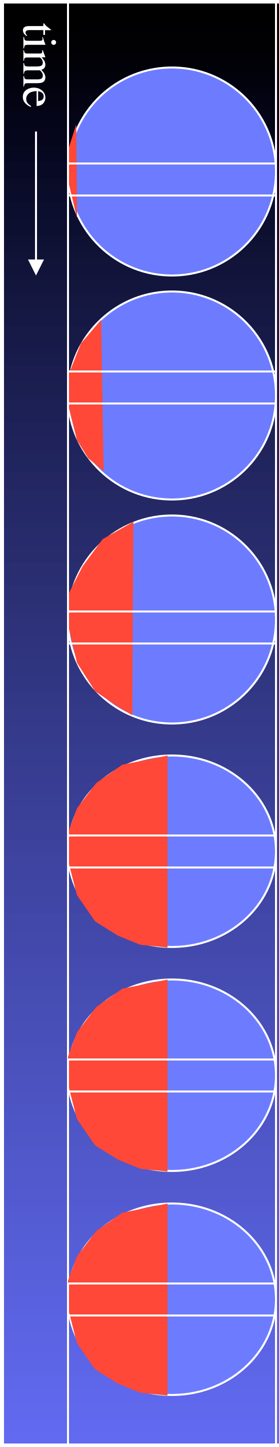
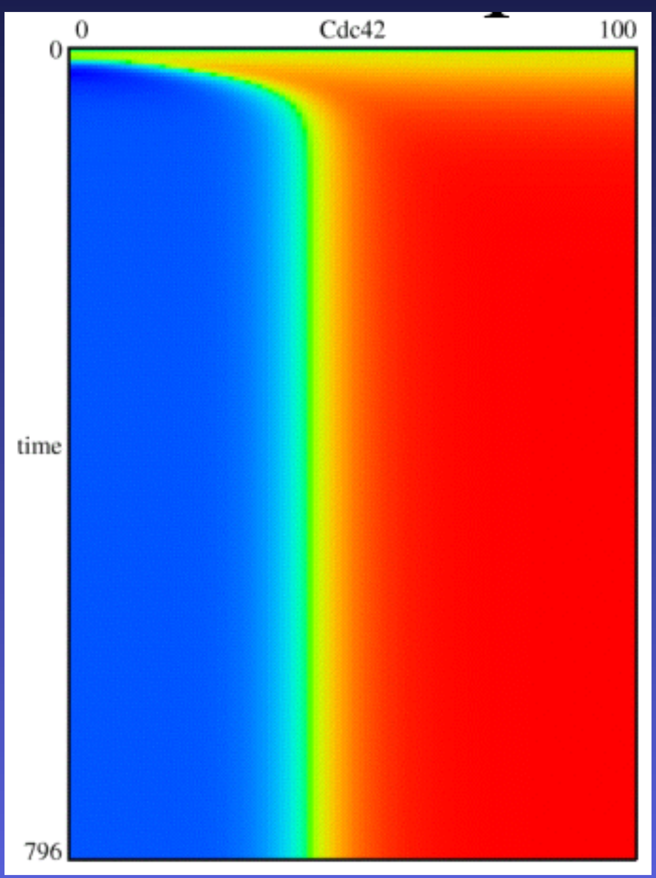
Mathematical Cell Biology Graduate Summer Course
University of British Columbia, May 1-31, 2012
Leah Edelstein-Keshet

Wave-pinning

Essential features



The behaviour



"Wave-pinning"

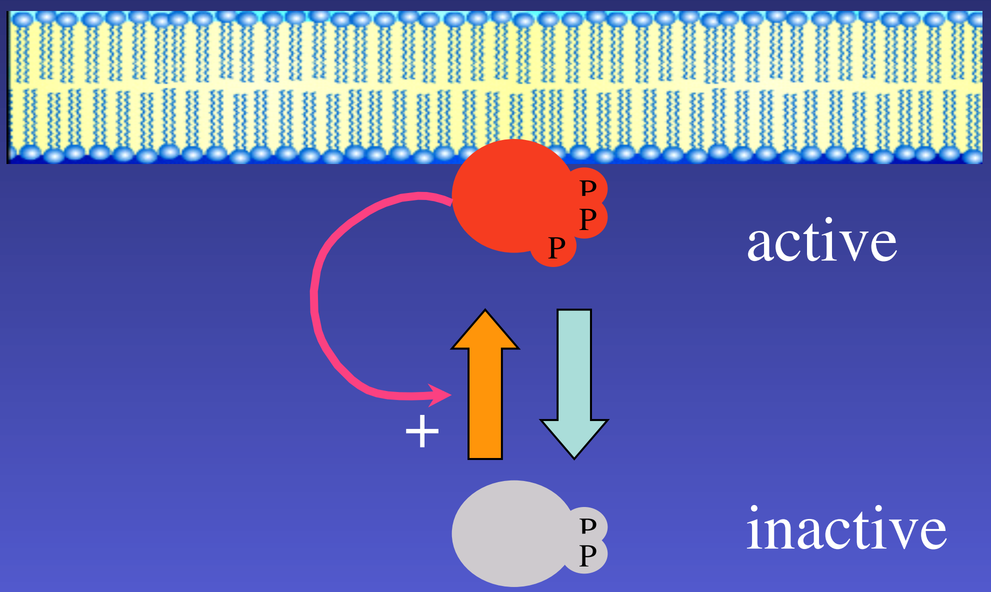
What is the underlying mechanism?

A Jilkine

Y Mori

Mori Y, Jilkine A, E-K L (2008) Biophysical Journal, 94: 3684-3697.

To investigate this, we study simple system:



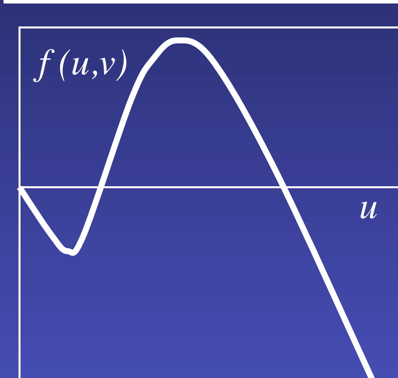
$D_{active} << D_{inactive}$

Mathematically:

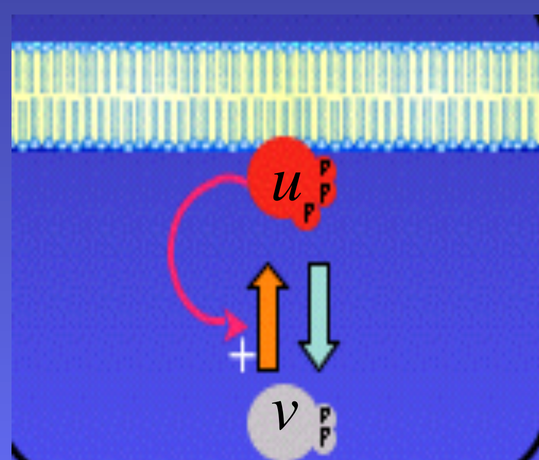
Reaction-diffusion eqns with positive feedback terms

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

$$f(u,v) = \eta \left(\delta + \frac{\gamma u^2}{m^2 + u^2} \right) v - \eta u$$

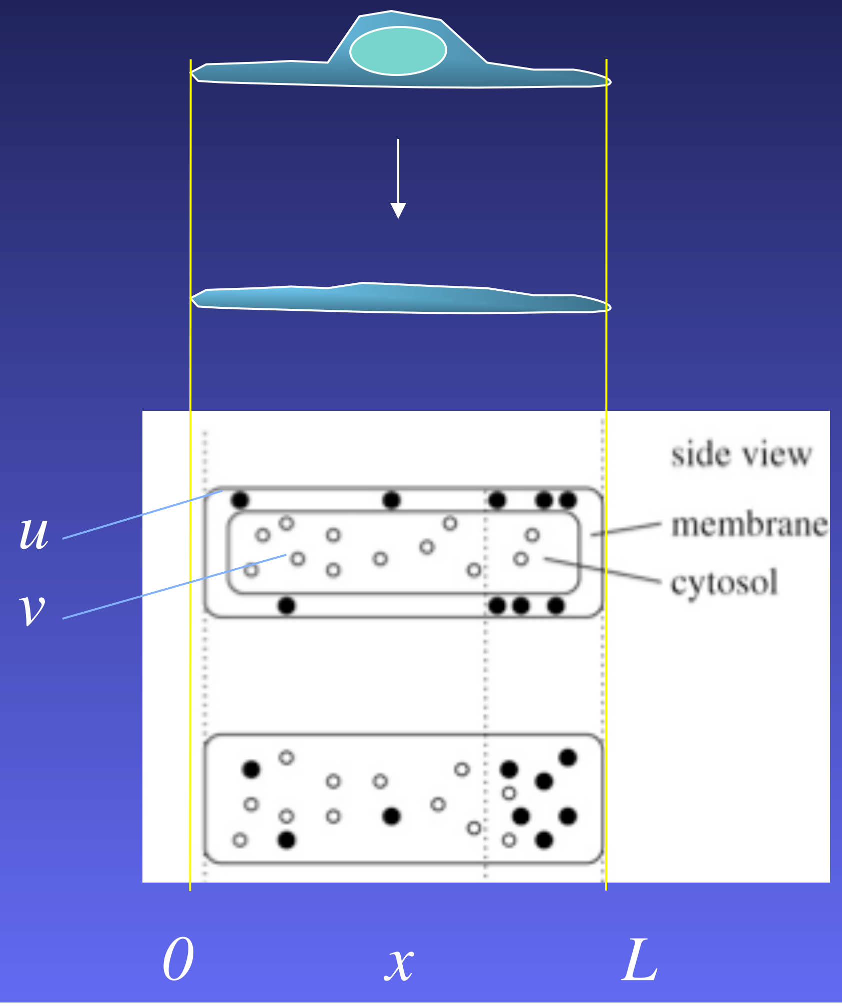


$\int u+v$ = Constant



$D_u << D_v$

Simplified 1D geometry:



$D_u << D_v$

Reduced model

Active form

Inactive form

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

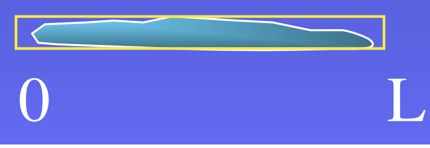
$D_u << D_v$

Typical kinetics

$$f(u,v) = \eta\left(\delta + \frac{\gamma u^2}{m^2+u^2}\right)v - \eta u$$

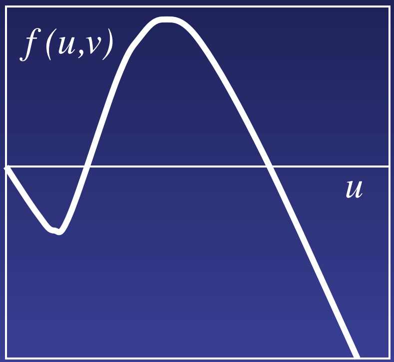
Neumann BCs

$$\frac{\partial u}{\partial x} = \frac{\partial v}{\partial x} = 0, \quad x = 0, L.$$



Moving fronts

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

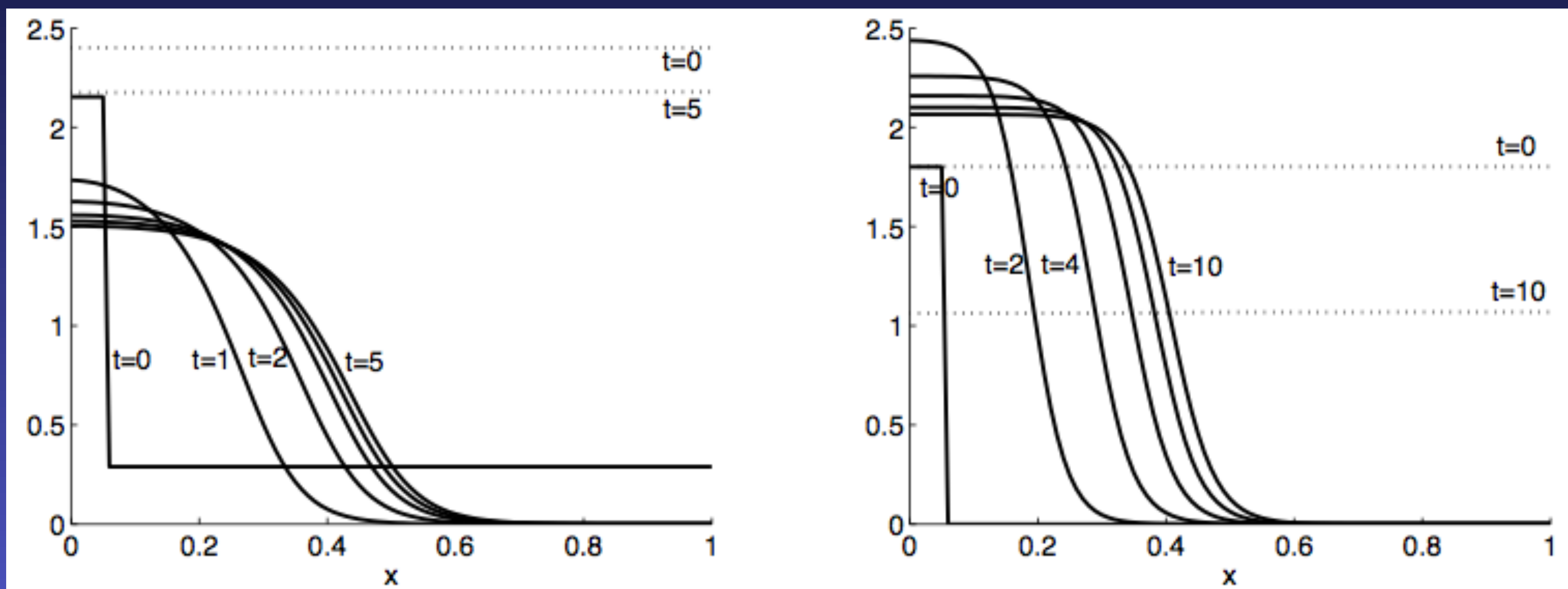


If *v* is fixed, and *u* eqn is on its own:

RD eqn with bistable kinetics.

This is known to have traveling wave solns (moving fronts).

When coupled with the eqn for *v*, get a wave pinning phenomenon:



$$f(u, v) = \left(\delta + \frac{\gamma u^2}{1 + u^2}\right) v - u.$$

$$f(u, v) = u(1 - u)(u - 1 - v)$$

Rescaled (there is a small parameter)

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

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

$$f(u, v) = \left(\delta + \frac{\gamma u^2}{1 + u^2} \right) v - u.$$

$D_u << D_v$

$$\epsilon^2 = \frac{D_u}{\eta L^2}, \quad D = \frac{D_v}{\eta L^2}$$

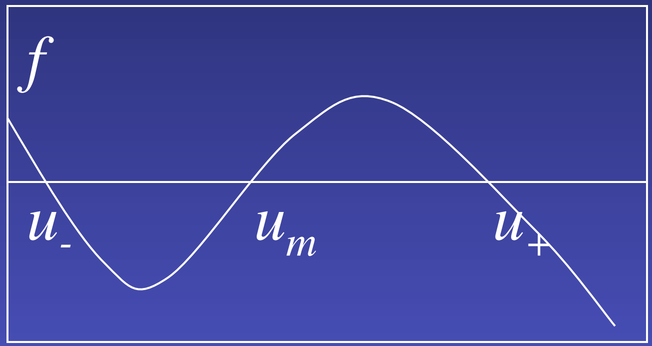
$$\int_0^1 (u + v) dx = K.$$

Conditions for Wave-pinning:

1. For v fixed in some range, $v_{min} < v < v_{max},$

   $f(u,v)=0$ has 3 roots

Shape of f:



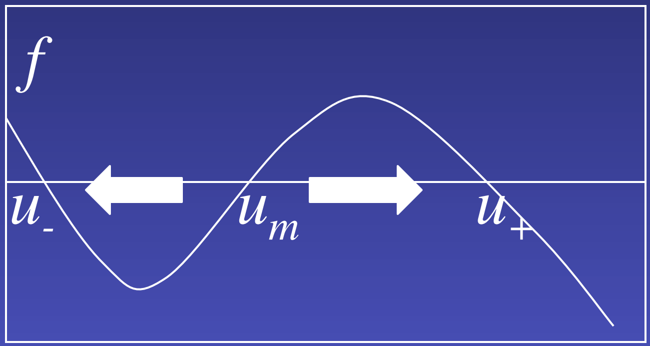
1. There is a v_c in the above range such that $\int_{u_-}^{u+} f(u,v_c)\,du = 0$
2. Conservation of $u+v$

Short time scale:

$$t_s = t/\epsilon$$

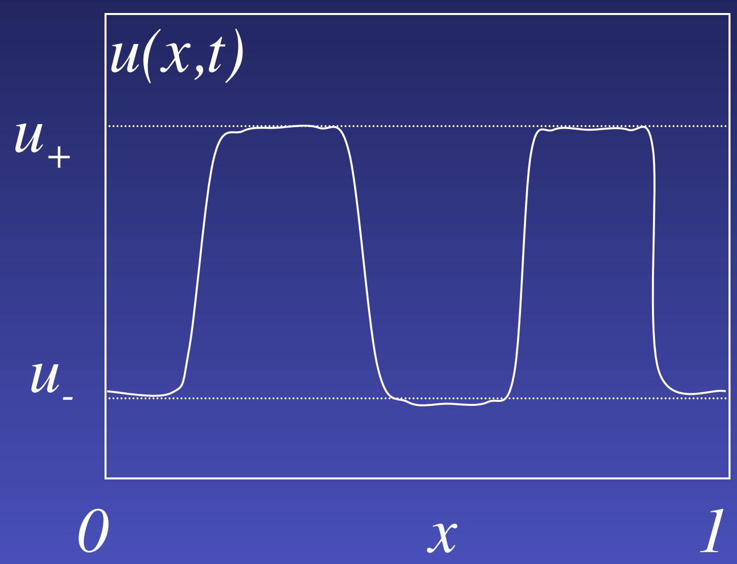
$$u = u_0 + \epsilon u_1, v = v_0 + \epsilon v_1$$

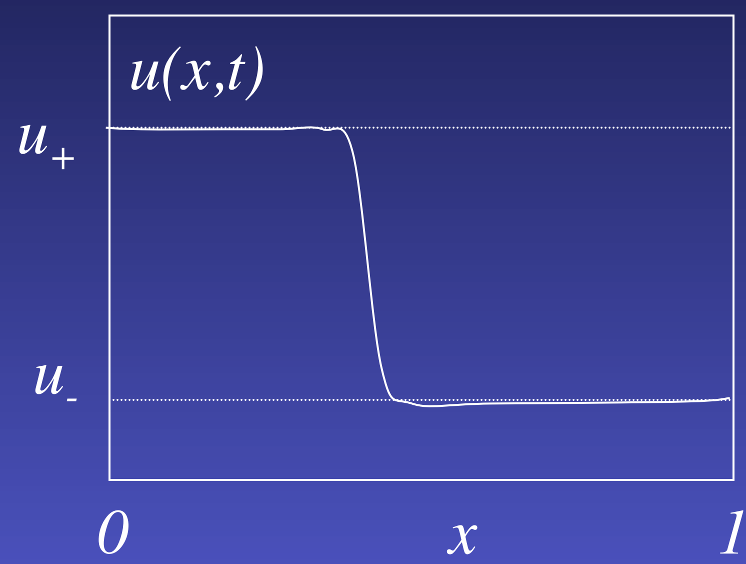
$$\frac{\partial u_0}{\partial t_s} = f(u_0, v_0),$$
$$\frac{\partial v_0}{\partial t_s} = D\frac{\partial^2 v_0}{\partial x^2} - f(u_0, v_0).$$



To leading order, u_o evolves to u_- or u_+
And v diffuses fast and attains uniform profile

Transition layers form on short timescale





Focus on single front solution (polarized domain)

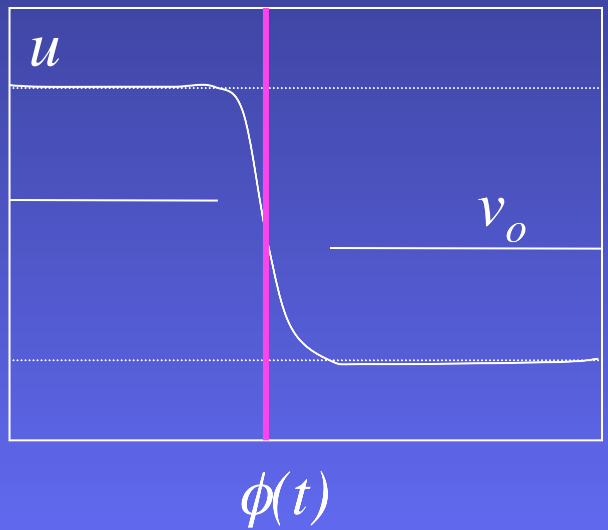
Intermediate time

Outer solution

$$0 = f(u_0, v_0),$$
$$0 = D\frac{\partial^2 v_0}{\partial x^2} - f(u_0, v_0).$$

Away from front $u = u_-$ or u_+

$$0 = D\frac{\partial^2 v_0}{\partial x^2}$$



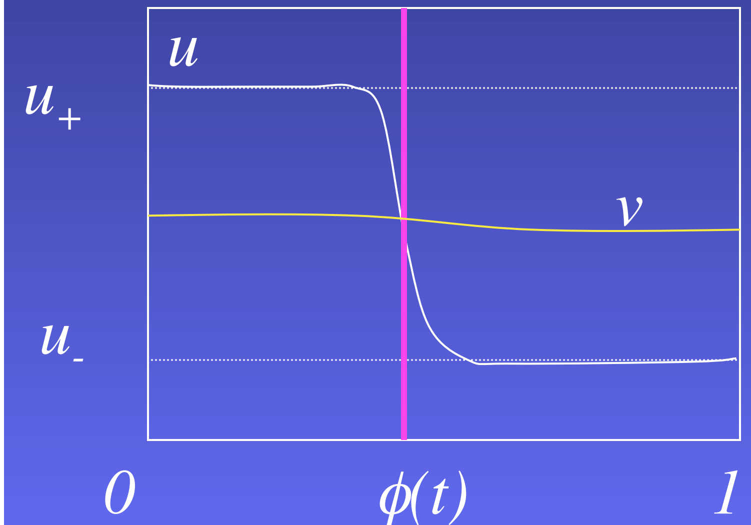
With BCs on [0,1], find that v_o is constant left and at right of front

Intermediate time scale

Stretched coordinate at the transition layer: $\xi = \frac{w}{\epsilon} = \frac{x-\phi(t)}{\epsilon}$

Inner solution
to leading order:

$$\frac{\partial^2 U_0}{\partial \xi^2} - \frac{d\phi_0}{dt}\frac{\partial U_0}{\partial \xi} + f(U_0, V_0) = 0,$$
$$\frac{\partial^2 V_0}{\partial \xi^2} = 0.$$



V_0 becomes spatially uniform.

Matching inner and outer sols:

$V_0 = v_0$

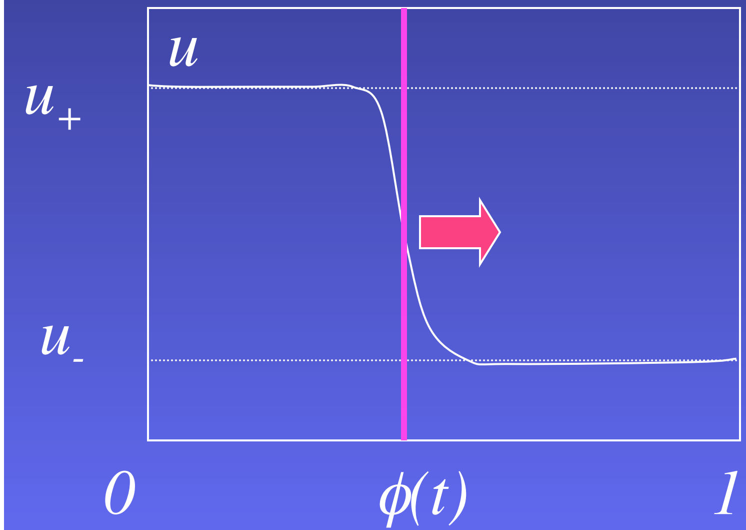
Front speed

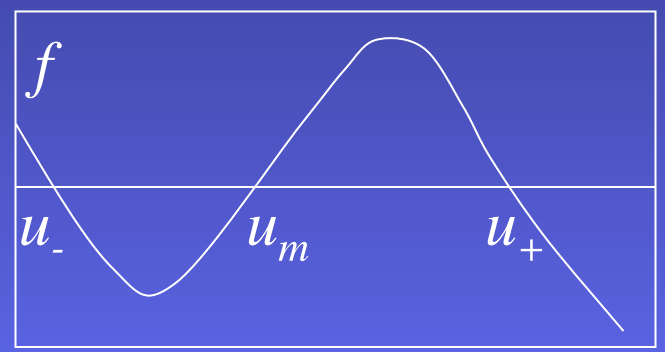
In inner layer, V_o is constant in space, so eqn for U_o depends only on U_o with V_o a time-varying parameter.

We are back to bistable scalar RD eqn.

Speed of the wave

$$\frac{d\phi_0}{dt} \equiv c(V_0) = \frac{\int_{u_-(V_0)}^{u_+(V_0)} f(s, V_0)ds}{\int_{-\infty}^{\infty} \left(\partial U_0^\phi(\xi, V_0)/\partial\xi\right)^2 d\xi}.$$

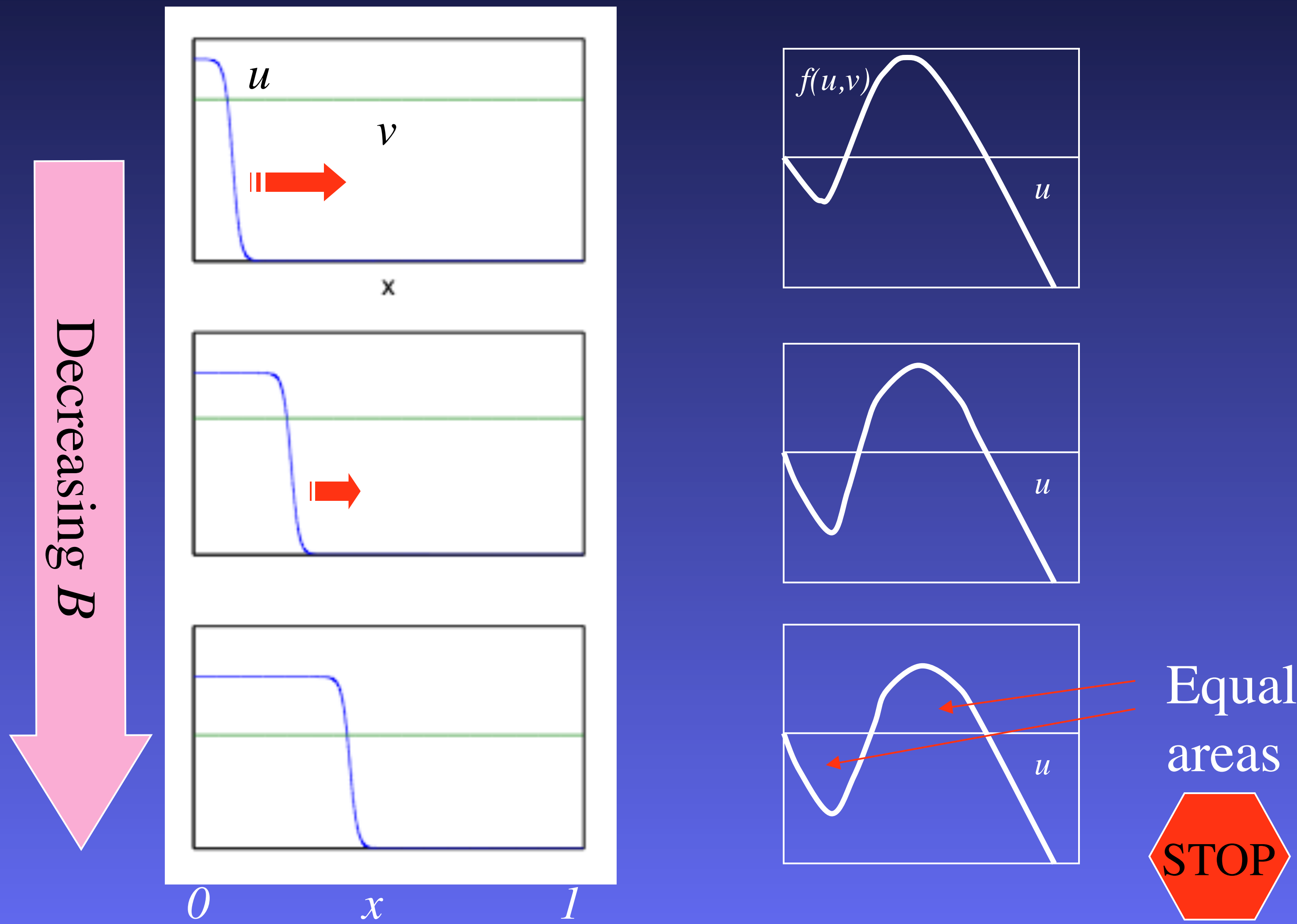




Front motion depletes *v*

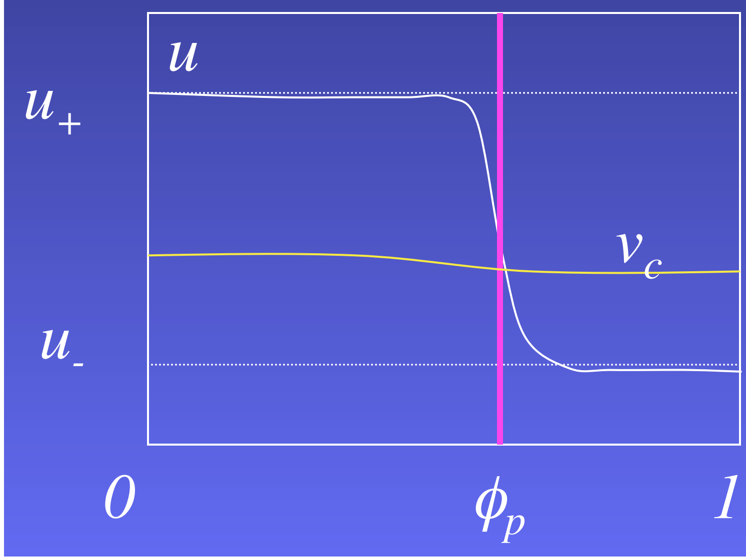
Front speed $d\phi_0/dt$, and dv_o/dt have opposite signs

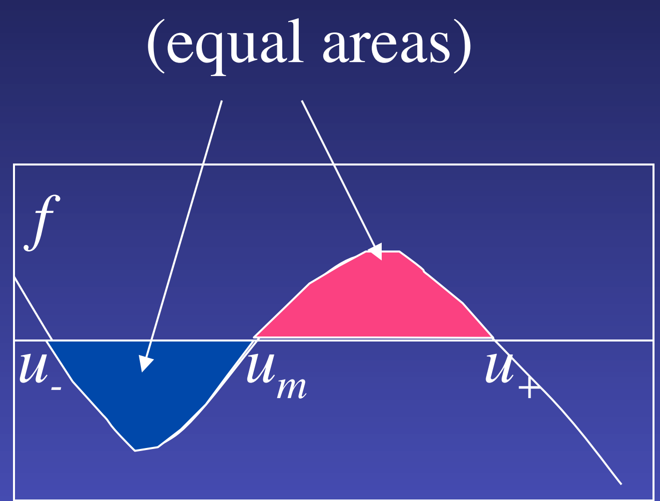
Stalling of the wave



Wave stalls when $\int_{u_-}^{u_+} f(u,v)\,du = 0$

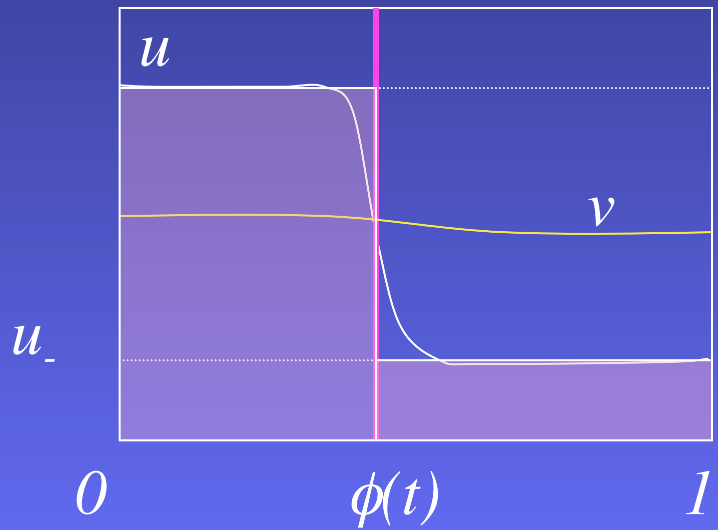
$$\frac{d\phi_0}{dt} \equiv c(V_0) = \frac{\int_{u_-(V_0)}^{u_+(V_0)} f(s,V_0)\,ds}{\int_{-\infty}^{\infty}\left(\partial U_0^{\phi}(\xi,V_0)/\partial\xi\right)^2 d\xi}. = 0$$

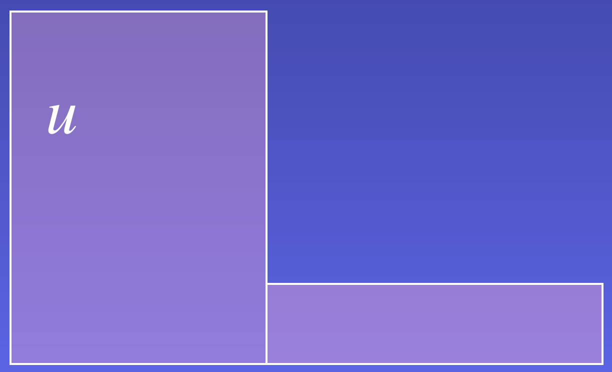




Where does the wave stop?

$$\int_0^1 (u+v)dx = K.$$





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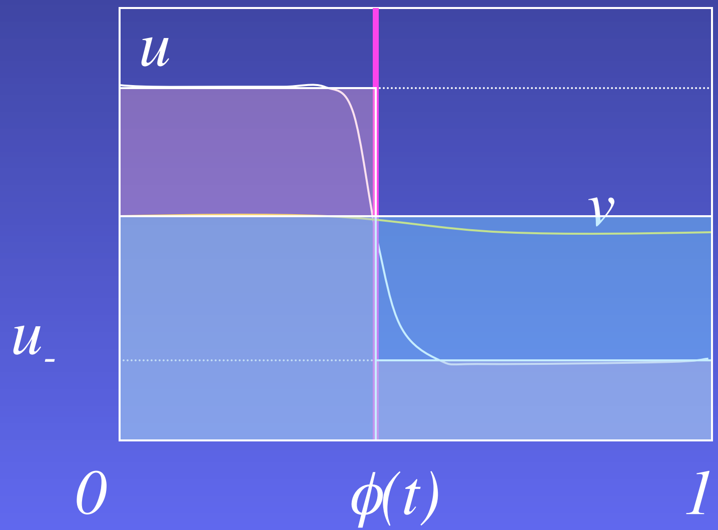
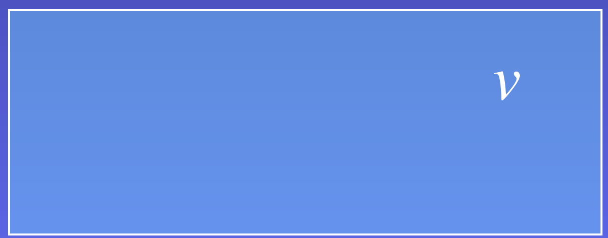
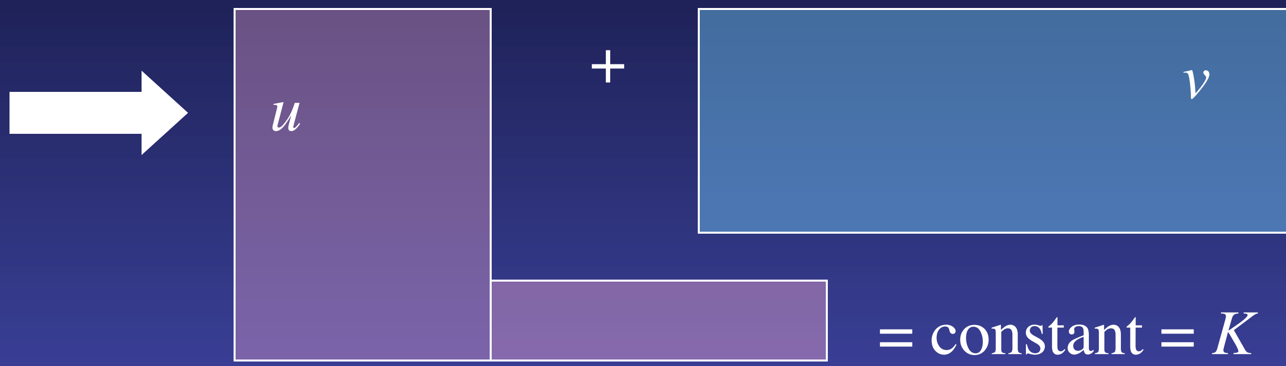
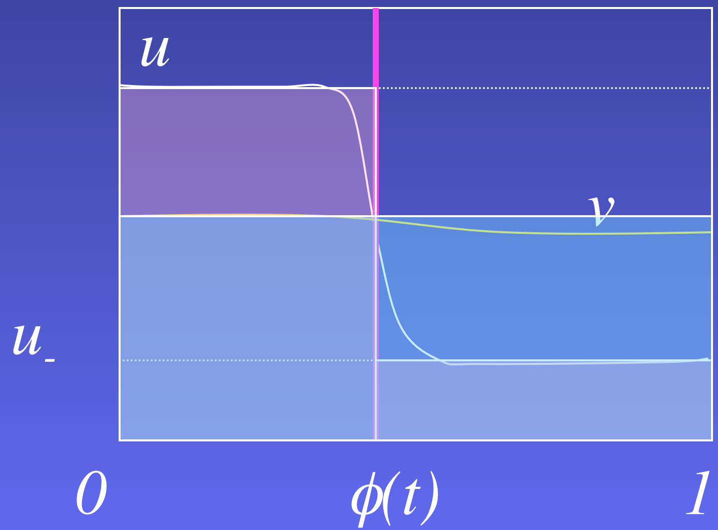




Conservation

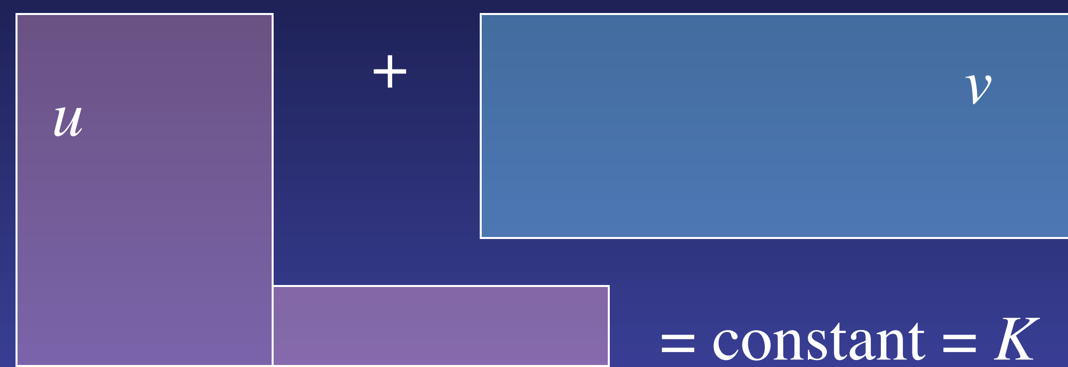
$$\int_0^1 (u+v)dx = K.$$



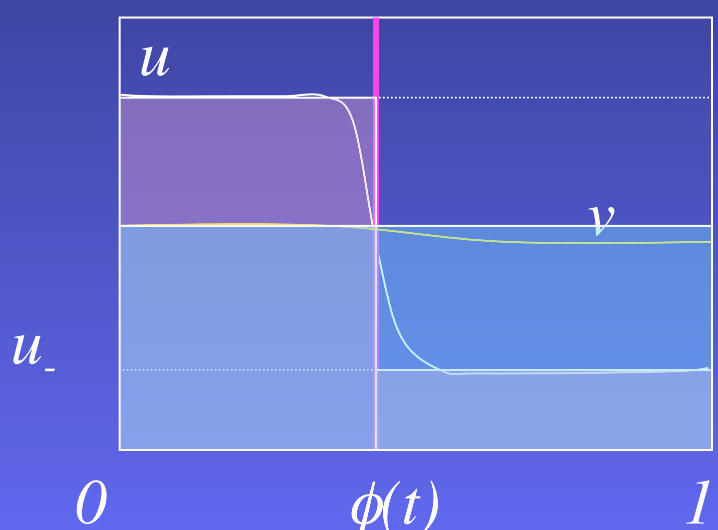


Conservation results in wave-pinning

$$\int_0^1 (u+v)dx = K.$$



= constant = K



Wave stops when

$$v_c = K - u_+(v_c)\phi_p - u_-(v_c)(1-\phi_p).$$

The mechanism:

Wave pinning results from the depletion of the inactive form and the fact that conservation of total amount of material is enforced.

Example: Cubic kinetics

$$f(u,v) = -(u - u_+(v))(u - u_m(v))(u - u_-(v))$$

Speed can be explicitly computed:

$$\frac{d\phi_0}{dt} \equiv c(V_0) = \frac{\int_{u_-(V_0)}^{u_+(V_0)} f(s,V_0)ds}{\int_{-\infty}^{\infty} \left(\partial U_0^\phi(\xi,V_0)/\partial\xi\right)^2 d\xi}.$$

Result:

$$c(v) = \frac{1}{\sqrt{2}}\left(u_+(v) - 2u_m(v) + u_-(v)\right).$$

Dynamics of front and stall position:

$$f(u,v) = u(1-u)(u-1-v)$$

Speed of the wave :

$$\frac{d\phi_0}{dt} = \frac{1}{\sqrt{2}}\left(\frac{K-\phi}{1+\phi} - 1\right), \quad v_0 = \frac{K-\phi_0}{1+\phi_0}$$

Stall position:

$$\phi_p = \frac{K-1}{2}.$$

Restriction for WP to occur:

$$\phi_p = \frac{K-1}{2}.$$

For wave to stall inside the domain: $0 < \phi_p < 1.$

This can only happen if: $1 < K < 3.$

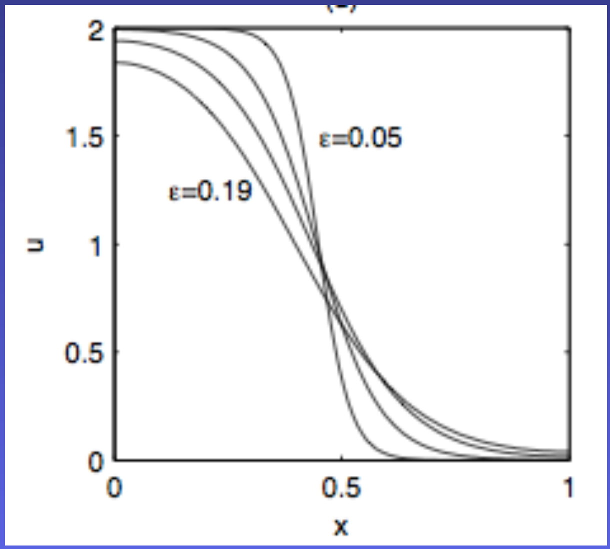
How does wave-pinning depend on parameters ?

$$\epsilon^2 = \frac{D_u}{\eta L^2}, \quad D = \frac{D_v}{\eta L^2}$$

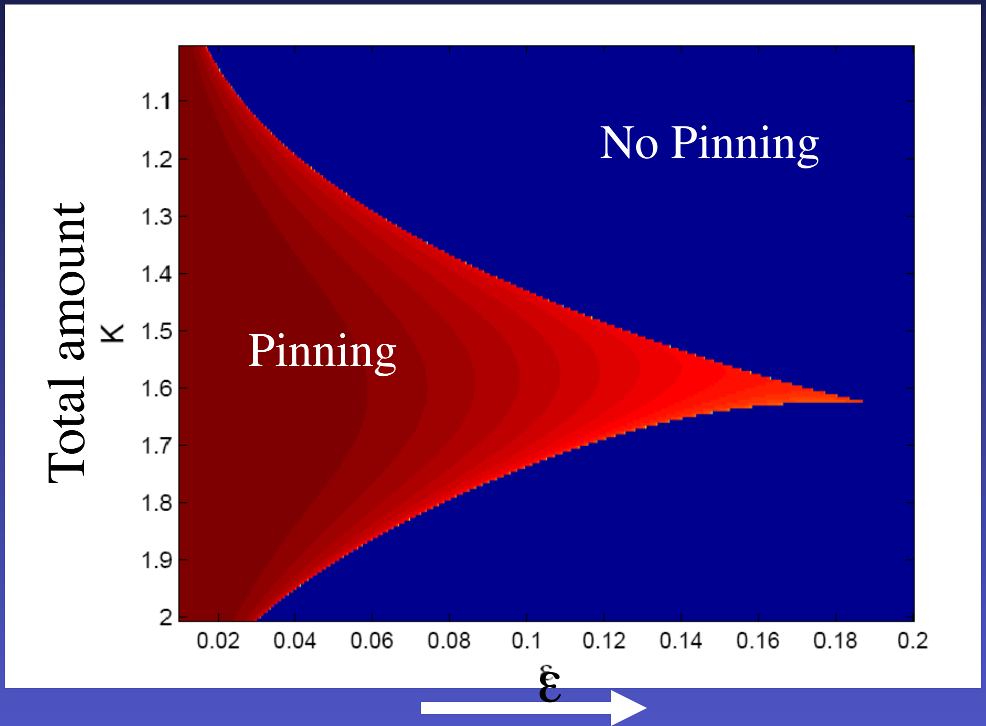
$$\int_0^1 (u+v)dx = K.$$

- For $D > 0$, $1 < K < 3$, and ε sufficiently small, there is a stable front solution. As ε increases, shape and stall position change.

- For $\varepsilon > \varepsilon_c(D,K)$ this solution no longer exists.



wave-pinning loss

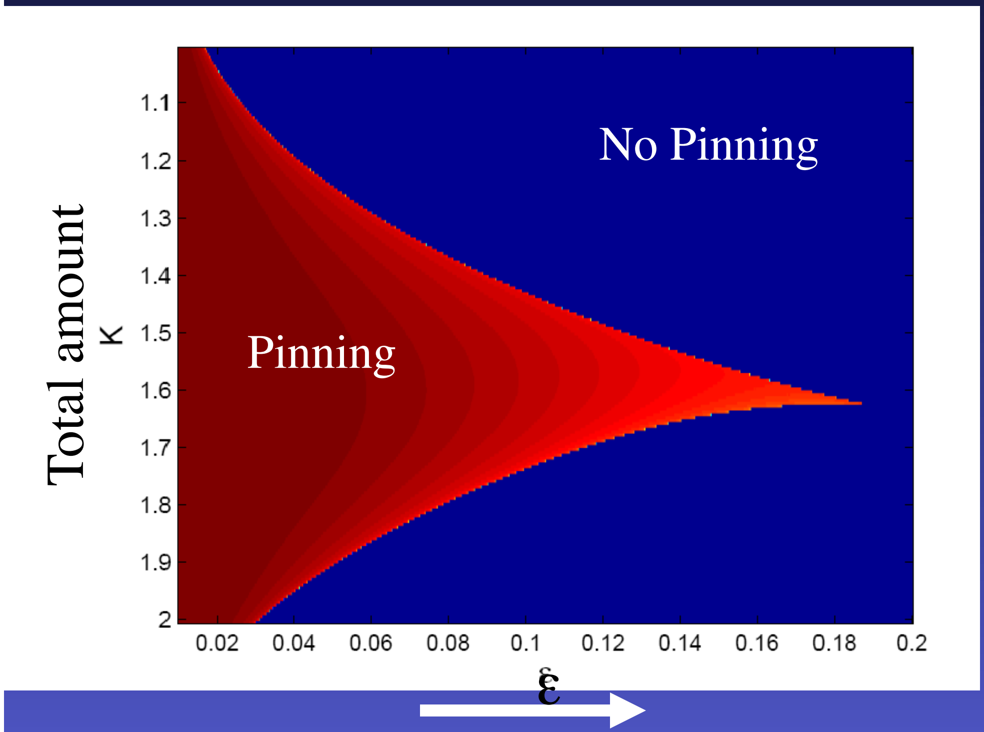


Diffusion D_u, ↑

Domain size L ↓

reaction rate ↓

Implications



If membrane diffusion too fast, or domain too small or reaction rate too slow, no wave-pinning so cell can't polarize.

Diffusion D_u, ↑

Domain size L ↓

reaction rate ↓