Chimera States and Seizures in a Mouse Neuronal Model

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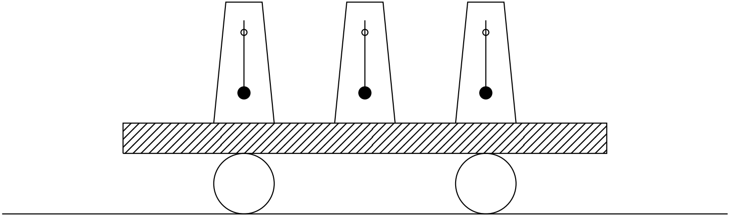
Roadmap

Synchronization

Huygens' pendulum clocks, fireflies, applauding crowds, people walking on London's Millenium Bridge, power grids, metronomes on a moving platform . . .



All provide examples of synchrony in surprising places.

The Kuramoto Model

A commonly-used model where synchrony arises is the Kuramoto model:

$$\frac{\partial}{\partial t}\phi(x,t) = \omega - \int G(x-x')\sin\big(\phi(x,t)-\phi(x',t)+\alpha\big)\,\mathrm{d}x' \quad (1)$$

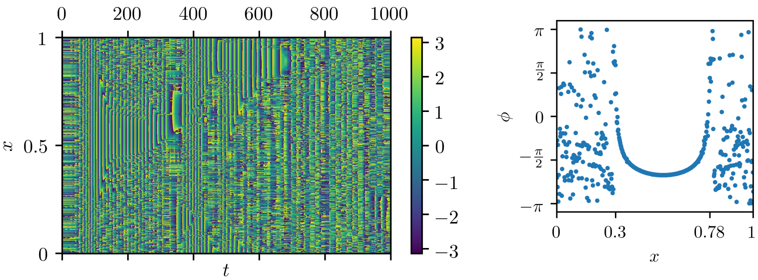
where

$$G(y) = \frac{\kappa}{2}e^{-k|y|} \quad (2)$$

It also exhibits some unexpected behavior...

Chimera States

Chimera states are **the coexistence of synchronous and asynchronous populations within a network of nonlocally-coupled oscillators** [1, 3].



(a) The time series of the Kuramoto simulation.

(b) A snapshot at $t = 120$.

Figure: An example of a chimera state in a network of Kuramoto oscillators (coupling is proportional to sine of phase difference).

Abrams Model

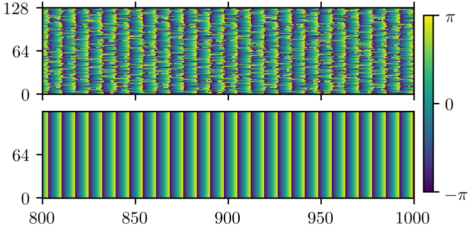
The Abrams Model is a network of Kuramoto oscillators divided into two populations. The coupling is stronger within populations than between them.

$$\frac{\mathrm{d}\theta_i^\sigma}{\mathrm{d}t} = \omega + \sum_{\sigma'=1}^{2} \frac{K_{\sigma\sigma'}}{N_{\sigma'}} \sum_{j=1}^{N_{\sigma'}} \sin\left(\theta_j^{\sigma'} - \theta_i^\sigma - \alpha\right) \tag{3}$$

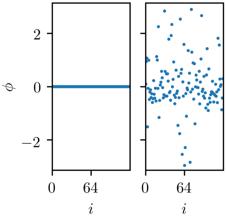
where

$$K = \begin{bmatrix} \mu & \nu \\ \nu & \mu \end{bmatrix} \quad \text{and} \quad \sigma \in \{1, 2\}. \tag{4}$$

Abrams Simulation



(a) The time series of the Abrams simulation.



(b) A snapshot at $t = 799.45$.

Figure: A simulation of the Abrams model for two populations of 128 oscillators. (a) the time series of the simulation for $t \in (800, 1000)$. (b) a snapshot at $t = 799.45$.

This is with $\mu = 0.6$, $\nu = 0.4$, $\alpha = \frac{\pi}{2} - 0.05$.

A Mechanical Example

Two swinging platforms tied together with springs, each holding 15 metronomes. For certain strengths of the spring (coupling strengths), chimera states appeared [5].

A mechanical example of a chimera state

Measures

A system's **order parameter** provides an instantaneous measure for how synchronous it is:

$$r(t) = \left| \left\langle e^{i\phi_k(t)} \right\rangle_{k \in C} \right|, \tag{5}$$

where ϕ_k is the phase of oscillator k, and $\langle f \rangle_{k \in C}$ is the average of f over all k in community C.

Measures

There are two useful measures for determining how chimeric a system is:

$$\chi = \langle \sigma_{\mathsf{chi}} \rangle_T \qquad \text{where} \quad \sigma_{\mathsf{chi}}(t) = \frac{1}{M-1} \sum_{c \in C} \left(r_c(t) - \langle r_c \rangle_C \right)^2 \tag{6}$$

$$m = \langle \sigma_{\mathsf{met}} \rangle_C \qquad \text{where} \quad \sigma_{\mathsf{met}}(c) = \frac{1}{T-1} \sum_{t \leq T} \left(r_c(t) - \langle r_c \rangle_T \right)^2 \tag{7}$$

The **chimera-like index** χ is the time average of the variance between communities of the order parameter. Its maximum value is $1/7$, and will be normalized as such.
The **metastability index** m is the average across communities of the variance over time of the order parameter. Its maximum value is $1/12$, and will be normalized as such.

Roadmap

Neurons

Neurons are cells which are specialized for communication. They *fire* by sending an electrochemical signal to other neurons. Internally, this *action potential* is a set of fast excitatory processes and slow inhibitory processes. Neural firings are *all-or-nothing*—a neuron can't half-fire.

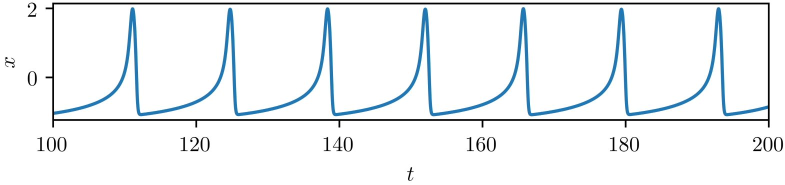


Figure: The membrane potential during a typical action potential.

Seizures

Seizures are **excessive(ly) synchronous neural activity** [8]. The two main types are:

Generalized The entire brain enters ictal stage simultaneously

Focal A subsection of the brain enters ictal stage while the rest remains asynchronous

Focal seizures often secondarily generalize.

Roadmap

Brain Models

We have extremely accurate models for the behavior of individual neurons. But, more is different, and modeling brains as collections of individual neurons is impractical. So, we use mean-field approximations (and the like).
This has two great benefits:

1. Simpler to simulate
2. Closer to observables

Epileptor

A famous phenomenological seizure model is called Epileptor [2]:

$$\dot{x}_1 = y_1 - f_1(x_1, x_2) - z + I_{\text{rest1}} \tag{8}$$

$$\dot{y}_1 = y_0 - 5x_1^2 - y_1 \tag{9}$$

$$\dot{z} = \frac{1}{\tau_0}(4(x_1 - x_0) - z) \tag{10}$$

$$\dot{x}_2 = -y_2 + x_2 - x_2^3 + I_{\text{rest2}} + 0.002g(x_1) - 0.3(z - 3.5) \tag{11}$$

$$\dot{y}_2 = \frac{1}{\tau_2}(-y_2 + f_2(x_1, x_2)) \tag{12}$$

where

$$g(x_1) = \int_{t_0}^{t} e^{-\gamma(t-\tau)} x_1(\tau)\, \mathrm{d}\tau \tag{13}$$

$$f_1(x_1, x_2) = \begin{cases} x_1^3 - 3x_1^2, & \text{if } x_1 < 0 \\ x_1\left(x_2 - 0.6(z-4)^2\right), & \text{if } x_1 \geq 0 \end{cases} \tag{14}$$

$$f_2(x_1, x_2) = \begin{cases} 0, & \text{if } x_2 < -0.25 \\ 6(x_2 + 0.25), & \text{if } x_2 \geq -0.25 \end{cases} \tag{15}$$

and $x_0 = -1.6$, $y_0 = 1$, $\tau_0 = 2857$, $\tau_1 = 1$, $\tau_2 = 10$, $I_{\text{rest1}} = 3.1$, $I_{\text{rest2}} = 0.45$, $\gamma = 0.01$.

Roadmap

Model Parameters

Symbol	Value	Meaning
x_j	—	**Membrane potential of the jth neural mass**
y_j	—	**Associated with the fast processes**
z_j	—	**Associated with slow processes**
b	3.2	Tunes the spiking frequency
I_j	4.4	External input current
x_{rev}	2	Ambient reverse potential
λ	10	Sigmoidal activation function parameter
θ	-0.25	Sigmoidal activation function parameter
μ	0.01	Time scale for variation of z
s	4	Governs adaptation
x_{rest}	-1.6	Resting/equilibrium potential
α	Varied	**Connection strength within cortices**
n'_j	Figure 4a	**Number of connections within a cortex from the jth neuron**
G'_{jk}	Figure 4a	**Intra-cortical connection matrix**
β	Varied	**Connection strength between cortices**
n''_j	Figure 4a	**Number of connections between cortices from the jth neuron**
G''_{jk}	Figure 4a	**Inter-cortical connection matrix**

Table: The list of parameters used in modeling the Hindmarsh-Rose network.

The Model

We used a network of modified Hindmarsh-Rose neurons [7]:

$$\dot{x}_j = y_j - x_j^3 + bx_j^2 + I_j - z_j - \frac{\alpha}{n'_j}\sum_{k=1}^{N} G'_{jk}\Theta_j(x_k) - \frac{\beta}{n''_j}\sum_{k=1}^{N} G''_{jk}\Theta_j(x_k) \tag{16}$$

$$\dot{y}_j = 1 - 5x_j^2 - y_j \tag{17}$$

$$\dot{z}_j = \mu(s[x_j - x_{\text{rest}}] - z_j) \tag{18}$$

where

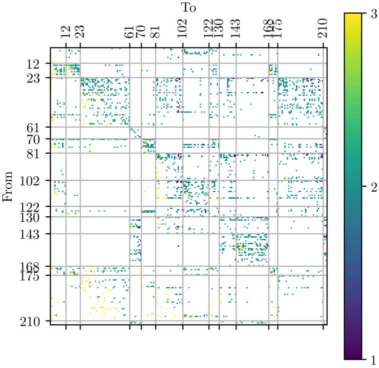
$$\Theta_j(x_k) = \frac{x_j - x_{\text{rev}}}{1 + e^{-\lambda(x_k - \theta)}} \tag{19}$$

This sigmoidal activation function helps make the model apply to groups of neurons (subcortices) instead of single neurons.

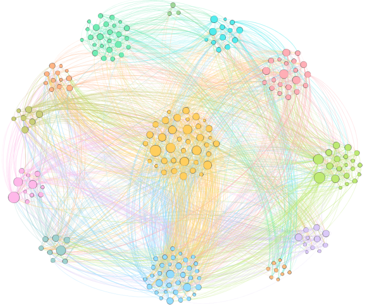
Roadmap

The Mouse Connectome

The oscillator network (fig. 4) was modeled after the mouse connectome [6].



(a)



(b)

Figure: (a) The mouse connectome represented as (a) a matrix and (b) a graph embedding.

Roadmap

The Implementation

The Hindmarsh-Rose model was coded up in Python, and integrated for various values of α and β. The initial conditions were drawn from uniform distributions:

$$x_j \in [-2, 2], \quad y_j \in [0, 0.2], \quad z_j \in [0, 0.2]$$

Integrated over $(-1000, 5000)$, keeping $t \in (0, 4000)$. The first 1000 time units are to eliminate transients, and the last 1000 are calculated but discarded to facilitate calculation of the phase:

$$\phi_j(t) = 2\pi \times \frac{t - t_i}{t_{i+1} - t_i} \tag{20}$$

Roadmap

Real EEG output

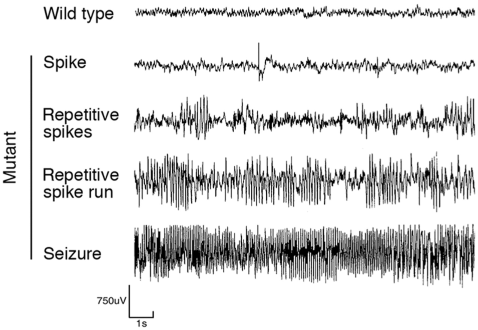


Figure: A typical EEG trace. The first row ("Wild type") shows a normal awake adult mouse EEG trace. The other four rows ("Mutant") show typical abnormal/epileptiform activity. Taken from [4].

Simulated EEG Output

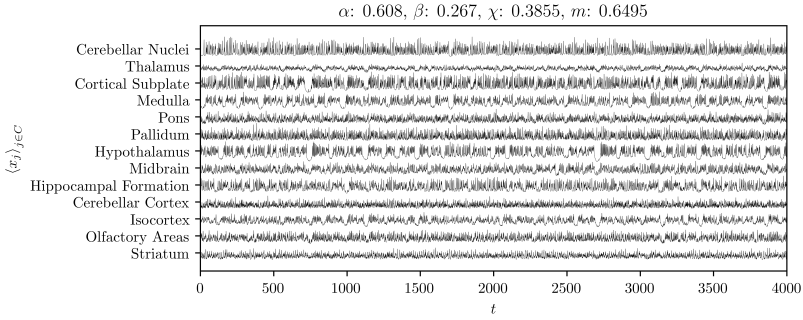


Figure: The mean membrane potential within each cortex.

Thalamus, Pons, Striatum — wild type
Cerebellar cortex — spiking behavior, spike runs
Medulla, Hypothalamus — repetitive spike runs
Cortical subplate — seizure-like behavior

Roadmap

Model Physicality

The neurons only collectively fired for certain values of α (intra-cortical coupling) and β (inter-cortical coupling).

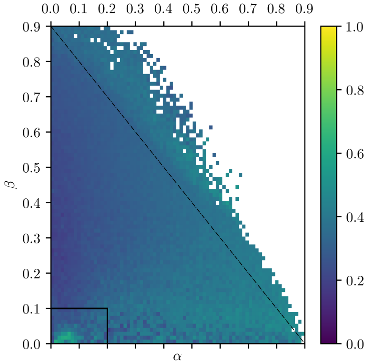
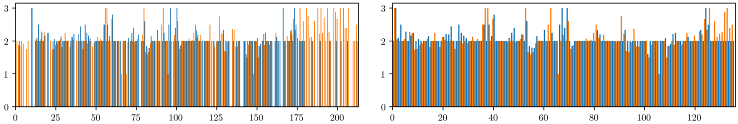


Figure: The chimera-like landscape of parameter space on $(\alpha, \beta) \in (0, 0.9) \times (0, 0.9)$. The aphysical region of the model is shown in white. The black rectangle in the bottom left corner indicates the region of parameter space shown in fig. 9.

Potential Explanation?

Physicality of the model depends more heavily on α than β. *Possibly* because $\overline{g}'_j = \sum_k (G'_{jk}/n'_j) > \sum_k (G''_{jk}/n''_j) = \overline{g}''_j$ for most j for which $0 \notin \left\{\overline{g}'_j, \overline{g}''_k\right\}$.



(a) All values

(b) Dropped zeros

Figure: The average connection strengths for each neuron j, within cortices (blue) and between them (orange). (a) All of the subcortices. (b) All of the subcortices for which neither intra- nor inter-cortical average strength was 0.

Roadmap

The Highly Chimeric Patch

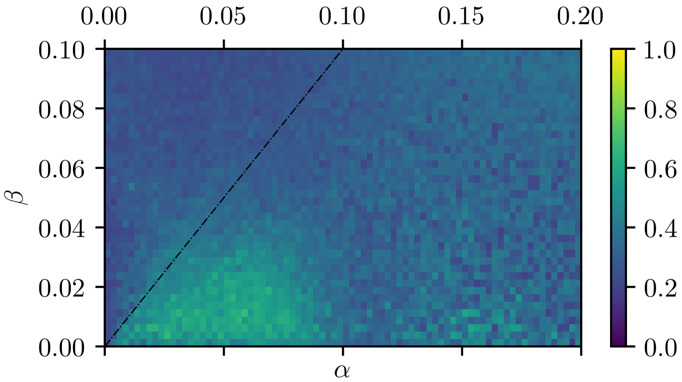


Figure: The chimera index of runs with $(\alpha, \beta) \in (0, 0.2) \times (0, 0.1)$. As before, the chimera-like index is normalized to $\frac{1}{7}$. The dashed line shows $\beta = \alpha$.

Yes, It's Real

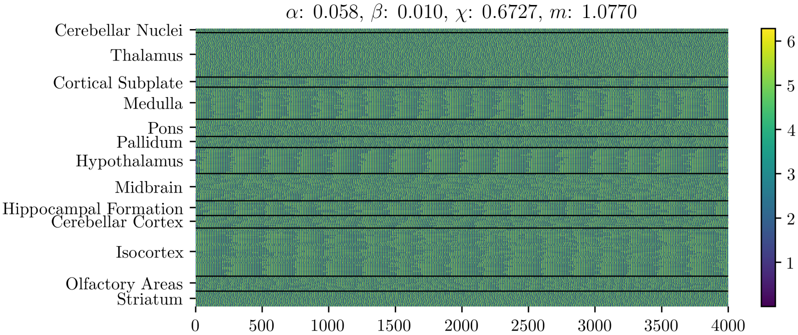


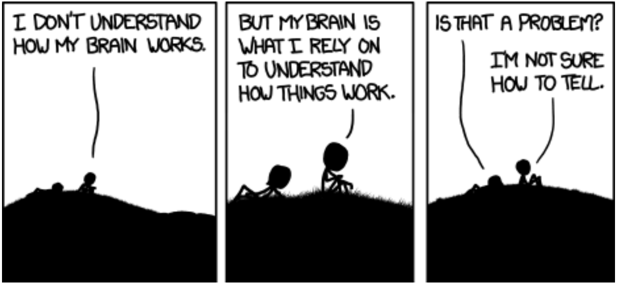
Figure: A run of the Hindmarsh-Rose simulation in the chimeric island. Synchronization is most consistently evident in the medulla, the hypothalamus, and the isocortex.

Another Viewpoint

An animation of the phase of the simulation.

Questions?

Because I've got plenty.



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