Electronic Supplementary Material (ESI) for Lab on a Chip.

SUPPLEMENTARY MATERIAL

Droplet Control Technologies for Microfluidic High Throughput Screening (μHTS)

Capillary Number

Between two immiscible fluids, interfacial tension, γ, defines the dynamics of the free surfaces and it plays an important role in two phase microfluidics. Interfacial tension acts to minimise the total surface area of an interface. In the absence of confinements, the minimum surface area is achieved by forming spheres, the shape of droplets in sufficiently big channels. A key parameter is the Capillary number which defines the balance of viscous forces to interfacial forces and it's given as:

$$Ca = \frac{\mu_{max} u}{\gamma} = \frac{viscous}{interfacial} \tag{1}$$

where μ_{max} is the viscosity of the more viscous fluid amongst the two immiscible phases and u is flow velocity. Capillary number plays an important role, especially in the formation and fusion of droplets.

Microvalve

A method that does not directly affect the droplets but rather disrupts the flow at a specific location has been developed with the use of thin membranes, referred to as microvalves. Valves date back to early civilisations such as Egyptians and Romans; they are fundamental components found in macrofluidics, the on-off switches that regulate the flow within vast networks. Early efforts to replicate this technology, on-chip, used Silicon Nitride Si_3N_4 as membrane material [1], however, soft lithography provided an easier alternative for fabrication of membranes for microfluidic systems[2]. Although it was later shown that such a membrane could be incorporated into a single layer chip offering simpler microfabrication[3], double layer designs are commonly preferred because their fabrication is not too arduous and they allow complex designs[4,5].

A double layer microfluidic chip usually consists of a gas layer and a liquid layer. Once there's an area where the two layers meet, a thin polydimethylsiloxane (PDMS) membrane is formed. By rapidly switching the pressure in the gas layer, usually controlled by solenoid valves and pneumatic pumps, the flow in the fluid layer could be manipulated. When the pressure in the gas layer is increased, the membrane deforms inward and plugs the fluidic channel (Fig. 1(a)). In other cases, when the gas layer pressure is similar to that of the fluidic layer, the flow is not disrupted (Fig. 1(b)), however, some studies have shown that a negative pressure could be applied to the gas layer for creating a suction effect[6] (Fig. 1(c)). Moreover, the membrane could be fluctuated to promote mixing within droplets[5].

Surface Acoustic Waves

SAWs are nm-scale amplitude acoustic waves that propagate at MHz frequencies on the near surface of piezoelectric substrates. They can be generated by actuation of electrode pairs de-

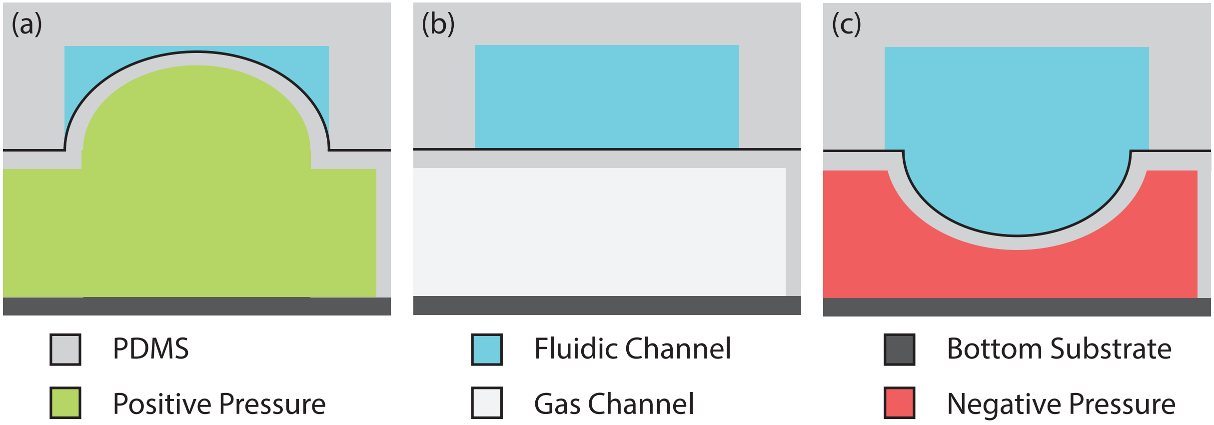

Figure 1: Cross sectional view of a representative microfluidic chip demonstrating microvalve working mechanism. (a) The membrane deforms outward and blocks the flow in the fluidic layer when positive pressure is applied. (b) The membrane is at rest when the pressure is neutral in the gas layer and (c) the membrane deforms inward creating suction when negative pressure is applied.

posited on piezoelectric substrate with constant spacing, often referred to as inter-digital transducers (IDTs) (Fig. 2). When a signal with matching frequency is applied across the electrode pairs, an electric field coupled to the piezoelectric material is produced which gives rise to SAWs. The resonant frequency of the IDTs, f, can be determined by using distance between each transducer pair, λ, (Fig. 2) and the speed of sound in the piezoelectric substrate, c_s:

$$f = c_s/\lambda \tag{2}$$

SAWs are classified as Rayleigh waves which do not penetrate deep into the substrate so they do not attenuate much in the absence of other substrates or liquids. Therefore they travel efficiently and easily couple into the fluids within microfluidic channels and transfer momentum to them (Fig. 2). This leads to interesting phenomena; to name a few relevant to the content of this review: acoustic streaming, acoustic radiation forces (ARF) and interface deformation.

SAWs refract upon contact with the fluid due to mismatch of sound speed in the media and they decay rapidly; often referred to as leaky SAW (Fig. 2). Due to the complexity of wave propagation and attenuation, there are spatial variations in the alternating pressure fields produced in the fluid, and non-linear effects mean forces are exerted on the fluid body which give rise to fluid flows, or acoustic streaming. In contrast, acoustic radiation force (ARF) only occurs when there are particles or droplets suspended in the fluid and act to displace them. Finally, in this context, another important phenomenon arises when an acoustic wave interacts with a fluid-fluid interface. If there's an acoustic impedance mismatch between the fluids that form the interface, a net radiation force is observed[7,8], this can be used to deform the interface towards or away from the incident wave depending on the properties of the fluids[9]. SAWs, in general, exhibit lower acoustic energy losses and power consumption, and, as such, are highly suitable for microfluidic actuation. Acoustic droplet actuation methods are compatible with integration into a lab-on-a-chip (LOC) devices and they do not involve any moving parts. Moreover, SAWs could be controlled accurately and easily with basic programming.

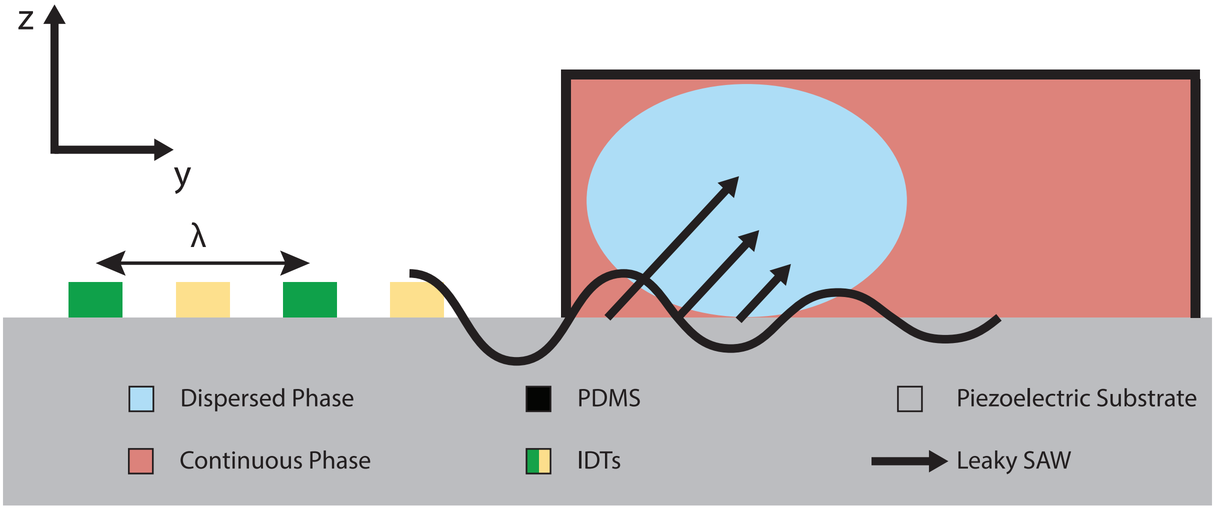

Figure 2: Surface acoustic waves generated by IDTs travel on piezoelectric substrate and couple into the fluid giving rise to pressure waves. SAWs can be used to manipulate droplets on demand.

Dielectric Heating

A dielectric material with a high electrical resistivity [10] has the potential to absorb electromagnetic (EM) energy when subjected to a time-varying electric field. The absorbed EM energy is uniformly converted to heat in this process called dielectric heating. Dielectric heating is the result of periodic molecular rotation where induced and intrinsic dipole moments in the material constantly (try to) align with the electric field [11]. Their ability to do so is quantified by the loss tangent, tan δ, of a material; in that case, the heat flux due to dipole heating, $\vec{q}_{DH}$ is given by: [12]

$$\vec{q}_{DH} = \omega |\vec{E}|^2 \varepsilon_r \varepsilon_0 \tan\delta h_s \tag{3}$$

where ω is the angular frequency, E is the electric field strength, h_s is the height of the material and ε_r, ε_0 are the relative permittivity of the material and free space, respectively.

Electric Fields

DC electric fields can be used to attract or repel droplets, however, the resulting body force is minuscule if the droplets do not carry a charge. For this reason, researchers have attempted to pre-charge droplets where one example shows that if an anode and a cathode are placed oppositely at a droplet splitting junction, the daughter droplets get charged up [13,14]. The charged droplets can then be significantly influenced by DC electric fields where they move towards the opposite charge while moving away from the same charge (Fig. 3(a)), this is referred to as electrophoresis [15].

The droplet charging step may not be ideal for a number of studies where charging a droplet might be harmful for droplet content, in such cases dielectrophoresis (DEP) can be preferred. When a droplet is subjected to an AC electric field, dipoles are created and they interact with the gradient of the electric field [15] (Fig 3(b)). This gives rise to DEP force, $\mathbf{F_{DEP}}$, a type of body force, given as:

$$\mathbf{F_{DEP}} = 2\pi\varepsilon_1 Re|\underline{K}(\omega)|r^3\nabla\mathbf{E}^2 \tag{4}$$

where ε_1 is the dielectric permittivity of the continuous media, $Re|\underline{K}(\omega)|$ is the real part of the Clausius-Mossotti function, $K(w)$, r is the droplet radius and $\mathbf{E}$ is electric field. It is important to note here that the attraction or repulsion depends on the sign of the real part of the Clausius-Mossotti function which almost always works to pull towards the high intensity region in the case of droplets. They could, however, push or pull depending on the AC frequency in the case of particles which are not covered in this review.

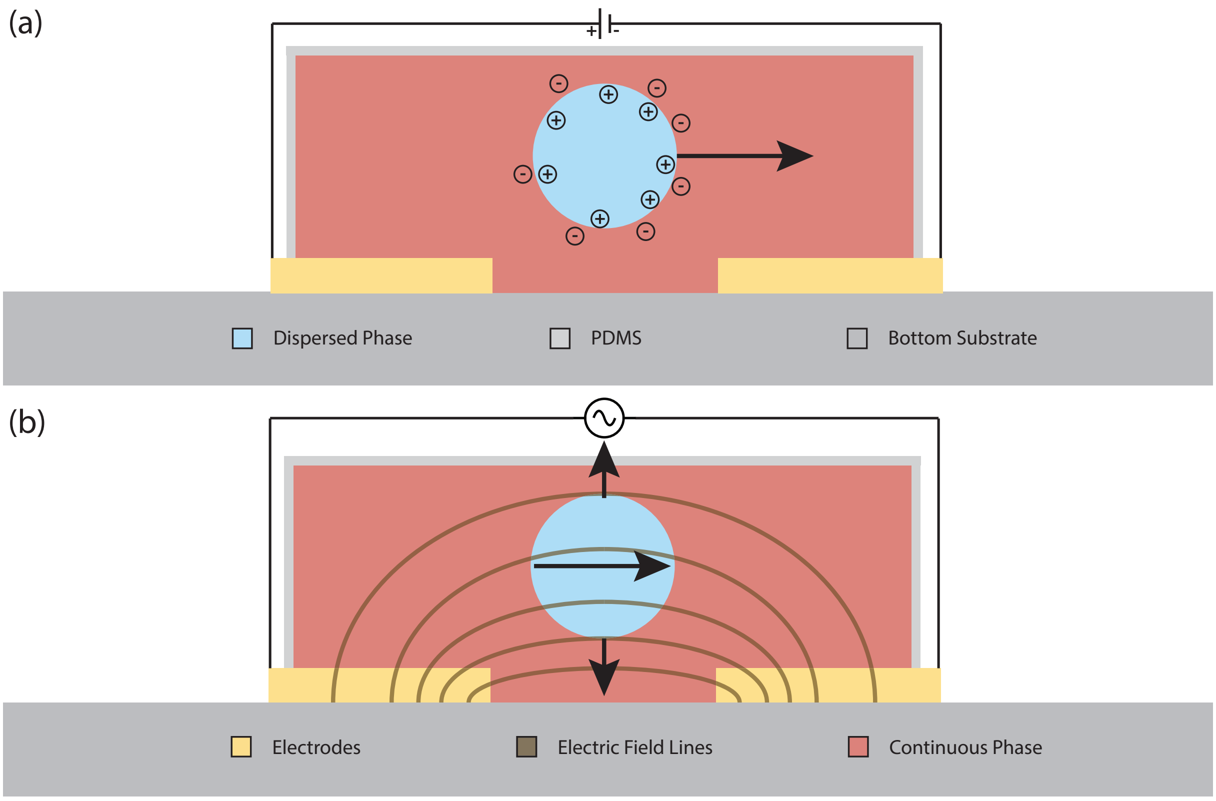

Figure 3: (a) Electrophoresis: Charged droplets migrate towards the electrode they are attracted to in a DC field. (b) Dielectrophoresis: Higher AC field intensity attracts droplets.

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