Self-sustained activity and intermittent synchronization in balanced networks

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Recent works

**Experimental Networks and Chimera States**

*Science* 371, 694 (2021)

**Scientific Reports** (2022) 12:21015

*Experimental Neurology* 373 (2024) 114652


*Chaos, Solitons and Fractals* 171 (2023) 113480


Computational modeling

- **Hodgkin-Huxley model or conductance-based model (Nobel 1963):**

  \[ C_m \frac{dV_i}{dt} = I - g_K n^4 (V_i - V_K) - g_{Na} m^3 h (V_i - V_{Na}) - g_l (V_i - V_l) \]

- **Adaptive exponential integrate-and-fire model:**

  \[ C \frac{dV}{dt} = -g_L (V - E_L) + g_L \Delta T \exp \left( \frac{V - V_T}{\Delta T} \right) \]

  \[ \tau_w \frac{dw}{dt} = a (V - E_L) - w \]

  - Low computational cost
  - Problems related to neural network
  - Describes biological patterns (Micro and Macro)
Spiral waves in IF model of CA1

- gexc = 0.125 nS
- gexc = 0.130 nS
- gexc = 0.135 nS
- gexc = 0.140 nS

Time = 2 ms
Microcircuit Reconstruction
Bulletin of the World Health Organization:

- Over 85 million people suffer from neurological diseases;
- ~50 million have epilepsy;
- The most common form is temporal lobe epilepsy (TLE);
- TLE presents high refractoriness to pharmacological treatment (~60%)
- What happens in the brain activity during an epileptic seizure?

Data from human hippocampal slices

Buchin et al. ENEURO, 2018.
Modelling epileptic seizures

- The pilocarpine model of temporal lobe epilepsy

- Pilocarpine acting through muscarinic receptors, causes an **imbalance between excitatory and inhibitory** transmission resulting in the generation of Status epilepticus

*In vivo*  
*In vitro*  
*In silico*
- Epileptic seizure ↔ normal neuronal activity
- How neuronal systems transit between these regimes?
- **Bistate firing patterns**
  I. Asynchronous firing (spikes)
  II. High synchronous firing (bursts)

**Resting state**

**Seizure (Pilo)**
Asynchronous firing in Rat

- Mean Fire Rate \(\sim 1\) Hz
- No External Noise
- Self-Sustained Activity (SSA)
Self-sustained activity of low firing rate in balanced networks

Increase the excitatory connection probability and synaptic conductance
Modelling Epileptic Networks

- Traub and Wong have proposed which epileptic synchronized burst are possible due three reasons:
  - (i) the capability of neurons to firing in burst,
  - (ii) the strong synaptic excitation, and
  - (iii) the relative disinhibition

- Epileptic and normal neuronal activity are support by the same physiological structure

- How neuronal systems transit between these regimes?
Inhibitory Effect on Synchronous Behavior

- The unbalance between excitation and inhibition generates synchronized bursts.
- Two types of loss of inhibition:
  - Decrease in synaptic strength (relative inhibitory synaptic conductance);
  - Dead of inhibitory neurons (fraction of inhibitory neurons).
Synchronization in function of $g$ (relative inhibitory synaptic conductance) and $g_{\text{exc}}$ (excitatory synaptic conductance).

The transition from desynchronous spikes to synchronous bursts of activity, induced by varying the synaptic coupling, emerges in a hysteresis loop due to bistability where abnormal (excessively high synchronous) regimes exist.
How epileptic seizures are triggered?

Mean Seizure Duration after applying SCP randomly (Asynchronous initial conditions)

Bistable Firing Pattern in a Neural Network Model


FIGURE 3 | Phase space $(w_1, V_1)$ (A,C) and time evolution of $w_1$ (B,D) for spikes (blue) and burst activity (red). The gray regions correspond to $dV_1/dt < 0$ and the black line represents $dV_1/dt = 0$ (V-nullcline).
Intermittency properties in a temporal lobe epilepsy model

And about Ion Channels?

The Roles of Potassium and Calcium Currents in the Bistable Firing Transition


Figure 2. Firing pattern for different $I_M$, $I_T$, and $I_L$ conductances. (A) Firing rate in colored ($g_T$, $g_L$)-diagram for $g_M = 0.03$ mS/cm$^2$. (B) The same as (A) for the CV. (C) Firing rate in colored ($g_M$, $g_L$)-diagram for $g_T = 0.4$ mS/cm$^2$. (D) The same as (C) for the CV. (E) Exemplar voltage traces considering different values of $g_M$, $g_L$, and $g_T$, where each parameter combination is shown atop and $V = -85$ mV before the depolarizing pulses. Other parameters are the same as Figure 1 with $I = 200$ pA.
Extracellular recording and stimulation
Large-scale biophysically detailed model of somatosensory thalamocortical circuits in NetPyNE

Fernando S. Borges1,2*, Joao V. S. Moreira1, Lavinia M. Takarabe1, William W. Lytroni1,3,4 and Salvador Dura-Bernal1,5

- > 26k neurons
- 249 populations
- > 60M synapses

In silico - high [Ca²⁺]₀
S1 model: LFP of 8k neurons (25%), running 15 sec simulations

Simulations: numprocs=1680, cell connection time = 3830.37 s, run time = 2052.19 s (15 sec), Total time = 7521.19 s

Human data: 64 events in 1200 sec ~ 17 in 300 sec

S1 model: 15 events in 300 sec
