **223**: 179-197). The aim of the modelling is to explore how intermittently toxic food sources (such as flowering crops that are periodically sprayed with insecticide) can impact on hive health and what factors determine when this type of environmental toxicity leads to hive death.

This project will suit someone who enjoys working with systems of nonlinear ODE's, including stability analyses, sketching phase planes, bifurcation analyses, and generating numerical solutions, and creating mathematical models for an biological system.