Neural oscillations level sets for activity constancy: from single neurons to networks

Guillermo Villanueva
Universitat Politècnica de Catalunya

Abstract

Neural oscillatory patterns can be characterized by a number of attributes, whose value is determined by the interplay of the participating currents. Experimental and theoretical work has shown that multiple combinations of parameters can generate patterns with the same attributes [1-4]. This endows neurons and networks with flexibility to adapt to changing environments and is substrate for homeostatic regulation [4].

At the same time, it presents modelers with the phenomenon of unidentifiability in parameter estimation. Attribute level sets (LSs) in parameter are manifolds on parameter space for which a given attribute is constant. Whether and under what circumstances the attribute LSs for individual neurons are conserved in the networks in which they are embedded and what additional network level sets emerge is not well understood.

In this work we describe a canonical (C-) model for oscillations LSs for single cells. Under certain conditions, the LSs for individual C-cells are preserved in networks of C-cells. Moreover new LSs emerge in these networks. We characterize them for both homogeneous and heterogeneous networks, where individual cells are identical or not.

Methods

The mathematical oscillator (C-model) used to represent the behavior of a neuron is given by

Neuron model
$$\begin{cases} \dfrac{dx}{dt} = \lambda x - \omega y - (bx + ay)(x^2 + y^2) \\ \dfrac{dy}{dt} = \omega x + \lambda x + (ax - by)(x^2 + y^2) \end{cases}$$

It is a type of the so-called Lambda-Omega systems with a single limit circle in which degeneracy is easily characterized. Amplitude and frequency LSs are given by

- Amplitude level sets $\rightarrow \dfrac{\lambda}{b} = K_a$
- Frequency level sets $\rightarrow \omega + a\dfrac{\lambda}{b} = K_f$

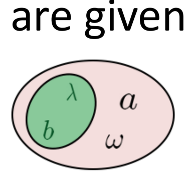


Figure 2. Degeneracy scheme

The general form of the linear connectivity networks of Lambda-Omega systems are

Network model
$$\begin{cases} \dfrac{dx_k}{dt} = \lambda_k x_k - \omega_k y_k - (b_k x_k + a_k y_k)(x_k^2 + y_k^2) + \sum_{j=1}^{N} \alpha_{k,j} x_j \\ \dfrac{dy_k}{dt} = \omega_k x_k + \lambda_k x_k + (a_k x_k - b_k y_k)(x_k^2 + y_k^2) \end{cases}$$

where $A = \{\alpha_{k,j}\}$ is the connectivity matrix

Introduction

Degeneracy in Biological Systems

The Activity-dependent homeostatic regulation (ADHR) mechanism constitute a negative feedback system through which neurons are able to restore their properties and compensate changes due to perturbations. It allows neurons to maintain their so-called target activity level.

The idea a given that target activity level can be achieved with different parameter combinations and that almost identical activity can arise from different intrinsic properties has both experimental and theoretical evidence [1,5].

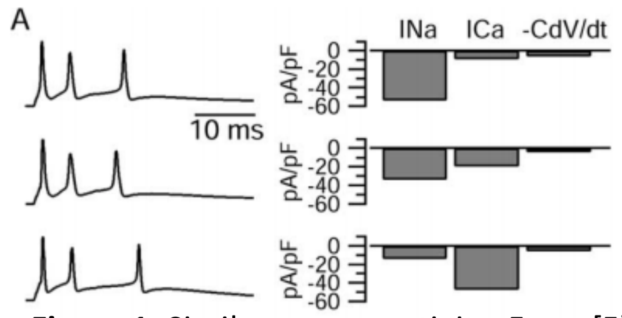


Figure 1. Similar neuron activity, From [5]

The fact that the target activity level of a neuron/networks is presumably an electrical activity pattern rather than a set of parameters on a given model give rise to the degeneracy in biological systems, which have important consequences on the modelling task.

Parameter Estimation Unidentifiability

Neuronal parameter optimization is the process of identifying sets of parameters that lead to a desired electrical activity pattern in a given neuron or neuronal network model that is not fully determined by experimental data.

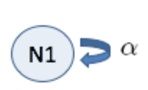
Structural degeneracy (of a given parameter model) refers to the situations where multiple sets of parameters values can produce the same observable output, therefore making the inverse problem ill-posed. It is only based on the inherent structure of a given model. If we create ground truth (fake) data using a particular set of parameters values, it is not clear (¿?) how to retrieve the biophysical parameter values used.

Attribute Level Sets (LSs) are the set of points on parameter space for which a given attribute is constant.

Results

Attribute Level Set Preservation

- The self-connected cell do not preserve LSs.



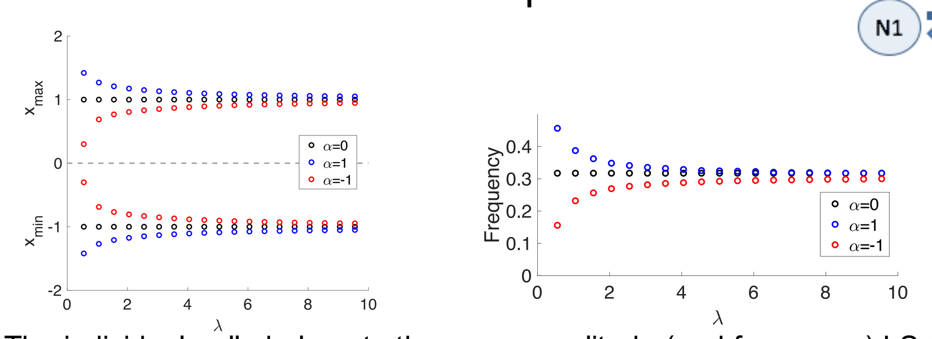


Figure 3. The individual cells belong to the same amplitude (and frequency) LS (K_a=1). Left: amplitude envelope diagram as a function of λ. Right: frequency diagram as a function of λ.

- Type-I (cells belong to the same amplitude and frequency LS) and type-II heterogeneous (cells belong to different amplitude LSs) two-cell networks preserve individual LSs on 2-dimmensional manifolds on parameter space.

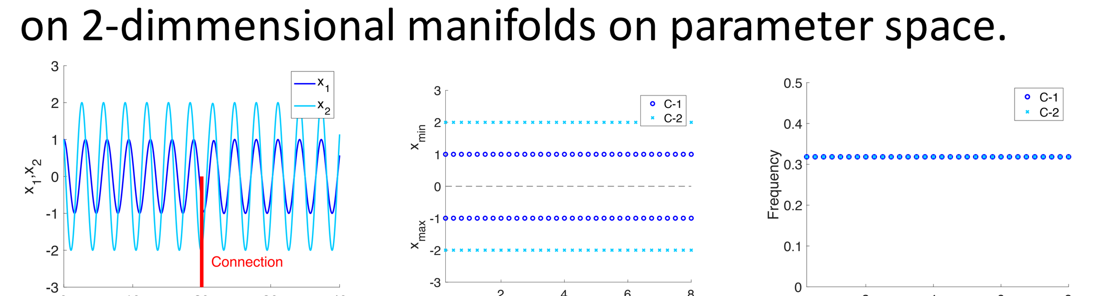
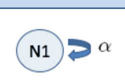
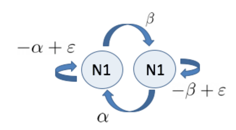


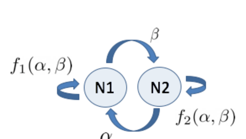
Figure 4. Synchronized network preserving LSs. Left: voltage traces before and after the connection. Middle: amplitude envelope diagram for values (λ_1, b_1) belonging to the same individual amplitude LS (K_a=1). Left: frequency diagram for the same values of (λ_1, b_1).

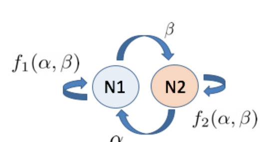
- Gap junctions preserve LSs in type-I heterogeneous networks. $A_{\text{gap-juntion}} = \begin{pmatrix} -\alpha & \alpha \\ \beta & -\beta \end{pmatrix}$

Newly Emerged Network Level Sets

- The self-connected cell
  

  - ✓ 2-dimensional total-degenerated LSs on the intrinsic parameter space.
- (Symmetrical) Homogeneous Networks
  

  - ✓ 2-dimensional total-degenerated LSs on connectivity parameter space.
- Type-I Heterogeneous Networks
  

  - ✓ 1-dimensional total-degenerated LSs on connectivity parameter space (Figure 5).
- Type-II Heterogeneous Networks
  

  - ✓ 1-dimensional total-degenerated LSs on the intrinsic parameter space of a single cell.

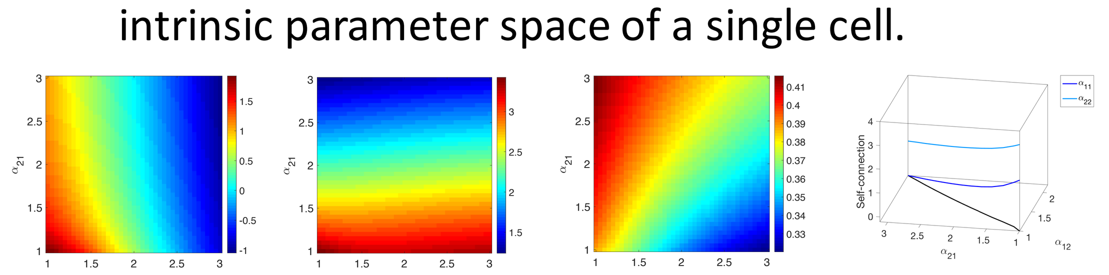


Figure 5.:Left and Middle-left: amplitude LS on connectivity parameter space. For each pair of cross-connectivity parameters there are the values of the self connectivity parameter α_{11} (Left) and α_{22} (Middle-left) such as the network amplitude is preserved. Middle-right: frequency for each point of the amplitude LS. Right: 1-dimensional total-degenerated LS on connectivity parameter space.

Conclusions

- ✓ Gap junctions do not preserve LSs on type-II heterogeneous networks (cells belong to different amplitude LS). However a readjust in self-connectivities guarantees LSs preservation.
- ✓ Several LSs have been computed (1,2-dimensional LSs on 1,2,3 or 4-dimensional parameter spaces).
- ✓ The type of network (homogeneous, heterogeneous, connectivity structure,…) does affect predictions in [3].
  *Prediction in [3]: If a particular homeostatic mechanism maintain m independent characteristics (or attributes) of neuronal activity, then at least m parameters must be changed as a response to a perturbation in one parameter of the system.

Future Work

- ✓ Relation between model symmetries and LSs preservation.
- ✓ Methods for disambiguation of degeneracy (noise, entrainment,…)
- ✓ Robust, non model-dependent and optimized algorithms to compute LSs
- ✓ New notions of a network LSs

Contact Information

Guillermo Villanueva
Universitat Politècnica de Catalunya
Email: guillermovillanuevabenito@gmail.com

References

[1] Prinz, A. A., Bucher, D. and Marder, E. Similar network activity from disparate circuit parameters. *Nat Rev Neurosci*, 7:1345-1352 (2004)
[2] Rotstein, H. G., Olarinre, M. and Golowasch, J. Dynamic compensation mechanism gives rise to period and duty cycle level sets in oscillatory neuronal models. *J Neurophysiol*, 116:2431-2452 (2016).
[3] Olypher, A. V. and Calabrese, R. L. Using constraints on neural activity to reveal compensatory changes in neuronal parameters. *J Neurophysiol*, 98:3749-3758 (2007).
[4] Olypher, A. V. and Prinz, A. A. Geometry and dynamics of activity-dependent homeostatic regulation in neurons. *J Comp Neurosci*, 28:361-374 (2010).
[5] Swensen AM, Bean BP. Robustness of burst firing in dissociated purkinje neurons with acute or long-term reductions in sodium conductance. J Neurosci. 2005 Apr 6;25(14):3509-20.