

## Stability of recurrent neural networks with activity-dependent homeostatic scaling of excitability

Michiel W.H. Remme<sup>1,2</sup> and Wytse J. Wadman<sup>1</sup>

<sup>1</sup> Center for NeuroScience, Swammerdam Institute for Life Sciences, University of Amsterdam, <sup>2</sup> Group for Neural Theory, Département d'Études Cognitives, École Normale Supérieure and Collège de France

Neuronal and synaptic properties show significant plasticity. At the same time, neurons have a limited dynamic range over which they are sensitive to changes in the synaptic input. Consequently, in order for neurons to remain functional, neural excitability needs to be continuously matched to the mean synaptic input level. Experiments have shown that neurons indeed regulate membrane conductances in response to altered input activity levels, thereby changing their excitability on the time scale of many hours up to days<sup>1</sup>. This homeostatic scaling of excitability (HSE) can also occur on time scales down to tens of minutes, suggesting that this process has a prominent role in neural functioning on different time scales<sup>2</sup>.

As neurons are embedded in networks, adaptation of the excitability at the single neuron level will affect the dynamics at the network level. This is especially relevant in highly recurrent networks of excitatory and inhibitory neurons, which are ubiquitous in the neocortex. Experimental and theoretical work has illustrated that such networks show a delicate balance between excitation and inhibition for maintaining network stability. Disturbance of this balance can lead either to quiescence or to runaway excitation.

Here we investigated the consequences of HSE for dynamics of recurrent networks, in particular its capacity to compensate for ongoing plasticity and maintain the network in a functional state where all cells function within their dynamic range. We addressed this issue using both mathematical analysis and numerical simulations. First, we analyzed the requirements for stability of adapting recurrent networks using a mean-field approach, describing the activity levels of interacting excitatory and inhibitory neurons at the population level. Based on experimental results, HSE is implemented as activity-dependent shifts of the input-output function<sup>2</sup>. The results show that stability of the adapting network depends critically on the relationship between the adaptation time scales of the two neuron populations combined with their respective input-output gains. We subsequently modeled recurrent networks consisting of excitatory and inhibitory leaky integrate-and-fire neurons showing HSE. The results confirm that stability of such networks requires a specific relationship between the time scales of adaptation: inhibitory neurons need to adapt sufficiently slow compared to the excitatory neurons. We find that in stable, adapting networks, HSE can maintain all neurons in the network in a functional state, rendering network activity robustly stable for varying levels of input. HSE can also, up to a certain limit, compensate for changes in network connectivity, e.g. resulting from synaptic plasticity or degenerative loss of neurons. However, while HSE can keep neurons in their dynamic range under such conditions, it will affect the risk of network instabilities. This suggests that the interplay of HSE (single cell intrinsic properties) and network level processes (connectivity changes) may play a significant role in pathological conditions, such as epilepsy.

[1] Desai et al. Plasticity in the intrinsic excitability of cortical pyramidal neurons. *Nat Neurosci*, 2(6):515–20 (1999).

[2] van Welie et al. Homeostatic scaling of neuronal excitability by synaptic modulation of somatic hyperpolarization-activated  $I_h$  channels. *Proc Natl Acad Sci U S A*, 101(14):5123–8 (2004).