PROBING THE ASSOCIATION BETWEEN AXONAL SPROUTING AND SEIZURE ACTIVITY USING A COUPLED NEURAL MASS MODEL

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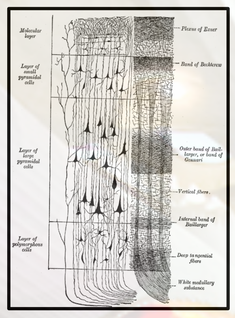
Computational Approach to Seizure Modeling

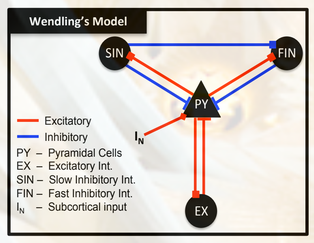
Generally believed mechanisms of seizure activity initiation

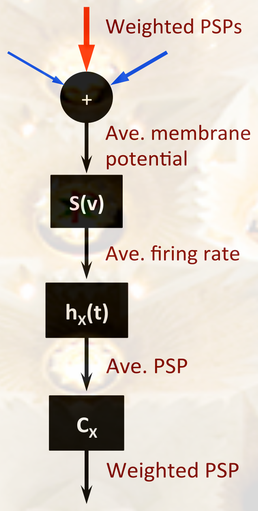
i. altered excitation-inhibition balance
   - Increased excitation (Wendling 2000)
   - Impaired dendritic inhibition (Wendling 2002)

Neural mass model

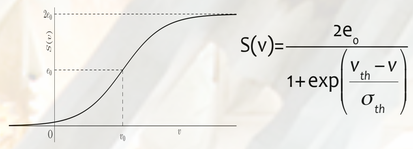


wikipedia.com

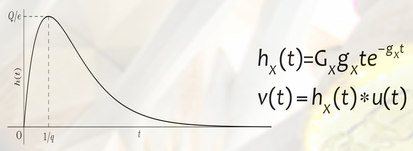




Firing response function



Post-synaptic impulse response



ii. synaptic reorganization of neuronal networks
   - Axon sprouting is a mechanism (Cavazos 1991)

Co-occurrence of axonal sprouting and seizure activity has been established in epilepsy and lesion models (Cavazos 1991, Sutula 2002, McKinney 1997)

i. sprouted axons made predominantly excitatory connections (Buckmaster 2002, Jin 2006)

ii. aberrant synaptic contacts were exhibited similar to those observed with LTP (Leite 2005)

Coupled neural mass model

Model Feature	Existing models		Proposed model
	Jansen and Rit (1995)	Goodfellow et al. (2012)	
Original context	Visual evoked potential	Seizure initiation	Seizure initiation
Propagation mechanism	Synaptic delay with longer latency	Pyramidal cell connections	Sprouted axons with longer latency
Dimensionality of coupling equation	Inconsistent	Consistent	Consistent
Interpretability of coupling parameter	Not physiological	Physiologically plausible	Density of sprouted axons

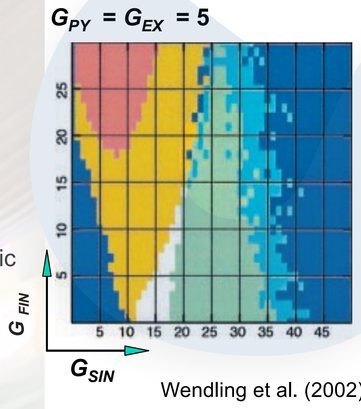
Goal of the study

To construct a physiologically-consistent generative model for seizure activity initiation, propagation, and termination

Low-voltage rapid

Slow rhythmic

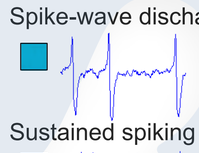
High-voltage periodic



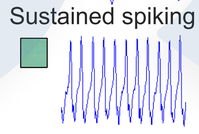
Wendling et al. (2002)

Normal Activity

Spike-wave discharges



Sustained spiking



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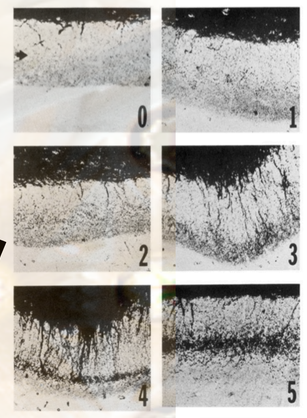
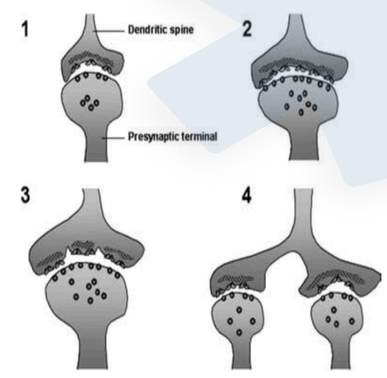
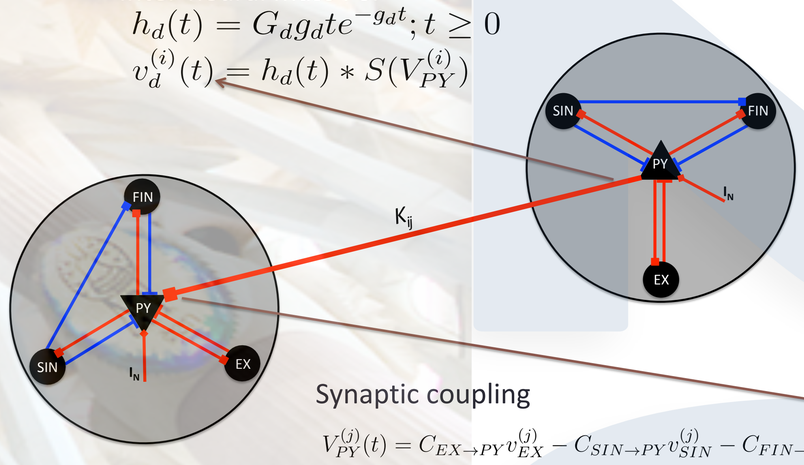




Leite (2005)

Inter-neural mass PSP

$$h_d(t) = G_d g_d t e^{-g_d t}; t \geq 0$$
$$v_d^{(i)}(t) = h_d(t) * S(V_{PY}^{(i)})$$

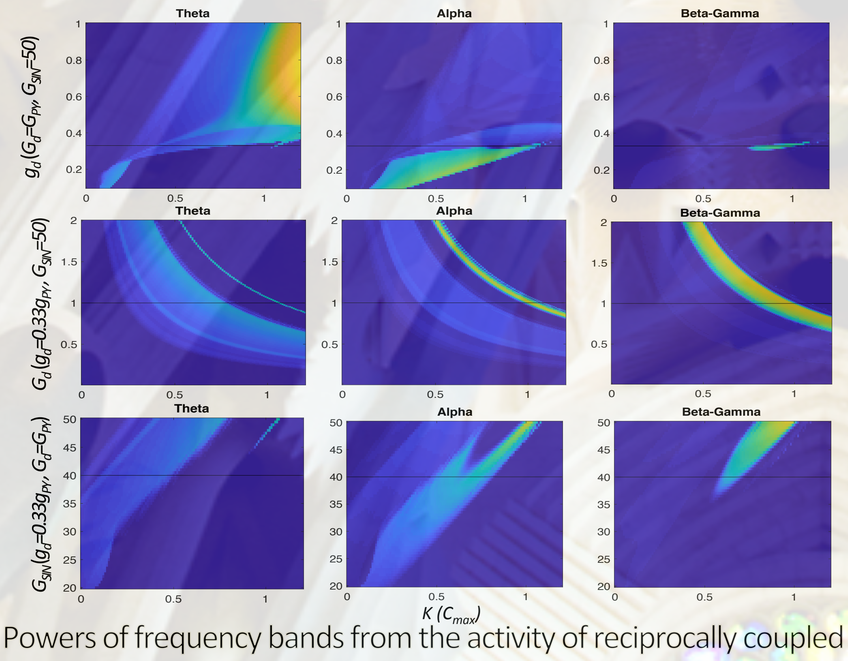


Synaptic coupling

$$V_{PY}^{(j)}(t) = C_{EX\to PY} v_{EX}^{(j)} - C_{SIN\to PY} v_{SIN}^{(j)} - C_{FIN\to PY} v_{FIN}^{(j)} + \sum_i K_{ij} v_d^{(i)}(t)$$

RESULTS

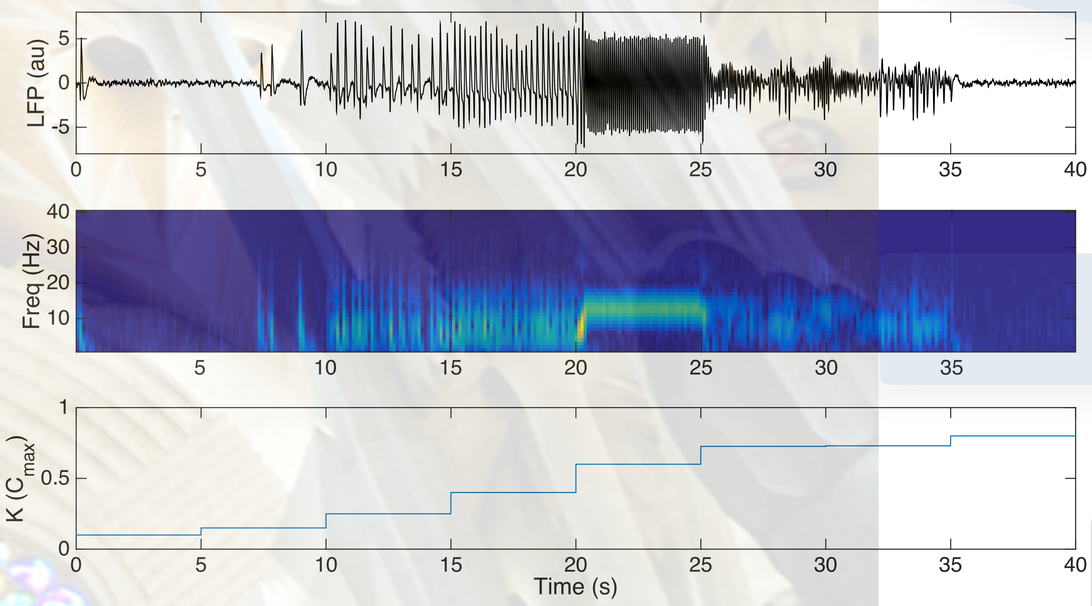
Activity maps with respect to model parameters



Powers of frequency bands from the activity of reciprocally coupled neural masses (K_{ij}=K_{ji}=K) suggest appropriate parameter settings.

Model reproduces different seizure activities at different coupling strength values (density of spouted axons)

(g_d=0.33g_{PY}, G_d=1.5G_{PY}, G_{SIN}=50)



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