Supporting Information

Partner-facilitating transmembrane penetration of nanoparticles: a biological test in Silico

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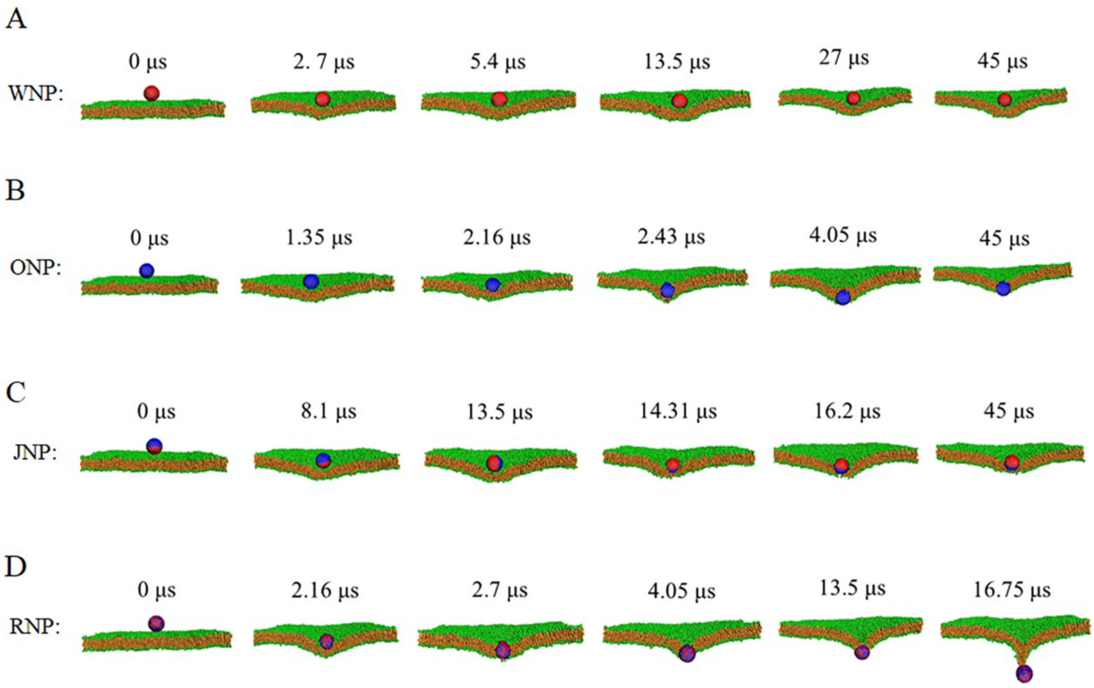

Figure S1. Representative translocation processes of the NPs into/across the lipid membranes. (A) WNP. It stays on the membrane surface at the end of the simulation; (B) ONP. It traps in the membrane at the end of the simulation; (C) JNP. It traps in the membrane at the end of the simulation; (D) RNP. It successfully translocates across the membrane during the simulation. In all cases, $F_s = 30\, {}^{k_BT}/_{r_c}, D_0 = 3\, r_c$.

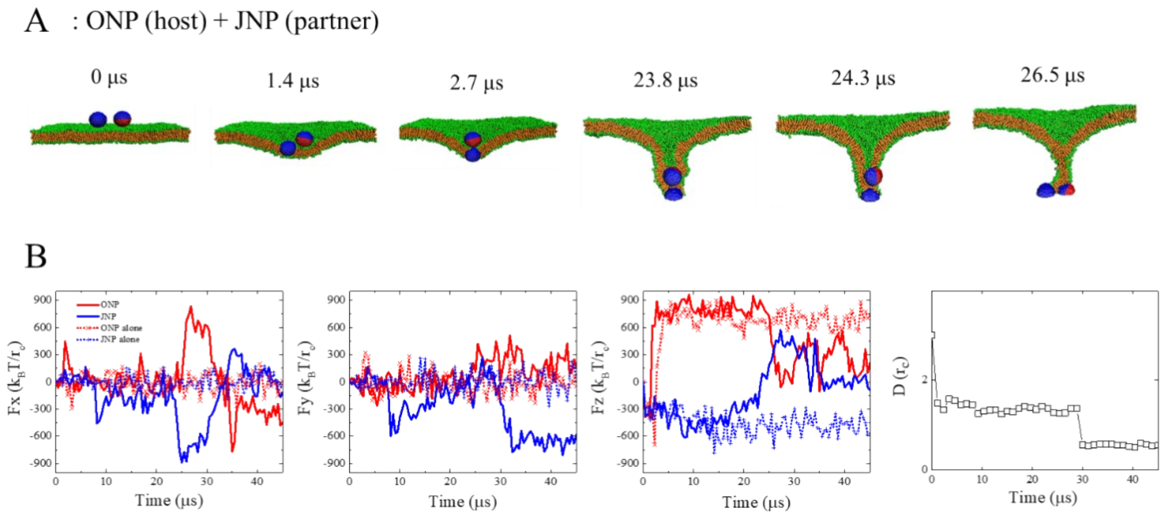

Figure S2. (A) Representative translocation process of a *host* ONP across a membrane with the help of a *partner* JNP. $F_s = 30\ {k_BT}/{r_c}$, $D_0 = 3\ r_c$ (B) Different components of NP-membrane forces and the inter-NP distance D in the translocation process. From left to right, figures correspond to x, y, and z components of the force and the final one is the evolution of D.

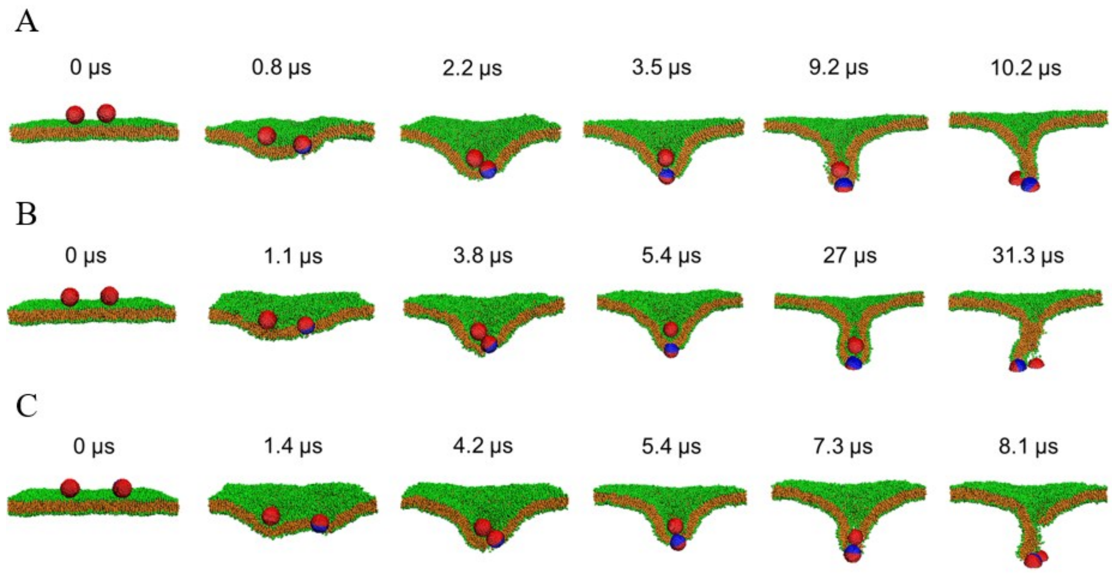

Figure S3. Representative translocation process of a WNP+JNP group across a membrane with varying initial separation D_0. (A) D_0=5 r_c, (B) D_0=8 r_c, and (C) D_0=12 r_c. $F_s = 35\ {k_BT}/{r_c}$.

WNP (host, $F_S = 35\ {}^{k_B\mathrm{T}}/_{r_c}$) + RNP (partner, $F_S = 30\ {}^{k_B\mathrm{T}}/_{r_c}$)

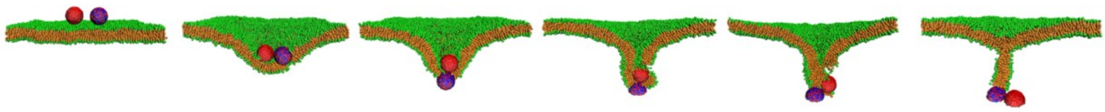

Figure S4. Representative translocation process of a *host* WNP across a membrane with the help of a *partner* RNP under the different driving forces. For the WNP, $F_s = 35\ {}^{k_BT}/_{r_c}$; For the RNP, $F_s = 30\ {}^{k_BT}/_{r_c}$, $D_0 = 3\ r_c$.

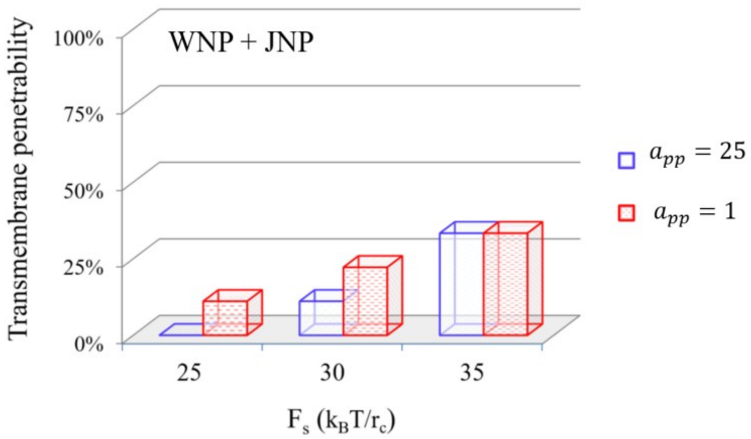

Figure S5. Transmembrane penetrability of a *host* WNP with the help of a *partner* JNP under the varying inter-NP affinity a_{pp}. In all cases here, $D_0 = 3\ r_c$.

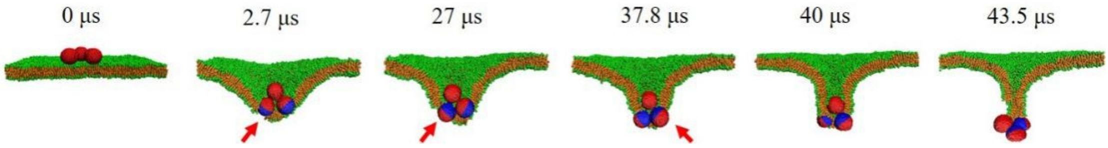

Figure S6. Representative translocation process of a *host* WNP across a membrane with the help of two *partner* JNPs. The arrows indicate the rotation of the JNP. $F_s = 30\, {}^{k_B T}\!/_{r_c}, D_0 = 3\, r_c$.

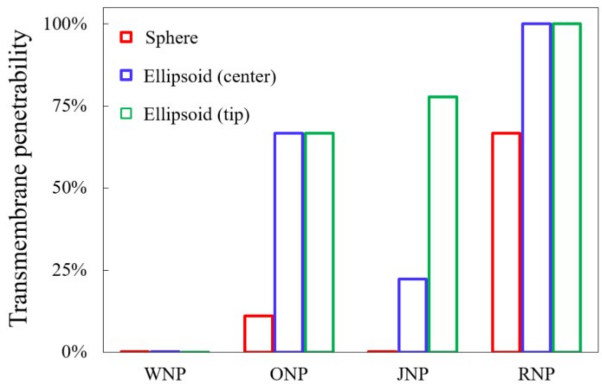

Figure S7. Transmembrane penetrability of one single NP with varying shape and the location of acting point of the driving force. In all cases, $D_0 = 3\ r_c$.

Table S1 Transmembrane penetrability of a NP (WNP, ONP, JNP or RNP) without or with a NP partner. $D_0 = 3\,r_c$.

Host NP	F_s (k_BT/r_c)	**Transmembrane penetrability** (n/m)*					
		Alone	+ *Partner* NP				
			+ WNP	+ ONP	+ JNP	+ RNP	**Total**
WNP	25	**0/3**	0/3	0/3	0/3	0/3	**0/12**
	30	**0/3**	0/3	0/3	1/3	0/3	**1/12**
	35	**0/3**	1/3	0/3	3/3	2/3	**6/12**
ONP	25	**0/3**	0/3	3/3	0/3	2/3	**5/12**
	30	**0/3**	0/3	3/3	2/3	3/3	**8/12**
	35	**1/3**	0/3	3/3	3/3	3/3	**9/12**
JNP	25	**0/3**	0/3	0/3	0/3	2/3	**2/12**
	30	**0/3**	1/3	2/3	2/3	0/3	**5/12**
	35	**0/3**	3/3	3/3	3/3	0/3	**9/12**
RNP	25	**0/3**	2/3	2/3	3/3	3/3	**10/12**
	30	**3/3**	3/3	3/3	3/3	3/3	**12/12**
	35	**3/3**	3/3	3/3	3/3	3/3	**12/12**

*Note: for n/m in the table, m stands for the total number of independent simulation events under a certain condition, while n refers to the successful times of transmembrane penetration of the *host* NP.

Table S2. Transmembrane penetrability of a *host* WNP with the help of a *partner* JNP under $a_{pp} = 1 {k_B T}/{r_c}$. $D_0 = 3\ r_c$.

Host NP	Fs ($k_B T/r_c$)	Transmembrane penetrability				
		+ *partner* NP				
WNP	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	1/3	0/3	**1/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	2/3	0/3	**2/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		1/3	0/3	3/3	2/3	**6/12**

Table S3. Transmembrane penetrability of a *host* WNP with two *partner* NPs. $D_0 = 3\ r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ Two *partner* NPs				
WNP	25	+ (WNP-WNP)	+ (ONP-ONP)	+ (JNP-JNP)	+ (RNP-RNP)	**Total**
		0/3	0/3	2/3	1/3	**3/12**
	30	+ (WNP-WNP)	+ (ONP-ONP)	+ (JNP-JNP)	+ (RNP-RNP)	**Total**
		0/3	3/3	2/3	1/3	**6/12**
	35	+ (WNP-WNP)	+ (ONP-ONP)	+ (JNP-JNP)	+ (RNP-RNP)	**Total**
		3/3	3/3	3/3	2/3	**11/12**

Table S4. Transmembrane penetration statistics of one single ellipsoidal NP with varying locations of acting point of the driving forces. $D_0 = 3\ r_c$.

NP Type	Fs (k_BT/r_c)	Transmembrane penetrability	
		ellipsoid (center)	ellipsoid (tip)
WNP	25	0/3	0/3
	30	0/3	0/3
	35	0/3	0/3
ONP	25	0/3	0/3
	30	3/3	3/3
	35	3/3	3/3
JNP	25	0/3	2/3
	30	0/3	2/3
	35	2/3	3/3
RNP	25	3/3	3/3
	30	3/3	3/3
	35	3/3	3/3

Table S5. Transmembrane penetrability of a *host* ellipsoidal WNP with a *partner* ellipsoidal NP (the driving forces act at the NP centers). $D_0 = 3\ r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ *partner* NP (ellipsoidal)				
WNP (ellipsoidal)	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	3/3	3/3	0/3	**6/12**

Table S6. Transmembrane penetrability of a *host* ellipsoidal WNP with a *partner* ellipsoidal NP (the driving forces act at the NP tips). $D_0 = 3\ r_c$.

<table>
<tr><td rowspan="2">Host NP</td><td rowspan="2">Fs (k_BT/r_c)</td><td colspan="5">Transmembrane penetrability</td></tr>
<tr><td colspan="5">+ partner NP (ellipsoidal)</td></tr>
<tr><td rowspan="6">WNP (ellipsoidal)</td><td rowspan="2">25</td><td>+ WNP</td><td>+ ONP</td><td>+ JNP</td><td>+ RNP</td><td>Total</td></tr>
<tr><td>0/3</td><td>0/3</td><td>0/3</td><td>0/3</td><td>0/12</td></tr>
<tr><td rowspan="2">30</td><td>+ WNP</td><td>+ ONP</td><td>+ JNP</td><td>+ RNP</td><td>Total</td></tr>
<tr><td>0/3</td><td>0/3</td><td>0/3</td><td>0/3</td><td>0/12</td></tr>
<tr><td rowspan="2">35</td><td>+ WNP</td><td>+ ONP</td><td>+ JNP</td><td>+ RNP</td><td>Total</td></tr>
<tr><td>1/3</td><td>0/3</td><td>2/3</td><td>0/3</td><td>3/12</td></tr>
</table>

Table S7. Transmembrane penetrability of a *host* spherical WNP with a *partner* prolate NP (the driving forces act at the NP centers). $D_0 = 3\,r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ *partner* NP (ellipsoidal)				
WNP (spherical)	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		1/3	0/3	0/3	0/3	**1/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	3/3	3/3	0/3	**6/12**

Table S8. Transmembrane penetrability of a *host* spherical WNP with a *partner* tilt-prolate NP (tilt angle: 45°, the driving forces act at the NP centers) . $D_0 = 3\ r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ *Partner* NP (ellipsoidal)				
WNP (spherical)	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	1/3	**1/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		1/3	3/3	3/3	0/3	**7/12**

Table S9. Transmembrane penetrability of a *host* spherical WNP with a *partner* oblate NP (the driving forces act at the NP centers) . $D_0 = 3\ r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ *Partner* NP (ellipsoidal)				
WNP (spherical)	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	2/3	2/3	0/3	**4/12**

Table S10. Transmembrane penetrability of a *host* spherical WNP (the driving forces act at the center) with a *partner* prolate NP (the driving forces act at the tip). $D_0 = 3\, r_c$.

Host NP	Fs (k_BT/r_c)	Transmembrane penetrability				
		+ *partner* NP (ellipsoidal)				
WNP (spherical)	25	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	30	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**
	35	+ WNP	+ ONP	+ JNP	+ RNP	**Total**
		0/3	0/3	0/3	0/3	**0/12**