

# Direct current coupled recordings of cortical spreading depression using silicone probes

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## Abstract

© 2017 Nasretdinov, Lotfullina, Vinokurova, Lebedeva, Burkhanova Chernova, Zakharov and Khazipov. Electrophysiological assessment of infraslow ( $< 0.1$  Hz) brain activities such as cortical spreading depression (SD), which occurs in a number of pathologies including migraine, epilepsy, traumatic brain injury (TBI) and brain ischemia requires direct current (DC) coupled recordings of local field potentials (LFPs). Here, we describe how DC-coupled recordings can be performed using high-density iridium electrode arrays (silicone probes). We found that the DC voltage offset of the silicone probe is large and often exceeds the amplifier input range. Introduction of an offset compensation chain at the signal ground efficiently minimized the DC offsets. Silicone probe DC-coupled recordings across layers of the rat visual and barrel cortices revealed that epidural application of KCl, dura incision or pinprick TBI induced SD which preferentially propagated through the supragranular layers and further spread to the granular and infragranular layers attaining maximal amplitudes of  $\sim -30$  mV in the infragranular layers. SD at the superficial cortical layers was nearly two-fold longer than at the deep cortical layers. Continuous epidural KCl evoked multiple recurrent SDs which always started in the supragranular layers but often failed to propagate through the deeper cortical layers. Intracortical KCl injection into the infragranular layers evoked SD which also started in the supragranular layers and spread to the granular and infragranular layers, further indicating that the supragranular layers are particularly prone to SD. Thus, DC-coupled recordings with silicone probes after offset compensation can be successfully used to explore the spatial–temporal dynamics of SD and other slow brain activities.

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## Keywords

Brain ischemia, DC recordings, Electroencephalography, Epilepsy, Migraine, Silicone probes, Spreading depression, Traumatic brain injury

## References

- [1] Akhmetshina D., Nasretdinov A., Zakharov A., Valeeva G., Khazipov R. (2016). The nature of the sensory input to the neonatal rat barrel cortex. *J. Neurosci.* 36, 9922–9932. DOI: 10.1523/JNEUROSCI.1781-16.2016
- [2] Ayata C., Lauritzen M. (2015). Spreading depression, spreading depolarizations, and the cerebral vasculature. *Physiol. Rev.* 95, 953–993. DOI: 10.1152/physrev.00027.2014.

- [3] Basarsky T. A., Duffy S. N., Andrew R. D., MacVicar B. A. (1998). Imaging spreading depression and associated intracellular calcium waves in brain slices. *J. Neurosci.* 18, 7189–7199.
- [4] Bragin A., Penttonen M., Buzsáki G. (1997). Termination of epileptic afterdischarge in the hippocampus. *J. Neurosci.* 17, 2567–2579.
- [5] Buzsáki G., Draguhn A. (2004). Neuronal oscillations in cortical networks. *Science* 304, 1926–1929. DOI: 10.1126/science.1099745
- [6] Canals S., Makarova I., López-Aguado L., Largo C., Ibarz J. M., Herreras O. (2005). Longitudinal depolarization gradients along the somatodendritic axis of CA1 pyramidal cells: a novel feature of spreading depression. *J. Neurophysiol.* 94, 943–951. DOI: 10.1152/jn.01145.2004
- [7] Colonnese M. T., Khazipov R. (2010). “Slow activity transients” in infant rat visual cortex: a spreading synchronous oscillation patterned by retinal waves. *J. Neurosci.* 30, 4325–4337. DOI: 10.1523/JNEUROSCI.4995-09.2010
- [8] Dreier J. P. (2011). The role of spreading depression, spreading depolarization and spreading ischemia in neurological disease. *Nat. Med.* 17, 439–447. DOI: 10.1038/nm.2333
- [9] Dreier J. P., Fabricius M., Ayata C., Sakowitz O. W., William Shuttleworth C., Dohmen C., et al. (2017). Recording, analysis, and interpretation of spreading depolarizations in neurointensive care: review and recommendations of the COSBID research group. *J. Cereb. Blood Flow Metab.* 37, 1595–1625. DOI: 10.1177/0271678X16654496
- [10] Dreier J. P., Reiffurth C. (2015). The stroke-migraine depolarization continuum. *Neuron* 86, 902–922. DOI: 10.1016/j.neuron.2015.04.004
- [11] Freeman J. A., Nicholson C. (1975). Experimental optimization of current source-density technique for anuran cerebellum. *J. Neurophysiol.* 38, 369–382.
- [12] Guedes R. C. A., Araújo M. D. G. R., Verçosa T. C., Bion F. M., de Sá A. L., Pereira A., Jr., et al. (2017). Evidence of an inverse correlation between serotonergic activity and spreading depression propagation in the rat cortex. *Brain Res.* 1672, 29–34. DOI: 10.1016/j.brainres.2017.07.011
- [13] Hartings J. A., Li C., Hinzman J. M., Shuttleworth C. W., Ernst G. L., Dreier J. P., et al. (2017a). Direct current electrocorticography for clinical neuromonitoring of spreading depolarizations. *J. Cereb. Blood Flow Metab.* 37, 1857–1870. DOI: 10.1177/0271678X16653135
- [14] Hartings J. A., Shuttleworth C. W., Kirov S. A., Ayata C., Hinzman J. M., Foreman B., et al. (2017b). The continuum of spreading depolarizations in acute cortical lesion development: examining Leao’s legacy. *J. Cereb. Blood Flow Metab.* 37, 1571–1594. DOI: 10.1177/0271678X16654495
- [15] Herreras O., Largo C., Ibarz J. M., Somjen G. G., Martín del Río R. (1994). Role of neuronal synchronizing mechanisms in the propagation of spreading depression in the in vivo hippocampus. *J. Neurosci.* 14, 7087–7098.
- [16] Herreras O., Somjen G. G. (1993a). Analysis of potential shifts associated with recurrent spreading depression and prolonged unstable spreading depression induced by microdialysis of elevated K in hippocampus of anesthetized rats. *Brain Res.* 610, 283–294. DOI: 10.1016/0006-8993(93)91412-I
- [17] Herreras O., Somjen G. G. (1993b). Propagation of spreading depression among dendrites and somata of the same cell population. *Brain Res.* 610, 276–282. DOI: 10.1016/0006-8993(93)91411-K
- [18] Joshi I., Andrew R. D. (2001). Imaging anoxic depolarization during ischemia-like conditions in the mouse hemi-brain slice. *J. Neurophysiol.* 85, 414–424. DOI: 10.1152/jn.2001.85.1.414
- [19] Kaufmann D., Theriot J. J., Zyuzin J., Service C. A., Chang J. C., Tang Y. T., et al. (2017). Heterogeneous incidence and propagation of spreading depolarizations. *J. Cereb. Blood Flow Metab.* 37, 1748–1762. DOI: 10.1177/0271678X16659496
- [20] Khazipov R., Sirota A., Leinekugel X., Holmes G. L., Ben-Ari Y., Buzsáki G. (2004). Early motor activity drives spindle bursts in the developing somatosensory cortex. *Nature* 432, 758–761. DOI: 10.1038/nature03132
- [21] Khazipov R., Zaynutdinova D., Ogievetsky E., Valeeva G., Mitrukina O., Manent J. B., et al. (2015). Atlas of the postnatal rat brain in stereotaxic coordinates. *Front. Neuroanat.* 9:161. DOI: 10.3389/fnana.2015.00161
- [22] Lauritzen M., Dreier J. P., Fabricius M., Hartings J. A., Graf R., Strong A. J. (2011). Clinical relevance of cortical spreading depression in neurological disorders: migraine, malignant stroke, subarachnoid and intracranial hemorrhage, and traumatic brain injury. *J. Cereb. Blood Flow Metab.* 31, 17–35. DOI: 10.1038/jcbfm.2010.191
- [23] Leão A. A. P. (1944). Pial circulation and spreading depression of activity in the cerebral cortex. *J. Neurophysiol.* 7, 391–396.
- [24] Leão A. A. P. (1947). Further observations on the spreading depression of activity in the cerebral cortex. *J. Neurophysiol.* 10, 409–414.
- [25] Makarova J., Gómez-Galán M., Herreras O. (2008). Variations in tissue resistivity and in the extension of activated neuron domains shape the voltage signal during spreading depression in the CA1 in vivo. *Eur. J. Neurosci.* 27, 444–456. DOI: 10.1111/j.1460-9568.2008.06022.x

- [26] Minlebaev M., Colonnese M., Tsintsadze T., Sirota A., Khazipov R. (2011). Early  $\gamma$  oscillations synchronize developing thalamus and cortex. *Science* 334, 226-229. DOI: 10.1126/science.1210574
- [27] Paxinos G., Watson C. (2007). *The Rat Brain in Stereotaxic Coordinates*. 6th Edn. San Diego, CA: Academic Press.
- [28] Pietrobon D., Moskowitz M. A. (2014). Chaos and commotion in the wake of cortical spreading depression and spreading depolarizations. *Nat. Rev. Neurosci.* 15, 379-393. DOI: 10.1038/nrn3770
- [29] Richter F., Lehmenkühler A. (1993). Spreading depression can be restricted to distinct depths of the rat cerebral cortex. *Neurosci. Lett.* 152, 65-68. DOI: 10.1016/0304-3940(93)90484-3
- [30] Somjen G. G. (2001). Mechanisms of spreading depression and hypoxic spreading depression-like depolarization. *Physiol. Rev.* 81, 1065-1096. DOI: 10.1152/physrev.2001.81.3.1065
- [31] Tallgren P., Vanhatalo S., Kaila K., Voipio J. (2005). Evaluation of commercially available electrodes and gels for recording of slow EEG potentials. *Clin. Neurophysiol.* 116, 799-806. DOI: 10.1016/j.clinph.2004.10.001
- [32] Vanhatalo S., Palva J. M., Andersson S., Rivera C., Voipio J., Kaila K. (2005a). Slow endogenous activity transients and developmental expression of K-Cl cotransporter 2 in the immature human cortex. *Eur. J. Neurosci.* 22, 2799-2804. DOI: 10.1111/j.1460-9568.2005.04459.x
- [33] Vanhatalo S., Voipio J., Kaila K. (2005b). Full-band EEG (fbEEG): a new standard for clinical electroencephalography. *Clin. EEG Neurosci.* 36, 311-317. DOI: 10.1177/155005940503600411
- [34] Wadman W. J., Jota A. J., Kamphuis W., Somjen G. G. (1992). Current source density of sustained potential shifts associated with electrographic seizures and with spreading depression in rat hippocampus. *Brain Res.* 570, 85-91. DOI: 10.1016/0006-8993(92)90567-s