Electronic supplementary information

Nanoplastics Penetration Across the Blood-Brain Barrier

Annemarie Ianos,[a,§] Jessica Zhou,[a,§] Tongxuan Qiao,[b] Tao Wei,[c] Baofu Qiao [a,*]

[§] A.I. and J.Z. contributed equally.

* Corresponding author: Baofu.Qiao@baruch.cuny.edu

Supporting Tables:

Table S1. Composition in each leaflet of the BBB apical bilayer. [a]

Type	POPC	CHOL	OSM	SLPC	SOPE	SAPE	SAPC	SAPS	SAPI
Number	4	28	18	8	6	14	8	8	2
Percent, %	4.2	29.2	18.8	8.3	6.2	14.6	8.3	8.3	2.1

[a] POPC = 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine,

CHOL = cholesterol,

OSM = N-oleoyl-d-erythro-sphingosylphosphorylcholine,

SLPC = 1-stearoyl-2-linoleoyl-sn-glycero-3-phosphocholine,

SOPE = 1-stearoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine,

SAPE = 1-stearoyl-2-arachidonoyl-sn-glycero-3-phosphoethanolamine,

SAPC = 1-stearoyl-2-arachidonoyl-sn-glycero-3-phosphocholine,

SAPS = 1-stearoyl-2-arachidonoyl-sn-glycero-3-phospho-L-serine,

SAPI = 1-stearoyl-2-arachidonoyl-sn-glycero-3-phosphoinositol.

Table S2. Area per lipid (APL, Å^2) at varying temperatures in the control systems (without polymers). [a]

BBB apical bilayer					
Temperature	**303 K**	**350 K**	**400 K**	**450 K**	**500 K**
APL (This work)	48.0 ± 0.7	53.5 ± 0.8	60.0 ± 1.2	67.5 ± 1.5	75.2 ± 3.3
Ref. [1]	45.3 @310K	52.3	60.6	67.1 @440K 70.3 @460K	73.9
POPC bilayer					
Temperature	**303 K**	**350 K**	**400 K**	**450 K**	**500 K**
APL (This work)	63.9 ± 1.2	69.5 ± 1.3	76.5 ± 1.3	85.6 ± 1.8	97.0 ± 2.6
Ref.	64.1 ± 0.1 [2] 64.3 [3] 68.3 ± 1.5 [2]	68.1 @333K [3]	-	-	-

a) The water-to-lipid number ratio is 50 : 1. [NaCl] = 150 mM. The simulations run 800 ns at 303K, 100 ns at 350 K and 400K, and 200 ns at 450 K and 500 K.

Table S3. Area per lipid (APL, Å^2) in different simulation conditions in the presence of nanoparticles.

		BBB_PE	**BBB_PP**	**BBB_PS**	**BBB_PET**	**Control**
Interior [a]	Steered MD [b]	51.7 ± 0.5	51.1 ± 0.5	50.2 ± 0.6	53.2 ± 0.7	-
	unbiased MD [c]	51.6 ± 0.6	50.5 ± 0.6	50.2 ± 0.7	52.8 ± 0.6	
Outside [a]	Steered MD [b]	47.9 ± 0.5	47.4 ± 0.6	47.4 ± 0.5	48.0 ± 0.7	48.0 ± 0.7 [e]
	unbiased MD [d]	47.9 ± 0.8	47.9 ± 0.6	47.8 ± 0.7	47.8 ± 0.7	

a) "Interior": polymer nanoparticle is in the interior of the BBB bilayer; "Outside": polymer nanoparticle is in the bulk water phase (*i.e.*, has no contact with the BBB).
b) Data were collected using the sMD simulations, with the first 20 ns trajectory abandoned.
c) Data are collected from the nanoparticle dissolution simulations (600 ns each).
d) Data in control simulations of the nanoparticles in the water phase (400 ns each).
e) Data of a control simulation of the BBB bilayer (*i.e.*, without nanoparticles). See Table S2.
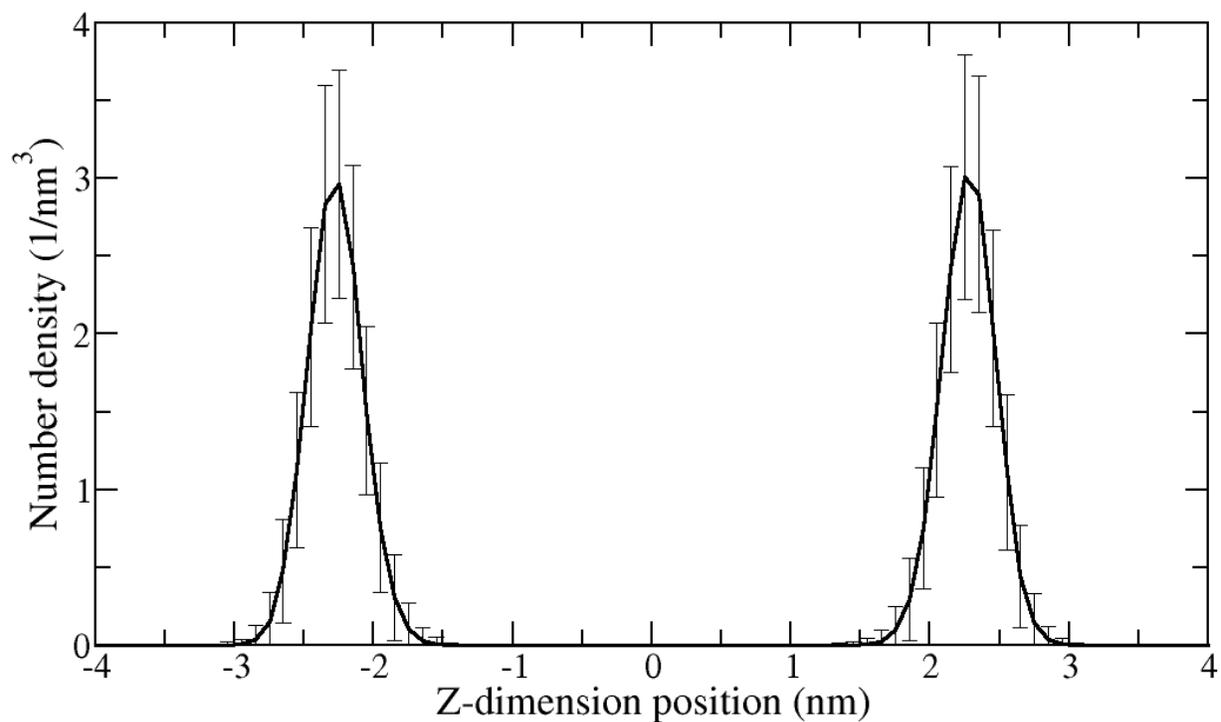
Supporting Figures:

Fig. S1. Number density profile of the lipid phosphorus atoms as a function of the distance to the BBB bilayer center in the control simulation (without polymers) at 303 K. The error bars stand for the standard deviations calculated from the last 0.75 μs of the 0.8 μs control simulation. The thickness of the BBB bilayer is thus estimated to be around 4.5 nm.
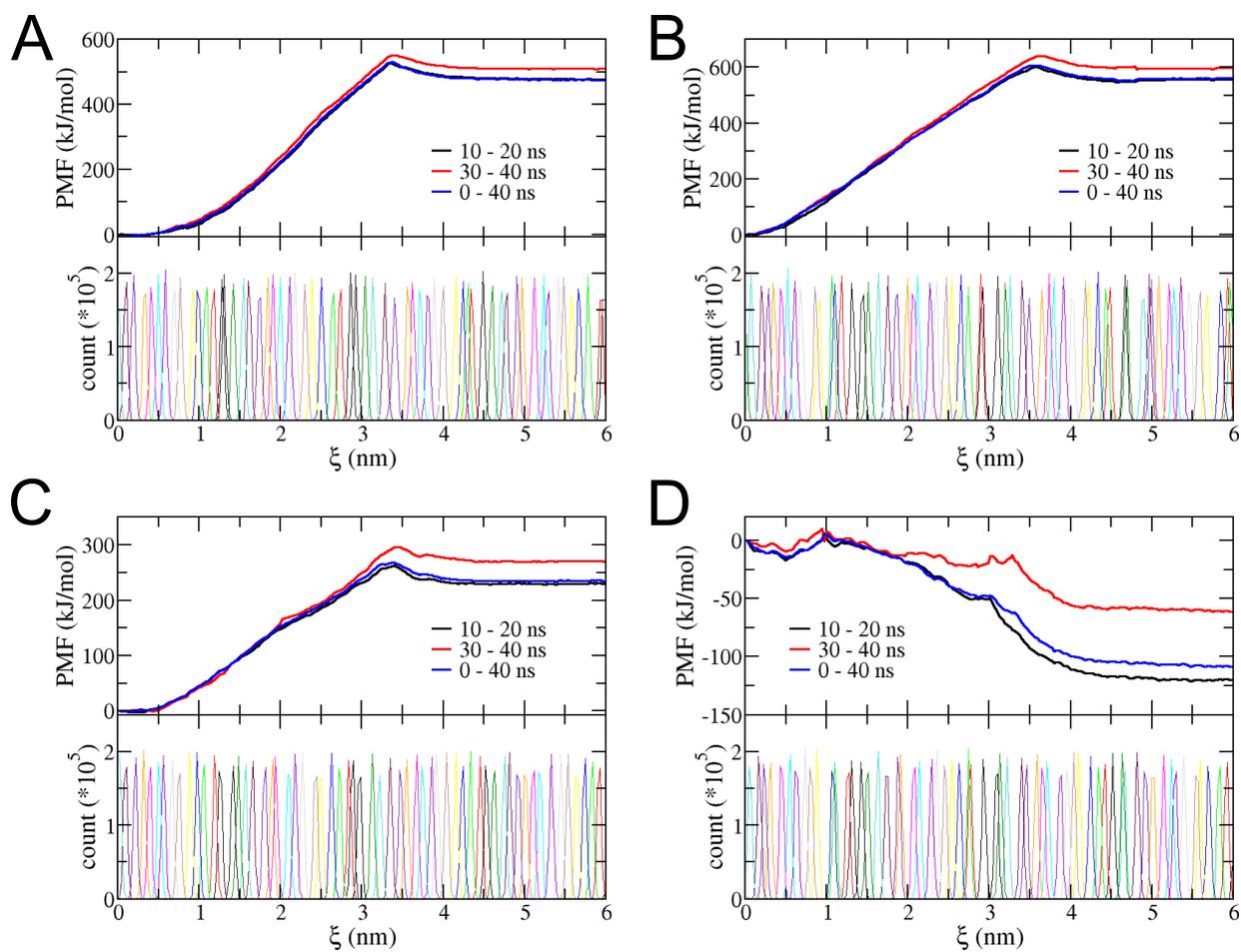
Fig. S2. Convergence of the PMF calculations for the polymer nanoparticles. (**A**) PE, (**B**) PP, (**C**) PS, and (**D**) PET. In each subplot, presented in the top one are the PMF profiles calculated at different simulation periods, with the histogram distribution of the WHAM analysis provided in the bottom one.
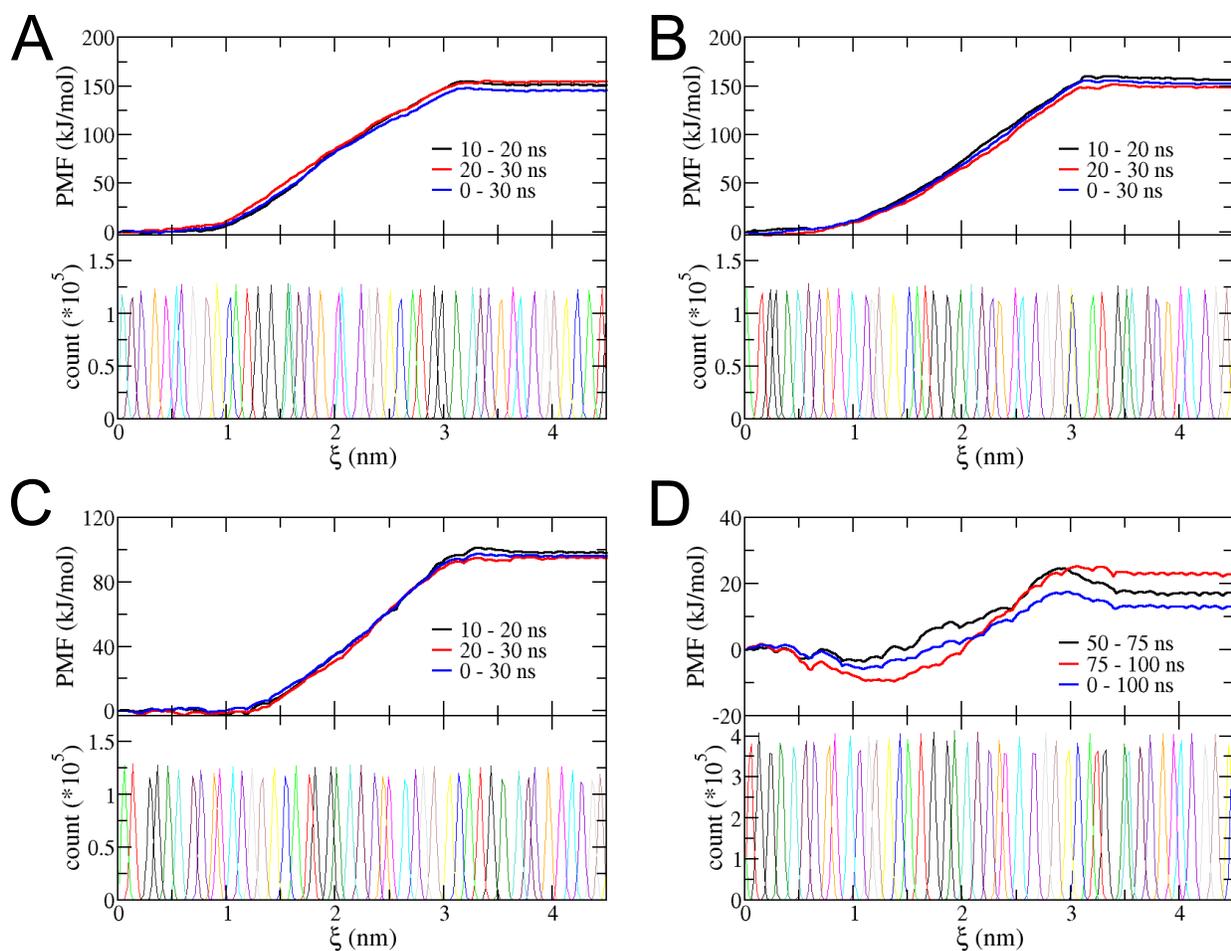
Fig. S3. Convergence of the PMF calculations for single polymer chains. (**A**) PE, (**B**) PP, (**C**) PS, and (**D**) PET. In each subplot, presented in the top one are the PMF profiles calculated at different simulation periods, with the histogram distribution of the WHAM analysis provided in the bottom one.

References:

1. Y. Wang, E. Gallagher, C. Jorgensen, E. P. Troendle, D. Hu, P. C. Searson and M. B. Ulmschneider, *Sci. Rep.*, 2019, **9**, 6117.
2. J. Lee, X. Cheng, J. M. Swails, M. S. Yeom, P. K. Eastman, J. A. Lemkul, S. Wei, J. Buckner, J. C. Jeong, Y. Qi, S. Jo, V. S. Pande, D. A. Case, C. L. Brooks, A. D. MacKerell, J. B. Klauda and W. Im, *J. Chem. Theory Comput.*, 2016, **12**, 405-413.
3. N. Kučerka, M.-P. Nieh and J. Katsaras, *Biochim. Biophys. Acta, Biomembr.*, 2011, **1808**, 2761-2771.