Excitable Systems

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MOL 410/510

Example — Action potentials in nerve cells

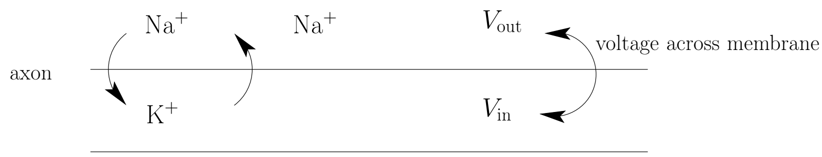
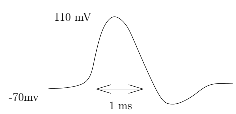


Figure 1: Nerve cell

Hodgkin-Huxley (1952)

- voltage ($V_{\text{in}} - V_{\text{out}}$) starts out negative ($\sim -70$ mV), a "resting potential"
- perturbation (e.g. injected current) increases voltage, which opens sodium channels
- Na^+ enters axon, increases voltage even more, to $\sim +100$ mV
- sodium channels close spontaneously in ~ 1 ms
- K^+ leakage returns voltage to ~ -70 mV
- sodium pumps restore Na^+ gradient and resting potential



The result is a transient depolarization wave that moves down the axon, though the wave doesn't spread. This is a "soliton."

Fitzhugh-Nagumo equation

A simplified model is the Fitzhugh-Nagumo equation:

$$\frac{\mathrm{d}V}{\mathrm{d}t} = I(t) - V(V-a)(V-1) - W \quad V = \text{voltage}$$
$$\frac{\mathrm{d}W}{\mathrm{d}t} = \varepsilon(V - \gamma W) \quad W = \text{recovery variable (like channels closing).}$$

Find nullclines:

Consider the phase plane for $I = 0$ (with parameters as in Kaplan and Glass: $\varepsilon = 0.008, a = 0.139, \gamma = 2.54$).

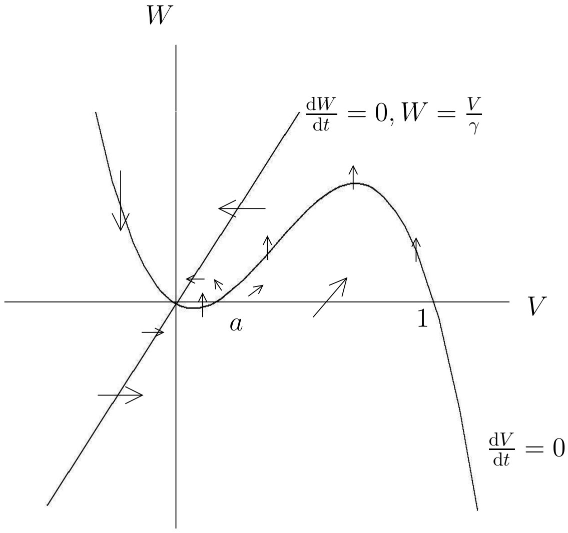


Figure 2: $I = 0$ phase plane

There is clearly a fixed point at the origin.

$$\begin{aligned} &\text{for } V > \gamma W, && \dot{W} > 0; \\ &\text{for } W > -V(V-a)(V-1), && \dot{V} < 0. \end{aligned}$$

Linear stability analysis of the fixed point at $(0,0)$:

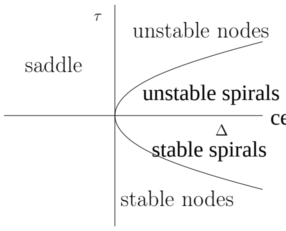
$$\begin{aligned} \dot{V} &= f(V,W) = -V(V-a)(V-1) - W \\ \dot{W} &= g(V,W) = \varepsilon(V - \gamma W) \end{aligned}$$

$$J = \begin{pmatrix} \frac{\partial f}{\partial V} & \frac{\partial f}{\partial W} \\ \frac{\partial g}{\partial V} & \frac{\partial g}{\partial W} \end{pmatrix}\Bigg|_{V=0,W=0}$$

$$\begin{aligned} &\frac{\partial f}{\partial V} = -(V-a)(V-1) - V(V-1) - V(V-a) = -a \text{ (with } V=0) && \frac{\partial f}{\partial W} = -1 \\ &\frac{\partial g}{\partial V} = \varepsilon && \frac{\partial g}{\partial W} = -\varepsilon\gamma. \end{aligned}$$

$$\text{Jacobian } J = \begin{pmatrix} -a & -1 \\ \varepsilon & -\varepsilon\gamma \end{pmatrix}$$

$$\begin{aligned} \Delta &= \det J = \varepsilon(1 + a\gamma) \\ \tau &= \operatorname{tr} J = -a - \varepsilon\gamma \\ \lambda_{1,2} &= \frac{1}{2}(\tau \pm \sqrt{\tau^2 - 4\Delta}) = -0.797 \pm 0.067i \end{aligned}$$



Which implies a stable focus at the origin.

But notice that flow along V-axis is away from origin for $a < V < 1$. So if a transient current $I(t)$ is enough to make $V > a$, then the trajectory will extend to $V \approx 1$ before returning to the origin. The action potential is "stereotyped": once $V > a$, the overall trajectory will be approximately independent of the precise initial value of V.

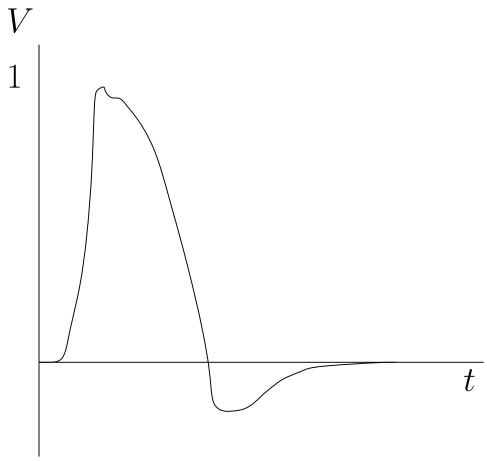


Figure 3: Action potential

Example — Competence in *Bacillus subtilis*

(cf. G.M Süel et al. *Nature* 23 March 2006.) Under certain conditions (e.g. starvation), a fraction ($\lesssim 20\%$) of the cells in a colony of the gram-positive bacterium *B. subtilis* become transiently competent to take up DNA from the medium — called "competence." This is an example of an excitable system:

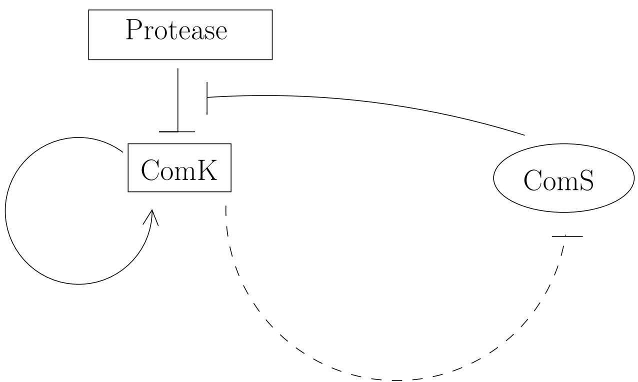


Figure 4: *B. subtilis* competence

- Com K positively autoregulated — "competence factor"
- protease acts on Com K *or* Com S

- Com K represses Com S (possibly with delay)

$$\dot{K} = a_k + \frac{b_k K^n}{k_0^n + K^n} - \frac{K}{1+K+S}$$
$$\dot{S} = \frac{b_S}{1+(\frac{K}{k_1})^\beta} - \frac{S}{1+K+S}$$

- Phase portraits for different parameter values (Figure 5).

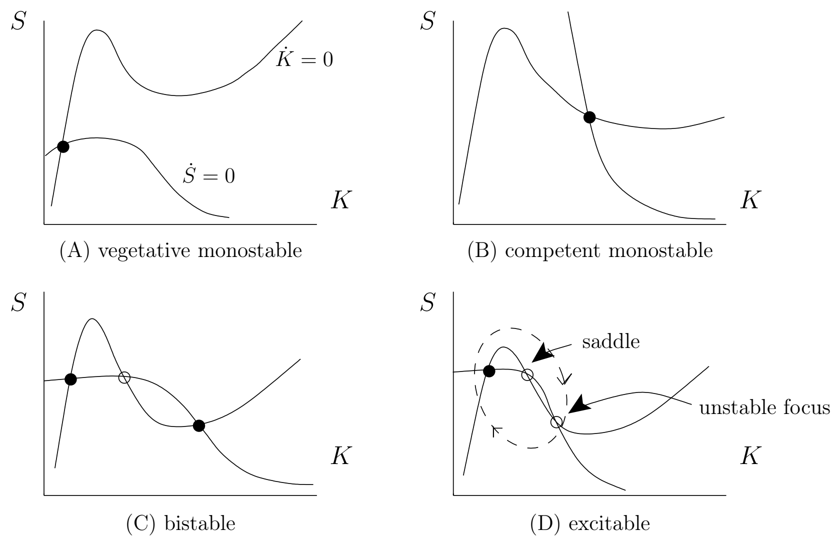


Figure 5: Phase portraits

Apparently, noise, e.g. in protein levels, excites the system out of a stable fixed point and produces era of competence.

The parameter range for excitable phase portrait is very small. But the range increases if a delay in Com S repression by Com K is included.

Qualitative effect of delay $K(t-\tau)$

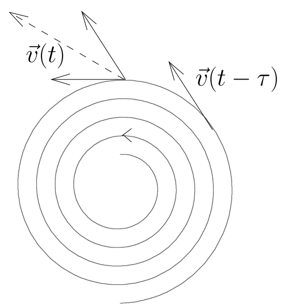


Figure 6: Delay effects

In the bistable region, we have stable focus at competent fixed point. Time delay includes some of velocity vector from time $t - \tau$. For large enough delays, the velocity vector begins to point outward, that is, stable focus becomes unstable focus.

Linear-stability analysis for time-delay differential equations

Example — Single time delay τ

$$\begin{aligned} \dot{\vec{x}} &= \vec{f}(\vec{x}(t), \vec{x}(t-\tau)) && \text{write } \vec{x}(t) = \vec{x}, \vec{x}(t-\tau) = \vec{x}_\tau \\ \vec{x} &= \vec{x}^* + \delta\vec{x} && \text{linear stability analysis} \end{aligned}$$

We have

$$\begin{aligned} \dot{\vec{x}} =& \delta\dot{\vec{x}} = \vec{f}(\vec{x}^* + \delta\vec{x}, \vec{x}^* + \delta\vec{x}_\tau) \\ & \delta\dot{\vec{x}} \approx \boldsymbol{J_0}\delta\vec{x} + \boldsymbol{J_\tau}\delta\vec{x}_\tau, \quad \text{since } \vec{f}(\vec{x}^*, \vec{x}^*) = 0. \end{aligned}$$

By linearity, $\delta\vec{x}(t) = \vec{A}e^{\lambda t}$. So

$$\lambda\vec{A} = (\boldsymbol{J_0} + e^{-\lambda\tau}\boldsymbol{J_\tau})\vec{A},$$

and so

$$\det\{\boldsymbol{J_0} + e^{-\lambda\tau}\boldsymbol{J_\tau} - \lambda I\} = 0$$

is an eigenvalue problem. We look to the characteristic equation. Unlike the ODE case, a DDE characteristic equation is *not* a polynomial in λ, but what's called a "quasi-polynomial."

If $\text{Re}\{\lambda\} > 0$ for any solution λ (and there are generally an infinite number of solutions!), then the fixed point $\vec{x}^*$ is unstable.

Delays, in other words, can destabilize otherwise stable fixed points.

Example — Linear system with delay

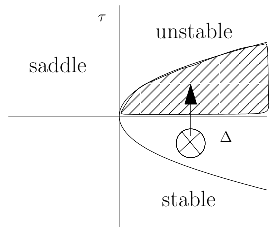
$$\begin{aligned} \dot{x} &= ax + by(t-\tau) \\ \dot{y} &= cx + dy \end{aligned}$$

A fixed point exists at the origin.

$$\boldsymbol{J_0} = \begin{pmatrix} a & 0 \\ c & d \end{pmatrix} \qquad \boldsymbol{J_\tau} = \begin{pmatrix} 0 & e^{-\lambda\tau}b \\ 0 & 0 \end{pmatrix}$$

Eigenvalue problem:

$$\begin{aligned} \det\begin{Bmatrix} a-\lambda & e^{-\lambda\tau}b \\ c & d-\lambda \end{Bmatrix} &= 0 \\ (a-\lambda)(d-\lambda) - bce^{-\lambda\tau} &= 0 \\ \lambda^2 - (a+d)\lambda + ad - bce^{-\lambda\tau} &= 0 \end{aligned}$$



No delay ($\tau = 0$)

$$\lambda_{1,2} = \frac{1}{2}(a + d \pm \sqrt{(a+d)^2 - 4(ad-bc)})$$

Assume $\det = ad - bc > 0$. If $a < 0, d < 0$, we cannot have an unstable cycle. (i.e., $\text{tr} < 0$)

Finite delay ($\tau > 0$)

For simplicity, we consider a short delay, with $\lambda\tau << 1$.

$$\lambda^2 - (a+d)\lambda + ad - bc(1 - \lambda\tau) = 0$$
$$\lambda^2 - (a+d-bc\tau)\lambda + ad - bc = 0$$

(This corresponds to a change from *trace* $\rightarrow$ *trace* $- bc\tau$.) And so,

$$\lambda_{1,2} = \frac{1}{2}(a + d - bc\lambda \pm \sqrt{(a+d+bc\tau)^2 - 4(ad-bc)})$$

If $a + d - bc\tau > 0, \mathrm{Re}\{\lambda_{1,2}\} > 0$. So even if $a < 0, d < 0$, a delay τ can make a stable cycle unstable. In practice, delays are often used in biology along with negative feedback to produce oscillations, e.g. circadian rhythms.