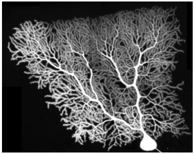
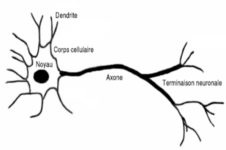
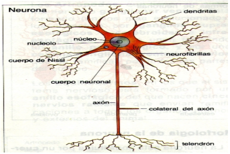
Integrate and Fire models for neural networks

and spontaneous activity

Benoît Perthame







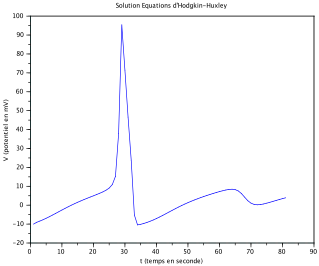
Introduction

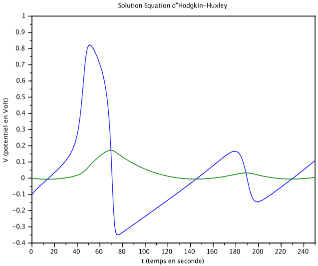
The electrically active cells are described by an **action potential**

- Hodgkin-Huxley
- FitzHugh-Nagumo
- Morris-Lekar
- Mitchell-Schaeffer

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

Introduction





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

- These models are accurate
- but very expensive/difficult to use for large assemblies of neurones.

Introduction

The Wilson-Cowan model (1972) describes the firing rates $N(x,t)$ of neuron assemblies located at position x through an integral equation

$$\frac{d}{dt}N(x,t) = -N(x,t) + \int w(x,y)\sigma\big(N(y,t)\big)\,dy + s(x,t)$$

- $\sigma(\cdot) =$ sigmoid
- $w(x,y) =$ connectivity matrix
- $s =$ source

Can be seen as a generic model of network.
Not physiologically based

Feature : multiple steady states and bifurcation theory
(Bressloff-Golubitsky, Chossat-Faugeras-Faye)

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Feature : multiple steady states and bifurcation theory (Bressloff-Golubitsky, Chossat-Faugeras-Faye)

Aim : large scale brain activity, visual hallucinations (Klüver, Oster, Siegel...)

OUTLINE OF THE LECTURE

Generic goal : understand physiologically based models of neural networks.

I. Principle of Noisy Integrate and Fire model

II. The nonlinear Noisy Integrate and Fire model

III. The voltage-conductance kinetic system for integrate&fire

IV. The elapsed time approach

Leaky Integrate and Fire

The Leaky Integrate & Fire model is simpler

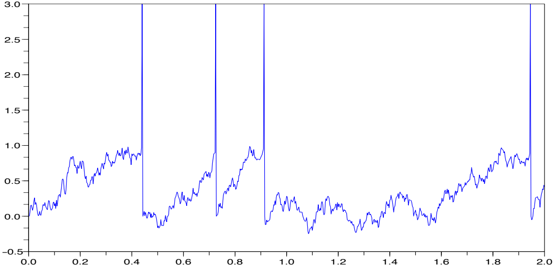
$$dV(t) = \big(- V(t) + I(t) \big) dt + \sigma dW(t), \qquad V(t) < V_{\mathrm{Firing}}$$

$$V(t_-) = V_{\mathrm{Firing}} \quad \Longrightarrow \quad V(t_+) = V_{\mathrm{reset}}$$

The idea was introduced by L. Lapicque (1907)

- $I(t)$ input current
- Noise or not
- Stochastic firing
- Much simpler that Hodgkin-Huxley/FitzHugh-Nagumo models

Leaky Integrate and Fire



Solution to the LIF model

- N. Brunel and V. Hakim, R. Brette, W. Gerstner and W. Kistler, Omurtag, Knight and Sirovich, Cai and Tao...
- Fit to measurements
- Explains quantitatively observations on the brain activity

Leaky Integrate and Fire

FIGURE 4 | Fitting spiking models to electrophysiological recordings. (A) The response of a cortical pyramidal cell to a fluctuating current (from the INCF competition) is fitted to various models: MAT (Kobayashi et al., 2009), adaptive integrate-and-fire, and Izhikevich (2003). Performance on the training data is indicated on the right as the gamma factor (close to the proportion of predicted spikes), relative to the intrinsic gamma factor of the neuron (i.e., proportion of common spikes between two trials). Note that the voltage units for the models are irrelevant (only spike trains are fitted). **(B)** The response of an anteroventral cochlear nucleus neuron (brain slice made from a P12 mouse, see Methods in Magnusson et al., 2008) to the same fluctuating current is fitted to an adaptive exponential integrate-and-fire [Brette and Gerstner, 2005; note that the responses do not correspond to the same portion of the current as in **(A)**]. The cell was electrophysiologically characterized as a stellate cell (Fujino and Oertel, 2001). The performance was $\Gamma = 0.39$ in this case (trial-to-trial variability was not available for this recording).

From C. Rossant et al, Frontiers in Neuroscience (2011)

Leaky Integrate and Fire

Open question :
Derive rigorously the Integrate and Fire model from the FHN system.

Leaky Integrate and Fire

The probability $n(v,t)$ to find a neuron at the potential v solves the Fokker-Planck Eq. for $v \le V_F$

$$\begin{cases} \frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v} \overbrace{\left[\big(-v + I(t) \big) n(v,t) \right]}^{\text{leak+external currents}} - a \overbrace{\frac{\partial^2 n(v,t)}{\partial v^2}}^{\text{Noise}} = \overbrace{N(t)\, \delta(v = V_R)}^{\text{neurons reset}}, \\ n(V_F, t) = 0, \qquad n(-\infty, t) = 0, \\ N(t) := -a \frac{\partial n(V_F,t)}{\partial v} \ge 0, \quad \text{(the total flux of neurons firing at } V_F\text{)}. \end{cases}$$

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$N(t)$ is also a Lagrange multiplier for the constraint

$$\int_{-\infty}^{V_F} n(v,t)dv = 1.$$

Leaky Integrate and Fire

$$
\begin{cases}
\frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\big(-v + I(t)\big) n(v,t)\right] - a\frac{\partial^2 n(v,t)}{\partial v^2} = N(t)\,\delta(v = V_R), \quad v \\
\\
n(V_F, t) = 0, \qquad n(-\infty, t) = 0 \\
\\
N(t) := -a\frac{\partial n(V_F,t)}{\partial v} \geq 0, \quad \text{(the total flux of firing neurons at } V_F\text{)}.
\end{cases}
$$

Properties (Cáceres, Carrillo, BP) For $I(t) \equiv 0$ the solutions satisfy

- $n \geq 0, \qquad \int_{-\infty}^{V_F} n(v,t)dv = 1,$
- $n(v,t) \underset{t\to\infty}{\longrightarrow} P(v)$ the unique steady state (probability density)
- The convergence rate is exponential

Conclusion Total desynchronization

Leaky Integrate and Fire

The proof uses

- the Relative Entropy. For $H(\cdot)$ convex,

$$\frac{d}{dt}\int_{-\infty}^{V_F} P(v)H\left(\frac{n(v,t)}{P(v)}\right)dv \leq 0,$$

- Hardy/Poincaré inequality,

$$\int_{-\infty}^{V_F} P(v)|u(v)|^2 dv \leq C\int_{-\infty}^{V_F} P(v)|\nabla u(v)|^2 dv,$$

when
$$\int_{-\infty}^{V_F} P(v)u(v)dv = 0, \qquad P(V_F) = 0$$

See : Ledoux, Barthe and Roberto

Noisy LIF networks

For networks, the current $I(t) = bN(t)$ is related to the network activity

$$
\begin{cases}
\frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\left(-v + bN(t)\right) n(v,t)\right] - a\left(N(t)\right)\frac{\partial^2 n(v,t)}{\partial v^2} = N(t)\,\delta_{V_R}(v), \\
n(V_F,t) = 0, \qquad n(-\infty,t) = 0, \\
N(t) := -a\left(N(t)\right)\frac{\partial}{\partial v} n(V_F,t) \geq 0, \quad \text{total flux of firing neurons at } V_F
\end{cases}
$$

Constitutive laws

- $b =$ connectivity
- $b > 0$ for excitatory neurones
- $b < 0$ for inhibitory neurones
- $a(N) = a_0 + a_1 N$

Noisy LIF networks

$$\begin{cases} \frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\left(-v + bN(t)\right) n(v,t)\right] - a\big(N(t)\big)\frac{\partial^2 n(v,t)}{\partial v^2} = N(t)\,\delta_{V_R}(v), \\ n(V_F,t) = 0, \qquad n(-\infty,t) = 0, \\ N(t) := -a\big(N(t)\big)\frac{\partial}{\partial v} n(V_F,t) \geq 0, \quad \text{total flux of firing neurons at } V_F \end{cases}$$

Can be derived from a large system of N interacting neurons, see Delarue, Inglis, Rubenthaler, Tanre : for $1 \leq i \leq N$

$$\frac{d}{dt}V_i(t) = -V_i(t) + \frac{\beta}{N}\sum_{j=1}^{N}\sum_{\tau_j}\delta(t-\tau_j) + \sigma dW_i(t), \qquad V_i(t) < V_F,$$

with τ_j the spiking times $V_j(\tau_j) = V_F$.

Noisy LIF networks

Theorem (J. Carrillo, D. Salort, BP, D. Smets)[inhibitory]
Assume

- $a = a_0 > 0$ and $b < 0$ (inhibitory)
- the initial data is bounded by a supersolution (in a certain sense)

Then,

- There are global solutions
- Uniformly bounded for all $t > 0$

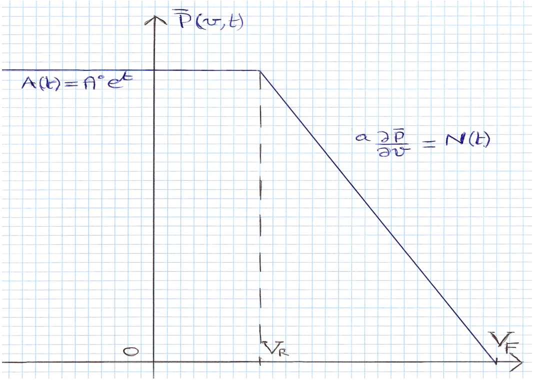
Open question Large time convergence to the unique steady state

See also Carrillo,Gonzalés, Gualdani, Schoenbeck for a reduction to Stefan problem

Noisy LIF networks

Proof Two ingredients :

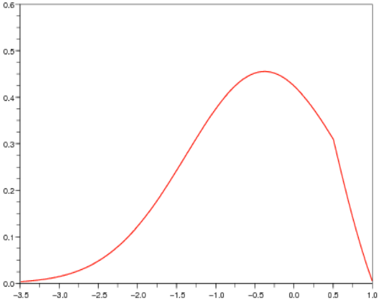
1. A universal supersolution (whatever is $N(t)$)

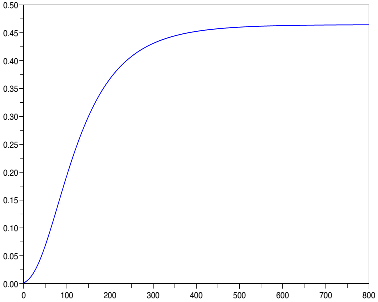


2. For the Fokker-Planck equation, regularizing effects $L^1 \to L^\infty$

Noisy LIF networks

$$\begin{cases} \frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\left(-v + bN(t)\right) n(v,t)\right] - a\left(N(t)\right) \frac{\partial^2 n(v,t)}{\partial v^2} = N(t)\, \delta_{V_R}(v), \\ n(V_F, t) = 0, \qquad n(-\infty, t) = 0, \qquad N(t) := -a\left(N(t)\right) \frac{\partial}{\partial v} n(V_F, t) \geq \end{cases}$$





Inhibitory case $b < 0$. Left $p(v,t)$, Right : N(t)

Noisy LIF networks

Theorem (M. Cáceres, J. Carrillo, BP) [excitatory, blow-up]
Assume $a \geq a_0 > 0$ and $b > 0$. Then the solution blows-up in finite time in the two cases

- the initial data is concentrated enough around $v = V_F$ (depending on b)
- initial data is given, b is large enough

Surprisingly

- Noise does not help
- value of b does not count

Noisy LIF networks

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- initial data is given, b is large enough

Possible interpretation

- $N(t) \to \rho\delta(t - t_{\mathrm{BU}})$ and $t_{\mathrm{BU}} > 0$,
- partial synchronization (S. Ha, Dumont-Henry, Giacomin, Pakdaman)

Noisy LIF networks

■ Noise does not help

Theorem (J. Carrillo, D. Salort, BP, D. Smets)[inhibitory]
Assume $a = a_0 + a_1 N$ and $b < 0$.
Then the solution blows-up in finite time when the initial data is concentrated enough around $v = V_F$

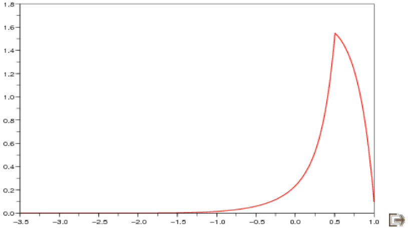
Noisy LIF networks

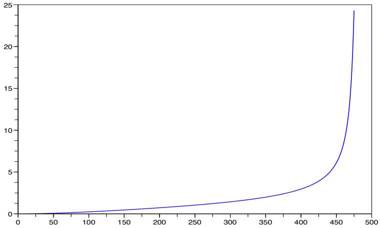
Theorem (J. Carrillo, D. Salort, BP, D. Smets) [excitatory, existence]

Assume $a \geq a_0 > 0$ and $b > 0$. Being given the initial data

- for b small enough, there is a solution
- it converges to the steady state

Noisy LIF networks





Excitatory integrate and fire model. Blow-up case. Left $p(v,t)$, Right : N(t)

Noisy LIF with refractory state

$$
\begin{cases}
\frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\left(-v+bN(t)\right)n(v,t)\right] - a\left(N(t)\right)\frac{\partial^2 n(v,t)}{\partial v^2} = \frac{R(t)}{\tau}\delta_{V_R}(v), \\
n(V_F,t) = 0, \qquad n(-\infty,t) = 0 \\
N(t) := -a\left(N(t)\right)\frac{\partial}{\partial v}n(V_F,t) \geq 0 \\
\frac{d}{dt}R(t) + \frac{R(t)}{\tau} = N(t). \qquad \text{Refractory state}
\end{cases}
$$

(See also Brunel for other versions)

Theorem (M.Cáceres, BP) [Refractory]

The solution blows-up in finite time in the 2 cases :

- $b > 0$ is fixed, if the initial data is concentrated enough around V_F.
- The initial data is given, if b large enough

Noisy LIF with refractory state

Proof. For $\mu = 2\max(\frac{1}{b}, \frac{V_F}{a_0})$, define

$$\phi(v) = e^{\mu v}, \qquad M_\mu(t) := \int_{-\infty}^{V_F} \phi(v) n(v,t).$$

For smooth solutions, we prove that $M_\mu(t)$ becomes larger than $e^{\mu V_F}$

$$\frac{dM_\mu}{dt} = \mu \int_{-\infty}^{V_F} (bN(t) - v + \mu a)\phi(v)p(v,t) - N(t)\phi(V_F) + \frac{R(t)}{\tau}\phi(V_R)$$

$$\geq N(t) \underbrace{\left[b\mu M_\mu(t) - \phi(V_F)\right]} + \mu \underbrace{\left[\mu a_0 - V_F\right]}_{\geq \mu V_F > 0} M_\mu(t)$$

> 0 is needed only initially

OK for b large enough or $M_\mu(0)$ large enough

To go further : the difficulty : no relation between M_μ and N

Noisy LIF with refractory state

Open question : coupling an inhibitory and excitatory network.

Spontaneous activity (regularized)

Assume refractory state and that the firing potential V_F is random.

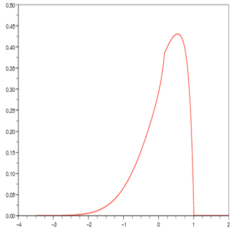
$$\frac{\partial n(v,t)}{\partial t} + \frac{\partial}{\partial v}\left[\left(-v+bN(t)\right)n(v,t)\right] - a\big(N(t)\big)\frac{\partial^2 n(v,t)}{\partial v^2} + \frac{n(v,t)}{\varepsilon}\mathbb{I}_{\{v>V_F\}}$$

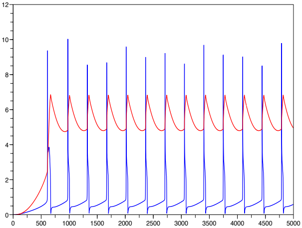
$$= \frac{R(t)}{\tau}\delta_{V_R}(v),$$

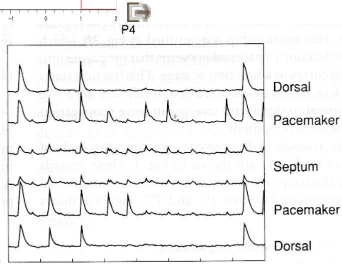
$$\begin{cases} N(t) := -\displaystyle\int \frac{n(v,t)}{\varepsilon}\mathbb{I}_{\{v>V_F\}}dv \\ \frac{d}{dt}R(t) + \frac{R(t)}{\tau} = N(t). \qquad \text{Refractory state} \end{cases}$$

Solutions are globally bounded.

Spontaneous activity (regularized)



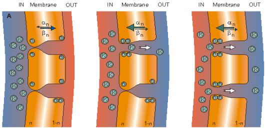




Left : Excitatory integrate and fire model with refractory state and random firing threshold

Right : Conhaim et al (2011) J. of physiology 589(10) 2529-2541.

Voltage-conductance I&F



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

Ion channels lead to ODE models *à la* Hodgkin-Huxley

$$\frac{\partial}{\partial t} p(v,g,t) + \frac{\partial}{\partial v}\left[\left(-g_L v + g(V_E - v)\right) p(v,g,t)\right]$$

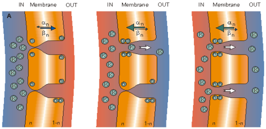
$$+\frac{\partial}{\partial g}\left[\frac{N(t)-g}{\sigma_E} p(v,g,t)\right] - \frac{a(t)}{\sigma_E}\frac{\partial^2}{\partial g^2} p(v,g,t) = 0,$$

$$v \in (0, V_F), \; g \geq 0,$$

Cai, Shelley, McLaughlin, Rangan, Kovacic, Ly, Trnachina...

Sub-elliptic fluxes

Voltage-conductance I&F



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$$v \in (0, V_F),\ \ g \geq 0,$$

Theorem (D. Salort, BP)

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

Elapsed time structured model

Based on K. Pakdaman, J. Champagnat, J.-F. Vibert

- s represents the time elapsed since the last discharge
- $n(s,t)$ probability of finding a neuron in 'state' s at time t
- $N(t)$ = activity of the network

$$\frac{\partial n(s,t)}{\partial t} + \overbrace{\frac{\partial n(s,t)}{\partial s}}^{\text{elapsed time advances}} + \overbrace{r(s, bN(t))\; n(s,t)}^{\text{firing neurons}} = 0,$$

$$N(t) := n(s=0,t) = \underbrace{\int_0^{+\infty} r(s, bN(t))\; n(s,t)ds}_{\text{neurons reset}},$$

Elapsed time structured model

$$\frac{\partial n(s,t)}{\partial t} + \overbrace{\frac{\partial n(s,t)}{\partial s}}^{\text{elapsed time advances}} + \overbrace{r(s,bN(t))\; n(s,t)}^{\text{firing neurons}} = 0,$$

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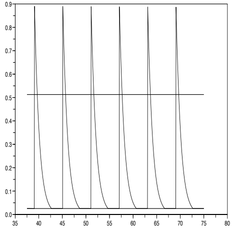

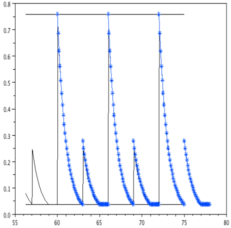

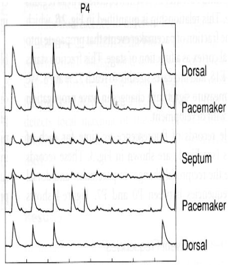

Right : Conhaim et al (2011) J. of physiology 589(10) 2529-2541.

Noisy LIF networks : CONCLUSION

- For the Noisy LIF model synchronization arises as a singularity of the total activity of the network

- But there are regimen with smooth solutions and total desynchronization

- Open problems
  - coupled inhibitory/excitatory
  - convergence to a steady state (inhibitory)
  - Derivation of LIF models

Noisy LIF networks : CONCLUSION

THANKS TO MY COLLABORATORS

M. J. Carceres, J. A. Carrillo

D. Smets, D. Salort

K. Pakdaman

Noisy LIF networks : CONCLUSION

THANKS TO MY COLLABORATORS

M. J. Carceres, J. A. Carrillo

D. Smets, D. Salort

K. Pakdaman

THANK YOU