Proc. Natl. Acad. Sci. USA
Vol. 90, pp. 1637–1638, March 1993

Commentary

Good vibes

Christof Koch

Computation and Neural Systems Program, 216-76, California Institute of Technology, Pasadena, CA 91125

Five years ago, two groups in Germany reported tantalizing evidence of stimulus-induced neuronal oscillations in the 30- to 70-Hz range (dubbed "40-Hz" oscillations) in striate cortex of the anesthetized cat (1, 2). This oscillatory firing can be phase-locked when recording from two distinct sites (3). These high-frequency oscillations and, in particular, the presence of stimulus-dependent synchronization among groups of neurons have given rise to a subculture of modelers and theoreticians arguing that these fast dynamic phenomena are the Rosetta stone of the brain and play a crucial role in figure–ground segmentation, perception, and even consciousness (4, 5). However, evidence for oscillations has been much less forthcoming in the monkey cortex, with some groups reporting them while other fail to find them.

Aficionados of 40-Hz neuronal oscillations and synchronization can now take heart by the latest of a string of publications by Llinás and colleagues in these pages (6–8). Use of a 37-channel magnetoencephalography (MEG) system (with a temporal resolution of 1 msec and a spatial resolution of a few millimeters at the cortical surface) allows them to scan the brain of healthy volunteers while they are relaxing or sleeping. After filtering the signal at 35–45 Hz, Llinás and Ribary find first that 40-Hz oscillatory activity throughout cortex is equally strong in the awake phase as in the rapid-eye-movement (REM) phase of sleep (during which dreams are most frequently reported). Activity in this frequency band is greatly reduced in deep sleep (delta-wave sleep). Second, following auditory stimulation (0.5-sec-long tones), 40-Hz activity can be reliably induced only in the awake state but not during REM sleep, although the thalamo-cortical resonance is not blocked as it is during delta sleep, supporting the idea that during dreaming less sensory information is made available to cortex. Their final result is the most intriguing. Detailed analysis of the MEG signal reveals an apparent phase shift totaling 12 msec among the 37 channels, an effect that can be interpreted as a wave of activity moving from the front to the back of cortex at 80 Hz.

Based on their previous findings (7) of a 3-msec phase shift between thalamic and cortical appearance of the 40-Hz activity, Llinás and Ribary argue that two systems are involved in expressing and controlling oscillations. One arises from specific sensory thalamic nuclei, their cortical targets in layer IV, and the projection back to the specific thalamic relay nucleus via layer VI. This system would be triggered upon specific sensory input. The second and more global system is represented by nonspecific intralaminar nucleus of the thalamus, not associated with any specific sensory or motor system and projecting to superficial cortical layers. It is this system which they believe causes the rostrocaudal sweep of 40-Hz activity. Unilateral lesion of the medial intralaminar nuclei in kittens and cats causes the animal to attend only little to visual stimuli presented in the contralateral hemisphere (9), while lesions of the intralaminar nucleus in humans lead to coma-like states. The function of these oscillations would be to temporally bind sensory events both within and across sensory modalities.

Galambos and colleagues (10) were among the first to report that auditory stimulation leads to the appearance of three or four cycles of a 40-Hz sine wave in the auditory evoked potential (AEP). The strength of this component is being explored by a number of anesthesiologists as the only reliable indicator of the presence of awareness in patients during general anesthesia (11, 12). Because this procedure usually induces paralysis and amnesia (as well as analgesia), it is difficult to assess to what extent different anesthetic agents actually lead to unconsciousness (patients might still be aware yet unable to either report or remember intraoperative events). The absence of strong 40-Hz oscillations in the MEG signal during deep sleep, when awareness is either reduced or absent altogether, is compatible with the practice of monitoring the AEP. Confirmation by recording MEG activity from subjects during various anesthetic states would be desirable.

What none of these electrophysiological or imaging studies address, however, is the functional relevance of oscillations. Intracellular recordings from thalamic and cortical neurons (14) have revealed the tendency of many neurons to generate activity at certain preferred frequencies (ranging from a few hertz to as high as 50–60 Hz). It may well be that, rather than reflecting binding or other high-level cognitive operations, the 40-Hz signal in the AEP and MEG data simply mirrors the natural resonant frequency of the brain, something that by itself may have no significance other than indicating that cortex is alive and well. By analogy, listening to the hum of the power transformer on my Macintosh tells me that the machine is operational without revealing anything about the machine's specific states. Relating the presence of high-frequency oscillations or synchronization among groups of neurons to perception will require studies of the type pioneered by Newsome and colleagues (13). They explored the quantitative relationship between the firing of single neurons in a motion-processing area in extrastriate cortex in the monkey with the simultaneous assessed psychophysical performance of the animal in a demanding motion-discrimination experiment.

During the previous two decades, Llinás and colleagues have provided us with ample evidence at the single-cell level (summarized in ref. 14) that the brain is not a system evolving towards a steady-state or fixed point. This report of 40-Hz waves criss-crossing the brain once more emphasizes the highly dynamic nature of cortex and its never ending ability to surprise us.

1. Eckhorn, R., Bauer, R., Jordan, W., Brosch, M., Kruse, W., Munk, M. & Reitböck, H. J. (1988) *Biol. Cybern.* **60**, 121–130.
2. Gray, C. M. & Singer, W. (1989) *Proc. Natl. Acad. Sci. USA* **86**, 1698–1702.
3. Gray, C. M., König, P., Engel, A. K. & Singer, W. (1989) *Nature (London)* **338**, 334–337.
4. von der Malsburg, C. & Schneider, W. (1986) *Biol. Cybern.* **54**, 29–40.
5. Crick, F. & Koch, C. (1990) *Sem. Neurosci.* **2**, 263–275.
6. Yamamoto, T., Williamson, S. J., Kaufman, L., Nicholson, C. & Llinás, R. (1988) *Proc. Natl. Acad. Sci. USA* **85**, 8732–8736.
7. Ribary, U., Ioannides, A. A., Singh, K. D., Hasson, R., Bolton, J. P. R., Lado, F., Mogilner, A. & Llinás, R. (1991) *Proc. Natl. Acad. Sci. USA* **88**, 11037–11041.
8. Llinás, R. R. & Ribary, U. (1993) *Proc. Natl. Acad. Sci. USA* **90**, 2078–2081.
9. Singer, W. (1982) *Hum. Neurobiol.* **1**, 41–49.

10. Galambos, R., Makeig, S. & Talmachoff, P. J. (1981) *Proc. Natl. Acad. Sci. USA* **78**, 2643–2647.
11. Madeler, C. & Pöppel, E. (1987) *Naturwissenschaften* **74**, 42–43.
12. Kulli, J. & Koch, C. (1991) *Trends Neurosci.* **14**, 6–10.
13. Newsome, W. T., Britten, K. H. & Movshon, J. A. (1989) *Nature (London)* **341**, 52–54.
14. Llinás, R. R. (1988) *Science* **242**, 1654–1664.