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Nanofluidics: a New Arena for Materials Science

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ADVANCED MATERIALS

Abstract

A significant growth of research in nanofluidics is achieved over the past decade, but the field is still facing considerable challenges toward the transition from the current physics-centered stage to the next application-oriented stage. Many of these challenges are associated with materials science, so the field of nanofluidics offers great opportunities for materials scientists to exploit. In addition, the use of unusual effects and ultrasmall confined spaces of well-defined nanofluidic environments would offer new mechanisms and technologies to manipulate nanoscale objects as well as to synthesize novel nanomaterials in the liquid phase. Therefore, nanofluidics will be a new arena for materials science. In the past few years, burgeoning progress has been made toward this trend, as overviewed in this article, including materials and methods for fabricating nanofluidic devices, nanofluidics with functionalized surfaces and functional material components, as well as nanofluidics for manipulating nanoscale materials and fabricating new nanomaterials. Many critical challenges as well as fantastic opportunities in this arena lie ahead. Some of those, which are of particular interest, are also discussed.

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1. Introduction

Nanofluidics is the study and application of fluids in and around geometries with nanoscale characteristic dimensions. The field of nanofluidics is not brand-new. Some issues associated with nanoscale fluidics have been occasionally dealt with by researchers in membrane science, colloid science, and chemical engineering for many decades. Nonetheless, nanofluidics has never attracted as much attention as it does now, owing to advances in nanofabrication, which give a boost to the recent growth of nanofluidics.[1–5] The increased availability of nanofabrication methods over the past two decades allows the fabrication of well-defined nanofluidic geometries such as nanochannels and nanopores to form novel nanofluidic devices.[6–8] Such devices, usually solid-state, planar, and transparent, are compatible with some available tools used in chemistry, physics, biology, and engineering. Such devices therefore provide accessible experimental platforms allowing the study of nanofluidics by researchers with different backgrounds, and in turn new tools and methodologies are increasingly being developed. As a result, exploration and application of nanoscale fluid behaviors and related phenomena in a controllable, reproducible, and predictable way gradually become possible.[9–17] In this article, the selected topics are mainly discussed in the context of nanofluidics confined in such nanofabricated devices with well-defined nanofluidic environments.

Nanofluidics is usually considered to be a realm evolved from microfluidics, but is obviously not just an extension of microfluidics. New physical phenomena and mechanisms which are not observed at microscales or in bulk start to emerge and dominate at nanoscales, opening up a virgin research territory to explore new scientific insights and applications of fluids. The representative phenomena and effects that have been unveiled include nonlinear transport (such as concentration polarization,[18–23] ion-current rectification[24–28]) and altered liquid properties of water (such as lower dielectric constant,[29,30] higher viscosity,[29–31] and higher proton mobility,[32–34] than in the bulk), mostly stemming from ultra-high surface-to-volume ratios, surface charge, and electric double layer overlap exhibited in nanochannels (Figure 1). The discussions of these phenomena, as shown in Figure 1, mainly focus on a range of length scales between 1 nm and 100 nm, which are the typical scales of nanofluidics (herein referred to as “classical nanofluidics”).[1,2,5] In many occasions, the discussions even extend scales over 100 nm to several 100 nm, which falls in a range of scales sometimes called “extended nanofluidics” (10–1000 nm; Figure 1).[4,35] From a perspective of application potential, the length scales of the so-called extended nanofluidics embrace a much wider range of nanometric objects, for example, nanoparticles, DNAs, viruses, exosomes, lipid vesicles, and polymers (Figure 1), which are of great interest in materials science, physics, chemistry, biology, energy, bioengineering, drug discovery, and clinical medicine. In addition, even though in the cases of handling such nanometric objects in extended nanofluidic environments with features larger than 100 nm (i.e., beyond the range of classical nanofluidics), the length scales of interspaces/fluids among the nanometric objects or between the channel walls and the nanometric objects often lie in the range of typical scales of classical nanofluidics (i.e., 1–100 nm). In such cases, physics and principles of classical nanofluidics can be of course applied or further explored. From these views, therefore, “nanofluidics” discussed in this Progress Report covers both regimes of “classical nanofluidics” and “extended nanofluidics” (Figure 1).

In the past decade, nanofluidic transport phenomena and effects have been intensively investigated, and a few striking applications (for example, nanopore-based DNA sequencing,[36–39] nanofluidic diodes or transistors[28,40–43], and resistive-pulse sensing[12,44–46]) have been demonstrated. The progress in these aspects has been reviewed extensively in the abovementioned recent publications and we will not go into details in this article. However, nanofluidics is still in its young stage, especially in comparison with its booming "brother" microfluidics. Because nanochannels are ultra-small closed space systems, most standard tools widely used in microfluidics as well as in nanosciences for open planar systems are difficult to directly apply to the field of nanofluidics. The technologies and methodologies enabling low-cost, high-throughput nanofabrication of nanochannels, nanofluidic control, nanofluidic measurement, function integration, molecular detection are still lacking. These major challenges not only hinder the involvement of much more researchers in many other fields to work with nanofluidics, but also impede the transition of nanofluidics research from the current physics-centered stage to the next application-oriented stage.

However, these challenges are also big opportunities for researchers with different backgrounds, for example, materials science. Materials science is expected to play an important role in not only nanofabrication, as it has already contributed to the field of nanofluidics, but also others. For example, well-defined nanofluidic environments would be a new arena to exploit possibilities of materials unachievable in the bulk and microscales. This is not only because of the aforementioned unique phenomena and effects of nanofluidic transport, but also because nanochannels are predicted to display unusual properties closely related to materials, due to their ultrahigh surface-area-to-volume ratios, ultra-short diffusion lengths, and ultra-short heat transfer distances. In addition, as listed in Figure 1, many important materials of great interest to the multidisciplinary community lie in the same length scales as nanofluidics, so nanofluidics opens up possibilities to separate, isolate, detect, manipulate, assemble, and organize these nanometric materials with a spatial and temporal resolution which is ever unattainable. Meanwhile, the assembly and manipulation of functional nanometric materials in nanochannels will in turn provide well-controlled additional functions and promise to greatly improve the capabilities of nanofluidics for the creation of versatile new systems and applications.

Some efforts and trials on the exploration of associating functional materials with nanofluidics have been carried out in the past few years, though not a lot. The goal of this article is to provide a selected overview of the recent progress, rather than a comprehensive review of the entire field. As conceptually depicted in Figure 2, the progress is summarized into five main directions: (1) materials and methods for fabricating nanofluidic devices (Figure 2a), (2) nanofluidics with functionalized surfaces (Figure 2b), (3) nanofluidics integrated with functional material components (Figure 2c), (4) nanofluidics for manipulating biological and nanoscale materials (Figure 2d), and (5) nanofluidics for the fabrication and synthesis of nanomaterials (Figure 2e). These five directions also form the following sections of this article, focusing on subjects of materials associated with the nanofluidic devices having well-defined nanochannel structures, as shown in Figure 2. To provide a full picture of recent progress in the first direction, new materials such as carbon nanotubes and two-dimensional materials to form alternative types of nanofluidic devices are also involved. In addition, in both past (as described in the very beginning of the article) and present, there is also a fairly significant intersection between micro-, meso-, and macroporous materials and nanofluidics, primarily driven by separations and catalysis, for example, molecular sieves (e.g., zeolites),[47–49] capacitive deionization,[50–52] metal–organic frameworks,[53–56] etc. These subjects are not covered here and interested readers are directed to other excellent reviews and articles on these subjects.

2. Materials and Methods for Fabricating Nanofluidic Devices

2.1. Major Materials and Methods

Out-of-plane nanopores and in-plane nanochannels are two typical nanofluidic structures. Nanopores can be biologically formed in lipid bilayers,[57] nanofabricated in thin solid-state membranes (for example, polymer membranes and silicon compound membranes such as silicon nitride membranes),[57–59] created in two-dimensional (2D) materials such as graphene,[60] or made in a hybrid of these materials. Nanopores have been applied to single molecule detection and DNA sequencing based on a principle of ionic or transverse tunneling current sensing through a nanopore. The materials, fabrication, and applications of nanopores have been well described in recent review articles[44,61–65] and will not be considered here.

Nanochannels are the core components of most nanofluidic devices. The methods for the fabrication of nanochannels vary depending on the substrate materials. Silicon was used to fabricate nanochannels in the early time via the direct transfer of nanofabrication technologies well established in the field of microelectronics.[66–68] In the past years, the fabrication of nanochannels in glass (fused-silica glass, in general) substrates was developed. Afterwards, glass became a major substrate material for the fabrication of nanofluidic devices, because of its excellent properties which are favorable for chemical and biological studies and applications. These excellent properties include superior optical transparency, thermal stability, chemical/biological inertness, mechanical robustness, and hydrophilic nature which is favorable for liquid introduction. However, besides the high cost of glass substrates, glass nanochannels are generally fabricated using expensive nanofabrication technologies such as e-beam (EB) lithography combined with plasma dry etching[69,70] or focused ion beam (FIB) lithography[71,72] through a series of delicate, sophisticated, and time-consuming processes conducted in high-class clean rooms. Such strict and expensive conditions have unfortunately restricted the development of glass nanofluidic devices to only a few research groups. Therefore, new alternative materials and methods for the fabrication of nanochannels are being explored for the purpose of efficient and economical promotion and acceleration of the development of nanofluidics.

2.2. Alternative Materials and Methods

Polymer-based materials are attractive alternatives, because of their low cost and flexible processing.[73–77] While polymer-based materials have been widely used to fabricate commercial microfluidic devices, their use in the fabrication of nanofluidic devices is still relatively rare. Unwanted deformation during the replication of nanochannel structures is a critical problem. Some groups have attempted to resolve the problem. For example, Park et al. achieved a significant reduction of unwanted substrate deformation during a direct single-step imprinting process by using a polymer stamp comprising a UV-curable resin.[73] The use of the technique enabled them to fabricate sub-100-nm nanochannels on poly(methylmethacrylate) (PMMA) substrates.

Similarly, fabricating nanochannels in soft materials like polydimethylsiloxane (PDMS) has faced many challenges, despite its popularity in the fabrication of microfluidic devices. A major challenge is dimensional instability and roof-collapse of channel structures after bonding, resulting from the low stiffness of regular PDMS (due to the low Young's modulus). While the use of hard-PDMS (h-PDMS) can somewhat alleviate the problem,[78–80] previous studies on the mechanism of such channel collapse have brought about new strategies of nanofluidic fabrication through active manipulation of the collapse.[81,82] Craighead et al. demonstrated the cost-effective fabrication of PDMS nanochannels based on the controlled collapse of microchannel structures.[83] PDMS nanochannels as small as 60 nm was achieved and DNA elongation experiments were demonstrated in the fabricated nanochannels.

However, due to the insufficient controllability of the geometric dimensions, further study is necessary to improve the fabrication repeatability and reproducibility of this technique.

In 2015, Kim et al. reported an alternative technique for fabricating PDMS nanofluidic devices based on another type of materials failure—cracks.[84] Cracks are often considered unfavorable especially in micro-/nanofabrication, but have been actively utilized to form micro-/nanopatterns sometimes. The technique developed by Kim et al., called cracking-assisted photolithography, overcome several crucial weakness and limitations of conventional cracking-based micro-/nanopatterning, such as limited substrate materials and incapability of manipulating crack development. In their study, to form cracks, micro-notch structures were first fabricated by using a standard photolithography process on a previously ultraviolet-exposed photoresist (SU-8) film (Figure 3a), which exhibited a gradient in cross-linking density (elastic thin layer and viscoelastic foundation) along the direction normal to the substrate (Figure 3b). These micro-notch structures as well as tensile stresses resulting from the gradient structures of the photoresist layer enabled well-controlled crack initiation, propagation, and termination (Figure 3a, b), during the development process. Nanopatterns resulting from the cracking could be easily controlled by the shape of the micro-notch structures and other process parameters. Hence, the technique allowed the production of various nanopatterns (for example, nanochannels) with accurately controlled geometric dimensions on a large area. The nanopatterns could be employed as master moulds to replicate complex nanofluidic devices using h-PDMS though soft lithography. A high-throughput nanofluidic device which has 1,000 pairs of microchambers connected through crack-assisted nanochannels for nanofluidic transport was also demonstrated (Figure 3c–g). Therefore, the cracking-assisted photolithography provides a promising way to fabricate nanofluidic devices without using high-cost conventional nanolithography. In addition, it also holds the potential to derive different approaches based on the same concept. For example, more recently, the fabrication of PDMS nanochannels with controllable channel size and spacing by taking advantage of solvent-induced crack formation was reported by Li et al.[85]

2.3. New Materials

Carbon nanotubes (CNTs) have emerged as new materials for studying unusual transport phenomena confined on length scales corresponding to molecular dimensions, because it can be directly employed as nanofluidic channels without complicated lithography processes.[86,87] In the early time, however, it was difficult to fabricate a CNT nanofluidic device, so researchers used molecular simulation as the first tool to study fluid characteristics in CNTs.[88–90] In the past few years, experimental studies were achieved first with CNT membranes and thereby opened up the road to exploit unique transport effects in CNTs and potential applications. Because the probed transport are averaged behaviors across numerous nanochannels in the CNT membrane, more recently there is a trend to experimentally study transport in isolated single CNTs to unveil detailed fluidic characteristics in CNTs. Some groups have built single-CNT nanofluidic platforms by overcoming the great challenge to embed single CNTs in micro/nano devices via various approaches.[91–95] These platforms offer great potentials to utilize CNTs as building blocks to flexible build devices with complex nanofluidic networks in the future.

Two-dimensional (2D) materials such as graphene, graphene oxide (GO), and other related materials are another new material family of great interest for nanofluidics.[96,97] Like CNTs, the layered structures of these 2D materials based large-scale membranes allow the fabrication of nanofluidic devices through non-lithography approaches. The concept stems from the fact that the interlayer spaces between 2D materials form nanoscale channel networks, allowing 2D confinement and transport of ionic species and molecules.

The concept was experimentally proved by Huang et al. in 2012.[98] They demonstrated the feasibility of fabricating cation selective nanofluidic devices through 2D layered materials. Large-scale arrays of nanochannels with height of ~1 nm were formed by restacking exfoliated GO sheets into a multilayer structure. GO sheets were negatively charged when dispersed in water, due to various oxygen containing groups presented on them. Surface-charge-governed nanofluidic ion transport (i.e., enhanced ionic conductivity) through such reconstructed layered GO sheets was observed for electrolyte concentrations as high as up to 50 mM. The work manifested that the use of 2D layered materials would be an innovative solution to the facile creation of flexible and large-scale (centimeter-long) nanofluidic devices.

The concept was also proved by others later.[99,100] For example, Jiang et al. constructed a macroscopic nanofluidic network in a layered graphene hydrogel membrane (GHM) with interlayer spacing of approximately 10 nm.[100] The layered GMH membrane was prepared through a simple solution process with low cost. In their design, electrolytes pass through the membrane vertically, generating a cross-membrane ionic current. The study also suggested that the layered GHM-based nanofluidic circuits could be used as fluidic energy conversion devices.

In 2015, Huang et al. further demonstrated the proof of concept of such kind of nanofluidic devices using more readily available clay layers rather than GO and graphene-based 2D materials.[101] They selected vermiculite as a model clay material in their study. Vermiculite is a layered magnesium aluminosilicate comprising two tetrahedral phyllosilicate sheets for every one magnesium-based octahedral sheet (Fig. 4a). The reassembly of chemically exfoliated vermiculite sheets by vacuum filtration created a thin vermiculite film (Fig. 4b) having a uniform lamellar microstructure with well-defined interlayer spacing (Fig. 4c), which forms nanochannels for experiments (Figure 4d). The vermiculite nanochannels showed higher-than-bulk proton conductivity (Figure 4e) and remarkable thermal stability greatly better than that of GO nanochannels. These features are favorable for the development of nanofluidic devices with low cost for long-term use.

More recently, Cheng et al. demonstrated that the interlayer spacing of layered graphene-based membranes can be continuously tuned by a solvent exchange method.[102] This made it possible to measure unusual scaling behaviors of both diffusive and electrokinetic ion transport in nanochannels with sizes across the entire range of sub-10-nm, which has been technical difficulties for conventional nanofluidic platforms.

The use of carbon nanotubes and 2D materials provides alternative ways to flexibly fabricate large-scale nanofluidic devices without using traditional nanolithography technologies. Considering these advantages, we can expect that these new materials will have a more and more important role in the field of nanofluidics in the future.

3. Nanofluidics with Functionalized Surfaces

Due to ultrahigh surface-to-volume ratios of nanochannels, surface properties dominate both “surface-charge-governed” and “geometry-governed” transport phenomena in nanofluidic devices, as well as capabilities and performance of various nanofluidic applications. Hence, the ability to modify and functionalize the surface characteristics of nanochannel walls is of great interest in the field of nanofluidics. The surface modification and functionalization are not only greatly helpful in the elucidation and exploration of unusual nanofluidic effects, but also indispensably crucial in the creation of novel devices and applications through making full use of the unusual effects. However, because nanochannels are ultra-small closed space systems, their surface modification and functionalization are not very easy. Especially, nanochannels tend to get clogged much more easily in comparison with microchannels, resulting in difficulties to use most useful methods of surface modification in microfluidics or for open surfaces.

Despite these challenges, some advances have been made recently. The major motivation of surface functionalization in most recent cases has been to obtain means to enable the "smart" control of nanofluidic transport behaviors (for example, ionic gating, ionic current rectification, nanofluidic diodes/transistors, and biomimetic ion channels), to response various environmental variables such as pH,[26,103–106][40] temperature,[40,107] ions,[104,108] specific molecules,[108–110][40] and electrochemical potential.[26] A variety of chemical substances including small molecules,[26,104,105] supramolecules,[108] biomolecules (for example, DNA),[110] and polymers[26,106,109] have been used to modulate surface charge,[104,106,111] wettability,[104,112] polarity,[106] functional groups,[26,103,105,106,109,110] through a wide range of methods such as chemical coupling,[26,103,104,108] ultraviolet (UV) irradiation,[105,112] physical adsorption,[111] self-assembly,[106,110,111] graft,[106,109] electrochemical polymerization,[26] spontaneous self-polymerization.[106] These advances have been reviewed elsewhere[24,113,114] and herein we will not further discuss in details.

As nanofluidics shows promise in single-molecule studies of biomolecules such as proteins and DNAs, the development of nanofluidic devices for these studies has increased recently and will attract more attention in the future. In comparison with ions and water molecules which have been the main players in previous studies of nanofluidic transport, biomolecules are usually larger molecules whose sizes approach characteristic dimensions of the nanochannels. Hence, surface effects get more dominant and hold greater impact on biomolecules. Then, intimate interactions between biomolecules and nanochannel walls simultaneously offer both opportunities and challenges. For example, the use of these interactions provides a promising way to directly observe, manipulate, and even probe organization of single biomolecules, but clogging, debris, and nonspecific adsorption resulting from undesired interactions are critical issues significantly affecting results. To tackle the challenges, surface modification of nanochannel walls is essential, but so far little progress (in terms of recent published papers) has been made because of difficulties. Herein, we select one impressive work reported by Tegenfeldt et al.[115] to make a simple introduction. To resolve the problem resulting from nanospecific protein adsorption in their study on the interaction of single DNA with proteins in nanochanenls, they developed a method for surface modification of nanochannels based on a lipid bilayer (LBL), which is a universal component of most cells and has ability to suppress non-specific bindings. In their method, they first introduced lipid vesicles (approximately 70 nm in diameter) to a microchannel (100 nm order), where the lipid vesicles ruptured, and formed a LBL to coat entire microchannels (Figure 5a). Then, the LBL in the microchannel spontaneously spread into nanochannels. As a result, a uniform lipid bilayer with fluidity and continuity formed in the nanochannels. Because the lipid bilayer exhibited high capability to avoid nonspecific adsorption of proteins (Figure 5b, c), it enabled the rapid movement of protein-DNA complexes in the nanochannels (Figure 5d). Therefore, the lipid bilayer-based coating is very useful to facilitate the direct visualization of the structure and the dynamics of protein-DNA complexes in nanochannels.[115–121] Last but not the least, it is worthy of attention that more recently Kitamori et al.[122] demonstrated that the use of a nanochannel coated with a lipid bilayer allowed sampling of a single cell content, which has been a challenge in single cell analysis because of the ultra-small volume.

Nonetheless, functionalization and modification of nanochannels are still facing considerable challenges. For example, solutions to accurate and selected modification of partial surface of nanochannel walls are still lacking, though some promising methods[123–126] have been reported (one of them, namely nano-in-nano integration,[126] will be described in the next section). In addition, due to quite large size of polymer molecules, surface functionalization with polymers is practically difficult, though many studies based on simulation and modeling have suggested that the involvement of polymers on nanochannel walls would bring about not only desired unusual effects on nanofluidic transport but also versatile nanofluidic applications.[127–131]

4. Nanofluidics Integrated with Functional Material Components

To advance the transition of nanofluidics research from the recent physics-centered phase to the next application-oriented phase, abilities allowing the integration of various kinds of functional material components into nanofluidic devices are indispensably required. Functional materials can serve as fluidic, chemical, biological, electrical, optical, thermal, and magnetic components in nanofluidic devices. Through the integration, unusual phenomena of nanofluidic transport and characteristic effects of confined nanospace are coupled with diverse properties of various functional materials. Synergy effects beneficial from such integration would offer formidable opportunities to create groundbreaking ideas as well as breakthrough applications. Hence, the integration possesses great potential to trigger formation of new fascinating interdisciplinary fields (for example, “nano-optofluidics”). However, the lack of methods for such integration has been one of the most critical bottlenecks in the field of nanofluidics, due to physical barriers arising from the ultrasmall and closed feature of nanochannels.

Integration before bonding and integration after bonding are considered to be two basic strategies. For integration after bonding, it is physically difficult to achieve by using current available nanofabrication approaches, due to the ultrasmall and closed feature of nanochannels. For integration before bonding, nanoscale-accuracy alignment and component material-friendly bonding are two significant technical hurdles. The first hurdle is because the integration of components in nanochannels usually requires multiple-step nanofabrication, which generally consists of a first step of nanofabrication of open nanochannels followed by steps of formation of dissimilar material components on exact locations in the open nanochannels in a controlled manner. Therefore, nanoscale-accuracy alignment during the multiple-step nanofabrication steps is necessary, but is greatly challenging. The second hurdle is because bonding of nanofluidic devices is usually performed under strict and harsh conditions, for example, harsh cleaning processes, high temperature, high pressure, as described in other excellent reviews[8][132][14][6] and articles[133,134] on bonding of nanofluidic devices. The conditions may bring about damage of the integrated components. Therefore, component material-friendly bonding is required for in situ integration of functional components in nanochannels.

4.1. Integration Bypassing Technical Hurdles

Despite the difficulty, some impressive works through bypassing the hurdles have been reported. Most of these works focused on the integration of electrical components (for example, electrodes) to enable electrical measurements (impedance[135] and resistance[136]), electrochemical reaction and detection,[137–139] or external physical operation[140,141] for nanofluidic devices.

Three major strategies which allow bypassing the hurdles have been demonstrated in the above-mentioned works. A first strategy is to place functional material components in microstructures (for example, microchannels and microchambers) which are connected to nanochannels, or in one separate layer (usually soft materials like PDMS) which can be easily bonded with another layer comprising nanochannels. Through certain transduction mechanism, the actuation of such components located around or in the outside of nanochannels allow the regulation of fluidic behaviors in the nanochannels. For example, surface acoustic waves (SAW)-actuated nanofluidic structures (Figure 6a–c) developed by Friend et al.[141] fall into this category. Their nanofluidic device (Figure 6a) was integrated with external interdigital electrodes (IDTs) to generate SAW (Figure 6b) along a nanochannel formed from bonded transparent lithium niobate (LN) wafers (Figure 6c). The use of SAW generated by the external IDTs enabled to fill and drain fluid from the nanochannel. In addition, a three-state nanofluidic field effect switch (Figure 6d–g) developed by Prakash et al.[140] also falls into this category. In their nanofluidic device, gold gate electrodes were fabricated on a second glass substrate and bonded to the glass substrate with channel network through an intermediate PDMS layer (Figure 6d, e). By controlling the gate potential (Figure 6f, g), field effect current switch with a forward (positive), off (zero), and a reverse (negative) current state for tunable control of ionic transport was demonstrated. A second strategy is to direct use nanoscale volumes enclosed by microfabricated planar electrodes which simultaneously act as electrochemical components. By using this smart strategy, Lemay et al. developed nanofluidic electrochemical systems for integrated detection of electrochemical processes and enzymatic reactions in sample volumes of few femtoliters (Figure 6h, i).[137,138] A third strategy is to fabricate nanochannels with embedded transverse electrodes, as presented by Ziaie,[135] Yamamoto,[136] and Bohn.[139] Because nanoscale accuracy alignment is not necessary for this case, conventional photolithography can easily meet the requirement of fabrication. Furthermore, PDMS is usually used to package the device so that device bonding can be achieved in a mild condition without bringing about damage to the integrated electrodes. These devices integrated with transverse electrodes have been applied to measurements of resistivity[135] and impedance[136] in nanochannels, as well as electrochemical generation of oxygen on chip (Figure 6j–m).[139]

4.2. In-situ Integration Surmounting Technical Hurdles

In contrast to these strategies bypassing the technical hurdles (i.e., nanoscale-accuracy alignment and material-friendly bonding), Xu et al. developed a new strategy (called 'nano-in-nano integration', Figure 7a) based on two key techniques which enable to direct surmount both hurdles. One is a technique allowing bonding of glass nanofluidic devices at low-temperature[70,126] or even room-temperature (25 °C)[142] through a simple surface activation using plasma treatments. Bonding of glass micro-/nanofluidic devices has been conventionally performed by using a fusion-bonding process at high temperatures (for example, ~1000 °C) and high vacuum;[133,134,143,144] such severe condition has been a major obstacle impeding nanofluidic integration. By using a two-step plasma surface activation process which consists of an O_2 reactive ion etching plasma treatment followed by a nitrogen microwave radical activation, they achieved a direct bonding of glass nanofluidic chips at around 200 °C in ambient air.[70] After that, the process was further modified. A strong, nanostructure-friendly, and high pressure-resistant room-temperature (25 °C) bonding method based on a one-step surface activation process with an O_2/CF_4 gas mixture plasma treatment was developed. These plasma treatments are able to adjust surface groups[145] as well as the wettability[146,147] of the substrates, which is considered to facilitate bonding in mild conditions, but the bonding mechanism is still not very clear and need further elucidate. The use of the new bonding techniques thoroughly eliminates the obstacle of bonding for functional component integration in nanochannels. Another is a technique capable of the placement control with a precision of several tens of nanometers for multiple-step nanofabrication.[126] The technique was based on accurate positioning of the fabrication placement assisted by a pair of gold reference marks, which could be searched manually and recognized by using a backscatter detector. The use of the technique allows the fabrication of arbitrary (for example, quasi-0D, quasi-1D, 2D, and 3D) features of functional materials in tiny open nanochannels, with nanoscale accuracy.

As conceptually depicted in Figure 7a, the nano-in-nano integration based on these two techniques comprises primary nano-in-nano patterning before bonding by using top-down approaches, low-temperature/room-temperature bonding, and/or secondary molecule patterning after bonding by using bottom-up approaches. As a versatile methodology and technique, the nano-in-nano integration open up a way to in situ integrate a wide range of functional material components (such as fluidic, chemical, biological, electrical, optical, thermal, and magnetic ones) in nanochannels. For example, fabrication of high-density gold nanoarrays for biomolecule immobilization and recognition in arrayed femtoliter nanochannels (Figure 7b, c),[126,148] integration of nanoscale probe electrodes enabling in situ probing of unusual effects of nanofluidic transport (Figure 7d–f),[29] and local assembly of soft matter-regulated nanovalves with nanoscale accuracy in nanochannels allowing the active regulation of femtoliter-scale fluid flows (Figure 7g–j),[149] have been demonstrated. Such integrated functional components are very useful for single cell omics studies, high-throughput single molecule detection, accurate operation of liquids of ultra-small volumes, and single molecule manipulation in the near future.

5. Nanofluidics for Manipulating Biological and Nanoscale Materials

Current understanding of nanoscale transport and knowledge of physics, biology and materials science allow us to envision new mechanisms and novel techniques to achieve fast , high-throughput manipulation of individual nanoscale objects—whether biological or non-biological entities—with super-high spatial–temporal resolution, rather than masses of all at once. To reach this goal, the considerable development of technology is required. Nanofluidic technology is of course necessary. This should come as no surprise, considering that the dimensions of nanochannels approach the dimensions of many biological and nanoscale objects of interest in a wide range of disciplines, as summarized in Figure 1. Therefore, in this section the current trend on 'manipulation' of 'single' nanoscale objects using well-defined nanochannels is focused, while many early works on analysis and separation of biological and nanoscale materials using nanofluidic devices, as well as nanoporous media in macroscopic and microfluidic channels, are not discussed here (review articles[1,6,12–14] can be referred to).

5.1. Manipulation of Single DNA Molecules

Nanochannels have been emerged as a promising tool to manipulate single DNA molecules.[150–153] Optical[154,155] and magnetic tweezers[156] are traditional tools capable of single DNA molecule manipulation, but the DNA molecule need to be tethered to solid surfaces or beads. In contrast, a single long DNA chain can be extensively confined and linearly stretched in a nanochannel without such tethering, allowing direct visualization,[157] probing,[158] mapping,[159] barcoding,[160,161] and in future sequencing of DNA on its own entire length scale. This advantage provides possibility to study single DNA molecules of any lengths, in a real-time, high resolution, high throughput, and massively parallel manner.

Thus far, a number of studies have been conducted towards this end,[150,159,162,163] but the flexible regulation of DNA translocation through nanochannels is still a critical one among various issues. Part of the motivation comes from developing nanochannel-based DNA sequencers, which are expected to enhance the sequencing performance by resolving typical challenging problems of current nanopore-based sequencing. The problems may involve, for example, DNA folding and extreme rapid DNA translocation across the nanopore, which either adversely affect the sequencing efficiency or impede the sequence from being identified at single-base resolution. The extensive confinement of the entire chain of a stretched DNA in a nanochannel having a diameter far below the persistence length of DNA, would refrain DNA from staying in a folded conformation, in terms of an energy favorable state. Furthermore, owing to ultrahigh surface-to-volume ratios of nanochannels, the DNA translocation speed could be reduced by surface functionalization to enhance interactions between DNA and the nanochannel wall. Such prediction has been supported by experiments recently. For example, Yobas et al. reported that DNA translocation through a nanochannel can be effectively slowed by electrically tuning the wall surface charge through an external gate bias (Figure 8).[164] The experiments were conducted on a nanofluidic field-effect transistor (NFET). The device involved a dielectric capillary (alumina; 50 nm in diameter), which was surrounded by an integrated gate electrode along its entire length (Figure 8a). The integrated gate electrode allowed for electrically modulating the surface charge of the dielectric alumina wall. In their experiments, a positive gate bias was observed to significantly reduce the translocation speed of DNA by one order of magnitude (Figure 8b), owing to enhanced electrostatic attraction between DNA chains and the capillary surface under the externally applied positive gate bias (Figure 8a). If the device could be further integrated with nanopores or tunneling electrodes in the future, it would be very promising for high-resolution DNA sequencing.

5.2. Manipulation and Tracking of Single Nanoparticles and Viruses

Recently, there is a trend towards the adoption of nanochannels to handle nanoparticles[165,166] and biological nanometric particles (for example, viruses[166,167]), despite potential issues posed by clogging. Manoharan et al. presented a high-speed tracking method of single dielectric nanoparticles and viruses by using optofluidic nanochannels (Figure 9a).[166] In their nanofluidic experimental platform, an open hollow cylindrical geometry inside the core of a single silica optical fiber was employed as a nanochannel (Figure 9b). Liquid containing unlabeled dielectric nanoparticles or viruses was introduced into the nanochannel by capillary forces. As claimed by the authors, clogging was not observed in their experiments, possibly because of repulsive electrostatic interactions between the channel wall and the nanoparticles or viruses. Then, light was guided into the core of the optical fiber to track the particles (Figure 9a, c). Because the diameter of the nanochannel (approximately 247 nm) is subwavelength of light, in the fiber a part of the optical mode overlaps with the cross-section of the nanochannel (Figure 9c). As a result, the guided light scatters off the nanoparticles or viruses. Through capturing scattered light by a microscope objective mounted perpendicular to the propagation direction (Figure 9a), tracking of individual unlabeled latex nanoparticles (as small as 19 nm in diameter; Figure 9d) and single cowpea chlorotic mottle virus virions (26 nm in size) was achieved, at high speeds of thousands of frames per second, for long durations of tens of seconds. These small viruses are usually difficult to track in the bulk using elastic scattering due to active Brownian motion. In contrast, a lowered diffusion coefficient was measured in the nanochannel, suggesting that Brownian motion of nanoparticles would be hindered due to the confinement[166] and thereby would contribute to the achievement of the unlabeled tracking. Hence, the study demonstrated an alternative method for tracking nanoscale particles which have been traditionally performed using confocal or fluorescence microscopy. Meanwhile, the study also suggests that through the combination with nanochannels, the performance of traditional techniques for manipulation or detection of nanoscale entities could be remarkably enhanced in terms of, for example, size, speed, resolution, duration, detection limit. Such enhanced performance would open up some new possibilities. For example, this reported method, owing to its high-speed and long-duration features of tracking, may allow the study of kinetics or dynamics of the assembly process of individual biological objects such as viruses. It is worthy of attention that in the same year Jacobson reported electrokinetic trapping of single virus (for example, hepatitis B virus) capsids in nanochannels (Figure 9e,f), allowing real-time monitoring kinetics of assembly reactions of single virus capsid formation (Figure 9g) via resistive-pulse sensing.[167]

6. Nanofluidics for the Fabrication and Synthesis of Nanomaterials

Nanofluidics can provide flow processes with features of nanoscale confinement, ultrasmall volumes below the picoliter scale, and strictly ordered steady streamlines, undergoing a variety of unusual fluidic and liquid effects as aforementioned. Such flow processes are very favorable for the fabrication or synthesis of nanomaterials with well-defined sizes and geometries, highly-ordered architectures, well-regulated orientation, and desired unusual properties, which are difficult or impossible to achieve via the bulk or microscale processes. It is a promising and exciting direction of nanofluidics, where a few exploratory studies have been reported recently.[168–173]

Serghei et al. presented the fabrication of polymer nanowires using a nanofluidic approach.[172] A main part of their nanofluidic device (Figure 10a) was a highly ordered nanoporous membrane (anodic aluminum oxide membrane) with a pore diameter of 40 nm and a typical length of 100 μm. Melting a bulk layer of the polymer (poly(vinylidenefluoride-co-trifluoroethylene), PVDF-TrFE), which was attached to the membrane, initiated flows of the melted polymer into nanochannels in the membrane (Figure 10a). After a certain time, the melted polymer confined in the nanochannels was crystallized during the flow process by cooling to room temperature, and as a result nanowires formed in the nanochannels. The formed polymer nanowires could be released from the nanofluidic device after partially or totally dissolving the membrane in a chemical solution. The obtained polymer nanowires exhibited a high aspect ratio and a well-defined diameter which is equal to the pore diameter of the membrane (Figure 10b). In addition, melting/crystallization of the polymer in the nanochannels could be real-time monitored in real time, by means of permittivity measurements. The measurements were achieved by using integrated electrodes, which were sputtered thin gold layers on the top and bottom surfaces of the porous membrane through a well-controlled sputtering process (Figure 10a). The information obtained via the real-time monitoring are very useful to manipulate the crystallization processes and optimize flow conditions, which would be helpful to facilitate the fabrication of nanowires with desired orientation and crystalline structures in the future.

The use of open nanochannels, despite simultaneously losing some advantages stemming from complete nanoconfiment of fluids, might be a smart strategy to synthesize nanomaterials using nanofluidic flows, as recently demonstrated by Horváth et al.[173] In their study, guided growth of nanowires of a photovoltaic compound ($CH_3NH_3PbI_3$) were achieved, by means of a process involving drop casting, solvent evaporation, metastable solvatomorph deposition, and crystallization in arrayed open nanochannels, which were easily formed by high resolution e-beam resist nanopatterns (Figure 10c–f). The method allows the synthesis of perovskite nanowires with controlled sizes, aspect ratios, cross-sectional shapes, and orientation on wafer-scale surfaces (Figure 10g, h), which have been difficult to achieve through traditional deposition techniques. The study offers a unique way to utilize nanofluidic flows, avoiding many difficult chip fabrication processes and complicated nanofuidic regulation. Such flexible way would be welcomed by some researcher (for example, materials scientists) who attempt to use nanofluidics but are hampered by technological barriers of fabricating nanofluidic devices.

Other interesting studies which have been reported in this direction may include the fabrication of nanoscale salt deposits,[171] nanofibers,[169] droplets,[170] nano-/microparticles,[170] and polymeric conical structures[168] by using nanofluidic flows. Although so far striking demonstrations are still lacking, much progress can be expected in the future. Of course, considerable development of nanofluidic methodologies and technologies, especially which enable versatile regulation of flows and powerful manipulation of materials in nanochannels, are required to reach the goal.

7. Outlook

We have witnessed a significant growth of nanofluidics over the past decade. Chemists, biologists, as well as mechanical scientists and engineers have contributed much to the growth but are still facing considerable challenges. Many of these challenges are associated with materials science, so meanwhile offer great opportunities for materials scientists to exploit. In addition, the use of unusual effects and confined spaces of nanofluidic environments opens up new mechanisms and technologies to manipulate nanoscale objects as well as to synthesize novel materials. Therefore, nanofluidics will be a new arena for materials science. Fortunately, we have experienced burgeoning progress which has been made towards this trend in the past few years, as partially summarized in this article. However, many challenges lie ahead. Some of particular interest are described as follows.

(1). Membranes of new materials (such as CNTs, 2D materials) can be directly used as nanofluidic devices without using expensive nanolithography technologies and are promising for applications such as separation, water purification, and high-efficient energy harvesting, but nanofluidic devices fabricated on solid-state substrates (such as glass) possess advantages in the ease of integration into a lot of available analytical methodologies and instruments, which would bring innovative devices and applications serving a variety of chemical, biological, and medical purposes. The development of new materials, low-cost nanolithography, and non-lithography technologies allowing the flexible fabrication of large-scale, high-throughput, three dimensional, solid-state in-plane nanochannels are required to broaden the commercial products and applications of the solid-state nanofluidic devices in the future.

(2). Clogging and fouling are critical issues occur in almost all applications of nanofluidics, due to the ultrasmall and closed feature of nanochannels. For fundamental studies on ionic transport in nanochannels, the use of ultrapure water and ultrapure solvents during the experiments as well as careful rinsing and drying after experiments is quite effective to avoid or alleviate clogging and fouling in nanochannels. However, for handling biological and nanoscale materials, clogging and fouling will frequently occur, due to the characteristic lengths of many biological and nanoscale materials are comparable to the dimensions of nanochannels, as shown in Figure 1. Clogging and fouling may be alleviated by delicate design of nanochannel structures and coating of channel walls to decrease interactions between these nanomaterials and channel walls as well as nonspecific adsorption of biomolecules. Coating with polymers widely used microfluidics usually bring about severe clogging, so coating with small molecules will be a feasible strategy. Therefore, synthesis of small molecules enabling to modulate surface energy and suppress nonspecific adsorption in nanochannels will be important in the future.

(3). To reach the goal of single cell omics which is a large-scale task in current biology and medicine, abilities allowing high-throughput manipulation and detection of subcellular entities are required. Nanofluidic devices are promising tools for these purposes due to subcellular volumes of nanochannels. The development of technologies and materials for fabricating nanoarray of functional surfaces or material domains in tiny nanochannels to selectively capture subcellular entities, as well as efficient mechanisms for simultaneously handling a large number of subcellular entities in nanochannels, would be an important direction in the future.

(4). If selective manipulating local fluids with ultrasmall volumes in nanochannels is achieved, accurate assembly of nanometric materials (ultimately single molecules) as building blocks in the liquid phase would become possible. This will revolutionarily impact on material fabrication and chemical synthesis in the future.

We expect materials science will have an important role in the future development of nanofluidics, since these challenges are difficult to resolve without the participation of materials scientists.

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References

[1] W. Sparreboom, A. van den Berg, J. C. T. Eijkel, *Nat. Nanotechnol.* **2009**, *4*, 713.

[2] L. Bocquet, P. Tabeling, *Lab Chip* **2014**, *14*, 3143.

[3] D. G. Haywood, A. Saha-Shah, L. A. Baker, S. C. Jacobson, *Anal. Chem.* **2015**, *87*, 172.

[4] K. Mawatari, Y. Kazoe, H. Shimizu, Y. Pihosh, T. Kitamori, *Anal. Chem.* **2014**, *86*, 4068.

[5] R. Mukhopadhyay, *Anal. Chem.* **2006**, *78*, 7379.

[6] P. Abgrall, N. T. Nguyen, *Anal. Chem.* **2008**, *80*, 2326.

[7] D. Mijatovic, J. C. T. Eijkel, A. van den Berg, *Lab Chip* **2005**, *5*, 492.

[8] C. Duan, W. Wang, Q. Xie, *Biomicrofluidics* **2013**, *7*, 26501.

[9] S. Prakash, A. Piruska, E. N. Gatimu, P. W. Bohn, J. V. Sweedler, M. A. Shannon, *IEEE Sens. J.* **2008**, *8*, 441.

[10] M. Rauscher, S. Dietrich, *Annu. Rev. Mater. Res.* **2008**, *38*, 143.

[11] M. L. Kovarik, S. C. Jacobson, *Anal. Chem.* **2009**, *81*, 7133.

[12] A. Piruska, M. Gong, J. V. Sweedler, P. W. Bohn, *Chem. Soc. Rev.* **2010**, *39*, 1060.

[13] M. Napoli, J. C. T. Eijkel, S. Pennathur, *Lab Chip* **2010**, *10*, 957.

[14] D. Xia, J. Yan, S. Hou, *Small* **2012**, *8*, 2787.

[15] Z. D. Harms, D. G. Haywood, A. R. Kneller, S. C. Jacobson, *Analyst* **2015**, *140*, 4779.

[16] Y. Xu, K. Jang, T. Yamashita, Y. Tanaka, K. Mawatari, T. Kitamori, *Anal. Bioanal. Chem.* **2012**, *402*, 99.

[17] T. Yasui, N. Kaji, M. R. Mohamadi, Y. Okamoto, M. Tokeshi, Y. Horiike, Y. Baba, *ACS Nano* **2011**, *5*, 7775.

[18] L. Cao, F. Xiao, Y. Feng, W. Zhu, W. Geng, J. Yang, X. Zhang, N. Li, W. Guo, L. Jiang, *Adv. Funct. Mater.* **2017**, *27*, 1604302.

[19] A. Syed, L. Mangano, P. Mao, J. Han, Y.-A. Song, K. Liu, Z.-Y. Wu, Y. Fouillet, *Lab Chip* **2014**, *14*, 4455.

[20] A.-C. Louër, A. Plecis, A. Pallandre, J.-C. Galas, A. Estevez-Torres, A.-M. Haghiri-Gosnet, *Anal. Chem.* **2013**, *85*, 7948.

[21] S. J. Kim, Y.-C. Wang, J. H. Lee, H. Jang, J. Han, *Phys. Rev. Lett.* **2007**, *99*, 44501.

[22] S. J. Kim, Y.-A. Song, J. Han, *Chem. Soc. Rev.* **2010**, *39*, 912.

[23] S. J. Kim, S. H. Ko, K. H. Kang, J. Han, *Nat. Nanotechnol.* **2010**, *5*, 297.

[24] H. Zhang, Y. Tian, L. Jiang, *Nano Today* **2016**, *11*, 61.

[25] T. Gamble, K. Decker, T. S. Plett, M. Pevarnik, J.-F. Pietschmann, I. Vlassiouk, A. Aksimentiev, Z. S. Siwy, *J. Phys. Chem. C* **2014**, *118*, 9809.

[26] M. Zhang, X. Hou, J. Wang, Y. Tian, X. Fan, J. Zhai, L. Jiang, *Adv. Mater.* **2012**, *24*, 2424.

[27] J. M. Perry, K. Zhou, Z. D. Harms, S. C. Jacobson, *ACS Nano* **2010**, *4*, 3897.

[28] I. Vlassiouk, Z. S. Siwy, *Nano Lett.* **2007**, *7*, 552.

[29] Y. Xu, B. Xu, *Small* **2015**, *11*, 6165.

[30] A. Hibara, T. Saito, H.-B. Kim, M. Tokeshi, T. Ooi, M. Nakao, T. Kitamori, *Anal. Chem.* **2002**, *74*, 6170.

[31] N. R. Tas, J. Haneveld, H. V. Jansen, M. Elwenspoek, A. van den Berg, *Appl. Phys. Lett.* **2004**, *85*, 3274.

[32] H. Chinen, K. Mawatari, Y. Pihosh, K. Morikawa, Y. Kazoe, T. Tsukahara, T. Kitamori, *Angew. Chemie Int. Ed.* **2012**, *51*, 3573.

[33] T. Tsukahara, A. Hibara, Y. Ikeda, T. Kitamori, *Angew. Chemie Int. Ed.* **2007**, *46*, 1180.

[34] S. Liu, Q. Pu, L. Gao, C. Korzeniewski, C. Matzke, *Nano Lett.* **2005**, *5*, 1389.

[35] T. Tsukahara, K. Mawatari, T. Kitamori, T. Tsukahara, T. Kitamori, N. Jing, J. Kameoka, T. A. Good, *Chem. Soc. Rev*. **2010**, *39*, 1000.

[36] Y. Feng, Y. Zhang, C. Ying, D. Wang, C. Du, *Genomics. Proteomics Bioinformatics* **2015**, *13*, 4.

[37] A. H. Laszlo, I. M. Derrington, B. C. Ross, H. Brinkerhoff, A. Adey, I. C. Nova, J. M. Craig, K. W. Langford, J. M. Samson, R. Daza, K. Doering, J. Shendure, J. H. Gundlach, *Nat. Biotechnol.* **2014**, *32*, 829.

[38] R. Marie, J. N. Pedersen, D. L. V Bauer, K. H. Rasmussen, M. Yusuf, E. Volpi, H. Flyvbjerg, A. Kristensen, K. U. Mir, *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110*, 4893.

[39] D. Branton, D. W. Deamer, A. Marziali, H. Bayley, S. A. Benner, T. Butler, M. Di Ventra, S. Garaj, A. Hibbs, X. Huang, S. B. Jovanovich, P. S. Krstic, S. Lindsay, X. S. Ling, C. H. Mastrangelo, A. Meller, J. S. Oliver, Y. V Pershin, J. M. Ramsey, R. Riehn, G. V Soni, V. Tabard-Cossa, M. Wanunu, M. Wiggin, J. A. Schloss, *Nat. Biotechnol.* **2008**, *26*, 1146.

[40] Y.-B. Zheng, S. Zhao, S.-H. Cao, S.-L. Cai, X.-H. Cai, Y.-Q. Li, *Nanoscale* **2017**, *9*, 433.

[41] L. Li, J. Mo, Z. Li, *Phys. Rev. Lett.* **2015**, *115*, 134503.

[42] W. Guan, R. Fan, M. A. Reed, P. Yang, A. Majumdar, *Nat. Commun.* **2011**, *2*, 506.

[43] E. B. Kalman, I. Vlassiouk, Z. S. Siwy, *Adv. Mater.* **2008**, *20*, 293.

[44] J. Kudr, S. Skalickova, L. Nejdl, A. Moulick, B. Ruttkay-Nedecky, V. Adam, R. Kizek, *Electrophoresis* **2015**, *36*, 2367.

[45] Z. D. Harms, D. G. Haywood, A. R. Kneller, L. Selzer, A. Zlotnick, S. C. Jacobson, *Anal. Chem.* **2015**, *87*, 699.

[46] K. Zhou, J. M. Perry, S. C. Jacobson, *Annu. Rev. Anal. Chem.* **2011**, *4*, 321.

[47] M. Moritz, M. Geszke-Moritz, *Mater. Sci. Eng. C* **2015**, *49*, 114.

[48] C. T. Kresge, W. J. Roth, J. Pérez-Pariente, J. Čejka, B. F. Chmelka, G. D. Stucky, E. W. Sheppard, B. F. Chmelka, R. Ryoo, J. Nicol, D. Marogloese, G. D. Stucky, B. F. Chmelka, *Chem. Soc. Rev.* **2013**, *42*, 3663.

[49] I. I. Ivanova, E. E. Knyazeva, G. Krishnaiah, A. Bonilla, K. Thomas, C. Fernandez, J.-P. Gilson, J. Pérez-Ramírez, *Chem. Soc. Rev.* **2013**, *42*, 3671.

[50] A. Subramani, J. G. Jacangelo, *Water Res.* **2015**, *75*, 164.

[51] M. E. Suss, S. Porada, X. Sun, P. M. Biesheuvel, J. Yoon, V. Presser, T. F. Baumann, J. Biener, A. Striolo, P. Simon, *Energy Environ. Sci.* **2015**, *8*, 2296.

[52] S. Porada, R. Zhao, A. van der Wal, V. Presser, P. M. Biesheuvel, *Prog. Mater. Sci.* **2013**, *58*, 1388.

[53] H. Furukawa, K. E. Cordova, M. O'Keeffe, O. M. Yaghi, *Science (80-.).* **2013**, *341*.

[54] N. C. Burtch, H. Jasuja, K. S. Walton, *Chem. Rev.* **2014**, *114*, 10575.

[55] Y. He, W. Zhou, G. Qian, B. Chen, P. Chen, T. Yildirim, W. Zhou, S. T. Nguyen, A. Ö. Yazaydın, J. T. Hupp, P. A. Georgiev, M. Eddaoudi, M. Schröder, Y. Han, Z. Shi, S. Feng, J. Li, *Chem. Soc. Rev.* **2014**, *43*, 5657.

[56] J. Liu, L. Chen, H. Cui, J. Zhang, L. Zhang, C.-Y. Su, X. Bao, J. Gascon, F. Kapteijn, B. Chaudret, R. A. Fischer, D. E. De Vos, M. Waroquier, V. Van Speybroeck, P. Van Der Voort, *Chem. Soc. Rev.* **2014**, *43*, 6011.

[57] F. Haque, J. Li, H.-C. Wu, X.-J. Liang, P. Guo, *Nano Today* **2013**, *8*, 56.

[58] C. Dekker, *Nat. Nanotechnol.* **2007**, *2*, 209.

[59] Y. He, M. Tsutsui, C. Fan, M. Taniguchi, T. Kawai, *ACS Nano* **2011**, *5*, 5509.

[60] H. Arjmandi-Tash, L. A. Belyaeva, G. F. Schneider, *Chem. Soc. Rev.* **2016**, *45*, 476.

[61] L. M. Baudhuin, M. J. Ferber, *Clin. Chem.* **2017**, *63*, 632.

[62] L. Liu, H.-C. Wu, *Angew. Chemie Int. Ed.* **2016**, *55*, 15216.

[63] S. Howorka, Z. Siwy, *ACS Nano* **2016**, *10*, 9768.

[64] D. Deamer, M. Akeson, D. Branton, *Nat. Biotechnol.* **2016**, *34*, 518.

[65] H. Arjmandi-Tash, L. A. Belyaeva, G. F. Schneider, *Chem. Soc. Rev.* **2016**, *45*, 476.

[66] J. L. Perry, S. G. Kandlikar, *Microfluid. Nanofluidics* **2006**, *2*, 185.

[67] J. Haneveld, H. Jansen, E. Berenschot, N. Tas, M. Elwenspoek, *J. Micromechanics Microengineering* **2003**, *13*, S62.

[68] J. Han, H. G. Craighead, *J. Vac. Sci. Technol., A* **1999**, *17*, 2142.

[69] W. Reisner, J. P. Beech, N. B. Larsen, H. Flyvbjerg, A. Kristensen, J. O. Tegenfeldt, *Phys. Rev. Lett.* **2007**, *99*, 58302.

[70] Y. Xu, C. Wang, Y. Dong, L. Li, K. Jang, K. Mawatari, T. Suga, T. Kitamori, *Anal. Bioanal. Chem.* **2012**, *402*, 1011.

[71] L. D. Menard, J. M. Ramsey, *Nano Lett.* **2011**, *11*, 512.

[72] Y. Xu, N. Matsumoto, *RSC Adv.* **2015**, *5*, 50638.

[73] J. Wu, R. Chantiwas, A. Amirsadeghi, S. A. Soper, S. Park, *Lab Chip* **2011**, *11*, 2984.

[74] R. Chantiwas, M. L. Hupert, S. R. Pullagurla, S. Balamurugan, J. Tamarit-López, S. Park, P. Datta, J. Goettert, Y.-K. Cho, S. A. Soper, *Lab Chip* **2010**, *10*, 3255.

[75] F. I. Uba, B. Hu, K. Weerakoon-Ratnayake, N. Oliver-Calixte, S. A. Soper, *Lab Chip* **2015**, *15*, 1038.

[76] Z. Yin, E. Cheng, H. Zou, L. Chen, S. Xu, *Biomicrofluidics* **2014**, *8*, 66503.

[77] J. Heo, H. J. Kwon, H. Jeon, B. Kim, S. J. Kim, G. Lim, *Nanoscale* **2014**, *6*, 9681.

[78] H. Kang, J. Lee, J. Park, H. H. Lee, *Nanotechnology* **2006**, *17*, 197.

[79] A. L. Thangawng, M. A. Swartz, M. R. Glucksberg, R. S. Ruoff, *Small* **2007**, *3*, 132.

[80] D. Huh, K. L. Mills, X. Zhu, M. A. Burns, M. D. Thouless, S. Takayama, *Nat. Mater.* **2007**, *6*, 424.

[81] Y. Y. Huang, W. Zhou, K. J. Hsia, E. Menard, J.-U. Park, J. A. Rogers, A. G. Alleyne, *Langmuir* **2005**, *21*, 8058.

[82] W. Zhou, Y. Huang, E. Menard, N. R. Aluru, J. A. Rogers, A. G. Alleyne, *Appl. Phys. Lett.* **2005**, *87*, 251925.

[83] S. Park, Y. S. Huh, H. G. Craighead, D. Erickson, *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 15549.

[84] M. Kim, D. Ha, T. Kim, *Nat. Commun.* **2015**, *6*, 6247.

[85] R. Peng, D. Li, *Lab Chip* **2016**, *16*, 3767.

[86] J. K. Holt, *Adv. Mater.* **2009**, *21*, 3542.

[87] S. Guo, E. R. Meshot, T. Kuykendall, S. Cabrini, F. Fornasiero, *Adv. Mater.* **2015**, *27*, 5726.

[88] X. Chen, G. Cao, A. Han, V. K. Punyamurtula, L. Liu, P. J. Culligan, T. Kim, Y. Qiao, *Nano Lett.* **2008**, *8*, 2988.

[89] S. Supple, N. Quirke, *Phys. Rev. Lett.* **2003**, *90*, 214501.

[90] A. Noy, H. G. Park, F. Fornasiero, J. K. Holt, C. P. Grigoropoulos, O. Bakajin, *Nano Today* **2007**, *2*, 22.

[91] H. Amiri, K. L. Shepard, C. Nuckolls, R. Hernández Sánchez, *Nano Lett.* **2017**, *17*, 1204.

[92] L. Liu, C. Yang, K. Zhao, J. Li, H.-C. Wu, *Nat. Commun.* **2013**, *4*, 2989.

[93] R. Singhal, Z. Orynbayeva, R. V. Kalyana Sundaram, J. J. Niu, S. Bhattacharyya, E. A. Vitol, M. G. Schrlau, E. S. Papazoglou, G. Friedman, Y. Gogotsi, *Nat. Nanotechnol.* **2011**, *6*, 57.

[94] W. Choi, Z. W. Ulissi, S. F. E. Shimizu, D. O. Bellisario, M. D. Ellison, M. S. Strano, *Nat. Commun.* **2013**, *4*, 2397.

[95] E. Secchi, S. Marbach, A. Niguès, D. Stein, A. Siria, L. Bocquet, *Nature* **2016**, *537*, 210.

[96] A. R. Koltonow, J. Huang, *Science (80-.).* **2016**, *351*, 1395.

[97] U. Mirsaidov, V. R. S. S. Mokkapati, D. Bhattacharya, H. Andersen, M. Bosman, B. Özyilmaz, P. Matsudaira, *Lab Chip* **2013**, *13*, 2874.

[98] K. Raidongia, J. Huang, *J. Am. Chem. Soc.* **2012**, *134*, 16528.

[99] M. R. Karim, K. Hatakeyama, T. Matsui, H. Takehira, T. Taniguchi, M. Koinuma, Y. Matsumoto, T. Akutagawa, T. Nakamura, S. Noro, T. Yamada, H. Kitagawa, S. Hayami, *J. Am. Chem. Soc.* **2013**, *135*, 8097.

[100] W. Guo, C. Cheng, Y. Wu, Y. Jiang, J. Gao, D. Li, L. Jiang, *Adv. Mater.* **2013**, *25*, 6064.

[101] J.-J. Shao, K. Raidongia, A. R. Koltonow, J. Huang, *Nat. Commun.* **2015**, *6*, 7602.

[102] C. Cheng, G. Jiang, C. J. Garvey, Y. Wang, G. P. Simon, J. Z. Liu, D. Li, *Sci. Adv.* **2016**, *2*.

[103] L. Wen, Y. Tian, Y. Guo, J. Ma, W. Liu, L. Jiang, *Adv. Funct. Mater.* **2013**, *23*, 2887.

[104] G. Xie, K. Xiao, Z. Zhang, X.-Y. Kong, Q. Liu, P. Li, L. Wen, L. Jiang, *Angew. Chemie Int. Ed.* **2015**, *54*, 13664.

[105] X. Sui, Z. Zhang, Z. Zhang, Z. Wang, C. Li, H. Yuan, L. Gao, L. Wen, X. Fan, L. Yang, X. Zhang, L. Jiang, *Angew. Chemie Int. Ed.* **2016**, *55*, 13056.

[106] G. Pérez-Mitta, J. S. Tuninetti, W. Knoll, C. Trautmann, M. E. Toimil-Molares, O. Azzaroni, *J. Am. Chem. Soc.* **2015**, *137*, 6011.

[107] X. Hou, F. Yang, L. Li, Y. Song, L. Jiang, D. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 11736.

[108] G. Pérez-Mitta, A. G. Albesa, W. Knoll, C. Trautmann, M. E. Toimil-Molares, O. Azzaroni, *Nanoscale* **2015**, *7*, 15594.

[109] Y. Xu, X. Sui, S. Guan, J. Zhai, L. Gao, *Adv. Mater.* **2015**, *27*, 1851.

[110] Y. Jiang, N. Liu, W. Guo, F. Xia, L. Jiang, *J. Am. Chem. Soc.* **2012**, *134*, 15395.

[111] D. Stein, M. Kruithof, C. Dekker, *Phys. Rev. Lett.* **2004**, *93*, 35901.

[112] R. Arayanarakool, L. Shui, A. van den Berg, J. C. T. Eijkel, *Lab Chip* **2011**, *11*, 4260.

[113] X. Hou, W. Guo, L. Jiang, *Chem. Soc. Rev.* **2011**, *40*, 2385.

[114] X. Hou, *Adv. Mater.* **2016**, *28*, 7049.

[115] F. Persson, J. Fritzsche, K. U. Mir, M. Modesti, F. Westerlund, J. O. Tegenfeldt, *Nano Lett.* **2012**, *12*, 2260.

[116] L. H. Fornander, K. Frykholm, J. Fritzsche, J. Araya, P. Nevin, E. Werner, A. Çakır, F. Persson, E. B. Garcin, P. J. Beuning, B. Mehlig, M. Modesti, F. Westerlund, *Langmuir* **2016**, *32*, 8403.

[117] K. Frykholm, R. P.-A. Berntsson, M. Claesson, L. de Battice, R. Odegrip, P. Stenmark, F. Westerlund, *Nucleic Acids Res.* **2016**, *44*, gkw352.

[118] D. E. Streng, S. F. Lim, J. Pan, A. Karpusenka, R. Riehn, *Lab Chip* **2009**, *9*, 2772.

[119] K. Jiang, C. Zhang, D. Guttula, F. Liu, J. A. van Kan, C. Lavelle, K. Kubiak, A. Malabirade, A. Lapp, V. Arluison, J. R. C. van der Maarel, *Nucleic Acids Res.* **2015**, *43*, 4332.

[120] C. Zhang, D. Guttula, F. Liu, P. P. Malar, S. Y. Ng, L. Dai, P. S. Doyle, J. A. van Kan, J. R. C. van der Maarel, *Soft Matter* **2013**, *9*, 9593.

[121] K. Frykholm, M. Alizadehheidari, J. Fritzsche, J. Wigenius, M. Modesti, F. Persson, F. Westerlund, *Small* **2014**, *10*, 884.

[122] L. Lin, K. Mawatari, K. Morikawa, Y. Pihosh, A. Yoshizaki, T. Kitamori, *Analyst* **2017**, *2*, 555.

[123] R. Karnik, Castelino, K., C. Duan, A. Majumdar, *Nano Lett.* **2006**, *6*, 1735.

[124] K. Shirai, K. Mawatari, T. Kitamori, *Small* **2014**, *10*, 1514.

[125] Q. Sheng, L. Wang, C. Wang, X. Wang, J. Xue, *Biomicrofluidics* **2014**, *8*, 52111.

[126] Y. Xu, N. Matsumoto, Q. Wu, Y. Shimatani, H. Kawata, *Lab Chip* **2015**, *15*, 1989.

[127] L. Cheng, D. Cao, *ACS Nano* **2011**, *5*, 1102.

[128] A. Poddar, D. Maity, A. Bandopadhyay, S. Chakraborty, R. Zimmermann, Á. V. Delgado, *Soft Matter* **2016**, *12*, 5968.

[129] A. Piruska, S. P. Branagan, A. B. Minnis, Z. Wang, D. M. Cropek, J. V. Sweedler, P. W. Bohn, *Lab Chip* **2010**, *10*, 1237.

[130] S. P. Adiga, D. W. Brenner, *Nano Lett.* **2005**, *5*, 2509.

[131] H. Ouyang, Z. Xia, J. Zhe, *Microfluid. Nanofluidics* **2010**, *9*, 915.

[132] R. Marie, A. Kristensen, *J. Biophotonics* **2012**, *5*, 673.

[133] P. Mao, J. Han, *Lab Chip* **2005**, *5*, 837.

[134] T. Tsukahara, K. Mawatari, A. Hibara, T. Kitamori, *Anal. Bioanal. Chem.* **2008**, *391*, 2745.

[135] T. Maleki, S. Mohammadi, B. Ziaie, *Nanotechnology* **2009**, *20*, 105302.

[136] R. Hatsuki, F. Yujiro, T. Yamamoto, *Microfluid. Nanofluidics* **2013**, *14*, 983.

[137] P. S. Singh, H.-S. M. Chan, S. Kang, S. G. Lemay, *J. Am. Chem. Soc.* **2011**, *133*, 18289.

[138] L. Rassaei, K. Mathwig, S. Kang, H. A. Heering, S. G. Lemay, *ACS Nano* **2014**, *8*, 8278.

[139] W. Xu, E. Foster, C. Ma, P. W. Bohn, *Microfluid. Nanofluidics* **2015**, *19*, 1181.

[140] M. Fuest, C. Boone, K. K. Rangharajan, A. T. Conlisk, S. Prakash, *Nano Lett.* **2015**, *15*, 2365.

[141] M. Miansari, J. R. Friend, *Adv. Funct. Mater.* **2016**, *26*, 7861.

[142] Y. Xu, C. Wang, L. Li, N. Matsumoto, K. Jang, Y. Dong, K. Mawatari, T. Suga, T. Kitamori, *Lab Chip* **2013**, *13*, 1048.

[143] J. S. Mellors, V. Gorbounov, R. S. Ramsey, J. M. Ramsey, *Anal. Chem.* **2008**, *80*, 6881.

[144] Y. Xu, K. Sato, K. Mawatari, T. Konno, K. Jang, K. Ishihara, T. Kitamori, *Adv. Mater.* **2010**, *22*, 3017.

[145] C. Wang, T. Suga, *ECS J. Solid State Sci. Technol.* **2016**, *5*, P393.

[146] C. Wang, Y. Wang, Y. Tian, C. Wang, T. Suga, *Appl. Phys. Lett.* **2017**, *110*, 221602.

[147] C. Wang, Y. Liu, T. Suga, *ECS J. Solid State Sci. Technol.* **2017**, *6*, P7.

[148] Y. Xu, Q. Wu, Y. Shimatani, K. Yamaguchi, *Lab Chip* **2015**, *15*, 3856.

[149] Y. Xu, M. Shinomiya, A. Harada, *Adv. Mater.* **2016**, *28*, 2209.

[150] S. K. Min, W. Y. Kim, Y. Cho, K. S. Kim, *Nat. Nanotechnol.* **2011**, *6*, 162.

[151] Y. Kim, K. S. Kim, K. L. Kounovsky, R. Chang, G. Y. Jung, J. J. dePablo, K. Jo, D. C. Schwartz, *Lab Chip* **2011**, *11*, 1721.

[152] C. Zhang, F. Zhang, J. A. van Kan, J. R. C. van der Maarel, *J. Chem. Phys.* **2008**, *128*, 225109.

[153] M. Tsutsui, Y. He, M. Furuhashi, S. Rahong, M. Taniguchi, T. Kawai, *Sci. Rep.* **2012**, *2*, 394.

[154] I. Heller, T. P. Hoekstra, G. A. King, E. J. G. Peterman, G. J. L. Wuite, *Chem. Rev.* **2014**, *114*, 3087.

[155] K. R. Chaurasiya, T. Paramanathan, M. J. McCauley, M. C. Williams, *Phys. Life Rev.* **2010**, *7*, 299.

[156] I. De Vlaminck, C. Dekker, *Annu. Rev. Biophys.* **2012**, *41*, 453.

[157] W. Reisner, J. N. Pedersen, R. H. Austin, *Reports Prog. Phys.* **2012**, *75*, 106601.

[158] X. Sun, T. Yasui, T. Yanagida, N. Kaji, S. Rahong, M. Kanai, K. Nagashima, T. Kawai, Y. Baba, *Sci. Technol. Adv. Mater.* **2016**, *17*, 644.

[159] E. T. Lam, A. Hastie, C. Lin, D. Ehrlich, S. K. Das, M. D. Austin, P. Deshpande, H. Cao, N. Nagarajan, M. Xiao, P.-Y. Kwok, *Nat. Biotechnol.* **2012**, *30*, 771.

[160] L. K. Nyberg, F. Persson, J. Berg, J. Bergström, E. Fransson, L. Olsson, M. Persson, A. Stålnacke, J. Wigenius, J. O. Tegenfeldt, F. Westerlund, *A Single-Step Competitive Binding Assay for Mapping of Single DNA Molecules*, **2012**.

[161] W. Reisner, N. B. Larsen, A. Silahtaroglu, A. Kristensen, N. Tommerup, J. O. Tegenfeldt, H. Flyvbjerg, *Proc. Natl. Acad. Sci. U. S. A.* **2010**, *107*, 13294.

[162] B. Zhang, M. Wood, H. Lee, *Anal. Chem.* **2009**, *81*, 5541.

[163] V. R. S. S. Mokkapati, V. Di Virgilio, C. Shen, J. Mollinger, J. Bastemeijer, A. Bossche, *Lab Chip* **2011**, *11*, 2711.

[164] Y. Liu, L. Yobas, *ACS Nano* **2016**, *10*, 3985.

[165] Y. Kazoe, K. Mawatari, T. Kitamori, *Anal. Chem.* **2015**, *87*, 4087.

[166] S. Faez, Y. Lahini, S. Weidlich, R. F. Garmann, K. Wondraczek, M. Zeisberger, M. A. Schmidt, M. Orrit, V. N. Manoharan, *ACS Nano* **2015**, *9*, 12349.

[167] Z. D. Harms, L. Selzer, A. Zlotnick, S. C. Jacobson, *ACS Nano* **2015**, *9*, 9087.

[168] H. J. Chung, X. N. Xie, C. H. Sow, A. A. Bettiol, A. T. S. Wee, *Appl. Phys. Lett.* **2006**, *88*, 23116.

[169] C. De Marco, E. Mele, A. Camposeo, R. Stabile, R. Cingolani, D. Pisignano, *Adv. Mater.* **2008**, *20*, NA.

[170] F. Malloggi, N. Pannacci, R. Attia, F. Monti, P. Mary, H. Willaime, P. Tabeling, B. Cabane, P. Poncet, *Langmuir* **2010**, *26*, 2369.

[171] J. Geerlings, E. Sarajlic, E. J. W. Berenschot, R. G. P. Sanders, M. H. Siekman, L. Abelmann, N. R. Tas, *Appl. Phys. Lett.* **2015**, *107*, 123109.

[172] A. Houachtia, P. Alcouffe, G. Boiteux, G. Seytre, J.-F. Gérard, A. Serghei, *Nano Lett.* **2015**, *15*, 4311.

[173] M. Spina, E. Bonvin, A. Sienkiewicz, B. Náfrádi, L. Forró, E. Horváth, *Sci. Rep.* **2016**, *6*, 19834.

Figures

Figure 1

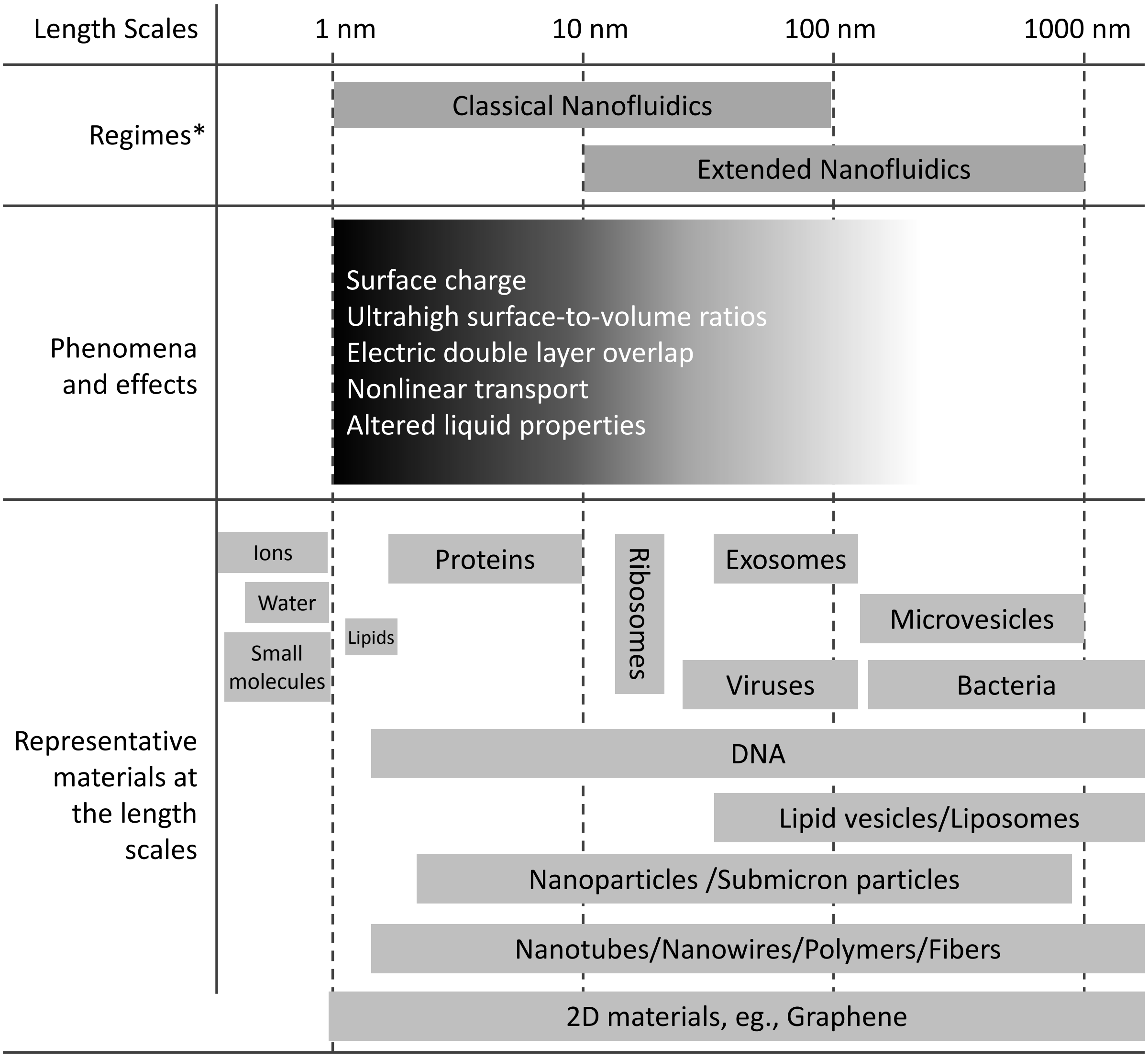

Figure 1. Representative materials and nanometric objects at the same length scales as nanofluidics, where unusual transport phenomena and effects occur.
*Sometimes, nanofluidics may also include flow through sub-nanometer channels like in zeolites, though there is no common definition. This regime is not included in the definition of nanofluidics in this article.

Figure 2

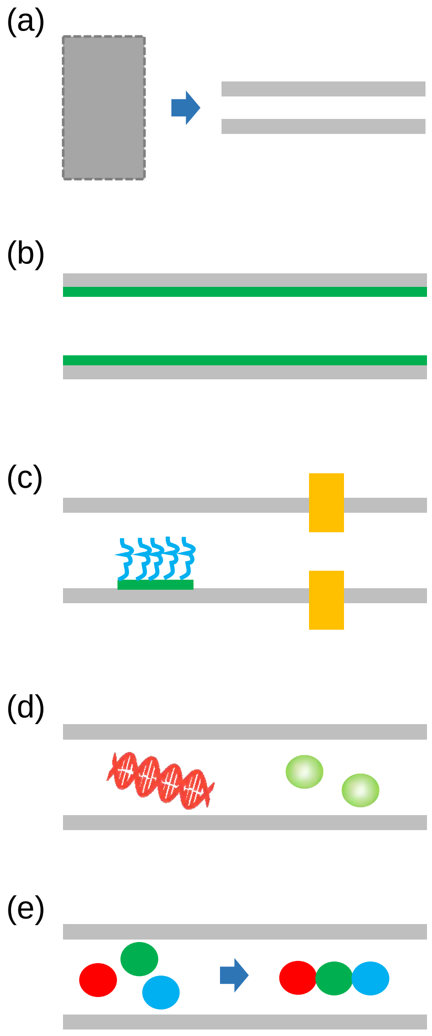

Figure 2. Conceptual drawing of nanofluidics associated with materials science. a) Materials for fabricating nanofluidic devices; b) nanofluidics with functionalized surfaces; c) nanofluidics integrated with functional material components; d) nanofluidics for manipulating biological and nanoscale materials; e) nanofluidics for the fabrication and synthesis of nanomaterials.

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Figure 3

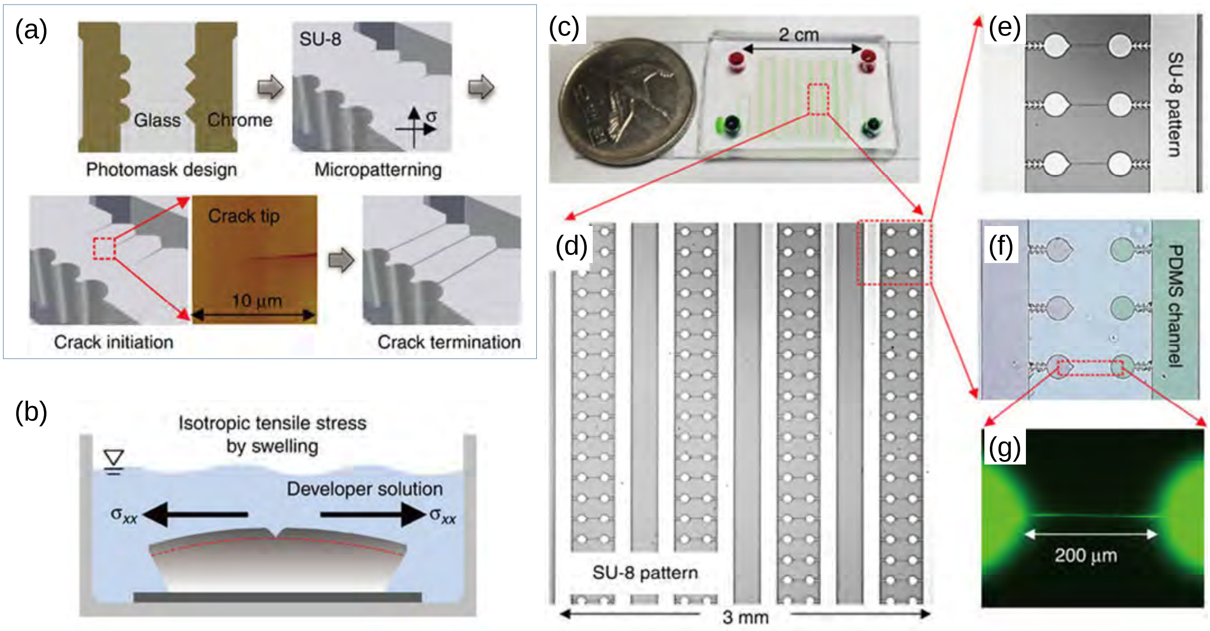

Figure 3. Fabrication of PDMS nanofluidic devices by taking advantage of well-controlled material cracking. a) Schematic drawing of the fabrication of the master mould with well-defined nanopatterns through cracking formation, b) resulting from the micropatterned notch structures in a SU-8 photoresist film undergoing isotropic tensile stress during swelling. c-f) A large-scale, high-throughput nanofluidic chip on PDMS replicated from a SU-8 mould which is fabricated using the cracking method; g) fluidic transport in the nanochannels is confirmed by introducing a solution of fluorescein isothiocyanate (FITC). Reproduced with permission.[84] Copyright 2015, Nature Publishing Group.

Figure 4

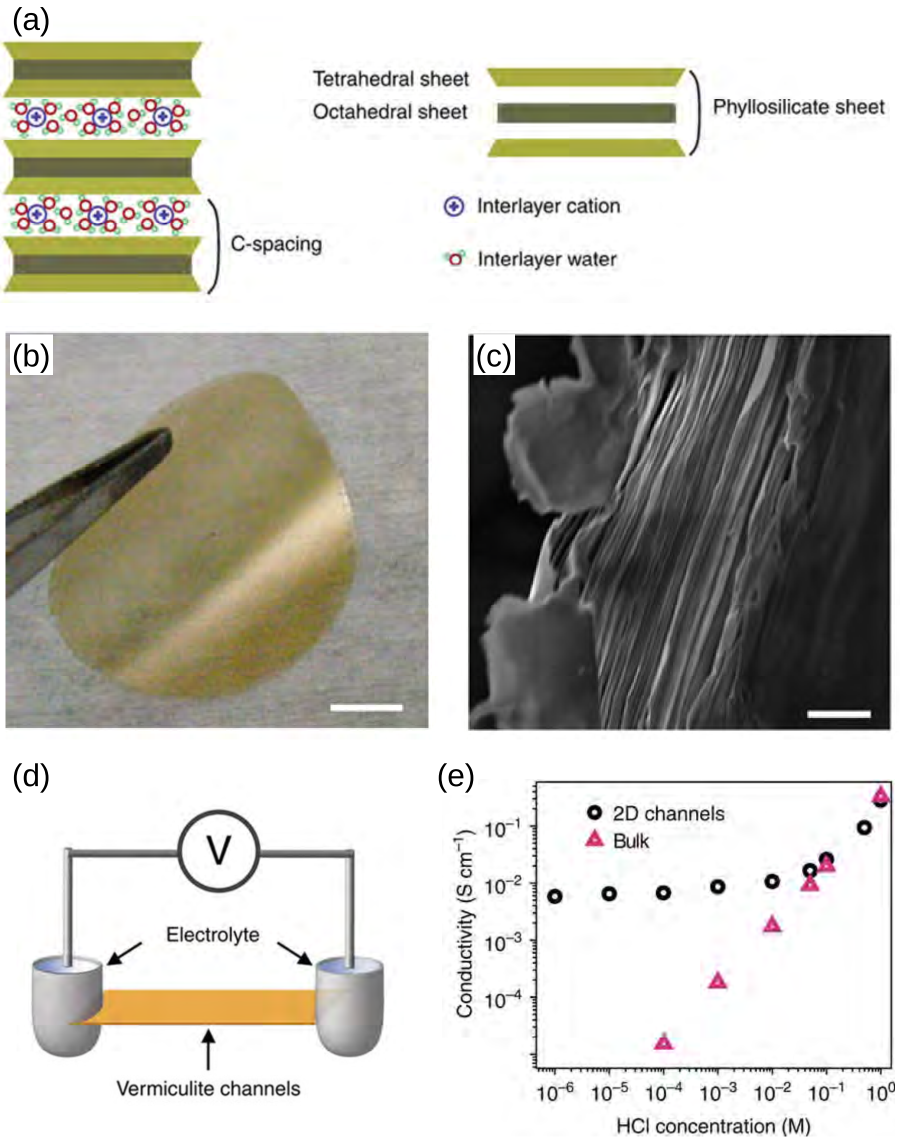

Figure 4. Nanochannels resulting from a) self-assembled interlayer spacing in b, c) a large-scale membrane of a 2D material (vermiculite) exhibits d, e) higher-than-bulk proton conductivity under d) a nanofluidic experimental setup. Scale bar in b) is 1 cm and scale bar in c) the cross-sectional SEM image of the vermiculite membrane is 1 µm. Reproduced with permission.[101] Copyright 2015, Nature Publishing Group.

Figure 5

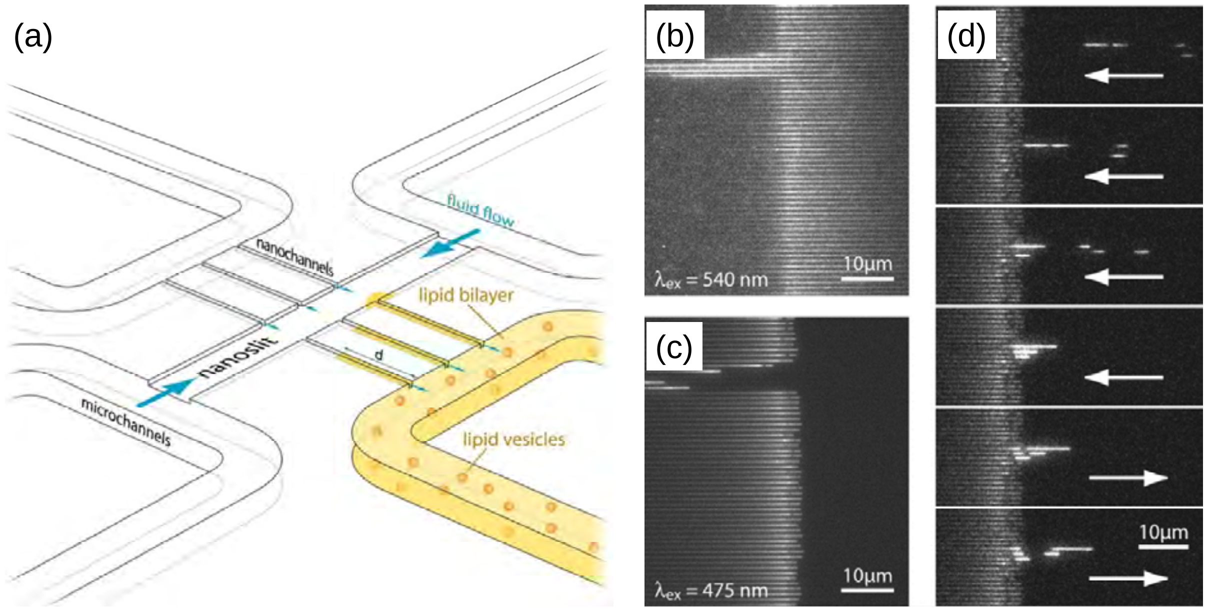

Figure 5. Lipid bilayer-based coating of channel walls to suppress nonspecific adsorption of proteins in the nanochannels. a) Schematic drawing of the coating process using lipid vesicles, which are first introduced into a microchannel, then rupture in the microchannel, and finally spontaneously spread into the nanochannels to form lipid bilayers in both the microchannel and the nanochannels. b) A fluorescence image of nanochannels partially (right-hand half) coated with fluorescently labeled lipid bilayer observed at 540 nm excitation. c) Nonspecific adsorption of RecA proteins, observed at 475 nm excitation, occur only in the uncoated area (left-hand half) of the nanochannels. d) RecA−DNA complexes nonspecifically bound to the uncoated area (left-hand half) of the nanochannels, due to the nonspecific adsorption of fluorescently stained RecA proteins to the channel walls, during motion of the DNAs driven by fluid flows, whose directions are indicated by the arrows. Reproduced with permission.[115] Copyright 2012, American Chemical Society.

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Figure 6

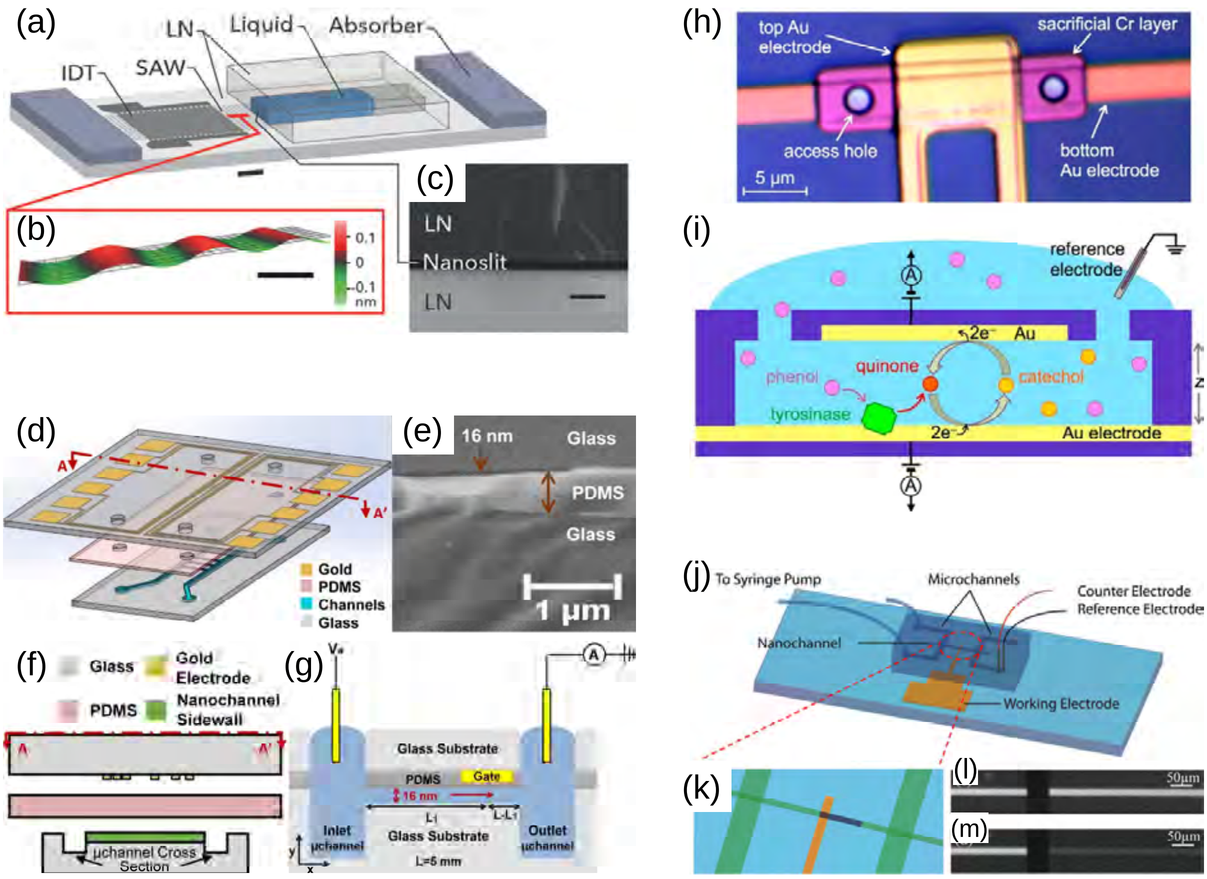

Figure 6. a-c) SAW-actuated nanofluidic device; a)schematic drawing of the device integrated with IDT to generate b) SAW along (c) an etched nanochannel (nanoslit) which was formed from bonded transparent LN wafers (SEM image). Reproduced with permission. Copyright 2016, Wiley-VCH.[141] d-g) A three-state nanofluidic field effect switch; d) schematic drawing of the device; gold gate electrodes were fabricated on a second glass substrate (top) and bonded to the glass substrate with channel network (bottom) through an intermediate PDMS layer; b) SEM image of the cross section of the nanochannel; f) exploded side view of the device; g) assembled side view of the experimental setup with the applied axial (Va) and gate (Vg) potentials. Reproduced with permission.[140] Copyright 2015, American Chemical Society. h) A nanofluidic electrochemical device for i) integrated detection of enzymatic reaction. Reproduced with permission.[138] Copyright 2014, American Chemical Society. j) A nanofluidic device consisting k) a nanochannel with embedded transverse electrode for electrochemical reaction; fluorescence images showing fluorescence intensity change due to electrochemical generation of H^+ during electrochemical oxidation of water l) before and m) after application of a working potential pulse. Reproduced with permission.[139] Copyright 2015, Springer.

Figure 7

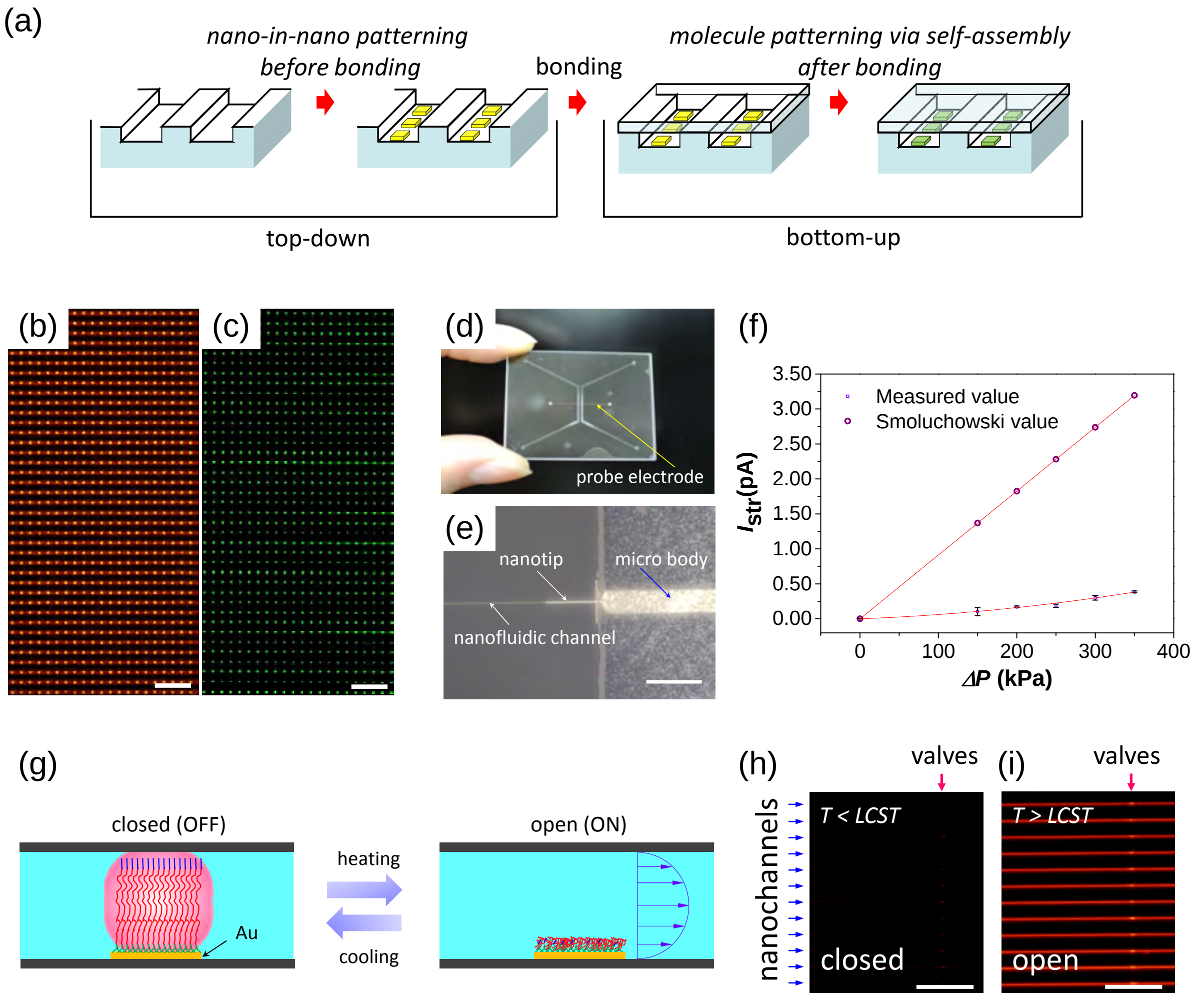

Figure 7. a) Nano-in-nano integration technology for b-h) the in situ integration of functional material components in nanochannels. a) Schematic drawing of the nano-in-nano integration process. b) A bright-field image of gold-nanopatterned nanochannels and c) a fluorescence image of a fluorescent molecular nanoarray formed on the gold nanopatterns via molecular self-assembly in the arrayed nanochannels. Reproduced with permission.[126] Copyright 2015, The Royal Society of Chemistry. d) A glass nanofluidic device with e) a pair of integrated probe electrodes f) for the in situ measurement of streaming currents in a single nanochannel. The measurements reveals a discrepancy between in situ nanoscopic experimental results and macroscopic laws of electrokinetic phenomena, suggesting unusual liquid properties confined in the nanochannel. Reproduced with permission.[29] Copyright 2015, Wiley-VCH Verlag GmbH & Co. KGaA. g) Conceptual drawing of an active nanofluidic valve using short-chain, thermoresponsive polymer brushes locally self-assembled in a nanochannel. The integrated nanovalves in femtoliter-scale nanochannels exhibit either h) a closed state above the lower critical solution temperature (LCST) of the polymer brushes or i) an open state below LCST, during flowing a solution of sulforhodamine B which can be observed by fluorescence

microscope. Reproduced with permission.[149] Copyright 2016, Wiley-VCH Verlag GmbH & Co. KGaA.

Figure 8

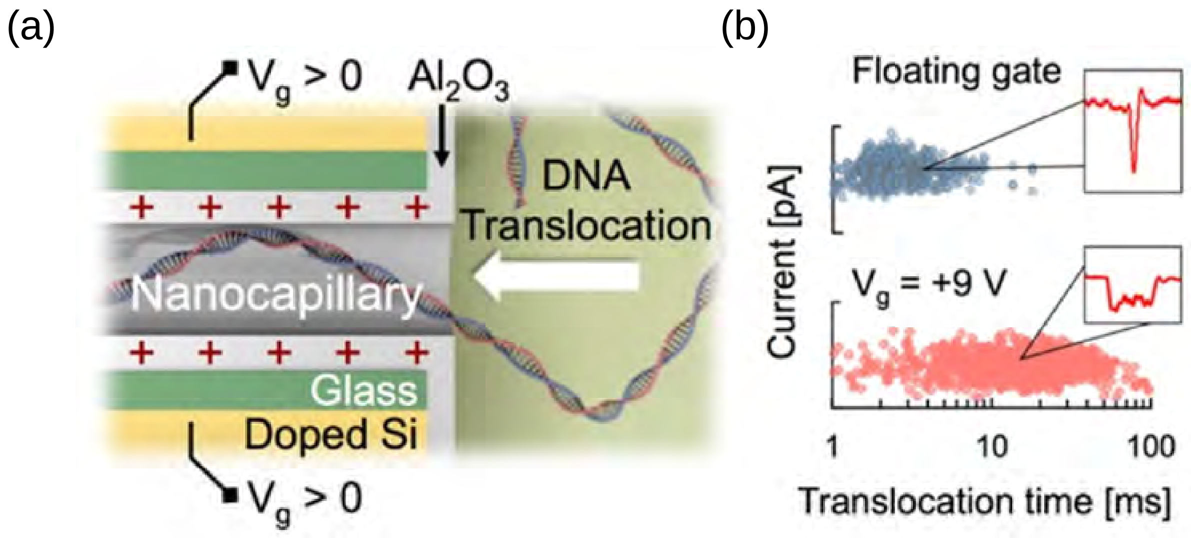

Figure 8. Manipulation of single DNA translocation in a nanofluidic field-effect transistor. a) Schematic drawing of the concept and b) translocation times of λ-DNA under a floating gate in comparison with those under a +9 V gate bias, experimentally observed during field-effect regulation of λ-DNA translocations with 1 M KCl buffer under a source-to-drain bias of 1 V. Reproduced with permission.[164] Copyright 2016, American Chemical Society.

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Figure 9

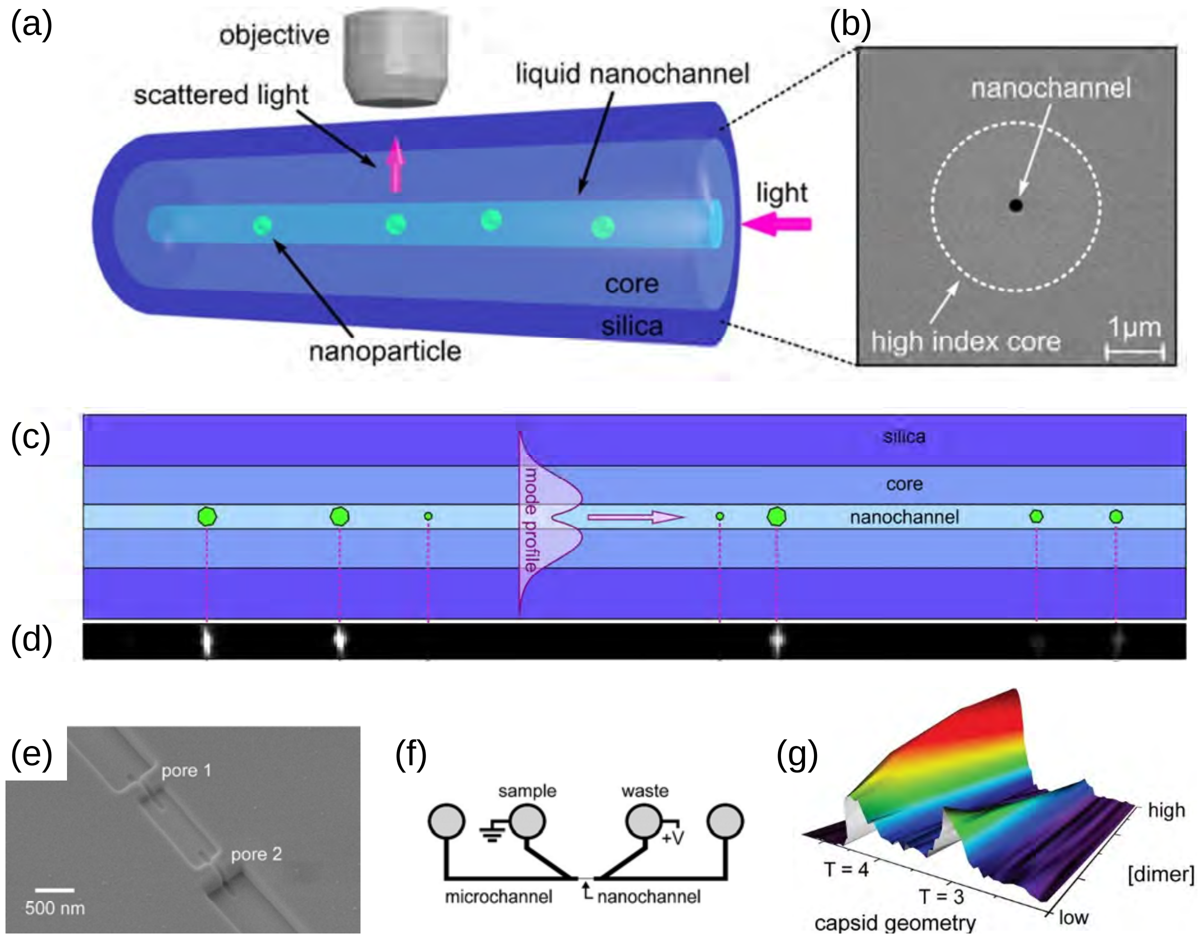

Figure 9. Manipulation and tracking of single nanoparticles and viruses in nanochannels. a) Tracking of single unlabeled latex nanoparticles (19, 25, and 51 nm) in b) a nanofluidic optical fiber by c, d) detecting weakly scattered light on the nanoparticles illuminated by a guided light, whose optical mode calculated at 670 nm is described in c). Reproduced with permission.[166] Copyright 2015, American Chemical Society. e) A glass nanofluidic device allowing f) electrokinetic manipulation and g) resistive-pulse monitoring the assembly of hepatitis B virus core protein dimers into T = 3 and T = 4 icosahedral capsids under biologically relevant concentrations. Reproduced with permission.[167] Copyright 2015, American Chemical Society.

Figure 10

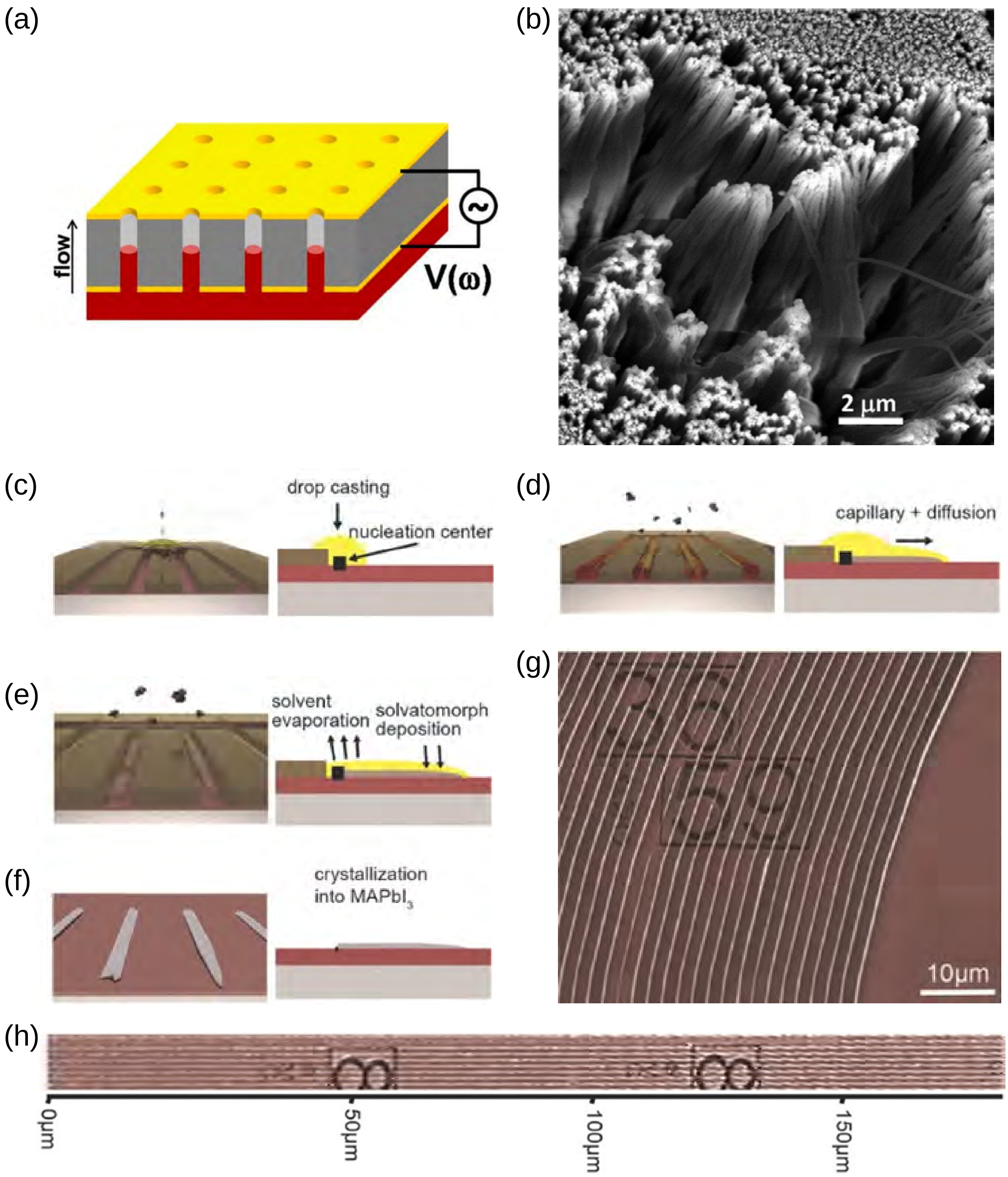

Figure 10. Fabrication of nanowires using nanofluidic approaches. a) Schematic drawing of the fabrication of PVDF-TrFE nanowires through melting/crystallization of the polymer in a highly ordered nanoporous membrane, which is integrated with electrodes allowing real-time monitoring the fabrication process; b) a SEM image of PVDF-TrFE nanowires fabricated by the method. Reproduced with permission.[172] Copyright 2015, American Chemical Society. c-

f) Schematic drawing of the sequential process of the fabrication of $CH_3NH_3PbI_3$ nanowires in open nanofluidic channels; Colored SEM images of g) curved $CH_3NH_3PbI_3$ nanowires and h) an array of extremely long $CH_3NH_3PbI_3$ nanowires on SiO_2 fabricated by the method. Reproduced with permission.[173] Copyright 2016, Nature Publishing Group.

Author Biography and Photograph

Yan Xu is an Associate Professor and the principal investigator of Nanofluidics Lab at Osaka Prefecture University, Japan. He received his bachelor's degree (2001) from Dalian University of Technology and his master's degree (2004) from Dalian Institute of Chemical Physics, Chinese Academy of Sciences. He completed his Ph.D. (2007) at The University of Tokyo. Research in his group is directed toward the use of nanofluidic devices for chemistry, biology, and materials science. His research group continues to involve the study and development of novel nanofluidic methods for single cell omics, single molecule chemistry, biomaterials, and nanomedicine.

ADVANCED MATERIALS

The use of nanofluidics opens up a new arena for materials science. Burgeoning progress is made, including new materials and methods for fabricating nanofluidic devices, nanofluidics with functionalized surfaces and functional material components, as well as nanofluidics for manipulating nanoscale materials and fabricating new nanomaterials..

Keywords: nanochannels, materials, surfaces, manipulation, fabrication

Y. Xu*

Nanofluidics: a New Arena for Materials Science

TOC image: