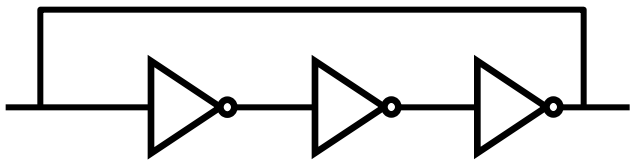
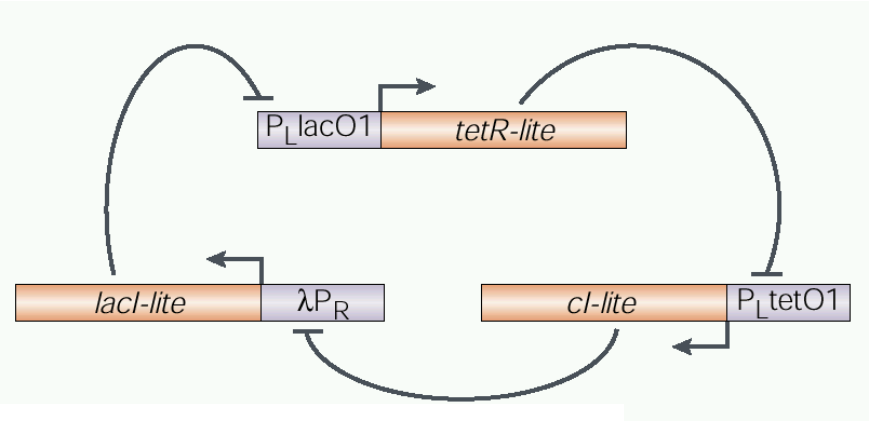
Evolution of synthetic oscillators

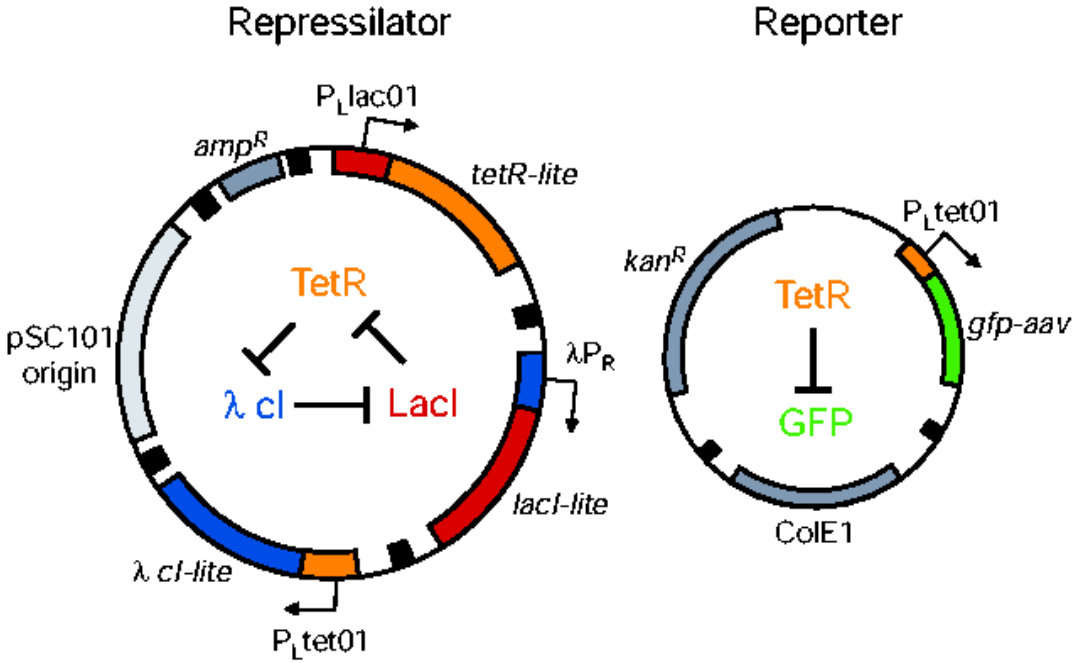
Year	Lab	Description
2000	Leibler	Repressilator
2003	Ninfa	Relaxation (activator/inhibitor)
2005	Liao	Metabollator
2009	Hasty	Tunable relaxation oscillator
2009	Fussenegger	Mammalian oscillator
2010	Hasty	Synchronized oscillator

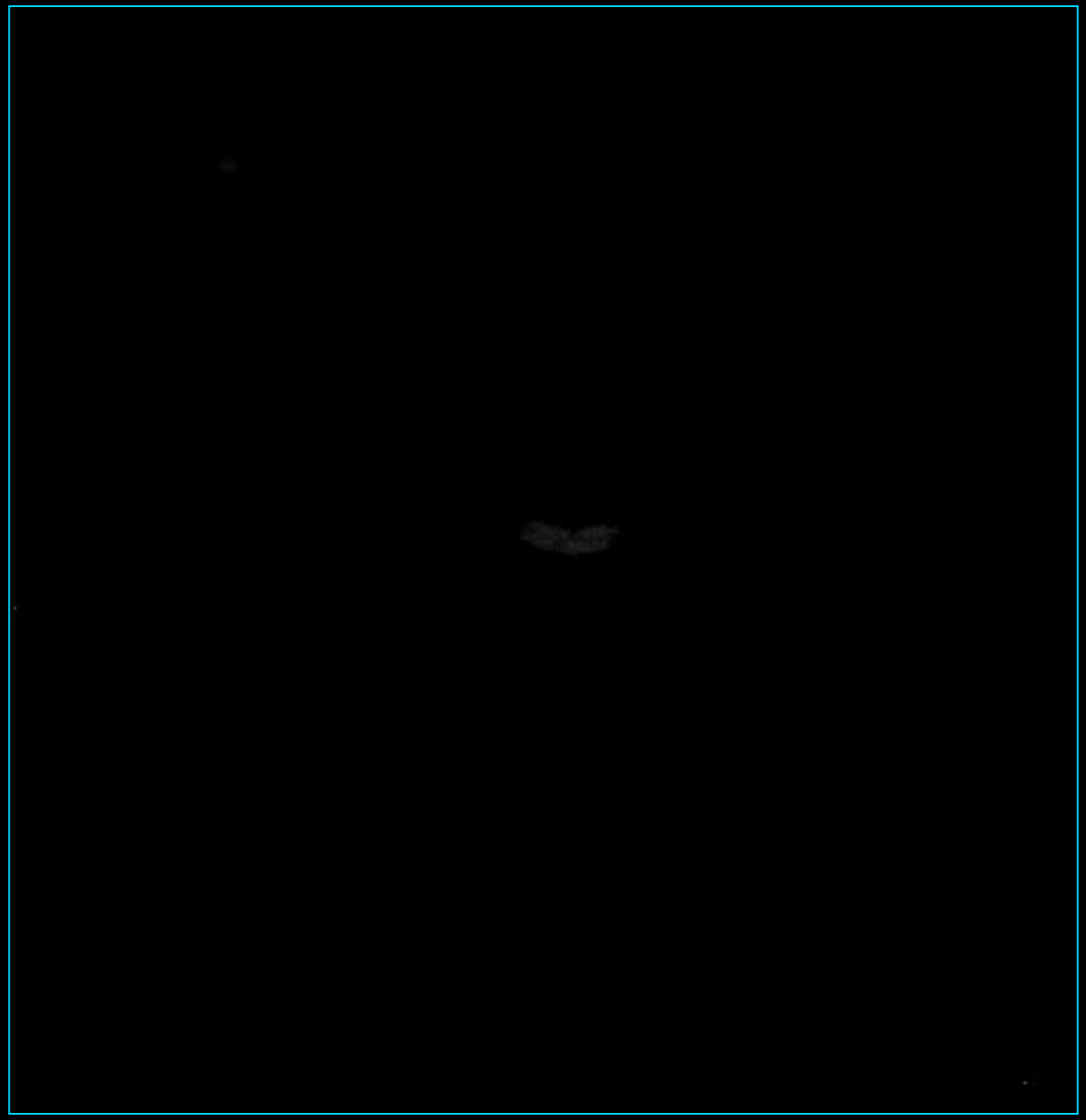
The Ring Oscillator

[Elowitz, Leibler 2000]



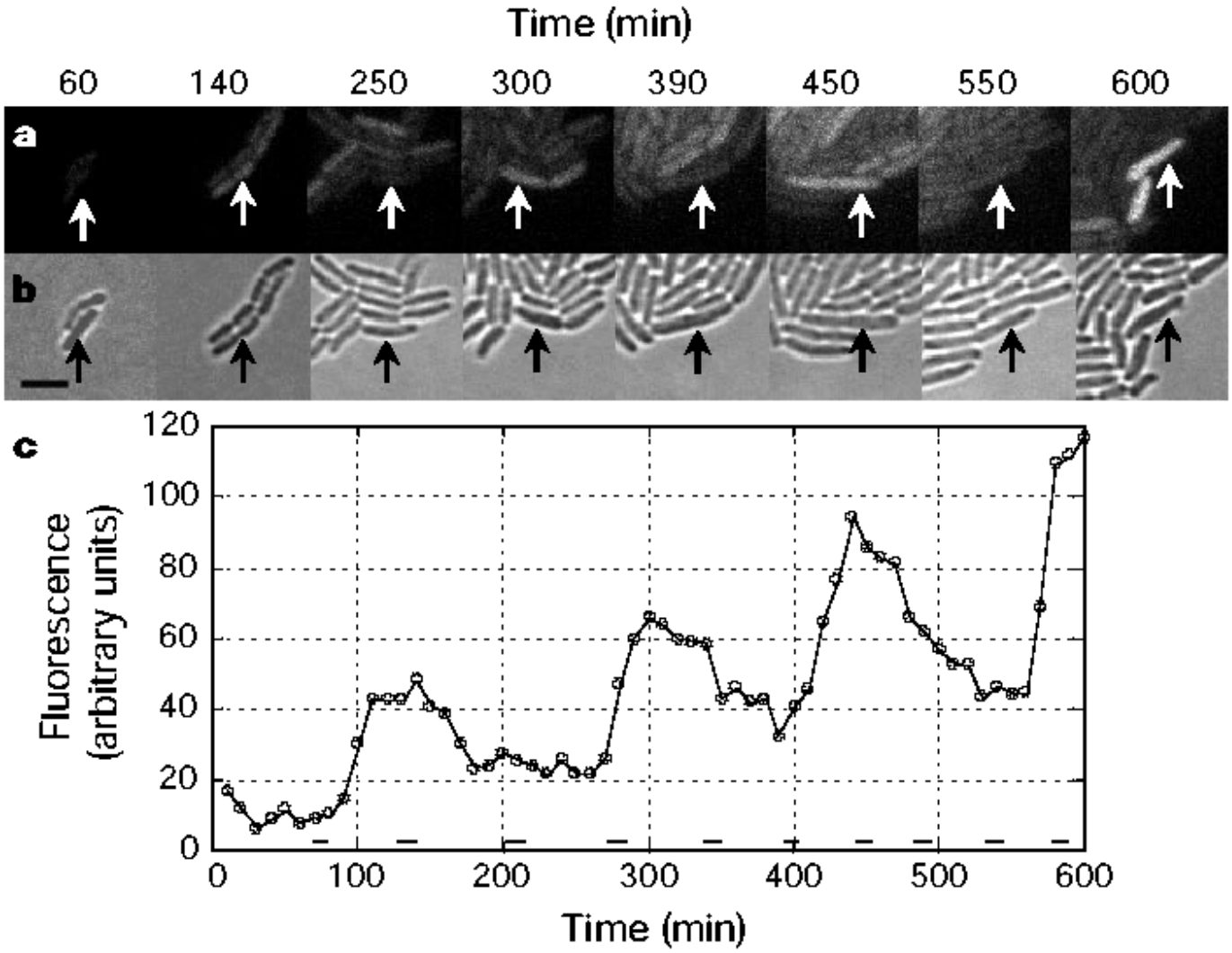




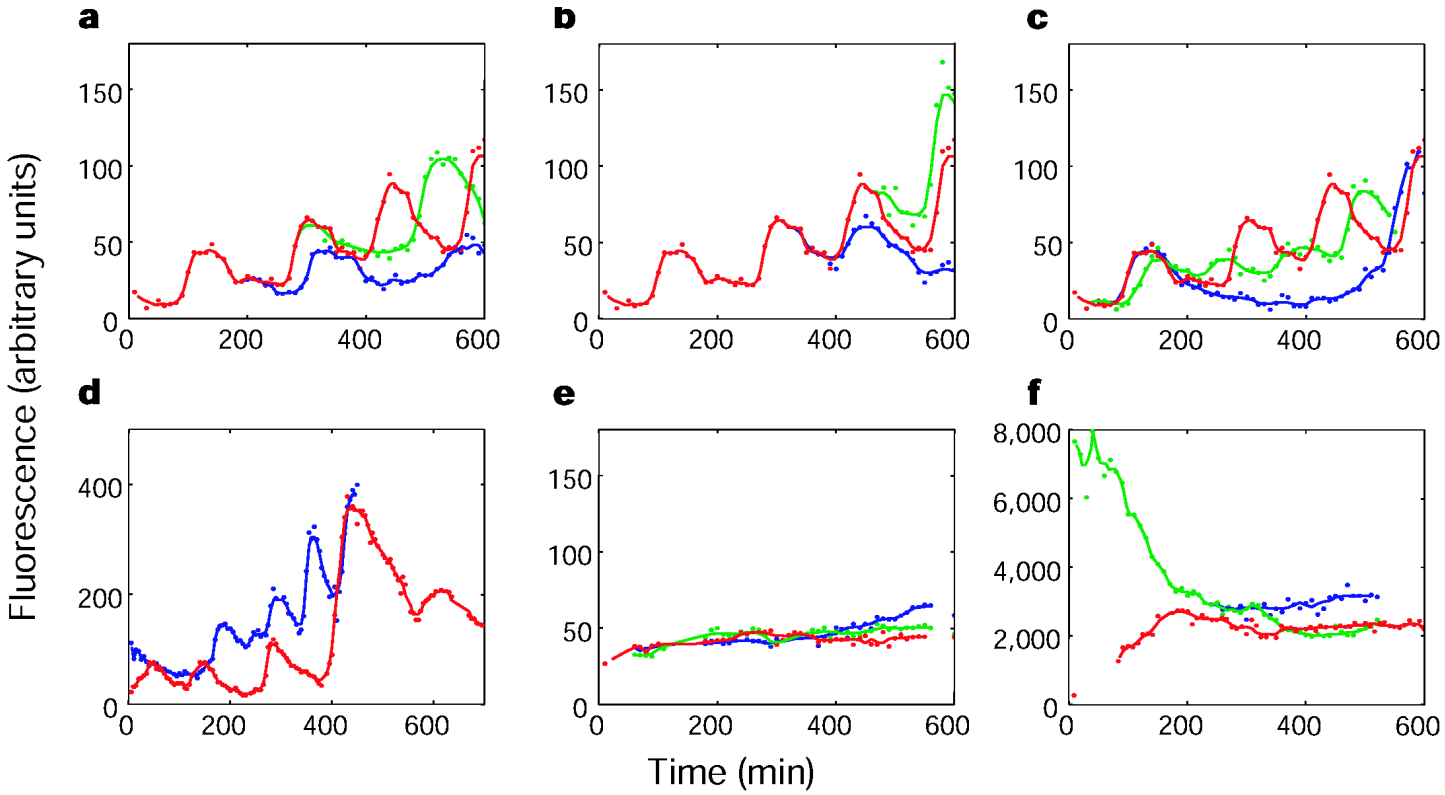


Courtesy: Michael Elowitz

Example of Oscillation



Evaluation of the Ring Oscillator



[Elowitz & Leibler, 2000]

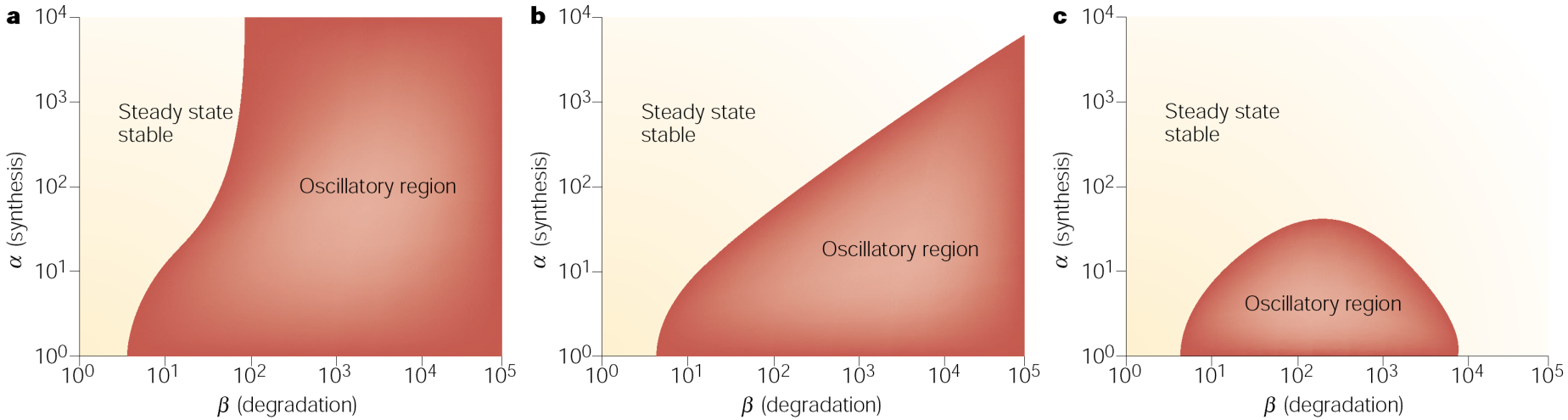
Reliable long-term oscillation doesn't work yet

➢ Need to match gates, maybe use other network motifs

Requirements for Oscillation

$$\frac{dm_i}{dt} = -m_i + \frac{\alpha}{(1+p_j^n)} + \alpha_0 \qquad \begin{pmatrix} i = lacI, tetR, cI \\ j = cI, lacI, tetR \end{pmatrix}$$

$$\frac{dp_i}{dt} = -\beta(p_i - m_i)$$

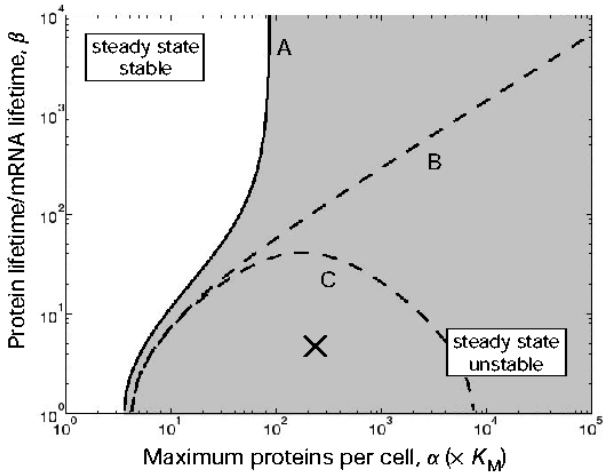


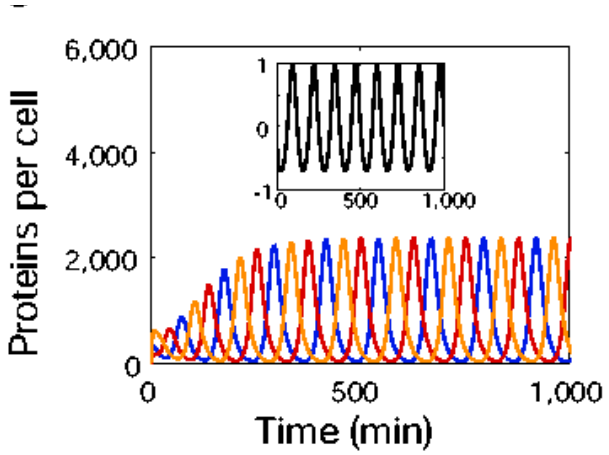
$n = 2.1, \ \alpha_0 = 0$ $\qquad$ $n = 2.0, \ \alpha_0 = 0$ $\qquad$ $n = 2.0, \ \alpha_0/\alpha = 10^{-3}$

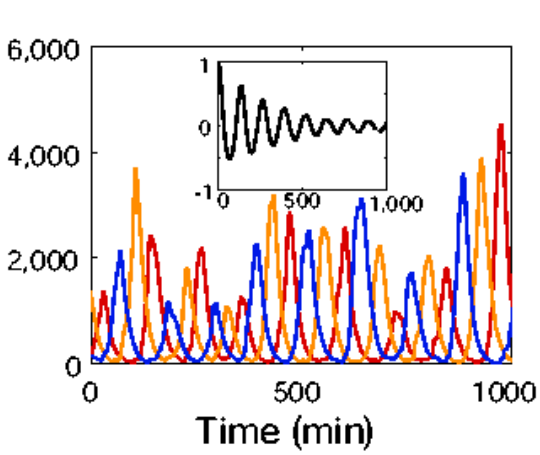
Analysis of Oscillation

$$\frac{dm_i}{dt} = -m_i + \frac{\alpha}{(1+p_j^n)} + \alpha_0 \qquad \begin{pmatrix} i = lacI, tetR, cI \\ j = cI, lacI, tetR \end{pmatrix}$$

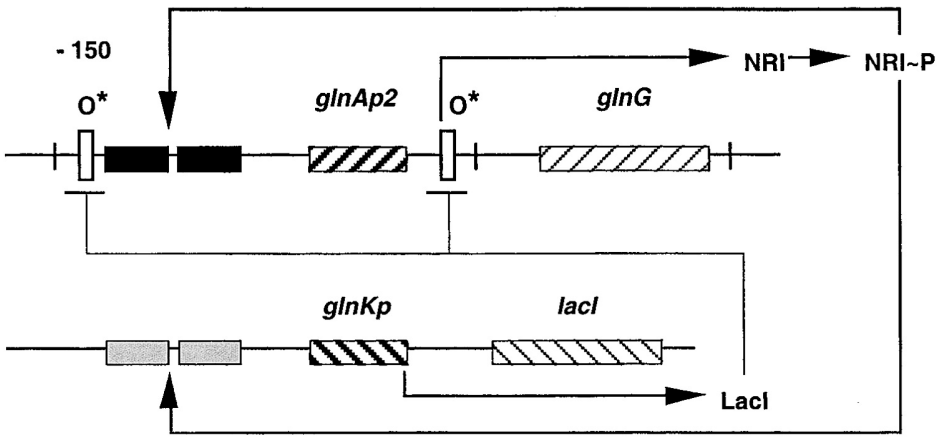
$$\frac{dp_i}{dt} = -\beta(p_i - m_i)$$

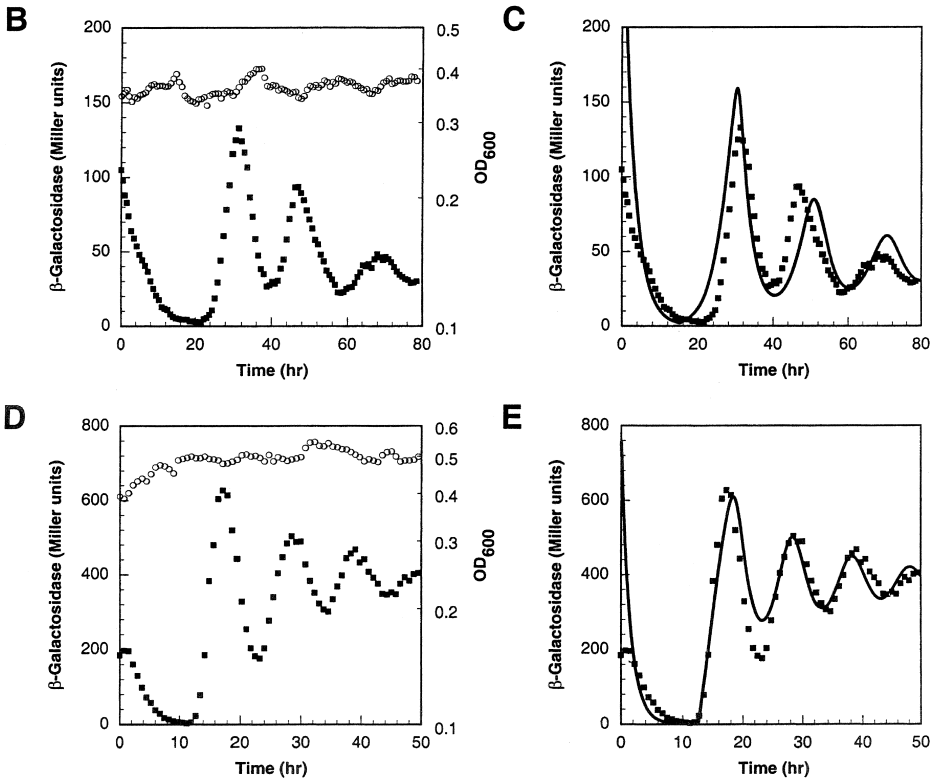






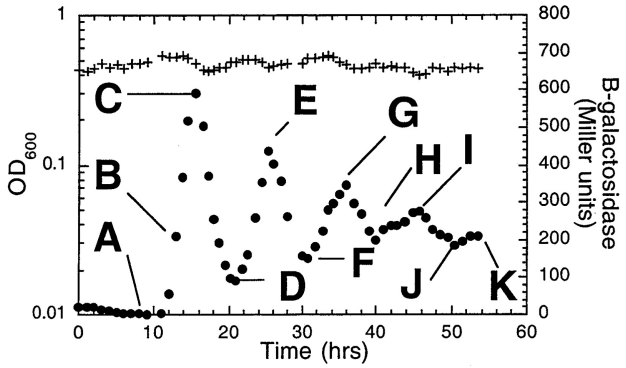
Ninfa's Genetic Clock

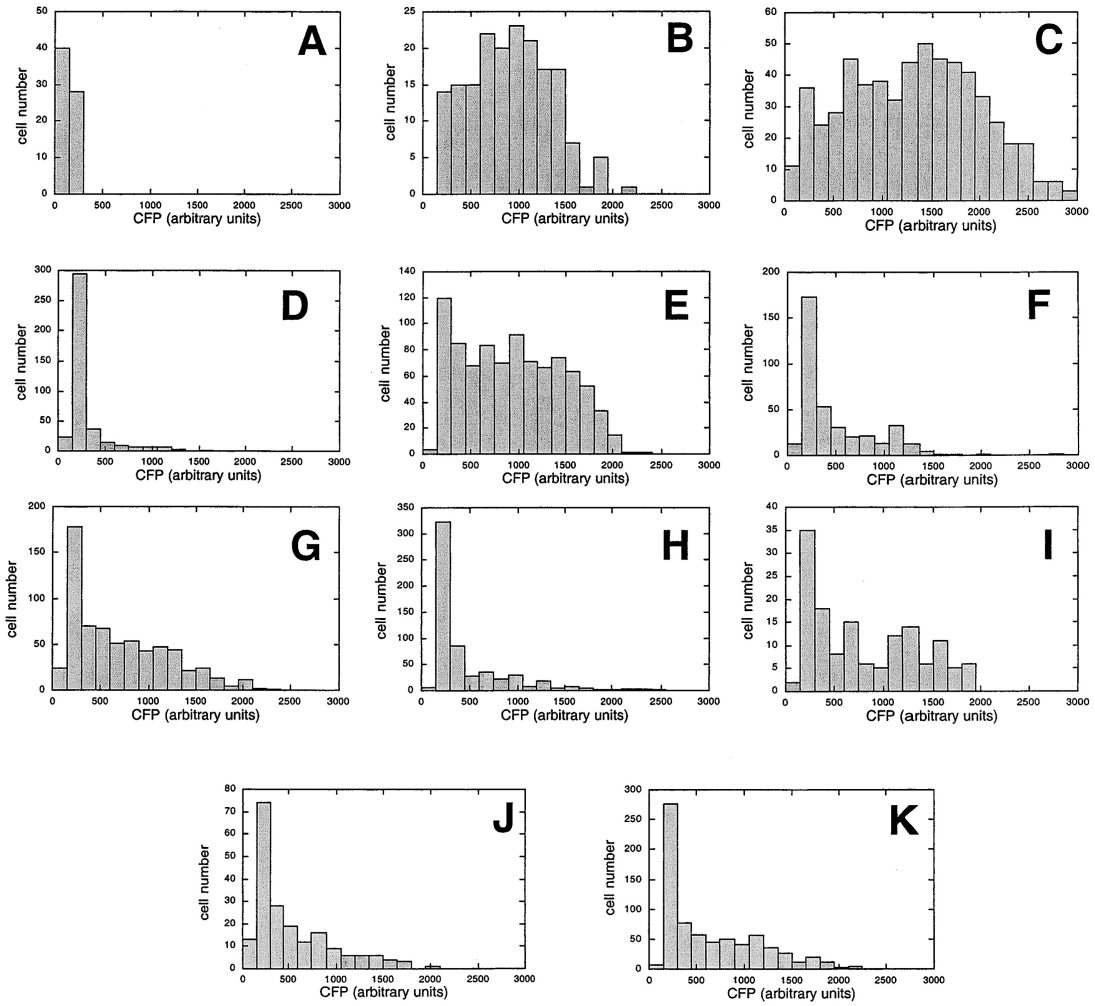




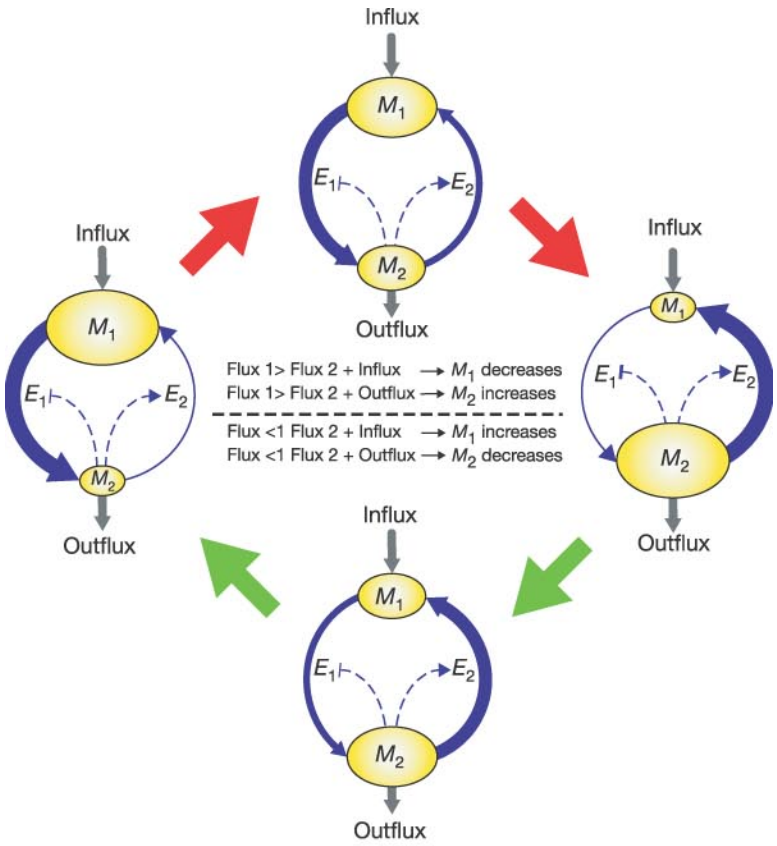
Mariette R. Atkinson, Michael A. Savageau, Jesse T. Myers,2,3 and Alexander J. Ninfa, Development of Genetic Circuitry Exhibiting Toggle Switch or Oscillatory Behavior in *Escherichia coli*, Cell, Vol. 113, 597–607, 2003

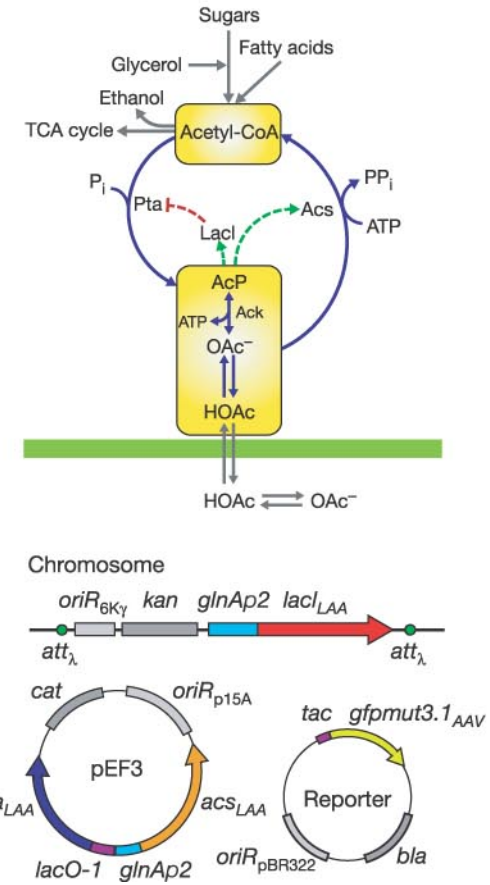
Single cell statistics





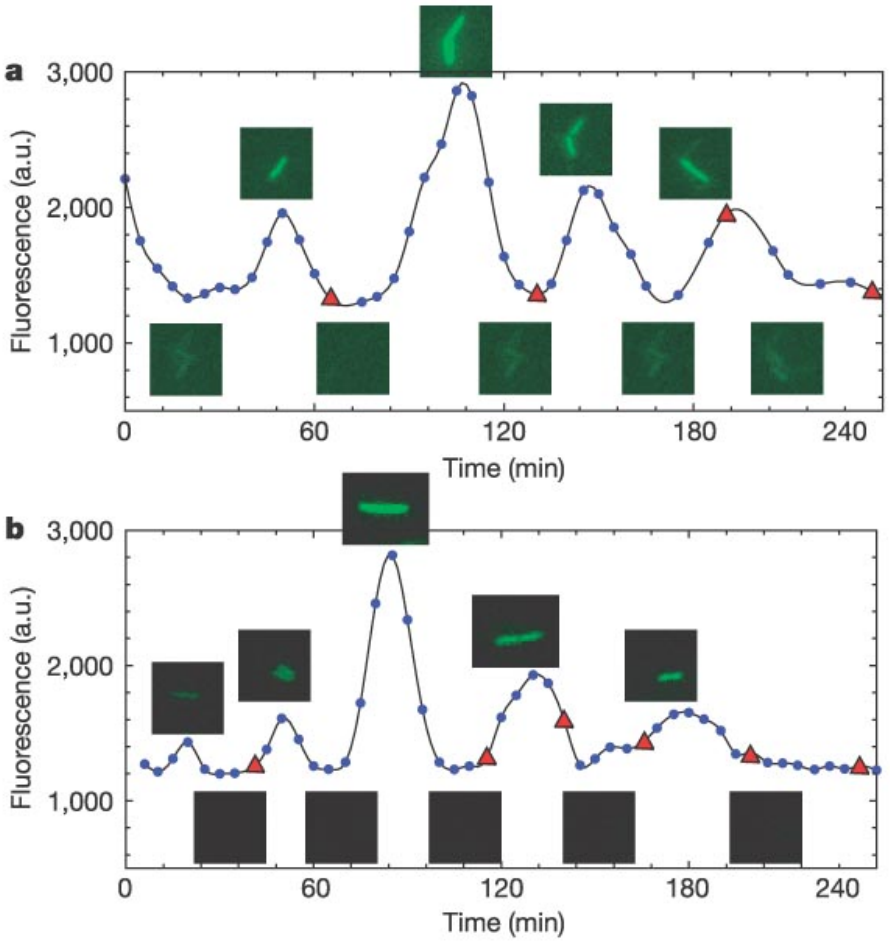
Metabolic Oscillator

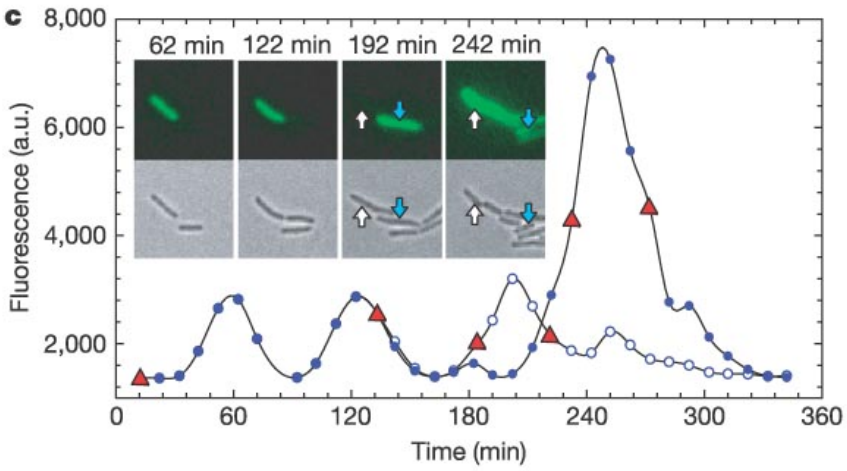




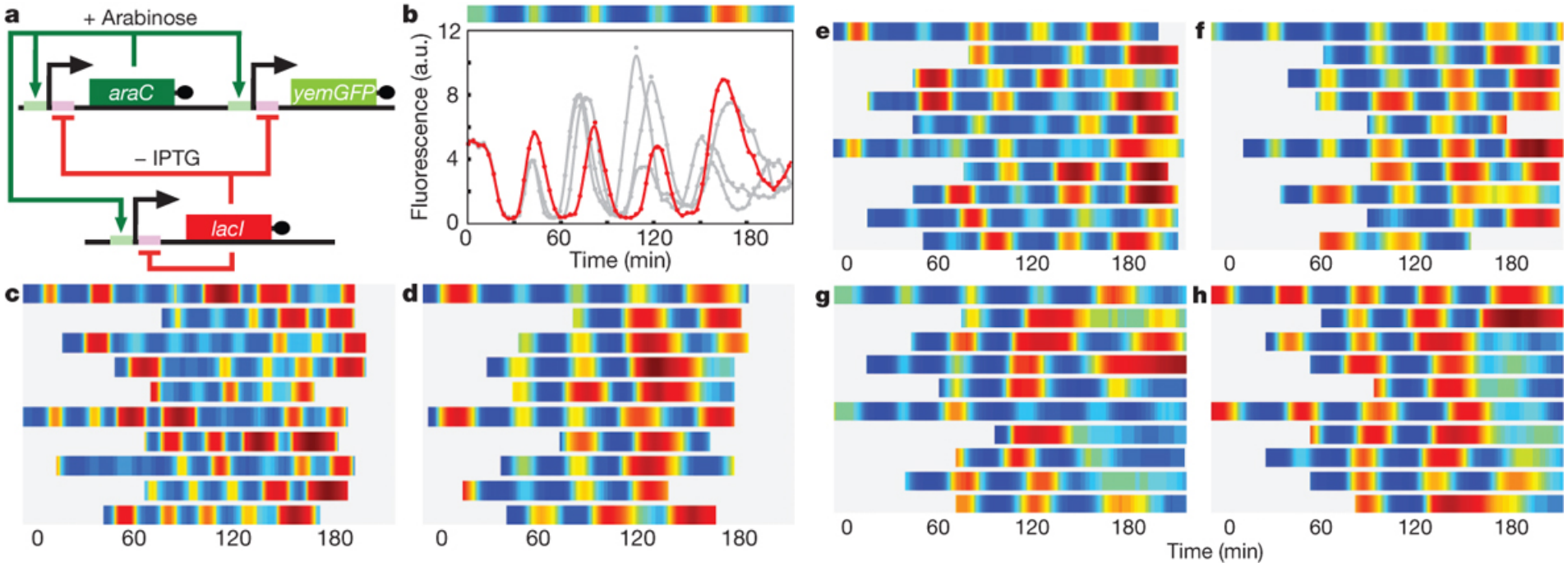
Eileen Fung, Wilson W. Wong, Jason K. Suen, Thomas Bulter, Sun-gu Lee & James C. Liao, A synthetic gene–metabolic Oscillator. Nature, VOL 435 (2005)

Metabollator Dynamics



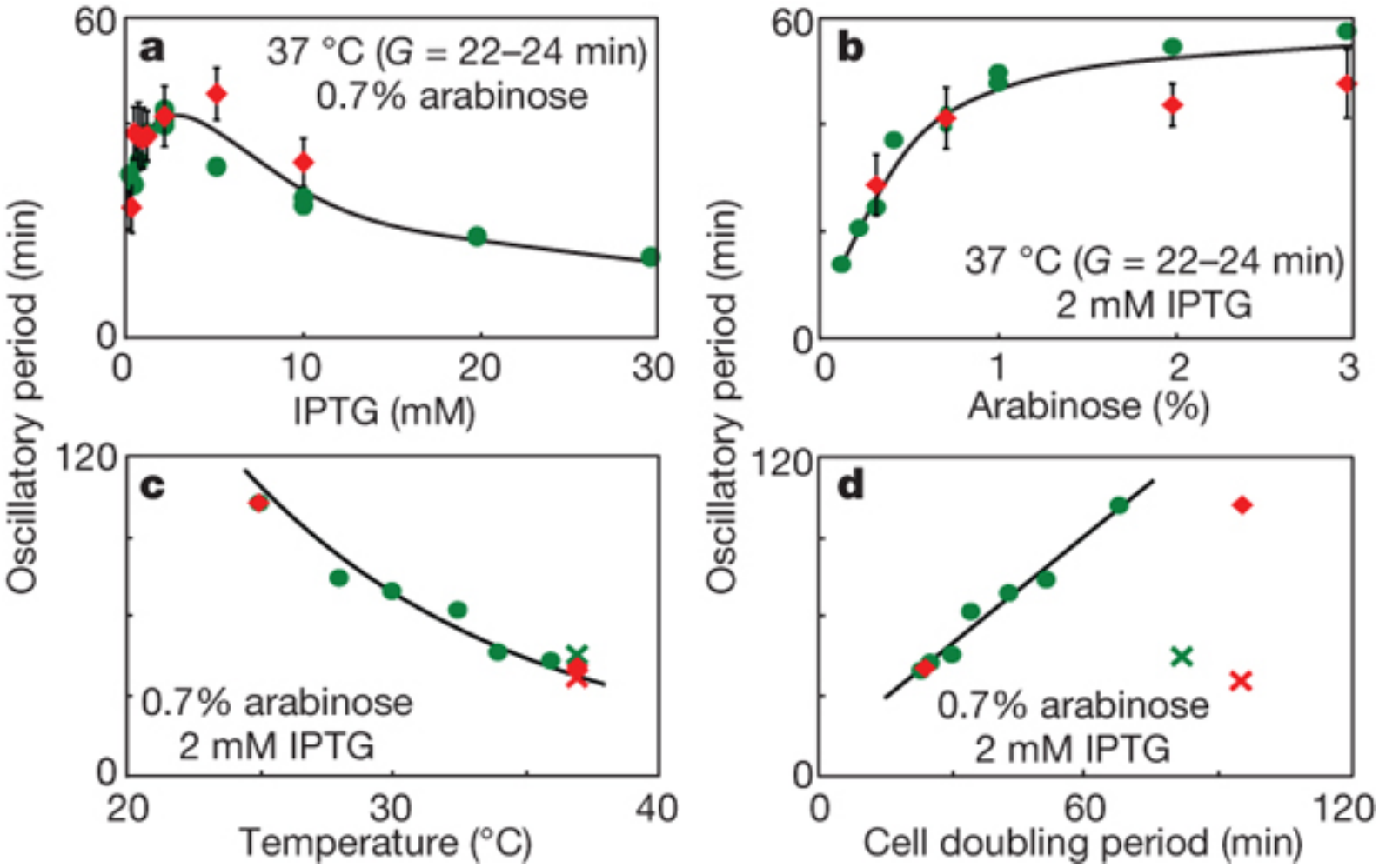


A Tunable Oscillator

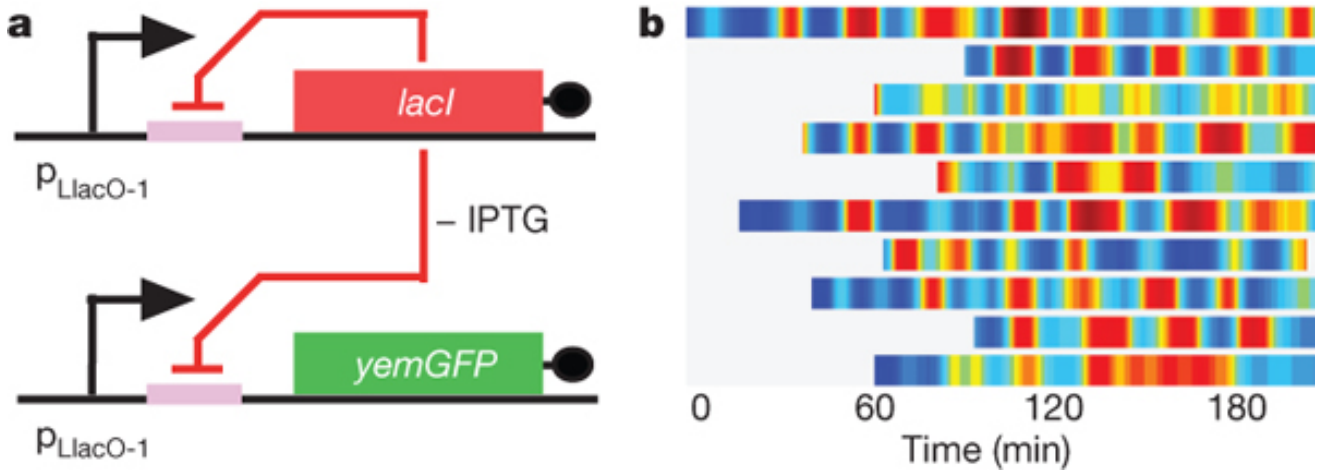


Jesse Stricker, Scott Cookson, Matthew R. Bennett, William H. Mather, Lev S. Tsimring & Jeff Hasty, A fast, robust and tunable synthetic gene oscillator Nature, Vol 456|27, 2008

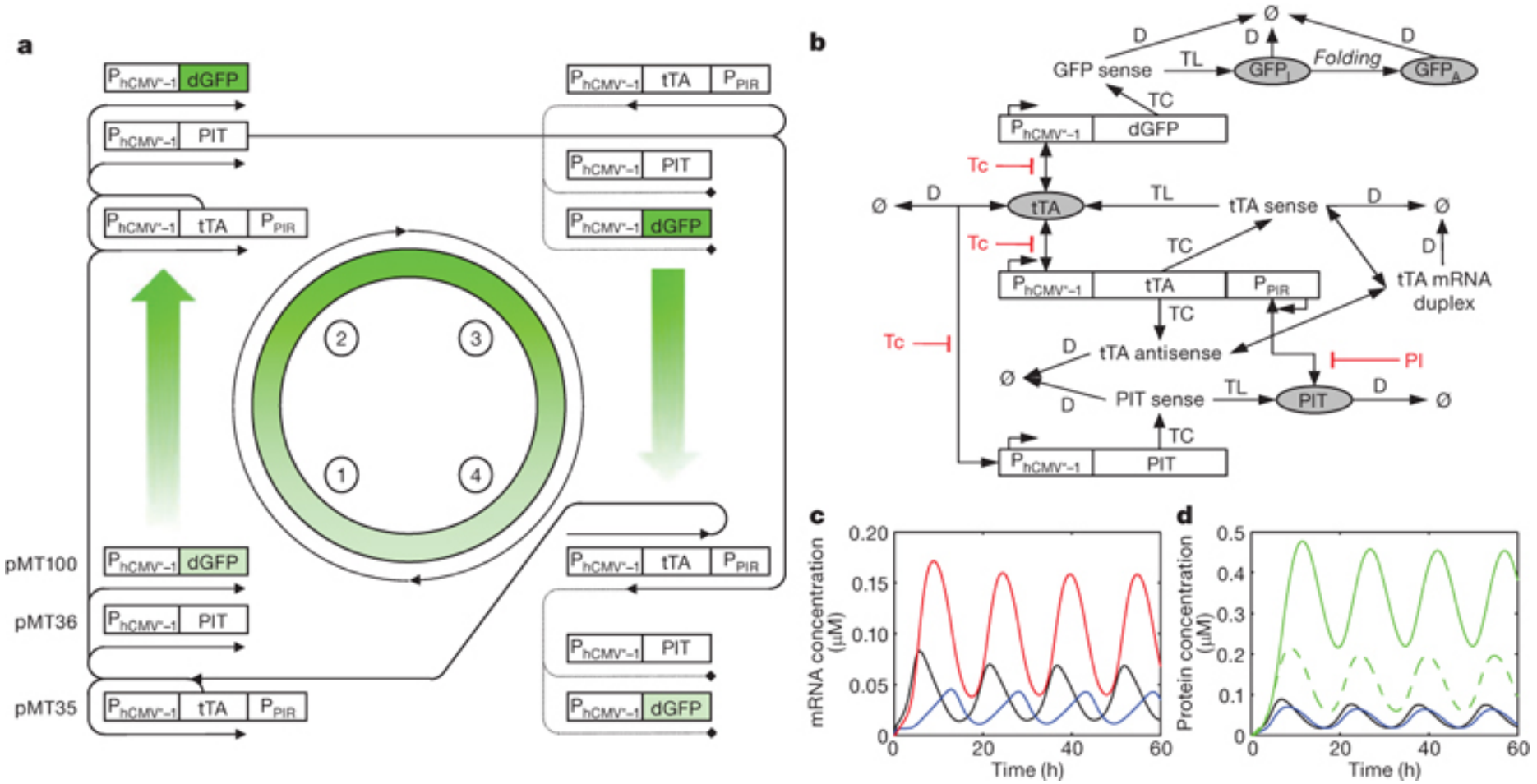
A Tunable Oscillator



An oscillator with no positive feedback loop

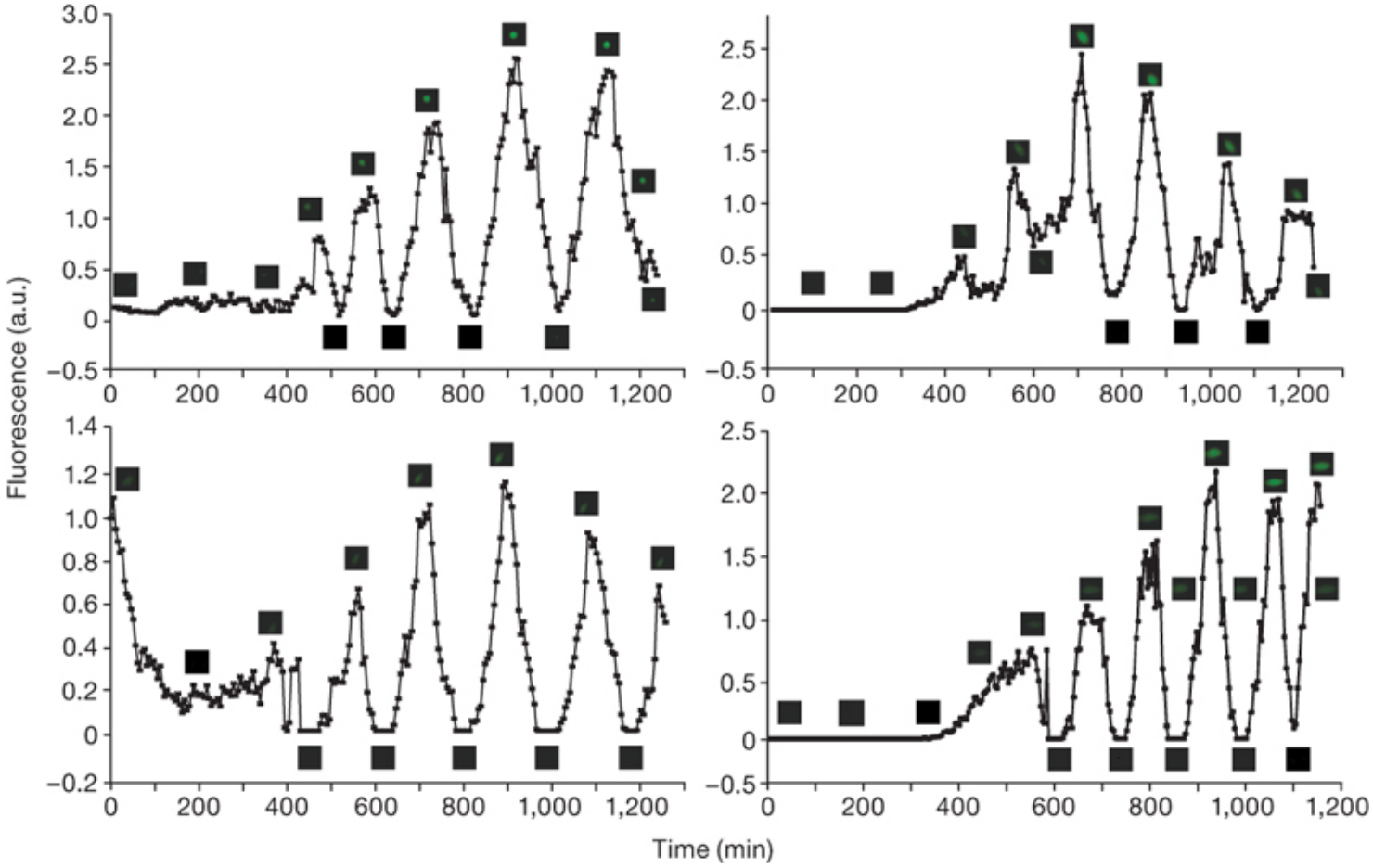


A mammalian oscillator

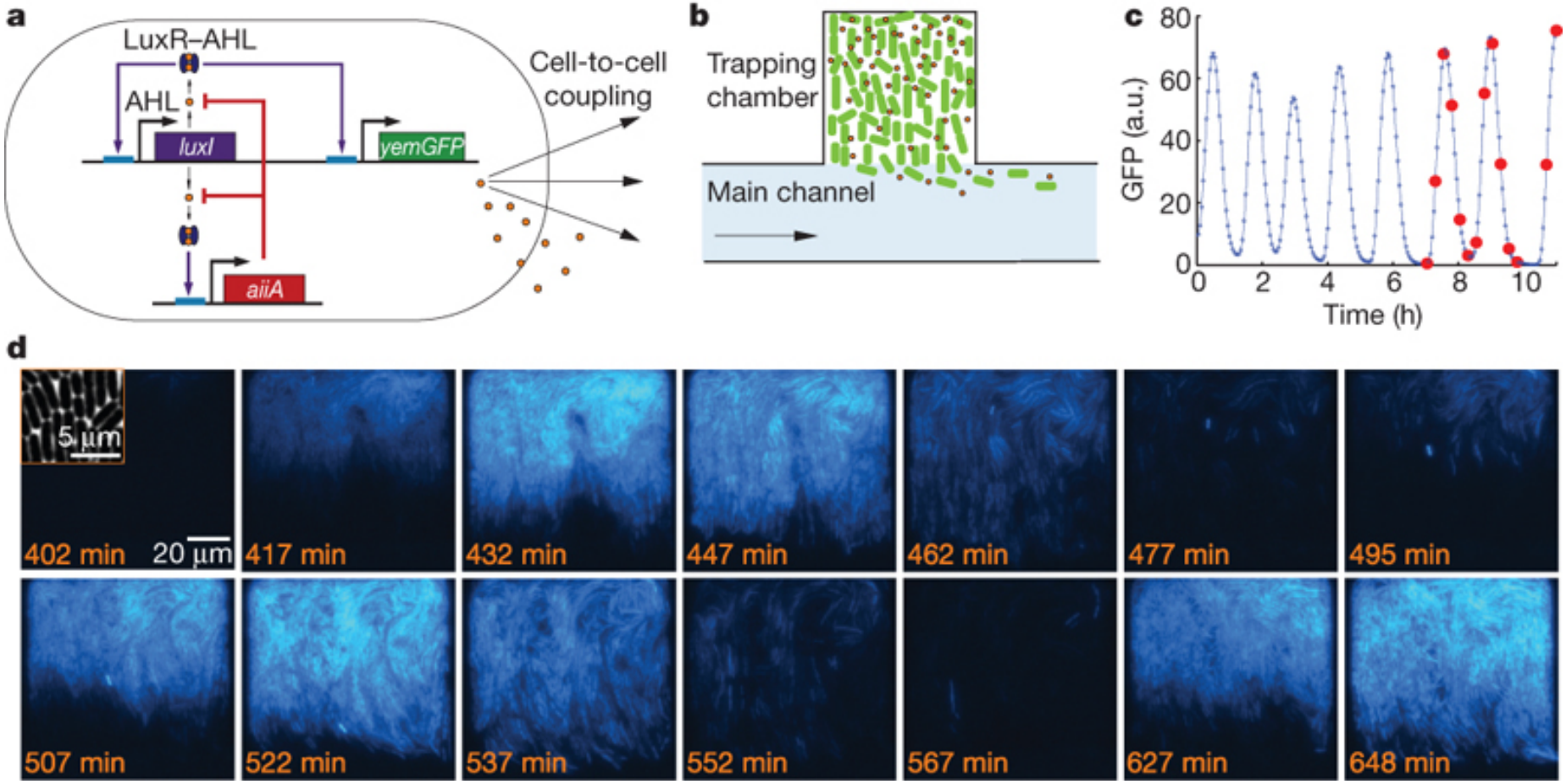


Marcel Tigges, Tatiana T. Marquez-Lago, Joerg Stelling & Martin Fussenegger, A tunable synthetic mammalian oscillator, Nature, Vol 457, 2009

Single cell behaviors

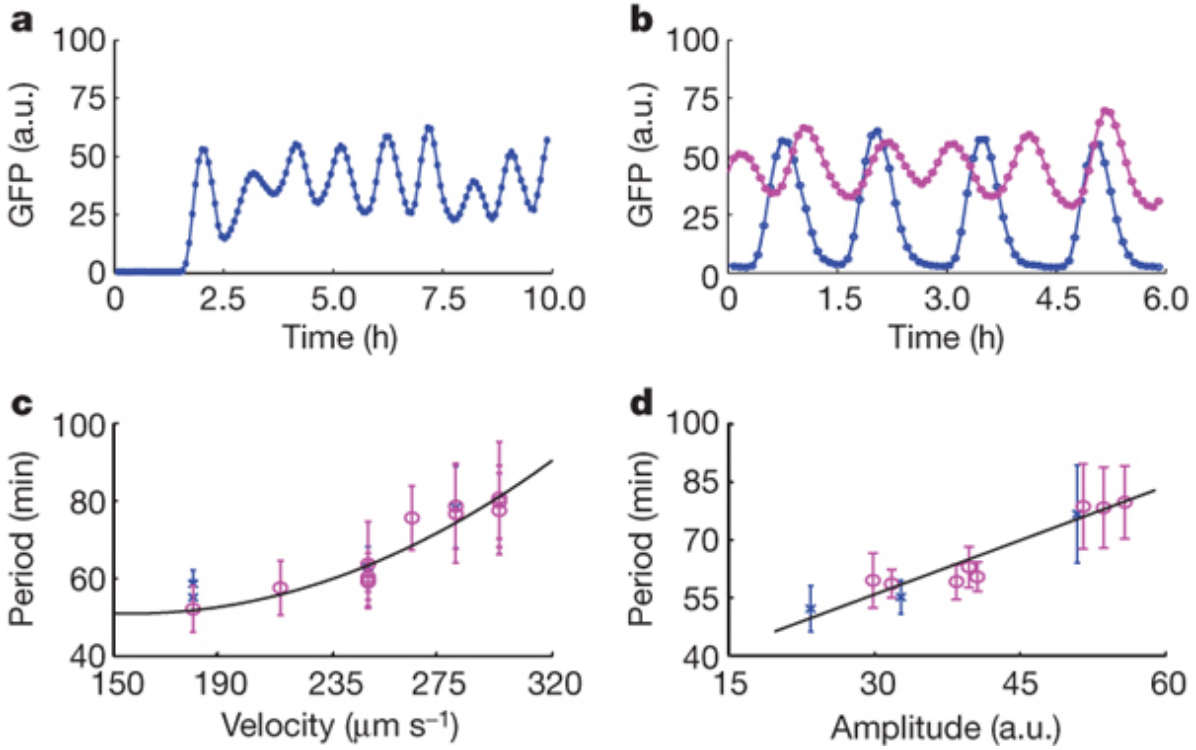


Synchronized oscillators

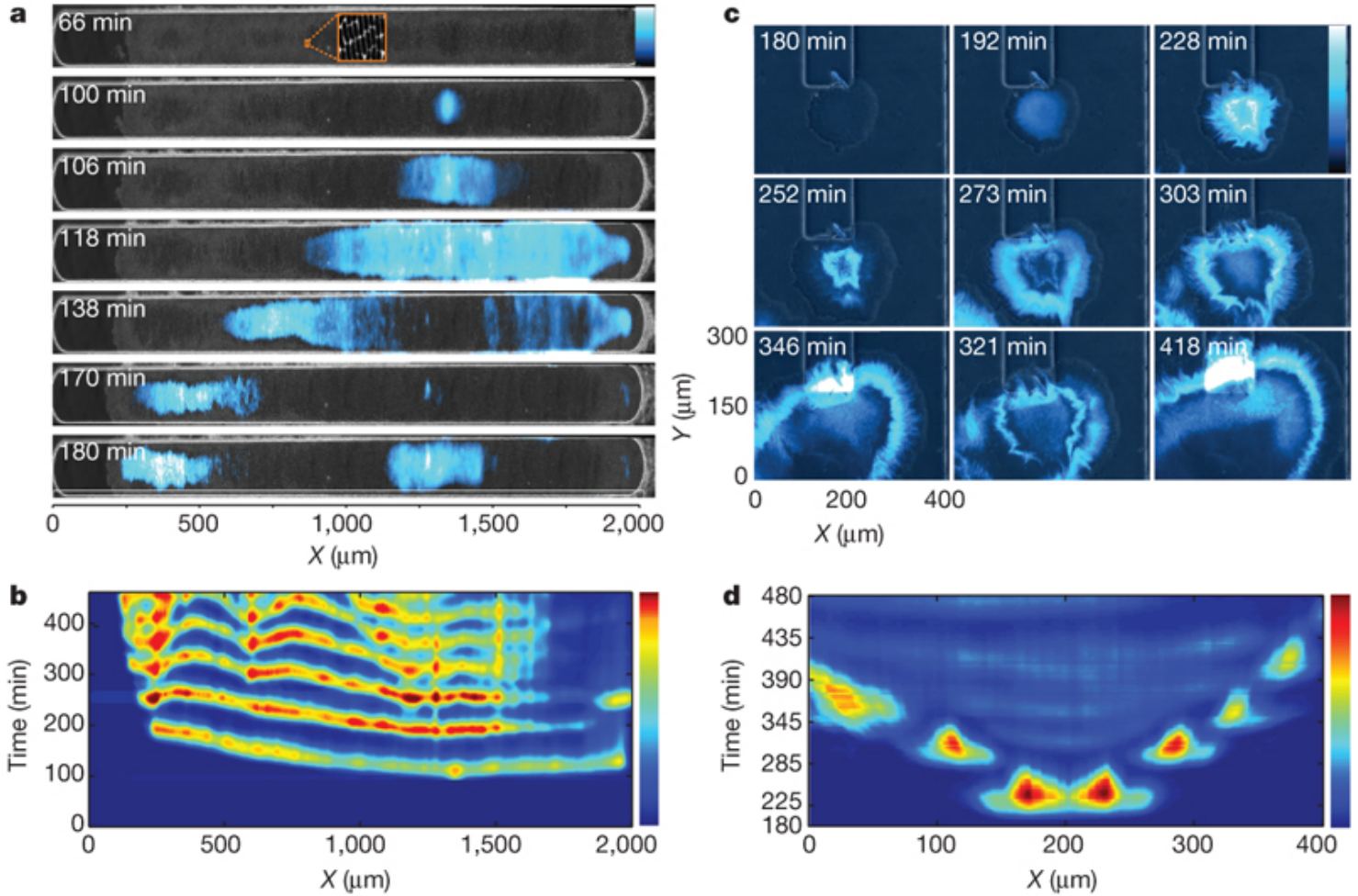


Tal Danino, Octavio Mondrago´n-Palomino, Lev Tsimring & Jeff Hasty, A synchronized quorum of genetic clocks, Nature, Vol 463| 21 (2010)

Dynamics under different microfluidic conditions



Spatiotemporal dynamics



Spatiotemporal models