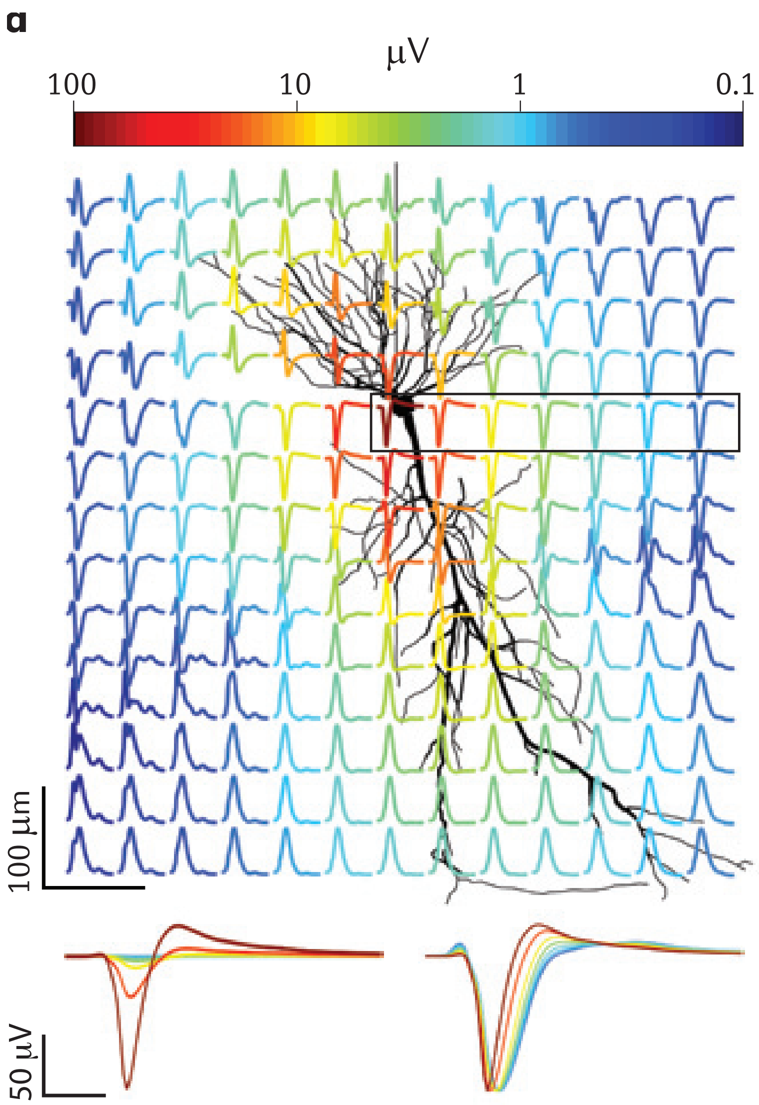
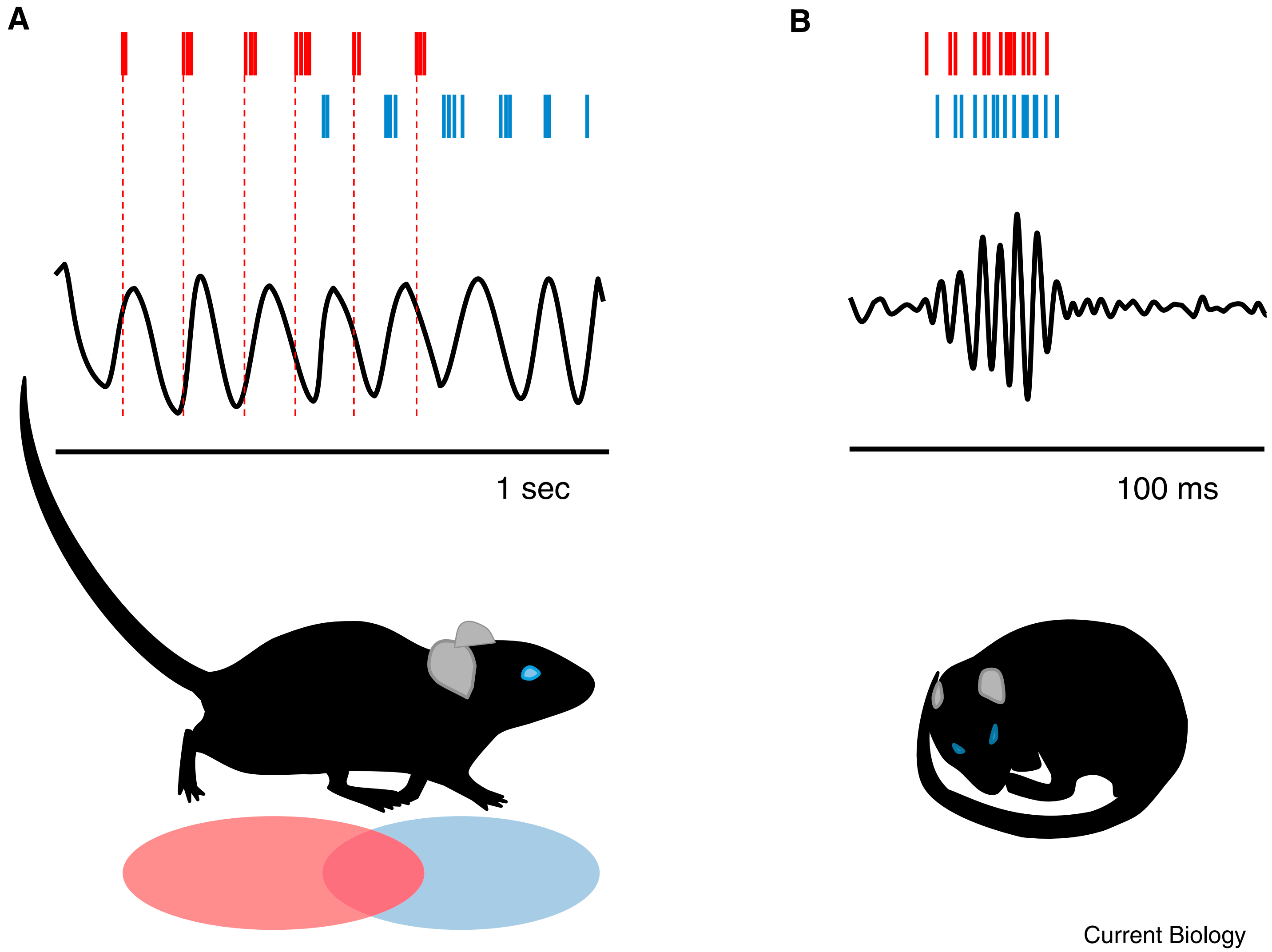
Cellular Biophysics & Modeling

Lecture 19

local field potentials, unit recordings, and hippocampal place cells





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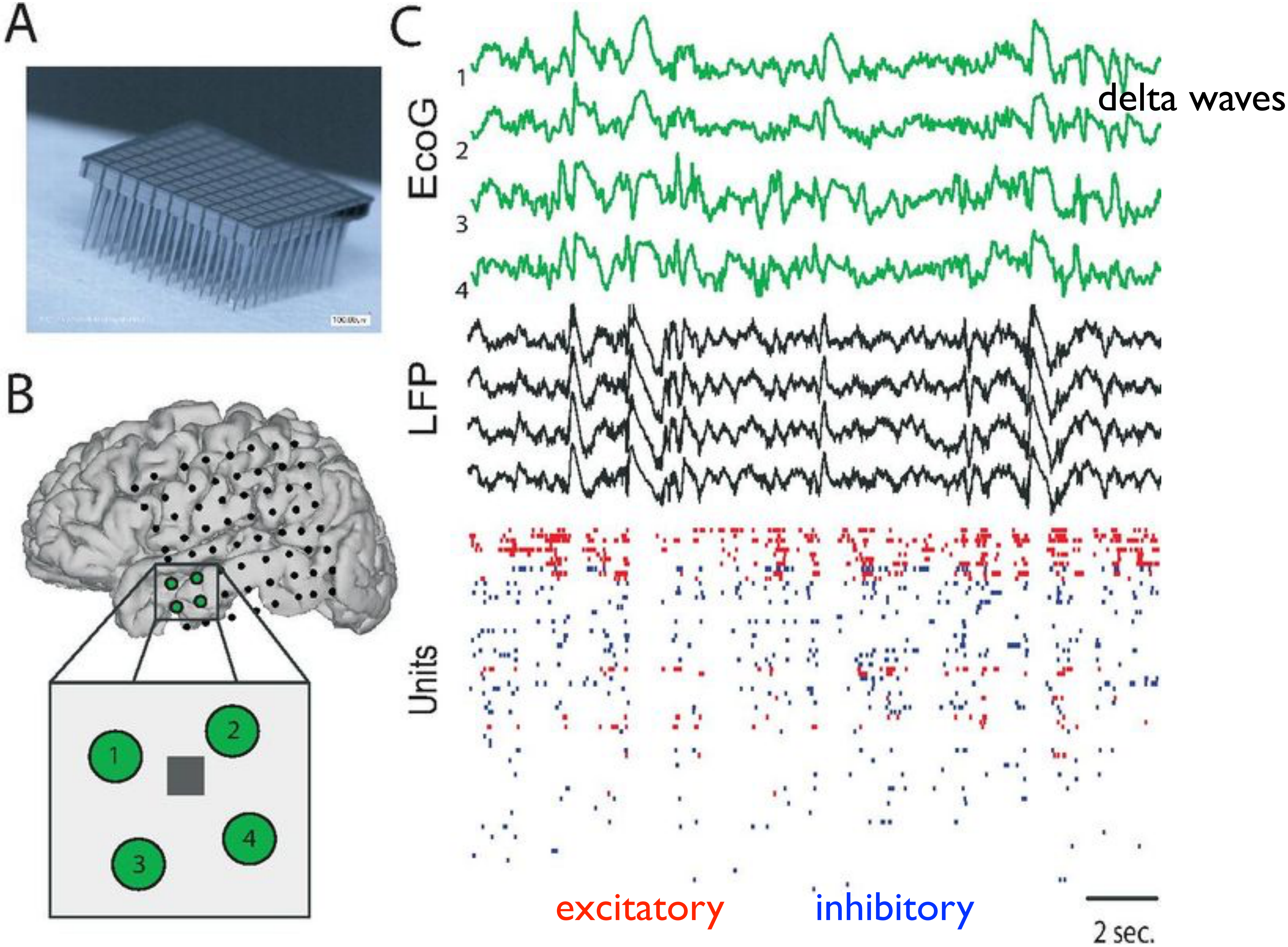
Electrocorticogram, local field potentials and **unit recordings**
during slow wave sleep in human recorded using extracellular electrode array



Intracellular recording of the transmembrane potential of an individual neuron has been the class focus. Simultaneous intracellular recordings are possible, but technically challenging. Intercellular recording can occur in various modes, e.g., voltage-clamp vs. current-clamp.

Electroencephalogram (EEG) recorded at surface of scalp with macro-electrodes. Low-frequency events like synaptic potentials propagate over large distances in extracellular space and are recordable on the surface of the scalp. Action potentials do not contribute much to the EEG signal.

Electro-corticogram (EcoG) is similar to EEG, but recorded from the surface of the brain using large subdural electrodes.

The **Local Field Potential (LFP)** is the electric potential recorded in the extracellular space in brain tissue, typically using micro-electrodes (metal, silicon or glass micropipettes). LFPs are recorded from depths of cortical or subcortical tissue.

Extracellular recording of "units": extracellular electrical potential recording of action potentials (spikes). APs are high frequency signals subject to steep attenuation in cortical tissue. APs are visible only for the cell(s) immediately adjacent to the electrode. Spikes are often "sorted" before making a "rastergram" that shows spike times.

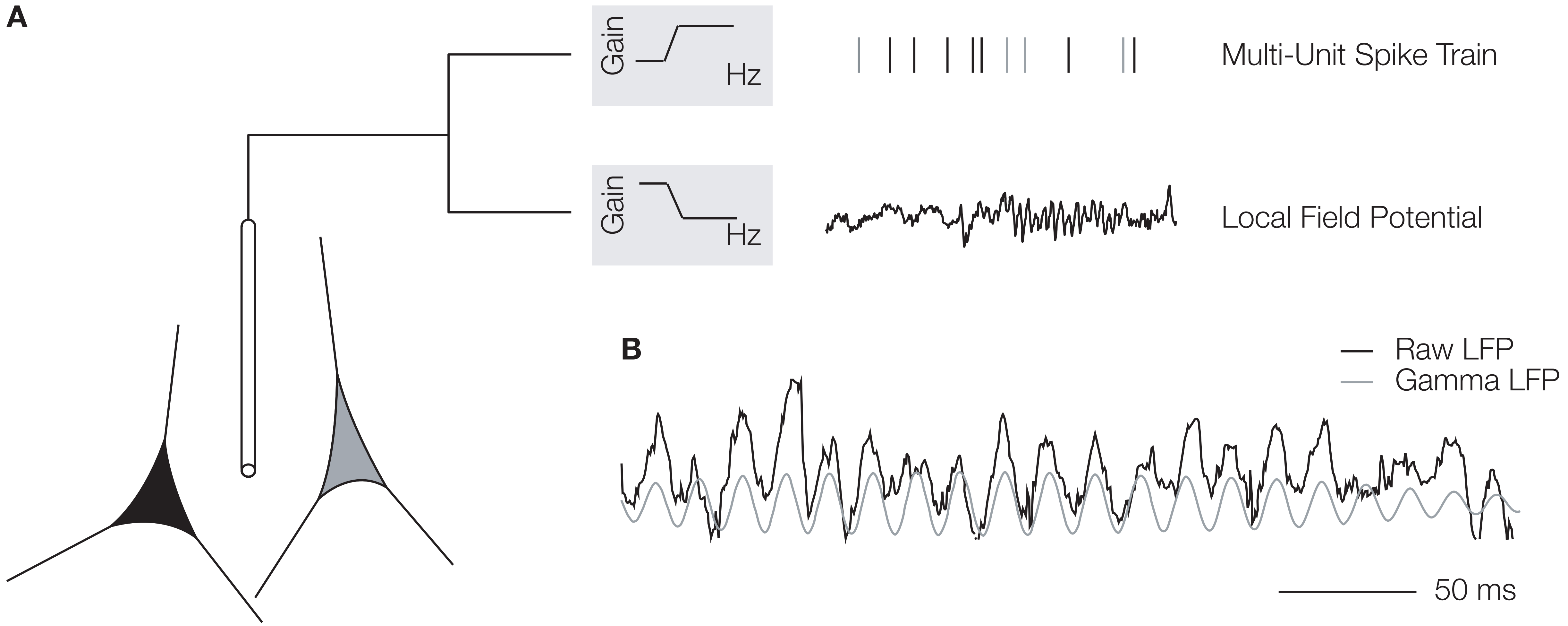
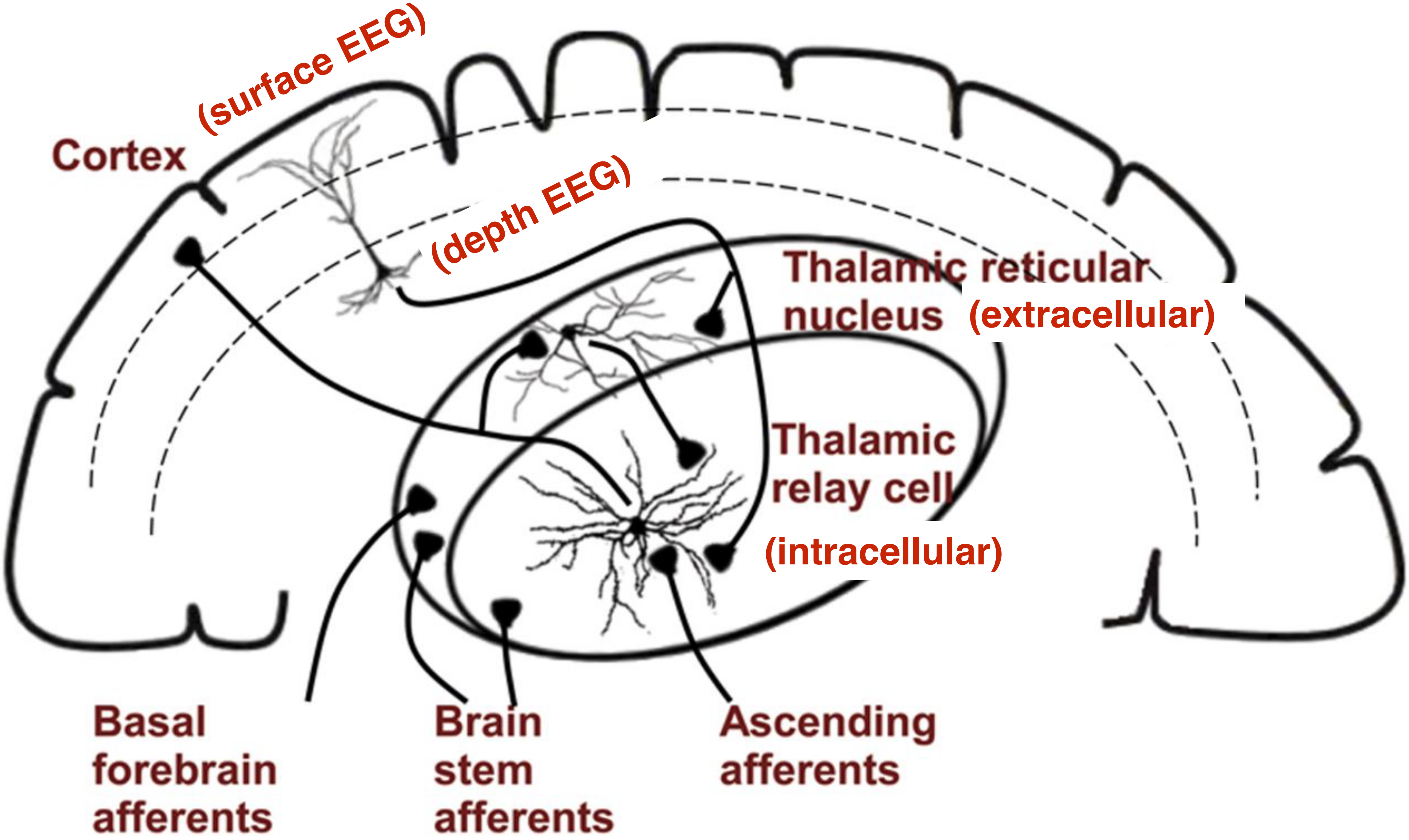
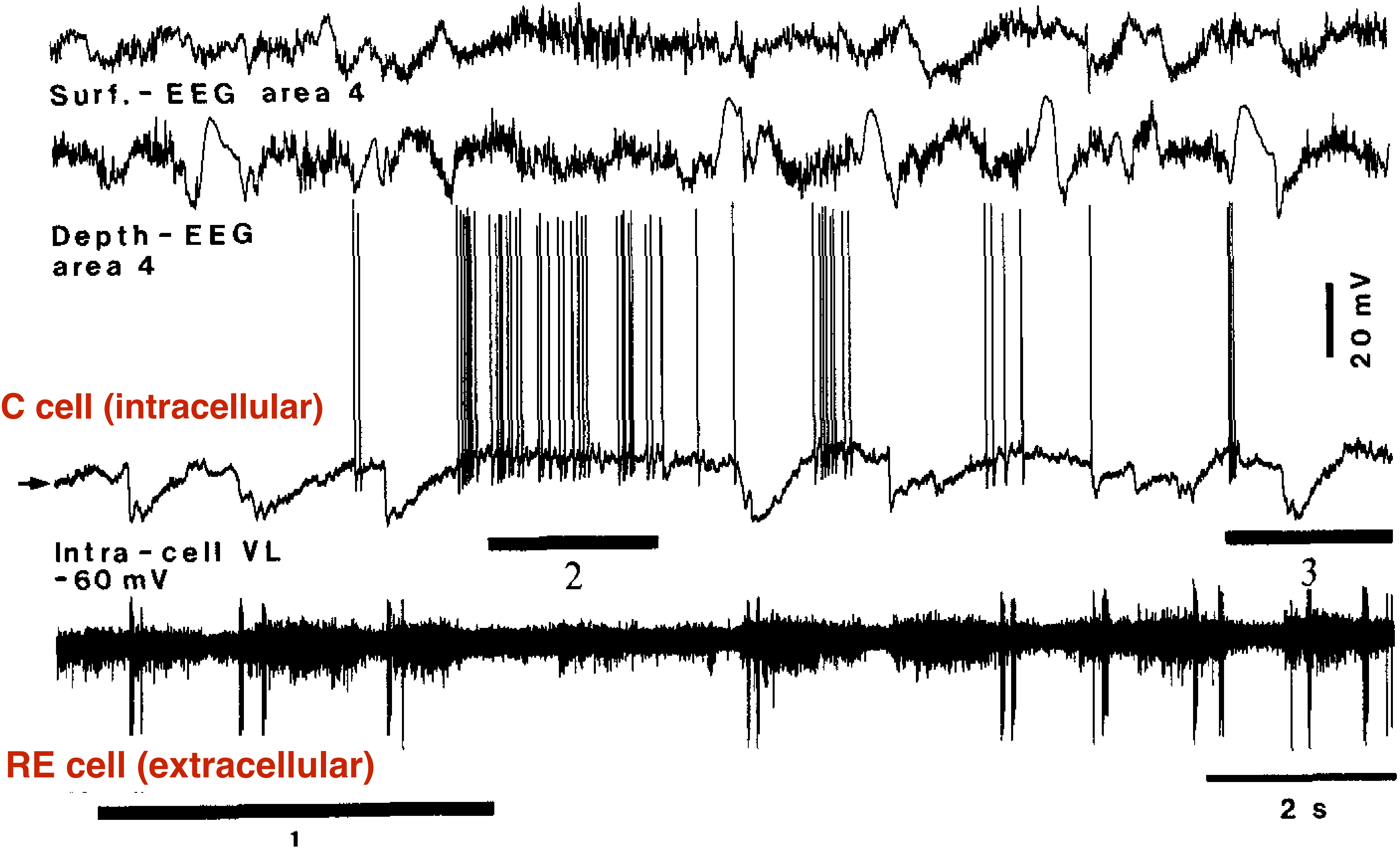


Figure 1 | (A) An extracellular electrode placed in the brain measures the mean extracellular field potential, an aggregate signal originating from the population of neurons in the vicinity of the electrode tip. To obtain multi-unit spiking activity, the recorded voltage trace is high-pass filtered and individual action potentials are detected (top). The local field potential (LFP) is comprised of the low frequency components of the extracellular field potential up to 200 Hz (bottom). Its frequency composition varies over time. In the example shown here, prominent oscillations in the frequency band between 30 and 90 Hz – called the gamma-band – are visible during the later part of the trace. **(B)** In primary visual cortex of awake primates, oscillations in the gamma-band of the local field potential are dominant during visual stimulation, as illustrated in the example. The raw signal (black) has been filtered in the gamma frequency range to obtain the gamma LFP (grey).

next slide shows simultaneous recording of motor cortex, ventral lateral thalamic nuclei, and thalamic reticular nucleus



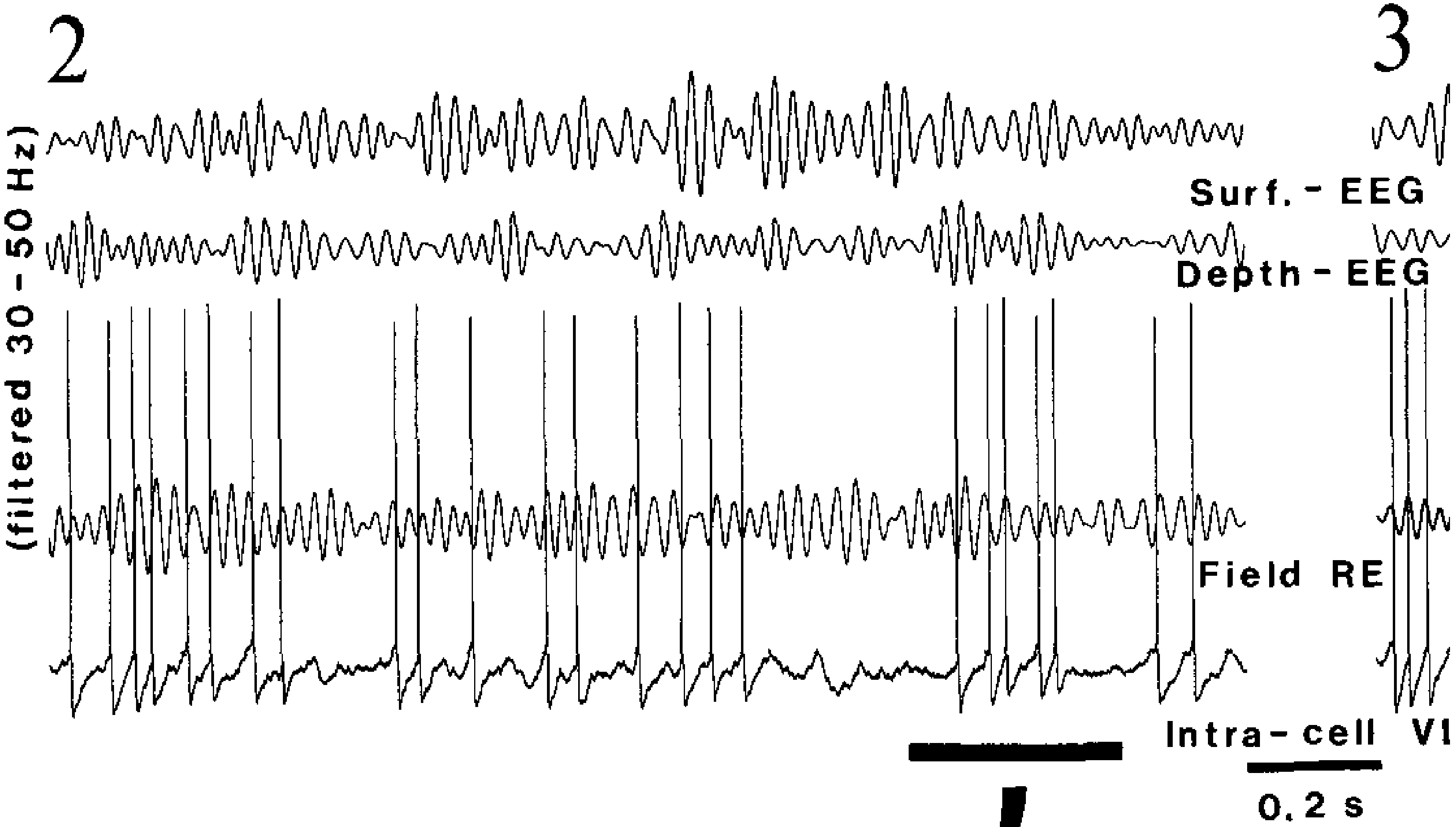
simultaneous recording of motor cortex (area 4), ventral lateral (VL) thalamic nuclei, and thalamic reticular nucleus (RE)



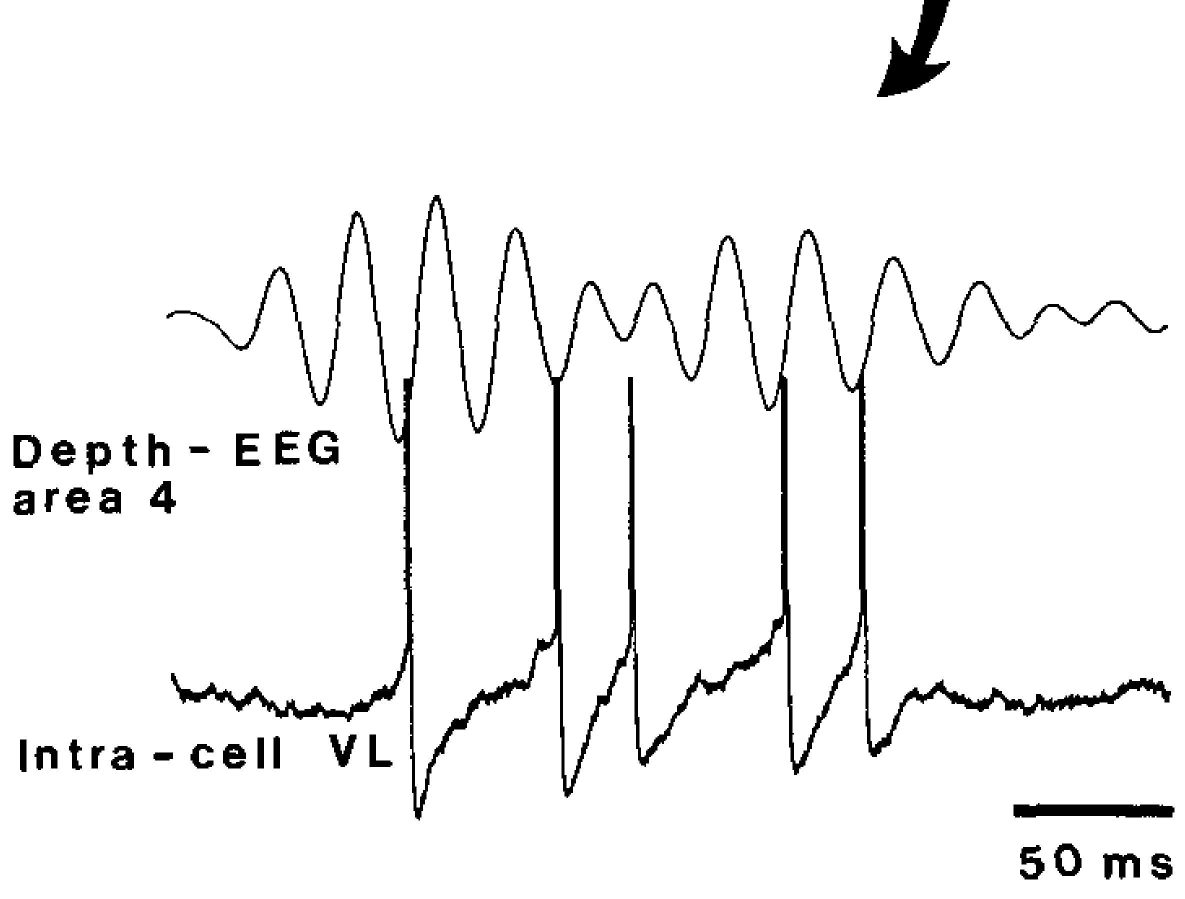
TC cell (intracellular)

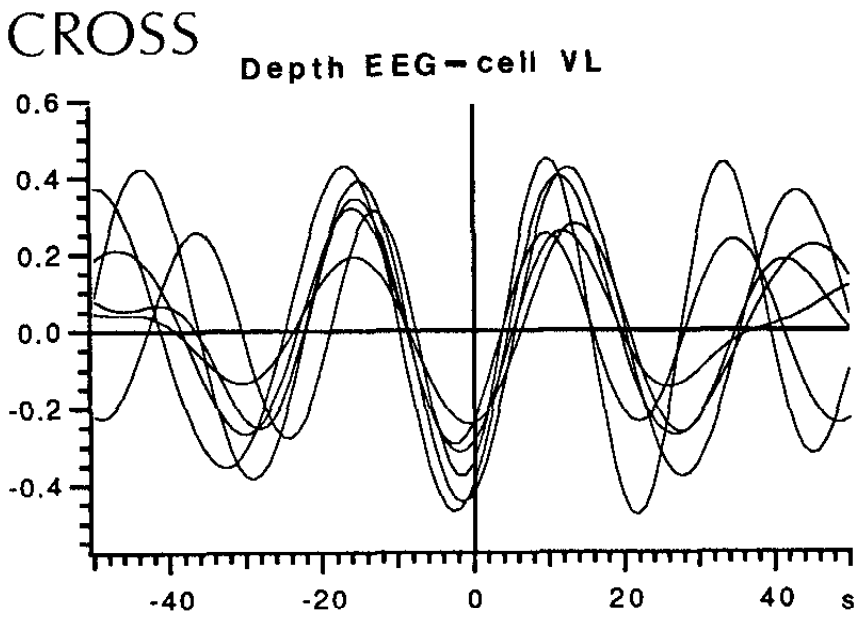
RE cell (extracellular)

Figure 5. Brief episodes of tonic activation are accompanied by sustained and correlated fast rhythms (40 Hz) in cortex and intracellularly recorded TC cell; ketamine and xylazine anesthesia. *Top left*, Four traces represent simultaneous recording of surface- and depth-EEG from precruciate area 4, intracellular activity of TC cell from the VL nucleus, and extracellular discharges of rostrolateral RE cell. EEG, VL, and RE cells display a slow oscillation (0.7–0.8 Hz) consisting of long-lasting, depth-positive EEG waves, leading to sharp depth-negative EEG potentials, related to the initiation of biphasic, long-lasting IPSPs in VL cell. The IPSPs are coincident with (and presumably generated by) spike-bursts in RE neuron. Panel marked by *1* is expanded



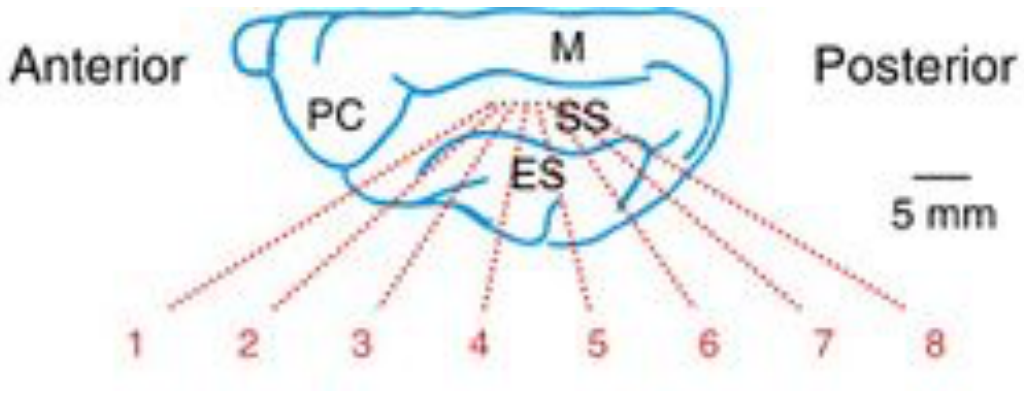
ventral lateral (VL) thalamocortical (TC) relay neurons spike with a particular phase relationship to the depth-EEG





correlogram measures cross-correlation

relationship between LFP and firing of neurons depends on brain state

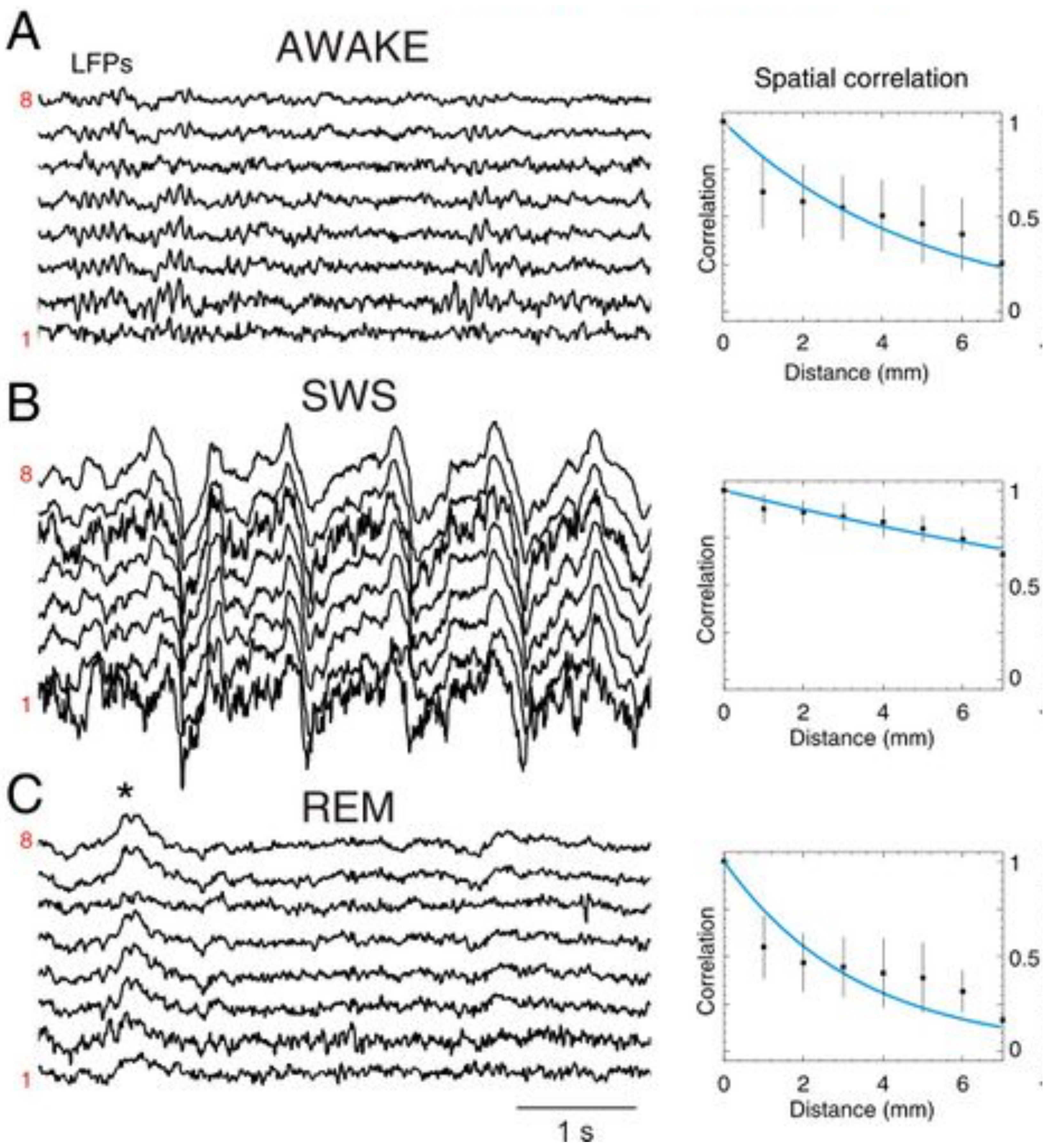


Local field potentials in cats during wake and sleep states. Eight electrodes were inserted into the depth (1 mm) of areas 5-7 of cat parietal cortex.

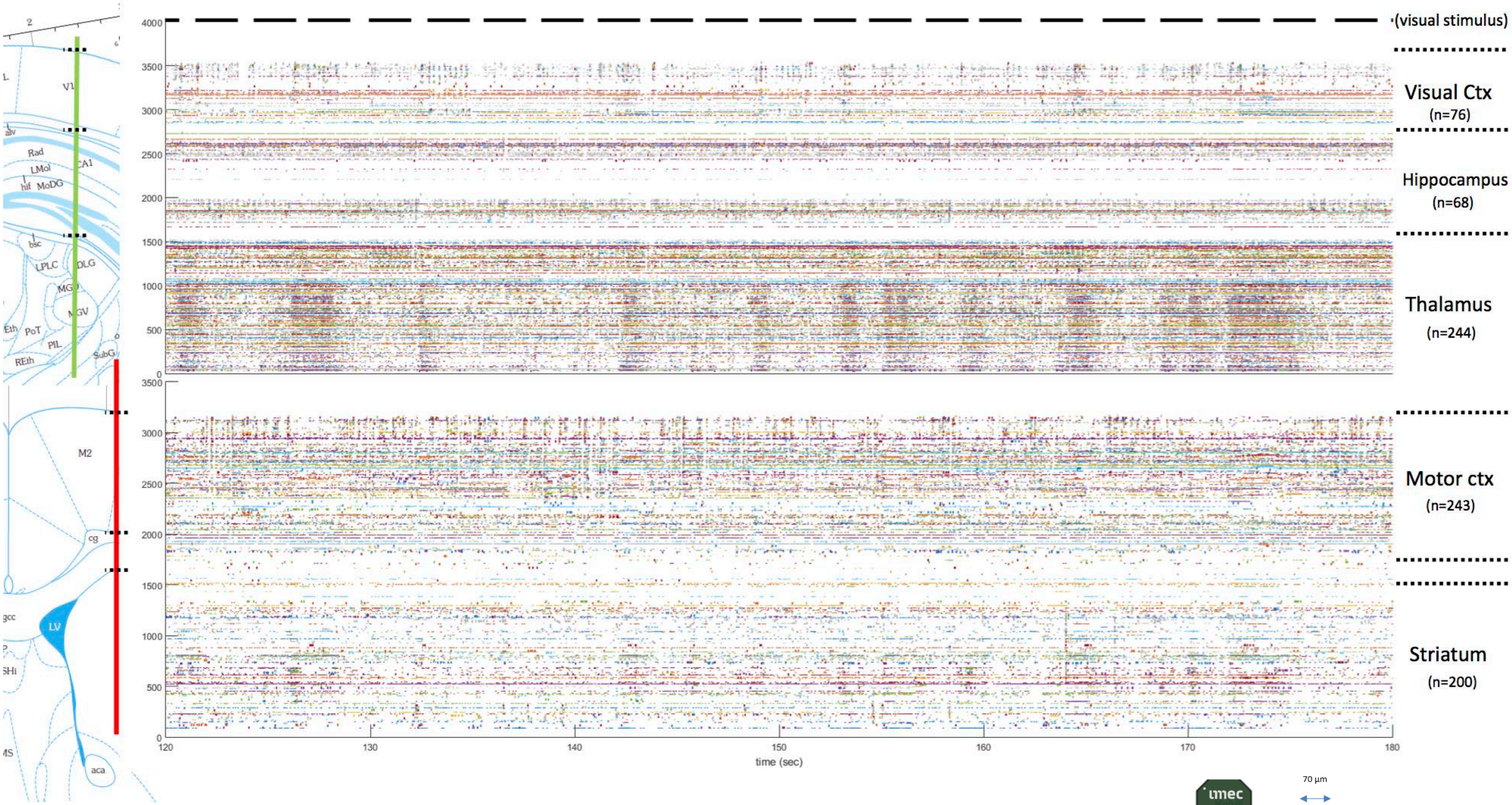
A. When the animal was awake, LFPs were characterized by low-amplitude fast activities in the beta/gamma frequency range (15-75 Hz). Correlations decayed steeply with distance.

B. During slow-wave sleep, the LFPs were dominated by large-amplitude slow-wave complexes recurring at a low frequency (<1 Hz; up to 4 Hz). Correlations stayed high for large distances.

C. During episodes of REM sleep, LFPs and correlations had similar characteristics as during wake periods.

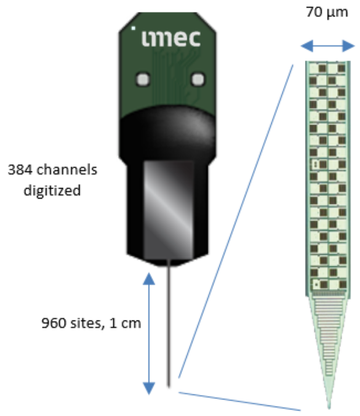


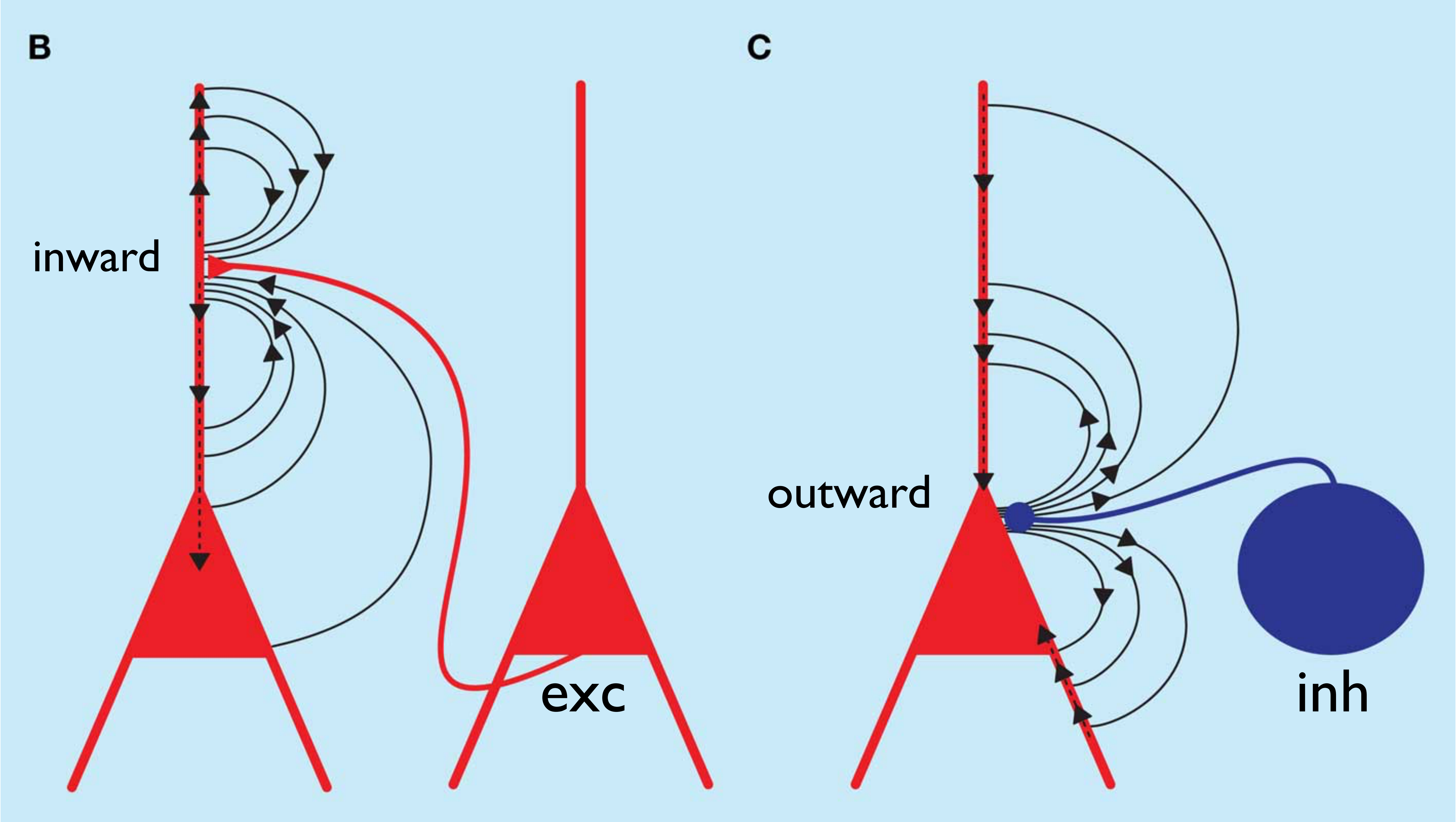
state-of-the-art multi-unit recordings


One minute of spike rasters from 831 sorted single neurons

simultaneous recording with two electrode arrays

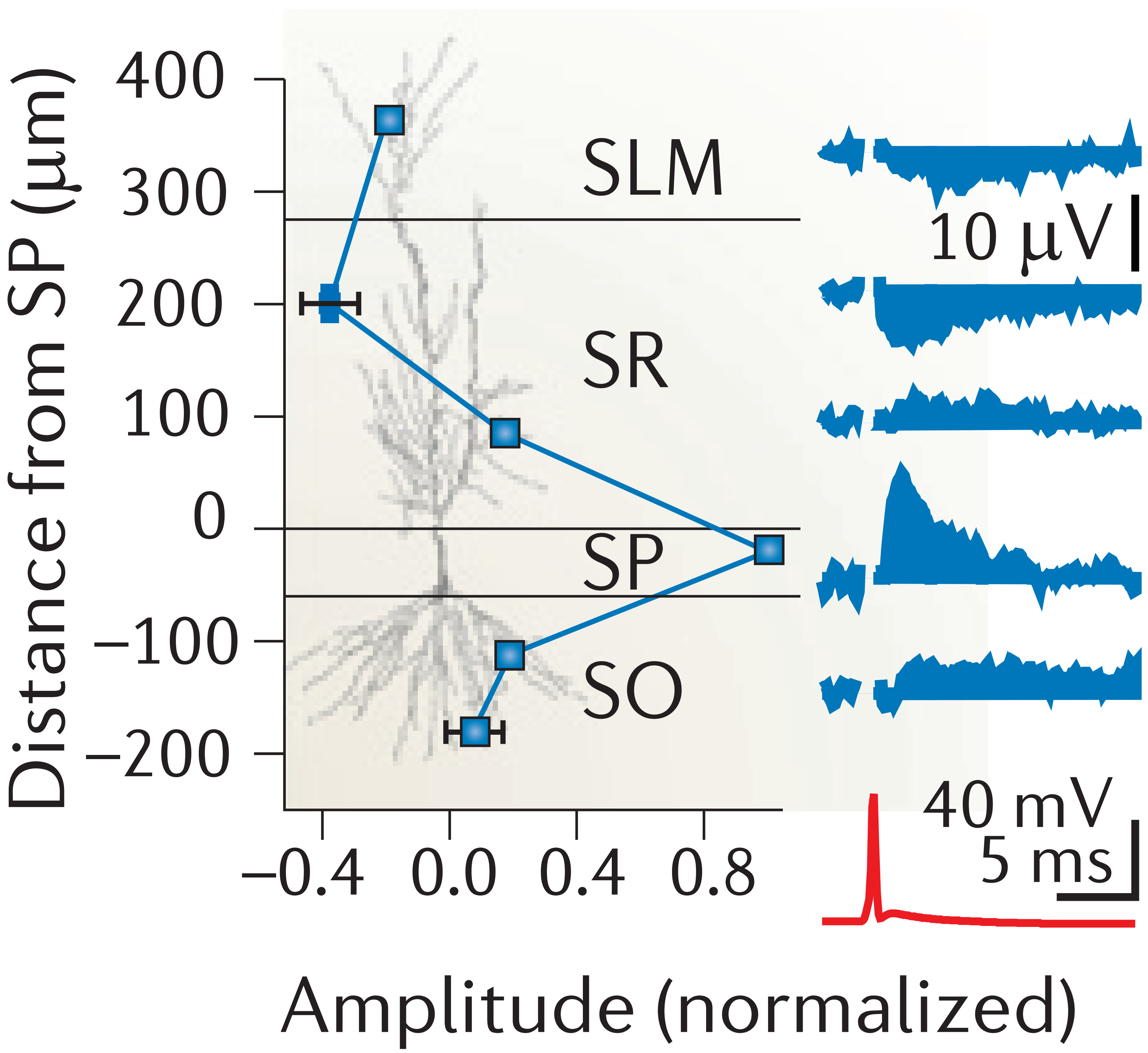
Recording, data processing, and documentation by Nick Steinmetz, nick[dot]steinmetz@gmail, in the CortexLab at UCL.



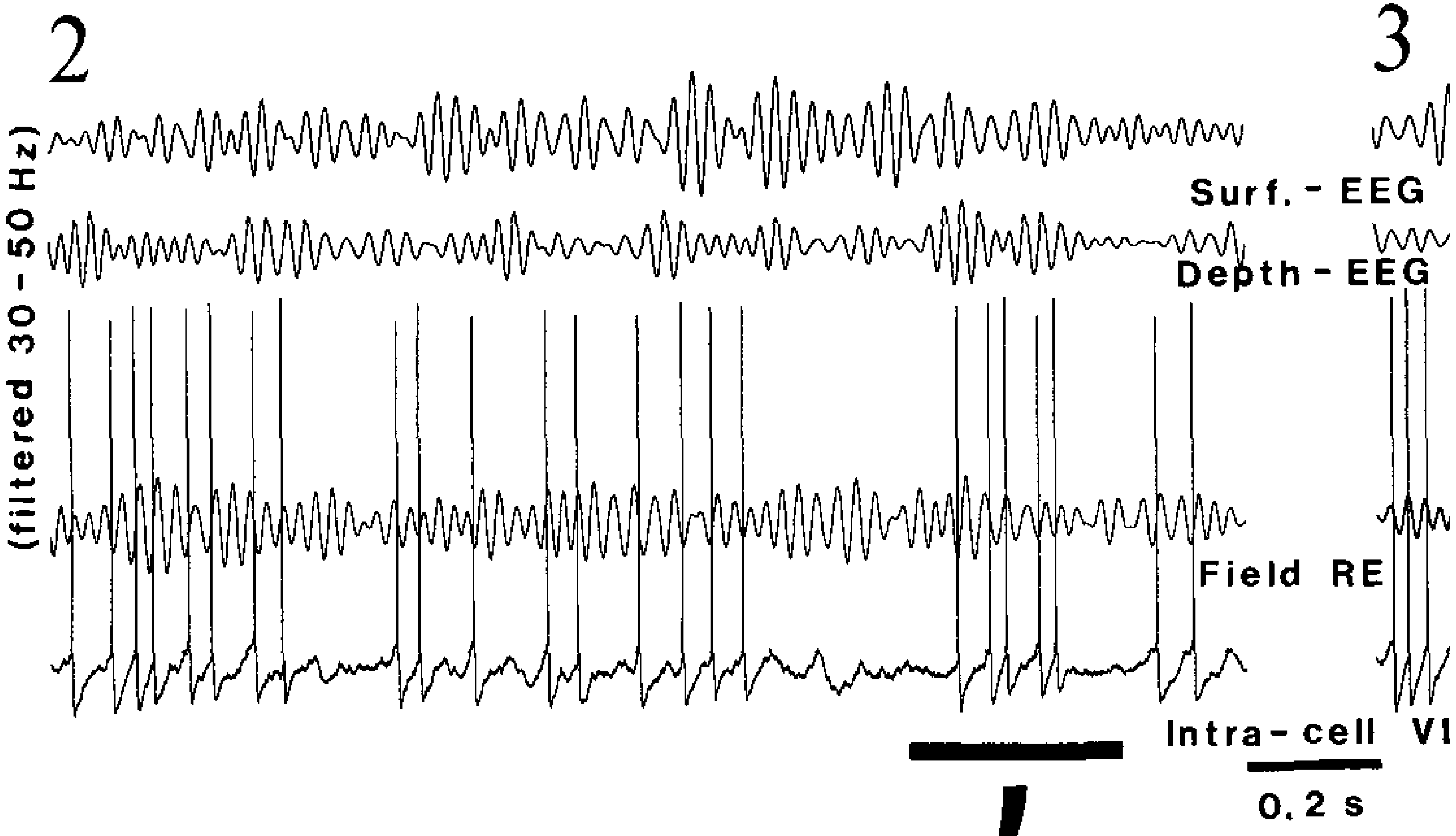


Local field potentials and underlying current sinks and sources.
(B) **Excitatory synaptic events** at the apical dendrite of pyramidal neurons generate an active current sink as positive ions flow into neurons; a concurrent passive source is recorded from the somatic region. (C) **Inhibitory synaptic events** at the perisomatic regions of pyramidal neurons generate an active source accompanied by a passive current sink at the dendrites.

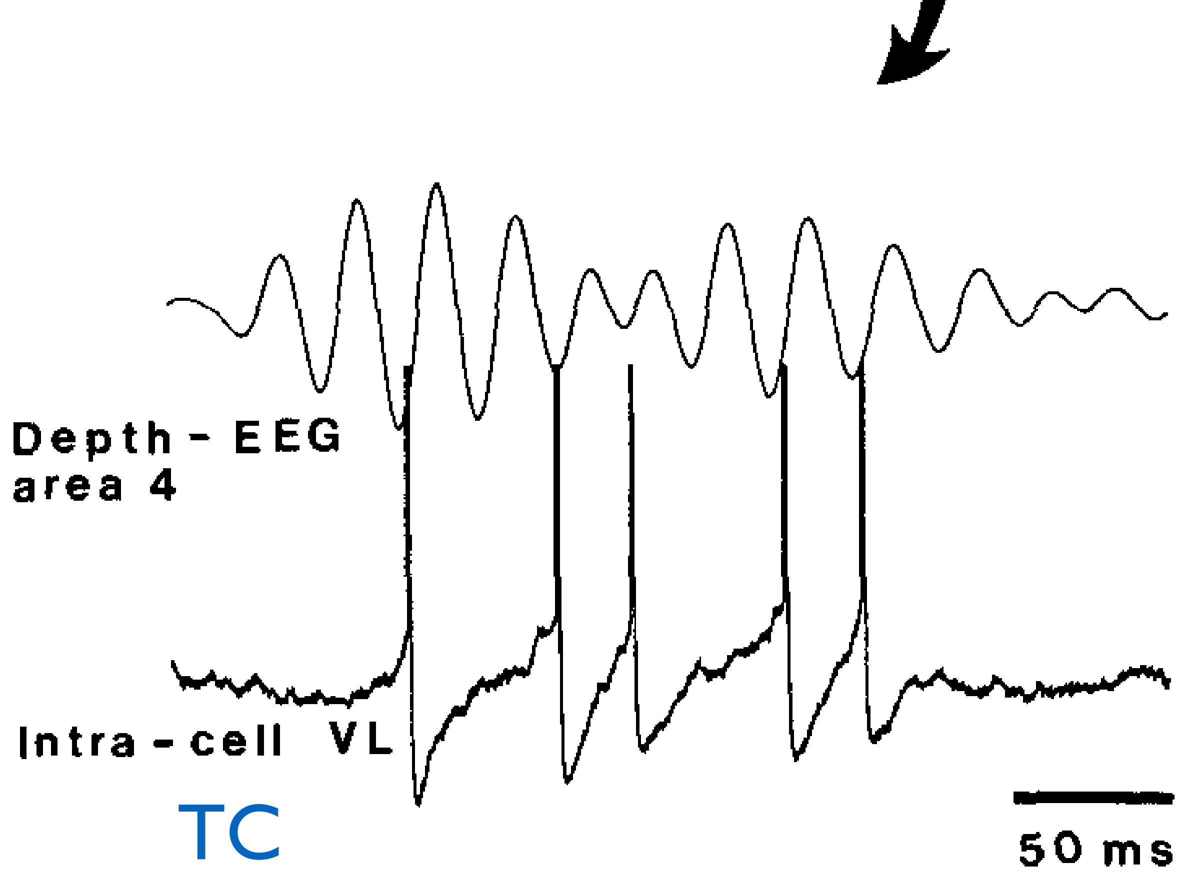
Inhibition-induced LFPs generated near a pyramidal neuron by lapp-induced action potentials in a nearby basket cell



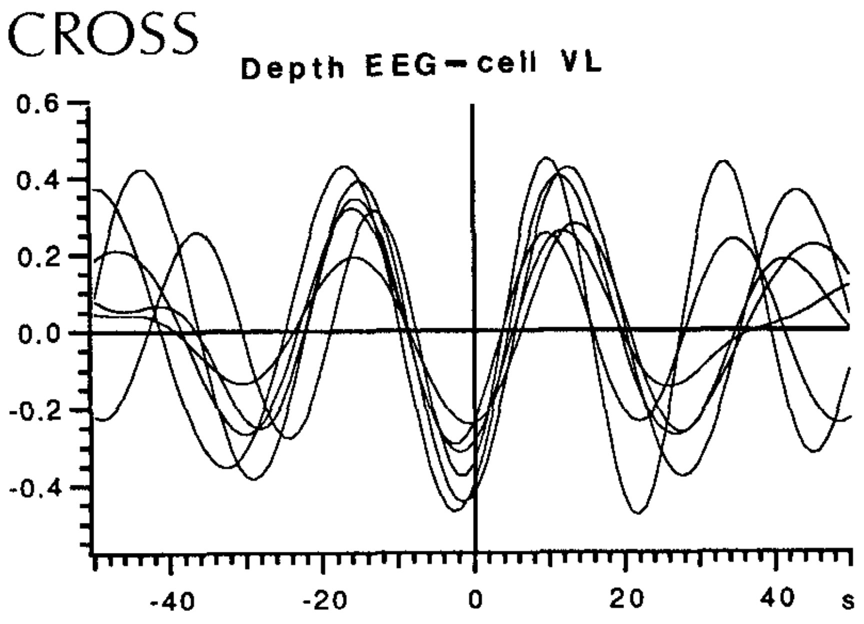
Inhibition-induced LFPs recorded extracellularly at six sites in multiple layers of the hippocampus. The mean LFP amplitude at each site is shown by the blue squares. Example LFP traces (blue) from six sites and the action potential of the basket cell (red trace) are shown on the right. Note that the largest positive response by inhibition-induced hyperpolarization occurs near the soma.



ventral lateral (VL) thalamocortical (TC) relay neurons spike with a particular phase relationship to local field potential (LFP) in thalamic reticular nucleus (RE) and depth-EEG

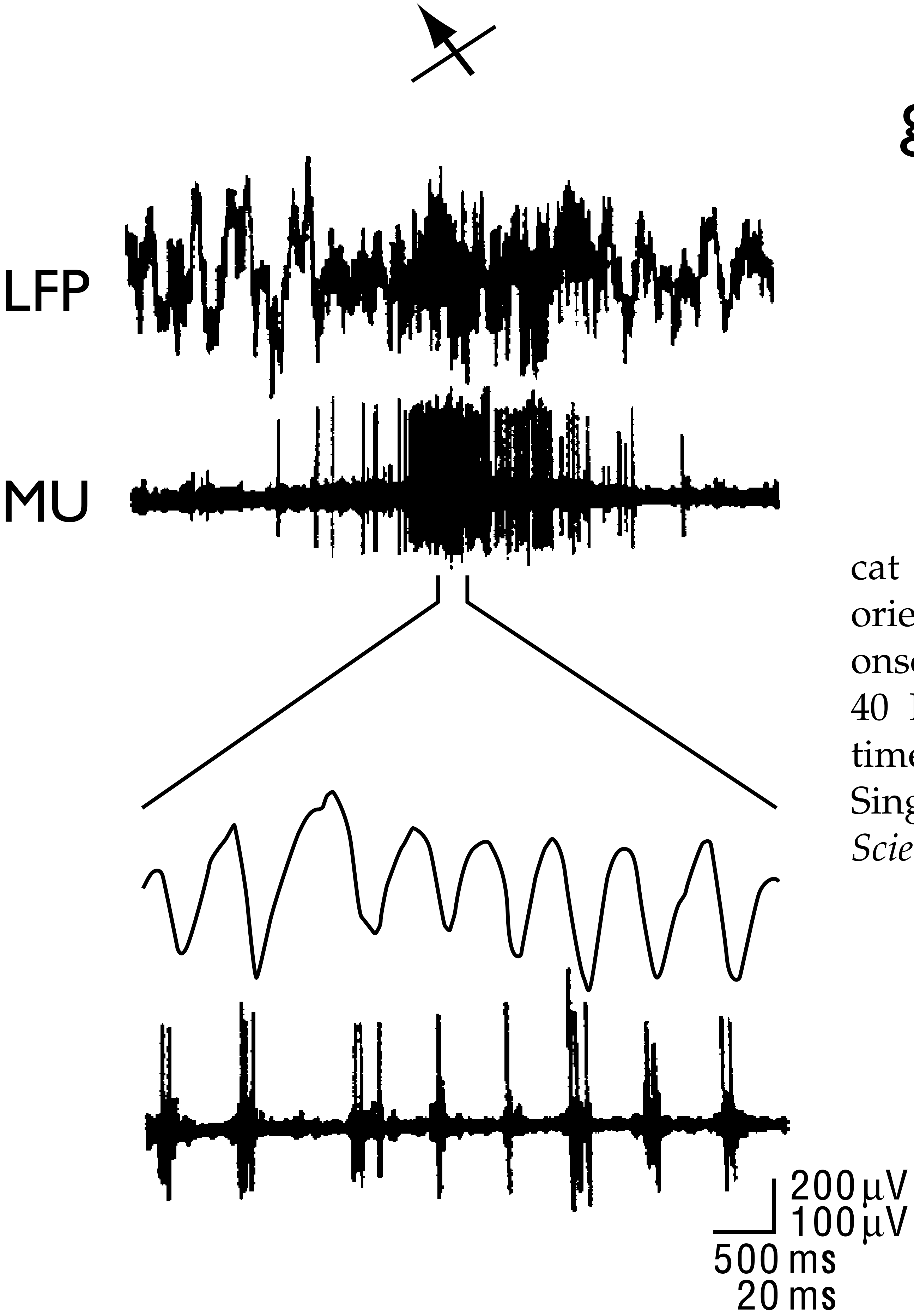


TC



correlogram measures cross-correlation

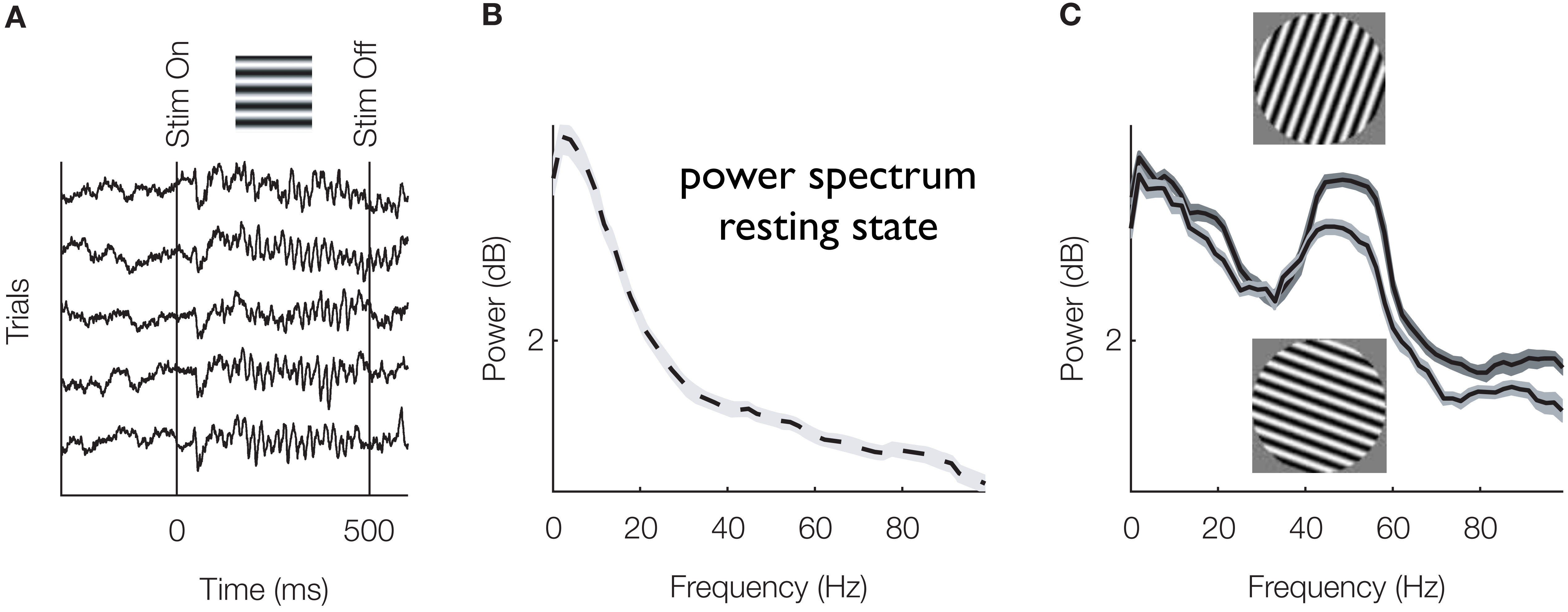
gamma oscillations (40 Hz) in primary visual cortex during visual stimulation



Multi-unit and local field potential from the cat primary visual cortex, in response to an optimally oriented light bar stimulus. In the upper two traces, the onset of the response is associated with an increase in *c*. 40 Hz oscillations, which are shown at an expanded timescale in the lower two panels. From Gray CM and Singer W (1989) *Proceedings of the National Academy of Sciences of the USA* **86**: 1698–1702.

drifting grating stimulus induces 40 Hz gamma oscillations

drifting gratings
different orientations



power spectrum
resting state

Figure 2 | (A) Exemplar raw traces showing the LFP during a typical trial. Before the onset of stimulation, low frequency fluctuations dominate the LFP. During stimulation with an oriented grating, however, strong gamma-oscillations are visible. **(B)** Typical power spectrum of the LFP during the resting state. Low frequency fluctuations dominate the spectrum, which follows roughly a 1/f decay. **(C)** Typical power spectra of the LFP during visual stimulation with two gratings of different orientation (differing colours). A pronounced power increase in the gamma-band is observed. In particular, this increase depends in strength on the orientation of the visual stimulus. All displays in this figure were adapted from (Berens et al., 2008).

place cells, grid cells, the theta rhythm and episodic memory

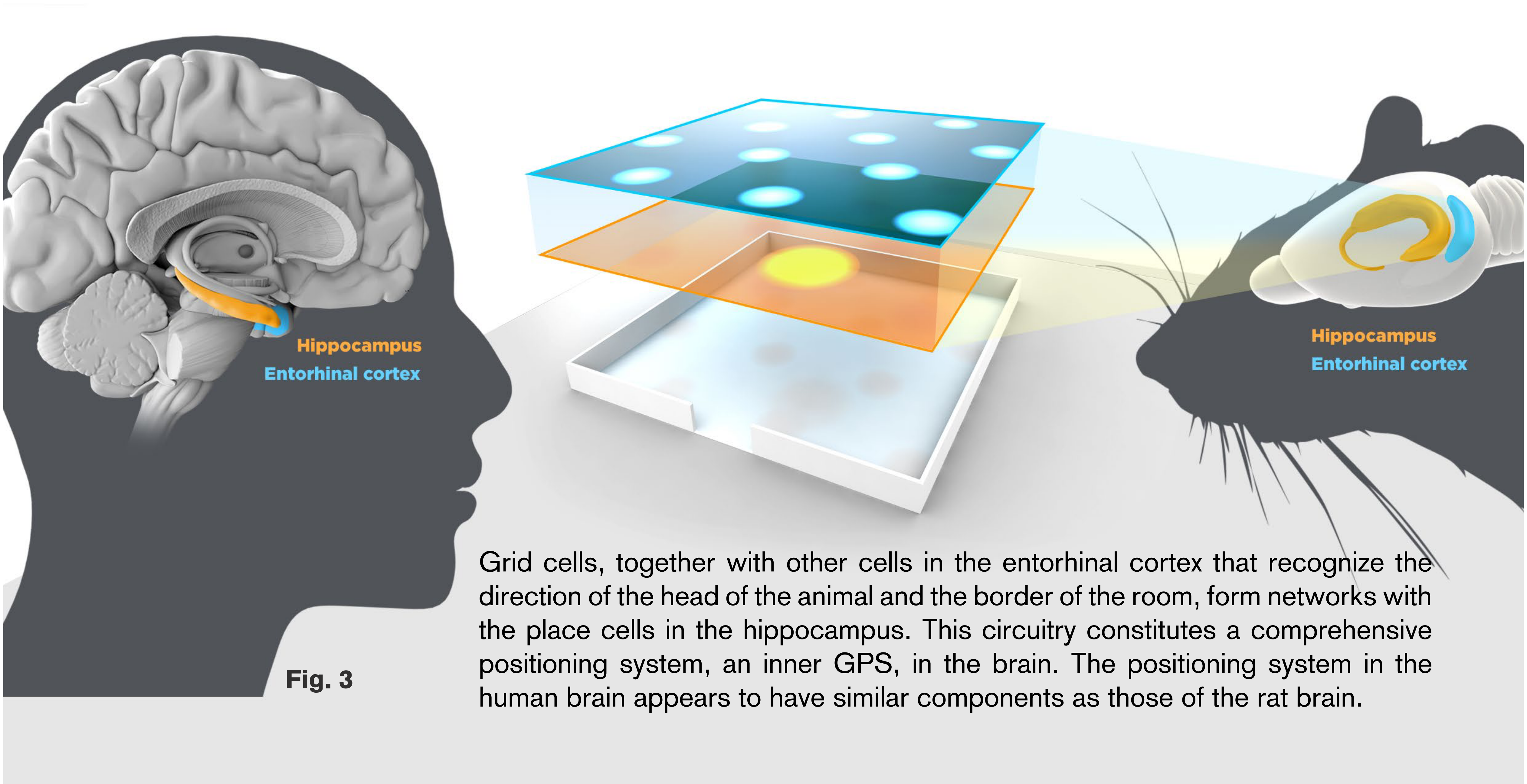


Fig. 3

Grid cells, together with other cells in the entorhinal cortex that recognize the direction of the head of the animal and the border of the room, form networks with the place cells in the hippocampus. This circuitry constitutes a comprehensive positioning system, an inner GPS, in the brain. The positioning system in the human brain appears to have similar components as those of the rat brain.

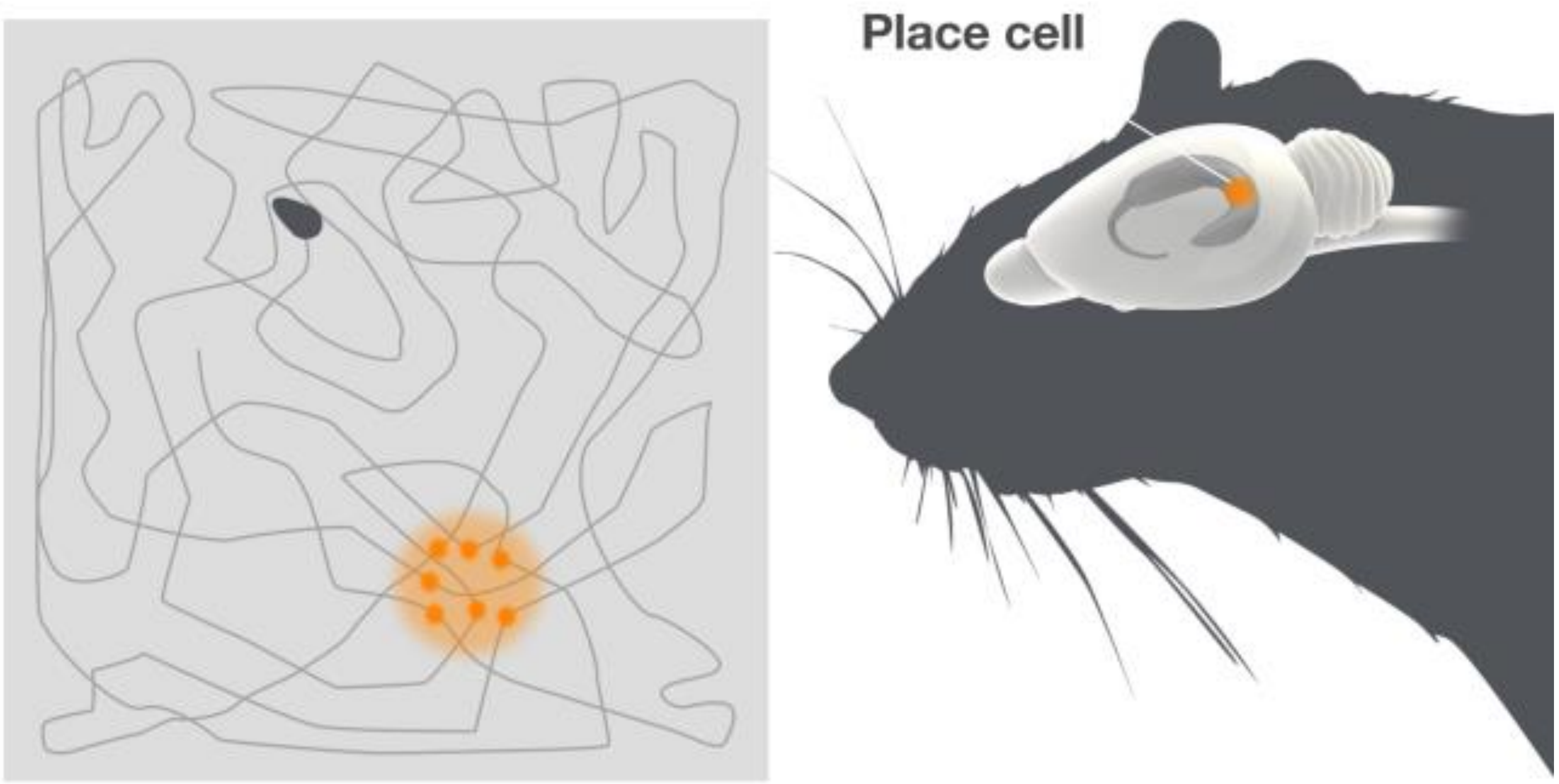
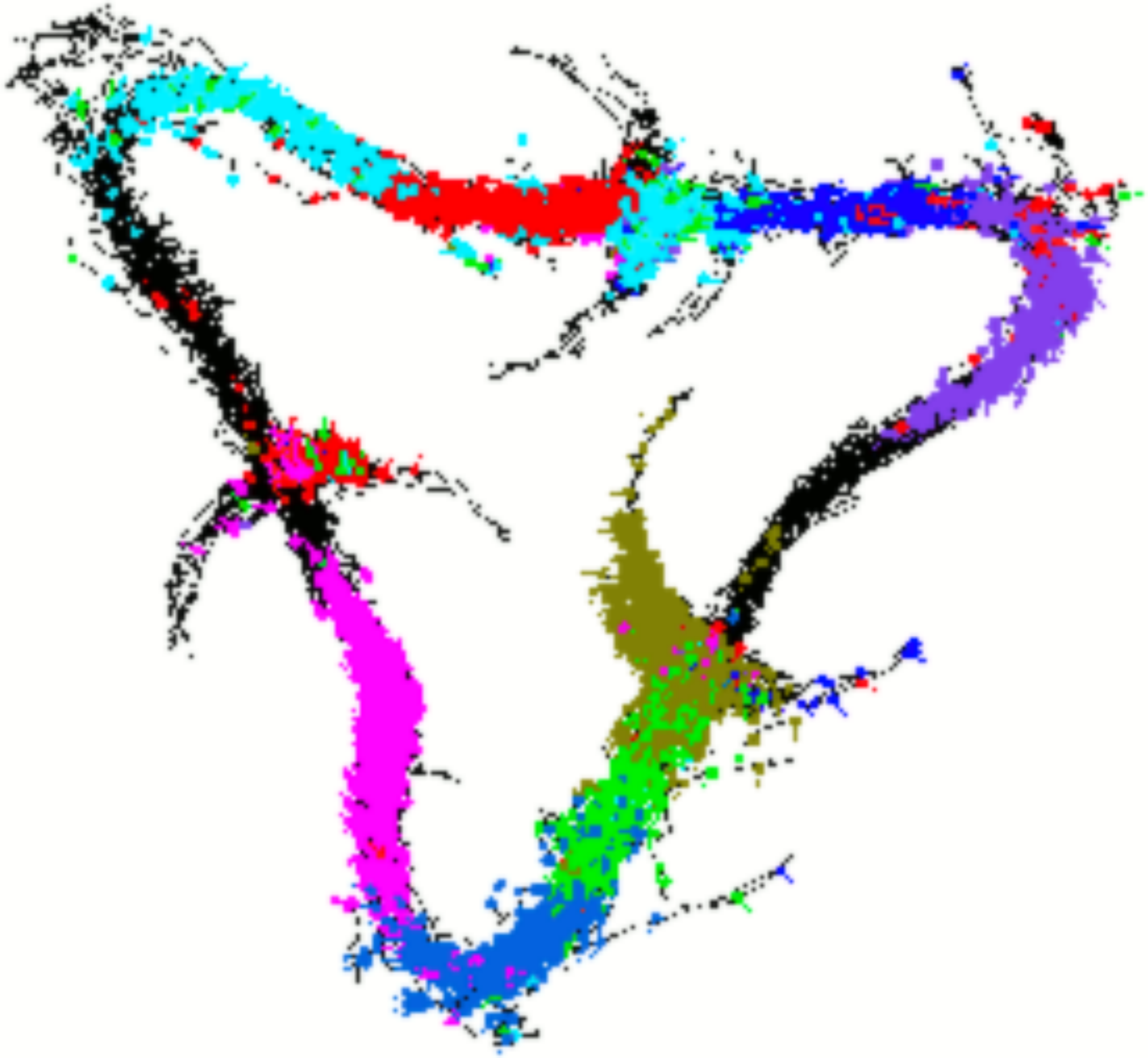


Figure 1. Place cells. *To the right is a schematic of the rat. The hippocampus, where the place cells are located is highlighted. The grey square depicts the open field the rat is moving over. Place cells fire when the animal reaches a particular location in the environment. The dots indicate the rat's location in the arena when the place cell is active. Different place cells in the hippocampus fire at different places in the arena.*

hippocampal
"**place cells**" are
active
when animal is within
a certain region of the
environment

this type of
receptive field was
never seen before



Spatial firing patterns of 7 **place cells** recorded from the CA1 layer of a rat. The rat ran several hundred laps clockwise around an elevated triangular track, stopping in the middle of each arm to eat a small portion of food. Black dots indicate positions of the rat's head; colored dots indicate action potentials, using a different color for each cell.

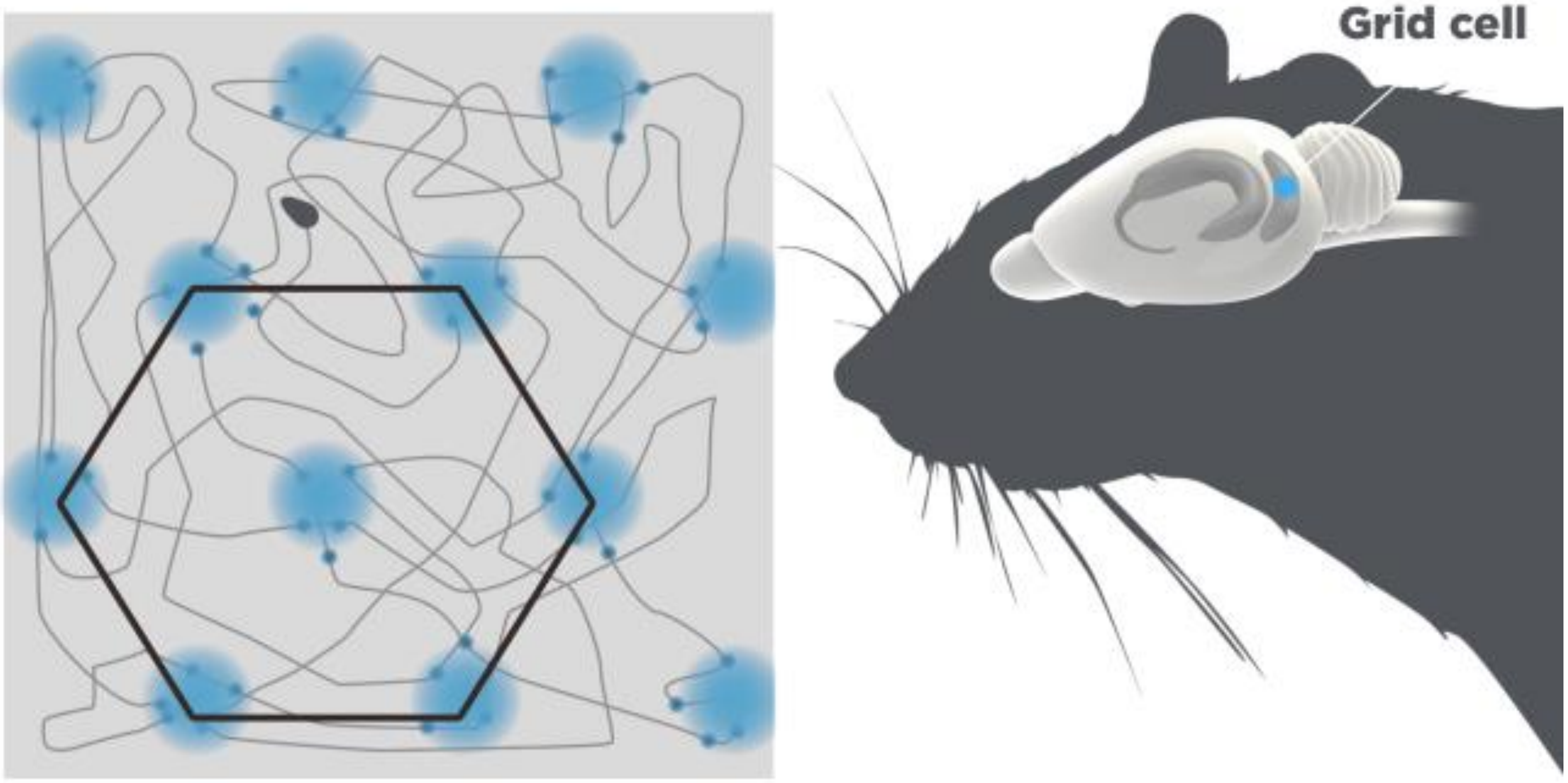


Figure 2. Grid cells. *The grid cells are located in the entorhinal cortex depicted in blue. A single grid cell fires when the animal reaches particular locations in the arena. These locations are arranged in a hexagonal pattern.*

Grid cells are active in multiple places forming nodes of a hexagonal grid.

Grid cells in same area of medial enthorinal cortex fire with same spacing and orientation of grid, but different phasing, together covering the environment.

Spacing of grid fields varies in medial entorhinal cortex w/ largest fields in the ventral part.

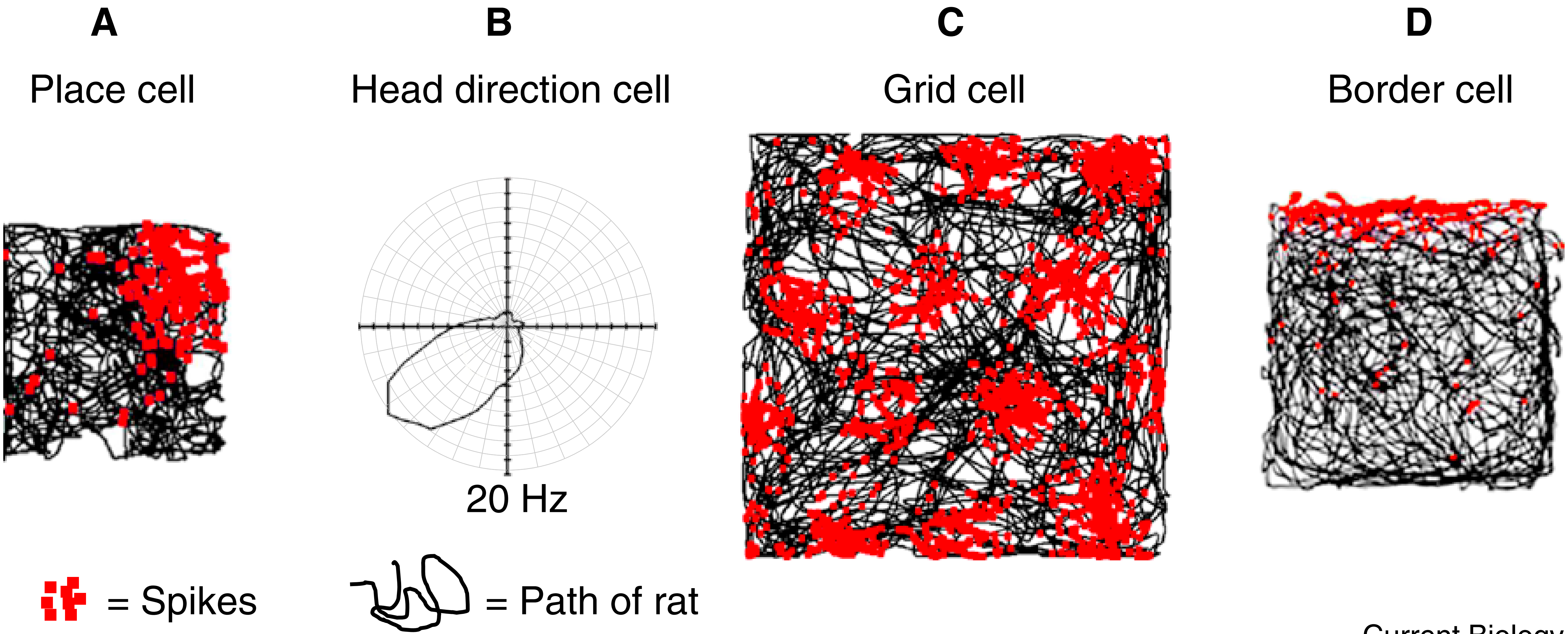


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Figure 2. Typical firing patterns of the major cell types in the cognitive map.
(A) A place cell, recorded by Elizabeth Marozzi (EM), which concentrated its firing in the Northeast corner of the enclosure. (B) A head direction cell, courtesy of Rebecca Knight, with a preferred firing direction to the Southwest of the enclosure. (C) A grid cell, recorded by EM, with firing fields evenly spaced in a close-packed hexagonal array across the surface of the arena. (D) A border cell, courtesy of Lin Lin Ginzberg, which only fired when the rat was in very close proximity to the North wall of the enclosure. For the spike plots (A, C and D), the neuronal action potentials (red squares) are superimposed on the path of the rat (black line) at the place where the rat was when the cell fired. These plots are not to scale, but the environment for the place cells was 60 x 60 cm, for the grid cell 120 x 120 cm, and for the border cell 100 x 100 cm. For the head direction cell (B), which fires everywhere in an environment, the firing is instead shown in the form of firing rate (distance from origin) as a function of head direction.

Place cells have **memory** functions! The rearrangement of **place fields** in different environments is called **remapping**.

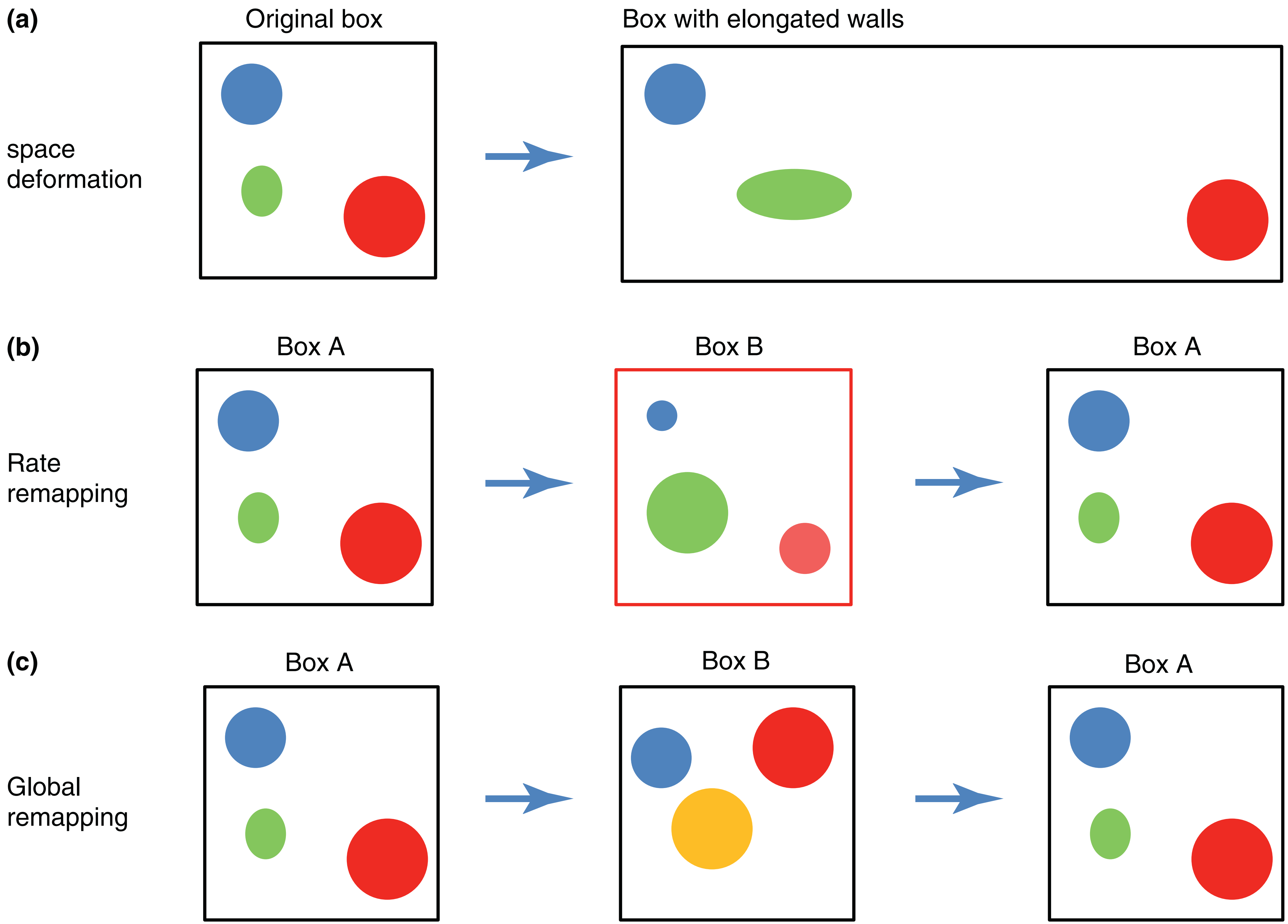


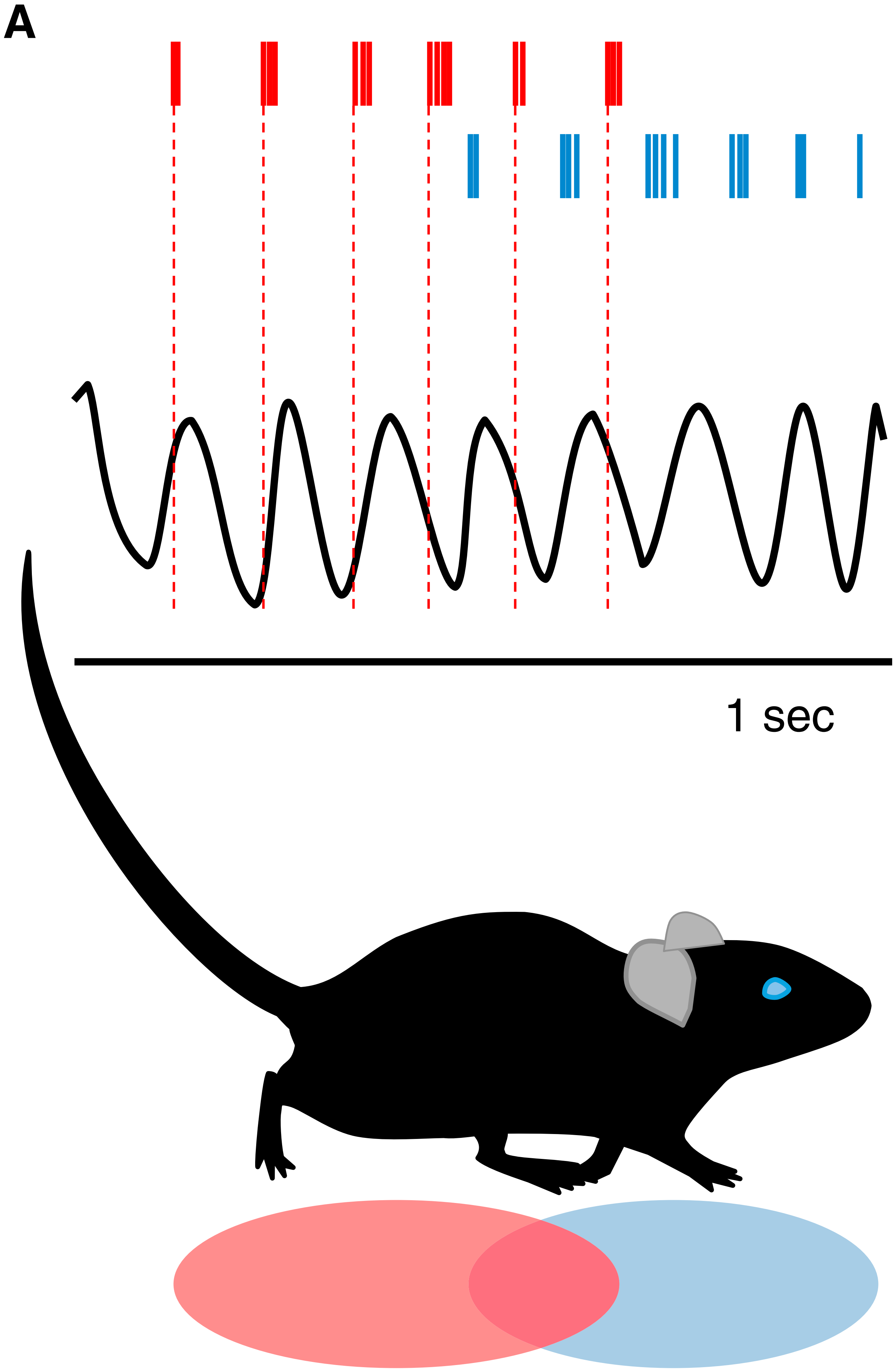
Figure I. Transformation of place cell maps. **(a)** Illustration of a place cell deformation. When the box is elongated, different cells change their firing position to correspond to the deformation of the box. For example, the blue cell anchors its firing field to the left wall, the red cell anchors to the right wall, and the green cell elongates itself. **(b)** Illustration of rate remapping. The different cells in box A continue to fire at a different firing rate in box B but at similar positions. When returning to box A the rates return to the original values. **(c)** Illustration of global remapping. Some cells fire in one room and not in another; other cells change the position of firing from one room to another in an unpredictable way.

Box 3. Remapping

Changes in the environment cause consistent changes in spatial maps in the hippocampus and the entorhinal cortex. These transformations are referred to as remapping [18].

Three main types of transformations can be considered:

- **Place cell deformations:** Squeezing or stretching the environment can cause a systematic move of the position of the place fields relative to the surrounding boundaries (Figure Ia). Such deformation was reported in 2-D boxes [50] but also along linear tracks [65]. In situations where place cells undergo spatial deformation, grid cells deform too [91].
- **Rate remapping:** In some cases, environmental transformations cause a dramatic change in the distribution of firing rates among place cells without an accompanying change in firing positions (Figure Ib). An example of a manipulation of the environment that induces rate remapping is to change the wall color of the box the rat is in from black to white [92]. When place cells undergo rate remapping, simultaneously recorded grid cells do not change their firing in a consistent way [68].
- **Global (place) remapping:** In some cases, environmental changes can change the position of the place fields in an unpredictable way. For example, when the rat is walking in a box in one room (room A) and then in a similar box in another room (room B), the positions and firing rates of the different place cells are apparently unrelated [93,94] (Figure Ic). Global remapping might also occur in the same location when the geometry or other salient properties of the environment change radically [18,68]. When place cells undergo global remapping, the firing vertices of grid cells undergo changes such as shifts in grid phase, grid orientation or grid scale [68]. Place cells do not preserve distance information during global remapping whereas grid cells do; that is, two place cells which had adjacent place fields in one environment might have very distant place fields in a second environment, whereas two grids with similar spacing will shift together such that the spatial phase relationships between the grid fields are conserved [30,68].



The **theta rhythm** is a sinusoidal **field potential oscillation** that is prominent when an animal runs through space.

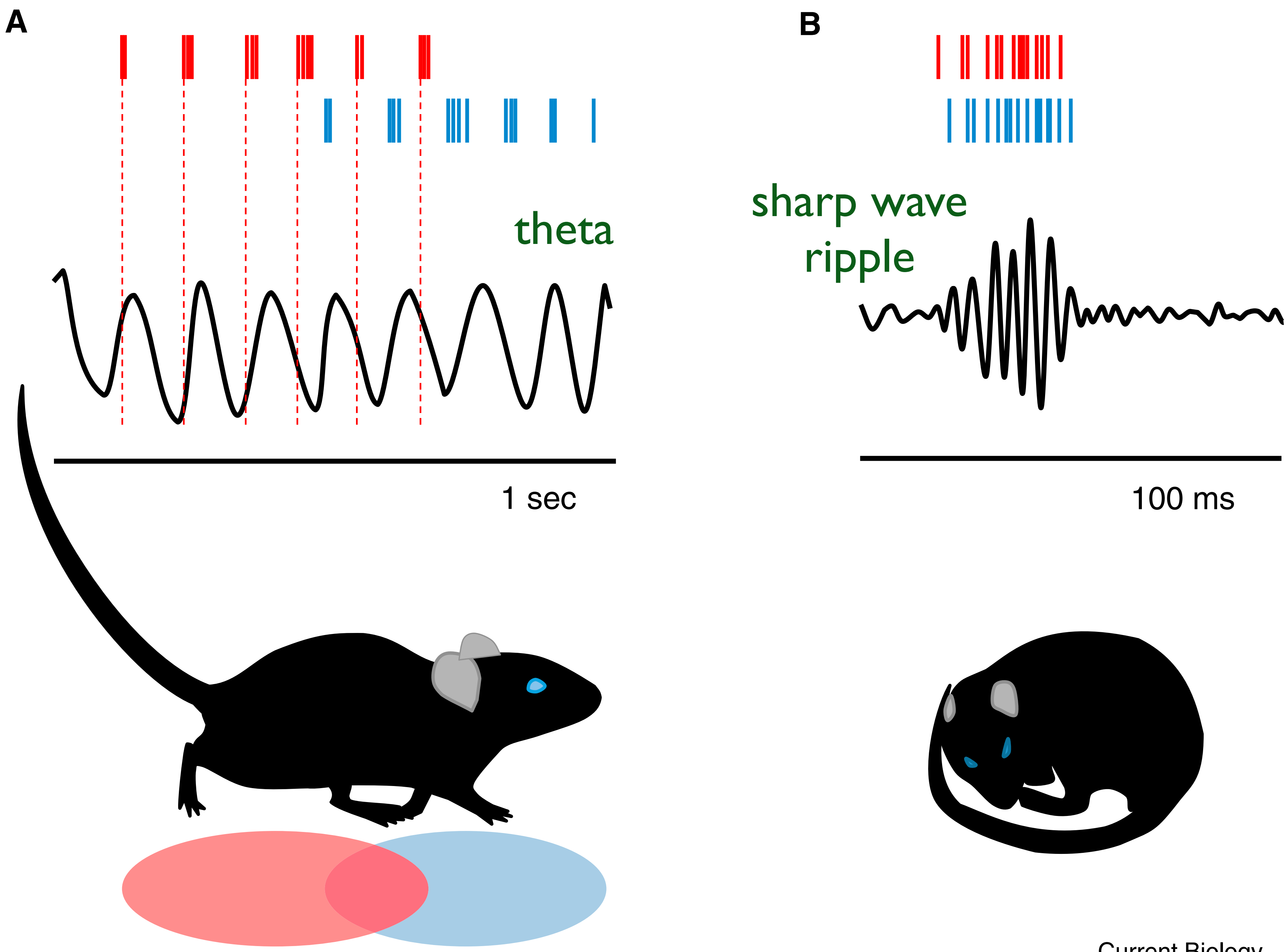
Left: the rat is running successively through the **place fields** of two **place cells** (red and blue). **Raster plots** show spike patterns (each spike is a vertical line).

The dotted lines show how the first spike in each burst corresponds to the phase of the ongoing theta rhythm — this line intersects theta wave at earlier and earlier phases of the cycle with each burst — this is **phase precession.**

Consequence: spikes occurring at entry to place field occur later in the cycle than spikes at exit of place field. When the rat enters the blue field it is exiting the red field and so its spikes occur at later phase of theta.

The brain may use the phase of theta to determine the relative locations of the two fields, which could help with self-localization.

two classes of **oscillations** in hippocampal system with same sequence of place cell activation during sleep



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Groups of place cells activated in a particular sequence during the behavior display the same sequence of activation in episodes during the subsequent sleep. This replay of place cell activity during sleep may be a **memory consolidation** mechanism, where the memory is eventually stored in cortical structures.

Figure 3. Two major classes of oscillation in the hippocampal spatial system, and patterns of associated cell firing.

(A) Theta rhythm, a sinusoidal field potential oscillation which is prominent when an animal runs through space. In the schematic example shown, a rat is running successively through the place fields of two place cells, shown in red and blue, respectively. The actual spike patterns of the two cells are shown in the raster plots at the top, with each spike shown as a vertical line. The dotted lines show how the first spike in each burst corresponds to the phase of the ongoing theta rhythm — note that this line intersects the theta wave at earlier and earlier phases of the cycle with each burst — this is *phase precession*. The consequence is that the spikes occurring at the entry to the place field occur later in the cycle than spikes as the rat exits the place field. The second cell, shown in blue, has a place field that overlaps — when the rat enters this field it is exiting the field of the red cell and so its spikes occur at a different (later) phase of theta. Thus, even within one theta cycle, by knowing the phase of theta the brain can determine the relative locations of the two fields, which could help with self-localization. (B) A sharp-wave ripple (SWR), occurring as a result of neuronal bursting when the rat rests or sleeps. Note the different timescale — SWRs occur in very short time-windows. Nevertheless, the sequence of spikes in the burst is similar to the sequence of the same cells that had fired during the previous run. This *replay* may have a role in consolidating memory of the waking experience.