Mathematical Cell Biology Graduate Summer Course

University of British Columbia, May 1-31, 2012

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An excitable contractile cell (Odell, Oster et al 1980)

mprime

PIMS

www.math.ubc.ca/~keshet/MCB2012/

Combined mechanical and chemical system

A contractile band of microfilaments and a chemical switch

A Mechanical Model for Epithelial Morphogenesis

G. Odell*, G. Oster, B. Burnside, and P. Alberch

J. Math. Biology 9, 291 – 295 (1980)

The Mechanical Basis of Morphogenesis

I. Epithelial Folding and Invagination

G. M. ODELL,[1] G. OSTER, P. ALBERCH, AND B. BURNSIDE

DEVELOPMENTAL BIOLOGY 85, 446–462 (1981)

See also: Oster, Odell, Alberch (1980) Mechanics, Morphogenesis and Evolution, Lectures on Mathematics in the Life Sciences Vol 13: 165-255
(Published by AMS)

Problem:

- How do local cell shape changes lead to overall morphogenetic changes in an embryo?

Cell sheet

Shape changes in cell sheet

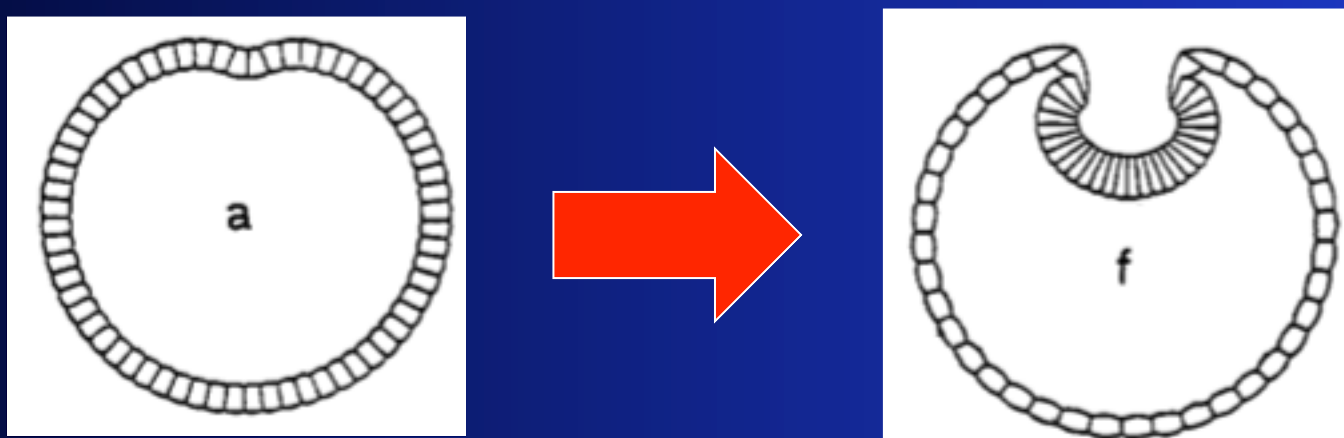


Fig 11 in: Oster et al (1980) Lectures on Mathematics in the Life Sciences Vol 13: 165-255

Local shape changes

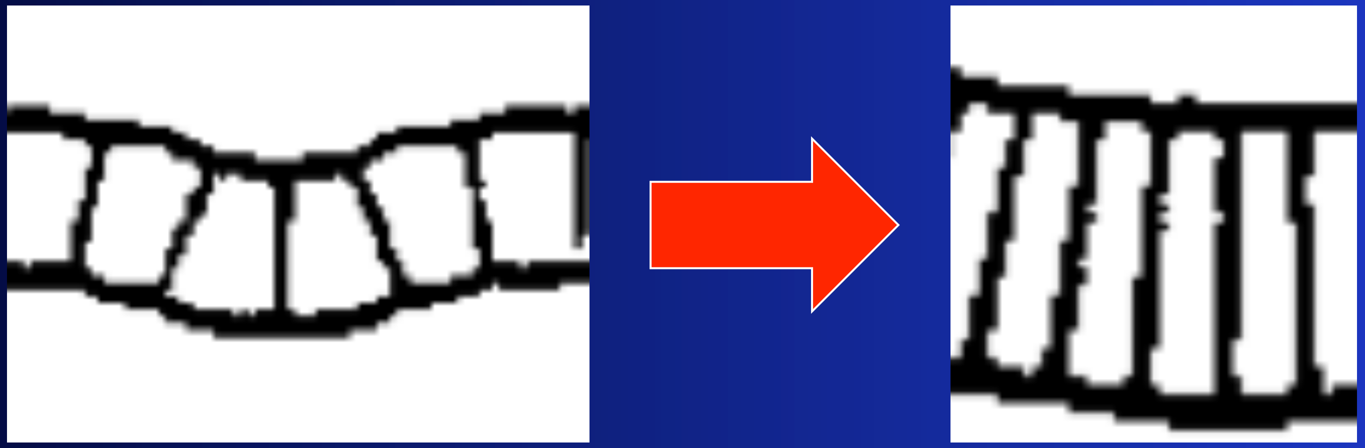
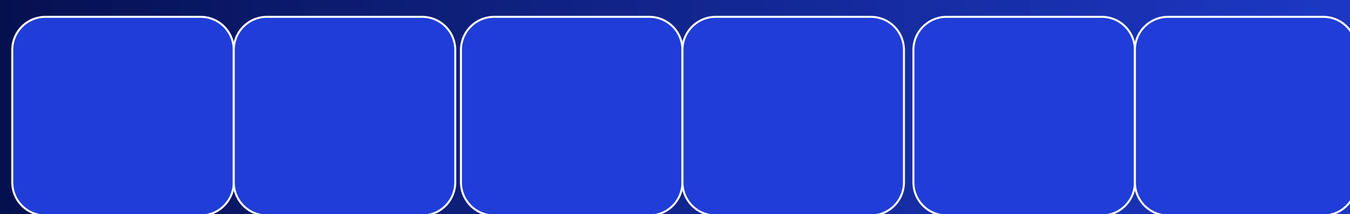


Fig 11 in: Oster et al (1980) Lectures on Mathematics in the Life Sciences Vol 13: 165-255

Assumptions

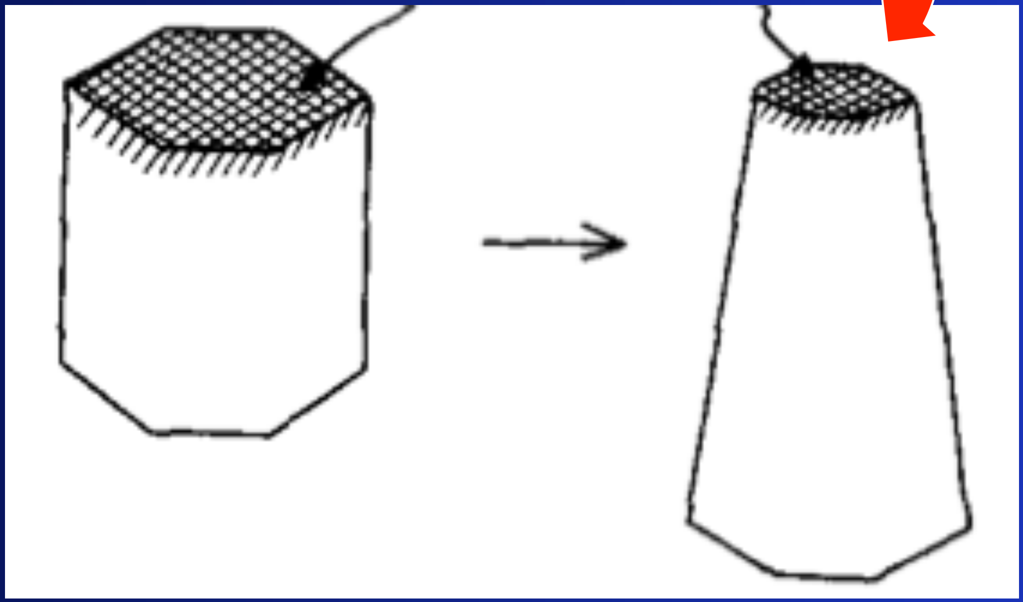
- Cells are attached to their neighbors



Cell sheet

Top surface has contractile fibers

- Apical filament bundle



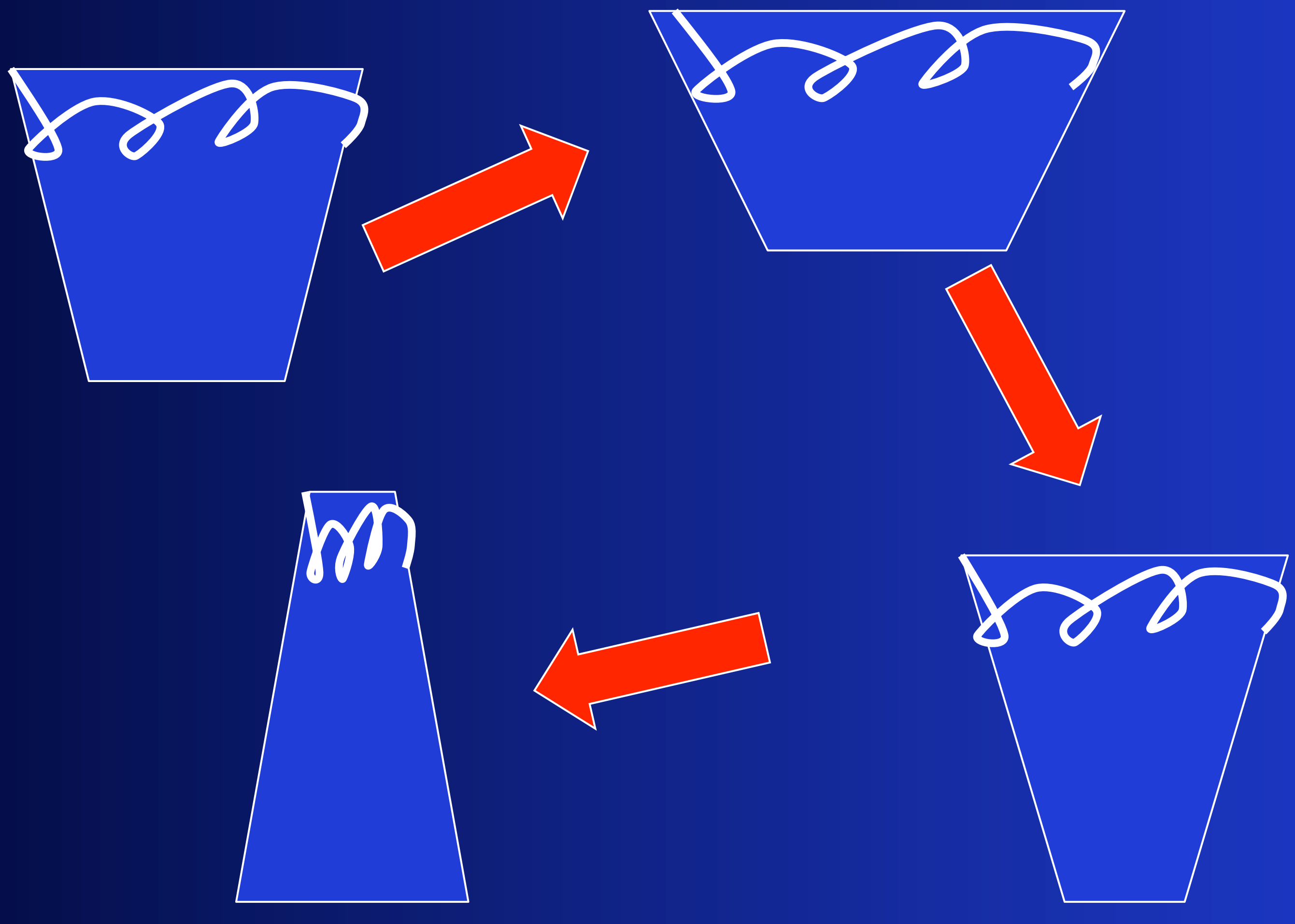
Cell volume is preserved

Cytoplasm acts like viscoelastic solid

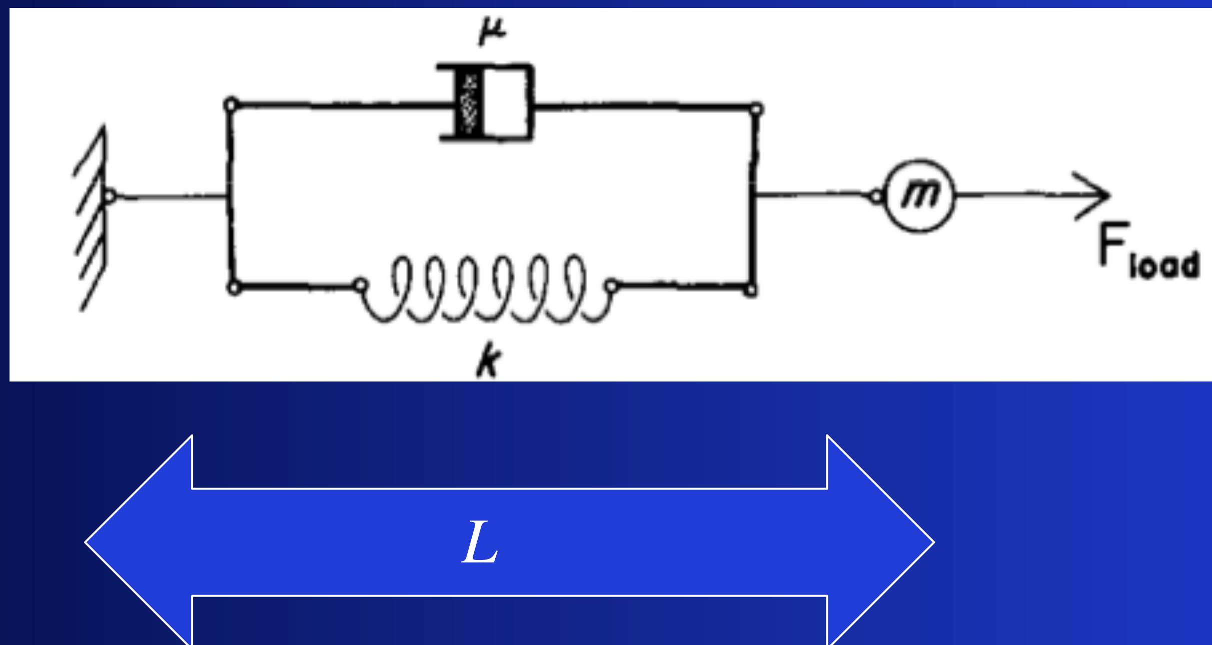
Hypothesis:

- The contractile fibers are excitable:
- A small deformation returns back to rest
- A large enough stretch leads to active contraction

Imposed stretch leads to sharp contraction

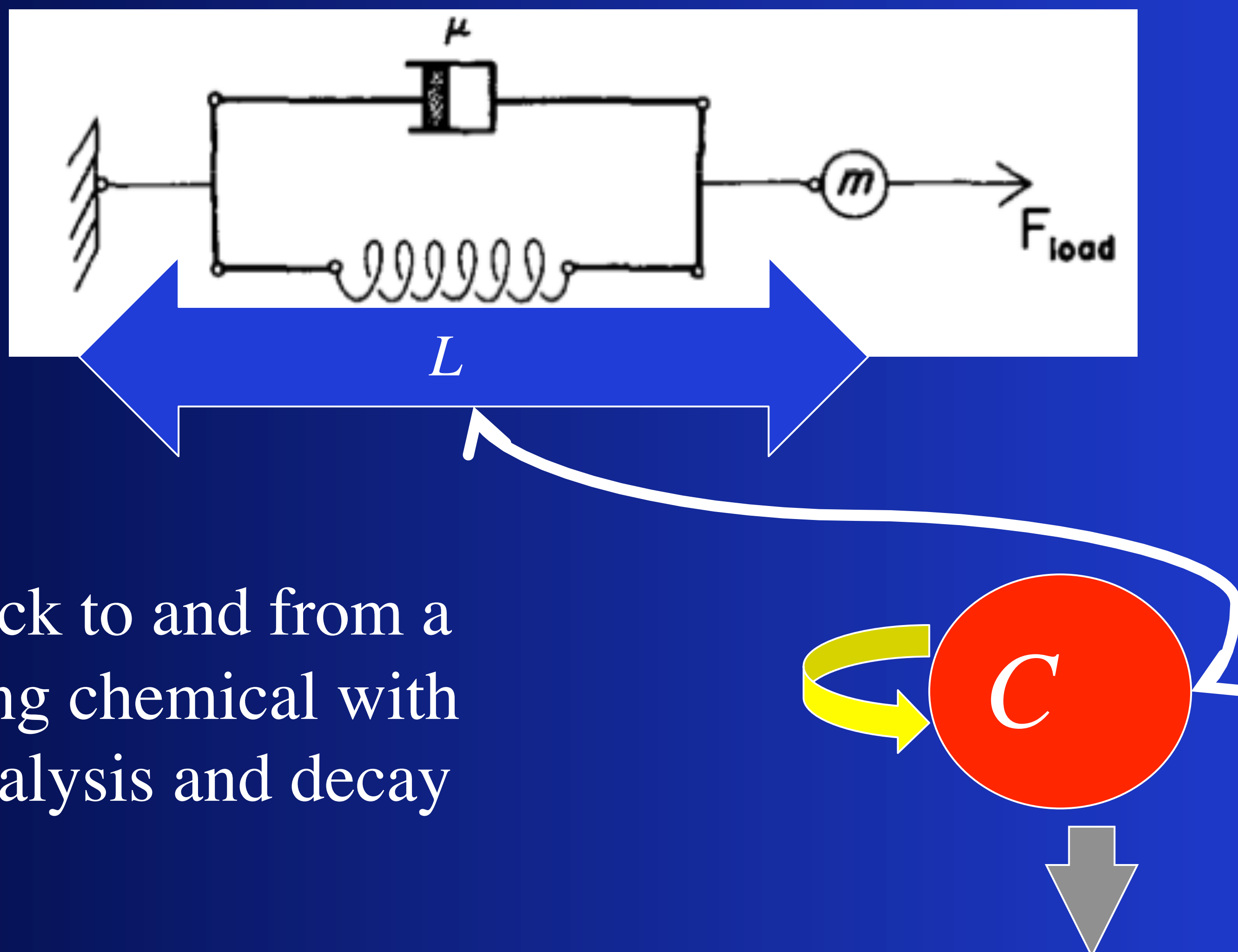


Model of single contractile element



Elastic spring in parallel with a resistance (“dashpot”)

Model of single contractile element



Feedback to and from a signaling chemical with autocatalysis and decay

Model equations

- Drag force proportional to contraction speed

$$F_{\mathrm{visc}} = -\mu \frac{dL}{dt}.$$

- Elastic force proportional to stretch of filament

$$F_{\mathrm{elas}} = -k(L - L_0),$$

Model equations

- Newton's Law: mass x acceleration = Σ forces

$$m \frac{d^2L}{dt^2} = F_{\text{elas}} + F_{\text{visc}} + F_{\text{load}},$$

Spring forces

- The equation for a deformed contractile "spring":

$$m \frac{d^2L}{dt^2} = -k(L - L_0) - \mu \frac{dL}{dt} .$$

Neglect inertial terms

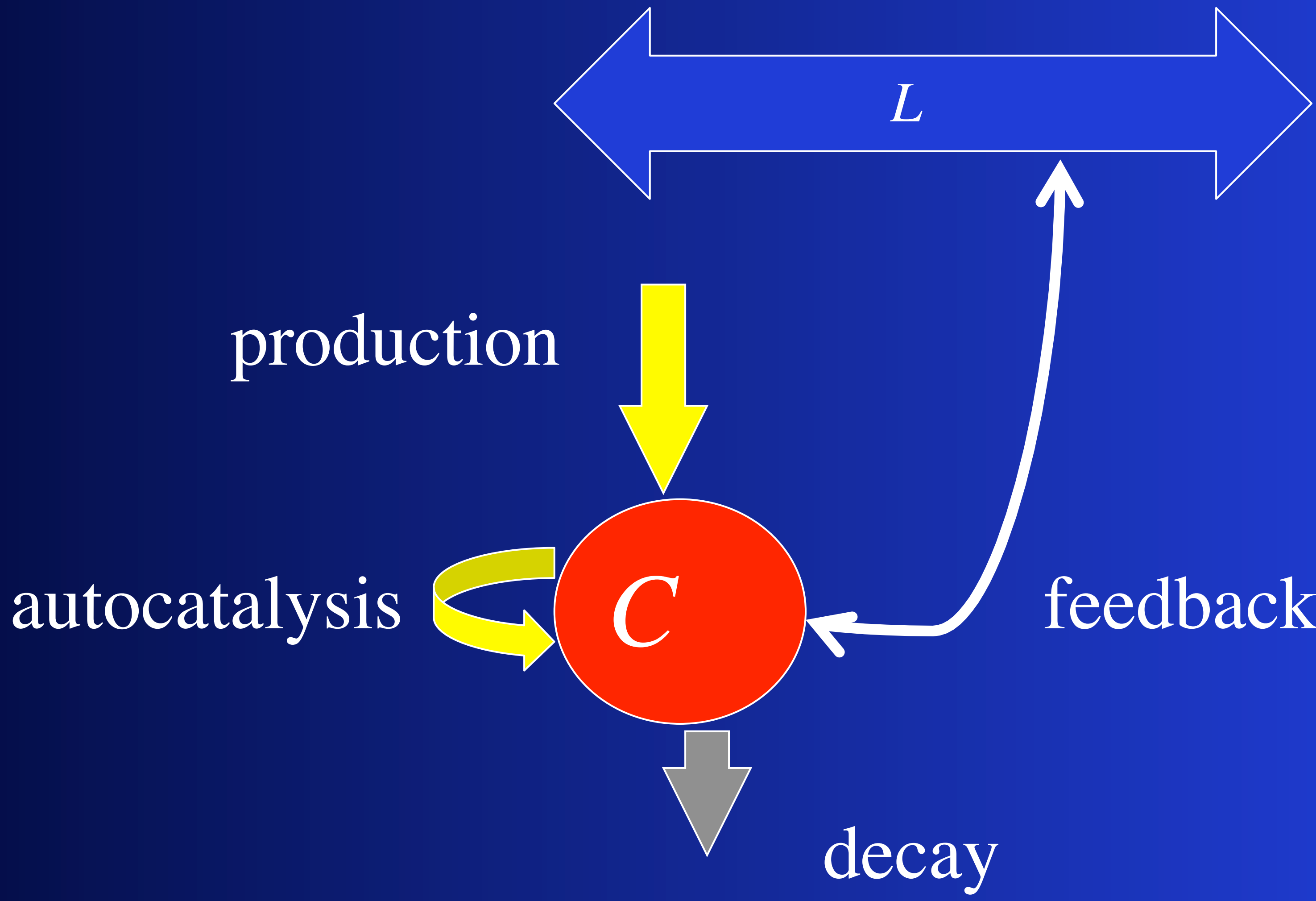
$$m\frac{d^2L}{dt^2} = -k(L - L_0) - \mu\frac{dL}{dt}.$$

Negligible

Viscous effects dominate on the cell size scale

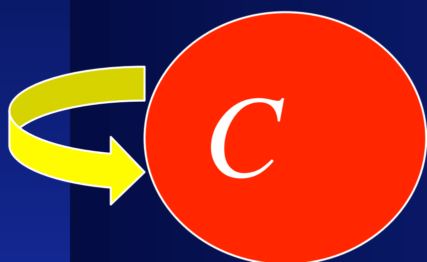
$$\frac{dL}{dt} = -\frac{k}{\mu}(L - L_0) + \frac{1}{\mu}F_{\text{load}}.$$

The chemical signal



Filament rest length can change

$$F_{\text{elas}} = -k(L - L_0),$$



$$L_0(c) = \varepsilon + \frac{1}{1 + \sigma c^2}$$

The chemical signal

$$\frac{dc}{dt} = -\upsilon c + S_c + J + \frac{\alpha c^2}{1 + \beta c^2}$$

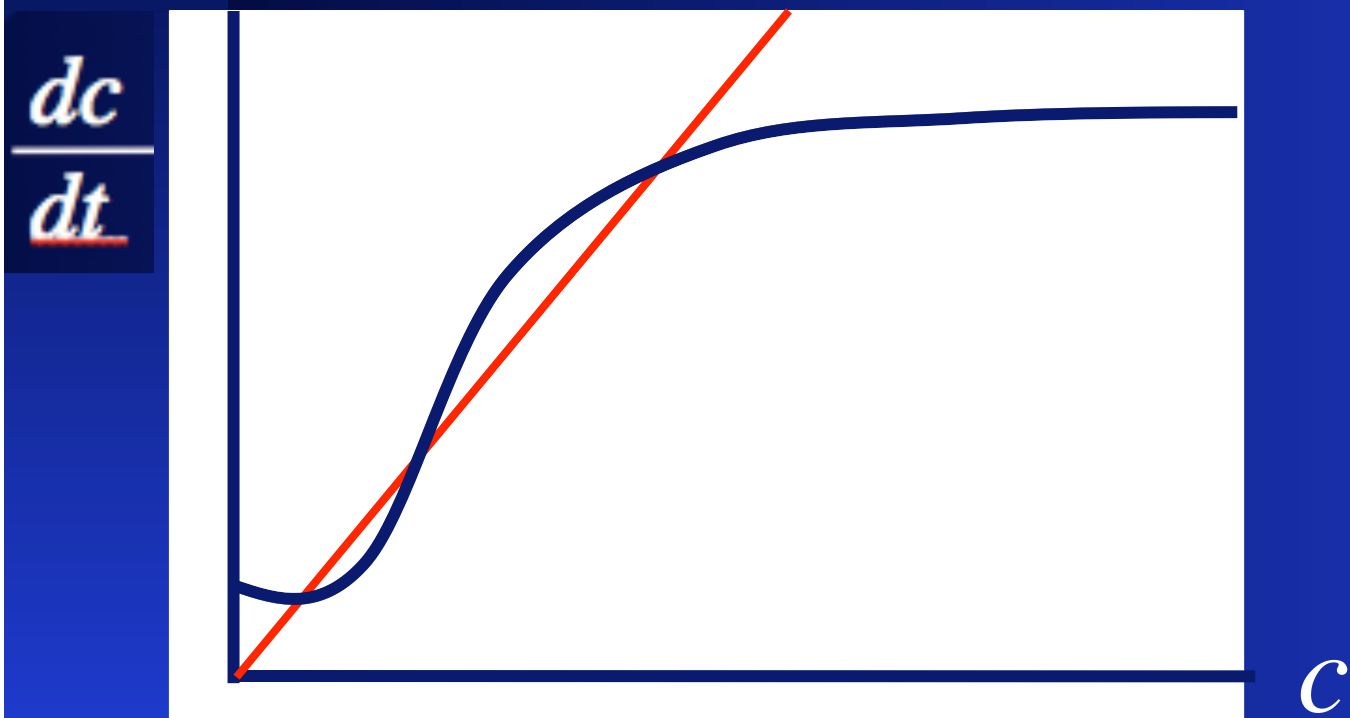
decay production autocatalysis

$$S_c = \gamma L$$

Chemical activated by the stretched length L

The chemical signal

$$\frac{dc}{dt} = -\upsilon c + S_c + J + \frac{\alpha c^2}{1 + \beta c^2}$$



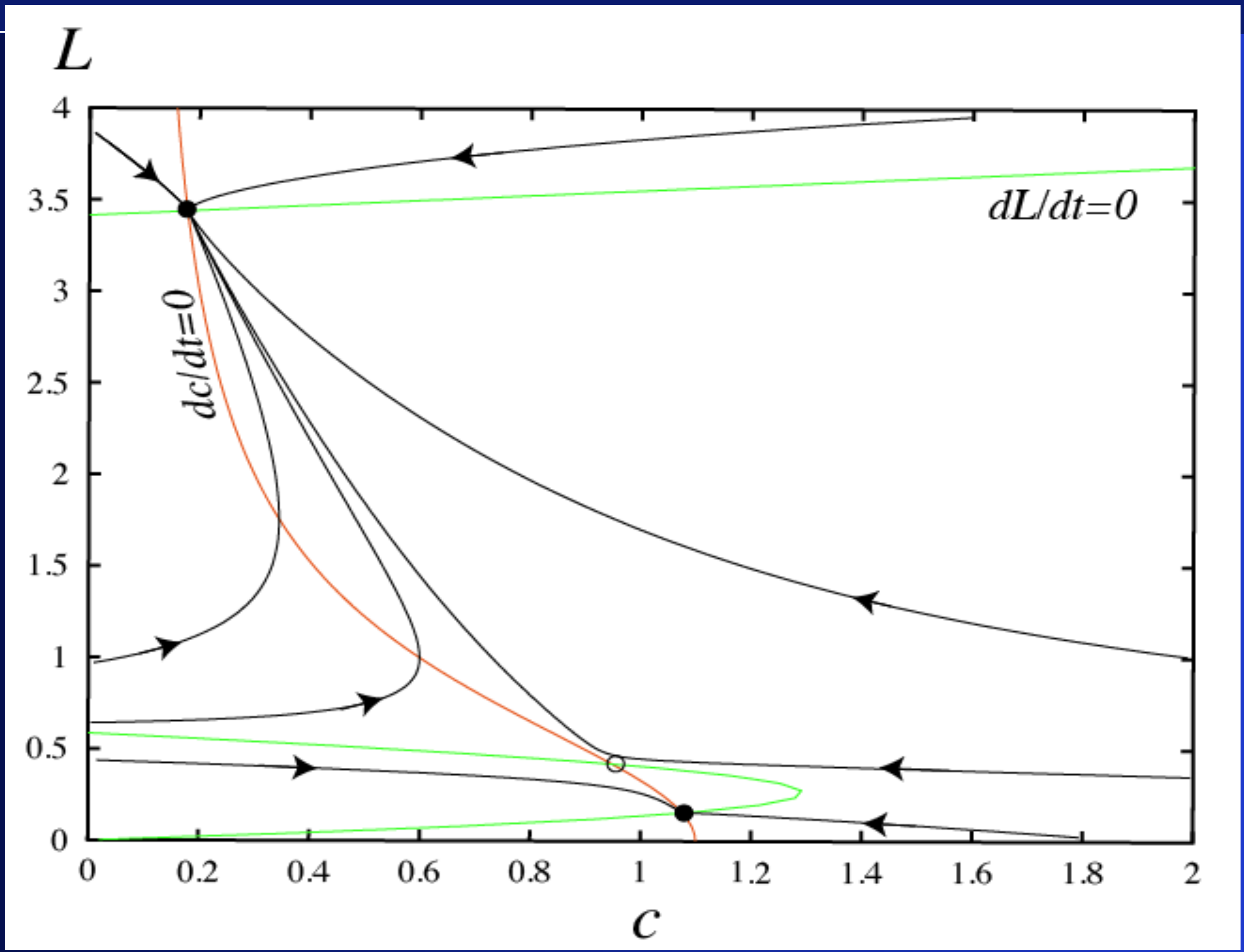
Full model for 1 cell

$$\frac{dL}{dt} = \frac{k}{m}\left(L - L_0(c)\right)$$

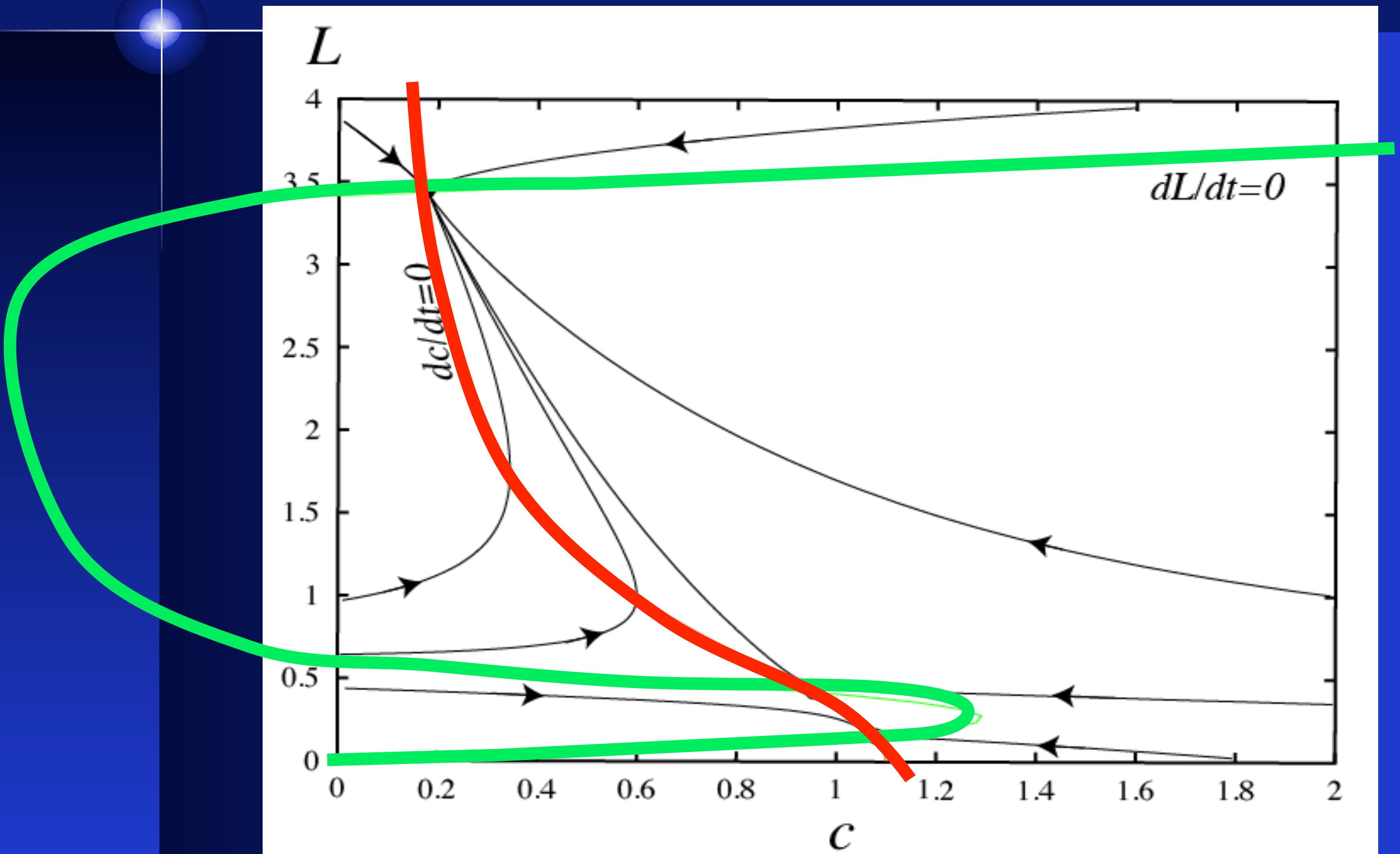
$$L_0(c) = \varepsilon + \frac{1}{1 + \sigma c^2}$$

$$\frac{dc}{dt} = -\upsilon c + \gamma L + \frac{\alpha c^2}{1 + \beta c^2}$$

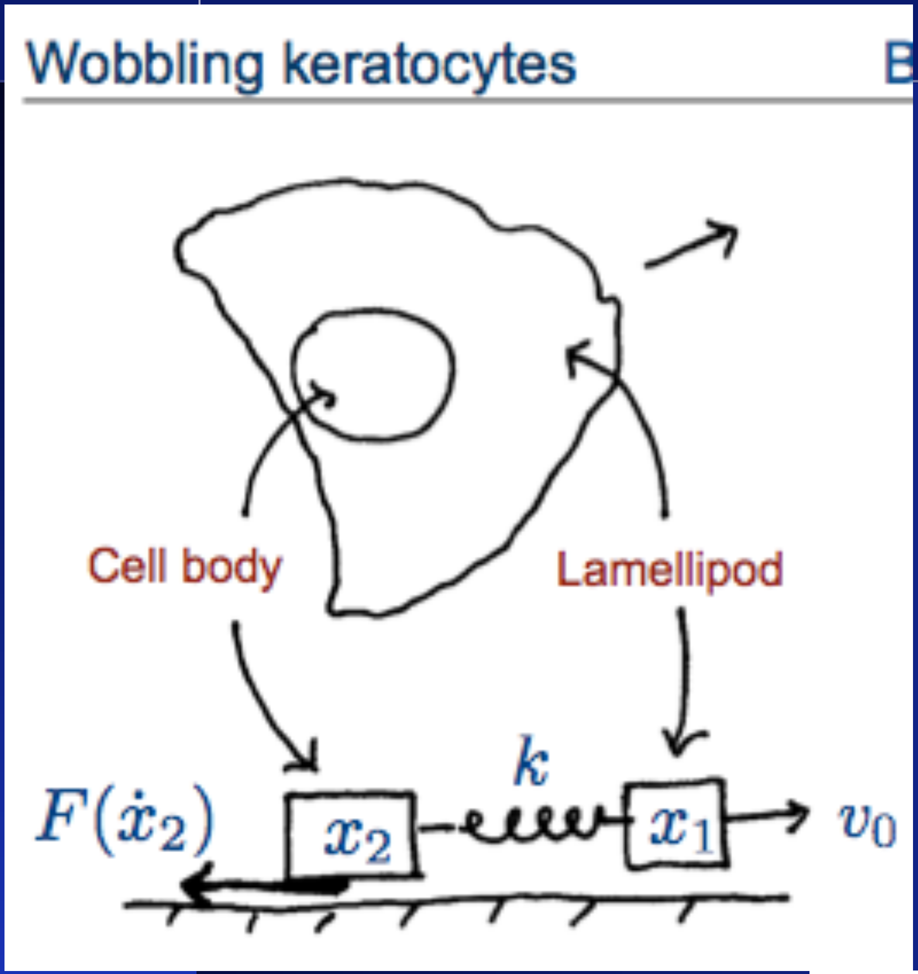
cL phase plane



“cubic nullcline”



Jun Allard's example: wobbly cell



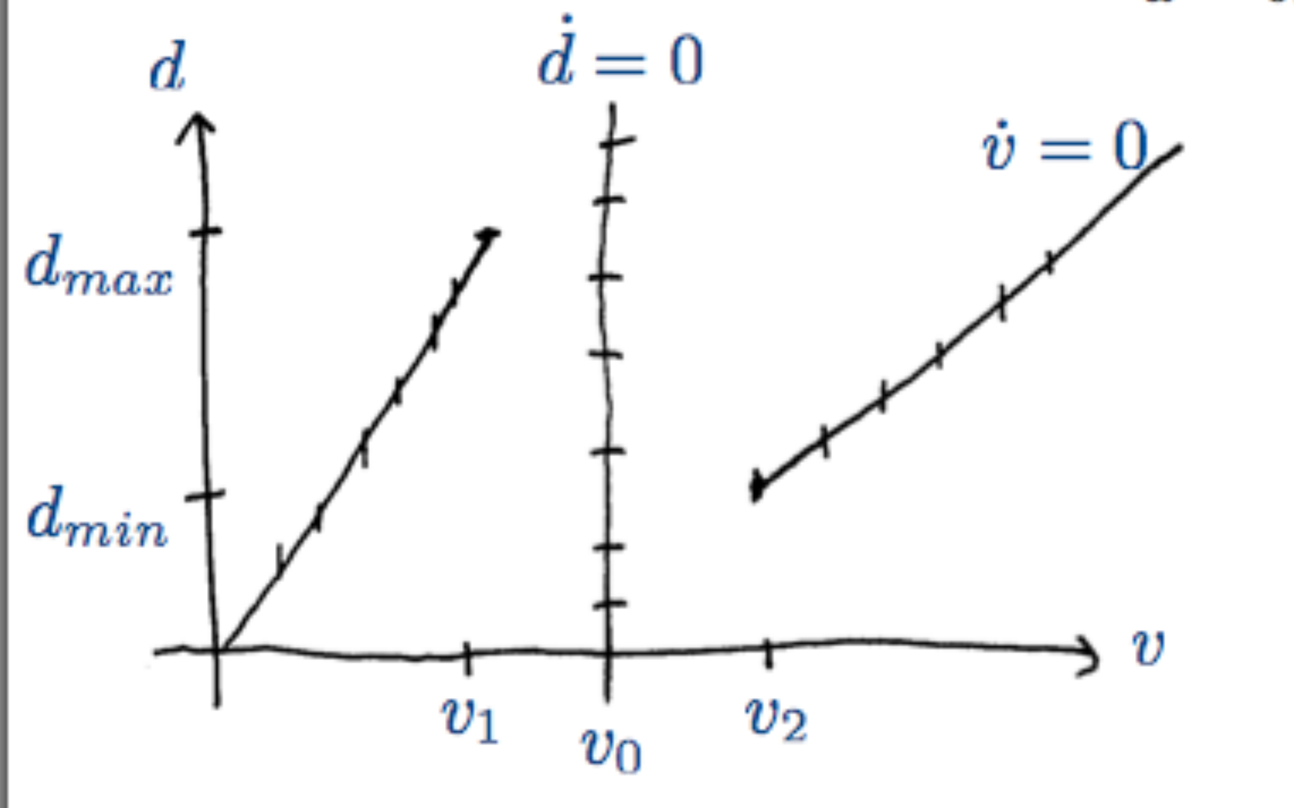
$$d = x_1 - x_2 - L_0 \qquad \Longrightarrow \qquad \epsilon \dot{v} = kd - \xi_i v$$

$$v = \dot{x}_2 \qquad\qquad\qquad \dot{d} = v_0 - v$$

Julicher's wobbly cell model (Jun's talk)

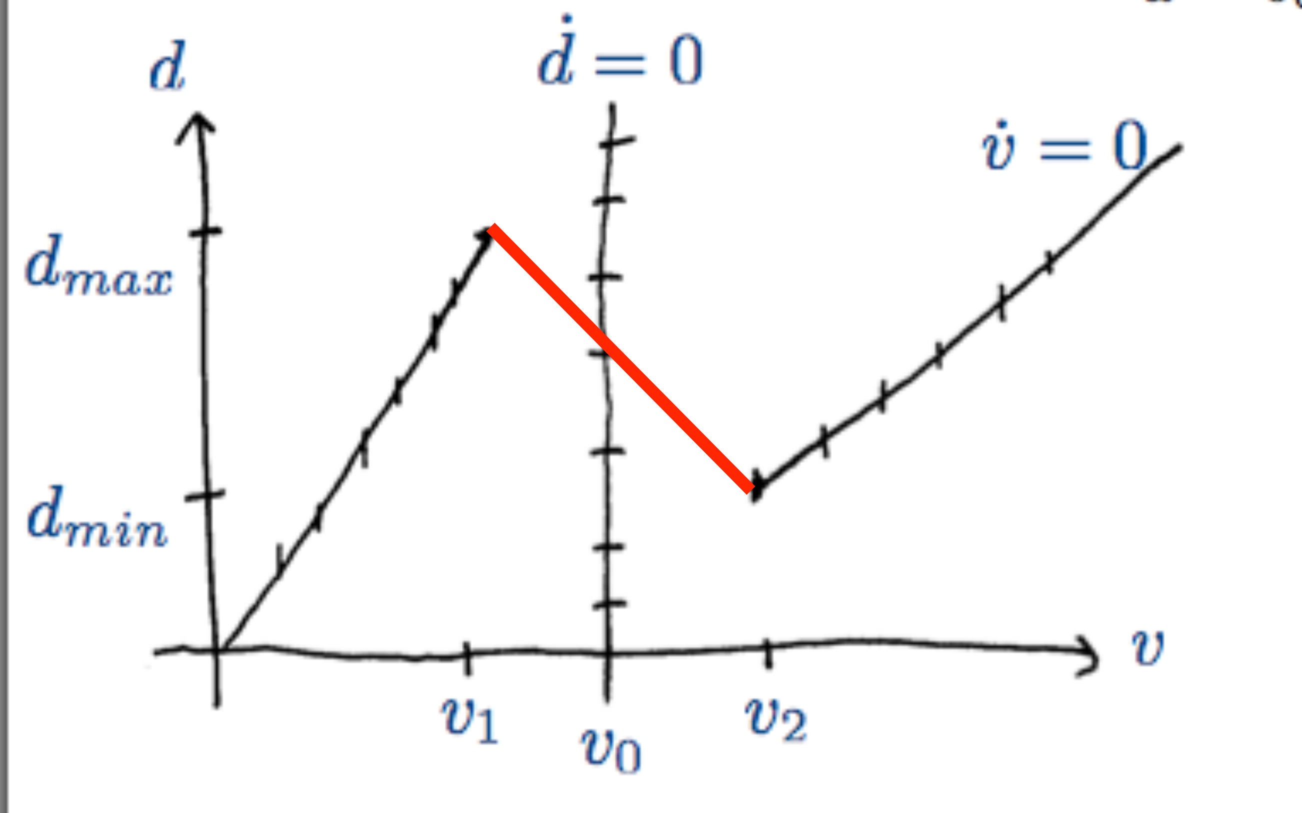
$$\epsilon \dot{v} = kd - \xi_i v$$

$$\dot{d} = v_0 - v$$

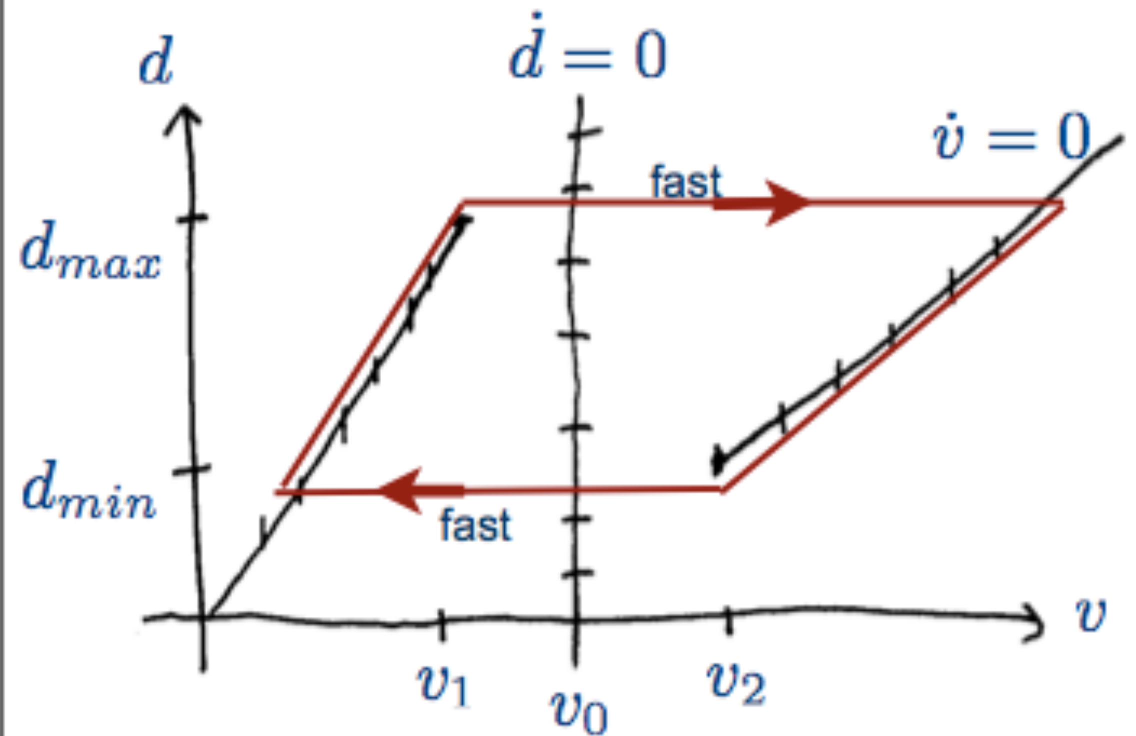


Piecewise linear "cubic" nullclines

$$\epsilon \dot{v} = kd - \xi_i v$$
$$\dot{d} = v_0 - v$$



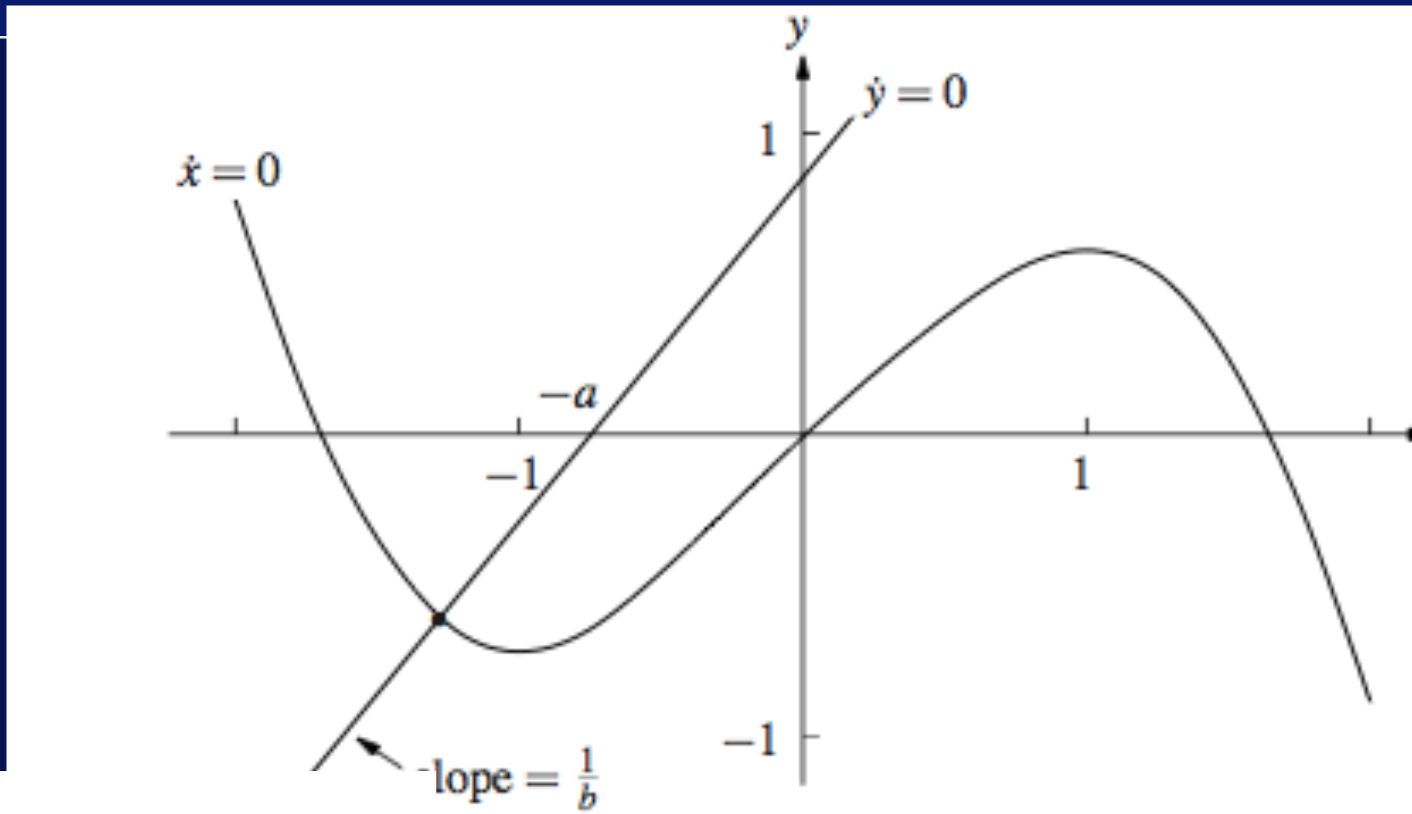
Oscillatory behaviour = "wobbling keratocyte"



$$\epsilon \dot{v} = kd - \xi_i v$$

$$\dot{d} = v_0 - v$$

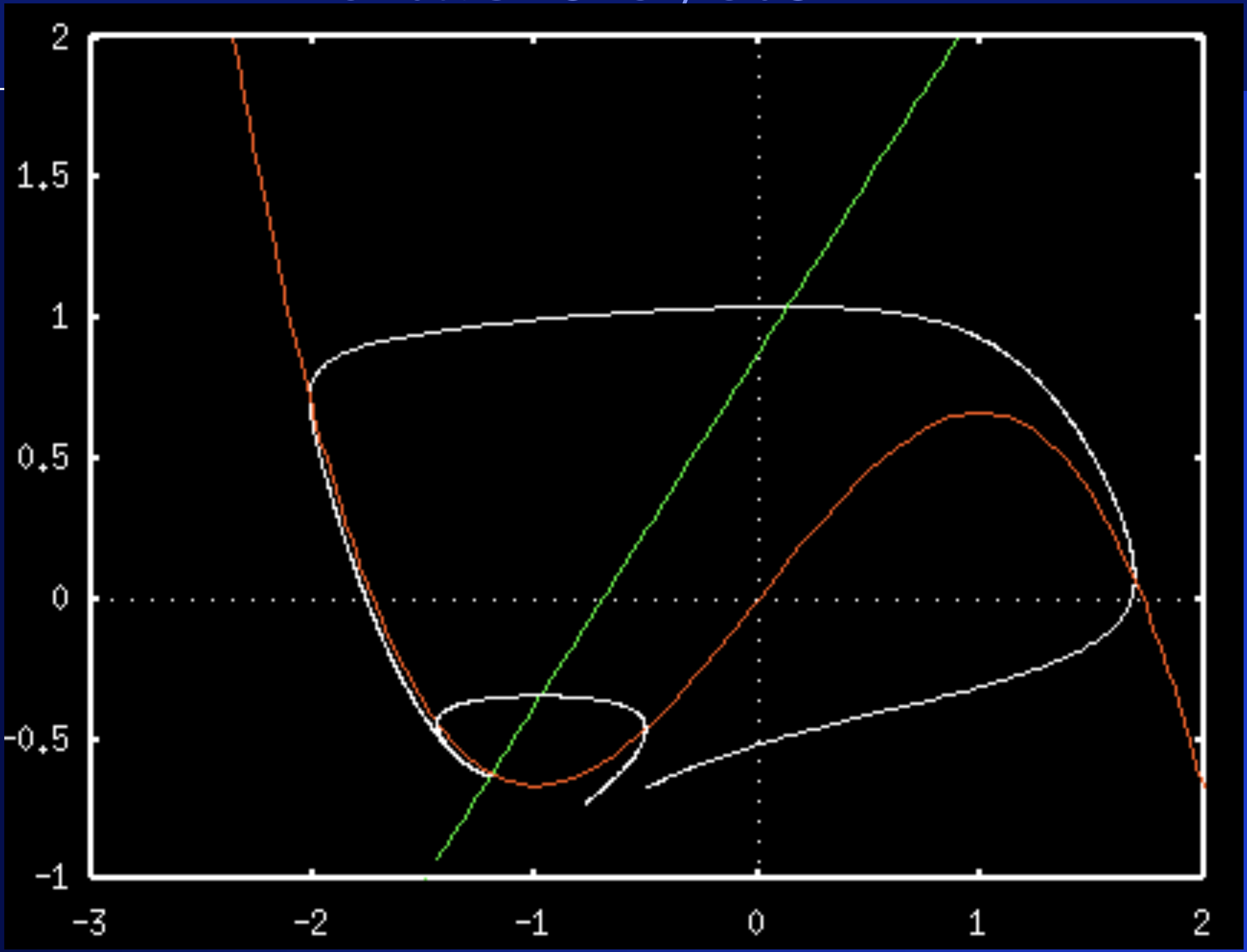
Compare with classic FitzHugh Model



$$\frac{dx}{dt} = c\left[x - \frac{1}{3}x^3 - y + j\right],$$

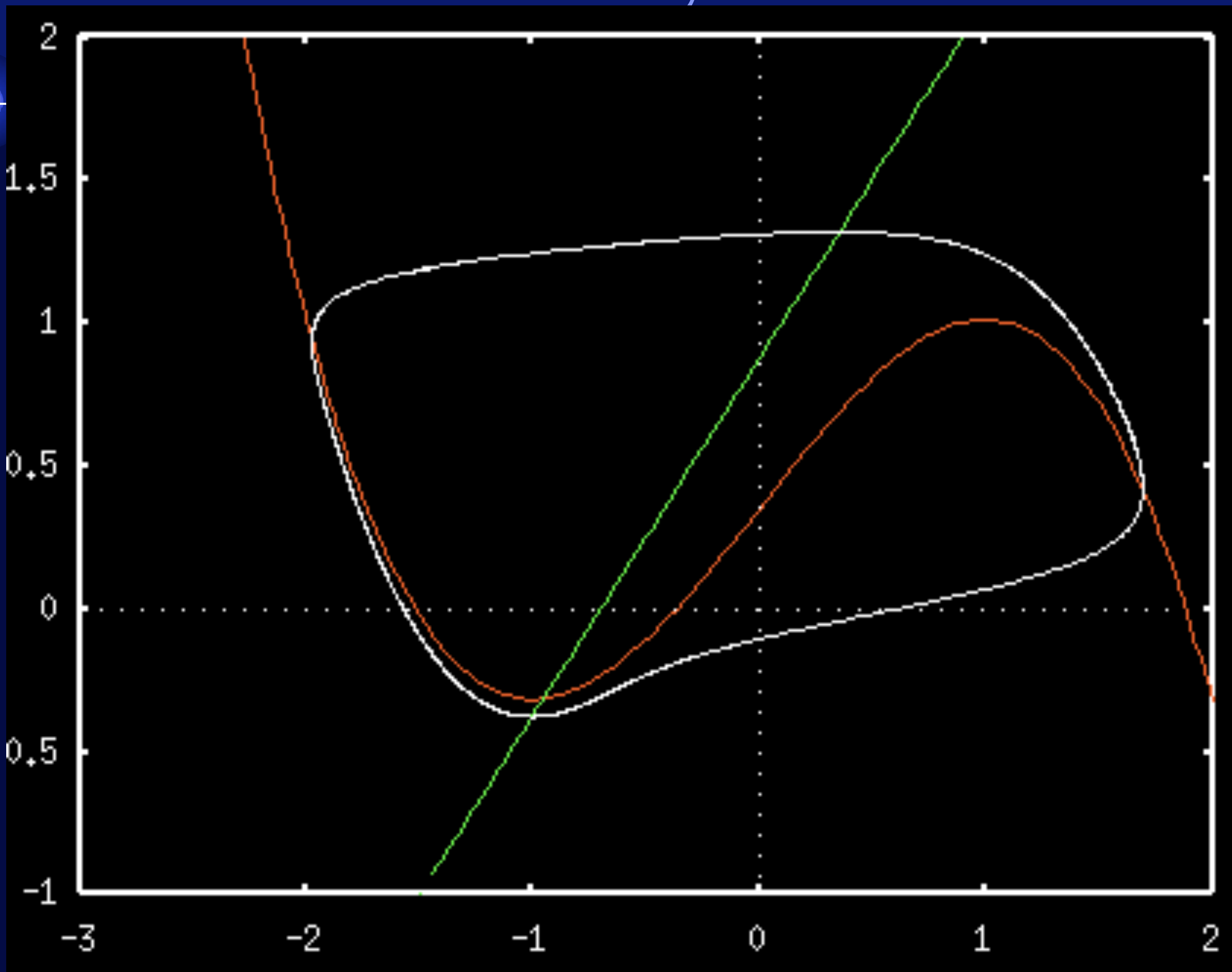
$$\frac{dy}{dt} = \frac{1}{c}[x + a - by]\,.$$

"Excitable system"



a=0.7, b=0.8, c=3, j=0

Limit cycle



a=0.7, b=0.8, c=3, j=0.35

Simulation of 1 excitable filament

```
#Odell_Oster.ode

dL/dt=-kmu*(L-L_0(c))
dc/dt=alpha*c^2/(1+beta*c^2)-eta*c+gamma*L
L_0(x)=eps+ 1/(1+sigma*c^2)

par kmu=1,alpha=2,beta=0.5,eta=1,eps=0.1,sigma=1,gamma=0.1
@xlo=0,xhi=2,ylo=0,yhi=4,xp=L,yp=c
done
```

Folding Epithelium

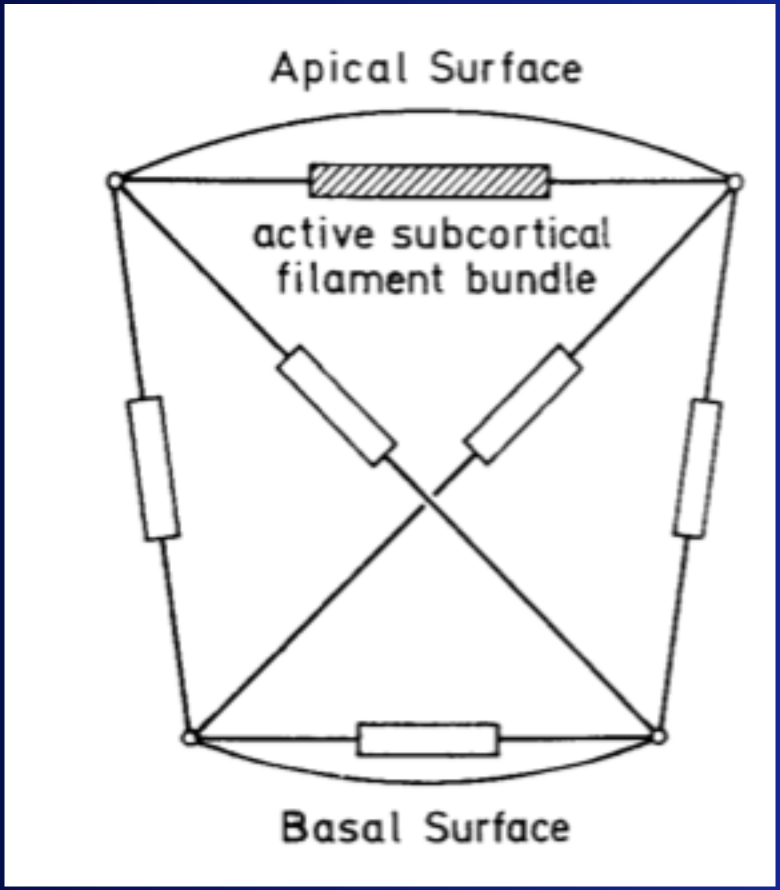
- Attach many cells together.
- Each cell pulls on its neighbors
- Each cell receives some chemical signal fro its neighbors

Full model for many cells

$$\frac{dL}{dt} = \frac{k}{m}(L - L_0(c)) + F$$

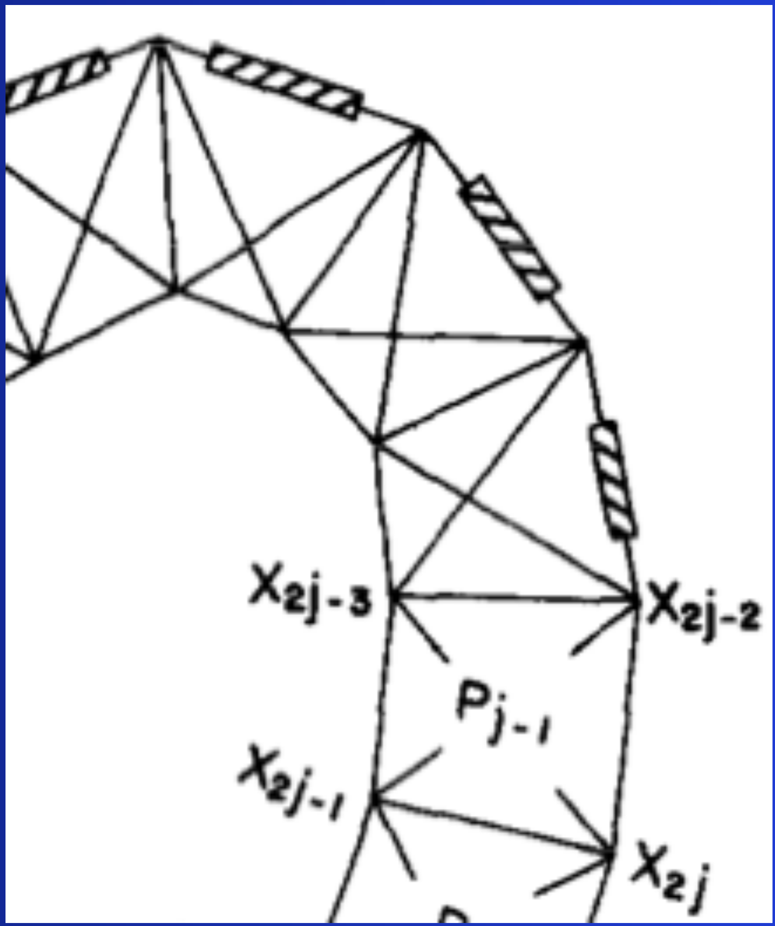
$$\frac{dc}{dt} = -v\,c + \gamma L + \frac{\alpha c^2}{1+\beta c^2} + J$$

Cortical Filament bundle



Cell sheet simulations

- Springs and dashpots and single excitable apical filaments in each cell.



Selection from Fig A3 in: Oster et al (1980) Lectures on Mathematics in the Life Sciences Vol 13: 165-255

Simulations (one of the earliest mechanochemical 2D sims)

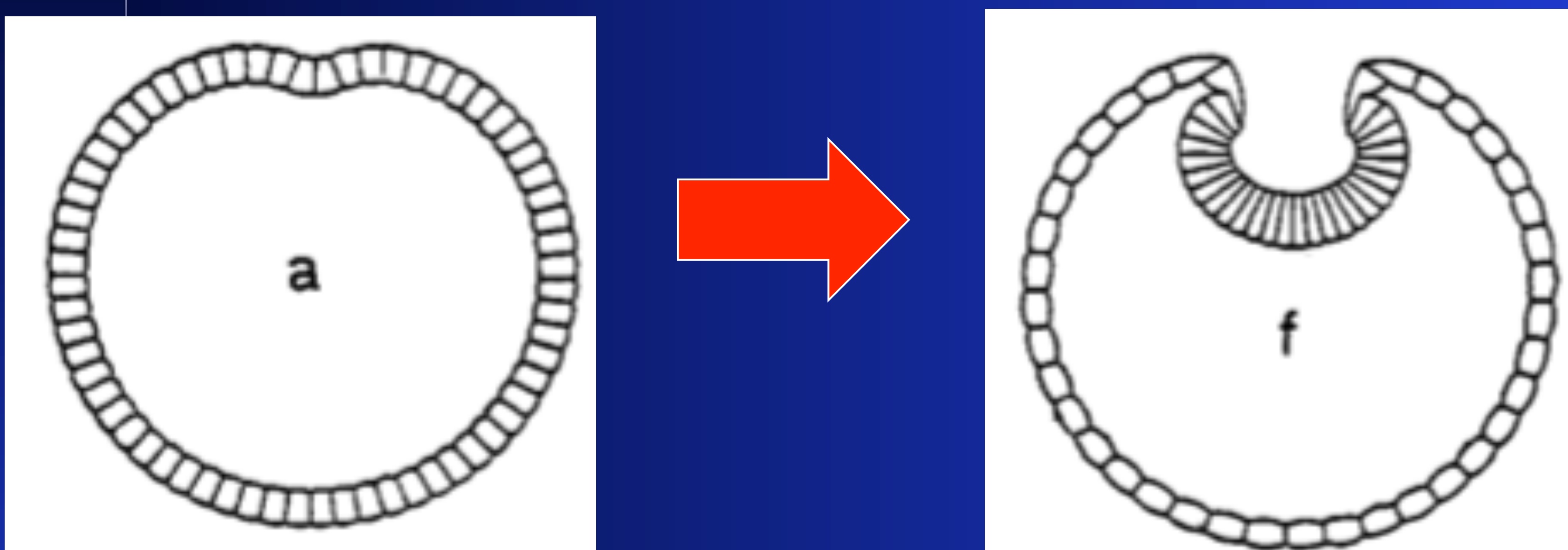


Fig 11 in: Oster et al (1980) Lectures on Mathematics in the Life Sciences Vol 13: 165-255

Take-home message:

- Use what you know about simple mathematical prototypes (switches, relaxation oscillators).. These reappear in many guises in modeling literature..
- Understand mini-model(s) before going to full (complex) systems
- Use simulations to study greater level of complexity, or behaviour of multiple units linked together.