



BUILDING A BETTER MODEL OF FRUIT FLY WING DEVELOPMENT

Rick Dilling
 CTMS Graduate Fellow (summer 2010)
 Advisors: Fred Nijhout (Biology), Tom Witelski (Mathematics)

The fruit fly, *Drosophila melanogaster*, is one of the most important model organisms used in biology. One of the ways fruit flies are being used is to determine the genetic and environmental factors that specify when the various parts, such as the wings, should stop growing so that their sizes are in correct proportion to the whole organism to allow them to function properly. One approach to studying fly wings has been to use the wealth of available empirical data to construct mathematical models of their growth. This is important not only to biologists who study normal growth and development but also to those who study cancer (abnormal growth) and evolution (driven by changes in development) because it allows us to use *in silico* manipulations to make *in vivo* and *in vitro* predictions. Unfortunately, none of the existing models takes into account the fact that wing growth is controlled by gene networks on two axes of development (anterior/posterior and dorsal/ventral) (see Fig. 1) that both feed into a common mechanism.

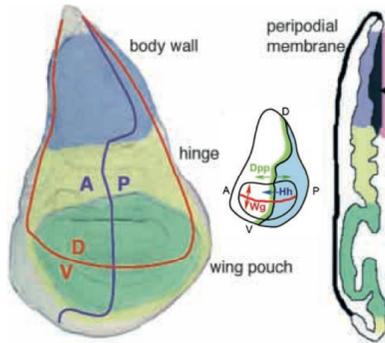


Fig. 1: A developing fruit fly wing (face-on and in cross-section) showing the two axes of development and the primary genes that are associated with them (from Butler *et al.* 2003, Crickmore and Mann 2008).

The distribution of genes being expressed in the growing wing can be modeled as a reaction/diffusion system with an added function, $\mathbf{a}(\mathbf{x},t)$, which represents how fast the different parts of the wing expand as it grows:

$$\frac{\partial c}{\partial t} = D\nabla_{\mathbf{x}}^2 c + R(c) - c \operatorname{div}_{\mathbf{x}} \mathbf{a}$$

We use another function, $\mathbf{\Gamma}(\mathbf{X},t)$, to find where each part of the wing grows to from its original position, \mathbf{X} , so that

$$\mathbf{x} = \mathbf{\Gamma}(\mathbf{X},t) \text{ and } \mathbf{a}(\mathbf{X},t) = \frac{\partial \mathbf{\Gamma}}{\partial t}$$

tell us, at time t , where each part of the wing has grown to and how fast and in what direction it will grow from there, respectively. How the different parts of the wing grow is specified by the Jacobian matrix $S = \partial \mathbf{a} / \partial \mathbf{x}$. The elements of S specify how different parts of the wing are growing (or shrinking) relative to their neighbors. Since the elements of S are themselves determined by either the absolute level or the slope of the level of gene expression (see Fig. 2), then we can solve for $\mathbf{\Gamma}$ by solving the following differential equation:

$$\frac{\partial}{\partial t} \left(\frac{\partial \mathbf{\Gamma}}{\partial \mathbf{X}} \right) = S \frac{\partial \mathbf{\Gamma}}{\partial \mathbf{X}}$$

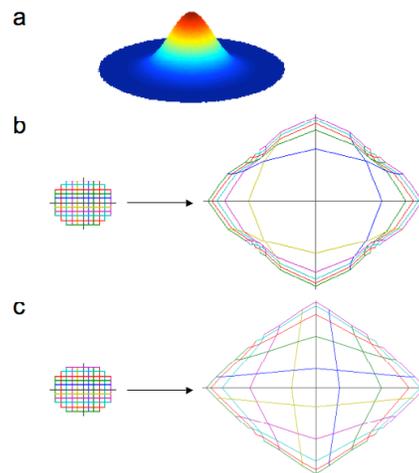


Fig. 2: (a) The level of expression in the growing wing of a gene controlling growth. (b) How the wing grows if the absolute level of gene expression determines growth. (c) How the wing grows if the gradient/slope of the level of gene expression determines growth.

Future work on this model will incorporate more genes in the reaction/diffusion system so that a more realistic S matrix can be constructed and the model can be verified against experimental data.