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Shantanu Bhattacharya
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Paper Microfluidics

Theory and Applications

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Advanced Functional Materials and Sensors

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Preface

Energy demand has been rising remarkably due to increasing population and urbanization. Global economy and society are significantly dependent on the energy availability because it touches every facet of human life and activities. Transportation and power generation are two major examples. Without the transportation by millions of personalized and mass transport vehicles and availability of 24×7 power, human civilization would not have reached contemporary living standards.

The International Society for Energy, Environment and Sustainability (ISEES) was founded at Indian Institute of Technology Kanpur (IIT Kanpur), India, in January 2014 with an aim to spread knowledge/awareness and catalyze research activities in the fields of energy, environment, sustainability, and combustion. The society's goal is to contribute to the development of clean, affordable, and secure energy resources and a sustainable environment for the society and to spread knowledge in the above-mentioned areas and create awareness about the environmental challenges, which the world is facing today. The unique way adopted by the society was to break the conventional silos of specializations (engineering, science, environment, agriculture, biotechnology, materials, fuels, etc.) to tackle the problems related to energy, environment, and sustainability in a holistic manner. This is quite evident by the participation of experts from all fields to resolve these issues. The ISEES is involved in various activities such as conducting workshops, seminars, and conferences in the domains of its interests. The society also recognizes the outstanding works done by the young scientists and engineers for their contributions in these fields by conferring those awards under various categories.

Third International Conference on "Sustainable Energy and Environmental Challenges" (III-SEEC) was organized under the auspices of ISEES from December 18 to 21, 2018, at Indian Institute of Technology Roorkee. This conference provided a platform for discussions between eminent scientists and engineers from various countries including India, USA, Norway, Finland, Sweden, Malaysia, Austria, Hong Kong, Bangladesh, and Australia. In this conference, eminent speakers from all over the world presented their views related to different aspects of energy, combustion, emissions, and alternative energy resource for

sustainable development and cleaner environment. The conference presented five high-voltage plenary talks from globally renowned experts on topical themes, namely "The Evolution of Laser Ignition Over more than Four Decades," by Prof. Ernst Wintner, Technical University of Vienna, Austria; "Transition to Low Carbon Energy Mix for India," by Dr. Bharat Bhargava, ONGC Energy Center; "Energy Future of India," by Dr. Vijay Kumar Saraswat, Hon. Member (S&T), NITI Aayog, Government of India; "Air Quality Monitoring and Assessment in India," by Dr. Gurfan Beig, SAFAR; and "Managing Large Technical Institutions and Assessment Criterion for Talent Recruitment and Retention," by Prof. Ajit Chaturvedi, Director, IIT Roorkee.

The conference included 24 technical sessions on topics related to energy and environmental sustainability including 5 plenary talks, 27 keynote talks, and 15 invited talks from prominent scientists, in addition to 84 contributed talks and 50 poster presentations by students and researchers. The technical sessions in the conference included advances in IC engines, solar energy, environmental biotechnology, combustion, environmental sustainability, coal and biomass combustion/gasification, air and water pollution, biomass to fuels/chemicals, combustion/gas turbines/fluid flow/sprays, energy and environmental sustainability, atomization and sprays, sustainable transportation and environmental issues, new concepts in energy conservation, waste to wealth. One of the highlights of the conference was the rapid fire poster sessions in (i) engine/fuels/emissions, (ii) renewable and sustainable energy, and (iii) biotechnology, where 50 students participated with great enthusiasm and won many prizes in a fiercely competitive environment. More than 200 participants and speakers attended this four days' conference, which also hosted by Dr. Vijay Kumar Saraswat, Hon. Member (S&T), NITI Aayog, Government of India, as the chief guest for the book release ceremony, where 14 ISEES books published by Springer, Singapore, under a special dedicated series "energy, environment, and sustainability" were released. This was the second time in a row that such significant and high-quality outcome has been achieved by any society in India. The conference concluded with a panel discussion on "Challenges, Opportunities, and Directions for National Energy Security," where the panelists were Prof. Ernst Wintner, Technical University of Vienna; Prof. Vinod Garg, Central University of Punjab, Bhatinda; Prof. Avinash K. Agarwal, IIT Kanpur; and Dr. Michael Sauer, University of Natural Resources, Austria. The panel discussion was moderated by Prof. Ashok Pandey, Chairman, ISEES. This conference laid out the roadmap for technology development, opportunities, and challenges in energy, environment, and sustainability domains. All these topics are very relevant for the country and the world in present context. We acknowledge the support received from various funding agencies and organizations for the successful conduct of the Third ISEES conference III-SEEC, where these books germinated. We would therefore like to acknowledge NIT Srinagar, Uttarakhand (TEQIP) (special thanks to Prof. S. Soni, Director, NIT, UK); SERB, Government of India (special thanks to Dr. Rajeev Sharma, Secretary); UP Bioenergy Development Board, Lucknow (special thanks to Sh. P. S. Ojha), CSIR; and our publishing partner Springer (special thanks to Swati Meherishi).

The editors would like to express their sincere gratitude to large number of authors from all over the world for submitting their high-quality work in a timely manner and revising it appropriately at a short notice. We would like to express our special thanks to Ms. Pulak Bhushan who reviewed various chapters of this monograph and provided their valuable suggestions to improve the manuscripts.

Recent advances in the field of paper microfluidics in innumerable research domains have stimulated considerable efforts to the development of rapid, cost-effective, and simplified point-of-care diagnostic systems. The book is divided into three parts, viz. theoretical background of paper microfluidics, fabrication techniques for paper-based devices, and broad applications. Each chapter of the book is self-explanatory and focuses on a specific topic and its relation to paper microfluidics. Each chapter starts with a brief description of the topic's physical background, essential definitions, and a short story of the recent progress in the relevant field. The book also covers the future outlook, remaining challenges, and emerging opportunities. This book shall be a tremendous up-to-date resource for researchers working in this area.

Kanpur, India — Shantanu Bhattacharya
Singapore — Sanjay Kumar
Kanpur, India — Avinash K. Agarwal

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About the Editors

Prof. Shantanu Bhattacharya (PhD) (ORCID ID: 0000-0002-7902-2119) is a Dr. Gurumukh T. and Veena M. Mehta Chair and Professor of Mechanical Engineering and the Head of Design Program at the Indian Institute of Technology Kanpur. Prior to this, he completed his MS in Mechanical Engineering from the Texas Tech University, Lubbock, Texas and a PhD in Bioengineering from the University of Missouri at Columbia, United States of America. He completed his postdoctoral training at the Birck Nanotechnology Center at Purdue University. Dr. Bhattacharya's main research interests are Design and development of micro-nanosensors and actuation platforms, nano-energetic materials, micro and nanofabrication technologies, water remediation using visible light photocatalysis and product design and development. He has many awards and accolades to his credit which includes the Institution of Engineers Young engineer award, the Institute of Smart structures and systems young scientist award, the national design research best mechanical engineering award, fellowship from the high energetic materials institute at Australia, fellowship of the Institution of Engineers of India etc. Dr. Bhattacharya has guided many PhD and masters' students and has many peer-reviewed international journal publications, patents, books, and conference proceedings.

Dr. Sanjay Kumar (ORCID ID: 0000-0001-8101-097X) is currently a Research Fellow at the National University of Singapore, Singapore. He received his PhD in design and fabrication of functionally engineered materials from the Department of Mechanical Engineering, Indian Institute of Technology Kanpur-208016 India. His research focuses on the development of design and development of acoustic metamaterials, acoustic wave control, paper-based analytical devices for point-of-care diagnostic applications, synthesis of nanoscale materials with controllable size and shape, design of multifunctional materials through self-assembly of nanoparticles, additive manufacturing processes, theoretical modeling and optimization, finite-element based numerical simulation, etc. He has published eight journal papers in peer reviewed international journals, six book chapters, and two US patent (filed). Along with Ms. Pulak Bhushan and Prof. Shantanu Bhattacharya, he received the Gandhian Young Technological Innovation (GYTI 2017) Award at Rashtrapati Bhavan, New Delhi, India for development of a dengue NS1 detection kit. He was also awarded the "IFMBE Young Investigator Award" at the 2nd International Conference for Innovation in Biomedical Engineering and Life Sciences (ICIBEL2017) held in conjunction with the 10th Asia Pacific Conference on Medical and Biological Engineering (APCMBE2017) Malaysia.

Prof. Avinash K. Agarwal joined IIT Kanpur in 2001 and prior to that, he worked at the Engine Research Center, University of Wisconsin, Madison, USA as a Post-Doctoral Fellow (1999–2001). His areas of interest are IC engines, combustion, alternative fuels, conventional fuels, lubricating oil tribology, optical diagnostics, laser ignition, HCCI, emissions and particulate control, and large bore engines. Prof. Agarwal has published more than 270 peer reviewed international journal and conference papers, 32 edited books, 55 books chapters and has 8000+ Scopus and 11100+ Google scholar citations. He is associate editor of ASME Journal of Energy Resources Technology. He has edited "Handbook of Combustion" (5 Volumes;

3168 pages), published by Wiley VCH, Germany. Prof. Agarwal is a Fellow of SAE (2012), Fellow of ASME (2013), Fellow of INAE (2015), Fellow of ISEES (2016), Fellow of RSC (2018), and Fellow of NASI (2018). He is recipient of several prestigious awards such as Clarivate Analytics India Citation Award-2017 in Engineering and Technology, NASI-Reliance Industries Platinum Jubilee Award-2012; INAE Silver Jubilee Young Engineer Award-2012; Dr. C. V. Raman Young Teachers Award: 2011; SAE International's Ralph R. Teetor Educational Award-2008; INSA Young Scientist Award-2007; UICT Young Scientist Award-2007; INAE Young Engineer Award-2005. Prof. Agarwal is the recipient of Prestigious Shanti Swarup Bhatnagar Award-2016 in Engineering Sciences.

Chapter 1
A Historical Perspective on Paper Microfluidic Based Point-of-Care Diagnostics

Sanjay Kumar, Pulak Bhushan, Avinash K. Agarwal and Shantanu Bhattacharya

Abstract Paper-based microfluidic systems have emerged as one of the most favorable technologies used in many potential applications such as point-of-care diagnostics, flexible electronics, energy storage, etc. From the past several decades, paper-based technology has readily accepted in the academic research lab and industries as well. The paper-based devices have changed the life of humankind. The distinguishing characteristics of paper substrate like low cost, biodegradability, biocompatibility, and ease of fabrication helped their adaptability in biosensing applications. This chapter gives a concise overview of the historical perspective of paper-based devices, classification of paper types, and their recent applications.

1.1 Introduction

In the past several decades, people have been migrating towards the most developed cities defying all cross-border concerns, making the world a 'global village'. The significant increase in the interaction between people from across the globe, has led to severe consequences for global health. These worldwide demo-graphical changes have steered the spreading of communicable diseases from one place to another through infected people (McMichael 2000; Pang and Guindon 2004; Tatem et al. 2006). For example, the severe acute respiratory syndrome (SARS), a respiratory viral disease was first recognized in 2003 in Guangdong Province, China and was

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spread out in over thirty countries within a year (World Health Organization 2003). Zika virus, a vector-borne flavivirus was first isolated in a monkey in 1947 in Uganda and reported in a human in 1953 in Nigeria and since then several outbreaks have been encountered in territories like America, Africa, Asia and Pacific (Hayes 2009; Petersen et al. 2016). Other such examples are the outbreak of human infection with avian influenza A (H7N9) virus in March 2013 in China, the epidemic of Ebola virus disease (EVD) in 2013 in West Africa and the dengue outbreak in Africa (Team 2016).

Conventional approaches used for diagnosis of infectious diseases is hindered by long turnaround times, skilled labor requirements, and sophisticated equipment requirements, imposing a financial liability on the healthcare system. According to a 2015 study by the World Health Organization (WHO), 1.8% of the population pays more than one quarter of their total expenditure on healthcare. Moreover, most of these infectious diseases originate in an underdeveloped/developing region where inadequate medical facilities render their timely diagnosis a difficult task. Due to the lack of proper diagnostic and medication facilities, these diseases claim thousands of human life annually (Lee et al. 2010). In 2003, the Bill and Melinda Gates Foundation in partnership with the National Institutes of Health identified the key challenges of diagnostics as, the lack of appropriate laboratory equipment and shortage of skilled personnel. They emphasized on the development of a simple, accurate, reliable and cost-effective strategy for rapid and point-of-care detection that would facilitate healthcare in resource-limited areas. In the context of early diagnostics of infectious diseases, WHO has released a set of guidelines termed ASSURED (i.e. affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free and deliverable to users) for developing point-of-care diagnostic devices (Peeling et al. 2006).

Point-of-care (POC) diagnostic devices enable the collection of a patient's health information at convenient locations generally outside of the main laboratory. They are low cost miniaturized systems integrated with complex functionalities facilitating timely diagnosis, health monitoring, clinical management, and dis-ease surveillance in both developing and developed countries (Wang et al. 2016). These devices have played a vital role in addressing global health needs by enabling early disease detection, preventing outbreaks and significantly affecting the medical outcome of disease treatment. According to the Coherent Market In-sights Analysis, the global POC diagnostic market was valued at US$1764.6 million in 2016 and is expected to witness a robust compound annual growth rate of 14.5% over the forecast period (2017–2025).

1.2 Paper Microfluidics: Historical Perspective

There are varieties of point-of-care technologies such as flow-through, agglutination assays, solid phase, and paper-based microfluidic device, etc. available in the market. The first three processes have been perceived as one of the most powerful

applications owing to their small size, portability, and low volume requirement for samples. Nevertheless, these systems require sophisticated equipment for fluidic handling and other attributes of diagnostic assays such as sample preparation and analyte detection, greatly limiting their usage in remote settings. Among these, paper-based microfluidics is the most widely used technique be-cause of its natural ability to passively transport fluid through capillary action or wicking, eliminating the need for external bulky pump or other equipment. Paper-based platforms possess several other distinguished characteristics such as rapid, inexpensive, ease of use, portability, affordability, low sample volume requirement, faster response, little interference, biodegradability, mass production capability, and external equipment-independent, which fulfills the WHO guidelines for POC (Yager et al. 2006).

From its first invention around 105 A.D. in ancient China (Temple 1998), paper has been used in many application areas. In the early 19th centuries Gay-Lussac developed a litmus paper (Crosland 2004). After that in 1850s to 1950s, researchers have developed paper-based sensors for various applications such as for radial paper chromatography (Weil 1953), urine test (Rocco 2005), detection of dyes and pigments (Müller and Clegg 1949), etc. However, paper-based sensors gained universal recognition after Martin and Synge were awarded Nobel Prize (chemistry) for their invention of paper chromatography in 1952. By the mid-1960s, commercialization of paper-based sensors had started such as, first dipstick assay for glucose detection in human blood, introduced by Ames company in 1964 (Rocco 2005), one-step lateral flow assay for the point-of-care pregnancy test kit launched by Unipath in 1988 (Chard 1992; Davies et al. 2007). Between mid-90s and 2000s, there was a progressive development of paper-based devices for detection of analytes such as diabetes, cholesterol, diagnostics of pathogens, and infectious diseases, etc. There was another major breakthrough in this field when two dimensional microfluidic paper-based analytical device (2D-μ PAD) was introduced by Whiteside's research group in 2007 (Martinez et al. 2007). Three distinguished branches with hydrophobic barriers made of SU-8 photoresist were patterned on chromatography paper using photolithography process and used for glucose and albumin detection. Since the development of 2D-μ PAD, extensive research has been carried out in device design, performance improvement and their utilization in various point-of-care applications in the past decades (Cate et al. 2014; Kumar et al. 2016a, b, 2017a, b, 2018; Morbioli et al. 2017; Li et al. 2017; You et al. 2017; Yeh et al. 2017; Whitesides 2018).

1.3 Outline

Paper microfluidics is one of the rapidly growing technology and shown a tremendous caliber in field of healthcare, biochemistry, environmental monitoring, analytical chemistry, etc. Owing to their distinct advantages such as rapid, easy-to-use, compatible with biological, organic and inorganic entities, chemical

inertness, robustness, economical, environment-friendly and easy disposal, paper microfluidic-based devices have become a prominent alternative for existing technologies POC technologies. In the past few decades, paper-based microfluidics has gained much attention in broad application areas such as point-of-care diagnostics, environmental monitoring, energy storage, fuel cell, flexible electronics, etc.

This monograph presents the different paper microfluidic-based technologies covering various applications such as point-of-care diagnostics, environmental pollution monitoring, public health monitoring, etc. Specific topics covered in the monograph include:

- Introduction to paper microfluidics
- Fluid transport mechanisms in paper-based microfluidic devices
- Fabrication techniques for paper-based microfluidic devices
- Flow control in paper-based microfluidic devices
- Sensing mechanisms in paper-based devices
- Advances in paper based point of care diagnostics for blood/plasma separation
- Evolution of paper microfluidics as an alternate diagnostic platform
- Paper-based microfluidic systems for detection of infectious diseases
- Paper-based microfluidic devices for detection of DNA
- Nucleic acid amplification on paper substrates
- Paper: A versatile material for the fabrication of low-cost wearable devices
- Paper-based devices for wearable diagnostic applications
- Paper-based devices for food quality control
- Environmental monitoring using paper-based devices
- Paper-based devices for energy storage applications
- Future of paper microfluidic systems.

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Chapter 2
Fluid Transport Mechanisms in Paper-Based Microfluidic Devices

Sanjay Kumar, Pulak Bhushan and Shantanu Bhattacharya

Abstract Paper microfluidics is one of the rapidly growing technology and shown a tremendous caliber in field of healthcare, biochemistry, environmental monitoring, analytical chemistry, etc. Owing to their distinct advantages such as rapid, easy-to-use, compatible with biological, organic and inorganic entities, chemical inertness, robustness, economical, environment-friendly and easy disposal, paper microfluidic-based devices have become a prominent alternative for existing technologies POC technologies. The challenge remains, however, in the designing of an efficient paper-based device for specific applications. A great deal of work has been done in this field to address the challenges in its two key enabling parameters namely 'materials properties' and 'fluid-transport mechanism' to achieve the functional paper device in an efficient and predictive way. Keeping in mind the previously published articles, the focus here is primarily on showcasing the fluid transport mechanisms through paper-based microfluidic devices. This chapter intends to provide an understanding towards theoretical modelling from a device perspective. The commonly used paper substrates and critical factors involved with any fluid transport phenomena is also covered.

Keywords Paper microfluidic · Fluid transport · Capillary flow · Lucas-Washburn equation · Paper types

S. Kumar and P. Bhushan have equal contribution in this chapter.

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2.1 Introduction

Paper is a thin, lightweight ($\sim$10 mg cm^{-2}) and flexible material, available in a wide range of thicknesses (Martinez et al. 2009). It is produced by pressing together multiple cellulose fibers with a porous structure (Altundemir et al. 2017). Although a variety of paper substrates is available in the market, among them, mainly two types of paper substrates are used in point-of-care diagnostics—pure cellulose fiber-based materials (filter paper, chromatography paper, etc.) and nitric acid treated cellulose-based materials (nitrocellulose membrane). Cellulose fiber is a linear chain macromolecule composed of β-D-glucopyranose units linked by glycosidic bonds (O'sullivan 1997). It is made from various raw sources such as wood, flax, cotton, jute, bamboo, grass, bagasse (Yetisen et al. 2013), etc. Cellulose is inherently fibrous, hydrophilic, tough, biodegradable and water-insoluble substance. In filter papers, fibers are randomly overlapped over each other (Fig. 2.1a–c) while in nitrocellulose membrane, fibers are granular in shape (Fig. 2.1d). Filter papers such as Whatman filter paper (grade 1–4) are generally used in qualitative analytical techniques for analyte detection. Owing to its wicking ability, filter paper is the most widely used substrate in the fabrication of paper-based devices (Martinez et al. 2009; Liana et al. 2012).

Nitrocellulose, is a microporous structure which is manufactured by partial nitration of refined cellulose (nitration ratio <2.3 substitutions per ring) (Mansfield 2005). Nitration alters the properties of cellulose such as from hydrophilic to hydrophobic and makes it highly adsorbable to proteins. Nitrocellulose membrane is widely used in lateral flow assay based biosensors (Fenton et al. 2008). Nitrocellulose membrane is brittle and weak. The lower tensile strength of nitrocellulose membranes (<2 lb/in) make them very difficult to handle. Therefore, adhesive polyester film backing is generally used to strengthen the nitrocellulose membrane (Mansfield 2009). Table 2.1 shows a summary of different types of paper substrate, their characteristics, and broad applications.

The selection of paper substrate in biosensing depends on various characteristics such as capillary flow time (the time required for a liquid sample to flow through the pores in the lateral direction), thickness of the paper, pore size, porosity (% of air present in porous structure) and surface quality. The capillary flow time is inversely related to the capillary flow rate and expressed as s cm^{-1}. Practically the capillary flow rate is difficult to measure accurately because the fluid flow rate through the nitrocellulose membrane decays exponentially as the fluid front transports along it. The estimation of capillary flow time helps in deciding the position of test line and control line on the membrane.

Paper thickness is another critical parameter for paper-based microfluidic devices for several reasons. The amount of sample required for a successful run of the assay depends on the pore volume. A thick membrane would need higher sample volume for the saturation of pores. But if the membrane thickness is too thin, then the membrane will be weak and might get damaged during handling. Also, when the known volume of capture reagent (Ab/Ag, in case of LFA) is either printed or

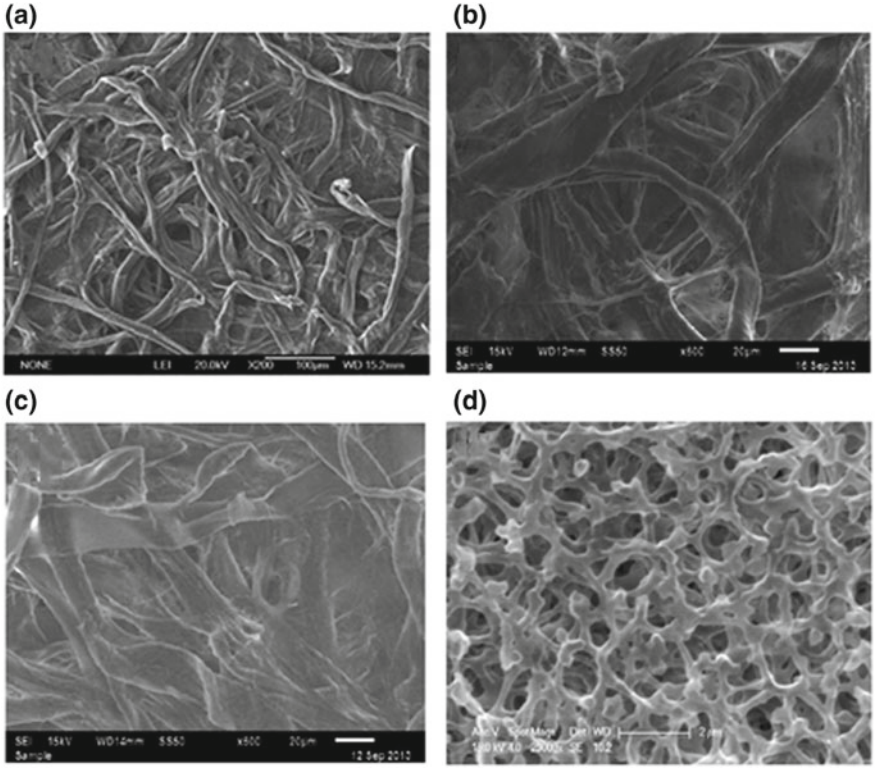

Fig. 2.1 SEM images of Whatman filter paper **a** Grade 1 at 200× magnification. Reprinted with the permission from Liu et al. (2015) ©Elsevier Ltd., 2014. **b** Grade 3 at 600× magnification (fiber thickness: 14.8 ± 1.4 μm) and **c** Grade 4 at 600× magnification (fiber thickness of 20.4 ± 3.6 μm). Adapted with permission from Evans et al. (2014) ©The Royal Society of Chemistry, 2014. **d** SEM images of nitrocellulose membrane with 0.2 μm pore size. Reprinted with the permission from Png et al. (2015) ©The Optical Society, 2015

pipetted onto the thin membrane, it will spread out resulting in poor color visibility. Commercially, the nitrocellulose membrane is available in the range of 100–150 μm thickness (Mansfield 2009).

Pore size is directly related to the particle retention capabilities of the paper. Pore size can be determined experimentally using the bubble point method (Yu et al. 2010). In this method, after soaking the porous structure of the membrane into liquid, air pressure is applied to transport the fluid into the pores of the membrane. The minimum pressure at which first air bubble is formed corresponds to the largest diameter of the pore in the filtration direction of the membrane, known as bubble point. At this point, the nominal pore size can be calculated from the following equation: $d = \frac{4\gamma \cos\theta}{P}$, where d is the average pore diameter, γ is the liquid surface tension, P is the minimum air pressure required to reopen the pore and θ is the

Table 2.1 Different types of paper substrates and their characteristics

Paper types	Characteristics	Applications
Whatman Filter paper grade 1	Fibrous structure, weight: 88 g m^{-2}, particle retention: >11 μm, thickness: 180 μm, porosity: 10.5 s	Detection of glucose (Kumar et al. 2017), lactate, uric Acid (Kumar et al. 2016)
Whatman Filter paper grade 2	Fibrous structure, weight: 103 g m^{-2}, particle retention: >8 μm, thickness: 190 μm	Monitoring of contaminants in the atmosphere, soil testing
Whatman Filter paper grade 3	Highly absorbent, Fibrous structure, weight: 187 g m^{-2} particle retention: >6 μm, thickness: 390 μm, porosity: 26 s	Suitable for suction filtration, used in Büchner funnels
Whatman Filter paper grade 4	Fibrous structure, weight: 96 g m^{-2}, particle retention: >25 μm, thickness: 205 μm, porosity: 3.7 s	Detection of nitrite ion (NO_2-) (Li et al. 2010)
Nitrocellulose membrane	Granular structure, reasonably uniform pore size, particle retention: >0.02 μm	Lateral flow assay, e.g. immobilization of antibody/antigen (Yen et al. 2015), DNA, enzymes, etc.
Cellulose glossy paper	Made of cellulose fiber blended with an inorganic filler, non-degradable and relatively smoother surface	Detection of ethanol (Arena et al. 2010)
Bioactive paper	Obtained by the modification of paper matrix with biomolecules	Detection of Pathogens (Pelton 2009)

contact angle between the liquid and pore wall. In actual condition, membranes contain a range of pore sizes known as pore size distribution (PSD) of the membrane. Using the PSD, the capillary flow rate can be estimated as a function of the pore size (Yetisen et al. 2013).

Porosity, a non-dimensional quantity is an inherent characteristic of the porous paper substrate. It is a measure of the extent to which its surface allows the penetration of a gas or liquid. It represents the volume fraction of open space in the paper substrate (Singh et al. 2017). Porosity can be obtained experimentally by measuring the volume of liquid absorbed by the paper substrate (Parolo et al. 2013). In this method, a paper strip of specific dimensions is dipped into a known amount of fluid such as phosphate-buffered saline (PBS). Then, the change in volume of liquid (pore volume) is measured after the strip is taken out. Finally, porosity can be calculated empirically by calculating the ratio of pore volume and the total volume of the paper.

The permeability of a porous substrate is a physical parameter that characterizes the degree of resistance to fluid flow (Rudman and Patterson 2001). The air permeability is partially dependent on the porosity. For fiber porous materials (Fig. 2.1a), it can be estimated using the following empirical relation (Van der Westhuizen and Du Plessis 1996):

$$k = r_f^2 \frac{\pi\varphi(1-\sqrt{1-\varphi})^2}{24(1-\varphi)^{1.5}} \tag{2.1}$$

where r_f is the average fiber radius. For random fibrous media, the permeability can also be calculated using the following permeability-porosity correlation (Nabovati et al. 2009).

$$k = C_1 r_f^2 \left(\sqrt{\frac{1-\varphi_c}{1-\varphi}} - 1 \right)^{C_2} \tag{2.2}$$

where φ_c is the critical value of porosity, and C_1 and C_2 are the geometrical factors of the network. Also, for the granular isotropic porous materials such as nitrocellulose membrane (Fig. 2.1d), permeability can be predicted through the Kozeny-Carman equation (Bear 2013; Choi et al. 2016).

$$k = \frac{d^2\varphi^3}{180(1-\varphi)^2} \tag{2.3}$$

2.2 Fluid Transport

Paper microfluidics deals with the fluid flow without any requirement of external force. The capillary action is the driving force for the passive movement of fluid through the paper substrate. The interaction between the paper and contacting surface of the fluid is generally governed by two opposite forces, i.e., cohesive force and adhesive force. When fluid is brought in contact with the paper, there is an intermolecular interaction between liquid molecules at the liquid–air interface (cohesion) and also between the solid-liquid interfaces (adhesion). The adhesive force is responsible for spreading of the liquid on to the porous substrate while the cohesive force such as surface tension is responsible for the reduction in the area of the liquid-air interface. So, the fluid flow occurs only when the effect of adhesion surpasses that of cohesion. The wicking depends on various physical and geometrical properties of porous media such as paper materials, the structure of the paper, pore size, permeability, paper size and shape and also on the physical properties of the liquid. In general fluid transport can be categorized in two groups namely, wet-out process and the fully wetted flow. In the first kind of flow, the fluid front is wicking along the dry porous media and can be modelled using the classical Lucas-Washburn equation. In the second case, the fluid transport occurs along the wetted porous media and is governed by the Darcy's law.

2.2.1 Classical Lucas-Washburn Equation (Capillary Flow)

Let us consider a rectangular porous paper strip of length L, uniform width w and thickness h. r_a is the average pore radius of the paper. When a small amount of liquid is dropped onto the paper substrate, three types of interfacial layer is formed due to surface tension, i.e., solid-liquid interface, liquid-vapor interface, and vapor-solid interface. The relationships between these interfacial surface tensions in an equilibrium condition (Fig. 2.2a) may be described as $\gamma_{SL} + \gamma_{LV} \cos\theta = \gamma_{SV}$, where γ_{SL},γ_{LV} and γ_{SV} are the interfacial surface tension (energy per unit area) between solid-liquid, liquid-vapor and vapor-solid interface respectively, and θ is the angle between the tangent of the liquid-vapor interface and the surface at the point of contact, known as contact angle. The contact angle is a measure of the shape of a liquid droplet on a solid surface. Generally, there are two types of liquid droplets, i.e., 'wetting' droplet $(\theta < 90°)$ and 'nonwetting' droplet $(\theta > 90°)$ and depending on its value, the surface can be either hydrophilic (liquid can wet the surface) or hydrophobic (liquid repellent surface). The chemical composition of the solid surface and liquid are the critical parameters for the contact angle.

The capillary pressure which is equal to pressure difference at liquid-solid (paper) interface in the wetted region is governed by the Laplace pressure (Washburn 1921),

$$\mathrm{P_c} = \frac{2\gamma\cos\theta}{\mathrm{r_a}} \tag{2.4}$$

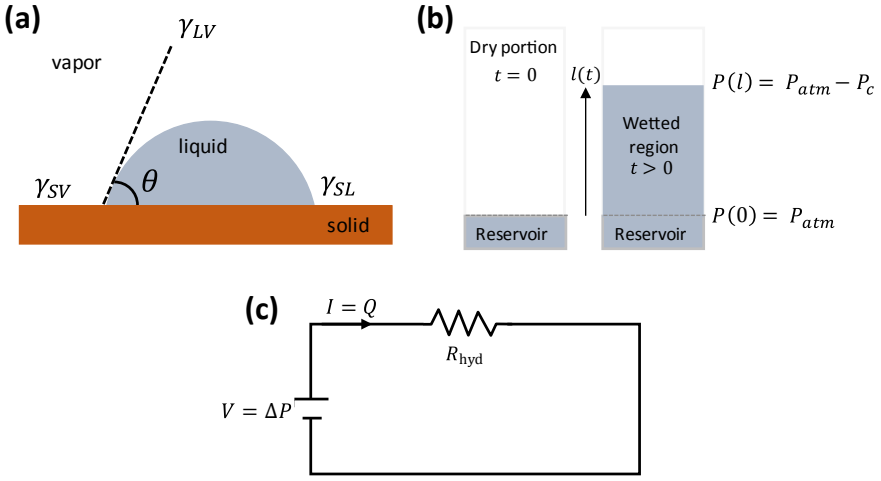

Fig. 2.2 **a** Surface tension force balance at a three-phase contact line between a liquid droplet, its vapor, and a non-deformable solid surface. **b** Schematic of fluid flow in a paper strip (porous media) through capillary action. **c** Electrical circuit analogy (Ohm's law) for fluid transport in a paper-based fluidic circuit