Cutting-edge brain research from a biophysical perspective: symposium synopsis of Session 1SCP at BSJ2019 in Miyazaki, Kyushu, Japan

Takashi Tominaga¹ • Bernd Kuhn²

Received: 14 January 2020 / Accepted: 5 February 2020 / Published online: 13 February 2020

© International Union for Pure and Applied Biophysics (IUPAB) and Springer-Verlag GmbH Germany, part of Springer Nature 2020

The organizers Takashi Tominaga (Tokushima Bunri University) and Bernd Kuhn (OIST Graduate University) planned the symposium with the idea that a biophysical perspective is essential to understand how the brain works. The brain is an amazingly complicated and sophisticated information processing device, consisting of billions of neurons and thousands of billions of connections in the mammalian brain. To understand how the brain processes information, it is essential to readout and manipulate neuronal activity on all different temporal and spatial scales. We asked three pioneering biophysicists (Prof. Nemoto, Dr. Tani, and Dr. Nakamichi) who have invented various state-of-the-art biophysical methods, especially optical methods, to share their ideas. Also, the symposium picked up two distinguished topics selected from the submitted poster abstracts (Ms. Wen and Prof. Toyota). The symposium “Cutting-edge brain research from a biophysical perspective” was held at the 57th Biophysical Society of Japan Annual Meeting.

The session started with a talk by Prof. Bernd Kuhn and Dr. Christopher J. Roome (OIST Graduate University) entitled “Simultaneous spatio-temporal dendritic voltage/calcium mapping and somatic recording from Purkinje neurons in awake mice.” Prof. Kuhn introduced the basic mechanism of voltage sensing with synthetic voltage-sensitive dyes (VSDs) and, specifically, their previously developed and well-studied ANNINE (ANellated hemicyanINE) dyes (Kuhn et al. 2004).

The use of the electrochromic dye in combination with state-of-the-art two-photon microscopy techniques allows them to record the activity of a single Purkinje cell dendrite in awake mice (Roome and Kuhn 2018; Kuhn and Roome 2019).

Prof. Nemoto (Research Institute of Electronic Science, Hokkaido University; now National Institute for Physiological Sciences, Okazaki) presented the second talk entitled “Novel *in vivo* two-photon microscopy for vast and longtime neural activity.” Prof. Nemoto presented their novel developments on two-photon microscopy that allows deep brain imaging. Also, their improved high-power laser enables them to expand the spatio-temporal observation range (Goto et al. 2019). Prof. Nemoto also introduced a unique nano-sheet (Iijima et al. 2019) that allows researchers to observe *in vivo* brain activity.

Dr. Nakamichi and Dr. Tanifuji (Riken Center for Brain Science (CBS)) presented the talk “Functional optical coherence tomography with Fourier imaging reveals three-dimensional and micro-scale brain functional structure.” Their pioneering work on the application of optical coherence tomography to study functional anatomy of brain activity revealed a unique three-dimensional operational structure of a “pin-wheel.” Pin-wheels in visual cortex have been known for decades; however, no one knew their 3D structure. In this talk, a precise analysis of the pin-wheel structure and its physiological implications was presented (Nakamichi et al. 2018, 2019).

The following speaker was Dr. Tomomi Tani (Marine Biological Laboratory, Woods Hole; now The National Institute of Advanced Industrial Science and Technology (AIST), Japan). Dr. Tani started the talk entitled “Dissecting nano-scale architecture and dynamics of molecular assemblies in living cells with polarized light” with an introduction of their unique strategy to use polarized light. Using this technology allows them to detect the rotation of polarized light in real-time. Single-molecule resolution enables them to determine the molecular orientation in complex assemblies such as living systems (Mehta et al. 2016; Ishii and Tani 2019). Dr. Tani also uses polarized light to read out brain activity by intrinsic optical signals from hippocampal

✉ Takashi Tominaga
tominagat@kph.bunri-u.ac.jp

✉ Bernd Kuhn
bkuhn@oist.jp

¹ Laboratory for Neural Circuit Systems, Institute of Neuroscience, Tokushima Bunri University, 1314-1 Shido, Sanuki, Kagawa, Japan

² Optical Neuroimaging Unit, Okinawa Institute of Science and Technology Graduate University (OIST), 1919-1 Tancha, Onna-son, Okinawa, Japan

slices. This will allow to gain new biophysical insight into brain function (Koike-Tani et al. 2019).

The first of the distinguished poster topics was presented by the graduate student Ms. Jierong Wen (RMIT University). Ms. Wen talked about “(1Pos005) The role of C-terminal carboxylation in alpha-conotoxin LsIA interactions with human alpha7 nicotinic acetylcholine receptor in silico.” The alpha7 nicotinic acetylcholine receptor (alpha7 nAChR) is one of the critical target receptors relating to human psychiatric diseases such as Alzheimer’s types of dementia. Ms. Wen introduced a detailed analysis of the interaction of a possible cure (alpha-conotoxin LsIA) to alpha7 nAChR using advanced homology modeling and molecular dynamics (MD) simulations (Wen and Hung 2019).

Prof. Takashi Tominaga and Dr. Yoko Tominaga (Tokushima Bunri University) introduced wide-field VSD imaging of brain slice preparations in their talk “Optical view of the brain neural circuit activity: Voltage-sensitive dye (VSD) imaging.” Prof. Tominaga introduced the present state of VSD imaging with their fast imaging system. The talk showed how improved VSD imaging (Tominaga et al. 2018, 2019) allows researchers to observe plastic changes in the propagation of voltage signals in a wide brain area (Kajiwarawa et al. 2019).

The second distinguished poster topic was presented by Professor Masatugu Toyota (Saitama University and Univ. Wisconsin-Madison) entitled “(1Pos266) Long-distance Ca^{2+} transmission via glutamate receptor channel in plants.” Prof. Toyota studies how cells in plants communicate with each other using Ca^{2+} imaging. This results in fascinating movies. The talk highlighted the universal importance of membrane potential and Ca^{2+} signaling across all cells in tissue showing that even the study of phylogenetically remote systems can shed new light on the understanding of the brain (Toyota et al. 2018; Toyota 2019).

Overall, the symposium covered many cutting-edge technologies that have revealed and will reveal many novel aspects of brain function.

References

- Goto A, Otomo K, Nemoto T (2019) Real-time polarization-resolved imaging of living tissues based on two-photon excitation spinning-disk confocal microscopy. *Aip Conf Proc* 7:56
- Iijima K, Oshima T, Kawakami R, Nemoto T (2019) Optical clearing of living brains with MAGICAL to extend in vivo imaging. *Biorxiv*:507426
- Ishii H, Tani T (2019) Spatial organization of cortical actin alignments for the ooplasmic segregation of ascidian *Ciona* eggs. *Biorxiv*:849323
- Kajiwarawa R, Tominaga Y, Tominaga T (2019) Network plasticity involved in the spread of neural activity within the rhinal cortices as revealed by voltage-sensitive dye imaging in mouse brain slices. *Front Cell Neurosci* 13:20
- Koike-Tani M, Tominaga T, Oldenbourg R, Tani T (2019) Instantaneous polarized light imaging reveals activity dependent structural changes of dendrites in mouse hippocampal slices. *bioRxiv*:523571
- Kuhn B, Roome CJ (2019) Primer to voltage imaging with ANNINE dyes and two-photon microscopy. *Front Cell Neurosci* 13:321
- Kuhn B, Fromherz P, Denk W (2004) High sensitivity of Stark-shift voltage-sensing dyes by one- or two-photon excitation near the red spectral edge. *Biophys J* 87:631–639
- Mehta SB, McQuilken M, Riviere PJ, Occhipinti P, Verma A, Oldenbourg R, Gladfelter AS, Tani T (2016) Dissection of molecular assembly dynamics by tracking orientation and position of single molecules in live cells. *Proc National Acad Sci* 113:E6352–E6361
- Nakamichi Y, Kalatsky VA, Watanabe H, Sato T, Rajagopalan U, Tanifuji M (2018) 3D topology of orientation columns in visual cortex revealed by functional optical coherence tomography. *J Neurophysiol* 119:1562–1575
- Nakamichi Y, Okubo K, Sato T, Hashimoto M, Tanifuji M (2019) Optical intrinsic signal imaging with optogenetics reveals functional cortico-cortical connectivity at the columnar level in living macaques. *Sci Rep-uk* 9:6466
- Roome CJ, Kuhn B (2018) Simultaneous dendritic voltage and calcium imaging and somatic recording from Purkinje neurons in awake mice. *Nat Commun* 9:3388
- Tominaga Y, Taketoshi M, Tominaga T (2018) Overall assay of neuronal signal propagation pattern with long-term potentiation (LTP) in hippocampal slices from the CA1 area with fast voltage-sensitive dye imaging. *Front Cell Neurosci* 12:389
- Tominaga Y, Taketoshi M, Maeda N, Tominaga T (2019) Wide-field single-photon optical recording in brain slices using voltage-sensitive dye. *J Vis Exp* 148:e59692. <https://doi.org/10.3791/59692>
- Toyota M (2019) SB-1 Long-distance Ca^{2+} signaling via glutamate receptor channels in plants. *Microscopy* 68:i13–i13
- Toyota M, Spencer D, Sawai-Toyota S, Jiaqi W, Zhang T, Koo AJ, Howe GA, Gilroy S (2018) Glutamate triggers long-distance, calcium-based plant defense signaling. *Science* 361:1112–1115
- Wen J, Hung A (2019) Effects of C-terminal carboxylation on α -Conotoxin LsIA interactions with human $\alpha 7$ nicotinic acetylcholine receptor: molecular simulation studies. *Mar Drugs* 17:206

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.