Intrinsic ionic dynamics, oscillations, and resonance are reflected in and can be extracted from neuronal spike-train cross-correlations

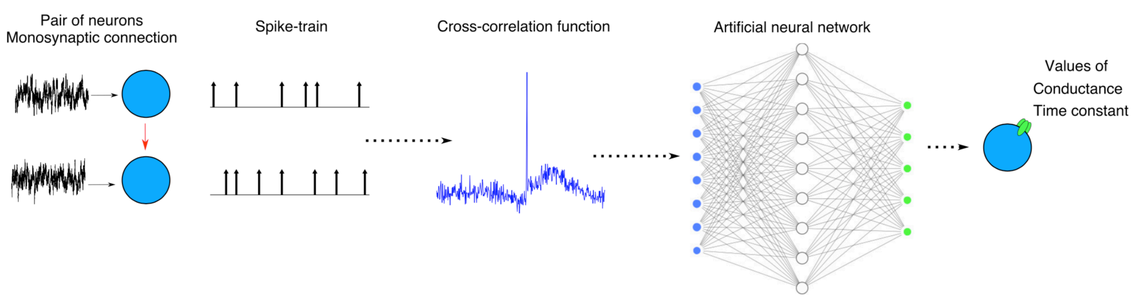
RUTGERS UNIVERSITY | NEWARK
Center for Molecular and Behavioral Neuroscience

Rodrigo FO Pena[1]
Martin V Ibarra[2]
Horacio G Rotstein[1]
[1]NJIT and Rutgers University, USA
[2]Universidad Nacional de la Patagonia San Juan Bosco & CONICET, Argentina

NJIT New Jersey Institute of Technology

Introduction

- Finely-timed spike relationships provide knowledge of **putative monosynaptic connections** in populations of neurons; Recent experiments involving hippocampal *in vivo* recordings were able to demonstrate such a relationship by means of the cross-correlation function (CCF).
- A **sharp peak within a few milliseconds** in the CCF indicates the presence of a connection.
- We have found that **postsynaptic intrinsic neuronal properties** such as the **ionic currents' nonlinearities** and **time constants** shape the CCFs between pre- and postsynaptic neurons (secondary peaks).
- It is not known whether **neuronal dynamics** in synaptically connected neurons can be **extracted** using this information;



to what extent can **CCFs** be used to capture **intrinsic neuronal dynamics**?

parameters of ionic currents such as **conductance** and **time constant**?

Model

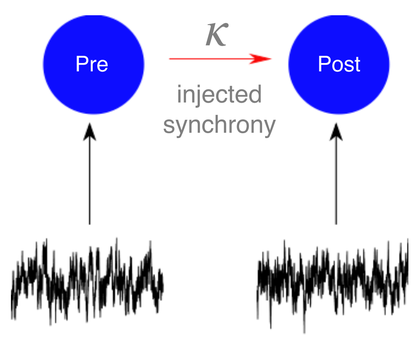
- **Neurons**

I_{NaP}+I_h model: Rotstein H.G., *J. Comput. Neurosci.* 43: 243–271 (2017)

$$C\frac{dV}{dt} = -I_L - I_h - I_{Nap} + I_{app} + I_{in}(t)$$
$$I_L = G_L(V - E_L)$$
$$I_h = G_h r(V - E_h)$$
$$I_{Nap} = G_p p_\infty(V)(V - E_{Na})$$

$x\ (= r, p)$

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}$$



The spike-train cross-correlation function is defined as

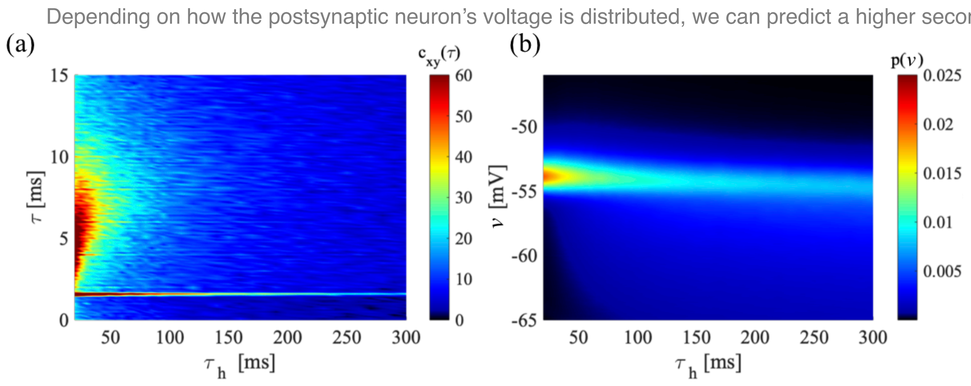
$$C_{ij}(\tau) = \langle x_i(t)x_j(t+\tau)\rangle - \langle x_i\rangle\langle x_j\rangle$$

where $\langle . \rangle$ is a time average.

- **Upon a presynaptic spike we test synapses**
  - Conductance-based: $I_{syn} = G_{ex}(V - E)$, $dG_{ex}/dt = -G_{ex}/\tau_{ex}$
  - Event-based: $V \leftarrow V + J$

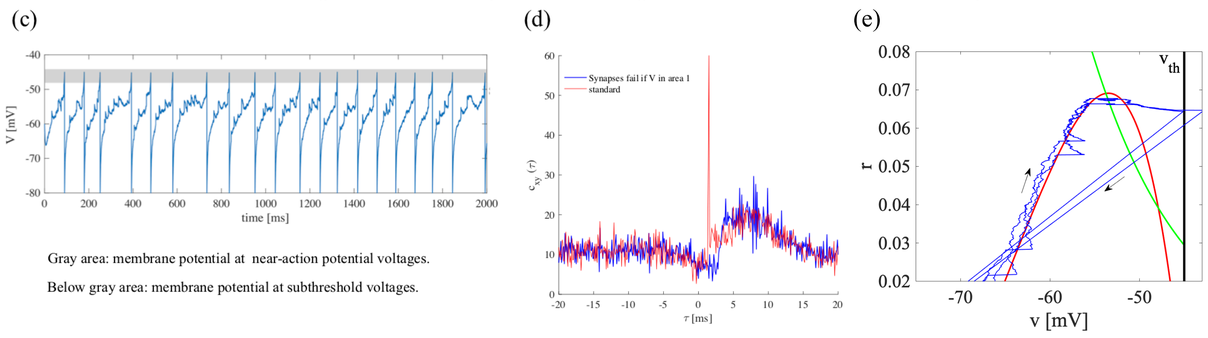
Second peak in c_{xy} is related to the voltage in which a postsynaptic event is perceived

Depending on how the postsynaptic neuron's voltage is distributed, we can predict a higher second peak:



p(v): membrane potential density.

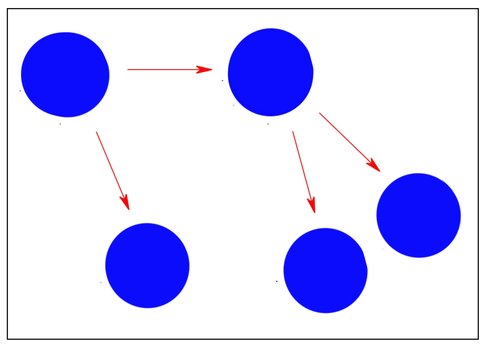
If we remove events arriving at near-action potential voltages, we are left with the second peak:



Gray area: membrane potential at near-action potential voltages.

Below gray area: membrane potential at subthreshold voltages.

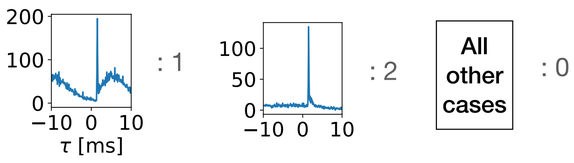
Construction of a database

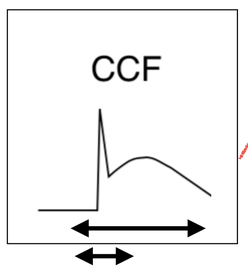


Random arrangements of a 5x5 network (always monosynapses)

- Each CCF 100 trials per network
- Database with 25,000 samples

Labeled data with different I_h properties





We also test if information around the first is enough;

In general, only first peak is considered.

Training

- Activation functions

Sigmoid
$\sigma(x) = \frac{1}{1+e^{-x}}$

tanh
$\tanh(x)$

ReLU
$\max(0, x)$

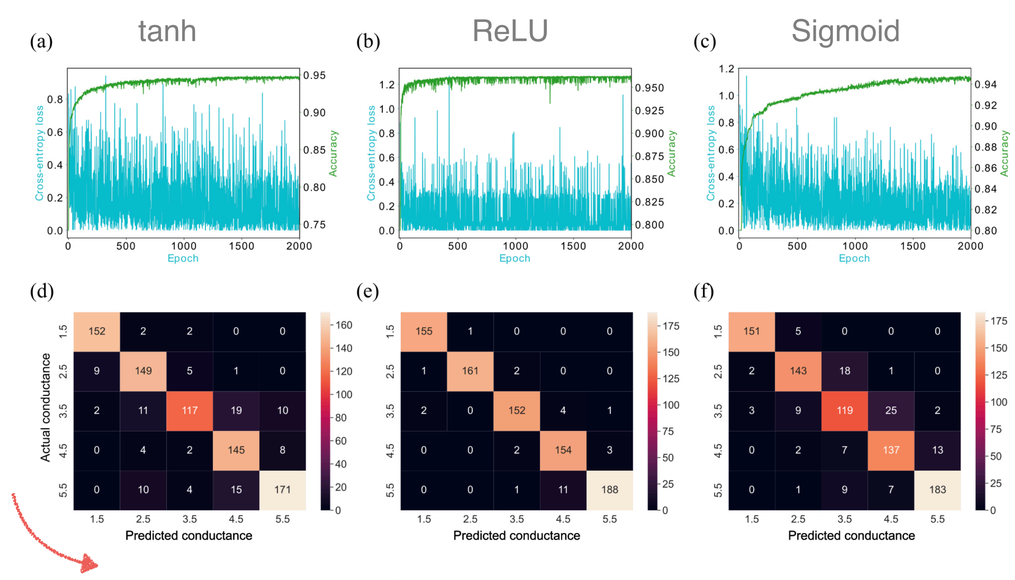
Training procedure:

- Training:validation is 80:20
- Backpropagation algorithm;
- Stochastic gradient descent;
- Cross-entropy loss function;

$$\mathcal{L} = -\frac{1}{m}\sum_{i=1}^{m} y_i \log(\hat{y}_i),$$

We measure:

$$\text{Precision} = \frac{TP}{TP+FP}.$$
$$\text{Recall} = \frac{TP}{TP+FN}.$$
$$\text{F1} - \text{score} = \frac{2 \times (\text{Precision} \times \text{Recall})}{\text{Precision} + \text{Recall}}.$$
$$MCC = \frac{(TP \times TN - FP \times FN)}{\sqrt{(TP+FP)(TP+FN)(TN+FP)(TN+FN)}}.$$

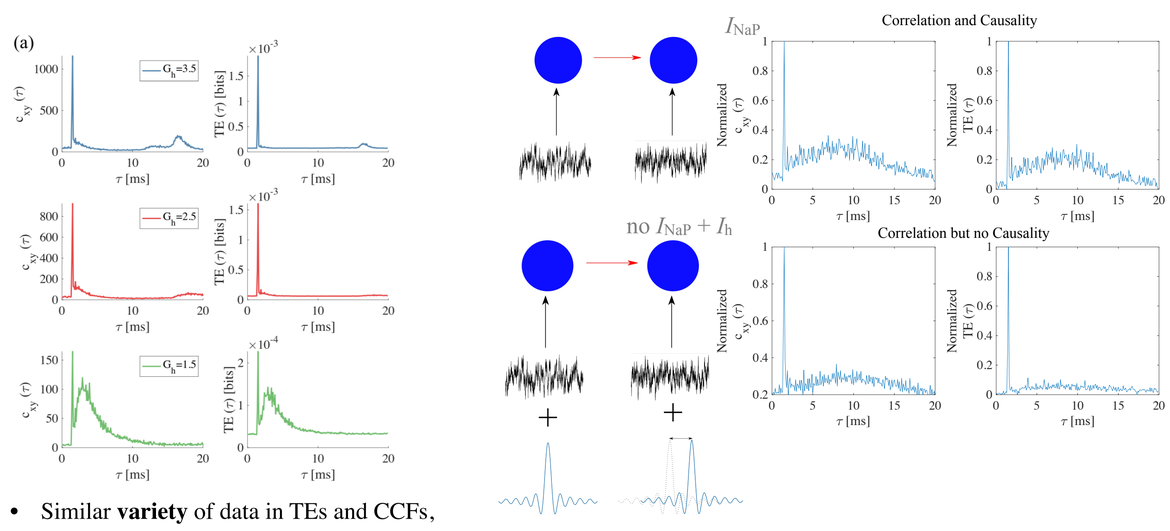


Good accuracy only if information around all cross-correlation is used.

Confounding factors

Let's compare with Transfer Entropy:

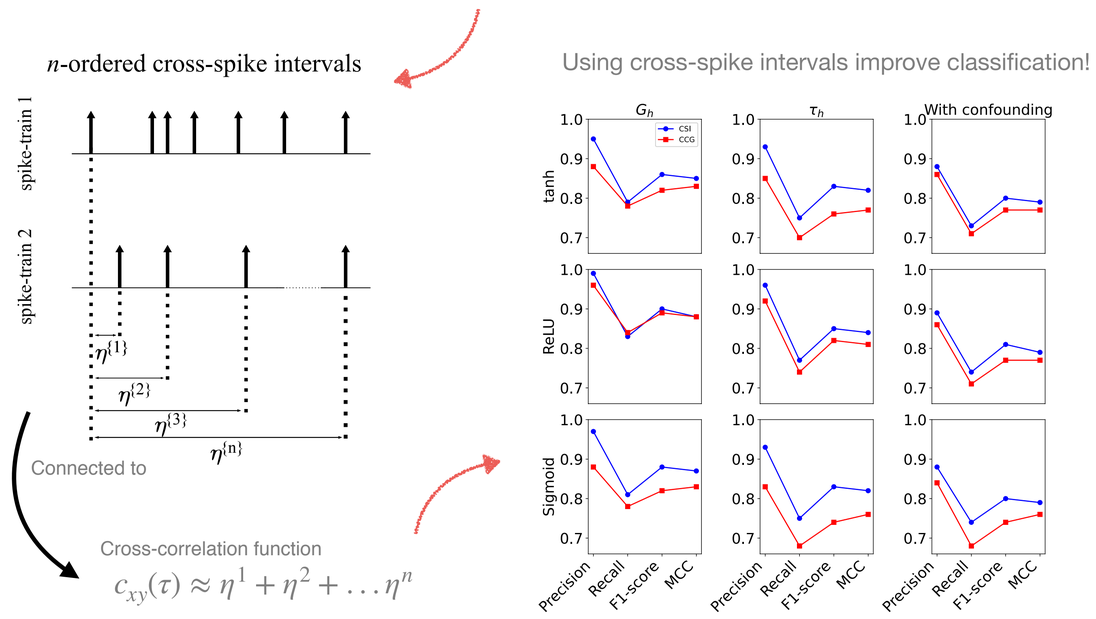
$$TE_{y\to x}(d) = \sum p(x_{t+1+d}, x_{t+d}, y_t)\log_2\left(\frac{p(x_{t+1+d}, x_{t+d}, y_t)p(y_t)}{p(y_{t+1}, y_t)p(x_t, y_t)}\right).$$



- Similar **variety** of data in TEs and CCFs,
- Variety is the only input necessary for a **supervised training algorithm.**

Confounding factors lower the accuracy

But how one could improve the classification without TE?



Conclusions

- Ionic properties can be extracted from CCFs (**F1-scores and Matthews correlation coefficient above 0.8**) only with information from lags beyond the first peak (**subthreshold dynamics**)
- Our results do not require sophisticated information-theoretic metrics such as **transfer entropy** but suffer from **confounding factors** provided by **background oscillations**.
- The **cross-spike intervals** is an alternative that improves the classification algorithms accuracy.

Acknowledgment

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