

## FUNDAMENTALS OF NEURONAL EXCITABILITY RELEVANT TO SEIZURES

# Neocortical synchronization

\*Igor Timofeev, †Maksim Bazhenov, \*José Seigneur, and ‡Terrence Sejnowski

\*Laval University, Québec, Canada; †University of California, Riverside, California, U.S.A.; and  
‡Salk Institute, La Jolla, California, U.S.A.

### SUMMARY

Neuronal synchronization occurs when two or more neuronal events are coordinated across time. Local synchronization produces field potentials. Long-range synchronization between distant brain sites contributes to the electroencephalogram. Neuronal synchronization depends on synaptic (chemical/electrical), ephaptic, and extracellular interactions. For an expanded treat-

ment of this topic see *Jasper's Basic Mechanisms of the Epilepsies, Fourth Edition* (Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV, eds) published by Oxford University Press (available on the National Library of Medicine Bookshelf [NCBI] at [www.ncbi.nlm.nih.gov/books](http://www.ncbi.nlm.nih.gov/books)).

**KEY WORDS:** Epilepsy, Extracellular conditions, Feedback loops, Local synchronization, Long-range synchronization, Oscillations, Propagating activities, Seizures.

Neuronal synchronization is a correlated appearance in time of two or more events associated with various aspects of neuronal activity. Neuronal synchronization depends on chemical synaptic interactions, electrical synaptic interactions, ephaptic interactions, and nonspecific interactions mediated by extracellular conditions that rest on activity-dependent changes in ionic concentrations. Herein, we consider two distinct types of neuronal synchronization (Timofeev et al., 2011): local synchronization that is responsible for the generation of local field potentials; and long-range synchronization, detected with distantly located electrodes and mediated primarily via chemical synaptic interactions. Neocortical synchronization during sleep is often associated with rhythmic oscillations of neuronal activity: slow oscillation, delta, spindle, beta, gamma, and ripples. In many cases, a primary oscillator generates a rhythm (example: spindle oscillation generated in thalamus) that projects and drives oscillations in target structures (such as neocortex). In other cases, different oscillations occur quasi-independently in different locations and can be synchronized in a particular pattern.

Normal thalamocortical oscillations during sleep or wake states (Steriade et al., 1993; Bazhenov & Timofeev, 2006) are generated as a result of both local and long-range synchronization. During paroxysmal (i.e., seizure) activity, the role of chemical synaptic interactions decreases because of depletion of extracellular  $Ca^{2+}$  that impairs synaptic transmission. Synchronized activities in

large populations of neurons (such as neocortex) may occur as nearly simultaneous patterns across an entire population or as propagating waves. When propagating activities occur, the synchronized activities appear with a distance-dependent phase shift. Neocortical synchronization also depends on extracortical mechanisms, since activation of cholinergic, noradrenergic, and serotonergic systems abolishes sleep synchronization patterns and generates activated cortical patterns. The presence of cortical–thalamic–cortical feedback loops contribute to the synchronization of cortical activities.

### ACKNOWLEDGMENTS

The authors acknowledge financial support from Canadian Institutes of Health Research (MOP-37862, MOP-67175), National Science and Engineering Research Council of Canada (grant 298475) and National Institute of Neurological Disorders and Stroke (1R01NS060870 and 1R01NS059740). I.T. is Fonds de la recherche en santé du Québec Research Scholar.

### DISCLOSURE

The authors declare no conflicts of interest.

### REFERENCES

- Bazhenov M, Timofeev I. (2006) Thalamocortical oscillations. [http://www.scholarpedia.org/article/Thalamocortical\\_Oscillations](http://www.scholarpedia.org/article/Thalamocortical_Oscillations).
- Steriade M, McCormick DA, Sejnowski TJ. (1993) Thalamocortical oscillations in the sleeping and aroused brain. *Science* 262:679–685.
- Timofeev I, Bazhenov M, Seigneur J, Sejnowski T. (2011) Neocortical synchronization. In Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV (Eds) *Jasper's basic mechanisms of the epilepsies*. 4th ed. Oxford University Press, New York [in press].

Address correspondence to Igor Timofeev, Laval University, QC G1J 2G3, Canada. E-mail: Igor.Timofeev@phs.ulaval.ca