Cooperativity in Reaction Rates

Consider another reaction network

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \overset{k_2}{\longrightarrow} E + P$$

$$C_1 + S \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_2 \overset{k_4}{\longrightarrow} C_1 + P$$

The reduced equations are

$$\frac{du}{d\tau} = f(u, v_1, v_2) \qquad \epsilon\frac{dv_1}{d\tau} = g_1(u, v_1, v_2) \qquad \epsilon\frac{dv_2}{d\tau} = g_2(u, v_1, v_2)$$

where $v_1 = c_1/e_0, v_2 = c_2/e_0$. Then,

$$\left.\frac{ds}{dt}\right|_{t=0} = e_0 s_0 \frac{(\alpha + \beta s_0)}{\gamma + \delta s_0 + s_0^2}$$

with a general result of a rate

$$rate \sim \frac{s^n}{K_m + s^n}$$

which is known as the *Hill equation*, with n being the *Hill coefficient*. The larger is n, the more sigmoidal and cooperative the reaction.

Slaving, Nonlinearities, and Fronts

A particularly simple example of nonlinearities arising from slaving fast variables to slow ones is seen in the scheme

$$\frac{dq}{dt} = \alpha q - \beta p q$$
$$\epsilon \frac{dp}{dt} = \gamma p - \delta q^2$$

In the steady state, $\gamma p \sim \delta q^2$, so $p \sim (\delta/\gamma) q^2$, and

$$\frac{dq}{dt} \simeq \alpha q - \frac{\beta\delta}{\gamma} q^3 = -\frac{\partial V}{\partial q} \qquad V(q) = -\frac{1}{2}\alpha q^2 + \frac{\beta\delta}{4\gamma} q^4$$

Looks like a potential. Bistability!

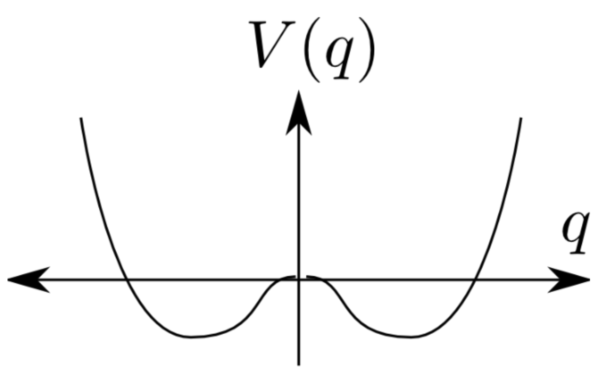
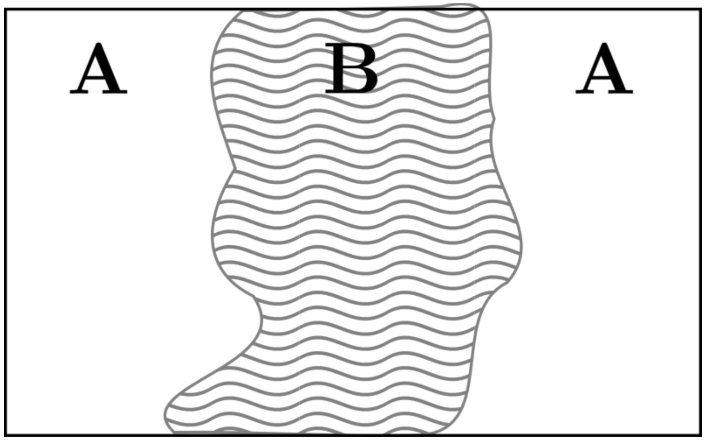


Fig. 20.2. Apprriximate chronological spread of the Black Death in Europe from 1347–50. (Redrawn from Langer 1964)

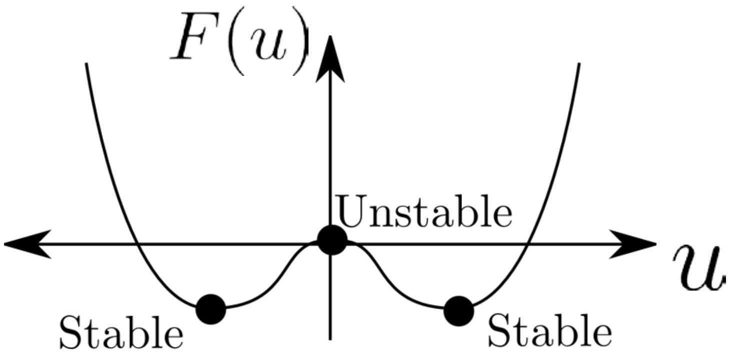
Front Propagation



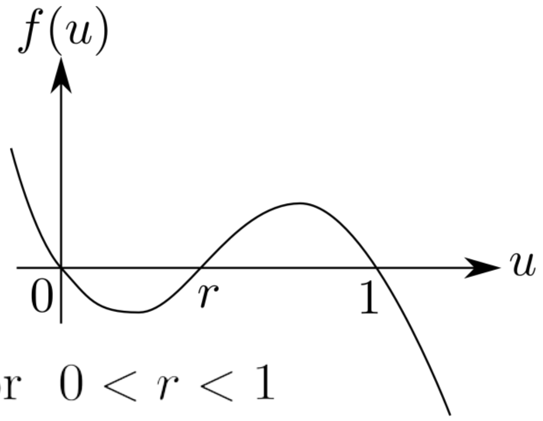
There are many many examples in biological physics in which problems of pattern formation are defined by the boundaries between regions of different behaviour of some generalized *field*, a chemical concentration, population level, etc.

To understand the general problem of *front propagation* we add diffusive effects to the nonlinearities considered so far. The simplest class of one-dimensional models takes the form

$$u_t = m u_{xx} + f(u) \ , \qquad \text{where} \qquad f(u) = -\frac{\partial F}{\partial u}$$



Front Propagation - continued



The fundamental question is:
How fast does the front move? A simple pedagogical model for $f(u)$ involves the cubic nonlinearity

$$\boxed{f(u) = -F'(u) = -u(u-r)(u-1)} \quad \text{for} \quad 0 < r < 1$$

Here, r is a control parameter that will tune the properties of the front, and

$$F(u) = \frac{1}{4}u^2(1-u)^2 + \left(r - \frac{1}{2}\right)\left(\frac{1}{2}u^2 - \frac{1}{3}u^3\right)$$

so that $F(0) = 0$ and $F(1) = (r - 1/2)/6$ and the energy difference between the two minima is

$$\Delta F = F(1) - F(0) = \boxed{\frac{1}{6}\left(r - \frac{1}{2}\right)}$$

For $r < 1/2$ the state $u = 1$ is the more stable, and for $r > 1/2$ the state $u = 0$ is more stable.

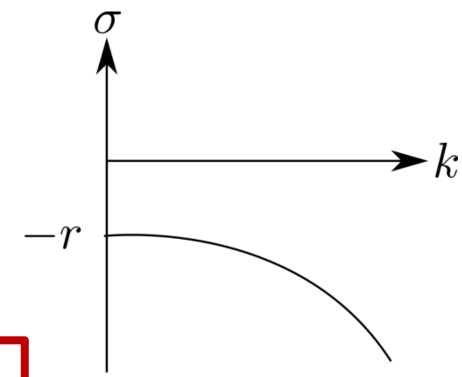
Linear Stability Analysis

Near $u = 0$,

$$u_t = mu_{xx} - ru + \ldots$$

and let $u = e^{ikx}e^{\sigma t}$. If $\sigma < 0$, u is stable, while if $\sigma > 0$ u is unstable. Substituting for u, we deduce that

$$\sigma = -r - mk^2 \ .$$



Near $u = 1$, let $u = 1 + \hat{u}$. Then

$$\hat{u}_t \sim m\hat{u}_{xx} - (1-r)\hat{u}$$
$$\sigma = -(1-r) - mk^2$$

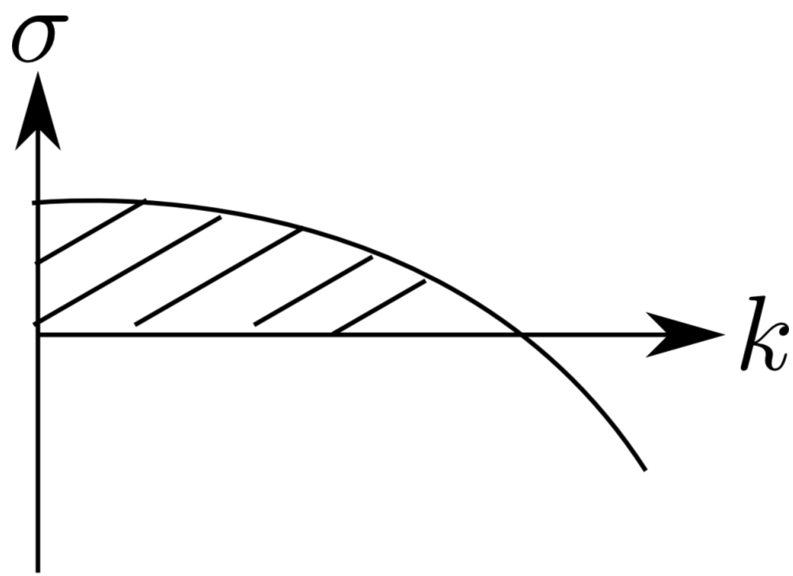
which is also always stable. Thus, both global minima are stable for all k.

Linear Stability Analysis – continued

Near $u = r$, we let $u = r + \tilde{u}$ and find

$$\tilde{u}_t = m\tilde{u}_{xx} + r(1-r)\tilde{u}$$
$$\sigma = r(1-r) - mk^2$$

and thus there is a band of unstable modes below a critical k. The obvious question is what happens between $u = 0$ and $u = 1$ when $r \sim 1/2$.



The Stationary Front (r=1/2)

Stationary front (r=1/2)

$$mu_{xx} - u\left(u - \frac{1}{2}\right)(u-1) = 0$$

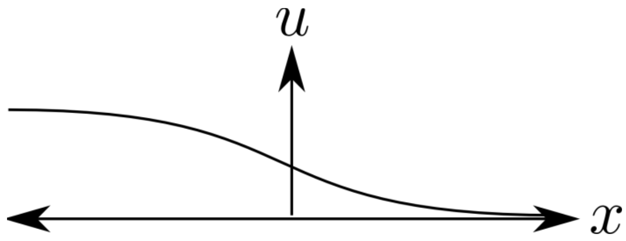
Multiplying through by u_x and integrating we find

$$\frac{1}{2}mu_x^2 - F(u) + C = 0$$

where the constant C can be seen to vanish from the boundary conditions ($u \to 1$ as $x \to -\infty$, $u \to 0$ as $x \to \infty$). This yields

$$u = \frac{1}{2}\left[1 - \tanh\left(\frac{x}{2\sqrt{2m}}\right)\right]$$

yielding a transition with a width controlled by m.



A Moving Front

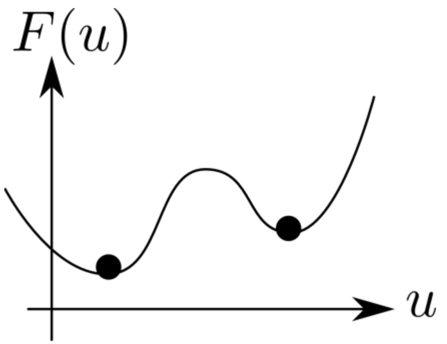
To determine the behavior of the case $r \neq 1/2$, a systematic perturbation theory is necessary. Here, instead, our goal is to derive heuristically the front motion of a 1D PDE with a generic nonlinearity. Consider

$$u_t = m u_{xx} - F'(u)$$

Imagine, after some transient period, a steady uniformly moving solution exists. We then seek a traveling solution of the form

$$u(x,t) = U(x - vt)$$

for some unknown v. The simplest case is for an $F(u)$:

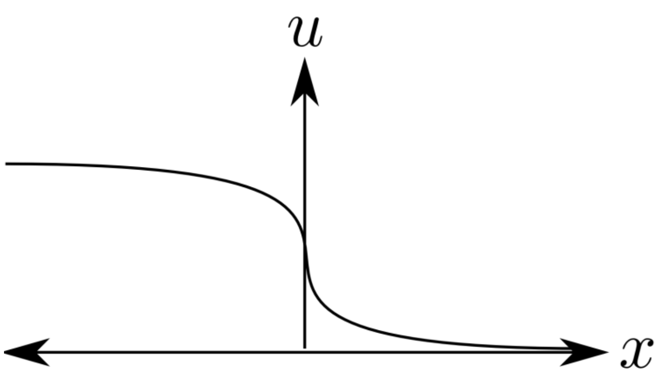


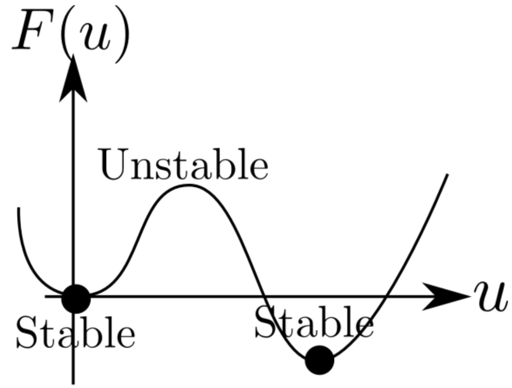
From the traveling-wave ansatz, we have

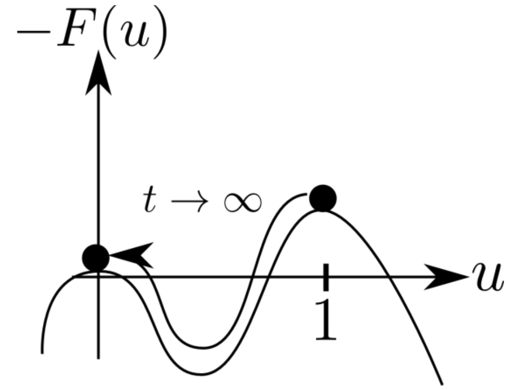
$$mU_{zz} + vU_z = -(-F'(U))$$

which is similar to Newton's second law ($m\ddot{q} + b\dot{q} =$ force) with m being the "mass" of a fictitious particle, U its "position", and z the "time", and with an effective potential $-F(U)$.

A Moving Front - continued



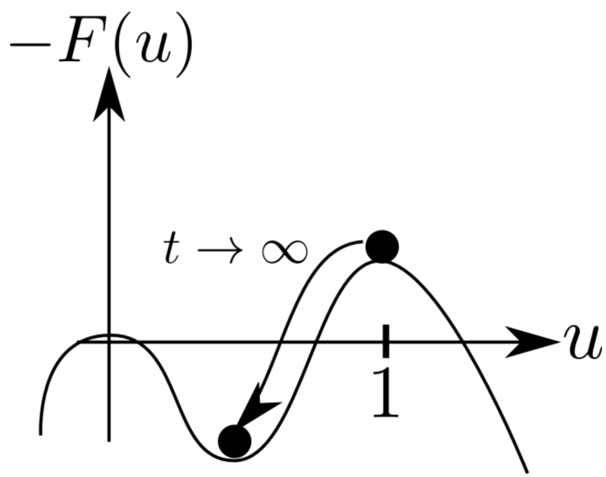




$$mU_{zz} + vU_z = -(-F'(U))$$

Now, looking at $-F$ instead of F, the situation can be viewed as a ball moving down a hill. The key point is that there exists a *unique* front speed v (a unique damping coefficient in the mechanical analogy), to achieve $u \to 0$ as $t \to \infty$.

If instead the front consists of a *stable-to-unstable* situation, the analogy will be In this case, any damping coefficient v greater than a critical value v_c will ensure $u \to 0$ as $t \to \infty$.



A Moving Front - continued

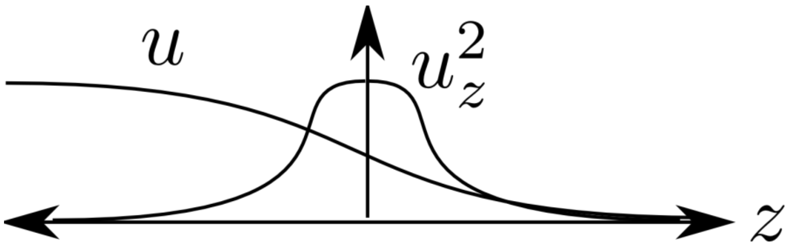
We now seek a first integral to the differential equation

$$mU_{zz} + vU_z = -(-F'(U))$$
$$mU_zU_{zz} + vU_z^2 = F'(U)U_z$$
$$\frac{1}{2}mU_z^2\Big|_{-\infty}^{\infty} + v\int_{\infty}^{\infty} dzU_z^2 = \int_{-\infty}^{\infty} \frac{dF}{dU}\frac{dU}{dz}dz = F(0) - F(1)$$

which is precisely the energy difference $-\Delta F$ between the two locally stable minima. We can then formally solve for the front velocity:

$$\boxed{v = \frac{-\Delta F}{\int_{-\infty}^{\infty} dzU_z^2}}$$

The denominator is like a drag coefficient, and is dominated by the front region.



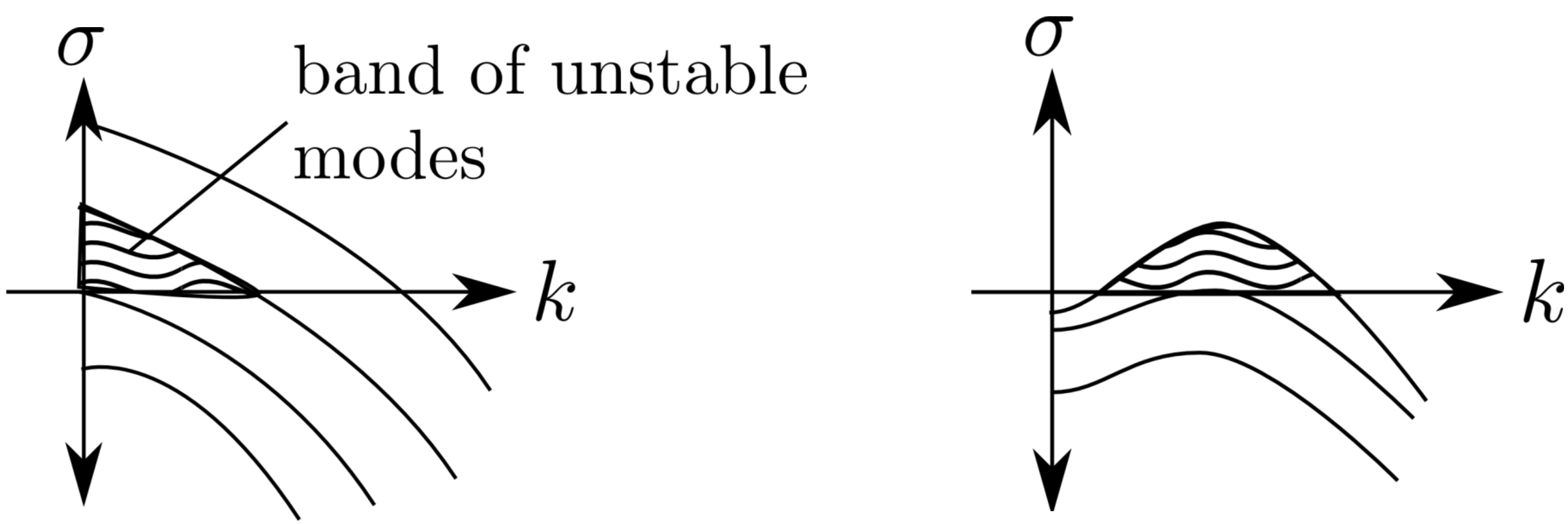
Phenomenology of Reaction-Diffusion Systems

We consider equations of the form

$$u_t = \mathcal{L}u + \mathcal{N}(u) \ , \qquad \mathcal{L}u = \alpha u + D u_{xx}$$

For solutions of the form $u \propto e^{ikx+\sigma t}$, $\sigma(k) = \alpha - Dk^2$. In k-space, the graph is simple (left) and corresponds to excitations of long wavelength. A more interesting possibility is when both long and short wavelength are damped (see the second plot). In this case, there is a well defined k^* corresponding to the fastest growing mode, leading to a pattern on that scale.

This leads to a fundamental question: *How can diffusion (governed by a second derivative) produce a k-dependence other than k^2?*.



Phenomenology of Reaction-Diffusion Systems

Since $\sigma = \sigma(k^2)$ (by left-right symmetry), we would require

$$\sigma(k) \sim \alpha + \beta k^2 - \gamma k^4 + \ldots$$
$$u_t = \alpha u - \beta u_{xx} - \gamma u_{4x} + \ldots$$

but such higher-order derivative theories for a single degree of freedom are rare. Instead, two *coupled* reaction-diffusion equations can produce this behavior.

The FitzHugh-Nagumo model. The FHN model was first developed as a simplification neuronal dynamics. Two chemical species are involved: u, the *activator*, and v, the inhibitor. Under suitable rescalings it typically takes the form

$$u_t = D\nabla^2 u + f(u) - \rho v$$
$$\epsilon v_t = \nabla^2 v + \alpha u - \beta v \ .$$

Notice that the inhibitor diffusion constant has been rescaled to unity. We may be interested in a whole range of values for ϵ, not necessarily small. The various terms on the RHS of the equations are:

$f(u)$	Autocatalysis & bistability
ρv	Inhibition
αu	Stimulation
βv	Self-limitation