Internal representation of hippocampal neuronal population span a time-distance continuum

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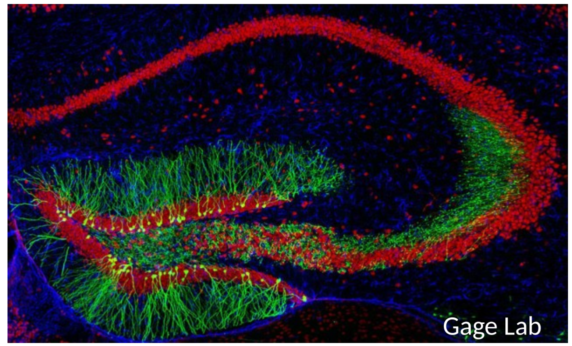
NeuroFrance, 2021

Hippocampus as a processor

Raw spatio-temporal data



Processed information

Space
Place Cells
Grid/border cells
Head direction cells

Context
Lateral Entorhinal Cortex

Timing
Theta rythm
Speed cells

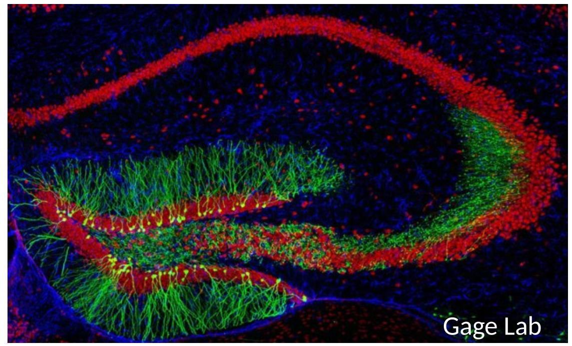
Place

Duration

Distance

Processing information in Hippocampus

Raw spatio-temporal data



Processed information

Space
Place Cells
Grid/border cells
Head direction cells

Context
LEC

Timing
Theta rythm
Speed cells

Bittner et al 2015
Milstein et al 2015

Place

Duration

Distance

Hippocampus as a processor

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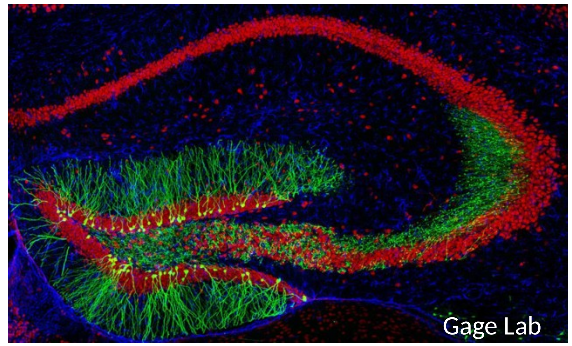

Processed information

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Timing
Theta rythm ia fundamental
Speed cells

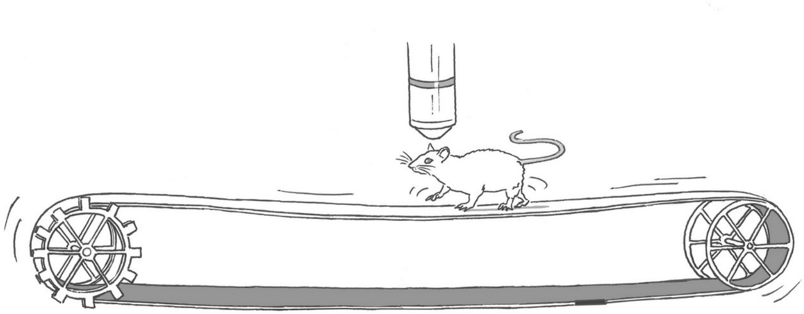
Place

Duration

Distance

Internally Generated Cell Assembly Sequences in the Rat Hippocampus
Pastalkova, Itskov, Amarasingham & Buzsáki, Science (2008)

New paradigm with spontaneous behavior



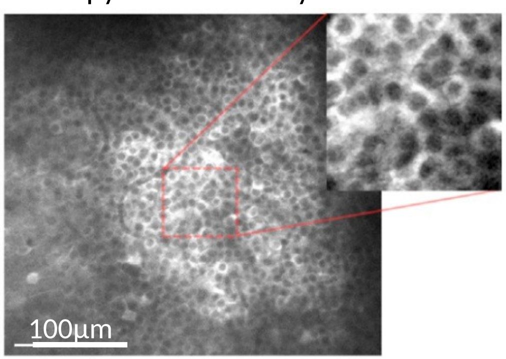
Headfixed mouse on a treadmill

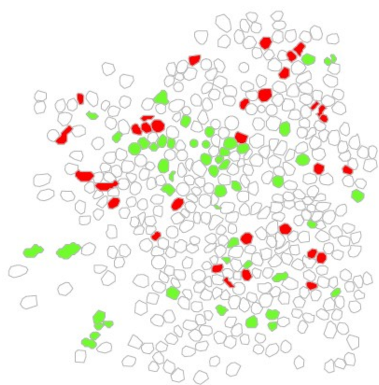
Minimize external information and constraints

- Non motorized
- No task, no reward
- No cues, experiment in the dark
- Neither water nor food deprivation
- N=7 mice

Large-scale calcium imaging

CA1 pyramidal cell layer

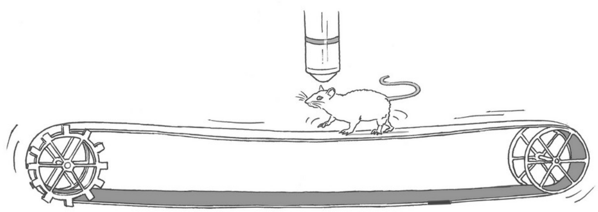


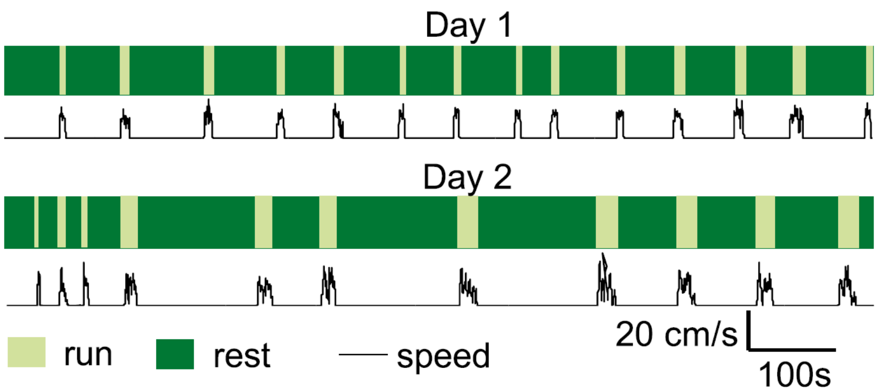


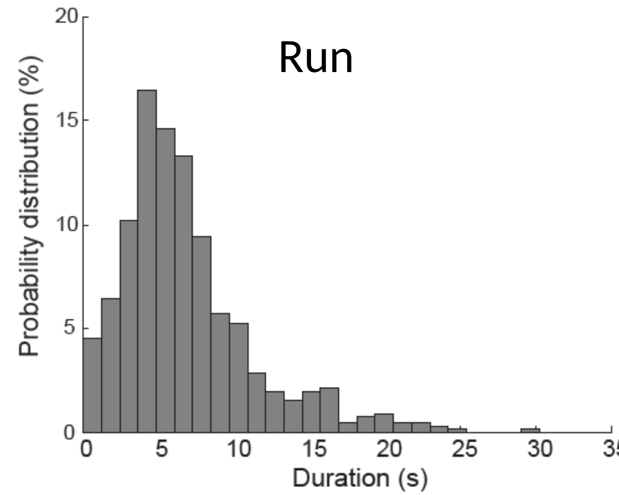
- Chronic implantation of
- cranial window
- 400x400µm² field of view
- 140+-47 active neurons over 1000
- 39+-11 % activated during run
- 34 imaging sessions of 20/30 min
- 2 consecutive days sessions

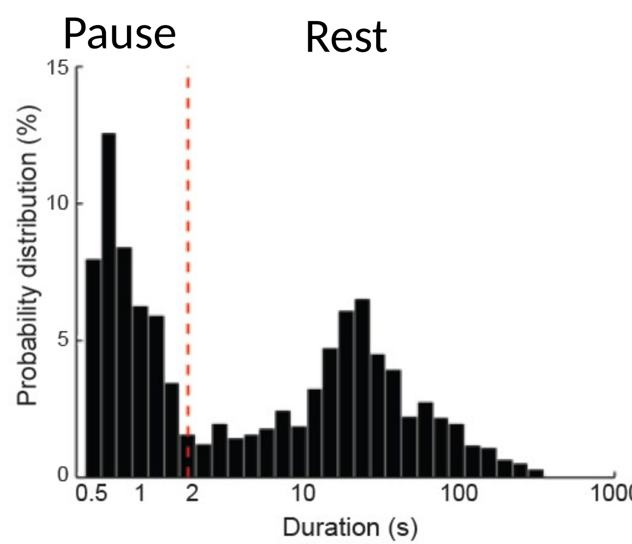
Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Spontaneous behavior









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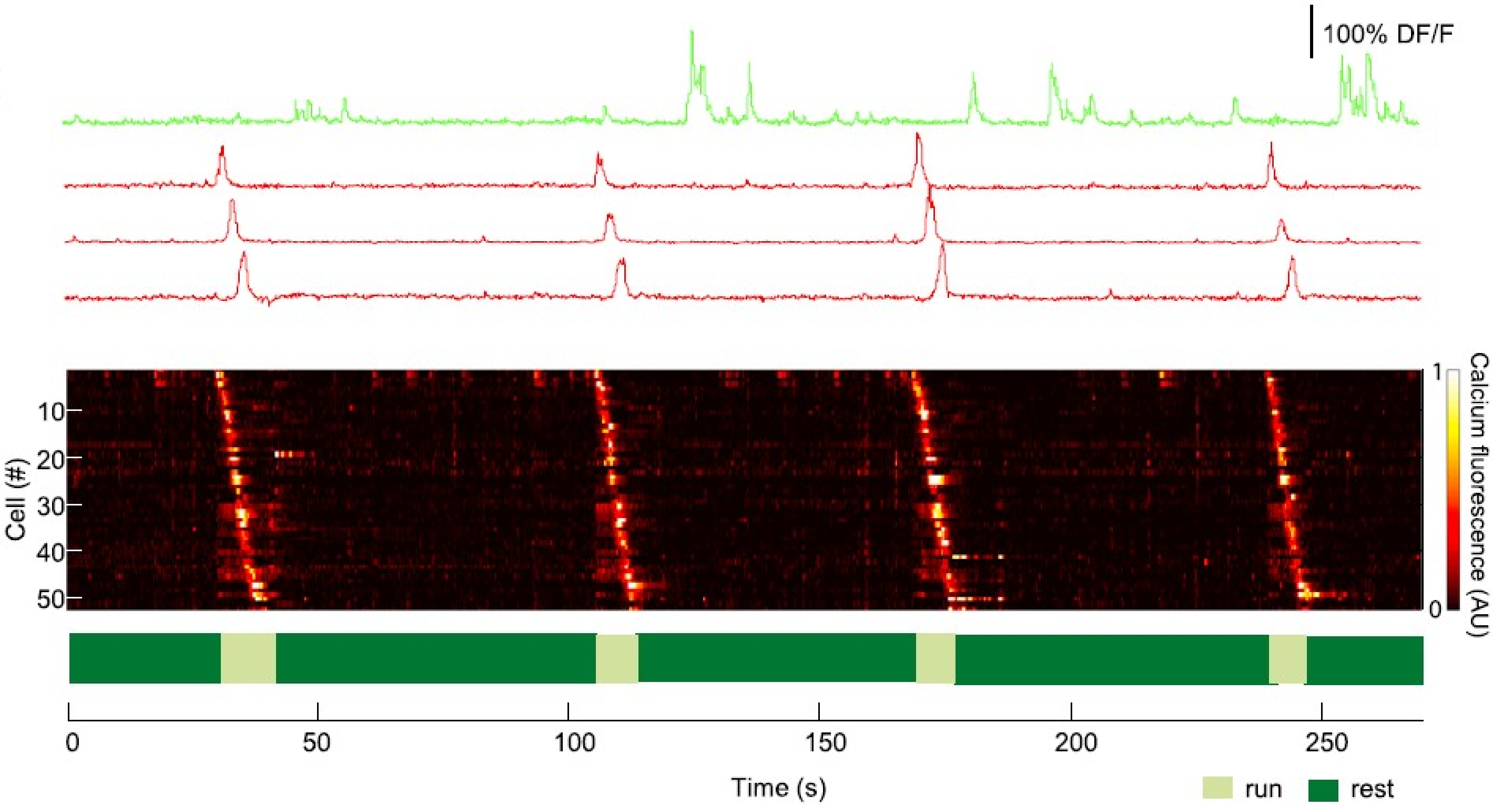
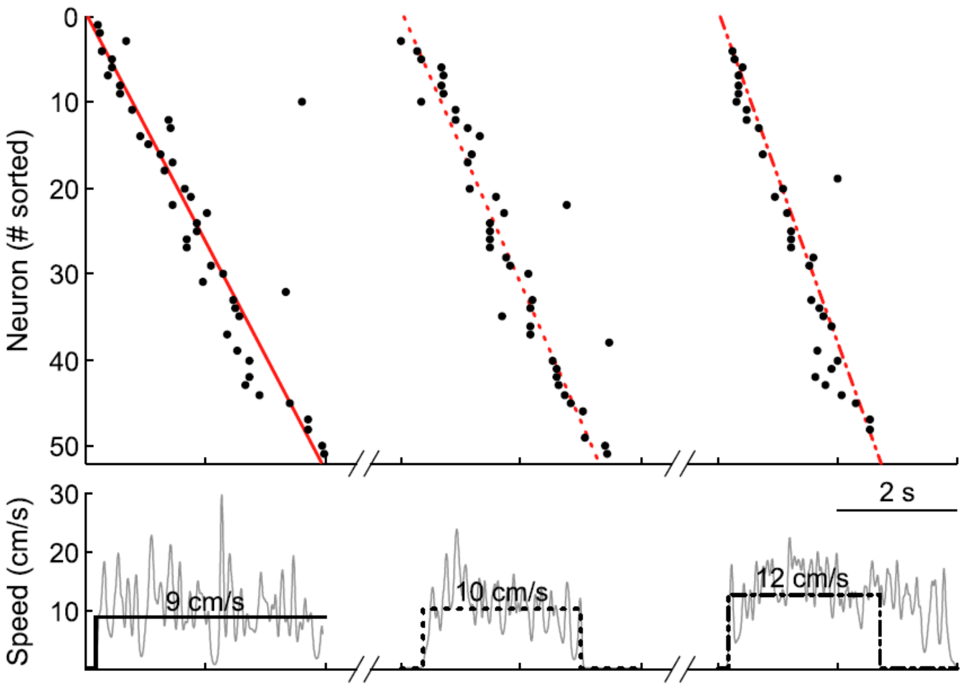
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

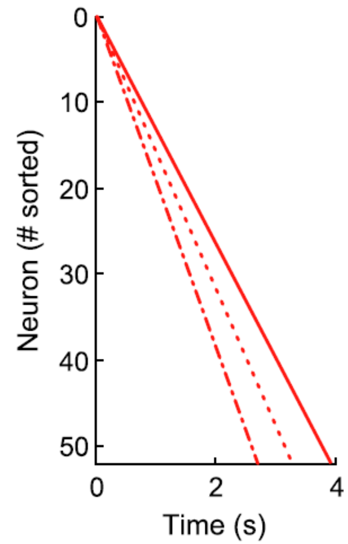
Sequences in the absence of task

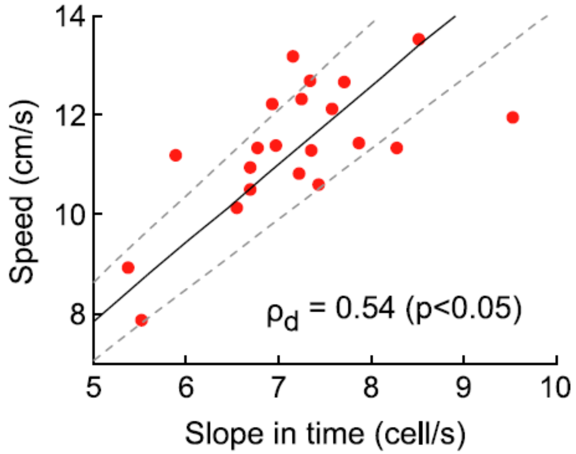


Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Sequence dynamics vs mouse speed



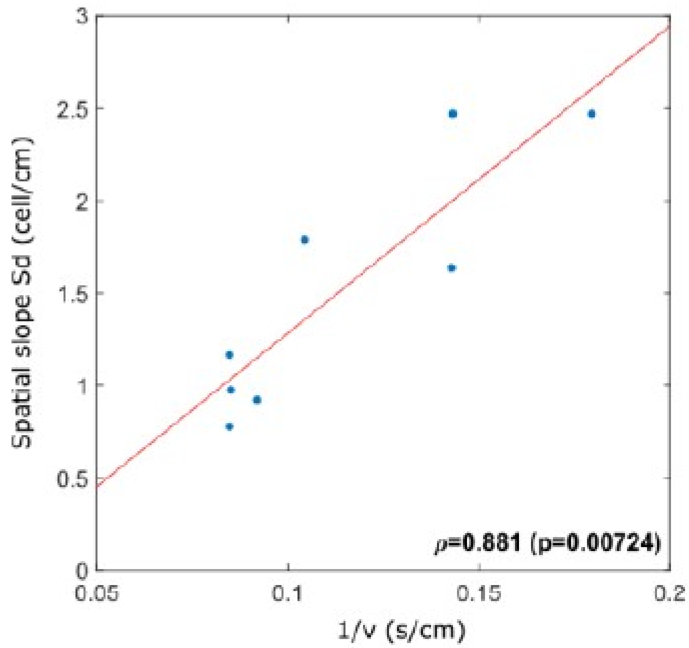


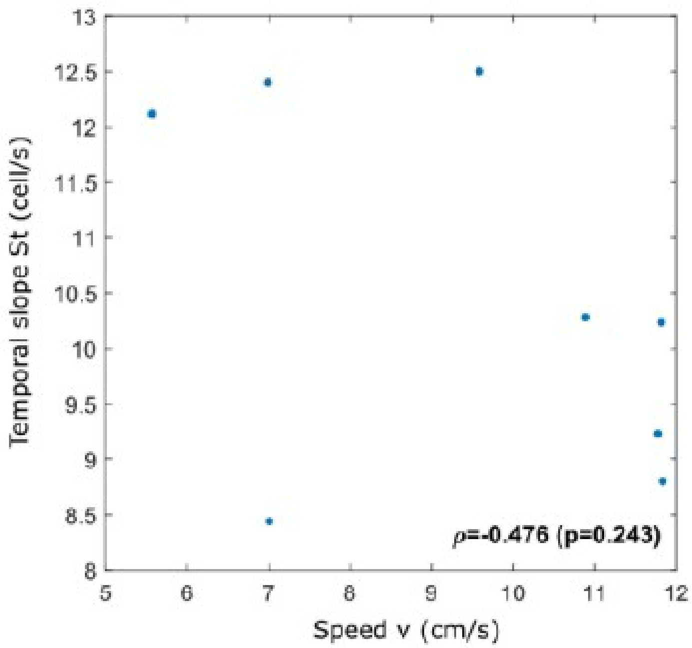


In this session, the temporal slope of the firing sequences is proportional to the mouse speed: neurons encode for run distance

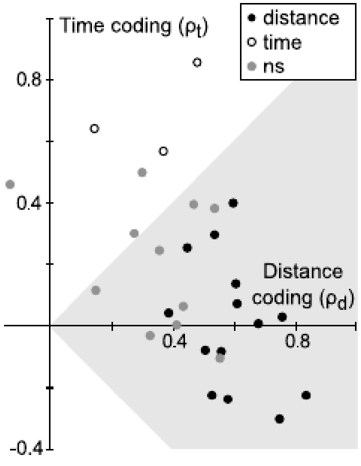
Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Sequence dynamics vs mouse speed



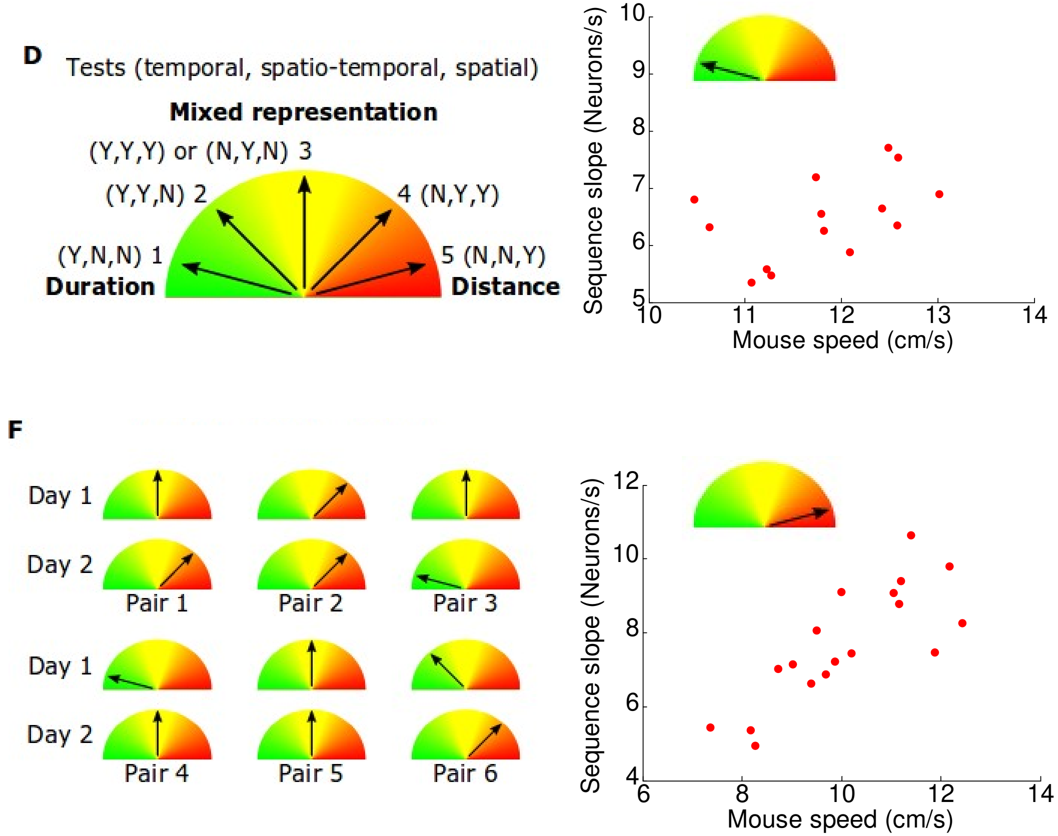


In this session, the spatial slope of the firing sequences is proportional to the mouse speed:
neurons encode for the run duration (elapsed time)



Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

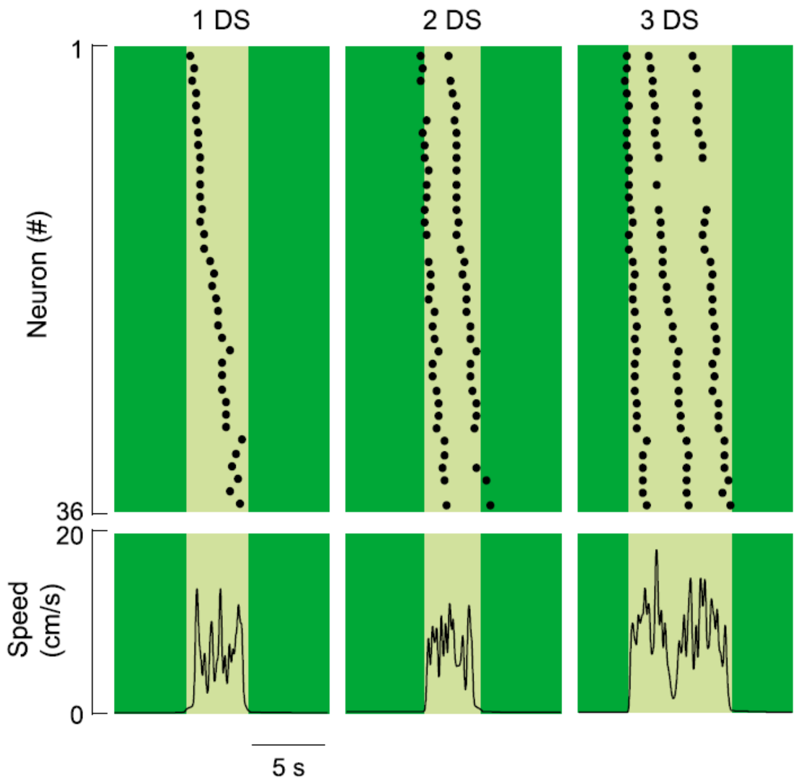
Analysis of distance and duration representation

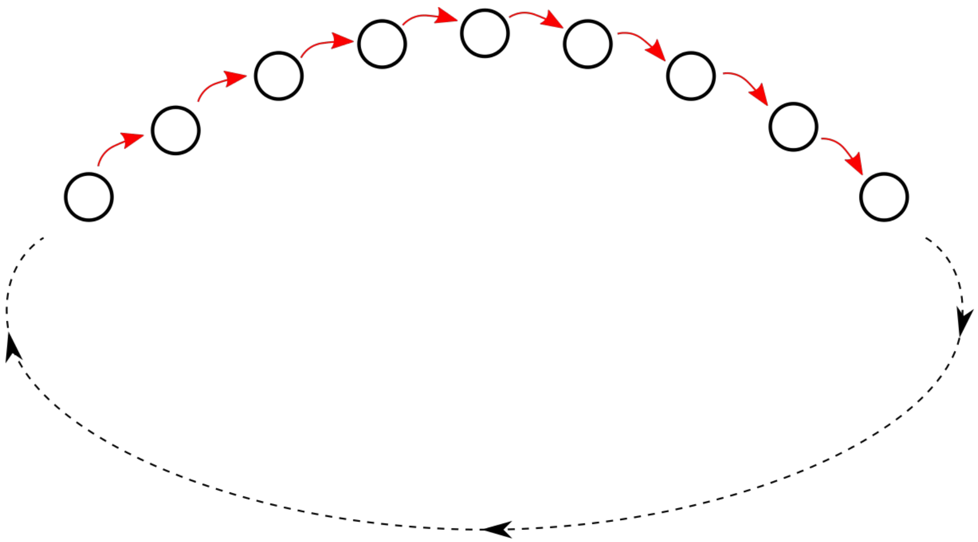


- Depending on the degree of correlation of the **temporal** (**spatial**) sequence slope and the **mouse speed** we have a **distance** (**duration**) representation
-
- A large part of the same neurons fires on Day 1 and Day 2, but they can modify their coding from Day 1 to Day 2
- Hippocampus can flexibly change the representation type from one day to the other

Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Underlying Network



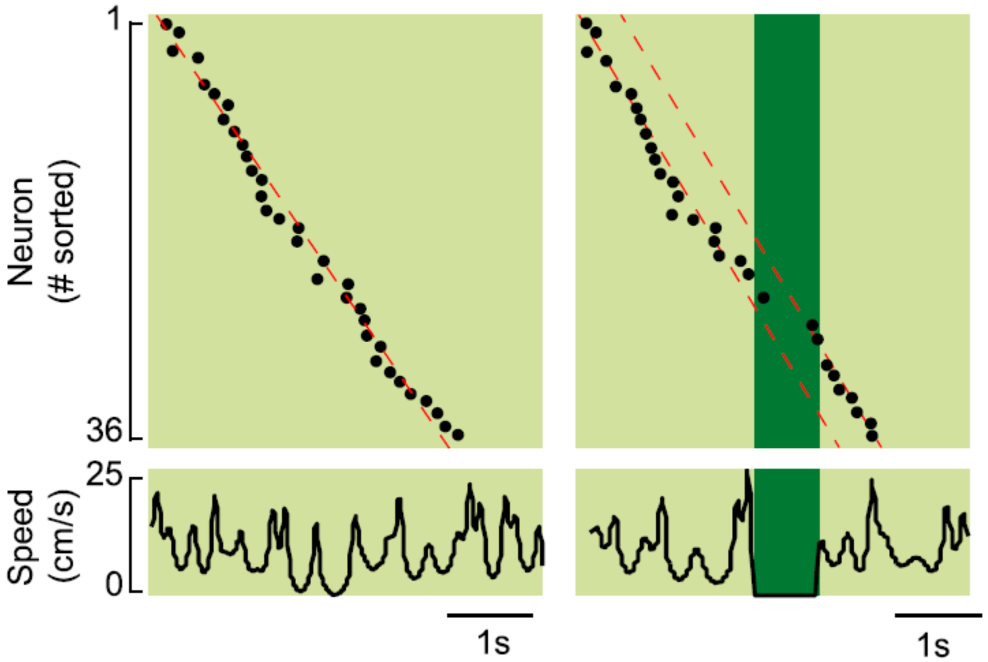


Sequences reboot within continuous run episodes

Recurrent functional network with PBCs

Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Sequences restart after short pause



Sequences do not reboot if pause < 2s

Short term plasticity

Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Model requirements

Outputs

- Neuronal sequences generated from non sequential inputs
- Duration and distance representation

Inputs

- Time and speed.

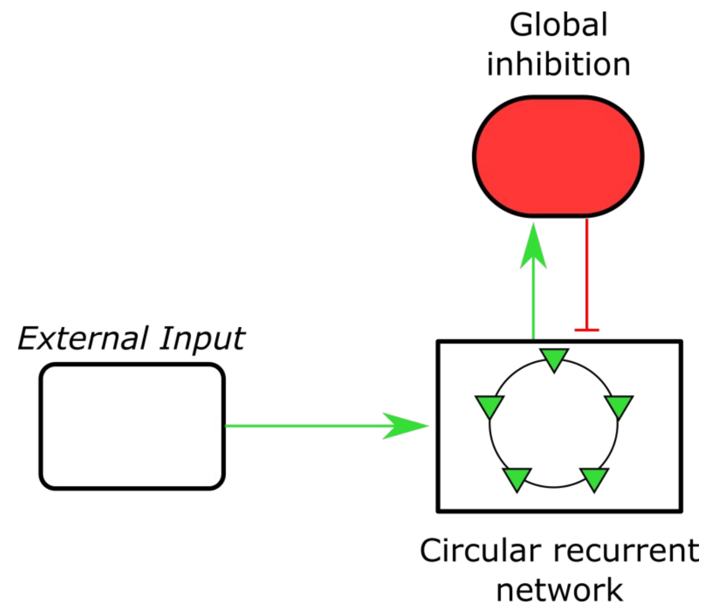
Theta oscillation with varying amplitude

Network

- Excitatory neurons with global inhibition
- Recurrent excitation => *circular network*
- Short term plasticity => *synaptic facilitation and depression*

Continuous Attractor Neural Network

Circular recurrent network
+ External excitatory input



Local excitation

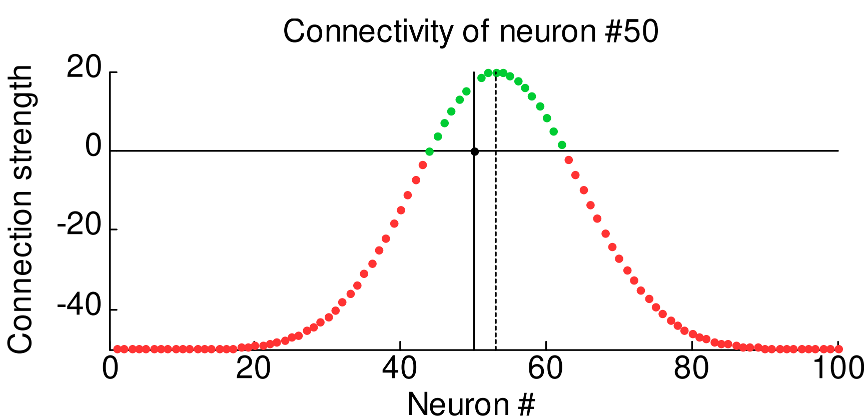
+ Global inhibition

→ Localized activity bump

Asymmetry of local connexions δ

→ Movement of activity bump

Neuronal sequences follows always same order



$$W_{i\rightarrow j} = J_1\, e^{-(i-j-\delta)^2/\sigma^2} - J_0$$

Romani & Tsodyks (2014), Wang et al (2015)

Continuous Attractor Neural Network

Firing rate model
Romani & Tsodyks (2014)

Threshold function

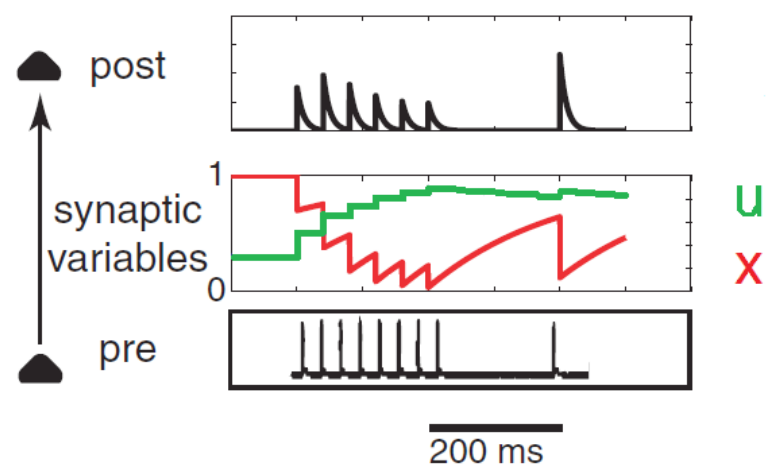
$$\tau \dot{m}\,(i,t) = -m(i,t) + f\big(I_R(i,t) + I_E(t)\big)$$

Recurrent input *External input*

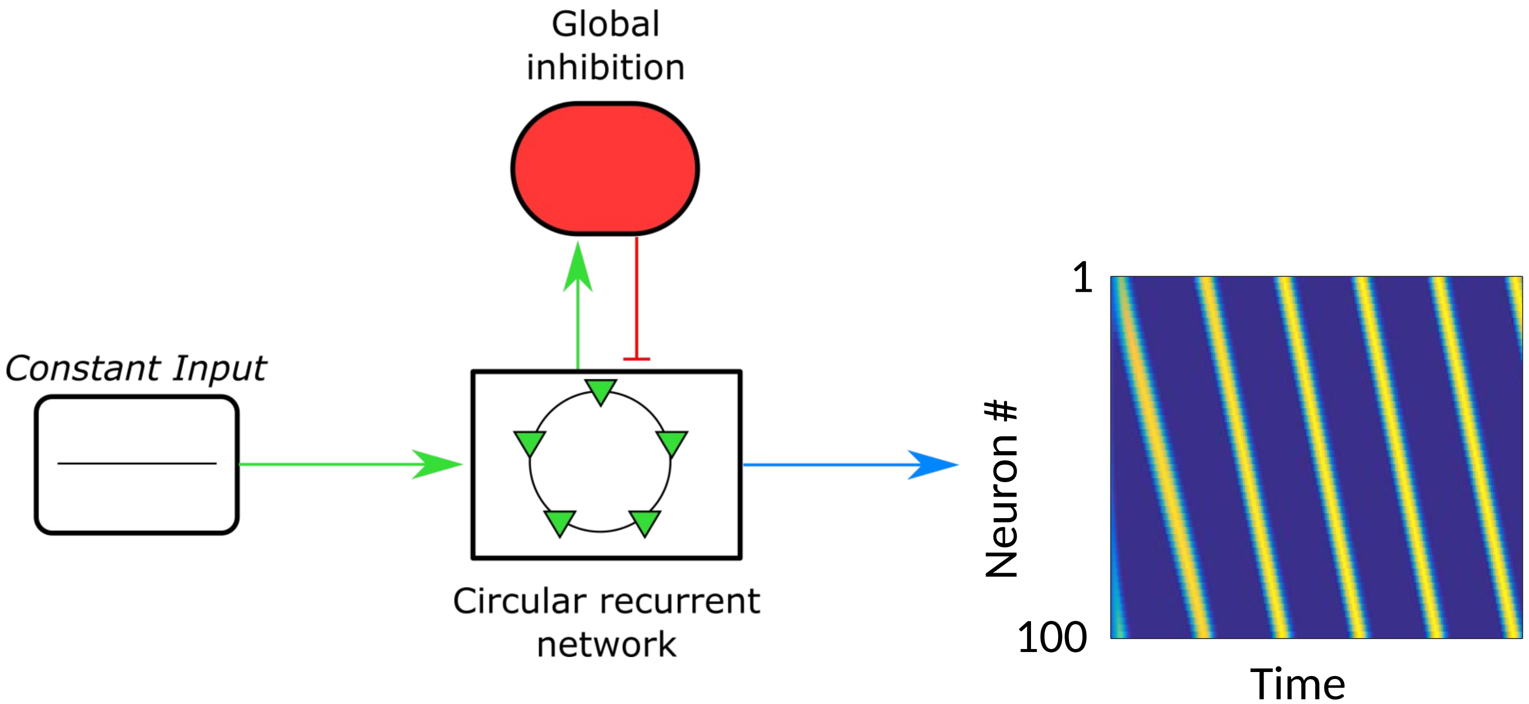
Synaptic plasticity
Mongillo et al (2008)

$$\frac{dx}{dt} = \frac{1 - x}{\tau_D} - u\ x\ \delta(t\text{-}t_{sp})$$

$$\frac{du}{dt} = \frac{U\ - u}{\tau_F} + U\ (1 - u\ )\ \delta(t\text{-}t_{sp})$$

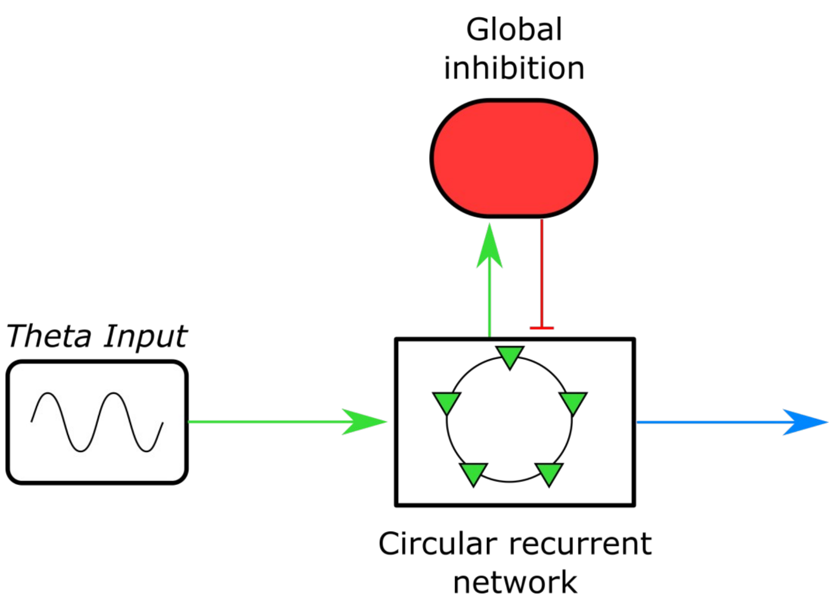


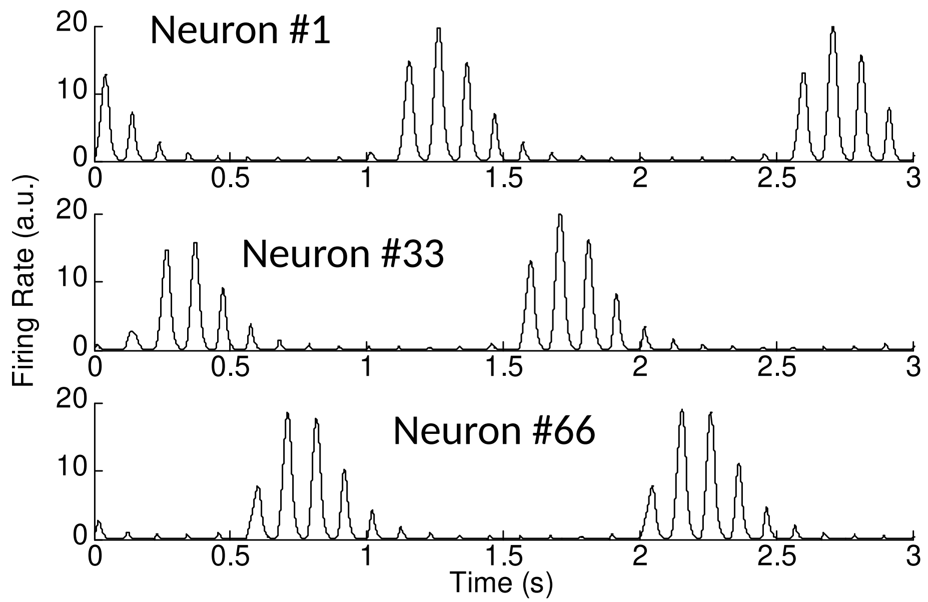
Constant input



Continuous sequences

Oscillatory input





Romani & Tsodyks (2014), Wang et al (2015)

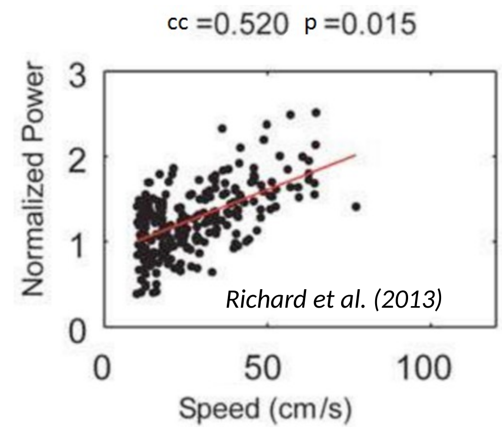
Theta modulated sequences

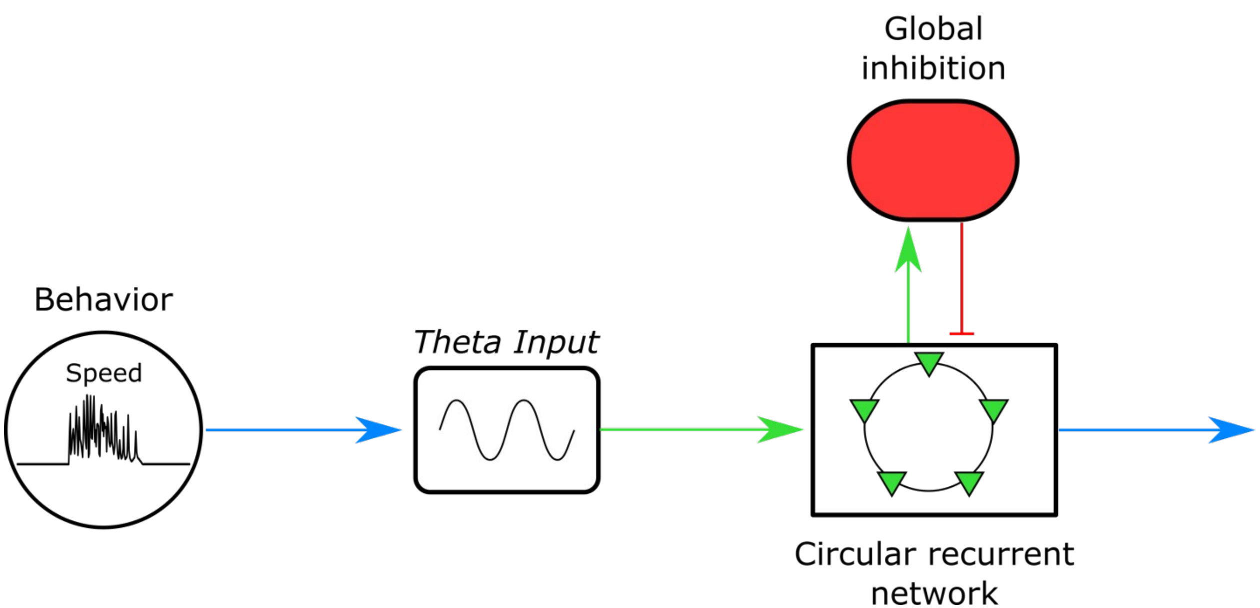
Speed-dependent input

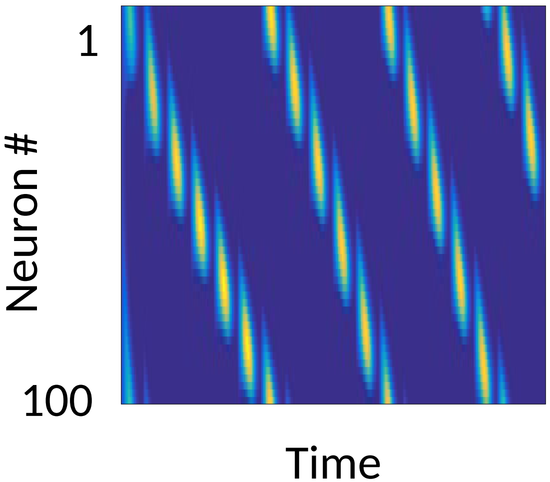
Working hypothesis : $\boxed{I_\theta = \alpha + \beta v}$

Linear relationship between theta amplitude and running speed

Richard et al. (2013), Fuhrmann et al. (2015), Bender et al .(2016)

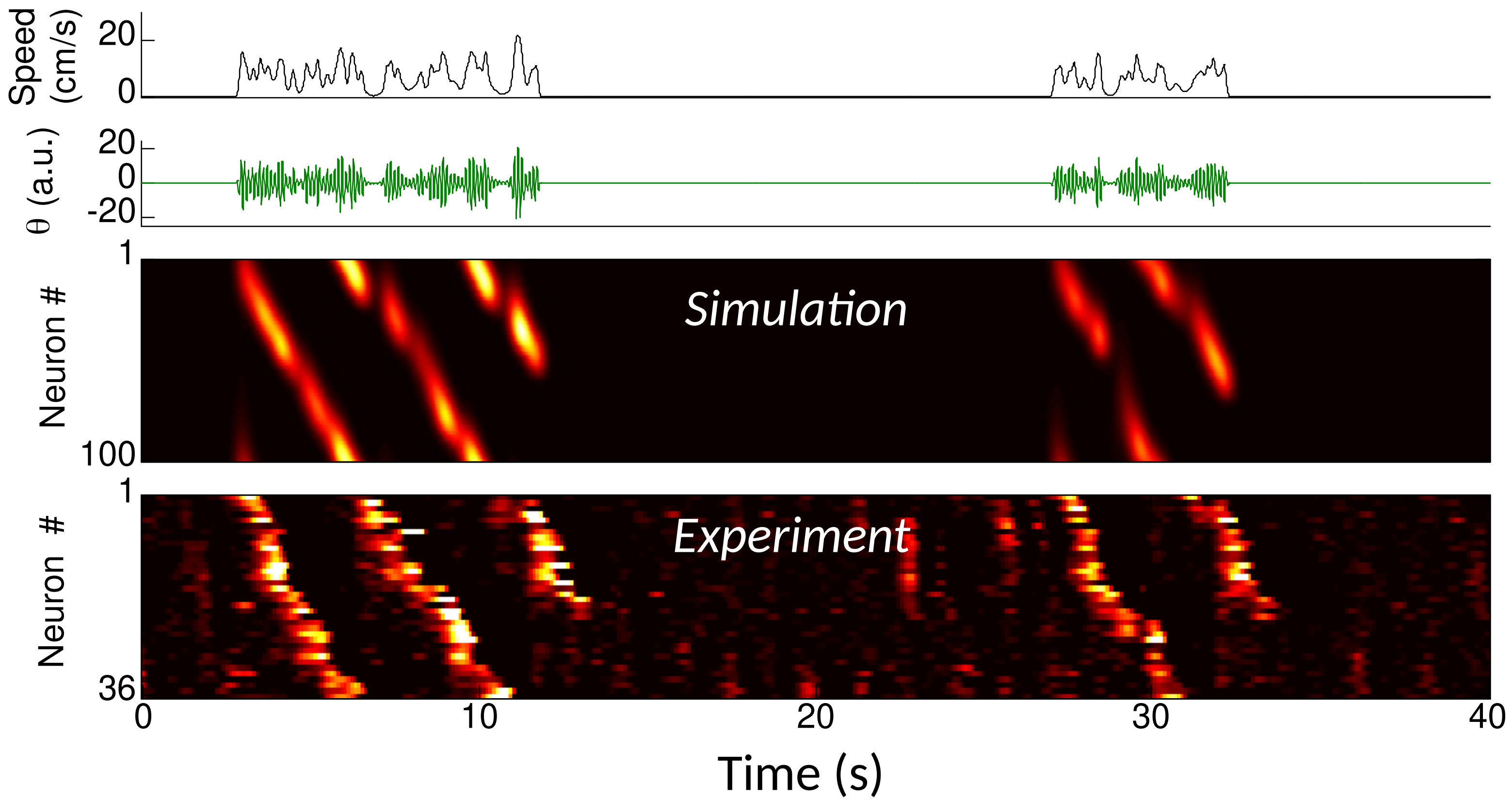






Haimerl*, Angulo-Garcia*,Vllette, Reichinnek , Torcini, Cossart & Malvache, PNAS (2019)

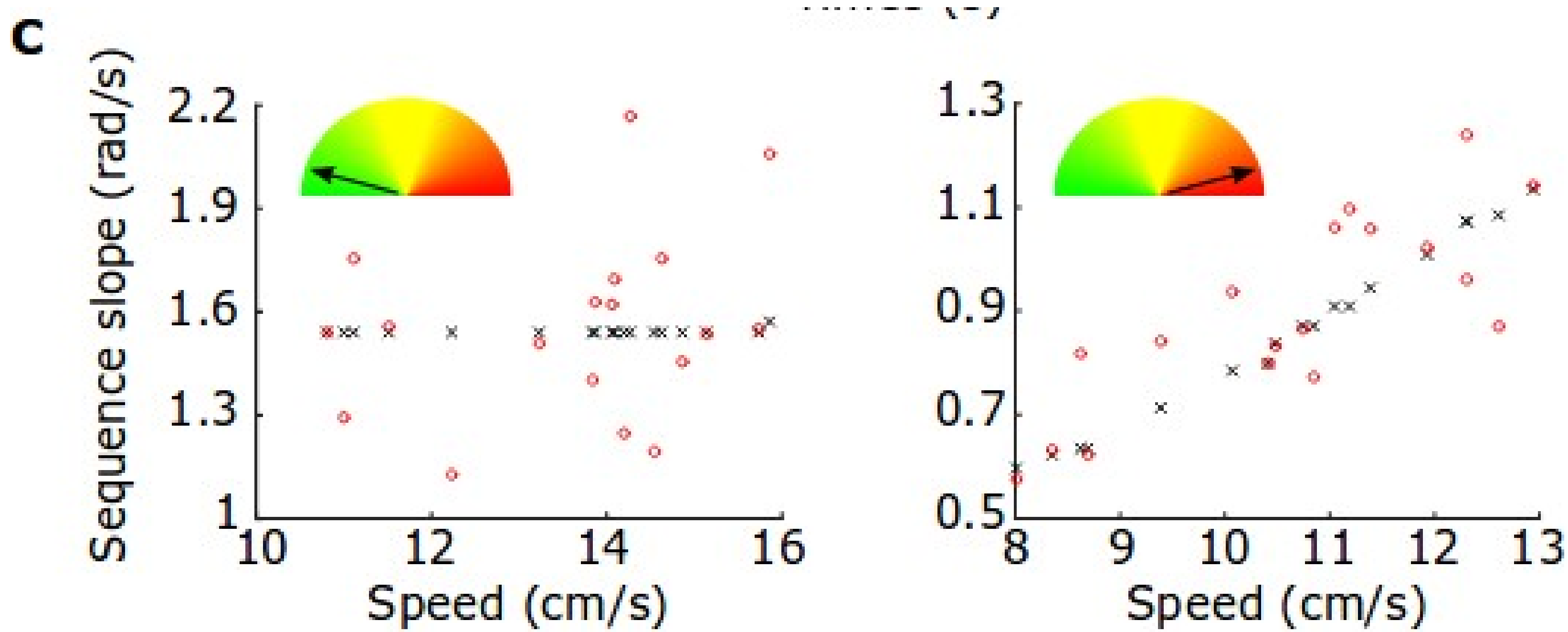
Speed-dependent input



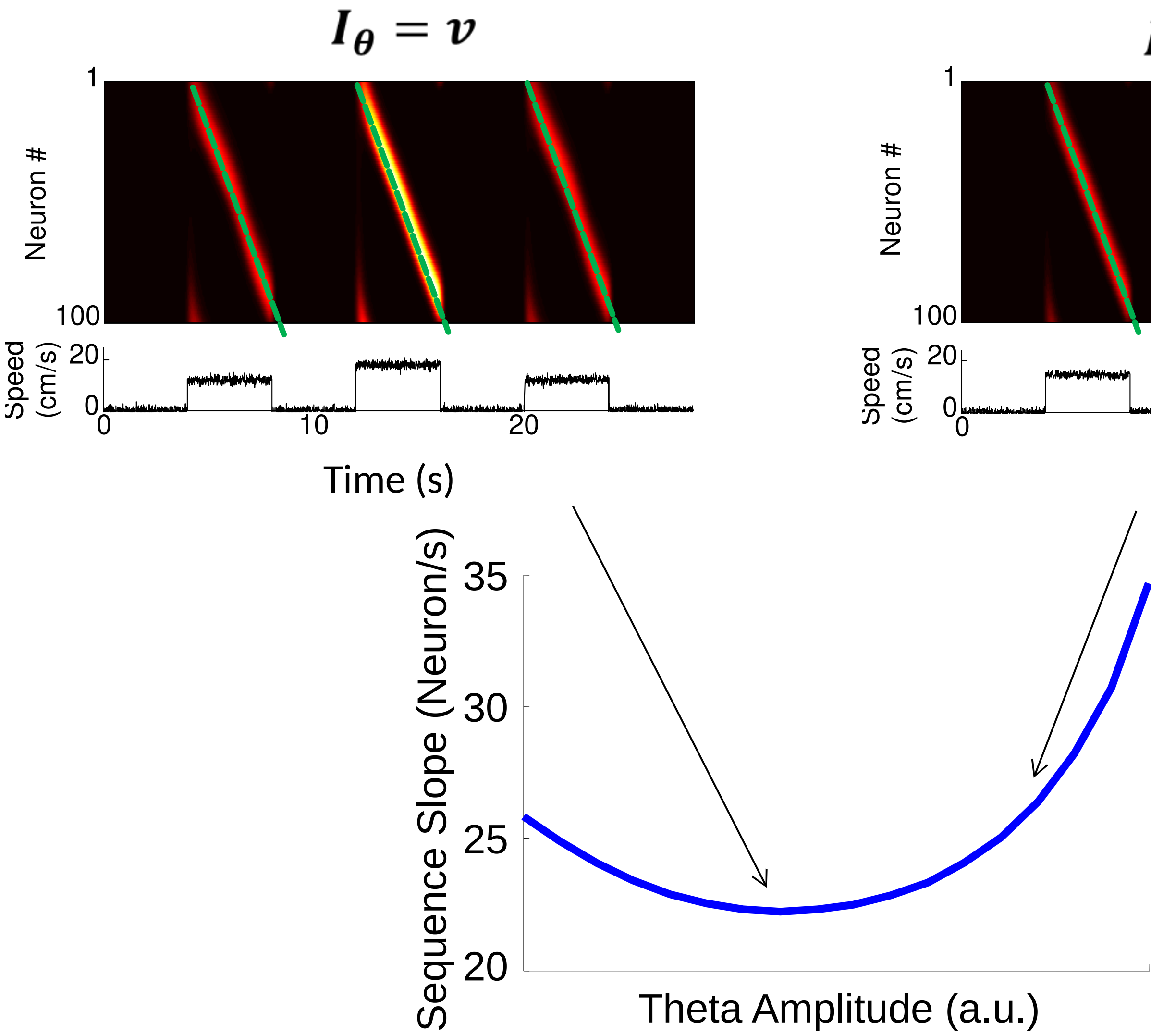
Haimerl*, Angulo-Garcia* , Villette, Reichinnek, Torcini, Cossart & Malvache, PNAS (2019)

Fitting to experimental data

We fitted the sequence slopes obtained from our model versus mouse velocity to the experimental data to obtain the mean input power I_0, the connectivity asymmetry Delta and the velocity gain Beta



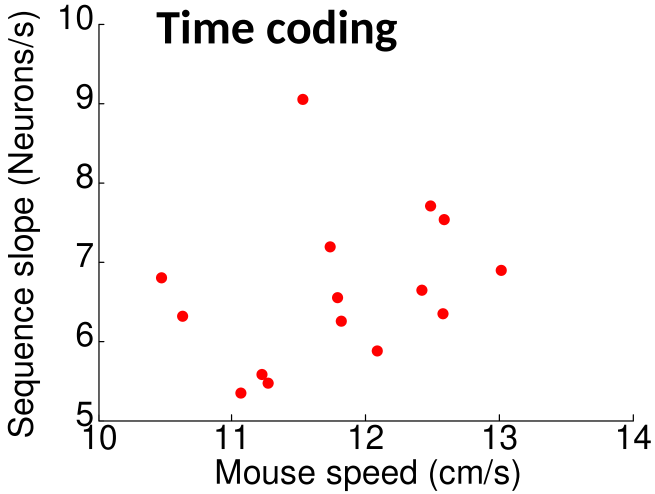
Neuronal sequences dynamics

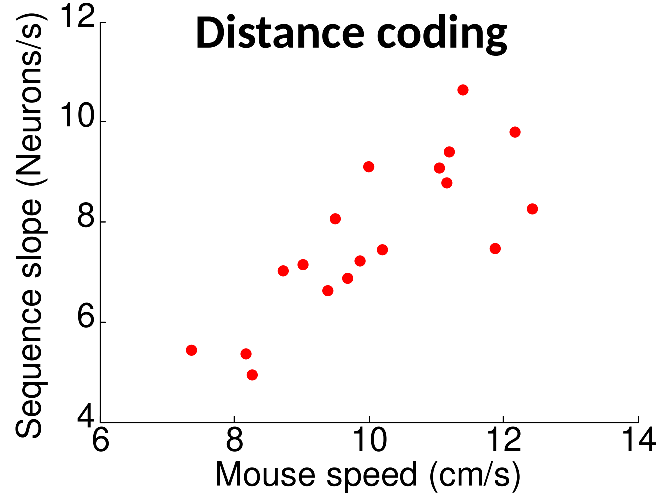


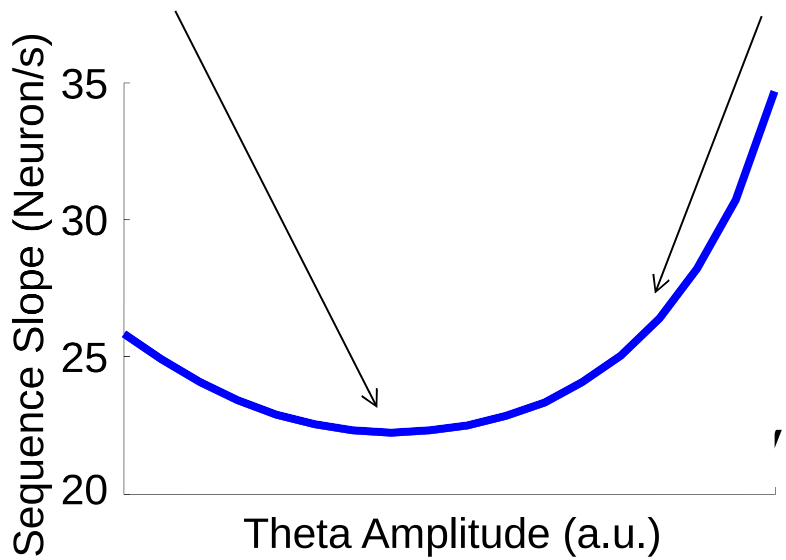
Nonlinear dependence induced by short-term plasticity

Facilitation is fundamental

Spatio-temporal coding







The same network can display both representations
y changing Theta Amplitude

Summary

- Experimental data suggest (functional) circular connectivity plus plasticity

- CANNs can encode both duration and distance, without modifying the
- network structure

- The dynamic range is sufficient for fitting the experimental data

The hippocampus is able to generate a spatiotemporal representation tuned to the task at hand

C. Haimerl, D. Angulo-Garcia, V. Villette, Su. Reichinnek, A. Torcini, R. Cossart, A. Malvache, "Internal representation of hippocampal neuronal population span a time-distance continuum" PNAS Proceedings of the National Academy of Sciences of the USA , 116, 7477-7482 (2019)

Acknowledgments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Thomas Tressard


Rosa Cossart

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ANR

INVESTISSEMENTS D'AVENIR

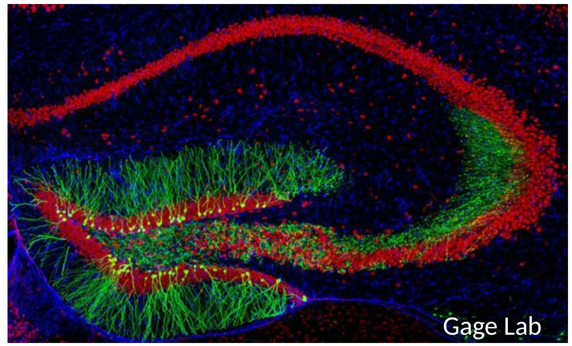
INVESTISSEMENTS D'AVENIR

Labex MME-DII

Modèles Mathématiques et Économiques de la Dynamique, de l'Incertitude et des Interactions

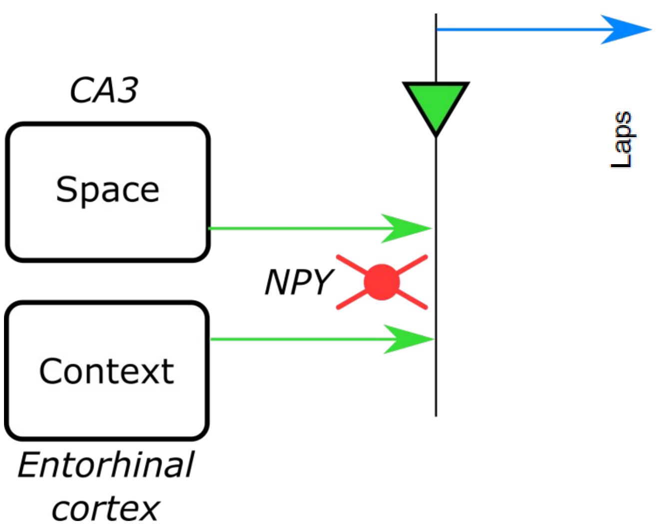
Place cell microcircuit

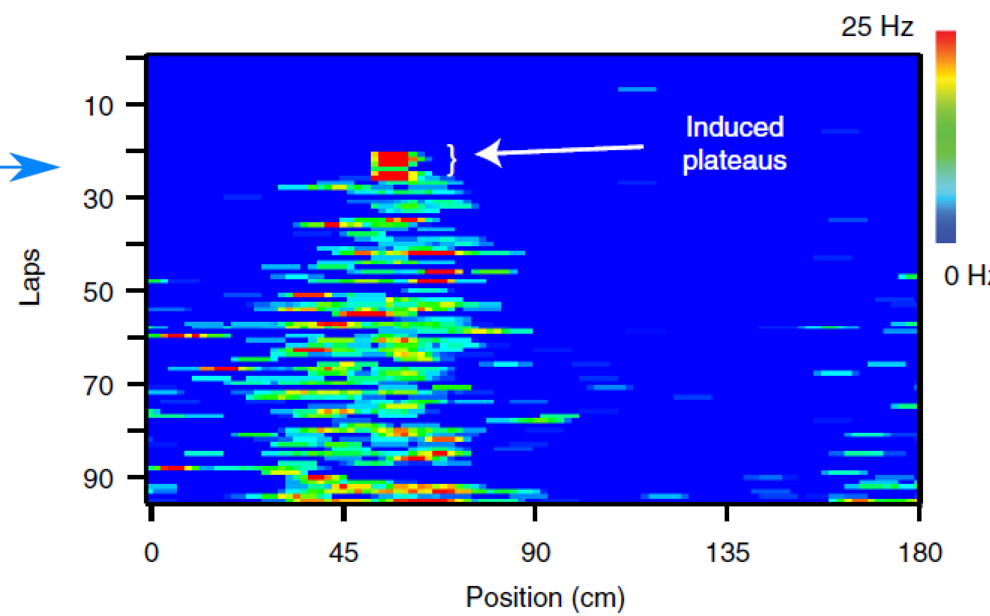
Raw spatio-temporal data



Processed information

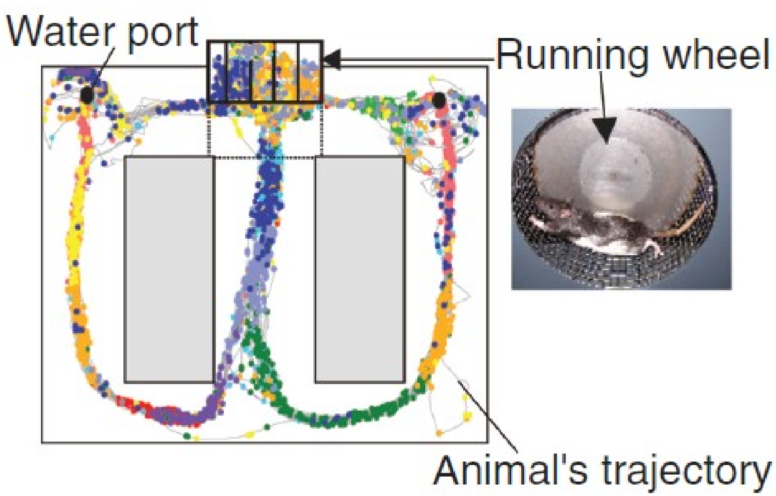
Bittner et al 2015
Milstein et al 2015

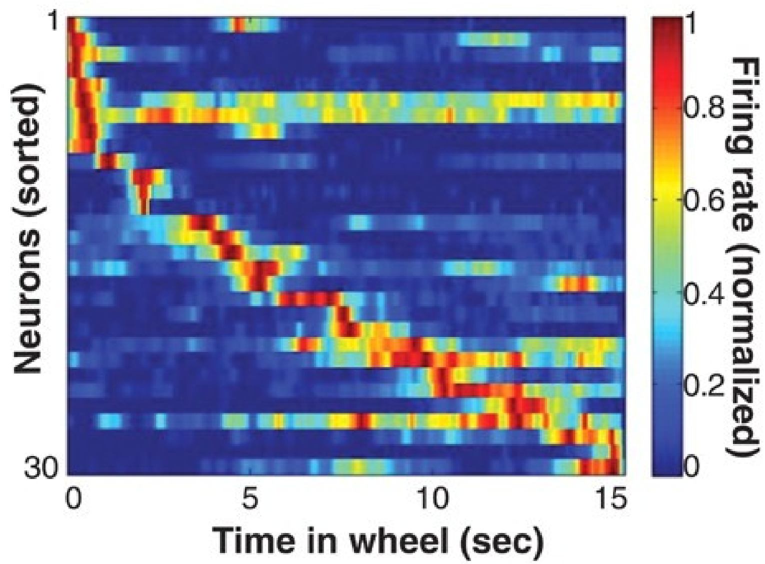




Time sequences

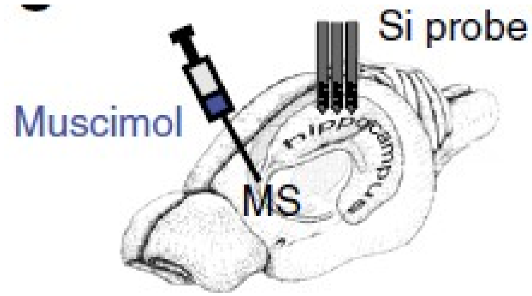
Time sequences in CA1 in a wheel during a delay task





Internally Generated Cell Assembly Sequences in the Rat Hippocampus
Pastalkova, Itskov, Amarasingham & Buzsáki, Science (2008)

Different mechanisms for place cells and time cells



Medial Septum inhibition

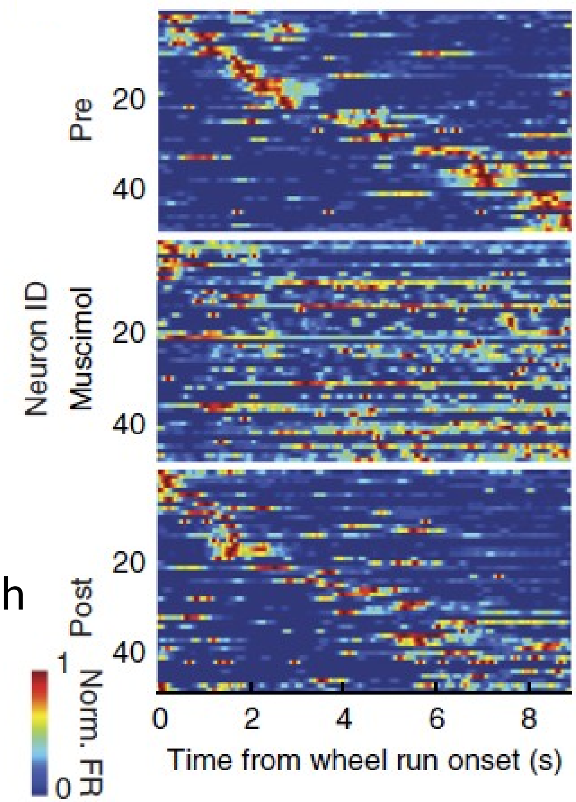
Decreases theta power

* Memory-dependent firing fields in the wheel are lost

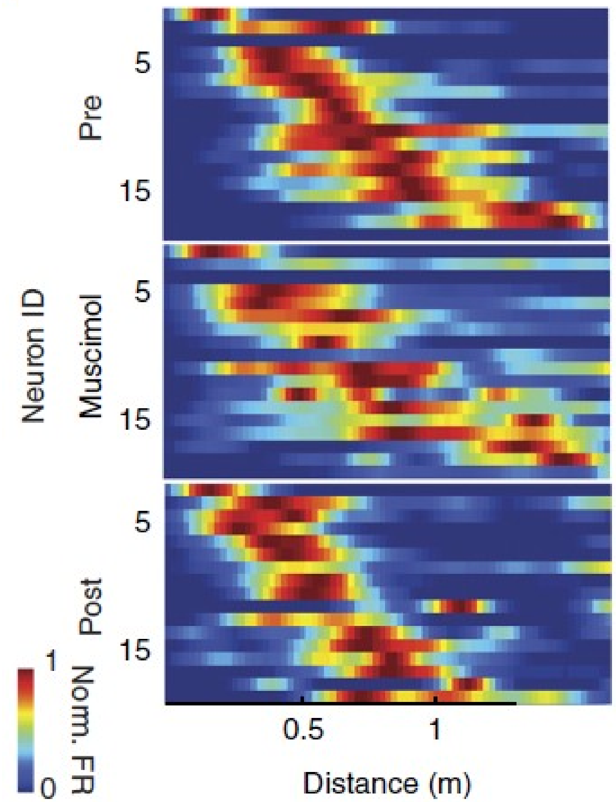
* Firing fields in the maze with sensory cues are maintained

* Theta sequences are lost

Time cells



Place cells

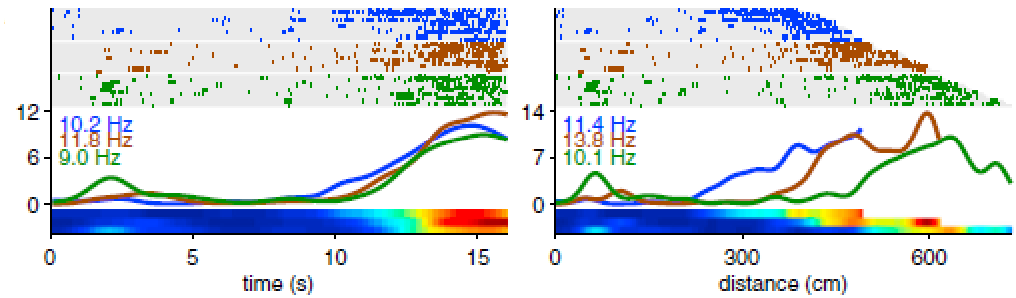


Theta sequences are essential for internally generated hippocampal firing fields. Wang, Romani, Lustig, Leonardo & Pastalkova, Nature Neuroscience (2015)

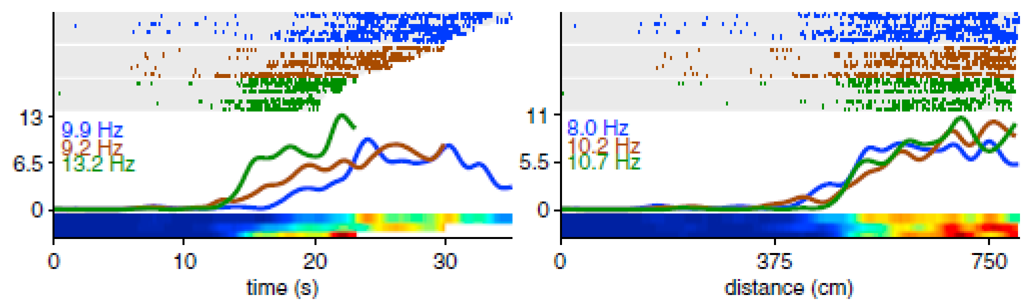
Disentangling time and distance

Treadmill with varying speed

Time-fixed sessions

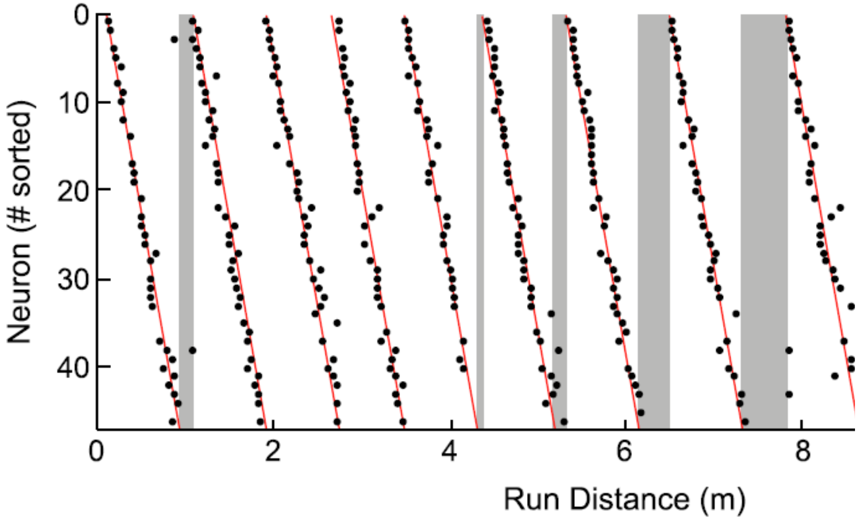


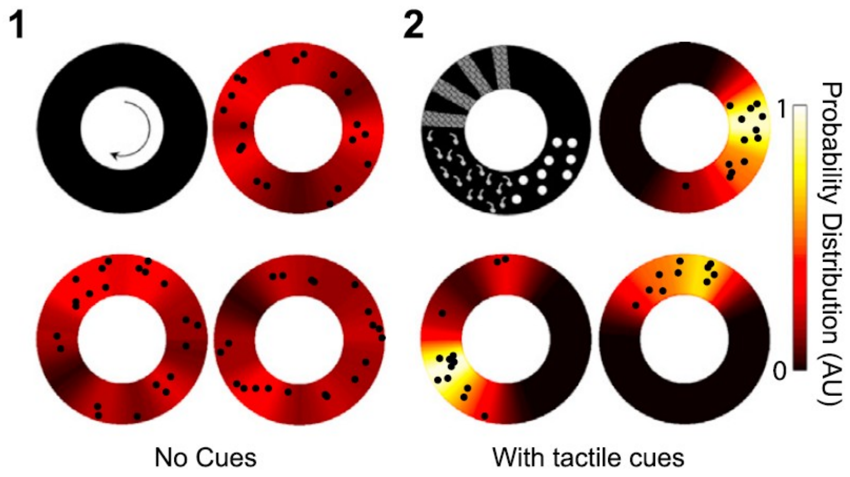
Distance-fixed sessions



Hippocampal ''Time Cells'': Time versus Path Integration
Kraus, Robinson, White, Eichenbaum & Hasselmo, Neuron (2013)

Sequence dynamics in spatial domain



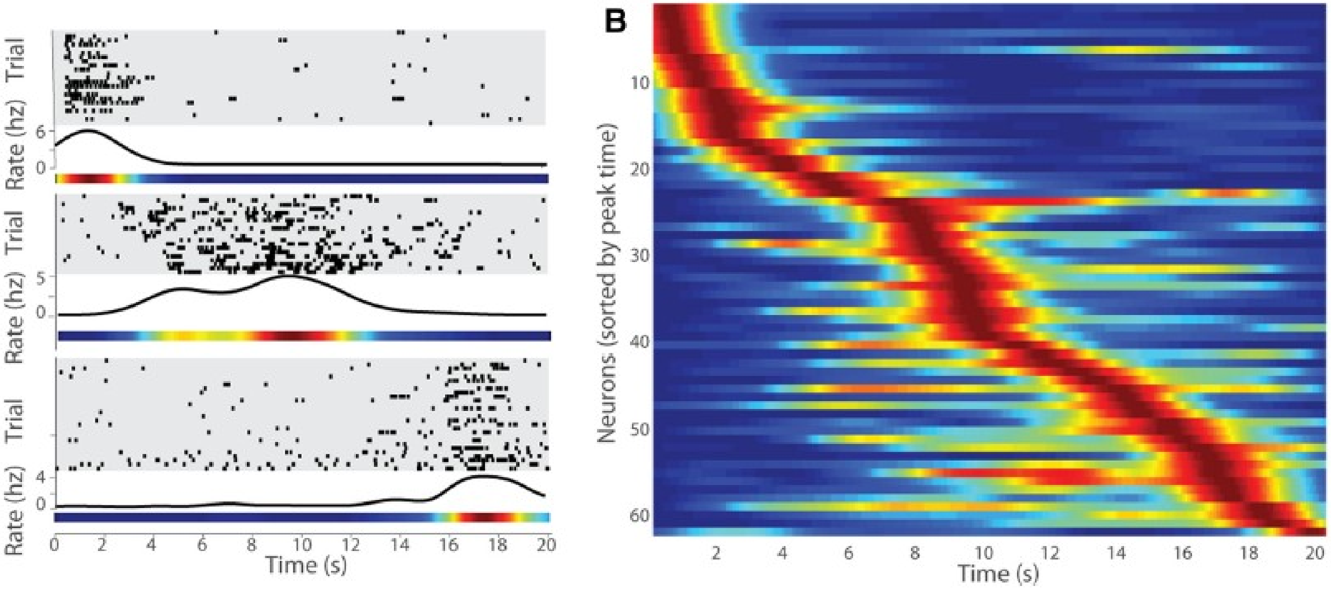


Distance representation but not place cells!

Internally Recurring Hippocampal Sequences as a Population Template of Spatiotemporal Information
Villette*, Malvache*, Tressard, Dupuy & Cossart, Neuron (2015)

Recurrent network to model CA1 ?!?

Hypothesis: CA1 reflects CA3 activity in the absence of external drive

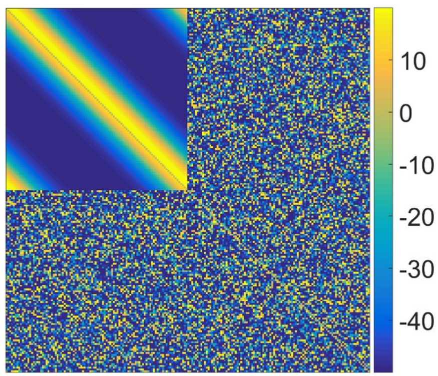


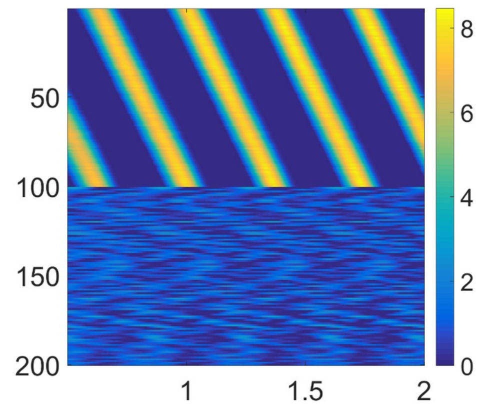
Time Cells in Hippocampal Area CA3
Salz, Tiganj, Khasnabish, Kohley, Sheehan, Howard & Eichenbaum, J. Neuro (2016)

Towards a more realistic model

Circular connectivity embedded in a random network

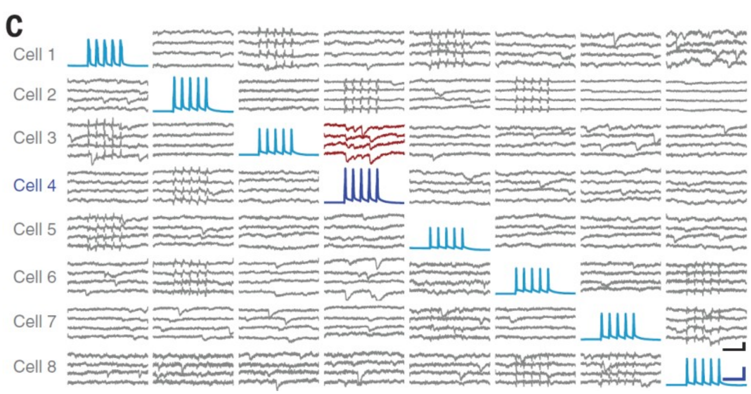
Connectivity matrix

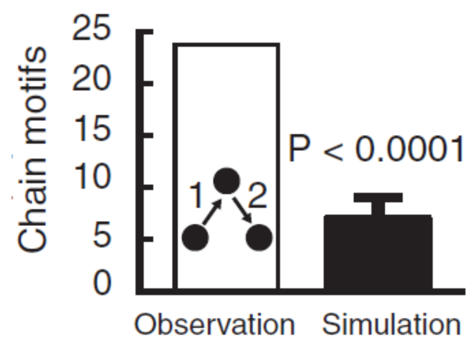




Model still valid for spatio-temporal coding

Connectivity in CA3 Guzman *et al* , *Science* (2016)





Haimerl*, Angulo-Garcia*, Torcini, Cossart & Malvache, in prep