Modeling the Arrest of Tissue Growth in Epithelia

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Short Abstract — **The mechanisms of growth control in tissues has received considerable attention, both experimentally and through quantitative models. In particular, the Drosophila wing disc appears to arrive robustly at a unique final size. Mechanical feedback from stresses induced by nonuniform growth has been experimentally implicated in growth arrest. Several computational models with different forms of this feedback have been proposed. We introduce an analytic framework that places different feedback mechanisms on compatible terms. This framework shows that only certain classes of models actually encode a unique final size. We estimate the size variability that arises without a unique fixed point.**

Keywords — **Growth control, mechanics, modeling, imaginal disc**

I. Background

THE arrest of tissue growth is a problem that any growth control system must be able to solve, and the mechanisms of growth control of any given system will determine how robust it is to different kinds of perturbation. If the control of growth in a tissue appears remarkably precise or robust this deserves a detailed explanation.

One example of such a tissue is the wing imaginal disk of *Drosophila*. Most growth occurs during the larval period, suggesting that adult wing size is largely determined at this stage. The two wings of a wildtype fly typically differ in area by less than 1%. While it is possible that some of this precision is due to non-disk-autonomous feedback processes, studies of wing disk dissected from a larva then grown and cultured in the abdomen of an adult fly [4] suggest a significant level of disk autonomous precision. These disks achieved the same size as the original disk to within 10%-20% error despite the dramatically different growth conditions and environment. This indicates that the final size of the disk is encoded in the growth control dynamics of the disk, at least to some extent.

There have been numerous efforts to model the dynamics of growth control in this tissue that focus on a broad range of possible mechanisms. One popular class of models, which will be our focus here, involves mechanical feedback. Among other classes of models, models that rely on

positional information encoded in cells currently lack a molecular foundation, and models that rely on cells' detecting time variation in morphogen concentrations are known not to have unique final sizes [5].

II. Models

We focus for this work on two models that have been presented, which we denote the "pressure threshold" model and the "compression gradient" model.

A. Pressure threshold model

The pressure threshold model, presented in different forms in [2,3], involves a central area where the growth occurs, with the outer area not contributing to the growth. This central area is constricted by the non-growing tissue and stops growing when the pressure from the non-growing tissue exceeds some threshold.

B. Compression gradient model

In the compression gradient model [6] a central area still grows with negative feedback but the other area of the disk grows with negative feedback from pressure and positive feedback from pressure gradients.

III. Conclusion

We find that the pressure threshold model does not encode a unique final size for the wing imaginal disk and is therefore susceptible to overgrowth in the event of removal of tissue (although it is relatively robust to transient variations in model parameters). We find that the compression gradient model does encode a unique final size for the wing imaginal disk.

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