Small Matters

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It might very well be a scene from the movie 'Honey I Shrunk the Kids', only perhaps the missus wouldn't have been too crossed to discover that I shrunk the lab instead. Microfluidics, which is the science of actuating fluids or manipulating particles at micron and sub-micron dimensions, is essentially in layman's terms, small scale plumbing. As a broad concept, microfluidics typically involves shrinking and connecting pipes, pumps, valves, reactors and separators, the very components that typically make up a laboratory or chemical plant, onto a microchip. Whilst that's a lot of real estate to fit onto a chip, advances in micro/nano-fabrication technology dating back to the integrated circuit revolution has made the 'lab-on-a-chip' concept a reality (Fig. 1).

The ability to miniaturise, parallelise and automate batch processes using microfluidic technology presents significant opportunities particularly for the healthcare, pharmaceutics, biomedical and energy industries. Instead of painful extractions of an entire test tube of blood that is then sent off to the pathology laboratory for days before the results of a blood test are returned, portable low cost and disposable point-of-care medical diagnostic devices could enable general practitioners to take tiny samples of blood (with volumes less than a hundredth of that from a needle prick) from a patient and obtain the results of the test almost immediately. Tiny biosensors that rapidly and accurately detect minute amounts of microbes can be deployed inconspicuously in high-density metropolitan areas as early warning systems that alert first responders in the event of a bioterrorist attack. Miniaturisation of the high throughput drug testing arrays presently employed in the identification of potential drug candidates cannot only reduce the amount of expensive samples and reagents used, but also allow the screening procedure to be carried out at a fraction of the time and cost as a consequence of shorter residence and response times. Concomitantly, microdevices are been developed for immunoassays, chemical analysis, drug delivery, public health and environmental monitoring, explosives detection, cell culture, and, polymerase chain reaction, amongst others (Craighead, 2006; deMello, 2006; El-Ali et al., 2006; Yager et al., 2006).

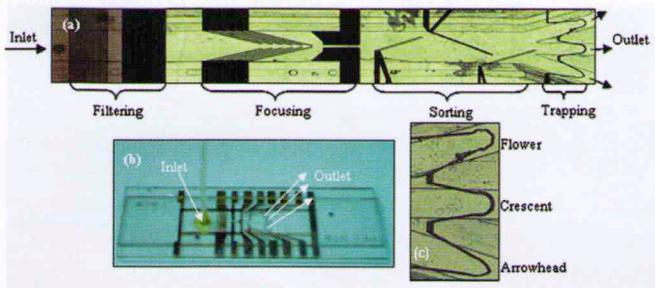


Fig. 1: (a) A microfluidic chip that filters, focuses, sorts and detects particles of different characteristics using dielectrophoresis (Cheng et al., 2007). (b) The chip comprises of a 25 micron high, 1 mm wide and 14.5 mm long fluidic channel enclosed by two glass microscope slides on which electrodes are patterned. (a,c) The electrode arrangements for the different particle processing stages are shown. In this case, the chip is configured to filter, sort and differentiate three different pathogenic species in a carrier liquid containing other particulate matter (debris). Figure courtesy of H-C Chang.

Scaling down the components required to store, load, actuate, meter, regulate, mix and react fluids or to separate/filter, manipulate and detect particles or microorganisms, however, is non-trivial. For a start, the surface area to volume ratio, which scales inversely with respect to the characteristic channel dimension, suggests the dominance of surface forces (such as viscous or capillary stresses, which, in general, tend to retard fluid motion) over body forces (such as inertial, gravitational or centrifugal stresses, which can generally be exploited to induce fluid motion) at very small scales. The resistance to fluid transport in pressure-driven flow scales inversely with the cube of the channel height in a long and wide rectangular microchannel and with the channel radius to the fourth power in a circular tube, typically rendering capillary syringe pumps ineffective for driving fluids in channels under 100 microns. Moreover, the large surface area to volume ratio characteristic of micron scale devices requires proper consideration of interfacial phenomena in their design. For example, microscopic effects such as disjoining pressure and wall shear pose significant design challenges during scale down.

Considerable progress in microfluidic research has been made in the past decade in addressing these challenges as well as those associated with the methods and materials for fabricating these small devices. In the latter, the development of soft lithography in poly(dimethylsiloxane) or PDMS, which is a soft elastomer that is optically transparent and biocompatible, has contributed significantly to the progress (Whitesides, 2006). In the former, there has emerged a large body of literature in which attempts to drive fluidic actuation and particle manipulation through various mechanisms (e.g., capillary, electric, magnetic and acoustic stresses) have been reported (Stone et al., 2004; Squires & Quake, 2005). With advances in micro/nano-fabrication technologies, it is also possible to drive microscale fluid and particle motion using tiny mechanical components, such as microgears and microactuators. Such micromachinery, known as micro-electro-mechanical systems (MEMS) (Ho & Tai, 1998) has not been widely implemented in microdevices due to the complexity, cost, reliability, and wear issues related with the tiny mechanically moving parts.

Fluid actuation via modulation of capillary stresses is mainly useful in open microfluidic systems (such systems are also described by the term digital microfluidics) that involve free drops discretely transported across the surface of the devices (Fig. 2); in contrast, closed microfluidic systems involve the continuous flow of liquids within closed microchannels. These open systems, although not particularly suited for large liquid volumes and continuous flow analysis, allow minimisation of liquid-surface contact, which is essential in systems involving biomolecules since surface adsorption is undesirable in these cases. In addition, open systems also eliminate attenuation of detection signals through channel walls and allow direct access to the samples. The downside of open systems, however, is the likelihood of contamination and evaporation.

The basic principle behind the use of capillary stresses for microfluidic actuation is the alteration of the wettability of the liquid on the substrate surface (Darhuber & Troian, 2005). There are two ways that this can be carried out. First, the surface tension or contact angle can be altered such that a capillary pressure difference is generated which, in turn, gives rise to fluid flow. This can be carried out by either applying a thermal gradient, or an electric field, the latter being known as electrowetting (Mugele & Baret, 2005; Yeo & Chang, 2006). Alternatively, chemical patterning or topological texturing of surfaces on which the liquid drops are placed can also be employed. The second method is to employ spatial gradients in the interfacial tension at a fluid-fluid interface. This gives rise to the so-called Marangoni stresses, inducing fluid flow towards regions of larger interfacial tension. These interfacial tension gradients can be produced by chemical (e.g., the use of surfactants), thermal, optical or electrical gradients. In either method, it has been a general view that with the exception of the use of electric fields, none of the techniques described above has yet to be developed into a practical method for rapid and sufficient manipulation or control of drop transport. Chemical modification of surfaces and interfaces allow for only passive control and could be incompatible with the working fluid. Temperature control, on the other hand, does not allow for sufficient local manipulation precision. Rapid switchability and long term reliability/reproducibility issues have also yet to be addressed.

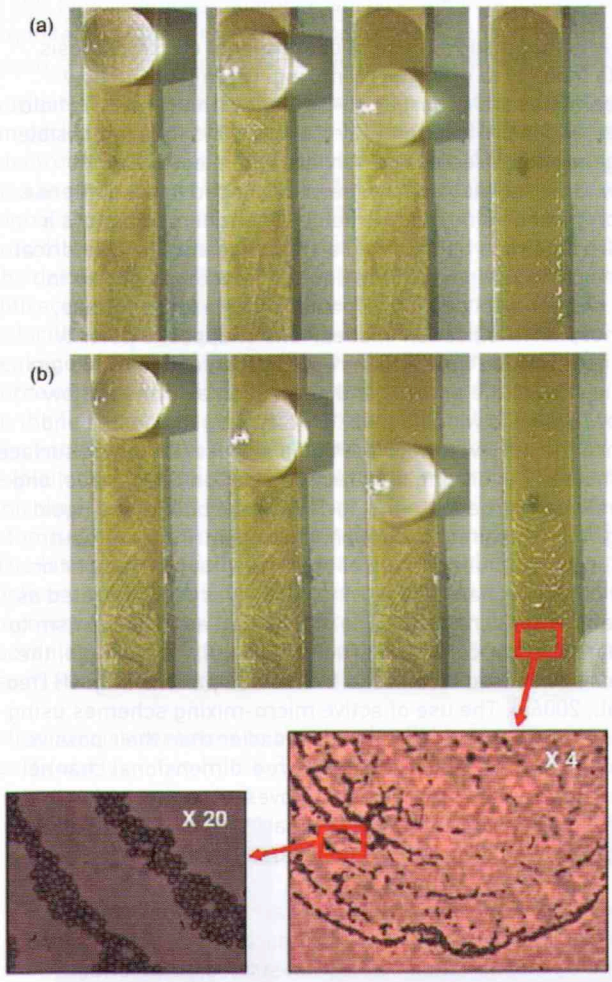


Fig. 2: (a,b) Droplet transport in an open microfluidic system driven by surface acoustic waves (Tan et al., 2007). The 10 microlitre liquid drop travels on a 3.5 mm wide and 17 mm long Teflon® track patterned onto the substrate. In this particular example, pollen particles roughly 20 micron in diameter were deposited on the track prior to the translation of the droplet. As the droplet is swept across the track, it picks up the pollen, thereby constituting an effective microparticle collection mechanism for biosensor sampling. Enlarged images of the particle footprints left behind the droplet are also shown.

To date, electrokinetics, which exploits the use of electric fields, has been the most popular way to induce microscale fluid flow and particle manipulation. There are many advantages of using electric fields, including the ease and low costs associated with the fabrication and incorporation of electrodes on microfluidic chips as well as the ability for precise fluid control and handling.

The underlying principle behind electrokinetic actuation lies in the formation of an electric double layer. When a surface is in contact with an electrolyte solution, i.e., an aqueous or polar solution containing ions, it acquires a net positive or negative charge either due to ionisation or dissociation of its chemical (e.g., carboxylate or silanol) groups, preferential adsorption of the ions in the solution onto it, or by some other surface charging mechanism. In any case, the charged surface attracts oppositely charged ions in the solution towards it and repels like charged ions, thus creating a polarised layer adjacent to it that is rich in counter-ions and lean in co-ions. This polarised layer is known as the electric (or Debye) double layer (Fig. 3a).

If an electric field were applied along the length of the microchannel, for example, the ions in the double layer will be attracted to the electrode with the opposite polarity. The Coulombic force arising from this interaction then induces the fluid in the double layer adjacent to the microchannel surface to flow, thus creating fluid motion known as electroosmotic flow akin to that which would arise if the sidewalls were moving like a conveyer belt dragging the rest of the fluid in the channel along with it (Fig. 3b). In the past 5 years, there has been significant research dedicated to developing electroosmotic micropumps that are efficient and reliable (Laser & Santiago, 2004).

Similarly, electric fields can be applied to move particles in a process known as electrophoresis (Fig. 3c). In fact, capillary electrophoresis, in which the concept was adapted to carry out separations in microanalytical devices during the 1960s, was one of the technologies that led to the emergence of microfluidics. Given its good reproducibility, sensitivity and wide applicability to both small and large molecular separation, capillary electrophoresis is currently a major workhorse in genomics, proteomics and metabolite profiling. Despite its widespread use in analytical chemistry applications, its insensitivity to particle size means that electrophoresis is unable to precisely manipulate particles particularly of nanoscale dimensions (Hughes, 2000).

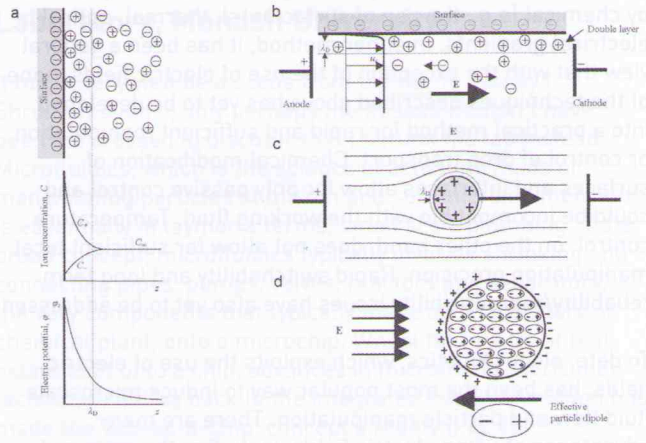


Fig. 3: (a) Schematic illustration of an electric double layer that arises when a surface is in contact with an electrolyte solution. The surface acquires charge (in this case, a negative charge) and hence attracts oppositely charged (in this case, positively charged) ions thus forming a polarised layer of thickness λ_D that is rich in counter-ions and lean in co-ions as seen in the sketch of the concentration profile below. There is also an increase in the electric potential close to the surface, as shown by the sketch of the potential distribution. (b) Principle of electroosmotic flow. Upon applying an electric field at two ends of a channel, the counter-ions (positively charged ions in this case) in the double layer are attracted to the electrode of opposite polarity, causing a net motion of the fluid in the double layer. This gives rise to a slip velocity at the walls which drags the rest of the fluid in the microchannel with it. For simplicity, only half the microchannel is shown. (c) Principle of electrophoresis. A particle immersed in an electrolyte solution acquires a charge (positive in this example) on its surface which leads to the formation of a double layer of negative charge around it. Upon applying an electric field, the ions in the double layer are attracted to the electrode of opposite polarity, thus generating a force on the particle in the opposite direction. (d) Principle of dielectrophoresis. A dielectric particle suspended in a dielectric medium upon application of an electric field develops an interfacial charge due to the difference in the electric permittivities between the particle and the medium, giving rise to an effective induced particle dipole. Applying a non-uniform electric field then produces a net force on the particle.

Alternative techniques such as dielectrophoresis and electrorotation, which rely on the effect of non-uniform electric fields to generate a net force on a dielectric particle suspended in a dielectric medium, are thus employed (Pohl, 1978; Jones, 2002). Such forces arise due to the net dipole induced on the particle due to the difference in electric permittivities between the particle and its surrounding medium (Fig. 3d).

An example of a microfluidic device that continuously sorts and detects different pathogenic species in a tiny fluid sample is shown in Fig. 1 (Cheng et al., 2007). Using a variety of three-dimensional electrode architectures, various sample/particle processing stages can be integrated onto the chip. Parallel arrays of planar electrodes are first employed to filter the sample in order to remove unwanted debris particulates. The remaining particles distributed throughout the channel width are subsequently focused using planar and interdigitated electrodes into a single line trajectory at the centre of the channel. Once the particles are aligned along the centre they are sorted by three-dimensional gate electrodes by deflecting particles of similar characteristics into the various bins where they are then trapped and concentrated using a variety of electrode shapes. In each stage, dielectrophoretic separation is employed for filtering, focusing, sorting and trapping the particles based on their size/shape and dielectric properties (electrical permittivity and conductivity) as well as that of the medium. Consequently, live and dead pathogens of different species can be filtered and sorted using dielectrophoresis, and finally differentiated using surface enhanced Raman spectroscopy.

A particular disadvantage of conventional electroosmosis is its inability to drive micro-mixing. Given that the flow streamlines are generally co-incident with the electric field lines, which are inherently irrotational, it is thus impossible to generate closed mixing vortices with electroosmotic flow. Other strategies have been developed to drive intense micromixing using electric fields. One scheme employs a sharp electrode tip mounted a small gap above a cylindrical microchamber in which the liquid is housed, as shown in Fig. 4a (Yeo et al., 2006b). Upon applying a large voltage, atmospheric ionisation ensues. Ions of opposite polarity to the electrode tip are then repelled, colliding into the air molecules in the process and generating a strong airflow known as ionic wind (Fig. 4b). By directing the needle and hence the airflow toward the liquid surface, the liquid surface is sheared generating fluid recirculation on the surface, and consequently, beneath the surface in the bulk of the liquid (Fig. 4c). This first concept of a microcentrifuge, without requiring the bulk rotation of the entire fluidic chamber or any other mechanically moving parts, was demonstrated as an effective micro-mixer (Fig. 4d) as well as a mechanism to separate or concentrate particles (Fig. 4e), for example, the separation of red blood cells from blood plasma (Fig. 4f) (Yeo et al., 2006a). The use of active micro-mixing schemes using electric fields are generally much easier than their passive counterparts, in which complex three-dimensional channel structures such as bends and grooves are patterned onto the microchannel to disrupt the laminarity of the flow (Ottino & Wiggins, 2004; Nguyen & Wu, 2005).

The 0.1 – 1 mm/s linear velocities achieved using electrokinetic devices, whilst comparatively fast with respect to the other microfluidic actuation strategies described above, nevertheless pale in comparison with acoustically driven microfluidics, which are typically one to two orders of magnitude quicker than the fastest electrokinetic devices due to the large sound velocities in liquids. For example, the same micro-mixing and particle concentration in Figs. 4d and 4e, which typically require one to several minutes, can be carried out in under 1 second using surface acoustic wave (SAW) devices (Fig. 5a) (Li et al., 2007a).

A SAW is essentially a 10 nm amplitude electroacoustic analogue of an earthquake wave that propagates along the

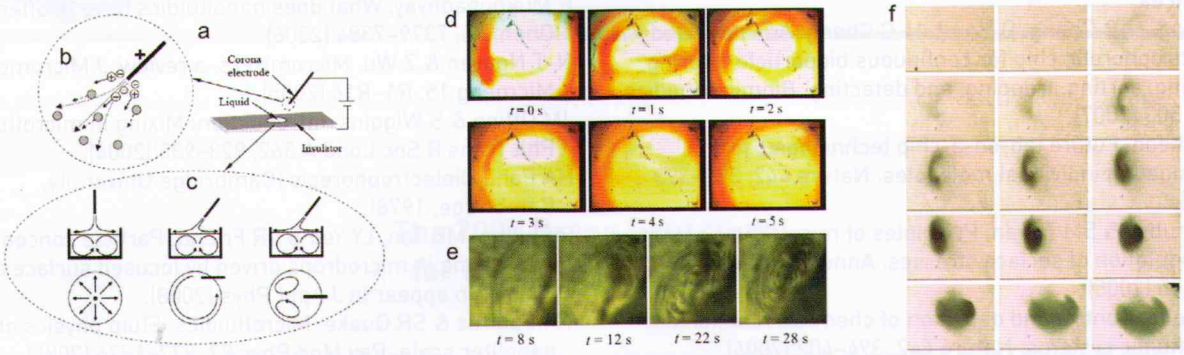
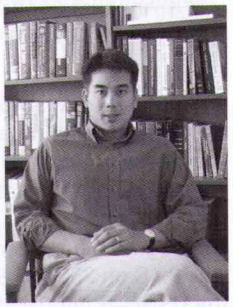


Fig. 4: (a) Schematic depiction of an electrohydrodynamically-driven microcentrifuge (Yeo et al., 2006b). (b) When a large voltage is applied across a sharp electrode tip (corona electrode), the air around it ionises. Oppositely charged ions (in this case, the negative ions) are repelled away from the electrode tip colliding into the air molecules and generating a bulk air thrust known as ionic wind. (c) By directing the electrode tip and hence the airflow at the surface of the liquid contained in a 5 mm diameter and 3 mm high cylindrical chamber, surface and bulk liquid recirculation patterns are observed. The surface recirculatory flows are exploited for (d) micro-mixing, and, (e) particle concentration. The bulk recirculatory flows are demonstrated for separating red blood cells from blood plasma, which was achieved in about 5 minutes (Yeo et al., 2006a).

surface of a piezoelectric substrate, generated by applying an oscillating electrical signal to the interdigital transducer electrodes patterned onto the substrate (Fig. 5b). SAW has been employed for decades for telecommunication signal processing and filtering. The ability for SAW to drive microfluidics, however, lies in the fluid-structural coupling of the device – the SAW which propagates along the substrate diffracts into the liquid due to the mismatch in the sound velocities in the liquid and in the substrate (Fig. 5c). This leakage of acoustic energy into the fluid generates a body force on the liquid and drives strong inertial recirculation in the fluid known as acoustic streaming (Li et al., 2007b). Recent studies have demonstrated that this can be exploited for fast microfluidic droplet transport (Fig. 2) and micropumping (Tan et al., 2007) as well as for rapid liquid atomisation and nanoparticle synthesis (Friend et al., 2008). The latter is potentially useful for portable pulmonary drug delivery applications; given that it is a rapid bulk atomisation technique, its ability for high throughput is a significant advantage over other point or nozzle atomisation techniques such as electrospraying (Yeo et al., 2004).

Microfluidics continues to be an active field of research, particularly on two fronts. There are continuing efforts to develop more effective mechanisms to drive fluid motion and particle manipulation. Efforts are also being undertaken to integrate these mechanisms for the development of on-chip mechanisms for a host of applications. However, few are simply contented to stop there – a growing number of microfluidics researchers are now exploring even smaller systems. Nanofluidics, which is the study of fluid mechanics in systems with dimensions under 100 nm, not only offers new insights due to the different physicochemical phenomena that arise as a result of molecular interactions but also presents many novel possibilities such as single cell manipulation and single-molecule DNA sequencing (Mukhopadhyay, 2006). Now, we're really getting into the small matters indeed... References over page....



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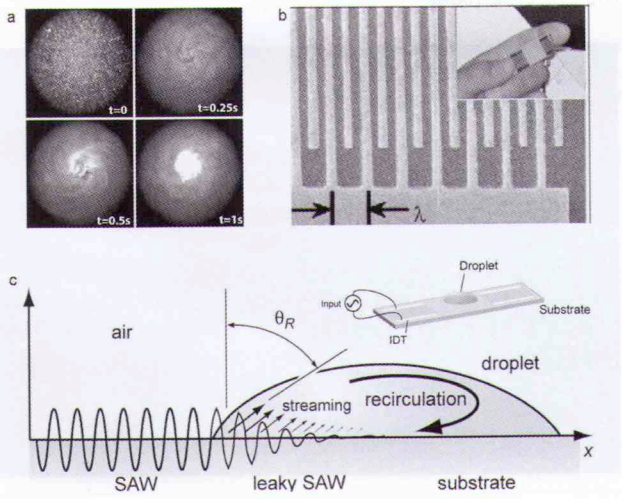

Fig. 5: Surface acoustic wave (SAW) microfluidics. (a) Rapid concentration of fluorescent 500 nm particles in under 1 second using focussed surface acoustic microfluidics (Shilton et al., 2008). (b) Interdigital transducer electrodes patterned via standard photolithography onto a piezoelectric substrate used to generate the SAW. The width and spacing of the electrodes λ determines the wavelength of the SAW; in this case, $\lambda \approx 200$ microns. (c) Leakage of the SAW into a fluid droplet placed on the piezoelectric substrate due to the difference in sound velocities between the phases. As a consequence, a body force is imparted onto the droplet which drives liquid recirculation within the droplet known as acoustic streaming. It is this fluid-structure interaction that enables SAWs to drive microfluidic actuation.

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Macedon Ranges Observatory discovers nova

According to AAVSO Special Notice #105 released on April 19, another possible nova event occurred in Sagittarius. Through their quick actions, Macedon Ranges Observatory in Central Victoria, Australia was on top of the alert and imaging.

No magnitude is given, but the original discovery magnitude was 8.4C on 20080418. No star close to this position is seen in the USNO-B nor 2MASS catalogs. Kato (VSNET-ALERT 10075) indicates that this new outbursting object has a pre-discovery observation by ASAS but was not visible 3 days earlier.

The quick acting staff at MRO immediately went to work imaging the area and comparing their results to the sky survey plates. The results are clear... Yet another new nova had been discovered.

Says Observatory Director Bert Candusio: "This was as exciting as the first Alert exercise done by the MRO only a few days ago. Although MRO tried to get the observation to the AASVO, we decided to supply the images to Universe Today so the general public could get the first glimpses of this exciting new object."

Once the coordinates were in place, Joe Brimacombe immediately set to work with a 12.5" Ritchey Chretien Optical Systems telescope and began imaging the target area with a STL 6303 CCD camera. Within 90 minutes the images were processed and the painstaking process of comparison began. By isolating certain star patterns within the area, the nova event was quickly confirmed.

The Universe Today