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## PHARMACEUTICAL BIOTECHNOLOGY

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**Design strategies for nanoparticles translocating through lipid bilayers**Vladimir A Baulin<sup>1</sup>, Marco Werner<sup>1</sup>, Yachong Guo<sup>1</sup>, Emmanuel Terazzi<sup>2</sup>, Ralf Seeman<sup>3</sup> and Jean Baptiste Fleury<sup>3</sup><sup>1</sup>Universitat Rovira i Virgili, Spain<sup>2</sup>University of Geneva, Switzerland<sup>3</sup>Universitat des Saarlandes, Germany

Design of nanomaterials able to cross lipid bilayers is a challenging task in nanotechnology. Large variety of shapes, sizes and surface coatings are used for the design of nanomaterials to overcome this barrier. However, the potential barrier is quite high for carbon nanotubes and nanoparticles to cross the lipid bilayer to translocate by thermal motion. It is generally accepted that small hydrophobic nanoparticles are blocked by lipid bilayers and accumulate in the bilayer core, while nanoparticles with sizes larger than 5 nm can only penetrate cells through a slow energy-dependent processes such as endocytosis, lasting minutes. In one example, we show how variation of hydrophobicity of the nanoparticles can lead to passive translocation of nanoparticles through lipid bilayer. This adsorption transition through reversible destabilization of the structure of the bilayer induces enhanced permeability for water and small solutes. In another example, we demonstrate that lipid-covered hydrophobic nanoparticles may translocate through lipid membranes by direct penetration within milliseconds. We identified the threshold size for translocation: nanoparticles with diameters smaller than 5 nm stay trapped in the bilayer, while nanoparticles larger than 5 nm insert into bilayer, open transient pore in the bilayer. Using the Single Chain Mean Field (SCMF) theory a mechanism of passive translocation through lipid bilayers is proposed. Observing individual translocation events of gold nanoparticles with 1-dodecanethiol chains through DMPC bilayers, we confirm the particle translocation and characterize the kinetic pathway in agreement with our numerical predictions. Mechanism relies on spontaneous pore formation in the lipid bilayer. The observed universal interaction behavior of neutral and chemically inert nanoparticles with bilayer can be classified according to size and surface properties.

**Recent Publications:**

1. S Pogodin and V A Baulin (2010) Can a Carbon Nanotube Pierce through a Phospholipid Bilayer? ACS Nano, 4: 5293–5300.
2. S Pogodin and V A Baulin (2011) Equilibrium Insertion of Nanoscale Objects into Phospholipid Bilayers. Curr. Nanosci. 7 (5): 721–726.
3. S Pogodin, M Werner, J U Sommer and V A Baulin (2012) Nanoparticle-Induced Permeability of Lipid Membranes, ACS Nano, p. 10555–10561.
4. Y Guo, E Terazzi, R Seemann, J B Fleury, and V A Baulin (2016) Direct proof of spontaneous translocation of lipid-covered hydrophobic nanoparticles through a phospholipid bilayer. Sci. Adv. 2 (11): 1600261.
5. S Pogodin and V A Baulin (2010) Coarse-Grained Models of Phospholipid Membranes within the Single Chain Mean Field Theory, Soft Matter. 6: 2216–2226.

**Biography**

Vladimir A Baulin has completed his graduation with honors from the Physics Department at Moscow State University in 2000. He spent three years in the Commissariat à l'Energie Atomique, Grenoble, France, pursuing his PhD in theory of polymer physics and received a PhD in Physics in 2003. In 2004-2006 he was a Postdoctoral Researcher at the Institut Charles Sadron, Strasbourg, France. Since 2008, he leads a group of Soft matter theory at the University Rovira i Virgili, Tarragona, Spain. He is a Coordinator of EU funded initial training network SNAL: smart nano-objects for alteration of lipid bilayers.

Vladimir.baulin@urv.cat