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Title: Modelling dorsal closure process of the fruit fly via coupled ODEs
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Development of the fruit fly's embryo has been extensively studied by the biologists. Among the stages of morphogenesis, dorsal closure involves dynamic signalling between various proteins and is important to the development of dorsal cells. This project aims to describe the dynamics of between the signalling proteins during the dorsal closure via coupled ODE system.

The prototype model developed via MATLAB establishes the structure of the dorsal amnioserosa tissue as 81 hexagonal cells, shown as Figure 1 below. Each cell consists of 12 mechanical springs, 6 edges and 6 spokes. The mechanical behaviour of all the springs is governed by the force ODE equations (Figure 2), with the force on spokes dynamically influenced by amount of protein myosin, via the myosin and signalling ODE equations (Figure 3). By decreasing the rest length of the mechanical springs over time, the prototype model artificially achieves cell constriction in agreement with experimental observation of the phase transition during dorsal closure.
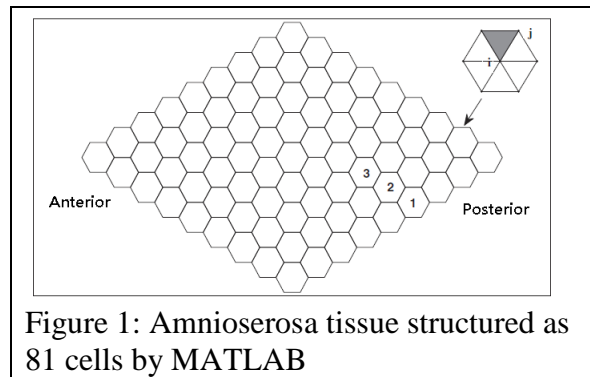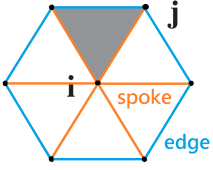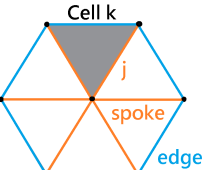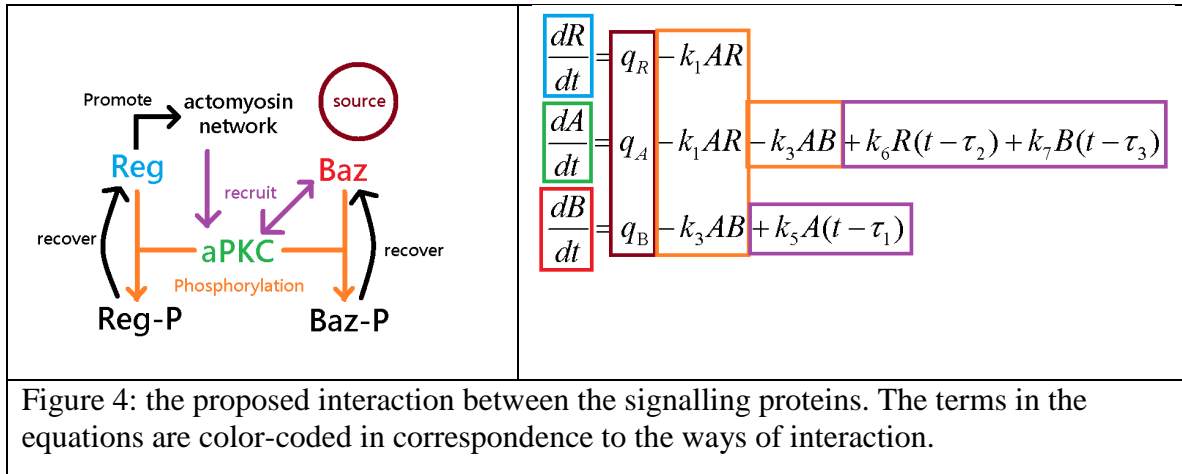

Figure 1: Amnioserosa tissue structured as 81 cells by MATLAB

Figure 2: Force equation for all edges and spokes		Figure 3: Myosin and signalling equation for spokes (in prototype model)	
	For each node i with adjacent nodes j $$f_{ij} = \mu\left(l_{ij} - l_{0ij}\right) + \beta m_{ij}$$ $$\eta\frac{d\boldsymbol{x}_i}{dt} = \boldsymbol{f}_i$$ $$\boldsymbol{f}_i = \sum_j f_{ij}\frac{\boldsymbol{x}_j - \boldsymbol{x}_i}{\left|\boldsymbol{x}_j - \boldsymbol{x}_i\right|}$$		For each spoke j in cell k $$\frac{dm_{kj}}{dt} = k^+ s_k h_{kj} - k^- m_{kj}$$ $$k^- = k_1\, e^{-k_2\left[\mu\left(l_{kj} - l_{0kj}\right) + \beta m_{kj}\right]}$$ $$\frac{ds_k}{dt} = q - k_0 M_k$$

However, we wish to accomplish a more natural phase transition without explicit mechanical manipulation. To improve upon the prototype model, this project expands the signalling equation by considering other signalling proteins--- Regulator, aPKC, and Bazooka as extra variables in the system. The dynamic interaction between the signalling proteins is examined in details, with the proposed equations illustrated by Figure 4 below.

Figure 4: the proposed interaction between the signalling proteins. The terms in the equations are color-coded in correspondence to the ways of interaction.

The introduction of delay in the recruitment terms plays an important role to result in oscillation in protein levels, as well as the cell area in early phase of dorsal closure. The presence of delay makes biological sense since the time scale for protein recruitments is significantly longer than spontaneous phosphorylation (consumption) between proteins. When we periodically decrease the delays, oscillation is successfully arrested, and all protein signals and cell areas reach a final steady-state value. Although decrease in delay can be attributed to cell contraction in the late phase of dorsal closure, further investigation is required to resolve potential chicken-egg reasoning.

All results were produced via MATLAB; while the prototype model used ode45 solver, the new model applies dde23 solver to accommodate for the delay terms. Running time is within few minutes for a simplified 4-cell tissue, up to several hours for the 81-cell tissue.

The main unresolved difficulty is to achieve cell contraction for the late stage of dorsal closure, with valid biological justification. One potential idea is to eliminate passive elasticity, with a fixed tissue boundary for early stage oscillation, and released boundary at late stage so that all spokes contract without spatial restriction. Another thought is to model the spokes and edges as asymmetric spring, of which only contraction is allowed. It is potential to encompass both ideas.