Digital virus manipulation chip with a large array of all-dielectric nanocavities

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Article

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Abstract

Spatial manipulation of a precise number of viruses for host cell infection is essential for the study of virus pathogenesis and evolution. Albeit optical tweezers have been advanced to the atomic level via optical cooling, it remains a formidable challenge to efficiently trap and move viruses in an aqueous environment, being restricted by insufficient strength of optical forces and a lack of precise spatial manipulation techniques. Here, we demonstrate giant optical forces produced by the enhancement of light in engineered arrays of nanocavities for trapping and digitally moving viruses down to 40 nm in size. By employing the virus hopping and flexibility of moving the laser position, we demonstrate a digital virus manipulation chip with a large trapping area, enabling single or massive virus transporting, positioning, and concentrating. Our work paves the way to efficient and precise manipulation of either single viruses or their massive ensembles, opening a wide range of novel opportunities for virus pathogenesis, virus diagnostics, vaccine, and antiviral drug development, being also important to tackle the current COVID-19 outbreaks.

Background

Near-field optics revolutionized optical tweezers¹⁻³ bringing this field to the nanoscale with low-heating effects and multiple functionalities¹⁻⁹. Nanowaveguides^{7, 8, 10-12}, photonic crystals with guided modes¹³, and ring resonators with whispering gallery modes^{11, 12, 14, 15} have been employed as prominent tools for manipulating small particles. However, these approaches are not very efficient for trapping nanoscale biological objects such as viruses being hampered by weak optical forces due to insufficient light confinement and low values of the quality factors (Q -factors) of the resonators. Plasmonic optical tweezers are usually accompanied by a huge amount of local heat, hindering practical biological applications¹⁶⁻¹⁹, which are sensitive to a slight increment of temperature (e.g., a few degrees). Slot waveguides and defect modes in photonic crystals were exploited to trap DNA with piconewton optical forces⁵ delivering simple proof-of-principle demonstrations which are not yet practical for precise manipulation. This approach relies on random diffusion of DNA molecules into the evanescence field region, and it is characterized by low trapping efficiency (less than 25%), so that optical extinction forces push DNA molecule along the slot lacking positioning capability. Precise manipulation of single viruses is important for the study of virus heterogeneity and evolution, i.e., hand-picking a specific virus mutant for host-cell infection; whereas the precise manipulation of massive viruses facilitates the studies of virus pathogenesis and influences of virus load in infection. Unfortunately, such virus digital manipulation technique is still lacking. To achieve robust virus manipulation, a strong subwavelength confinement in resonant cavities with large trapping area is required. Here, we propose a digital virus manipulation chip based on all-dielectric nanocavities to trap, move, position and concentrate viruses digitally.

Recently, efficient trapping of light inside nanostructures has raised immense attention due to the broad range of applications in lasing, nonlinear optics, and sensing. Among many different mechanisms, the optical bound state in the continuum (BIC) shows unprecedentedly large quality factors (Q factors)²⁰ that

may stipulate enormous response of a photonic structure to incident electromagnetic waves and strong enhancement of near-fields, being an efficient tool to engineer leaky modes and their strength. In practice, BICs are realized with high but finite values of the Q factors due to structural losses and imperfections, and they are usually termed “quasi BICs” or “supercavity modes”²¹, and some of the quasi-BIC applications have been demonstrated for lasing²², sensing²³, and other effects²⁴⁻²⁷. Importantly, quasi-BIC states can be employed for an efficient control of leaky modes in a variety of photonic structures. Here, we employ the BIC-inspired physics of the leaky-mode control to manipulate tiny bioparticles, as small as viruses down to 40 nm in size. After a vigorous calculation of optical forces from different nanocavities in the band structure, we reveal that the BIC nanocavities are accompanied with weak optical forces due to the perfect confinement of light in nanostructures without leakage. However, some of Trapping modes in the reflection spectrum serve as a perfect paradigm for competent candidates because of their highly localization of light inside nanoholes and some energy leakage outside nanoholes. Those Trapping modes enhance optical forces at the nanoscale by at least two orders of magnitude. More specifically, we demonstrate a digital virus manipulation chip for the trapping and manipulation of 100-nm adenoviruses in large arrays of nanocavities, paving the way for precise manipulation of viruses such as SARS-CoV-2 to study virus pathogenesis and mutation, innovate virus diagnostic toolkits, and develop vaccine and antiviral drugs, which are important to combat virus outbreaks, evidently demonstrated in the current COVID-19 outbreak.

Our demonstrated functions require several elegant implementations at the same time, such as the tight confinement of light in nanoholes to generate huge optical force, all-dielectric material to prevent absorption, exquisite hopping mechanisms to ensure precise positioning in the central of laser spot, shallow microchannel to guarantee the immersion of virus in the near field, and optical microscope with dark field imaging and removable stage. Thus, the demonstrate functions (e.g., transporting, positioning, patterning, sorting, and concentrating) are not attainable by previous methods. Our approach opens a range of novel opportunities to handle exosomes, lysosomes, lipid droplets, etc. in similar size range with important biomedical information for disease diagnostics, prognosis, and therapeutic guidance.

Results

Nanocavity integrated virus digital chip

The 110-nm-diameter silicon nitride (Si_3N_4) nanocavity array on a silicon oxide substrate is illuminated by a projected large-sized Gaussian beam (wavelength: 532 nm; diameter > 10 μm) to excite the Trapping mode in the dielectric nanocavities (Fig. 1a). The Trapping mode confines the light field tightly in the holes of the nanocavities, generating isolated hotspots with high light intensities. When a virus particle flows to the light illuminating area, it is trapped in the beam and hops between isolated hotspots. The virus also experiences an optical gradient force that pushes it towards the nanohole²⁸. Viruses with size smaller than the nanoholes will eventually be caged inside the nanoholes, while bigger viruses will be released by the microfluidic drag force when the laser is switched off. To ensure that the viruses flowing to the laser illuminating area experience enough optical forces to pull them to the surface and nanoholes,

we fabricate an optofluidic virus digital chip (VDC) with a 1- μm shallow microchannel as shown in Fig. 1b. The shallow microchannel is fabricated by spin-coating a 1- μm Polydimethylsiloxane (PDMS) onto the surface of a quartz block and ablating the pattern of microchannel using the laser engraving. The detailed fabrication process is discussed in Methods.

The nanocavities are designed to have the Trapping mode being confined inside the nanoholes (Fig. 1c), which is used to trap viruses as the light is tightly focused to generate a strong optical gradient force. On the other hand, the Futile mode is guided along the dielectric layer, leading to a much weaker optical gradient force that is incapable of trapping viruses. Figure 1d presents the simulated resonances of the TE polarized field when the hole radius and gap are 55 nm and 295.1 nm, respectively. The Q -factor plot (Supplementary Fig. 2) shows that mode 3 and mode 4 at point Γ have Q -factor up to 10^9 . The mode 1 has a quality factor $< 10^3$ but has the largest optical gradient force (Fig. 1e) on the polystyrene nanoparticle (radius: 50 nm; Refractive index R_I : 1.58) placed right above the nanohole (Supplementary Fig. S2c). This is because perfect BIC mode traps light without leakage, resulting in a relatively small optical gradient force. On the other hand, the leaking mode 1 obtains a balance between light confinement and leakage to achieve a strong optical gradient force, creating optical trapping potential wells in the nanocavities for virus trapping. Mode 2 (at point Γ) has the smallest optical attractive force towards the hole, resulting from light wave deflecting from the hole. More simulations of the resonances and optical forces of the TM modes (Supplementary Figs. 2-5). Since the nanocavities are made of dielectric material (Si_3N_4), it does not absorb light efficiently and therefore does not generate heat during virus trapping (Supplementary Movie 1), conserving the properties and viability of trapped viruses.

Figure 2a shows the reflection spectrum of the nanocavities with different nanohole radii and intervals g under an illumination of a 532 nm laser. The strong coupling in the parametric space produces an avoided resonance crossing with low- Q (modes 1, 3 and 5) and high- Q (modes 2, 4 and 6) modes on the left and right sides of the spectrum, respectively. Modes 1 and 6 traps light inside the holes so that they can generate large optical forces on the nanoparticle. And modes 2 and 5 disperse light in the solid Si_3N_4 so that the optical force is small. Figure 2b shows the enhancement factor S which is defined as $S = |\max E_{\text{hole}}|/|E_{\text{in}}|$ where $|\max E_{\text{hole}}|$ is the maximum normalized electric field inside the nanohole and $|E_{\text{in}}|$ is the incident electric intensity. S reaches a maximum of 73, showing that the laser intensity can be enhanced by approximately 5,300 folds. Meanwhile, as light is tightly confined in a circle with a diameter $D_h \leq 110$ nm (D_h is the diameter of the hole), the optical gradient force, which is proportional to the intensity gradient (related to the maximum value in the hole), is hugely enhanced²⁹. Meanwhile, the distribution of the Poynting vector shows that the optical scattering forces acted on a particle placed above nanohole are also pointed towards the nanohole (Fig. 2c), double ensuring the caging of viruses into the nanoholes with the optical force. To explore the trapping limit of the nanocavities, we investigate the trapping force on viruses with diameter ranging from 20 to 100 nm and R_I of 1.4 (virus) and 1.58 (polystyrene nanoparticle) in Fig. 2d. Two cases are simulated (see the sketch in Fig. S10a): (1) the nanohole diameter is set to 110 nm, and (2) nanohole diameter $D_h = D + 10$ nm, where D is the diameter of the nanoparticle. Different intervals are chosen according to the radii of holes to match the Trapping modes in Figs. 2a and

2b. The trapping force is negligible when $D < 40$ nm but remains relatively large when $D \geq 40$ nm. Therefore, the trapping limit of the Trapping mode nanocavities is 40 nm. The abrupt reducing of optical force when $D < 40$ nm is partly because that the optical gradient force decreases with D^3 , and because the interference of cavity resonance from the trapped nanoparticle will become prominent when both the particle size and hole size are very small. Above the surface, some weaker light spots occur and generate sub-potential wells for the 100-nm polystyrene nanoparticle, as shown in Fig. 2e. The refractive index of the nanoparticle and laser wavelength are 1.58 and 532 nm, respectively. Nanoparticles and viruses will hop from the sub-potential wells to the central deep potential well. More importantly, the change of temperature is negligible (< 0.01 K) when illuminated with a laser intensity of $1 \text{ mW}/\mu\text{m}^2$ (Fig. 2f), making it suitable to manipulate viruses without heating them up and altering their viability.

Manipulation of adenoviruses

With a Gaussian beam (wavelength 532 nm) being projected on the nanocavity array, the virus tends to hop from the side lobe potential well to the deeper potential well in the centre (Fig. 3a) at nanoscale ($g = 295.1$ nm). In the scale of a few micrometres, the virus gradually moves to the nanohole in the centre of the beam by multiple hopping, showing the principle of precise positioning by optical hopping. Simultaneously, the virus is attracted towards the nanohole by the optical gradient force. The hopping time of virus ($D = 100$ nm; $RI = 1.4$) from the side hotspot to the central hotspot is less than 10 ms (Fig. 3b). Figure 3c shows the scanning electron microscope (SEM) image of the fabricated nanocavities with a diameter of 110 nm and an interval g of 295.1 nm, realizing the designed Trapping mode. Since we can flexibly move the laser beam, we can easily trap and position viruses in the array of nanocavities based on the virus hopping mechanism. Four prominent Movie frames are shown in Fig. 3d to illustrate the caging process. An adenovirus (yellow circle) was first spotted at $t = 0$. Meanwhile, the laser spot (green circle) was moved to the path of the virus. Then, the adenovirus was trapped and ready to be transported at $t = 2.5$ s. It started to be caged when reaching the target position at $t = 5.5$ s and remained caged inside the hole when the beam is moved away at $t = 20.1$ s. 50-nm upconversion particles, 70- and 100-nm polystyrene nanoparticles, and adenoviruses are easily patterned in various signs in the nanocavity array (Fig. 3e and Supplementary Movies 2,3). The stable caging of nanoparticles or viruses smaller than the nanohole can be verified by experimentally flushing the surface with an extremely fast flow stream (e.g., 2.5 mm/s in Fig. 21). The nanoparticles will be easily flushed away if their sizes are larger than the hole because of the perfect surface treatment (see Methods) to avoid surface adhesion.

Since the diameter of the nanoholes is 110 nm, only viruses smaller than 110 nm can be efficiently caged in the nanoholes. Larger viruses will be flushed away by the fluidic drag force when the laser is switched off. Sorting of nanoparticles and adenoviruses can be achieved whereby larger nanoparticles and adenovirus could only be temporarily trapped by the laser spot. Once the laser spot was moved away, these larger nanoparticles and adenoviruses were released and eventually flushed away by the microflow. This size-selective mechanism is demonstrated by the nanoparticles and adenovirus, as shown in Figs. 4a and 4b, respectively. The 100-nm nanoparticle can be caged and patterned. However, the big nanoparticle conjugate will be released when the beam is moved swiftly at $t = 47.4$ s in Fig. 4a

(Supplementary Movie 5). Similarly, adenovirus larger than 110 nm can be trapped above the hole at $t = 26.0$ s in Fig. 4b (Supplementary Movie 6) and released at $t = 29.4$ s. Some adenoviruses were not caged in the nanocavity array because of the broad size distribution of adenoviruses, measured by the Nanosizer (Fig. 4c). Based on the sorting mechanism, the nanocavity array is also capable to measure the size distribution of adenoviruses using different designs with various nanohole sizes. For instance, the 90-nm nanoholes can determine the percentage of viruses larger or smaller than 90 nm. We fabricate holes with different sizes (i.e., 90, 100, 110, and 120 nm) in different areas in one chip, then use them to trap viruses to determine how much percentage of viruses are larger than 90, 100, 110, and 120 nm. The comparison of the size distribution using the Trapping mode nanocavity array and Nanosizer is shown in Fig. 4d. The results from the nanocavity array and Nanosizer are comparable, but the nanocavity array has higher measured percentage. This is caused by the unexpected escape of adenoviruses smaller than the size of the holes due to the less trapping time and Brownian motion.

We can also concentrate massive viruses in the nanocavity array (Fig. 5a) by continuously illuminating the array with a high laser power (e.g., 60-100 mW, equivalent laser intensity ~ 1 mW/ μm^2). In the higher laser power, instead of a single nanohole, more nanohole (hotspots) will have stronger optical gradient forces to attract the viruses inside. The experimental results in Fig. 5b shows the caging of dozens of adenoviruses within the laser spot when the laser power is 100 mW. Instead of being concentrated within a circle, the virus will move to the nanohole in the centre of the beam by optical hopping when illuminated with a lower laser intensity. This is because the input Gaussian beam has a gradient. Thus, only the nanohole in the centre of the beam has enough optical gradient force for the caging when the laser power is low, while more nanoholes are capable of caging viruses when the laser power is high. Figure 5c illustrates the motion trajectories of adenoviruses being flushed to the laser spot by the fluidic drag force³⁰, and subsequently, hopping to the centre of the laser spot under a laser power of 10 mW (equivalent laser intensity ~ 0.1 mW/ μm^2). The SEM image of caged 87-nm nanoparticles is shown in Fig. 5d. Most nanoparticles reside at the bottom of the hole (depth 240 nm), so they appear a little bit dim. The nanoparticle can be brighter when it sticks to the side wall of the hole and resides close to the upper surface of hole. Each hole tends to trap one nanoparticle when the sizes of particle and hole are close because the trapped nanoparticle can disturb the light field and weaken the optical force from the hole, causing difficulties in trapping more nanoparticles. The probability of a virus going into the nanohole (P_{trapping}) depends on the trapping time. In principle, a virus has a higher probability to be caged in the nanohole with a longer the trapping time. However, in some cases, the virus was not caged in the nanohole for a long trapping time (Supplementary Movie 7). P_{caging} also depends on the beam moving velocity when the virus is transported. When the beam velocity $v_b > 10$ $\mu\text{m/s}$, $P_{\text{caging}} < 3\%$ because the virus does not have sufficient time to be caged. Meanwhile, the probability of virus being transported with the beam ($P_{\text{transporting}}$) is $> 80\%$ when $v_b < 20$ $\mu\text{m/s}$. When the beam moves too fast, e.g., $v_b > 20$ $\mu\text{m/s}$, the virus is unlikely to be transported because of the inertia. Therefore, the optimal v_b for the transporting of the adenovirus is between 10-20 $\mu\text{m/s}$ (Fig. 5e). P_{caging} for the adenovirus is $> 95\%$ when the trapping time is longer than 20 s (laser beam holding still) and the laser power is larger than 80 mW (Fig. 5f). The

high caging efficiency demonstrates a high reliability that the Trapping mode nanocavity array can be used to efficiently localize single viruses in the nanoholes. This probability of virus caging is done by measuring the viruses with relatively weak intensity to guarantee that their sizes are smaller than the hole size. The intensity can be easily visualized because most of the viruses have similar scattering intensity because their sizes are close. It shows a high caging probability given certain power and flow velocity when the virus size is smaller than the hole.

Discussion

We have demonstrated the efficient manipulation of both single (as small as 40 nm) and massive viruses using the novel physics of Trapping mode-empowered nanocavity arrays. The achieved balance between the subwavelength confinement and leakage of light has led to 100-fold stronger optical forces than that in conventional photonic crystals, representing a major step towards virus manipulation. The nanocavity array is fabricated into an optofluidic chip with a shallow microchannel (1 μm in depth) to ensure a high-efficiency ($\sim 100\%$) trapping of nanoparticles and viruses. Our design can be easily adapted to the infra-red transparency window by changing the radii and intervals of nanoholes obtained from the calculated spectrum for a certain wavelength. Our results demonstrate the unprecedented capabilities of either single virus trapping, transporting, positioning, and patterning, virus sorting by size, or concentration of massive viruses down to a single virus precision, which open new opportunities in a wide range of practical applications in virus research. Single virus infection on a few host cells is essential for the studies of virus heterogeneity and evolution driven by high mutation rate. Spatial patterning of virus particles may reveal how viruses infect specific host cells and spread to the neighbouring host cells, quantifying the multiplicity of infection and infectivity rate. Sorting and concentrating viruses allow direct counting of virus particles to investigate the effect of virus loading on infectivity, as opposed to the current plaque-based indirect quantification methods. Coupled with the mature microfluidics and lab-on-a-chip technologies, precise control of the micro-environment conditions during host-cell infection and drug testing potentially improves the efficiency in vaccine and anti-viral drug development. All these possibilities accelerate the development of virus diagnostics, vaccines, and anti-viral drugs to combat unknown pathogenic outbreaks such as COVID-19. Our results also pave the way for other biomedical and clinical applications in disease diagnostics, prognosis and theragnostic, targeting on exosomes, liposomes, and lipid droplets which fall under the same size regime of viruses.

Methods

Chip fabrication and image acquisition

The Si_3N_4 layer with a thickness of 240 nm was first spin coated with the photoresist (ZEP520A) at a speed of 4000 rpm for 120 s to get a target thickness of 330 nm. The Si_3N_4 layer was then exposed by the electron lithography (Vistec EBPG5200, Germany). After the writing of the pattern, the chip was developed by the developer (ZED-N50) for 60 s. The developed chip was etched by RIE etching machine (Oxford Plasmalab80 RIE, UK). After fabrication, the Si_3N_4 chip is then bound with a quartz square coated

with a 1- μm PDMS layer using the plasma treatment. The 1- μm PDMS layer is laser engraved by the laser engraving machine (Universal, USA) to form the microchannel. Therefore, the depth of the microchannel is the same as the 1- μm PDMS layer, which facilitates the optical trapping of viruses in the near field. The quartz square was also drilled with two holes using the sonic drilling machine (SOM-121, Drill Master, Japan) with a drill head diameter of 1.5 mm. To inset and fix the tubes, the chip was eventually bound with two PDMS cuboids which were also drilled with two holes connecting to holes in the quartz square. A Single-Photon-Sensitive EMCCD (iXon Ultra 888) plus the dark field excitation was used to observe the single virus. Meanwhile, because our optofluidic chip was specially designed to let the images only penetrate a thin quartz glass (1 mm, shown in Fig. 1b) and the microchannel is only 1 μm (Fig. 1b), we can easily observe single viruses in our nanophotonic chop. The viruses can also be labeled with fluorescence staining for virological applications.

Sample preparation

Before the injecting of viruses in serum, the surface of the Si_3N_4 layer needs to be treated with multiple chemical and biological solvent to prevent the surface adhesion. The PEG-silane (PG1-SL-2k, Nanocs, USA) and Startingblock (Thermo Fisher, Singapore) solutions were used to prevent the binding of nanoparticles and viruses. The newly bonded chip was treated with the PEG-silane, with concentration of 2.11 mg/mL in absolute ethyl alcohol (EtOH) with an injection rate of 1 $\mu\text{L}/\text{min}$ for 2 hours. Then the channel was washed with absolute EtOH for 1 hour with a flow rate of 2 $\mu\text{L}/\text{min}$. Finally, the Starting Block solution was 1:1 diluted in Phosphate-buffered saline (PBS) and was injected with flow rate of 2 $\mu\text{L}/\text{min}$ for 1 hour. Then the surface of chip was ready for carry on experiment with nanoparticles and viruses.

Human adenovirus 5 was purchased from ATCC (catalogue number ATCC® VR-1516™). Goat serum was from Gibco (16210-064). Adenovirus stock samples were aliquot and stored at -80 °C until use. The virus concentration 5.8×10^{11} particles/mL from stock vial was thaw to room temperature in biosafety cabinet. The virus stock was diluted 1000 times to 5.8×10^8 particles/mL in 1 mL goat serum ($R/I \sim 1.34$) or PBS ($R/I \sim 1.33$) solution. The virus solution was then filtered, passing through a portable membrane filter with a pore size of 200 nm to filter out the large viruses. Because the filtration using the pressure to force the viruses passing through the 200-nm pore, the viruses may be squeezed, and some viruses larger than 200 nm may also pass through. After the filtration, the virus solution was ultrasonicated in 1 minute to avoid potential aggregation. Then the solution was ready for injection into the optofluidic chip.

$\text{YCl}_3 \cdot 6\text{H}_2\text{O}$ (99.99%), $\text{YbCl}_3 \cdot 6\text{H}_2\text{O}$ (99.9%), $\text{TmCl}_3 \cdot 6\text{H}_2\text{O}$ (99.99%), NaOH (98%), NH_4F (99.99%), oleic acid (OA, 90%), 1-octadecene (ODE, 90%) were purchased from Sigma-Aldrich. Unless otherwise noted, all the chemicals were used as raw materials without further purification.

Synthesis of $\text{NaYF}_4:20\%\text{Yb}^{3+}, 4\%\text{Tm}^{3+}$ upconversion nanoparticles

The NaYF₄:20%Yb³⁺, 4%Tm³⁺ upconversion nanoparticles were synthesized using a coprecipitation method. In a typical procedure, 1 mmol RECl₃·6H₂O (RE=Y, Yb and Tm) with doped ratios of 0.78 : 0.2 : 0.04 together with 6 mL oleic acid and 15 mL 1-octadecene were added to a 50 ml three-neck round-bottom flask under vigorous stirring. The resulting mixture was heated at 160 °C for 30 mins to form clean lanthanide oleate complexes. The solution was cooled down to under 50 °C, and 6 mL methanol solution containing 2.5 mmol NaOH and 4 mmol NH₄F was added with vigorous stirring for 30 mins. Then the mixture was slowly heated to 150 °C and kept for 20 mins under argon flow to remove methanol and residual water. Next, the solution was quickly heated at 300°C under argon flow for 1.5 h. Finally, the reaction solution was cooled down to room temperature. The products were precipitated by ethanol and centrifuged at 9000 rpm for 5 min, then washed for three times with cyclohexane, ethanol and methanol to get the nanoparticles. The resulting nanoparticles were collected and redispersed in cyclohexane with 10 mg/mL concentration.

Simulation of band structures, optical forces, and temperatures of the VDC

The band structure and quality factor of silicon nitride nanowell plate are calculated using three-dimensional finite element method in COMSOL. The refractive indices of the liquid medium (water), the silicon nitride and silicon oxide are set to be 1.3337+1.4992×10⁻⁹i, 2.056+0i and 1.4607+0i, respectively. The nanoparticles are diluted in the PBS (*R*/*I* ~ 1.33). And the adenoviruses are diluted in either goat serum (*R*/*I* ~ 1.34) or PBS. It is noted that the slight difference of experimental solutions (goat serum or PBS) for virus with the simulation medium (water) does not have a large influence on the resonance of the spectrum or optical forces. Period boundary conditions are applied to the *x*- and *y*-directions and perfectly matched layers (PML) is constructed along the *z*-direction are constructed. The band structure is calculated using eigen frequency solver with gradual change of the incident angle.

The optical force is calculated by integrating the Minkowski Stress tensor over the surface the nanoparticle which is placed above the surface (Supplementary Fig. 2). The Minkowski stress tensor is expressed as⁷,

$$\langle T_{ij} \rangle = \frac{1}{2} Re \left[D_i E_j^* + B_i H_j^* - \frac{1}{2} (D \cdot E^* + B \cdot H^*) \delta_{ij} \right] \quad (1)$$

where $\langle \cdot \rangle$ means the time average operation over an oscillation period. And $\hat{n}$ is the unit vector normal to the enclosing surface. The optical force is simulated either using the eigen frequency solver (Fig. 1d) or frequency solver (Fig. 2d) in COMSOL.

The simulation of temperature in the VDC is also performed in COMSOL with the combination of three modules, e.g., Electromagnetic Waves (Frequency Domain), Laminar Flow and Heat Transfer in Fluids. Two multiphysics are configurations are set, which are Electromagnetic Heat Source and Non-Isothermal

Flow. The maximum mesh in each component of the model is set to $\lambda/10/R$, where λ is the wavelength of the laser and R is the refractive index of each component. The minimum temperature interval is set to 10^{-8} s to investigate the time-dependent temperature distribution in the VDC.

Declarations

Data availability

All data needed to evaluate the conclusions in this paper are available in the main text or the supplementary materials.

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Author contributions

Y.S., A.Q.L., D.P.T. and Y.K. conceived this idea; Y.S., Y.W., M.-K.C., S.W., Y.Y., C.T.C., Y.K., D.P.T. and A.Q.L. performed theoretical analysis and numerical simulations; Y.S. fabricated the nanophotonic chips. Y.S., Z.L., H.C., J.L., F.W. and T.T.B.N. conducted experimental studies; Y.S., Y.W., M.-K.C., L.K.C., S.W., Y.Z., Z.L., X.Z., H.C., Y.Y., P.H.Y., W.S., T.T.B.N., J.L., F.W., C.T.C., Y.K., D.P.T. and A.Q.L. involved in the discussion and data analysis. Y.S., L.K.C., S.W., C.T.C., Y.K., D.P.T. and A.Q.L. wrote the manuscript. L.K.C., C.T.C., D.P.T., Y.K. and A.Q.L. supervised this project.

Competing interests: The authors declare no competing interests.

Additional information

Supplementary Information is available for this paper at

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Figures

Figure 1

Concept of virus manipulation with resonator nanohole arrays. **a** Schematic illustration of nanocavities. The nanocavities are illuminated with a projected Gaussian beam with a diameter $> 10\ \mu\text{m}$. Viruses smaller than the nanohole size ($D_h = 110$ nm) are caged inside the nanoholes when flowing to the laser illumination area. **b** Illustration of the packaged VDC. The nanochannel has a depth of $1\ \mu\text{m}$ so that the nanoparticle and virus are immersed in the near-field light wave to experience strong optical force. The images of virus can be captured through the (1 mm) quartz glass. Multiple layers from the top to bottom are PDMS (thickness 5 mm), Quartz (1 mm), PMDS (1 μm), Si_3N_4 (250 nm), SiO_2 (2 μm) and Silicon (730 μm). **c** Illustration of the normalized electric field $|E|$ of the Trapping mode with light trapped inside the hole and the Futile mode with light trapped inside the solid Si_3N_4 . **d** Dispersion relation around 532 nm for laser resonances in both ΓX and ΓM directions. **e** Calculated optical forces in the z-direction of four resonances with TE modes. The radius and refractive index of nanoparticle are 50 nm and 1.58. The particle is placed right above the hole. Insets show the normalized electric fields.

Figure 2

BIC-empowered nanocavities for virus trapping. a-b Reflection (a) and Electric field (b) enhancement ($S = |\max E_{\text{hole}}|/|E_{\text{in}}|$) spectra of the nanocavities as a function of radii and intervals. The insets in (a) show the normalized electric field in the y - z planes. The electric field is enhanced by 73-fold. The two red lines in (b) with mode 1 and mode 6 are the Trapping mode with light trapped inside the hole and can be used for the trapping. The blue lines with mode 2 and 5 are Futile modes with light dispersed in the solid Si₃N₄ and cannot be used for the trapping. c Poynting vector distributions in the y - z plane with a particle placed on top of the nanohole (red circle). The scale bar is 200 nm. d Calculated trapping force for nanoparticles with refractive index of 1.4 and 1.58 when $D_h = D + 10$ nm and $D_h = 110$ nm. e Simulated optical trapping potential well landscapes of a 100-nm nanoparticle at $z = 115$ nm (particle centre). f Temperature increase as a function of laser intensity. The temperature increase induced by the laser used in the experiment is less than 0.01 °C. The left and right insets show the temperature distribution of the x - z plane in steady state with flow velocities of 0 $\mu\text{m/s}$ and 10 $\mu\text{m/s}$, respectively. Two insets share the same colour legend.

Figure 3

Demonstration of virus hopping and caging. **a** Schematic illustration of adenovirus hopping from the adjacent hotspot to the central hotspot with higher laser intensity. **b** Simulation of virus hopping along the diagonal direction. **c** Scanning electron microscopic image of the fabricated Si_3N_4 nanocavity array. **d** Trapping, transporting, positioning, and caging of adenoviruses < 110 nm. **e** Patterning of nanoparticles and adenoviruses.

Figure 4

Demonstration of sorting of adenoviruses by their size. a Sorting of the nanoparticles. The 100 nm polystyrene nanoparticles can be caged inside the nanoholes with a diameter of 110 nm, while the nanoparticle complex will escape from the beam when the beam is shifted swiftly. b Experimental demonstration of the trapping of big adenovirus inside the beam and releasing when the beam is shifted. c Size distribution of adenovirus measured by Nanosizer. d Size distribution comparison measured by quasi-BIC nanocavity array and Nanosizer.

Figure 5

Demonstration of virus hopping and caging. a Schematic illustration of adenovirus hopping from the adjacent hotspot to the central hotspot with higher laser intensity. b Simulation of virus hopping along the diagonal direction. c Scanning electron microscopic image of the fabricated Si₃N₄ nanocavity array. d Trapping, transporting, positioning, and caging of adenoviruses < 110 nm. e Patterning of nanoparticles and adenoviruses.

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