Integrating stimulus responsive materials and microfluidics – The key to next generation chemical sensors

Bartosz Ziółkowski[1], Monika Czugala[1] and Dermot Diamond

CLARITY Centre for Sensor Web Technologies, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland

[1]Both authors contributed equally to this work.

Abstract

New generations of chemical sensors require both innovative (evolutionary) engineering concepts and (revolutionary) breakthroughs in fundamental materials chemistry, such as the emergence of new types of stimuli responsive materials. Intensive research in those fields in recent years have brought interesting new concepts and designs for microfluidic flow control and sample handling that integrate high quality engineering with new materials. In this paper we review recent developments in this fascinating area of science, with particular emphasis on photoswitchable soft actuators and their incorporation into fluidic devices that are increasingly biomimetic in nature.

Introduction

In a utopian future, water quality will be monitored through large numbers of densely deployed sensors that are capable of detecting key quality parameters with exquisite selectivity and sensitivity, and of functioning reliably in an autonomous manner for long periods of time (years). The information generated by these sensor networks will be analysed and filtered, and key events flagged in real time to key stakeholders (agency enforcement officers, water treatment specialists, and the general public). However, in reality, issues like biofouling and surface degradation mean that sensor characteristics change rapidly in real samples, and consequently, chemical sensors must be regularly recalibrated to ensure the information they send is reliable. This results in complex and very costly devices that must integrate fluidics, standards, and waste storage, as well as sampling and analytical procedures. Consequently, monitoring programmes are dominated by manual grab sampling at a relatively small number of locations, with a frequency often restricted to 3 or 4 times per year. Scale up in terms of sampling frequency and number of locations is dictated by cost, and therefore the key to significant movement towards the utopian vision is to drive down the cost base of environmental monitoring.

Analysis of the component cost base of autonomous analysers we have built (Gen1[1] and Gen2), together with a speculated cost analysis of a future platform based on fully integrated polymer actuator valves and pumps are presented in Figure 1. These show clearly for Gen1 and Gen 2, that the single greatest contribution to the cost base is the fluidic handling category. In the first generation (Gen1) design, this amounted to over 80% of the total cost of ca. €2,000, and while this dropped in the second generation design through good engineering and careful choice of components, it was still almost 2/3 of the total component cost of ca. €180. These are accurate figures based on platforms that we are currently making. We have also made a 'concept' integrated analyser with integrated polymer actuator pumps and estimate the total cost to be in the region of €20-50 per unit, of which we estimate ca. 50% is costs related to fluid handling components. The figures here are more speculative, but there is no doubt that if the fluid handling components could be fully integrated into the fluidic system, for example using highly automated in-situ photopolymerisation of the key liquid handling components, the unit cost would be considerably lower. Furthermore, if the control stimulus for valve actuation/fluidic control does not require physical contact (e.g. light, heat, magnetism..) then manufacturing would be further simplified, as the fluid handling layer could be produced as an entirely stand-alone unit. Therefore in this contribution, we will review strategies for making and integrating polymer actuators in microfluidic systems, and speculate on how the field may progress over the coming years.

Polymer Actuator Valves in Microfluidic Systems

Valves are one of the most important components within microfluidic systems, since they provide directional control of flow and facilitate essential actions, such as sample/standard selection and addition of reagents. Some key requirements of an ideal microvalve are;

- Zero flow resistance in the open position;
- Zero leakage in the closed position;
- Infinite tolerance to high pressure in the closed position;
- Instant response to switching between the open and closed positions
- Simple routes to fabrication and integration in-situ within the microfluidic system
- Prepared from readily available and processable materials.

Many different types of microvalves have been demonstrated, and while none of these can be described as totally satisfactory, they do present significant advances in the realisation of

[1] These are 1st and 2nd Generation versions of fluidic based colorimetric chemical analysers targeting analytes such as phosphate, nitrate, pH, COD etc.

some of these ideal characteristics.[1] In most conventional systems a diaphragm is coupled to an actuator, powered from an external source, which deflects the diaphragm via a magnetic field, high voltage or heating.

Magnetically actuated valves

Flow regulation in microfluidic devices by magnetic forces has many advantages, such as capability of generating large angular displacement as well as possibility of using very strong magnetic force to drive actuation. Satarkar and co-workers developed the nanocomposite hydrogel valve, in which magnetic nanoparticles were dispersed in temperature-responsive N-isopropylacrylamide (NIPAAm) polymer matrix[2] (Figure 2). The swelling and collapse of the hydrogel nanocomposite can be remotely controlled by application of an alternating magnetic field (AMF) at a frequency 293 kHz. The disadvantage of this hydrogel microvalve is that its response as reported is sluggish, but this can be improved by moving to smaller valve dimensions, as gel processes are typically diffusion driven, and smaller feature sizes reduce the diffusion pathlength. Similar oscillating magnetic field actuated valves were prepared by Ghosh *et al.*[3]

Pneumatic valves

Pneumatic microvalves represent another type of fluid handling, however, they require external laboratory infrastructure – gas cylinders, computers, ground electricity, for their operation which makes it difficult to incorporate them into autonomous monitoring instruments. The development of PMMA/PDMS pneumatic valves and pumps for disposable microfluidics was reported by Zhang *et. al.*[4]. Pneumatic microstructures were fabricated by sandwiching a PDMS membrane between PMMA fluidic channel and manifold wafers, as in Figure 4. Valve control was obtained by applying pressure on the pneumatic layer sited in a displacement chamber using a computer regulated solenoid. Apart from providing fluid pressure up to 15.4 mL/s at 60 kPa, the valve seals reliably against forward fluid pressures as high as 60 kPa. A PMMA diaphragm pump was presented based by connecting three valves in series. Simultaneously, the fluid flow rate could be accurately controlled from nL to mL per second, simply by changing the valve actuation time, the displacement chamber volume, and the applied pressure. Go and Shoji presented a three-dimensional in-plane hemisphere PDMS microvalve without dead volume and leakage flow.[5] A closing time of 0.1 s and an opening time of 0.5 s were obtained by applying a pneumatic pressure of 10 kPa to the PDMS membrane. Even though a faster response for closing was possible, it took a longer time to release the membrane for opening.

Electrothermal valves

In contrast to many other technologies, electrothermally actuated phase change microvalves developed by Kaigala *et. al.* can be readily scalable to smaller dimensions, allowing the fabrication of a portable and inexpensive genetic analysis platform.[6] This easily integrated, reusable microvalve technology that can be easily incorporated within standard lab on a chip (LOC) technologies is based on the polyethylene glycol polymer (PEG) that exhibits a large volumetric change between its solid and liquid phases**.** The volumetric expansion, thermally controlled by applying thin film resistive elements that are patterned with standard microfabrication techniques, switches a flexible PDMS membrane between opened or closed state between two discontinuous channels (Figure 5). The switching time for opening/closing, was on the order of minutes, and the microvalve was reported to be leakage-free to a pressure of 30 psi at a temperature of 50 ˚C in the PEG reservoir. Selvaganapathy *et. al.* realized normally open electrothermally actuated inline microvalve for liquid regulation[7]. The actuation mechanism was based on a thermally activated phase change in the Paraffin layer resulting in a high volumetric expansion. The microvalve was surface micromachined on top of preformed flexible microfluidic channels using a low temperature fabrication process. As the Paraffin was heated beyond its melting point using the microheaters underneath them, it undergoes a volume expansion, which deflects the flexible diaphragm of the piston, closing the microchannel beneath it. Actuation was achieved at power as low as 35 mW with the response times of 15 ms. Similar valves opened by melting a polymer with heat provided from a laser were demonstrated by Garcia-Cordero *et al.*[8] These valves were fully integrated into a microfluidic platform and are characterised by very low cost. The disadvantage is that they can be used only once.

Soft polymer valves

Most conventional microvalves coupled to piezoelectric, thermopneumatic, electrostatic or electromagnetic actuators require high power consumption, which is highly unfavourable for autonomously deployed instruments. Soft polymer actuators offer an alternative approach that is more biomimetic in nature, and in principle can require relatively low energy for actuation. For example, hydrogels swell and contract significantly due to water movement into/out of the gel. These volume changes are associated with phase transition behaviour triggered by small alterations of certain external stimuli. These materials can respond to a variety of external stimuli, such as pH, temperature, or light. Among these hydrogels, pH responsive materials have been the focus of particular attention. By converting chemical energy into mechanical work, pH sensitive hydrogels can exhibit both sensing and actuating functions simultaneously. For example, for the pH-sensitive hydrogel poly(2-hydroxyethyl methylacrylate-co-acrylic acid) or poly(HEMA-co-AA), the movement of water is initiated by

the ionization of the polymer backbone[9]. Beebe *et. al.* reported a channel with two strips of poly(HEMA-co-AA) deposited along the walls using the laminar flow characteristics to enable polymer precursors to be restricted only to the channel wall region (Figure 6)[10]. Under conditions of high pH, swelling of the hydrogel structures occurred and blocked the channel. As the pH in the sensing channel was changed from 11 to 2, the hydrogel contracted to open the flow in the adjacent channel. Although swelling and shrinkage of the hydrogel in response to pH change are reversible and repeatable, reopening of the channel from the closed state (at which point the hydrogel is fully expanded) may limit the use of this design in some applications. In general it is found that the dynamics of reswelling in hydrogels are much slower than contraction, due to the inherent asymmetry of diffusion in these materials.[11, 12]

Since diffusion is the rate-limiting factor governing the swelling process of hydrogels, the response time can be improved by reducing the size of hydrogel microstructures. In order to fabricate stable hydrogel actuators with fast response times, hydrogel films were photopolymerized using a photomask around prefabricated posts (Figure 6)[13]. At pH 11, the films expanded, closing the channel, whereas flushing the channel with solution at pH 2 resulted in the valves opening, with response time of 12 s. Based on the valve mechanism described above, a pH-dependent flow sorter was also demonstrated (Figure 7)[10]. The entrance to each branch of 'T' channel was gated with hydrogel microstructure that expanded in one branch of the channels at high pH and contracts in low pH, whereas a hydrogel of different composition in another branch exhibited an inverse behaviour. In this way, the microfluidic device directed the flow to the appropriate branch, depending on the pH of the solution.

Yu *et. al.* presented a biomimetic bistrip valve capable of directional flow control in response to changes in the local fluid environment[14], [15]. The valve structure is similar to the venous valve, consisting of a pair of pH sensitive poly(HEMA-co-AA) hydrogel strips overlapped by the pair of pH-insensitive strips (Figure 8). When exposed to high pH, dissimilar expansion to adjacent hydrogel strips caused the valve to bend during swelling, thus forming a normally closed check valve allowing only forward flow of pressure above the threshold value. If low pH solution enters the channel, the pH sensitive strips shrink, allowing both forward and backward flow. In comparison to traditional microfluidic valves where actuation occurs very rapidly, here the activation and deactivation times are quite slow, at 6 and 3 minutes respectively. However, this slow operating valve can be successfully applied in drug delivery and bioassay devices, where timescales for events can be of the order of hours.

However, in order to handle biological cells and proteins, manipulation of fluids with neutral pH is desired. In order to minimize the complexity of fully polymeric integrated fluidic circuits (IFC), all electronically controllable components should ideally be made with one type of hydrogel. This can be achieved with poly(N-isopropylacrylamide) (PNIPAAm), one of the best-known temperature-sensitive multifunctional hydrogels. At a temperature above the lower critical solution temperature (LCST) of 32^{o}C PNIPAAm chains undergo rapid and reversible entropy driven phase transition from extended hydrated coils to collapsed hydrophobic globules that precipitate in water.[16, 17] The temperature-sensitive PNIPAAm hydrogel, which is typically controlled by electronic heating elements, has been used widely for fabrication of not only the standard elements of liquid handling, such as microvalves [18 19 20] and micropumps [21], but also specific active components such as chemostat valves [18] and chemical sensors [22].

Although robust valves with fast response to external stimuli and successful performance of repeated "open-close" cycles have been reported [19], their transition temperature (slightly above 30^{o} C causes shrinkage and valve opening) is too low for some applications, such as on-chip PCR, for which the valves must remain closed at much higher temperatures. Frechet *et. al.* realized thermally actuated valves by crosslinking NIPAAm with N-ethylacrylamide (NEAAm), for which the LCST can be adjusted within a wide temperature range to meet the specific requirements of some applications[23]. In order to avoid valve displacement during operation, the microchannels were vinylized to enable covalent attachment of the photopolymerized gels. As a result, a 5 mm long poly(NIPAAm-co-NEAAm) (1:1 molar ratio) valve holds pressure up to 18 MPa without noticeable dislocation, leakage or structural damage in closed mode. Although the authors demonstrated the versatility of the valve and its ability to perform well under conditions typical of numerous microfluidic processes, displaying actuation times in the range of 1-4 s, there is still the need for thermoelectrical elements to implement temperature control. What is more, application of heat induced phase transition is not suitable for samples containing heat sensitive materials, such as protein and cells.

Micropumps in fluidic systems

In contrary to widely researched and tested microvalves, there is not much interest in hydrogel-based electronically controllable micropumps. Richter *et. al.*[21] presented diffusion micropump (Figure 9a), which peristaltic operation provides a continuous and relatively homogeneous pumping. The flow rate obtained for this device is 2.8±0.35 μl min^{-1}, with the maximum flow rate of pumping stroke determined by the shrinking kinetics of the hydrogel.

This process is strongly dependent on the heating power of the heating meanders in addition to the properties of the elastic PDMS membrane. The higher the pressure of the membrane (directly proportional to its increasing thickness), the faster actuator shrinks. On the other hand, the increase of membrane thickness significantly influences the reload time of the pump and decreases the maximum swelling volume of hydrogel.

However, this kind of micropump is unsuitable for some applications. For example, some solvents can destroy the hydrogel structure, particles cannot pass the actuation chamber, since the monolithic PNIPAAm actuator is placed directly in the pump chamber, or the pumping pressure can be not sufficient enough. Another pump described by this group based on displacement (Figure 9b), provides higher performance (flow rate of 4.5 ul min-1 and a back pressure of 1.28 kPa) based on a hydrogel actuator separated from the process medium by a movable membrane. Inexpensive design, simple control and soft lithographic fabrication makes these hydrogel pumps a significant advance towards the realisation of disposable microfluidic components.

Photoswitchable Polymer Actuators

In recent years, the range of applications for lab-on-a-chip systems has significantly increased due to several promising aspects, such as smaller sample and reagent volume consumption and less wastage produced, which is cost-effective and environmental friendly. Since it is possible to place many microfluidic architectures in a relatively small area, it enables complex sample processing operations with rapid analysis times to be performed, due to the large increase in the surface area to volume ratio associated with reduction in dimensions. Because of the numerous advantages offered by the microscaled channels, the concept of microfluidic “lab on a chip” has triggered significant effort in development of materials and their employment in miniaturized devices. In particular, switchable materials offer intriguing possibilities and the potential to integrate sophisticated functions in a simple overall design. Because of their relative ease of fabrication and simple control, stimuli responsive materials integrated with microfluidic manifolds could significantly advance the development of fully integrated microfluidic systems.

Smart engineering of analytical fluidic devices can generate improvements up to a limit, beyond which new, robust and smart materials are needed for further progress.[24] One of the most attractive strategies to implement fluid manipulation on integrated microfluidic platforms is light irradiation, which allows not only for non-contact operation but also independent and remote manipulation of multiple fluids. Photoresponsive polymer materials have been studied by many research groups, and many polymers and polymer gels

functionalized with azobenzene [25-27], leukochromophore [28] [29], and spirobenzopyran [30] [31] have been examined. Valves can be controlled with IR[32], blue [33, 34] or white [24, 35] light.

IR-responsive materials

The performance of microvalves based on the volumetric change due to infrared (IR) light illumination was reported by Lo *et. al*.[32] They presented an IR-light responsive hydrogel based on thermo-responsive pNIPAAm hydrogels incorporating glycidyl methacrylate functionalized graphene-oxide (GO–GMA). The valve operates in two states – closed, adopted when the IR source is turned off, and opened, adopted when the IR source is turned on, due to absorbance of the IR light by the GO–GMA sheets, which triggers the hydrogel to contract, allowing for fluidic flow. The performance of the hydrogel microvalve is shown in Figure 10. When the infrared light is switched off, the heat is dissipated to the surrounding environment, and the hydrogel absorbs water, expanding its volume and blocking the microchannel again.

Spiropyran-based photocontrolled soft actuators.

One of the first reports of a spiropyran monomer copolymerised with vinyl monomers to obtain a photoresponsive polymer was published by Smets[36] *et. al.* in 1978. The author synthesised a crosslinker consisting of two connected spiropyran molecules each having one vinyl group attached. They showed that the spiropyran-crosslinked poly-bisphenol-A-pimelate or polyethyleneglycol tere/isophthalate rubbers contracted as the sample is irradiated with light, and the spiropyran opened into a merocyanine form. Furthermore, they showed that the opening of the spiropyran and consequential colour change was not directly linked with the polymer contraction. Figure 11 shows that when the samples are exposed to light in the range 290nm < λ < 400nm the polymer does not contract significantly, but colouration appears. Illuminating the sample with the light above 472nm wavelength produces a rapid contraction reaching a maximum when the light wavelength matches the merocyanine absorption wavelength (Figure 12.)

Therefore, the authors claimed that[36]:

- The irradiation wavelength dependence of the contraction corresponds closely with the absorption spectrum of the merocyanine.
- The rates of ring opening/closure in the spiropyran ↔ merocyanine equilibrium do not control the rates of dilatation/contraction. The contribution of ring opening/closure is of secondary importance, except for the initial formation of the merocyanine.
- The isomerisation between different open merocyanine forms forces conformation changes in the neighbouring polymer units and this results in shrinkage

Another report from the same group claimed that the viscosity of solutions of poly(methylmethacrylate-co-1,3,3-trimethylindolino-6'-nitro-8'(methacryloxy)methyl]spirobenzopyran) can also be altered with light irradiation λ>310 nm.[37] This is ascribed to the polar neighbouring methacrylate groups solvating the polar merocyanine form of the photochrome co-monomer. This effect decreases as the solvent polarity is increased and disappears in dichloromethane.

In more recent work, on spiropyran (3mol%) copolymers of pNIPAM, by Sumaru[38] *et al* presented an actuation mechanism based on the lower critical solubility temperature (LCST) of poly(N-isopropylacrylamide)[17] and the fact that it changes depending on the chromophore state. Figure 13 shows the copolymer used in this study, and the effect of switching. When the copolymer is immersed in an acidic (0,26 mM HCl) solution the spiropyran part of the polymer changes to the open merocyanine form, and becomes protonated. When this polymer is irradiated with light at 422 nm, which matches the absorbance of the protonated merocyanine form, the polymer chains collapse and the proton is released. A correlated change in both absorbance at 422 nm and ionic conductivity is observed.

In a parallel publication Sumaru[39] investigated this system further. Solutions of pNIPAM-co-acrylated spiropyran were analysed at acidic, basic and neutral pH with respect to the temperature and light induced precipitation of the polymer. The following observations were reported:

- The protonated merocyanine (MC-H^+) pNIPAM copolymer absorbs at 422nm. The uncharged merocyanine copolymer absorbs strongly at 530nm and weakly around 370nm.
- Without light irradiation the acidified pNIPAM solution becomes turbid around 32˚C however the turbidity increase is not significant due to the remaining protonated MC-H^+ chromophores that stabilise the polymer
- With light irradiation at 422nm (absorption band of MC-H^+) the acidified polymer solution becomes turbid at 29˚C and increases with increasing temperature. Also the absorption intensity at 422nm is decreasing as the merocyanine chromophore reverts to the spiropyran form
- A significant turbidity increase is also observed when the same sample is kept at 31,5˚C in the dark and then irradiated with 422nm light
- Little precipitation is observed when the pNIPAM solutions are neutral or basic due to the fact that at these conditions the chromophore is mostly in the spiropyran (SP) form

These results suggest that the status of the SP⇔MC equilibrium in the copolymer chain, which is controlled by light irradiation, changes the hydrophobic-hydrophilic character of the whole polymer, leading to changes in the LCST. The system works best in acidic pH because under these conditions, the equilibrium predominantly favours the formation of MC. Based on this work of Sumaru, it seems that the LCST is lowered as the equilibrium shifts towards the closed-hydrophobic SP form. This implies that the hydrophilic merocyanine form raises the entire copolymer's LCST. However it should be noted that the opposite effect has been reported by Ivanov[40] *et al*. In this case, a 10˚C downward swift of the LCST was reported when the sample was irradiated with UV light in deionised water, and the merocyanine absorption at 450nm became apparent. However, Ivanov used a spiropyran molecule functionalised with a methacryloyl group through the indoline nitrogen linker, in contrast with Sumaru, who acrylated the spiropyran through the 6-hydroxybensopyran group.

Important claims in Sumaru's papers[38, 39, 41] are as follows:

- No protonation at the tertiary amine of spirobenzopyrans with electron-withdrawing substituents in the closed-ring form was detectable by NMR even at acidic conditions.[38]
- The open merocyanine form of the chromophore used by Sumaru has a $pK_a \approx 6\text{-}7$ and is not strong enough base to remove protons from water molecules[39]

Aditionally, Krüger *et al*[41] shows that the LCST can be shifted as much as by 20 ˚C in acrylamide copolymerised with monomers containing azobenzenes.[41] Here, a similar explanation for the phenomena seen by Sumaru[38, 39] is also suggested.

To optimise the actuation of spiropyran functionalised pNIPAM polymers one needs to consider not only changes happening at the chromophore modified units, but also the contraction and swelling processes throughout the entire pNIPAM polmer. It is well known that pNIPAM collapses from an expanded coil to a compact globule form when heated above ~ 32˚C and the opposite happens when cooled down. Wang[11] *et al* showed that there is a particle diameter-temperature hysteresis when pNIPAM is precipitated and left to reswell (Figure 14).

The authors claim that the pNIPAM chains collapse above the LCST and form intrachain hydrogen bonds that make the resulting globule difficult to dissolve once the temperature decreases.[11] Moreover, according to Sun[12] *et al.,* during heating the backbone chains collapse first, the side isopropyl groups react next and then water is expelled last. On the other hand, during cooling the globule swells once water becomes again a sufficiently good solvent for the polymer chains and diffuses in between the collapsed pNIPAM chains. After

the water has diffused into the polymer network the intrachain hydrogen bonds break and the side chains reswell first and then the backbone follows.[11, 12]

On a macroscopic scale, one way to increase the speed of reswelling of pNIPAM hydrogels is to modify the morphology of the bulk material and increase the polymer surface area in contact with water. An effective way of using the inherent LCST pNIPAM property to make macroporous hydrogels was developed by Wu *et al*. [42] In this work the NIPAM is polymerised and crosslinked above its LCST with and without hydroxypropyl cellulose. As a result NIPAM polymerised in its precipitated state and a porous network was formed in which swelling/deswelling ratio and rates were significantly higher than for the conventional hydrogel. The cellulose additive improved the gel performance even further (Figure 15).

Although all those approaches improve the characteristics of pNIPAM-spiropyran system little has been done to optimise the fundamental phenomenon at the very core of the actuation process. Satoh *et al*[43] prepared spiropyran monomers with different electron donating and electron withdrawing groups and demonstrated that the spiropyran opening in HCl can be drastically improved by certain substituents on the pyran-benzene ring (Figure 16).

With this approach it was demonstrated that pNIPAM-spiropyran hydrogels can collapse and reswell within 15 min.[44] However, the authors themselves admit that the “fastest” hydrogels did not return to the original size. This was ascribed to photo-induced decomposition of the polymer. As for other systems mentioned above, the LCST driven collapse of the gel is rather fast but the reswelling of the gel is comparatively slow and problematic.[33] This is because the actuation of the pNIPAM-spiropyran gel is a two-step process. For the shrinking the protonated merocyanine has to be first isomerised to the hydrophobic SP form. This increase in the hydrophobicity of the chain induces its collapse and water ejection.[33, 39] The reverse process is more difficult as after conversion of SP to the charged MC form, protonation occurs followed by diffusion of water into the collapsed polymer globules before the chains can reorder and swell.[11, 12] A manifold with microvalves made from such material was demonstrated by Sagiura *et al* (Figure 17).[33] The maximum pressure the pSPNIPAAm gel microvalves could withstand was determined to be 30 ± 6.6 kPa. At pressures in excess of this, the gels deformed and leakage occurred.

A similar approach was presented by Benito-Lopez *et. al.*[24, 35]. However, in this case, an ionic liquid (IL) was incorporated within a poly(N-iso-propylacrylamide) polymer matrix copolymerised with acrylated benzospiropyran. Using various IL components within the gels allows the kinetics of valve actuation to be controlled, and the IL mediates the rate of protonation/deprotonation and movement of counterions and solvent (water). Different

ionogels were photo-polymerised *in situ* in the channels of a poly(methyl methacrylate) (PMMA) microfluidic platform. After immersion for 2 h in 0.1 mM HCl aqueous solution, in which the ionogel exhibits a rapid swelling effect due to protonation of the polymer backbone, the rate of photo-induced shrinking due to dehydration of the ionogel was measured. The required light intensity is so low that low cost LEDs can be employed for successful valve actuation. Results showed that trihexyl-tetradecylphosphonium dicyanamide based ionogel produced the fastest valve-opening kinetics, opening 4s after light irradiation (Figure 18). Although it is possible to reuse the valves several times, the time to re-close the ionogel valve is relatively long (ca. 30 min) and requires re-immersion in an acidic solution.

An innovative approach to microfluidics incorporating photoresponsive pSPNIMAAm hydrogels was described by Sugiura *et. al*[34] The group demonstrated on-demand formation of microchannels with arbitrary pathways using micropatterned light irradiation of (initially planar) hydrogel sheets. After light irradiation through an appropriately designed mask, a microchannel between adjacent inlet/outlet ports spontaneously formed under the irradiated area, allowing for fluid flow between a designated input and output and the channels rapidly became filled with reagent within a few minutes of illumination (Figure 19). The effect was repeated for several channel configurations – straight, bent or serpentine. What is more, the authors demonstrated independent and parallel flow control in a polydimethylsiloxane (PDMS) microchannel network by micropatterned light irradiation of photoresponsive microvalves prepared from the same 200 μm thick hydrogel sheet. As a result of light irradiation, the gel in the irradiated area adjacent to the through-holes shrank, thus opening the valve within several minutes.

Azobeznene based polymeric actuators

Another interesting class of photoactuated materials is based on azobenzenes[27, 45-48]. These molecules are in a trans configuration in the ground state but when irradiated with UV light they isomerise to the cis orientation.[26, 27] The structural reorganisation of the molecule and the attached chains can have a significant macroscopic effect on the host material.[27] This phenomenon was greatly enhanced by D. Broer's group by incorporation of azobenzenes in liquid crystal structures.[25, 49] When the azobeznene molecule isomerises to the cis form under UV light there is an increase in disorder resulting in shrinkage along the direction of the liquid crystal structure and expansion in the perpendicular direction. When the white light is used the molecules and the polymer return to the initial state.[49] This shows a reversible and quick photoactuation of the polymeric material (Figure 20).

The speed of actuation and strength of this material must be emphasised. The films reach 70% of the maximum deformation within 7 seconds and take the same to return to the original shape while having over 1GPa of elastic modulus. This material is therefore much suitable to generate mechanical work and displace fluids than considerably softer gels. Coupled with biomimetic approaches such as artificial cilia[25] these azobenzenes-ordered materials open new perspectives in microfluidic and lab-on-a-chip devices. The field of photomechanical actuators containing azobenzenes is covered in a review by Barrett *et al.*[27]

Table 1. Approximate ranges for the characteristics of microvalves.

Actuator type	Energy requirement	Applied Pressure (kPa)	Actuation time	Generated deflection or volume change	Measured flow (μl min-1)	References
Pneumatic	0.04–0.5 W	20-230	<25 s	3.5 -150 μm	$3{\cdot}10^3$ - $1{\cdot}10^6$	50-52
Magnetic gels	59.5 kA/m		<13 min		0.2 - 100	2, 53
Chemically responsive gels	none		12 s – 30 min	<200 μm	10-150	10, 13, 54
Thermoresponsive gels	0.2-0.4 W		1 - 9 s	<30 %	1 - 50	23, 55
Spiropyran based photoactive gels	1-20 mW/cm2	3.4-69	30 s -1hr	<60 %	30± 6.6	33, 35, 56
Azobenzene based photoactive polymers	10mW/cm^2		<15 s	100 m^{-1} (curvature[26])		26

Conclusions

Table 1. summarises the features of the presented classes of actuators. There are so many exciting developments happening in materials chemistry that one can only 'touch the surface' in a review paper of this type. The potential range of stimuli responsive materials is virtually unlimited, and this, coupled with new deposition techniques that offer unsurpassed control of feature offer a tremendously rich research landscape for science to explore. The potential benefits to society emerging from this research are truly enormous. Perhaps the great issue of biofouling will finally be put to rest, opening up new opportunities in long-term implantable chem/bio-sensors that can monitor, report, and ultimately control the levels of key biomarkers. Similarly, reliable low cost sensors could open the way to environmental monitoring on a massive scale. Stimuli-responsive polymers could form the basis of new generations of biomimetic sensing based on polymer pumps and valves incorporated in

microfluidic platforms much more reminiscent of our own circulation systems. The convergence of technologies that facilitate the control of micro/nano-structured surfaces coupled with these new materials is a powerful combination – materials chemistry now must be recognised as the core foundation underpinning these exciting possibilities.

Acknowledgements:

This work was performed as part of the EU Framework 7 project “ATWARM” (Marie Curie ITN, No. 238273)”. D. D. acknowledges funding from Science Foundation Ireland (SFI) under the CLARITY CSET award (Grant 07/CE/I1147).

References:

1. K. G. Kovacs, *Microfluidic devices. In Micromachined Transducers - Sourcebook*, WCB/McGraw-Hill, Boston:, 1998.
2. N. S. Satarkar, W. Zhang, R. E. Eitel and J. Z. Hilt, *Lab on a Chip*, 2009, **9**.
3. S. Ghosh, C. Yang, T. Cai, Z. B. Hu and A. Neogi, *J. Phys. D: Appl. Phys.*, 2009, **42**.
4. W. Zhang, S. Lin, C. Wang, J. Hu, C. Li, Z. Zhuang, Y. Zhou, R. A. Mathies and C. J. Yang, *Lab on a Chip*, 2009, **9**, 3088.
5. J. S. Go and S. Shoji, *Sensors and Actuators A: Physical*, 2004, **114**, 438-444.
6. G. V. Kaigala, V. N. Hoang and C. J. Backhouse, *Lab on a Chip*, 2008, **8**, 1071.
7. P. Selvaganapathy, E. T. Carlen and C. H. Mastrangelo, *Sensors and Actuators A: Physical*, 2003, **104**, 275-282.
8. J. L. Garcia-Cordero, D. Kurzbuch, F. Benito-Lopez, D. Diamond, L. P. Lee and A. J. Ricco, *Lab Chip*, 2010, **10**, 2680-2687.
9. J. Moorthy and D. J. Beebe, *Analytical Chemistry*, 2003, **75**, 292 A-301 A.
10. D. J. Beebe, J. S. Moore, J. M. Bauer, Q. Yu, R. H. Liu, C. Devadoss and B.-H. Jo, *Nature*, 2000, **404**, 588-590.
11. X. Wang, X. Qiu and C. Wu, *Macromolecules*, 1998, **31**, 2972-2976.
12. S. Sun, J. Hu, H. Tang and P. Wu, *J. Phys. Chem. B*, 2010, **114**, 9761-9770.
13. R. H. Liu, Y. Qing and D. J. Beebe, *Microelectromechanical Systems, Journal of*, 2002, **11**, 45-53.
14. J. S. M. David J. Beebe, Qing Yu, Robin H. Liu, Mary L. Kraft, Byung-Ho Jo, and Chelladurai Devadoss, *Proceedings of National Academy of Sciences of the United States of America*, 2000, **97**, 13488-13493.
15. J. M. B. Q. Yu, J. S. Moore and D. J. Beebe, *Appl. Phys. Lett*, 2001, **78**, 2.
16. Dusek, in *Adv. Polym. Sci.*, ed. D. K., 1993, vol. 110, pp. 1-261.
17. H. G. Schild, *Prog. Polym. Sci.*, 1992, **17**, 163-249.
18. D. K. A. Richter, S. Howitz, T. Gehring and K.-F. Arndt, *J. Microelectromech. Syst*, 2003, **12**.
19. S. M. C. Yu, P. Selvaganapathy, C. H. Mastrangelo, F. Svec, J. J.. Fréchet, *Anal. Chem*, 2003, **75**, 1958-1961.
20. L.-J. Y. Jiun-Min Wang, *Tamkang Journal of Science and Engineering*, 2005, **8**, 231-236.
21. A. Richter, S. Klatt, G. Paschew and C. Klenke, *Lab on a Chip*, 2009, **9**.
22. M. G. n. G. Gerlach, J. Sorber, G. Suchaneck, K.-F. Arndt, A. Richter, *Sens. Actuat. B*, 2005, **555**, 111-112.
23. Q. Luo, S. Mutlu, Y. B. Gianchandani, F. Svec and J. M. J. Fréchet, *Electrophoresis*, 2003, **24**, 3694-3702.
24. R. Byrne, C. Ventura, F. B. Lopez, A. Walther, A. Heise and D. Diamond, *Biosens. Bioelectron.*, 2010, **26**, 1392-1398.

25. C. L. van Oosten, C. W. M. Bastiaansen and D. J. Broer, *Nat Mater*, 2009, **8**, 677-682.
26. K. D. Harris, R. Cuypers, P. Scheibe, C. L. van Oosten, C. W. M. Bastiaansen, J. Lub and D. J. Broer, *J. Mater. Chem.*, 2005, **15**, 5043-5048.
27. C. J. Barrett, J.-i. Mamiya, K. G. Yager and T. Ikeda, *Soft Matter*, 2007, **3**, 1249-1261.
28. D. K. M.Irie, *Macromolecules*, 1986, **19**, 2476–2480.
29. M. H. M. Irie, *Makromol. Chem. Rapid Commun.*, 1985, **6**, 533–536.
30. A. M. M. Irie, K. Hayashi, *Macromolecules* 1979, **12**, 1176–1180.
31. K. H. A. Menju, M. Irie, *Macromolecules* 1981, **14**, 755–758.
32. C.-W. Lo, D. Zhu and H. Jiang, *Soft Matter*, 2011, **7**, 5604-5609.
33. S. Sugiura, K. Sumaru, K. Ohi, K. Hiroki, T. Takagi and T. Kanamori, *Sensors and Actuators A: Physical*, 2007, **140**, 176-184.
34. S. Sugiura, A. Szilagyi, K. Sumaru, K. Hattori, T. Takagi, G. Filipcsei, M. Zrinyi and T. Kanamori, *Lab Chip*, 2009, **9**, 196-198.
35. F. Benito-Lopez, R. Byrne, A. M. Raduta, N. E. Vrana, G. McGuinness and D. Diamond, *Lab Chip*, 2010, **10**, 195-201.
36. G. Smets, J. Braeken and M. Irie, *Pure Appl. Chem.*, 1978, **50**.
37. M. Irie, A. Menju and K. Hayashi, *Macromolecules*, 1979, **12**, 1176-1180.
38. K. Sumaru, M. Kameda, T. Kanamori and T. Shinbo, *Macromolecules*, 2004, **37**, 7854-7856.
39. K. Sumaru, M. Kameda, T. Kanamori and T. Shinbo, *Macromolecules*, 2004, **37**, 4949-4955.
40. A. E. Ivanov, N. L. Eremeev, P. O. Wahlund, I. Y. Galaev and B. Mattiasson, *Polymer*, 2002, **43**, 3819-3823.
41. R. Kröger, H. Menzel and M. L. Hallensleben, *Macromol. Chem. Phys.*, 1994, **195**, 2291-2298.
42. X. S. Wu, A. S. Hoffman and P. Yager, *J. Polym. Sci., Part A: Polym. Chem.*, 1992, **30**, 2121-2129.
43. T. Satoh, K. Sumaru, T. Takagi, K. Takai and T. Kanamori, *Phys. Chem. Chem. Phys.*, 2011, **13**, 7322-7329.
44. T. Satoh, K. Sumaru, T. Takagi and T. Kanamori, *Soft Matter*, 2011, **7**, 8030-8034.
45. K. N. Long, T. F. Scott, H. Jerry Qi, C. N. Bowman and M. L. Dunn, *Journal of the Mechanics and Physics of Solids*, 2009, **57**, 1103-1121.
46. K. M. Lee, H. Koerner, R. A. Vaia, T. J. Bunning and T. J. White, *Macromolecules*, 2010, **43**, 8185-8190.
47. H. Wang, K. M. Lee, T. J. White and W. S. Oates, *Macromol. Theory Simul.*, 2011, n/a-n/a.
48. K. M. Lee, N. V. Tabiryan, T. J. Bunning and T. J. White, *J. Mater. Chem.*, 2012, **22**, 691-698.
49. C. L. van Oosten, D. Corbett, D. Davies, M. Warner, C. W. M. Bastiaansen and D. J. Broer, *Macromolecules*, 2008, **41**, 8592-8596.
50. X. Yang, C. Grosjean, Y.-C. Tai and C.-M. Ho, *Sensors and Actuators A: Physical*, 1998, **64**, 101-108.
51. C. A. Rich and K. D. Wise, *Microelectromechanical Systems, Journal of*, 2003, **12**, 201-208.
52. H. Takao, K. Miyamura, H. Ebi, M. Ashiki, K. Sawada and M. Ishida, *Sensors and Actuators A: Physical*, 2005, **119**, 468-475.
53. G. Santaneel and C. Tong, *Journal of Physics D: Applied Physics*, 2010, **43**, 415504.
54. A. Baldi, G. Yuandong, P. E. Loftness, R. A. Siegel and B. Ziaie, *Microelectromechanical Systems, Journal of*, 2003, **12**, 613-621.
55. A. Richter, S. Howitz, D. Kuckling and K.-F. Arndt, *Sensors and Actuators B: Chemical*, 2004, **99**, 451-458.
56. S. Sugiura, A. Szilagyi, K. Sumaru, K. Hattori, T. Takagi, G. Filipcsei, M. Zrinyi and T. Kanamori, *Lab on a Chip*, 2009, **9**.