Mathematical modeling in biology.

D. Salort, LBCQ, Sorbonne University, Paris

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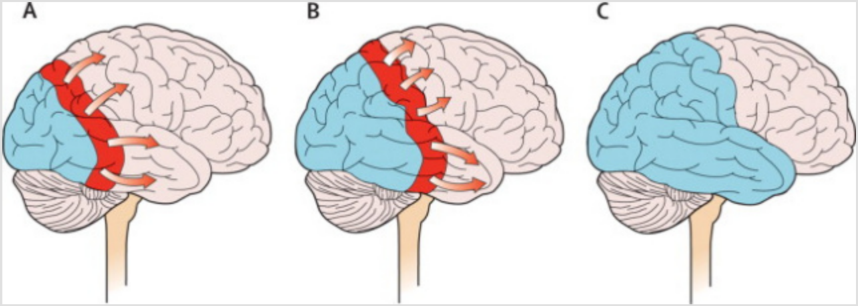
Spatial mathematical models in neurosciences

Spatial mathematical models : Those models appear to be very relevant to describe some specific dynamics as for example

- observation of some wave propagation on the brain (as for migraine for example)



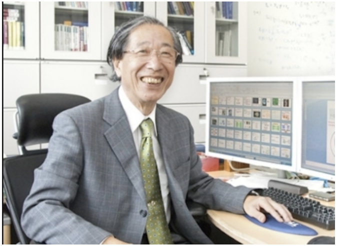
Cortical spreading depression (CSD) is a slowly propagated wave of depolarization followed by suppression of brain activity.

http://www.edmontonneurotherapy.com/

- Modeling of synaptic plasticity and phenomena of learning processes ?

Shun-ichi Amari model

Shun-ichi Amari model (1977) :



$$\partial_t u(t,x) = -u(t,x) + \int_\Omega K(x,y)F(u(t,y))dy + I(t,x).$$

- $u(t,x)$ models the average membrane potential or activity of the network
- $K(x,y)$ is a kernel which models the weight connectivity from the neuron at position y to the neuron at position x.
- F is a sigmoid fonction. On of the simplest example is the case where F is a Heaviside function

There exists a huge literature around this pionnier work, with many extensions.

Shun-ichi Amari model (1977).

Questions :

- Does this model exhibit stationary states with different intensity of activity with respect to the aera of the brain ?
- Can we exhibit traveling wave with this model ?

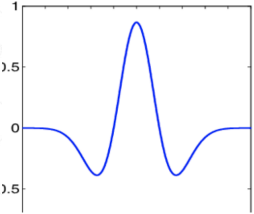
Study of the stationary states of Amari model.

Stationary equation in the homogenous case:

$$u(x) = \int_{\Omega} K(x-y)F(u(y))dy + h.$$

Choice of the kernel :

- We often use a ”mexican hat”



- But we can perform also studies for example with only excitatory weights

Study of the stationary states of Amari model.

As, a neuron at position x receive the activity of a neuron at position y, only if $u(t, y) > 0$, we define "the excited region" of the brain as follows

Definition

The excited region of a stationary state $E(u)$ is given by

$$E(u) = \{x \in \mathbb{R}, \quad \text{such that } u(x) > 0.\}.$$

We can then expect to have four type of stationary states

- 1) Stationary states where there do not exists excited region
- 2) Stationary states with only excited regions
- 3) Stationary states with a localized excited region
- 4) Stationary states of wave type of speed 0.

Stationary states for cases 1) and 2).

Case with no excited region. We must have

$$u(x) = h, \quad \text{that is} \quad h \leq 0.$$

Case with only excited region. We must have

$$u(x) = \int_{-\infty}^{+\infty} w(x-y)dy + h > 0, \quad \text{that is} \quad h > -\int_{-\infty}^{+\infty} w(y)dy = -2W_\infty.$$

Stationary states with local excited regions

Stationary states with local excited regions.

- We search regular solutions such that $u(x) > 0$ on (a, b) and $u(x) \leq 0$, else.
- By invariance by translation, we can assume that (a, b) is of the form $(0, a)$ with $a > 0$.

We have existence of a stationary state with local excited region iff

$$h < 0 \quad \text{and} \quad W(a) = -h.$$

$$\text{where } W(x) := \int_0^x w(y)dy.$$

Stationary states of wave type of speed 0.

Stationary states with local excited regions.

- We search regular solutions such that $u(x) > 0$ on $(0, +\infty)$ and $u(x) < 0$ on $(-\infty, 0)$.

We have existence of a stationary state with of wave type of speed 0 iff

$$h < 0 \quad \text{and} \quad W_\infty = -h.$$

Evolution dynamic

The evolution of neural fields models is widely studied. One of the first main questions that we can set are

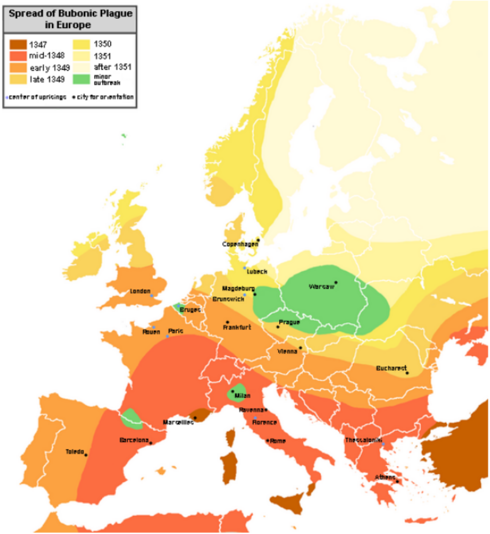
- Is there traveling wave ?
- What is the behavior of the solution with respect to the initial data ?
  - Does we converge to a fully excited region ? (invasion phenomena)
  - Does we converge to the extinction of activity ?
  - Does we converge to more complex patterns as periodic solutions or locally excited solutions ?

Evolution dynamic

Study of traveling waves

- There is a very large class of models which exhibit traveling waves.
- One of the reference model which exhibit this dynamic is the Fisher KPP Equation (explicit solutions)
- The case of neural fields may be complex
- There are some specific cases where we can make explicit computations (see for example Faye and Kilpatrick).

The Fisher KPP Equation



The Fisher KPP Equation

The Fischer KPP Equation ($d = 1$ with analatycal computations)

$$\partial_t u(t,x) - \partial_{xx} u(t,x) = f(u(t,x))$$

with, for $0 < \theta < 1$

$$f(y) = 0 \quad \text{if} \quad y < \theta \quad \text{and} \quad f(u) = (1-u) \quad \text{if} \quad \theta < y \leq 1.$$

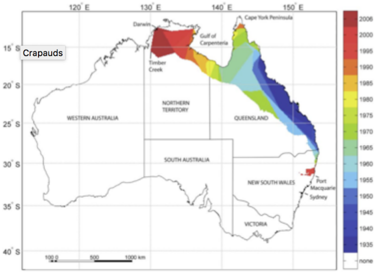
Traveling wave

There exists a unique c^* and a unique decreasing function v with $v(0) = \theta$, $v(-\infty) = 1$, $v(+\infty) = 0$ and such that $v(x - c^* t)$ is solution of the Fischer KPP equation.

- In the above example, the speed of propagation is constant.
- There are some example in biology where we search non constant speed of propagation.

Traveling wave (with non constant speed of propagation

Example with non constant speed of propagation : cane toads in Australia (O. Benichou, E. Bouin, V. Calvez, N. Meunier, S. Mirrahimi, B. Perthame, G. Raoul, and R. Voituriez)



Traveling wave with non constant speed of propagation

Example with non constant speed of propagation : cane toads in Australia (O. Benichou, V. Calvez, N. Meunier and R. Voituriez)

- A few cane toads where introduced in Austria in the 1930th
- The speed of propagation observed is bigger than the constant speed of propagation predicted by classical Fisher KPP equations.
- Taking into account that, with time cane toads gets bigger and smaller, a new model has been proposed.
- This model include a new variable of morphology : the coefficient of diffusion of the cane toads depends on this parameter.
- This allows to recover the observations

Traveling wave for neural field model

To construct explicit solutions, we consider the following neural fields model (Faye and Kilpatrick)

$$u'(t,x) = -u(t,x) + \int_{y=-\infty}^{+\infty} K(x-y)H(u(y) - \frac{1}{4})dy, \quad K(x) = \frac{1}{2}e^{-|x|}.$$

- The active region is given by the set of positions x such that $u(t,x) > \frac{1}{4}$
- The inactive region is given by the set of positions x such that $u(t,x) \leq \frac{1}{4}$.
- We can again study the steady states and we see the emergence of different patterns (as constant solutions, bumps, periodic solution).

Traveling wave (Faye and Kilpatrick)

There exists a unique $c > 0$ and a decreasing function v with $v(0) = \frac{1}{4}$ $v(-\infty) = 1$, $v(+\infty) = 0$ with $v(x - ct)$ solution of the neural field equation.

Propagation or asymptotic extinction of the activity

To understand the behavior of the solution with respect to the initial data, we again consider the following neural fields model (Faye and Kilpatrick)

Behavior with respect to the initial data (Faye and Kilpatrick)

Consider a smooth initial data u_0, even ($u_0(x) = u_0(-x)$) with $u_0' > 0$ if $x < 0$ and $u_0' < 0$ if $x > 0$. Assume that $\ell > 0$ such that $u_0(\ell) = \frac{1}{4}$. Then the following holds

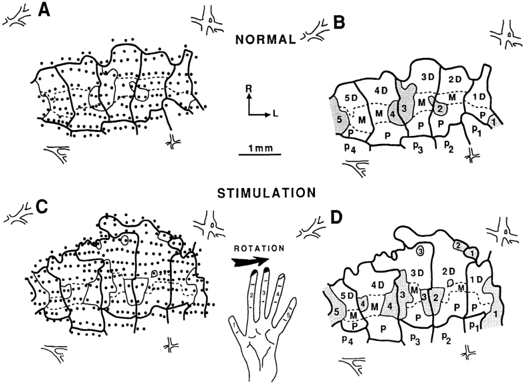
- If $\ell > W^{-1}(\frac{1}{4})/2$, then $u \to 1$ locally uniformly on $\mathbb{R}$
- If $\ell < W^{-1}(\frac{1}{4})/2$, then $u \to 0$ locally uniformly on $\mathbb{R}$
- If $\ell = W^{-1}(\frac{1}{4})/2$, then u converges to a bump function.

How the brain learn ?

How the brain learn ? :

- Since the ends of the XIX century, the notion of plasticity synaptic emerges
- The brain is always remodeling with respect to the stimuli that we receive, our experience
- This remodeling is made, in particular via the emergence of new connections (or depletions of connections) and via the change of strength of interconnections between the neurons

How the brain learn



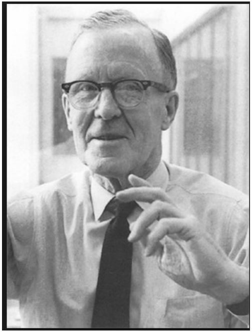
from W. M. Jenkins, M. M. Merzenich, M. T. Ochs, T. Allard and E. Guic-Robles, ÒFunctional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulationÓ

Questions

What are the rules which are behind those remodeling ?

How the brain learn ?

The Hebbian rule :



"Neurons that fire together, wire together" (Hebb, 1904-1985)

How the brain learn

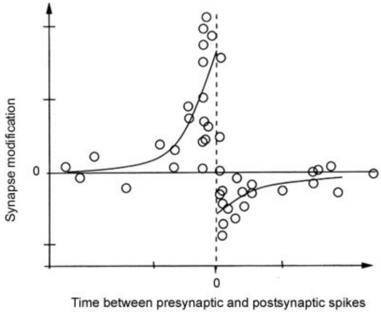
Typical simple modeling including the Hebbian rule :

$$u'(t,i) = -u(t,i) + \sum_{j=1}^{N} K_{ij}(t) S(u(t,j) + I(t,i)$$

$$\frac{1}{\varepsilon} K'_{ij}(t) = -\alpha K_{ij}(t) + F(K_{ij}(t)) u(t,i) u(t,j).$$

How the brain learn ?

The Spike Time Dependent plasticity rule :



- The connections are reenforced if the presynaptic neuron discharge before the post-synaptic neuron.
- The opposite happens if the postsynaptic neuron discharge before the presynaptic neuron
- no or very low synaptic modification if the delay between spikes are to long.

Typical simple modeling including the Hebbian rule :

$$u'(t,i) = -u(t,i) + \sum_{j=1}^{N} K_{ij}(t) S(u(t,j) + I(t,i)$$

$$\frac{1}{\varepsilon} K'_{ij}(t) = C_1 u_i(t) u_j \star g(t) - C_2 u_j(t) u_i \star g(t)$$

where typically,

$$g(t) = Ce^{-\alpha t} H(t).$$