

Moving-part-free microfluidic systems for lab-on-a-chip

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Abstract

Microfluidic systems are part of an emerging technology which deals with minute amount of liquids (biological samples and reagents) on a small scale. They are fast, compact and can be made into a highly integrated system to deliver sample purification, separation, reaction, immobilization, labelling, detection, etc, and thus are promising for applications such as lab-on-a-chip and handheld healthcare devices. Miniaturized micropumps typically consist of a moving-part component, such as a membrane structure, to deliver liquids, and they are unreliable, complicated in structure and difficult to be integrated with other control electronics circuits. The trend of new-generation micropumps is moving-part-free micropumps operated by advanced techniques, such as electrokinetic force, surface tension/energy, acoustic waves, etc. This paper reviews the development and advances of the relevant technologies, and introduces the electrowetting-on-dielectrics and acoustic wave-based microfluidics. The programmable electrowetting micropump has been realized to dispense and manipulate droplets in 2D with up to 1000 addressable electrodes and electronics built underneath. The acoustic wave-based microfluidics can be used not only for pumping, mixing and droplet generation but also for biosensors, suitable for single-mechanism-based lab-on-chips application.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Microfluidics refers to a set of technologies that control the flow of minute amounts of liquids—typically from a few picolitres (pL) to a few microlitres (μL) in a miniaturized system [1, 2]. Such systems hold the promise of combining multiple functions on a single chip, including purification, separation, reaction, immobilization, labelling and detection. Rapid advances in microfluidics have sparked their tremendous widespread applications in pharmaceuticals, biotechnology, life sciences, defence, public health and agriculture [3].

Microfluidics includes micropumps, micromixers, microchannels, check valves and microchambers. Among them, micropumps and micromixers are the most important components for microfluidic applications as they are the active

components. The types of micropumps vary widely in design and application but can be categorized into two main groups: mechanical and non-mechanical pumps. Conventional mechanical micropumps represent smaller versions of macro-sized pumps that typically consist of a microchamber, check valves, microchannels and an active diaphragm to induce displacement for liquid transportation. Thermal bimorph, piezoelectric, electrostatic and magnetic forces, as well as shape memory mechanisms, have been utilized to actuate the diaphragm [1–3]. These micropumps are complicated, expensive, typically made by multi-wafer processes and difficult to be integrated with other systems such as integrated circuits (IC) for control and signal processing due to incompatible processes and structures [1, 2, 4]. They generally have a large dead volume, leading to excessive

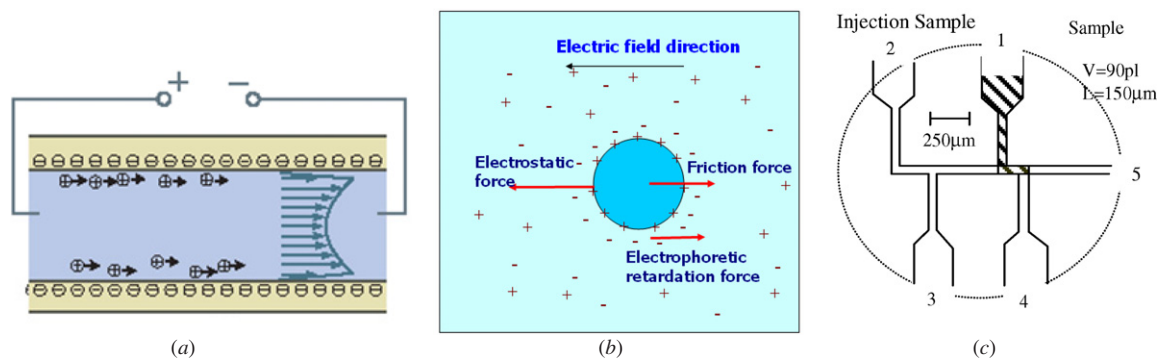


Figure 1. Schematic drawings of (a) EO and (b) EHD pumps, and an (c) EHD-based microfluidic chip (after [28]).

waste of biosamples and reagents which are very expensive and precious in biological analysis, especially for the forensic investigation. These micropumps typically have moving parts which lead to low production yields in fabrication, high failure rates and poor reliability in operation.

Recently there has been a trend to develop non-mechanical or moving-part-free micropumps such as electroosmotic (EO) [5], electrophoresis (EP) [6], dielectrophoresis (DEP) [7, 8], asymmetric electric field, electrowetting-on-dielectrics (EWOD) [9, 10], electrostatic pumps [11, 12], etc. The main mechanisms used for these moving-part-free micropumps are electrokinetic force and surface tension- or surface energy-related force. The former ones typically require electric/magnetic fields to mobilize ionic or polarized particles and species in liquid which can drag liquid through friction forces and form continuous flow *albeit* with some exceptions as discussed later. The latter ones are based on the modification of surface tension/energy by external stimuli to manipulate discrete droplets. Electric field, thermal and concentration gradients generated by localized heating or optical beams, photosensitization and capillary forces are used for these micropumps. The key characteristic of the micropumps of the latter category is that they can transport discrete droplets, the so-called digital micropumps, on channel-less (or wall-less) planar surfaces with no check valves. The fabrication process is simple and requires no special substrate. Therefore, these pumps can be easily integrated with ICs. Recently, a new generation of micropumps has emerged using a surface acoustic wave (SAW) generated on a piezoelectric substrate as an actuation force [13]. SAW micropumps can manipulate discrete liquid droplets from a picolitre to a few tens of microlitres and can also pump a continuous fluid.

Mixing liquids in small dimensions is a great challenge for microfluidics due to their inherent low-Reynolds-number flow conditions [14]. Currently, micromixing is dominated by passive mixing in microchannels through capillary phenomenon and static structures [15, 16]. Complete mixing is found difficult for these microfluidic systems, leading to an incomplete reaction and false readings in biochemical detection. Therefore, improving the diffusion-dominated passive mixing in microfluids has become a crucial issue for the development of microfluidics and lab-on-a-chip. Various technologies have been developed for active mixing such as cantilevers and membranes [17]. They are complicated, of

high cost and are not reliable. Acoustic streaming is the most effective mixer for liquids in small dimensions as it is quick and efficient typically taking less than a few seconds to reach >95% mixing [14, 18]. It is an active mixing method with no moving component, possessing great advantages over the other passive and active micromixers currently used in microfluidics.

This paper reviews the development of moving-part-free microfluidics, focusing more on the micromixers and nanopumps realized using electrokinetic force, surface tension and acoustic waves.

2. Electrokinetic microfluidics

Ionic species, charges or dipoles in liquid can gain electrokinetic energy from the applied electric field, and move along the electric field. When they move in the liquid, a dragging force is produced through friction of the particles with liquid surrounding them and induces a liquid flow. A few micropump technologies using the electrokinetic force have been developed including electroosmosis and electrophoresis (these two are considered as part of the electrohydrodynamic (EHD) phenomena), DEP, asymmetric electric field [19–21]. Magnetohydrodynamic (MHD) pumps also belong to this category though an external magnetic field is applied to produce the flow [22].

When liquid and solid come together, a charge layer is generated at the interface with opposite charges existing in the liquid and solid, forming an electric double layer (EDL) with a thickness of ~10 nm in the liquid. The thin layer of liquid next to the channel wall will have a net positive charge (see figure 1(a)). When an electric field parallel to the wall is applied, the ions are dragged along, resulting in a fluid flow with a flat plug flow profile in a narrow channel (from tens of nanometres to a few micrometres). When the channel is wide, the flow in the middle of the channel drops rapidly away from the wall surface as shown in figure 1(a). The flow profile strongly depends on liquid conductivity, strength of the electrical field applied and pressure generated [23, 24]. This is the principle for electroosmosis pumping. Since the charge layer in the liquid is very thin, it is only suitable for narrow channel applications, and the flow velocity is small, typically less than 1 mm s⁻¹ [2]. The differential pressure produced between the channels is the highest among the

Q1

currently available micropumps, in the range of 0.1–1 atm. With the application of porous frit or nanoporous structures for the channel wall, or packing of nanoparticles in the channel, EO pumps with differential pressure up to 20 atm have been developed [25–27], which is suitable for high volumetric pumping. The voltage used for EO micropumps is in the range of a few tens of volts and increases up to 1.5 kV for those with high differential pressure.

An electrophoretic micropump works by either injecting ions or inducing the production of ions in a fluid and then using an electric field to drag those ions. This dragging induces friction between the ions and fluid and produces a flow (see figure 1(b)). Since the fluids used for biological and medical research and life science are mostly biofluids containing various ions such as Na^+ , K^+ and Cl^- , electrophoretic micropumps are very useful in microfluidics and lab-on-chips. Electroosmosis and electrophoresis are part of the EHD effect and co-exist in most microfluidic systems. The combined electrokinetic forces are more effective in transporting the liquids. EP micropumps require high electric field intensity, typically in the range of tens to hundreds of volts. With modern microfabrication technology, electrodes with a gap of tens of micrometres can be easily achieved. Thus the operating voltage has been substantially reduced to a few tens of volts. Figure 1(c) is an example showing the design of an EHD pump [28]. By applying an electric field in the horizontal direction, the liquid is pumped along the horizontal channel (between terminals 2 and 5). When an electric field is applied to the vertical channels (e.g. between terminals 1 and 4), samples or reagents can be introduced into the horizontal channel, and waste can be disposed into the reservoir. Using this technique, sectioned samples or reagents with a fixed quantity can be generated for analysis, a pre-condition for quantitative microfluidics and lab-on-a-chip. EHD micropumps require no special substrate; they are typically made on low-cost glass substrates with polymers forming the channel wall which can be obtained by moulding or embossing. Substantial progress has been made recently to develop EHD micropumps on flexible and low-cost substrates such as parylene substrates [29, 30], making them possible for a disposable lab-on-a-chip.

DEP is a phenomenon in which the uncharged but polarized particles can be pumped into the regions of high electric field intensity. It has been considered as part of the EHD phenomena for transporting dielectric liquids. Original DEP device structures were not good enough for fluidic application due to excessive Joule heating and easy electrolysis as the electrodes directly contact the liquid. With the application of advanced dielectric coatings, ac voltage and miniaturized microelectrodes, these problems have been solved [31, 32]. DEP-based micropumps have become one of the most popular electrokinetic force-based microfluidic systems [8] as they can not only pump mass flow, but also dispense and manipulate droplets on the wall-less surface with a speed up to 5 cm s^{-1} , more than one order of magnitude higher than the other micropumps [31, 32]. They have also been utilized to separate particles and bio-species in the liquids [33–36]. DEP micropumps can only be used in liquids with low conductivity, $\sim 10^{-4} \text{ S m}^{-1}$ to avoid Joule heating. For

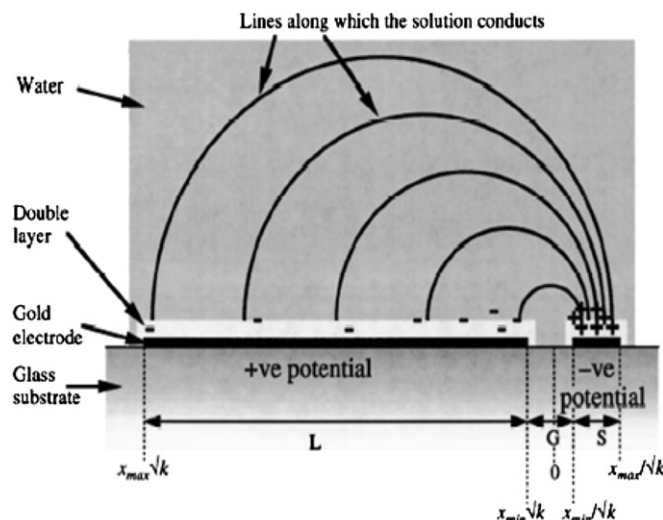


Figure 2. Electric field distribution of an asymmetric electrode-based micropump [19].

biofluids of conductivity higher than $\sim 10^{-4} \text{ S m}^{-1}$, an ac voltage with extremely high frequency $\sim 10^8 \text{ Hz}$ is needed to minimize Joule heating [34, 35]. Therefore, this limits their applications in biological analysis [8].

A MHD micropump is based on the Lorentz force to move ions in liquids and to produce flow through a dragging force. An electric current is passed across a channel forming ions in the liquid. A magnetic field oriented perpendicular to the channel will produce a force acting on ions along the channel direction, mobilizing the ions and inducing a liquid flow along the channel [22]. An ac current has been used to minimize electrolytic reaction which may produce gas bubbles and impede the fluidic flow [37]. The MHD mechanism produces a much bigger force than other EHD pumps [2, 26, 36] and is suitable for high volumetric pumping. However, in addition to the requirement for an external magnetic field, it requires a substantially higher conductivity for the liquid than those used in the other pumps.

Since the microchannel is relatively long, a large electric field is typically required to produce sufficient forces for EHD and DEP micropumps to produce the fluidic flow. MHD pumps require high current and high magnetic field to generate sufficient ion movement for pumping and consume high power. These problems can be solved by using an asymmetric arrangement of electrodes which produce a large localized electric field pointing in one direction with one example shown in figure 2 [19–21]. Non-uniform electric field distribution by an ac electric voltage produces a net electrokinetic force acting on ionic species, and moves liquid in the same manner as in the other electrokinetic force-based micropumps. However, this can be operated at an ac voltage typically less than 1 V, more than one order of magnitude smaller than those used in most other electrokinetic micropumps. The devices have high pump power and are able to deal with liquids with volume up to several hundreds of μl , but the velocity is low, typically in the range of a few tens to hundreds of $\mu\text{m s}^{-1}$. The pumping power can be increased significantly, when the two substrates with the

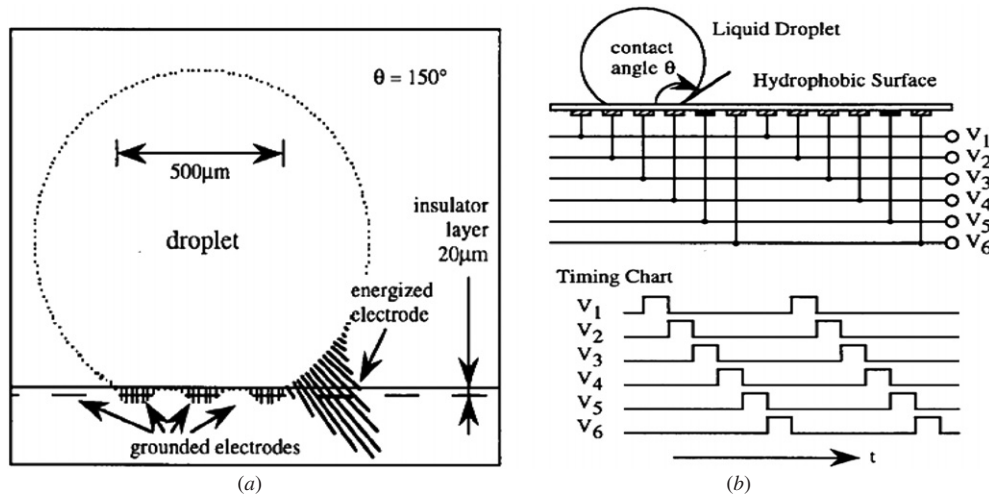


Figure 3. Schematic drawing of an electrostatic micropump and an array of electrodes for operation [38].

electrodes form a symmetric structure with the microchannel sandwiched between them [19].

Most electrokinetic pumps can only be used for continuous flow application which typically requires channels with walls to confine the liquid. This limits their applications for quantitative analysis. Among the above-mentioned pumping mechanisms, DEP micropumps can be made on a droplet basis and are called digital microfluidics. The electrostatic force-based micropump is another type of the electrokinetic force-based micropump [11, 12, 38, 39] though it is thought to be a more surface tension-related one. The electrostatic pump having a structure schematically shown in figure 3(a) consists of an array of electrodes covered by a dielectric layer. A hydrophobic surface with a contact angle larger than 90° is required for this droplet-based pump. An electric field is applied to the electrode next to the droplet, with the others grounded. This electric field induces negative charges on one side of the droplet surface closest to the electrode and positive charges on the other side. The induced charges create the Maxwell stress through the electrostatic force. If the static force is large enough to overcome the surface tension of the droplet, the droplet moves onto the electrode with voltage applied [38, 39]. By applying a sequential electric field to the electrode array, discrete droplets can be manipulated and transported to where they are required. The operation is schematically shown in figure 3(b). The drawback of the electrostatic pump is that a high electrical voltage up to a few hundreds of voltages is required to generate a sufficient force to move the liquid. This may cause breakdown of the dielectric layer, leading to leakage and electrical shock to biological species. A simplified fishbone design has been developed which can accurately move and guide the droplet by an ‘inchworm’ technique at a relatively low field, and with a low pumping velocity, in the order of a few hundreds of $\mu\text{m s}^{-1}$ [40].

Although the electrokinetic pumps can transport liquid, they are not good for mixing liquids in the channels due to low-Reynolds-number flow conditions. Liquids from different channel sections entering into the main channel

remain separated. Although passive mixing structures such as posts and serpentine structures have been used to increase the mixing [15, 16], a complete mixing is still one of the main challenges for these micropumps.

3. Surface tension-based microfluidics

Liquid on the surface of a solid substrate has a fixed shape, determined by its surface energy between the liquid and solid. When the surface energy of the solid substrate is high, the droplet has a small contact angle. It has a cap-like shape, or even spreads on the whole surface, forming a ‘wet’ surface. It acquires a ball-like shape when the surface energy of the substrate is low. The contact angle of the droplet on the substrate is determined by the balance of interfacial energies between the solid and liquid, γ_{SL} , the solid and gas, γ_{SG} , and the liquid and the gas, γ_{LG} , and is expressed by Young’s equation [5]:

$$\cos \theta = \frac{\gamma_{SG} - \gamma_{SL}}{\gamma_{LG}} \tag{1}$$

Static capillary force has recently become a popular actuation mechanism for microfluidics [41, 42]. This is particularly useful for one-time-use disposable devices. When liquid is introduced into microchannels, the capillary force will ‘pull’ the liquid into the microchannel if its surface is hydrophilic, with a contact angle of less than 90°, delivering samples or reagents to where they are designed. This process can be accomplished and enhanced by surface chemical treatment which typically increases the surface energy of the channel wall. The surface energy can be controlled by various stimuli such as electric field, optical beam and chemical treatment. If the surface energy of the substrate is increased artificially on one side close to the droplet, the liquid ball will spread out in this direction, leading to motion of the droplet. This phenomenon has been utilized for various surface tension-based micropumps.

Electrowetting (EW) or EWOD micropumps are devices for moving discrete droplets on a channel-less flat surface using an electrical field to alter the surface tension of the substrate.

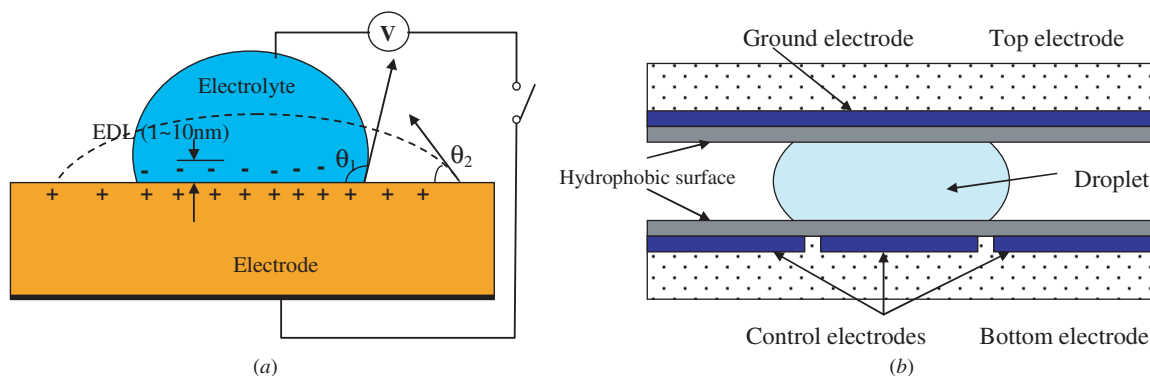


Figure 4. (a) Alteration of the surface contact angle by an electropotential. The droplet becomes flat (the broken line) when a voltage is applied, and (b) an EW-based micropump (after [9]).

As shown in figures 4(a) and (b), when a voltage potential is applied to a droplet deposited on a dielectric substrate, it energizes the substrate surface, and increase its surface energy, γ_{SL} , according to Lippman's equation [5]:

$$\gamma_{SL} = \gamma_{V0} - \frac{C}{2} V^2. \quad (2)$$

Here γ_{V0} and γ_{SL} are the interfacial energies between the surface solid and liquid before and after applying a voltage V , and C is the specific capacitance of the dielectric layer as shown in figure 4(a). The device is designed such that only the surface energy of the substrate on one side of the droplet is increased. As the voltage increases, the droplet moves to where the surface energy of the substrate is high. In order to facilitate this droplet for microfluidic application, an EW pump typically consists of two parallel electrodes with the droplet sandwiched between them as shown in figure 4(b). The electrodes are covered with a thin dielectric material and the surface is treated to have a high hydrophobicity with a contact angle larger than 90° . Activating an electrode next to one side of the droplet deforms the droplet asymmetrically and produces a pressure gradient in the droplet which causes movement of the droplet. If the surface force of the droplet is overcome, the droplet moves towards the activated electrode [5]. EW pumps typically use a grid or an array of electrodes to realize liquid transportation. The EW micropump consumes little power as there is no current involved.

By manipulating and changing the shape of droplets, EW/EWOD technology has been applied in areas such as lab-on-a-chip [9, 43]. The early reported EWOD-based microfluidic lab-on-a-chip platform for clinical diagnostic was presented in [44, 45]. It details the ability to perform glucose concentration measurements on a droplet-based lab-on-a-chip. Figure 5 shows an improved system developed with the ability to analyse human physiological solutions [46]. Kim's group has demonstrated the application of EWOD technology in proteomics, and the EWOD electrode array system realized multiplexed sample preparation on a digital microfluidic chip [47, 48]. Figure 6 shows the multiplexed sample preparation and analysis (with an ability to perform sample purification) which has a much higher throughput than conventional methods [47].

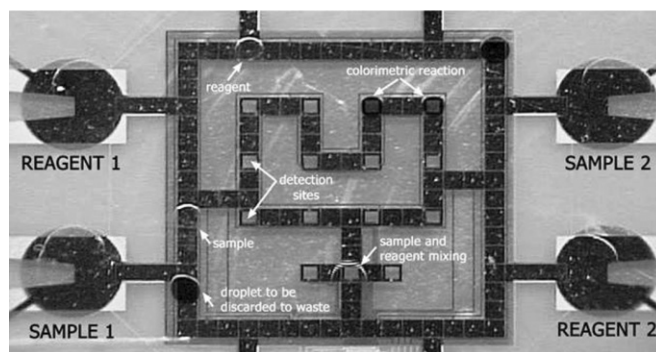


Figure 5. Lab-on-a-chip system for analysing human physiological solutions designed [46].

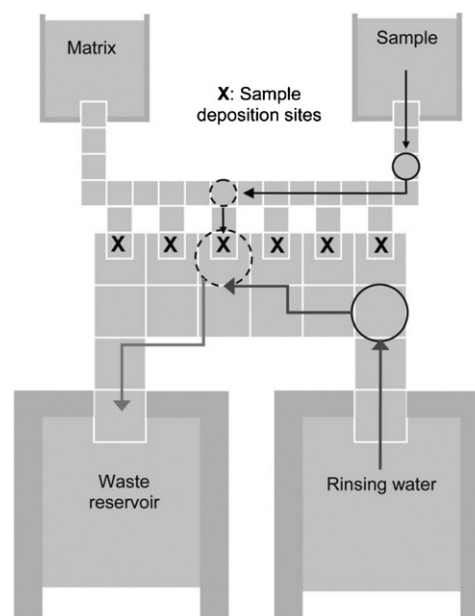


Figure 6. A schematic view of the EWOD system with function of sample preparation and analysis [47].

Recently, Gong *et al* have demonstrated EWOD devices fabricated on a printed circuit board (PCB) with 8×8 large electrode array and land grid array connection to the control circuit [49]. This enables EWOD devices with up

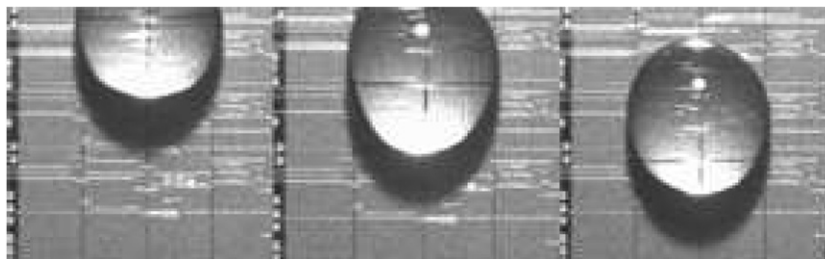


Figure 7. A moving droplet on the post-processed EWOD electrode array controlled by an integrated CMOS circuit underneath [51].

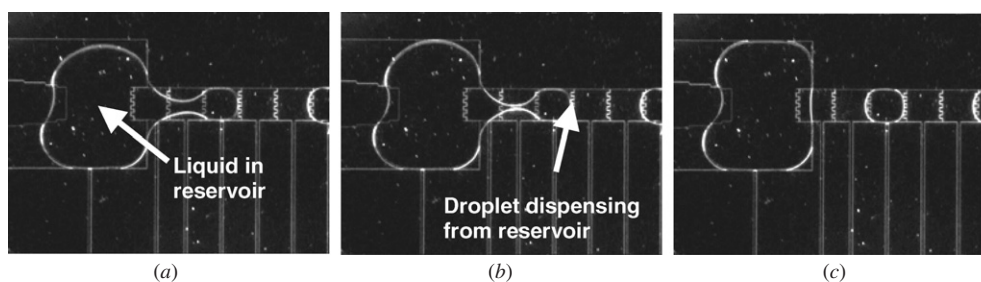


Figure 8. Top view of an EWOD device, showing (a) a 1 μl droplet on the reservoir electrode is being pulled out on to a small electrode array, (b) both the reservoir electrode and a small electrode are switched on to pull both sides of the liquid to split it, and (c) 80 nl droplet is dispensed after the splitting [54].

to 1000 individually addressed electrodes to be achieved at a reasonable price. The ability of addressing large EWOD electrode arrays enables more complex systems including a higher droplet volume resolution, throughput and reconfiguration possibility [49]. Based on the PCB EWOD systems, on-chip sensing has been presented by Luan *et al* aiming at integrating an optical sensing system with digital microfluidics [50]. Driven by similar motivations, Li *et al* has reported the integration of EWOD and CMOS technology by post-processing standard foundry-fabricated chips [51], which potentially enables both electrode arrays and sensor arrays to be controlled by integrated addressing CMOS circuit. Figure 7 shows a 1 μl droplet being manipulated on an EWOD electrode array controlled by an ‘underneath’ circuit fabricated using 100 V CMOS foundry technology.

One of the key parameters in EW/EWOD technology is the driving voltage. Earlier work on EW arrays required driving voltages in the range 80–100 V [52]. Recently, with a more judicious choice of high dielectric constant materials (i.e. barium strontium titanate (BST) and bismuth zinc niobate (BZN) [53]) and the dielectric thickness, the voltage required to manipulate droplets has been reduced below 15 V. More recently, Li *et al* developed a room temperature-grown anodic Ta_2O_5 process and a robust low-voltage EWOD operation which can be integrated with PCB and CMOS technology [54]. The anodic Ta_2O_5 with a typical dielectric constant of around 20 has been used widely in electrolyte capacitors. The ability of robustly providing high charge density at a low voltage enabled sub-15 V EWOD manipulation [53]. EWOD devices which consist of a combination of one large electrode and several smaller electrodes can realize a microdispensing (droplet generation) and micromanipulation function with one example shown in figure 8.

In addition to the planar structure, an electrocapillary pump has the combined effect of EW and capillary force, which can be used to construct 3D micropumps. It consists of multichannels with electrodes inside covered by a thin dielectric layer. By applying a voltage between the electrode and the liquid, it produces a dramatic change in the surface energy between liquid and channel wall, and thus can pump liquid up to a height of a few centimetres vertically [55, 56].

The surface energy of a solid surface can be modified by thermal flux [57, 58] or an optical beam [59, 60], which introduces a localized heating effect. The surface energy of the substrate and the liquid increases as the temperature of the substrate rises. Localized heating generates a temperature gradient and propels the droplet towards the colder region. Thermal gradient micropumps, also called thermal capillaries, consist of an array of microchannels and microheaters. The microheater raises the temperature locally and generates a temperature gradient, hence a surface tension gradient. The droplet moves from the high-temperature zone to low-temperature zone. Using the same thermal capillary force, it is also possible to generate/separate droplets. A temperature gradient of 1 $^\circ\text{C mm}^{-1}$ was reported to be sufficient to modify the surface tension to mobilize the droplets [57, 58]. The system must be so designed that it limits the temperature below 50 $^\circ\text{C}$ for biological analysis. Another form of heating effect-based micropump is the vapour bubbles-based pump [61, 62], though it does not entirely utilize a surface force-driven mechanism. It consists of an array of microheaters embedded under the microchannel. By heating the liquid to a boiling point, bubbles are generated within the channel. Pulsed electrical signals are sent to the microheaters in sequence and the bubbles are moved from one electrode to another, pushing

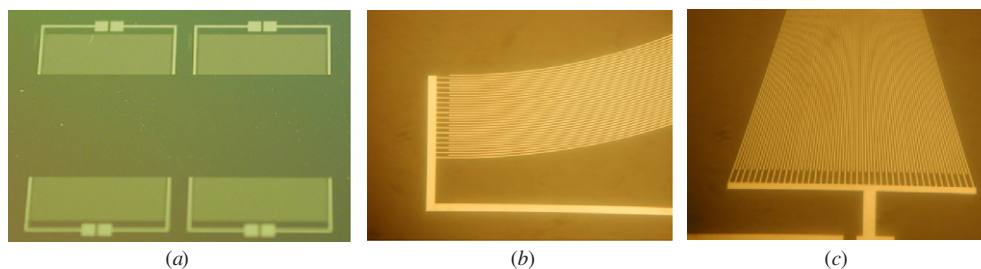


Figure 9. Photos of a pair of SAW transducers made on LiNbO_3 (a), SAW with circular (b) and slanted (c) IDT electrode structures fabricated by the authors.

the liquid forward. However, the overheating of the liquid is a problem for biological application and the power consumption is higher than those for other micropumps.

An optical-wetting micropump has a structure similar to that of an EW device with a transparent top electrode as shown in figure 4(c), typically with a conductive film on a glass substrate for the application of electric field [59, 60]. A focused optical beam from a laser or LED passes through the electrode to modify the surface tension of the inner surface of the electrodes. An area is ‘warmed up’ and induces a thermal gradient which deforms the droplet on one side and manipulates the droplet as in an EW micropump. A droplet immersed in another liquid can also be manipulated by surface energy alteration [63]. By focusing a laser beam near a droplet in the liquid, the surface tension of the droplet is modified due to the thermal gradient. Based on this principle, the microdroplet can be manipulated by the laser beam, which has a great potential for its application in droplet-based flow-through polymer chain reaction (PRC) systems for DNA amplification and detection [64]. An optical beam can also be used to modify the surface energy using photosensitive or photo-absorption materials deposited on a solid substrate to form a light-driven micropump [65–67]. A photoresponsive surface was achieved using photochromic azobenzene units. Under the incident light, the surface undergoes a chemical reaction. The surface tension changes in the order of milliseconds, leading to manipulation of droplets. Garnier *et al* have also demonstrated that liquid can climb vertically, forming a spatial distribution in two dimensions by varying the intensity of the incident light [65]. The limitation for optical micropumps is that they require an external optical system to control the droplet motion, which might hinder their applications.

Surface energy-based micropumps transport liquids in a discrete droplet form, suitable for the development of digital microfluidics. EW-based micropumps are simple in structure and operation and can be integrated with control electronics with advantages of simplicity, compactness and low cost. They use a very small amount of liquid and reagents and consume little power. They can also be controlled by an electronic signal. Using a grid pattern and computer control, the droplets can be programmed to move independently and in any direction on a 2D plane with a high level of controllability. Being able to move droplets around on a chip without channels creates an opportunity for automated lab-on-a-chip applications without requiring complicated fabrication

that has plagued other continuous flow microfluidic systems. Mixing in EW droplet-based microfluidics is better than those in continuous flow electrokinetic pumps. The electrokinetic pumps mostly rely on dynamic mixing caused by the additional kinetic energy generated when two droplets are merged together (reduced surface area). However, once the droplets are merged, mixing in the formed droplets is extremely difficult due to the low-Reynolds-number condition. Mixing or stirring within a droplet is often required for the effective immobilization of biomarkers and minimization of non-specific binding for biological analysis.

4. Acoustic microfluidics

When an alternating electric field is applied to a piezoelectric material, a mechanical wave is generated that propagates in the substrate or on the surface of the materials through the piezoelectric effect, in either a Rayleigh mode (vertical and surface normal) or a shear mode wave (horizontal in-plane). A wave propagating through the whole substrate thickness is called a bulk wave which introduces a displacement normal to the surface of the substrate with amplitude in the order of a few tens of angstroms. The mechanical wave propagating on the surface of the materials (within a few wave lengths depth) is called the surface acoustic wave (SAW) either in a Rayleigh mode (vertical and surface normal) or shear mode wave (horizontal in-plane).

SAW devices typically consist of a pair of interdigitated transducers (IDT) as shown in figure 9(a): one IDT electrode is the transmitter and the other one is the receiver. The resonant frequency of the device is determined by the periodicity of the electrode and the acoustic velocity of the substrate. For SAW microfluidics, one IDT electrode is normally used. For sensing application, two IDTs can be used together to form a pair of electrodes. When the Rayleigh acoustic wave generated by the IDT meets a liquid droplet deposited on its wave path, the momentum and energy of the acoustic waves are coupled to the droplet as schematically shown in figure 10(a). Depending on the surface tension and the pressure gradient generated by the acoustic wave, three situations arise: streaming (mixing), pumping and atomization [68–71]. If the surface is hydrophilic and the acoustic pressure is insufficient to push the liquid forward, the kinetic energy will only induce internal acoustic streaming, thus realizing the mixing function in the droplet as well as in the liquid mass. If the power is large enough and the SAW device surface is hydrophobic, the liquid can be

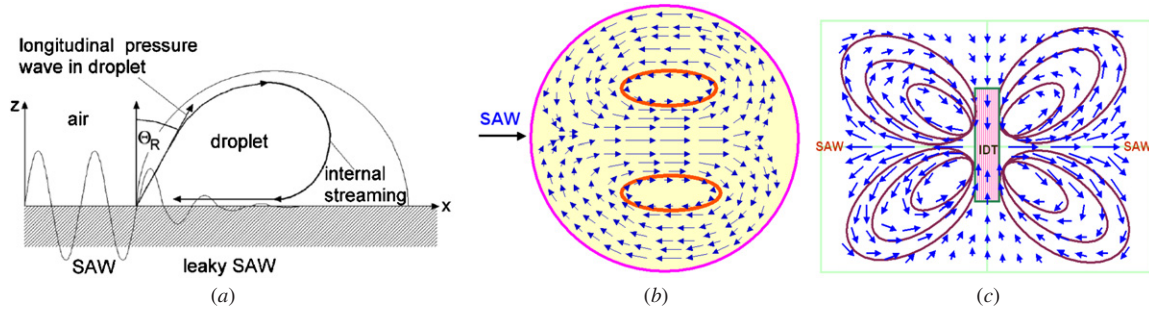


Figure 10. Schematic drawing of acoustic streaming (a), top view of the acoustic streaming pattern within a droplet (b) and in a liquid tank (c) [74, 75].

pushed forward as will be discussed later. Further increase in the acoustic wave power transfers high moment and energy to the liquid, and tiny droplets in the sizes of picolitres or smaller can be generated and ejected from the surface of the parent droplet, forming a mist [70, 72] which can be used for spray application. It is difficult to control the size by this atomization process; therefore, it is not suitable for microfluidic application.

The acoustic wave generates a force acting on the droplet at a fixed angle, which is determined by the properties of the piezoelectric material and liquid. The force direction corresponds to the Rayleigh diffraction angle θ_R , which is expressed as follows [13]:

$$\theta_R = \arcsin \left(\frac{V_{\text{liq}}}{V_{\text{sub}}} \right). \quad (3)$$

Owing to the Rayleigh angle, the acoustic force is applied to liquid locally at a fixed direction, causing streaming within the droplet or the continuous liquid. The Rayleigh angle is even visible from the acoustic streaming within a droplet by the addition of nanoparticles or ink in the liquid [14].

Figures 10(b) and (c) show the acoustic streaming patterns induced in a droplet and in a liquid tank when the SAW device is immersed in it. The droplet, located in the middle wave path of the IDT electrode, has a symmetrical streaming pattern, semi-circulating within the droplet and forming a vortex shape. The symmetrical pattern breaks when the droplet locates off the central wave path, and could even produce a single circulated streaming in the droplet. The latter has been utilized to concentrate particles [73]. When a SAW with one standard IDT electrode is immersed in the liquid, it induces a symmetrical butterfly streaming pattern because acoustic waves produced by standard IDT electrode can be transmitted bi-directionally [74–76].

Figure 11 shows the dependence of the streaming velocity at the middle of the droplet as a function of the applied RF signal voltage for a LiNbO₃ SAW pump with wavelengths of 32 μm . The streaming velocity reaches 18 cm s^{-1} at an RF voltage of ~ 2.25 V by a fundamental Rayleigh wave, more than two orders of magnitude higher than most of other micropumps. The third harmonic mode wave can also be used to pump liquid, but the streaming velocity is typically five to ten times smaller than that produced by the fundamental mode wave. With its high acoustic streaming speed, the SAW is superior in performing effective mixing. An effective and

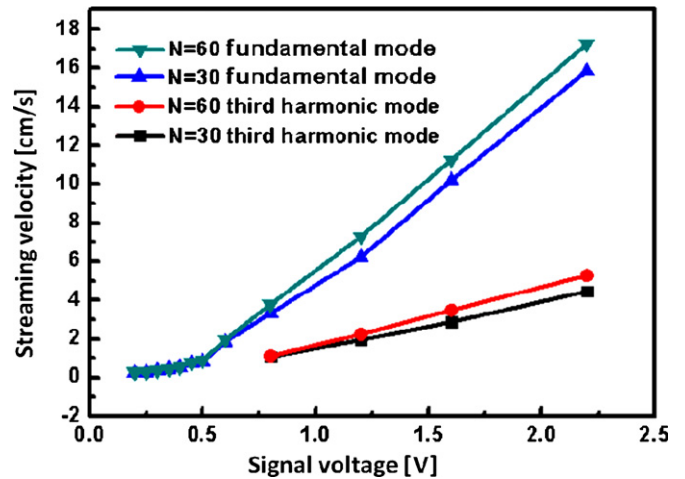


Figure 11. Dependence of acoustic streaming velocities at the middle of the droplet as a function of applied signal voltage from a LiNbO₃ SAW micropump [75].

completed mixing in less than 2 s within a narrow channel and in a microdroplet has been obtained [14, 77], demonstrating its superiority over the passive micromixers and other droplet-based micropumps. SAW devices with an array of sectored Fresnel annular ring electrodes can even generate high ‘waves’, providing much better mixing functionality for large-quantity liquids [18, 78, 79].

When the acoustic force is large enough, it induces an acoustic pressure gradient and deforms the droplet. The acoustic force, F_s , applied on the droplet can be measured through the deformed shape of the droplet by the following equation [71, 80, 81]:

$$F_s = 2R\gamma_{LG} \sin \left(\frac{\theta_1 + \theta_2}{2} \right) (\cos \theta_1 - \cos \theta_2) \quad (4)$$

where θ_1 and θ_2 are the advancing and receding contact angles of the droplet as illustrated in figure 12(a), and R is the radius of the droplet. If the acoustic force is larger than the surface force, the droplet can be pushed forward; otherwise the droplet remains in the original position. Figure 12(a) shows the deformed droplet on a LiNbO₃ SAW device under an acoustic pressure. The droplet deforms with asymmetric contact angles on both sides. From the contact angles of the deformed droplet, it is possible to find the acoustic force using equation (4).

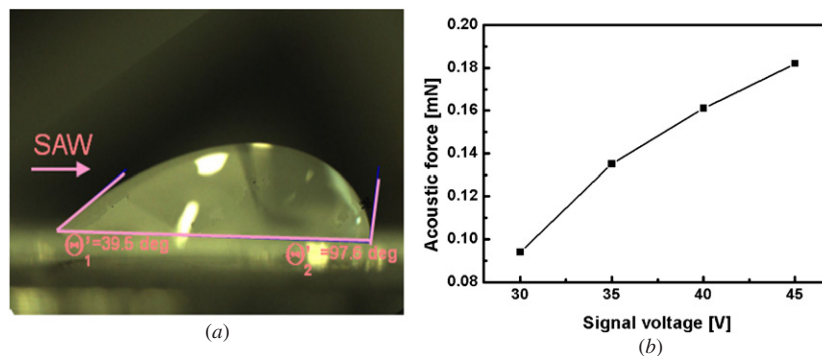


Figure 12. A photo of a deformed liquid droplet under an acoustic pressure and the measured acoustic force as a function of RF signal voltage [75].

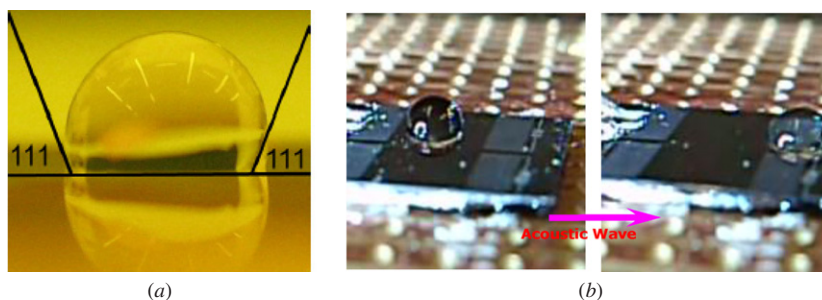


Figure 13. A photo of a droplet on the OTS-treated LiNbO₃ surface with a contact angle of 111° (a) [75], and photos of a droplet (10 μl) moved before and after applying a pulsed RF signal to a thin film ZnO SAW (b) [90].

Figure 12(b) shows the dependence of the acoustic force acting on a 10 μl droplet as a function of the RF signal voltage for a LiNbO₃ SAW device. The acoustic force increases almost linearly with the voltage and reaches 180 μN at a voltage of 45 V. This generates a pressure of over 80 Pa on the droplet, comparable to pressures obtained in some mechanical micropumps [1–4]. With such a large acoustic force produced, the SAW pump can manipulate droplets more efficiently than many of the droplet micropumps discussed above. It can also be used to pump a continuous flow in a channel. The microchannels could be physical walls made of various polymers [14] or invisible surface tracks with different hydrophobicities [82]. For continuous flow systems, the channel width should be kept smaller than the vortices of the streaming to minimize reverse flow which reduces the acoustic pressure and pumping speed. One of the advantages of the SAW-based pumps and mixers is that IDT electrodes can be built outside of the microchannels without direct contact with the fluid, and the IDT electrode can remotely manipulate the liquids, a characteristic which no other micropumps possess. This ‘remote’ pumping capability is very important and useful in developing flow-through PCR [83, 84].

Since most of the piezoelectric substrates (such as LiNbO₃) are hydrophilic with contact angles less than 90°, the surface force is so high that the liquid on their surface cannot be propelled by an acoustic wave even when a high RF signal up to 45 V is applied. For droplet manipulation, the surface of SAWs must be hydrophobic with a sliding force smaller than the acoustic force generated. The sliding force of a water droplet on a piezoelectric substrate can be modified by

coating the substrate with a hydrophobic layer such as HMDS, Teflon, PVDF or octadecyltrichlorosilane (OTS). PVDF has the smallest sliding force of ~85 μN, but a thick layer is normally obtained by spin coating which damps the acoustic wave significantly, leading to failure of droplet manipulation by acoustic waves. Teflon coating is hydrophobic with a contact angle larger than 100°. Plasma deposition of a thin CFx layer results in a sliding force in the range of 85–140 μN [71], sufficiently good for droplet-based micropump applications. However, this requires a plasma process and may damage other components on the same substrate. Self-assembly mono-layer OTS was found to be the best material for the formation of a very thin hydrophobic surface used for droplet-based micropumps [82, 85]. OTS has a layer of thickness of ~10 nm, with a contact angle of ~110° for water as shown in figure 13(a), suitable for droplet-based liquid transportation [82, 86]. The sliding force for such surfaces is in the range of 80–140 μN depending on the processing conditions, but much smaller than the achievable acoustic forces as shown in figure 12(b). This clearly indicates that an RF signal with medium voltage (<35 V) is sufficient to overcome the surface tension and mobilize the droplet.

Figure 13(b) shows two photos of a 10 μl water droplet on an OTS-treated ZnO SAW device before and after applying an RF signal of 45 V. The acoustic wave can manipulate droplets with size up to 50 μl (easier for smaller droplets), demonstrating its superiority over other moving-part-free micropumps. For the precise control of displacement and location of the droplet, pulsed RF signals are normally used to manipulate droplets. An RF signal with pulse widths of

Q4

200–600 ms was found to move a droplet at a rate of 30–100 $\mu\text{m}/\text{pulse}$, largely depending on the RF voltage applied. Pulsed RF signal can also minimize the acoustic heating, a common phenomenon for SAW devices, making SAW pumps more effective, efficient and precise. Digitized programmable SAW microfluidics have been realized by many groups for biological and chemical analyses. [68, 71, 75].

SAW-based micropumps and micromixers have often been realized using piezoelectric substrates such as LiNbO_3 and LiTaO_3 [68, 73]. These are bulk materials, expensive and fragile, and most importantly they cannot be integrated with other control and signal processing electronics. Piezoelectric thin films such as ZnO and AlN have been used for SAW devices in the communication sector for a long time, and demonstrated excellent performance [87, 88]. We have recently developed SAW microfluidics using piezoelectric thin film ZnO on Si substrates, and have demonstrated streaming and pumping functions [74, 89–92]. For microfluidic application, SAW devices with a medium operational frequency (for example, a few tens of MHz) are sufficient. This requires a ZnO piezoelectric film with a thickness of a few micrometres. Magnetron sputtering was used to deposit the high-quality ZnO films on Si substrates at room temperatures, and high-performance SAW devices were prepared based on the ZnO thin films [74, 92, 93].

When a piezoelectric layer has a lower acoustic velocity than that of the substrate, a higher order Sezawa mode acoustic wave co-exists with the Rayleigh-mode wave, and it becomes the dominant transmission signal with higher resonant frequency. Similar to the R-wave, the Sezawa wave is also a longitudinal wave with a substantial wave component penetrating into the Si substrate. The resonant frequency of the S-wave decreases with the increase in the overlayer thickness and the acoustic speed reaches that of the Si substrate. The interaction of liquid with the S-wave is similar to that of the R-wave but at a different Rayleigh angle. It was found that the Sezawa wave is more effective in acoustic streaming and droplet-based pumping owing to its much larger transmission amplitude than the Rayleigh wave in ZnO/Si SAW devices [74]. A streaming velocity of $\sim 5 \text{ cm s}^{-1}$ was obtained by Sezawa waves from a ZnO SAW. Although this is much smaller than 18 cm s^{-1} streaming velocity obtained from LiNbO_3 SAWs, it is still one order of magnitude higher than most of other micropumps, and is more than enough for microfluidic applications as most of microsystems do not need such high pumping and mixing speed. Figure 14 is a comparison of streaming velocities driven by the Sezawa and Rayleigh waves, demonstrating the potential of the Sezawa mode wave for microfluidic application [75]. ZnO is a hydrophilic material with a contact angle of $\sim 70^\circ$ for water, and the contact angle strongly depends on the surface condition and exposure of light [94]. It was found that OTS treatment resulted in a contact angle of $\sim 110^\circ$, similar to that obtained from the LiNbO_3 substrate as shown in figure 13(a), and the surface of the OTS-treated ZnO SAW device is stable and reliable, suitable for droplet-based liquid transportation. Figures 13(b), and (c) are photos of a droplet (10 μl) before and after applying a pulsed RF signal with a voltage of 45 V on a ZnO SAW

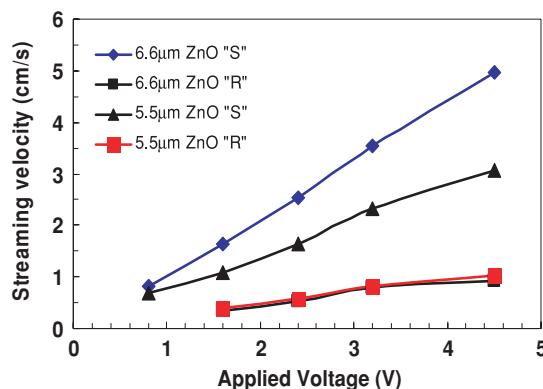


Figure 14. Streaming velocity as a function of RF signal voltage with wave mode as a parameter. 'S' and 'R' stand for Sezawa and Rayleigh mode waves, respectively [74].

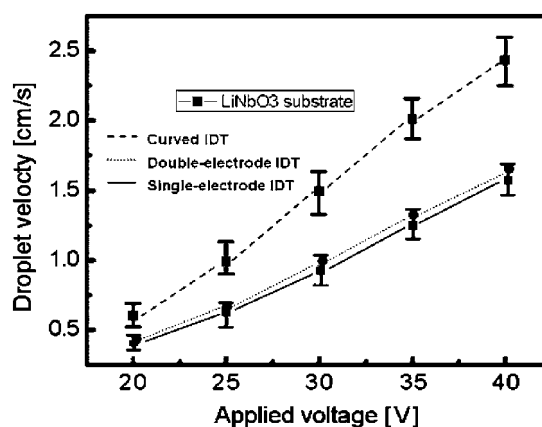


Figure 15. Comparison of droplet velocities driven by an acoustic wave for SAW devices with a standard and a curved IDT structure [86].

device. These clearly demonstrated the potential of the ZnO thin film for SAW-based microfluidics, with full integration of electronics for control and signal processing.

Acoustic waves generated by IDT electrodes in a standard SAW will travel in both directions with half the energy wasted. IDT electrodes can be modified to transmit acoustic waves in one direction by using reflector IDTs, splitting gate (or double electrode) and single-phase unidirectional transmission [95, 96], thus increasing the pumping and streaming efficiency. The streaming velocity can be improved by 10–30% compared with that of a standard SAW pump. Further enhancement of streaming and pumping velocities can be achieved by using a semi-circular IDT configuration (figure 9(b)) which can focus the acoustic wave energy, thereby increasing the pumping efficiency [86]. Figure 15 is a comparison of the droplet velocities for SAW pumps with a standard and semi-circular IDT structure. The maximum droplet velocity obtained by a semi-circular IDT SAW is 60–70% higher than that by a standard SAW IDT. SAW devices with a slanted IDT electrode as shown in figure 9(c) have a broad range of resonant frequencies, and can be used to alter the directions of streaming and droplet movement by changing the operating frequency [97].

Since acoustic waves can travel for a long distance without decaying significantly, thin film-based SAW pumps can be fabricated away from the microchannels and microchamber to 'remotely' control pumping and mixing. We also found that acoustic waves generated on a ZnO film can continuously travel in the Si substrate without ZnO film on top of the wave path. This offers a great flexibility to fabricate highly integrated microfluidics with the SAW devices built on isolated ZnO islands while other components such as microchannels, chamber and sensors are fabricated on the Si substrate directly. This configuration can avoid the direct contact of the biofluid and IC control circuit with the ZnO layer, which is very reactive, and a protection layer must be used.

It is worth mentioning another form of acoustic wave-based microfluidic system: flexural plate acoustic devices. Acoustic waves generated by IDT travelling through a thin plate can induce flexural motion of the plate normal to its surface which can be used for pumping and mixing [98–101]. This type of microfluidic devices has a moving membrane with a complicated process to make a thin plate. They will not be introduced in detail here, and readers may find more information through the references cited above.

Acoustic microfluidic pumps have the advantages that no other actuation mechanism can deliver. The acoustic wave can be used for both continuous flow and discrete droplets with sizes from a few picolitres to tens of microlitres. It can be used not only as a micropump, but also as an *in situ* active micromixer for droplets and continuous flow. Furthermore, SAW devices can be used as sensors, which can detect biological substances through biological recognition system [102, 103]. These have clearly demonstrated the potential for highly integrated lab-on-a-chip systems using a single acoustic actuation/sensing mechanism on a low-cost substrate, a characteristic that no other microfluidic systems possess. With the successful demonstration of the detection of antibody–antigen pairs by a thin film ZnO SAW biosensor [90, 104], the SAW-based microfluidics and lab-on-a-chip integrated with ICs can be soon realized on low-cost Si or glass substrates.

5. Conclusion

Microfluidic systems are one of the emerging technologies handling small amount of liquids. Since they are fast, compact and can be made into a highly integrated system, they are promising for biological and medical research and life science applications. The new trend for microfluidics is to develop moving-part-free micropumps operated by electrokinetic force, surface tension and surface acoustic waves. By using discrete unit-volume droplets, a microfluidic function can be reduced to a set of repeated basic operations, which facilitates the use of hierarchical and cell-based approaches for microfluidic biochip design. Therefore, digital microfluidics offers a flexible and scalable system architecture as well as high fault-tolerance capability. Since each droplet can be controlled independently, these systems have dynamic reconfigurability, whereby groups of unit cells in a microfluidic array can be reconfigured to change their functionality during

the concurrent execution of a set of bioassays. One common actuation method for the digital microfluidics is EWOD, which can be digitally programmed for droplet generation, merging and movement with electronics built underneath. Another advanced technology is based on acoustically induced droplet transport employing surface acoustic waves. SAWs can not only be used for pumping, mixing and droplet generation, but can also be used for biosensing; thus, they are suitable for the development of single-mechanism-based lab-on-a-chip systems for bioanalysis and healthcare devices.

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system *Lab Chip* submitted

Queries

- (1) Author: The sense of the sentence ‘A few micropump technologies using . . .’ is unclear. Please check.
- (2) Author: Please check whether the edits made in the sentence ‘A simplified fishbone design has . . .’ retain your intended sense.
- (3) Author: The sense of the expression ‘delivering samples or reagents to where they are designed’ is unclear. Please check.
- (4) Author: Please check whether the edits made in the sentence ‘The sliding force of a water . . .’ retain your intended sense.
- (5) Author: Please update references [35, 51, 54, 75, 82, 92, 104].
- (6) Author: The sense of the text in the caption to figure 8 is unclear. Please check.
- (7) Author: Please be aware that the colour figures in this article will only appear in colour in the Web version. If you require colour in the printed journal and have not previously arranged it, please contact the Production Editor now.

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