Cortical rhythms and interneurons for reading working memory
(a computational study of laminar DLPFC)

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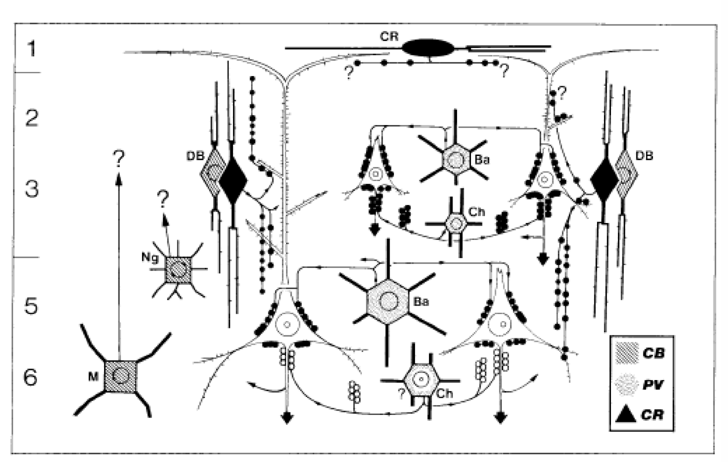
Introduction

Dorsolateral prefrontal cortex (DLPFC) maintains working memory (WM) in the persistent spiking of pyramidal cells. Experimental and theoretical studies have shown this activity depends on slow excitation between recurrently connected neurons [1]. Increasingly, working memory studies are characterizing network oscillations in the local field potential that are coincident with persistent activity. Relatively little is known about the generation of these rhythms, their relationship to persistent spiking, or the mechanisms that gate and appropriately direct communication of working memory to other cortical and subcortical areas. In many paradigms, DLPFC activity is partially driven by anterior cingulate cortex (ACC), which selectively synapses on superficial calbindin-positive (CB) interneurons. We hypothesize that ACC-mediated CB inhibition can coordinate persistent subassemblies to drive deep-layer DLPFC principal cells in asynchronous and rhythmic modes. To investigate potential mechanisms, we developed a computational model of laminar DLPFC including multiple classes of interneurons, superficial and deep layers, and mechanisms providing persistence & rhythmicity.

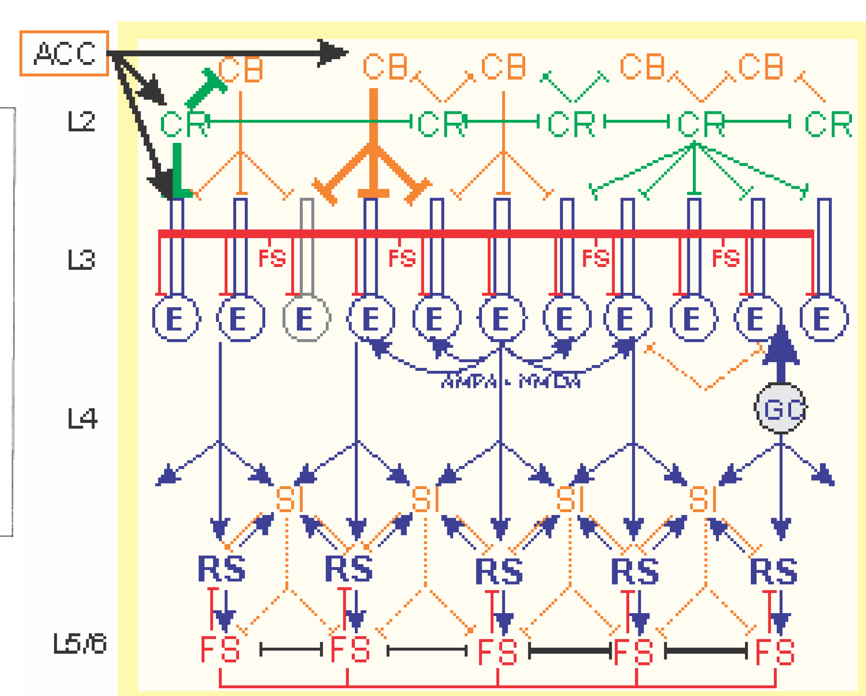
Methods

Laminar DLPFC



Ref [3], Figure 29.

Computational model



Population	Intrinsic currents	Inputs
CB	$NaF + KDR + L$	$\boldsymbol{I_{ACC}}$
E	$Na, K, leak, \frac{d}{dt}[Ca^{2+}]$, Ca, Can	$\boldsymbol{I_{Cue}}$
Edend	NaP, Ks, leak	
FS	Na, K, leak	
RS	Na, K, leak	
LTS/SI	Na, K, h, leak	$\boldsymbol{I_{ACC}}$

$$\dot{V} = -\sum_{channels} I_{int} - \sum_{channels} I_{int} + \boldsymbol{I_{ACC}} + I_{Cue} + \eta,$$

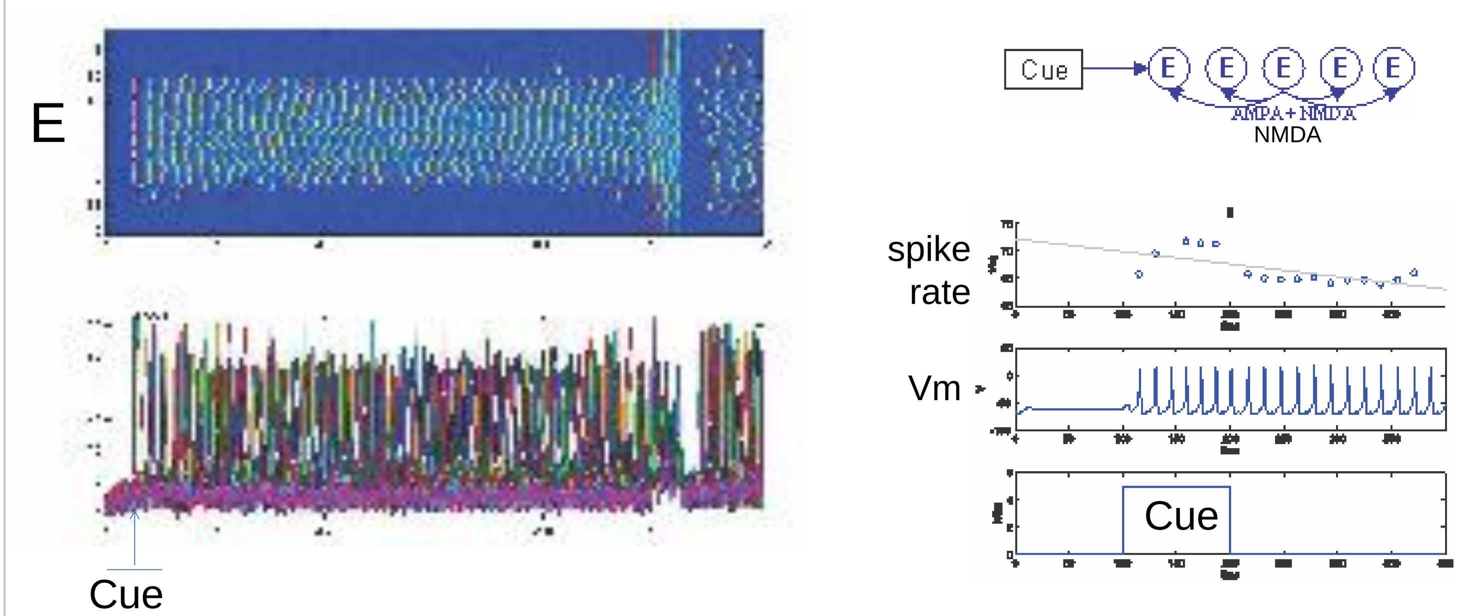
$$I_{int} = \boldsymbol{g_{int}} m^M h^H (V - E_{int})$$

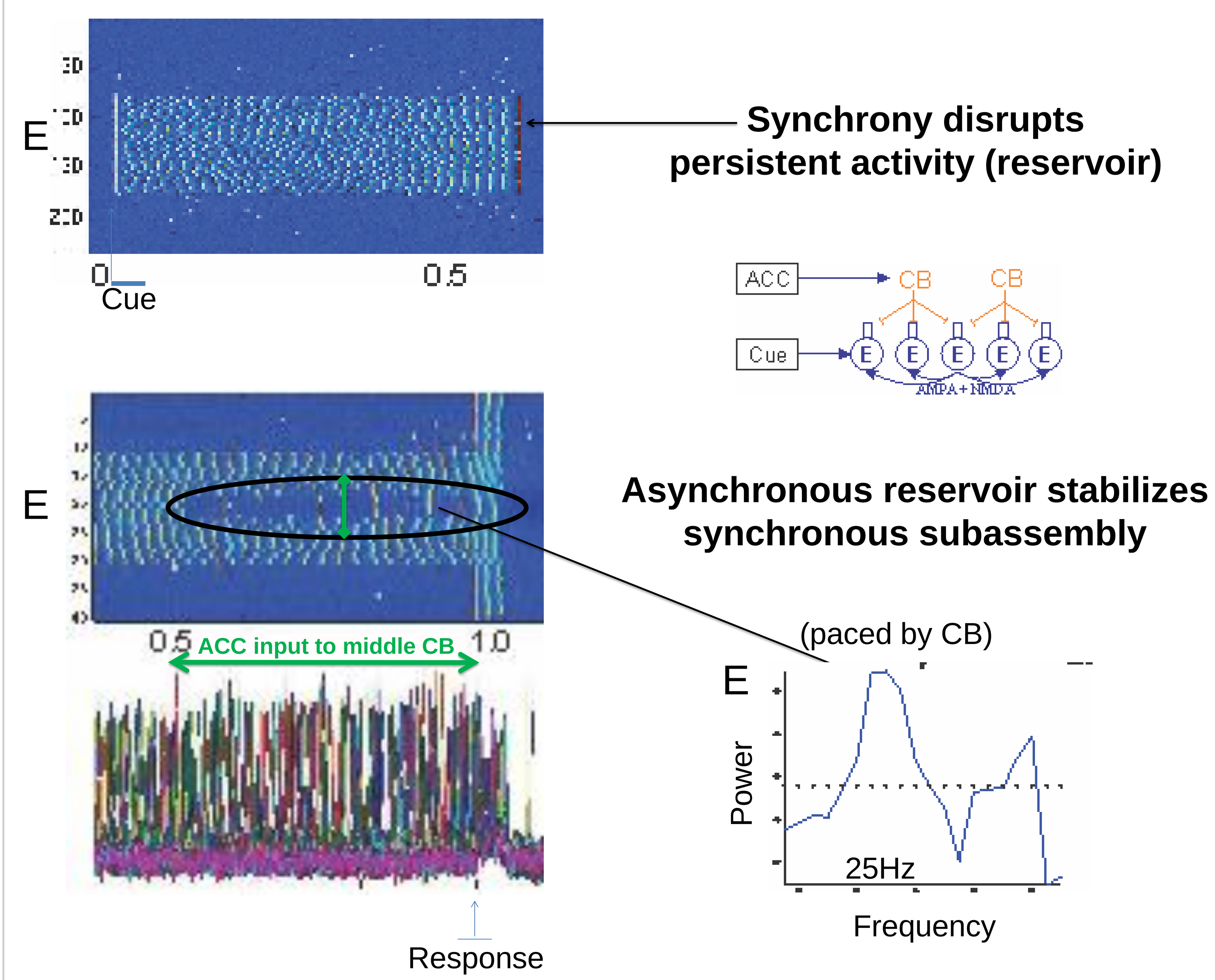
$$I_{syn} = g_{syn} s K^{XY} (V - E_{int}), \dot{s} = f(V, \boldsymbol{\tau_{syn}})$$

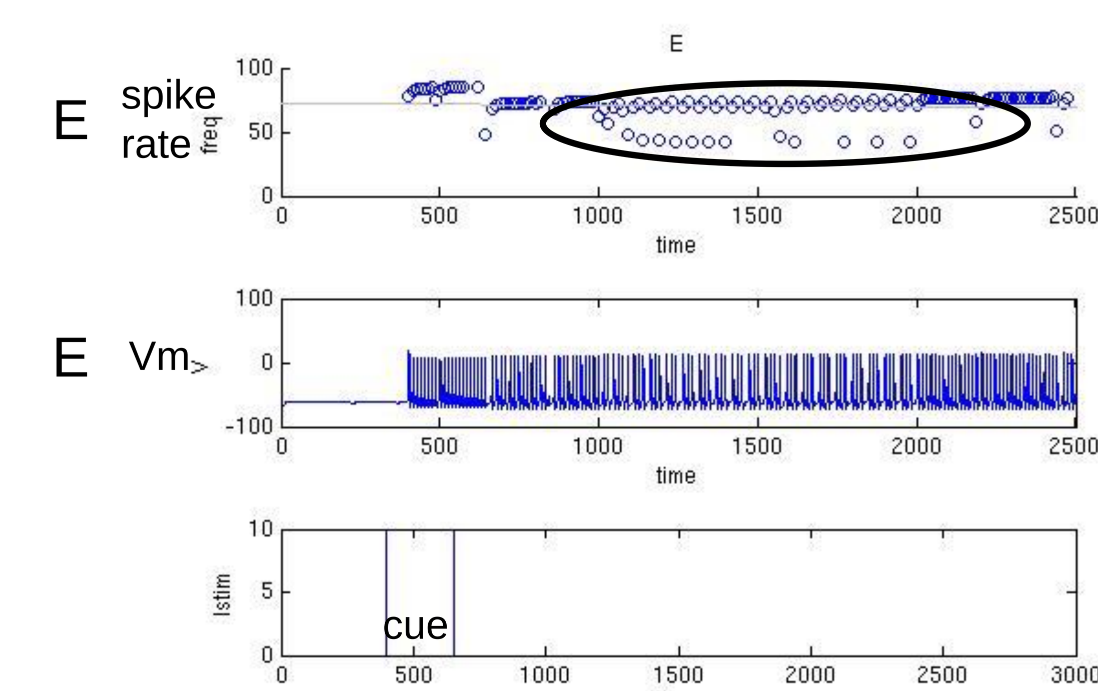
$$K^{XY} = c_{XY} e^{-\left\|\frac{x-y}{\sigma_{XYs}}\right\|^2}, \eta \sim N(0,\sigma)$$

Working memory maintenance in L2/3 DLPFC

Persistent spiking maintained by slow recurrent excitation

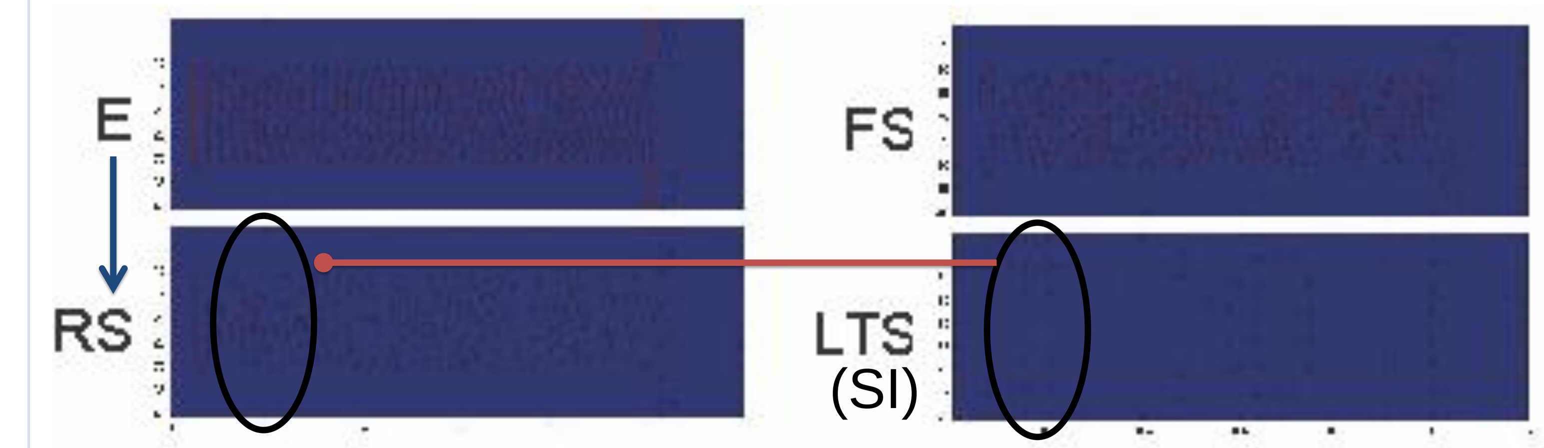




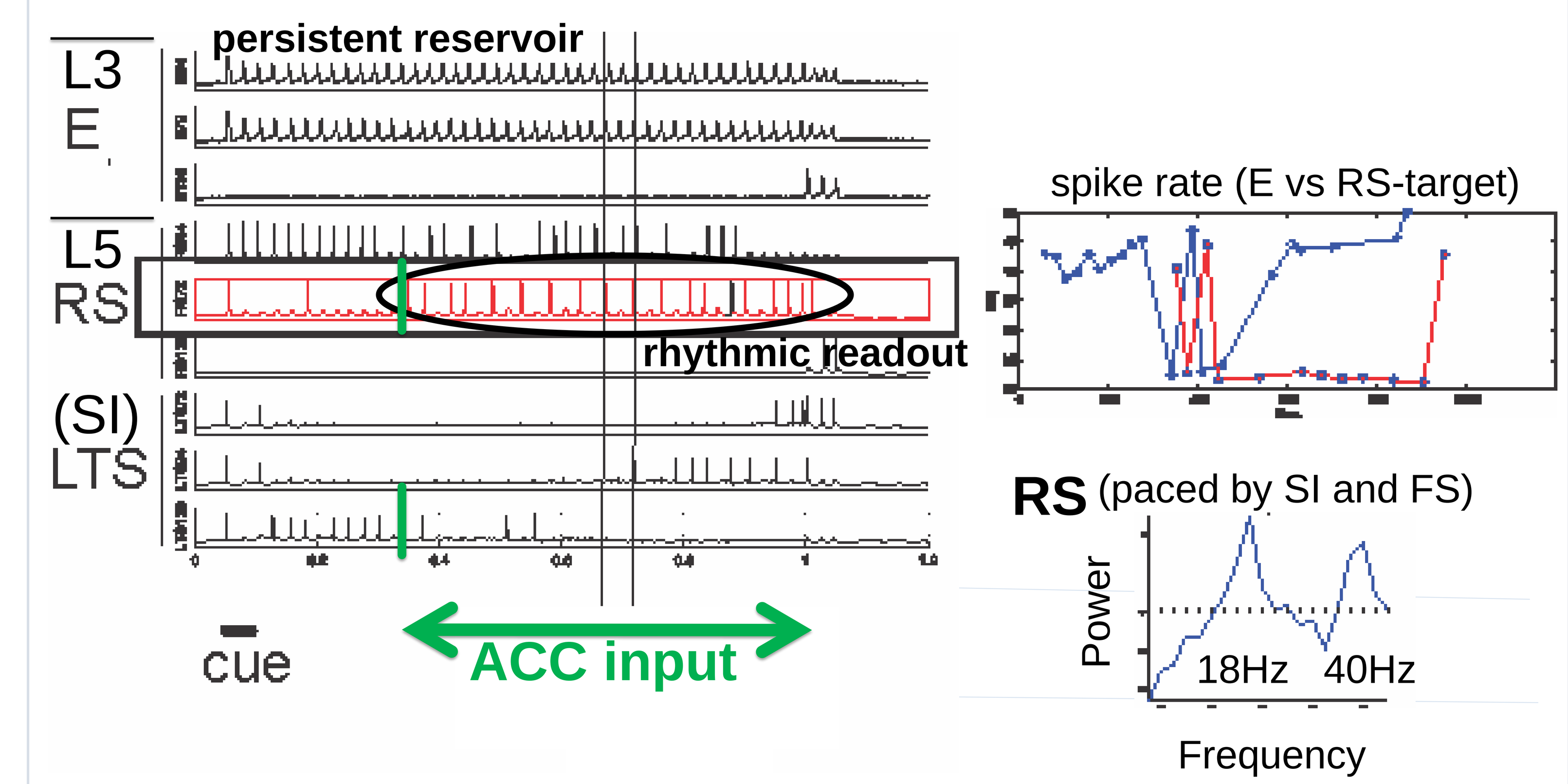


ACC control mechanisms for WM readout

Persistent reservoir-driven SI interneurons gate RS spiking



Rhythmic subassembly readout of asynchronous reservoir



ACC-targeted CB disinhibit RS by silencing SI/LTS

Conclusions

- Persistent activity in DLPFC can be stably maintained in asynchronous spiking and rhythmic subassemblies; the latter requires additional asynchronous drive from a larger reservoir of persistent activity.
- Interneurons targeted by ACC can gate readout of persistent activity in DLPFC by disinhibiting response cells driven by the persistent reservoir.
- Asynchronous activity can be read-out in asynchronous or rhythmic modes paced by either slow or fast interneurons.

References

1. Wang, Min, et al. *Neuron* 77.4 (2013): 736-749.
2. Barbas, Helen, J. Bunce, and Maria Medalla. *Principles of Frontal Lobe Functions* (2013): 31-48.
3. Gabbott, Paul LA, and Sarah J. Bacon. *Journal of Comparative Neurology* 364.4 (1996): 567-608.