



# Stellate Cell Responses to Conductance Input: Reliability Resonance in the Theta Frequency Band

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## Introduction

We applied current ( $I_{\text{clamp}}$ ) and conductance ( $G_{\text{clamp}}$ ) inputs to stellate cells (SCs) of the medial entorhinal cortex. For constant and fluctuating stimuli, responses to  $I_{\text{clamp}}$  and  $G_{\text{clamp}}$  differed in two fundamental ways:

- $G_{\text{clamp}}$  induced less membrane variance ( $\sigma_v^2$ ) than  $I_{\text{clamp}}$ .
- $G_{\text{clamp}}$  elicited longer inter-spike intervals ( $T_{\text{isi}}$ ) than  $I_{\text{clamp}}$ .

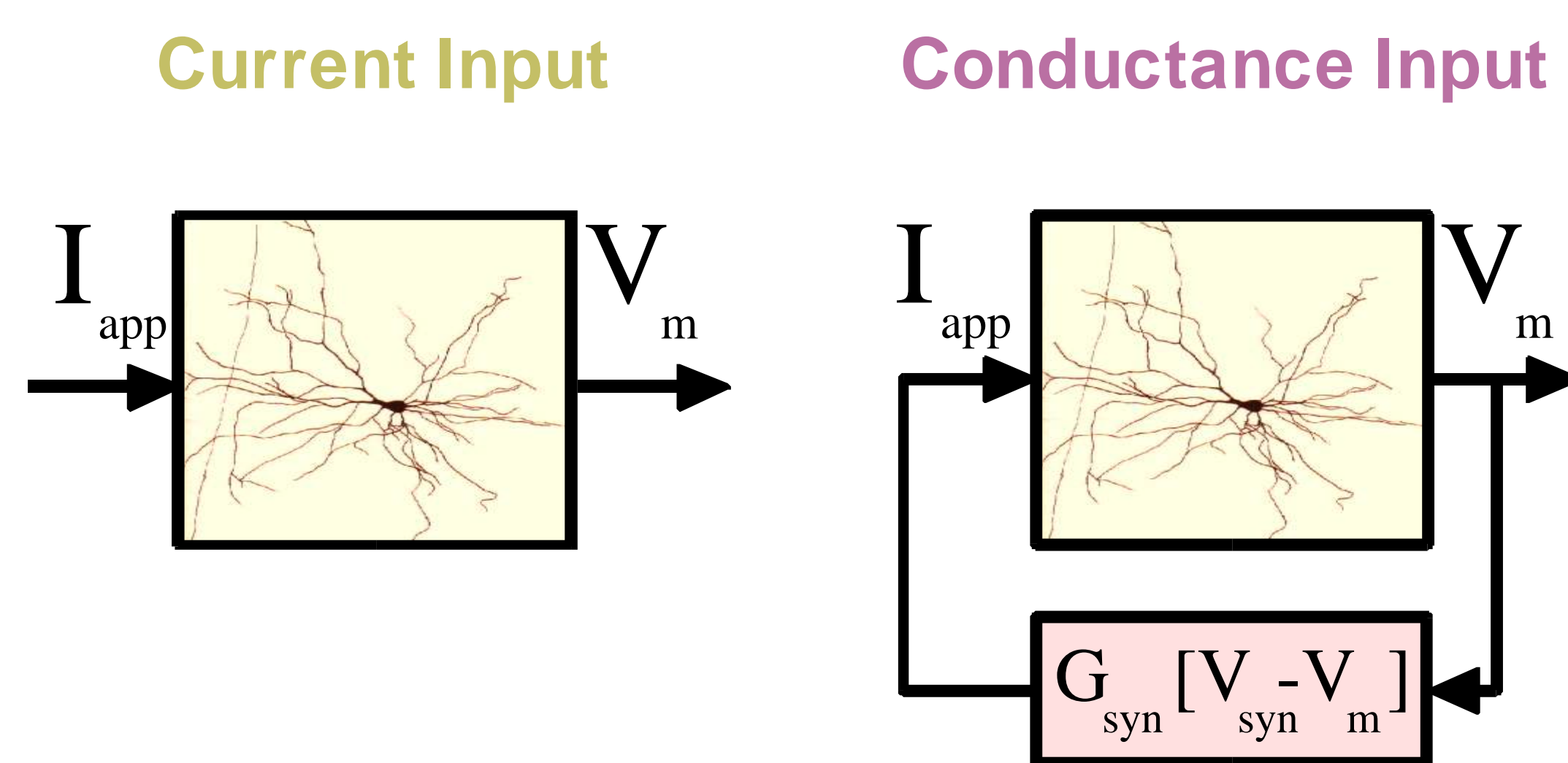
We subsequently asked how reliably SCs fired in response to repeated presentations of identical fluctuating stimuli. In general, reliability covaried with firing rate, but:

- $G_{\text{clamp}}$  revealed a resonant peak in reliability in the theta frequency range (4-12 Hz), not present with  $I_{\text{clamp}}$ .

In this poster, we present the experiments and results which lead to these conclusions, and offer some theoretical insights to explain them. We hypothesize that the decreased  $\sigma_v^2$  and increased  $T_{\text{isi}}$  of  $G_{\text{clamp}}$  allow stellate cells to respond reliably to input events in the range of frequencies that these cells are exposed to *in vivo*.

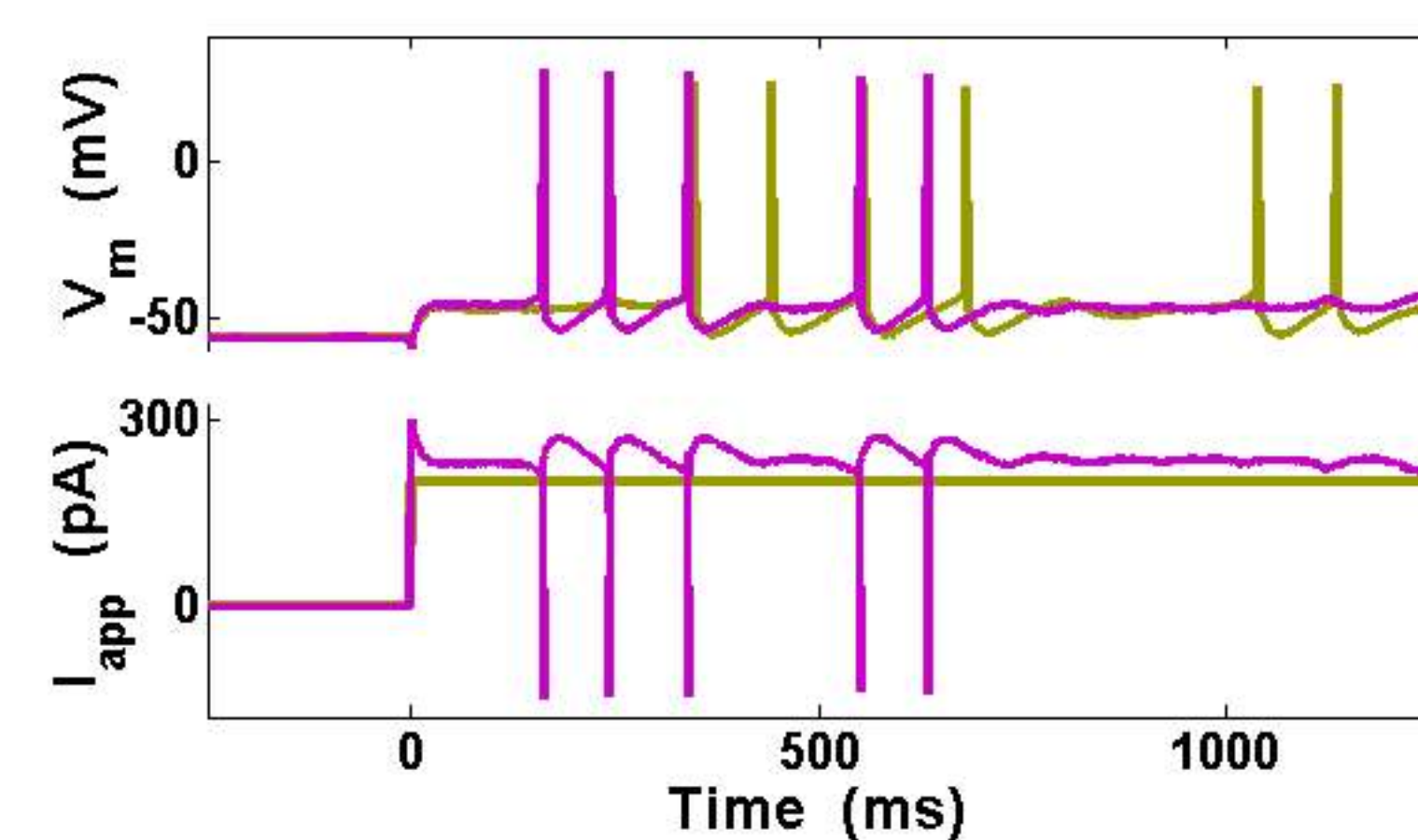
## Methods

Tissue was prepared according to approved protocols. Briefly, 14-22 day Long Evans rats were anesthetized with  $\text{CO}_2$  and euthanized via decapitation. Brains were immediately immersed in  $0^\circ\text{C}$  artificial cerebral-spinal fluid and sliced into  $350\ \mu\text{m}$  thick sections of the hippocampus and entorhinal cortex. Neurons were visualized with an infra-red digital interference contrast equipped microscope, and whole cell patches were made with 4-7 M electrodes filled with artificial neuroplasm. Stellate cells were identified by the presence of a bidirectional  $V_m$  sag in response to both depolarizing and hyper-polarizing current.

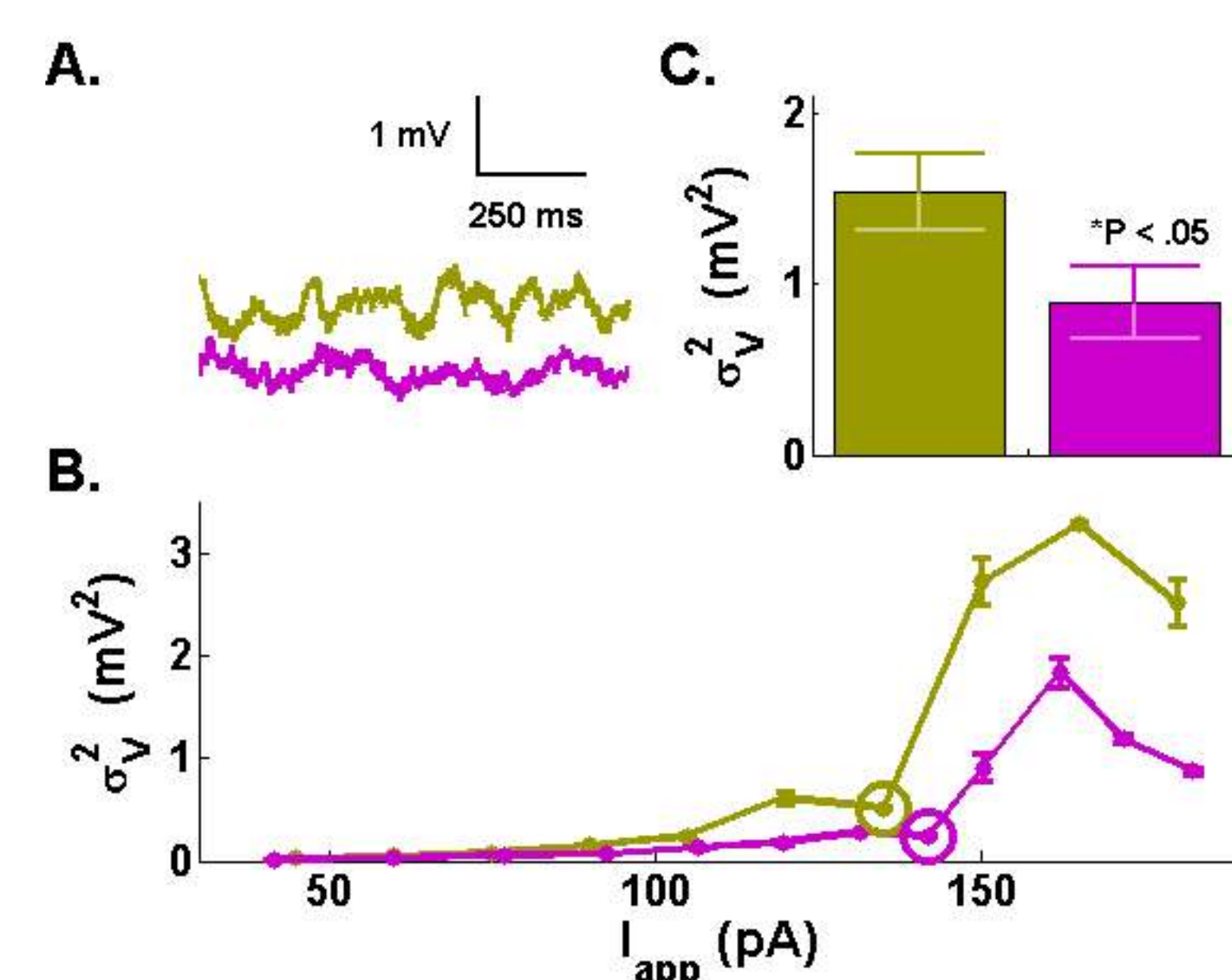


**Figure 1.** Input schematics for the two different modalities. *Left*) For current input ( $I_{\text{clamp}}$ ), predefined current waveforms were provided directly to SCs, and  $V_m$  was only recorded. *Right*) For conductance input ( $G_{\text{clamp}}$ ), applied current was calculated from a predetermined conductance waveform and the instantaneous  $V_m$ . The Real Time Linux Dynamic Clamp used in these experiments has a loop delay of less than  $50\ \mu\text{s}$  and operates in excess of 20 kHz.

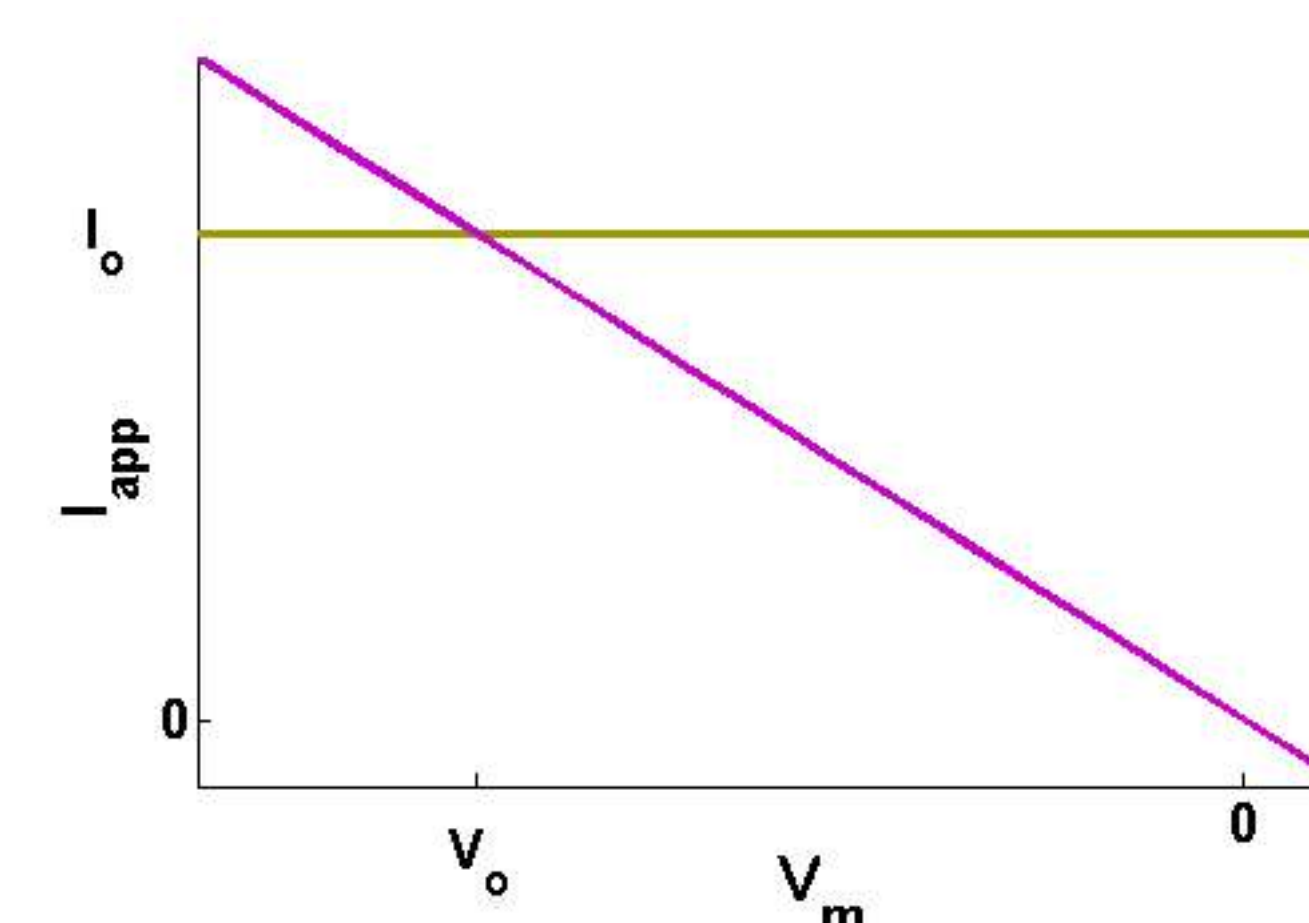
## Results



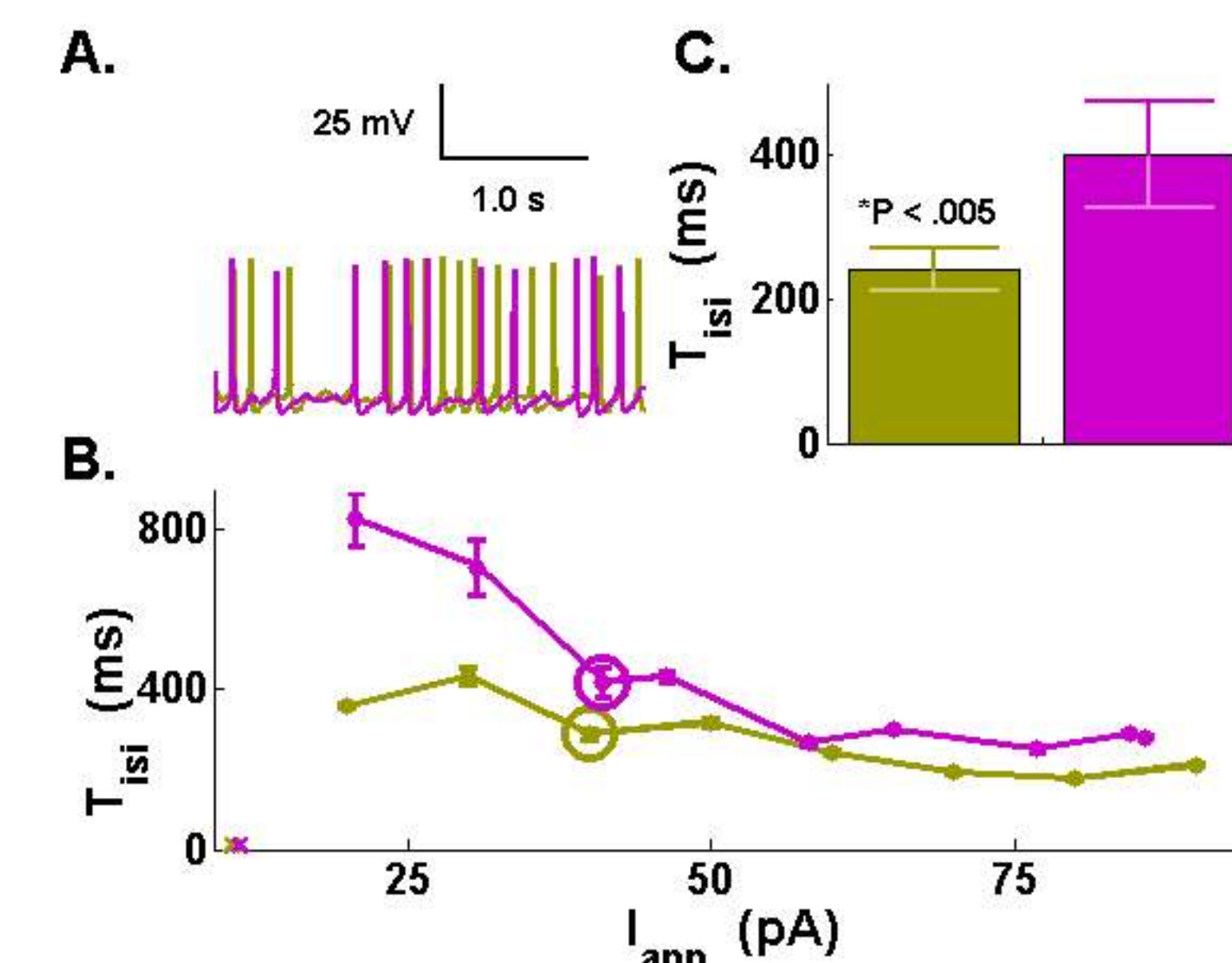
**Figure 2.** Steps of **current** ( $I_{\text{clamp}}$ ) and **conductance** ( $G_{\text{clamp}}$ ) presented to SCs. *Top*) Induced membrane potential for one instance of each modality. *Bottom*) Applied current for the two modalities look similar except during spikes.



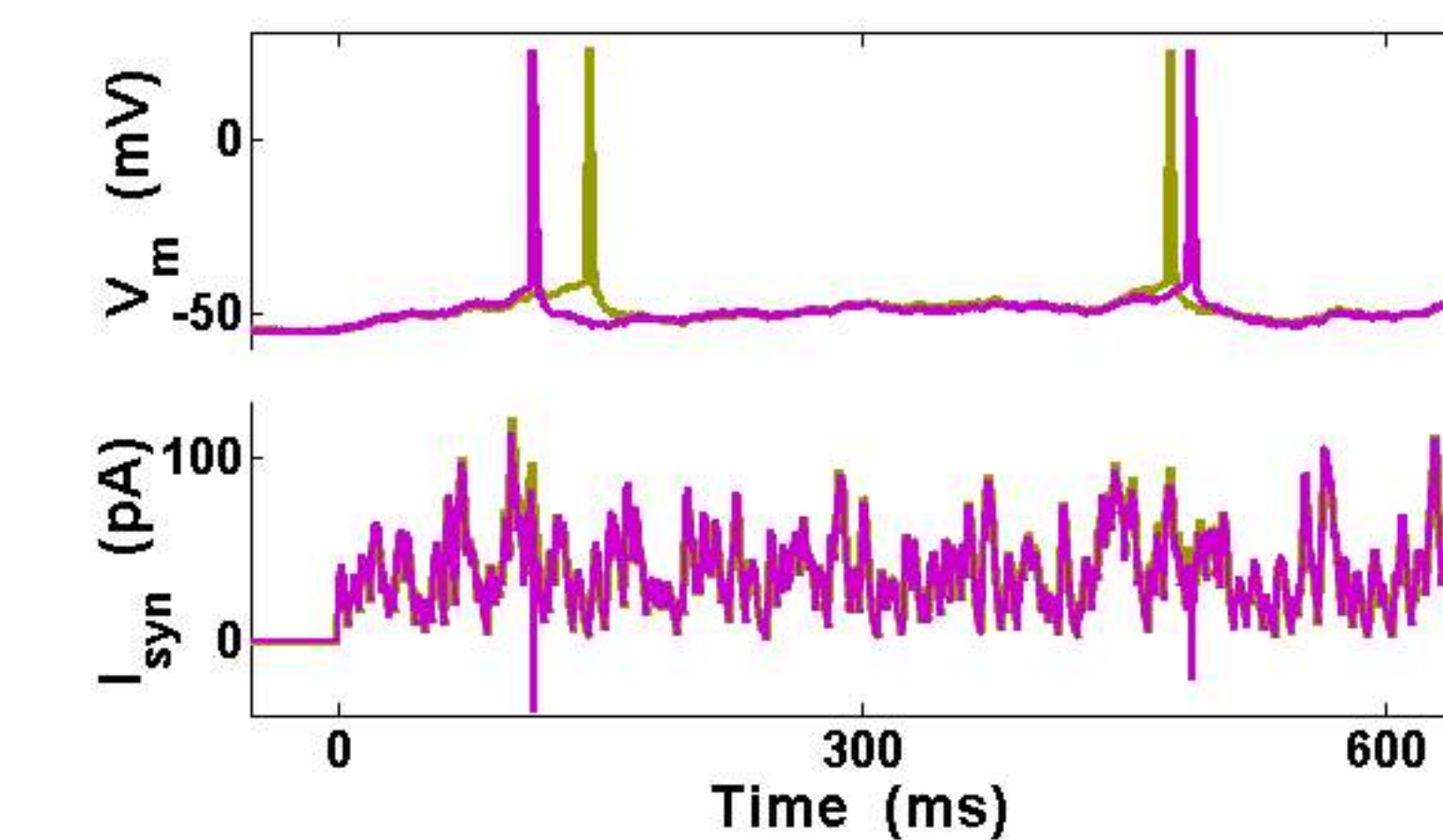
**Figure 3.**  $G_{\text{clamp}}$  typically induced less membrane potential variance ( $\sigma_v^2$ ) than  $I_{\text{clamp}}$ . *A*) Example  $V_m$  from one trial of each modality. *B*)  $\sigma_v^2$  grew with input strength for both modalities, but was always larger for  $I_{\text{clamp}}$ . Circles indicate largest subthreshold data, depicted in *A*, and used to lump cells in *C*. *C*) For 20 SCs,  $\sigma_v^2$  was greater in response to  $I_{\text{clamp}}$  than to  $G_{\text{clamp}}$ .



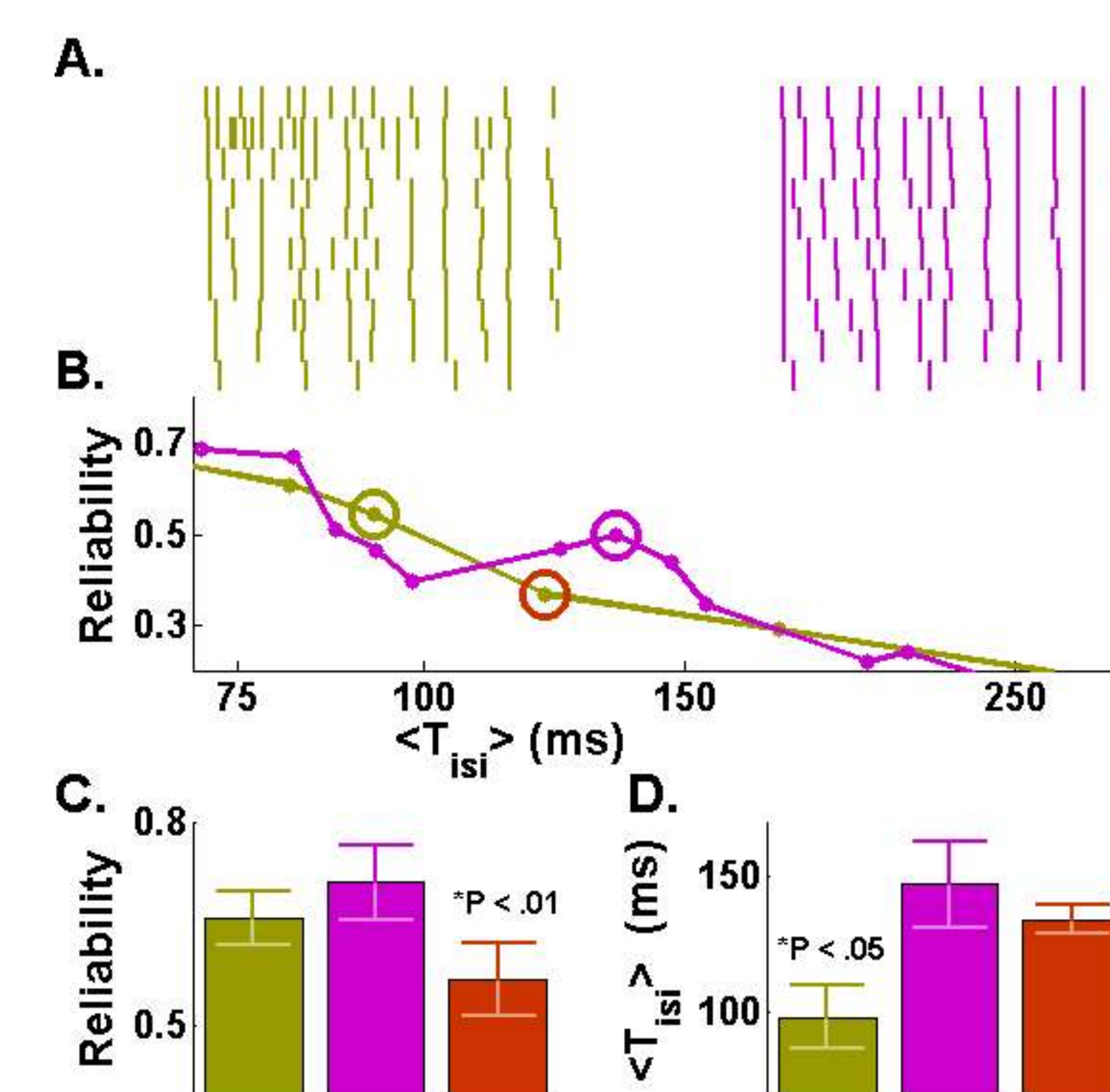
**Figure 4.** Proposed mechanism whereby  $G_{\text{clamp}}$  reduces  $\sigma_v^2$ . Consider two inputs,  $I_{\text{clamp}}$  and  $G_{\text{clamp}}$ , of the same average current  $I_o$ . The two inputs induce the same average potential  $V_o$ . The graph shows  $I_{\text{app}}$  as a function of  $V_m$  for both cases. For  $G_{\text{clamp}}$ , the negative relationship indicates that a conductance allows deviations from  $V_o$  to be smaller and occur less often. Additionally,  $V_m$  will cross spiking threshold less frequently (Fig. 5).



**Figure 5.**  $G_{\text{clamp}}$  elicited longer inter-spike intervals ( $T_{\text{isi}}$ ) than  $I_{\text{clamp}}$ . *A*) Example  $V_m$  from one trial of each modality. *B*) For both modalities,  $T_{\text{isi}}$  decreased with increasing  $I_{\text{app}}$ , but was greater for  $G_{\text{clamp}}$ . Circles indicate data in *A* and used to lump cells in *C*. *C*) For 20 SCs,  $T_{\text{isi}}$  was significantly longer in response to  $G_{\text{clamp}}$  than to  $I_{\text{clamp}}$ .



**Figure 6.** Pseudo-synaptic waveforms of **current** ( $I_{\text{clamp}}$ ) and **conductance** ( $G_{\text{clamp}}$ ) presented to SCs. *Bottom*) Applied current for the two modalities. *Top*) Induced membrane potential for one instance of each modality. Results from Figs. 3 & 5 are similar for step and pseudo-synaptic inputs.



**Figure 7.**  $G_{\text{clamp}}$  unmasks reliability peak at theta frequencies (4-12 Hz). *A*) Rastergram of spike times in response to identical inputs of  $I_{\text{clamp}}$  (*left*) and  $G_{\text{clamp}}$  (*right*). *B*) Example reliability as a function of average  $T_{\text{isi}}$ . Circles denote data from *A*, and represent data used to lump cells: maximum  $I_{\text{clamp}}$  reliability in theta range; peak  $G_{\text{clamp}}$  reliability in theta range;  $I_{\text{clamp}}$  reliability nearest to  $\langle T_{\text{isi}} \rangle$  of peak  $G_{\text{clamp}}$ . *C*) For 8 cells, peak reliability in the theta range is higher for  $G_{\text{clamp}}$ . *D*) Reliability peaks at longer  $\langle T_{\text{isi}} \rangle$  for  $G_{\text{clamp}}$  inputs.

## Conclusions

We compared the effects of current ( $I_{\text{clamp}}$ ) and conductance ( $G_{\text{clamp}}$ ) inputs on stellate cells of the medial entorhinal cortex. Our results indicate that:

- $G_{\text{clamp}}$  induces less membrane variance ( $\sigma_v^2$ ) than  $I_{\text{clamp}}$ .
- $G_{\text{clamp}}$  elicits longer inter-spike intervals ( $T_{\text{isi}}$ ) than  $I_{\text{clamp}}$ .
- $G_{\text{clamp}}$  reveals a resonant peak in reliability in the theta frequency range (4-12 Hz), not present with  $I_{\text{clamp}}$ .

The first result can be understood in terms of control theory: the conductance based negative feedback keeps membrane potentials more stable. The second result follows from the first: if  $V_m$  deviates from rest less frequently, it will reach threshold and thus spike, less frequently.

The third result is more complex, and needs to be explored in other cell types. We speculate that longer inter-spike intervals give the slow membrane mechanisms enough time to recover between action potentials and the decreased membrane variance reduces the probability of accidentally triggering an action potential. These two effects leave the cell primed and sensitive to quick input changes for long periods of time. Thus, repeated events are more likely to induce more reliable responses.

Because conductance clamp inputs are similar to neuronal inputs *in vivo*, this work suggests that stellate cells naturally fire more reliably but less frequently than previous current clamp work indicates. This finding may have implications for both information processing and metabolic efficiency in this and other central nervous system regions.

## Acknowledgments

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