Systems Biology: Theoretical Biology

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Excitable Media

Contents

- Excitable media
    - Action potential propagation.
    - Waves in 1D and 2D.
    - Spiral waves and turbulence.
    - Waves and cardiac arrhythmias.
    - Waves and slime moulds.

Excitable media

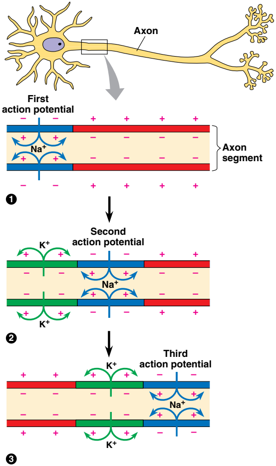
A neuron is an example of an excitable medium.

General excitable medium properties:

- An activation threshold.
- An all-or-none response.
- Refractoriness.
- Wave propagation.

How wave propagation works:

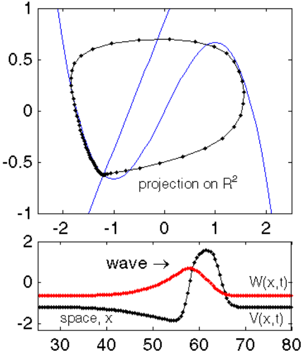
1. Activations spreads *passively* to a nearby spot.
2. The threshold at this spot is exceeded.
3. A new *active* response is generated.
4. Refractoriness prevents a backwards wave.



Modeling wave propagation in an excitable medium

We can use the Fitzhugh-Nagumo model with diffusion:

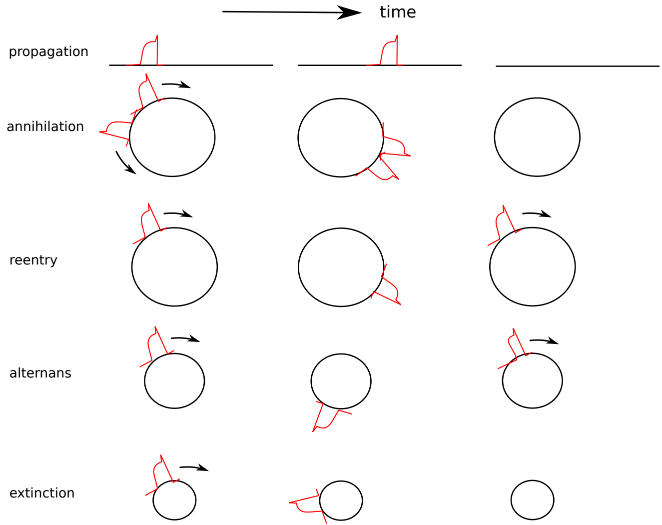
$$\frac{\partial V}{\partial t} = -V(V-a)(V-1) - W + D\frac{\partial^2 V}{\partial x^2}$$
$$\frac{\partial W}{\partial t} = c(V - bW)$$



- The wave-front *activates* points in front.
- The wave-tail is *refractory*.

http://www.scholarpedia.org/article/FitzHugh-Nagumo_model

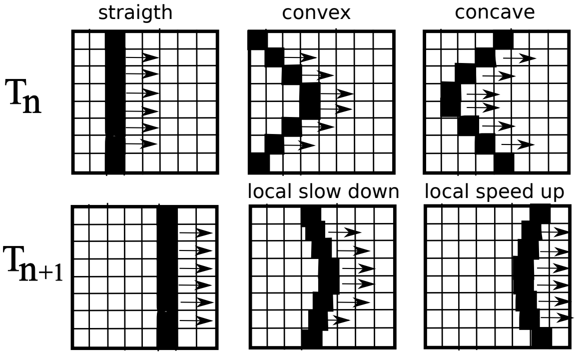
Wave propagation in 1D



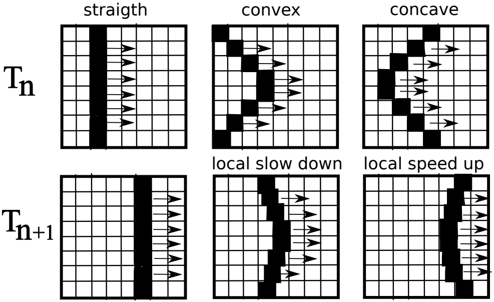
Wave propagation in 2D, curvature effects

$$\frac{\partial V}{\partial t} = -V(V-a)(V-1) - W + D\left(\frac{\partial^2 V}{\partial x^2} + \frac{\partial^2 V}{\partial y^2}\right)$$

$$\frac{\partial W}{\partial t} = c(V - bW)$$

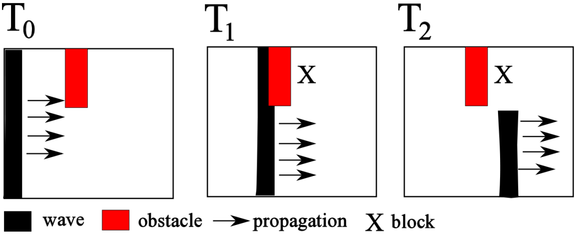


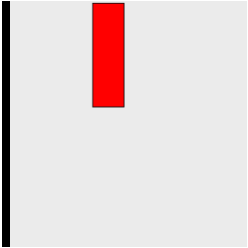
Curvature effects



Curvature affects the *local propagation speed* of waves.
The net effect is the *straigthening* of wavefronts.

Wave propagation in 2D: Wave break and free ends

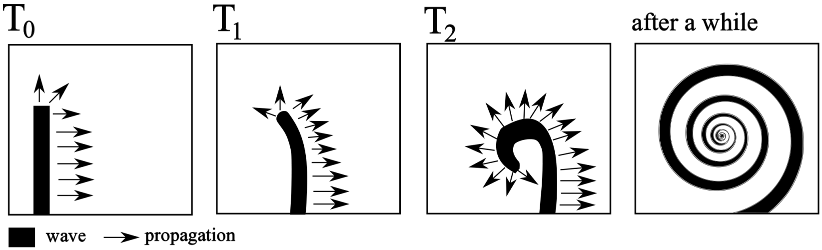




The presence of an **inexcitable obstacle** or a **refractory region** will cause a wave to break and produce a free wave end.

Wave propagation in 2D: Spiral Formation

So what happens if we have a free wave end?

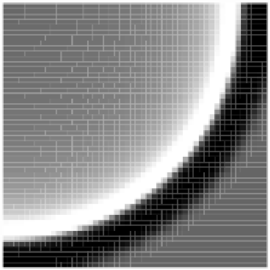


Curvature at the free wave-end locally slows propagation.
This causes the wave to **curl back**, which in turn
results in **spiral wave formation**.

Note the direction of curling and wave propagation!

Wave propagation in 2D: waves, spirals and turbulence

target waves



wave propagation

spiral waves

wave reentry

turbulence

wave alternans

Planar waves: single trigger produces a single wave, which **terminates**.
Spirals & turbulence: re-entry allows for re-excitation, **perpetual** pattern.

Other ways to model excitable media

A CA model can also be used to model an excitable medium.

Rules:

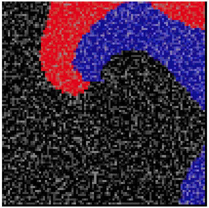
1. Excite if 3 or more excited neighbours.
2. Remain excited for 5 timesteps.
3. Become refractory for 3 timesteps.

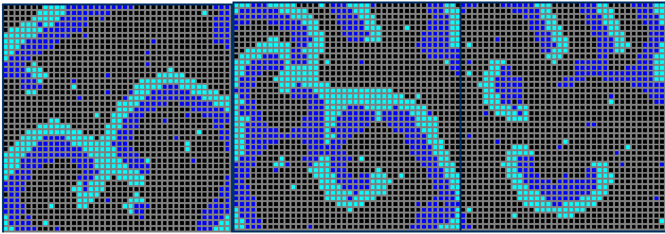
variable states

- 0 rest
- 1 excited
- 2 refractory

update rules

input ind. state	duration own state neighbor states	output new ind. state
0	3 or more 1's	1
0	less than 3 1's	0
1	5 steps	2
1	less than 5 steps	1
2	4 steps	0
2	less than 4 steps	2



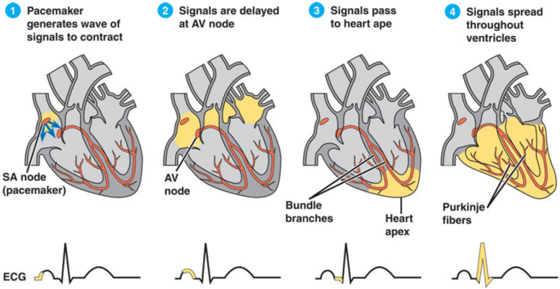


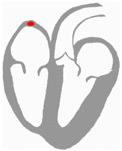
From: http://www.cnd.mcgill.ca/bios/bub/CAs.html

Cardiac tissue

The heart is an **electro-mechanical** pump:

- Cells generate and conduct action potentials.
- Cells contract in response to action potentials.





Fast wave propagation ensures timed, coordinated contraction

Cardiac arrhythmias

Arrhythmias

Abnormalities in *rate* and/or *coordination* of cardiac contraction, caused by abnormality of the **excitation wave**.

normal sinus rhythm

ventricular tachycardia

ventricular fibrillation

Tachycardia is an increased contraction rate, which leads to incomplete filling with blood and less efficient pumping.

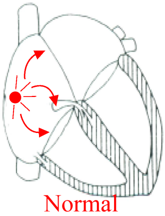
Fibrillation is an increased rate without coordination, and with hardly any pumping. It is lethal within minutes.

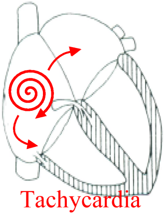
What is the cause of these abnormalities?

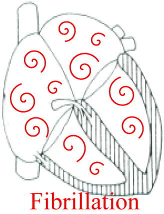
Cardiac arrhythmias

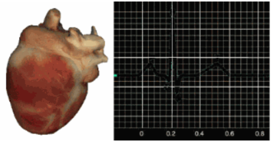
Hypothesis

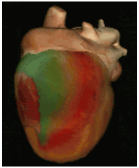
Ventricular tachycardia and fibrillation could be caused by spiral waves and turbulence (broken spirals).

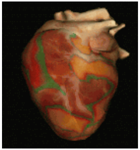












Experimental proof of hypotheses

From: http://www.vet.cornell.edu/news/FentonCherry/Media/main.html

Curing Fibrillation?

We can use our knowledge about excitable media to:

- invent new cures
- understand existing ones

We will examine this in the exercises.

Dictyostelium discoidum

The heart is not the only excitable medium.

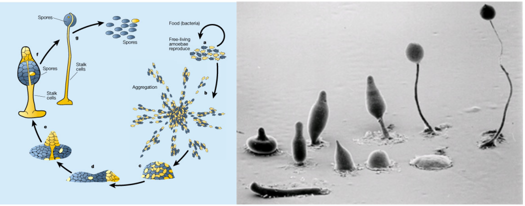
The slime mould *Dictyostelium discoidum* is a species of amoeba. Individual cells can communicate using **cyclic-AMP**.

Cellular signalling system:

- c-AMP is produced by cells in response to stress.
- c-AMP acts as a chemo-attractant for other cells.
- c-AMP makes cells produce more c-AMP.
- c-AMP production becomes refractory.

There is positive feedback and refractoriness, which suggests that a group of *Dictyostelium* cells can also act as an excitable medium!

Modelling Dictyostelium discoidum

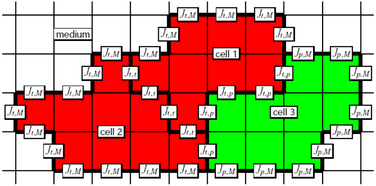


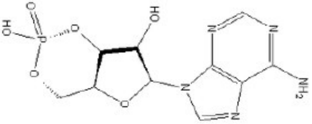
How does cAMP cause otherwise free-living cells to form a “super-organism”?

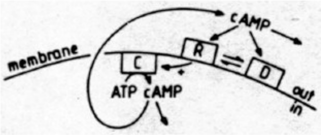
To understand this, a 3D spatial model of *Dictyostelium discoidum* was created by Stan Mareé, Paulien Hogeweg, and Nick Savill.

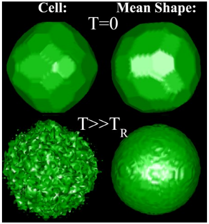
Modelling an Organism

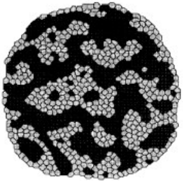
Stan Mareé, Paulien Hogeweg, and Nick Savill











$$\frac{\partial c}{\partial t} = D_c \Delta c - f(c, a_\tau, \cdots) - r \quad ,$$

$$\frac{\partial r}{\partial t} = \varepsilon(c)(kc - r) \quad .$$

Dictyostelium discoidum

Modelling an Organism

Stan Mareé, Paulien Hogeweg, and Nick Savill