Outline

1. Chemotaxis-driven linear instability
2. Diffusive instability
3. Bistable kinetics and fronts
4. Pulses, wavetrains and spirals
5. Autosolitons

Chemotaxis-driven Linear Instability (1)

Keller & Segel, 1971: cells migrate in a self-imposed field of chemoattractant

$$\frac{\partial n}{\partial t} = -\frac{\partial}{\partial x}\left(-m\frac{\partial n}{\partial x} + cn\frac{\partial c}{\partial x}\right), \qquad \left.\frac{\partial n}{\partial x}\right|_{0,L} = 0$$

$$\frac{\partial c}{\partial t} = -\frac{\partial}{\partial x}\left(-D\frac{\partial c}{\partial x}\right) + fn - kc, \qquad \left.\frac{\partial c}{\partial x}\right|_{0,L} = 0$$

$$s.s.: \bar{n} = N/L, \bar{c} = \bar{n}f/k$$

$$n(x,t) = \bar{n} + n'(x,t)$$

$$c(x,t) = \bar{c} + c'(x,t)$$

Linearized equations:

$$\frac{\partial n'}{\partial t} = m\frac{\partial^2 n'}{\partial x^2} - c\bar{n}\frac{\partial^2 c'}{\partial x^2}$$

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c'}{\partial x^2} + fn' - kc'$$

Solution:

$$\begin{pmatrix} n'(x,t) \\ c'(x,t) \end{pmatrix} = \sum_{i=1}^{\infty} \begin{pmatrix} A_i \\ B_i \end{pmatrix} \cos(q_i x)\exp(l_i t)$$

why $i \neq 0$?

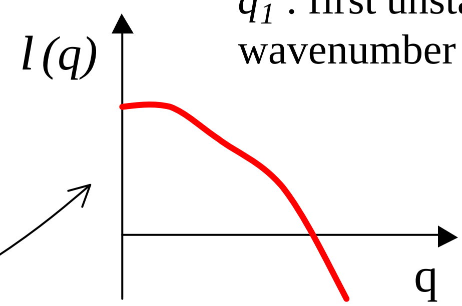
Linear instability of uniform state: $l_i > 0$

Keller-Segel (2)

For every wavenumber q : $\begin{bmatrix} l + mq^2 & -c\bar{n}q^2 \\ -f & l + Dq^2 + k \end{bmatrix} \begin{pmatrix} A \\ B \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

Nontrivial solutions $(A \neq 0, B \neq 0)$ when $\det(M) \neq 0$

$l_{1,2}$ satisfy $(l + mq^2)(l + Dq^2 + k) - c\bar{n}q^2 f = 0$



Condition for instability : $m(Dq^2 + k) < c\bar{n}f$

Using the B.C. : $m\left[\dfrac{D(pi)^2}{L^2} + k\right] < c\bar{n}f$

Interpretation :

1) small m, D, k, i

2) large L

3) large $c, \bar{n}, f$

This is just linear analysis ...

Keller-Segel (3)

- Instability is promoted by

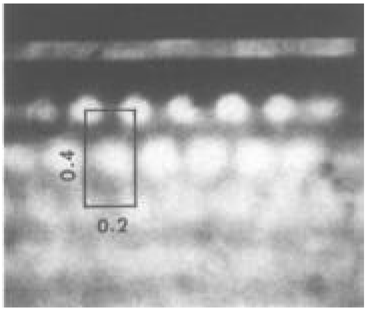
  low random motility & chemoattractant degradation
  high chemotactic sensitivity, secretion rate, cell density

- Problems

  no saturating effect: $\lim_{t \to \infty} n(x,t) = d(x)$
  instability does not appear to involve linear mechanism
  mechanism is more complicated

References:
1. E.F. Keller and L.A. Segel, J. theor. Biol. (26), 399-415, 1970
2. T. Hillen and K. Painter, Adv. Appl. Math. (26), 280-315, 2001

Linear Transport
+ Nonlinear Chemistry



Castets et al,
PRL, 64, 2953 (1990)

"… a mathematical model of the growing embryo will be described. This model will be a simplification and an idealization, and consequently a falsification. It is to be hoped that the features retained for discussion are those of greatest importance in the present state of knowledge"

1. Diffusion can have a destabilizing effect
2. Nonlinear chemistry can generate patterns
3. These mechanisms operate in development

A.M. Turing, "The Chemical Basis of Morphogenesis", Phil. Trans. Roy. Soc. B 237 (1952)

Diffusive Instability: The Model

$$\frac{\partial C_1}{\partial t} = D_1 \frac{\partial^2 C_1}{\partial x^2} + R_1(C_1, C_2); \qquad \left.\frac{\partial C_1}{\partial x}\right|_{0,L} = 0$$

$$\frac{\partial C_2}{\partial t} = D_2 \frac{\partial^2 C_2}{\partial x^2} + R_2(C_1, C_2); \qquad \left.\frac{\partial C_2}{\partial x}\right|_{0,L} = 0$$

uniform s.s.:

$$R_1(\bar{C}_1, \bar{C}_2) = 0, \quad R_2(\bar{C}_1, \bar{C}_2) = 0$$

perturbations:

$$C_1'(x,t) = C_1(x,t) - \bar{C}_1$$

$$C_2'(x,t) = C_2(x,t) - \bar{C}_2$$

Linearize around uniform steady state

$$\frac{\partial C_1'}{\partial t} = D_1 \frac{\partial^2 C_1'}{\partial x^2} + a_{11} C_1' + a_{12} C_2'$$

$$\frac{\partial C_2'}{\partial t} = D_2 \frac{\partial^2 C_2'}{\partial x^2} + a_{21} C_1' + a_{22} C_2'$$

$$a_{ij} \equiv \left.\frac{\partial R_i}{\partial C_j}\right|_{\bar{C}_1, \bar{C}_2}$$

Only “chemistry”

L.A. Segel and J.L. Jackson, “Dissipative Structure: An Explanation and an Ecological Example”, J. theor. Biol., 1972, 37, 545-559

Diffusive Instability: Linear Analysis

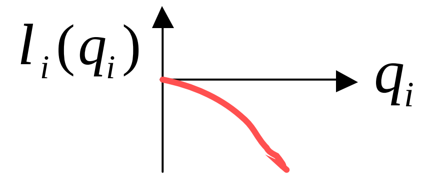
Linear dynamics: $\begin{pmatrix} C_1'(x,t) \\ C_2'(x,t) \end{pmatrix} = \sum_{i=0}^{\infty} \begin{pmatrix} A_i \\ B_i \end{pmatrix} \cos(q_i x) \exp(l_i t)$

Stability: $l_i < 0 \; \forall i$

$$(l_i - a_{11} + D_1 q_i^2)(l_i - a_{22} + D_{22} q_i^2) - a_{12} a_{21} = 0$$

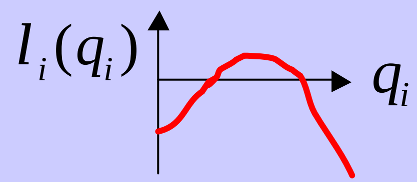
uniform perturbations decay when

1. $a_{11} + a_{22} < 0$
2. $a_{11} a_{22} - a_{12} a_{21} > 0$



only diffusion

Can nonuniform perturbations grow under these conditions?



diffusion + reaction

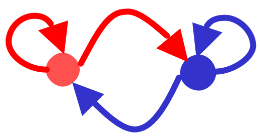
Diffusive Instability: Conditions

Necessary and sufficient conditions

1. $a_{11} + a_{22} < 0$	}	uniform SS is stable
2. $a_{11}a_{22} - a_{12}a_{21} > 0$	}	(only chemistry)
3. $a_{11}D_2 + a_{22}D_1 > 0$		chemistry + transport

Possible Jacobians:

$$\begin{bmatrix} + & - \\ + & - \end{bmatrix} \rightarrow$$



activator/inhibitor system

$$\begin{bmatrix} + & + \\ - & - \end{bmatrix}$$

What does this mean?

1. One substance is an "inhibitor" (pick 2)
2. The other one is an "activator" (1)
3. Range of activator is less than the range of inhibitor

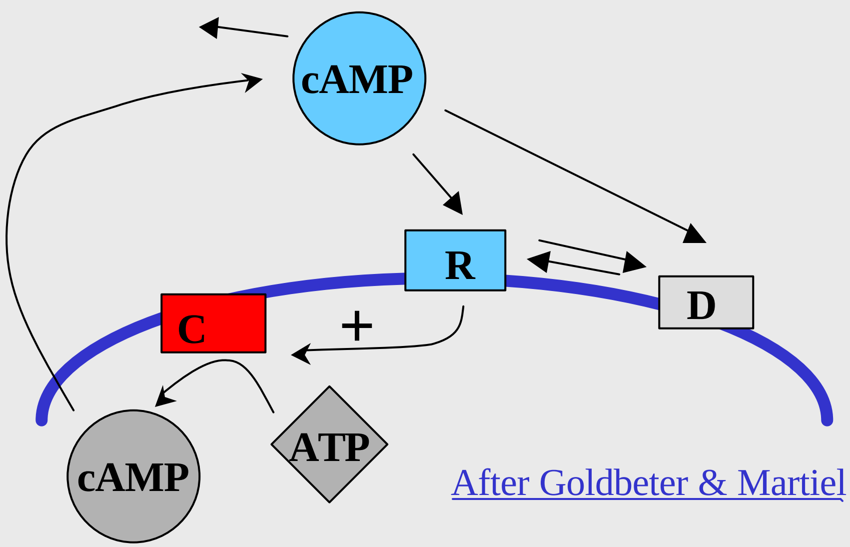
$$\frac{D_1}{a_{11}} < \frac{D_2}{|a_{22}|}$$

More species and dimensions:

1) Satnoianu RA, Menzinger M, Maini PK. "Turing instabilities in general systems". J Math Biol. 2000, 41, 493

2) De Wit A, "Spatial patterns and spatiotemporal dynamics in chemical systems" Adv. Chem. Phys., (109), 435, 1999

cAMP Network: Cartoon



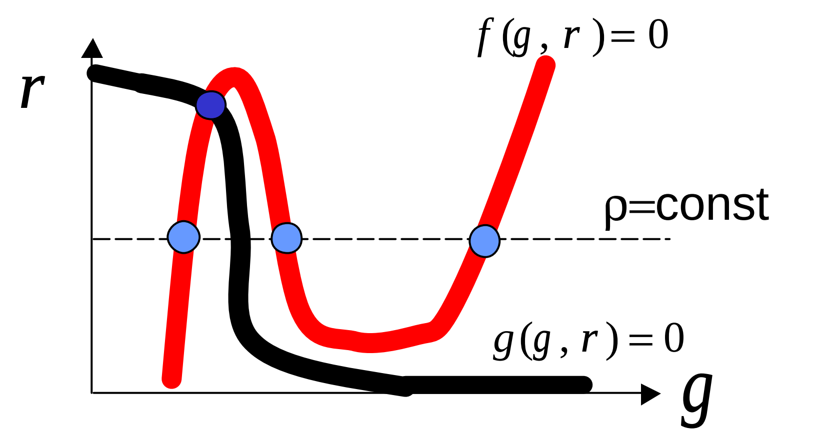
Variables:

r – fraction of receptors in the active state

g – extracellular cAMP

$$\frac{\partial g}{\partial t} = \Delta g + \frac{1}{e} f(g, r) \quad \text{- "fast" \& diffusing}$$

$$\frac{\partial g}{\partial t} = g(g, r) \quad \text{- "slow" \& localized}$$



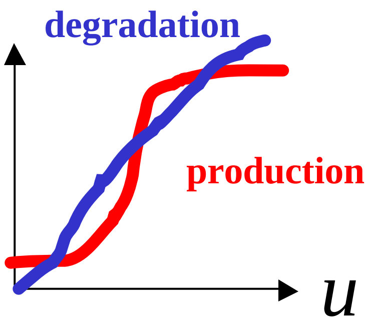
Fix ρ ⇒ γ has 3 steady states

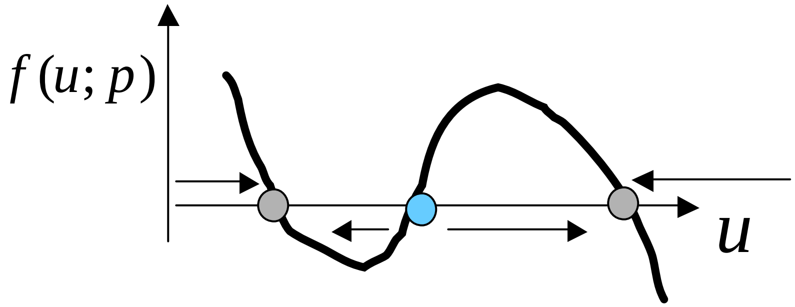
Other examples: Ca induced calcium release
Growth factor-induced growth factor release

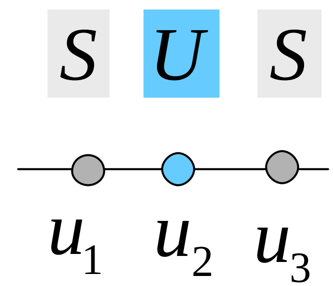
JL Martiel, A. Goldbeter, "A model based on receptor desensitization for cAMP signaling in Dictyostelium cells", Biophys.J. , 52, 807, 1987

Positive Feedback Alone: Bistability

Two stable steady states



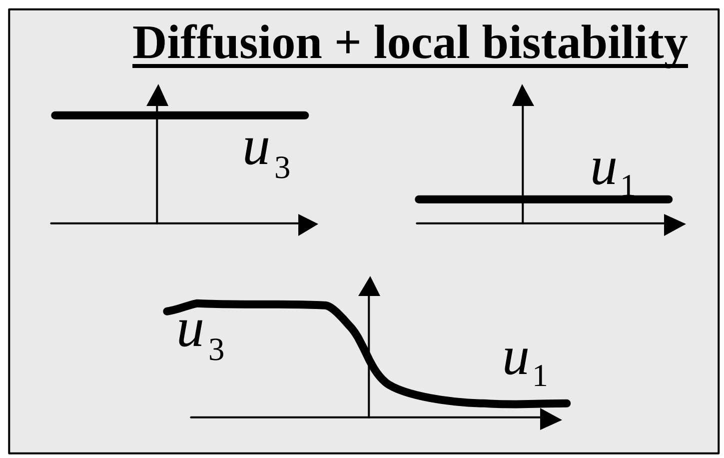




$$\frac{du}{dt} = f(u;p) \equiv P(u;p) - R(u;p)$$

balance of production & degradation

$$\frac{\partial u}{\partial t} = f(u;p) + D\frac{\partial^2 u}{\partial x^2}$$ - with diffusion

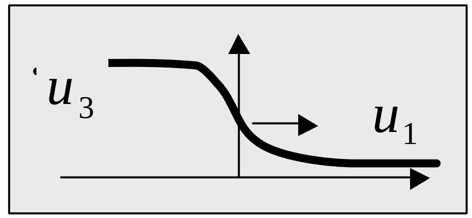


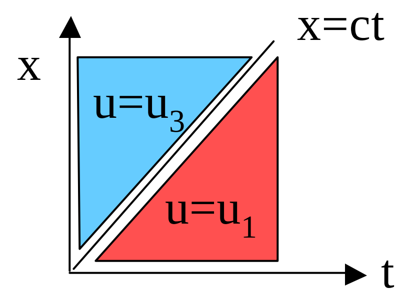
Nonuniform transitions between uniform steady states

AS Mikhailov, “Foundations of Synergetics-I”, Springer, 1994

Bistable Media: Propagating Fronts

$$\frac{\partial u}{\partial t} = f(u;p) + D\frac{\partial^2 u}{\partial x^2}$$





Look for self-similar solutions:

wave propagating to the right

$$u(x,t) = u(x-ct); x \equiv x - ct$$

$$\lim_{x\to-\infty} u(x) = u_3; \lim_{x\to+\infty} u(x) = u_1$$

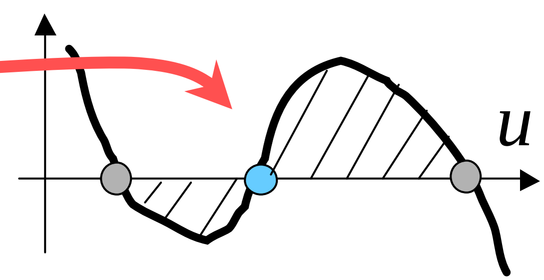
Change variables:

$$-cu_x = f(u) + Du_{xx}$$

Both the propagation speed (c) and its profile are uniquely determined by the properties of the medium : all fronts in a bistable medium have the same profile, independently of initial conditions

What determines the direction and speed of propagation?

$$\int_{-\infty}^{+\infty} \left(-cu_x = f(u) + Du_{xx}\right) u_x \Rightarrow c = \frac{\int_{u_1}^{u_1} f(u;p)\,du}{\int_{-\infty}^{+\infty} (\frac{du}{dx})^2\,dx}$$

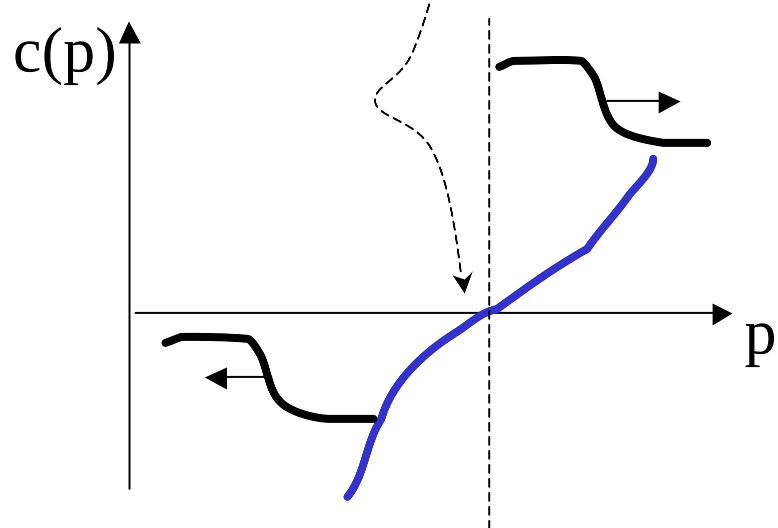


AS Mikhailov, “Foundations of Synergetics-I”, Springer, 1994

Bistable Media: Front Speed

$$\int_{u_1}^{u_1} f(u;p)\,du = 0$$

Front stationarity ($c = 0$) is determined by kinetics alone:



The front is stationarity only for a single parameter value:

Expressions for speed are available only for 2 cases:

$$f(u) = -k(u-u_1)(u-u_2)(u-u_3) \Rightarrow c = \frac{1}{2}\sqrt{kD}(u_1+u_3-u_2)$$

$$f(u) = k[(u_1-u)+(u_3-u_1)H(u-u_2)] \Rightarrow c = \frac{\sqrt{kD}(u_1+u_3-u_2)}{\sqrt{(u_2-u_1)(u_3-u_2)}}$$

AS Mikhailov, "Foundations of Synergetics-I", Springer, 1994

Bistable Media: Conclusions

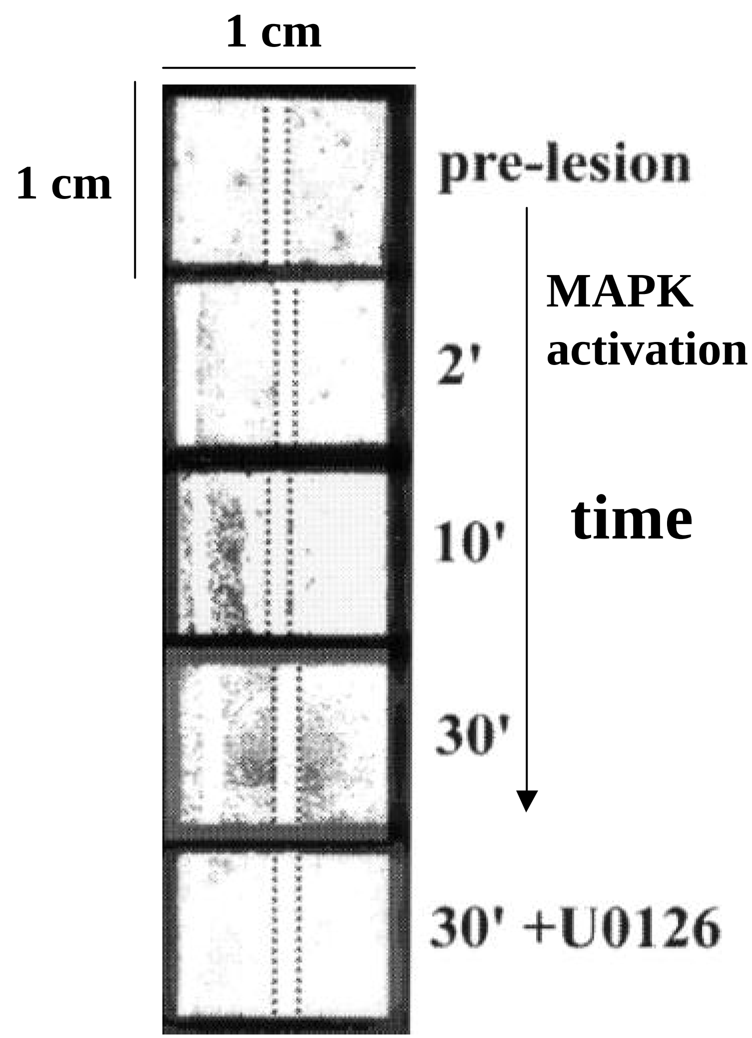
$$c = \sqrt{D} \times chemistry$$

Diffusion can be a very fast way to propagate signals, when coupled to positive feedback

Time to reach a point:

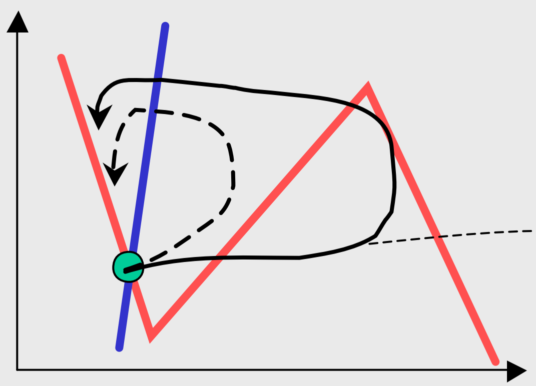
$$T = L / c = \frac{L}{(\sqrt{D} \times chemistry)}$$

Pure diffusion in 1D: $T = L^2 / 2D$



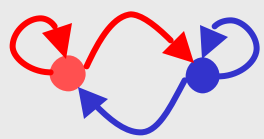
JM Mandell, NC Gocan, SR, Vandenberg, "Mechanical Trauma Induces Rapid Astroglial Activation of ERK/MAP Kinase: Evidence for a Paracrine Signal", GLIA, 34, 283, (2001)

Excitability



$$\frac{\partial u}{\partial t} = f(u,v) + D\Delta u$$

$$\frac{\partial v}{\partial t} = e(-v+u)$$



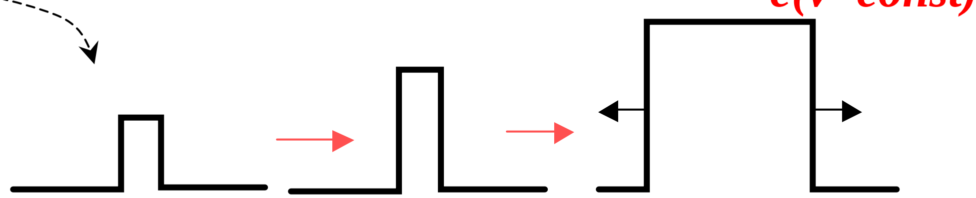
activator/inhibitor system

Slow variable with characteristic time scale e^{-1}

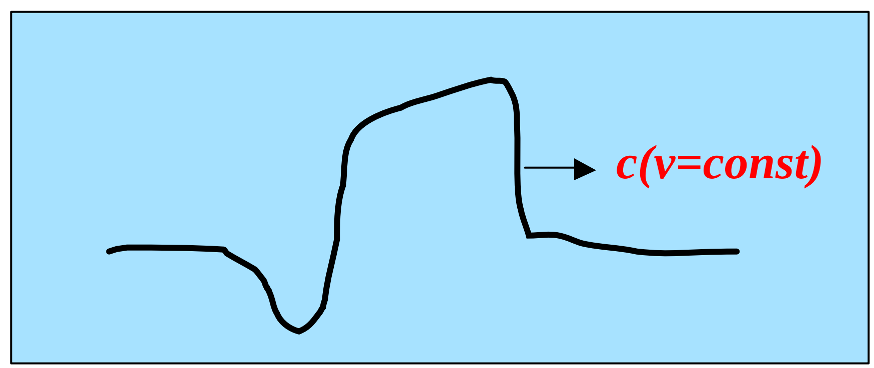
T~O(1): *v* = const – <u>bistable medium</u>

There are superthreshold excitations

How do they propagate?



At longer times *v* starts to decrease:



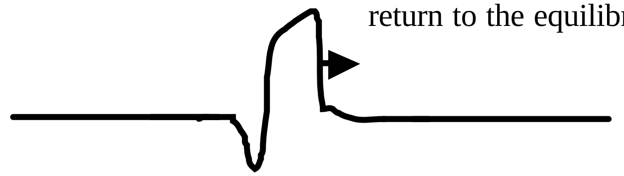
Patterns in 1D Excitable Media

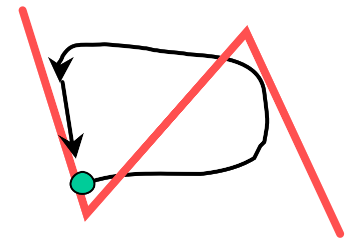
Solitary pulse

$u(x), v(x)$

$x = x - ct$

Excitation,
return to the equilibrium





Periodic Wave

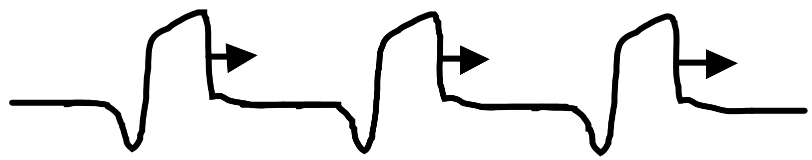
$u(x), v(x)$

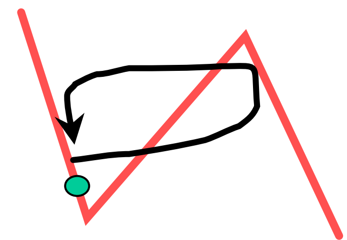
$u(x + 2p) = u(x),$

$v(x + 2p) = v(x)$

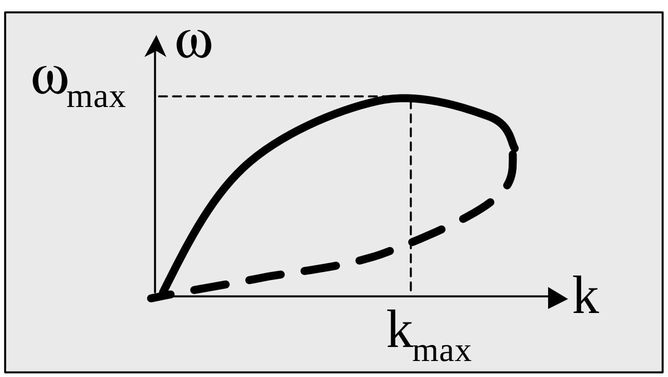
$x = kx - wt$

New excitation,
before return to equlibrium





Group velocity: ***w/k***



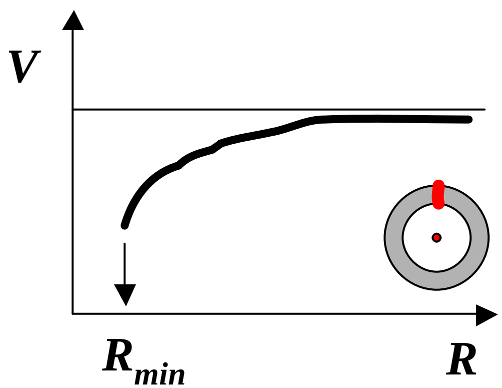
Group velocity of a wave train is less than velocity of a solitary pulse (Why?)

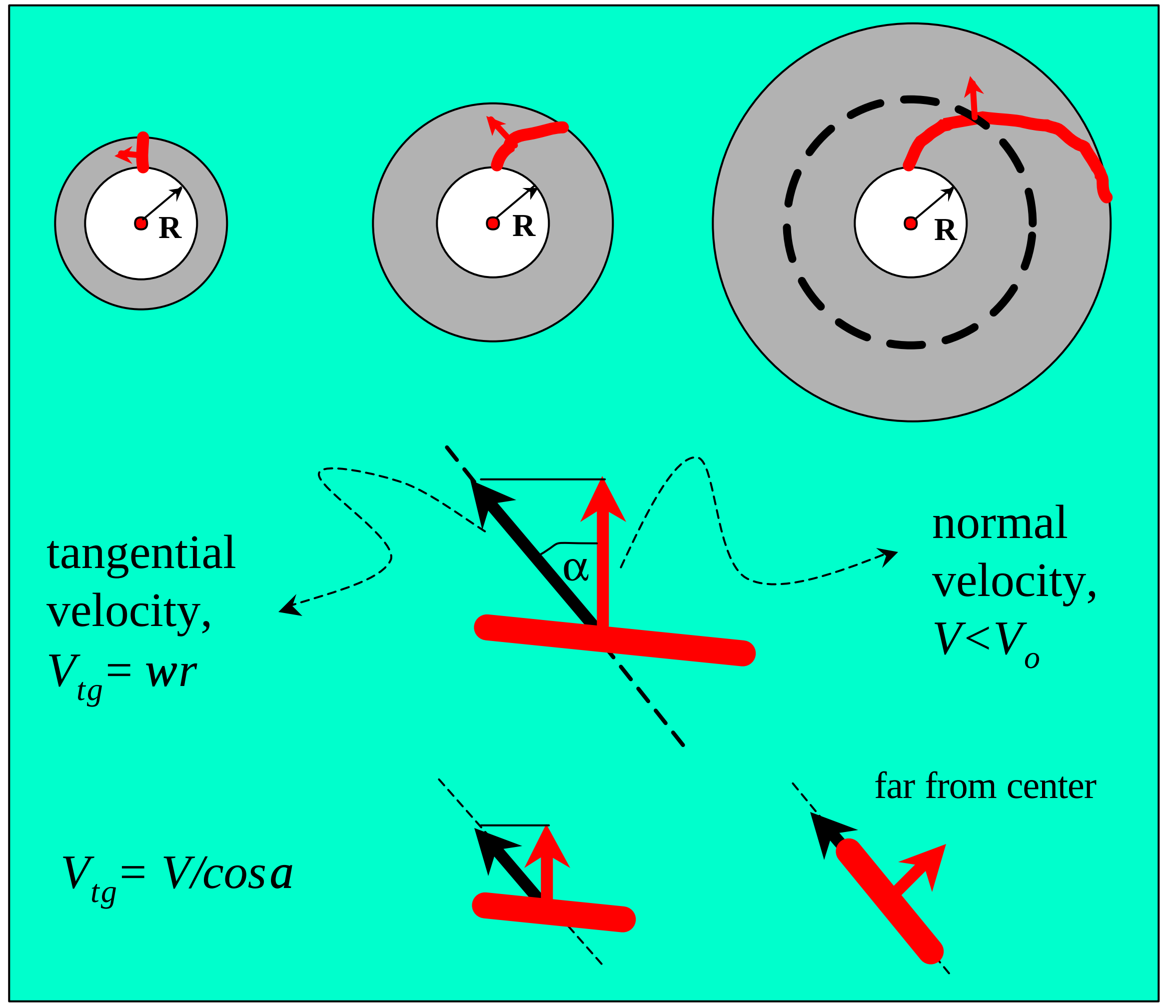
AS Mikhailov, “Foundations of Synergetics-I”, Springer, 1994

Spiral Waves

Periodic wave train, period ***L***:

Pulse in a thin ring, ***R=2p/L***:

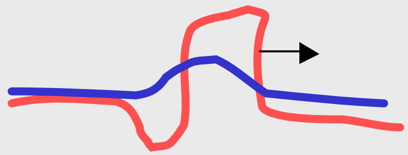




E. Meron, “Pattern formation in Excitable Media”, Phys. Rep., 218, 1-66, 1992

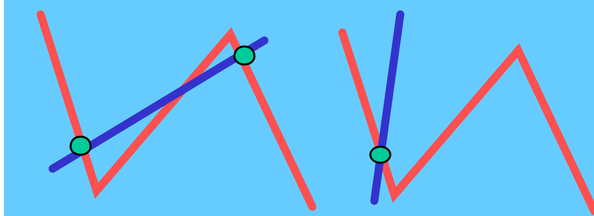
New Stationary Patterns

Traveling: Solitary or Periodic

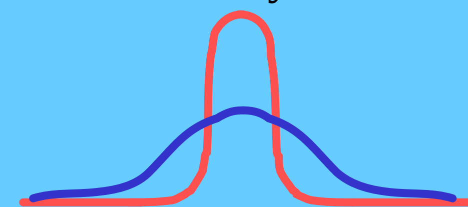


fast diffusing activator/
slow localized inhibitor

Reverse properties of
activator and inhibitor



Stationary Pulse



localized activator/
fast diffusing inhibitor

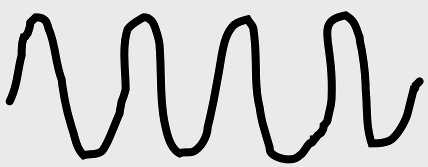
$$t_u \frac{\partial u}{\partial t} = f(u,v) + l^2 \Delta u$$

$$t_v \frac{\partial v}{\partial t} = g(u,v) + L^2 \Delta v$$

$$t_u < t_v \qquad l \ll L$$

different

Stationary & Periodic



S. Koga and Y. Kuramoto, "Localized Patterns in Reaction-Diffusion Systems", Prog. theor. Phys., 1980, 63, 106-121.

Meinhardt H, Gierer A. "Pattern formation by local self-activation and lateral inhibition", Bioessays. 2000, 22, 753-60.