SYNTHESIS OF TIOPHENE MODIFIED BODIPY BASED POLARITY SENSORS AND THEIR PHOTOPHYSICAL PROPERTIES IN LIPID MEMBRANES

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Lipid raft hypothesis suggests that cell membrane is composed of rigid compartments (liquid-ordered phase Lo) enriched with sphingolipids and cholesterol floating in the sea of glycerophospholipids (liquid-disordered phase Ld) [1]. It has been shown that Lo phase is involved in many normal cellular processes such as signal transduction and cholesterol homeostasis, while also being significant in evolution of neurodegenerative diseases such as Alzheimer's [2]. To elucidate the importance of lipid rafts for cellular processes it is important to visualize these domains in living cells. This can be achieved by environment-sensitive dyes that can discern between Ld and Lo phases based on their ability to sense differences in polarity [3]. Probes that sense polarity by their fluorescence lifetime are immensely useful in cell imaging by using FLIM (*fluorescence lifetime imaging microscopy*) [4]. In this communication we report four red-emitting BODIPY polarity sensors that were synthesized and tested in model lipid membranes (Fig. 1.). Initial BODIPY fluorophores were synthesized by methods well described in literature [5]. Afterwards we introduced bromine atoms into the 2,6 and 2,3,5,6 positions of BODIPY core to produce brominated dyes. Finally, Pd-catalyzed cross-coupling reaction between brominated dyes and 2-(tributylstannyl)tiophene was employed to produce red-emitting polarity probes. After synthesis, fluorophores were inserted into LUV's (large unilamellar vesicles) that were produced by extrusion. Ld liposomes were formed from DOPC, while Lo phase was obtained from a mixture of DOPC/DPPC and cholesterol. The fluorescence lifetime of all the probes was shorter in Ld phase. This can be explained by the fact that our probes have faster decays in polar environments. On the other hand, the difference of fluorescence lifetimes was higher for disubstituted probes (-$OC_{10}H_{21}$: 0.314 ns; -$OC_{16}H_{33}$: 0.439 ns) than for the tetrasubstituted ones (-$OC_{10}H_{21}$: 0.084 ns; -$OC_{16}H_{33}$: 0.129 ns), meaning that BDP-$(Tioph)_2$ fluorophores can discriminate lipid rafts from the Ld phase more effectively than BDP-$(Tioph)_4$ probes. Also, it is important to notice that the length of the alkoxy group at the meso position does not significantly affect the photophysical properties of these dyes.

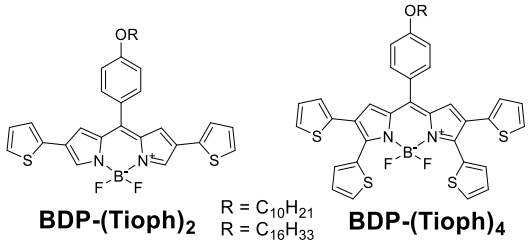

Fig. 1. Di- and tetra- substituted BODIPY polarity sensors.

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