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Relating firing rate codes and oscillations to function and pathology of neural circuits

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Questions

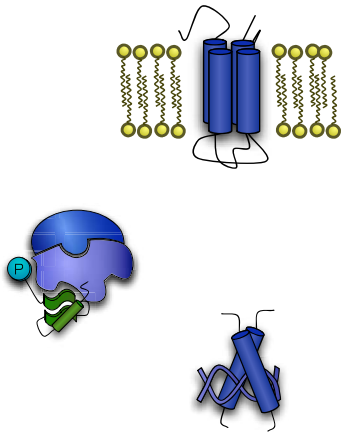
1. Are rate-coded computations and gamma frequency network oscillations generated from the same neural hardware?

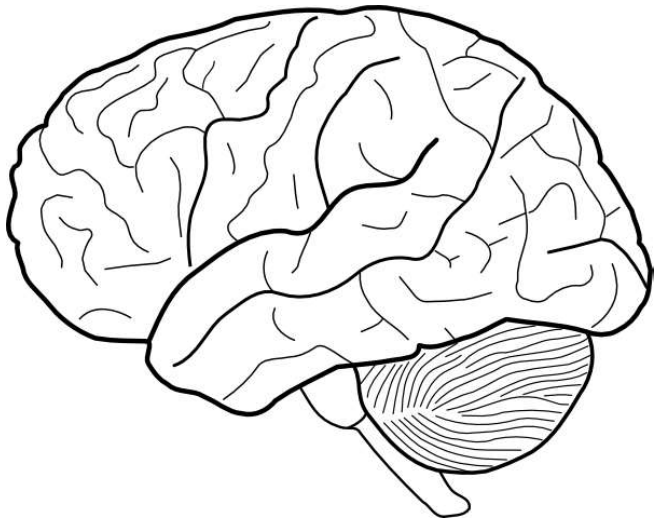
2. How does excitatory and inhibitory synaptic strength influence rate-coded computation and gamma oscillations?

3. Can rate-coded computation and gamma oscillations be differentially modulated? Or, do gamma oscillations index rate coded computations?

What are the key biological mechanisms that determine cognitive functions?

Molecules



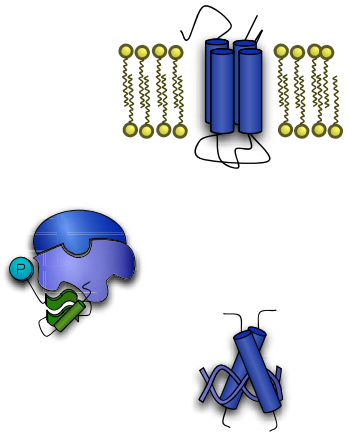


Behaviour

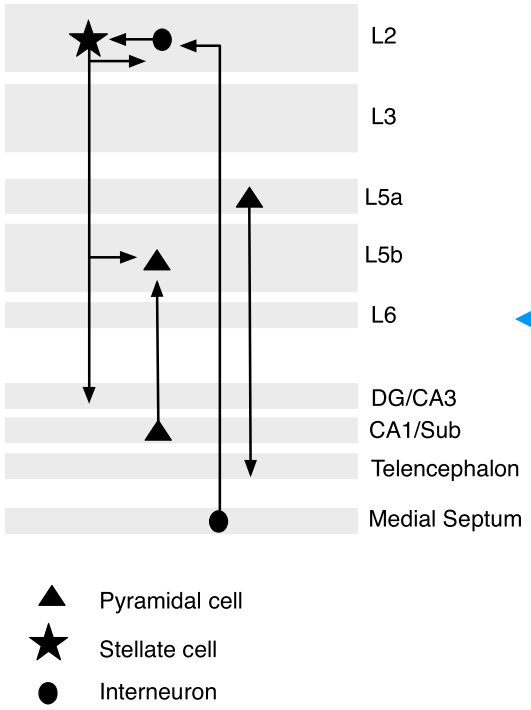
Disorders

What are the key biological mechanisms that determine cognitive functions?

Molecules



Circuits



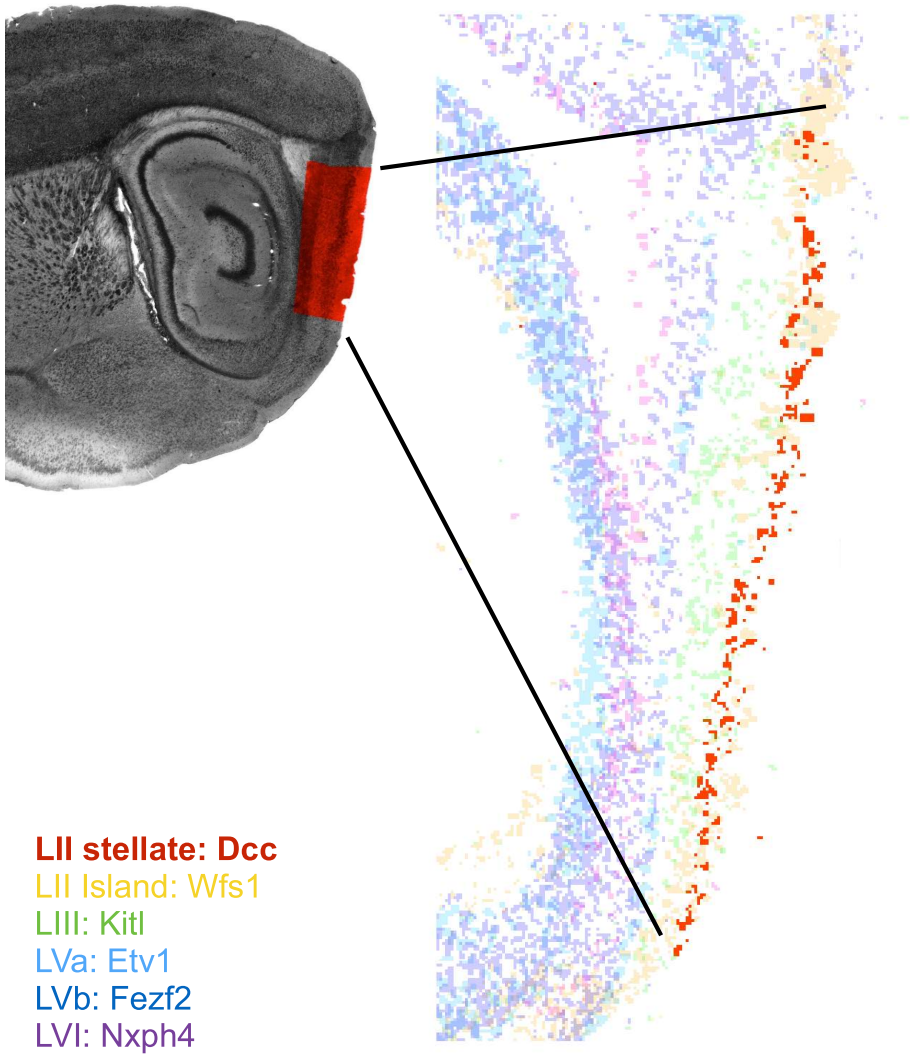
Algorithms

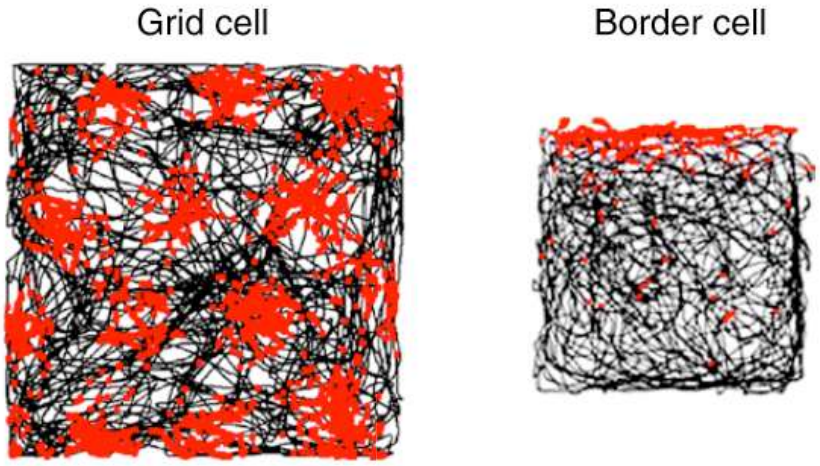
$$p(t) = p_0 + \int_o^t v(t)\partial t$$

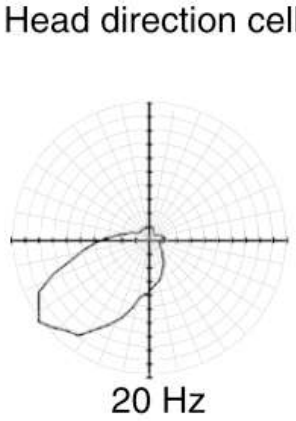
Behaviour

Disorders

The medial entorhinal cortex contains multiple molecular and functional cell types





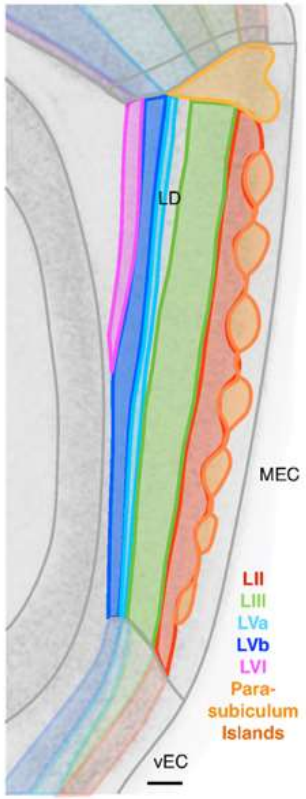


Ramsden, Sürmeli, McDonagh & Nolan,
PLoS Comp. Biol. (2015)

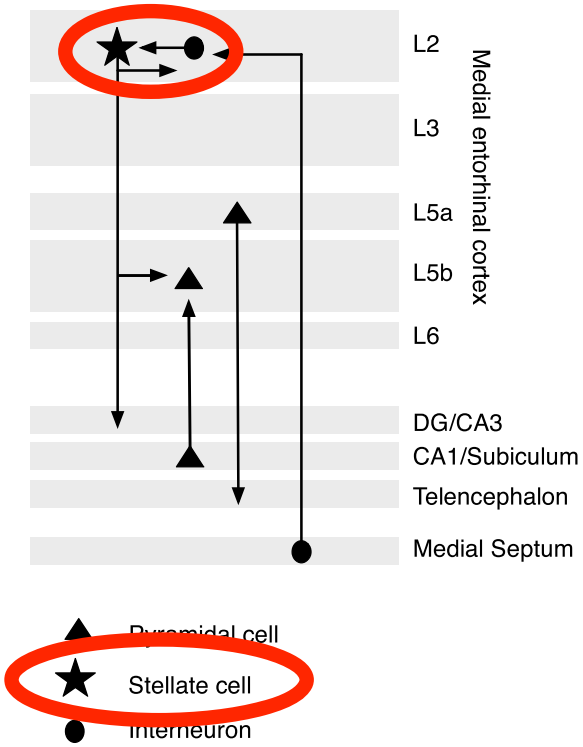
Marozzi and Jeffery, Current Biology (2012)

Molecular, circuit and theoretical approaches to mechanisms of entorhinal computation

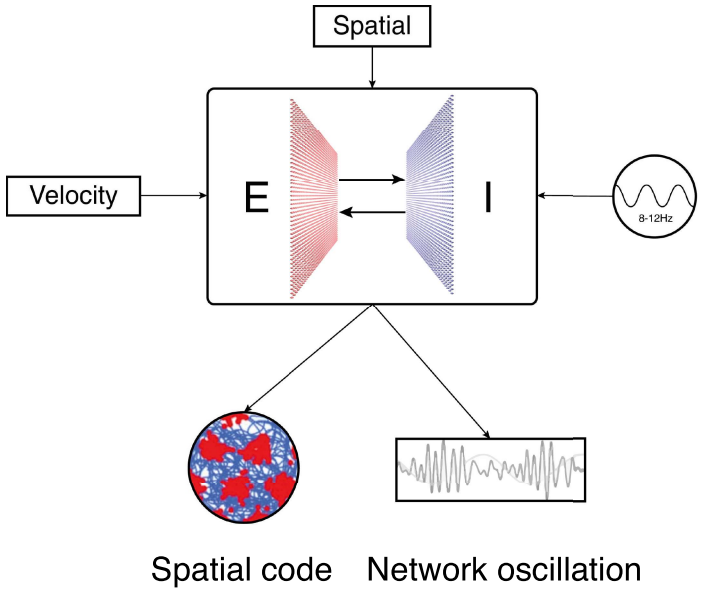
Molecular topography



Circuit connectivity



Circuit models and analysis



Ramsden et al. PLoS Comp. Biol. (2015)
Sürmeli et al. Neuron (2015)

Pastoll et al. Neuron (2013)
Gonzalez-Sulser et al. J. Neurosci. (2014)
Sürmeli et al. Neuron (2015)

Pastoll et al. Neuron (2013)
Solanka et al. eLife (2015)
Chadwick et al. eLife (2015)

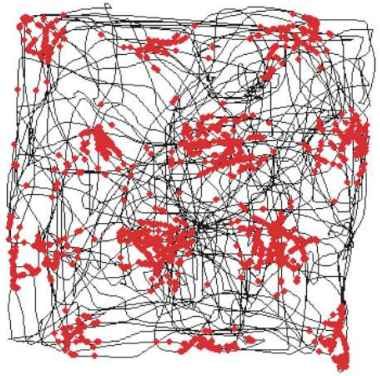
1. Organisation of circuits within layer 2 of the MEC

2. A shared circuit mechanism for grid firing and theta-nested gamma oscillations

3. Model-based predictions for relationships between rate coded computations and network oscillations

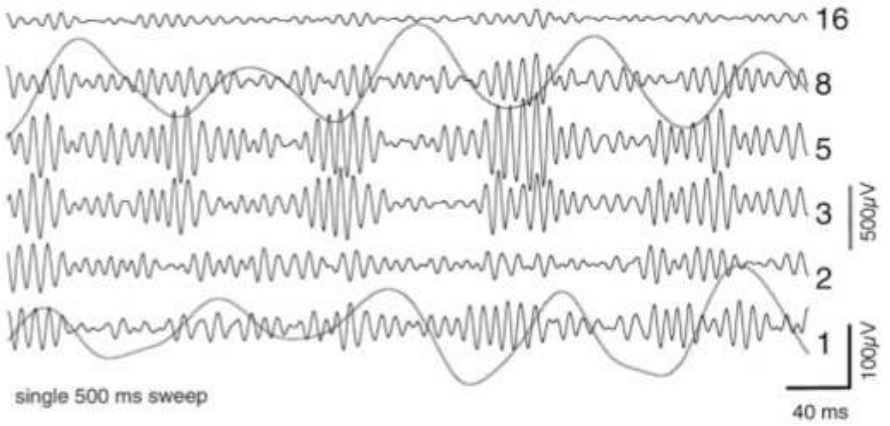
In vivo ‘read outs’ of circuit activity in the medial entorhinal cortex

Spatial firing fields



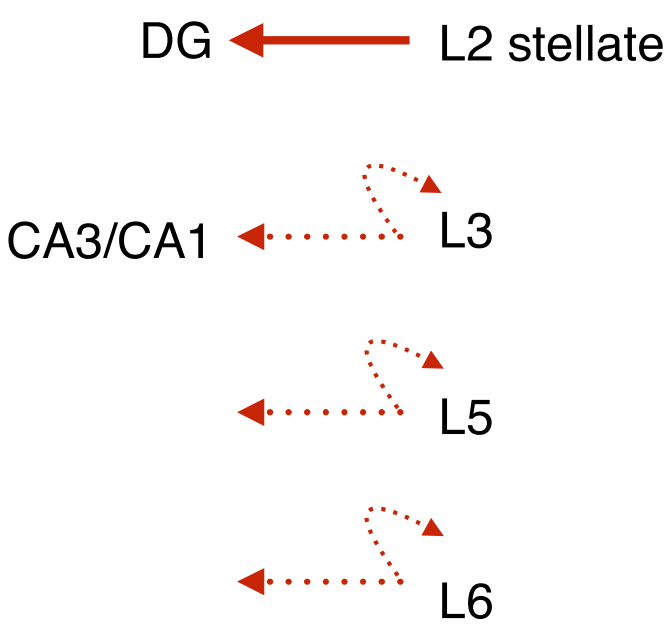
Hafting et al., 2005

Theta (4-12 Hz) and gamma (30 - 100 Hz) activity



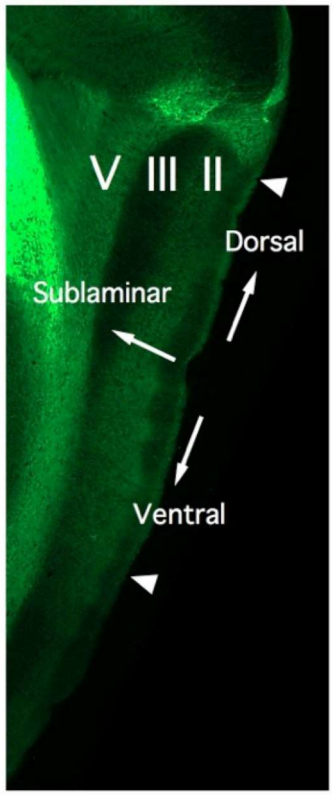
Chrobak and Buzsaki, 1998

A view of intra-laminar connectivity in the MEC based on simultaneous recordings from pairs of neurons

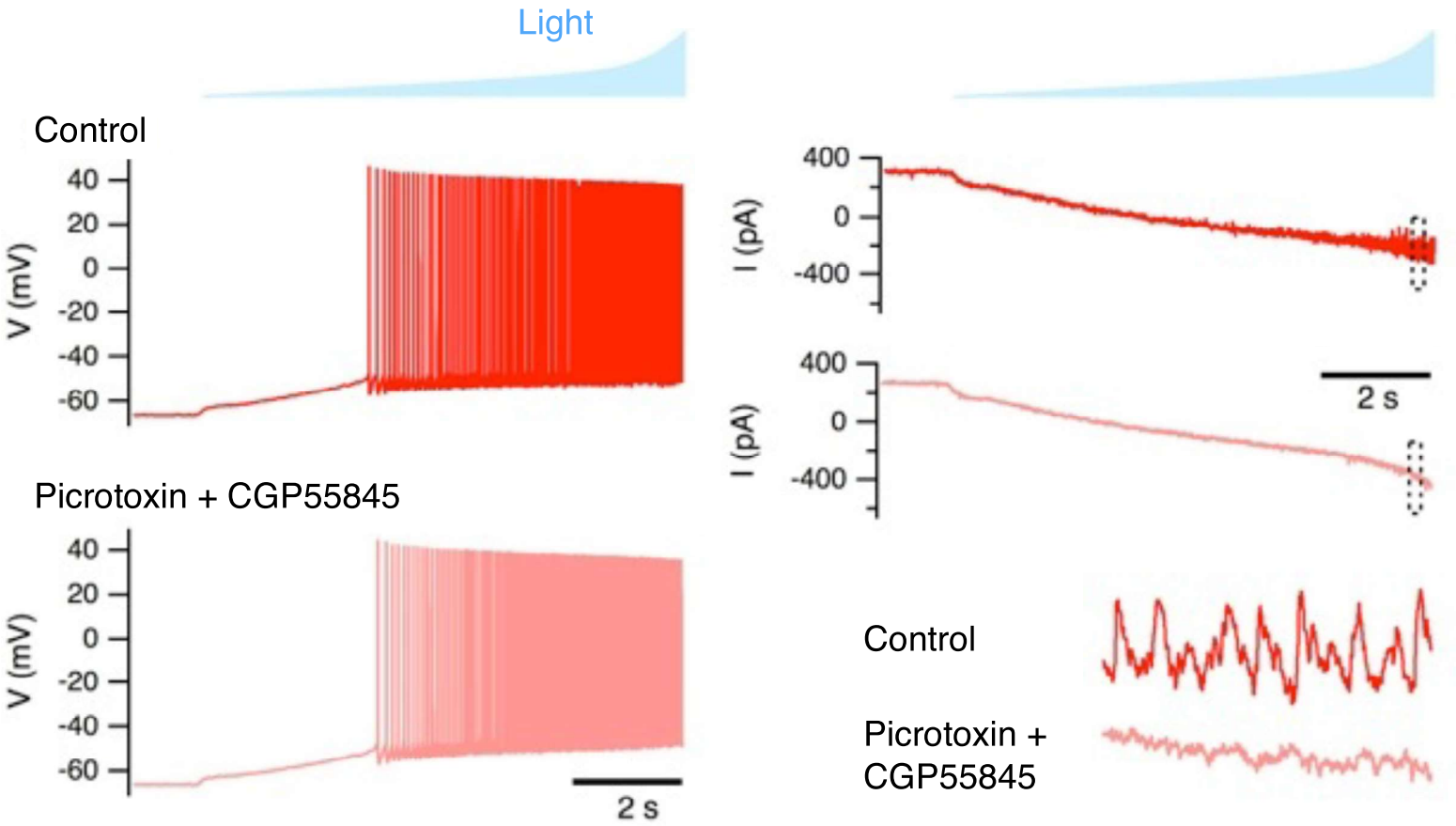


Dhillon and Jones, Neuroscience (2000)

Stellate cells do not interact through local excitatory connections

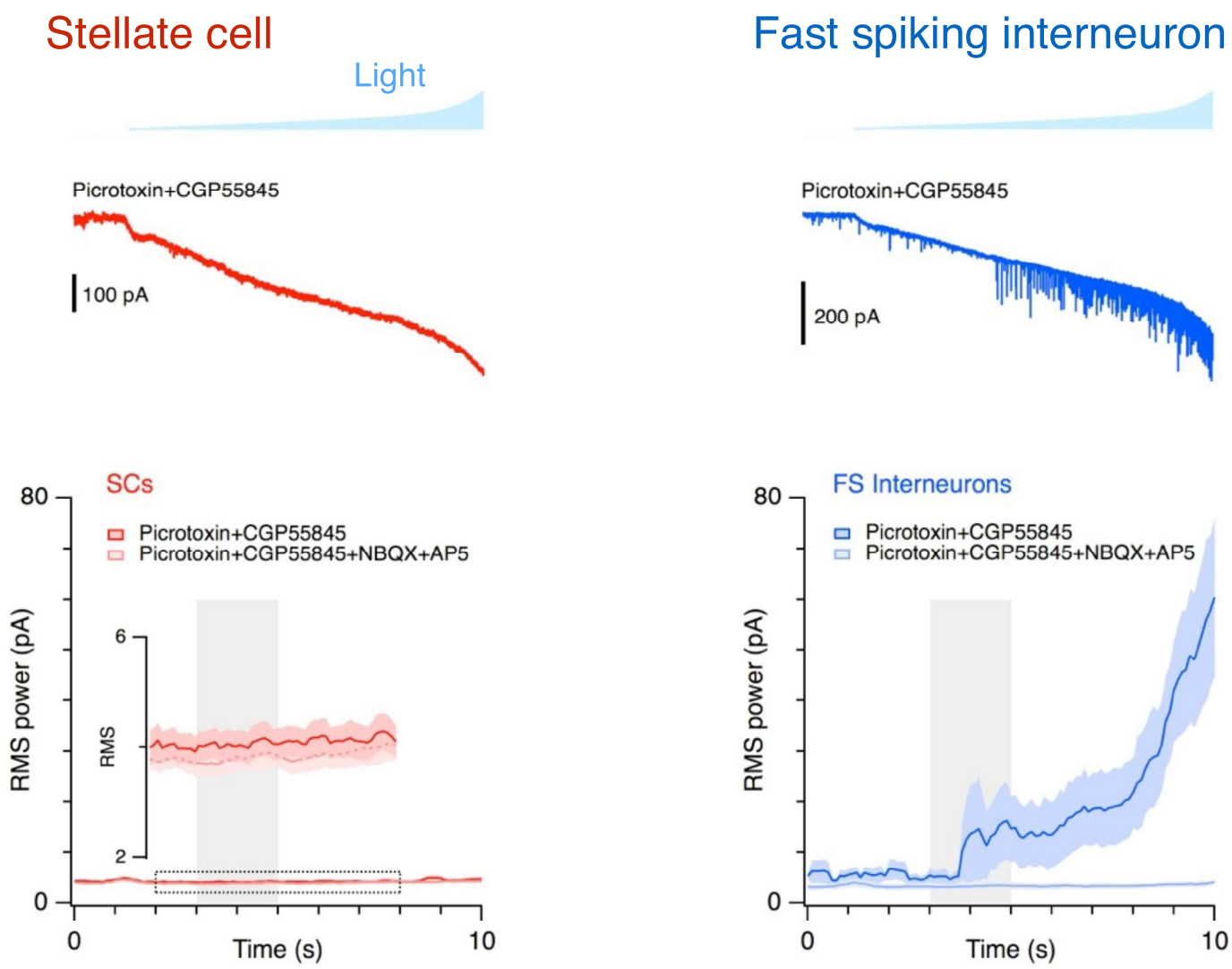


Thy1-ChR2-YFP
(Arenkiel et al., 2007)



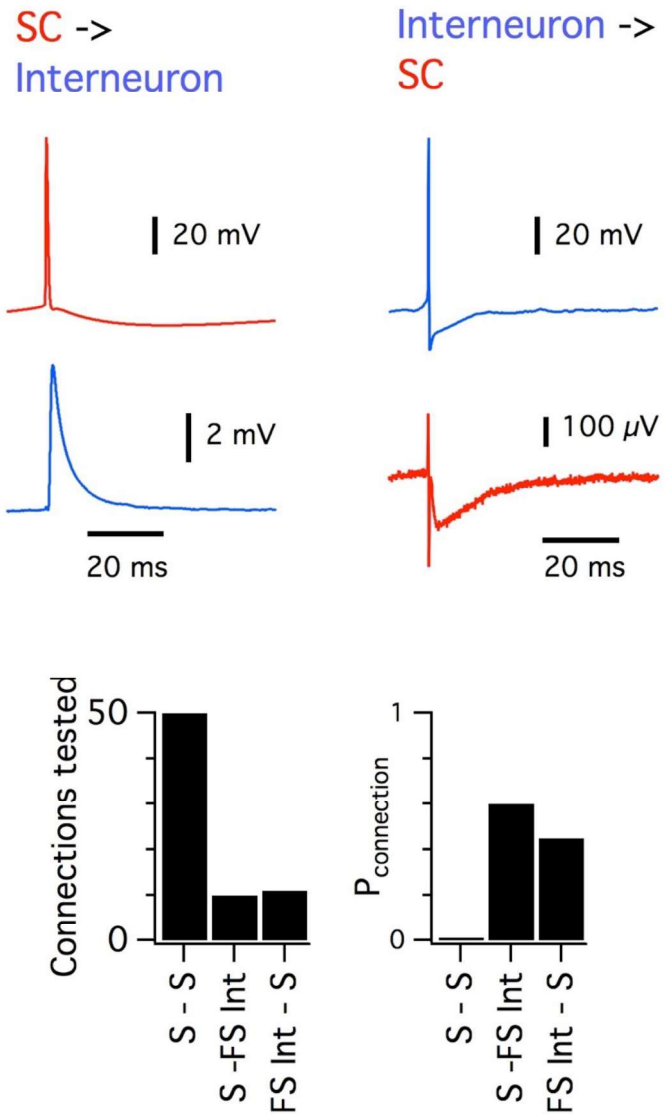
Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)

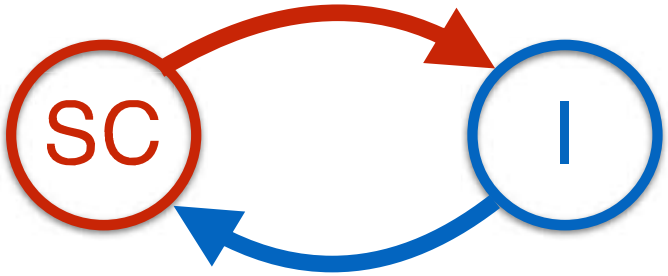
Stellate cells provide excitatory input to fast spiking interneurons



Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)

Stellate cells communicate via inhibitory interneurons

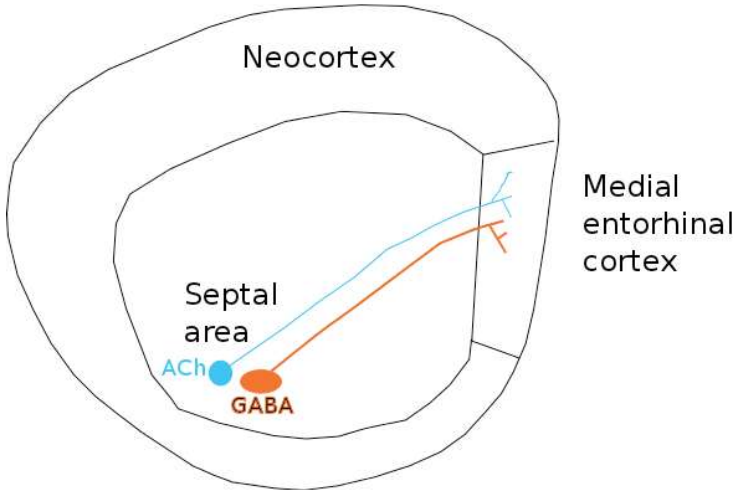


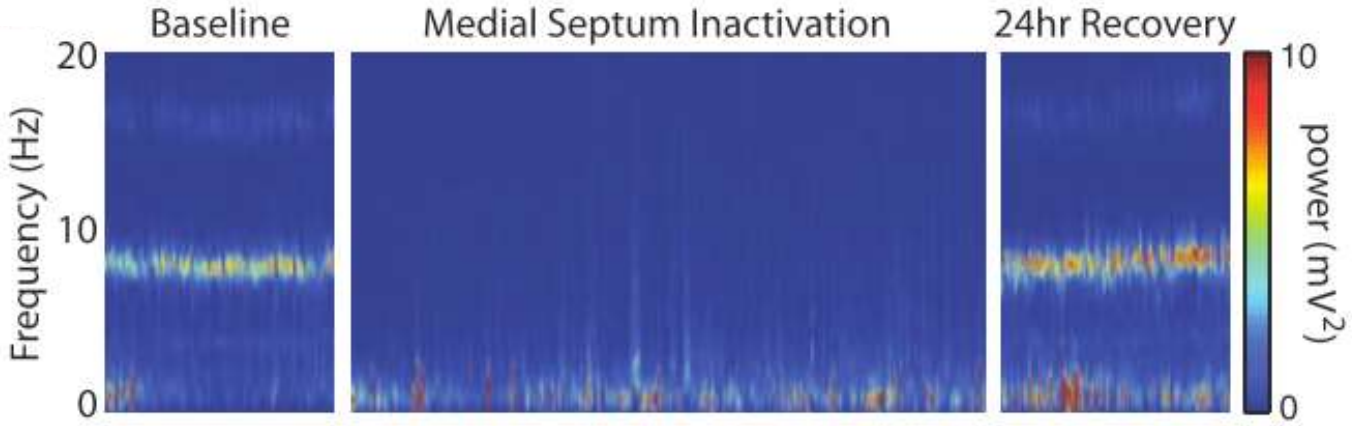


See also:
Dhillon and Jones, Neuroscience (2003)
Couey et al. Nature Neuroscience (2013)

Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)

Is theta frequency input sufficient to elicit nested gamma?

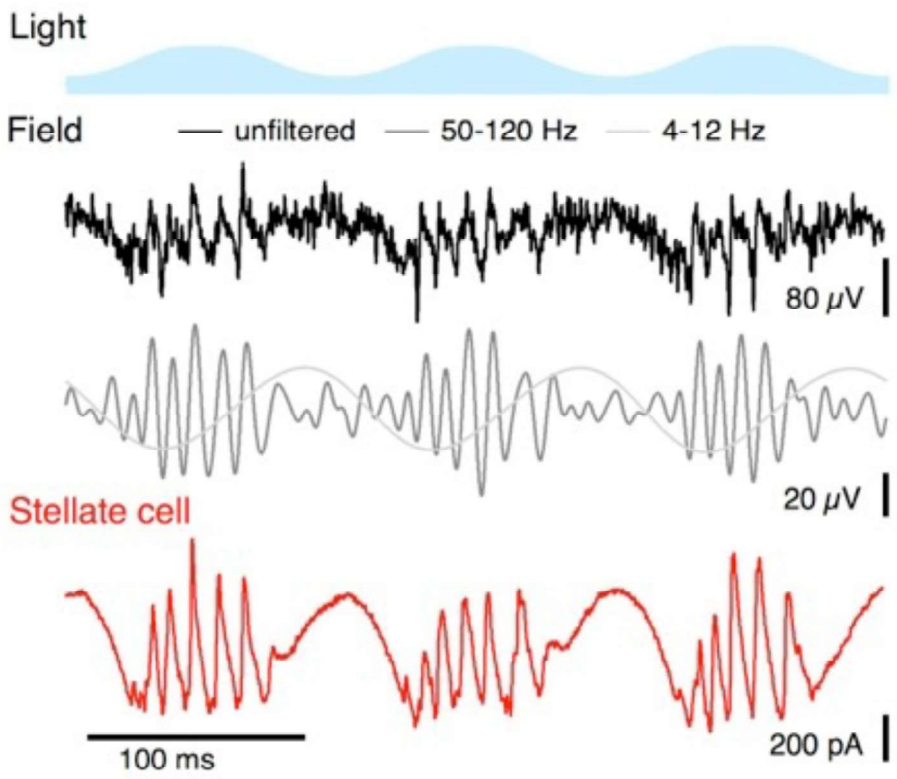




Theta activity requires external drive from the septum

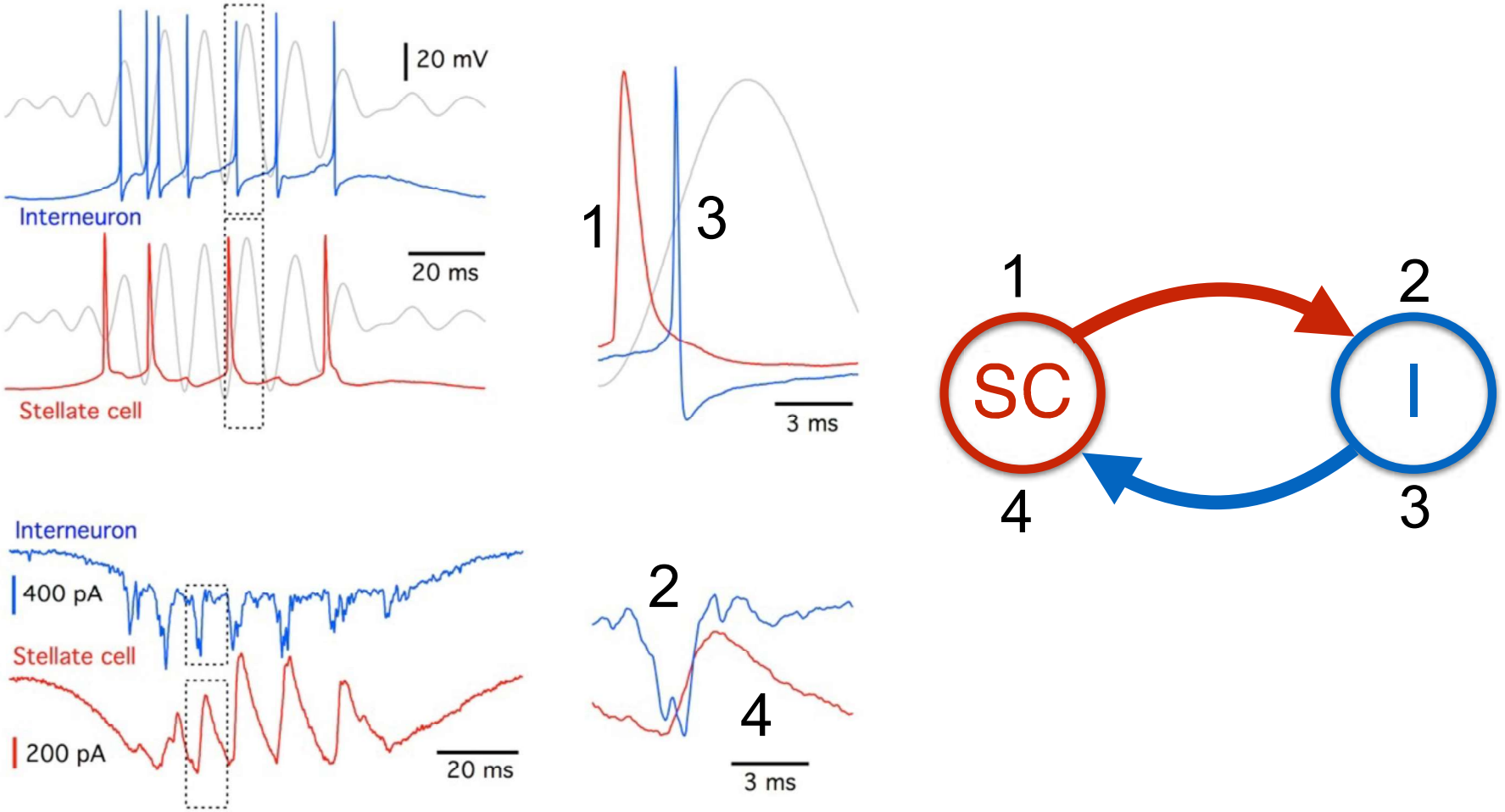
Brandon et al. Science (2011)
see also Koenig et al. Science (2011)

Theta drive is sufficient for emergence of nested gamma oscillations



Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)

Nested gamma involves recurrent interactions between interneurons and stellate cells



Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)

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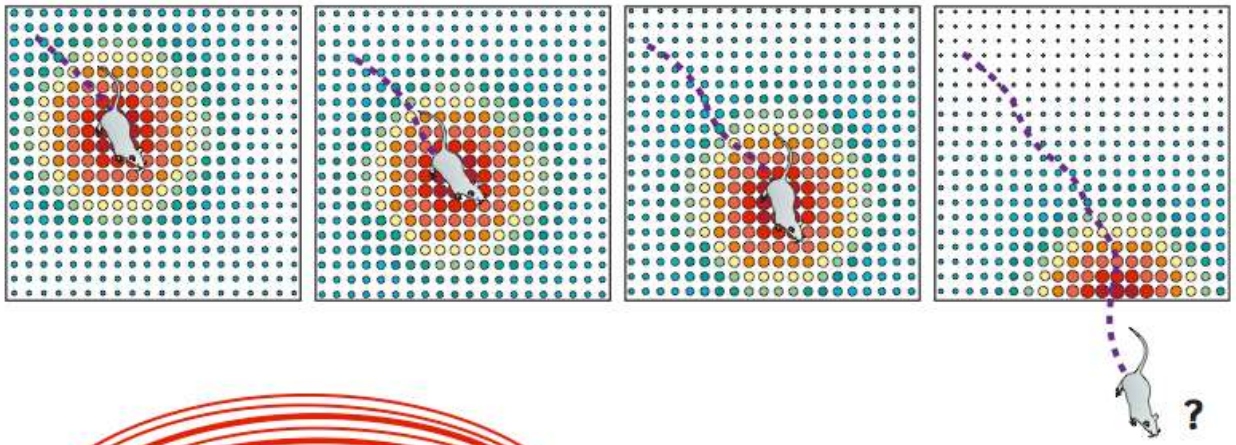
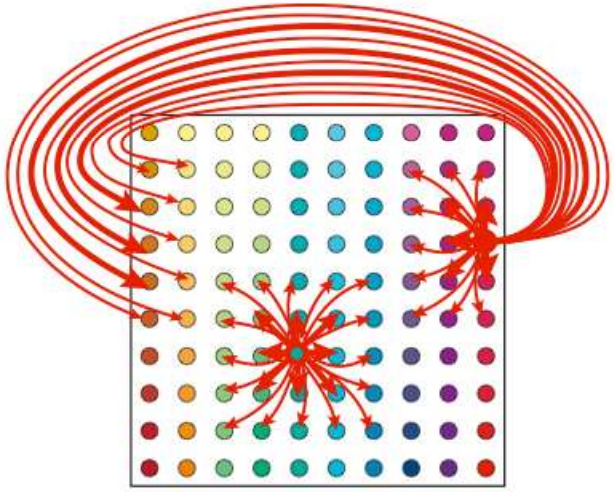
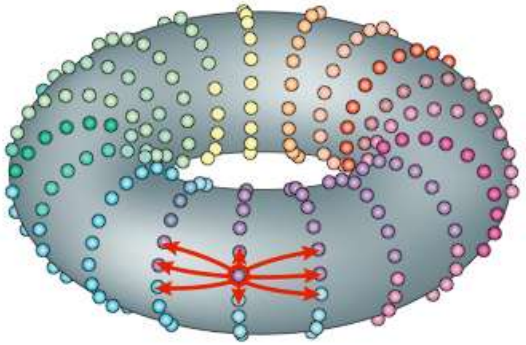
Representation of space using ‘attractor maps’







McNaughton et al., Nature Reviews Neuroscience (2006)

Path integration attractor models with E-E connections:
Samsonovich and McNaughton J. Neurosci. (2006)
Fuhs, Touretzky J. Neurosci. (2006)
Guanella, Kiper, Verschure Int J Neural Syst (2007)

Models with exclusively I-I connections:
Burak, Fiete PLoS Comput Biol (2009)

E-I connectivity multiplexes gamma oscillations and rate codes

Theta

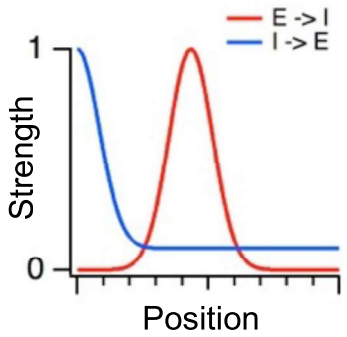
Place cells
(active 100 ms / 10 s)

Direction x
speed cells

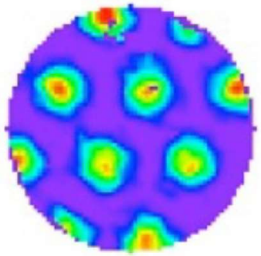
E

I

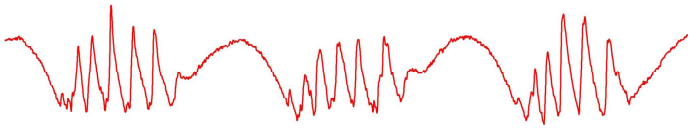
E cells: 68 x 58 sheet
I cells: 33 x 29 sheet



Grid fields / network
attractor states



Clock-like theta-nested
gamma oscillations

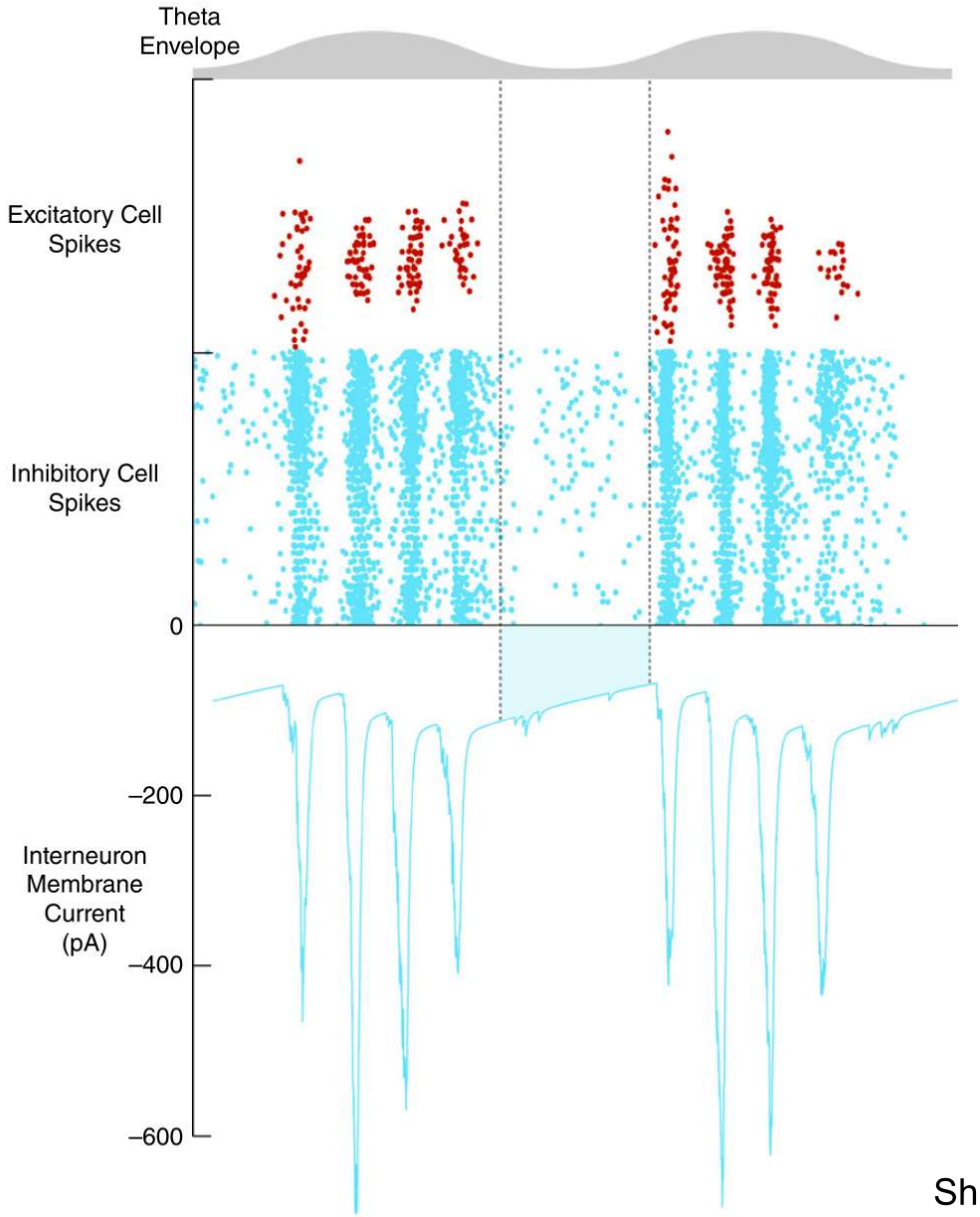


Timing code

Rate code

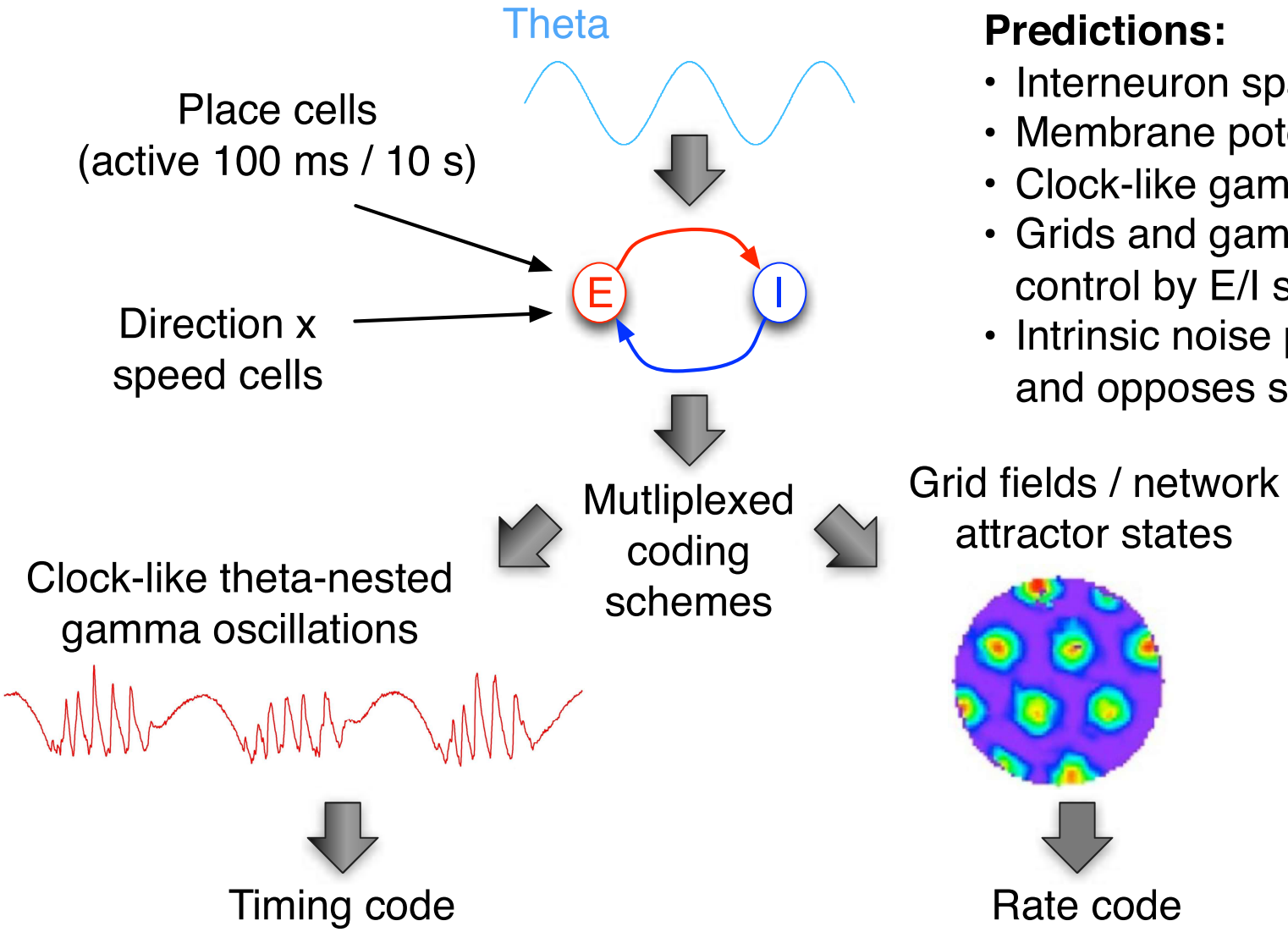
Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)
Solanka, van Rossum and Nolan, eLife (2015)

Activity bumps are maintained across theta cycles by slow synaptic currents



Shipston-Sharma et al., J. Physiol. (2016)

E-I models predict circuit dynamics and organisation



Predictions:

- Interneuron spatial firing fields.
- Membrane potential dynamics.
- Clock-like gamma.
- Grids and gamma differentially control by E/I synaptic strength.
- Intrinsic noise promotes grid firing and opposes seizures.

Pastoll, Solanka, van Rossum and Nolan, Neuron (2013)
Solanka, van Rossum and Nolan, eLife (2015)

1. Organisation of circuits within layer 2 of the MEC

2. A shared circuit mechanism for grid firing and theta-nested gamma oscillations

3. Model-based predictions for relationships between rate coded computations and network oscillations

What is the relationship between gamma oscillations and normal cognition / cognitive disorders?

Gamma oscillations correlate with various measures of cognitive activity, ability and dysfunction. What this means mechanistically is unclear.

Hypothesis 1: Computations are rate coded. Gamma may index circuit computation, but is not functionally important.

Hypothesis 2: Gamma and rate codes implement distinct computations. E.g. communication through coherence may operate orthogonally to rate coded computations.