Synaptic activity and excitability modulates information transfer in Purkinje cells: a modeling study

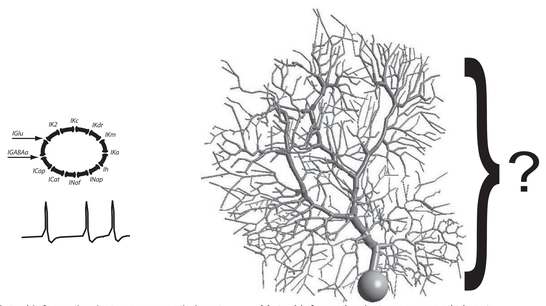
Allan D. Coop[1], Hugo Cornelis[1], Fidel Santamaria[2]

1 Department of Epidemiology and Biostatistics,University of Texas Health Sciences Center at San Antonio, San Antonio, TX 78229;
2 Department of Biology, SiViRT and Neurosciences Institute, University of Texas at San Antonio, San Antonio, TX 78249

SiViRT CENTER FOR SIMULATION, VISUALIZATION, AND REAL TIME PREDICTION

Introduction

Synaptic information is transfered from synapses, to dendrites, to the soma. This is particularly true in Purkinje cells, since there are no backpropagating action potentials.



Mutual information between synaptic input:
Spikes

Mutual information between synaptic input:
Dendritic segments
Dendritic currents
Whole dendrite
Soma

Traditional approaches collapse the information capacity of a neuron into a point source process at the soma. Here we want to understand how the membrane excitability and synaptic activity affect how synaptic information is coded in a large dendritic tree.

Methods

Purkinje cell model

The simulations consisted in randomly activating all the excitatory and inhibitory synapses at constant Poisson firing rates. We used four different combinations of excitatory and inhibitory synaptic activity that resulted in the same firing rate at the soma of the Purkinje cell. We ran simulations for up to 400 s saving the value of all dendritic and synaptic currents every 100 µs. In order to avoid initial condition effects the first 5 seconds of all traces were not used for the analysis. Simulations were run with a pre-release version of the new GENESIS 3 software (http://www.genesis-sim.org/) in a cluster at UTSA (http://www.cbi.utsa.edu).

Statistical analysis

In order to simplify the analysis we monitored the total value of the synaptic or dendritic currents. We also chose to use the total excitatory current because then the results of our study could be mapped to dynamic current clamp experiments.

For the purposes of comparing the changes due to background activity we normalized the value of all currents from 1-100 and binned the data in 1000 equally spaced bins. All the analyses described here were performed with the normalized current values.

Initial characterization of currents was done by calculating the histograms under all the different combinations of synaptic activity. Further analysis consisted in calculating the cross-correlation between the excitatory synaptic input (IGlu) and dendritic currents.

Mutual information

The entropy was calculated as

$$H(x) = \sum_i p(x_i) \log_2 P(x_i)$$

where p is the probability of seeing value x_i. The conditional entropy was calculated as

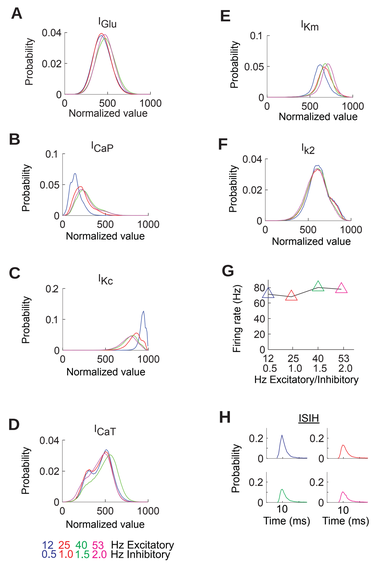
$$H(y|x)=\sum_j \sum_i p(x_i,y_j) \log_2 p(y_j|x_i)$$

In our case, x is the input signal (IGlu) and y any of the dendritic currents. Conditional probability distributions matrices were calculated based on the binned traces. Finally, the mutual information was calculated:

$$I(y|x)=H(y)-H(y|x)$$

It is well known that the value of I can be biased due to the binning process and finite size of the data being analyzed (Panzeri et al., 2007). We used a recently developed toolbox in Matlab (Natick, MA) that allows the accurate calculation of the different information measurements and compensation for potential biases (Magri et al., 2009). The value of I can be biased if the joint probability distribution of the two traces being analyzed is scattered and does not fill out the joint probability space (1000 x 1000 entries). The ratio N/m has been shown to determine the strength of such a bias, where N is the number of non-zero entries in the joint probability distribution and m number of non-zero entries of probability distribution of the stimulus. If N/m is less than 1 then the value obtained from calculating the mutual information is biased. All our simulations had an N/m > 1.

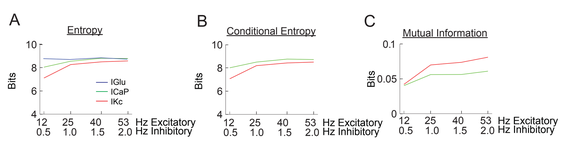
1 ICaP and IKc are strongly modulated by synaptic activity



Probability distribution of synaptic and dendritic currents. **A**: The Purkinje cell model was stimulated with pairs of excitatory and inhibitory synaptic activity. The total excitatory synaptic current (IGlu) remained practically constant for all the combinations of excitatory and inhibitory activity (activity in Hz). **B**: Probability distribution of the ICaP in response to the different combinations of excitatory and inhibitory activity in A. **C**: Probability distribution of IKc for the same simulations in B. **D-F**: The probability distribution of the other dendritic currents remained practically independent of level of synaptic activity. **G**: The average firing rate at the soma remains constant for all combination of synaptic activity. **H**: The Purkinje cell inter-spike distributions for each combination of synaptic activity in A have the same mean and standard deviation.

2 Modulation of information content by synaptic activity

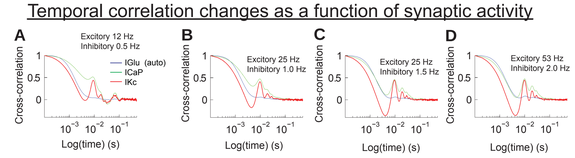
Mutual information ratios change as a function of synaptic activity



Calculating the amount of excitatory synaptic information being carried by dendritic currents. **A**: Entropy of the IGlu, ICaP, and IKc. **B**: Conditional entropy of H(ICaP|IGlu) and H(IKc|IGlu). **C**: Mutual information for I(ICaP,IGlu) and I(IKc, IGlu) calculated from A and B; e.g. I(ICaP,IGlu)=H(ICaP)-H(ICaP|IGlu). B and C were calculated with a 1 ms time difference between IGlu and the dendritic currents. All calculations were bias corrected using the Panzeri-Treves method.

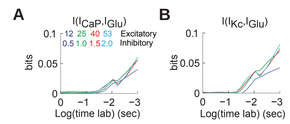
3 Temporal correlation of information content

Temporal correlation changes as a function of synaptic activity



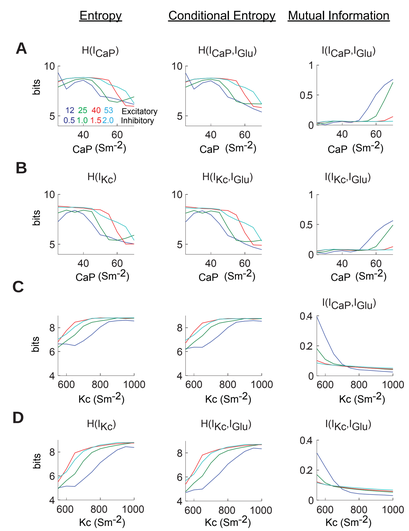
Cross-correlation analysis of total synaptic excitatory input and dendritic currents. The figures show the auto-correlation of the synaptic current (IGlu, blue), and the cross-correlation of IGlu with ICaP (green), and IKc (red). We repeated this analysis for all the combinations of synaptic activity (**A-D**).

This correlation is also reflected in Mutual Information



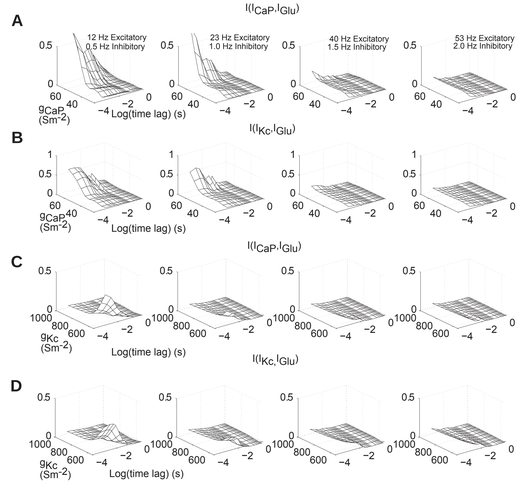
Dependence of mutual information to previous activity. **A**: I(ICaP(t),IGlu(t-Δt)) for Δt between 0-1 s. **B**: I(IKc(t),IGlu(t- Δt)) for Δt between 0-1 s. The different traces correspond to different combinations of synaptic activity. Mutual information was bias corrected using the Panzeri & Treves method.

4 Dendritic excitability shifts information content



Excitatory synaptic current information content in dendritic currents as a function of dendritic excitability. **A**: Calculations H(ICaP), H(ICaP|IGlu) and I(ICaP,IGlu) as a function of gCaP. **B**: Similar to A but with respect to IKc. **C-D**: Identical calculations as A and B but varying gKc. Mutual information was bas corrected using the Panzeri & Treves method.

5 Dendritic currents as information channels modulated by membrane excitability and synaptic activity



Excitatory synaptic current information content in dendritic currents as a function of dendritic excitability and time lags. **A**: I(ICaP(t),IGlu(t- Δt)) for Δt from 0-1 s and varying gCaP. **B**: As in A for IKc. **C-D**: Identical calculations as in A-B but varying gKc. The different panels correspond to different combinations of synaptic activity. Mutual information was bias corrected using the Panzeri & Treves method.

Conclusions

- Excitability of the dendritic tree modulates the information content of the total excitatory input in conjunction with the amount of synaptic activity.
- Treating each dendritic conductance as an information channel could constrain the value and distribution of dendritic currents in encoding synaptic information when building models.
- Although no apparent information is encoded at the soma (constant firing rate) dendritic information content is a function of the level of synaptic activity.

References

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Acknowledgments

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