

March 30, 2023

RE: Manuscript submission

Dear editor of PLOS Computational Biology

We would like to submit our manuscript **“Towards a unified framework for metastability in neuroscience”** for consideration as a Perspective article in *PLOS Computational Biology*.

In the article, we start by arguing that the currently existing formulations for metastability, a phenomenon characterized essentially by a succession of transient states CITE, have several conceptual differences, as they are mostly restricted to specific contexts, and a general framework is still missing. To defend this, we review some major works studying metastability in the brain.

As a solution to this, we propose a general, **context-independent, framework for metastability**. First, we provide a general definition of metastability, which acts as an umbrella term that encompasses most of the existing formulations and observations in neuroscience.

This definition naturally connects to the theory of dynamical systems, which allows us to extract a **general dynamical principle for metastability.** This principle can be implemented in a variety of specific mechanisms, which we then discuss and illustrate with didactic examples. Some of these mechanisms have been proposed in the literature, but in less theoretical detail, and some are new.

We believe that, by unifying experimental observations to rigorous theory, this framework can be adopted and extended by a wide range of researchers in both experimental and theoretical neuroscience, and also in dynamical systems theory. We have taken care to write the Perspective in a didactic way that will be clear to researchers in all these areas. We hope this will help to unite neuroscience and dynamical systems theory, which can open the way for several lines of research, such as identifying dynamical mechanisms from experiments and using this knowledge to improve tools for predicting and controlling brain behavior.

Thank you very much for considering our manuscript. We look forward to further correspondence on this submission.

Sincerely,

Kalel Luiz Rossi, on behalf of all co-authors

Reviewer suggestions:

Good:

**Neuroscience**

- Giancarlo La Camera: important work on metastability, published in Plos Comp Bio this year (2023); has the recent review on metastability also; if not him also Braden A. W. Brinkman (co-worker)

- Mikhail Rabinovich: work on heteroclinic cycles/metastability; published in plos comp bio

- Valentin Afraimovich: work on heteroclinic cycles/metastability; published in plos comp bio

- Scott Kelso: a lot of works on metastability; we complement/extend his views

**Dynamics:**

- Peter Ashwin: very good researcher in dynamics, work on heteroclinic cycles and transients

Unsure:

- Fingelkurts: lot of works on metastability, no clue about them though

- Karl Friston: we agree a lot, but he might just be too busy

Probably bad:

* Steven schiff: seemed to like the work, but not very related; Lyle didnt like his talk also
* Gustavo deco: I'd avoid, since their group is pretty much the only that we disagree with; what about Viktor Jirsa and Morten Kringelbach?
* Hastings: understands transients, but not very strong in neuro or dynamics
* Tsuda and Kaneko: better not I think

Editor:

Alireza Soltani, Dartmouth College, UNITED STATES -- editored camera's recent paper on metastability