Supplementary Information for Nanoparticle-Blockage-Enabled Rapid and Reversible Nanopore Gating with Tunable Memory

Rami Yazbeck, a,1 Yixin Xu, a,1 Tyrone Porter, b and Chuanhua Duan, a,2

a Department of Mechanical Engineering, Boston University, Boston, MA, 02215, USA.
b Department of Biomedical Engineering, University of Texas at Austin, Austin, TX, 78712, USA.

1 R.Y and Y.X contributed equally to this work.
2 To whom correspondence may be addressed. Email: duan@bu.edu.

This PDF file includes:

Supplementary text: sections S1 to S14
Figures S1 to S14 (not allowed for Brief Reports)
Tables S1 (not allowed for Brief Reports)
SI References
**Supplementary Information Text**

**S1. Mechanism of trapping blockage mode**

The total force $F_t$ acting on a particle placed in an ionic solution near a nanopore through which an electric field is applied consists of an electrical force $F_e$, and a hydrodynamic force $F_h$, arising from the fluid motion around the particle. The most accurate method of determining both forces is by integrating the Maxwell stress tensor $T_e$ and the hydrodynamic stress tensor $T_h$ over the particle surface, respectively (1).

$$F_t = F_e + F_h$$  

(s1)

$$F_e = \int T_e \cdot n \, dA = \int [\varepsilon \vec{E} \vec{E} - \frac{1}{2} (\varepsilon \vec{E} \cdot \vec{E}) \delta] \cdot n \, dA$$  

(s2)

$$F_h = \int T_h \cdot n \, dA = \int [\eta (\nabla \vec{u} + \nabla \vec{u}^T) - p \delta] \cdot n \, dA$$  

(s3)

In Eq. (s2) and (s3), $n$ is the unit vector normal to the particle surface (directed outward from the particle surface to the fluid), $A$ is the surface area of the particle, $\vec{E}$ is the electric field intensity, $\varepsilon$ represents electric permittivity of the fluid, $\delta$ denote the identity tensor, $\vec{u}$ represents the fluid velocity, and $p$ is the pressure.

The electric field ($\vec{E}$) in Eq. (s2) and the velocity field ($\vec{u}$) in Eq. (s3) can be obtained by simultaneously solving the Navier-Stokes (neglecting inertial term) and continuity equations for liquid flow throughout the pore (Eq. s4), Poisson equation for electric potential (Eq. s5), and Nernst-Plank equation for the ionic mass transport within the electrolyte solution (Eq. s6) at the steady state.

$$0 = -\nabla p + \eta \nabla^2 \vec{u} + \rho_e \vec{E} , \quad \nabla \cdot \vec{u} = 0$$  

(s4)

$$\rho_e = \nabla \cdot \varepsilon \vec{E} = \sum_i c_i z_i F$$  

(s5)

$$0 = \nabla \left( -D_i \nabla c_i - F z_i \frac{D_i}{RT} c_i \vec{E} \right) + \vec{u} \cdot \nabla c_i$$  

(s6)

In these equations, $\rho_e$ is the net charge density in solution, $c_i$ is the molar concentration of species $i$, $z_i$ is the valence of species $i$, $F$ is Faraday’s constant, $D_i$ is the diffusion coefficient of species $i$, $R$ is the universal gas constant, and $T$ is the temperature. To solve the strongly coupled equations (s4, s5 and s6) we established a two-dimensional axi-symmetrical multi-physical model in COMSOL using the following modules: creeping flow (spf), electrostatics (es) and transport of diluted species (chds).

The boundary conditions associated with the spf module include no-slip boundary condition on the surface of the nanopore and the nanoparticle, a normal flow with pressure = 0 atm is applied at the ends of both reservoirs. The boundary conditions associated with the es module, include specified surface charge densities on the particle surface ($\sigma_2 = -41.85 \text{ mC/m}^2$ which is equivalent to a zeta potential of $-42.5 \text{ mV}$; conversion done by using Grahame Equation) and the nanopore ($\sigma_1 = -3.13 \text{ mC/m}^2$), electric potential of 200 mV at the end of lower reservoir (The end of reservoir that contains the nanoparticle is grounded). All other boundaries were insulated. The boundary conditions associated with the chds module include a concentration of 150 mM NaCl (which is equivalent to 1x PBS) at the end of both reservoirs, no flux through the nanoparticle, the nanopore and the side edges of the reservoirs (see Figure S1a). In addition, we set the initial concentration...
of the solution in both reservoirs to be 150 mM NaCl. The axis of symmetry is a vertical line through
the center of the pore.

Figure S1b shows the total force $F_t$ applied on a nanoparticle with diameter $d_{np} = 390 \text{ nm}$
and pore $d_{np} = 115 \text{ nm}$ with diameter with respect to $\Delta z$, distance from the particle lower edge to
the pore entrance. When $F_t > 0$, the nanoparticle is moving toward the pore. As the particle moves
closer to the pore, $F_t$ switches polarity becoming a repulsive force that pushes the particle away.
So, the particle will be trapped at the equilibrium position where the transition happens ($F_t = 0$). In
this case trapping (equilibrium position) happens at $\Delta z = -0.15 \text{ nm}$

The major contributions to the electrical force $F_e$ in this work are the electrophoretic force $F_{EP}$, the
dielectrophoretic force $F_{DEP}$ which acts on the nanoparticle due to non-uniform DC electric field.
On the other hand, the only major contributing force to the hydrodynamic force $F_h$ is the
electroosmotic drag force $F_{EO}$ (see Figure S1c) (2).

S2. Full trapping/ releasing current trace

Trapping/releasing of a nanoparticle near a nanopore is highly repeatable and can be
achieved as many times as desired. Figure S2a shows the current trace of more than 200
continuous trapping/ releasing cycles of 390 nm PS-COOH particles suspended in 1x PBS using a
115 nm silicon nitride nanopore. The input voltage function consists of a 2s +200 mV pulse which
allows the particle to be driven toward the pore and get trapped, and a 2s -200 mV pulse for
releasing. Figure S2a also shows that the opening/ closing current does not fluctuate over the +200
trapping/releasing cycles. For a zoom-in view on the current trace, the signal inside the dashed box
in Figure S2a is plotted in Figure S2b. The large transient current occurring during sign reversal of
the voltage is a result of charges stored at the silicon nitride membrane and at the solution electrode
interfaces which migrates upon changing the direction of the electric field.

S3. Volatile memory in trapping blockage mode

Figure S3a shows the current trace of two continuous trapping cycles without applying
release pulses. Between the two cycles, the voltage pulse was completely removed for around 2
minutes in order to relax the system. As the zoom-in current traces show, after the first +200 mV
capture pulse successfully trapped a nanoparticle (Figure S3b), the second trapping event still
started with an open nanopore (Figure S3c) when the voltage was added. This proves that once
the capture voltage is removed, the trapped nanoparticle will be released without the aid of the
reverse bias, leaving the nanopore open until the next capture pulse is applied to trigger the
blockage event. This indicates that the closed state in the trapping mode cannot be maintained
without a voltage hence the trapping closed state has volatile memory.

S4. Concentration dependence study

We defined the closing response time ($t_{\text{closed}}$) as the time it takes to reach a closed/partially
closed state after the voltage stimulus is applied (Figure S4a). As Figure S4b shows, in the trapping
mode experiments, the closing response time decreases linearly as nanoparticle concentration
gets higher until it reaches the limit induced by the capacitance response. This is because higher
nanoparticle concentration will bring more available nanoparticles present within the nanopore
capture radius. The trend of the closing response time matches the theoretical prediction (3):

$$ t_{\text{closed}} = \frac{1}{f} = \frac{\eta (4L + \pi D)}{\pi N_c \varepsilon V D^2} \left| \frac{1}{k_{\text{pore}}} - \frac{1}{k_{\text{particle}}} \right| $$
where \( f \) is the capture rate and \( V \) is the magnitude of the driven voltage, while \( \eta, \varepsilon, L, D, N_\varepsilon \), refer to the solution viscosity, permittivity, nanopore thickness, diameter and nanoparticle concentration respectively. \( \zeta_{\text{pore}} \) and \( \zeta_{\text{particle}} \) are the zeta potential of the nanopore and nanoparticle.

**S5. Nanopore surface charge density calculation**

The surface charge density, \( \sigma \), of the nanopore is determined by measuring the pressure-induced streaming current. Silanol (SiOH) groups on the nanopore inner pore surface tend to become negatively charged when in contact with the aqueous solution, which induces an electrical double layer (EDL) in the solution near the inner pore walls. The surface charges repel the co-ions and attract excess counter-ions within the electrical double layer. A streaming current will hence be generated when pressure-driven fluid flow passing through the nanopore. Considering the electrical double layer is extremely thin (thickness \( \lambda_D \approx 0.83\text{nm} \) in our case) comparing to the nanopore diameter in the 1xPBS buffer solution, the streaming current \( I_{\text{str}} \) can be predicted as (4):

\[
I_{\text{str}} \approx \frac{\sigma \lambda_D \Delta P}{\eta} \frac{L}{A}
\]

where \( L, A \) refers to the thickness and diameter of the nanopore, respectively. \( \eta \) is the viscosity of the solution and \( \Delta P \) is the external pressure. The Debye length, \( \lambda_D \), characterizes the thickness of EDL. The testing setup is the same as the one used nanopore gating experiment introduced in the Methods. The nanopore chip is sandwiched between two separated reservoirs containing 1xPBS buffer, with two immersed Ag/AgCl electrodes on both sides for current measurement and a pressure outlet mounted in one of the reservoirs. To gain the streaming current, we applied a pressure sweep from 0 to 2 atm and each pressure step lasted for 1s. As the corresponding current trace is shown in Figure S5a, the streaming current \( I_{\text{str}} \) increases with the pressure, showing a linear dependency (Figure S5b). Here we estimated the surface charge density by fitting the streaming current with Eq. (s12). The SiN nanopores used in our experiment show a surface charge density \( \sigma_{\text{SiN}} = -3.1 \pm 0.5 \text{mC/m}^2 \) and it turns to \( \sigma_{\text{PLL}} = +5.8 \pm 2.1 \text{mC/m}^2 \) after coated with poly-l-lysine (PLL).

**S6. Non-volatile memory in contact blockage mode**

Figure S6 shows the current trace of a 115 nm silicon nitride nanopore coated with PLL physically blocked by a 390 nm PS-COOH nanoparticle. The input voltage function consists of a 3s +200 mV pulse, a 3s -200 mV and are each intermediated by a 10 s -25 mV to monitor the status of the pore. Unlike trapping/releasing of a nanoparticle near a nanopore which is highly repeatable, a nanoparticle in contact with the nanopore cannot be reversed by simply reversing voltage polarity. Moreover, unlike trapping mode which exhibits volatile memory, this contact blockage mode shows a permanent non-volatile memory since the closed state (gating efficiency 70%) is maintained even after replacing the forward and reverse voltages (± 200 mV) with a small monitoring voltage which would not affect the particle motion (- 25 mV).

**S7. Ionic current rectification in contact blockage mode**

Figure S7a shows the current trace of a 115 nm silicon nitride nanopore coated with poly-l-lysine (PLL) permanently blocked with a 390 nm PS-COOH nanoparticle and the corresponding open state current along with the applied voltage pulse. The magnitude of the ionic current for the open state is symmetric for voltages with same magnitude but opposite polarity. This is not the case for the contact blockage mode for which the magnitude of the ionic current is higher for -200 mV (16 nA, gating efficiency ~38%) compared to the magnitude of the current recorded for +200 mV (9.5 nA, gating efficiency ~70%). This non-linearity observed transpires from the permanent presence of a nanoparticle at the entrance of the nanopore which introduces a surface charge
discontinuity and asymmetry in the pore geometry resulting in a rectified, diode-like current behavior \((5, 6)\). However, this non-linearity is not observed when a smaller voltage was applied \((25 \text{ mV})\) due to the significantly reduced ion concentration polarization (Figure S7b). For both forward and reverse \(25 \text{ mV}\), the permanent blockage current is \(~1.2 \text{ nA} \) (gating efficiency of \(~70\%\)). This proves that there is an enhancement of ionic current flow in reverse bias and no depletion in the forward bias for the case of \(200 \text{ mV}\) and the actual gating efficiency of the contact blockage system is about \(70\%\).

**S8. Contact blockage mode experimental result summary.**

Table S1 tabulates the contact blockage mode results obtained using different experimental settings: particle type (i.e. rigid or soft), particle diameter and pore diameter. The results include the gating efficiency which account for the average of at least 5 different blockage events in each case and the corresponding standard deviation. The results displayed are rounded to the nearest integer. By analyzing the data displayed in Table S1 for both rigid and soft nanoparticles, we have found that particle size and pore diameter does not affect the gating efficiency significantly.

**S9. Possible mechanisms for incomplete blockage of the contact blockage mode**

Achieving contact blockage mode by physically blocking the pore with a hard nanoparticle yields a high but not a complete gating. We hypothesize that such incomplete blockage is from the leakage gap which remains open and allows ion/molecule transport. This gap possibly results from imperfect shape of the circular nanopore or the spherical nanoparticle. Figure S8a is a TEM image of a typical nanopore used in our experiments. The nanopore morphology is highly circular however it is not perfectly circular, and its eccentricity is measured to be 0.3. Figure S8b is an SEM image of the PS-COOH particles used in our experiment which clearly shows they are also not perfect spheres. Moreover, the gap could also stem from imperfect blockage position (the center of the nanopore may not be in coaxial with the nanoparticle). To estimate how much of shift would lead to a gating efficiency of \(70\%\), we have used COMSOL to calculate the corresponding current as a perfectly spherical particle is horizontally shifted from the center of a perfectly circular pore. We have found that a horizontal shift of only \(4.7 \text{ nm}\) from the center of a \(115 \text{ nm}\) pore can result in a significant leakage and a \(70\%\) gating efficiency (Figure S8c).

**S10. Reversing the LBE gating by voltage stimulus**

Liposome-blockage-enabled gating shows non-volatile memory as the nanopore maintains closing state after the voltage stimulus is removed. This gating process is hard to be reversed only by voltage stimulus. As Figure S9 shows, a \(700 \text{ mV}\) voltage pulse fails to re-open the nanopore as the corresponding current stays around zero while the stimulus is applied.

**S11. Fluorescence measurements**

To quantify chemical release rate through a nanopore we have used a \(2.7 \text{ mM}\) solution of fluorescein sodium salt (MW: 376.27 Da, excitation/emission \(460/515 \text{ nm}\)) diluted in \(1 \times \text{ PBS}\). The dye placed in the top chamber (this is the flat side of the device) diffuses through the nanopore to the lower chamber where it can be detected within the field of view (FOV) of the camera in terms of an increase in the fluorescence intensity value by an inverted fluorescence microscope. Figure S10a shows a plot for the “mean fluorescence intensity value” detected over time within a \(330\times330 \text{ µm}^2\) FOV, for a single \(150 \text{ nm}\) silicon nitride nanopore, a completely LBE gated \(150 \text{ nm}\) nanopore and a silicon nitride membrane with no pore. Mean fluorescence intensity value is the sum of the intensity in the image divided by the total number of pixels, it is measured with an arbitrary scoring system (a.u.) and normalized by the exposure time. Our results show that releasing of the fluorescent dye from single open state nanopore via pure diffusion resulted in an increase of
fluorescence intensity. In addition, we have also tested chemical releasing for a pore completely blocked with a liposome. In this case the “mean fluorescence intensity value” did not increase overtime (like the no pore case) indicating that the liposome entirely sealed the pore and completely stopped the diffusion of the dye through the pore.

The mean fluorescence intensity per unit time (a.u. / ms) is related to the concentration of fluorophores (µM) present in the corresponding FOV (Figure S10b). The slope of the best fit line of Figure S10b (154.25 a.u.ms⁻¹.µM⁻¹) was therefore used to relate the mean fluorescence intensity per unit time to the concentration of dyes. The actual amount of fluorescence (fMole) was then obtained by simply multiplying the concentration by the volume of the solution within the FOV of the camera (Figure 10c).

To account for the dye that has diffused outside of the detection window, we have used finite element analysis simulation to numerically measure the amount of dye that has diffused with respect to time in the FOV (Figure S11a) and in the entire reservoir (Figure S11b) for a 150 nm pore. For the numerical simulation we have used diffusion coefficient of 4.3*10⁻¹⁰ (m²/s). From the numerical result, the releasing for 150 nm pore through entire reservoir is linear, and the release rate obtained from the slope of Figure S11b is 0.137 fMole/s. Figure S10c is a plot of the ratio of the amount of dyes in the FOV to the total amount of dyes that has diffused. We were able to fit a second order exponential line to this correlation which suggests that there is a relationship between the amount of dyes in the FOV and the total amount of dyes that has diffused. We note that this relationship is not dependent on the pore radius. The coefficient of determination (R²), which is an indication of how well the theoretical model fits the experimental data, is 0.999. The numerical fitted expression is given as:

\[
y = A_1 \times \exp\left(-\frac{t}{t_1}\right) + A_2 \times \exp\left(-\frac{t}{t_2}\right) + y_0
\]

Where t is the time, A1, A2, t1, t2 and y0 are all constants and their corresponding values are 0.43331 ± 0.01299, 0.57472 ± 0.01506, 98.62896 ± 2.12873, 683.26546 ± 69.34745, 0.03093 ± 0.0279. Using this numerically fitted expression and our result shown in Figure S9c, we can estimate the total amount of dyes that has diffused to the bottom chamber (Figure S11d). Our results show that releasing of the fluorescent dyes from single nanopore results in a linear increase of fluorescence intensity, indicating that a constant releasing rate is achieved, and the slope of the line characterizes the release rate. In this case for 150 nm pore, we measure the release rate by diffusion to be 0.13 fMole/s which quantitatively match the simulation result further validating our approach.

S12. Multi-cycle controlled fluorescein releasing from single nanopore using LBE gating

Figure S12 shows several consecutive on/off cycles of the fluorescein releasing via a 150 nm nanopore using the rapid, reversible, and complete LBE nanopore gating and the associated non-volatile memory. For this experiment, liposomes with an average diameter of 327 nm were used to gate the pore reversibly upon the applied closing (voltage) and opening (pressure) stimuli. We observe the amount of dye in the field of view (FOV) change with the ON and OFF state of the nanopore. After the opening voltage pulse, the dye intensity is continuously increased in the cis reservoir until the closing pulse is applied, after which the amount of fluorescence in the FOV starts to decrease because diffusion-based releasing from the nanopore stops and the fluorescein in the FOV diffuses out. The results in Fig. S12 further demonstrate the reversibility of the LBE gating strategy and the enabled controlled chemical releasing.

S13. Mechanism of LBE gating

Figure S13a is a SEM image of a nanopore device after the LBE-gating experiment. In this case, all the nanopores are milled inside the membrane. We clearly observe a spanned lipid layer covering the nanopores. Figure S13b is a SEM image of the 10x10 150 nm nanopores (total 100
nanopores) used to check if the LBE gating is a result of liposome deformation or rupture. The nanopores are > 2 µm apart. We have used an array as it is easier to pinpoint the location of an array in comparison to a single nanopore. Figure S13c is a bright-filed microscope image of the nanopore array gated with the fluorescent liposomes using an upright optical microscope (Olympus BH2) at 80x magnification. Given that under fluorescent microscope we cannot see the liposomes (see Figure 4b), the dark spots observed in Figure S13c, which cover more than 95 of the 100 nanopores are a result of ruptured liposome, hence the name black lipid membrane (BLM). At first glance, the BLMs in Figure S13c appears to be the nanopore themselves. However, at this magnification we cannot see the nanopores. Figure S13d is a microscope image of the same device after removing the BLMs by immersing the device in chloroform and then cleaning in a hot piranha solution. In that case we do not see individual nanopores probing, thus what we observe in Figure S13c is a result of the LBE gating. Figure S13e is a fluorescent image of 400 nm PS-COOH fluorescent particles (Ex: 480 nm, Em: 520 nm) blocking the nanopore array. This is a solid proof that if the fluorescent liposomes did not rupture, they would be clearly distinguished.

S14. Investigating the thickness of the suspended lipid layer across nanopore

To further investigate the mechanism of LBE gating, we used high-resolution Atomic Force Microscope (AFM) imaging to examine the nanopore after LBE gating. First, we achieved complete gating of a silicon nitride (SiN) nanopore using DPhPC liposome and then carefully dried the gated nanopore device for AFM imaging. The resultant AFM image is shown in Fig. S14a. The AFM image was obtained with the tapping mode using a conical silicon cantilever with a radius of 8 nm. We can clearly observe from Fig. S14a a flat supportive film of lipids spanned across the nanopore. This confirmed the presence of the lipid bilayer over the SiN surface.

We also investigate the thickness of the lipid bilayer covering the nanopore. It is worth noting that the lipid layer seems to be deflecting down across (and in close proximity to) the nanopore. This is because the lipid layer is suspended across the pore and does not have solid support, which makes it susceptible to vibration and deflection from the force exerted on it by the AFM tip. Thus, to obtain the thickness of the ruptured lipid layer, we measured the height profile along the horizontal lines shown in Fig. S14a. These lines are chosen to span from a flat SiN surface to the lipid layer on SiN solid support (i.e., not in close proximity to the nanopore). The height profile measurements plotted in Fig. S14b show that the thickness of the lipid supportive film is approximately 5 nm, which according to literature, corresponds to the measured thickness of a single lipid bilayer (7, 8). Hence, from AFM imaging we can conclude that the liposome driven to gate the pore results in a single lipid bilayer rather than multilayer.
Figures

Figure S1. Mechanism of trapping blockage mode, (a) Schematic showing simulation parameters. (b) Plot of the numerically obtained net total force $F_t$ applied on a nanoparticle with diameter $d_{np} = 390 \, nm$ and pore $d_{np} = 115 \, nm$ with respect to $\Delta z$, distance from the particle lower edge to the pore entrance. (c) Plot of the major forces (electrophoretic, electro-osmotic and dielectrophoretic) acting on a 390 nm particle that acts on particle with $r_p = 195 \, nm$ approaches a pore with $d_{pore} = 115 \, nm$ with respect to distance from the center of the pore to the center of the particle.
Figure S2. (a) Ionic current trace for more than 200 continuous trapping/releasing experiment of 390 nm PS-COOH particles suspended in 1x PBS, at 200 mV and using a 115 nm silicon nitride pore. (b) Zoom-in-view on the current signal.
Figure S3. (a) Ionic current and voltage trace of two continuous trapping cycles obtained from a 115 nm silicon nitride nanopore by 390nm PS-COOH nanoparticles. (b) Zoom-in signal of the first trapping cycle. (c) Zoom-in signal of the latter trapping cycle.
Figure S4: Concentration dependence study using various concentrations of 390 nm PS-COOH particles tested with a 115 nm silicon nitride pore, (a) example of ionic current trace used for the capture rate measurements and the corresponding voltage pulse. (b) Log-scale plot of the experimental and theoretical capture rate at different nanoparticle concentrations.
Figure S5. (a) Ionic current trace vs time for various applied pressure. (b) Average ionic current values vs applied pressure.
Figure S6. Ionic current trace obtained from a 115 nm silicon nitride nanopore coated with PLL physically blocked by a 390 nm PS-COOH nanoparticle and the corresponding applied voltage pulse.
Figure S7. Ionic current trace for a 115 nm silicon nitride nanopore coated with PLL permanently blocked with a 390 nm PS-COOH nanoparticle and the corresponding open state current. The input voltage function consists of (a) 3 s +200 mV pulse followed by a 3 s -200 mV pulse. (b) 2 s +25 mV followed by a -25 mV.
Figure S8. (a) TEM image of a typical silicon nitride nanopore used in our experiments. (b) SEM image of the PS-COOH nanoparticles used in this study. (c) Plot of the gating efficiency (%) obtained numerically with respect to nanoparticle horizontal shift from the pore radius as shown in the inset.
Figure S9. Ionic current signal obtained for liposome-blockage-enabled gating and the corresponding applied voltage pulse.
Figure S10. Quantifying chemical releasing from single nanopores using inverted fluorescence microscope, (a) plot of the mean fluorescent intensity value over time for open state (150 nm pore), no pore, and liposome blockage enable gating (100% gating efficiency). (b) Mean fluorescence intensity (a.u. / ms) v.s Na-FI concentration (µM), and corresponding error bars. (d) Plot of the amount of dye in fMole over time for the three different cases tested.
Figure S11. Numerical and experimental results of the amount of dye released from single nanopores, (a) Numerical results of the amount of dye that has diffused within the FOV. (b) Numerical results of the total amount of dye that has diffused from the nanopore. (c) Ratio of the amount of dye in FOV to the total amount of dye released from the nanopore and the numerically fitted line. (d) Experimental approximation of the total amount of dye released from a nanopore as a function of time for the different studied cases; open state (150 nm pore), no pore, and liposome blockage enable gating (100 % gating efficiency).
Figure S12. Results for multi-cycle LBE-gating-controlled fluorescein releasing from single 150 nm nanopore with the corresponding applied stimuli.
Figure S13. Exploring the mechanism of LBE gating. (a) SEM image of a nanopore array device after the LBE-gating experiment; nanopores are all inside the free-standing silicon nitride membrane. (b) SEM image of the 10 by 10 array of 150 nm nanopores (location inside the dashed rectangle); the nanopores are > 2 µm apart. (c) Bright-field microscope image of the nanopore array device after achieving LBE gating with fluorescent liposomes. The dark spots distinctively observed are BLMs. (d) Bright-field microscope image of the nanopore array device after removing the BLMs by immersing the device in chloroform then cleaning with piranha solution. (e) Fluorescent image of 400 nm PS-COOH fluorescent particles (Ex: 480 nm, Em: 520 nm) blocking the nanopore array.
Figure S14. Investigating the thickness of the suspended lipid layer across nanopore (a) AFM image of dried nanopore after achieving complete gating with DPhPC liposome. (b) Image of the height profile corresponding to the horizontal lines in (a).
Table S1: Result summary of the contact blockage mode experiments using different experimental settings.

| Particle type       | Particle diameter (nm) | Pore diameter (nm) | Gating efficiency (%) |
|---------------------|------------------------|--------------------|-----------------------|
| PS-COOH             |                        |                    |                       |
| 105                 | 60                     | 62% ± 2%           |                       |
|                     | 90                     | 60% ± 3%           |                       |
| 390                 | 60                     | 64 ± 2%            |                       |
|                     | 90                     | 66 ± 2%            |                       |
|                     | 150                    | 70 ± 3%            |                       |
| DPhPC liposome      |                        |                    |                       |
| 327                 | 90                     | 100%               |                       |
|                     | 150                    | 100%               |                       |
| 800                 | 90                     | 100%               |                       |
|                     | 150                    | 100%               |                       |
SI References

1. Ai Y & Qian SZ (2011) Electrokinetic particle translocation through a nanopore. Phys Chem Chem Phys 13(9):4060-4071.
2. Kang KH, Xuan XC, Kang YJ, & Li DQ (2006) Effects of dc-dielectrophoretic force on particle trajectories in microchannels. J Appl Phys 99(6).
3. Davenport M, et al. (2012) The Role of Pore Geometry in Single Nanoparticle Detection. Acs Nano 6(9):8366-8380.
4. Kirby BJ & Hasselbrink EF, Jr. (2004) Zeta potential of microfluidic substrates: 1. Theory, experimental techniques, and effects on separations. Electrophoresis 25(2):187-202.
5. Karnik R, Duan C, Castelino K, Daiguji H, & Majumdar A (2007) Rectification of ionic current in a nanofluidic diode. Nano Lett 7(3):547-551.
6. Ali M, et al. (2014) Current rectification by nanoparticle blocking in single cylindrical nanopores. Nanoscale 6(18):10740-10745.
7. Teschke O & de Souza EF (2002) Liposome structure imaging by atomic force microscopy: Verification of improved liposome stability during adsorption of multiple aggregated vesicles. Langmuir 18(17):6513-6520.
8. Regan D, Williams J, Borri P, & Langbein W (2019) Lipid Bilayer Thickness Measured by Quantitative DIC Reveals Phase Transitions and Effects of Substrate Hydrophilicity. Langmuir 35(43):13805-13814.