Chapter

Microfluidic Devices: Applications and Role of Surface Wettability in Its Fabrication

Shivanjali Saxena and Rakesh Joshi

Abstract

Microfluidic devices are based upon the behavior of fluids at the microenvironment level. They offer innumerable applications in the field of science and technology. Their scope is not limited to single field and now have applications in various fields such as biomedical, energy, chemicals and environment as well. Their major advantages are low experiment to cost ratio, and fast response time. Surface wettability is one of the factors contributing to the working of microfluidic devices. Surface wettability measurement is a very critical technique to measure the flow of micro fluids in microfluidic applications. In microfluidic devices the detection of small volume change with change in fluid properties is very minor because of the micrometer range. In order to detect this small change in micrometer range, an *in situ* wetting measurement is required. In this chapter, we have discussed about types of taxis, microfluidic devices: an application of taxis, microfluidic applications and role of surface wettability in microfluidic devices.

Keywords: microfluidic, devices, surface wettability, lab-on-chip, applications, biomedical

1. Introduction

The era of microfluidics started in 1980s with the development of silicon etching procedures which were made for microelectronics industry. This paved way for manufacturing of first of its kind devices called Micro Electro Mechanical Systems (MEMS). In these devices mechanical microelements were integrated together on a silicon wafer. In the 1990s, researchers explored applications of these devices in the field of biology, chemistry and biomedical. They used these devices for controlling liquid's movement in micro channels which paved way for microfluidics. Laboratories on chip were developed for incorporating all the major procedures of biology, chemistry or biomedical on single platform. But, this use to come with huge cost and infrastructure for microelectronics industry. In 2000s a new era of microfluidics was started with the development of molding micro channels in polymers. This lead to decrease in cost as well as manufacturing time that caused the boom in the area of microfluidics and motivated researchers of all fields to work using them [1]. In the era of fast pacing science, microfluidic are devices to enhance pace of research and decrease the experimental cost. They run on principle of various types of taxis, majorly chemotaxis. Taxis is the

movement of particles according to some external guiding agent. This agent can be heat, oxygen, pressure, electric field or chemical, etc. Various types of taxis, their applications and microfluidics are discussed in this chapter. Microfluidic is the technology where movement of the particles is on the basis of microenvironment consisting of viscosity, surface tension and pressure. In microfluidics, micro channels are molded or etched over the silicon, glass or various polymer materials such as PolyDimethylSiloxane. These types of devices are vastly being used in all the fields of research, diagnostics and therapeutics. In microfluidics, the micro channels are formed to attain the desired result which can consist of: mixing, sorting, pumping or controlling the biochemical microenvironment. They have the advantage of decreasing the response time and experimental consumables and overall cost. They have the potential to perform large scale experimentation in small scale. Important factors to be considered for fabrication of microfluidic devices are temperature resistance, superior optical transparency of the material, high hardness, excellent electrical isolation, thermal stability, chemical inertness to many fluids, biocompatibility, and surface wettability. The performance of microfluidic device depends majorly upon etched or molded micro channel's surface properties. Therefore surface modification is an important factor to improve overall performance of microfluidic devices. Surface roughness, surface heterogeneity and solution impurity are the key parameter which affects the wettability of microfluidic device.

2. Introduction to taxis

Molecules are always in motion irrespective of their state. Molecules in solid state have least freedom while in gaseous state have maximum freedom. Freedom of movement of molecules in liquid phase lies between molecules in solid and gaseous phases. Heat and temperature are factors that affect the movement of molecules. Enhance temperature increases the translational movement of molecules. Movement of molecules can be random or directed towards certain stimuli. Random movement is termed as "kinesis" while directed movement towards certain stimuli is termed is "taxis". For taxis, there is sensory component to detect the attractant and motor component to enable the movement towards the stimuli [2]. Taxis are classified on the basis of the stimulus into various categories.

3. Types of taxis

3.1 Aerotaxis

Aerotaxis is the movement of molecules where oxygen acts as stimulant [3]. It has been observed in bacteria and other microorganisms. Active movement of cells is observed along the gradient of oxygen. Aerotaxis plays role in cell survival as optimal concentration of oxygen is required for cell metabolism and growth [4].

3.2 Anemotaxis

Anemotaxis is the movement towards wind. It is observed in drosophila and some terrestrial mammals such as rats which tend to follow the wind. Drosophilla has been observed to move against the air current [5]. Rats were also observed to follow anemotaxis as air current carries information regarding location and odor content [6].

3.3 Barotaxis

Barotaxis is the movement towards stimulus that is pressure. Movement due to hydraulic resistance (resistance to flow as a result of liquid) is also termed as barotaxis. This type of movement is observed in the neutrophils, a type of immune cell. Neutrophils follows path of least hydraulic resistance.

3.4 Chemotaxis

Chemotaxis can be defined as the movement of cells towards the higher chemical concentration gradient [7]. It is directional locomotion of cells and was first described in the bracken fern spermatozoa in 1884 by Pfeffer. Later in 1888, this phenomenon was described by Leber in mammalian leukocytes in response to an injury. Chemotaxis is an important process required for the growth and development of multicellular organism, immune response and cancer metastasis [8].

3.5 Durotaxis

Durotaxis is the movement of cells towards more rigid gradient which is a result of variation in the structural property of the extracellular matrix. This type of motion implies movement towards more stiffness [9]. This type of motion has been observed in various cell types such as human fibroblast cells, mesenchymal cells and cancer cells. Substrate rigidity is the stimulus that initiates the movement in durotaxis [10].

3.6 Electrotaxis/galvanotaxis

Electrotaxis is also termed as galvanotaxis and implies movement guided through electric field or current [11]. Living cells have the tendency to sense and follow direct current electric field. This type of movement is observed in both *in vitro* and *in vivo* conditions although the mechanism behind sensing of electric field by cells remains unclear [11]. Its applications are observed in wound healing and development. Disruption of an epithelial layer in wound leads to generation of an endogenous electric field which guides migration of cells towards the wound for regeneration [12].

3.7 Gravitaxis

Gravitaxis is characterized by directional movement in response to gravity [13]. This type of movement is observed in the motile microorganisms such as euglena where gravity acts as stimulus to select their niche in environment. It can be both positive and negative. Positive gravitaxis implies movement towards water while negative gravitaxis implies movements towards the surface [14]. This type of motion is observed in *Drosophila melanogaster* and around 18 genes have been identified that mediate this gravitational motion in them [15]. To elucidate the mechanism of this type of motion, asymmetric self-propelled particles were studied for this motion. It was observed that shape anisotropy alone is sufficient to induce such type of motion [16].

3.8 Hydrotaxis

Moisture acts as stimulus in hydrotaxis. Movement of cells, animals or plants towards more moisture is termed as positive hydrotaxis and towards less moisture

is termed as negative hydrotaxis. Hydrotaxis is observed in the *C. elegans* as they move towards their preferred water content for mating, geographical distribution and reproduction [17]. It is also observed in the cyanobacterium in desert crusts. Cyanobacteria colonies are observed 1.5–2.0 mm deep into the desert crust but when crust surface is saturated with water, cyanobacterium moves towards the surface having higher moisture content [18].

3.9 Magnetotaxis

Magnetotaxis is the movement due to magnetic field. This type of movement is a character of diverse group of gram-negative bacteria that perform their orientation and coordination movements according to earth's magnetic field [19]. They are majorly aquatic and swim along the geomagnetic field lines. These types of bacteria are also termed as magnetotactic bacteria [20]. Supramolecular adaptive nanomotors have been developed that exhibit magnetotactic behavior and their guided motion is observed in the tissue model [21].

3.10 Phototaxis

Phototaxis is the movement towards or away from the light source. This type of movement is characteristic of phototrophic organisms and is also observed in plants. Prokaryotes use type-I sensory rhodopsin photoreceptors for phototaxis and it allows them movement towards steep light gradient. Cyanobacteria can also perform phototaxis but they also can perform it in two-dimension only through gliding on the surface. Eukaryotes have the ability to navigate through light vector in three-dimension in open water [22].

3.11 Rheotaxis

Rheotaxis is the movement in response to water or air current. This type of motion is observed in aquatic animals where their movement occurs in response to water current [23]. When movement is towards oncoming water current, it is termed as positive rheotaxis while movement opposite of oncoming water current is termed negative rheotaxis [24]. This type of motion is observed in zebrafish, Crustaceans and American lobsters [25].

3.12 Thermotaxis

Thermotaxis is the movement towards or away from temperature gradient. In this motion, organism move towards temperature source. Slime molds and nematodes are known to move along shallow temperature gradient [26, 27]. Mammalian sperm is also observed to perform theromtaxis to reach towards the oviduct in the female body [28].

4. Microfluidic devices: an application of Chemotaxis

Microfluidics is the technology based upon behavior of fluids in the microenvironment. Fluids tend to behave very differently in micrometric scale as compared to macro scale. These characteristics of fluids are now been used for various studies based upon taxis. In macroscopic system, pressure, volume and temperature are the key players whereas viscosity, surface tension, high shear rate and geometric effects (high surface to volume ratios, constriction, and bifurcation) are the key drivers

of the microfluidic system [29]. Microfluidics is the integration of fluids physically restricted to sub-millimeter dimensions with micro/nanostructures and devices [30]. Microfluidics is an emerging interdisciplinary field consisting of engineering, physics, chemistry, microtechnology, biotechnology and material sciences [31]. The reason for its emergence is miniaturization of operational unit in the microfluidic devices. Miniaturization is preferred as all operations can be packed in small form that can be automated and is portable [32]. Low amount of materials and chemicals are required for development and samples required is also less. Automation enables widespread use of the system without any special training requirements. Easy disposals, low cost, reduction of cross-contamination and fast response time are other benefits of the microfluidic system [33].

The global size of microfluidic devices was USD 13.5 billion in 2019 and is supposed to have a compound annual growth rate of 11.3%. The large market size is due to its multi-application and ease of usability. Basic layout of microfluidic devices consist of incorporated fluid channels in at least one direction. These channels provide high surface to volume ratio which is useful in applications such as biochemical analysis, antimicrobial susceptibility test and heat exchange modules. This field started with applications in chromatography and electrophoresis [34]. With time it has evolve and currently it has vast applications due to development of new fabrication materials and technologies [31]. Its applications include environmental sensing, biomedical applications, drug discovery, drug delivery, micro scale energy systems, artificial organs, micro scale chemical testing and production, micro propulsion, combinatorial synthesis and assays. These applications have been classified under broad categories for discussion in this chapter.

4.1 Biomedical applications

Microfluidics can be used in biomedical field as analytical arrays, gradients, separators, microdiluters, gel structures, droplets, painting cells and devices [35]. In arrays, a set of multiple microchannels is used to study the relationship between different cells with proteins or chemicals within a combinatorial system. This type of system can be used for detection of specific proteins in large number of samples, antibiotic resistance testing, etc. Microfluidics can be used for generation of very steep gradients that cannot be created using other macro techniques [35]. These gradients are useful in the study of macromolecules and cells in response to their varying environment. Biochemical gradients are useful in dictating physiological processes such as proliferation, differentiation and migration. These gradients play an important role in tissue generation as well. They are used for organ on chip techniques also. Phil et al. used drug gradients for activity measurement over CHO cells [36]. Migration and behavior of neutrophils according to protein gradient has also been studied [37]. Chung et al. used growth factor gradient to study the differentiation of human neural stem cells [38].

Microfluidics can be used as diluters where solution is passed through series of controlled dilutions to be used in a specific assay. Ainla et al. have shown use of pulse width flow modulation based designing of microdiluter [39]. They used this microfluidic diluter for analyzing the effect of Ca(2+) concentration over phospholipid bilayer spread onto a SiO2 surface. Microdiluters can also be used as immunoassays for detection of multiple antigens at a same time [40]. Microfluidics can be used in conjunction with gels or microchannels can be made in gels using soft lithography technique. Various types of gels in which microfluidic can be fabricated are agarose, agar and calcium alginate. These types of systems can be used to study complex microenvironment of cells. Takeuchi et al. used microchannels fabricated in agarose to grow *Escherichia coli* in presence of various molecules that can alter

their phenotype [41]. Cabodi et al. used alginate based microchannels for study of mass transfer in channels [42]. Complex Microfluidic systems are now being highly researched and commercialized to develop point of care/lab-on-chip (LOC) devices and organ on chip. These devices have high potential as they can provide the customer with the easy of usability, less sample requirement, time and cost efficiency.

Point of care devices are diagnostic measures that are directly used by patients and without requirement of medical staff. A simple paper based microfluidic that can be used as point of care device are known as lateral flow test (LFT). Porous material such as glass fiber, nitrocellulose and cellulose paper can be used for fabrication of LFT. The components on microfluidic LFT device are sample collection pad, a dried conjugate pad followed by a reaction area and an absorbent wicking pad. This is incorporated within a plastic housing and plastic barriers throughout to maintain one dimensional flow. The best example of LFT is dipstick pregnancy test kit. This test works on the principle of an immunoassay. Sample which is urine is applied to the sample pad and rehydrates the goldnanoparticles conjugated detection antibodies [43]. These rehydrates antibodies bind to the target antigen present in the sample. Together they flow to the capture region which consists of control and test line. At the test line, non-labeled antibodies specific for the detection antigen are immobilized. When rehydrated labeled antibodies conjugated with the sample antigen reaches test line, it binds to the non-labeled antibodies specific for that same antigen. This interaction gives visual color change thereby making test line visible in case of positive results. This process is depicted through **Figure 1a** and **b**. The wicking pad in the device performs function of attracting the sample through LFT. After reaction membrane is completely wetted, the capture region functions through capillary action.

Paper microfluidics has also been used to provide point of care diagnostics for non-communicable diseases such as cardiovascular disease and cancer. In this

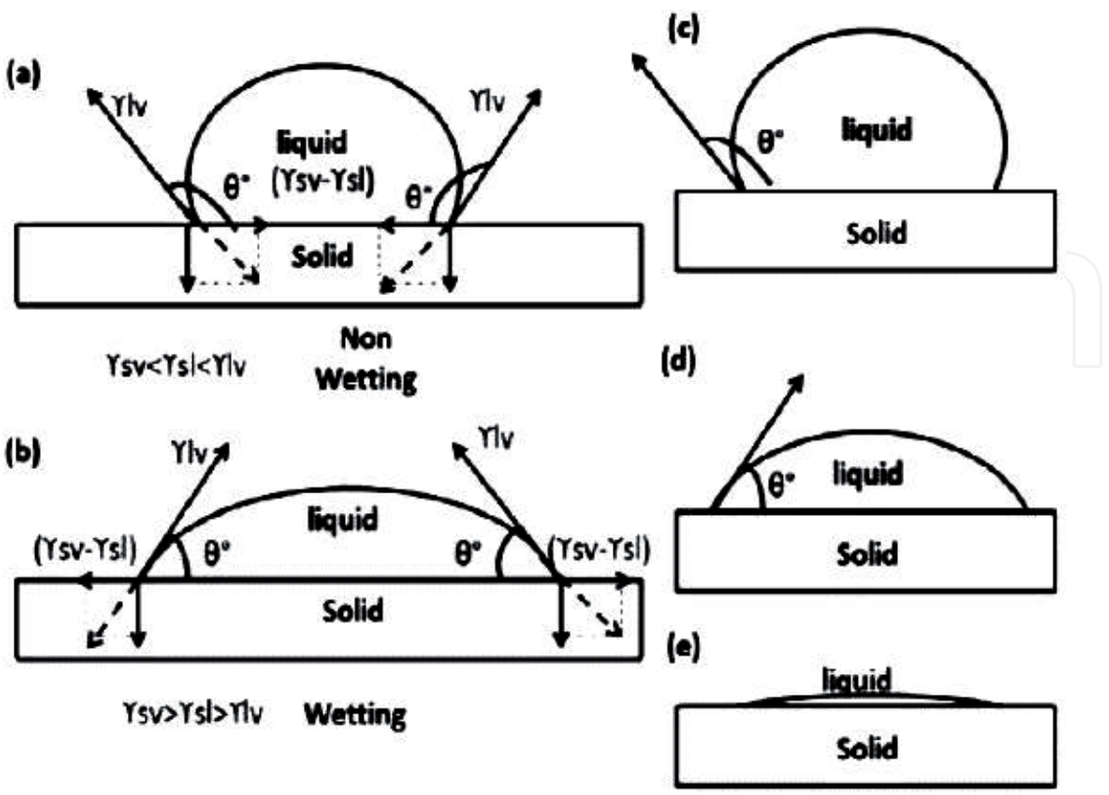

Figure 1.
(a) Non-wetting phenomenon, (b) wetting phenomenon, (c) larger contact angle (non wetting), (d) wetting, (e) angle close to zero complete (wetting).

work, synthetic urinary biomarker is used which is detected through paper microfluidics [44]. These types of devices are also being used for saliva based detection of oral diseases. In the research work by Amy et al. point of care diagnostic device for oral diseased was developed using monolithic disposable cartridge. It was designed in a compact analytical device. This device combined sample pre-treatment procedure of filtering, enrichment and mixing of sample with electrophoretic immunoassays. It can efficiently and quickly measure analyte concentration in the minimally treated and very low volume (20 μl) of saliva sample [45]. Microfluidic devices are also used for digital polymerase chain reaction (PCR) which is a very powerful gene expression analytical tool. Christina et al. showed use of microfluidic based digital PCR for prenatal detection of fetal aneuploidy. Fetal Aneuploidy is the presence of an abnormal number of chromosomes (structures that contain genetic information) in the fetus [46].

Organ on chip is the new class of laboratory models that have advantages of both *in vivo* and *in vitro* models. These chips are microfluidic devices in which tissue of interest is cultured in the favorable microenvironment simulating the actual physiological conditions efficiently. These types of devices can also be used in the field of personalized medicine. For personalized medicine, cells from specific donor patients and healthy patients can be studied under the same environment. Various examples of such devices are lung on a chip [47], atherosclerosis on a chip that made study of physiological functions of an organ and its response to various stimuli feasible [48]. Other examples are bacteria inhabited gut on a chip [49] and blood brain barrier on a chip [50]. This field of organ on chip is emerging rapidly and showcasing various organs' culture and their physiological microenvironment simulation on these microfluidic chips.

4.2 Energy applications

The development in the field of integrated microfluidics was successfully laid by its incorporation with the optical elements such as plasmonic surfaces [51] and waveguides [52]. In 2000s, the development of liquid-crystal switchable gratings, microfluidically tunable photonic crystal fibers and bubble switch laid the foundation of using microfluidics as an essential part of the photonic devices. During mid-2000s a new field of "optofluidics" was evolved from the existing technologies in the field of photonics and microfluidics. Using microchannels and photonic elements, optofluidics has the strength of having precise control over light and fluidics at small scale [53]. Microfluidic systems are being used for development of photocatalytic microreactor. A planar microfluidic reactor was developed by Lei et al. It consisted of the small planar chamber where two TiO2 coated slides were used as top cover and bottom substrate. Microstructured UV-cured NOA81 layer was used as the sealant and flow input/output. This reactor has advantages of microfluidics such as easy control of flow, rapid fabrication and large surface/volume ratio. It is the key to more efficient photocatalytic water treatment [54]. TiO2 based microreactor has been developed by Matic et al. for photocatalytic applications. This system was fabricated on metal-titanium foil. Titania nanotubes were mechanically engraved in the substrate foil. Using anodization & hydrothermal treatment TiO2 anatase film was immobilized over the inner layer of these tubules. An additional TiO2 anatase layer was added on top of the film to provide larger photocatalytic area. This microreactor depicted enhanced durability and efficiency [55]. Meng et al. also developed microfluidic based photocatalytic microreactor. They used nanofibrous TiO2 through electrospun to develop this photocatalytic microreactor. It depicted enhance efficiency as compared to TiO2 film based microreactor [56].

Recently, applications of microfluidics have been developed in the form of microfluidic fuel cells. In these cells, all the systems such as fluid delivery, removal, etc. is confined to the microfluidic channel only. These cells do not require a physical barrier for separation of fuel and oxidant species and therefore they operate in co-laminar flow mode. Whereas, in conventional fuel cell a physical barrier such as proton exchange membrane is required. They can be used to power microsystems, generate on-chip power and in consume electronics as well [31]. Microfluidic fuel cells have attracted huge researchers as they are portable power sources with short startup time and environment friendly nature. Microfluidic fuel cell using laminar air flow had been developed by Eric et al. (**Figure 2a**). It was made through a Y-shaped microchannel consisting of two catalyst covered electrodes on opposite walls. Through these channels, fuel and oxidant merge and flow laminarly parallel between these two electrodes without turbulent mixing. They showed that this type of system can be effectively used to generate microscopic power source for room temperature [57]. There is patented microfluidic fuel cell system for portable energy applications. In this system, microfluidic container, substrate for catalytic composition, a liquid/gas separator, a fuel cell consisting of anode and cathode and electrical connections were all assembled to form this portable energy system [58]. The design of the system and fuel cell components is depicted through **Figure 2b** and **c**, respectively [58]. Luke et al. also developed these microfluidic cells based on microbial fuel that can be used to provide power supply to integrated biosensors. This system was developed in polydimethylsiloxane. Here, two carbon cloth electrodes and proton exchange membrane was used. *Shewanella oneidensis* MR-1 was used in anode chamber as electrogenic bacterial strain and ferricyanide was used in cathode chamber (**Figure 2d**). Maximum current of 2.59 μA was generated using this miniature microbial fuel cell [59]. Svetlana et al. developed a microfluidic cell for energy conversion. They developed hydrogen and oxygen based microfluidic cell using polydimethylsiloxane (PDMS) device. In this

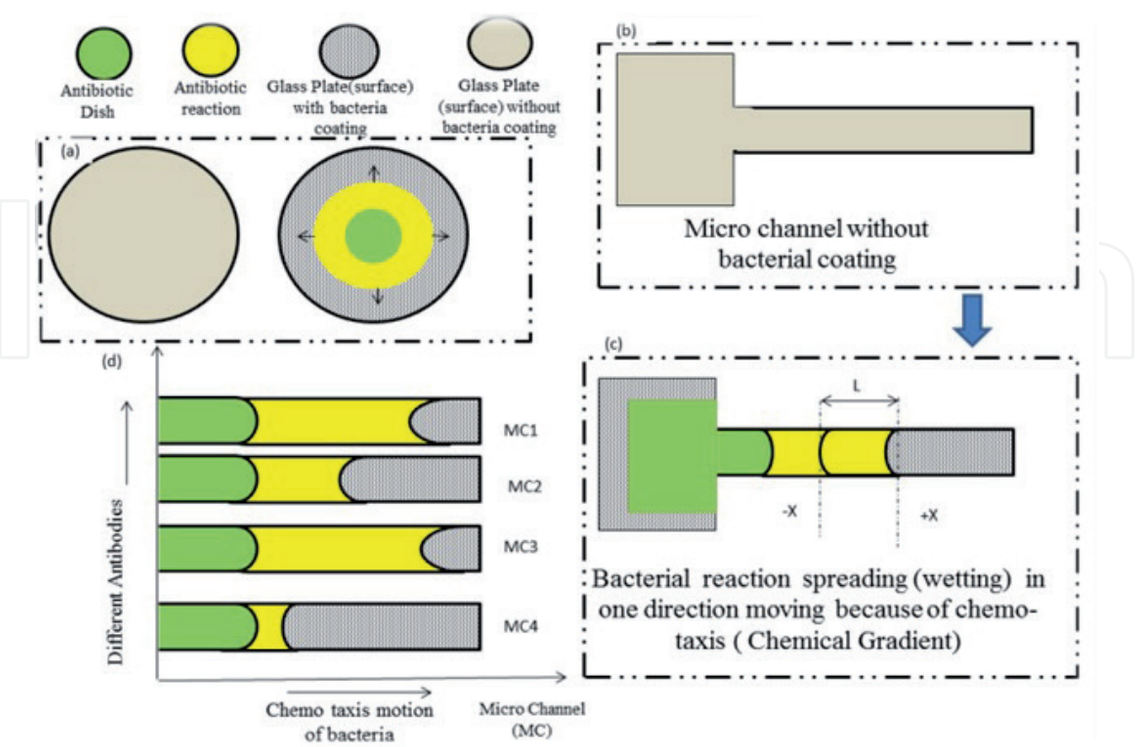

Figure 2.
(a) The reaction of antibiotic dish with bacteria, (b) glass microchannel without bacterial coating, (c) reaction of antibiotic with bacteria in microchannel, and (d) the spreading of chemical reaction in microchannel with different antibodies.

device Pt/quartz electrodes in the form of thin film were embedded into the device. The PDMS microchannel network containing liquid electrolyte was used for immersion of electrode array into it. This also performs the function of thin glass permeable membrane for feeding reactants to the electrodes. This fuel cell operated at room temperature with the maximum power density of 700 $\mu W/cm^2$. The overall lifetime of this cell was comparatively higher to the exiting higher surface electrodes based fuel cells [60].

4.3 Chemical and environmental applications

Recent growth in the field of microfluidics has been observed in the field of environmental assessment. Microfluidics is advantageous as multiple processes such as pre-treatment, pre-concentration, separation and detection are incorporated at the same platform. It is used for trace analysis of materials as less risk of contamination is there due to preclusion of sample transportation process. Microfluidics play role in the development of subsurface energy based technologies in the future. Mark et al. developed a microfluidic system based upon high temperature and pressure. Within geo-material micromodels such as rock, cement, clay, etc., direct observations for flow and transport can be made using this system and that too in reservoir conditions. In this micromodel fabrication method, 3D tomography images of real fractures were used as micromodel template. This provided better representation of the pore space and fracture geometries in subsurface formations [61]. Several microfluidic devices can be used for detection and analysis based upon electrochemistry, surface enhanced Raman spectroscopy, chemiluminescence, absorbance and laser-induced fluorescence. These electrochemical and optical based systems can be conjugated on a single micro platform to perform environmental monitoring. These labs on chip systems can be used for real time tracking of pollutants in the environment. Major advantages of these systems are portable compact size, better process control, low-cost production, real-time analysis, low sample consumption and fast response. LOC is used for real-time analysis of pollutants in wastewater. Combining it with the wireless communication, make it a strong tool for modifying data acquisition parameters and data transfer [62].

Microfluidic systems are being used for detection of formaldehyde as well. Formaldehyde is the organic volatile compound found in many household products. It is associated with health risk factors and is also a cause of sick building syndrome. Therefore its detection at real-time in the surroundings is essential for a healthy living. Liu et al. developed a paper based microfluidic system for detection of formaldehyde. Acetoacetanilide reagent is used to implant paper-based chip at reaction site. Concentration of formaldehyde is detected using UV light which induces fluorescence intensity in the dihydropyridine. Dihydropyridine is the complex of formaldehyde with acetoacetanilide. This method was used to detect formaldehyde in the commercial food samples and proved to be an efficient method for detection of formaldehyde concentration [63]. Similarly, Czugala et al. developed a fully integrated microfluidic device to provide wireless and portable analytical platform. This system can be used for detection of nitrite anions in the water. Nitrite anions are one of the water contaminants along with lead, cadmium and nitrate. In this system detection is done through analysis of color intensity of complex formed between nitrite anions and Griess reagent. This color intensity was assessed using low cost Paired Emitter Detector Diode. Biomimetic photoresponsive ionogel microvalve controlled by LED was used for manipulation of on-chip fluid. This system was one of its type that conjugated fully functional microfluidics with photobased valving and photo detection [64]. Microfluidic devices along with porous plugs have also been developed. This device can be used

for size based separation of particles including microorganisms and therefore have implications as miniature filter for analysis of water samples. Living radical photo-polymerization technique using wide range of polymers was used for fabrication of these devices. Salt-leaching technique was used for placement of porous plug in the microfluidic channels. Pore size of the porous plug in this device was determined using flow field-flow fractionation. It is a new and cost efficient simple tool for water assessment [65]. Research is moving at a fast pace for development and commercialization of such paper based microfluidic devices that can be conjugated with other existing techniques.

5. Role of In situ surface wettability for the development of microfluidic devices

Surface wettability or wetting is the ability of the liquid to maintain contact and interact with the solid surface over which it is flowing. It results from the interaction of intermolecular forces between the molecules of liquid and molecules over the surface of the solid. Surface wettability measurement is a very critical technique to measure the flow of micro fluid in microfluidic applications. In microfluidic devices the detection of small volume change with change in fluid properties is very small because of the micrometer range. In order to detect this small change in micrometer range *in situ* wetting measurement is required. Microfluidic devices offer innumerable application in the field of science and technology. The scopes of these types of devices have been increasing for recent decades. For example, in clinical trials for drug development the amount of antibodies used is very high and cover large cost. On the other hand microfluidic devices reduce amount and cost of antibodies as well as time.

In microfluidic devices the motion of chemical reaction governed by chemo taxis gradient and this gradient is responsible for the motion of droplet. The motion of droplet generally measured with the help of wettability and wettability of droplet depends upon the surface. Wettability has a dynamic impact on the displacement of fluid inside micro fluidic device. The change in displacement of any fluid inside any microfluidic device measured in term of spreading of fluid. The spreading behavior of any flowing liquid measured with its wetting behavior and it is generally measured in term of contact angle. The magnitude of contact angle formed by micro fluid with micro-channel wall has great importance to study the characteristics of micro fluidic device.

Example: Suppose a static fluid is placed at the center of any plate and we apply taxis gradient at the two end of plate. The taxis gradient (magnetic, chemotaxis) is responsible for the displacement of fluid inside. The fluid try to spread both in linear (parallel to gradient axis) and lateral (perpendicular to direction of applied gradient) direction. The two directional spreading of liquid makes difficulty in the quantitative measurement in displaced liquid. In order to overcome this issue microfluidic devices play the important role in various scientific testing applications.

The contact angle measurement is carried out using young's equation is given in Eq. (1). The equation is derived by balancing different interfacial energy in all direction.

$$\cos\theta = \left(\sigma_{sv} - \sigma_{sl}\right) / \sigma_{lv} \tag{1}$$

where θ = contact angle
σ_{sv} = solid/vapor interfacial energy

σ_{sl} = solid/liquid interfacial energy
σ_{lv} = liquid/vapor interfacial energy.

Wettability of fluid over the solid surface is measured in terms of contact angle (θ). The higher value of contact angle leads to lower wettability (low spreading area of displaced fluid) as shown in **Figure 1c**. The contact angle close to 0°, as droplet turns into flat puddle shows complete wetting (highest spreading area) as shown in **Figure 1e**, if angle exceeds zero but is less than 90° as shown in **Figure 1d** shows wetting [66].

In microfluidic devices the fluid displacement takes place only in linear direction because of micro channel cavity. The quantitative measurement of displaced fluid inside micro channel can be made by measuring the dimension of micro channel and displace length of fluid. The measurement of displace volume with little change in taxis gradient improves the overall sensitivity of device. Sensitivity of device is defined as the measurement of small change in the system by varying input parameter.

5.1 Case study 1

The existing process of antibiotic susceptibility measurement uses Petri dish coated with bacteria and divides the Petri dish into required number of segment using marker. An antibiotic dish (different concentrations) is then placed over the bacterial coated Petri dish. The petri dish is then placed over incubator for 24–48 hours. The reaction of bacteria with antibiotic takes place in petri dish and reaction takes place in radial outward direction as shown in **Figure 1a**. The measurement of reaction in radial direction is difficult to quantify in required scale. To overcome this issue a microfluidic device can be used as antibiotic susceptibility testing device. In this type of device, glass slide micro channel is coated with bacterial coating like petri dish as shown in **Figure 1b**. Different antibodies are then placed over bacterial coated micro channel for measuring the spreading of reaction

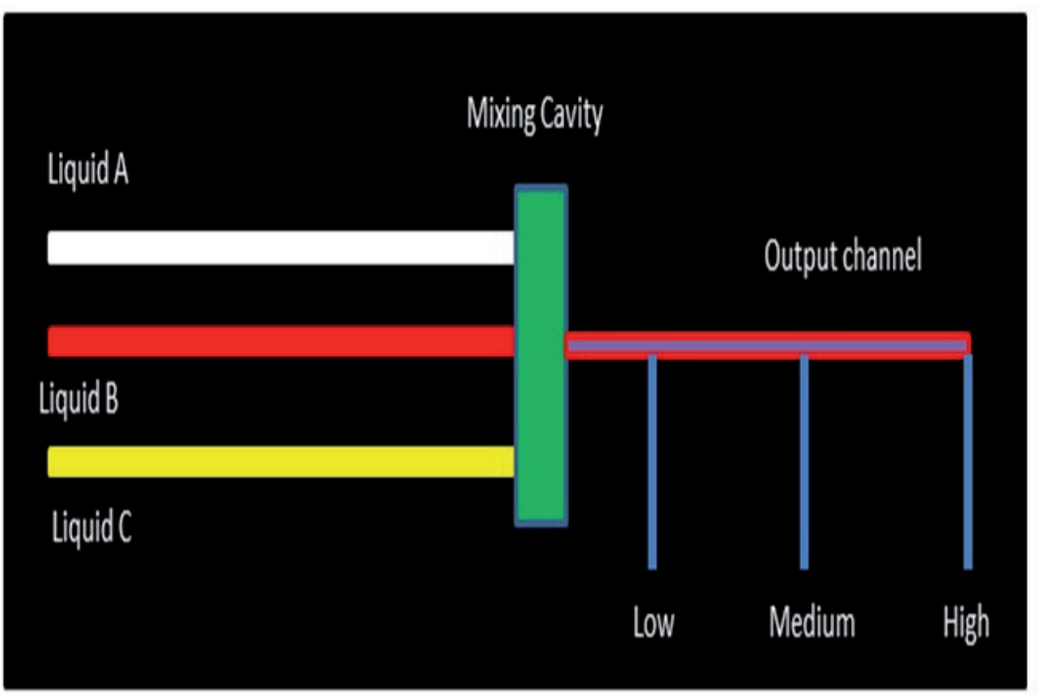

Figure 3.
Microfluidic device for mixing different liquid.

due to chemo taxis in one direction and chemo taxis spreading phenomenon can be quantify using microfluidic chip time lapse microscopy as shown in **Figure 1d**. The spreading of reaction is then measured by the dimension of micro channel as shown in **Figure 1c**.

5.2 Case study 2

In this study, microfluidic device for mixing three liquid is used. In this device, three different liquid A, B and C is used to mix in different concentration and their mixing reaction is measured with the range of output mixing micro channel as shown in **Figure 3**. In this type of device the change in output parameter can be detect significantly my using small volume of liquid droplet. These devices are very useful to measure mixing behavior of two or more liquid for various chemical mixing applications.

6. Factor affecting wettability

The wettability is generally are properties of displaced liquid measured in term of contact angle. The surface morphology, material impurity and porosity are the properties which affect the wettability.

Effect of surface roughness: All smother surfaces look rough in microscopic level. The rough surface of solid specimen affects the wettability of liquid over the solid surface. The contact angle formed with flat surface is called apparent contact angle θ_a and it is consider by considering ideal surface condition. The actual contact angle θ_A is generally higher than that of apparent contact angle θ_a as shown in **Figure 4a,b**. To calculate real surface free energies of liquid actual contact angle is used. Generally hydrophilic surface is considered to be the best surface where lower

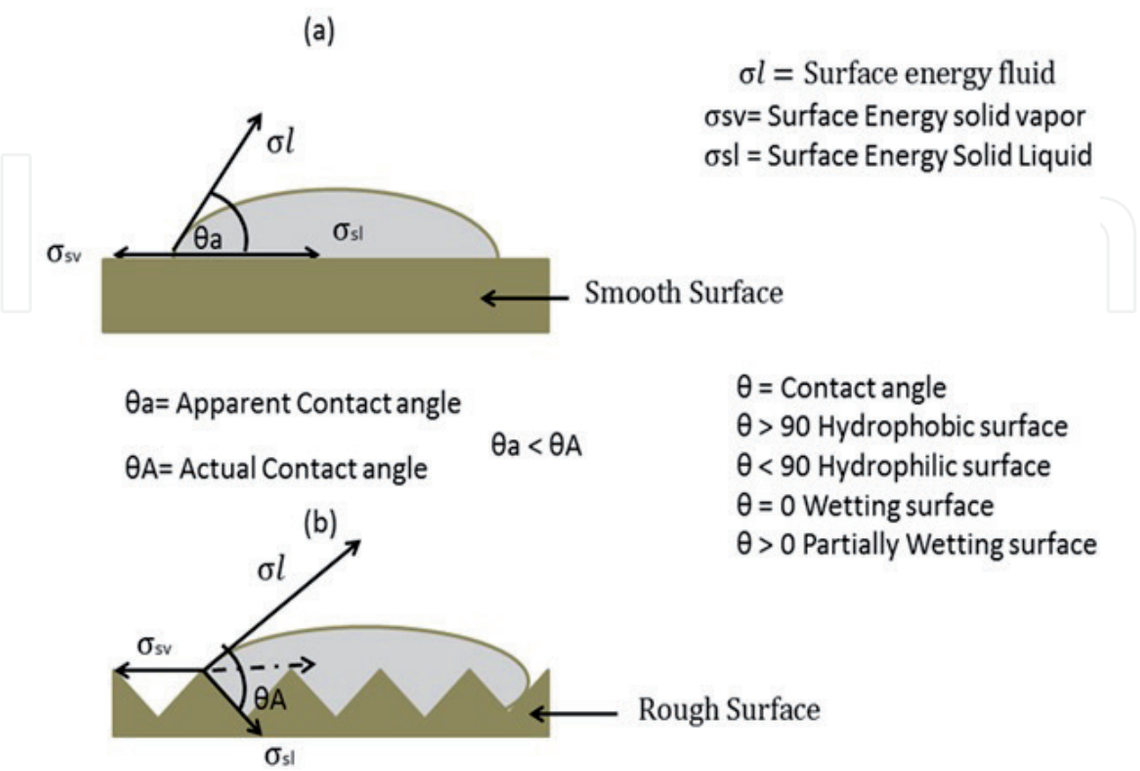

Figure 4.
Effect of surface roughness on the wettability of fluid.

value of contact angle is obtain. The wettability of liquid surface generally increases as we decrease the surface roughness of solid surfaces. The relation between roughness and wettability was explained by Wenzel and stated that if the surface is chemically hydrophobic it will become more hydrophobic when surface roughness is added. According to Wenzel,

$$\cos\left(\theta_A\right) = R\cos\left(\theta_a\right) \tag{2}$$

R is the surface ratio between actual and projected area of solid surface over which fluid is flowing. For smother surface R = 1 and apparent contact angle becomes equal to actual contact angle. Other than surface roughness, impurity and porosity in solid surface effect wettability.

7. *In situ* wettability measurement in microfluidic devices

In microfluidic device, the displacement of fluid takes place continuously, and it is very difficult to measure wettability (contact angle formed by moving fluid with the wall of micro channel). The Sessile drop method and image analysis techniques are the method used only for measuring the static contact angle of liquid in micro channel device. For biomedical and clinical application the chemotaxis reaction takes place continuously and required continuous monitoring of contact angle *in situ* image capturing system is used. In this technique the position of chemical reaction captured with the help of microscope and high speed camera installed over the viewing point of microscope [67]. The camera records the position of reaction in different time interval and measured the contact angle and contact angle is further used to measure interfacial energy of fluid in microfluidic devices. The schematic of *in situ* image capturing system is as shown in **Figure 5**.

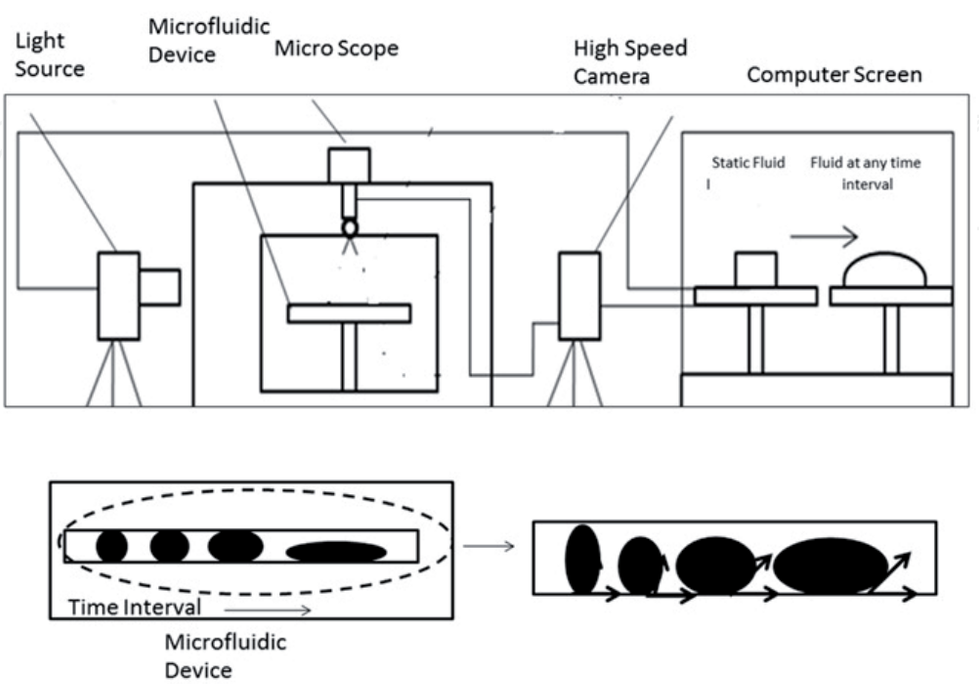

Figure 5.
In situ image capturing system for measuring wettability of microfluid devices.

In this system a microscope is just place at the top of microfluidic device and it captures the motion of chemical reaction change in micro channel. A light source is applied from the side to capture the video with more celerity with the help of high speed camera and store video into computer. The video is than sliced into image in required time interval as shown in lower left corner of figure. The Enlarge version of captured screen is shown in lower right corner of **Figure 5** which shows the measurement of contact angle variation at different time interval.

8. Fabrication process of microfluidic devices

The selection of microfluidic fabrication process is dependent on type of material selection for different microfluidic application. The special grade stainless steel, borosilicate glass, PDMS (polydimethylsiloxane), PMMA(Poly methyl metacrylate) copper, aluminum and Acrylic have been used as solid material for microfluidic device fabrication. Chemical etching, 3D printing, Additive manufacturing, micromachining are the common manufacturing practices for the development of different microfluidic devices [68–70].

9. Conclusion

Microfluidic devices are one of the most widely used devices of twenty-first century. They are being used in almost all the fields including biomedical, energy, chemical, environmental, etc. Microfluidics is the technology based upon various types of taxis, specifically chemotaxis. Surface wettability is an essential factor in the development of microfluidics. Elucidating mechanisms to improve surface wettability will help in the betterment of microfluidic devices. There are still unexplored applications of microfluidics such as in paint industry: to study the mixing and spreading of paints. Initially, microfluidics developed due to advancement in the field of silicon etching and molding of micro channels technique. The further advancement in the fabrication techniques will pave way for development of high-leveled microfluidic devices that will open a new era of research in all the fields.

Acknowledgements

We would like to acknowledge DARVUN India for providing us the opportunity of working for them.

Conflict of interest

The authors declare no conflict of interest.

IntechOpen

Author details

Shivanjali Saxena and Rakesh Joshi*
Research Scientist, DARVUN India, Patiala, Punjab, India

*Address all correspondence to: joshi.1@iitj.ac.in

IntechOpen

References

[1] Casquillas GV, Houssin T, Durieux L. Microfluidics and microfluidic devices: A review. Elveflow Microfluidic Instruments RSS. 2018

[2] Delves PJ, Roitt IM. Encyclopedia of Immunology. Academic Press; 1998

[3] Mazzag B, Zhulin I, Mogilner A. Model of bacterial sband formation in aerotaxis. Biophysical Journal. 2003;**85**:3558-3574

[4] Taylor BL, Zhulin IB, Johnson MS. Aerotaxis and other energy-sensing behavior in bacteria. Annual Reviews in Microbiology. 1999;**53**:103-128

[5] Kalmus H. Anemotaxis in *Drosophila*. Nature. 1942;**150**:405

[6] Yan S, Graff MM, Bresee CS, Man YB, Hartmann MJ. Whiskers aid anemotaxis in rats. Science Advances. 2016;**2**:e1600716

[7] Lauffenburger DA, Zigmond SH. Chemotactic factor concentration gradients in chemotaxis assay systems. Journal of Immunological Methods. 1981;**40**:45-60

[8] Clark AG, Simon A, Aizel K, Bibette J, Bremond N, Vignjevic DM. 3D cell migration in the presence of chemical gradients using microfluidics. Methods in cell biology: Elsevier. 2018;**147**:133-147

[9] Plotnikov SV, Pasapera AM, Sabass B, Waterman CM. Force fluctuations within focal adhesions mediate ECM-rigidity sensing to guide directed cell migration. Cell. 2012;**151**:1513-1527

[10] DuChez BJ, Doyle AD, Dimitriadis EK, Yamada KM. Durotaxis by human cancer cells. Biophysical Journal. 2019;**116**:670-683

[11] Cortese B, Palama IE, D'Amone S, Gigli G. Influence of electrotaxis on cell behaviour. Integrative Biology. 2014;**6**:817-830

[12] Tai G, Reid B, Cao L, Zhao M. Electrotaxis and wound healing: experimental methods to study electric fields as a directional signal for cell migration. Chem: Springer. 2009:77-97

[13] Adams C, Paul A. Phototaxis and geotaxis of light-adapted zoeae of the golden king crab lithodes aequispinus (anomura: *Lithodidae*) in the laboratory. Journal of Crustacean Biology. 1999;**19**:106-110

[14] Häder D-P, Hemmersbach R. Gravitaxis in *Euglena*. Euglena: Biochemistry, Cell and Molecular Biology. Advances in Experimental Medicine and Biology; Springer. 2017;**979**:237-266

[15] Armstrong J, Texada M, Munjaal R, Baker D, Beckingham K. Gravitaxis in *Drosophila melanogaster*: A forward genetic screen. Genes, Brain, and Behavior. 2006;**5**:222-239

[16] Ten Hagen B, Kümmel F, Wittkowski R, Takagi D, Löwen H, Bechinger C. Gravitaxis of asymmetric self-propelled colloidal particles. Nature Communications. 2014;**5**:4829

[17] Wang W, Qin L-W, Wu T-H, Ge C-L, Wu Y-Q, Zhang Q, et al. cGMP signalling mediates water sensation (hydrosensation) and hydrotaxis in *Caenorhabditis elegans*. Scientific Reports. 2016;**6**:19779

[18] Pringault O, Garcia-Pichel F. Hydrotaxis of cyanobacteria in desert crusts. Microbial Ecology. 2004;**47**: 366-373

[19] Lefèvre CT, Bazylinski DA. Ecology, diversity, and evolution of magnetotactic bacteria. Microbiology

and Molecular Biology Reviews. 2013;**77**:497-526

[20] Parker G. Encyclopedia of Materials: Science and Technology. Elsevier; 2001

[21] Peng F, Tu Y, Men Y, van Hest JC, Wilson DA. Supramolecular adaptive nanomotors with magnetotaxis behavior. Advanced Materials. 2017;**29**:1604996

[22] Jékely G. Evolution of phototaxis. Philosophical Transactions of the Royal Society, B: Biological Sciences. 2009;**364**:2795-2808

[23] Suli A, Watson GM, Rubel EW, Raible DW. Rheotaxis in larval zebrafish is mediated by lateral line mechanosensory hair cells. PLoS One. 2012;**7**

[24] Baxendale S, Whitfield T. Methods to study the development, anatomy, and function of the zebrafish inner ear across the life course. Methods in Cell Biology: Elsevier. 2016:165-209

[25] Queiroga H, Blanton J. Interactions between behaviour and physical forcing in the control of horizontal transport of decapod crustacean larvae. Advances in Marine Biology. 2005;**47**:107-214

[26] Poff KL, Skokut M. Thermotaxis by pseudoplasmodia of *Dictyostelium discoideum*. Proceedings of the National Academy of Sciences. 1977;**74**:2007-2010

[27] Pline M, Diez JA, Dusenbery DB. Extremely sensitive thermotaxis of the nematode *Meloidogyne incognita*. Journal of Nematology. 1988;**20**:605

[28] Bahat A, Eisenbach M. Sperm thermotaxis. Molecular and Cellular Endocrinology. 2006;**252**:115-119

[29] Xue X, Patel MK, Kersaudy-Kerhoas M, Desmulliez MP, Bailey C, Topham D. Analysis of fluid separation in microfluidic T-channels. Applied Mathematical Modelling. 2012;**36**:743-755

[30] Zhang M, Gong X, Wen W. Manipulation of microfluidic droplets by electrorheological fluid. Electrophoresis. 2009;**30**:3116-3123

[31] Lin B. Microfluidics: Technologies and Applications. Springer; 2011

[32] Aryasomayajula A, Bayat P, Rezai P, Selvaganapathy PR. Microfluidic Devices and their Applications. Springer Handbook of Nanotechnology. Berlin, Heidelberg: Springer; 2017. pp. 487-536

[33] Igata E, Arundell M, Morgan H, Cooper J. Interconnected reversible lab-on-a-chip technology. Lab on a Chip. 2002;**2**:65-69

[34] Seeley JV, Micyus NJ, Bandurski SV, Seeley SK, McCurry JD. Microfluidic deans switch for comprehensive two-dimensional gas chromatography. Analytical Chemistry. 2007;**79**:1840-1847

[35] Weibel DB, Whitesides GM. Applications of microfluidics in chemical biology. Current Opinion in Chemical Biology. 2006;**10**:584-591

[36] Pihl J, Sinclair J, Sahlin E, Karlsson M, Petterson F, Olofsson J, et al. Microfluidic gradient-generating device for pharmacological profiling. Analytical Chemistry. 2005;**77**:3897-3903

[37] Irimia D, Liu S-Y, Tharp WG, Samadani A, Toner M, Poznansky MC. Microfluidic system for measuring neutrophil migratory responses to fast switches of chemical gradients. Lab on a Chip. 2006;**6**:191-198

[38] Chung BG, Flanagan LA, Rhee SW, Schwartz PH, Lee AP, Monuki ES, et al.

Human neural stem cell growth and differentiation in a gradient-generating microfluidic device. Lab on a Chip. 2005;**5**:401-406

[39] Ainla A, Gözen I, Orwar O, Jesorka A. A microfluidic diluter based on pulse width flow modulation. Analytical Chemistry. 2009;**81**:5549-5556

[40] Jiang X, Ng JM, Stroock AD, Dertinger SK, Whitesides GM. A miniaturized, parallel, serially diluted immunoassay for analyzing multiple antigens. Journal of the American Chemical Society. 2003;**125**:5294-5295

[41] Takeuchi S, DiLuzio WR, Weibel DB, Whitesides GM. Controlling the shape of filamentous cells of *Escherichia coli*. Nano Letters. 2005;**5**:1819-1823

[42] Cabodi M, Choi NW, Gleghorn JP, Lee CS, Bonassar LJ, Stroock AD. A microfluidic biomaterial. Journal of the American Chemical Society. 2005;**127**:13788-13789

[43] Hu J, Wang L, Li F, Han YL, Lin M, Lu TJ, et al. Oligonucleotide-linked gold nanoparticle aggregates for enhanced sensitivity in lateral flow assays. Lab on a Chip. 2013;**13**:4352-4357

[44] Warren AD, Kwong GA, Wood DK, Lin KY, Bhatia SN. Point-of-care diagnostics for noncommunicable diseases using synthetic urinary biomarkers and paper microfluidics. Proceedings of the National Academy of Sciences. 2014;**111**:3671-3676

[45] Herr AE, Hatch AV, Throckmorton DJ, Tran HM, Brennan JS, Giannobile WV, et al. Microfluidic immunoassays as rapid saliva-based clinical diagnostics. Proceedings of the National Academy of Sciences. 2007;**104**:5268-5273

[46] Fan HC, Blumenfeld YJ, El-Sayed YY, Chueh J, Quake SR. Microfluidic digital PCR enables rapid prenatal diagnosis of fetal aneuploidy. American Journal of Obstetrics and Gynecology. 2009;**200**:543.e1-543.e7

[47] Huh D, Matthews B, Mammoto A, Montoya-Zavala M, Hsin H, Ingber D. A mechanosensitive transcriptional mechanism that controls angiogenesis. Science. 2010;**328**:1662-1668

[48] Westein E, van der Meer AD, Kuijpers MJ, Frimat J-P, van den Berg A, Heemskerk JW. Atherosclerotic geometries exacerbate pathological thrombus formation poststenosis in a von Willebrand factor-dependent manner. Proceedings of the National Academy of Sciences. 2013;**110**:1357-1362

[49] Kim HJ, Huh D, Hamilton G, Ingber DE. Human gut-on-a-chip inhabited by microbial flora that experiences intestinal peristalsis-like motions and flow. Lab on a Chip. 2012;**12**:2165-2174

[50] van Der Helm MW, Van Der Meer AD, Eijkel JC, van den Berg A, Segerink LI. Microfluidic organ-on-chip technology for blood-brain barrier research. Tissue barriers. 2016;**4**:e1142493

[51] Lee HJ, Goodrich TT, Corn RM. SPR imaging measurements of 1-D and 2-D DNA microarrays created from microfluidic channels on gold thin films. Analytical Chemistry. 2001;**73**:5525-5531

[52] Pawlak M, Schick E, Bopp MA, Schneider MJ, Oroszlan P, Ehrat M. Zeptosens' protein microarrays: A novel high performance microarray platform for low abundance protein analysis. Proteomics. 2002;**2**:383-393

[53] Erickson D, Sinton D, Psaltis D. Optofluidics for energy applications. Nature Photonics. 2011;**5**:583-590

[54] Lei L, Wang N, Zhang X, Tai Q, Tsai DP, Chan HL. Optofluidic planar reactors for photocatalytic water treatment using solar energy. Biomicrofluidics. 2010;**4**:043004

[55] Krivec M, Žagar K, Suhadolnik L, Čeh M, DraŽić G. Highly efficient TiO2-based microreactor for photocatalytic applications. ACS Applied Materials & Interfaces. 2013;**5**:9088-9094

[56] Meng Z, Zhang X, Qin J. A high efficiency microfluidic-based photocatalytic microreactor using electrospun nanofibrous TiO2 as a photocatalyst. Nanoscale. 2013;**5**:4687-4690

[57] Choban ER, Markoski LJ, Wieckowski A, Kenis PJ. Microfluidic fuel cell based on laminar flow. Journal of Power Sources. 2004;**128**:54-60

[58] Gervasio D, Zenhausern F. Microfluidic fuel cell system and method for portable energy applications. Google Patents; 2006

[59] Wagner LT, Yang J, Ghobadian S, Montazami R, Hashemi NN. A microfluidic reactor for energy applications. Open Journal of Applied Biosensor. 2012;**1**:21

[60] Mitrovski SM, Elliott LC, Nuzzo RG. Microfluidic devices for energy conversion: Planar integration and performance of a passive, fully immersed H2-O2 fuel cell. Langmuir. 2004;**20**:6974-6976

[61] Porter ML, Jiménez-Martínez J, Martinez R, McCulloch Q, Carey JW, Viswanathan HS. Geo-material microfluidics at reservoir conditions for subsurface energy resource applications. Lab on a Chip. 2015;**15**:4044-4053

[62] Lin Y, Gritsenko D, Feng S, Teh YC, Lu X, Xu J. Detection of heavy metal by paper-based microfluidics. Biosensors & Bioelectronics. 2016;**83**:256-266

[63] Liu C-C, Wang Y-N, Fu L-M, Huang Y-H. Microfluidic paper-based chip platform for formaldehyde concentration detection. Chemical Engineering Journal. 2018;**332**:695-701

[64] Czugala M, Fay C, O'Connor NE, Corcoran B, Benito-Lopez F, Diamond D. Portable integrated microfluidic analytical platform for the monitoring and detection of nitrite. Talanta. 2013;**116**:997-1004

[65] Chon K, Moon J, Kim S, Kim S-D, Cho J. Bio-particle separation using microfluidic porous plug for environmental monitoring. Desalination. 2007;**202**:215-223

[66] Joshi R, Chhibber R. Effect of surface roughness and oxidation conditions on wettability of borosilicate glass sealant. Materials Science Forum: Trans Tech Publ. 2017;**909**:61-66

[67] Joshi R, Chhibber R. Development and interface characterization of unmatched glass-metal joint. Journal of Manufacturing Processes. 2018;**31**:787-800

[68] Ackermann KR, Henkel T, Popp J. Quantitative online detection of low-concentrated drugs via a SERS microfluidic system. ChemPhysChem. 2007;**8**:2665-2670

[69] Bruzzone A, Costa H, Lonardo P, Lucca D. Advances in engineered surfaces for functional performance. CIRP Annals. 2008;**57**:750-769

[70] Ungerböck B, Mistlberger G, Charwat V, Ertl P, Mayr T. Oxygen imaging in microfluidic devices with optical sensors applying color cameras. Procedia Engineering. 2010;**5**:456-459