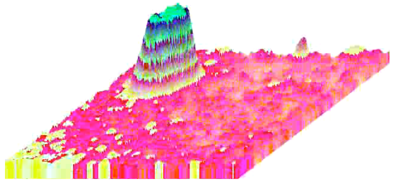
Travelling waves in biology: Lecture 1

1 Examples

Spiral waves of calcium activity in a Xenopus oocyte

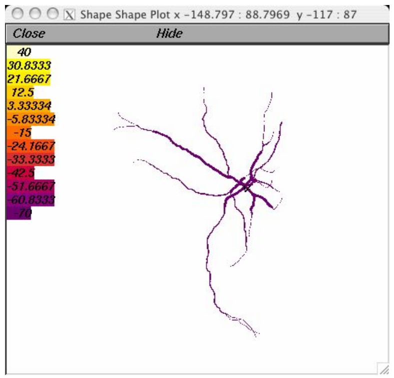
from Jim Lechleiter's lab http://www.uthscsa.edu/csb/faculty/lechleiter.asp

Stochastic intracellular waves



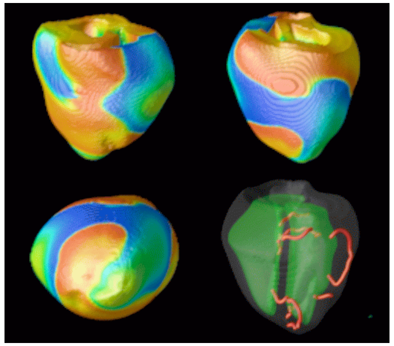
IP_3-evoked calcium puffs and waves in a Xenopus oocyte from Ian Parkers lab http://parkerlab.bio.uci.edu/

Action potentials in a branched neuron



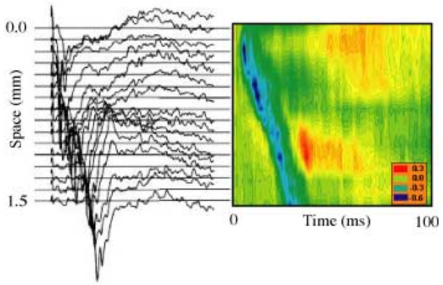
Action potential propagation in a branched dendrite from Yulia Timofeeva http://www.dcs.warwick.ac.uk/people/academic/Y.Timofeeva/

Cardiac waves

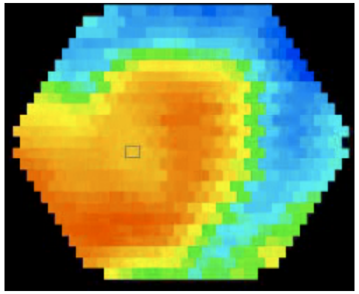


Evolution of ventricular fibrillation from Flavio Fenton's lab http://arrhythmia.hofstra.edu/

Epileptic waves



Synaptic waves in neuronal issue from Dave Pinto's lab
http://www.bme.rochester.edu/bmeweb/faculty/pinto.html



Waves in rat neocortical slices
from Jian-YoungWu's lab http://www.georgetown.edu/faculty/wuj/

Many spatially extended dynamical systems support travelling waves. For example, action potentials on axons, spiral waves of electrical activity on hearts, flame fronts in forest fires, etc. It is quite often possible to calculate the properties of such waves by constructing an associated homoclinic or heteroclinic connection.

Global connections

Consider a continuous-time dynamical system defined by

$$\dot{x} = f(x), \qquad x \in \mathbb{R}^n$$

with equilibria $x^{(0)}, x^{(1)}, x^{(2)}, \ldots$ and *flow* $\phi(x,t)$.
An orbit Γ starting at a point $x \in \mathbb{R}^n$ is called *homoclinic* to the equilibrium point $x^{(0)}$ if $\phi(x,t) \to x^{(0)}$ as $t \to \pm\infty$.
An orbit Γ starting at a point $x \in \mathbb{R}^n$ is called *heteroclinic* to the equilibrium points $x^{(1)}$ and $x^{(2)}$ if $\phi(x,t) \to x^{(1)}$ as $t \to -\infty$ and $\phi(x,t) \to x^{(2)}$ as $t \to +\infty$

A detailed discussion about waves in mathematical biology can be found in the textbook by Keener and Sneyd [1].

Many biological systems are *excitable* (e.g. cardiac and neural tissue).

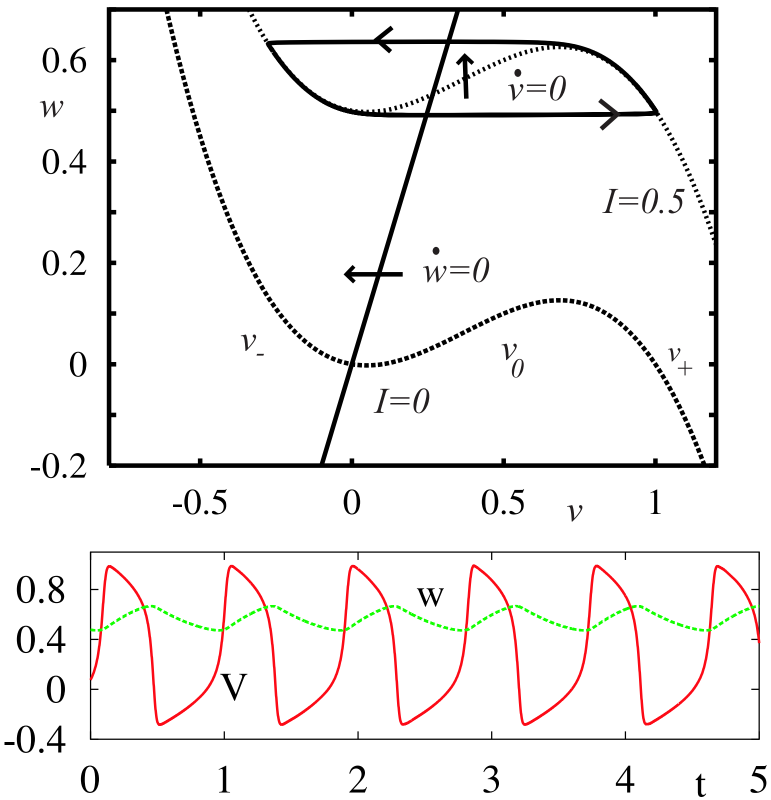
2 The geometry of excitability – `FitzHughNagumo.ode`

The FitzHugh-Nagumo equations capture the essential features of an excitable system:

$$\begin{aligned} \mu\dot{v} &= f(v) - w + I \equiv f_1(v,w), \qquad f(v) = v(a-v)(v-1) \\ \dot{w} &= v - \gamma w \equiv f_2(v,w) \end{aligned}$$

where $0 < a < 1$ and $\gamma, \mu > 0$. In a neural context v is like the membrane potential and w plays the role of a recovery or gating variable. Linear stability analysis: fixed point $(\overline{v}, \overline{w})$ is unique and defined by the real solution of the cubic equation

$$f(\overline{v}) - \frac{\overline{v}}{\gamma} + I = 0, \qquad \overline{w} = \frac{\overline{v}}{\gamma}$$



Nullclines for the FitzHugh-Nagumo model with $a = 0.1$ and $\gamma = 0.5$. Periodic orbit with $I = 0.5$ and $\mu = 0.001$.

The Jacobian is given by

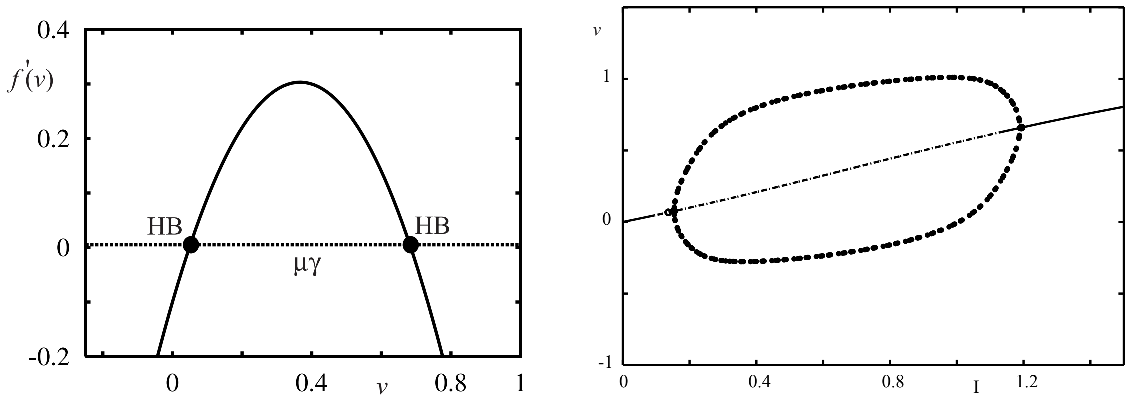
$$L = \begin{bmatrix} f'(\overline{v})/\mu & -1/\mu \\ 1 & -\gamma \end{bmatrix}, \qquad f'(v) = v(a-v) + v(1-v) + (v-a)(1-v)$$

For $I = 0$ $(\overline{v}, \overline{w}) = (0, 0)$ and the fixed point is stable since $\text{Tr}\, L = f'(0)/\mu - \gamma < 0$ (since $f'(0) = -a$) and $\det L = (1 + a\gamma)/\mu > 0$ and $(\text{Tr}\, L)^2 - 4 \det L = (a/\mu - \gamma)^2 - 4/\mu > 0$ if $\mu \ll 1$.

With non-zero I we look for Hopf bifurcations defined by $\text{Tr}\, L = 0$ and $\det L > 0$, which gives

$$f'(\overline{v}) = \mu\gamma$$

A plot of the quadratic $f'(v)$ shows that there may be two Hopf bifurcation points. Since for $I = 0$ the fixed point is stable we expect an instability of the fixed point with increasing I and a restabilisation for some even larger value of I. To prove the existence of a stable limit cycle when the fixed point is unstable we appeal to the Poincaré Bendixson theorem. If we pick a large enough box ($|v|, |w| \to \infty$) then it is a simple matter to show that all trajectories are *inwards*.



Left: Conditions for Hopf bifurcation ($f'(\overline{v}) = \mu\gamma$). Right: Bifurcation diagram for $\mu = 0.01$, $\gamma = 0.5$.

The system is said to be *excitable* when the fixed point is stable and on the left branch of the cubic v nullcline and *oscillatory* when the fixed point is unstable and on the middle branch of the cubic v nullcline.

When $\mu \ll 1$ the variable v is said to be *fast* and w *slow*. This means that v may adjust rapidly and maintain a pseudo-equilibrium along the stable branches of $f_1(v, w) = 0$. Along these branches the dynamics of w are governed by the reduced dynamics

$$\dot{w} = f_2(v_\pm(w), w) = G_\pm(w)$$

When it is not possible for v to be in quasi-equilibrium, the motion is governed by

$$\frac{dv}{d\tau} = f_1(v, w), \qquad \frac{dw}{d\tau} = 0$$

where τ is the fast time scale $\tau = \mu t$. On this time scale w is a constant while v equilibrates to a solution of $f_1(v, w) = 0$.

The curve $v = v_0(w)$, the middle branch, is a *threshold* curve.

The period of oscillation of a stable orbit around an unstable fixed point on the middle branch can be approximated by the time spent on the slow branches. If we denote the value of w at the lower knee of the cubic by w_* and at the upper by w^* then the period of oscillation is given by

$$T = \int_{w_*}^{w^*} \left(\frac{1}{G_+(w)} - \frac{1}{G_-(w)} \right) dw$$

3 Waves in a bi-stable system

Let us consider the simple example of a spatially extended bi-stable system of the form

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

where $f(v) = v(v-1)(\alpha - v)$. By a travelling wave we mean solutions of the form

$$v(x,t) = V(x+ct) = V(\xi)$$

for some undetermined *speed* c. $\xi = x + ct$ is called the travelling wave variable. When written as a function of ξ the wave appears stationary. Substitution into the bistable equation yields a second order ODE

$$V_{\xi\xi} - cV_\xi + f(V) = 0$$

Equivalently we have

$$\begin{aligned} V_\xi &= W \\ W_\xi &= cW - f(V) \end{aligned}$$

The fixed points are $(V,W) = (0,0)$ (saddle) and $(V,W) = (1,0)$ (saddle). To find travelling fronts we look for a heteroclinic trajectory that connect these equilibria. The equilibria at $V = \alpha$ is either a node or a spiral (since the eigenvalues of the linearisation have the same sign). Our goal is to choose a value of c such that the trajectory that leaves the saddle $V = 0$ at $\xi = -\infty$ can be made to connect with the saddle $V = 1$ at $\xi = +\infty$. This is known as *shooting*. Since we expect $V_\xi \to 0$ as $\xi \to \pm\infty$ we try solutions of the form

$$W = BV(V-1)$$

implying that $W_V = B(2V-1)$. From the first order form we may take the ratio of W_ξ and V_ξ to obtain

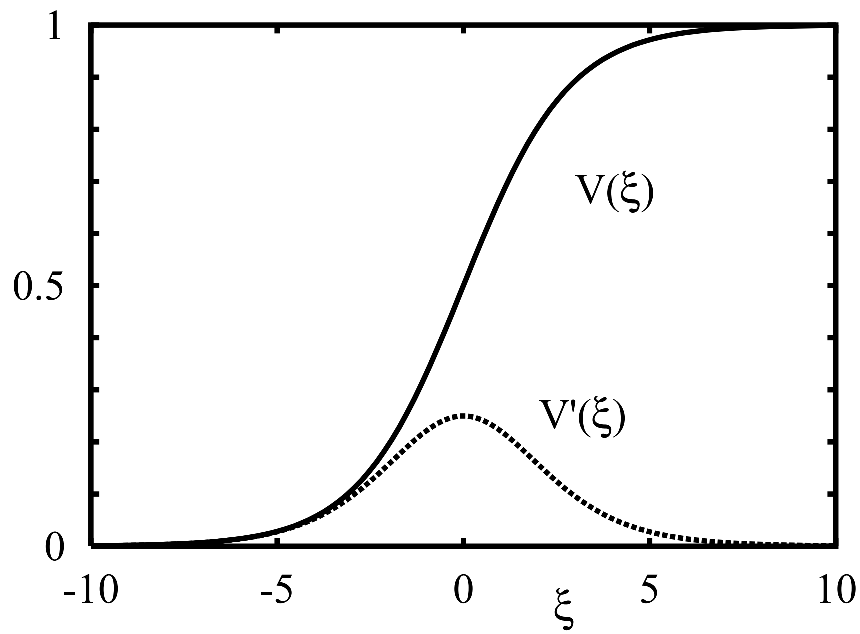
$$W_V = c - \frac{\alpha - V}{B}$$

where we use $f(V) = W(\alpha - V)/B$. Comparing the two forms for W_V and equating powers of V yields $B = \pm 1/\sqrt{2}$ and

$$c = \pm \frac{2\alpha - 1}{\sqrt{2}}$$

Finally solving $V_\xi = W$ we have an exact form of the solution given by

$$v(x,t) = \frac{1}{1 + \exp[-(x + ct)/\sqrt{2}]}$$



4 Waves in a threshold model

$v = v(x,t)$, $x \in \mathbb{R}$, $t \in \mathbb{R}^+$.

$$v_t = -\frac{v}{\tau} + v_{xx} + H(v-h). \tag{1}$$

Here, H is a Heaviside step function, and h is a constant threshold.

Introduce $\xi = x - ct$. In a co-moving frame (1) becomes

$$-cv_\xi + v_t = -\frac{v}{\tau} + v_{\xi\xi} + H(v-h). \tag{2}$$

where $v = v(\xi, t)$. A travelling wave solution $q(\xi)$ is obtained upon letting $\partial_t v \to 0$, such that

$$q_{\xi\xi} + cq_\xi - \epsilon q = -H(q-h), \qquad \epsilon = \frac{1}{\tau}.$$

Now consider a front solution where $q(\xi) \geq h$ for $\xi \geq 0$ and $q(\xi) < h$ for $\xi < 0$. In this case

$$q(\xi) = \begin{cases} \tau + Ae^{m_-\xi} & \xi \geq 0 \\ Be^{m_+\xi} & \xi < 0 \end{cases},$$

where

$$m_\pm = \frac{-c \pm \sqrt{c^2 + 4\epsilon}}{2}$$

Continuity of q and q' at $\xi = 0$ gives the coefficients A and B as

$$A = \frac{m_+\tau}{m_- - m_+}, \qquad B = \frac{m_-\tau}{m_- - m_+}.$$

The speed of the front is then determine by demanding that $q(0) = h$, so that

$$h = \frac{m_-\tau}{m_- - m_+}.$$

This may be re-arranged to give the speed explicitly as

$$c = \frac{1/h - 2/\tau}{\sqrt{1/h - 1/\tau}}, \qquad h < \tau.$$

4.1 Evans function

Consider perturbations of the form $v(\xi, t) = q(\xi) + u(\xi, t)$. To first order we have from (2) that

$$-cu_\xi + u_t = -\frac{u}{\tau} + u_{\xi\xi} + \delta(q - h)u.$$

Perturbations of the form $u(\xi, t) = u(\xi)e^{\lambda t}$ lead to the eigenvalue problem

$$Qu = \delta(q - h)u, \qquad Q = -d_{\xi\xi} - cd_\xi + \lambda + \epsilon. \tag{3}$$

The Green's function, η, of the linear differential operator Q ($Q\eta = \delta$) may be calculated (using Fourier transforms) as

$$\eta(\xi) = \int_{-\infty}^{\infty} \frac{dk}{2\pi} \frac{e^{ik\xi}}{k^2 - ick + \lambda + \epsilon} = \frac{1}{k_+(\lambda) - k_-(\lambda)} \begin{cases} e^{k_-(\lambda)\xi} & \xi \geq 0 \\ e^{k_+(\lambda)\xi} & \xi < 0 \end{cases},$$

where

$$k_\pm(\lambda) = \frac{-c \pm \sqrt{c^2 + 4(\epsilon + \lambda)}}{2}.$$

Here we have assumed that $\lambda + \epsilon > 0$ (i.e we are to the right of the essential spectrum). We may now solve (3) in the form

$$u = \eta * [\delta(q - h)u],$$

where $*$ denotes convolution. Using the result that $\delta(q - h) = \delta(\xi)/|q'(0)|$ we have that

$$u(\xi) = \mathcal{A}(\lambda, \xi)u(0), \qquad \mathcal{A}(\lambda, \xi) = \frac{\eta(\xi)}{|q'(0)|}.$$

Demanding a non-trivial solution at $\xi = 0$ gives the condition $\mathcal{E}(\lambda) = 0$, where

$$\mathcal{E}(\lambda) = 1 - \mathcal{A}(\lambda, 0) = 1 - \frac{m_+ - m_-}{k_+(\lambda) - k_-(\lambda)} = 1 - \frac{\sqrt{c^2 + 4\epsilon}}{\sqrt{c^2 + 4(\epsilon + \lambda)}}.$$

We identify $\mathcal{E}(\lambda)$ as the Evans function of the front. Note that $\mathcal{E}(0) = 0$, as expected for a system with translation invariance. Moreover, for $\lambda + \epsilon > 0$ there are no solutions of $\mathcal{E}(\lambda) = 0$ in the right hand complex plane. Since $\mathcal{E}'(0) > 0$ the zero-eigenvalue is simple, and so the travelling front solution is stable.

For a proper discussion of the Evans function see the lectures of Professor Sandstede, and take a look at the review article by Kapitula [2].

References

[1] J Keener and J Sneyd. *Mathematical Physiology*. Springer-Verlag, New York, 1998.

[2] T Kapitula. *Dissipative Solitons*, chapter Stability analysis of pulses via the Evans function: dissipative systems, pages 407–428. Springer-Verlag, 2005.