Probing neuronal activity using membrane interfacial water

S. Roke

Laboratory for fundamental BioPhotonics (LBP), Institute of Bio-engineering (IBI), and Institute of Materials Science (IMX), School of Engineering (STI), and Lausanne Centre for Ultrafast Science (LACUS), École Polytechnique Fédérale de Lausanne (EPFL), CH-1015, Lausanne, Switzerland, E-mail: sylvie.roke@epfl.ch

Abstract

Neurons communicate through electrochemical signalling within a complex network. These signals are composed of spatiotemporal changes in membrane potentials that are traditionally measured by electrical recordings or using optical probes. Since probes are inevitably invasive and damaging to the cells, label-free imaging approaches are sought for. For many years second harmonic (SH) imaging has been a promise for delivering direct label-free neuronal membrane potential information. However, to date this promise has not been delivered, owing to the intrinsic low sensitivity of the method.

Here, we demonstrate an improvement in label-free second harmonic neuroimaging sensitivity by ~3 orders of magnitude using a wide-field medium repetition rate illumination [1-4]. We perform a side-by-side patch-clamp and second harmonic imaging comparison to demonstrate the theoretically predicted linear correlation between whole neuron membrane potential changes and the square root of the second harmonic intensity. We assign the ion induced changes to the SH intensity to changes in the orientation of membrane interfacial, which is used to image spatiotemporal changes in the membrane potential and K^+ ion flux. We observe a non-uniform spatial distribution and temporal activity of ion channels in the mouse brain neurons.

References

[1] - Optical Imaging of Surface Chemistry and Dynamics in Confinement, C. Macias-Romero, I. Nahalka, H. I. Okur, S. Roke, *Science* (2017) 357, 784-788

[2] - A label-free and charge-sensitive dynamic imaging of lipid membrane hydration on millisecond time scales, O. Tarun, C. Hannesschläger, P. Pohl, and S. Roke, *Proc. Nat. Acad. Sci. USA* (2018) 115, 4081-4086.

[3] - Membrane water as a probe for neuronal membrane potentials and ionic flux at the single cell level, M. Didier, O. Tarun, P. Jourdain, P. Magistretti, S. Roke, *Nat. Commun*. (2018), 9, 5287.

[4] - Endogenous SHG and 2PEF coherence imaging of substructures in neurons in 3D, C. Macias-Romero, C. Teulon, M. E. P. Didier and S. Roke, *Opt. Express* (2019), 27, 2235-22