The science of sleep in myWaves

Saclay, 5 February 2025.

Alain Destexhe research team is responsible for the R & D in myWaves. This CNRS laboratory is located at the Paris-Saclay University Institute of Neuroscience (NeuroPSI) and has a solid experience in studying sleep oscillations and brain waves, as outlined here.

Sleep spindles of intermediate sleep

Spindle oscillations are slow-wave sleep oscillations that appear in the intermediate sleep stage (N2). These oscillations are known to be generated in the thalamus, a central brain structure. In our past work, we found that spindle oscillations, although generated in the thalamus, depend on the feedback between thalamus and cerebral cortex, to reach synchrony over the entire brain (Contreras et al., *Science* 1996). We investigated various aspects of sleep spindles, such as their spatiotemporal distribution (Contreras et al. *J Neurosci*. 1997), spindles during spreading depression (Contreras et al., *Neuroscience* 1997), how spindles are synchronized by cortex (Destexhe et al. *J. Neurophysiol*. 1998) and how inhibition is key during sleep spindles (Peyrache et al., *PNAS* 2011).

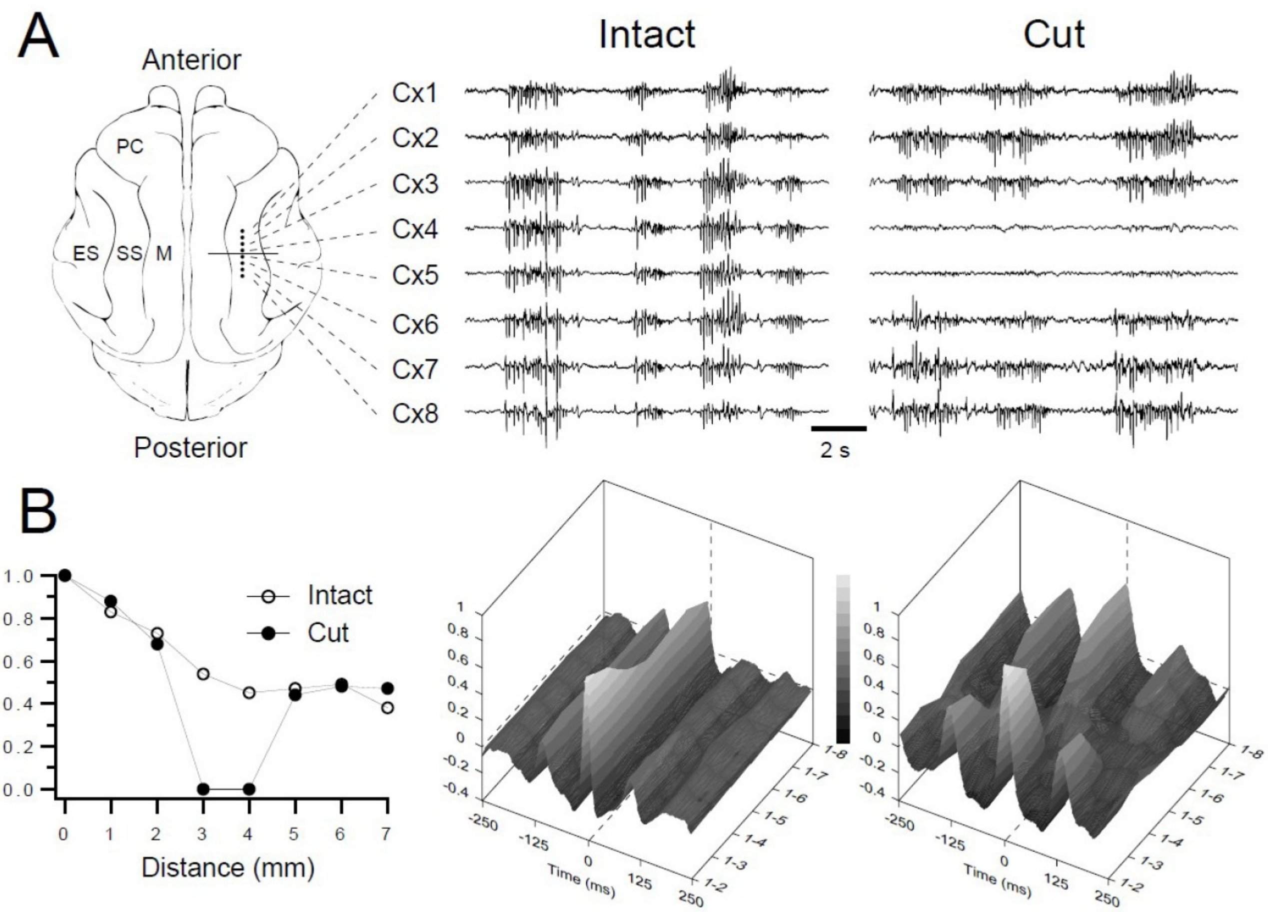

Figure 1 : Multi-electrode recordings during sleep spindles. A. Recordings in parietal cortex show that sleep spindles are generally synchronized (Intact), but after inactivation in the middle of the gyrus (Cut), the spindle synchrony still remains. B. Quantification of this phenomenon by showing the synchrony with distance. Modified from Contreras et al. *Science* 1996.

Slow (delta) waves of deep sleep

Sleep slow waves, or delta waves, constitute the hallmark of the deepest phase of sleep (N3). The study of slow waves began with the first spatio-temporal characterization of cellular and electro-corticogram (EcoG) activity during sleep slow waves (Destexhe et al., *J. Neurosci* 1999). This cellular/EcoG correlates was later studied in humans (Peyrache et al., *PNAS* 2012), which remains today the only investigation of excitatory and inhibitory neurons during human slow-wave sleep. In particular, one aspect that appeared is that neurons exhibit special correlation properties during sleep, first found in animals (Marre et al., *Phys. Review Lett.* 2009) and later in human.

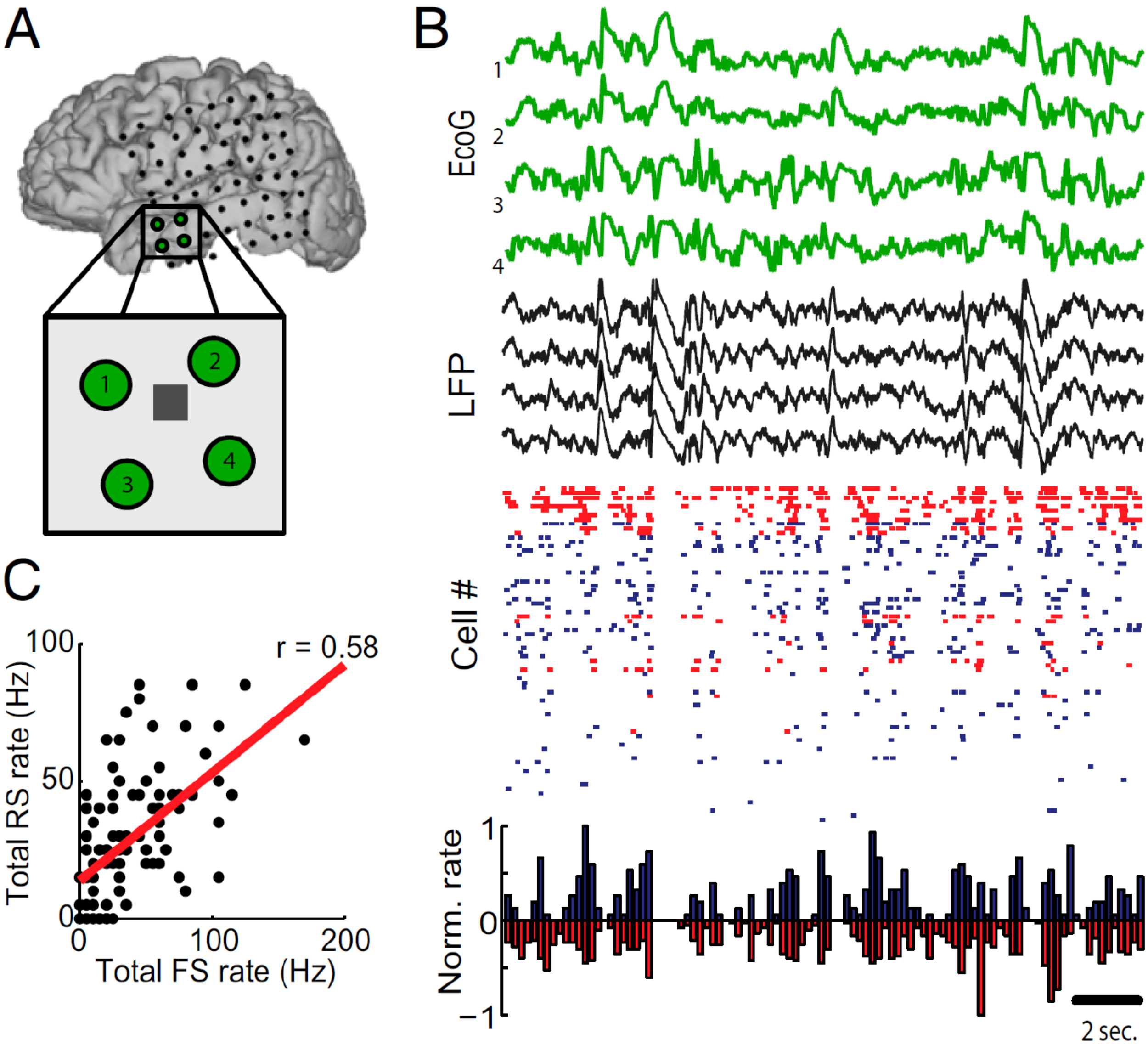

Figure 2 : Multilevel recordings of slow-waves in human. A. Placement of microelectrodes in temporal cortex (gray box), together with EcoG (green). B. EcoG signals (green) together with micro-electrode signals (LFP) during slow-wave sleep. The cells shown are single neuron spikes (blue=excitatory, red=inhibitory). Bottom : firing rates showing that there is a balance between excitation and inhibition. C. Correlation between the two cell types. Modified from Peyrache et al. *PNAS* 2012.

The Peyrache et al. 2012 study was extended to all states of the brain, including REM sleep (Dehghani et al., *Sci. Reports* 2016). It was suggested that the microstates between slow waves may represent « fragments of wakefulness » (Destexhe et al., *TINS* 2007). We also analyzed the production of slow waves in various conditions, comparing natural sleep and anesthesia, in vivo and in vitro, and found that although slow-wave sleep and deep anesthesia produce similar slow waves, they have different properties (Nghiem et al., *Cereb. Cortex* 2020).

Slow-wave sleep was also investigated intracellularly (Rudolph et al., *J Neurosci* 2007), which remains to date the most detailed investigation of the excitatory and inhibitory synaptic inputs during slow wave sleep and REM sleep. The cellular correlates of sleep oscillations were reviewed more recently (Susin and Destexhe, *Curr. Opinion. Physiol.* 2020).

Fast (beta, gamma) waves during sleep

Sleep is also characterized by the production of fast oscillations, beta (15-25 Hz) and gamma (40-80 Hz) waves. These oscillations are also present in human slow-wave sleep (Le Van Quyen et al. *PNAS* 2016), and were shown to be essentially organized by inhibitory neurons. This is also so far the only study that demonstrated the involvement of inhibitory neurons in sleep oscillations in human.

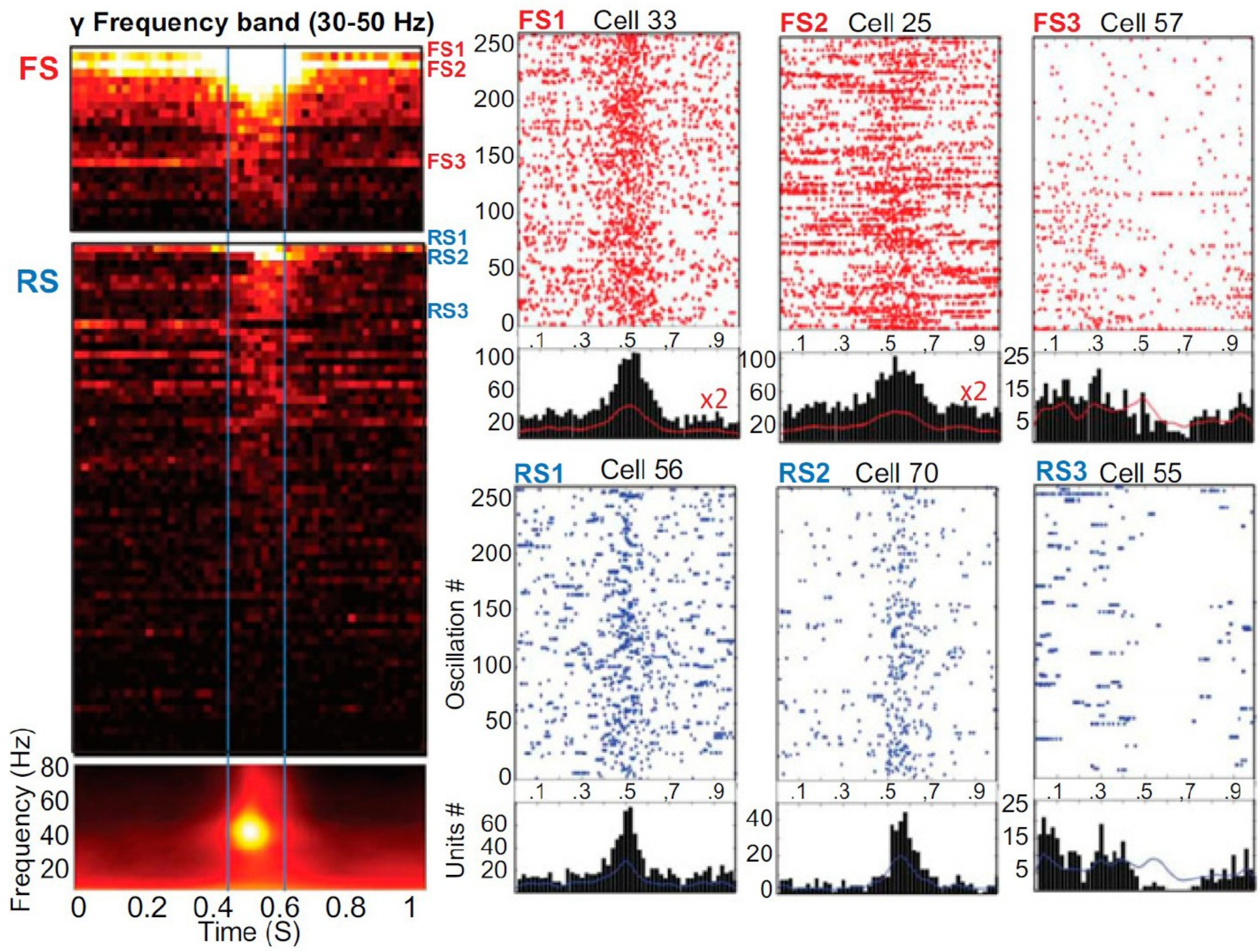

Figure 3 : Firing of single neurons in human during slow-wave sleep gamma oscillations. A few example cells are shown (red=inhibitory ; blue=excitatory) with respect to gamma oscillations. Left : diagram of all cell types showning that gamma oscullations are correlated essentially with inhibitory neurons. Modified from LeVanQuyen et al. *PNAS* 2016.

Computational aspects of sleep

A very powerful method to investigate sleep mechanisms is to design computational models. We have designed models of various types of sleep oscillations, such as sleep spindles and slow oscillations, which are summarized in a monograph (« *Thalamocortical Assemblies* », Destexhe and Sejnowski, Oxford University Press, 2023). We also proposed cellular mechanisms that could be at play during the different types of sleep oscillations, in an attempt to explain why we sleep (Sejnowski and Destexhe, *Brain Res*. 2000).

More recently, slow-wave sleep was modeled in whole-brain models of human (Goldman et al., *Frontiers Comp Neuro* 2023) and animals (Sacha et al., *Applied Sci*. 2024 ; Montagni et al., *iScience* 2024). One of the highlight of such whole-brain models is that they provide a mechanistic explanation of the reduced responsiveness to sensory stimuli in slow-wave sleep.

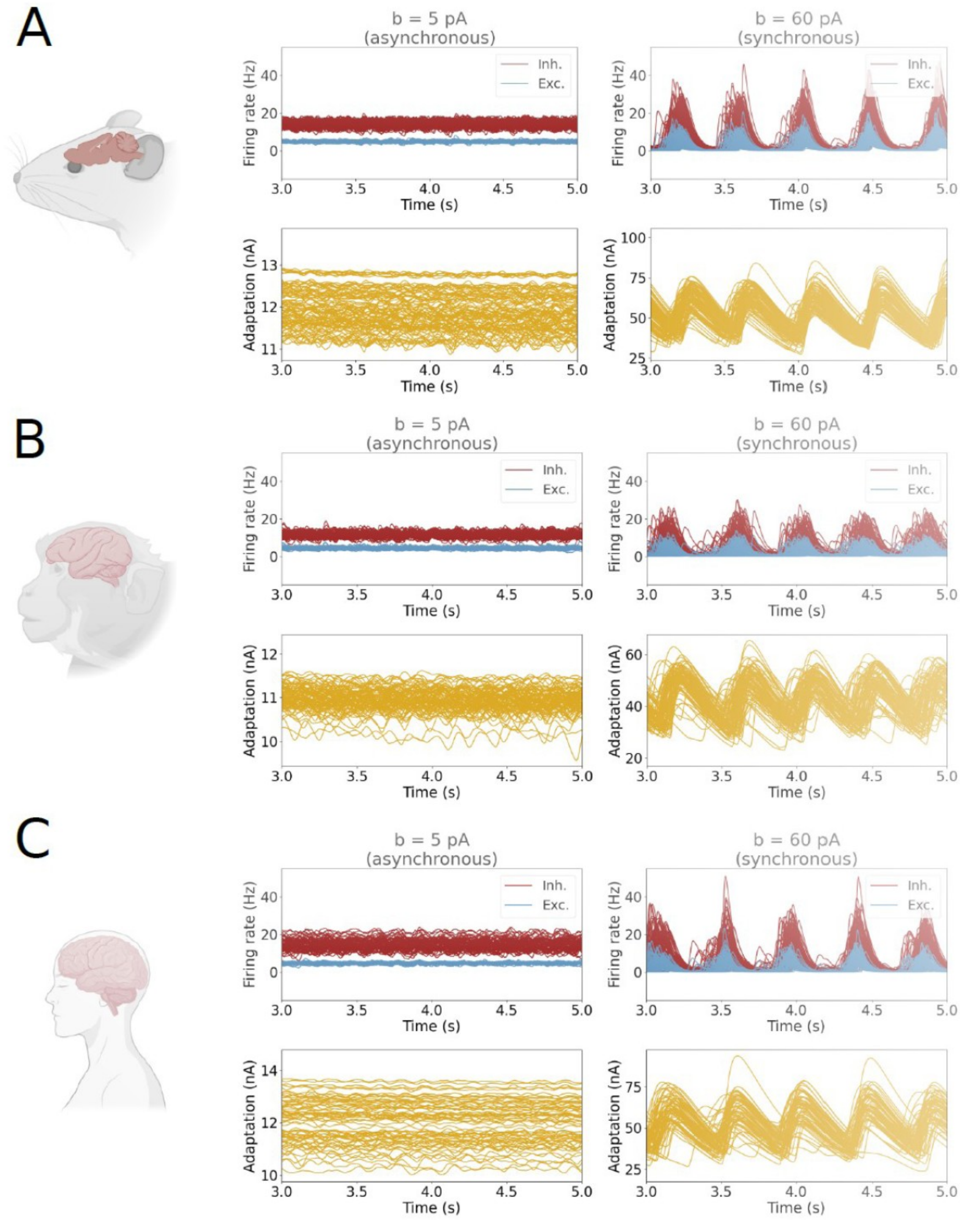

Figure 4 : Whole-brain computational models of awake and slow-wave sleep. Whole-brain models were developed for mice (A), macaque monkey (B) and human (C). The activity of different brain regions is shown for simulated wakefulness (asynchronous) and simulated slow-wave sleep (synchronous). Modified from Sacha et al., *Applied Sci*. 2024.

Sleep and music

Finally, another computational approach is to parametrize sleep oscillations to convert them into sound sequences (Destexhe and Foubert, *J. Acoust. Soc. Am.* 2022). This approach was also elaborated in a book chapter (Destexhe and Foubert, « Composing music from brain activity – The Spikiss Project », In : Exploring Transdisciplinarity in Art and Sciences, Springer, 2018).

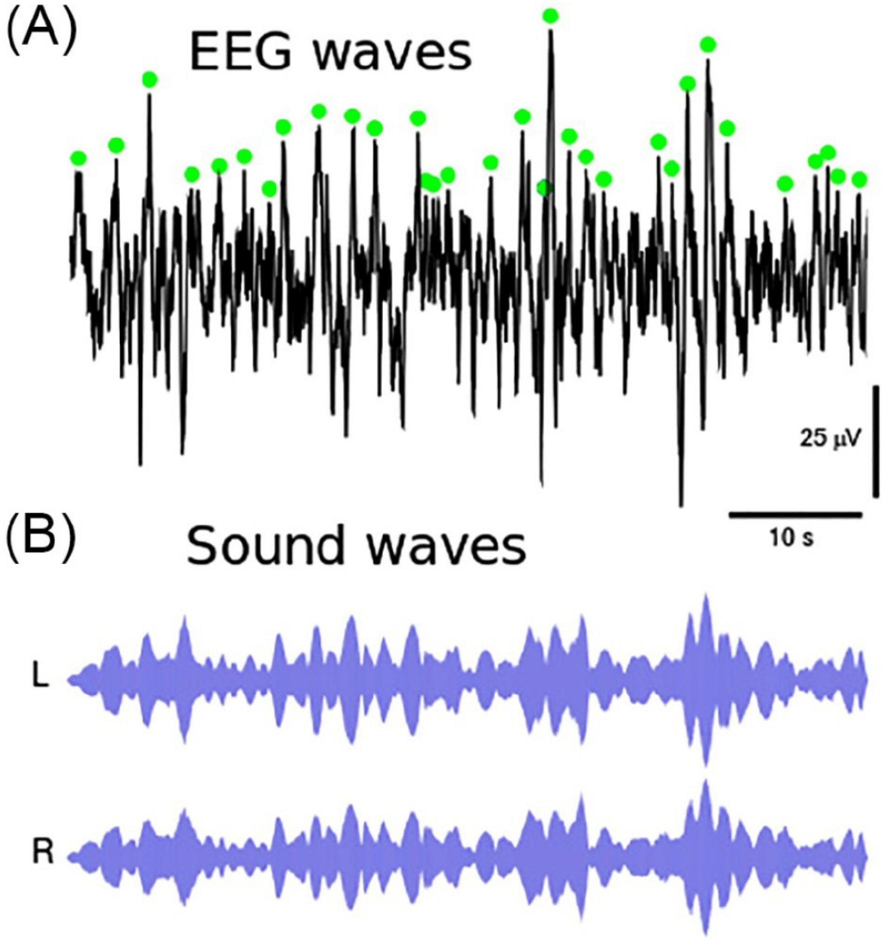

Figure 5 : Conversion from EEG waves into sound waves. EEG waves are shown during slow-wave sleep (A), and were converted into sound waves (B). Each detected delta wave (green dots) initiates a sound wave, leading to the sound sequence shown in (B). Modified from Destexhe and Foubert, *J. Acoust. Soc. Am.* 2022.

Converting brain activity during sleep into sounds is a subject that was further developed together with the myWaves startup company, funded in 2023.

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