How are position and context simultaneously encoded in the mammalian brain?

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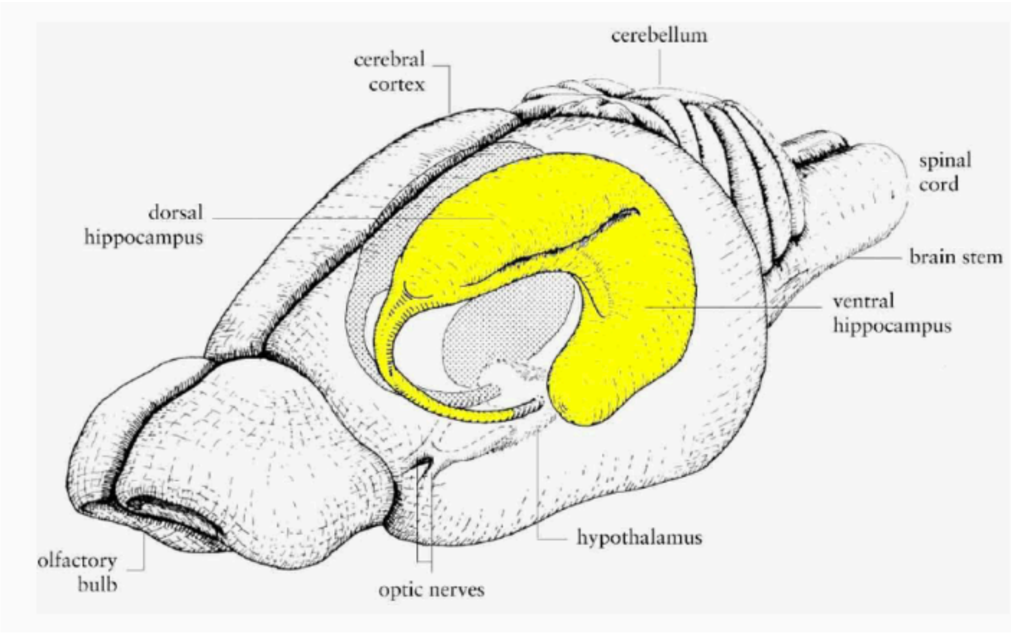
Saint Petersburg, September 2017

Representation of space in the brain



Human : 30 million neurons

Rat : 0.3 million neurons

'present' in all vertebrates

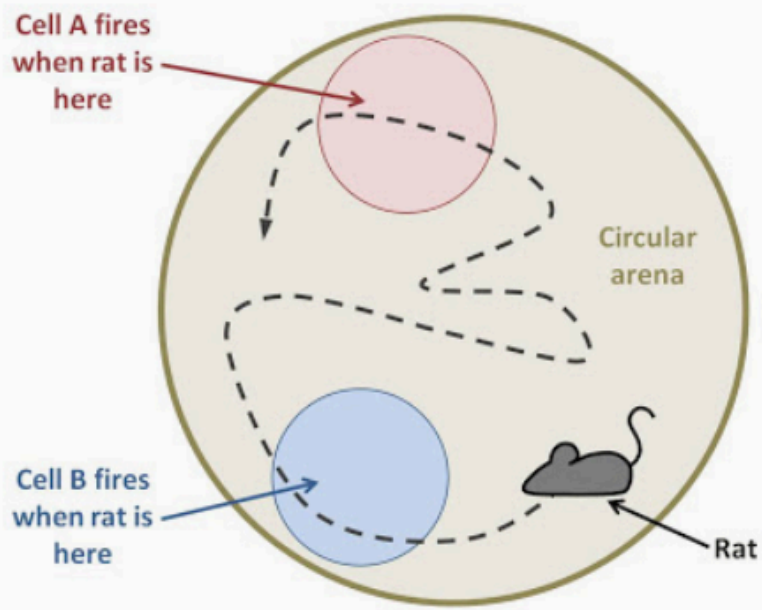
Recordings of electrical activity:

O'Keefe & Dostrovsky (1971)
[Nobel Prize 2014]

Neural cells in the hippocampus respond to position in space (called place cells)

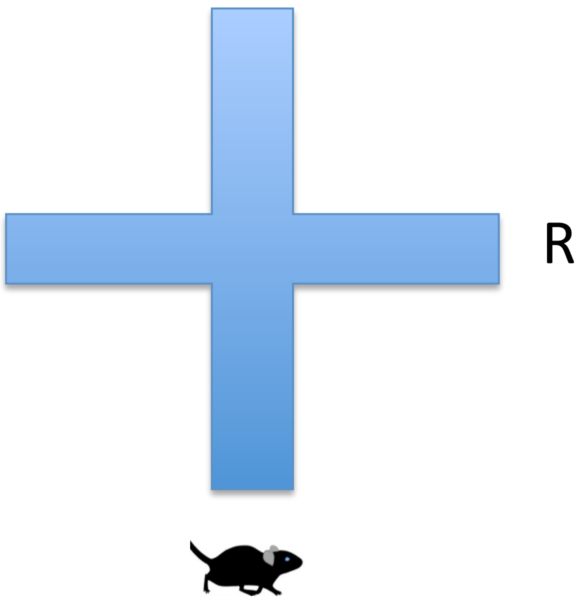
Place cells and fields

Place cells in the hippocampus regions CA1 and CA3 present spatially-located firing fields.



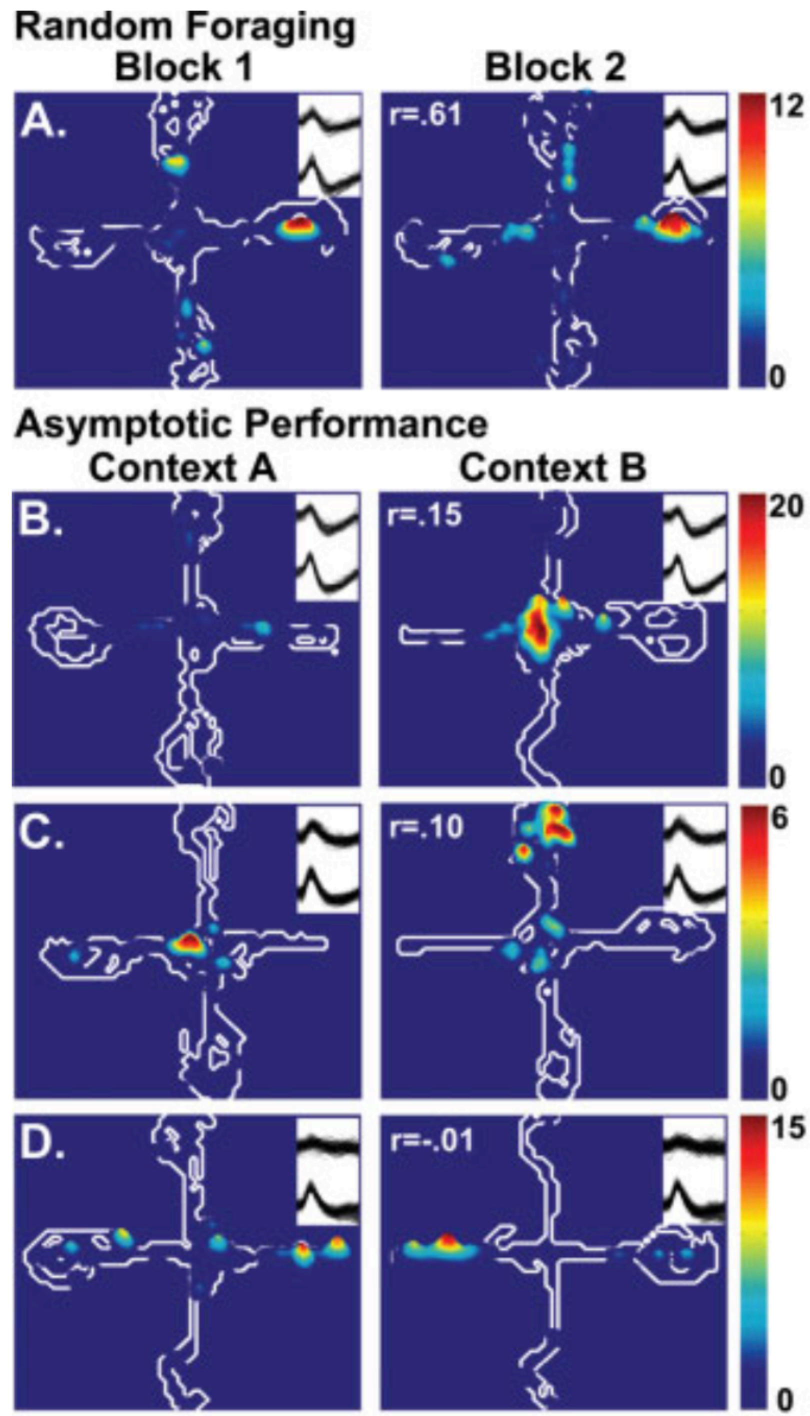
- Place fields are retrieved when the animal is placed in the same environment after days
- Stable in dark and against limited changes of environment
- Low-dimensional projections of <u>context-dependent</u> place fields in complex, high-D space

Place cells and fields

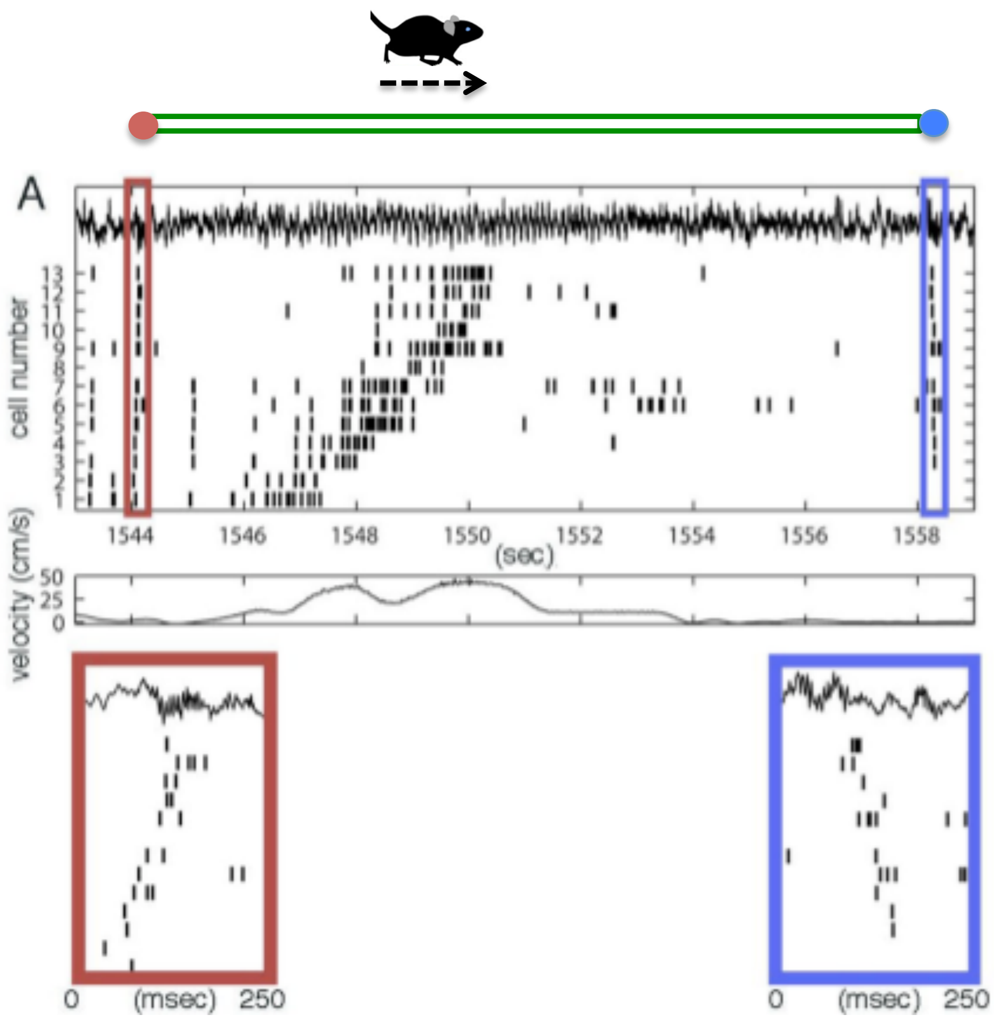


Random reward experiment
(Half East, half West arm)

Smith, Mizumori, Hippocampus (2006)



Place cells and fields



Diba, Buzsaki, *Nat. Neuroscience* (2007)

Place-cell activity can take place on compressed time scales

⟹ Internally generated (input independent) network activity

Main question

How can position(s) and context(s) (task, emotional state, …) be encoded in the (unique) hippocampal neural network?

- Data Analysis: multi-electrode recording of neural cells in rats

  Inference of effective network, and

  Decoding of cognitive maps

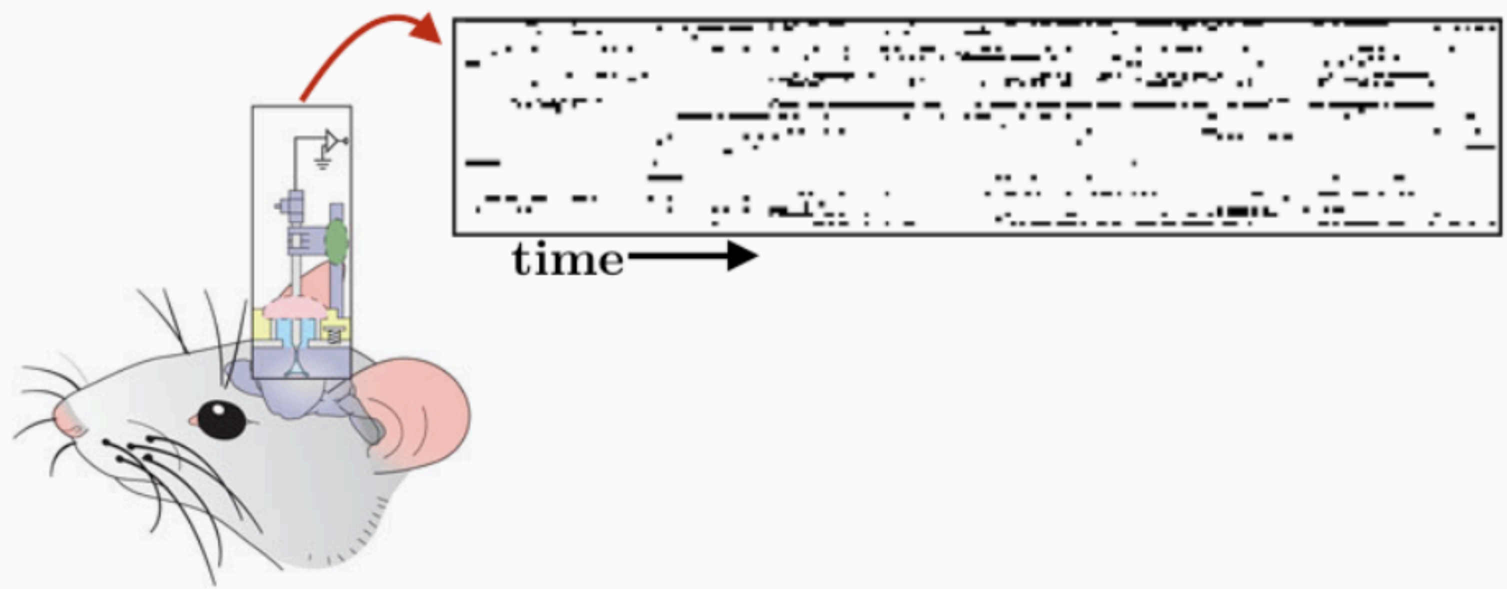
- Theory: Single network « storing » multiple context-dependent maps

  Memory of continuous attractors (cf. Hopfield model for point attractors)

  Transitions between attractors

Teleportation experiment (1)

Data Structure

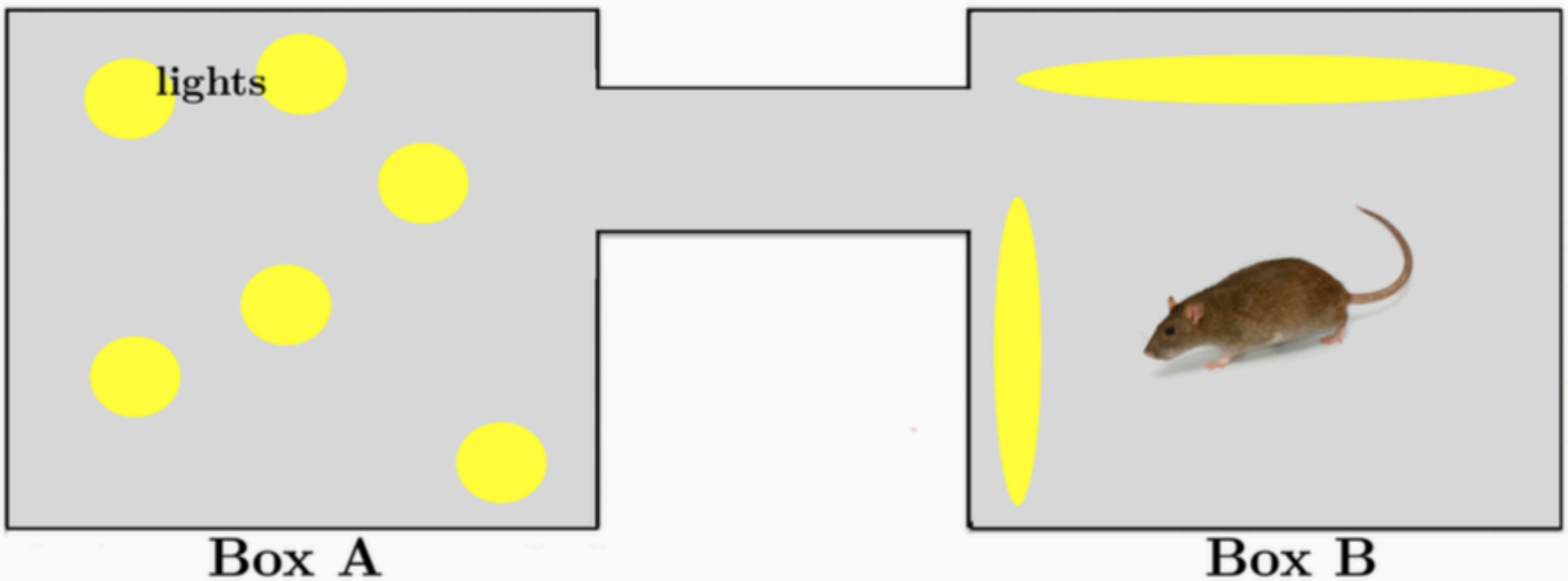


Microarray recordings of brain activity $\sim$ 30 recorded neurons

Jezek, Henriksen, Treves, Moser & Moser, Nature 478, 246 (2011)

Teleportation experiment (2)

Data Structure

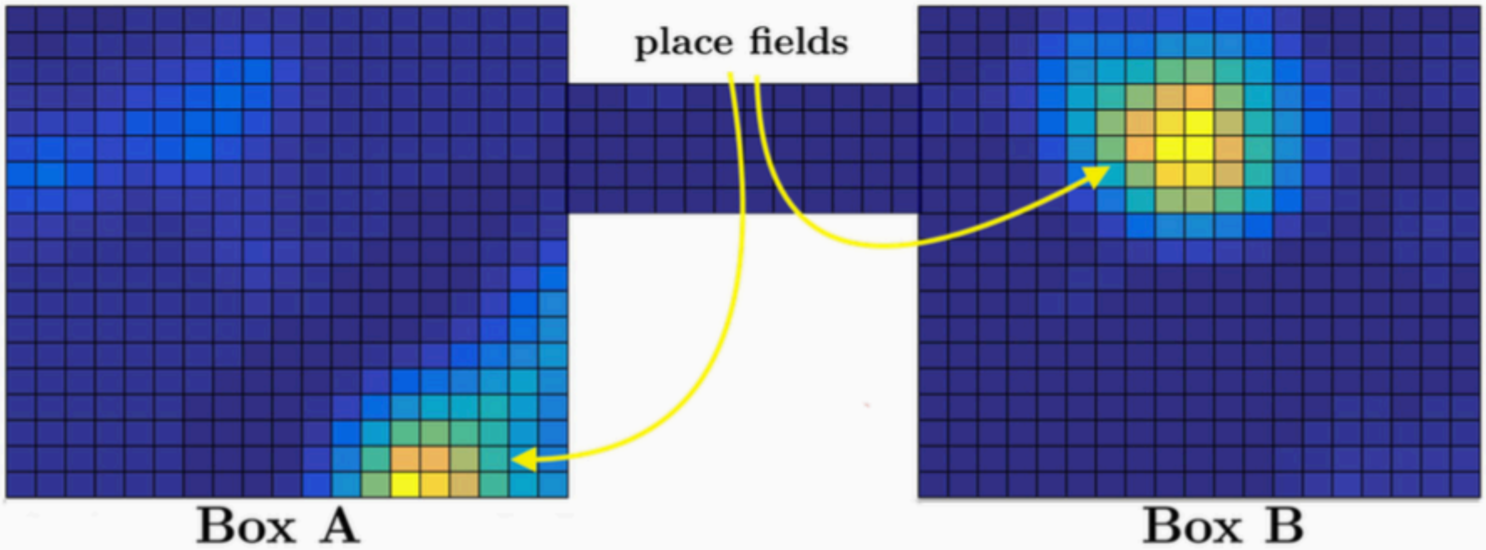


Rat trained to memorize two environments (A and B)

Two reference sessions are recorded (one for each environment).

Teleportation experiment (3)

Data Structure

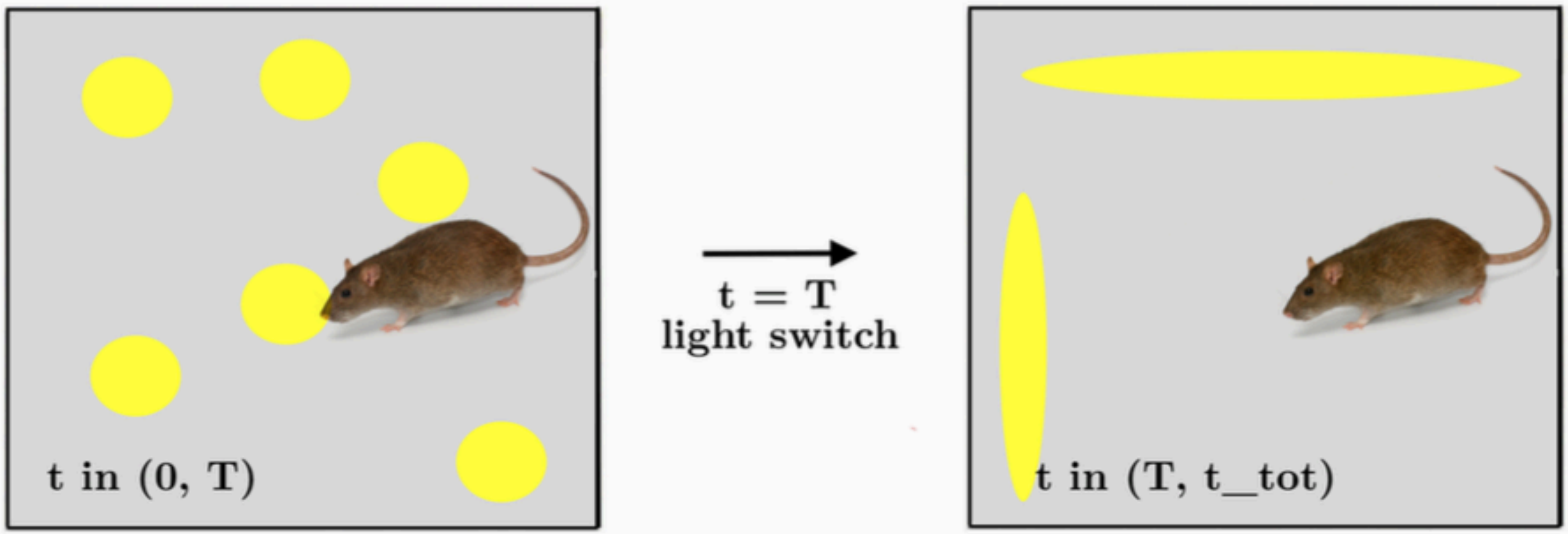


Experiment is conducted such that remapping takes place

[CA3 : global remapping, CA1 : rate remapping]

Teleportation experiment (4)

Data Structure



Test session: light cues are suddenly changed from one box to the other (teleportation)

Teleportation experiment (5)

Decoder: procedure to translate brain activity $\vec{s}(t)$ into one of the memorized states

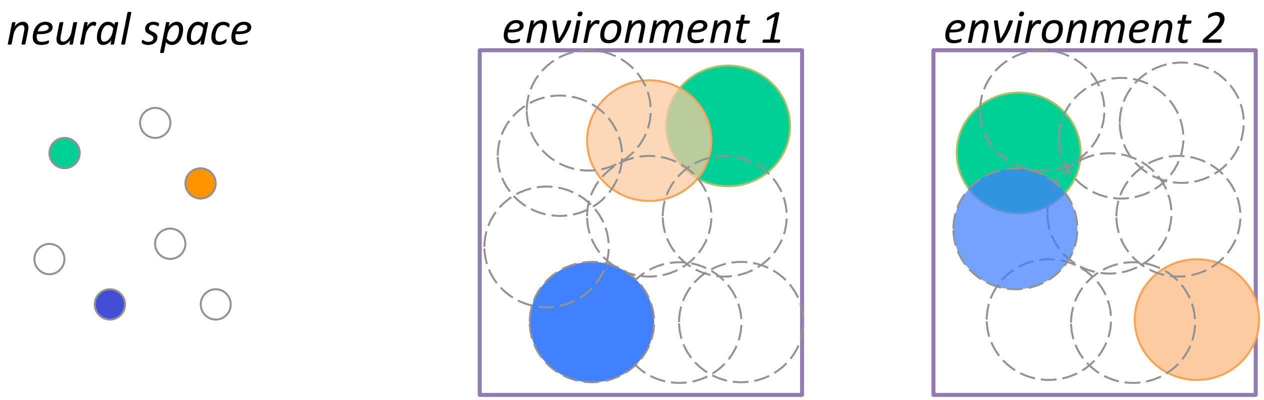
$$\vec{s} \to \{\text{environments}\} \tag{1}$$

- from two reference sessions we infer two parametric probabilistic models for the activity $P(\vec{s} \mid M = A, B)$
- at each time in the test session we compute log-likelihood difference for map given the activity:

$$\Delta\mathcal{L}(t) = \log\left(\frac{P(A \mid \vec{s}(t))}{P(B \mid \vec{s}(t))}\right) \tag{2}$$

NB: if bin width Dt small enough, s=0,1 ➔ binary valued activities (Ising «spins»)

Teleportation experiment (6)



Effective Ising model captures pattern of correlations:

$$P(M \mid \vec{s}) \;\propto\; P(\vec{s} \mid M) \;=\; \frac{1}{\mathcal{Z}^M} \exp\left(\sum_i h_i^M s_i + \sum_{i<j} J_{ij}^M s_i s_j\right) \qquad (3)$$

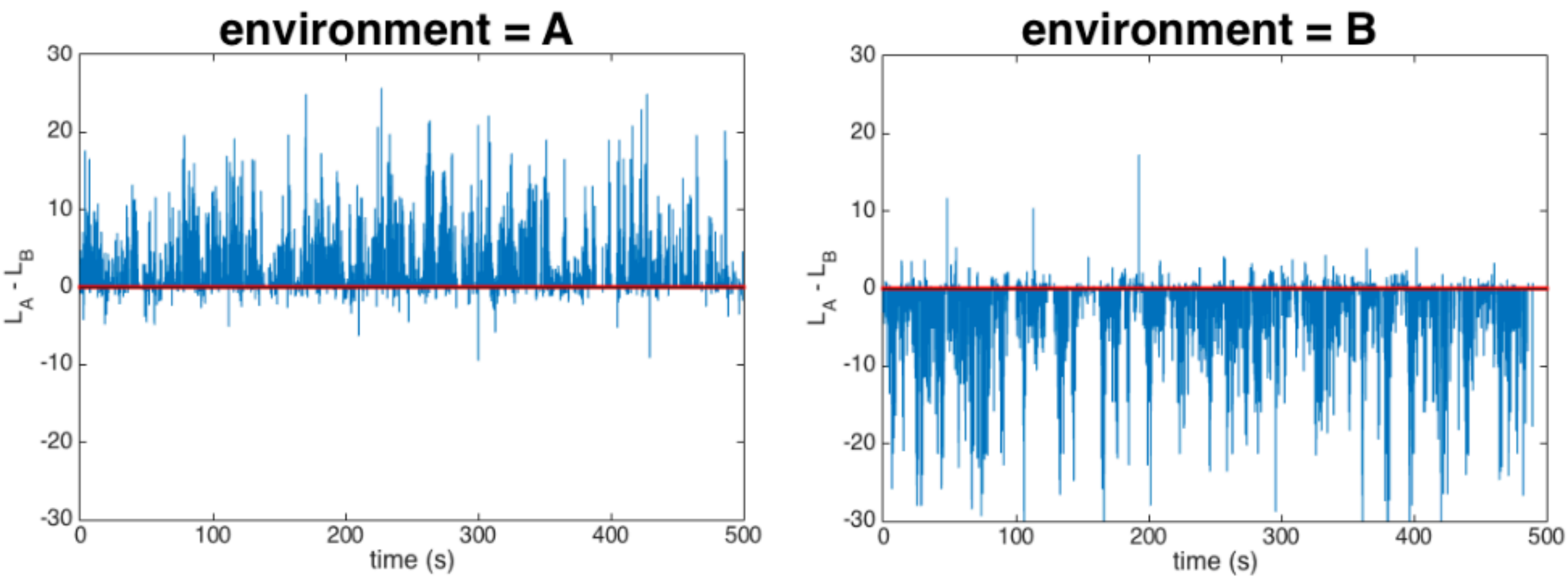
Inference procedure:

- solve the inverse problem to infer couplings $J_{ij}^{A,B}$ and fields $h_i^{A,B}$ from reference sessions A and B with A.C.E. (Cocco & Monasson 2011)
- compute likelihoods for A and B in the test session

$$\mathcal{L}_{Ising}^{A,B}(t) \;:=\; \sum_i h_i^{A,B} s_i(t) + \sum_{i<j} J_{ij}^{A,B} s_i(t) s_j(t) - \log(\mathcal{Z}^{A,B}) \qquad (4)$$

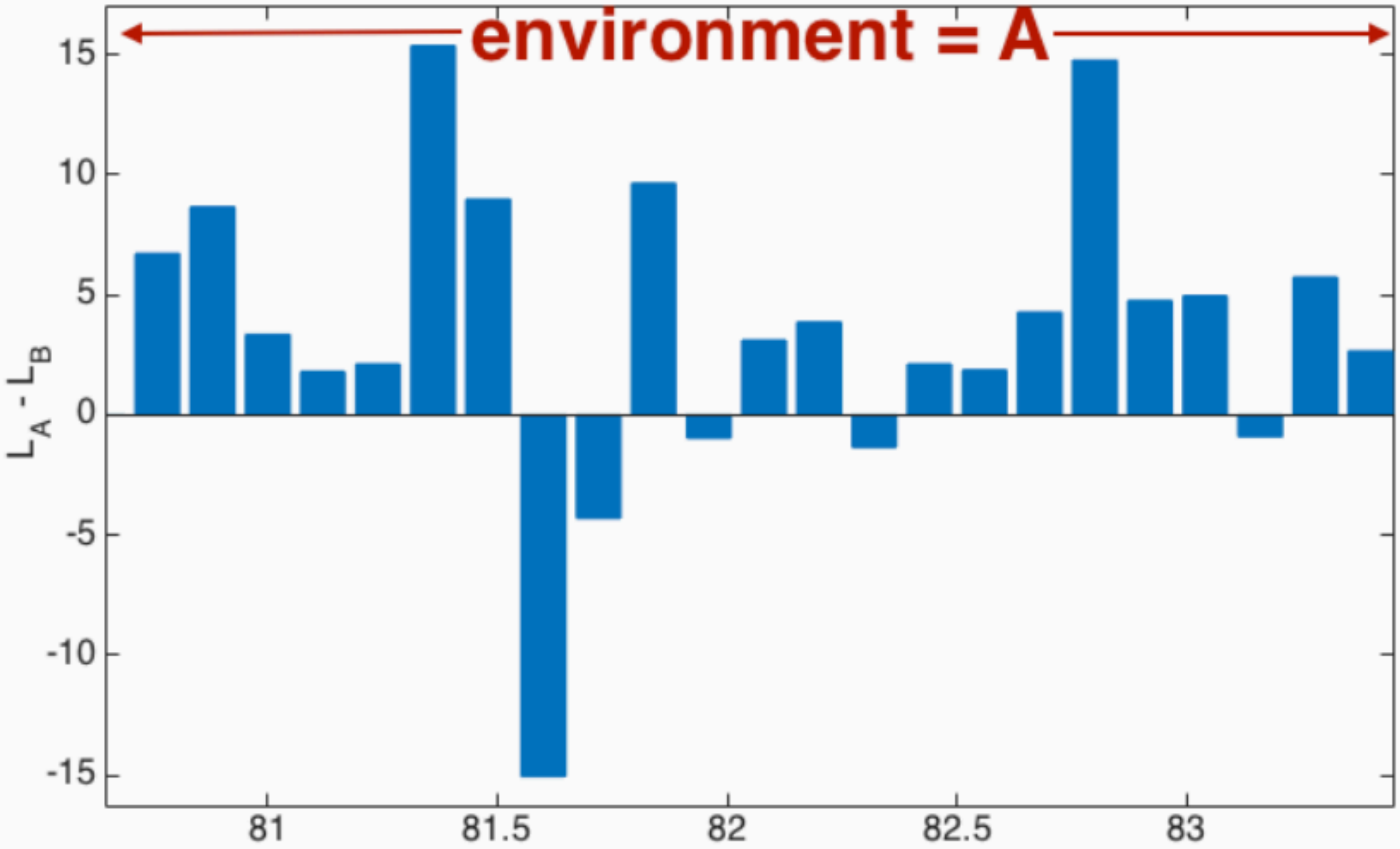
Cross-validation of decoding method (1)

- perform decoding on constant-environment test sessions



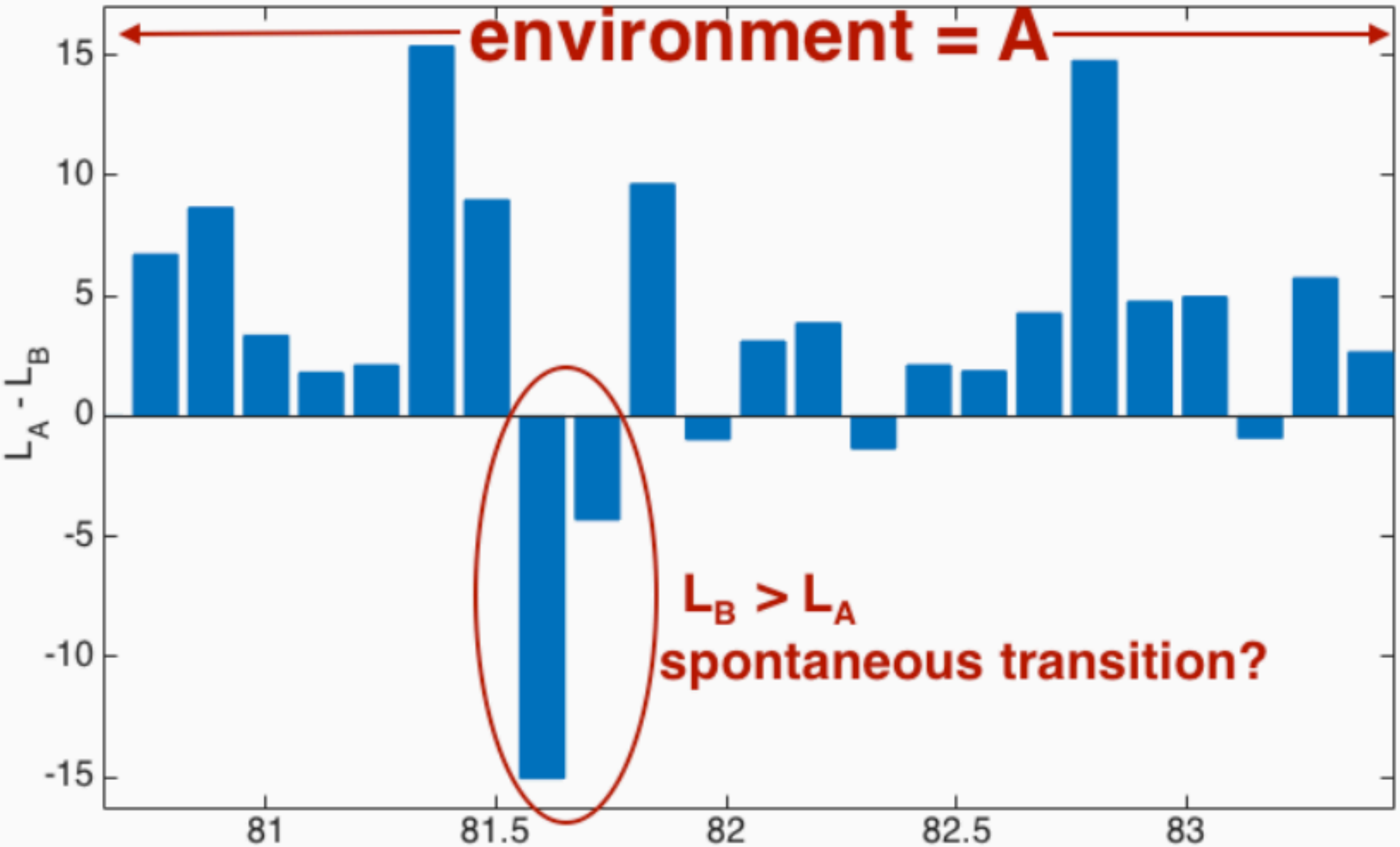
Transitions (1)

Sometimes the Ising decoder suggests that the represented environment in the brain is not the physical external one

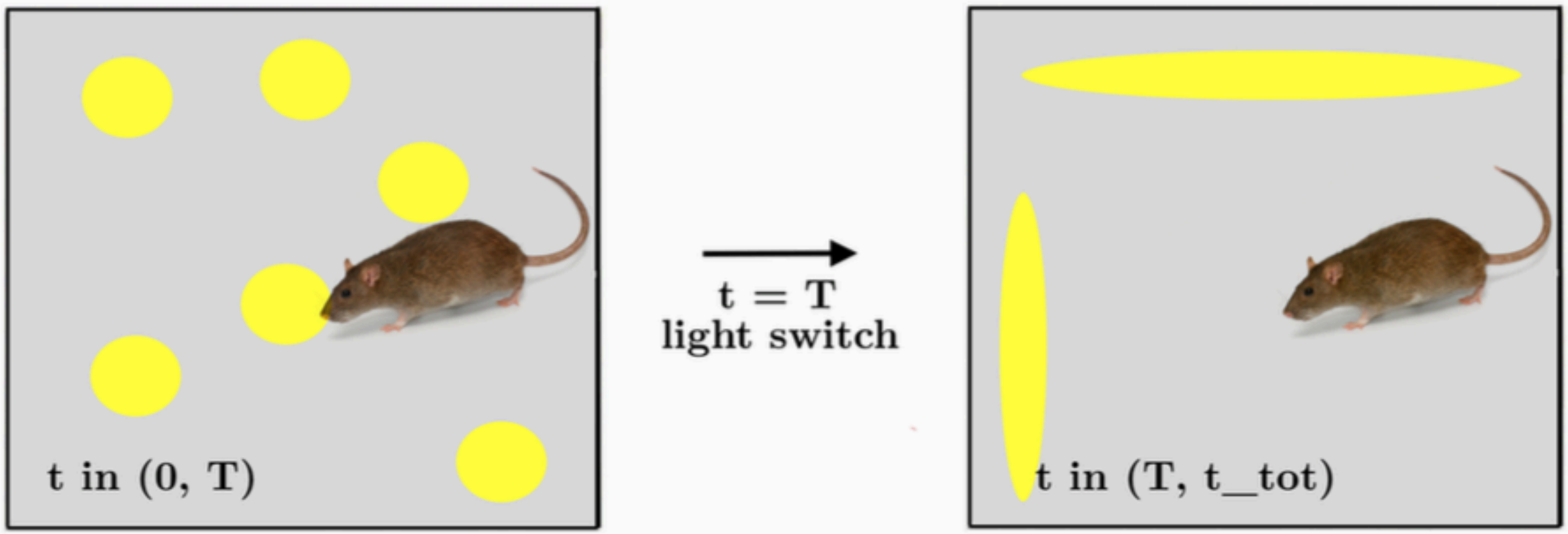


Transitions (2)

Sometimes the Ising decoder suggests that the represented environment in the brain is not the physical external one



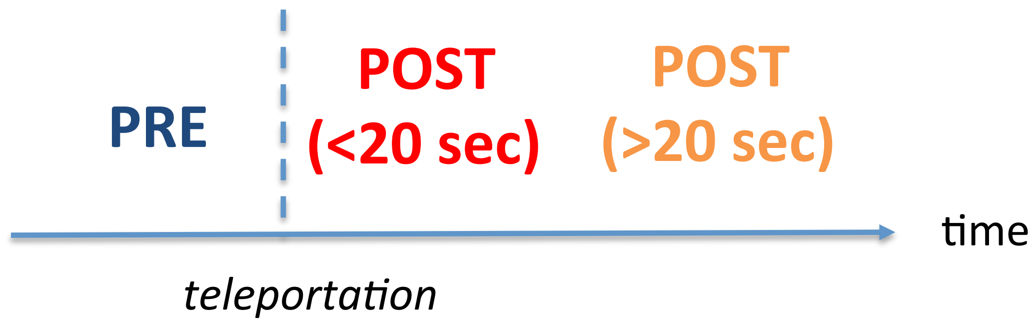
Reminder: Teleportation experiment

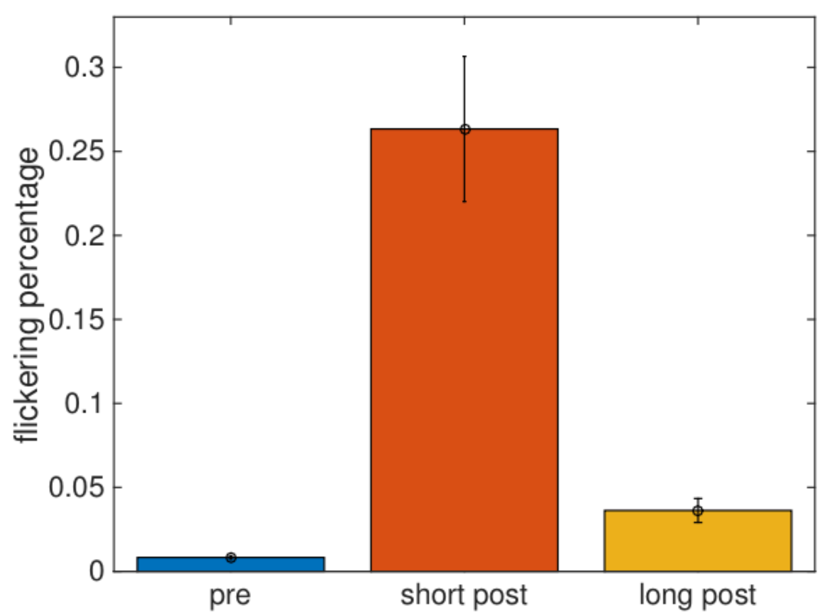


Test session: light cues are suddenly changed from one box to the other (teleportation)

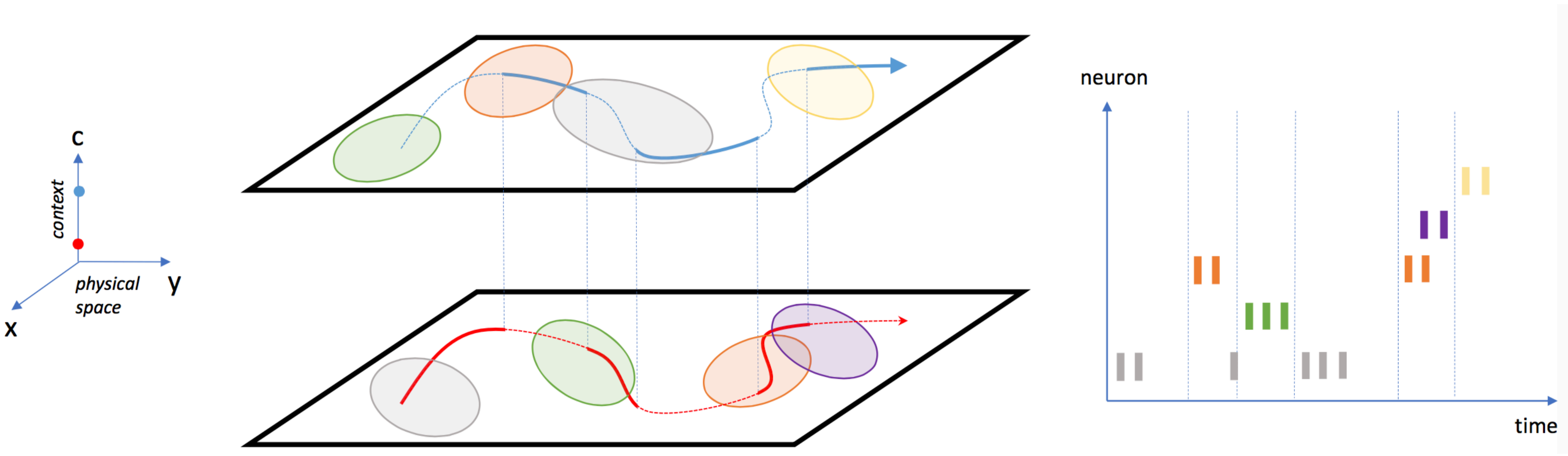
Transitions: Results (1)

Teleportation enhances network instability over both short and long term periods





Transitions: Results (2)



Is spatial position accurately encoded at all times despite the presence of fast contextual flickerings?

Transitions: Abstract model of map memory

In decoding so far: one Ising model for each map, but there is a single hippocampus …
Can we have a model storing all maps in a single set of interactions?

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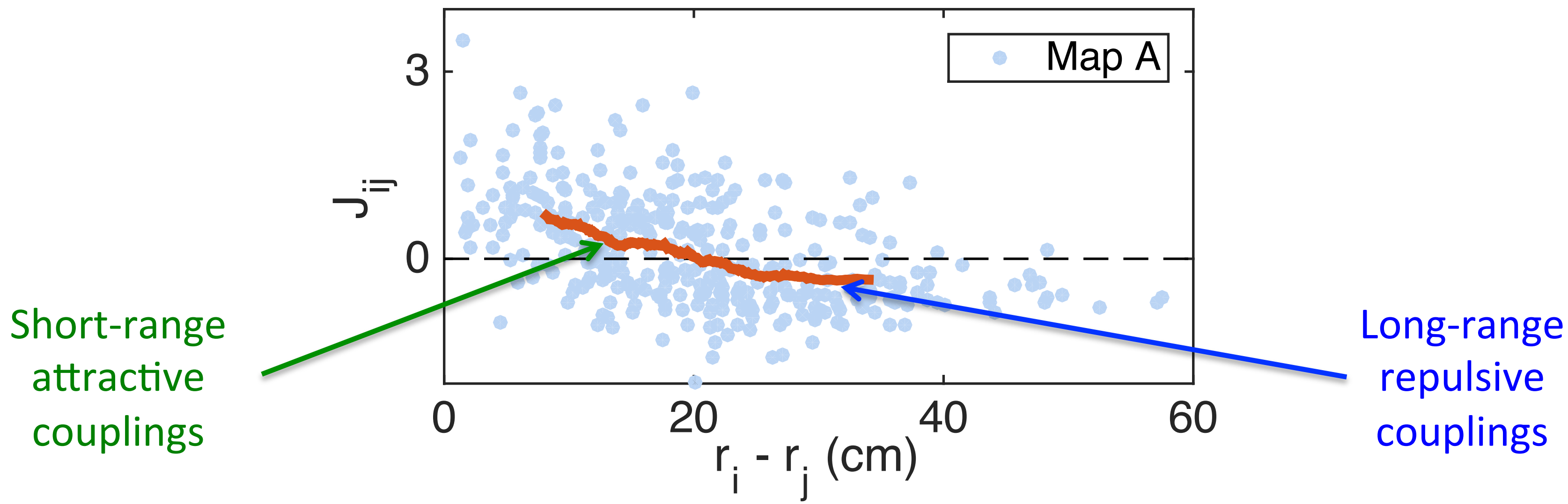
In decoding so far: one Ising model for each map, but there is a single hippocampus …
Can we have a model storing all maps in a single set of interactions?

Draw some inspiration from inferred Ising models:

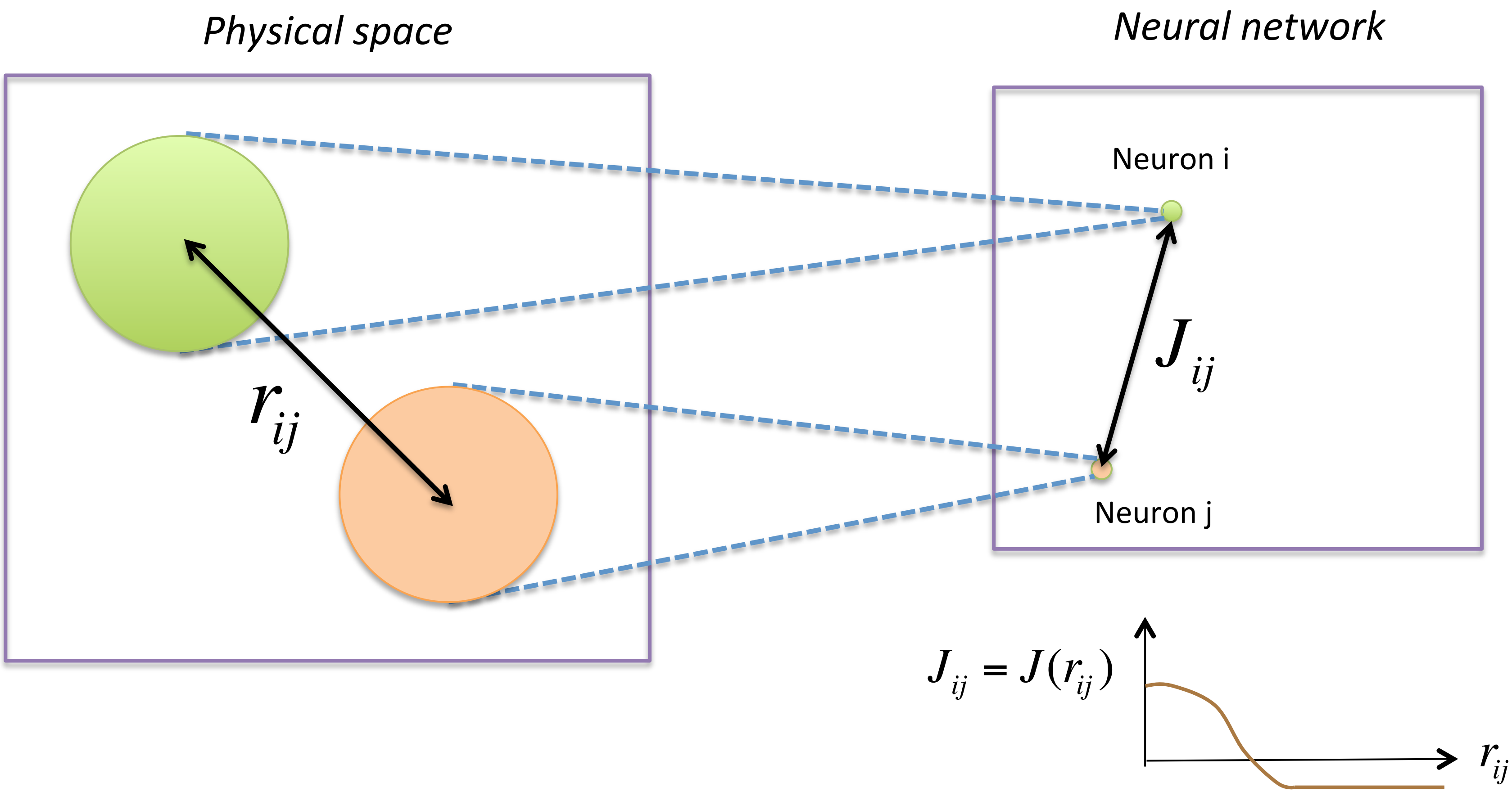


Similar to Lebowitz-Penrose model for liquid/vapor transition ….

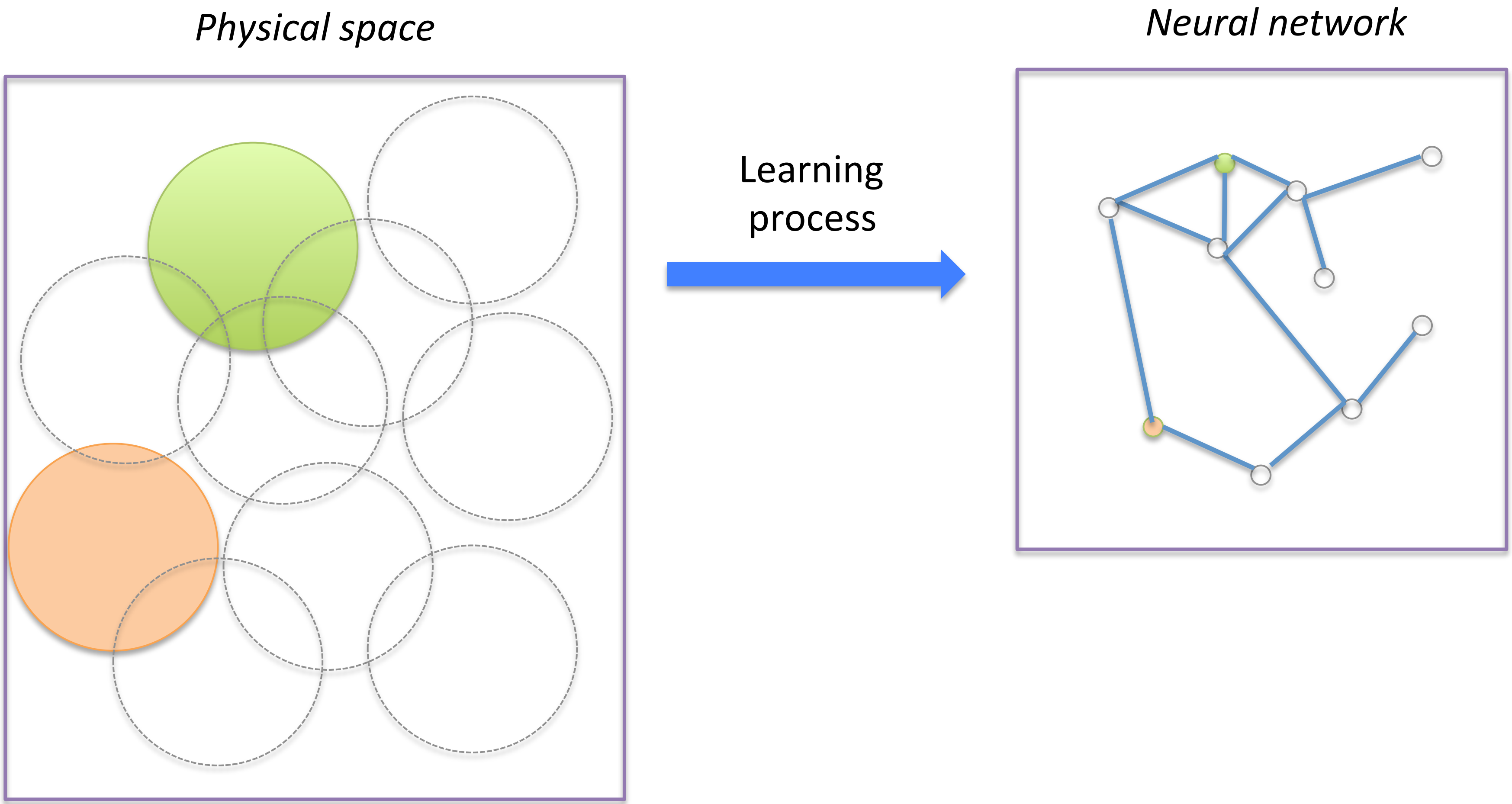
Neural network model (1)

Neuron = binary state, silent or active: $\sigma_i = 0,1$

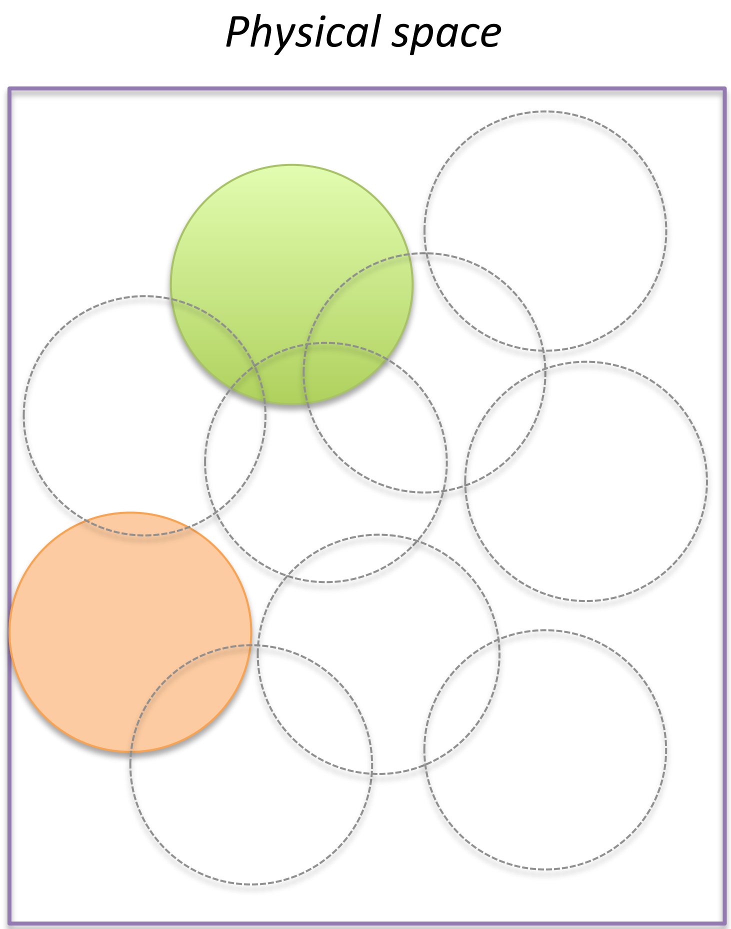
Interactions J_{ij}:

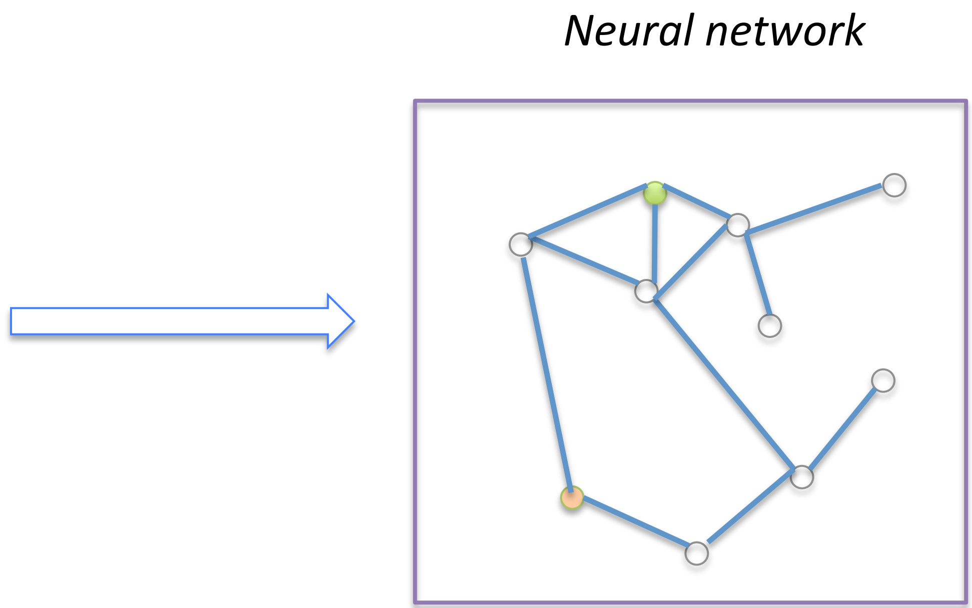


Neural network model (2)



Neural network model (2)





Distribution of neural activity configurations?

Neural network model (3)

- **Dynamical rules:** (on the N-dimension hypercube)

$$\sigma_1,\ldots,\sigma_i=0,\ldots,\sigma_N \underset{1/R}{\overset{R}{\rightleftarrows}} \sigma_1,\ldots,\sigma_i=1,\ldots,\sigma_N \qquad \text{with} \qquad \log R=\frac{1}{2T}\sum_{j(\neq i)} J\left(\left|\vec{x}_i-\vec{x}_j\right|\right)\sigma_j$$

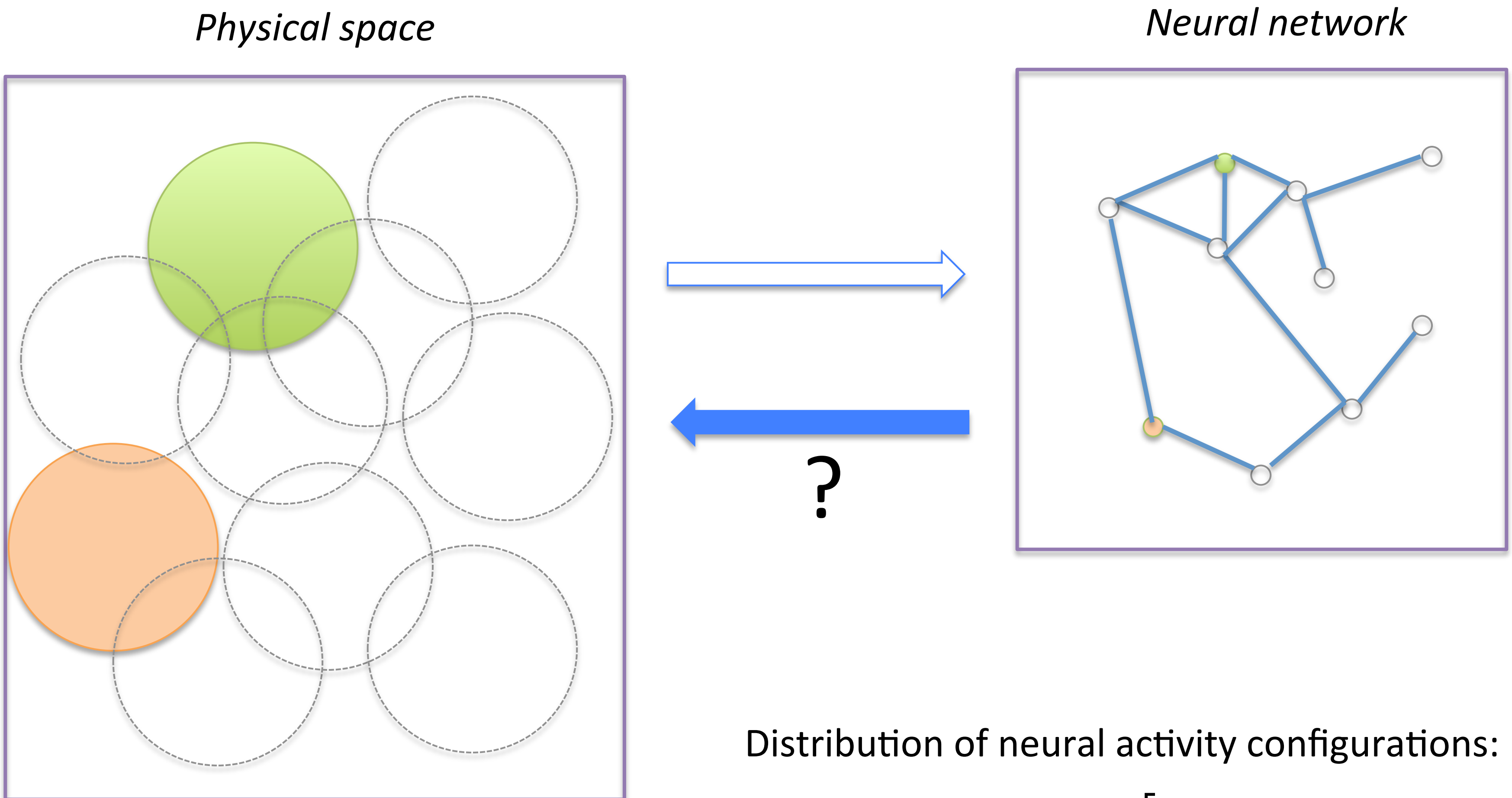
Noise level

- **Stationary distribution of neural activity configurations:**

$$P(\sigma_1,\sigma_2,\ldots,\sigma_N)\propto \exp\left[\frac{1}{T}\sum_{i<j} J\left(\left|\vec{x}_i-\vec{x}_j\right|\right)\sigma_i\sigma_j\right]$$

i.e. Gibbs measure associated to MCMC dynamics with rates

Neural network model (4)



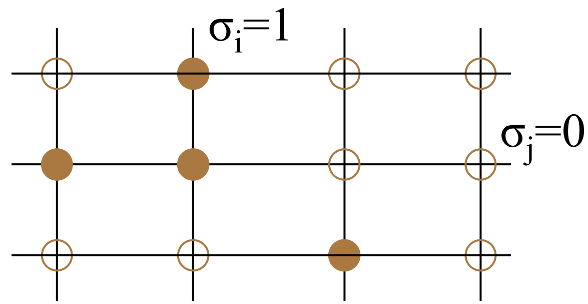
Distribution of neural activity configurations:

$$P(\sigma_1,\sigma_2,\ldots,\sigma_N) \propto \exp\left[\frac{1}{T}\sum_{i<j} J\left(\left|\vec{x}_i - \vec{x}_j\right|\right)\sigma_i\sigma_j\right]$$

Lattice gas model and continuous attractor

Lattice-gas model for the liquid/vapor transition :

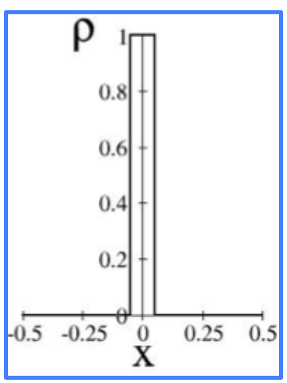
Lebowitz and Penrose (1966)

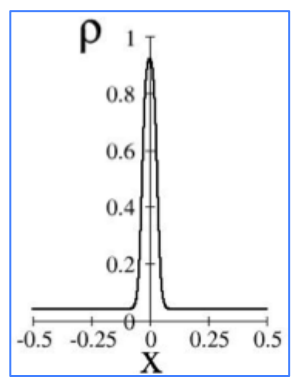


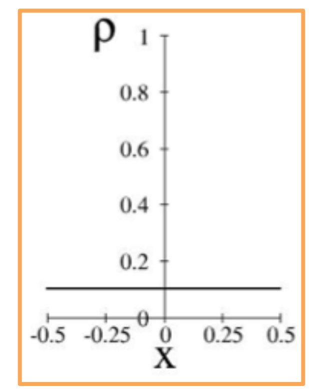
$$J_{ij} = J\left(\left|\vec{x}_i - \vec{x}_j\right|\right)$$

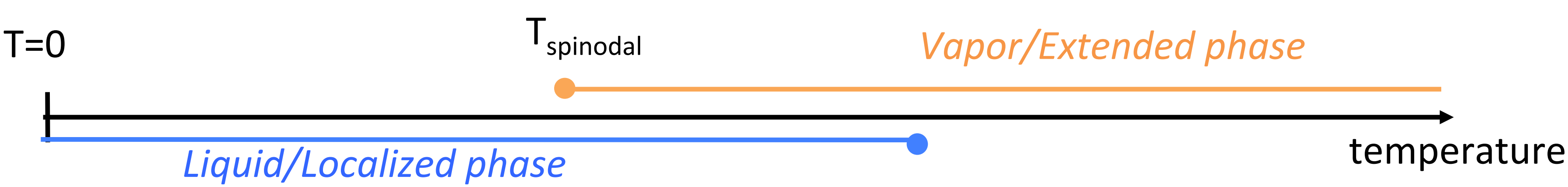
Order parameter =
Coarse-grained density:

$$\rho(x) \equiv \lim_{\epsilon\to 0} \lim_{N\to\infty} \frac{1}{\epsilon N} \sum_{(x-\frac{\epsilon}{2})N \leq i < (x+\frac{\epsilon}{2})N} \langle \sigma_i \rangle$$







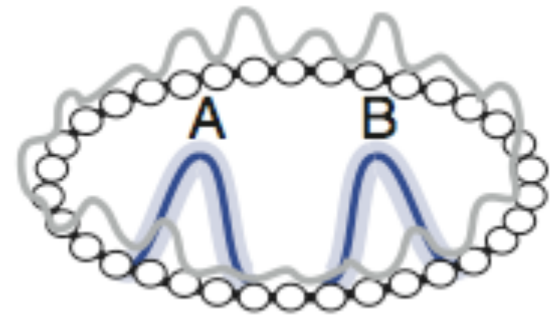


Continuous attractors & « population » coding

- successive firing of neurons along the ring in 1D or higher D = continuous attractor

- active bump = collective coordinate $\vec{x}$ for the neural activity (robust encoding)

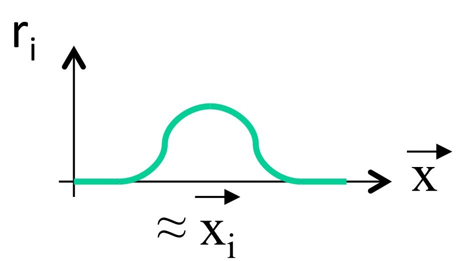
- bump persists *without* any input, but may be *driven by* an input (stimulus or other neural activity)



[Yoon et al., 2013]

- 2 points of view:

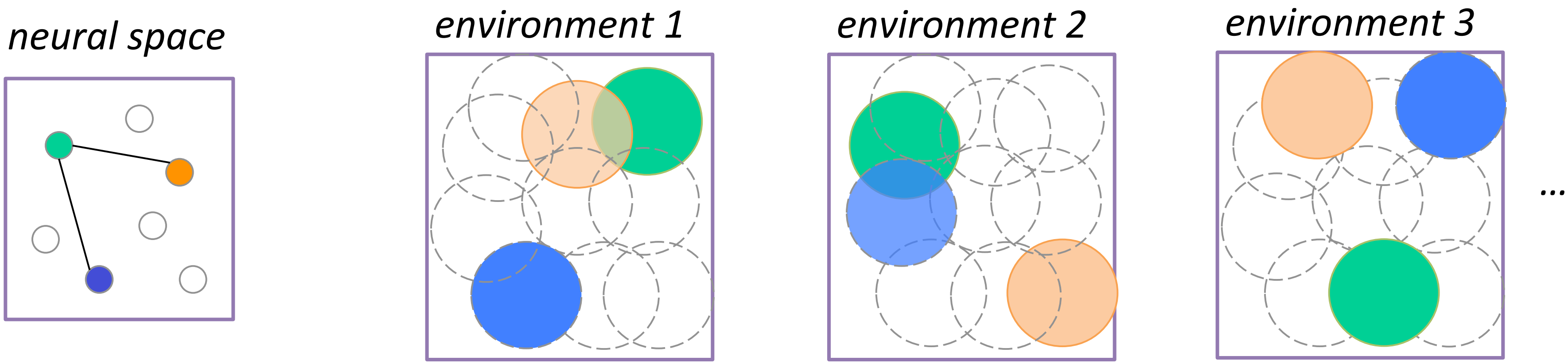
fixed time



fixed neuron

(place field)

Transitions: Abstract model of map memory



Distribution of neural activity configurations:

$$P(\sigma_1, \sigma_2, \ldots, \sigma_N) \propto \exp\left[\sum_{i<j} J_{ij}\sigma_i\sigma_j + h\sum_i \sigma_i\right]$$

Samsonovitch & McNaughton (1997)

with $$J_{ij} = \sum_e J\left(\left|\vec{x}_i^e - \vec{x}_j^e\right|\right)$$

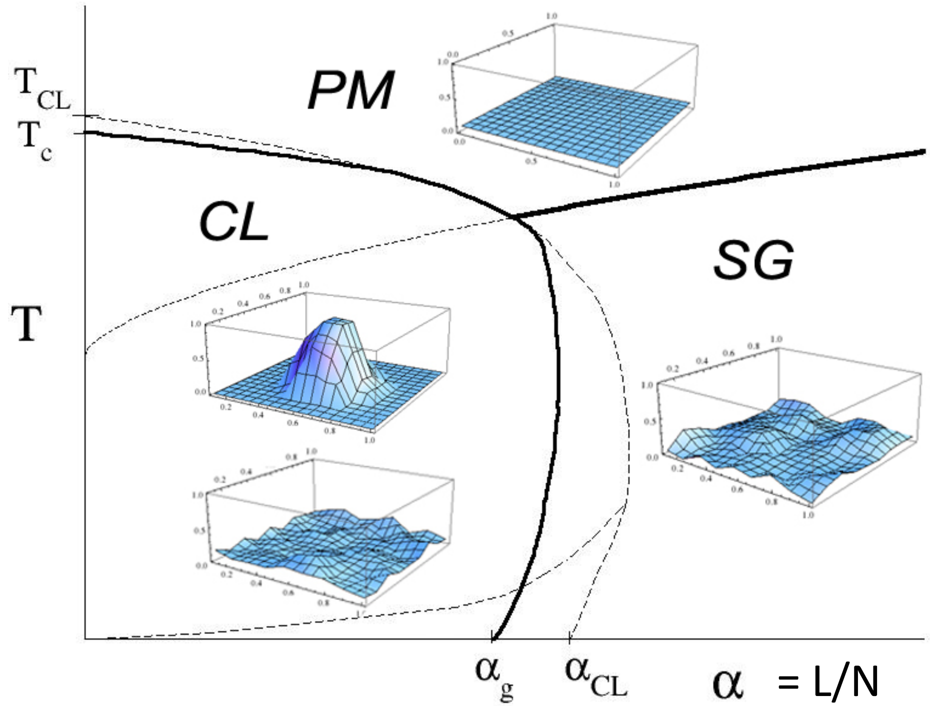
R.M. & Rosay (2013-2015)

<u>In the model:</u> New environment *e* = random permutation π

Transitions: Abstract model of map memory

Hamiltonian $$H = -\sum_{i<j}\sum_{l} J^0_{\pi^l(i),\pi^l(j)}\sigma_i\sigma_j$$

R.M., Rosay (2015)

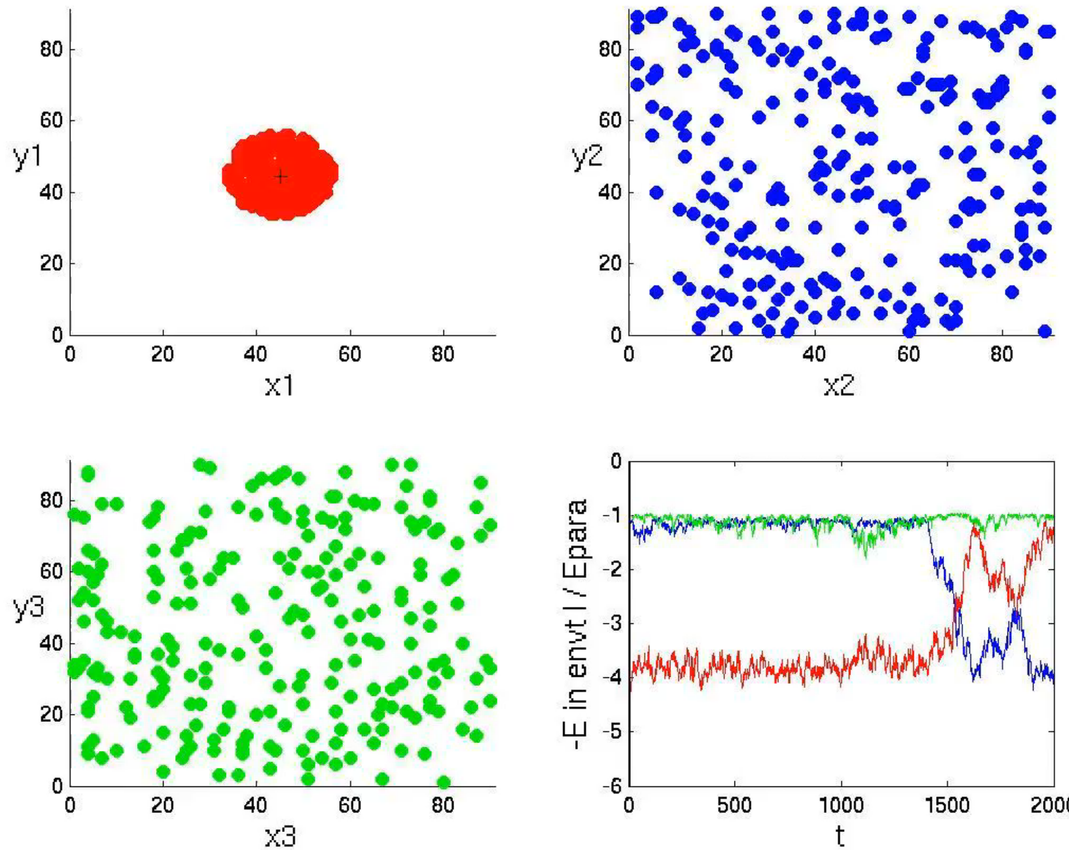


➔ Storage of activity configurations: 'finite' basin of attractions (Hopfield model)

➔ Storage of spatial maps: basins of attractions ≈ space of configurations !!

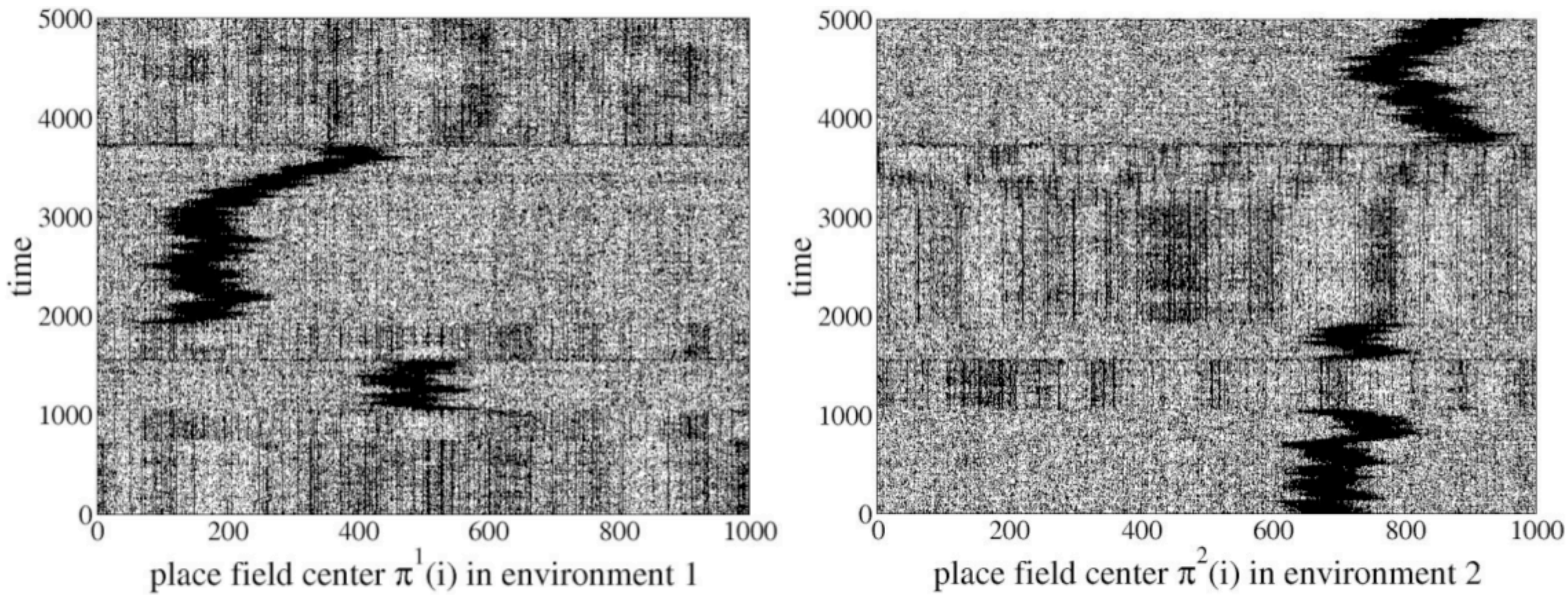
Scenarios for spontaneous transitions?

MCMC simulations (90x90 neurons, D=2)



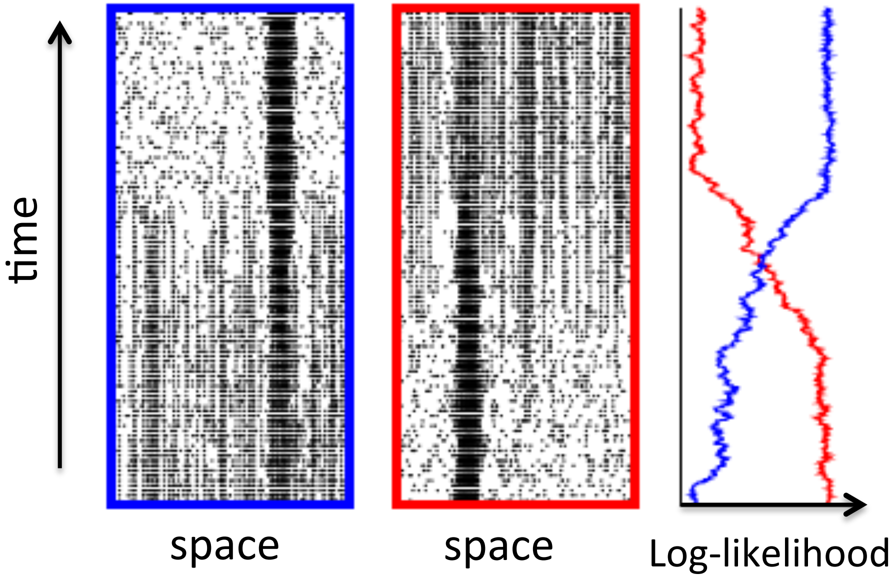
Scenarios for spontaneous transitions?

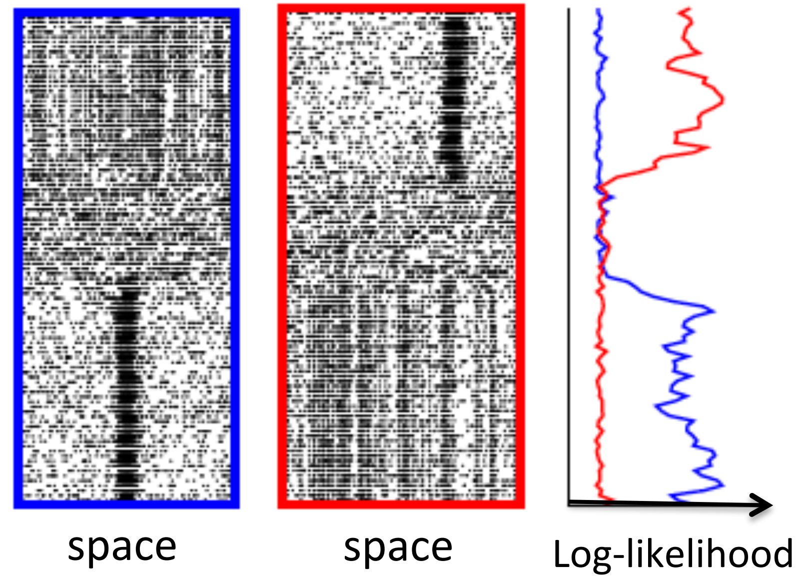
MCMC simulations (1000 neurons, 10% active at any time, D=1)



- ‘Diffusion’ of bumps within maps (quasi-particle obeys Stokes-Einstein!!)
- Spontaneous transitions from one map to another. Mechanism(s) ??

Scenarios for spontaneous transitions?



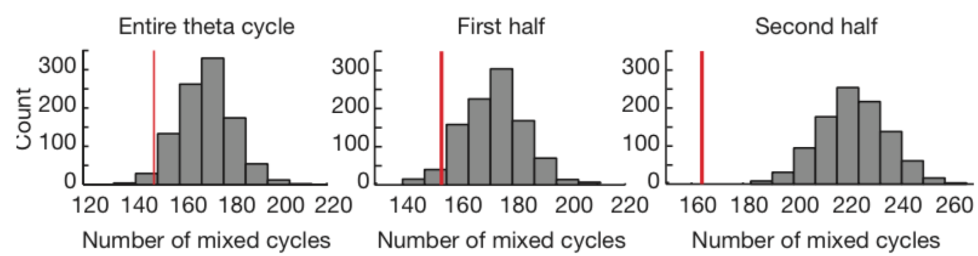


Transition facilitated by local similarities between maps (Wormhole)

Transition through ‘evaporation’ and ‘condensation’

In real recordings??

Relevance of Theta oscillations



Conclusions & Perspectives

Open neuroscience issues:

biological constraints (realistic aspects, e.g. adaptation, imperfect learning,…)

effects of rhythms? *(exploration of activity landscape)*

Statistical physics:

- optimal storage of D-dimensional attractors?

- bumps: detection, interactions, computations, …?

- bumps in « complex » spaces?

\+ Phenomenology of multiple continuous attractor network model compatible with experiments. Can we get further evidence from real data?

A few references

<u>Experiments:</u> A Sense of Where You Are, New York Times, April 30th, 2013

<u>Some references:</u>

Amari. *Biological cybernetics* 27, 77 (1977)

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<u>Self citations:</u> (available from my web page)

With S. Rosay: *Physical Review E* 87, 062813 (2013) (storage capacity)

Physical Review E 89, 032803 (2014) (dynamics)

Physical Review Letters 115, 09810 (2015) (transitions)

With S. Cocco, K. Jezek & L. Posani: *J. Comput. Neurosci. Doi:10.1007/ s10827-017-0645-9* (2017)

With S. Cocco, L. Posani, G. Tavoni: *Current Opinion in Systems Biology 3, 103* (2017)