Hallmarks of habituation: a biochemically-plausible model

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Living systems have complex information processing capabilities. Arguably the most remarkable is learning, which enables organisms to modify their behavior in response to past stimuli. In this work we focus on habituation, one of the non-associative forms of learning. Habituation is commonly defined as a progressive decrease in response upon repetitive sensory stimulation (Fig. 1). A multitude of different organisms, behaviors, and experimental approaches have been used to study habituation, but still surprisingly little is known about the underlying mechanisms [1].

There are several characteristics of habituation that are widely conserved from single cell organisms to invertebrates and vertebrates. For example, the dynamics of habituation is not solely determined by the number of stimuli but additionally depends on the frequency and intensity of stimulation. These hallmarks are called frequency and intensity sensitivity [2].

Frequency sensitivity means more frequent stimulation produces more rapid and/or more pronounced habituation. On the other hand, more intense stimuli generates less rapid and/or less pronounced response decrement (intensity sensitivity).

In this study we have set a biochemically-plausible mechanistic model that can account for the frequency and intensity sensitivity hallmarks of habituation in an unified framework, which has not been done yet to our knowledge.

Following an idea of a habituation model in a discrete time setting [3], we show that concatenation of two incoherent feedforward motifs (IFF) can explain the central effects of the stimulation frequency on the dynamics of habituation, *i.e.*, frequency sensitivity. The primary characteristic lies in the different timescales of the two cascaded motifs, resulting in a distinct pattern of memory formation based on the frequency of stimulation. Additionally, our concatenated IFF model comprehensively obeys the intensity sensitivity hallmark of habituation.

On the other hand, we have also examined a negative feedback architecture (NF), which has been previously suggested as a possible circuit underlying habituation [4]. As with the IFF model, we concatenated two NF circuits. We have found a region in the parameters' space that exhibits robust solutions, which account for the nontrivial hallmarks of frequency and intensity sensitivity.

Our biochemically inspired model of habituation sheds some light on the possible mechanisms underlying the well-conserved frequency and intensity sensitivity hallmarks.

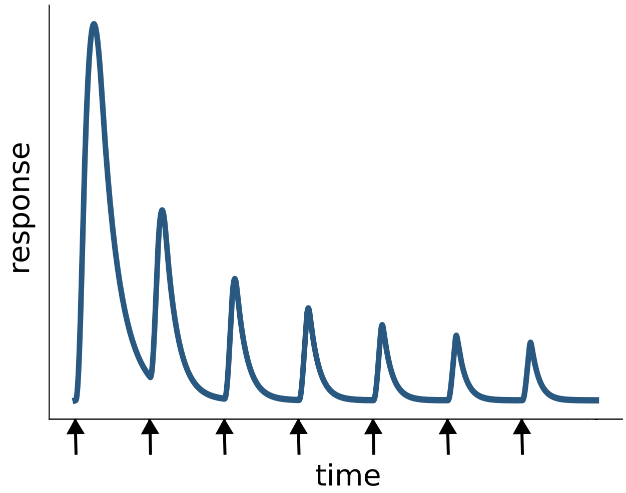

Fig. 1. Schematic illustration of habituation. The response diminishes upon repeated stimuli (black arrows). For additional properties of habitation, see [2].

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