From Genes to Organisms *via* the Cell

Modeling Biological Growth in Plant Science and Biomedicine

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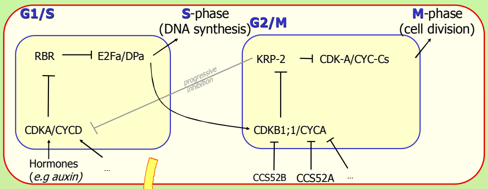
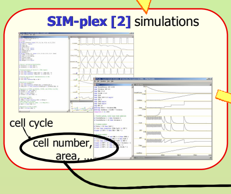
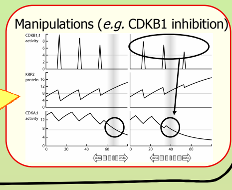
Now that the DNA sequences of many crop species and biomedically relevant animals are available, we are ready for the next challenge:
how does the genetic code control the dynamic mechanisms leading to biological form and function?

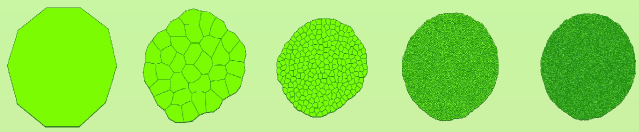
Single cell modeling



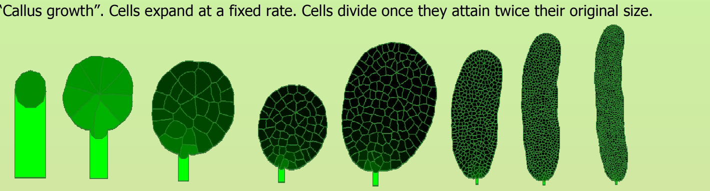




Plant tissue modeling



"Callus growth". Cells expand at a fixed rate. Cells divide once they attain twice their original size.



"Meristematic growth". Leaf stalk secretes decaying plant hormone; the expansion rate is proportional to the concentration of the hormone. Cells divide once they attain twice their original size.

A deterministic model of the plant cell cycle predicts single-cell parameters, including cell expansion and division rates.

Cell wall

The cell as the central actor of morphogenesis

To understand how the linear information in the DNA describes three-dimensional growth and form, it helps to look at multicellular organisms as huge, highly organized colonies of individual cells; each of the organisms' myriad cells contains an identical copy of DNA orchestrating the cells behavior depending on signals from the neighboring cells. Thus we can distinguish two questions [1]:

1. How do genes regulate cell behavior, and
2. How do those strictly regulated, collective cell behaviors (*e.g.* patterned cell divisions, cell expansion, cell shape changes) drive biological development?

Thus to evaluate the mechanism behind a knock-out phenotype, we would characterize 1) how it affects *cell behavior* (*e.g.* faster or slower cell division), and 2) test how these cell behavioral changes affect morphogenesis.

A better understanding of the mechanisms controlling growth and form, will helps us to more specifically **improve crop yield** or to better **control blood vessel growth**.

plant / animal

plant / animal

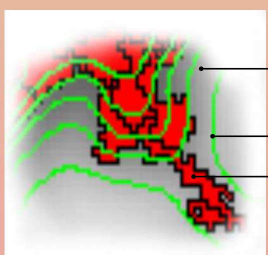
Pseudopods

A stochastic model of plant cell mechanics predicts growth and form of plant tissues depending on single-cell parameters, including cell division rates, mechanical properties of the cell wall and response to plant hormones.

***In vitro* observations and literature data give behavioral rules for endothelial cells (blood vessel cells), including response of filopodia to chemoattractants (*e.g.* VEGF)**

A stochastic model of animal cell mechanics (Glazier and Graner's Cellular Potts Model [1]) predicts the collective behavior of cell clusters (pattern formation) depending on single cell behavioral parameters, including cell shape, chemotaxis and secretion of chemoattractants.

Observations of cell behavior



Grey-scale indicates chemoattractant concentration

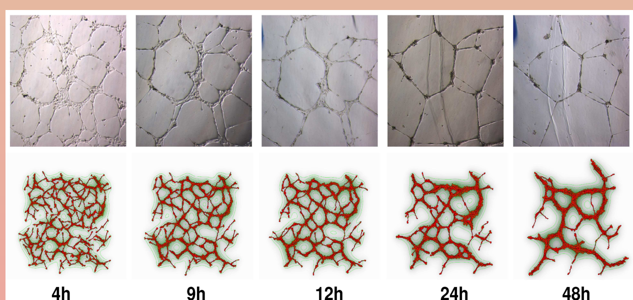
chemoattractant concentration isoline

Endothelial cell

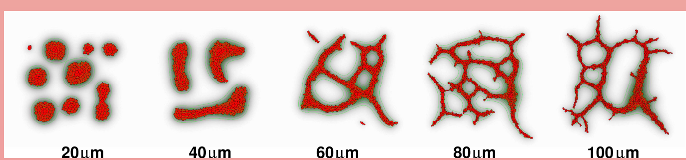
Endothelial cells
- Probe environment with filopodia
- Secrete chemoattractants
- Preferentially extend filopodia towards chemoattractant, and consequently move up gradients
- Have an elongated shape

Chemoattractant
- Diffuses through extracellular matrix
- Degrades rapidly in ECM

In silico cell culture experiments



Manipulating cell shape



References

[1] Merks, R.M.H. and Glazier, J.A. A cell-centered approach to developmental biology. *Phys. A*, 2005, 352, 113-130.

[2] Vercruysse, S. and Kuiper, M. Simulating genetic networks made easy: network construction with simple building blocks. *Bioinformatics*, 2005, 21, 269-271.

[3] Merks, R.M.H., Brodsky, S.V., Goligorksy, M.S., Newman, S.A, and Glazier, J.A. Cell elongation is key to in silico replication of in vitro vasculogenesis and subsequent remodeling. *Dev. Biol.,*2006, 289, 44-54.

Acknowledgments

This project is funded by a Marie Curie Intra-european Fellowship to Roeland Merks (LeafMorphoSim). R. Merks carried out the biomedical simulations at the Biocomplexity Institute, Indiana University Bloomington, USA with Prof. James Glazier.

MARIE CURIE ACTIONS