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Coarse-grained molecular dynamics simulations study on localized membrane curvature induced by the tetanus toxin and lipid composition

G. Mahamithawa and S.P. Rajapaksha*

Department of Chemistry, Faculty of Applied Sciences, University of Sri Jayewardenepura, Gangodawila, Sri Lanka

Tetanus toxin (Tetanospasmin), a proteinaceous toxin secreted by Clostridium tetani bacteria, is responsible for the inactivation of inhibitory interneurons leading to tetanus. The internalization mechanism of the toxin into the neurons has not yet been definitively identified. The focus of this coarse-grained molecular dynamics (CGMD) simulation study was to determine the capability of the tetanus toxin to generate localized membrane curvatures that could act as the trigger to clathrin mediated endocytosis. CGMD simulations were carried out with protein attached and detached membranes to identify the toxin's capability of inducing membrane curvatures. A dipalmitoylphosphatidylcholine (DPPC) membrane (>1700 DPPC residues) with the potential of -70 mV yielded a 0.004 $Å^{-1}$ positive curvature after 400 ns, and reversed potentials (+70 mV) yielded a -0.002 $Å^{-1}$ curvature. Increment of the applied potential to +/- 140 mV leads to produce rapid curvatures (0.003 $Å^{-1}$ and -0.007 $Å^{-1}$ after 50 ns, respectively). Increasing the membrane negative charge by introducing 1,2-dioleoyl-snglycero-3-phosphoserine (DOPS), dipalmitoylphosphatidyl -inositol (DPPI) lipids and additional monosialotetrahexosylganglioside (GM1a) toxin receptors at -70 mV resulted a higher induced curvature, which was highly pronounced with the presence of the toxin. Unsaturated lipid tails showed a drastic increase in the curvature of 0.006 $Å^{-1}$ after 115 ns at -70 mV. Incorporation of large headgrouped lipids into the bilayer showed a -0.007 $Å^{-1}$ curvature even in the absence of the toxin at -70 mV producing a reduced curvature even with a higher overall charge and unsaturations in the membrane. The study suggests that the tetanus toxin is capable of inducing membrane curvatures, and the magnitude of the curvature depends on the applied potential, membrane charge and nature of the lipids.

Keywords: Tetanus toxin, molecular dynamics simulations, membrane curvature

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E-mail: suneth@sjp.ac.lk