A course on physical models of living systems

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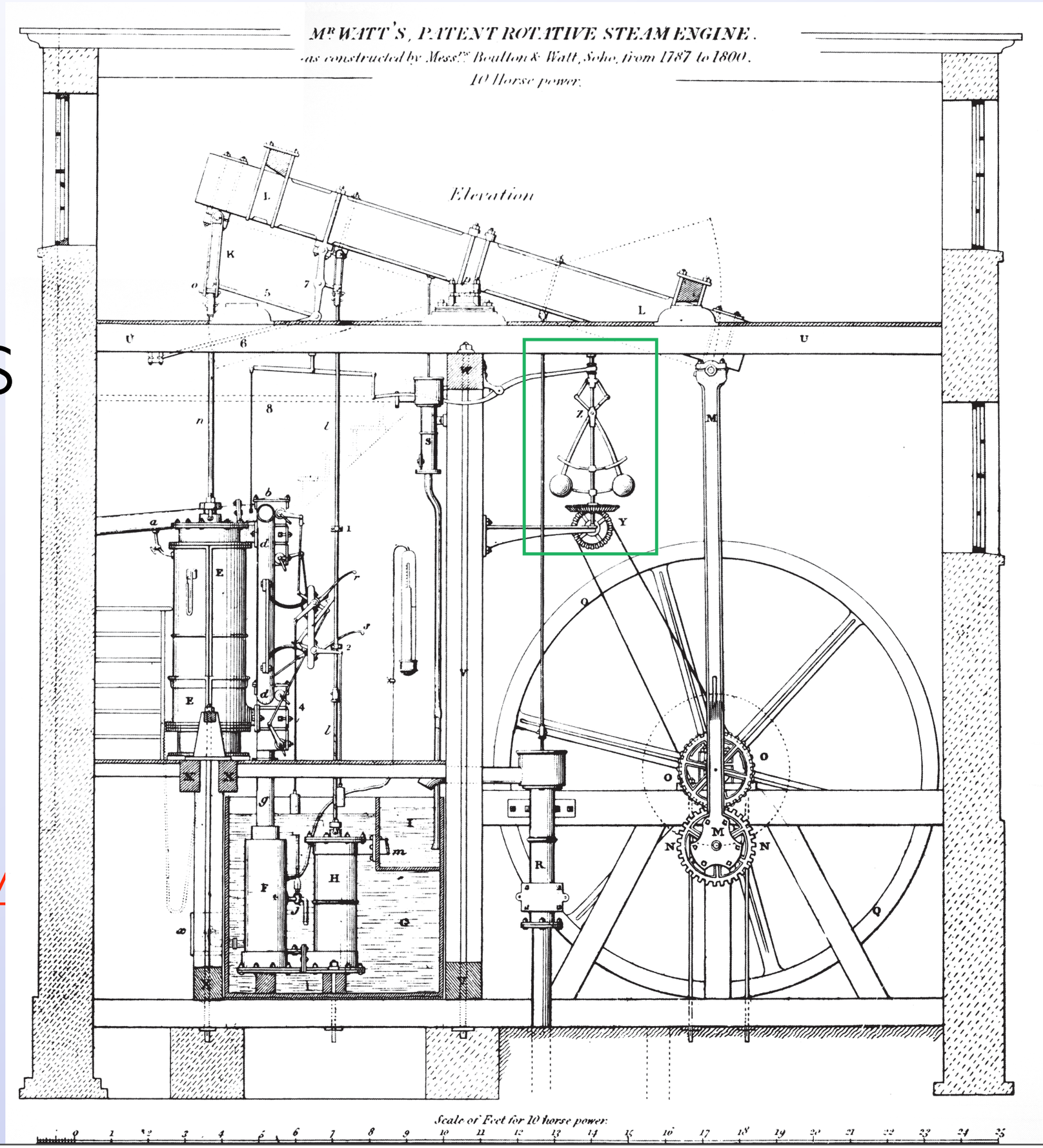
These slides will appear at
www.physics.upenn.edu/



Message

✳ **Students are excited about synthetic biology ("Build life to understand it").**

✳ **All natural living systems employ feedback control.**

✳ **Physicists can illuminate these subjects with a little dynamical systems theory.**

✳ **Students, especially engineering students, like that.**

✳ **Out of the welter of zillions of articles, I chose *three* concepts. For each, I follow the same three steps:**

- Introduce a *biological problem* cells face.
- Find a *mechanical mechanism* that addresses an analogous problem.
- Describe a *synthetic biology implementation* that is simple enough to admit a quantitative prediction.
- Return to a natural example.

Biological problem I: Homeostasis

Chemical reactions in cells are random. Environmental fluctuations are random. **How can a cell do anything organized in the face of all that randomness?**

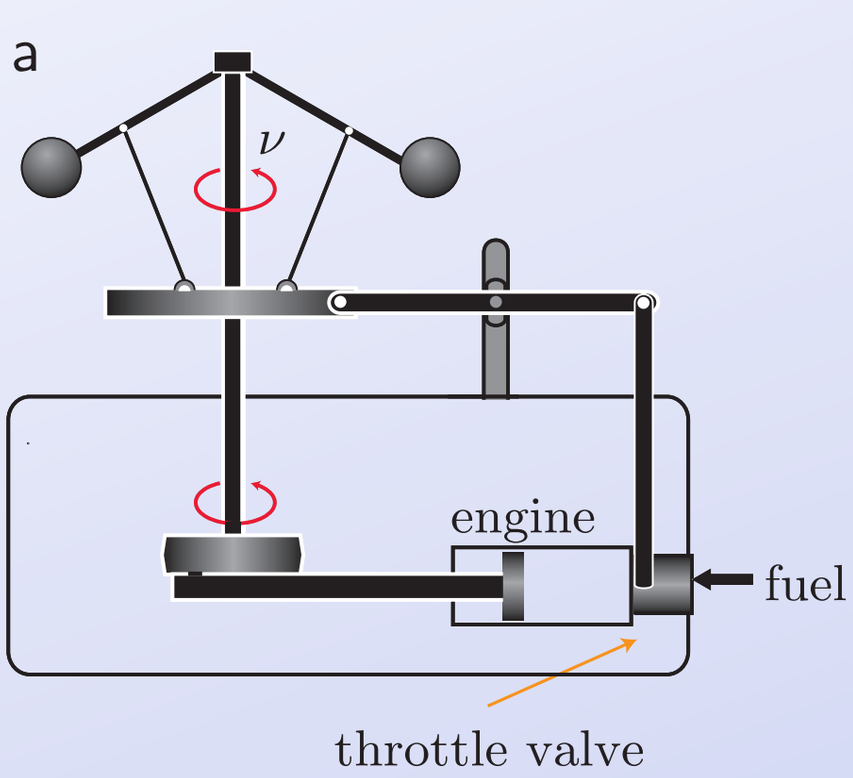
✳**A cell does not have 6×10^{26} copies of each relevant molecule.**
Fluctuations are significant.

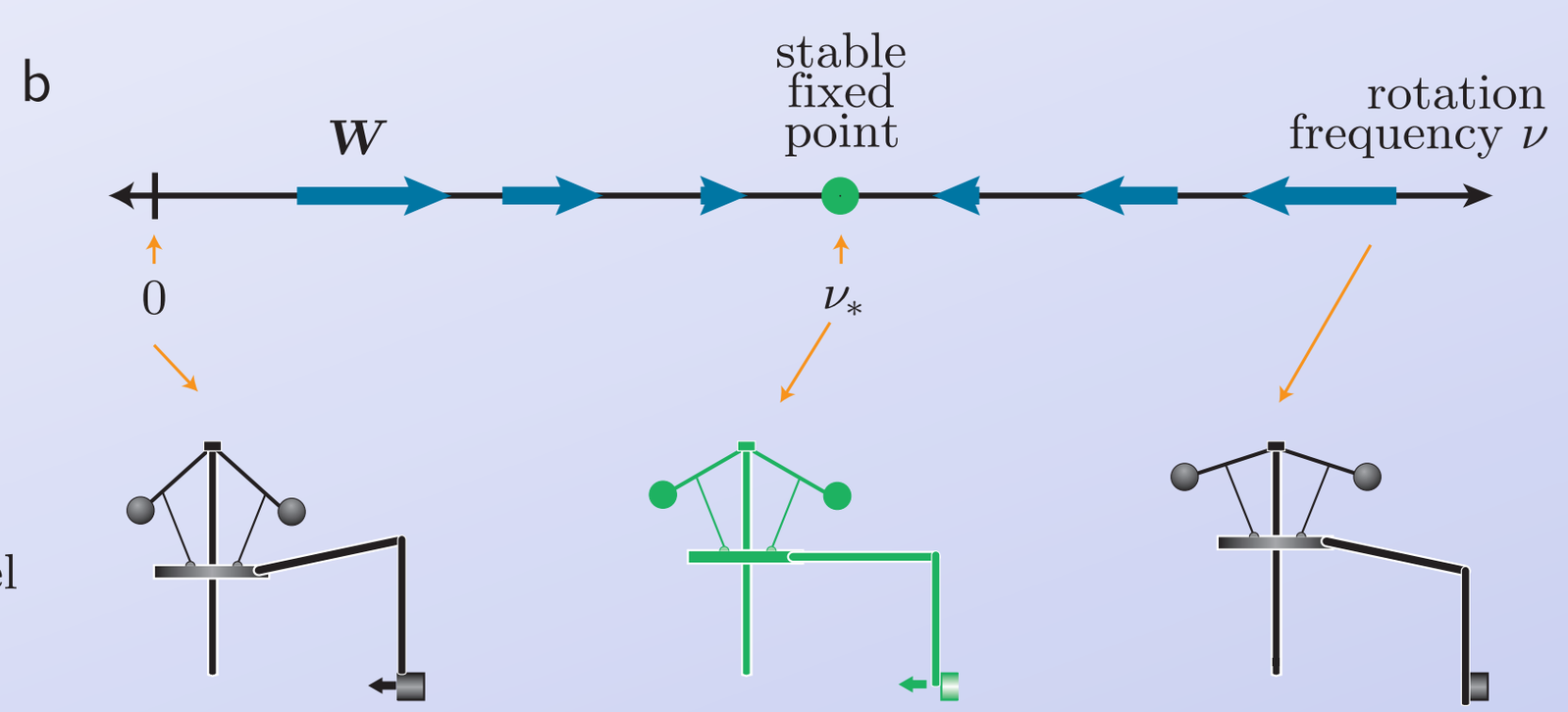
✳**Cells must also respond to variations of small numbers of external signal molecules.**

To get started, how does a cell even maintain a roughly constant composition (homeostasis)?

Biological problem I: Homeostasis

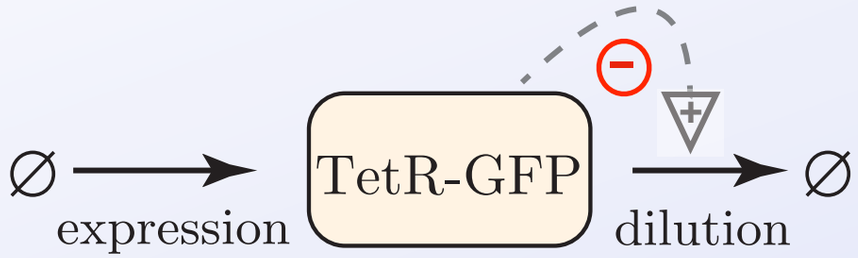
Mechanical analogy 1: Governor

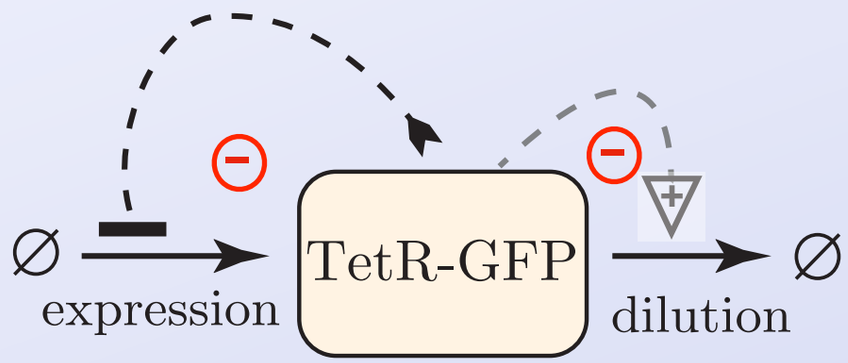


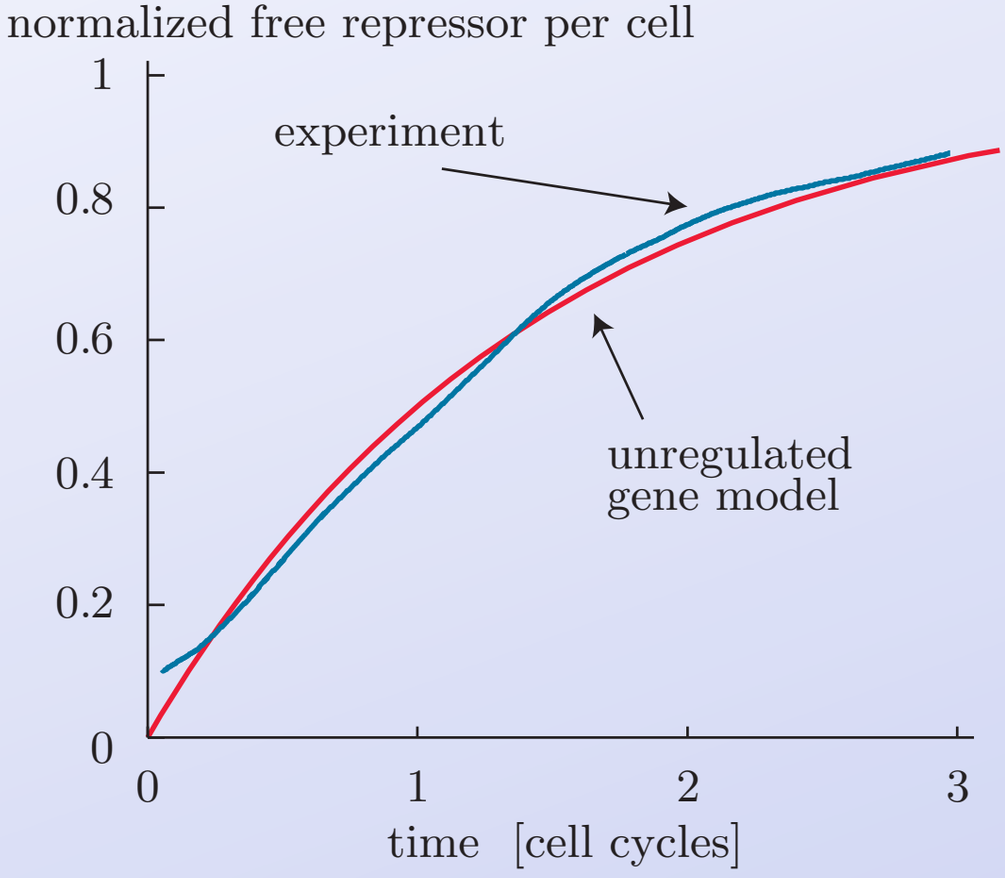


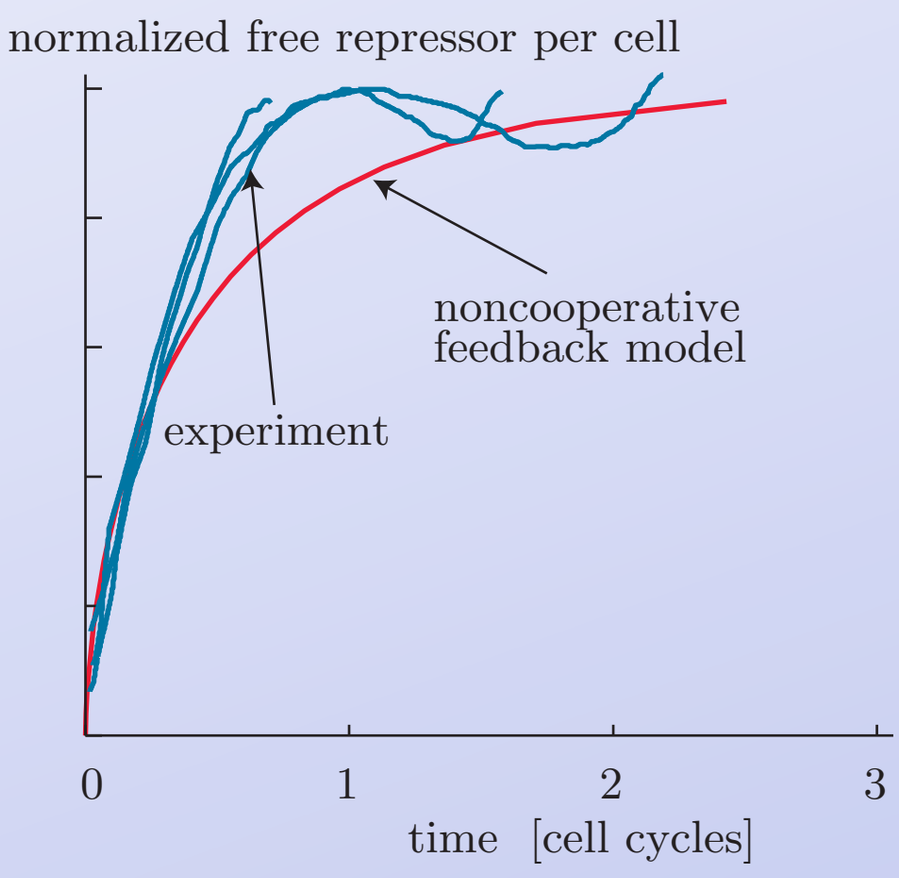
From P Nelson, *Physical models of living systems* (WH Freeman, to appear).

Biological problem I: Homeostasis
Mechanical analogy 1: Governor
Synthetic biology 1: Governor circuit









From P Nelson, *Physical models of living systems* (WH Freeman, to appear). Data from: N Rosenfeld et al. J Mol Biol (2002) vol. 323 (5) pp. 785-93

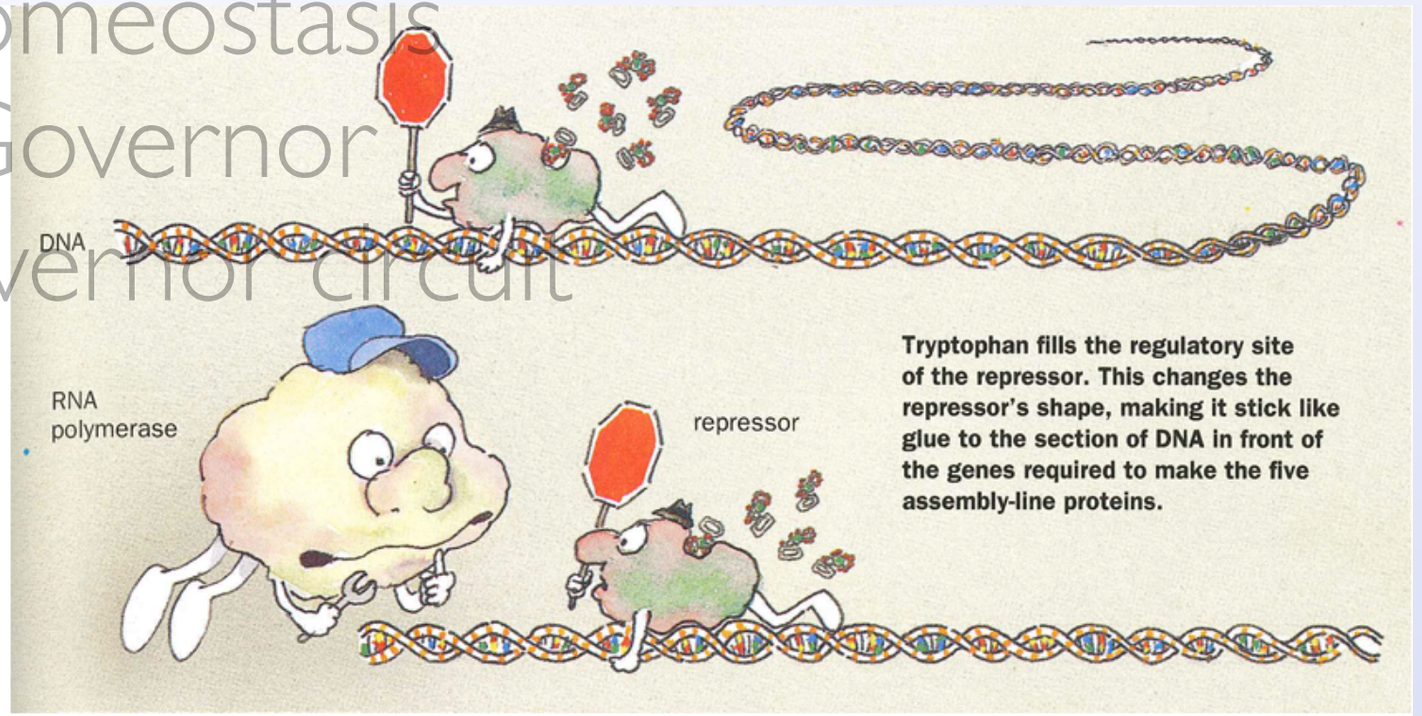
Biological problem I: Homeostasis

Mechanical analogy I: Governor

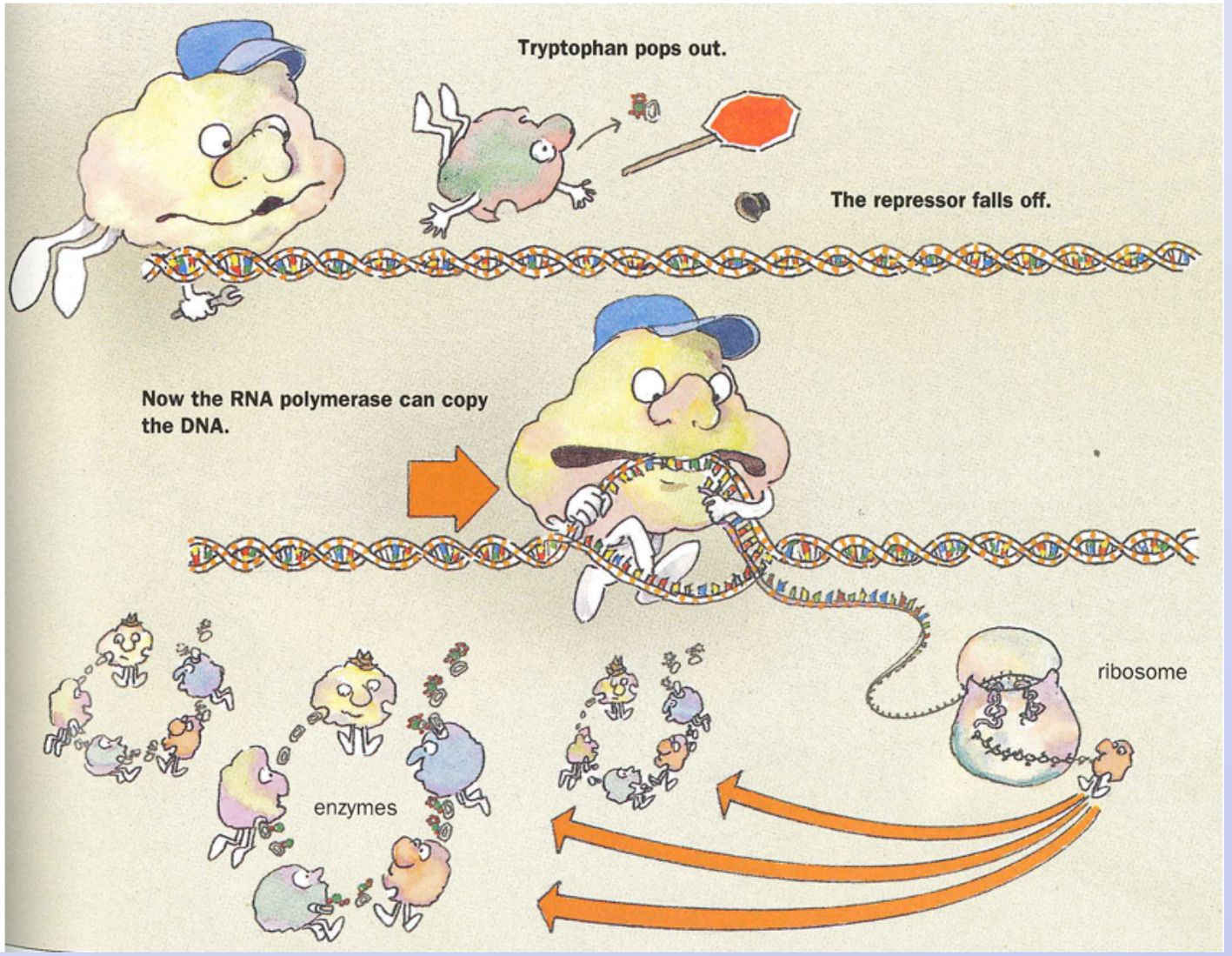
Synthetic biology I: Governor circuit

Natural realization I: *trp* regulation circuit

a



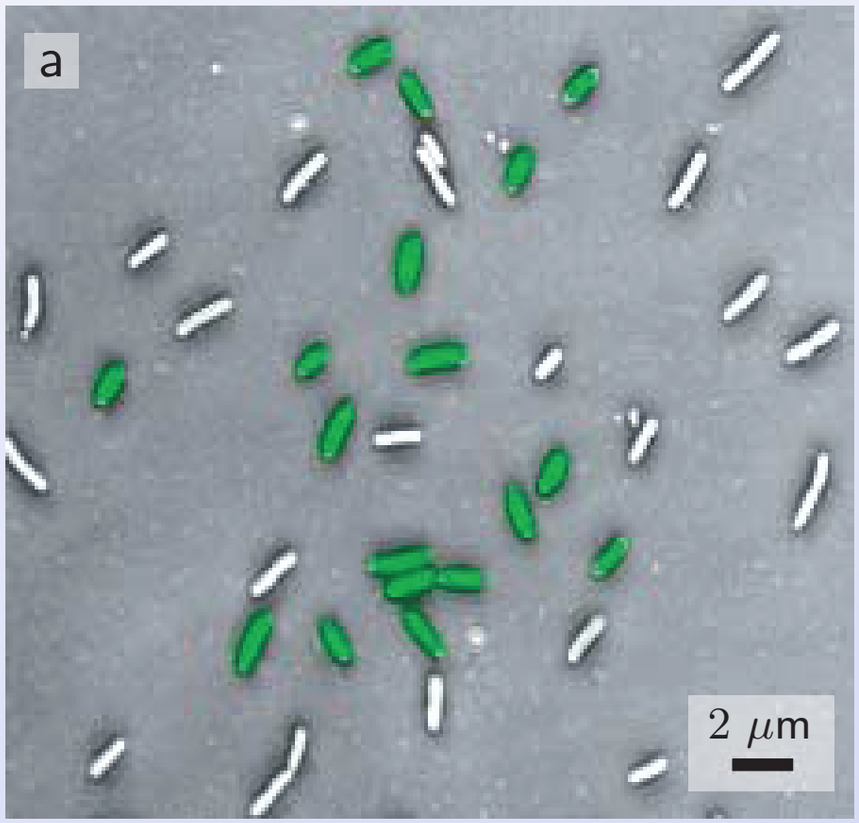
b

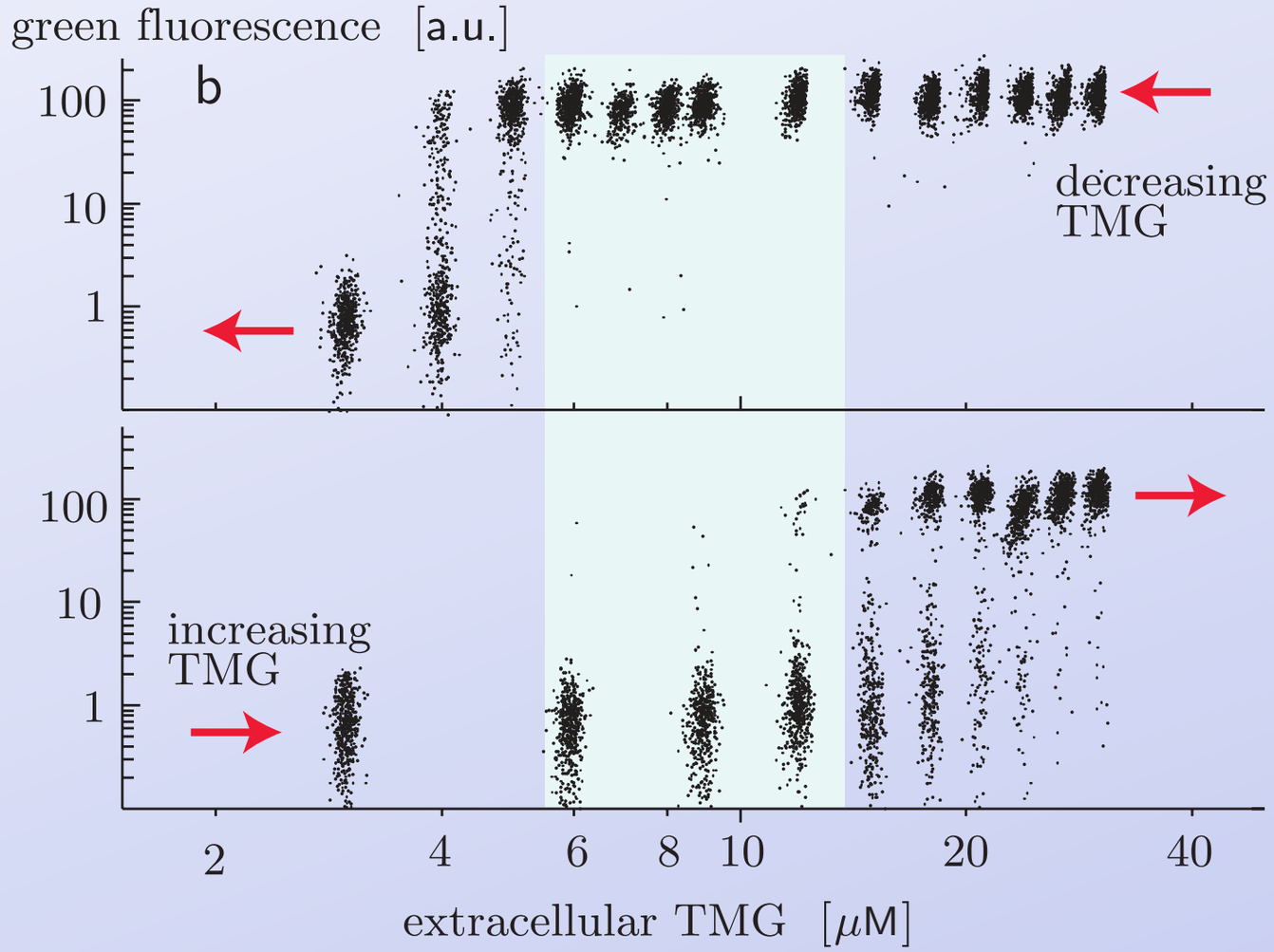


From Hoagland and Dodson, *The way life works*.

Biological problem 2: Switch response

How do you make decisions without a brain?

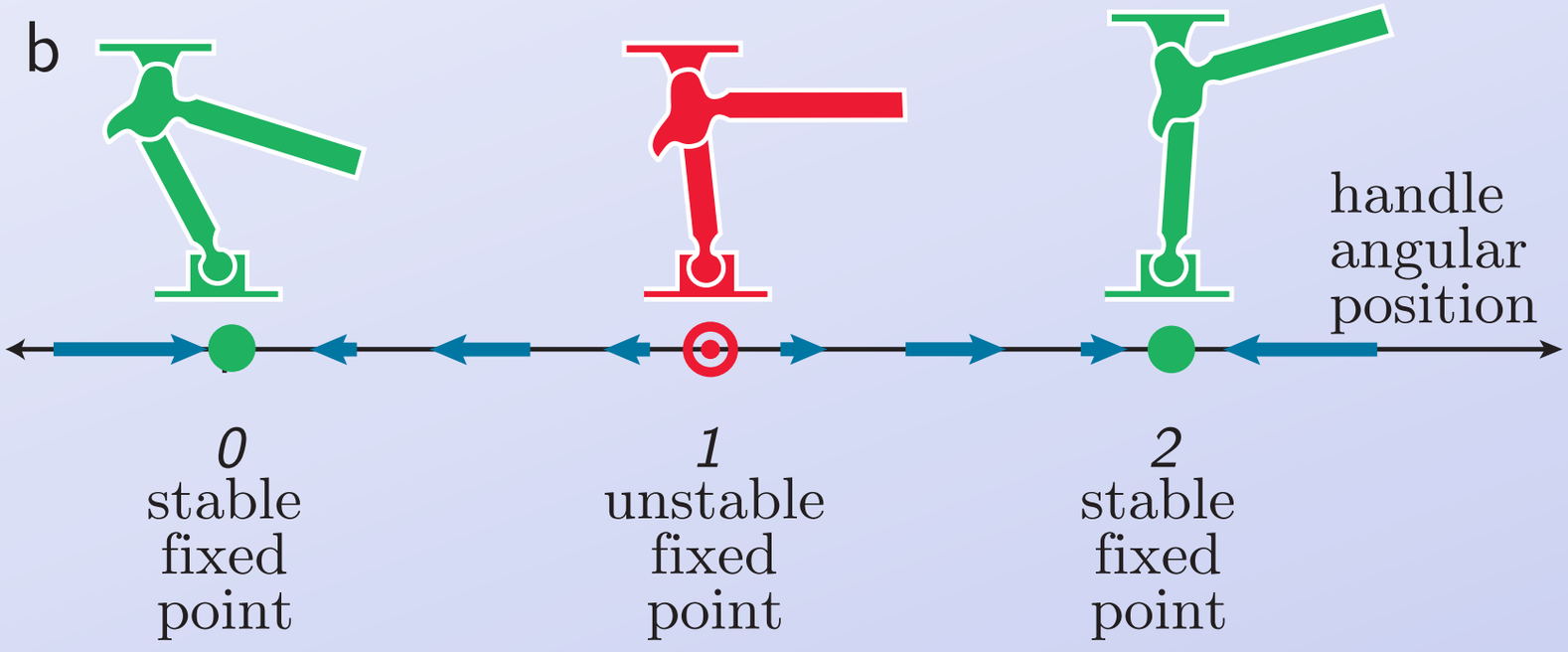




From P Nelson, *Physical models of living systems* (WH Freeman, to appear). Data and image from: Ozbudak et al., Nature (2004) vol. 427 (6976) pp. 737-740.

Biological problem 2: Switch response

Mechanical analogy 2: Toggle

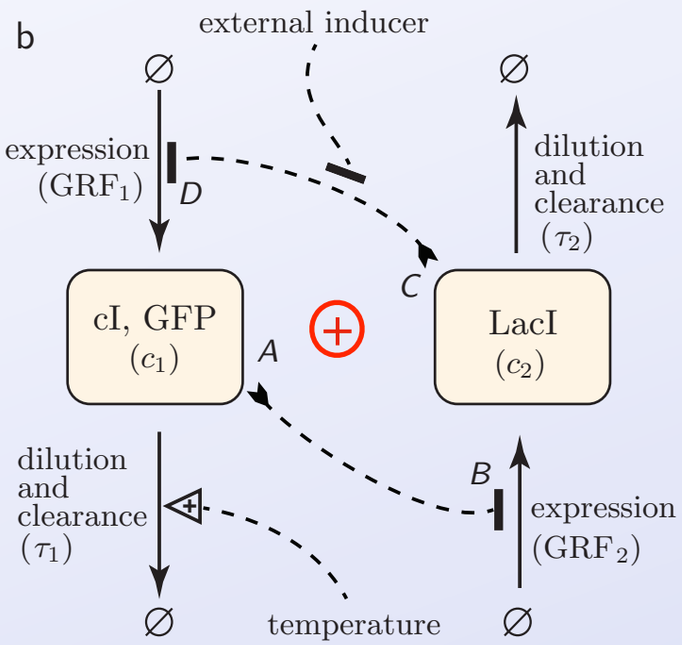


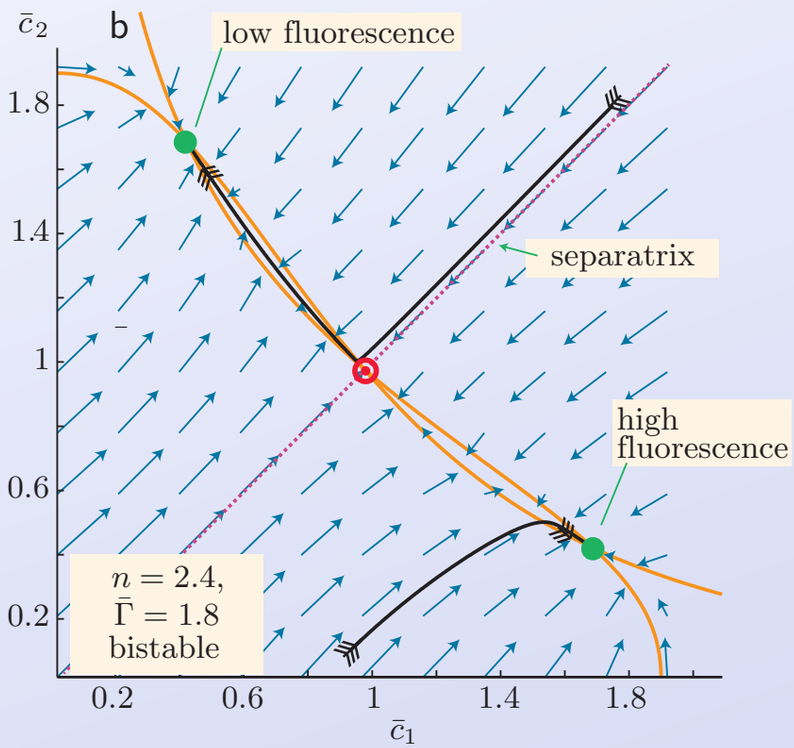
From P Nelson, *Physical models of living systems* (WH Freeman, to appear).

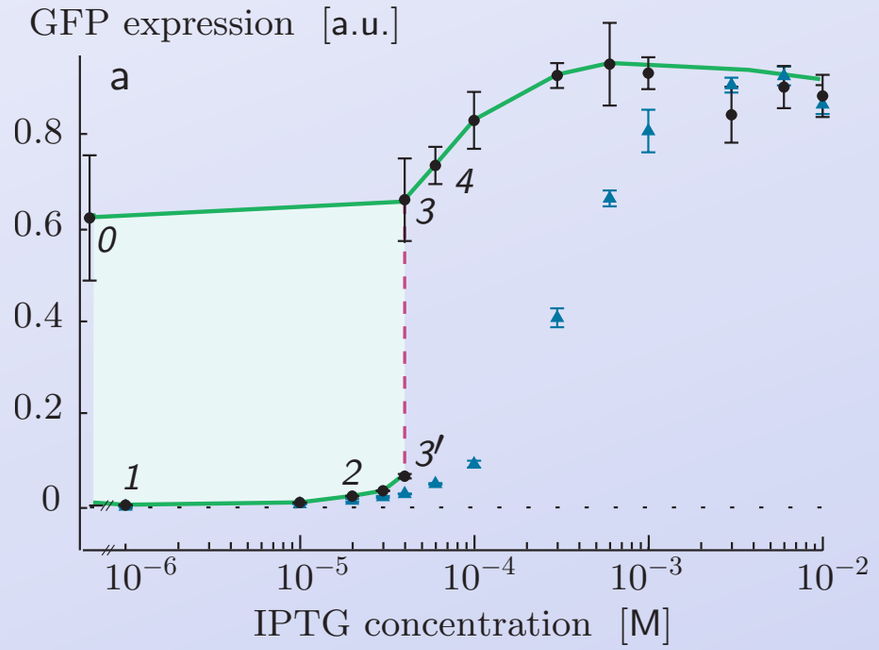
Biological problem 2: Switch response

Mechanical analogy 2: Toggle

Synthetic biology 2: Two-gene switch







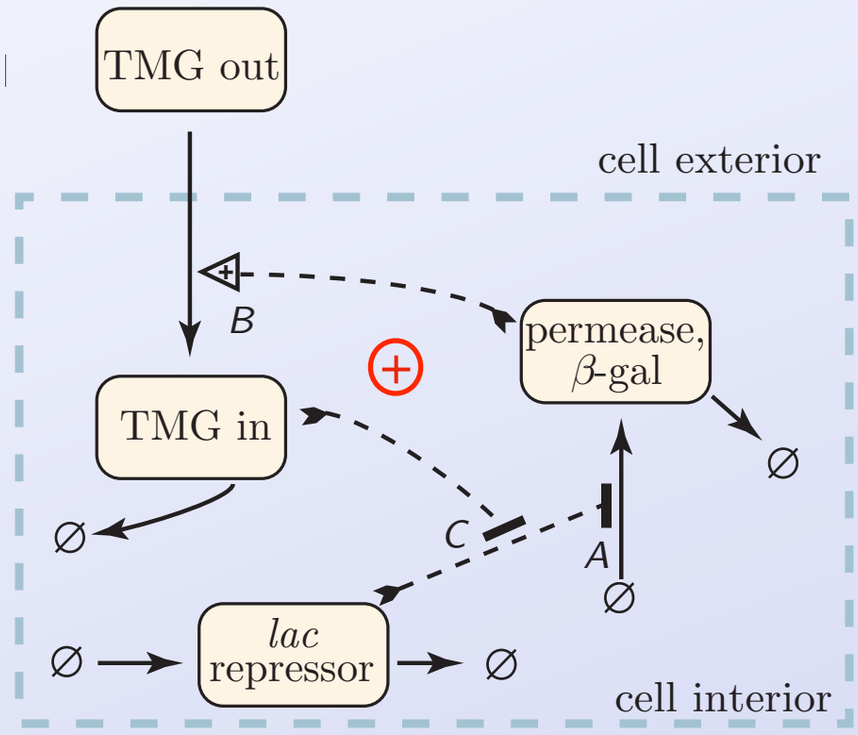
From P Nelson, *Physical models of living systems* (WH Freeman, to appear). Data from: Gardner et al., Nature (2000) vol. 403 (6767) pp. 339-42.

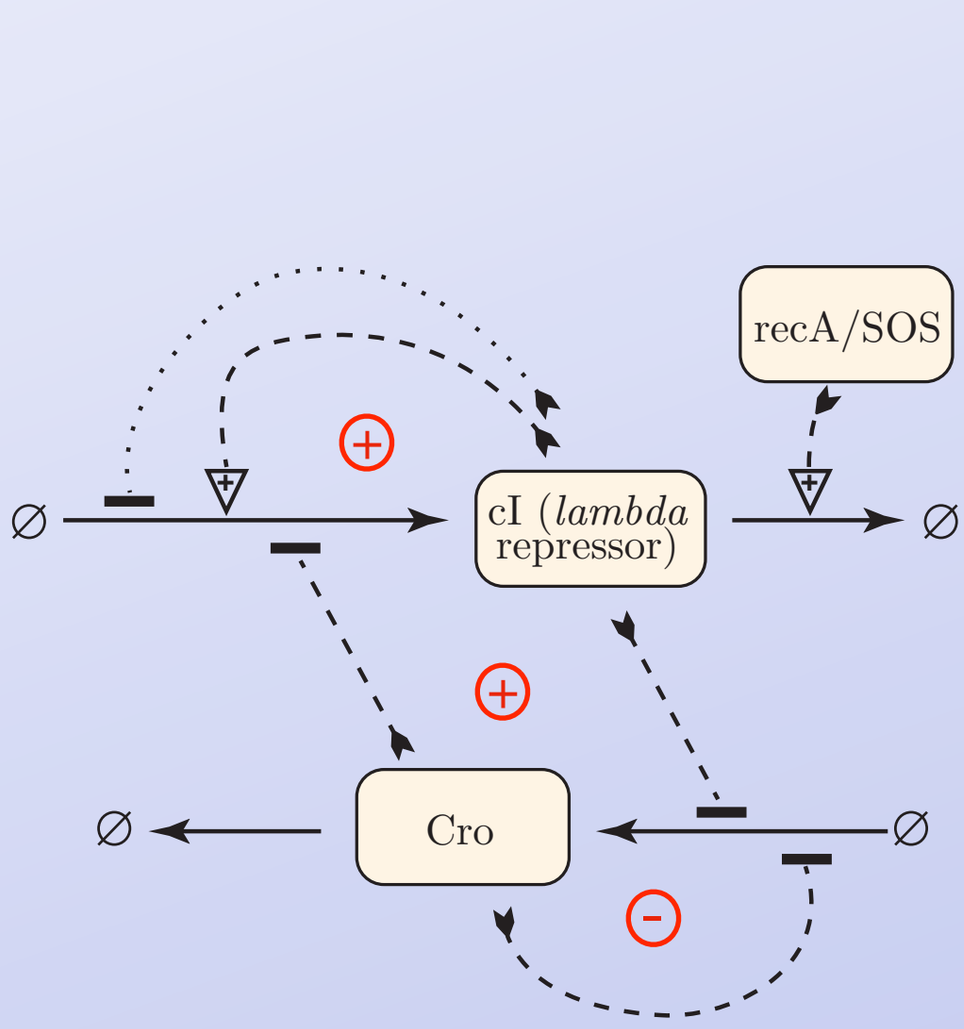
Biological problem 2: Switch response

Mechanical analogy 2: Toggle

Synthetic biology 2: Two-gene switch

Natural realization 2: *lac* and *lambda* switches

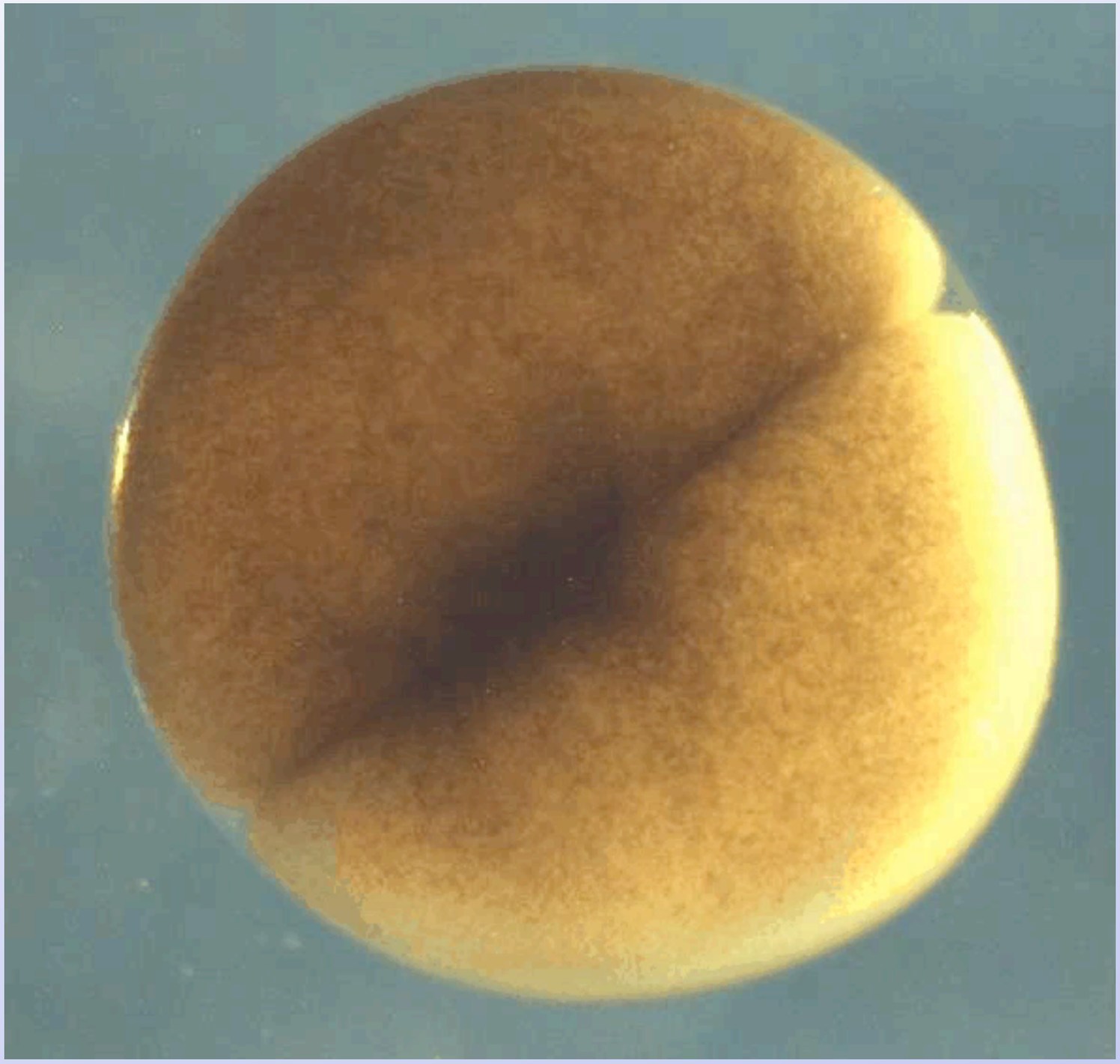




From P Nelson, *Physical models of living systems* (WH Freeman, to appear).

Biological problem 3: Periodic behavior

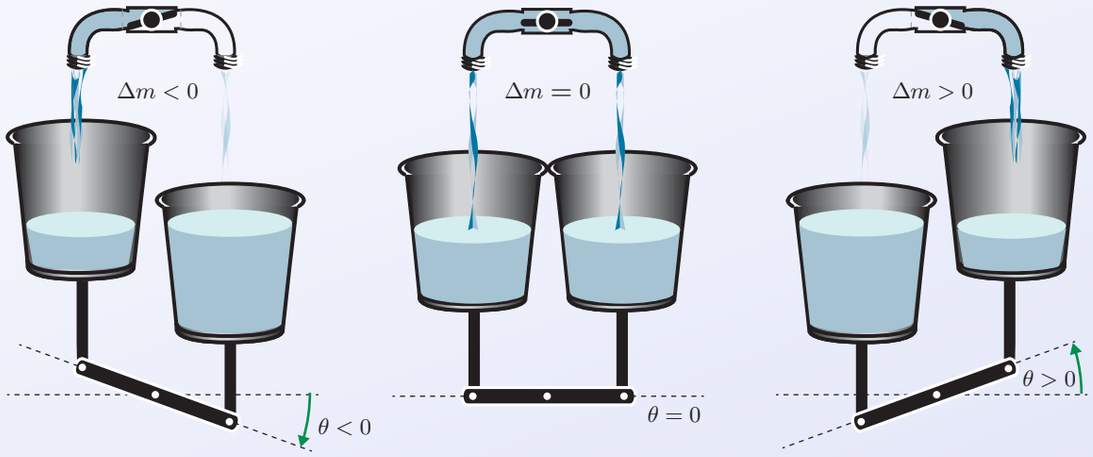
How do these cells stay in sync without communicating?



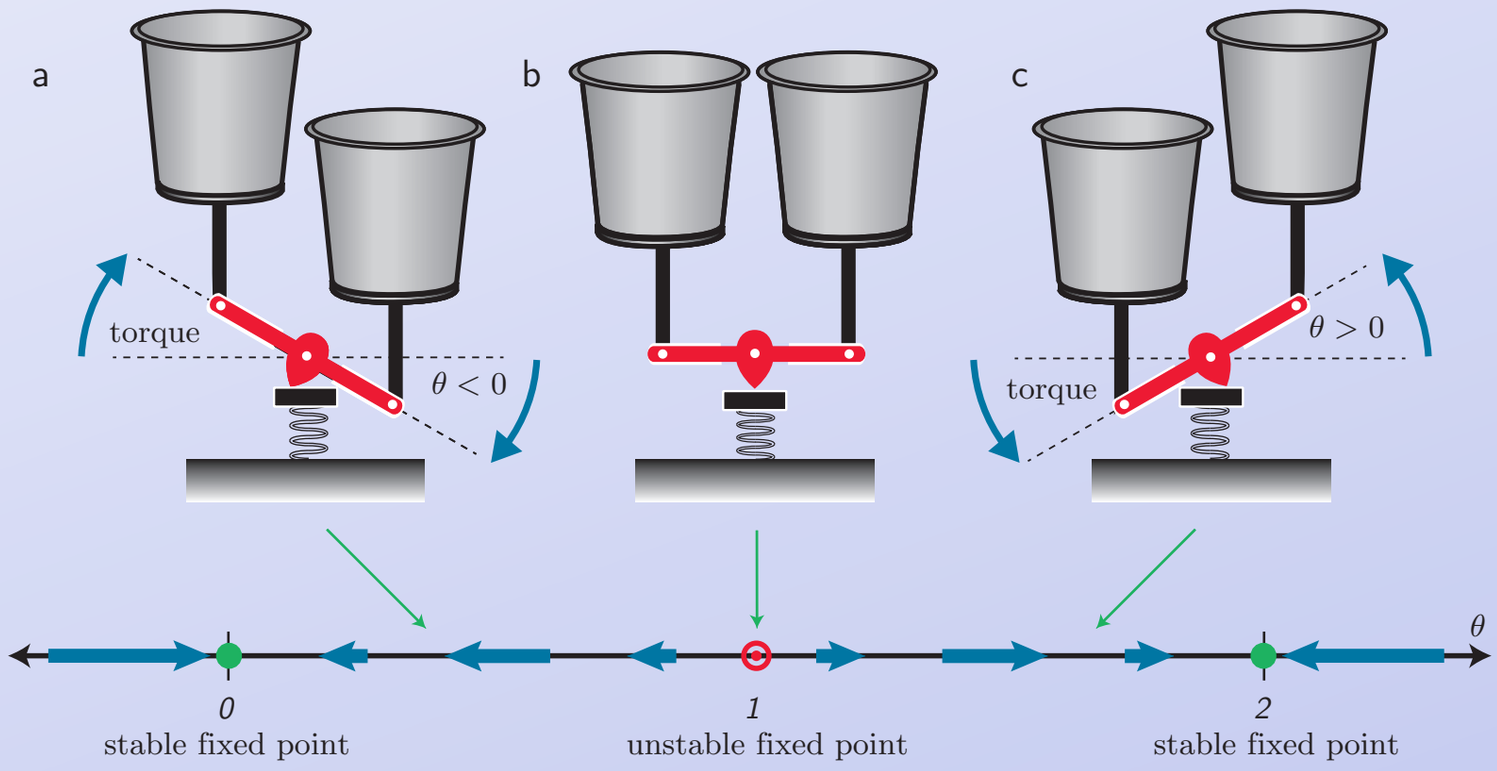
Video courtesy Tony Tsai.

Biological problem 3: Periodic behavior

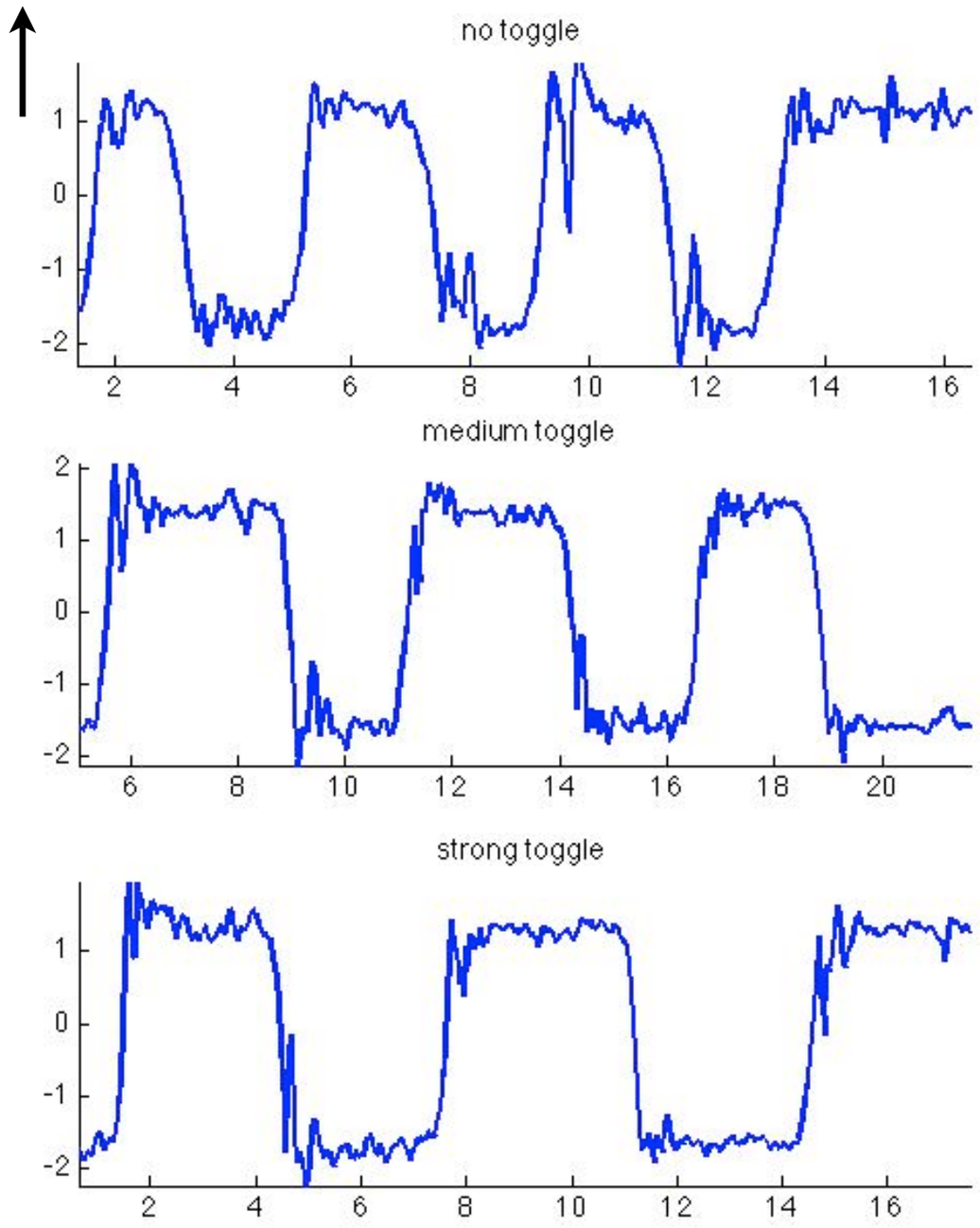
Mechanical analogy 3: Relaxation oscillator



From P Nelson, *Physical models of living systems* (WH Freeman, to appear).

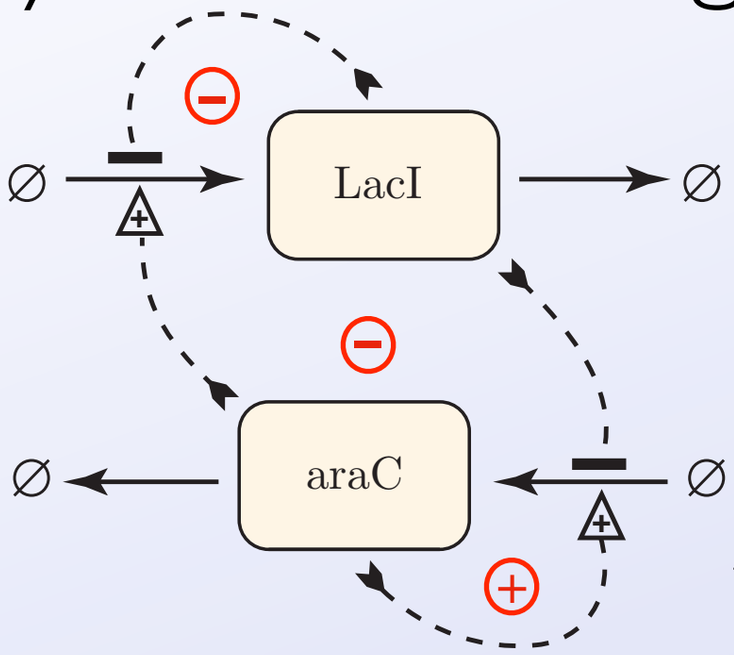


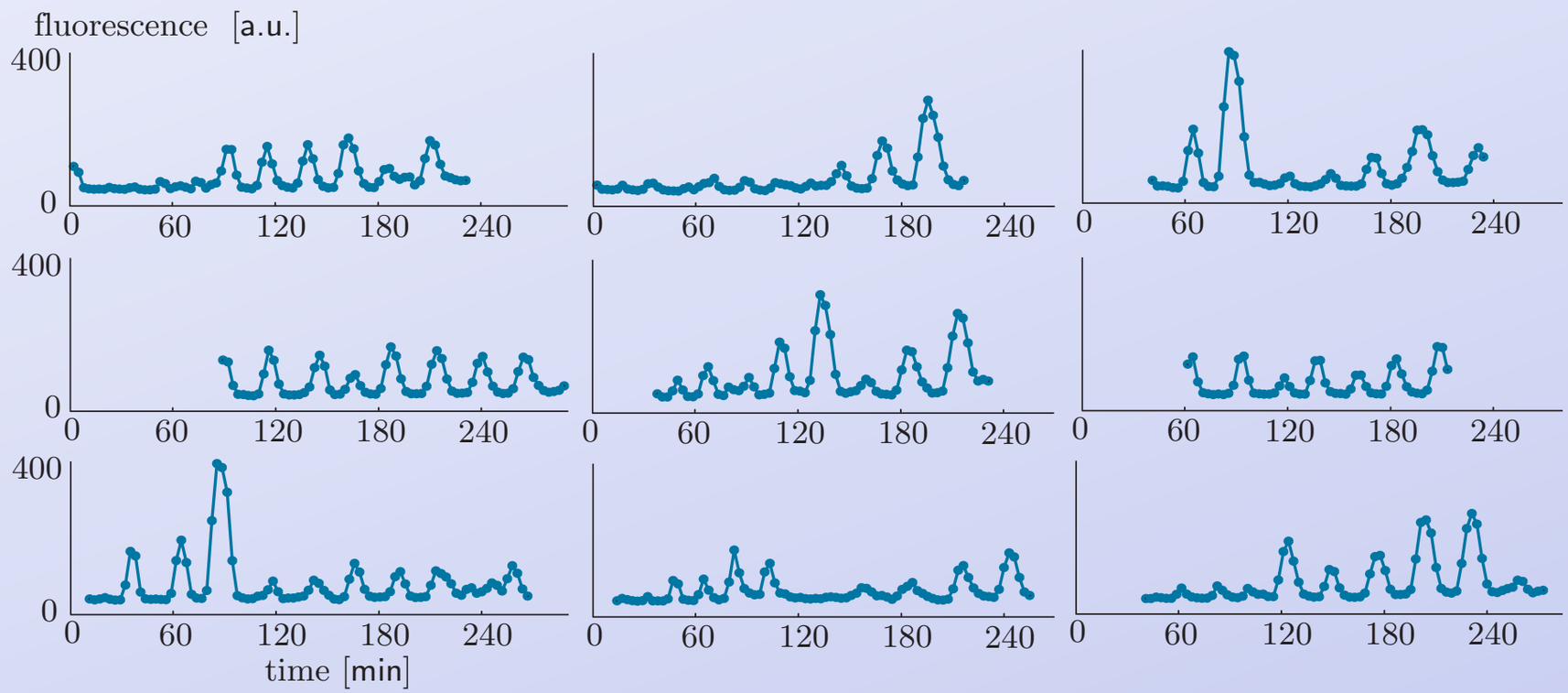
displacement



time

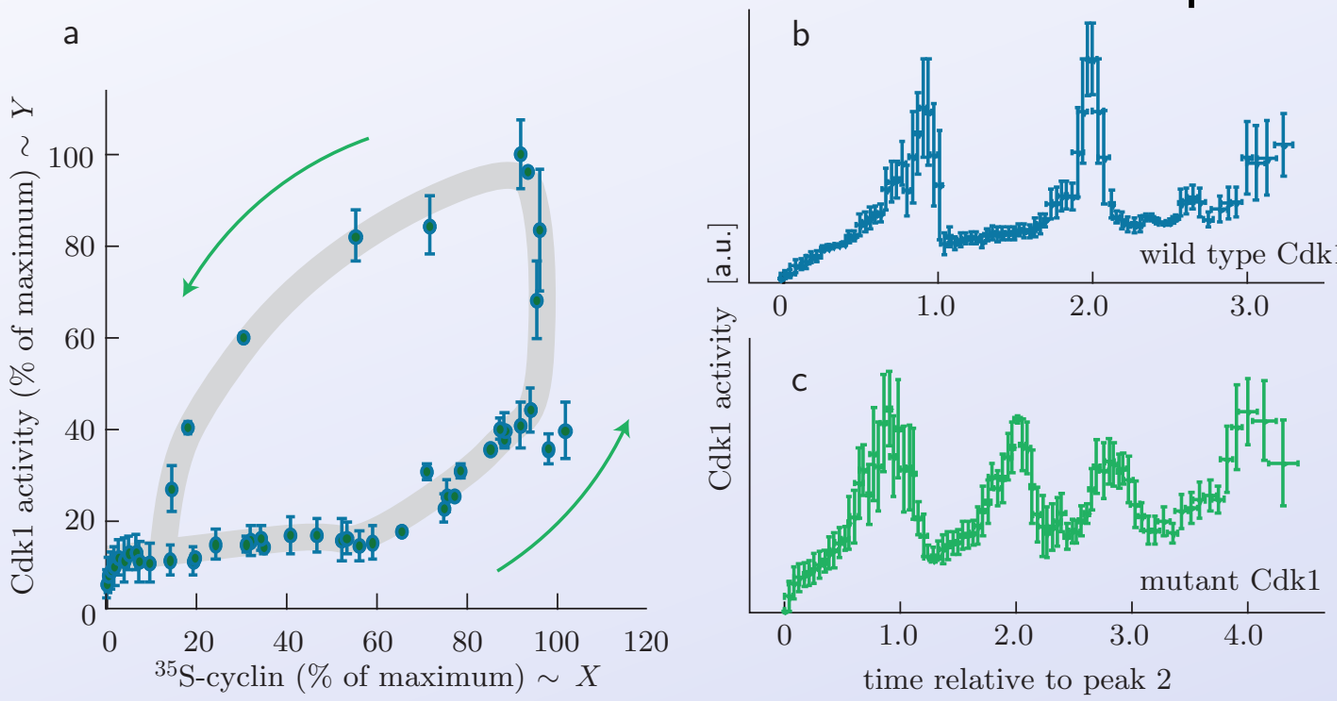
Biological problem 3: Periodic behavior
Mechanical analogy 3: Relaxation oscillator
Synthetic biology 3: Oscillation via linked +/- feedback loops

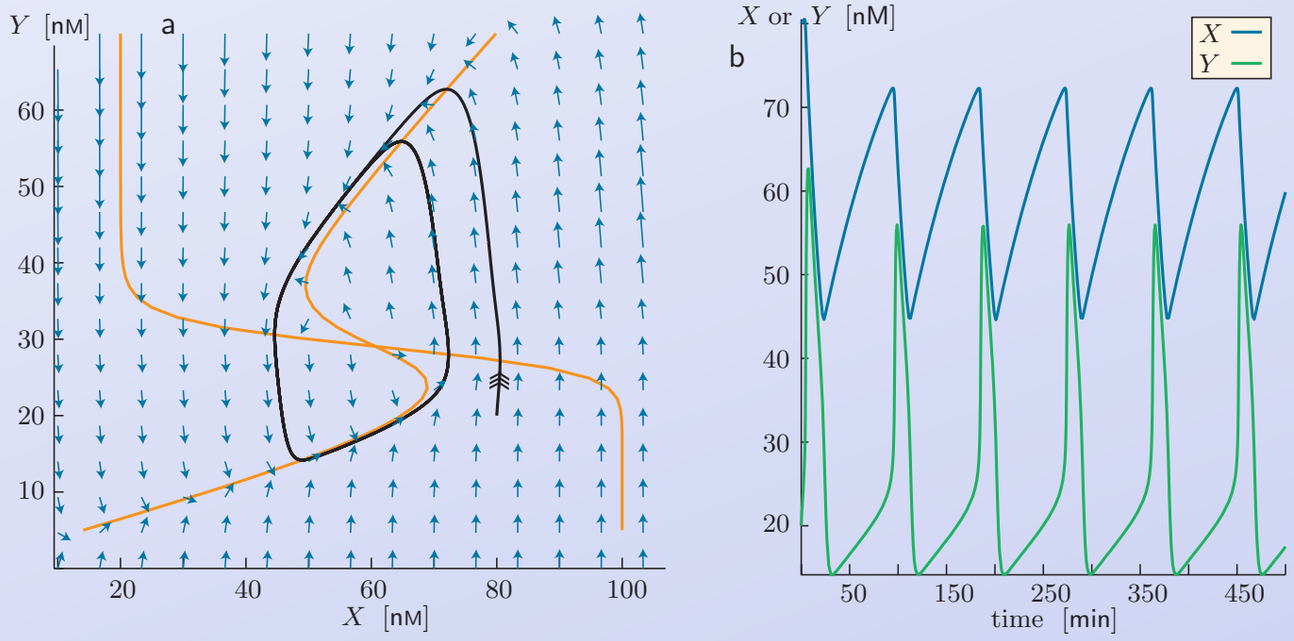




From P Nelson, *Physical models of living systems* (WH Freeman, to appear). Data from: Stricker et al., Nature (2008) vol. 456 (7221) pp. 516-519.

Biological problem 3: Periodic behavior
Mechanical analogy 3: Relaxation oscillator
Synthetic biology 3: Relaxation oscillator
Natural realization 3: Xenopus oocyte





From P Nelson, *Physical models of living systems* (WH Freeman, to appear). Data from: Pomerening et al., Cell (2005) vol. 122 (4) pp. 565-78.

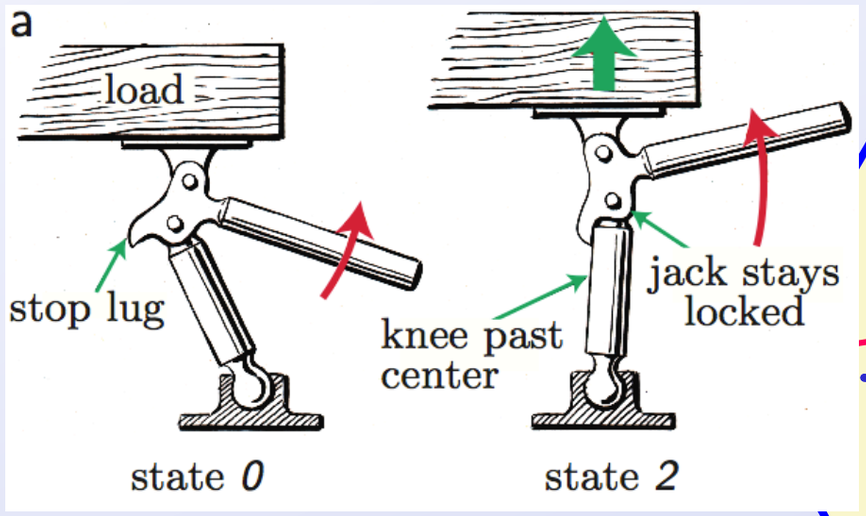
Wrap

So what is modeling anyway?

screed

Answer: ***It's a Tetrahedron***

[cf Rob's talk]:



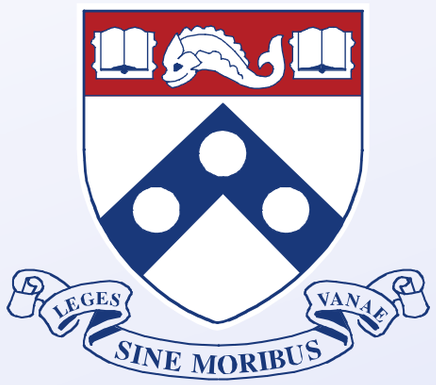

```
Nf1=figure(1);
quiver(dm,theta,dmdot.*scaling,thetadot.*scalin
g,1);
% nullclines
hold on;
smalltg = [-1.2:.02:1.2];
```

data

$$\frac{\mathrm{d}c_1}{\mathrm{d}t} = -\frac{c_1}{\tau_1} + \frac{\Gamma_1/V}{1+(c_2/K_{\mathrm{d},2})^{n_1}}$$
$$\frac{\mathrm{d}c_2}{\mathrm{d}t} = -\frac{c_2}{\tau_2} + \frac{\Gamma_2/V}{1+(c_1/K_{\mathrm{d},1})^{n_2}}$$

"Yadda, yadda... feedback, yadda... bistability, hysteresis, yadda,... bifurcation...

Thanks



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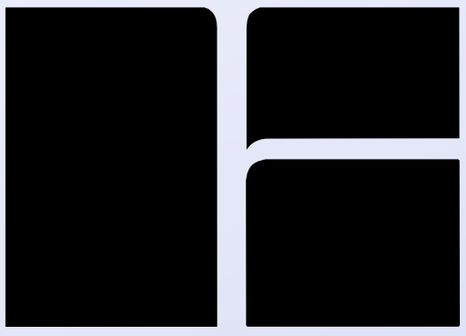
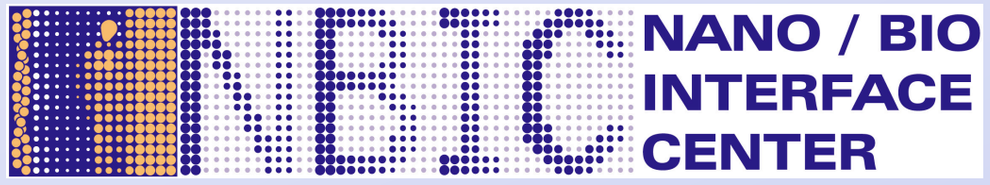


W H Freeman and Co.



NSF NSEC

For these slides see:

www.physics.upenn.edu/~pcn

Why do we even have classes at all?

✳**To tell them facts?**
No -- facts are now free in infinite quantity.

✳**To tell them the latest, most trustworthy facts?**
No -- none of us can be as up to date as Wikipedia.

Well -- *skills and habits* still matter a lot. When you walk into a room with your toolbag and encounter a problem you've never seen, which tool should you pull out of your bag? Knowing where to begin is a difficult but learnable skill.

Students need to develop the right skills and habits for that, but many (most?) courses don't really help.

A class should help them do that -- in some specific context. ***Biological physics is an interesting context for that purpose***, regardless whether a student goes on in that field.

The interesting questions in science are those where we shake our heads and ask, ***"How could anything like that possibly happen at all?"*** And biophysics is full of such questions.

wrap