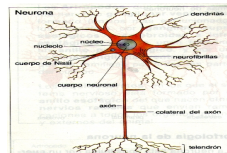
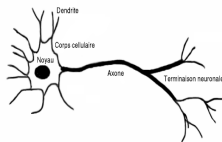
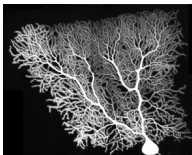


# PDEs for neural networks analysis, simulations and behaviour

Benoît Perthame  
UIMP, august 2018



- I. The single neuron,
  - I. 1. Excitable systems
  - I. 2. slow-fast dynamics,
  - I. 3. Integrate&Fire model, role of noise
  - I. 4. Distribution of neurons
  
- II. Networks, examples
  
- III. Networks, Leaky noisy I&F
  
- IV. Networks, time elapsed models

Electrically active cells are described by an **action potential**  $V(t)$

Models are well established

■ Hodgkin-Huxley

■ FitzHugh-Nagumo

■ Morris-Lecar

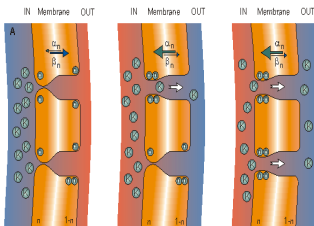
■ Mitchell-Schaeffer

$$\begin{aligned}C \frac{dv}{dt} &= I - g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) \\ \frac{dm}{dt} &= a_m(V)(1 - m) - b_m(V)m \\ \frac{dh}{dt} &= a_h(V)(1 - h) - b_h(V)h \\ \frac{dn}{dt} &= a_n(V)(1 - n) - b_n(V)n \\ a_m(V) &= .1(V + 40)/(1 - \exp(-(V + 40)/10)) \\ b_m(V) &= 4 \exp(-(V + 65)/18) \\ a_h(V) &= .07 \exp(-(V + 65)/20) \\ b_h(V) &= 1/(1 + \exp(-(V + 35)/10)) \\ a_n(V) &= .01(V + 55)/(1 - \exp(-(V + 55)/10)) \\ b_n(V) &= .125 \exp(-(V + 65)/80)\end{aligned}$$

The class of Morris-Lecar is typically

$$\left\{ \begin{array}{l} \frac{dV(t)}{dt} = \sum_{k=1}^I g_k(t)(V_k - V(t)) + I(t), \\ \frac{dg_k(t)}{dt} = \frac{G_k(V(t)) - g_k(t)}{\tau_k}, \quad g_k(0) \geq 0, \quad k = 1, 2, \dots, k_M, \end{array} \right.$$

■ The index  $k$  refers to ionic channels/conductances along the nerve (Ca, K, Na, Cl...)



From J. Malmivuo and R. Plonsey, Principles and Appl. of bioelectric and biomagnetic fields, OUP 1995

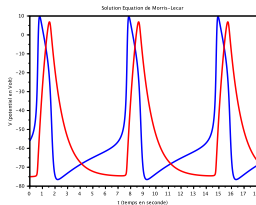
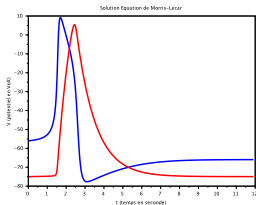
The class of Morris-Lecar is typically

$$\begin{cases} \frac{dV(t)}{dt} = \sum_{k=1}^I g_k(t)(V_k - V(t)) + I(t), \\ \frac{dg_k(t)}{dt} = \frac{G_k(V(t)) - g_k(t)}{\tau_k}, \quad g_k(0) \geq 0, \quad k = 1, 2, \dots, k_M, \end{cases}$$

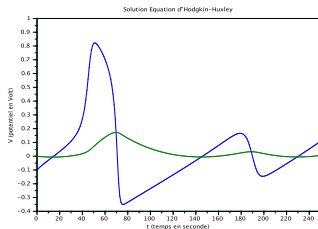
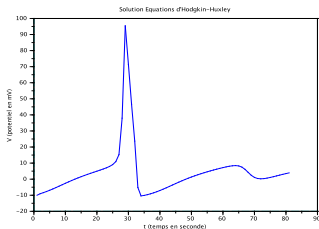
- The index  $k$  refers to ionic channels/conductances along the nerve (Ca, K, Na, Cl...)
- The  $V_k$  are called the “reversal potentials” (Nernst-Planck theory)
- The leak  $V_L$  is used to aggregate some of them
- $\tau_k$  can be  $\ll 1$
- Sharp nonlinearities  $G_k$  (sigmoids)

The class of Morris-Lecar is typically

$$\left\{ \begin{array}{l} \frac{dV(t)}{dt} = \sum_{k=1}^I g_k(t)(V_k - V(t)) + I(t), \\ \frac{dg_k(t)}{dt} = \frac{G_k(V(t)) - g_k(t)}{\tau_k}, \quad g_k(0) \geq 0, \quad k = 1, 2, \dots, k_M, \end{array} \right.$$

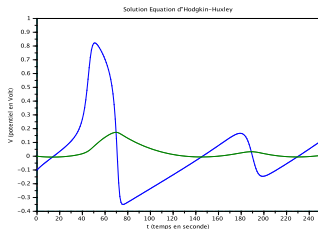
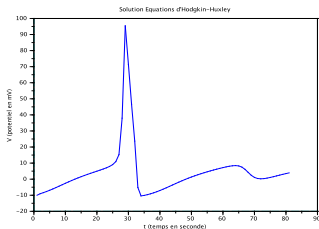


↑ spike    ↑ Hyperpolarisation



Solutions of Hodgkin-Huxley's model and of FitzHugh-Nagumo's model

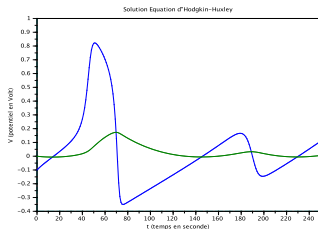
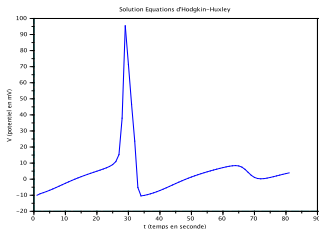
- these models are accurate
- represent the property of **excitability** and **hyperpolarization**



Solutions of Hodgkin-Huxley's model and of FitzHugh-Nagumo's model

- these models are accurate
- represent the property of **excitability**
  - A small perturbation generates a large trajectory
  - Return to equilibrium
  - The trajectory depends very little on the perturbation





Solutions of Hodgkin-Huxley's model and of FitzHugh-Nagumo's model

- These models are accurate BUT
- difficult to understand why they are **excitable**
- expensive for large assemblies of neurones
- do not explain properties of large assemblies
- This motivates using simpler models

FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), & v(t=0) = v^0, \\ \dot{w}(t) = v(t) - v^* - \alpha w(t) & w(t=0) = w^0. \end{cases}$$

It can be derived from the Morris-Lecar model

$$\begin{cases} \frac{dV(t)}{dt} = g_L(V_L - V(t)) + G_{Na}(V(t))(V_{Na} - V(t)) + g_K(t)(V_K - V(t)) \\ \frac{dg_K(t)}{dt} = \frac{G_K(V(t)) - g_K(t)}{\tau_K} \end{cases}$$

$$V_K < V_L < V_{Na}$$

FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), & v(t=0) = v^0, \\ \dot{w}(t) = v(t) - v^* - \alpha w(t) & w(t=0) = w^0. \end{cases}$$

It can be derived from the Morris-Lecar model

$$\begin{cases} \frac{dV(t)}{dt} = g_L(V_L - V(t)) + G_{Na}(V(t))(V_{Na} - V(t)) + g_K(t)(V_K - V(t)) \\ \frac{dg_K(t)}{dt} = \frac{G_K(V(t)) - g_K(t)}{\tau_K} \end{cases}$$

$$v(t) = \ln(V(t) - V_K)$$

FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), & v(t=0) = v^0, \\ \dot{w}(t) = v(t) - v^* - \alpha w(t) & w(t=0) = w^0. \end{cases}$$

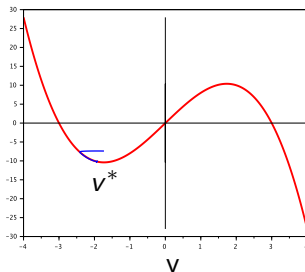
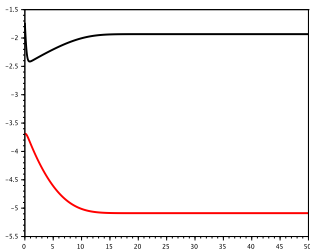
It can be derived from the Morris-Lecar model

$$\begin{cases} \frac{dV(t)}{dt} = g_L(V_L - V(t)) + G_{Na}(V(t))(V_{Na} - V(t)) + g_K(t)(V_K - V(t)) \\ \frac{dg_K(t)}{dt} = \frac{G_K(V(t)) - g_K(t)}{\tau_K} \end{cases}$$

$$\frac{dv(t)}{dt} = \underbrace{\frac{g_L(V_L - V(t)) + G_{Na}(V(t))(V_{Na} - V(t))}{V(t) - V_K}}_{:=F(v(t))} - g_K(t)$$

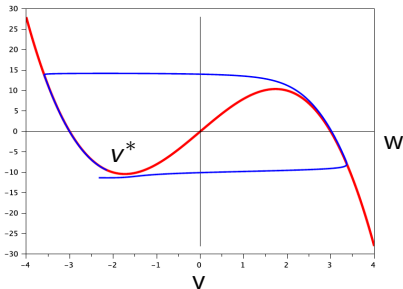
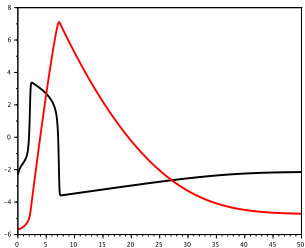
## FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), \\ \dot{w}(t) = v(t) - v^* \end{cases} \quad \begin{cases} v(t=0) = v^0, \\ w(t=0) = w^0. \end{cases}$$



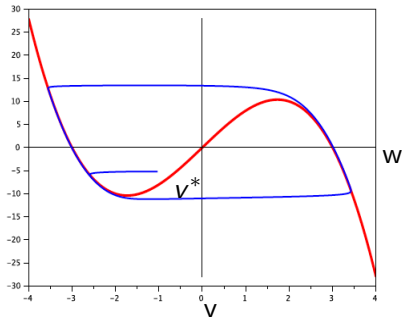
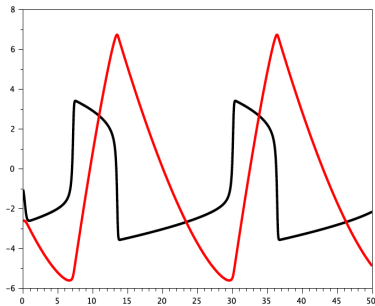
## FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), \\ \dot{w}(t) = v(t) - v^* \end{cases} \quad \begin{cases} v(t=0) = v^0, \\ w(t=0) = w^0. \end{cases}$$

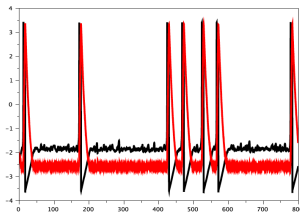
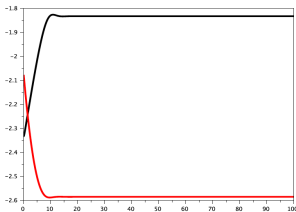


## FitzHugh-Nagumo

$$\begin{cases} \varepsilon \dot{v}(t) = f(v(t)) - w(t), \\ \dot{w}(t) = v(t) - v^* \end{cases} \quad \begin{cases} v(t=0) = v^0, \\ w(t=0) = w^0. \end{cases}$$



# Single neuron : Role of noise



$$\begin{cases} \frac{dv(t)}{dt} = f(v(t)) - w(t), \\ \frac{dw(t)}{dt} = v(t) - v^* + \sigma \frac{dB(t)}{dt}. \end{cases}$$



Slow-fast dynamics

$$\begin{cases} \varepsilon \dot{v}_\varepsilon(t) = f(v_\varepsilon(t)) - w_\varepsilon(t), & v_\varepsilon(t=0) = v^0, \\ \dot{w}_\varepsilon(t) = v_\varepsilon(t) - v^* & w_\varepsilon(t=0) = w^0. \end{cases}$$

**Theorem** As  $\varepsilon \rightarrow 0$ , we have

- $v_\varepsilon(t) \rightarrow v(t)$  a.e.,
- $w_\varepsilon(t) \rightarrow w(t)$  uniformly (locally)

$$\frac{dw(t)}{dt} = Q_\pm(w(t)) - v^*, \quad v(t) = Q_\pm(w(t)) \Leftrightarrow f(v) = w$$

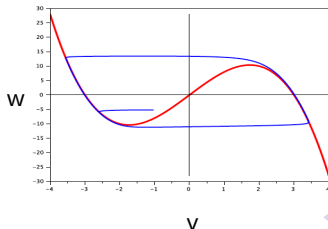
Slow-fast dynamics

$$\begin{cases} \varepsilon \dot{v}_\varepsilon(t) = f(v_\varepsilon(t)) - w_\varepsilon(t), & v_\varepsilon(t=0) = v^0, \\ \dot{w}_\varepsilon(t) = v_\varepsilon(t) - v^* & w_\varepsilon(t=0) = w^0. \end{cases}$$

**Theorem** As  $\varepsilon \rightarrow 0$ , we have

- $v_\varepsilon(t) \rightarrow v(t)$  a.e.,
- $w_\varepsilon(t) \rightarrow w(t)$  uniformly (locally)

$$\frac{dw(t)}{dt} = Q_\pm(w(t)) - v^*, \quad v(t) = Q_\pm(w(t)) \Leftrightarrow f(v) = w$$



$$\begin{cases} \varepsilon \dot{v}_\varepsilon(t) = f(v_\varepsilon(t)) - w_\varepsilon(t), & v_\varepsilon(t=0) = v^0, \\ \dot{w}_\varepsilon(t) = v_\varepsilon(t) - v^* & w_\varepsilon(t=0) = w^0. \end{cases}$$

Proof (1)

$$\begin{aligned} |f(v_\varepsilon(t)) - w_\varepsilon(t)|^2 &= \varepsilon \dot{v}_\varepsilon(t) [f(v_\varepsilon(t)) - w_\varepsilon(t)] \\ &= \varepsilon \frac{d}{dt} [F(v_\varepsilon(t)) - v_\varepsilon(t)w_\varepsilon(t)] + \varepsilon v_\varepsilon \frac{dw_\varepsilon}{dt} \end{aligned}$$

with  $F' = f$

$$\begin{cases} \varepsilon \dot{v}_\varepsilon(t) = f(v_\varepsilon(t)) - w_\varepsilon(t), & v_\varepsilon(t=0) = v^0, \\ \dot{w}_\varepsilon(t) = v_\varepsilon(t) - v^* & w_\varepsilon(t=0) = w^0. \end{cases}$$

Proof (1)

$$\begin{aligned} |f(v_\varepsilon(t)) - w_\varepsilon(t)|^2 &= \varepsilon \dot{v}_\varepsilon(t) [f(v_\varepsilon(t)) - w_\varepsilon(t)] \\ &= \varepsilon \frac{d}{dt} [F(v_\varepsilon(t)) - v_\varepsilon(t)w_\varepsilon(t)] + \varepsilon v_\varepsilon \frac{dw_\varepsilon}{dt} \end{aligned}$$

$$\frac{1}{\varepsilon} \int_0^T |f(v_\varepsilon(t)) - w_\varepsilon(t)|^2 dt = F(v_\varepsilon) - v_\varepsilon w_\varepsilon \Big|_0^T + \int_0^T v_\varepsilon (v_\varepsilon - v^*) dt$$

and this is bounded (assuming solutions are bounded).

$$\begin{cases} \varepsilon \dot{v}_\varepsilon(t) = f(v_\varepsilon(t)) - w_\varepsilon(t), & v_\varepsilon(t=0) = v^0, \\ \dot{w}_\varepsilon(t) = v_\varepsilon(t) - v^* & w_\varepsilon(t=0) = w^0. \end{cases}$$

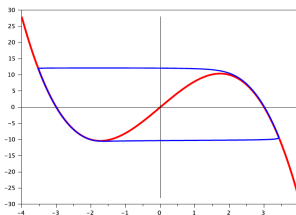
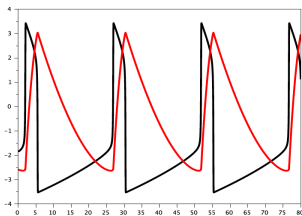
Proof (2)

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_0^{v_\varepsilon(t)} |f(z) - w_\varepsilon(t)|^2 dz &= \dot{v}_\varepsilon(t) |f(v_\varepsilon(t)) - w_\varepsilon(t)|^2 + Bdd \\ &= \underbrace{\varepsilon \dot{v}_\varepsilon(t)}_{\text{bounded}} \underbrace{\frac{|f(v_\varepsilon(t)) - w_\varepsilon(t)|^2}{\varepsilon}}_{\text{step 1}} + Bdd \end{aligned}$$

Which means that, after extraction

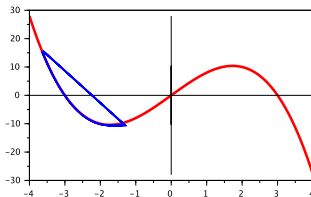
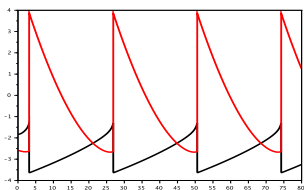
$$\int_0^{v_\varepsilon(t)} |f(z) - w_\varepsilon(t)|^2 dz$$

converges a.e.

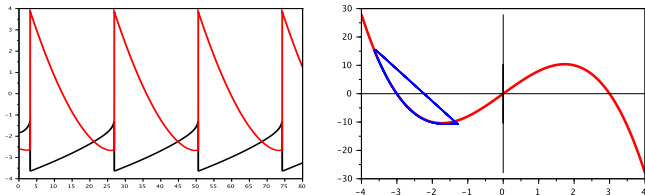


(FitzHugh-Nagumo, fast discharge) solution of a variant of the FitzHugh-Nagumo system

$$\begin{cases} \frac{dv(t)}{dt} = h(v(t)) + I(t), & \tau_i \leq t < \tau_{i+1}, \\ v(\tau_i^+) = V_R, & \lim_{t \rightarrow \tau_{i+1}} v(t) = v(\tau_{i+1}^-) = V_F. \end{cases}$$



Solution of the integrate-and-fire system



Solution of the integrate-and-fire system

$$\begin{cases} \frac{dV(t)}{dt} = h(V(t)) + I(t), & \tau_i \leq t < \tau_{i+1}, \\ V(\tau_i^+) = V_R, & \lim_{t \rightarrow \tau_{i+1}^-} V(t) = V(\tau_{i+1}^-) = V_F. \end{cases}$$

With  $h \leq 0$

When  $I(t) = 0$ .  $V(t) \rightarrow V_R$  (relaxation)

When  $I(t) \gg 1$  periodic solutions appear

Vlasov type equation

$$\begin{aligned} \frac{\partial}{\partial t} p(v, g, t) + \frac{\partial}{\partial v} [(g_L(V_L - v) + g(V_E - v))p(v, g, t)] \\ + \frac{\partial}{\partial g} \left[ \frac{G(v, t) - g}{\sigma_E} p(v, g, t) \right] - \frac{a}{\sigma_E} \frac{\partial^2}{\partial g^2} p(v, g, t) = 0, \\ v \in (V_L, V_E), g \geq 0, \end{aligned}$$

Boundary conditions :

- Zero flux at  $V_L < V_E$
- No flux condition at  $g = 0$

Mathematical interest : Sub-elliptic fluxes



Similar to the Kinetic Fokker-Plack model of interacting particles

$$\frac{\partial}{\partial t} p(x, v, t) + v \cdot \nabla_x p - \operatorname{div}_v (vp) - \Delta_v p = 0$$

Regularizing effects, time decay  $M = \exp(-|v|^2/2)$ ,  $u = p/M$

$$\frac{1}{2} \frac{d}{dt} \int M |\partial_v u + \partial_x u|^2 \leq - \int M |\partial_v u + \partial_x u|^2.$$

Bouchut, Desvillettes, Villani, Hérau

Dolbeault, Mouhot, Schmeiser, Herda, Arnold

Càceres, Carrillo, Goudon

Liu Liu and S. Jin

$$\begin{cases} \frac{dv(t)}{dt} = h(v(t)) + I(t), & \tau_i \leq t < \tau_{i+1}, \\ v(\tau_i^+) = V_R, & \lim_{t \rightarrow \tau_{i+1}^-} v(t) = v(\tau_{i+1}^-) = V_F. \end{cases}$$

$$\begin{aligned} \frac{\partial}{\partial t} p(v, t) + \frac{\partial}{\partial v} [(h(v) + I)p(v, t)] &= 0, \quad 0 < V_R < V_F, \\ (h(V_R) + I)p(V_R, t) &= N(t) := (h(V_F) + I)p(V_F, t) \end{aligned}$$

Assuming  $(h(V_R) + I) > 0$ ,

$$(h(V_F) + I) > 0$$

$$\begin{aligned} \frac{\partial}{\partial t} p(v, g, t) + \frac{\partial}{\partial v} [(-g_L(V_L - v) + g(V_E - v))p(v, g, t)] \\ + \frac{\partial}{\partial g} \left[ \frac{G(t) - g}{\sigma_E} p(v, g, t) \right] - \frac{a}{\sigma_E} \frac{\partial^2}{\partial g^2} p(v, g, t) = 0, \\ v \in (V_L, V_F), g \geq 0, \end{aligned}$$

Boundary conditions :

- outgoing Flux  $N(g, t)$  at  $V_F < V_E$  enters at  $v = V_L$
- No flux condition at  $g = 0$
- $G(t) = \mathcal{G} \left( \int N(g, t) dg \right)$

D. Cai, Shelley, McLaughlin, Rangan, L. Tao, Kovacic, Ly, Trnachina...

$$\begin{aligned} \frac{\partial}{\partial t} p(v, g, t) + \frac{\partial}{\partial v} [(-g_L(V_L - v) + g(V_E - v))p(v, g, t)] \\ + \frac{\partial}{\partial g} \left[ \frac{G(t) - g}{\sigma_E} p(v, g, t) \right] - \frac{a}{\sigma_E} \frac{\partial^2}{\partial g^2} p(v, g, t) = 0, \\ v \in (V_L, V_F), g \geq 0, \end{aligned}$$

Boundary conditions :

- outgoing Flux  $N(g, t)$  at  $V_F < V_E$  enters at  $v = V_L$
- No flux condition at  $g = 0$
- $G(t) = \mathcal{G} \left( \int N(g, t) dg \right)$

### Theorem (D. Salort, BP)

- Stationary solutions belong to  $L^{\frac{8}{7}-}$
- Evolution solutions are globally bounded in  $L^p$  (no blow-up)

**Open questions** : Long time asymptotic, regularity

- Single neurone models are numerous and complex
- They share the property to describe excitability
- The I&F model is derived has a double Slow-Fast limit
- PDEs come as Eulerian versions