

The non linear dynamics of retinal waves Bruno Cessac

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The non linear dynamics of retinal waves

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Contributors

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Retinal waves

<u>Spontaneous</u> spatio-temporal waves during development Disappear short after birth when vision is functional



MEA recording of the voltage from a mouse retina (courtesy E Sernagor).

Recordings from the retina



Variability within retinal waves



Variability within retinal waves



Retinal waves require three components:

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Experiment for coupled and isolated neurons, Zheng et al., 2006, Nature

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Retinal waves require three components:

Several models of stage II retinal waves have been already proposed:

ii)Refractory mechanism (slow After HyperPolarisation- sAHP)

- Feller et all Neuron, 1997.
- Eglen et al, J. Neuroscience 2000.
- Godfrey & Swindale. PLoS Comput Biol, 2007.
- Hennig et al, J. Neuroscience, 2009
- Lansdell et al, PLoS Computational Biology, 2014.

But none of them as studied simultaneously these 3 aspects:

(i) realistic model of spontaneous bursting
 (ii) sAHP biophysical modelling
 (iii) realistic Ach interaction.

Experiment for coupled and isolated neurons, Zheng et al., 2006, Nature

Membrane potential dynamics







Set of equations for sAHP current

Activated Ca-gated K+ channel



Gating mechanism

All 4 subunits R of the channel are bound to activate the channel

Saturated Calmodulin molecule (CaM) bind to each channel subunit

4 Calcium ions bound to each saturated Calmodulin complex S Set of equations for sAHP current

Activated

$$\tau_R \frac{dR}{dt} = a_R S(1 - R) - R$$

$$\tau_{S} \frac{dS}{dt} = -S + a_{S}C^{4}(1 - S)$$

S : Fraction of saturated calmodulin concentration (CaM)

$$\tau_{Ca} \frac{dC}{dt} = -a_R \frac{C}{H_x} + C_o + \delta_{Ca} I_{Ca}(V)$$

C : Intracellular Calcium concentration

SACs Network

Model synaptic interactions



Fig 7. Starbust amonime cells as stained with tucher yellow in whitemoxim rabbit retruit

SACs on a lattice

SACs become points on a lattice

SACs realistic connections

Acetylcholine current

- Molecular nicotinic receptors (nAchR)
- Two molecules of acetylcholine bind to open a nicotinic channel
- The nicotinic conductance depends on the second power of the acetylcholine neurotransmitter concentration A

$$g_{Ach} = g_{Ach}^{m} \frac{A^{2}}{K_{d}^{2} + A^{2}}$$





$$C_{m} \frac{dV_{i}}{dt} = -g_{L}(V_{i} - V_{L}) - g_{C}M_{\infty}(V_{i})(V_{i} - V_{C}) - g_{K}N_{i}(V_{i} - V_{K}) -G_{sAHP}(R_{i})(V_{i} - V_{K}) - G_{A}(\{A_{k}\}_{k\in\mathcal{B}_{i}})(V_{i} - V_{A})$$

$$\tau_{N} \frac{dN_{i}}{dt} = \Lambda(V_{i})(N_{\infty}(V_{i}) - N_{i})$$

$$\tau_{C} \frac{dC_{i}}{dt} = -\frac{\alpha_{C}}{H_{X}}C_{i} + C_{0} - \delta_{C}g_{C}M_{\infty}(V_{i})(V_{i} - V_{C})$$

$$\tau_{S} \frac{dS_{i}}{dt} = \alpha_{S}(1 - S_{i})C_{i}^{4} - S_{i}$$

$$\tau_{R} \frac{dR_{i}}{dt} = -\mu A_{i} + \beta_{A}T_{A}(V_{i}),$$

N neurons, 6 N equations

$$C_{m} \frac{dV_{i}}{dt} = -g_{L}(V_{i} - V_{L}) - g_{C}M_{\infty}(V_{i})(V_{i} - V_{C}) - g_{K}N_{i}(V_{i} - V_{K}) - G_{s}AF20 \text{ parameters per neuron}(V_{i} - V_{A})$$

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$$\tau_{N} \frac{dN_{i}}{dt} = (But neurons are assumed identical) + (V_{i})(N_{\infty}(V_{i}) - N_{i})$$

$$\tau_{C} \frac{dC_{i}}{dt} = -\frac{\alpha_{C}}{H_{X}}C_{i} + C_{0} - \delta_{C}g_{C}M_{\infty}(V_{i})(V_{i} - V_{C}) - Time scale separation$$

$$\tau_{S} \frac{dS_{i}}{dt} = -\alpha_{C}(1 - S_{i})C^{4} - S_{i}$$

$$T_{R} \frac{dR_{i}}{dt} = Medium C, A. \ \tau_{C} = 2 \text{ s}, \ \tau_{A} = 1.86 \text{ s}.$$

$$\frac{dA_{i}}{dt} = Slow S, R. \ \tau_{R} = \tau_{S} = 44 \text{ s}.$$

Fast time scale

On the fastest time scale, the sAHP conductance $G_{S_i} = g_S R_i^4$

and the Acetylcholine conductance $G_{A_i} = g_A \sum_{j \in \mathcal{B}_i} \frac{A_j^2}{\gamma_A + A_j^2}$

are, as slow variables, essentially constant =>

control parameters of the fast dynamics.

$$\begin{cases} C_m \frac{dV}{dt} = -g_L (V - V_L) - g_C M_\infty (V) (V - V_C) - g_K N (V - V_K) - G_S (V - V_K) - G_A (V - V_A) \\ \\ \tau_N \frac{dN}{dt} = \Lambda (V) (N_\infty (V) - N) \end{cases}$$

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$$\begin{cases} C_m \frac{dV}{dt} = -g_L(V - V_L) - g_C M_\infty(V)(V - V_C) - g_K N(V - V_K) - G_S V - V_K) + G_A V - V_A) \\ \tau_N \frac{dN}{dt} = \Lambda(V)(N_\infty(V) - N) \end{cases}$$











Noise induced bursting



Noise induced bursting





Noise induced bursting





Spontaneous Bursting Mechanism of SACs



The sAHP cycle




Probability to trigger a burst



Probability to trigger a burst



Probability to trigger a burst





Bursting cells produce Ach

$$G_{A_i} = g_A \sum_{j \in \mathcal{B}_i} \frac{A_j^2}{\gamma_A + A_j^2}$$

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The mechanism of retinal waves



The mechanism of retinal waves



The mechanism of retinal waves



Variability <u>within</u> retinal waves



Non linear coupling and feedback



















$$r(t) = c.t^z$$











250

200

150 100

> 50 0

> > 0

c (μ m/s)

 g_{A_0}

0.05

For $g_A < g_{A0}$, no propagation is possible. Individual cells can burst but gA is not large enough to trigger a wave.

I. A bursting cell can induce bursting of a neighbour, but transition is driven by noise. Transport is sub-ballistic.







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 \mathbf{g}_{A} (nS)



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5 0.2 0.25 0

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Variability <u>within</u> retinal waves



iv) Spatial Variability



Variability within retinal waves

Simulations made by L. Gil



https://www.youtube.com/ watch?v=shMR3NMCBDE



iv) Spatial Variability



1. The leading parameters are the Ach conductance G_A and the sAHP conductance G_s .

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- 2. Waves history generates transient refractory zones of sAHP which constrain the forthcoming waves propagation.

Assume:

- Nearest neighbours interaction;
- Continuous space limit ;
- GS, GA are considered as spatio-temporal fields ;
- Mean-field approximation to Ach production



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$$\begin{split} \frac{\partial G_A}{\partial t} &= g_A D_A \, \Delta \, \Omega + S. \\ S &= - \mu_A G_A + g_A \, \frac{d \, \beta_A}{\sqrt{\gamma_A}} \, \Omega \end{split}$$







1) Minimal g_A value for wave propagation

$$g_{A_0} \equiv \frac{2\,\mu_A\,\sqrt{\gamma_A}}{\beta_A\,\Omega}\,\,\frac{I_{SN} + G_{S_2}\,(V_{Si_2} - V_K)}{V_A - V_{Si_2}},$$



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2) Wave speed in the ballistic range

$$c = \frac{a}{t_C - \frac{1}{\mu_A} \log \left[1 + \frac{1}{g_A} \frac{2\mu_A \sqrt{\gamma_A}}{n\beta_A \Omega} \frac{I_{SN} + G_{S_2} (V_{Si_2} - V_K)}{V_{Si_2} - V_A} \right]}$$



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3) g_A value to enter in regime III

$$g_A = \frac{g_{A_0}}{1 - \frac{1}{2d}}$$



$$\frac{\partial G_A}{\partial t} = g_A D_A \left[\left(\nabla G_S, \nabla G_A \right) H_\Omega \left(\begin{array}{c} \nabla G_S \\ \nabla G_A \end{array} \right) + \frac{\partial \Omega}{\partial G_S} \Delta G_S + \frac{\partial \Omega}{\partial G_A} \Delta G_A \right] + S$$

Links with :

Kardhar, Parisi, Zhang

Self-Organised criticality



