LEVENTE CSERI PhD
Biological Chemistry Department, BrainVisionCenter
6/1 43-46. Liliom Str., 1094 Budapest, HUNGARY
+36 70 594 9413 / levente.cseri@brainvisioncenter.com / www.brainvisioncenter.com

Molecular probes with extended conjugation for the monitoring of neuron membrane potential

Zsófia Horváth,[1,2] Réka Lányi,[3] Zoltán Mucsi,[1] Levente Cseri[1,2]

[1]Biological Chemistry Department, BrainVisionCenter, 6/1 43-46. Liliom Str., 1094 Budapest, Hungary; E-mail: levente.cseri@brainvisioncenter.com

[2]Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, 3. Muegyetem rakpart, 1111 Budapest, Hungary

[3]Department of Biology, BrainVisionCenter, 6/1 43-46. Liliom Str., 1094 Budapest, Hungary

Introduction

The detailed understanding of neuron activity and network structures holds the promise of new treatments for neurological diseases and the development of the next generation of brain–computer interfaces. To effectively study neurons, the spikes of swift membrane potential change should be detectable and observable over time. Voltage sensitive dyes (VSDs) enable the fast non-invasive simultaneous monitoring of membrane potential in a large number of neurons with fluorescence microscopy, but the currently available sensors are limited by their low fluorescence enhancement and brightness. A better understanding of the voltage sensing mechanism and a facile screening method of candidate molecules could lead to the development of more efficient VSDs.

Methods

VSDs were synthesized from commercially available chemicals in 6–8 synthetic steps. Time-dependent density functional theory (DFT) calculations were carried out in Gaussian 16 with B3LYP method and 6-311+G(d,p) basis set to predict spectroscopic properties. Two-photon microscopy experiments were conducted on a 3D acousto-optic laser-scanning microscope (ATLAS, Femtonics). Femtosecond laser pulses were provided by a Chameleon Discovery laser (Coherent) operated at 840 nm. Voltage signals were induced in HEK cells using whole-cell patch-clamp method.

Results & Discussion

This work focuses on several aspects of VSD development. First, the role of the lipophilic wire part of a prominent VSD were systematically modified synthetically and studied by computational methods to explore its role in the voltage sensing

LEVENTE CSERI PhD
Biological Chemistry Department, BrainVisionCenter
6/1 43-46. Liliom Str., 1094 Budapest, HUNGARY
+36 70 594 9413 / levente.cseri@brainvisioncenter.com / www.brainvisioncenter.com

mechanism and to identify a pathway to property improvements. Second, novel VSDs were synthesized based on a tetraoxaazapentacene fluorophore to acheive high photostability and improved two-photon fluorescence properties. Finally, the novel VSDs were tested in single-photon spectroscopic experiments using a liposomal system and two-photon microscopic experiments with HEK cells.