BMC Neuroscience

Lecture presentation

Open Access

Single-molecule tracking of raft-based signal transduction: a system of digital signal transduction?

Akihiro Kusumi

Address: Membrane Mechanisms Project, ICORP-JST, Institute for Integrated Cell-Material Sciences (iCeMS); Research Center for Nano Regenerative Medical Engineering, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan

Email: Akihiro Kusumi - akusumi@frontier.kyoto-u.ac.jp

from Seventeenth Annual Computational Neuroscience Meeting: CNS*2008
Portland, OR, USA. 19–24 July 2008

Published: 11 July 2008

BMC Neuroscience 2008, **9**(Suppl 1):L6 doi:10.1186/1471-2202-9-S1-L6

This abstract is available from: http://www.biomedcentral.com/1471-2202/9/S1/L6

The plasma membranes of neuronal cells contain high concentrations of glycosphingolipids and glycosylphosphatidylinositol-anchored receptors (GPI-ARs), as well as cholesterol, which suggests important roles played by hypothetical microdomains, called raft domains in these membranes. Using simultaneous two-color single-molecule tracking of GPI-ARs, as well as intracellular lipid-anchored signaling molecules, Gαi, Lyn, and PLCγ, we have obtained results showing that the plasma membrane is poised for assembly of these molecules, upon the external stimulation that initiates oligomerization of 3–9 GPI-AR molecules.

The receptor-cluster-induced, cholesterol-dependent assembly, termed receptor-cluster raft (RCR), works as a platform for the signal transducton of GPI-AR. Gαi2 and Lyn (GFP conjugates) are recruited to RCRs frequently, but transiently (100–200 ms), based on protein-protein and lipid-lipid (raft) interactions. Gαi2 binding to and its subsequent activation of Lyn are likely to take place within the same RCR, resulting in actin-dependent temporary immobilization (0.57-s lifetime, called Stimulation-induced Temporary Arrest of LateraL diffusion or STALL, every 1.3 s), inducing the temporary (250 ms) recruitment of PLCγ2, for IP_3 production. Therefore, the RCR in STALL is a key, albeit transient, platform for transducing the extracellular GPI-AR signal to the intracellular IP_3-Ca^{2+} signal, via PLCγ2 recruitment.

The bulk activation of IP_3-Ca^{2+} signaling and Src-family kinases persists over several minutes to several 10 s of minutes. Meanwhile, single-molecule events, such as STALL and the recruitment of PLCγ2, Gαi2, and Lyn to RCR, lasted only for a fraction of a second. Namely, individual single-molecule events may occur like a digital pulse, and the bulk analogue-type activation of signaling molecules may be the result of superposition of these pulse-like signals. In this sense, the basic signaling mechanism in the raft-based signaling system could be called digital or frequency-modulated.