

SCIENTIFIC SEMINAR



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How is neurotransmitter release triggered in microseconds

Great advances have been made to understand the molecular mechanisms underlying neurotransmitter release, but two central questions have remained unanswered: how is membrane fusion induced and how does Ca^{2+} help to trigger fusion in microseconds. Thus, it is known that the SNARE proteins syntaxin-1, SNAP-25 and synaptobrevin form a tight four-helix bundle called the SNARE complex that brings the synaptic vesicle and plasma membranes together, but bringing membranes into contact is not sufficient for fusion. It is also clear that the Ca^{2+} sensor synaptotagmin-1 triggers fast release in cooperation with the SNAREs, but the mechanism of action of synaptotagmin-1 is unknown. Our all atom molecular dynamics simulations now suggest that extension of the SNARE helices into the juxtamembrane sequences preceding their transmembrane regions initiates fast, microsecond scale membrane fusion because it catalyzes encounters of the hydrophobic acyl chains of lipids from both membranes at the polar bilayer interface. Our simulations, together with NMR and FRET data, also suggest that helical extension into the juxtamembrane regions is hindered by energy barriers and that synaptotagmin-1 acts as a lever that, upon Ca^{2+} influx, facilitates such extension by re-orienting on the membrane and pulling the SNARE complex.

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Wednesday

July 16

Atrio 800

12.00H



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