Chapter 10

Opto-Smart Systems in Microfluidics

Larisa Florea
Centre for Data Analytics, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland

Dermot Diamond
Centre for Data Analytics, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland

Fernando Benito-Lopez
Microfluidics UPV/EHU Cluster, Analytical Chemistry Department, University of the Basque Country UPV/EHU, Spain

ABSTRACT

The possibility of using photo-stimulus to control flow in microfluidics devices is very appealing as light can provide contactless stimulation, is biocompatible and can be applied in a non-invasive and highly precise manner. One of the most popular ways to achieve photo-control flow in microfluidic channels is throughout the use of photo-responsive molecules. We review here the different principles and strategies of using photo-responsive molecules to induce or control liquid motion using light, which include the use of photo-controlled polymeric actuators, photo-sensitive coatings, or photo-sensitive surfactants. We further analyse the capability of these approaches to induce flow control throughout the photo-operation of valves, photo-control of electro-osmotic flows or photo-manipulation of discrete microliter-sized droplets.

INTRODUCTION

The intrinsic features of microfluidic devices ensure two main characteristics during an analytical process: low consumption of reagents and sample as well as rapid and repeatable analysis protocols (Martinez, Phillips, Whitesides, & Carrilho, 2010). However, to date, extensive chemical and biological tasks need to be carried out outside the microfluidic device to prepare and pre-process samples prior microfluidic manipulation as conventional lab-on-a-chip devices are not yet suitable for non-ideal sample analysis (Gonzalez Crevillen, Hervas, Angel Lopez, Cristina Gonzalez, & Escarpa, 2007). These tasks include

DOI: 10.4018/978-1-5225-0066-7.ch010

sampling, pre-concentration, fluorescence labelling, filtration, mixing, sample analysis, as well as many other techniques that require manpower and are very time-consuming (Argentiere, Gigli, Mortato, Gerges, & Blasi, 2012).

Therefore, the main aim is to realise downscaling of these conventional tasks within the microfluidic devices and consequently develop innovative systems capable of preparing and/or analysis of samples "on-chip". If these functions could be integrated within the microfluidic device, then time and costs would be reduced and high throughput and high degree of automation would be realised (R. Byrne, Benito-Lopez, & Diamond, 2010). For this purpose two main ways of investigation are considered: an "evolutionary" and a "revolutionary" approach.

The "evolutionary" approach involves tremendous downscale of conventional units, and their assembly level by level to achieve the desired functionalities (Abgrall & Gue, 2007; Laser & Santiago, 2004; Psaltis, Quake, & Yang, 2006). However, microfluidic systems developed to date according to this approach, generally require complicated control systems and are by far from being trivial and widely accessible.

The "revolutionary" approach in the area of microfluidics is recently emerging and consists in the incorporation of stimuli-responsive materials into microfluidic devices, to obtain smart, functional, highly controllable components integrated in the microfluidic device (F. Benito-Lopez et al., 2010; M. Czugala, Ziolkowski, Byrne, Diamond, & Benito-Lopez, 2011; Florea, Diamond, & Benito-Lopez; Florea, Hennart, Diamond, & Benito-Lopez, 2012; Ziółkowski, Czugala, & Diamond, 2012). For instance, the use of a light stimulus in microfluidic systems is appealing because it can be applied precisely in different sections within a microdevice, in a non-invasive manner.

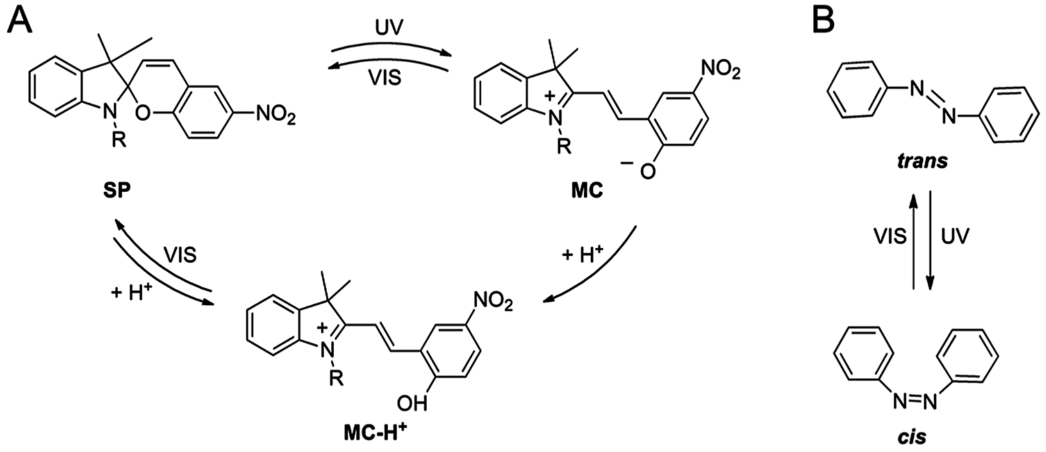
The possibility of controlling flow in microfluidics using opto-stimulus will offer new platforms with unprecedented flexibility and improved versatility. Some recent reviews have already been devoted to specific aspects of this field (R. Byrne et al., 2010; M. Chen et al., 2011; M. Czugala et al., 2011; Padgett & Di Leonardo, 2011). The use of holographic optical tweezers for optical manipulation, actuation and sensing in lab-on-chip systems was described by Padgett and Di Leonardo (Padgett & Di Leonardo, 2011). Other recent review by Baigl (Baigl, 2012) describes in detail strategies to photo-actuate microfluidic systems, such as the application of the chromocapillary effect, light-induced Marangoni effects, optically induced dielectrophoresis, digital optofluidics, light-induced electro-osmosis and optoelectrowetting, among others.

Here we review the possibility of controlling flow in closed microchannels, and manipulating discrete microliter-sized droplets by employing photo- and thermo-responsive materials incorporated in microfluidic units in the form of polymeric actuators, photo-responsive coatings or photo-sensitive surfactants.

OPTO-SMART SYSTEMS INTEGRATION IN MICROFLUIDIC DEVICES

The most widely used photo-sensitive molecules for photo-actuation of liquids in microfluidics are spiropyrans and azobenzenes. These are photochromic units that change their characteristics (conformation, polarity) reversibly in response to light of particular wavelengths. When incorporated in functional units, these changes in conformation/polarity of the photochromic unit induce in turn "on demand" changes in volume (Bassetti, Chatterjee, Aluru, & Beebe, 2005; Beebe et al., 2000; Kwon, Jeong, Park, Moon, & Lee, 2011; Richter, Klatt, Paschew, & Klenke, 2009), surface chemistry (Fernando Benito-Lopez et al., 2009; Garcia et al., 2007; Higuchi et al., 2004; Samanta & Locklin, 2008), surface charge, wettability (Anastasiadis, Lygeraki, Athanassiou, Farsari, & Pisignano, 2008; Dattilo, Armelao, Fois, Mistura, &

Figure 1. Reversible structural transformations of (A) spiropyran derivatives and (B) azobenzene in response to light



Maggini, 2007; Samanta & Locklin, 2008) or interfacial tension (Diguet et al., 2009; Diguet, Li, Queyriaux, Chen, & Baigl, 2011). Spiropyrans have been investigated extensively as active components in soft photo-actuators for microfluidic valves (F. Benito-Lopez et al., 2010; S. Sugiura et al., 2007). The light-stimulated switching of spiropyran is due to the photo-cleavage of the C_{spiro}-O bond upon irradiation with UV light (Hirshberg, 1956; Minkin, 2004). This cleavage allows a conformational rearrangement between a closed, colourless spiropyran form and an opened, colourful merocyanine (MC) form (Dürr & Bouas-Laurent, 2003; Minkin, 2004) with the colour arising from a strong absorption band in the visible spectral region (Figure 1A). In contrast, exposure of the MC isomer to visible light induces reversion to the closed spiropyran form (SP); therefore, it is possible to reversibly switch between the polar (or zwitterionic), coloured MC and colourless uncharged SP forms using light irradiation. Another interesting property of spiropyrans is its sensitivity towards pH (Doron, Katz, Tao, & Willner, 1997; Lee, Song, Lee, Ryu, & Chi, 2009), under acidic conditions, the MC isomer is converted to the protonated merocyanine (MC-H^+) form (Figure 1A).

Azobenzenes are another widely used class of photochromic molecules (Gaonkar, Kumar, & Neckers, 1990; Ide, Ozama, & Matsui, 2011). Under dark conditions, azobenzene preferentially exists in its *trans*, less polar configuration. Under UV light irradiation (350–370 nm) it undergoes photo-isomerisation to its *cis*, more polar form (Figure 1B). The reverse *cis* → *trans* isomerisation can be driven by visible light or occurs thermally in the dark. It is known that azobenzenes reversibly change their geometry from a planar to a non planar upon UV irradiation, generating a width decrease in the distance between the *para* carbon atoms from 9.9 Å to 5.5 Å and a corresponding increase in the dipole moment from 0.5 D to 3.1 D (Nicoletta et al., 2012). One of the most important advantages of azobenzenes is their stability over many illumination cycles, which makes them ideal components of numerous molecular devices and functional materials (Hoffmann, Resch-Genger, & Marlow, 2000; Singleton, Ramsay, Barsan, Butler, & Barrett, 2012).

Another approach to opto-actuation in microfluidics is through photo-thermal activation. The novelty of these systems relies on using light absorbance to generate localised heating (G. Chen, Svec, & Knapp, 2008; Hua, Pal, Srivannavit, Burns, & Gulari, 2008; Lo, Zhu, & Jiang, 2011).

This chapter will discuss recent trends for the incorporation of thermo- and photo-responsive moieties (in particular spiropyrans and azobenzene) into functional units in microfluidic devices capable of responding to an external opto-stimulus. The chapter will be structured into three main sections based on different microfluidic operations that can be controlled by light, *i.e.*:

- Photo-controlled polymeric actuators,
- Photo-controlled electro-osmotic flow,
- Photo-manipulation of droplets.

Specific examples will be discussed in terms of the technique used for integration of the photo- activated or photo-thermo- activated unit into the microfluidic device, the impact of the photo-stimulus and the applicability of these approaches for photo-actuation of liquids or droplets in microfluidics.

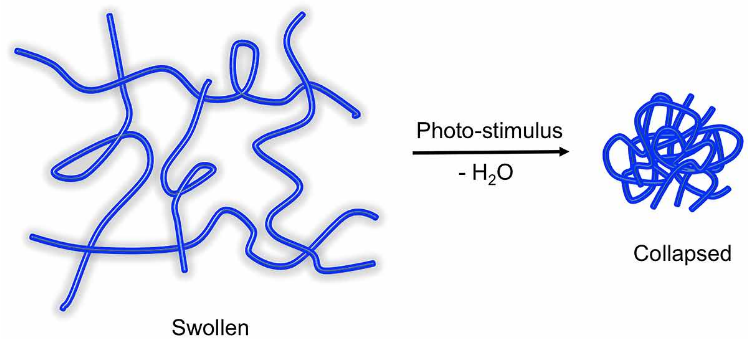
PHOTO-CONTROLLED POLYMERIC ACTUATORS

Stimuli-responsive polymers present all the advantages of polymeric materials, such as versatility, processability, low cost and amplified response to weak stimuli. Stimuli-responsive materials produce many useful effects in microfluidic systems, such as “on-demand” changes in volume (Bassetti et al., 2005; Beebe et al., 2000; Kwon et al., 2011; Richter et al., 2009), optical proprieties (Angiolini, Benelli, Giorgini, & Raymo, 2009; Ivanov, Eremeev, Wahlund, Galaev, & Mattiasson, 2002; Levy et al., 1997; Lin & Chiu, 2003; Samoladas, Bikiaris, Zorba, Paraskevopoulos, & Jannakoudakis, 2008; Stitzel, Byrne, & Diamond, 2006; Such, Evans, & Davis, 2006), permeability (Chung, Ito, & Imanishi, 1994; Park, Ito, & Imanishi, 1998) and surface chemistry (Fernando Benito-Lopez et al., 2009; Garcia et al., 2007), which in turn activate/deactivate different functions such as the capability of molecular recognition (Fernando Benito-Lopez et al., 2009; R. J. Byrne, Stitzel, & Diamond, 2006) (including capture, release and detection of analytes), autonomous control of flow rate and direction (Beebe et al., 2000; Dong & Jiang, 2007), and wettability switching (Anastasiadis et al., 2008).

The most commonly used opto-actuators in microfluidics are photo-responsive hydrogels as they have the ability to undergo volumetric changes in response to an external light stimulus (F. Benito-Lopez et al., 2010; S. Sugiura et al., 2007). A hydrogel is defined as a network of hydrophilic polymer chains that is able to swell and retain large amounts of water. In a fully-swollen hydrogel, up to 95% of its mass can consist in water that was absorbed into its three dimensional network (Alvarez-Lorenzo & Concheiro, 2008; Yoshida, Yang, Kumakura, Hagiwara, & Katakai, 1991). Hydrogels possess excellent biocompatibility and a degree of flexibility, very similar to natural tissue, due to their significant water content (He, Zuo, Xie, Huang, & Xue, 2011; Kim & Shin, 2007). Photo-responsive engineered hydrogels can be made to collapse and thereby release a percentage of their water content upon light irradiation (Figure 2).

In this context, polymeric actuators are commonly employed in microfluidic devices to provide the functionality of micro-valves. Valves are central components within microfluidic systems, being essential for directional control and movement of flows while enabling important actions, such as flow regulation, flow diversion and addition of reagents. The micro-valves developed to date can be classified in two categories, active and passive, employing mechanical, non-mechanical and external control systems (Oh & Ahn, 2006).

Figure 2. Photo-induced hydrogel shrinkage



In the case of passive valves, which do not have any moving components and are easy to fabricate, hydrogel based materials have received special attention. These valves change volume in response to external stimuli to stop/open the flow (Beebe et al., 2000; G. Chen et al., 2008; Dong & Jiang, 2007; Geiger, Pisano, & Svec, 2010).

Incorporation of photo-responsive units within hydrogel-based valves allows non-invasive, external control of the valve based on the intrinsic responsiveness of the polymer to an optical stimulus. Photo-responsive polymer materials for micro-valve applications have been studied by many research groups, and many polymers and polymer gels functionalised with azobenzene (D. Kungwatchakun, 1988), leukochromophore (M. H. M. Irie, 1985; M.Irie, 1986), and spirobenzopyran (A. Menju, 1981; F. Benito-Lopez et al., 2010; A. M. M. Irie, K. Hayashi, 1979; S. Sugiura et al., 2007) have been examined.

This section is organised as follows: Firstly, we show how smart micro-valves can be actuated by light using a light-to-heat energy conversion mechanism. In this case, a localised temperature increase is caused by light irradiation, which in turn induces volume changes of the micro-valve (usually based on hydrogels). Then, we review how photo-responsive moieties like spiropyrans and azobenzenes are incorporated into polymers to achieve photo-precise manipulation of micro-valves.

Chen *et al.* (G. Chen et al., 2008) developed a light-actuated micro-valve via photoinitiated patterned polymerisation of *N*-isopropylacrylamide (NIPAAm) within microfluidic channels. PNIPAAm is one of the best-known temperature-sensitive hydrogels, having the ability to shrink and expand due to its lower critical solution temperature (LCST)(Harmon, Kucking, & Frank, 2003; Kuckling, Harmon, & Frank, 2002; Xu, Wei, Zhang, Cheng, & Zhuo, 2007). Below the LCST (32 °C), PNIPAAm chains are hydrated by water due to the hydrogen bondings between the amide residue and on the polymer chains and the water molecules, and therefore the gel is swollen. Above this temperature hydrogen bonds between solvent molecules and water are gradually broken and polymer-polymer interactions become thermodynamically favored compared with polymer-solvent interactions. As a consequence, the PNIPAAm chains collapse sharply from a hydrophilic coil into a hydrophobic globule that precipitates in water (Dusek, 1993; Schild, 1992) and the PNIPAAm hydrogels shrink rapidly. The novelty of the approach used in Chen's PNIPAAm micro-valve relies on heating the valve from the absorption of light provided by a quartz halogen illuminator. The pressure-tolerance of the micro-valve can be tuned by changing the mechanical strength of the polymer monolith inside the microchannel through the choice of a suitable amount of monomer and crosslinker. In addition, the response time and pressure resistance of a PNIPAAm valve can be optimised by varying the tetrahydrofuran (THF) content in the polymerisation mixture. In these conditions, opening and closing response times of the valve can be modulated in the range of 4.0 to 6.2 s. The on/off switching of the valve using the quartz halogen was repeated multiple times and show no deterioration after at least 9 irradiation cycles (G. Chen et al., 2008).

Using a different approach, Lo *et al.* (Lo et al., 2011) reported the performance of an IR light-responsive micro-valve. The valve consisted of PNIPAAm hydrogel nanocomposite incorporating glycidyl methacrylate functionalised graphene oxide (GO– GMA) sheets. The valve operated in two states – OFF (closed) - adopted when the IR source is turned off and the hydrogel completely blocks the channel, and ON (opened), adopted when the IR light is turned on, due to shrinking of the hydrogel upon absorbance of the IR light by the GO–GMA sheets. The ON state could be explained as follow: GO–GMA sheets absorbed the IR radiation converting it into heat. During this process, the temperature of the system is increased above the LCST of PNIPAAm, which triggers the hydrogel to contract, allowing for fluidic flow. When the IR light is switched off the heat dissipated to the surrounding environment, the hydrogel absorbed water and expanded its volume back to the original size, blocking the flow. The performance of the hydrogel micro-valve is shown in Figure 1. The intensity of the IR light reaching the hydrogel sample in order to induce actuation is 1.21 W cm^{-2} and causes a temperature increase of the valve from 25 °C to 40 °C after 2 min of IR irradiation, which might make this type of material not appropriate for several applications including some bioanlysis. Moreover, the reversability of the photo-induced actuation is not discussed by the authors in the present paper, suggesting that this valve might be suitable for one-use only.

Independent optical control of microfluidic valves composed of optomechanically responsive nanocomposite hydrogels (poly-*N*-isopropylacrylamide-co-acrylamide) was achieved using strongly absorbing gold nanoparticles or nanoshells embedded in the actuator polymer (Figure 4). These nanocomposite materials respond to different wavelengths of light: while gold-colloid nanocomposite hydrogel collapses in response to green light, the gold-nanoshell nanocomposite hydrogel collapses in response to near-IR light. In both cases, the valves opened completely in less than five seconds. This approach has the advantage of allowing independent control of valves formed from composites with different nanoparticles depending on the illumination wavelength. As the phase changes in these thermo-responsive polymers are reversible, these type of valves are suitable for multiple use applications (Sershen et al., 2005).

Figure 3. A micro-valve made of GO–GMA IR-responsive hydrogel. Top- views of the micro-valve are on the left. Respective images taken under a microscope are on the right. (a) GO–GMA hydrogel micro-valve before actuated by IR irradiation (OFF state) and (b) after exposure to IR light (ON state).
Reproduced by permission of The Royal Society of Chemistry

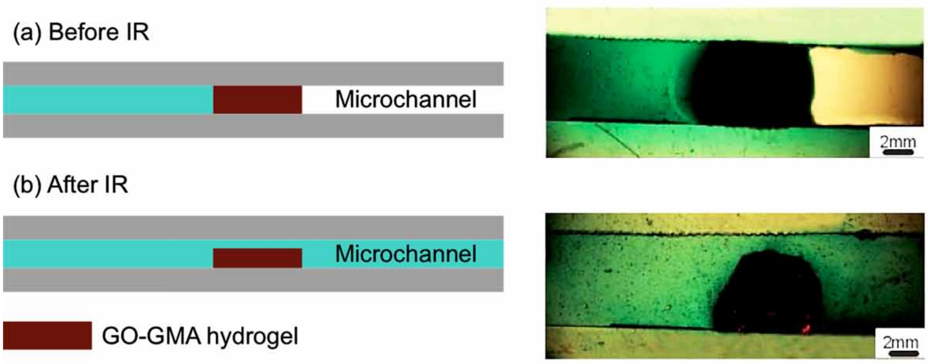
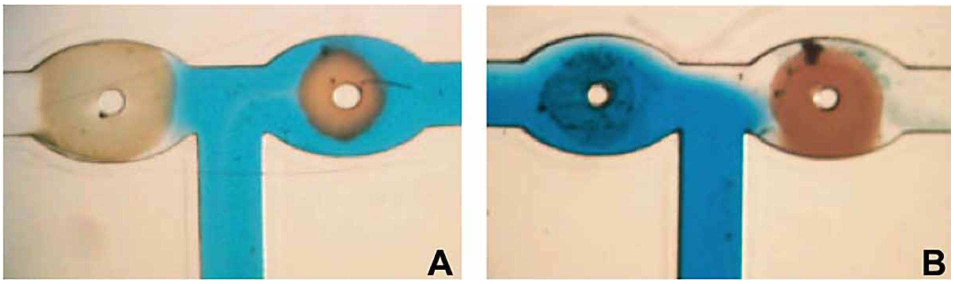


Figure 4. Two valves formed at a T-junction in a fluidics device, one made of a gold-colloid nanocomposite hydrogel and the other a gold- nanoshell nanocomposite hydrogel. The channels are 100 μm wide. a) When the entire device was illuminated with green light (532 nm, 1.6 W cm^{-2}), the gold colloid valve opened while the nano-shell valve remained closed. b) However, when the device was illuminated with near infrared light (832 nm, 2.7 W cm^{-2}), the opposite response was observed. In both cases, the valves opened within 5 s.

Sershen et al., 2005 Copyright © 2005 WILEY-VCH Verlag GmbH & Co

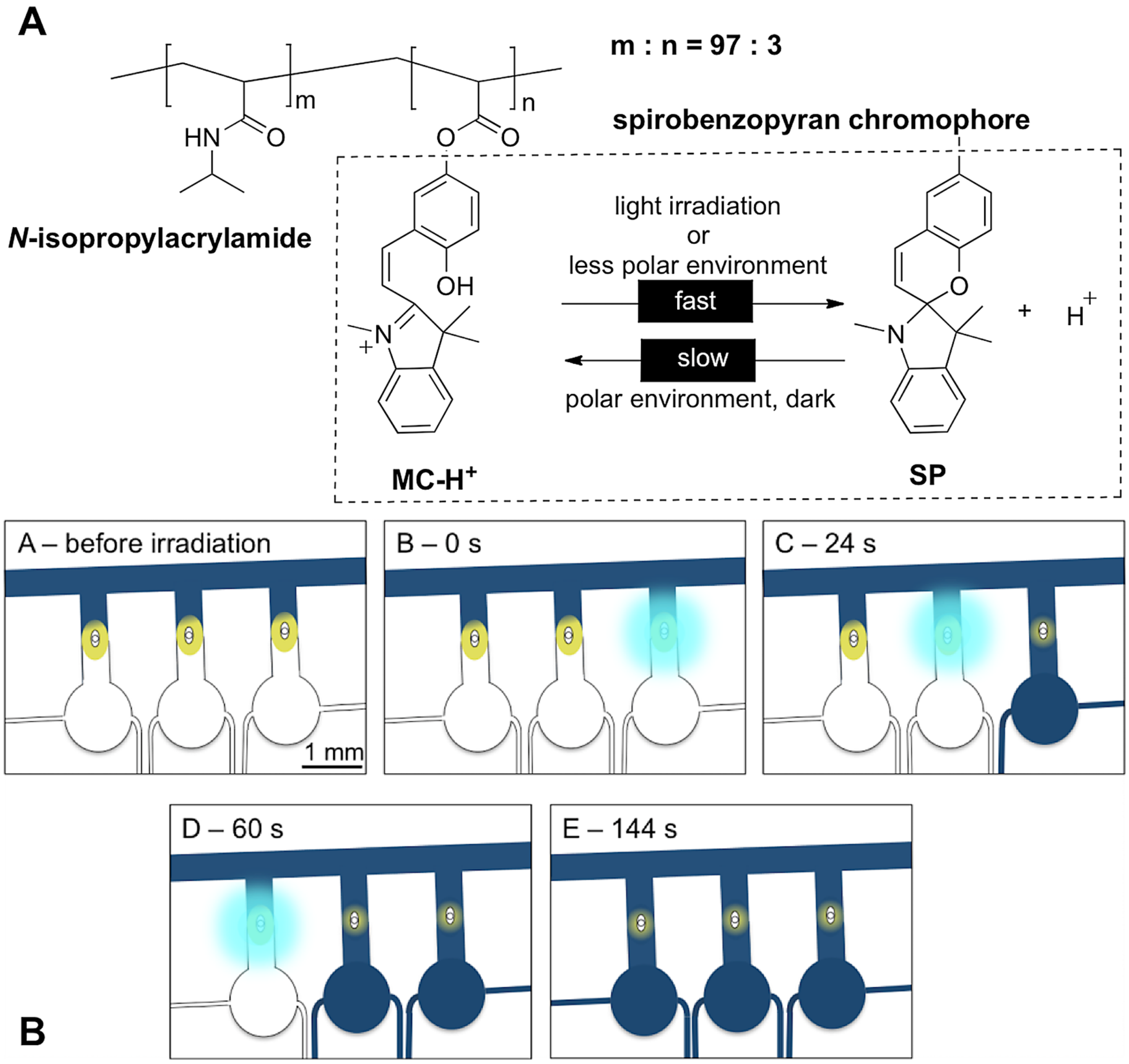


A different optically addressable micro-actuator array (microfluidic “flash memory”) with latched operation was proposed by Hua *et al.* (Hua et al., 2008). The micro-actuator array consists of individual phase-change based actuators addressed by localised heating through focused light patterns provided by a modified projector or high power laser pointer. After the initial light “writing” during which the phase is temporarily changed to a liquid form, the actuated status is self-maintained by the solid phase of the actuator without power and pressure inputs. The micro-fluidic flash memory can be re-configured by a new light illumination pattern and common pressure signal providing a flexible, energy-efficient, and low cost multiplexing solution for microfluidic applications based on physical displacements. The advantage of this approach is that the phase-change wax is fully encapsulated and thus immune from contamination issues in fluidic environments. Moreover, compared to other systems previously discussed, this optically-addressed microactuator array is reusable and thermal simulation shows that the temperature rise in the microfluidic channels when the wax melts was less than 10 °C, which should not be considered an issue for most applications.

While in all the examples described so far the key of the opto-stimulation is the conversion of photo-energy to thermal energy, photo-stimulation can also be achieved by incorporation of photo-responsive moieties in microfluidic units.

In 2004, Sumaru *et al.* (Sumaru, Kameda, Kanamori, & Shinbo, 2004) presented an actuation mechanism based on the lower critical solubility temperature (LCST) of spiropyran (3 mol %) copolymers of poly(*N*-isopropylacrylamide) (pSPNIPAM). Figure 5a shows the chemical structure of pSPNIPAM and the reversible isomerisation of the photochromic unit from the protonated merocyanine (MC-H$^+$) to the closed spiropyran form (SP) under white light irradiation. In acidic conditions (0.26 mM HCl), the spiropyran unit present in the copolymer changed from SP to the MC-H$^+$ form, which presents a strong absorption band around 422 nm. When the copolymer was irradiated with light matching the absorbance of MC-H$^+$, the MC-H$^+$ is switched back to the closed hydrophobic SP form, releasing one proton in the process (Figure 3a); As result of the formation of the more hydrophobic SP isomer, dehydration of the main polymer chain occurs. A correlated change in both absorbance at 422 nm (particular to MC-H$^+$) and specific conductance was recorded when pSPNIPAAm aqueous solution (0.10 wt %) was repeatedly irradiated with white light over three cycles.

Figure 5. (A) Chemical structure of pSPNIPAAm and characteristics of its components: pNIPAAm main chain and spirobenzopyran side chain (Sumaru et al., 2004). Copyright (2004) American Chemical Society. (B) Schematic representation of a micro-fluidic platform that contains multiple pSPNIPAAm hydrogel micro-valves. These micro-valves can be independently controlled by means of local light irradiation. A - A solution containing blue dye was introduced into the main micro-channel. B - Blue light was locally irradiated to the right side pSPNIPAAm gel micro-valve. C - The right side micro-valve was opened after 18 s blue light irradiation and after 24 s from start, the center micro-valve was locally irradiated with blue light. D - The center micro-valve was opened after 30 s blue light irradiation and after 60 s from start, blue light was locally irradiated to the left side micro-valve. E - The left side micro-valve was opened after 24 s blue light irradiation and it is shown that after 144 s from start all the chambers were filled with the blue dye solution. Adapted from ref. (Shinji Sugiura et al., 2007)



Independently controlled micro-valves made from such material, capable of photo-actuation in acidic media (0.5 mM HCl), were later demonstrated by Sugiura *et al.* (Shinji Sugiura et al., 2007). These micro-valves (Figure 5b) were fabricated through in situ polymerisation at desired positions in the micro-channels and later opened by local light irradiation. This process was found to be rather fast, with each valve opening within 18 to 30 s of light irradiation. The maximum pressure the pSPNIPAAm gel micro-valves could withstand was determined to be 30 ± 6.6 kPa. Over this pressure the gels deformed and leakage occurred.

A similar approach was presented by Benito-Lopez *et al.* (F. Benito-Lopez et al., 2010) in our laboratories, with the difference that in this case, an ionic liquid (IL) was incorporated within the pSPNIPAAm polymer matrix to produce microfluidic valves. Four different phosponium based ionic liquids incorporating different anions (dicyanoamide ($[dca]^-$), bis(trifluoro methanesulfonyl)-amide ($[NTf_2]^-$), dodecylbenzenesulfonate ($[dbsa]^-$), tosylate ($[tos]^-$)) were used and the micro-valves were produced throughout *in situ* polymerisation of the ionogels (IL + pSPNIPAAm) in micro-channels fabricated in poly(methyl methacrylate) (PMMA). After immersion of the ionogels for 2 h in 0.1 mM HCl aqueous solution, in order to allow protonation of the photochromic unit to the MC-H^+ form and to obtain a fully swollen ionogel, photo-induced dehydration kinetics were measured. It was found that the incorporation of different ILs causes different actuation behaviours of the ionogels. When used for the production of micro-valves, by simply varying the IL-component of the ionogel, different micro-valves can be tuned to open at different times using a single light source. Results showed that in the particular configuration used by the authors, the IL-free polymer gel micro-valve opens after 2 s of light irradiation, followed by the $[dca]^-$ based ionogel (4 s), the $[tos]^-$ based ionogel (18 s) and the $[dbsa]^-$ based ionogel (44 s). The slowest kinetics are given by the $[NTf_2]^-$ based ionogel (49 s) (Figure 6).

Recently, ionogel actuator microstructures based on pSPNIMAAm have been thoroughly characterized in our laboratories and their potential for micro-valve fabrication has been investigated. It was found that the photo-induced swelling and shrinking behaviour of the ionogels is strongly dependent on the nature of the ionic liquid. For example, when the $[NTf_2]^-$ based phosphonium ionogel was used, the ionogel reached the highest degree of swelling (up to 180% of its initial size) and showed rhe fastest shrinkage rate ($k_{sh} = 29 \pm 4 \times 10^{-2}\ s^{-1}$)(Monika Czugala et al., 2014)

An original approach for photo-control of fluid in microfluidics incorporating pSPNIMAAm hydrogels was described by Sugiura *et al.* (S. Sugiura et al., 2008; Shinji Sugiura et al., 2009). The authors demonstrated on-demand formation of micro-channels with arbitrary pathways by micro-patterned light irradiation of a 200 µm thick pSPNIMAAm hydrogel sheet prepared by *in situ* free radical polymerisation (Figure 7). The hydrogel layer was covalently attached to a glass slide while another glass slide containing multiple inlets and outlets was placed on top of the hydrogel sheet. Micro-patterned light irradiation was realised by means of computer-controlled maskless micro-pattern projection unit. As a result of micro-patterned light irradiation, the pSPNIMAAm hydrogel gel in the irradiated area between adjacent inlet/outlet ports shrank, forming a micro-channel between the two glass plates and allowing for fluid to flow. The effect was repeated for several channel configurations – straight, bent or serpentine. Furthermore, authors also demonstrated, in the same publication, independent and parallel flow control in a polydimethylsiloxane (PDMS) micro-channel network through the opening of targeted microvalves created with the same photoresponsive hydrogel sheet. In this system, a microfluidic device containing multiple photoresponsive micro-valves was constructed by stacking a PDMS micro-channel chip and a glass slide with mechanically fabricated through-holes on pSPNIPAAm hydrogel sheet attached to a glass plate. Parallel control of multiple micro-valves was also successfully demonstrated as two micro-valves

Figure 6. Performance of the ionogel microfluidic valves: (a) micro-valves closed; the applied vacuum is unable to pull the dyes through the microchannels. White light is applied for the time specified in each picture (b). 'No I.L.' valve is first to actuate followed by ionogels incorporating [dca]- (c), [tos]- (d), [dbsa]- (e), [NTf2]- (f), all valves are open. Numbers and arrows indicate when the channel is filled with the dye because of micro-valve actuation
F. Benito-Lopez et al., 2010. Reproduced by permission of The Royal Society of Chemistry

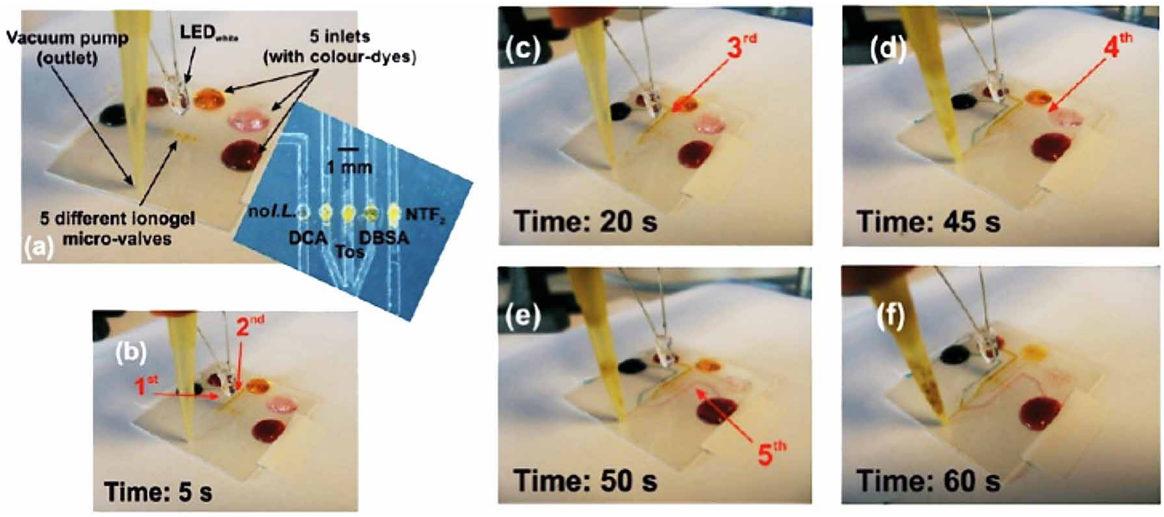
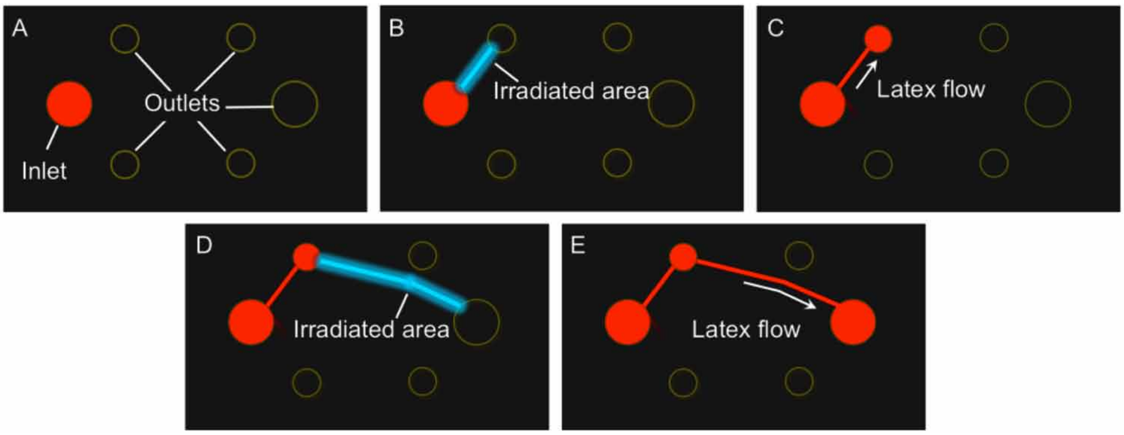


Figure 7. Schematic showing on-demand formation of microchannels with arbitrary pathways in a "universal" microfluidic system by micro-patterned light irradiation. White arrows indicate the flow direction of a fluorescently labelled latex bead suspension. A - pSPNIMAAm hydrogel sheet having one inlet and multiple outlets; B - Microchannel formation by micro-patterned light irradiation of the pSPNIPAAm hydrogel sheet; C - Latex bead suspension flowing through the microchannel after irradiation. Flow of the red coloured latex bead suspension from the inlet to the upper-left-side outlet is visible. D,E - A different sequence of micro-patterned light irradiation and microchannel formation
Adapted from S. Sugiura et al., 2008



were simultaneously opened within several minutes by micro-patterned light irradiation. As this system works in “photon mode” in contrast with “heat mode”, no interference between adjacent micro-valves was observed. Although, the isomerisation of the SP unit is a reversible phenomenon, the reswelling of the gel is still diffusion limited due to the requirement for re-protonation of SP for valve closing. As a consequence, the reswelling process takes more than one hour.

However, the main disadvantages of pSPNIMAAm based hydrogels and ionogels has been the long reswelling times (up to one hour) and the need for an external acidic source (typically HCl solution 10^{-3} M) in order to induced reprotonation of the spiropyran photochromic unit to induce reswelling of the gel. This has made pSPNIMAAm materials suitable mainly for single use application.

Recently, the need for an external acidic source has been eliminated by introducing acrylic acid (AA) as a comonomer in the polymeric chain (Ziółkowski, Florea, Theobald, Benito-Lopez, & Diamond, 2013). The newly synthesised p(SP-AA-NIPAAm) hydrogels work on the same principle as described above, however, the reswelling times become comparable with the shrinking times. Micro-valves based on this material are considered to be capable of multiple operations as the shrinking and reselling of the hydrogel is fully reversible. Moreover, the pH operation range has been extended to up to pH 7-8, making p(SP-AA-NIPAAm) based actuators suitable for biological applications.

In a different approach, a new micro-valve membrane actuator for microfluidic system applications was realised by using a crosslinked liquid-crystalline polymer (CLCP) incorporating azobenzene moieties (M. Chen et al., 2011). It was found that under UV light irradiation the valve is open while under white light irradiation the valve is closed. The time to open and close the valve can be as short as 8 s and 6 s, respectively.

PHOTO-CONTROL OF ELECTRO-OSMOTIC FLOW

When an electric field is applied along a micro-channel or micro-capillary having a charged wall, the motion of mobile counter-ions in the diffuse counter-ion layer near the channel wall induces a spontaneous global liquid motion. This movement is called electroosmotic flow (EOF) (Huang, Gordon, & Zare, 1988; Y. Liu, Fanguy, Bledsoe, & Henry, 2000; Rathore & Horvath, 1997). EOF constitutes an important component in certain chemical separation techniques, notably capillary electrophoresis (Huang et al., 1988; Y. Liu et al., 2000). There has been an increased interest in EOF in the recent years, in parallel with the development of microfluidic systems and EOF has been exploited in microfluidics to provide a degree of flow control. This approach offers a range of advantages compared to more established pumps based technologies, such as peristaltic pumps, as it creates a constant pulse-free flow in which the magnitude and direction of the flow are controlled externally, without the use of any mechanically moving parts.

EOF is strongly sensitive to the zeta potential of the channel wall and the key requirement to realise photo-controlled EOF is the ability to optically change the zeta potential of the micro-channel/micro-capillary wall. Moorthy *et al.* (Moorthy, Khoury, Moore, & Beebe, 2001) demonstrated this type of approach by using micro-channels (1000 µm wide, 20 µm deep) coated with titanium dioxide (TiO_2). TiO_2 is a direct semiconductor that exhibits a change in surface charge upon radiation with UV light, leading to variations in the zeta potential. In these conditions, electroosmotic flow modulation was recorded in the presence/absence of UV radiation. The magnitude of the change in electroosmotic flow rate due to UV irradiation was found to be pH dependent. Under optimal conditions (pH = 4.7), the authors report a change in EOF from 0 (no light) to -242 ± 60 µm s^{-1} (with light). Another strategy was later proposed by Oroszi *et al.* (L. Oroszi, Der, Kirei, Ormos, & Rakovics, 2006) who used micro-channels formed between PDMS and glass coated with cadmium sulfide (CdS) photoactive layer. Light illumination (provided by a mercury lamp filtered to 400 – 725 nm) resulted in a decreased electric field accompanied by a reduction of electroosmotic flow. Specifically, at a driving voltage of 100 V, photo-irradiation of the photo-conductor for periods of 30 s caused a decrease in the average flow velocity from 45 $\mu m\ s^{-1}$ (in the dark) to 8 $\mu m\ s^{-1}$ (under illumination). The same group later on demonstrated that introducing a pattern into the photosensitive layer enables the generation of complex flow profiles upon illumination (L. s. Oroszi, Der, Kirei, Rakovics, & Ormos, 2009).

Spiropyrans have also been used to modify the electroosmotic flow. It has recently been demonstrated in our laboratories by Scarmagnani *et al.* (Scarmagnani et al., 2010) that, under acidic conditions, electroosmotic flow (EOF) generated in a spiropyran-modified acrylate based monoliths could be modulated using light irradiation (Figure 6). In an acidic environment (HCl 1 mM) The SP-modified acrylate based monolith gained a positively charged surface due to the protonation of the SP unit to MC-H^+ (Figure 8A) and the micro-capillary adopted a yellow colour (Figure 6B). Upon irradiation with white light, MC-H^+ converted back to the non-polar SP form (Figure 6A) indicated by the change in colour of the microcapillary to colourless (Figure 6B). When the MC-H^+ form is dominant, it produces a charged surface, which enables a relatively high flow rate (up to 1.6 $\mu L\ min^{-1}$) to be generated under electroosmotic conditions. Upon exposure to white light, the concentration of MC-H^+ decreases due to the photo-conversion to the uncharged SP form, with up to 20% reduction of the EOF. The process is reversible, and removal of the light source results in a flow increase back to the original rate. A schematic of the microchip used in these experiments is shown in Figure 6C.

The ability to alter flow rates in microfluidic channels using light has very significant implications, as it could dramatically simplify the manner in which micro-flow systems are controlled.

PHOTO-MANIPULATION OF DROPLETS

Digital or droplet-based microfluidics involves the generation and manipulation of discrete droplets inside micro-devices (Teh, Lin, Hung, & Lee, 2008) and unlike continuous-flow systems, droplet-based microfluidics allows for independent control of each droplet. Droplet microfluidics encompasses two different approaches;

- Mechanisms that are much more similar to traditional microfluidics, in which droplets are carried by a carrier flow, and;
- More innovative mechanisms like electrowetting for droplet transport or the use of stimuli-responsive surfactants for directed droplet movement at the air-liquid interface.

Photo-manipulation of droplets for microfluidic purposes can be realised through the use of photosensitive molecules incorporated in surface (channel) coatings or surfactants.

In 1992 Chaudhury and Whitesides (Chaudhury & Whitesides, 1992) showed that a wettability gradient on a surface is able to induce droplet motion. In this context, if a wettability gradient of a microfluidic platform could be optically induced, then droplet movement could be realised. Given the fact that light intensity is easily manipulated, a gradient can be created by partially illuminating a substrate that exhibits photo-responsive wettability behaviour.

Figure 8. (A) SP acrylate switching in acidic environment between the MC-H$^+$ form (right) and the SP form (left) when irradiated with white light. (B) Picture of the spiropyran acrylate monolith flushed with HCl 10^{-3} M switched between the MC-H$^+$ form, in the absence of light exposure and the SP form when irradiated with white light. (C) Schematic representation of the cross section of the microchip: 1) Electrode; 2) 1.5 ml 10^{-3} M HCl reservoir; 3) PEEK tubing; 4) epoxy glue; 5) PMMA sheet 5 mm thickness; 6) layer of PSA; 7) second sheet of PMMA (0.5 mm thickness); 8) SP acrylate monolith 8 mm length; 9) white LEDs (430-760 nm)

Scarmagnani et al., 2010. Copyright © 2010 Trans Tech Publications Inc.

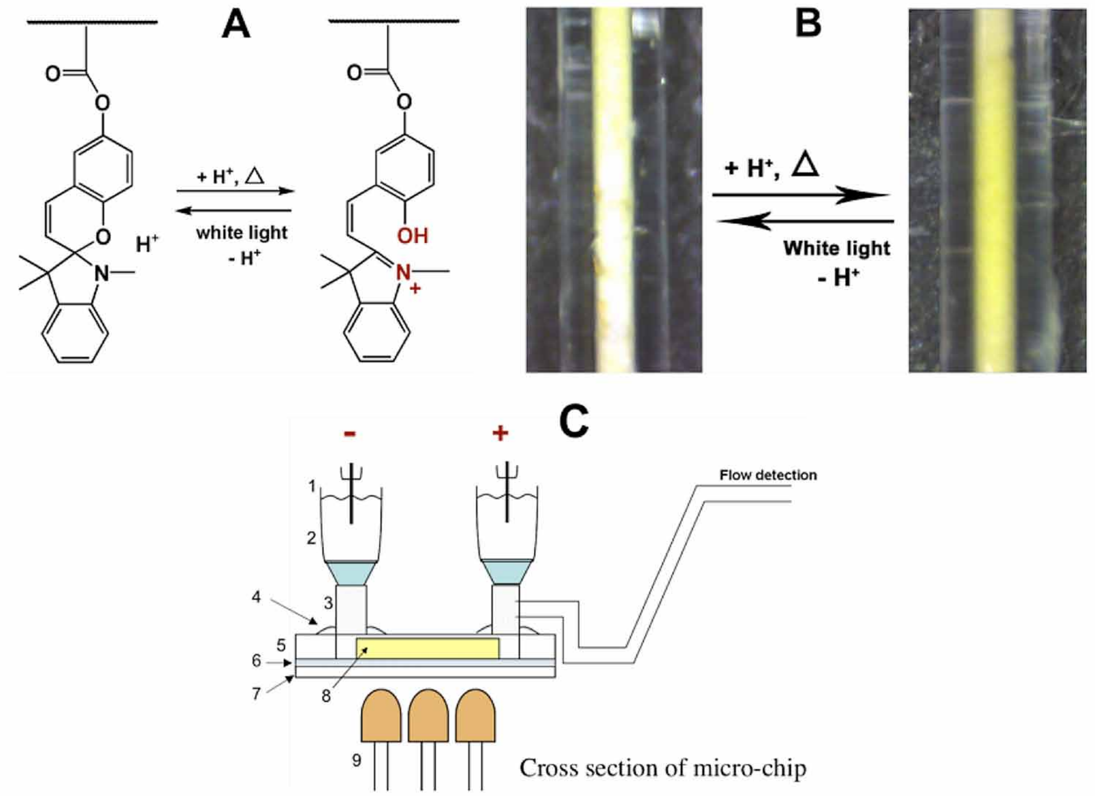


Photo-responsive surface wettability is usually achieved by functionalising with a photochromic moiety, most often azobenzenes and spiropyrans that dramatically change polarity upon photo-irradiation. Although a vast variety of photochromic coated substrates have shown to exhibit significant changes in wettability upon photo-stimulation (Anastasiadis et al., 2008; Fries, Samanta, Orski, & Locklin, 2008; Lygeraki et al., 2008; Samanta & Locklin, 2008; Wang et al., 2012), so far only a few have demonstrated droplet photo-manipulation.

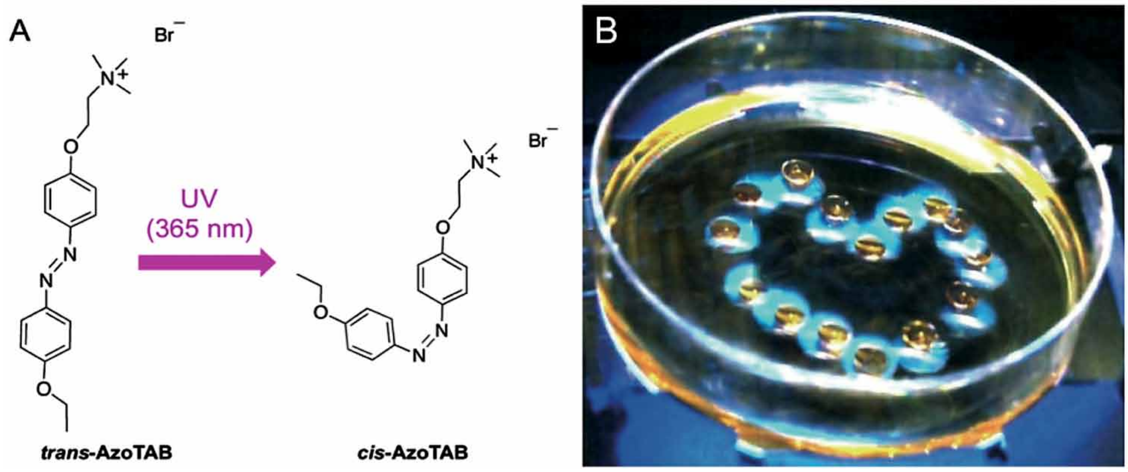
Ichimura *et al*. (Ichimura, Oh, & Nakagawa, 2000) showed the movement of an oil droplet on a flat surface modified with calix[4]resorcinarene derivative having photochromic azobenzene units. Asymmetrical photo-irradiation of this surface with different UV and visible light fluxes caused a gradient in the surface free energy due to the isomerisation of the azobenzene-containing monolayer, leading to a directional droplet movement. Although the velocity of the droplet depended intrinsically on the intensity and gradient of the light, a typical speed of 35 μL min^{-1} was observed for the motion of a 2 μL olive oil droplet. Authors also demonstrated the photo-manipulation of fluid inside a surface-modified glass tube, showing the applicability of this technique for fluid manipulation in microfluidics. Although there is no theoretical limitation in movement distance for this approach, the surface-assisted method was only demonstrated for liquids that exhibited both small-hysteresis and large photo-induced changes in contact angles upon photo-isomerisation.

More recently, similar results were reported by Yang *et al.* (D. Yang et al., 2007) using a flat surface functionalised with an azobenzene monolayer, and also by Berna *et al.* (Berna et al., 2005), using a photo-sensitive rotaxane-modified substrate (flat or tilted by 12 °C). Although promising, these photo-droplet manipulations were only demonstrated for olive oil, a few organic compounds (benzonitrile, diiodomethane, 1-Methylnaphthalene, 1,1,2,2 - Tetrachloroethane), some nematic liquid crystals, but never for water. At this stage, photo-manipulation of surface wettability cannot produce fast manipulation of a large number of individual droplets, which is required for delivering real-life applications of digital microfluidics.

Another interesting means of transporting μL-sized droplets that has been explored in recent years is the use of photo-sensitive surfactants (Diguet et al., 2009; Diguet et al., 2011). These are surfactants that incorporate a photochromic moiety, most often spiropyrans (S. L. Liu, Fujihira, & Saji, 1994; H. Sakai et al., 2007; K. Sakai, Imaizumi, Oguchi, Sakai, & Abe, 2010; Takagi, Kurematsu, & Sawaki, 1995; Takumi et al., 2007) or azobenzenes (Diguet et al., 2009; Diguet et al., 2011; Eastoe, Dominguez, Wyatt, Beeby, & Heenan, 2002; L. Yang, Takisawa, Hayashita, & Shirahama, 1995; Zhang, Wang, & Lee, 2009), although other photoswitchable moeties have also been investigated (Bonini et al., 2005; Eastoe et al., 2002).

For linear surfactants functionalised with spiropyrans or azobenzenes, UV irradiation induces isomerisation of the photochromic unit to the more polar form which causes an increase in air–water interfacial tension of up to 10 mN m^{-1} (Baigl, 2012). Diguet *et al.* (Diguet et al., 2009) explored the use of a cationic photo-sensitive surfactant that incorporates an azobenzene unit for photo-manipulation of droplets. The first demonstration was performed with an oil droplet floating on a water bath containing a cationic photo-sensitive azobenzene trimethylammonium bromide surfactant AzoTAB (Figure 7A) that is initially in the trans configuration. Partial illumination of the solution containing AzoTAB with UV light, next to the droplet, resulted in a higher surface tension in the illuminated area and the droplet could be 'pushed' along by the UV light. Contrariwise, by changing the light source to blue light, the surface tension gradient formed is in the opposite direction, causing the droplet to be 'pulled' along by the blue light. This type of droplet manipulation can be performed repeatedly, with droplet velocities of up to 300 μm s^{-1}. The authors also demonstrated that greater precision of droplet manipulation can be achieved by using simultaneous two-color illumination, wherein the center part of the droplet is under blue illumination (attraction) while the droplet periphery is surrounded by a UV light (repulsion). This two-color illumination creates a 'trap' for the droplet and therefore by moving the two-color source, the droplet can be moved at will around a desired trajectory. Figure 9B shows a superposition of a set of images which follows the path of a single droplet as it is moved along a heart-shaped trajectory at a speed of about 300 μm s^{-1}. This type of precise and fast droplet manipulation is very appealing for droplet-based analytical/microfluidic applications, as now one can imagine parallel and complex manipulation of a large number of individual μL-sized droplets using two-color location control.

Figure 9. A-Molecular structure of the photo-sensitive surfactant AzoTAB. Upon illumination at 365 nm, trans-AzoTAB isomerises to cis configuration, resulting in a more polar tail
Adapted from Diguet et al., 2009. B-Photomontages of the motion of a droplet along a heart shape trajectory. Reproduced with author's permission from www.baigllab.com



Another fascinating way of using photo-sensitive surfactants to control liquid behavior was recently demonstrated by the same group. In this case, AzoTAB was used to provide photo-induced reversible switching between a continuous two-phase laminar flow and a droplet generating regime, in microfluidic devices employing a typical water-in-oil flow focusing geometry (Diguet et al., 2011). Based on the same principle, they demonstrated that interfacial energy between flowing liquids and the microfluidic substrate could be photo-modulated. When AzoTAB was added to the aqueous phase of a two-phase laminar-flow regime (water/oil) in a microfluidic system, UV light induced fragmentation of the flow, to a regime where mono-dispersed droplets were formed. When the light stimulus was removed, the system reverted to the laminar regime. This strategy was applicable to different device morphologies and allowed many cycles of reversible and rapid switches as well as spatio-temporal control of flow regime localisation.

More recently, we have demonstrated that surfactant type molecules can be on-demand released from organic based droplets (*e.g.* droplets made of dichloromethane) through photo-manipulation of the pH of the external solution (Florea et al., 2014). This process causes a propulsion-type movement, much faster than previously reported photo-induced droplet movement with speeds up to 4000 $\mu m\ s^{-1}$. This is the first example of photodriven chemopropulsion (photo-chemopropulsion), in which photo irradiation in close proximity to the micro-vehicle (lipophilic droplet) initiates a rapid pH change in the aqueous channel fluid in which the vehicle (droplet) sits. This causes rapid solubilisation of the released lipophilic surfactant type molecule in the channel fluid and an immediate change in surface tension of the fluid surrounding the droplet resulting in fast movement (ca. 100–4000 $\mu m\ s^{-1}$) of the droplet away from the light source. Although this movement is reversible it requires a rather complex system in order to achieve photo-chemopropulsion. In this case particular chemicals are required for both the droplet and the surrounding solution making this system rather specific and not easily implemented for wide applications. Moreover, the droplet (made of dichloromethane) is susceptible to evaporation and therefore not likely to be used for long-time applications. Several approaches have been made in order to overcome these problems and chemo-propelled droplet made of ionic liquids (ILs) have been recently demonstrated by us (Francis, Fay, Florea, & Diamond, 2015). Due to the inherited no vapour pressure of the IL, these droplets are not subject to evaporation, are environmentally stable, can dissolve a vast range of chemicals and have been shown to spontaneously move in a wide range of chemical gradients in open fluidic channels, following the source of a chemoattractant (*eg*. HCl, NaCl, Na_2SO_4). Several strategies to photo-induce chemopropulsion of these IL droplets are currently under investigation in our laboratories.

CONCLUSION

The examples presented here give some indication of the potential of using an optical stimulus for photo-modulation of flow behavior in micro-fluidics by incorporating photo-responsive units into polymeric actuators, coatings, or surfactants. Although these examples can only hint at the possibilities, such as photo-modulation of flows or photo-induced droplet formation in microfluidics, the reader can gain some knowledge of the tools now available to achieve these effects. Incorporation of photo-responsive or photo-thermo-responsive molecules in microfluidics together with smart engineering of the opto-functional unit can provide switchable characteristics that have great potential for many target applications. Opto-controlled microfluidics can open new possibilities based on unprecedented flexibility, versatility, reduced costs and simplicity. Moreover, advanced features such as parallel manipulation of multiple spatially resolved photo-responsive units through the use of patterned light exposure, variable light intensities, user selectable wavelengths, and excellent temporal control, become practically realisable. This clearly opens great advantages over standard actuation methods that rely on highly complex arrays of actively moving components (pumps, valves) based on individually addressable electronic or pressure based control.

We believe that the use of opto-responsive units in microfluidics could form the basis of the new types of autonomous microfluidic-based analytical devices that are much more biomimetic in nature, and lower cost than current technologies. However, the future of opto-manipulated microfluidics relies on convincing demonstrations of their application to real scenarios in which their unique photo-controlled characteristics lead to truly disruptive platforms for studying chemical or biological processes compared to existing technologies. As for now, this field is still at an early stage and the functionality of these photo-responsive materials in real-life scenarios is yet to be demonstrated. Issues like biocompatibility, environmental stability, environmental safety and contamination are still to be addressed before these disruptive technologies can become competitive on the microfluidics market.

ACKNOWLEDGMENT

This work was partially supported by Science Foundation Ireland under INSIGHT Award SFI/12/RC/2289. F.B.-L. wants to thanks the Ramón y Cajal Programme (Ministerio de Economía y Competitividad) and the European Union's Seventh Framework Programme for research, technological development, and demonstration under Grant Agreement No. 604241.

REFERENCES

Abgrall, P., & Gue, A. M. (2007). Lab-on-chip technologies: Making a microfluidic network and coupling it into a complete microsystem - a review. *Journal of Micromechanics and Microengineering*, *17*(5), R15–R49. doi:10.1088/0960-1317/17/5/R01

Alvarez-Lorenzo, C., & Concheiro, A. (2008). Intelligent Drug Delivery Systems: Polymeric Micelles and Hydrogels. *Mini Reviews in Medicinal Chemistry*, *8*(11), 1065–1074. doi:10.2174/138955708785909952 PMID:18855723

Anastasiadis, S. H., Lygeraki, M. I., Athanassiou, A., Farsari, M., & Pisignano, D. (2008). Reversibly Photo-Responsive Polymer Surfaces for Controlled Wettability. *Journal of Adhesion Science and Technology*, *22*(15), 1853–1868. doi:10.1163/156856108X320014

Angiolini, L., Benelli, T., Giorgini, L., & Raymo, F. M. (2009). Optical and chiroptical switches based on photoinduced photon and proton transfer in copolymers containing spiropyran and azopyridine chromophores in their side chains. *Polymer*, *50*(24), 5638–5646. doi:10.1016/j.polymer.2009.10.013

Argentiere, S., Gigli, G., Mortato, M., Gerges, I., & Blasi, L. (2012). Advances in Microfluidics. In R. Kelly (Ed.), *Advances in Microfluidics*. InTech.

Baigl, D. (2012). Photo-actuation of liquids for light-driven microfluidics: State of the art and perspectives. *Lab on a Chip*, *12*(19), 3637–3653. doi:10.1039/c2lc40596b PMID:22864577

Bassetti, M. J., Chatterjee, A. N., Aluru, N. R., & Beebe, D. J. (2005). Development and modeling of electrically triggered hydrogels for microfluidic applications. *Journal of Microelectromechanical Systems*, *14*(5), 1198–1207. doi:10.1109/JMEMS.2005.845407

Beebe, D. J., Moore, J. S., Bauer, J. M., Yu, Q., Liu, R. H., Devadoss, C., & Jo, B. H. (2000). Functional hydrogel structures for autonomous flow control inside microfluidic channels. *Nature*, *404*(6778), 588–590. doi:10.1038/35007047 PMID:10766238

Benito-Lopez, F., Byrne, R., Raduta, A. M., Vrana, N. E., McGuinness, G., & Diamond, D. (2010). Ionogel-based light-actuated valves for controlling liquid flow in micro-fluidic manifolds. *Lab on a Chip*, *10*(2), 195–201. doi:10.1039/B914709H PMID:20066247

Benito-Lopez, F., Scarmagnani, S., Walsh, Z., Paull, B., Macka, M., & Diamond, D. (2009). Spiropyran modified micro-fluidic chip channels as photonically controlled self-indicating system for metal ion accumulation and release. *Sensors and Actuators. B, Chemical*, *140*(1), 295–303. doi:10.1016/j.snb.2009.03.080

Berna, J., Leigh, D. A., Lubomska, M., Mendoza, S. M., Perez, E. M., Rudolf, P., & Zerbetto, F. et al. (2005). Macroscopic transport by synthetic molecular machines. *Nature Materials*, *4*(9), 704–710. doi:10.1038/nmat1455 PMID:16127455

Bonini, M., Berti, D., Di Meglio, J. M., Almgren, M., Teixeira, J., & Baglioni, P. (2005). Surfactant aggregates hosting a photoresponsive amphiphile: Structure and photoinduced conformational changes. *Soft Matter*, *1*(6), 444–454. doi:10.1039/b511544b

Byrne, R., Benito-Lopez, F., & Diamond, D. (2010). Materials science and the sensor revolution. *Materials Today*, *13*(7-8), 9–16. doi:10.1016/S1369-7021(10)70124-3

Byrne, R. J., Stitzel, S. E., & Diamond, D. (2006). Photo-regenerable surface with potential for optical sensing. *Journal of Materials Chemistry*, *16*(14), 1332–1337. doi:10.1039/b516400a

Chaudhury, M. K., & Whitesides, G. M. (1992). How to make water run uphill. *Science*, *256*(5063), 1539–1541. doi:10.1126/science.256.5063.1539 PMID:17836321

Chen, G., Svec, F., & Knapp, D. R. (2008). Light-actuated high pressure-resisting microvalve for on-chip flow control based on thermo-responsive nanostructured polymer. *Lab on a Chip*, *8*(7), 1198–1204. doi:10.1039/b803293a PMID:18584098

Chen, M., Huang, H., Zhu, Y., Liu, Z., Xing, X., Cheng, F., & Yu, Y. (2011). Photodeformable CLCP material: Study on photo-activated microvalve applications. *Applied Physics. A, Materials Science & Processing*, *102*(3), 667–672. doi:10.1007/s00339-010-6103-4

Chung, D. J., Ito, Y., & Imanishi, Y. (1994). Preparation of porous membranes grafted with poly(spiropyran-containing methacrylate) and photocontrol of permeability. *Journal of Applied Polymer Science*, *51*(12), 2027–2033. doi:10.1002/app.1994.070511207

Crevillen, A., Hervas, M., Lopez, M., Gonzalez, M., & Escarpa, A. (2007). Real sample analysis on microfluidic devices. *Talanta*, *74*(3), 342–357. doi:10.1016/j.talanta.2007.10.019 PMID:18371648

Czugala, M., O'Connell, C., Blin, C., Fischer, P., Fraser, K. J., Benito-Lopez, F., & Diamond, D. (2014). Swelling and shrinking behaviour of photoresponsive phosphonium-based ionogel microstructures. *Sensors and Actuators. B, Chemical*, *194*, 105–113. doi:10.1016/j.snb.2013.12.072

Czugala, M., Ziolkowski, B., Byrne, R., Diamond, D., & Benito-Lopez, F. (2011). *Materials science: the key to revolutionary breakthroughs in micro-fluidic devices.*

Dattilo, D., Armelao, L., Fois, G., Mistura, G., & Maggini, M. (2007). Wetting properties of flat and porous silicon surfaces coated with a spiropyran. *Langmuir*, *23*(26), 12945–12950. doi:10.1021/la7024878 PMID:18027976

Diguet, A., Guillermic, R. M., Magome, N., Saint-Jalmes, A., Chen, Y., Yoshikawa, K., & Baigl, D. (2009). Photomanipulation of a Droplet by the Chromocapillary Effect. *Angewandte Chemie International Edition*, *48*(49), 9281–9284. doi:10.1002/anie.200904868 PMID:19890927

Diguet, A., Li, H., Queyriaux, N., Chen, Y., & Baigl, D. (2011). Photoreversible fragmentation of a liquid interface for micro-droplet generation by light actuation. *Lab on a Chip*, *11*(16), 2666–2669. doi:10.1039/c1lc20328b PMID:21727984

Dong, L., & Jiang, H. (2007). Autonomous microfluidics with stimuli-responsive hydrogels. *Soft Matter*, *3*(10), 1223–1230. doi:10.1039/b706563a

Doron, A., Katz, E., Tao, G. L., & Willner, I. (1997). Photochemically-, chemically-, and pH-controlled electrochemistry at functionalized spiropyran monolayer electrodes. *Langmuir*, *13*(6), 1783–1790. doi:10.1021/la960729e

Durr, H., & Bouas-Laurent, H. (2003). *Photochromism: Molecules and Systems*. Elsevier.

Dusek, K. (1993). Responsive gels, volume transitions I and II. In D. K. (Ed.), *Adv. Polym. Sci.* (Vol. 109 & 110).

Eastoe, J., Dominguez, M. S., Wyatt, P., Beeby, A., & Heenan, R. K. (2002). Properties of a stilbene-containing gemini photosurfactant: Light-triggered changes in surface tension and aggregation. *Langmuir*, *18*(21), 7837–7844. doi:10.1021/la0257384

Florea, L., Diamond, D., & Benito-Lopez, F. Polyaniline Coated Micro-capillaries for Continuous Flow Analysis of Aqueous Solutions. *Analytica Chimica Acta*. doi:10.1016/j.aca.2012.11.027 PMID:23260671

Florea, L., Hennart, A., Diamond, D., & Benito-Lopez, F. (2012). Synthesis and characterisation of spiropyran-polymer brushes in micro-capillaries: Towards an integrated optical sensor for continuous flow analysis. *Sensors and Actuators. B, Chemical*, *175*, 92–99. doi:10.1016/j.snb.2011.12.055

Florea, L., Wagner, K., Wagner, P., Wallace, G. G., Benito-Lopez, F., Officer, D. L., & Diamond, D. (2014). Photo-Chemopropulsion–Light-Stimulated Movement of Microdroplets. *Advanced Materials*, *26*(43), 7339–7345. doi:10.1002/adma.201403007 PMID:25236879

Francis, W., Fay, C., Florea, L., & Diamond, D. (2015). Self-propelled chemotactic ionic liquid droplets. *Chemical Communications*, *51*(12), 2342–2344. doi:10.1039/C4CC09214G PMID:25562698

Fries, K., Samanta, S., Orski, S., & Locklin, J. (2008). Reversible colorimetric ion sensors based on surface initiated polymerization of photochromic polymers. *Chemical Communications*, 47, 6288–6290. doi:10.1039/b818042c PMID:19048131

Gaonkar, S. R., Kumar, G. S., & Neckers, D. C. (1990). Photochromism of azobenzene-containing polymers. 4. effect of spacer groups. *Macromolecules*, *23*(24), 5146–5148. doi:10.1021/ma00226a018

Garcia, A., Marquez, M., Cai, T., Rosario, R., Hu, Z., Gust, D., & Park, C.-D. et al. (2007). Photo-, thermally, and pH-responsive microgels. *Langmuir*, *23*(1), 224–229. doi:10.1021/la061632n PMID:17190508

Geiger, E. J., Pisano, A. P., & Svec, F. (2010). A Polymer-Based Microfluidic Platform Featuring On-Chip Actuated Hydrogel Valves for Disposable Applications. *Journal of Microelectromechanical Systems*, *19*(4), 944–950. doi:10.1109/JMEMS.2010.2048702

Harmon, M. E., Kuckling, D., & Frank, C.W. (2003). Photo-cross-linkable PNIPAAm copolymers. 5. Mechanical properties of hydrogel layers. *Langmuir*, *19*(26), 10660–10665. doi:10.1021/la030232m

He, L., Zuo, Q., Xie, S., Huang, Y., & Xue, W. (2011). Intelligent hydrogels for drug delivery system. *Recent Patents on Drug Delivery & Formulation*, *5*(3), 265–274. doi:10.2174/187221111797200533 PMID:21834779

Higuchi, A., Hamamura, A., Shindo, Y., Kitamura, H., Yoon, B. O., Mori, T., & Umezawa, A. et al. (2004). Photon-modulated changes of cell attachments on poly(spiropyran-co-methyl methacrylate) membranes. *Biomacromolecules*, *5*(5), 1770–1774. doi:10.1021/bm049737x PMID:15360286

Hirshberg, Y. (1956). Reversible formation and eradication of colors by irradiation at low temperatures - a photochemical memory model. *Journal of the American Chemical Society*, *78*(10), 2304–2312. doi:10.1021/ja01591a075

Hoffmann, K., Resch-Genger, U., & Marlow, F. (2000). Photoinduced switching of nanocomposites consisting of azobenzene and molecular sieves: Investigation of the switching states. *Microporous and Mesoporous Materials*, *41*(1-3), 99–106. doi:10.1016/S1387-1811(00)00277-8

Hua, Z., Pal, R., Srivannavit, O., Burns, M. A., & Gulari, E. (2008). A light writable microfluidic "flash memory": Optically addressed actuator array with latched operation for microfluidic applications. *Lab on a Chip*, *8*(3), 488–491. doi:10.1039/b712983a PMID:18305870

Huang, X. H., Gordon, M. J., & Zare, R. N. (1988). Current-monitoring method for measuring the electroosmotic flow-rate in capillary zone electrophoresis. *Analytical Chemistry*, *60*(17), 1837–1838. doi:10.1021/ac00168a040

Ichimura, K., Oh, S. K., & Nakagawa, M. (2000). Light-driven motion of liquids on a photoresponsive surface. *Science*, *288*(5471), 1624–1626. doi:10.1126/science.288.5471.1624 PMID:10834837

Ide, T., Ozama, Y., & Matsui, K. (2011). Photochemistry of azobenzene in sol-gel systems. *Journal of Non-Crystalline Solids*, *357*(1), 100–104. doi:10.1016/j.jnoncrysol.2010.09.009

Irie, M., & Hosoda, M. (1985). Photoresponsive polymers—reversible solution viscosity change of poly(N,N-dimethylacrylamide) with pendant triphenyl- methane leucohydroxide residues in methanol. *Die Makromolekulare Chemie. Rapid Communications*, *6*(8), 533–536. doi:10.1002/marc.1985.030060803

Irie, M., & Kunwatchakun, D. (1986). Photoresponsivepolymers.8.Reversiblephoto- stimulated dilation of polyacrylamide gels having triphenylmethane leuco derivatives. *Macromolecules*, *19*(10), 2476–2480. doi:10.1021/ma00164a003

Irie, M., Menju, A., & Hayashi, K. (1979). Photoresponsive polymers. reversible solution viscosity change of poly (methyl methacrylate) having spiroben- zopyran side groups. *Macromolecules*, *12*(6), 1176–1180. doi:10.1021/ma60072a032

Ivanov, A. E., Eremeev, N. L., Wahlund, P. O., Galaev, I. Y., & Mattiasson, B. (2002). Photosensitive copolymer of N-isopropylacrylamide and methacryloyl derivative of spyrobenzopyran. *Polymer, 43*(13), 3819-3823. doi:10.1016/s0032-3861(02)00191-x

Kim, B., & Shin, Y. (2007). pH-sensitive swelling and release behaviors of anionic hydrogels for intelligent drug delivery system. *Journal of Applied Polymer Science*, *105*(6), 3656–3661. doi:10.1002/app.26450

Kuckling, D., Harmon, M. E., & Frank, C. W. (2002). Photo-cross-linkable PNIPAAm copolymers. 1. Synthesis and characterization of constrained temperature-responsive hydrogel layers. *Macromolecules*, *35*(16), 6377–6383. doi:10.1021/ma0203041

Kungwatchakun, D., & Irie, M. (1988). Photoresponsive polymers—photocontrol of the phase-separation temperature of aqueous-solutions of poly N-isopropylacrylamide-co-N-(4-phenylazophenyl)acrylamide. *Die Makromolekulare Chemie. Rapid Communications*, *9*(4), 243–246. doi:10.1002/marc.1988.030090408

Kwon, G. H., Jeong, G. S., Park, J. Y., Moon, J. H., & Lee, S.-H. (2011). A low-energy-consumption electroactive valveless hydrogel micropump for long-term biomedical applications. *Lab on a Chip*, *11*(17), 2910–2915. doi:10.1039/c1lc20288j PMID:21761057

Laser, D. J., & Santiago, J. G. (2004). A review of micropumps. *Journal of Micromechanics and Microengineering, 14*(6), R35-R64. doi:10.1088/0960-1317/14/6/r01

Lee, C. W., Song, Y. H., Lee, Y., Ryu, K. S., & Chi, K. W. (2009). Reversible photochromic switch ensemble and its photoimaging using H+ transfer between spiropyran and fluorescein in a polymer matrix. *Chemical Communications*, 41, 6282–6284. doi:10.1039/b913096a PMID:19826695

Levy, D., DelMonte, F., Oton, J. M., Fiksman, G., Matias, I., Datta, P., & Lopez-Amo, M. (1997). Photochromic doped sol-gel materials for fiber-optic devices. *Journal of Sol-Gel Science and Technology*, *8*(1-3), 931–935. doi:10.1007/BF02436963

Lin, J. S., & Chiu, H. T. (2003). Photochromic behavior of spiropyran and fulgide in thin films of blends of PMMA and SBS. *Journal of Polymer Research-Taiwan*, *10*(2), 105–110. doi:10.1023/A:1024940921678

Liu, S. L., Fujihira, M., & Saji, T. (1994). Formation of an organic thin-film by photochemical isomerization of a surfactant with a spiropyran moiety. *Journal of the Chemical Society. Chemical Communications*, 16, 1855–1856. doi:10.1039/c39940001855

Liu, Y., Fanguy, J. C., Bledsoe, J. M., & Henry, C. S. (2000). Dynamic coating using polyelectrolyte multilayers for chemical control of electroosmotic flow in capillary electrophoresis microchips. *Analytical Chemistry*, *72*(24), 5939–5944. doi:10.1021/ac000932l PMID:11140760

Lo, C.-W., Zhu, D., & Jiang, H. (2011). An infrared-light responsive graphene-oxide incorporated poly(N-isopropylacrylamide) hydrogel nanocomposite. *Soft Matter*, *7*(12), 5604–5609. doi:10.1039/c1sm00011j

Lygeraki, M. I., Tsiranidou, E., Anastasiadis, S. H., Fotakis, C., Pisignano, D., Cingolani, R., & Athanassiou, A. (2008). Controlling the reversible wetting capability of smart photochromic-polymer surfaces by micro patterning. *Applied Physics. A, Materials Science & Processing*, *91*(3), 397–401. doi:10.1007/s00339-008-4473-7

Martinez, A. W., Phillips, S. T., Whitesides, G. M., & Carrilho, E. (2010). Diagnostics for the Developing World: Microfluidic Paper-Based Analytical Devices. *Analytical Chemistry*, *82*(1), 3–10. doi:10.1021/ac9013989 PMID:20000334

Menju, A., Hayashi, K., & Irie, M. (1981). Photoresponsive polymers. 3. Reversible solution viscosity change of poly(methacrylic acid) having spirobenzopy- ran pendant groups in methano. *Macromolecules*, *14*(3), 755–758. doi:10.1021/ma50004a055

Minkin, V. I. (2004). Photo-, thermo-, solvato-, and electrochromic spiroheterocyclic compounds. *Chemical Reviews*, *104*(5), 2751–2776. doi:10.1021/cr020088u PMID:15137806

Moorthy, J., Khoury, C., Moore, J. S., & Beebe, D. J. (2001). Active control of electroosmotic flow in microchannels using light. *Sensors and Actuators. B, Chemical*, *75*(3), 223–229. doi:10.1016/S0925-4005(01)00557-3

Nicoletta, F. P., Cupelli, D., Formoso, P., De Filpo, G., Colella, V., & Gugliuzza, A. (2012). Light Responsive Polymer Membranes: A Review. *Membranes*, *2*(1), 134–197. doi:10.3390/membranes2010134 PMID:24957966

Oh, K. W., & Ahn, C. H. (2006). A review of microvalves. *Journal of Micromechanics and Microengineering*, *16*(5), R13–R39. doi:10.1088/0960-1317/16/5/R01

Oroszi, Laszlo, Der, Andras, Kirei, Huba, Ormos, Pal, & Rakovics, Vilmos. (2006). Control of electroosmostic flow by light. *Applied Physics Letters, 89*(26). doi:10.1063/1.2424648

Oroszi, L., Dér, A., Kirei, H., Rakovics, V., & Ormos, P. (2009). Manipulation of microfluidic flow pattern by optically controlled electroosmosis. *Microfluidics and Nanofluidics*, *6*(4), 565–569. doi:10.1007/s10404-008-0346-9

Padgett, M., & Di Leonardo, R. (2011). Holographic optical tweezers and their relevance to lab on chip devices. *Lab on a Chip*, *11*(7), 1196–1205. doi:10.1039/c0lc00526f PMID:21327211

Park, Y. S., Ito, Y., & Imanishi, Y. (1998). Photocontrolled gating by polymer brushes grafted on porous glass filter. *Macromolecules*, *31*(8), 2606–2610. doi:10.1021/ma9605199

Psaltis, D., Quake, S. R., & Yang, C. (2006). Developing optofluidic technology through the fusion of microfluidics and optics. *Nature*, *442*(7101), 381–386. doi:10.1038/nature05060 PMID:16871205

Rathore, A. S., & Horvath, C. (1997). Capillary electrochromatography: Theories on electroosmotic flow in porous media. *Journal of Chromatography. A*, *781*(1-2), 185–195. doi:10.1016/S0021-9673(97)00627-4 PMID:9368385

Richter, A., Klatt, S., Paschew, G., & Klenke, C. (2009). Micropumps operated by swelling and shrinking of temperature-sensitive hydrogels. *Lab on a Chip*, *9*(4), 613–618. doi:10.1039/B810256B PMID:19190798

Sakai, H., Ebana, H., Sakai, K., Tsuchiya, K., Ohkubo, T., & Abe, M. (2007). Photo-isomerization of spiropyran-modified cationic surfactants. *Journal of Colloid and Interface Science*, *316*(2), 1027–1030. doi:10.1016/j.jcis.2007.08.042 PMID:17884070

Sakai, K., Imaizumi, Y., Oguchi, T., Sakai, H., & Abe, M. (2010). Adsorption Characteristics of Spiropyran-Modified Cationic Surfactants at the Silica/Aqueous Solution Interface. *Langmuir*, *26*(12), 9283–9288. doi:10.1021/la100161a PMID:20225812

Samanta, S., & Locklin, J. (2008). Formation of photochromic spiropyran polymer brushes via surface-initiated, ring-opening metathesis polymerization: Reversible photocontrol of wetting behavior and solvent dependent morphology changes. *Langmuir*, *24*(17), 9558–9565. doi:10.1021/la8017387 PMID:18642863

Samoladas, A., Bikiaris, D., Zorba, T., Paraskevopoulos, K. M., & Jannakoudakis, A. (2008). Photochromic behavior of spiropyran in polystyrene and polycaprolactone thin films - Effect of UV absorber and antioxidant compound. *Dyes and Pigments*, *76*(2), 386–393. doi:10.1016/j.dyepig.2006.09.012

Scarmagnani, S., Walsh, Z., Benito-Lopez, F., Macka, M., Paull, B., & Diamond, D. (2010). Incorporation of acrylate based spiropyran monoliths in micro-fluidic devices for photo-controlled electroosmotic flow. *Advances in Science and Technology*, *76*, 100–105. doi:10.4028/www.scientific.net/AST.76.100

Schild, H. G. (1992). Poly (n-isopropylacrylamide) - experiment, theory and application. *Progress in Polymer Science*, *17*(2), 163–249. doi:10.1016/0079-6700(92)90023-R

Sershen, S. R., Mensing, G. A., Ng, M., Halas, N. J., Beebe, D. J., & West, J. L. (2005). Independent optical control of microfluidic valves formed from optomechanically responsive nanocomposite hydrogels. *Advanced Materials, 17*(11), 1366. doi:10.1002/adma.200401239

Singleton, T. A., Ramsay, K. S., Barsan, M. M., Butler, I. S., & Barrett, C. J. (2012). Azobenzene Photoisomerization under High External Pressures: Testing the Strength of a Light-Activated Molecular Muscle. *The Journal of Physical Chemistry B*, *116*(32), 9860–9865. doi:10.1021/jp3060872 PMID:22799454

Stitzel, S., Byrne, R., & Diamond, D. (2006). LED switching of spiropyran-doped polymer films. *Journal of Materials Science*, *41*(18), 5841–5844. doi:10.1007/s10853-006-0289-z

Such, G. K., Evans, R. A., & Davis, T. P. (2006). Rapid photochromic switching in a rigid polymer matrix using living radical polymerization. *Macromolecules*, *39*(4), 1391–1396. doi:10.1021/ma052002f

Sugiura, S., Sumaru, K., Ohi, K., Hiroki, K., Takagi, T., & Kanamori, T. (2007). Photoresponsive polymer gel microvalves controlled by local light irradiation. *Sensors and Actuators. A, Physical*, *140*(2), 176–184. doi:10.1016/j.sna.2007.06.024

Sugiura, S., Sumaru, K., Ohi, K., Hiroki, K., Takagi, T., & Kanamori, T. (2007). Photoresponsive polymer gel microvalves controlled by local light irradiation. *Sensors and Actuators. A, Physical*, *140*(2), 176–184. doi:10.1016/j.sna.2007.06.024

Sugiura, S., Szilagyi, A., Sumaru, K., Hattori, K., Takagi, T., Filipcsei, G., & Kanamori, T. et al. (2009). On-demand microfluidic control by micropatterned light irradiation of a photoresponsive hydrogel sheet. *Lab on a Chip*, *9*(2), 196–198. doi:10.1039/B810717C PMID:19107273

Sugiura, S., Szilágyi, A., Sumaru, K., Takagi, T., Zrínyi, M., & Kanamori, T. (2008). On-demand fluid control on microchip by micro-patterned light irradiation using photo-responsive hydrogels. *Paper presented at the Twelfth International Conference on Miniaturized Systems for Chemistry and Life Sciences*, San Diego, California, USA.

Sumaru, K., Kameda, M., Kanamori, T., & Shinbo, T. (2004). Reversible and Efficient Proton Dissociation of Spirobenzopyran-Functionalized Poly(N-isopropylacrylamide) in Aqueous Solution Triggered by Light Irradiation and Temporary Temperature Rise. *Macromolecules*, *37*(21), 7854–7856. doi:10.1021/ma0487249

Takagi, K., Kurematsu, T., & Sawaki, Y. (1995). Photochromic behavior of surfactant spiro 2h-1-benzopyran-2,2' 2,3 -dihydroindole s (spiropyrans) adsorbed into clay interlayers. *Journal of the Chemical Society-Perkin Transactions*, *2*(8), 1667–1671. doi:10.1039/p29950001667

Takumi, K., Sakamoto, H., Uda, R. M., Sakurai, Y., Kume, H., & Kimura, K. (2007). Photocontrol of anionic micelles containing lipophilic crowned spirobenzopyran. *Colloids and Surfaces a-Physicochemical and Engineering Aspects, 301*(1-3), 100-105. doi:10.1016/j.colsurfa.2006.12.029

Teh, S.-Y., Lin, R., Hung, L.-H., & Lee, A. P. (2008). Droplet microfluidics. *Lab on a Chip*, *8*(2), 198–220. doi:10.1039/b715524g PMID:18231657

Wang, D., Jiao, P., Wang, J., Zhang, Q., Feng, L., & Yang, Z. (2012). Fast photo-switched wettability and color of surfaces coated with polymer brushes containing spiropyran. *Journal of Applied Polymer Science*, *125*(2), 870–875. doi:10.1002/app.36254

Xu, X.-D., Wei, H., Zhang, X.-Z., Cheng, S.-X., & Zhuo, R.-X. (2007). Fabrication and characterization of a novel composite PNIPAAm hydrogel for controlled drug release. *Journal of Biomedical Materials Research. Part A*, *81A*(2), 418–426. doi:10.1002/jbm.a.31063 PMID:17117471

Yang, D., Piech, M., Bell, N. S., Gust, D., Vail, S., Garcia, A. A., & Picraux, S. T. et al. (2007). Photon control of liquid motion on reversibly photoresponsive surfaces. *Langmuir*, *23*(21), 10864–10872. doi:10.1021/la701507r PMID:17803327

Yang, L., Takisawa, N., Hayashita, T., & Shirahama, K. (1995). Colloid-chemical characterization of the photosurfactant 4-ethylazobenzene 4'-(oxyethyl)trimethylammonium bromide. *Journal of Physical Chemistry*, *99*(21), 8799–8803. doi:10.1021/j100021a054

Yoshida, M., Yang, J. S., Kumakura, M., Hagiwara, M., & Katakai, R. (1991). Artificially intelligent hydrogels responding to external stimuli such as temperature and ph. *European Polymer Journal*, *27*(9), 997–1005. doi:10.1016/0014-3057(91)90048-S

Zhang, J., Wang, S.-C., & Lee, C. T. Jr. (2009). Photoreversible Conformational Changes in Membrane Proteins Using Light-Responsive Surfactants. *The Journal of Physical Chemistry B*, *113*(25), 8569–8580. doi:10.1021/jp807875u PMID:19485396

Ziółkowski, B., Czugala, M., & Diamond, D. (2012). Integrating stimulus responsive materials and microfluidics – The key to next generation chemical sensors. *Journal of Intelligent Material Systems and Structures*.

Ziółkowski, B., Florea, L., Theobald, J., Benito-Lopez, F., & Diamond, D. (2013). Self-protonating spiropyran-co-NIPAM-co-acrylic acid hydrogel photoactuators. *Soft Matter*, *9*(36), 8754–8760. doi:10.1039/c3sm51386f