QUANTITATIVE CHARACTERISATION OF INFORMATION TRANSMISSION IN A SINGLE NEURON

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ABSTRACT

In this work, information theory has been employed to study the information transmission at the mossy fibre-granule cell synaptic relay of the cerebellum. Granule cells (GCs) are characterised by a limited number of excitatory and inhibitory synaptic inputs (4 typically), which allowed us to investigate the cell's input space extensively. Here, we present some results of our information theoretic analysis (mutual information, and stimulus-specific information) of the transmission properties of a single GC obtained by using both a detailed mathematical model and whole-cell patch recordings in slices. Our findings indicate that a major amount of information is conveyed by the spike time correlations across the inputs and that long-term synaptic plasticity affects the information transmission process significantly. Interestingly, long-term synaptic potentiation (LTP) increases the average amount of information transmitted, but not necessarily the contribution of the most informative set of stimuli. In addition, the effect of Golgi cell inhibition on mossy fibre-granule cell information transfer has been investigated using numerical simulations only. Synchronisation of Golgi cells improved information transmission through the mossy fibre-granule cell relay. This observation suggests that theta-frequency oscillations (3-12 Hz), which are observed in the granular layer in vivo and are thought to reflect a high level of Golgi cell synchronisation, may enhance information transmission along the mossy fibre pathway.

KEY WORDS

Information transmission, cerebellum, long-term plasticity

1 Introduction

Neurons process input spike information in complex ways and many factors enter into play. Synapse dynamics include numerous interacting mechanisms as neurotransmitter release, diffusion and post-synaptic receptor activation, and intrinsic electroresponsiveness. Many of these factors may undergo activity-dependent changes, which have major effects on the neuron transmission properties.

This complex neural processing can be analysed by comparing the information content in the neuron inputs with that in its output, i.e. by quantifying how much information the neural responses convey about the input stimuli. In this approach, neurons are considered as stochastic communication devices and information theory [1] provides the mathematical framework, e.g. mutual information (MI), to quantify their transmission properties. Estimating MI requires to determine the probability distribution of the output spike trains given any input spike train. This method implies to sample the cell's input space exhaustively and is usually unfeasible even for a single neuron due to: (i) the complexity of the nonlinear processing at the level of individual synapses, (ii) the large number of synaptic inputs (typically 10^3-10^4), and (iii) their location on spatially extended dendritic trees with active transmission properties[1]. A remarkable exception is provided by cerebellar granule cells (GCs). These neurons are characterised by a compact electrotonic structure [3] and a very low number of synapses receiving mossy fibre (MF) afferents (4 on average). Moreover, their synaptic transmission dynamics and plasticity have been extensively studied (see [4] and references therein). In this study we present an information theoretic analysis (mutual information and stimulus-specific information) of the transmission properties of a single GC using both a detailed mathematical model and whole-cell patch recordings in slices. In particular, we focus on how the information transmitted by a GC is regulated by long-term synaptic plasticity occurring at the MF-GC synapses.

2 Information transmission in the cerebellar granular layer

The cerebellar input layer is of particular interest: it is characterised by a huge number (10^{11}) of tiny cells (granule cells) that, according to the classical theories by Marr

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[1] Previously, approximations via dimensionality reduction have been attempted, focusing on the effect of an individual synapse while considering the rest of the dendritic inputs as background noise [2].

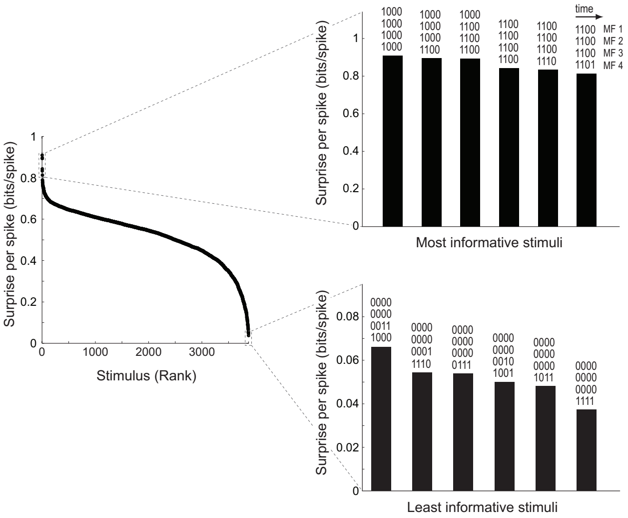

Figure 1. We assessed the surprise per spike of all stimuli (left diagram) and examined in more detail the set of stimuli providing the largest (and the smallest) contribution to the overall information. The upper-right panel shows that the 6 most informative stimuli were those having multiple coincident spikes across the four mossy fibres. The lower-right panel displays the least informative input patterns.

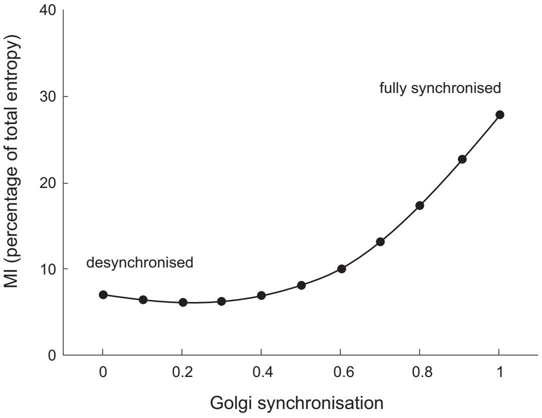

Figure 2. MI computed between the mossy fibre inputs and the granule cell responses as a function of the synchronisation of the Golgi cell inhibition onto granule cells.

and Albus [5, 6], are able to encode afferent information into a sparse representation that facilitates discrimination of very similar inputs. In this study, we focus on the MF-GC synapse, which is an important site of plasticity of the cerebellar granular layer. MFs are the primary afferents to the cerebellar cortex and convey multimodal sensory inputs to the GCs. Despite their relative simplicity, GCs play an important role in the cerebellum processing. Indeed, they are characterised by a complex temporal dynamics [7, 8] capable of regulating the input-output relationship via synaptic gain modulation [6, 9]. GCs are inhibited by the activity of the Golgi interneurons, which are thought to be responsible for the theta-frequency oscillations (3-12 Hz) observed in the granular layer in vivo. We will disregard the effects of Golgi inhibition in the first part of this paper; then, we will show some preliminary analysis of the effect of Golgi activity in the last part.

Induction of long-term synaptic potentiation (LTP) at MF-GC synapses alters the spiking response of GCs [4]. We have measured the information transmitted through a single GC before and after induction of LTP at MF-GC synapses, a condition that modifies the neutransmitter release probability p at the MF synaptic terminals [10]. Experimental data were obtained by in vitro whole-cell patch recordings of GCs. To measure MI, one to four of the MFs were stimulated by a set of spike trains that mimicked the discharge of GCs following punctuate tactile stimulation in vivo [11]. Moreover, we have developed a Hodgkin-Huxley model of a single GC, in which the stochasticity of neurotransmission is accurately reproduced [4]. The same stimulation protocol was employed to run numerical simulations and MI was measured while varying the release probability p at the MF-GC synapses [12].

In a typical experiment or simulation all spike trains were digitalised (using 10 ms time bins for the input, and 6 ms for the output), and a controlled set of stimuli $\mathcal{S}$ (each stimulus being formed by 4 input spike trains) was chosen. Then, we recorded the elicited neural responses $r \in \mathcal{R}$ when one stimulus $s \in \mathcal{S}$ was repeatedly presented with a known a priori probability $p(s)$. Once we collected all the data, we estimated the corresponding joint probabilities, $p(r, s)$, and the probability distribution of the responses averaged over the stimuli, $p(r)$. The mutual information was then computed:

$$I(\mathcal{R};\mathcal{S}) = \sum_{s\in\mathcal{S}}\sum_{r\in\mathcal{R}} p(r,s)\ \log_2\left[\frac{p(r,s)}{p(r)p(s)}\right] \tag{1}$$

Because limited sampling induces a positive bias in MI values, we corrected our MI estimates by means of a second order extrapolation [13].

We observed, both in the experiments and in the simulations, that MI increased as a function of p. This corroborated the working hypothesis that LTP would enhance MI and suggested that optimal transmission may correspond to large p values. To further investigate this hypothesis, we performed a series of simulations to assess the effect of LTP upon the information transmitted by the subset of the most informative stimuli [14]. MI is an average measure of *informativeness* of a set of stimuli. In order to isolate the contribution of a single stimulus, we used the stimulus specific information measure (*surprise*)[15, 16]:

$$I(s) = \sum_{r\in\mathcal{R}} p(r|s)\log_2\frac{p(r|s)}{p(r)} \tag{2}$$

By measuring the surprise of the most informative stimuli as a function of the average release probability p, we found that it initially grew exponentially, and then it saturated at a plateau for $p >= 0.5$. So, although MI was maximised by LTP, the efficient transmission of the most informative stimuli already occurred at intermediate p values. These values are of the same order to those measured in vitro in standard conditions [10]. It also suggests that at higher p values, it is the least informative stimuli that increased their overall contribution to MI and not the most informative ones. These theoretical findings indicate that neurons as well as synaptic plasticity mechanisms may have evolved for optimising the transmission of a limited set of relevant stimuli.

We then inspected the input spike train patterns to identify those features (e.g. discharge frequency and spatio-temporal structure) that characterise efficient information transfer in the GC. By measuring the contribution of single stimuli to information as a function of the correlation across the MFs, we found that the most informative stimuli were characterised by the presence of multiple coincident spikes across the four MFs (Fig. 1), whereas no coincident spikes were observed in the least informative inputs. Notice that the most informative stimulus of Fig. 1 has the same number of spikes of the least informative one. Our results showed that the spatio-temporal structure of the input spike train is more relevant than the input spike count to information transmission. Indeed, correlated activity across the MF afferents largely contributed to information transmission in the GC. This findings extends a previous study showing that the GC firing requires the co-activation of two or more MFs [3].

We also ran a series of numerical simulations to study the effect of Golgi inhibition on information transmission. We considered four Golgi cells (GoCs), one for each MF-GC synapse, firing periodically with a frequency of 10 Hz with different random phases. We then measured the impact of the synchronisation of the four GoCs on the amount of information transmitted by the GC. As shown in Fig. 2, the synchronisation of GoCs largely improved information transmission through the MF-GC relay. This preliminary result supports the hypothesis that a synchronous oscillatory behaviour of the GoCs might be relevant to the regulation of information transmission at the level of the MF-GC synaptic relay.

To summarise, we adopted an information theoretic approach to characterise the transmission properties of a single GC by means of both numerical simulations and whole-cell patch clamp recordings in slices. Our findings indicate that a major amount of information is conveyed by the spike time correlations across the inputs and that long-term synaptic plasticity affects the information transmission process significantly. Interestingly, although LTP increases the average amount of information transmitted, it does not necessarily increase the contribution of the most informative stimuli.

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