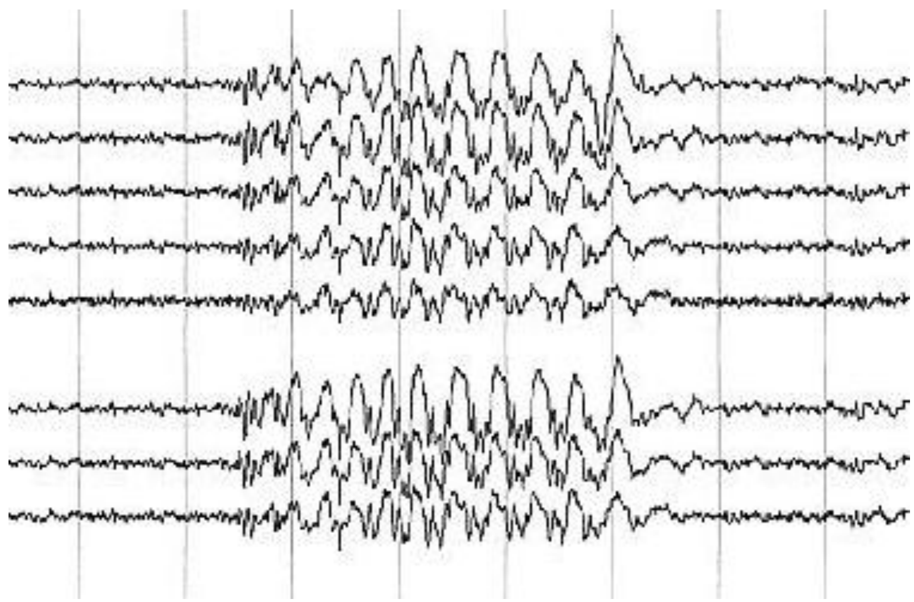
Role of dendrites in noise-induced synchronization

Alla Borisyuk

University of Utah

Epilepsy: synchrony

- Seizures: excessive or synchronous activity of populations of neurons

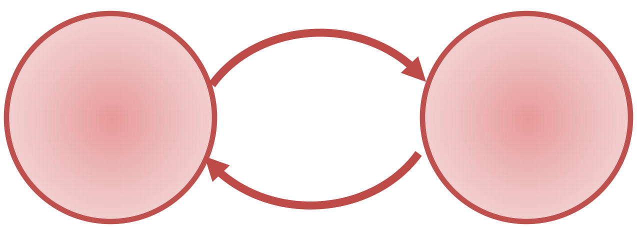


Casaubon et al 2003

Two types of synchronization

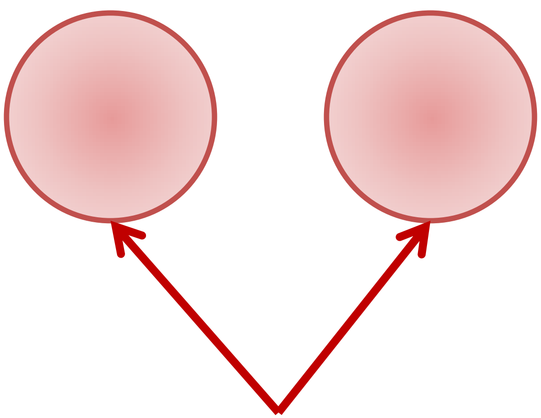
Synchronization of coupled cells

(seizure focus)



Synchronization to a common noisy source

(secondary epileptogenesis)



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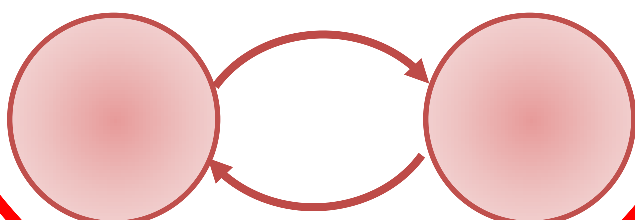

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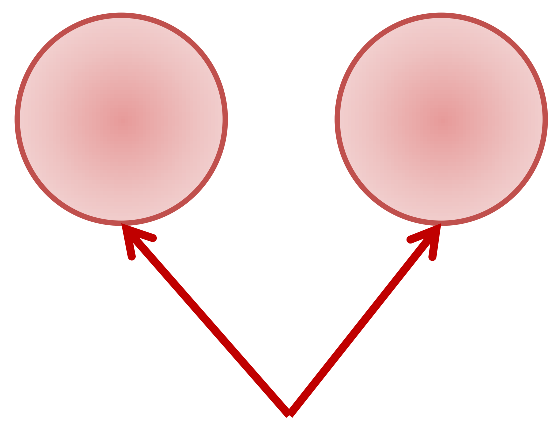

Two types of synchronization

Synchronization of mutually coupled cells

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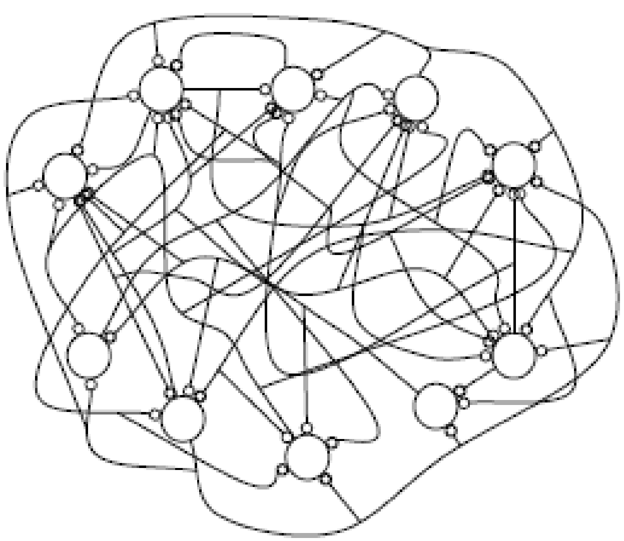

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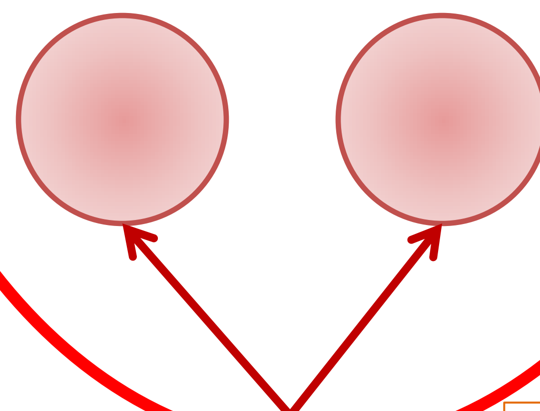
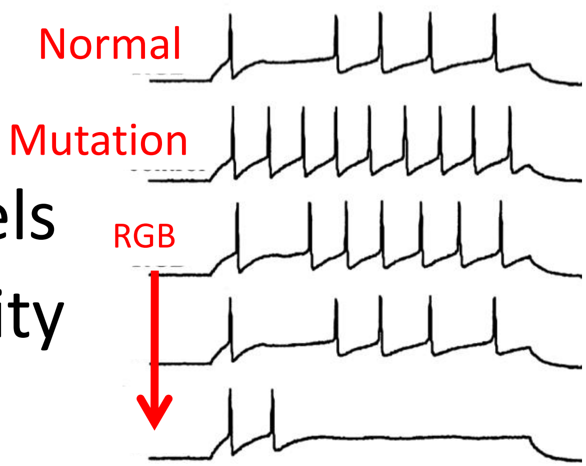


"Reliability"

Epilepsy: channels

- Many types of epileptic seizures have been traced to genetic mutations of ion channels
- Some of the drugs for epilepsy target the same channels
- <u>Example:</u>

- M-current: KCNQ2/KCNQ3 K^{+} channels
- Mutations lead to increased excitability
- Benign familial neonatal convulsions
- Drug retigabine – current activator

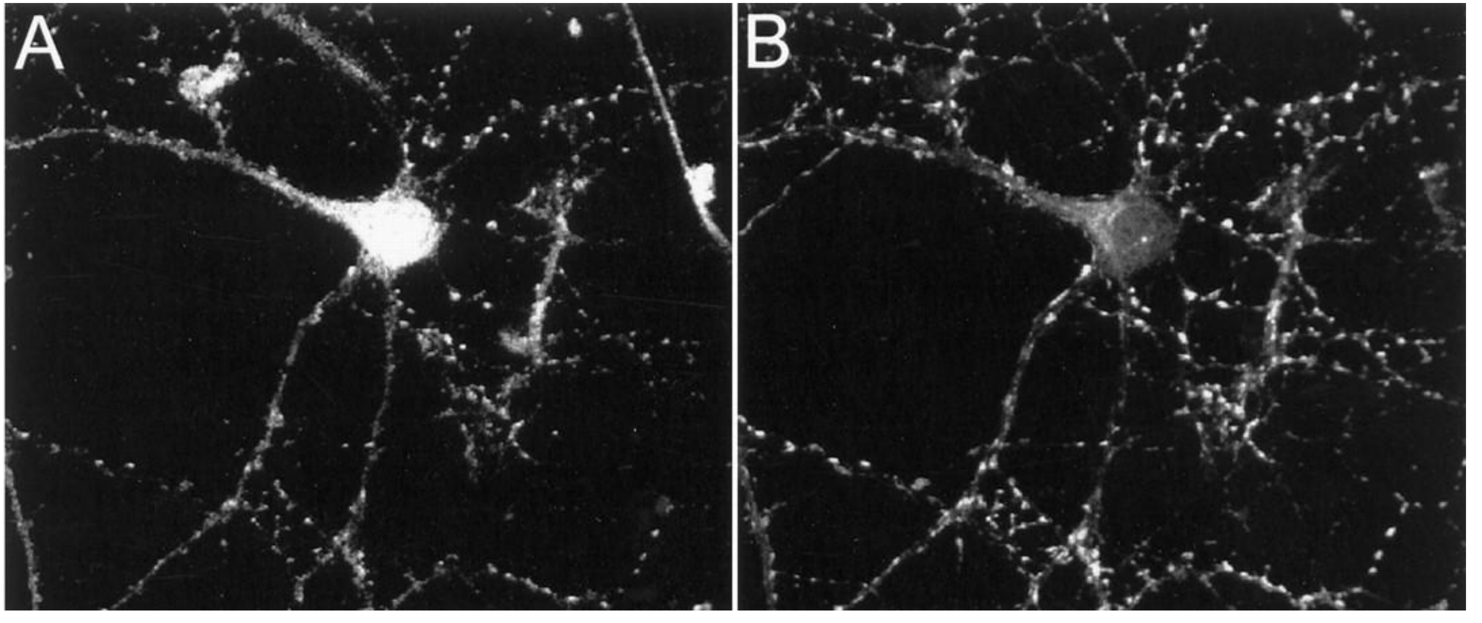


Otto et al. 2002

Epilepsy: dendrites

- Some of the epilepsy- implicated channels are located in dendrites

Kv4.2 channel (Temporal lobe epilepsy)



Petrecca et al 2000

Link between channels and synchrony

- **Big goal:** how changes in (dendritic) ionic channels affect synchronization
- **Data** (Netoff: slice, single-cell)

  - epileptogenic mutations may mean less synchrony

  - anti-epileptic drugs – more synchrony
- **Tools:**

- phase response curves
- Lyapunov exponents

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- Characteristic of an oscillator;
- Phase shift as a function of perturbation time

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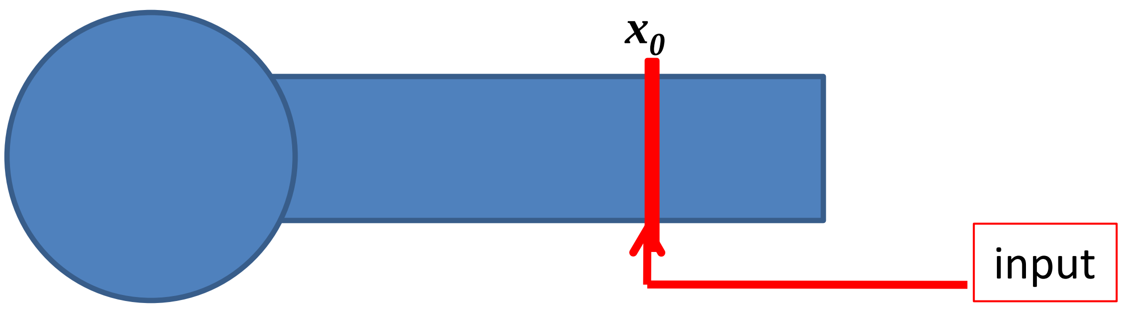
- Negative: measure of trajectories' convergence rate (rate of synchronization)
- Positive: indicator of chaos

In this work: synchrony to noise, dendrites, channels

- Develop mathematical framework for quantifying the ability of cells to synchronize to common noisy input
- Develop 2 semi-analytical approaches, compare with numerical simulations
- Model: oscillating soma, white noise input, (initially passive) cable dendrite



Synchronization to noise

- Phase oscillators with white noise (Teramae and Tanaka 2004): Ability to synchronize can be quantified by Lyapunov exponent

$$\lambda = -\frac{\varepsilon^2}{2T}\int_0^T (PRC'(\theta))^2 d\theta$$

- Extended (Galan, Ermentrout, Urban 2008) to non-white noise:

$$\lambda = \varepsilon^2 \lim_{t\to\infty}\frac{1}{t}\int_0^t PRC''(s)\int_0^s PRC(s')C(s-s')ds'ds$$

Synchronization to noise

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Strength of input

Oscillator period

Phase response curve

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Noise autocorrelation function

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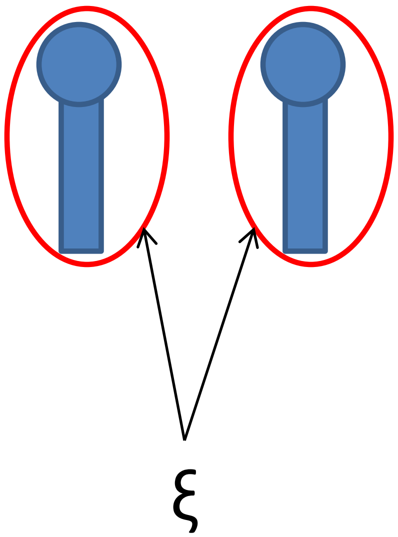
With non-white drive oscillators may not synchronize (unreliable)

Approach 1: “White Noise Approach”

- Consider soma and dendrite as one oscillator, compute its PRC (Goldberg et al. 2007): dPRC
- Formulate synchronization problem as synchronization of somato-dendritic oscillators by white noise



$$\lambda_{d,white}(x_0) = -\frac{\varepsilon^2}{2T}\int_0^T ((dPRC(\theta, x_0))')^2 d\theta$$

Approach 1: "White Noise Approach"

$$\lambda_{d,white}(x_0) = -\frac{\varepsilon^2}{2T}\int_0^T ((dPRC(\theta, x_0))')^2 d\theta$$

$$dPRC = \frac{\kappa}{C}\int_0^\infty PRC(t_0 + t)\frac{\partial}{\partial x}G(x = 0, t; x_0, t_0)dt$$

$$G_{si}(x, t; x_0, t_0) = G_\infty(x - x_0, t - t_0) - G_\infty(x + x_0, t - t_0)$$

$$G_\infty(x, t) = \frac{1}{\sqrt{4\pi t/\tau}}\exp(-\frac{t}{\tau} - \frac{x^2\tau}{4D^2 t})$$

Approach 1: "White Noise Approach"

$$\lambda_{d,white}(x_0) = -\frac{\varepsilon^2}{2T}\int_0^T ((dPRC(\theta, x_0))')^2 \, d\theta$$

Green's function

$$dPRC = \frac{\kappa}{C}\int_0^\infty PRC(t_0 + t)\frac{\partial}{\partial x} G(x = 0, t; x_0, t_0)\, dt$$

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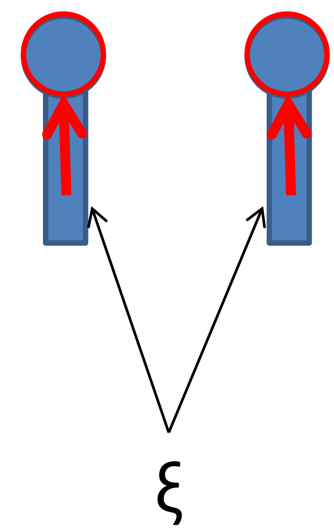
$$G_\infty(x,t) = \frac{1}{\sqrt{4\pi t/\tau}}\exp\left(-\frac{t}{\tau} - \frac{x^2\tau}{4D^2 t}\right)$$

Approach 2: "Colored noise approach"

- Consider somas as oscillators receiving noise filtered by the dendrite

$$\lambda_{colored}(x_0) = \varepsilon^2 \lim_{t\to\infty} \frac{1}{t} \int_0^t PRC''(s) \int_0^s PRC(s')C(s-s')ds'ds$$



Approach 2: “Colored noise approach”

- Consider somas as oscillators receiving noise filtered by the dendrite

$$\lambda_{colored} = \varepsilon^2 \lim_{t\to\infty} \frac{1}{t} \int_0^t PRC''(s) \int_0^s PRC(s')C(s-s')ds'ds$$

- C(x,y) is the correlation function and for input into the soma it can be found as

$$C(s,s') = \left(\tfrac{\kappa}{C}\right)^2 \int_0^{s\wedge s'} \frac{\partial}{\partial x} G(0,s;x_0,t) \frac{\partial}{\partial x} G(0,s';x_0,t)dt$$

Example

Passive semi-infinite cable dendrite with Hodgkin-Huxley oscillating soma attached at the boundary

<u>Cable</u>

$$\tau \frac{\partial v(x,t)}{\partial t} = D^2 \frac{\partial^2 v(x,t)}{\partial x^2} - [v(x,t) - v_L]$$

Example

Cable

$$\tau \frac{\partial v(x,t)}{\partial t} = D^2 \frac{\partial^2 v(x,t)}{\partial x^2} - [v(x,t) - v_L]$$

Boundary at ∞

$$\frac{\partial v(\infty,t)}{\partial x} = 0$$

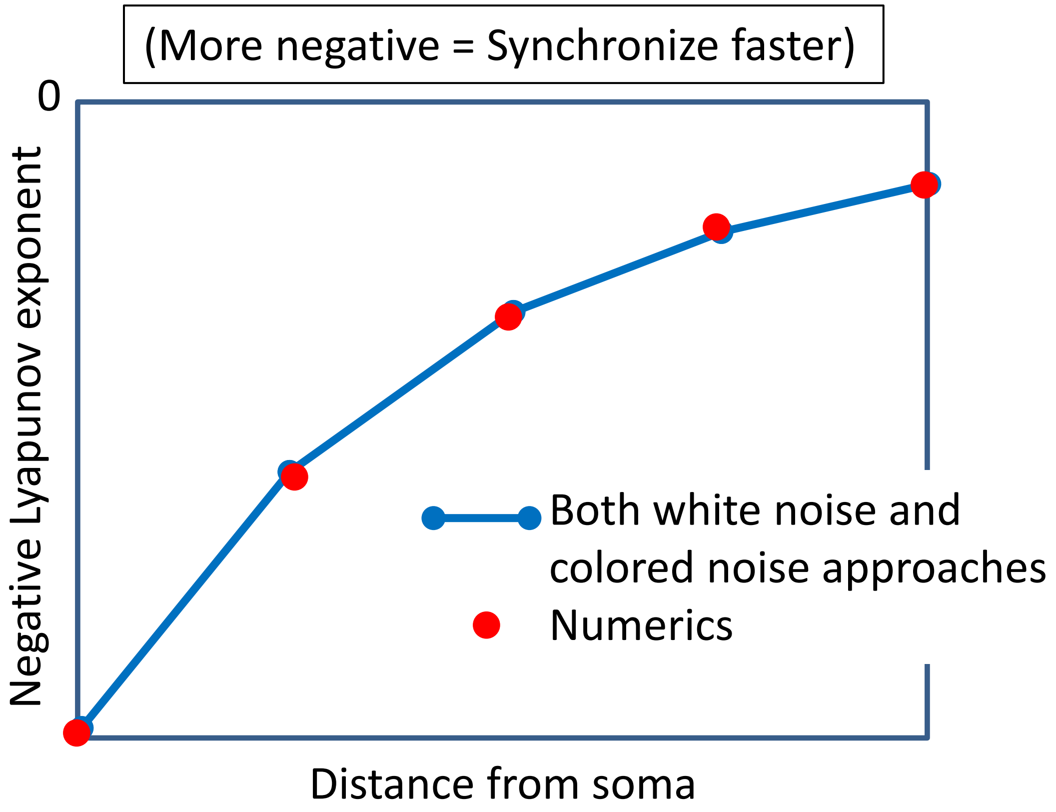
Boundary at 0: *v(0,t)=V*

$$C\frac{dV}{dt} = I - g_{Na} h m^3 (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + \kappa \frac{\partial}{\partial x} v(0.t)$$

$$\frac{dX}{dt} = a_X(V)(1 - X) - b_X(V)X, \qquad X = m, n, h$$

Crook et al. 1998

Both approaches work



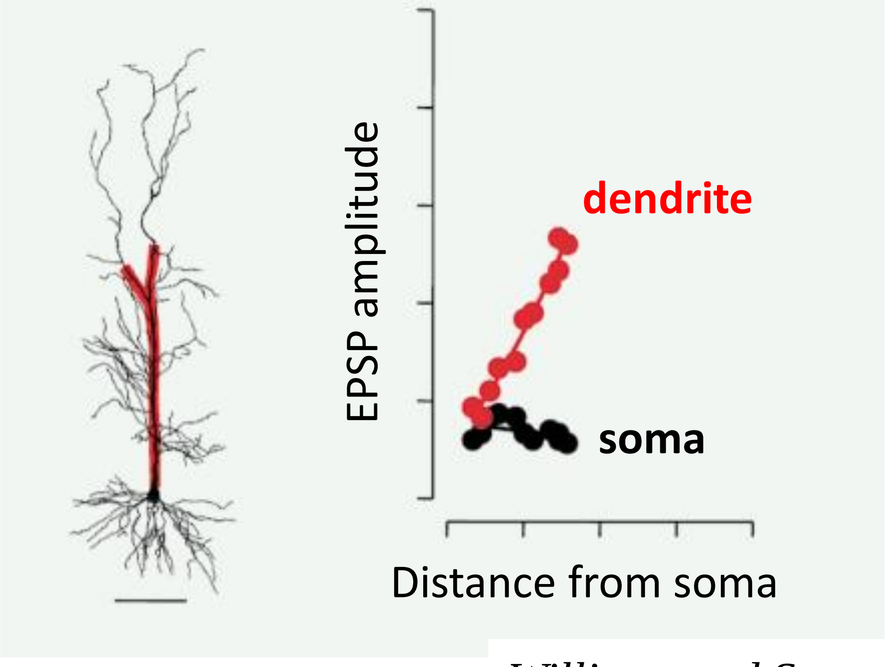
Observations

- White noise approach is computationally more efficient
- Colored noise approach is more robust with other models
- Works for a variety of models
- Expected to fail sometimes (unreliability)

Dendritic democracy

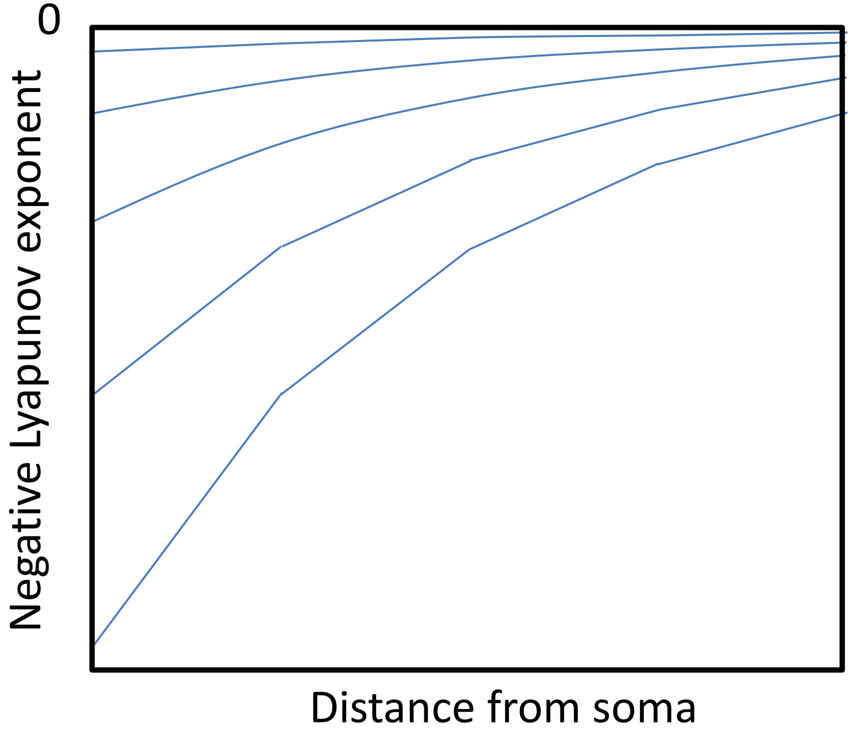
- Increase in synaptic efficacy with distance along the dendrite
- Equalizing the effect of synaptic inputs on the soma

CA1 hippocampal pyramidal neuron



Williams and Stuart, 2003

Numerics: distal inputs can be more synchronizing than proximal ones, if dendritic democracy is included



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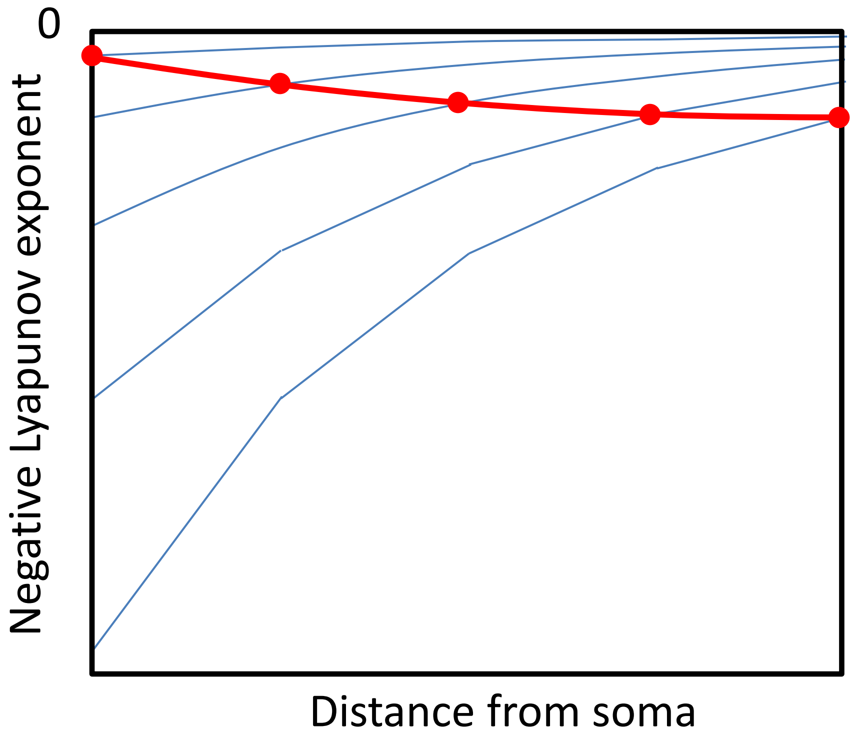


Dendritic democracy: analytic computation

- Current seen by the soma can be computed as

$$I(t) = p(x_0)\frac{\partial G}{\partial x}(0,t;x_0,0)$$

- Fixing the amplitude of this current, solve for the strength of stimulus as a function of location

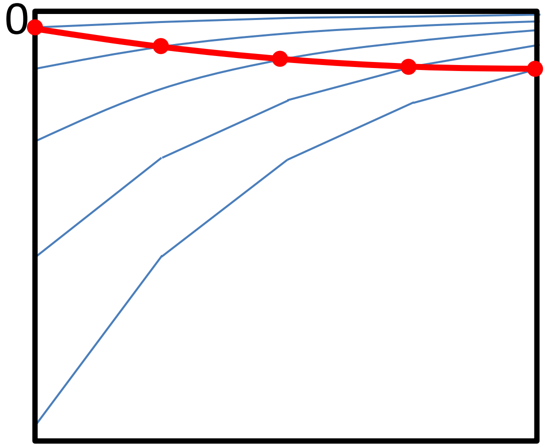
$$\max_t(I(t)) = \delta_{PSP} \qquad \Rightarrow \qquad p(x_0)$$

Dendritic democracy: analytic computation

- Lyapunov exponent

$$\lambda(x_0;\delta_{PSP}) = -\frac{(p(x_0))^2}{2T}\int_0^T \left(dPRC'(\theta;x_0)\right)^2 d\theta$$

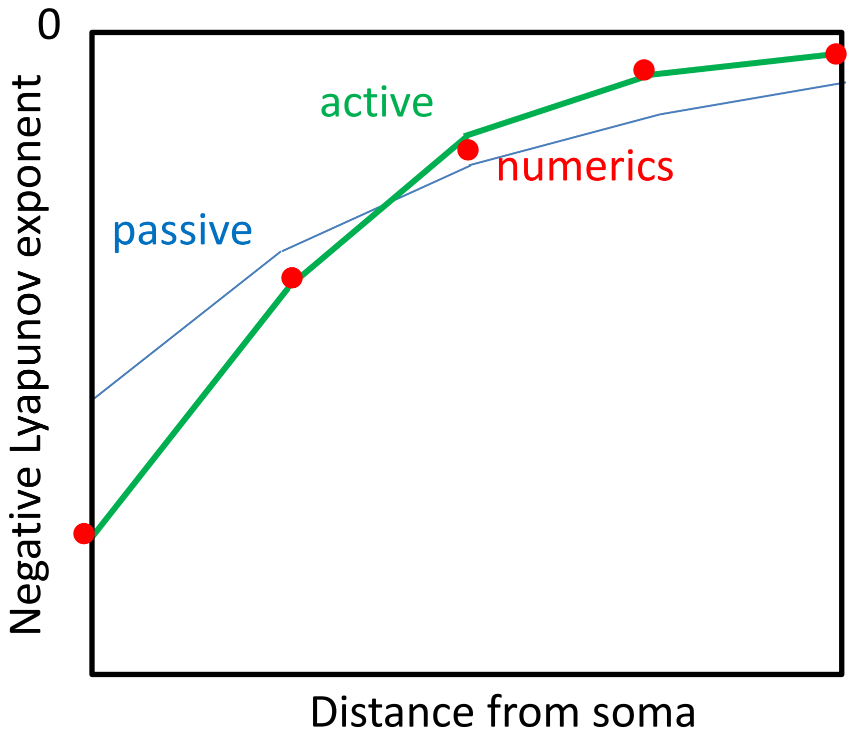
Always decreasing for a passive cable



Active dendrite: linear approximation

- Active dendritic currents: linearize around rest (Bressloff 1999)
- Green’s function can still be found (Goldberg et al 2007)
- Spatially nonuniform channel distribution can be considered

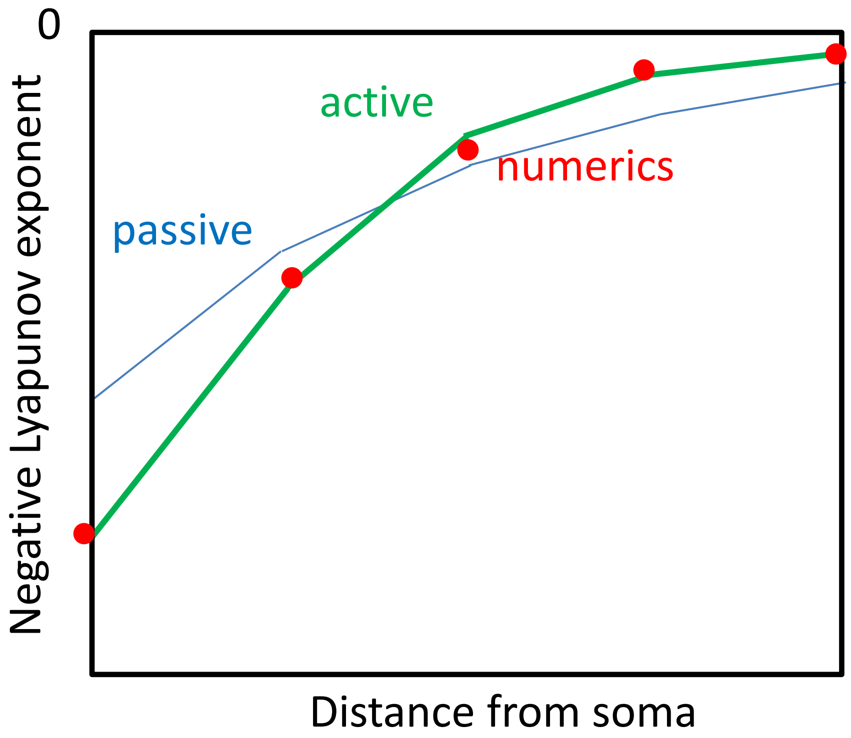
Example (hcn current)



- But: linearization fails in interesting cases

Other approaches are needed

Example (hcn current)



Presence of active currents may facilitate or decrease synchrony, depending on where the inputs are located

Conclusion: Part II

- Both “white noise” and “colored noise” analytical approaches work for passive dendrite and some active dendrite cases
- Distal inputs can be more efficient at synchronizing than proximal ones, if synaptic democracy is included
- Whether the active dendritic conductances have synchronizing or desynchronizing effect, may depend on the location of the inputs

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- Theoden Netoff, University of Minnesota

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