Computational estimates of the effect of asynchronous synaptic activity on fluctuations in the membrane potential of motoneurons

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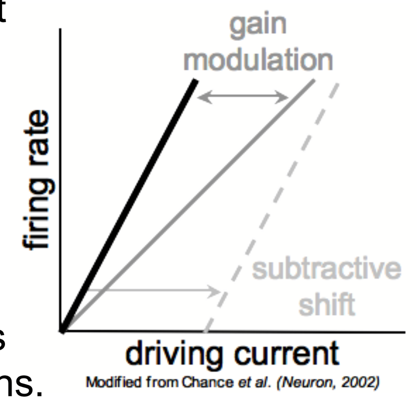
BACKGROUND AND AIM

- **Gain modulation** is a change in slope in a neuron's input-output curve. It is distinct from the subtractive shift resulting from hyper-polarizing or shunting inhibition alone.
- Previous studies have found that the noise in somatic membrane potential resulting from background synaptic activity modulates the gain of firing rate in cortical neurons (Chance *et al.*, 2002; Prescott and De Koninck, 2003).
- However the synaptic and voltage-gated ion channel distributions and parameters used in these studies are specific to cortical neurons. It is not straightforward to apply their conclusions to motoneurons.



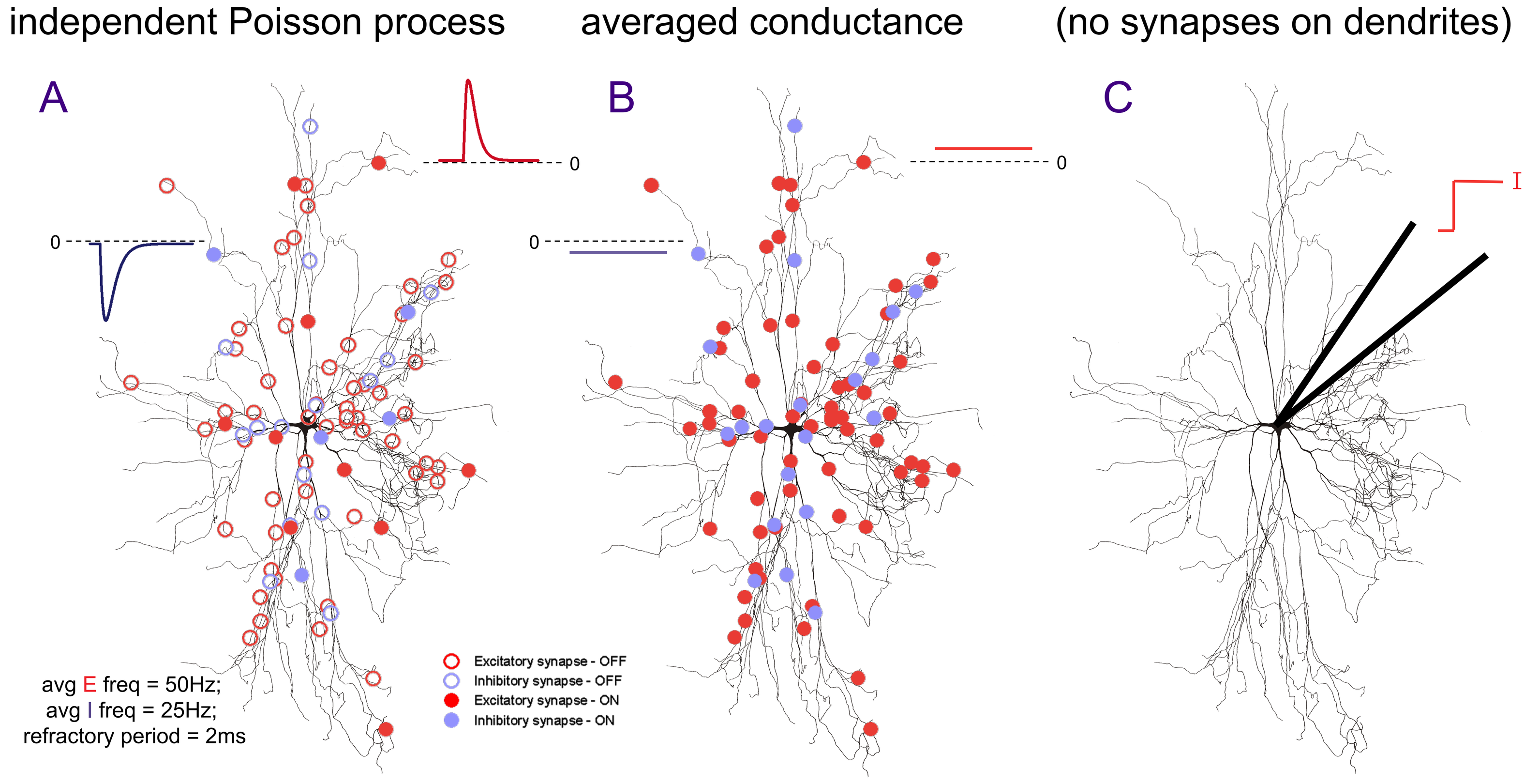
Modified from Chance et al. (Neuron, 2002)

Question: Does asynchronous background synaptic activity lead to gain modulation of firing rate in motoneurons?

Three compartmental models of a feline neck motoneuron

- *Synapses:* **background synapses** (balanced excitatory and inhibitory, i.e. no net current) and **signal synapses** (excitatory only); all uniformly distributed wrt surface area.
- *Voltage-gated ion channels:* Hodgkin and Huxley Na^+ and K^+ channels and slow and delayed-rectifier K^+ channels on the soma and axon (ElBasiouny, 2006)

Asynchronous Synapse Model	Constant Conductance Synapse Model	Current Injection Model
Synapses each release transiently with an independent Poisson process	Synapses each release tonically with a time-averaged conductance	Constant current injection at soma (no synapses on dendrites)

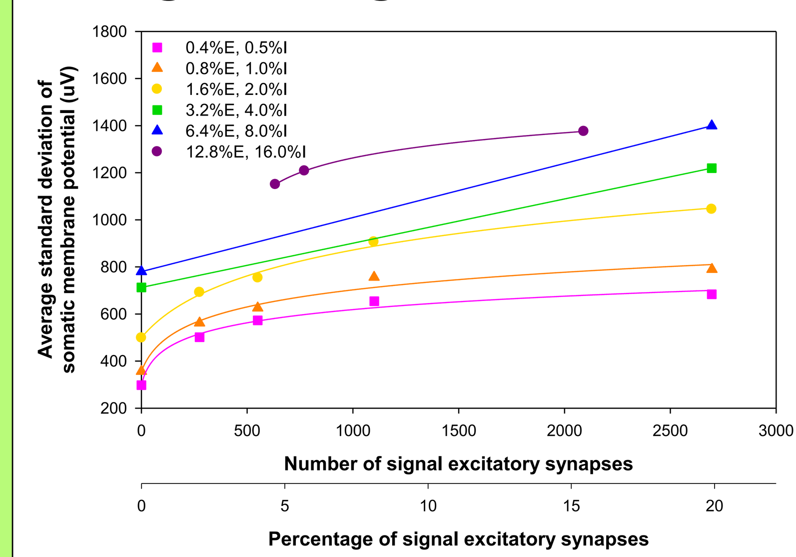


Model generation:

A → Time-average synaptic conductances. A & B…
* Have the same conductance
* Differ with respect to noise
→ B

B → Voltage clamp soma at resting membrane potential, inject the measured current at soma. B & C…
* Have same current at soma
* Differ in conductance alone
→ C

Firing rate & gain modulation vary with background synaptic activity



A passive asynchronous synapse model shows that noise (std. dev. of somatic membrane potential):
- Increases with increasing background
- Increases with increasing signal, but saturates

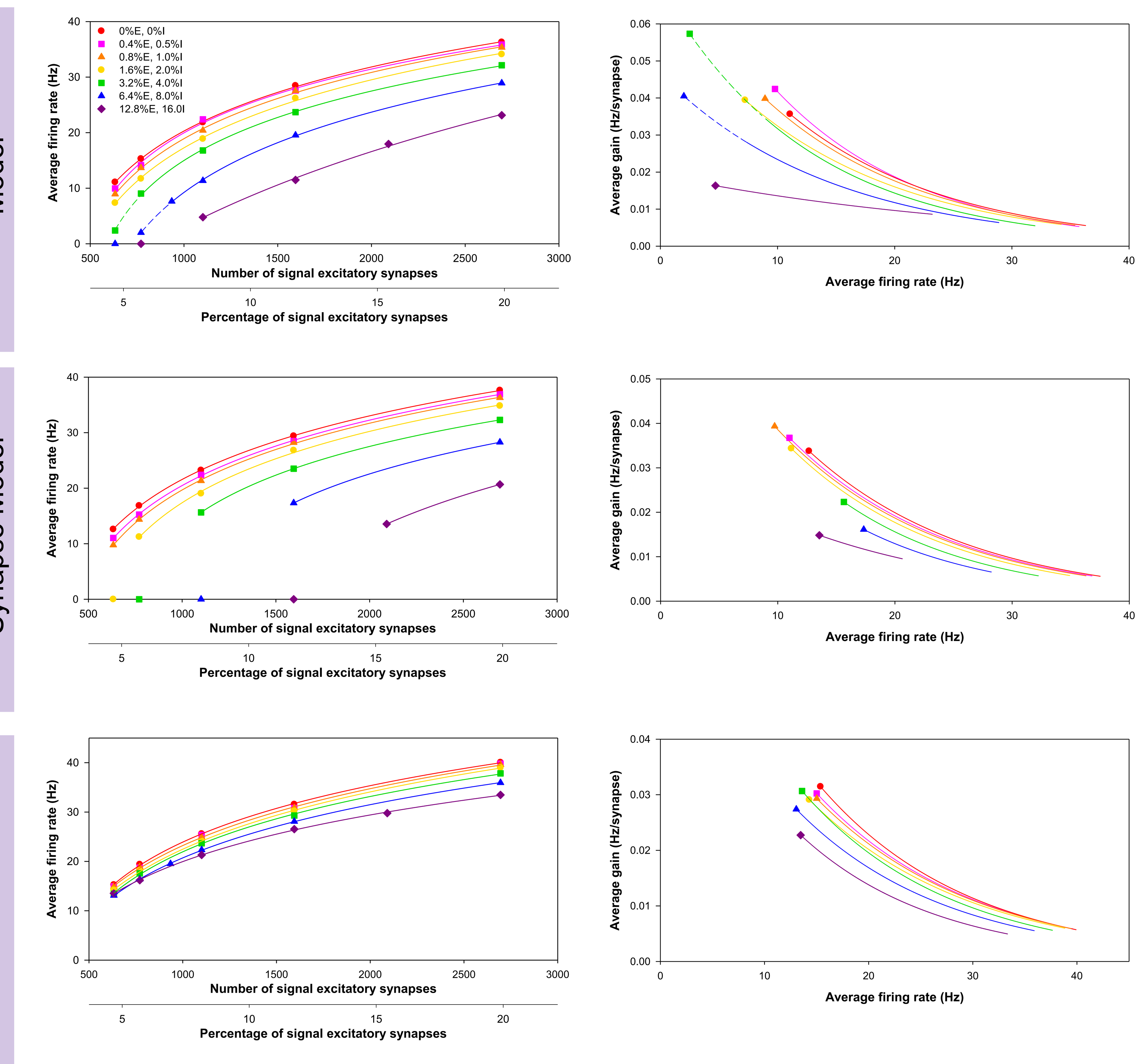
Analysis: To calculate the average firing rate for active models, the average interspike interval (ISI) was calculated over all ISIs over five 500 ms trials. If a trial had only one spike, an ISI of 0.4 ms was used (indicated by a dashed line in the curve fit). All curve fits shown are regressions to the third order logarithmic equation $y = y_0 + a\ \ln(x - x_0)$ ($R > 0.97$ for all fits). Gain was calculated as the first-order derivative of the regression for each firing rate curve fit.

Firing Rate:	Gain Modulation:
- Increases with increasing signal - Decreases with increasing background	- Gain decreases with increasing background

Asynchronous Synapse Model

Constant Conductance Synapse Model

Current Injection Model



CONCLUSIONS

Increasing asynchronous background synaptic activity does lead to gain modulation of firing rate in motoneurons.

- The firing rate curves for the asynchronous synapse model clearly show a change in slope with increasing background synaptic activity.
- Noise from relatively high asynchronous background synaptic activity increases firing rate compared to the constant conductance model when excitatory signal input is low. However, this effect disappears at higher levels of excitatory signal input.

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If asynchronous background synaptic activity is high enough, noisy somatic membrane potential increases firing rate during low excitatory signal input

- The gains of the asynchronous synapse model and constant conductance synapse model are different only at very high background