Answers That Matter.

Wireless Recording Of The Electrophysiology Of Cognition In Psychiatric Disease Models

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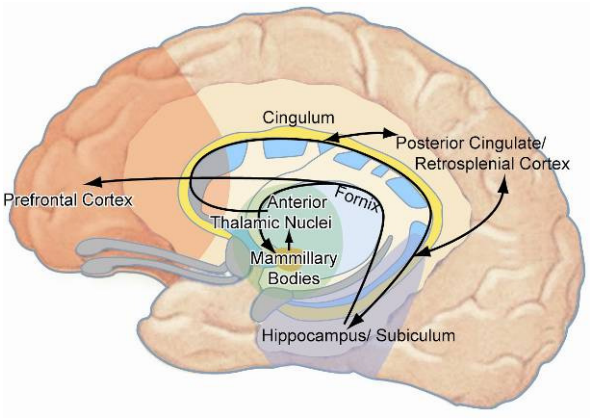
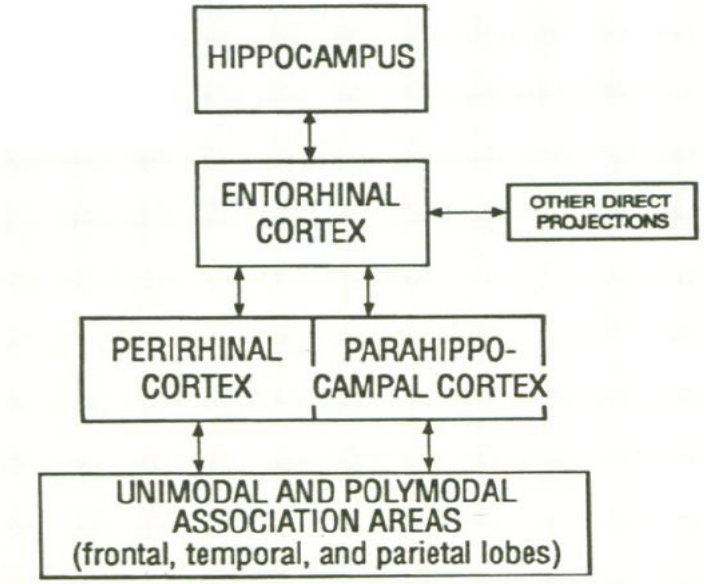
The hippocampus is:

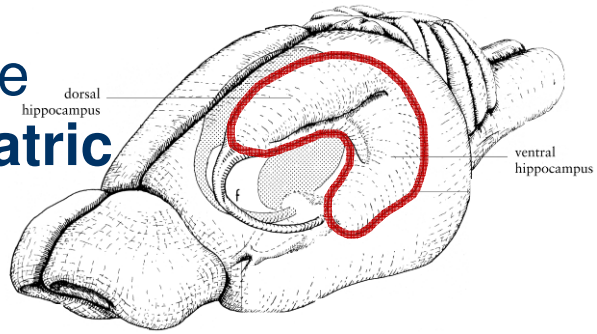
- part of the temporal lobe





- vital for declarative/episodic memory , working memory and spatial memory

- Hippocampal memory deficits are a key feature of a number of **neurodegenerative** and **psychiatric disorders**



The standard T-Maze rewarded alternation task is highly sensitive to **hippocampal** manipulations (e.g. lesion studies)

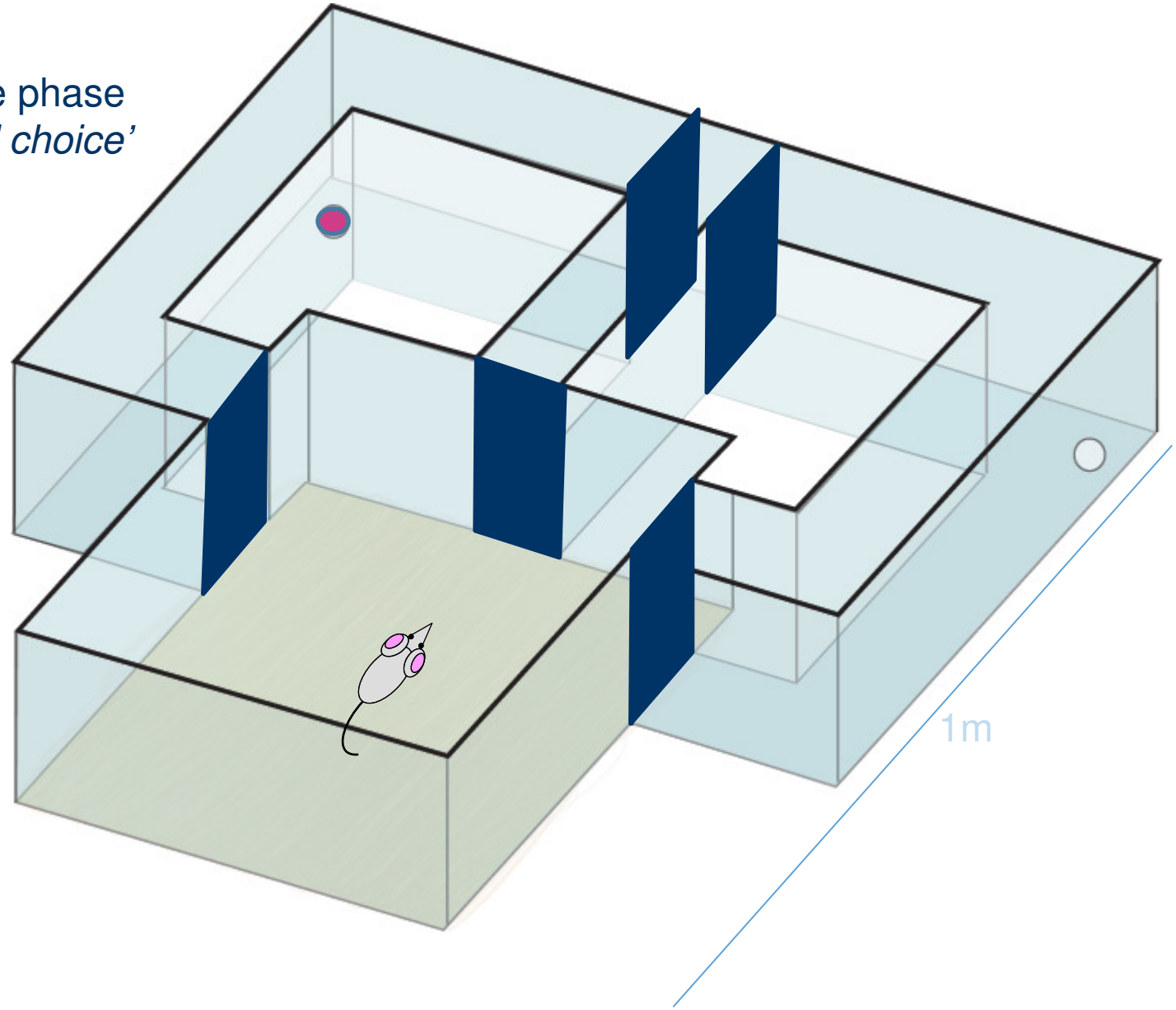
- Movie unavailable online

√

Animals must be handled between the two phases and between trials

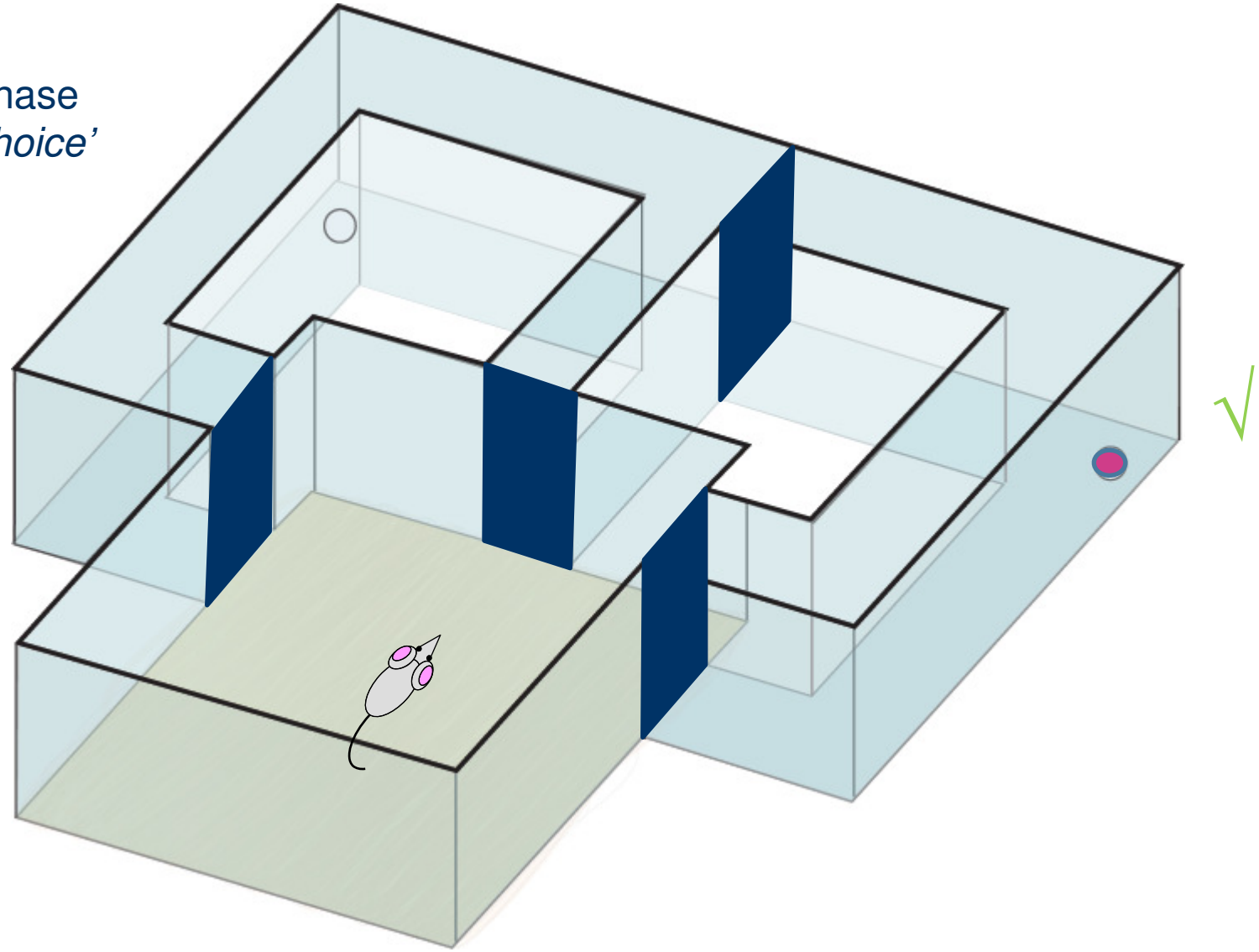
Automated T-Maze: Rewarded alternation task

Sample phase
'Forced choice'



Automated T-Maze: Rewarded alternation task

Test phase
'Free choice'

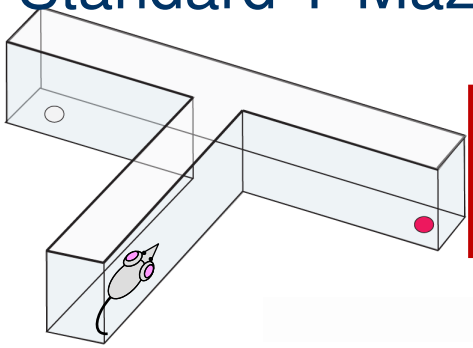


Validation of the Automated T-Maze: Hippocampal lesions

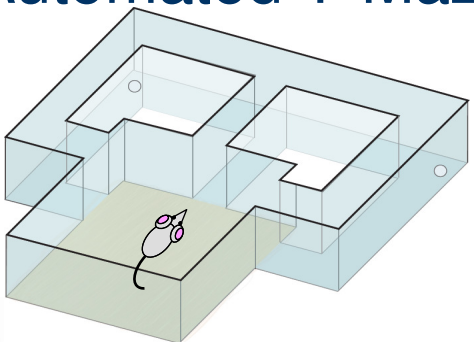
Standard T-Maze

60 trials

Automated T-Maze



Both tasks are Hippocampus-dependent



2 weeks

2 days

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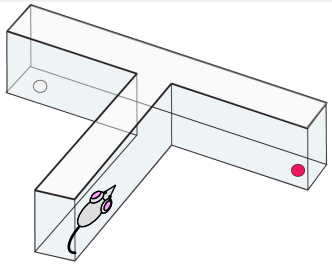
Standard T- Maze versus Automated T-Maze

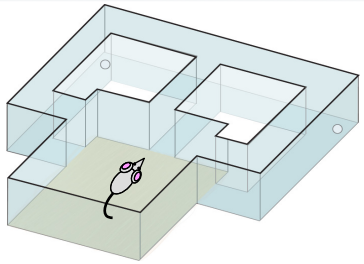
Standard T-Maze



- Manual
- Behaviour output:
  correct/incorrect response
- Intense handling:
  - stress
  - performance
- Low throughput: 2 weeks

X 3Rs benefits

Automated T-Maze



- Automated and computerised
- Behaviour output:
  correct/incorrect response,
  latency (+ lights and tones)
- No handling:
  - stress
  - performance
- High throughput: 2-3 days

➢ **Overall, the Automated T-Maze provides greater statistical power from fewer animals**

√ **3Rs benefits**

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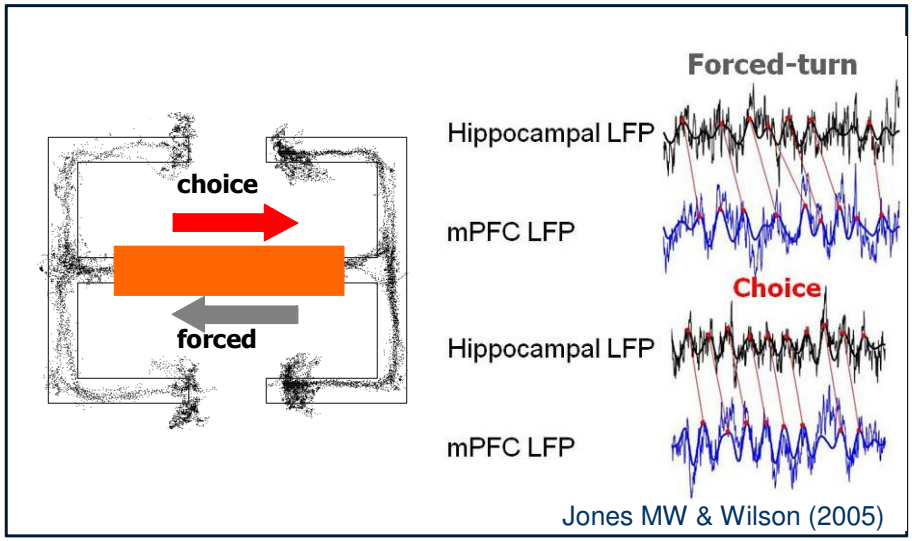
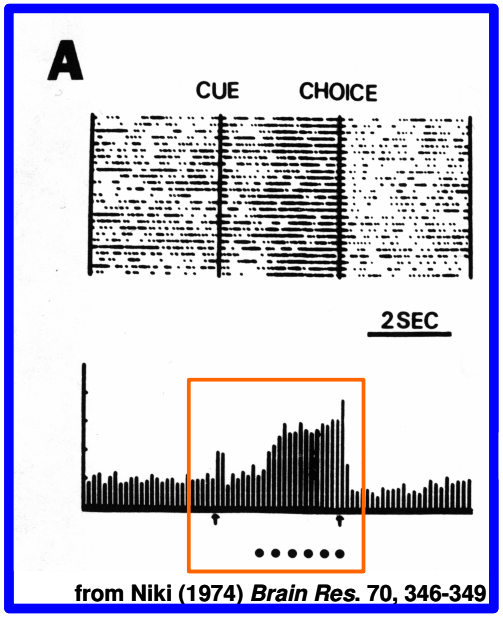
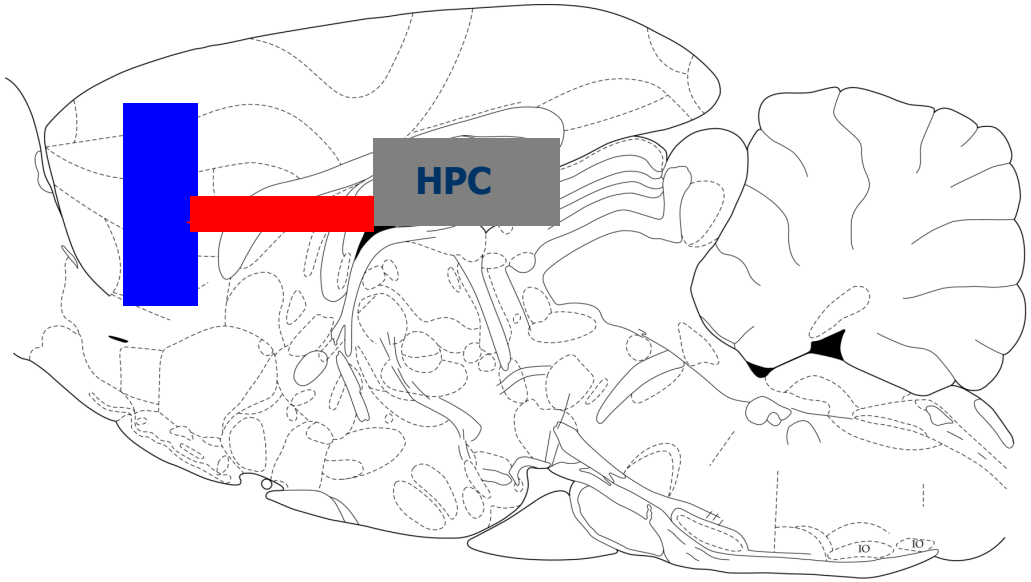
Electrophysiological recordings reveal the neuronal activity supporting performance on these tasks, while the animal is performing them

- The firing rate of single cells in the hippocampus can encode spatial information (place cells)
- While in the prefrontal cortex "delay firing working memory cells" can encode short term memory.







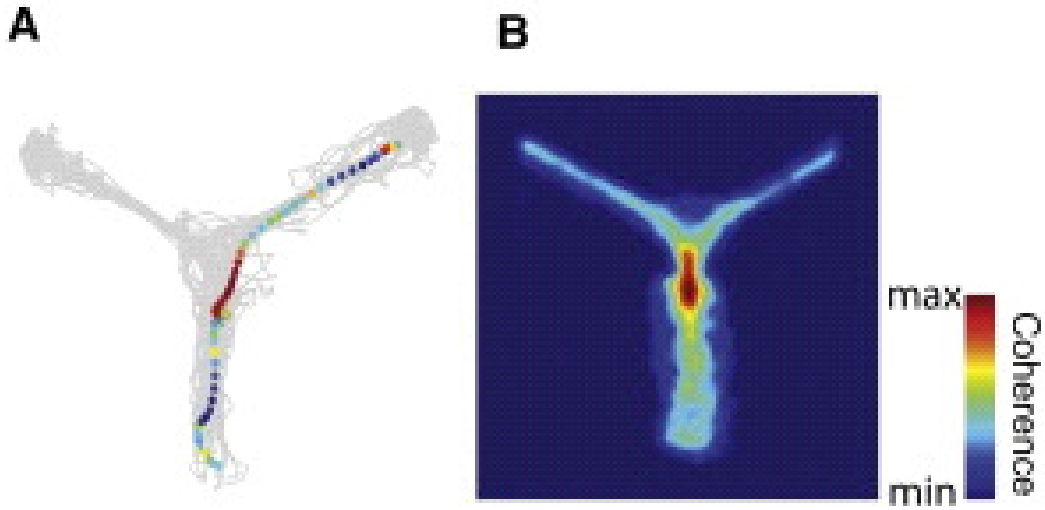
Hippocampal-prefrontal interactions

- **Hippocampal-prefrontal recordings have shown that neuronal networks in these areas synchronise at the choice point in spatial working memory tasks (single unit and EEG)**

Neuron
Article

Coherent Theta Oscillations and Reorganization of Spike Timing in the Hippocampal-Prefrontal Network upon Learning

Karim Benchenane,[1,7,*] Adrien Peyrache,[1] Mehdi Khamassi,[1,2] Patrick L. Tierney,[3,4] Yves Gioanni,[3] Francesco P. Battaglia,[1,5,6,*] and Sidney I. Wiener[1,6]



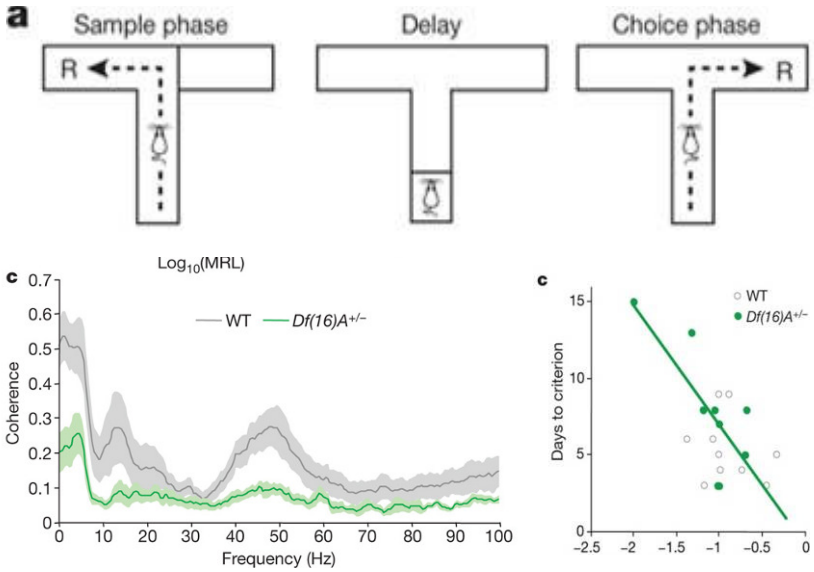
Prefrontal-hippocampal synchrony is impaired in both a genetic mouse model of schizophrenia and in patients during high working memory load

Vol 464|1 April 2010|doi:10.1038/nature08855 nature

LETTERS

Impaired hippocampal–prefrontal synchrony in a genetic mouse model of schizophrenia

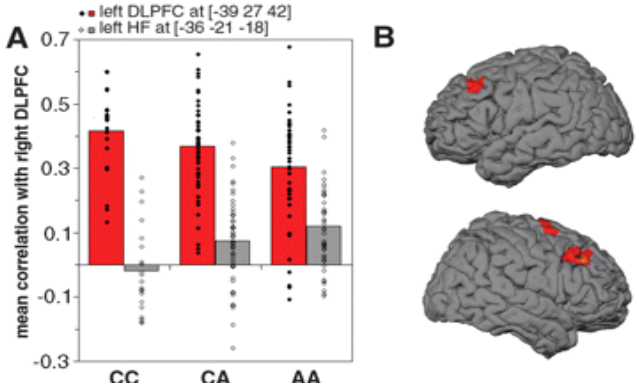
Torfi Sigurdsson[1], Kimberly L. Stark[1,2], Maria Karayiorgou[1,4], Joseph A. Gogos[2,3] & Joshua A. Gordon[1,4]



1 May 2009 | $10
Science

Neural Mechanisms of a Genome-Wide Supported Psychosis Variant

Christine Esslinger,[1*] Henrik Walter,[2,3*] Peter Kirsch,[1*] Susanne Erk,[3] Knut Schnell,[2,3] Claudia Arnold,[3] Leila Haddad,[1] Daniela Mier,[1] Carola Opitz von Boberfeld,[3] Kyeon Raab,[1] Stephanie H. Witt,[4] Marcella Rietschel,[4] Sven Cichon,[5] Andreas Meyer-Lindenberg[1]†



- Prefrontal-hippocampal coherence was reduced and could be used to **predict t-maze learning deficit.**

- Disrupted prefrontal synchrony in schizophrenic patients

Can we modulate these network impairments to provide new therapies?

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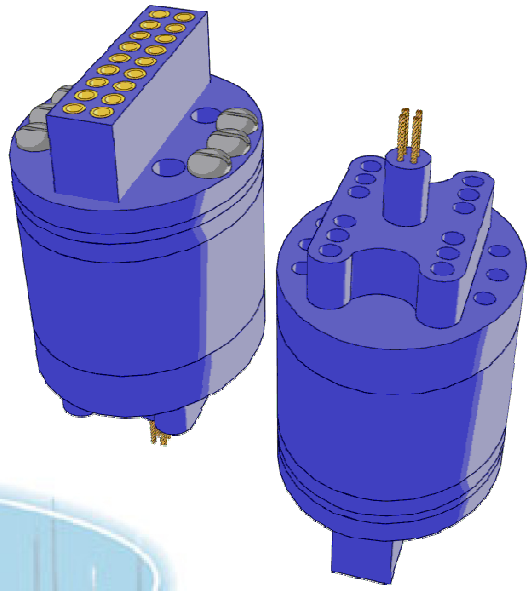
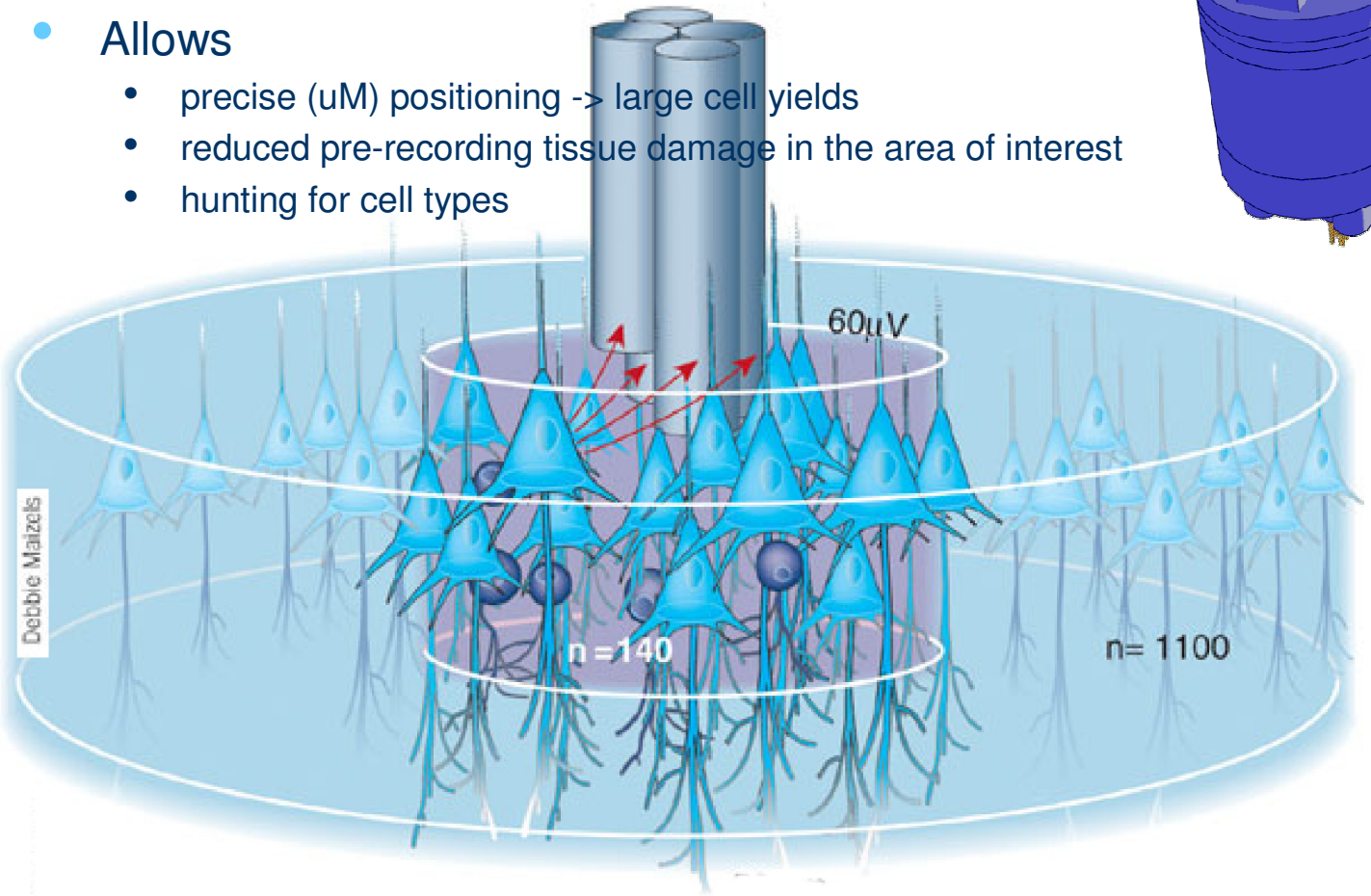
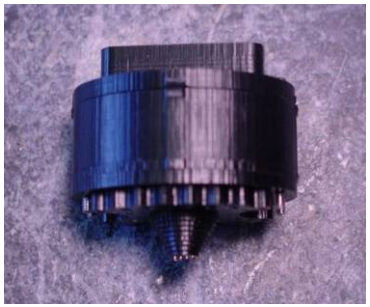
Electrophysiology methodology

- Chronic implants contain moveable arrays of
  - twisted 4-wire electrodes (tetrodes), or
  - multi-site silicone probes
- Position is adjusted after recovery from surgery
- Allows
  - precise (uM) positioning -> large cell yields
  - reduced pre-recording tissue damage in the area of interest
  - hunting for cell types







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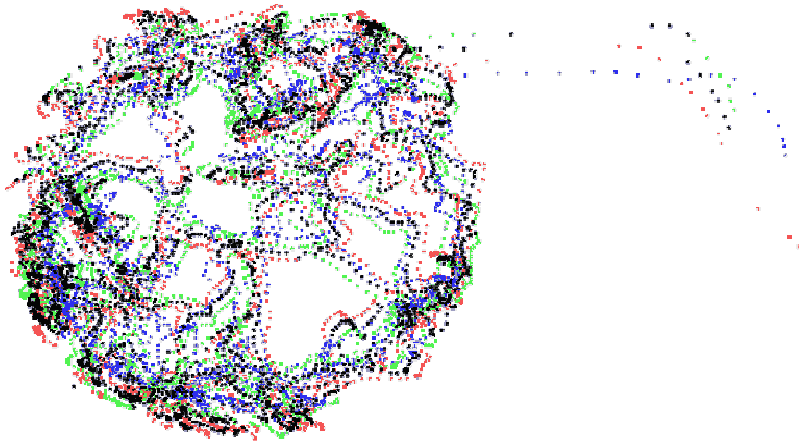
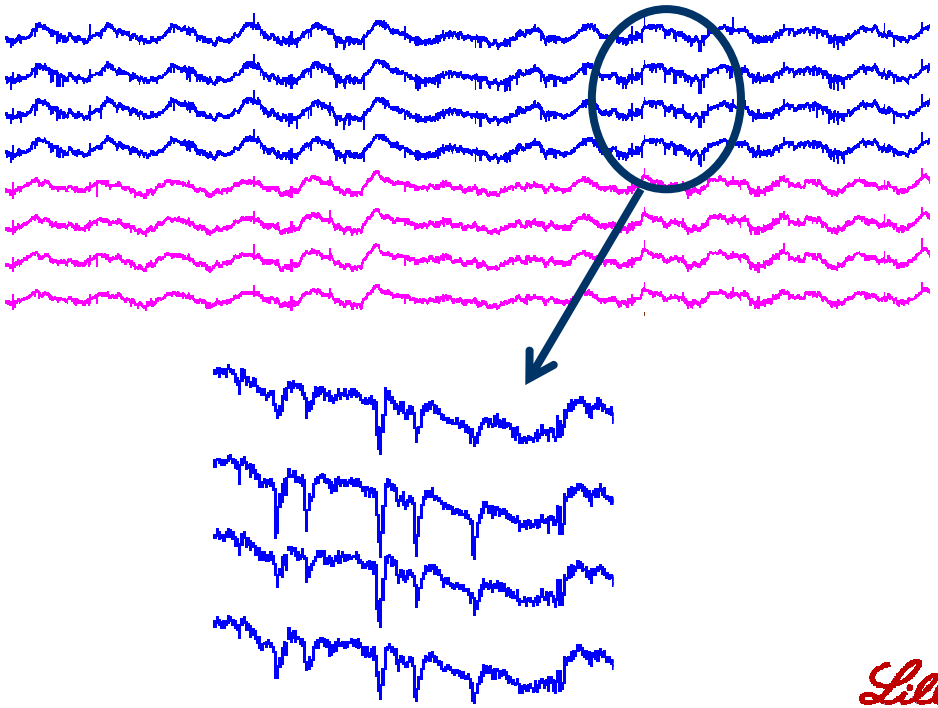
What can we measure?

- Combine different types of information
  [Within and between regions]



- Behaviour
  - **Position**, heading, **speed**

- EEG / Local field potentials (LFP)
  - **Theta**/gamma power spectrum
  - **Cycle detection**
  - Ripple/sharp-wave events



- Spiking
  - Action potential **waveforms**
  - **Activity levels** (firing rates)
  - **Temporal properties** (e.g. bursting)
  - **Behavioural correlates** (e.g. place fields)
  - **Relationship to LFP**

Benefits of a wireless system

Classical tethered system

- Additional training to accustom to presence of the cable
- Potential restriction of movement
- Limited to experiments using either
  - heavy cable (to turn a commutator)
  - -or-
  - simple open-top mazes but with constant monitoring to prevent cable-twisting

X 3Rs benefits

Wireless system

- Freedom of movement
- Reduced animal handling
- Reduced burden of weight for the animal
- Capacity to run more animals simultaneously, reducing duration of experiment
- Ability to use a wider variety of more naturalistic paradigms

√ **3Rs benefits**

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The challenge...

Overall objectives

To develop a prototype of a wireless 16-32 channel recording system that can acquire and transmit data for a minimum of 24h, that can be replaced or recharged with minimal discomfort for the animal and is small enough to be carried by a mouse without affecting its behaviour or welfare.

Key requirements

A wireless recording device that has the following specifications:

- Capability equivalent to recording 16 channels at 32kHz (ideally 32-64 channels).
- Any part of the system carried by the mouse must not weigh more than 3g
- Battery life of at least 24 hours to allow mice to learn multiple tasks within the T-maze, uninterrupted and without stressful insults.
- Event tracking integration, at least 8 independent event inputs to allow the behavioural data to be linked to the electrophysiological data.
- Scalable; must be ultimately possible to record from 8 animals in a single room.
- Interface with other commercially available electrodes, hardware and software
  - **(e.g. Neuronexus, Neuralynx, etc).**
- Flexibility in recording time and sampling rate.

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