

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*.

Recently in the literature, many studies have pointed to empirical evidence of the metastable functioning of the brain. Interestingly, across such studies, the formulations for metastability have several conceptual differences, as they are mostly restricted to specific contexts. Therefore, a unifying framework for metastability –able to reach a broad audience-- is still missing in the literature. First, to illustrate this deficiency, we review various studies containing observations, and formulations, of metastability in the brain.

As a solution, we propose a general, context-independent framework for metastability. We start by providing a general definition of metastability, which acts as an umbrella term encompassing 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.

By unifying experimental observations to rigorous theory, this framework can be adopted and extended by a wide range of researchers in experimental and theoretical neuroscience and dynamical systems theory. We have written the Perspective in a didactic way that will be clear to researchers in all these areas. Our framework 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