A Tug-of-War Mechanism for Pattern Formation in a Genetic Network

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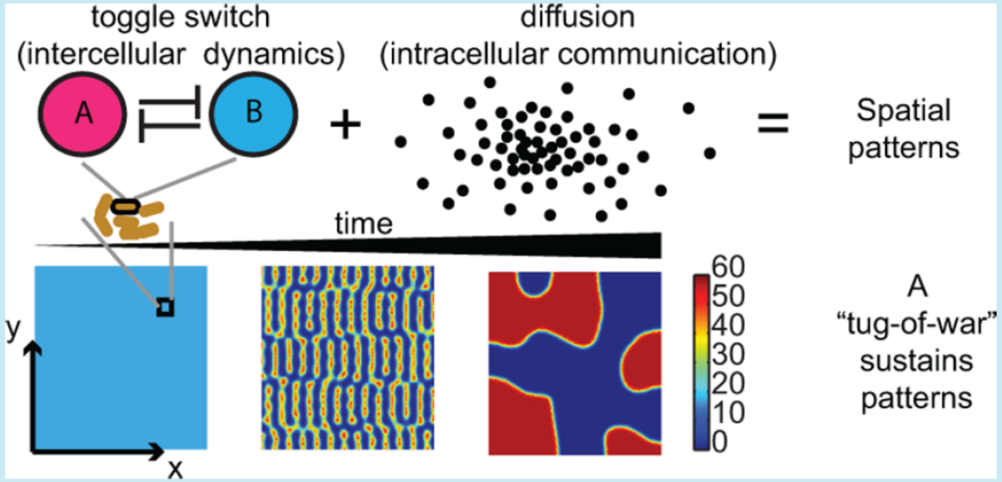
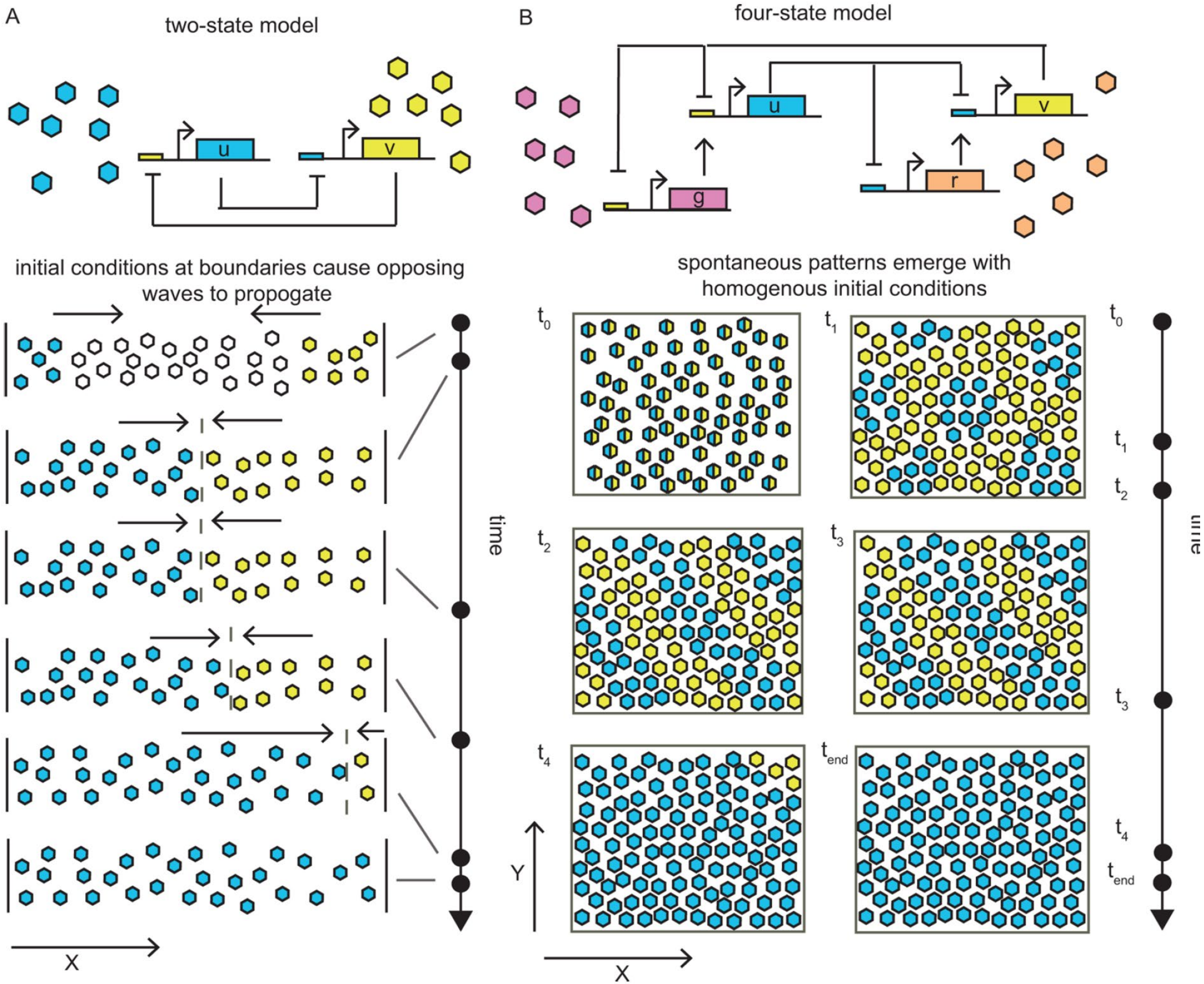
Supporting Information

ABSTRACT: Synthesizing spatial patterns with genetic networks is an ongoing challenge in synthetic biology. A successful demonstration of pattern formation would imply a better understanding of systems in the natural world and advance applications in synthetic biology. In developmental systems, transient patterning may suffice in order to imprint instructions for long-term development. In this paper we show that transient but persistent patterns can emerge from a realizable synthetic gene network based on a toggle switch. We show that a bistable system incorporating diffusible molecules can generate patterns that resemble Turing patterns but are distinctly different in the




A
two-state model
u
v
initial conditions at boundaries cause opposing waves to propogate
time
X
B
four-state model
u
v
g
r
spontaneous patterns emerge with homogenous initial conditions
t0
t1
t2
t3
t4
tend
Y
X

Equation for Toggle switch with diffusion

$$\frac{\partial u(t,x)}{\partial t} = D\frac{\partial^2 u(t,x)}{\partial x^2} + f(v(t,x)) - \gamma u(t,x)$$

$$\frac{\partial v(t,x)}{\partial t} = D\frac{\partial^2 v(t,x)}{\partial x^2} + f(u(t,x)) - \gamma v(t,x)$$

With nonlinearity

$$f(z) = \alpha\frac{1}{1+z^2}$$

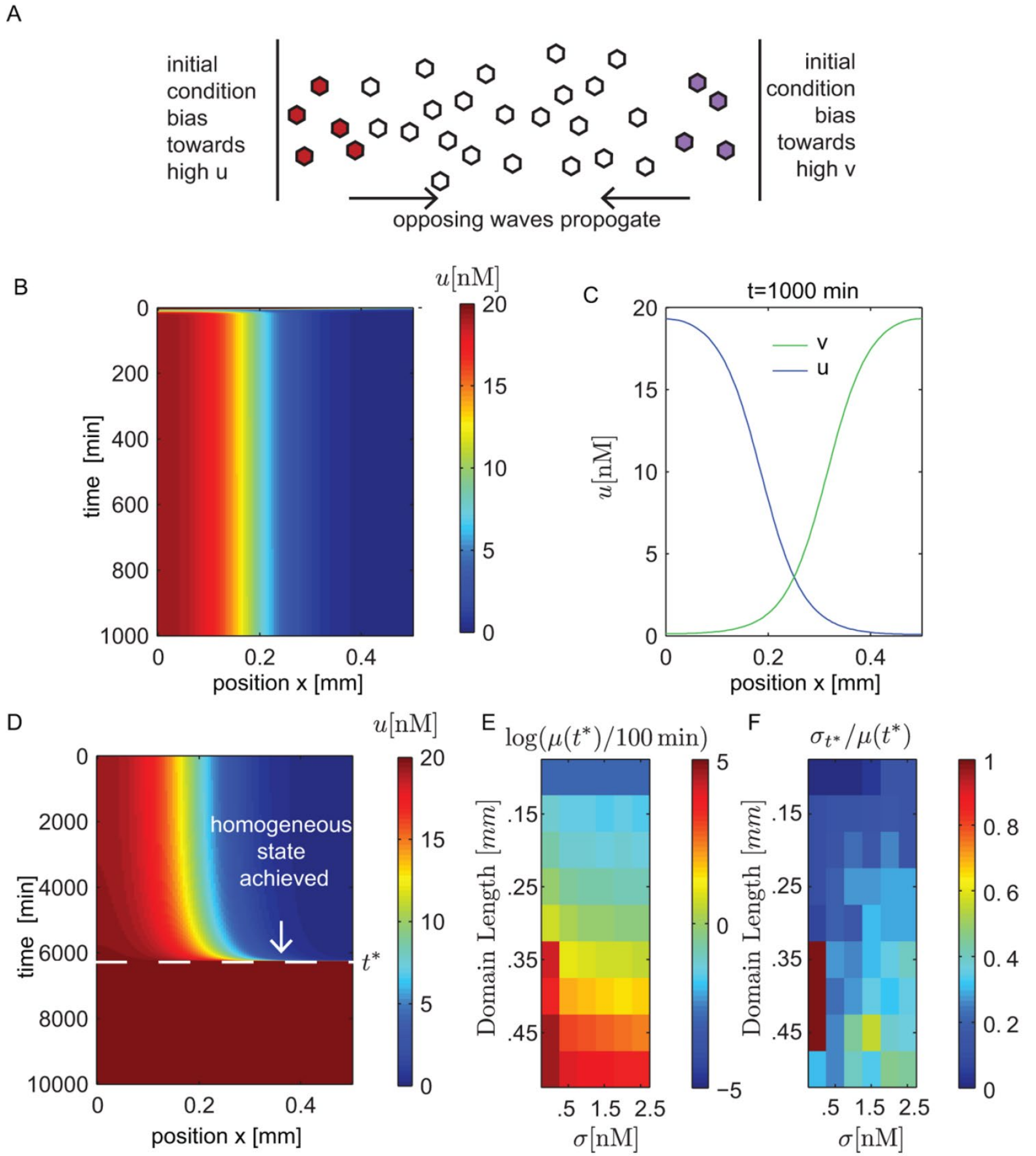
And boundary conditions

$$\frac{\partial u(t,0)}{\partial x} = \frac{\partial u(t,L)}{\partial x} = \frac{\partial v(t,0)}{\partial x} = \frac{\partial v(t,L)}{\partial x} = 0$$

Initial condition already has a bias:

$$u(0,x) = u^* + A_0 e^{\mu(-x)} + \mathrm{randn}(\sigma, x)[\mathrm{nM}]$$

$$v(0,x) = v^* + A_0 e^{\mu(x-L)} + \mathrm{randn}(\sigma, x)[\mathrm{nM}]$$



Why is it instable in the long run?

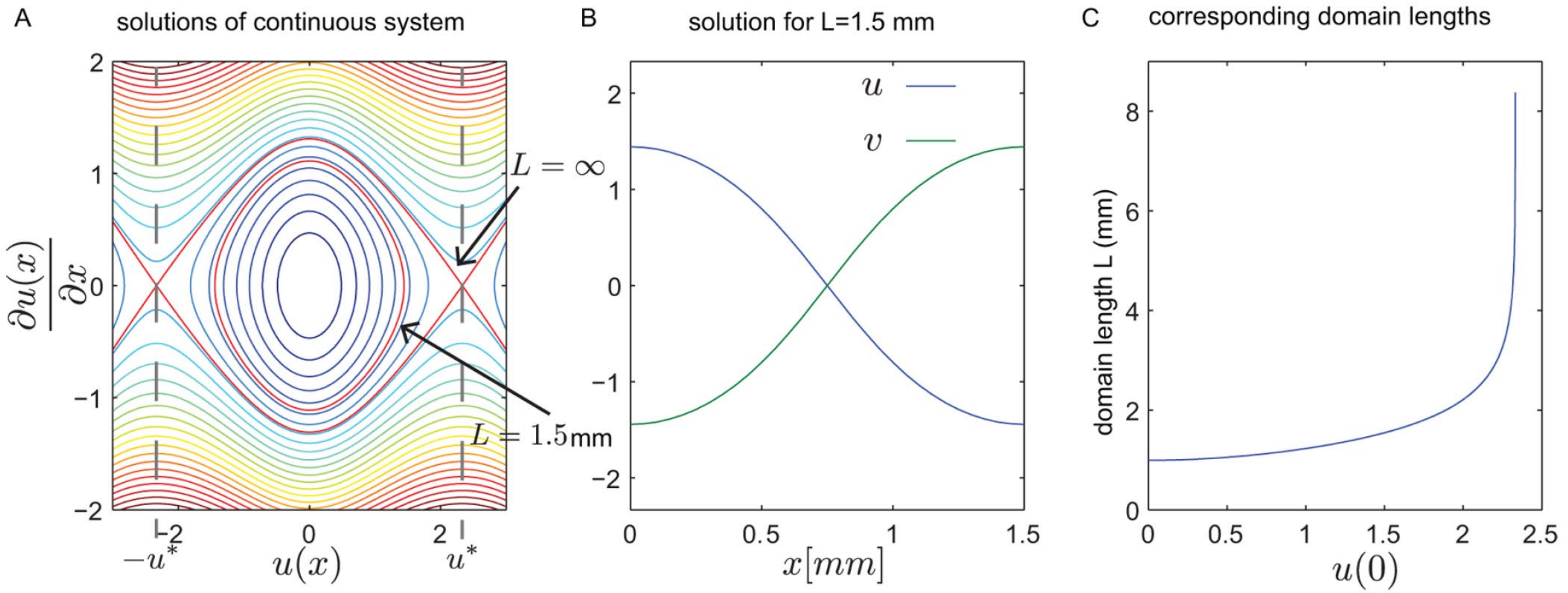
Looking at more simple bistable system:

we set $\gamma = 1$. $\qquad f(z) = -\alpha \tan^{-1}(z)$

Leads to stability condition
(here zero mode is unstable!) $\quad \gamma > \alpha - D\left(\frac{k\pi}{L}\right)^2$

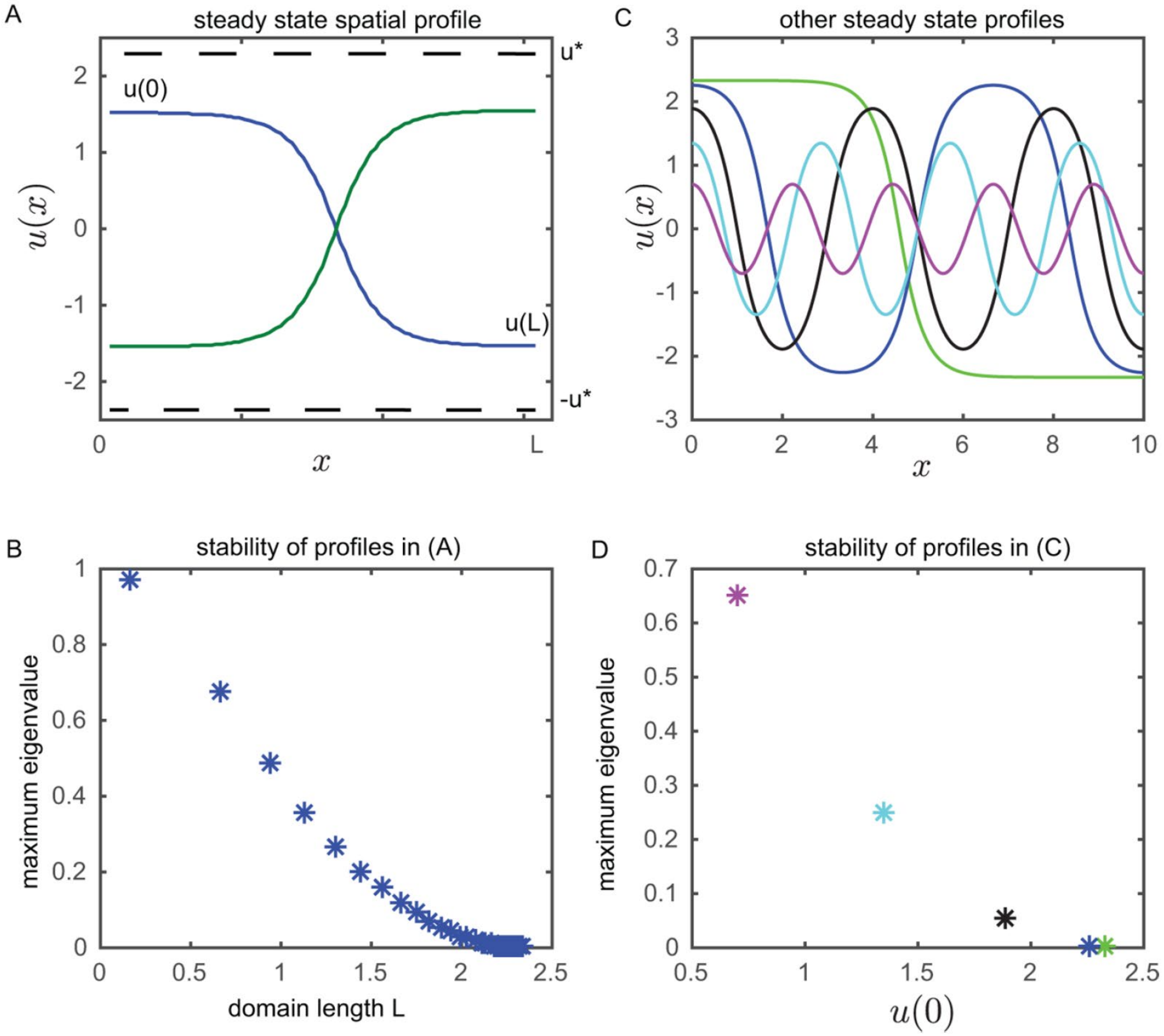
$$\frac{\mathrm{d}}{\mathrm{d}x}\begin{bmatrix} u(x) \\ v(x) \end{bmatrix} = \begin{bmatrix} u'(x) \\ v'(x) \end{bmatrix}$$

$$\frac{\mathrm{d}}{\mathrm{d}x}\begin{bmatrix} u'(x) \\ v'(x) \end{bmatrix} = -D^{-1}\begin{bmatrix} f(u(x)) \\ f(v(x)) \end{bmatrix} + D^{-1}\begin{bmatrix} u(x) \\ v(x) \end{bmatrix}$$



Half circle in phase plot before

Other solutions are possible



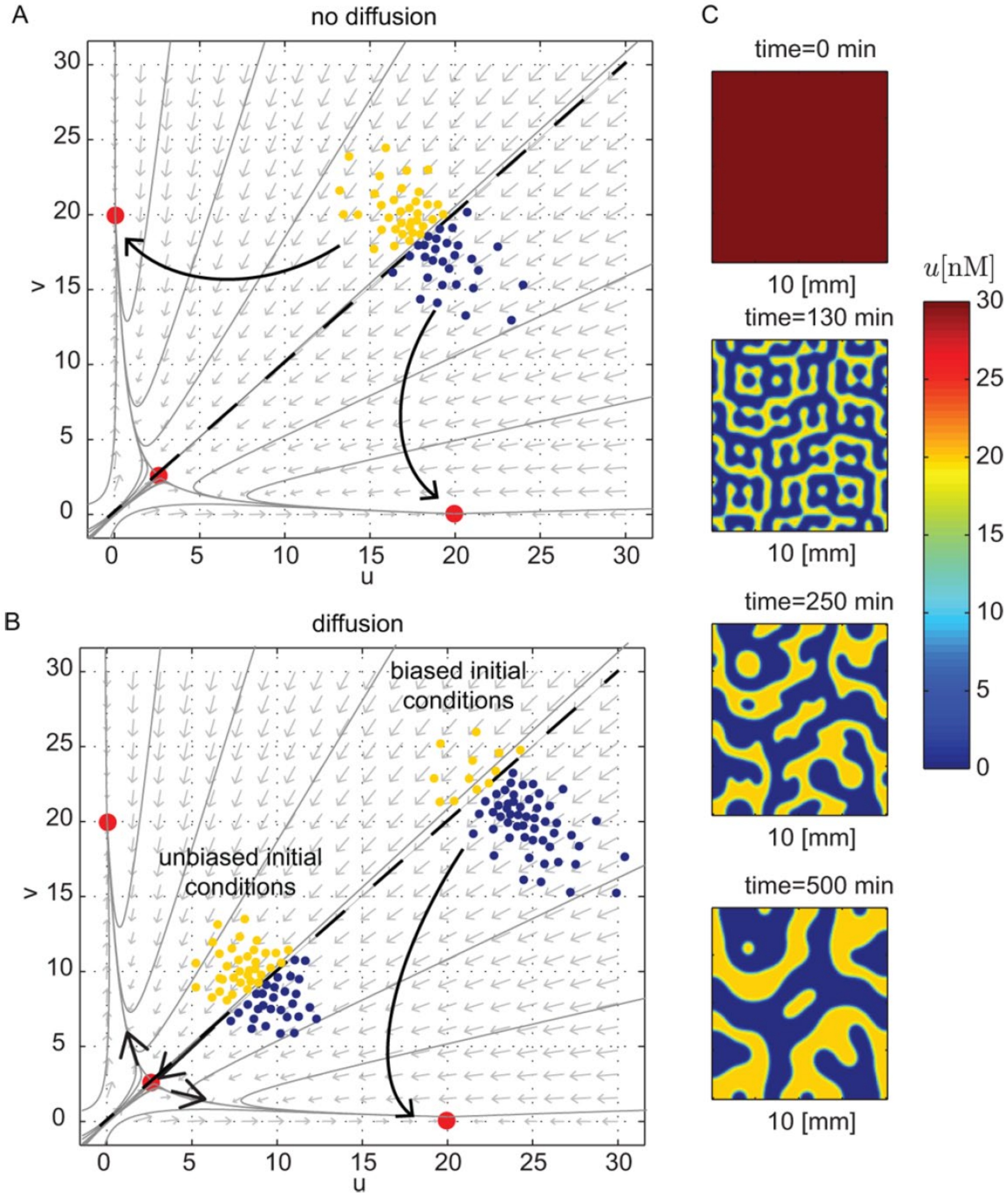
The shorter the domain, the more unstable

Higher frequencies are more unstable

2D Toggle switches and instabilities

$$\frac{\partial u(t,x,y)}{\partial t} = D_u \frac{\partial^2 u(t,x,y)}{\partial x^2} + D_u \frac{\partial^2 u(t,x,y)}{\partial y^2} + \frac{\alpha_u}{1+v(t,x,y)^2} - \gamma_u u(t,x,y)$$

$$\frac{\partial v(t,x,y)}{\partial t} = D_v \frac{\partial^2 v(t,x,y)}{\partial x^2} + D_v \frac{\partial^2 v(t,x,y)}{\partial y^2} + \frac{\alpha_v}{1+u(t,x,y)^2} - \gamma_v v(t,x,y)$$



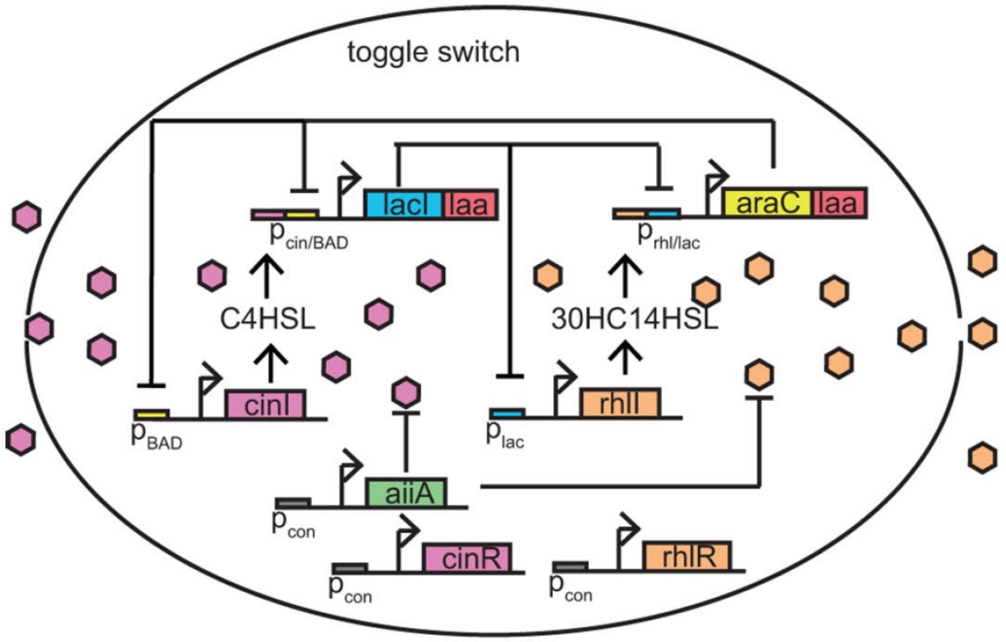
Toggle switch with quorum sensing

$$\frac{\partial u(t,x,y)}{\partial t} = \frac{a_{lacI}}{1+v(t,x,y)^2} + \frac{a_2(g(t,x,y)+\delta r(t,x,y))}{1+g(t,x,y)+\delta r(t,x,y)} - \gamma_p u(t,x,y)$$

$$\frac{\partial v(t,x,y)}{\partial t} = \frac{a_{araC}}{1+u(t,x,y)^2} + \frac{a_2(r(t,x,y)+\delta g(t,x,y))}{1+r(t,x,y)+\delta g(t,x,y)} - \gamma_p v(t,x,y)$$

$$\frac{\partial g(t,x,y)}{\partial t} = D_{C14}\frac{\partial^2 g(t,x,y)}{\partial x^2} + D_{C14}\frac{\partial^2 g(t,x,y)}{\partial y^2} + \frac{a_{lacI}}{1+v(t,x,y)^2} + l - \gamma_g g(t,x,y)$$

$$\frac{\partial r(t,x,y)}{\partial t} = D_{C4}\frac{\partial^2 r(t,x,y)}{\partial x^2} + D_{C4}\frac{\partial^2 r(t,x,y)}{\partial y^2} + \frac{a_{araC}}{1+u(t,x,y)^2} + l - \gamma_s r(t,x,y).$$



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