Acquisition of first datasets of electrophysiological recordings of hippocampal cells in VR environment (D3.3.1 – SGA2)
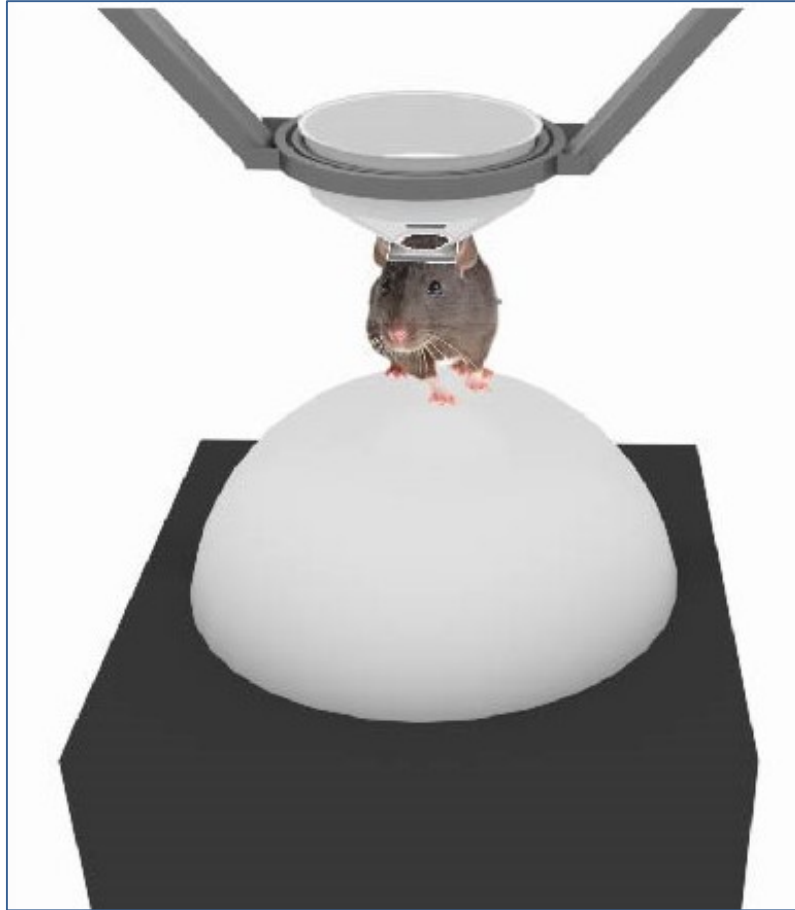
Figure 1: A mouse attached to the head-holder for a virtual reality (VR) task

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Author(s):	Guifen CHEN, UCL (P82)
Compiled by:	Guifen CHEN, UCL (P82)
Contributor(s):	Guifen CHEN, UCL (P82) Francesca CACUCCI, UCL (P82) Neil BURGESS, UCL (P82)
SciTechCoord Review:	Martin TELEFONT, EPFL (P1)
Editorial Review:	Annemieke MICHELS, EPFL (P1), Guy WILLIS, EPFL (P1)
Description in GA:	Report on acquisition of first datasets (T.3.3.2)
Abstract:	We present a mouse virtual reality (VR) system which restrains head-movements to horizontal rotations, compatible with multi-photon imaging. We are able to record place cells and grid cells in the virtual environments that we have developed.
Keywords:	Virtual reality, place cells, grid cells
Target Users/Readers:	neuroscience community, HBP partners, general public.

Table of Contents

Table of Figures

1.   Two-dimensional virtual reality setup

We designed and tested a virtual reality system for a mouse subject. In this Deliverable, we show the methods that we developed for this virtual reality system, as well as the data we collected on mouse hippocampus formation using this system.
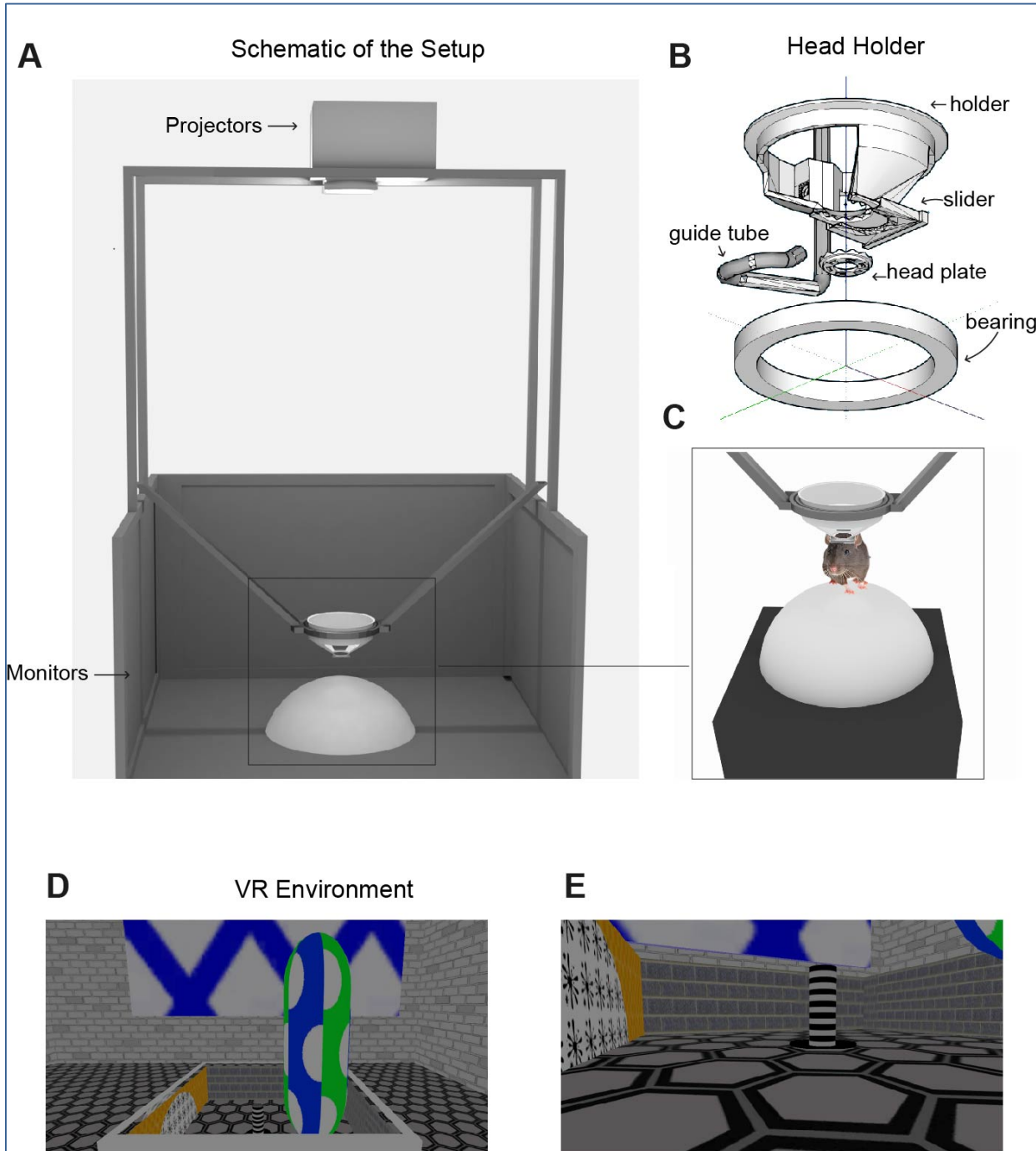

Figure 2 Virtual reality setup

(A) Schematic of the Virtual Reality (VR) setup (VR square). (B) A rotating head-holder. (C) A mouse attached to the head-holder. (D-E) Side views of the VR environment.

A circular head-plate made of plastic (Stratasys Endur photopolymer) is chronically attached to the skull of the mouse subject, with a central opening allowing the implant of tetrodes for electrophysiological recording. The head-plate makes a self-centring joint with a holder mounted in a bearing (Kaydon reali-slim bearing KA020XP0) and is clipped into place by a slider. The bearing is held over the centre of an air-supported Styrofoam ball. Four LCD screens placed vertically around the ball and two projectors directed downwards onto a horizontal floor provide the projection of a virtual environment.

The virtual environment runs on a Dell Precision T7500 workstation PC running Windows 7 64-bit on a Xeon X5647 2.93 GHz CPU, displayed using a combination of four Acer B236HL LCD monitors mounted vertically in a square array, plus two LCD projectors (native resolution 480 × 320, 150 lumens) mounted above to project floor texture. The head-holder is at the centre of the square and 60 mm from the bottom edge of the screens, and 9,500 mm below the projectors. The LCD panels are 514 mm x 293 mm, plus bezels of 15 mm all around. These six video feeds are fed by an Asus AMD Radeon 6900 graphics card and combined into a single 5,760 × 2,160 pixel virtual display using AMD Radeon Eyefinity software. The VR is programmed using Unity3d v5.0.2f1, which allows virtual cameras to draw on specific regions of the virtual display, with projection matrices adjusted to the physical dimensions and distances of the screens, and also to offset the vanishing point from the centre. For example, a virtual camera facing the X-positive direction renders its output to a portion of the virtual display which is known to correspond to the screen area of the physical monitor facing the X-negative direction.

Translation in the virtual space is controlled by two optical mice (Logitech G700s gaming mouse), mounted with orthogonal orientations at the front and side of a 200 mm-diameter hollow polystyrene sphere, which floats under positive air pressure in a hemispherical well. The optical mice drive X and Y inputs respectively by dint of their offset orientations, and gain can be controlled using the Unity software. Gain is adjusted such that real-world rotations of the sphere are calibrated so that a desired environment size (e.g. 600 mm across) corresponds to the appropriate movement of the surface of the sphere under the mouse subject (i.e. moving 600 mm, or just under one rotation, on the sphere takes the mouse across the environment). Mouse pointer acceleration is disabled at operating system level to ensure that movement of the sphere is detected in a linear fashion, independent of running speed.

The mouse subject is able to freely rotate in the horizontal plane, which has no effect on the VR display (but brings different screens into the mouse's view). Vertical movement is constrained by the fixed holder to which the mouse's head plate is clipped. Rotation is detected and recorded for later analysis using an Axona dacqUSB tracker which records the position of two LEDs mounted at ~25 mm offset to left and right of the head stage amplifier. Rotation is sampled at 50 Hz by detection of the LED locations using an overhead video camera, while virtual location is sampled and logged at 50 Hz.

Behaviour is motivated by the delivery of milk rewards (SMA, Wysoy) controlled by a Labjack U3HD USB Data Acquisition device. A digital-to-analogue channel applies 5V DC to a control circuit driving a 12V Cole-Parmer 1/16″ solenoid pinch valve, which is opened for 100 ms for each reward, allowing for the formation of a single drop of milk (5 uL) under gravity feed at the end of a 1/32″ bore tube held within licking distance of the animal's mouth.

Control of the Labjack and of reward locations in the VR is via UDP network packets between the VR PC and a second experimenter PC, to which the Labjack is connected by USB. Software written in Python 2.7 using the Labjack, tk (graphics) and twistd (networking) libraries provide a plan-view graphic interface in which the location of the animal and reward cues in the VE can be easily monitored and reward locations manipulated with mouse clicks.

2. Data description

With the virtual reality system we developed, we were able to record neural activity of spatial cells [1], [2] from mice while they were exploring in a 60 x 60 cm virtual square.

Place cells recorded from the CA1 region of the hippocampus showed spatially localized firing in the virtual environment, with similar firing rates in the virtual and real square environments (Figure 3). Grid cells recorded in the dorsal medial entorhinal cortex, showed similar grid-like firing patterns in virtual reality as that in reality (Figure 4).

Importantly, we demonstrated that the VR system allows expression of the characteristic spatially modulated firing patterns of place, grid and head-direction cells in open arenas. Thus, it passes the first pre-requisite as a tool for studying the mechanisms behind the two-dimensional firing patterns of these spatial cells. By using VR, the system presented here offers advantages over traditional

paradigms by enabling manipulations that are impossible in the real-world, allowing visual projection of an environment that need not directly reflect a physical reality or the animals' movements. By working for mice and by constraining the head to rotation in the horizontal plane, our system has the potential for future use with multi-photon imaging using genetically encoded calcium indicators. The use of multiple screens and floor projectors is not as elegant as the single projector systems, but allows the possible future inclusion of a two-photon microscope above the head without interrupting the visual projection, while the effects of in-plane rotation on acquired images should be correctable in software.
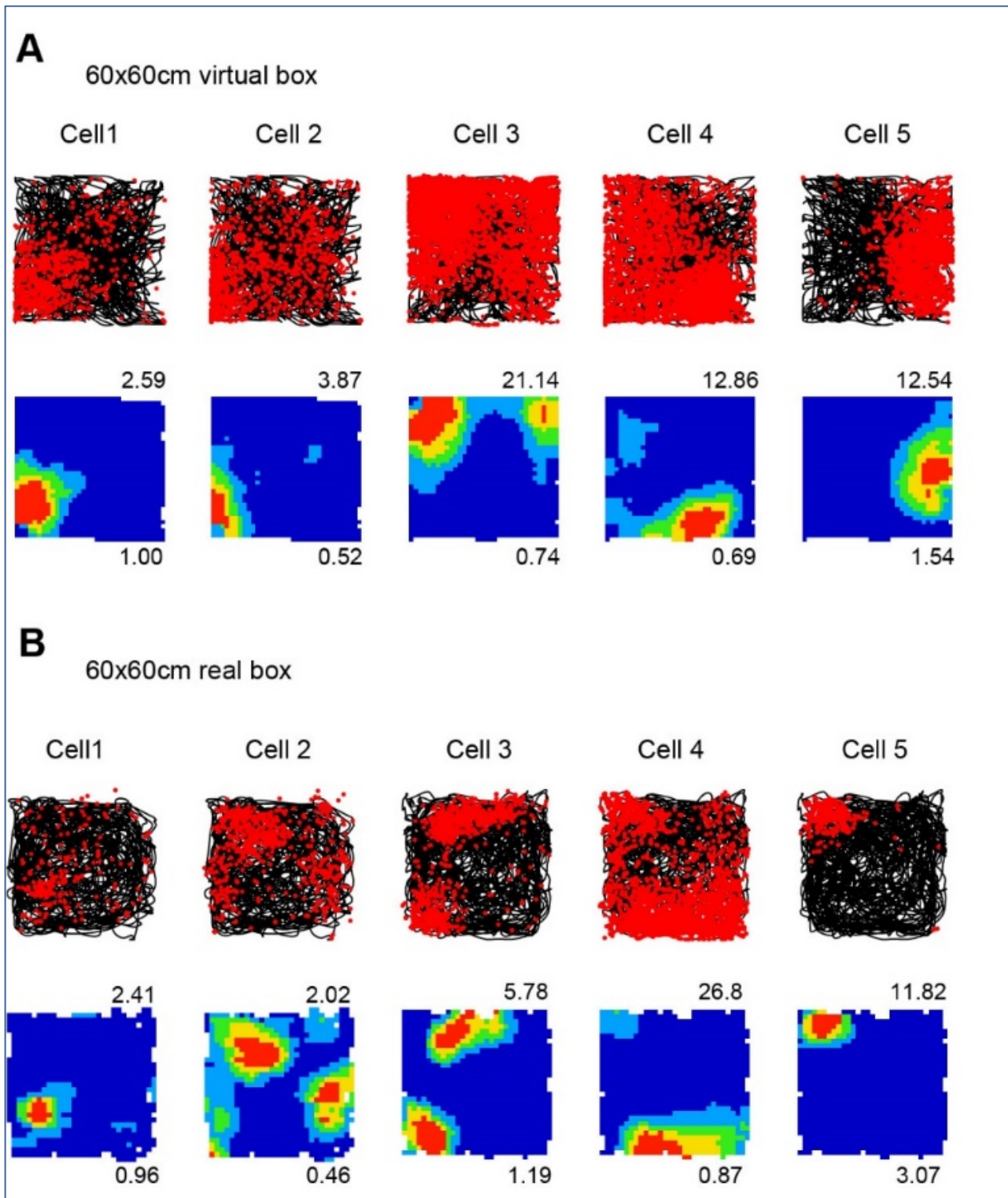

Figure 3 Place cell firing in real and virtual environments

(A-B) The same five place cells recorded in a 60 × 60 cm virtual square (A) and in a 60 × 60 cm real square (B, one cell per column). Top row: 40 min running trajectory (black line) with red dots showing the locations of spikes; 2nd row, firing rate maps, maximum firing rate (Hz) shown at top right, spatial information (bits/spike) bottom right.
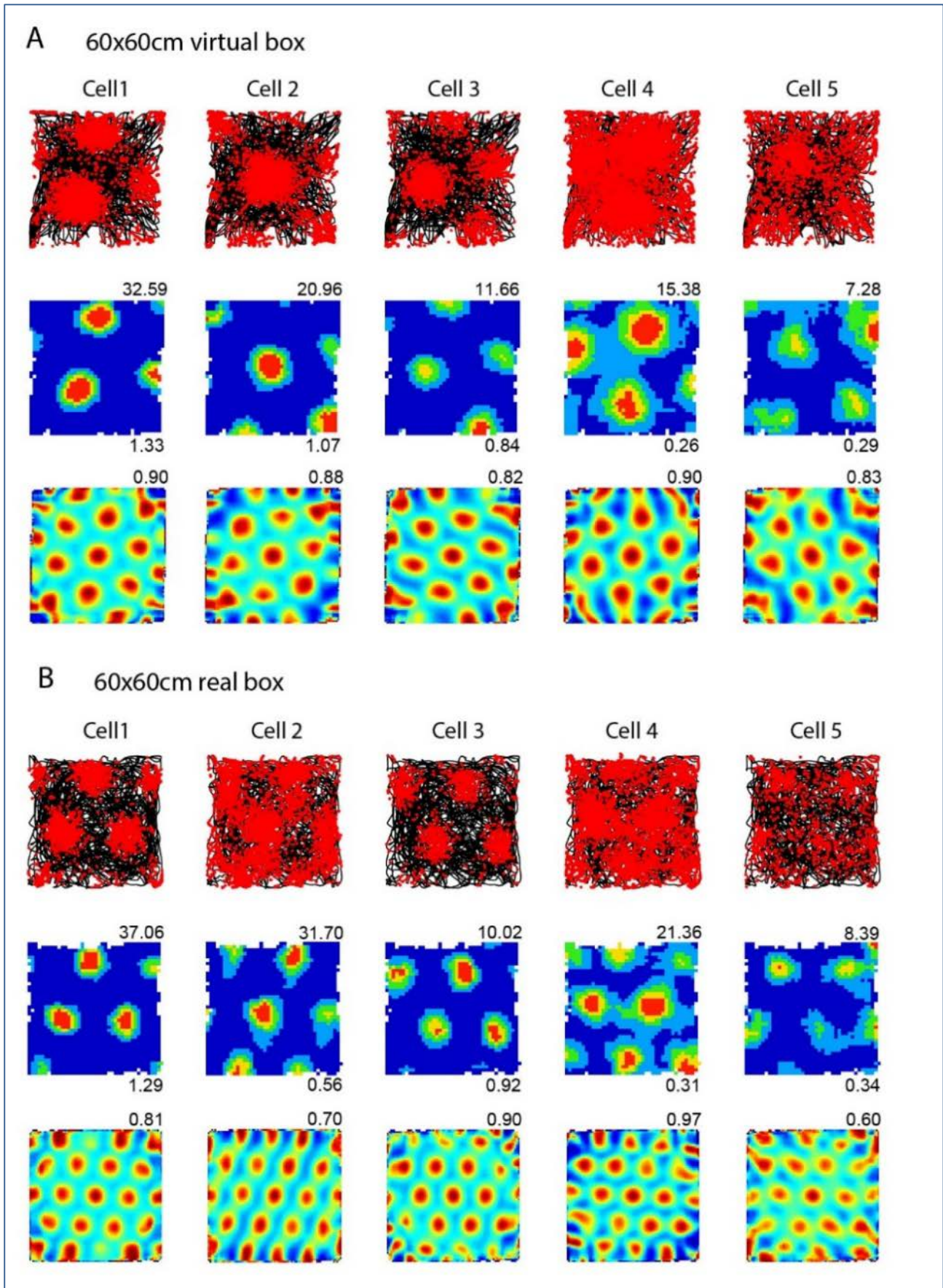
Figure 4 Grid cell firing in real and virtual environments

(A–B) The same five grid cells simultaneously recorded in a 60 × 60 cm virtual square (A) and in a 60 × 60 cm real square (B, one cell per column). Top row: 40 min running trajectory (black line) with red dots showing the locations of spikes; second row, firing rate maps, maximum firing rate (Hz) shown top right, spatial information (bits/spike) bottom right; third row: spatial autocorrelations, gridness scores top right.

3.   Publications and impacts

We have published the research results on eLife [3] and presented the results in various national and international conferences, including the SfN 2018 neuroscience conference.

We have uploaded matlab files of our data to Open Science Framework: https://osf.io/yvmf4/ and it will be available in the HBP Neuroinformatics Platform by 1 December 2019.

We have demonstrated the ability of a novel mouse virtual reality (VR) system to allow expression of spatial learning and memory in open environments. Importantly, we also demonstrated that the VR system allows expression of the characteristic spatially modulated firing patterns of place, grid and head-direction cells in open arenas. This provides a new technique to study the contributions of different sensory inputs to forming spatial representations in the brain. With the potential to integrate two-photon microscopy, this technique offers a powerful tool for monitoring large population of neurons over a long period of time in behaving animals, and opens a new window for studying spatial cognition.

4.   References

[1] Hafting, T., Fyhn, M., Molden, S., Moser, M. B. & Moser, E. I. Microstructure of a spatial map in the entorhinal cortex. *Nature* **436**, 801-806, doi:10.1038/nature03721 (2005).

[2] O'Keefe, J. & Dostrovsky, J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res* **34**, 171-175 (1971).

[3] P1340 Chen, G., King, J. A., Lu, Y., Cacucci, F. & Burgess, N. Spatial cell firing during virtual navigation of open arenas by head-restrained mice. *Elife* **7**, doi:10.7554/eLife.34789 (2018).