Supporting Information

Electrophysiological Characterization of Membrane Disruption by Nanoparticles

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Nanoparticles - The relationship between particle size, concentration and surface area is given in Table S1. The silica nanosphere diameters were measured with dynamic light scattering; the calculations are based on an ideal spherical geometry and a silica density of 2.0 g/cm^3. The volume of the droplets is 2 μL for electrophysiology experiments and 1 μL for confocal fluorescence microscopy of individual droplets.

Table S1 – Concentration and total surface area of silica nanospheres

Nominal particle diameter [nm]	Measured particle diameter [nm]	Particle concentration [μL^{-1}]	Particle molar concentration [M]	Weight/volume concentration [μg/mL]	Total particle surface area [$\mu m^2/\mu L$]
50	61	5,000	$8.3 \cdot 10^{-15}$	$1.2 \cdot 10^{-3}$	$5.8 \cdot 10^{1}$
500	462	5,000	$8.3 \cdot 10^{-15}$	$5.2 \cdot 10^{-1}$	$3.4 \cdot 10^{3}$
	490	5,000	$8.3 \cdot 10^{-15}$	$6.2 \cdot 10^{-1}$	$3.8 \cdot 10^{3}$
50	61	500,000	$8.3 \cdot 10^{-13}$	$1.2 \cdot 10^{-1}$	$5.8 \cdot 10^{3}$
50	61	5,000,000	$8.3 \cdot 10^{-12}$	1.2	$5.8 \cdot 10^{4}$
500	462	5,000,000	$8.3 \cdot 10^{-12}$	$5.2 \cdot 10^{2}$	$3.4 \cdot 10^{6}$
	490	5,000,000	$8.3 \cdot 10^{-12}$	$6.2 \cdot 10^{2}$	$3.8 \cdot 10^{6}$

Diffusion model - We solved the diffusion equation $c_t = D\ \nabla^2 c$ in spherical coordinates, with the diffusion coefficient D calculated using the Stokes-Einstein relation for each nanoparticle species. On the surface of the droplet we used the zero sink boundary condition, *i.e.* $c = 0$, which essentially assumes that any nanoparticle that becomes in contact with the droplet boundary (i.e. the lipid layer) is instantaneously and irreversibly adsorbed to it. The analytic solution for this problem is presented in Crank[1] and we implemented this in Matlab. The zero sink boundary condition is appropriate for a situation where the nanoparticles have a strong tendency to associate with the lipids and where crowding effects on the lipid membrane are negligible. In Figure S1, the flux represents the average number of particles diffusing into the lipid layer as a function of time, while the cumulative flux represents the average number of particles that has become associated with the lipid layer. The maximum number of particles that could have crossed the lipid bilayer was taken as the value of the cumulative flux (mol μm^{-2}) multiplied by the bilayer area (0.06 mm^2). Some key parameters are given in Table S2 and S3, for electrophysiology and cross-over experiments, respectively.

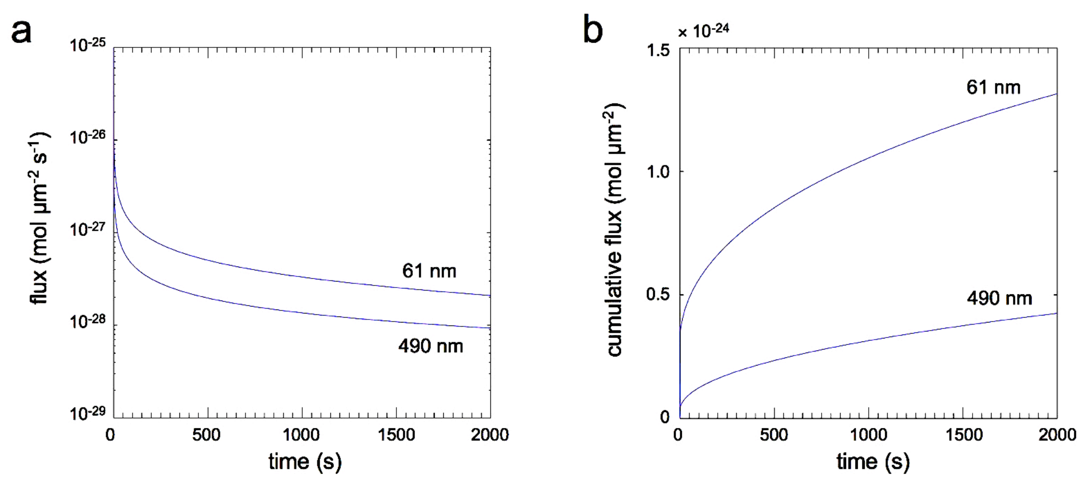

Figure S1 – Time dependence of (a) the flux and (b) the cumulative flux of 61-nm and 490-nm diameter particles at the droplet boundary according to the zero sink diffusion model. The initial nanoparticle concentration is 8.3 pM ($5 \cdot 10^6$ particles/μL) and the droplet volume is 2 μL.

Table S2 – Particle flux at the lipid bilayer, fraction of particles present at the droplet boundary, fraction of the boundary area occupied by nanoparticles, and number of nanospheres at the lipid bilayer area, calculated from the flux and the cumulative flux at t = 2000 s. The initial nanoparticle concentration is 8.3 pM ($5 \cdot 10^6$ particles/μL), the droplet volume is 2 μL, and the bilayer area is 0.06 mm^2.

Nominal particle diameter [nm]	Measured particle diameter [nm]	Flux at droplet boundary [mol μm^{-2} s^{-1}]	Flux at bilayer area [particles s^{-1}]	Cumulative flux at droplet boundary [mol μm^{-2}]	Fraction of particles at boundary	Surface coverage by nano-spheres	Number of particles at bilayer
50	61	$2.10 \cdot 10^{-28}$	8.47	$1.31 \cdot 10^{-24}$	60 %	0.3 %	$5.29 \cdot 10^4$
500	462	$9.57 \cdot 10^{-29}$	3.86	$4.59 \cdot 10^{-25}$	21 %	5.9 %	$1.85 \cdot 10^4$
	490	$9.32 \cdot 10^{-29}$	3.76	$4.44 \cdot 10^{-25}$	20 %	6.1 %	$1.71 \cdot 10^4$

Table S3 – Cumulative particle flux at the lipid bilayer area at t = 2000 s for the particle concentration as used for the fluorescence microscopy experiments. The initial nanosphere concentration is 58 pM ($3.8 \cdot 10^7$ particles/μL), the droplet volume is 2 μL, and the bilayer area is 0.06 mm^2.

Nominal particle diameter [nm]	Measured particle diameter [nm]	Flux at droplet interface [mol μm^{-2} s^{-1}]	Cumulative flux at droplet interface [mol μm^{-2}]	Cumulative flux at bilayer	
				Number of particles	Fraction of total particles
50	61	$1.47 \cdot 10^{-27}$	$9.18 \cdot 10^{-24}$	$3.70 \cdot 10^5$	0.53 %
500	462	$6.68 \cdot 10^{-28}$	$3.07 \cdot 10^{-24}$	$1.24 \cdot 10^5$	0.18 %
	490	$6.51 \cdot 10^{-28}$	$2.97 \cdot 10^{-24}$	$1.20 \cdot 10^5$	0.17 %

Reference

1. Crank, J. *The Mathematics of Diffusion*; Oxford University Press: Oxford, 1975.