Population-based signal processing and stimulus-response in oxytocin neurons

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Introduction

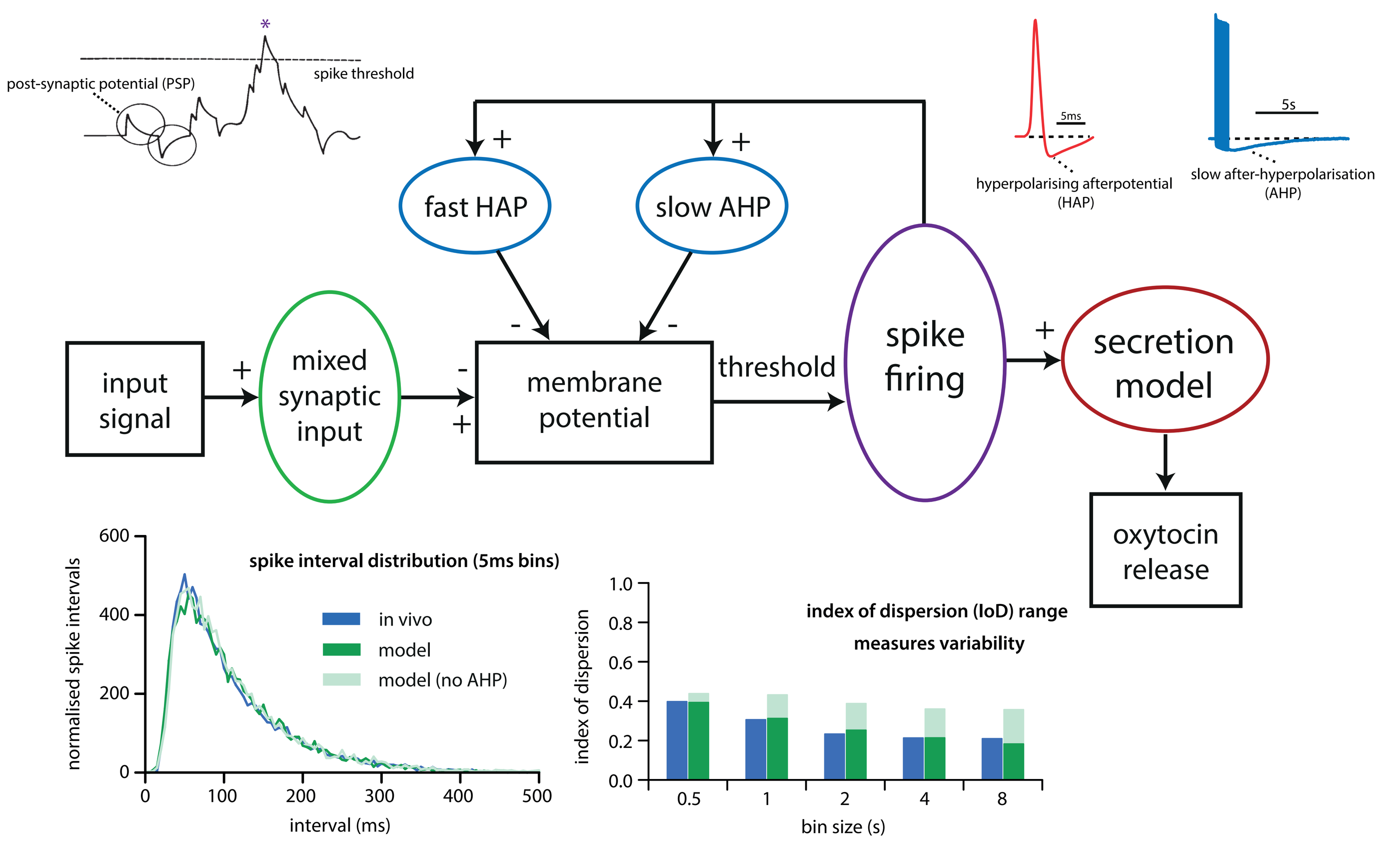
Oxytocin neurons are known for their role in milk-ejection and in homeostatic regulation of osmotic pressure, but they also function as part of appetite regulation, signalling satiety in response to the gut hormone CCK. They respond to multiple signal types, secreting oxytocin both peripherally into plasma, from posterior pituitary axonal terminals, and centrally, via dendritic secretion. Blood plasma oxytocin gives the most accessible measure of oxytocin neuronal activity, but the relationship between input stimulus and plasma output response is complex and highly non-linear.

In milk-ejection, where a large short pulse of oxytocin is required, the neurons act as a coordinated network, but in other roles spiking activity is asynchronous, and the heterogeneous neurons act as a population of independent cells producing a summed output signal. The oxytocin neurons must act both individually and as a population to process noisy synaptic inputs into a robust output signal.

We have previously developed an integrated input, (integrate-and-fire based) spiking, secretion, and plasma diffusion single oxytocin neuron model, accurately simulating *in vitro* and *in vivo* response. This model showed how intrinsic mechanisms such as the after-hyperpolarisation (AHP) act to reduce signal noise. Here we study a model neuron population, with varied levels of heterogeneity and independence of input signals in order to understand the relationship between single cell properties and action as a population in producing a robust signal response.

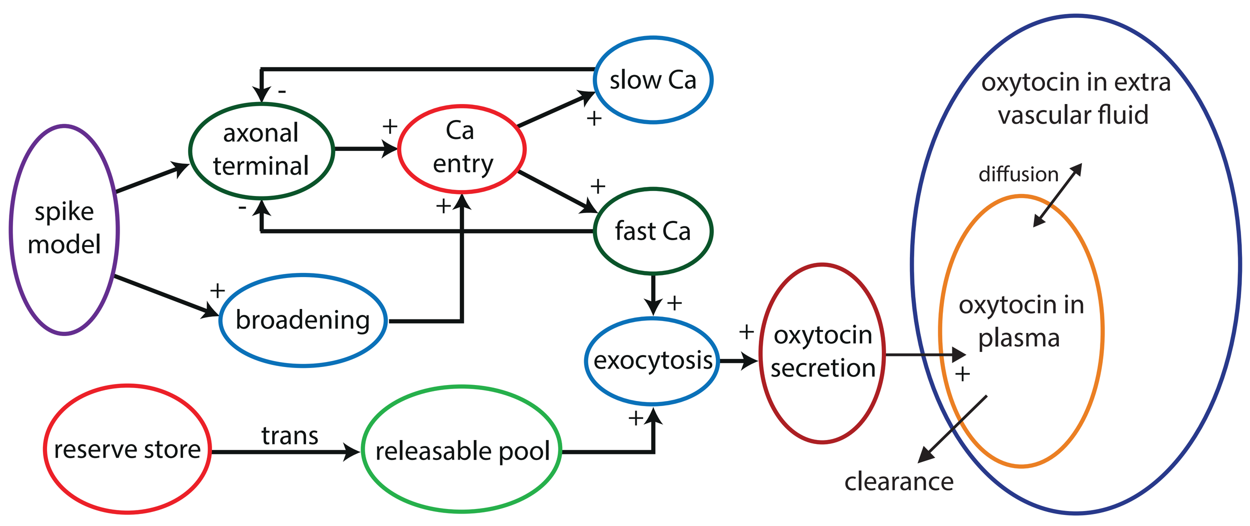
The Spiking Model

A heavily modified 'integrate-and-fire' model simulates synaptic input and the resulting spike activity, modulated by a set of hyperpolarising and depolarising post-spike potentials.

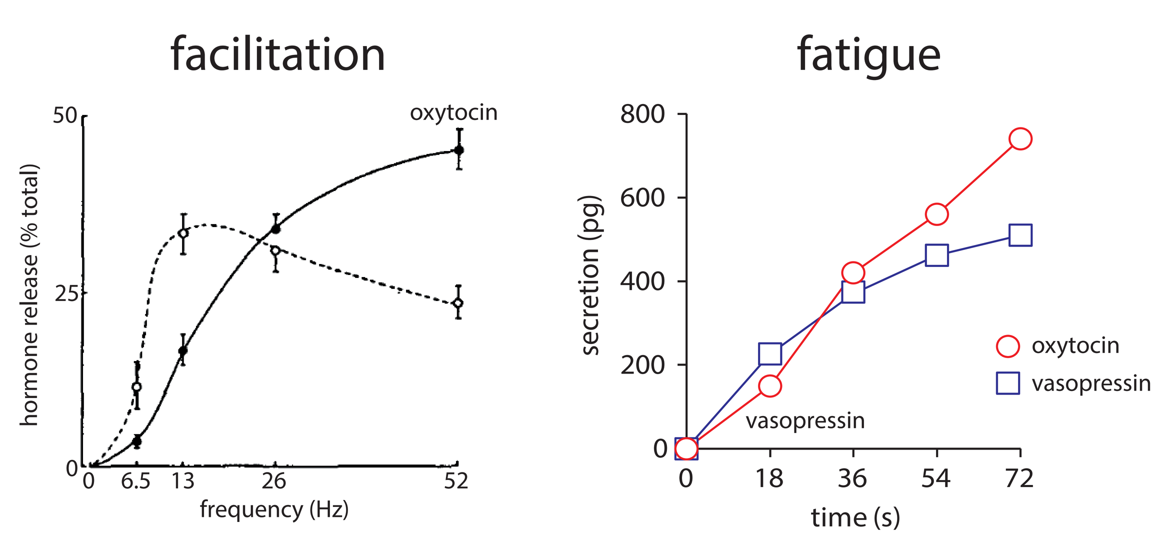


The Secretion and Plasma Model

The secretion model simulates the stores and spike stimulated exocytosis of vesicles from the axonal terminals, matching the experimentally observed facilitation and fatigue effects that result in a secretion response that is dependent on spike patterning as well as frequency, and sensitive to noise.

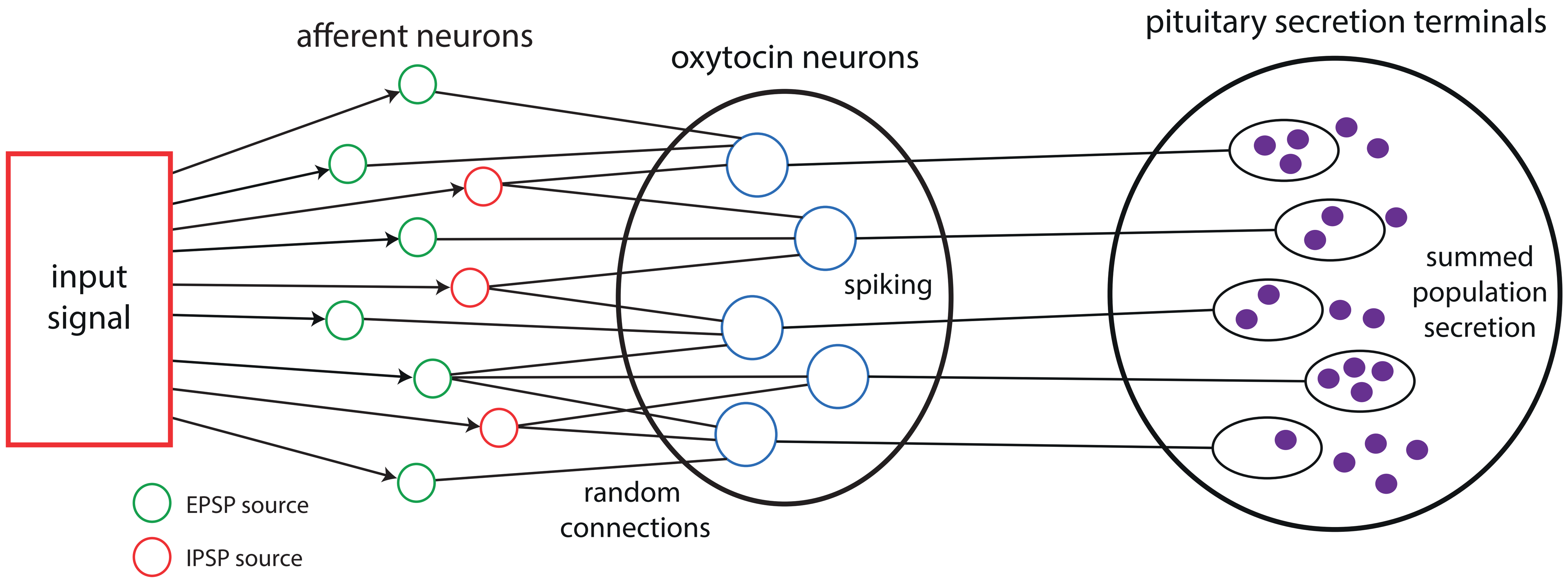


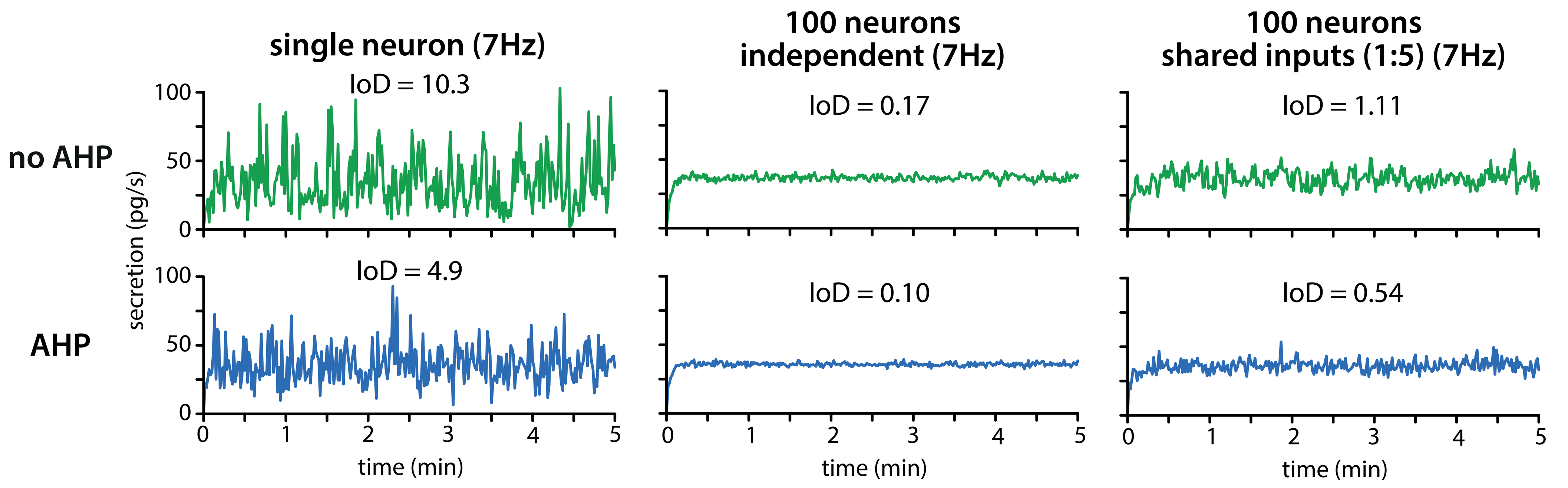
non-linear relationship between spiking and secretion



Input Signal Independence

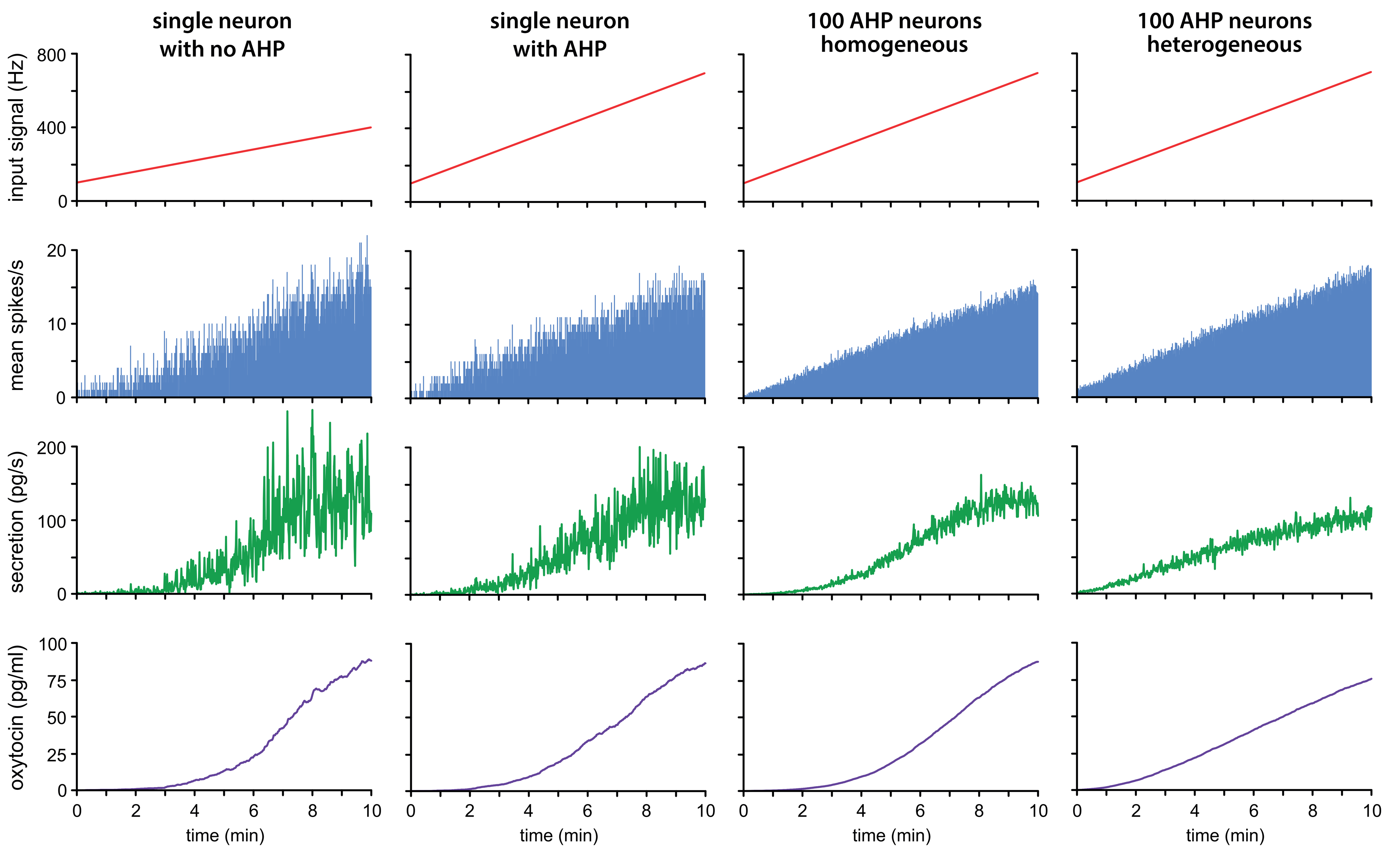
The non-linear secretion response in the single neuron model produces a noisy secretion signal. The AHP acts to reduce this noise. However, the summed secretion of a population also produces a much smoother output signal. Does this make the AHP redundant? What if we don't assume that neuron input is independent?





Heterogeneity

We add heterogeneity by randomly varying the number of input connections per neuron. The AHP moderates heterogeneity by having a weaker and stronger effect on slower and faster neurons. A ramped input signal simulates experiments where osmotic pressure slowly rises.



Conclusion

The AHP acts to reduce noise in the secretion signal. A simple summed population model suggests that this effect is lost beyond single neurons, but it becomes important again when we consider the shared input signals across the population. The AHP also acts to increase the linearity of the signal response. Population heterogeneity has a strong effect on linearising the signal response, and increases the dynamic range.

References

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