Bistable firing patterns: one way to understand how epileptic seizures are triggered

Fernando S. Borges[1], Ewandson L. Lameu[2], Kelly C. Iarosz[3], Paulo R. Protachevicz[4], Iberê L. Caldas[3], Alexandre H. Kihara[1], Antonio M. Batista[1,4]

[1]Federal University of ABC, [2]National Institute for Space Research, [3]University of São Paulo, [4]State University of Ponta Grossa

Abstract

- Excessively high, neural synchronisation has been associated with epileptic seizures.
- Epileptic and normal neuronal activity are support by the same physiological structure.
- How neuronal systems transit between these regimes?
- We verify that the decrease in the influence of inhibition can generate synchronisation originating from a pattern of desynchronised spikes.
- In the transition from desynchronous spikes to synchronous bursts of activity, emerges a bistability where a square current pulse can:

  I - trigger abnormal synchronisation (epileptic seizures);

  II - suppress abnormal synchronisation by applying on less than 10% of the neurons.

Introduction

Epileptic seizures are associated with excessively high synchronous activities of neocortex regions or other neural populations [1]. In experiments and simulations, the reduction of excitatory and the increase of inhibitory influence have been effective in suppressing and preventing synchronized behaviors. Traub and Wong [2] showed that synchronized bursts that appear in epileptic seizures depend on neural dynamics.

Recurrent seizures can kill neurons and lead to chronic epilepsy. Evidence that supports this further is provided by abnormal anatomical alterations, such as dendritic reconfigurations, synaptogenesis, and neurogenesis. In fact, such alterations change the balance between inhibition and excitation. Several studies showed that epileptiform activities are related not only with unbalanced neural networks, but also with highly synchronous regimes.

In this work, we build a random network with neural dynamics to study synchronization induced in a bistable state which is related to epileptic seizures.

Neural Network

We consider a network composed of N=1000 (80% excitatory) adaptive exponential integrate-and-fire (AEIF) neurons coupled by means of inhibitory and excitatory synapses. Borges et al. [3,4] verified that depending on the excitatory synaptic strength and connection probability, a network of coupled AEIF neurons can exhibit transitions between desynchronized spikes and synchronized bursts. The dynamics of each neuron in the network is given by the set of equations

$$C_{\rm m}\frac{dV_i}{dt} = -g_L(V_i-E_L)+g_L\Delta_T\exp\left(\frac{V_i-V_T}{\Delta_T}\right) + I_i - w_i + \sum_{j=1}^{N}(V_{\rm REV}^j - V_i)M_{ij}g_j + \Gamma_i,$$

$$\tau_w\frac{dw_i}{dt} = a_i(V_i-E_L)-w_i$$

The membrane potential V_i and adaptation current w_i represent the state of each neuron i. The synchronous behavior in the network can be identified by means of the complex phase order parameter **R** (=1 for fully synchronized patterns). Using the mean value of ISI (inter-spike interval), and its standard deviation, we calculate the coefficient of variation **CV** (spike when CV<0.5 and burst fire patterns when CV≥0.5) [3,4].

$$R \equiv \frac{1}{N}\sum_{j=1}^{N}\exp({\rm i}\psi_j(t)) \qquad \overline{\rm CV} = \frac{1}{N}\sum_{i=1}^{N}{\rm CV}_i$$

Inhibitory Effect on Synchronous Behavior

The unbalance between excitation and inhibition generates synchronized bursts.

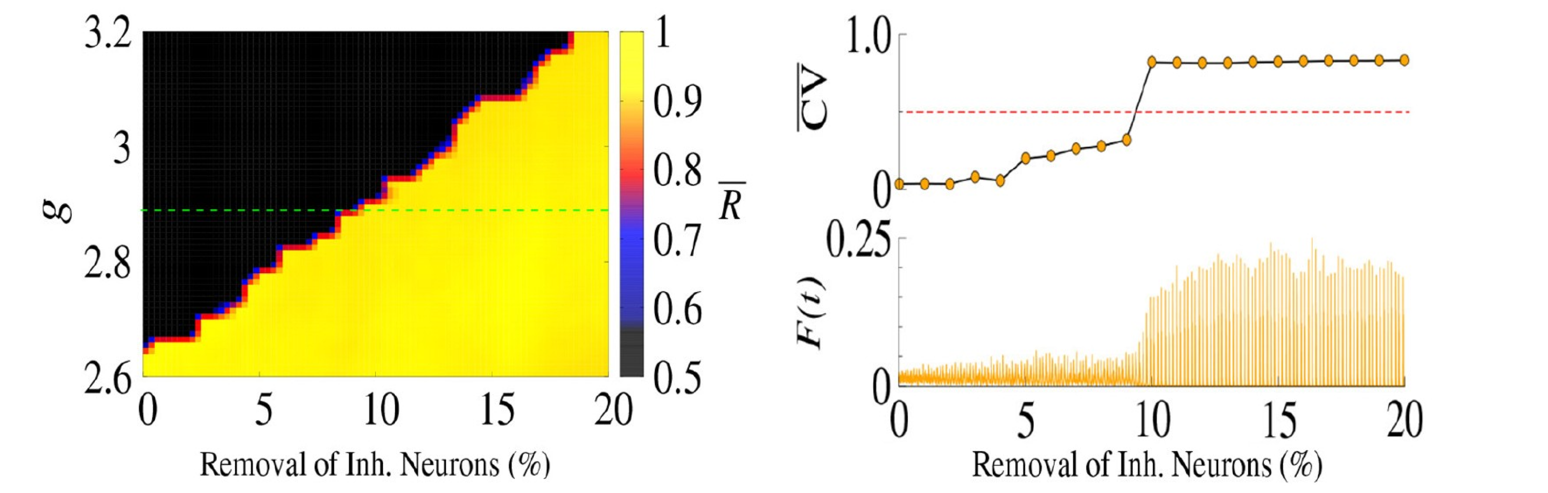

Figure 1. The time-average order parameter for g (relative inhibitory synaptic conductance) vs. the percentage of inhibitory neurons removed from the network.

Bistable Regime

We analyse synchronization in function of g and g_{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.

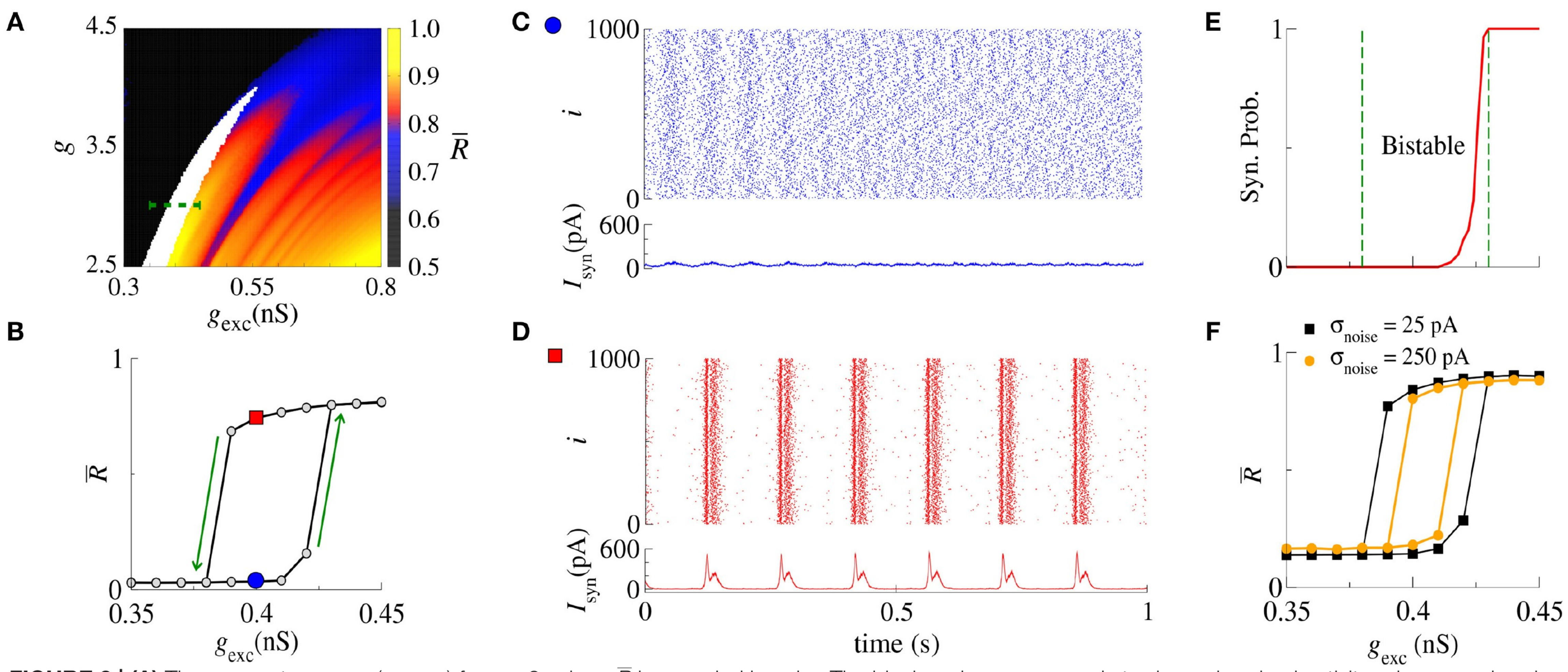

FIGURE 2 | (A) The parameter space (g, g_{exc}) for $r = 2$, where $\overline{R}$ is encoded in color. The black region corresponds to desynchronized activity, whereas colored regions indicate $\overline{R} > 0.6$ and the white region represents the bistable regime. **(B)** The bistable region indicated in the parameter space of **(A)** by means of a green dashed line. **(C,D)** Show the raster plots and I_{syn} for desynchronized spikes (blue circle) and synchronized bursts (red square), respectively. We identify bistability by checking when $\overline{R}_{backward} - \overline{R}_{forward} > 0.4$ and consider two trials for each set of parameter values. **(E)** The synchronization probability as a function of g_{exc}. **(F)** $\overline{R} \times g_{exc}$ for σ_{noise} equal to 25 pA and 250 pA.

External Square Current Pulse

We verify that a square current pulse can trigger excessively high (abnormal) synchronization.

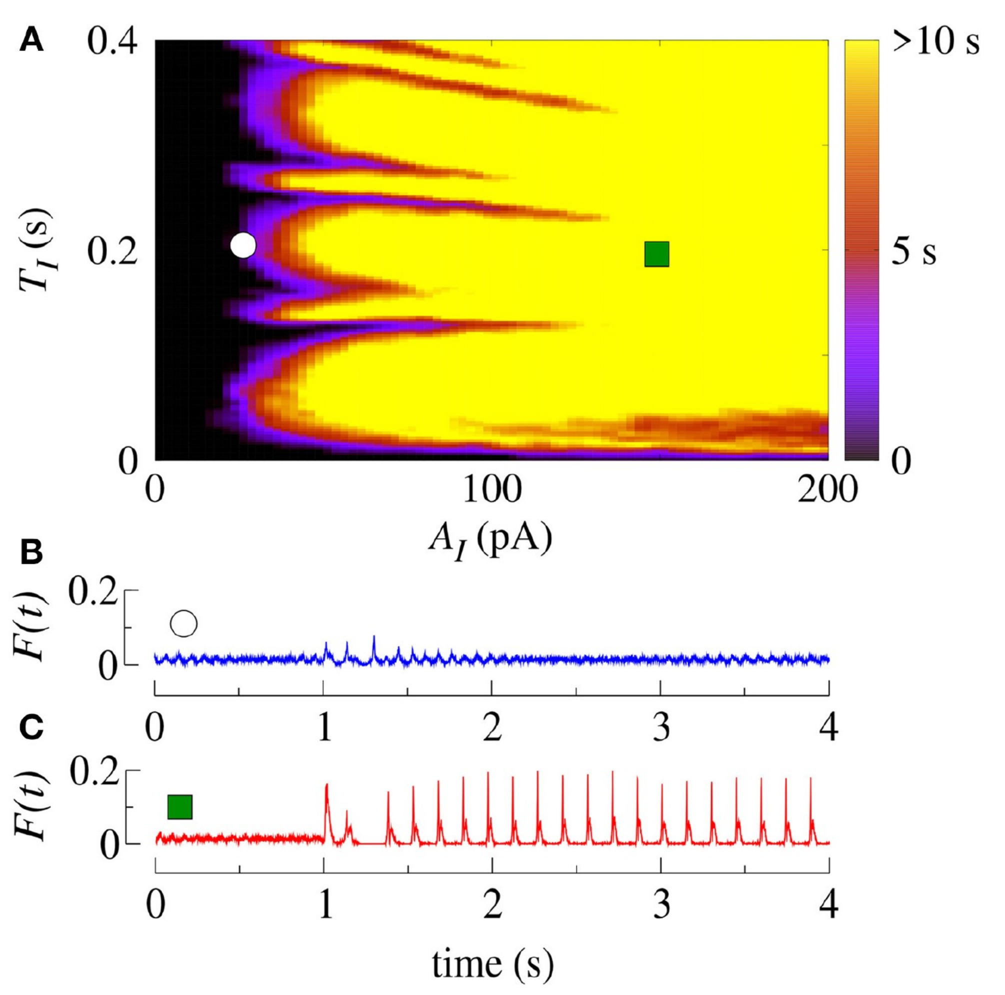

FIGURE 4 | (A) The parameter space (T_I, A_I) in the bistable regime, where the color bar indicates the time the system shows synchronized burst behavior after the application of SCP. Instantaneous firing-rate for values for **(B)** white circle ($A_I = 25$pA, $T_I = 0.2$s) and **(C)** green square ($A_I = 150$pA, $T_I = 0.2$s). Note that in this figure $g_{exc} = 0.4$nS, $g = 3$ and $r = 2$.

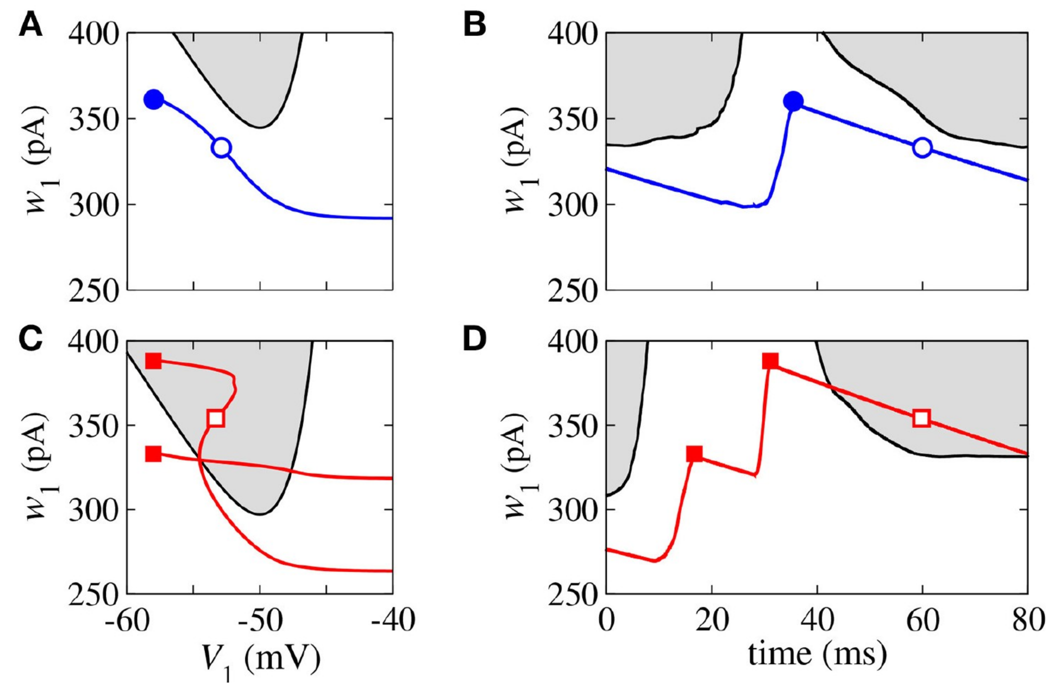

FIGURE 3 | Phase space (w_1, V_1) **(A,C)** and time evolution of w_1 **(B,D)** for spikes (blue) and burst activity (red). The gray regions correspond to $dV_1/dt < 0$ and the black line represents $dV_1/dt = 0$ (V-nullcline).

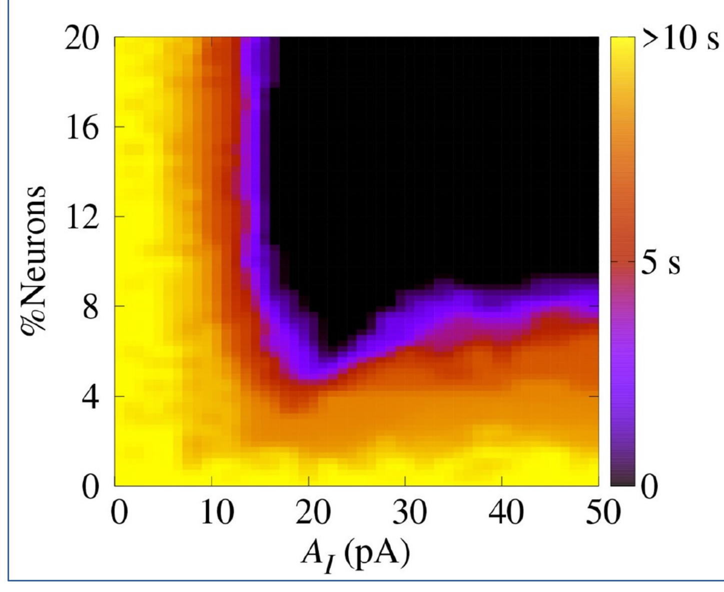

FIGURE 5 | The parameter space, where the color bar indicates the time the system shows synchronized burst behavior after the application of SCP. Number of perturbed neurons as a function of A_I. Note that in this figure we consider $g_{exc} = 0.4$nS, $g = 3$ and $r = 2$.

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