# Dendritic subunits: the crucial role of input statistics and a lack of two-layer behavior

**DJ Strouse*, Balázs Ujfalussy, and Máté Lengyel**

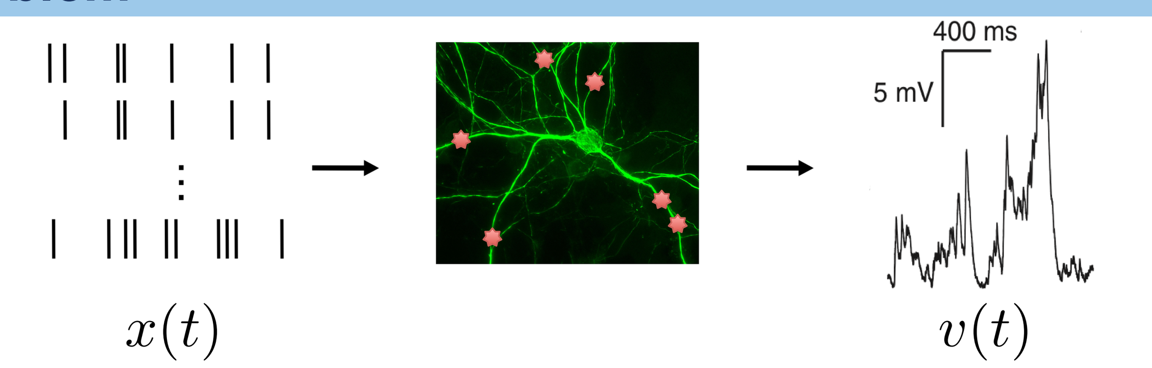
Computational and Biological Learning Lab, Department of Engineering, University of Cambridge, UK

*Present address: Department of Physics, Princeton University, USA

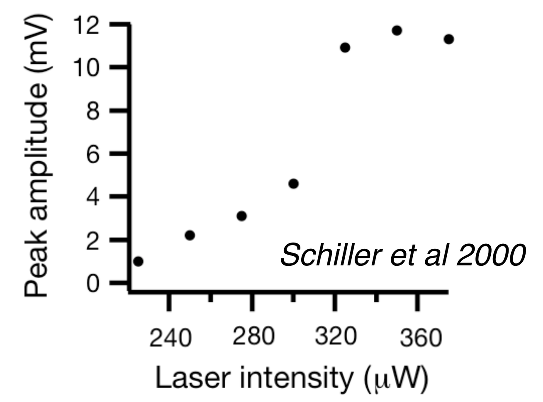
Computational and Biological Learning, University of Cambridge

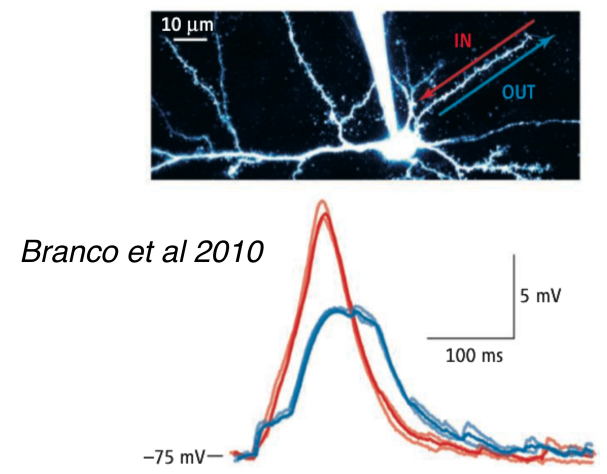
UNIVERSITY OF CAMBRIDGE

## The problem




**Peak somatic membrane potential is a nonlinear function of dendritic stimulation...**

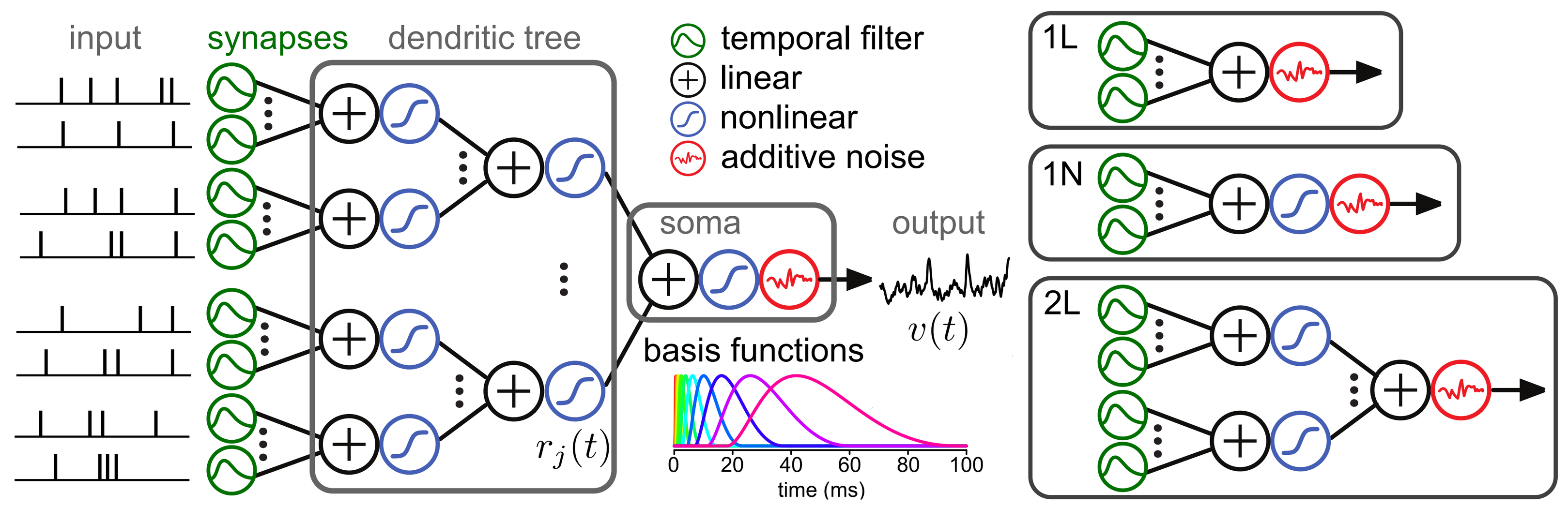



**...and sensitive to temporal order of inputs.**

## The model: hierarchical linear-nonlinear cascade (hLN)

**We have developed a dynamic, analytically tractable, and computationally interpretable model for dendritic computation which can be fit to arbitrarily complex dendritic trees.**




**response of subunit j**

$$r_j(t) = g_j\left(\sum_{k\in c_{\mathrm{sub}}(j)} w_k r_k(t) + \sum_{i\in c_{\mathrm{syn}}(j)} \mathbf{b}_i^T \tilde{\mathbf{x}}_i(t)\,;\boldsymbol{\theta}_j\right)$$

**somatic membrane potential**

$$v(t) = w_1 r_1(t) + v_0 + \eta(t)$$

- **sets of subunits and synapses providing input to subunit j**: $c_{\mathrm{sub}}(j)$, $c_{\mathrm{syn}}(j)$
- **basis weights for synapse i**: $\mathbf{b}_i$
- **nonlinearity of subunit j...**: $g_j$
- **baseline membrane potential**: $v_0$
- **weight on output of subunit k**: $w_k$
- **spike input to synapse i convolved with basis functions**: $\tilde{\mathbf{x}}_i(t)$
- **...and its vector of parameters**: $\boldsymbol{\theta}_j$
- **Gaussian noise and its std**: $\eta(t)$, $\sigma$

**m^th basis function** (*Pillow et al 2008*)

$$f_m(t') = \begin{cases} \frac{1}{2}\cos(a\log[t'+c]-\phi_m)+\frac{1}{2} & t' \text{ s.t. } a\log[t'+c]\in[\phi_m-\pi,\phi_m+\pi] \\ 0 & \text{otherwise} \end{cases}$$

## Fitting the model to data

**random initialization (constrained to not saturate the nonlinearities)** → **maximum likelihood via (subunit-wise) coordinate gradient ascent** ← **synthetic or compartmental model data**

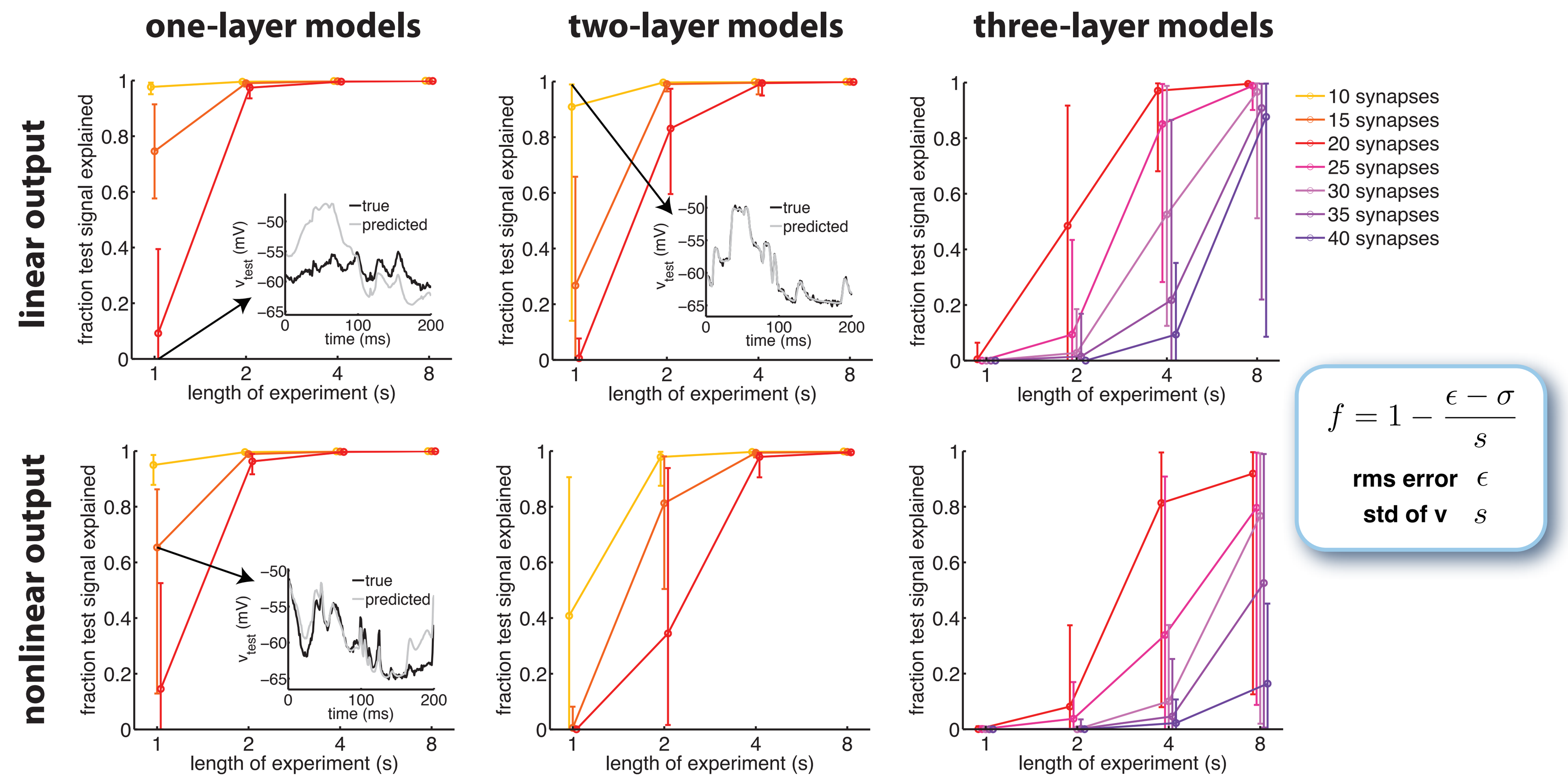
## Comparison to other modeling approaches

**"two-layer network" perceptron model** *Poirazi et al 2003* → generalization → **hLN model** ← simplification ← **multi-compartment models (e.g. Neuron)** *Hines et al 1997*

Generalization:
- handles dynamic inputs and outputs
- flexibly models different cells/conditions

Simplification:
- computational interpretability
- ease of fitting
- analytic tractability

## Validation of fitting

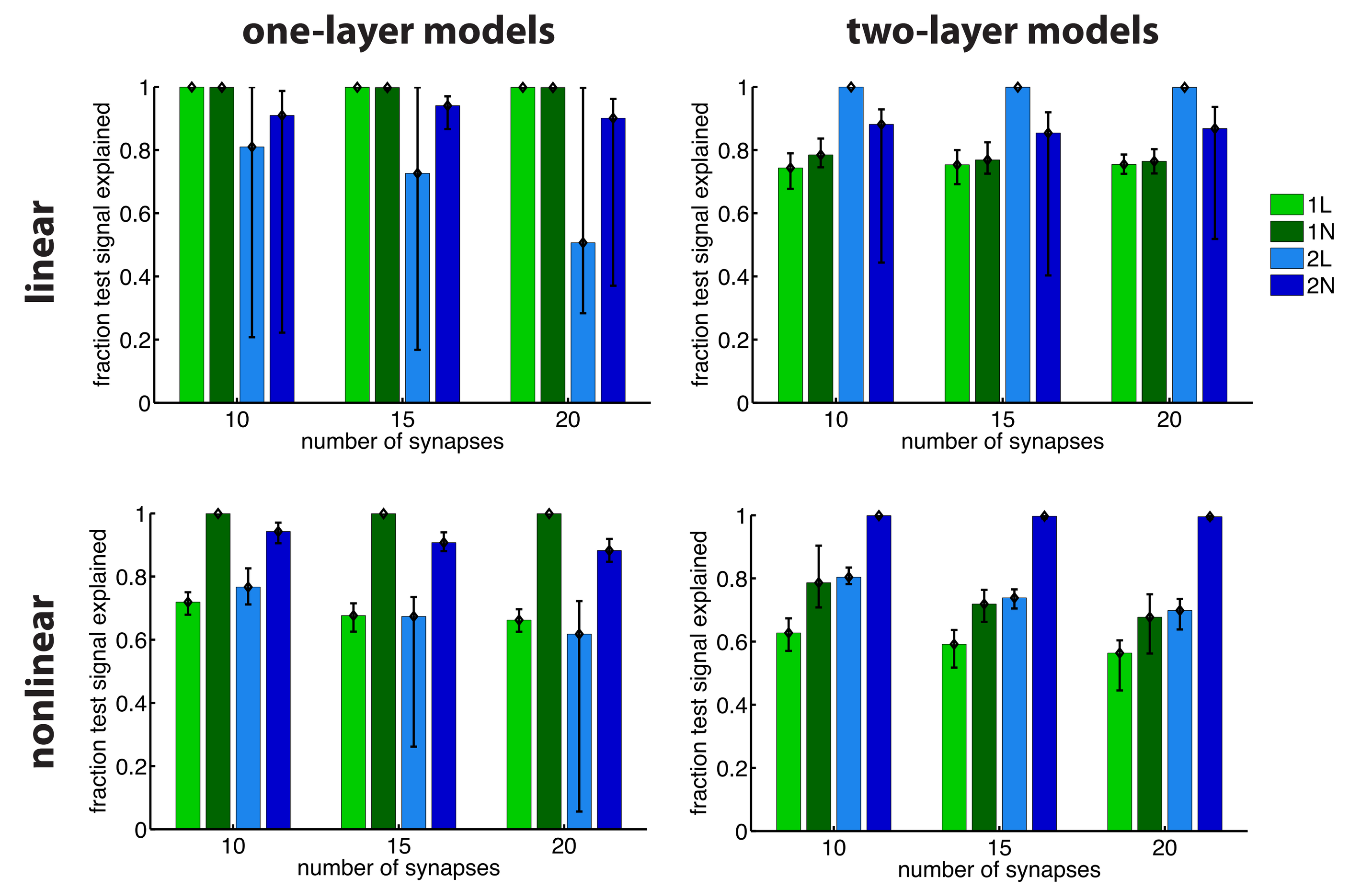



$f = 1 - \frac{\epsilon - \sigma}{s}$

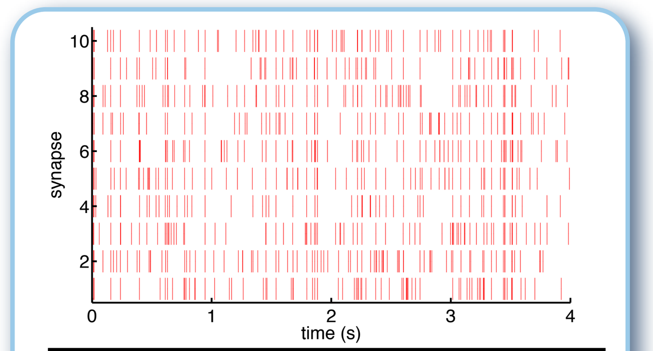
rms error $\epsilon$

std of v $s$

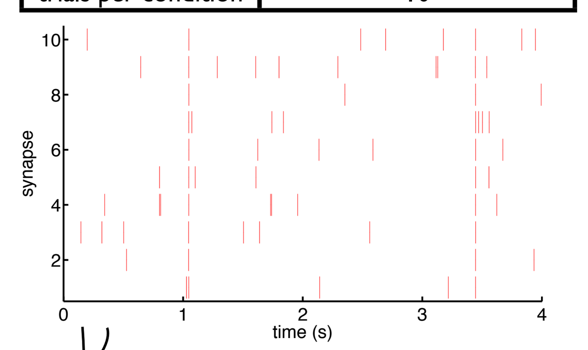
## Validation of model selection

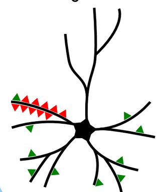



## Experiment 1: role of input statistics




| | |
|---|---|
| number of synapses | 10 |
| location of synapses | distributed or clustered |
| input firing rate | 20Hz (above), 2Hz (below) |
| correlations? | yes, due to shared spikes |
| conductances | passive only (inc. NMDA) |
| size of training set | 32s |
| size of test set | 8s |
| trials per condition | 10 |



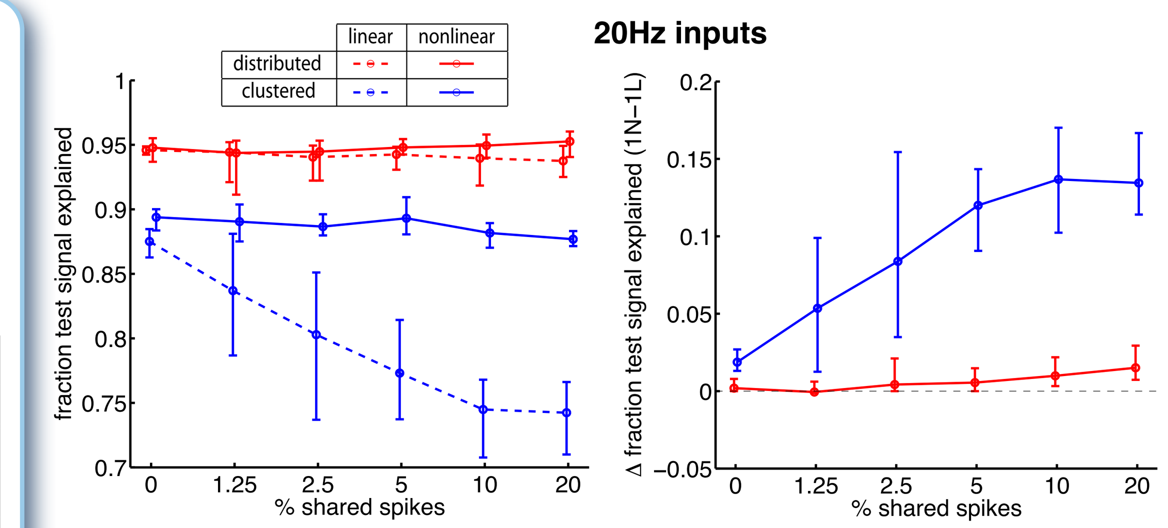




$f^* = 1 - \frac{\epsilon}{s}$

rms error $\epsilon$

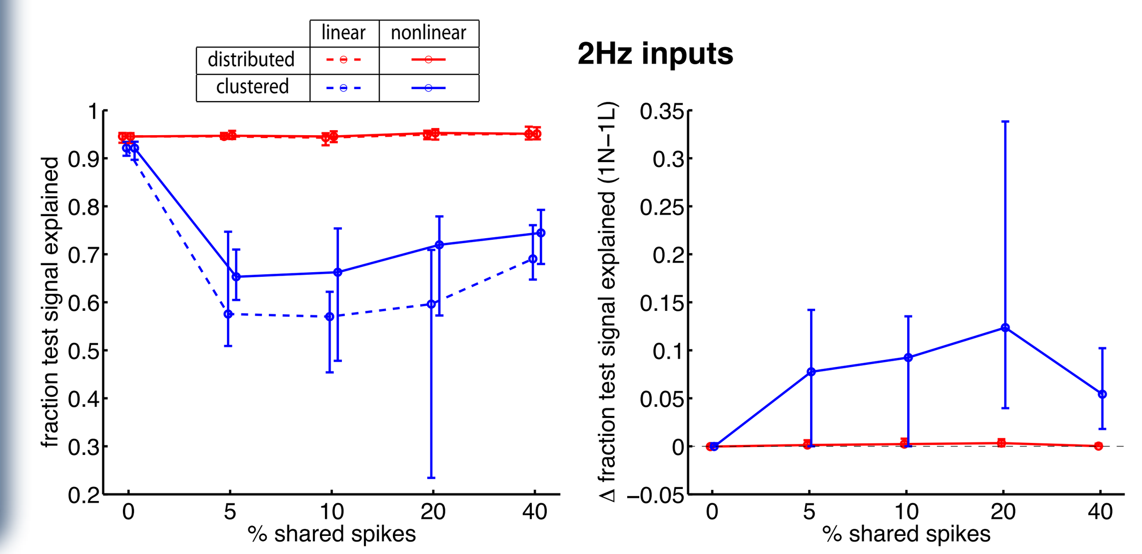
std of v $s$

**20Hz inputs**



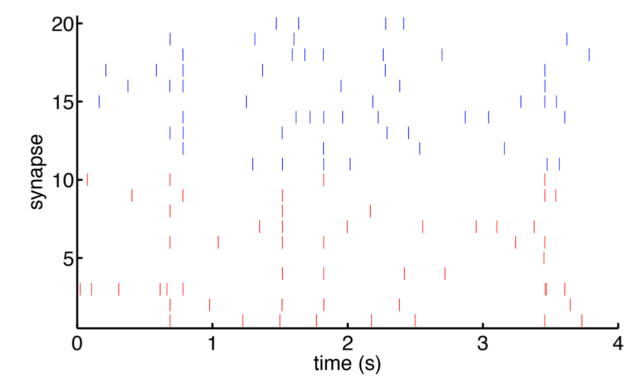

**Both spatial and temporal clustering necessary to elicit nonlinear behavior.**

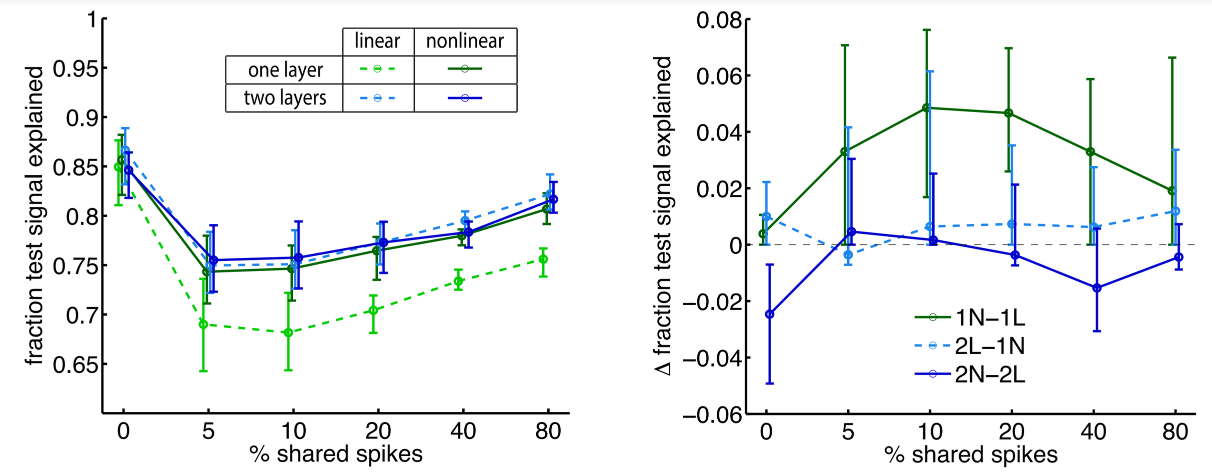
**2Hz inputs**




## Experiment 2: lack of two-layer behavior

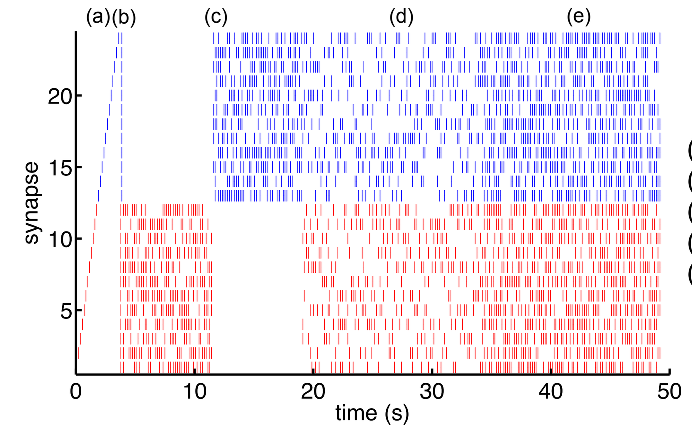
| | |
|---|---|
| number of synapses | 20 |
| location of synapses | 10 each on 2 branches |
| input firing rate | 2Hz |
| correlations? | yes, within- and across-branch |
| conductances | passive only (inc. NMDA) |
| size of training set | 32s |
| size of test set | 8s |
| trials per condition | 12 |



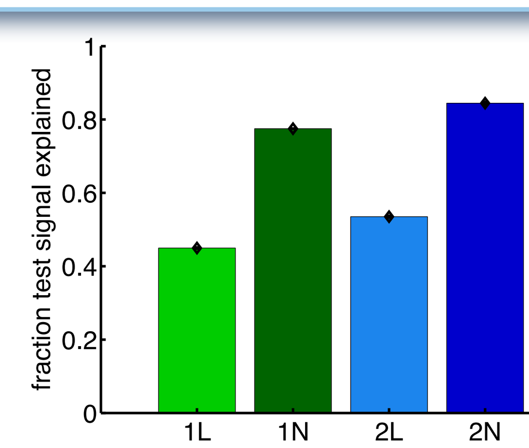

**Two-layer models do not perform significantly better than single global nonlinearity.**

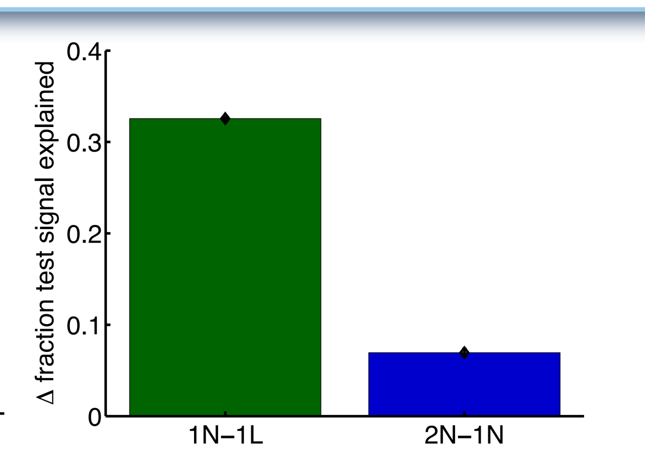
| | |
|---|---|
| number of synapses | 24 |
| location of synapses | 12 each on 2 branches |
| input firing rate | varies in time |
| correlations? | yes, varies by event type |
| conductances | active and passive |
| size of training set | 50s |
| size of test set | 50s |
| trials per condition | 2 |




**event types**

(a) each synapse alone (24 events)
(b) all 12 on one branch (2)
(c) 6 random on one branch (100)
(d) 3 random on each branch (100)
(e) 6 random on each branch (100)




## Compartmental model details

- cortical pyramidal neuron with AMPA and NMDA synapses of Branco et al 2010
- soma, axon, and 69 dendritic compartments
- active channels: Hodgkin-Huxley type Na+ and K+ channels, M-type K+ channel (slow, non-inactivating), Ca2+-dependent K+ channel, high-threshold Ca2+ current, and T-type Ca2+ channel
- all simulations performed in NEURON simulation environment (Hines & Carnevale 1997)

## Future work

- smarter structure learning
- alternative basis functions (dendritically filtered alpha kernels)
- output feedback filter (to model temporally extended responses)
- extension to hidden state space models
- use of more natural synaptic inputs
- fit data from glutamate uncaging experiments
- comparing functional architecture (inferred by the model) to anatomical morphology

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## Acknowledgements

We thank Maneesh Sahani, Jonathan Pillow, Zoubin Ghahramani, Judit Makara, and Tiago Branco for useful discussions. This work has been supported by the Winston Churchill Foundation of the United States (DJ), the University of Cambridge Department of Engineering (DJ), the Wellcome Trust (ML), and OTKA MB08-84471 (BU).