

To the Editor:

We attach for your consideration our manuscript, *Homeostatic mechanisms may shape the type and duration of oscillatory modulation*, for publication as a **Regular Research** article in *Journal of Neurophysiology*. This work was previously reviewed as **Rapid Report**, under JN-00259-2019. It was felt though the work was promising and appropriate the paper required major revisions, which have now undertaken leading to this new submission.

Oscillations are nearly as ubiquitous in the mammalian brain as chemical neuromodulators, like Acetylcholine. Both can control neural excitability. However unlike neuromodulators—whose interactions with homeostasis are well established—the interplay between oscillations and homeostasis is not well understood.

We conducted a computational study of hippocampal pyramidal cells to answer three basic questions. One, do tonic oscillations--generated with biologically-consistent parameters--engage homeostatic mechanisms? Two, does homeostasis in turn change the oscillation's function? Three, do short bursts of oscillation have distinct effects from tonic oscillations?

We report a surprising—even paradoxical—result: Ca^{2+} -mediated homeostasis causes normally synchronizing AMPAergic oscillations to become inhibitory and desynchronizing. We conjecture this is an answer to the fundamental question of why the theta rhythm is inhibitory. In pyramidal cells GABA doesn't generate new action potentials and so provokes no homeostatic response. This leaves hippocampus cells with the largest possible dynamic range. Likewise in our model, bursts of excitatory oscillation minimally interact with the slow homeostasis time constant and so retain their typical excitatory effects. That is, homeostasis might also explain why AMPAergic oscillations in cortex tend to appear as bursts.

We use a small set, of admittedly simple, simulations to speak to fundamental questions about why oscillatory dynamics appears as they do in the mammalian brain. Our results suggest the interplay between oscillations and homeostasis might be as complex, and as important, as the well known interplay between neuromodulators and homeostasis.

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