UC Merced Center for Computational Biology

Applied Mathematics & Center for Computational Biology Joint Seminar

Biomolecular Manipulations With Nanosecond Pulsed Electric Fields — In Cells and In Silico

Presented by

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Abstract

Alterations in the asymmetric arrangement of phospholipids in the plasma membrane serve as both semaphore and structural framework in platelet activation, lymphocyte signal transduction, angiogenesis, and the phagocytotic clearance of apoptotic cells and aging erythrocytes. Nanosecond, megavolt-per-meter electric pulses — high instantaneous power but low total energy — induce phosphatidylserine (PS) externalization without physically disrupting the membrane, providing a means for manipulating a key biomolecular structure in living cells through a remote, non-contact agent. Effects of nanoelectropulse exposure include not only phospholipid translocation but also, with doses appropriate for the cell type and the physical and chemical environment, intracellular calcium release, activation of neural cells, chromatin structural modifications, and apoptosis. Experimental evidence is consistent with electrophysical models that predict the penetration of electrical pulses with durations shorter than the charging time of the cell membrane (< 100 ns) into the cell interior. Real-time fluorescence microscopic observations and molecular dynamics (MD) simulations associate membrane perturbation directly and immediately with nanoelectropulse exposure and support the hypothesis that PS externalization is driven by the porating potential that develops across the lipid bilayer as the membrane capacitance charges during a pulse. Nanometer-diameter hydrophilic pores form within nanoseconds of the application of megavolt-per-meter electric fields normal to the lipid bilayer in MD simulations, and PS migrates electrophoretically through the pores in the direction of the anode, consistent with imaging analysis of PS externalization using the fluorescent dye FM1-43 and fluorescent conjugates of the PS-binding protein annexin V. MD simulations are facilitating investigations of nanopore initiation mechanisms and lifetime, and the behavior of biomolecules in high electric fields. Because of the present inaccessibility of the nanosecond time scale to real-time cell biological investigations, the development of effective nanoelectropulse therapeutic regimens for cancer may depend on the accuracy of fine-grained simulations of systems of cells and tissues, a challenge for both modelers and experimentalists.

P. Thomas Vernier is Engineering Manager of MOSIS and Research Scientist at the University of Southern California Information Sciences Institute. His research and industrial experience includes ultraviolet microscopy analysis of S-adenosylmethionine metabolism in the yeast Rhodotorula glutinis, molecular biology of the temperature-sensitive host restriction of bacterial viruses in Pseudomonas aeruginosa, low-level environmental gas monitoring, wide-band instrumentation data recording, and semiconductor device modeling and electrical characterization. He currently concentrates on the effects of nanosecond, megavolt-per-meter electric fields on biological systems, combining experimental observations with molecular dynamics simulations, and on the integration of cellular and biomolecular sensors, carbon nanotubes, and quantum dots with commercial integrated electronic circuit fabrication processes.

Vernier received his Ph.D. in Electrical Engineering from the University of Southern California in 2004, and is a member of the American Chemical Society, American Society for Cell Biology, American Society for Microbiology, Bioelectrochemical Society, Bioelectromagnetics Society, and Institute of Electrical and Electronics Engineers.

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