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# Modular microfluidic valve structures based on reversible thermoresponsive ionogel actuators

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This paper reports for the first time the use of a crosslinked poly(*N*-isopropylacrylamide) ionogel encapsulating the ionic liquid 1-Ethyl-3-methylimidazolium ethyl sulphate as a thermoresponsive and modular microfluidic valve. The ionogel presents superior actuation behaviour over its equivalent hydrogel. The ionogel swelling and shrinking mechanisms and kinetics are investigated as well as the performance of the ionogel when integrated as a valve in a microfluidic device. The modular microfluidic valve demonstrates fully reversible *on-off* behaviour without failure for up to eight actuation cycles and a pressure resistance of 1100 mbar.

*Keywords:* microfluidic, valve, ionic liquid, ionogel, thermoresponsive, reversible actuation.

## Introduction

Stimuli responsive hydrogel materials respond to environmental stimuli such as temperature, pH, light, solvent composition, chemicals and an electric or magnetic field, by an abrupt change in volume, accompanied by intake or release of a large amount of water.[1] This volume change is often reversible, returning back to the original configuration when the stimulus is removed.[2] These hydrogels are able to directly translate chemical energy into mechanical energy, without the need for any sophisticated external power other than a simple light source such as an LED,[3] or a heater,[4] making them advantageous in applications like point-of-care devices. For instance, these devices can often require smart and integrated fluid handling systems, incorporating pumps and valves, in order to support their operation. In this context, low cost energy sources are preferred to actuate the hydrogels.[4] [5]

Advances in stimuli responsive materials based on hydrogels have enabled new functionalities through the incorporation of smart micro/nano-structures in microfluidic channels for fluidic control and manipulation.[6] [7] Furthermore, when hydrogels are patterned within microchannels, they can be utilised to manipulate important characteristics of microfluidic devices such as transport, reaction, and encapsulation. In particular, patterned hydrogel valves have the advantage of combining miniaturised scale with small dead volume, it is a simple set-up and they can be integrated into Microsystems easily.[8]

In particular, poly(*N*-isopropylacrylamide) (NIPAAm) hydrogels shrink and expand due to dramatic structural changes that occur at the so-called lower critical solution temperature (LCST), which is around 32 ºC in water. In an aqueous environment, individual NIPAAm chains show a hydrophilic behaviour with an expanded coil structure below the LCST, but as the temperature increases above 32 ºC, hydrophobic isopropyl groups are exposed undergoing a reversible conformational change to form compact globule shapes. Because of the thermoresponsive properties of NIPAAm-based gels, they have been extensively used and investigated for different applications such as transdermal drug delivery systems,[9] smart surfaces and coatings for cell tissue engineering[10] and also as valves in microfluidic devices,[11] among others. Nevertheless their practical applicability in microfluidic devices is limited due to their discrete shrinking with increasing temperature, low material robustness, rather slow kinetics (particularly of expansion) and degree of actuation.[12]

Improvements in the physical robustness of hydrogels were reported by us when using ionogels instead.[13] An ionogel is a polymer gel that incorporates an ionic liquid (IL) within its polymer matrix. Two main advantages arose from this approach; firstly, the tendency of conventional hydrogels to become brittle when stored under standard ambient conditions was avoided, due to the low vapour pressure of the ionic liquids and their ability to plasticise the gel polymer structure. And secondly, the swelling and shrinking kinetics (and consequently the ionogel actuation kinetics) were strongly influenced by the ionic liquid used to form the ionogel. Ionic liquids have attracted much attention because of the potential applications in many fields of chemistry and industry due to their chemical and thermal stability, low vapour pressure, high ionic conductivity properties, and tuneable hydrophobic and hydrophilic nature.[14] Incorporating ILs into polymer gels is also attractive as this generates materials with the inherent advantages of ILs within a solid or semi-solid gel-type structure.

In the Lab-on-a-Chip field, most efforts to date have been focused on the generation of integrated systems that enable complex flow control and large scale integration. In contrast, there have been relatively few investigations into the generation of modular flow control systems, which are capable of being integrated into more than one microfluidic configuration.[15] Modular systems are attractive alternatives for integration because they can be tailored for different applications as building blocks, avoiding redesigning of every single element of the microfluidic device.

The development of microfluidic devices capable of performing complex functions requires the integration of microvalves with an appropriate performance, as they are essential tools for the control and manipulation of flows within microchannels.[5] Liquid handling in microfluidics is a recurrent issue that has still not been completely solved. Therefore the possibility of generating modular valve components that are capable of being integrated within a pre-existing device configuration is very appealing.

Applications of valves include flow regulation, on/off switching and sealing of liquids, gases or vacuums. Valves have been developed in the form of active or passive structures employing mechanical, non-mechanical and externally (to the microfluidic chip) located systems. 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 since these valves change volume in response to external stimuli to stop/enable the flow. Nevertheless, the fabrication of hydrogels inside microfluidic channels with precise control of position and composition is challenging.[13]

Here we present the synthesis, characterisation and actuation kinetics of a crosslinked poly(*N*-isopropylacrylamide) ionogel encapsulating the ionic liquid 1-Ethyl-3-methylimidazolium ethyl sulphate. The ionogel has been integrated and tested as a thermoresponsive material in a modular microfluidic valve fabricated using a fast prototyping technique with cyclic olefin polymer (COP) films.

## Experimental

### Materials

*N*-isopropylacrylamide (NIPAAm) (Sigma-Aldrich, Ireland), *N,N'*-methylene-bis(acrylamide) (MBAAm), 2,2-5 dimethoxy-2-phenyl-acetophenone (DMPA) and the ionic liquid 1-Ethyl-3-methylimidazolium ethyl sulfate (EMIES) [$C_2$mIm][$EtSO_4$] were obtained from Sigma Aldrich (Spain) and used for ionogel preparation. All chemicals were used without further purification.

Isopropyl alcohol (IPA) was purchased from Panreac Química S.L.U. (Spain). Rolls of 100 µm thick COP films (ZeonorFilm®) were obtained from Zeon Chemicals (Düsseldorf, Germany).

### Modular microfluidic valve fabrication

Three different valves were envisioned and fabricated by rapid prototyping using the cutting plotter FC8000-60 from Graphtec. The 3D design of the valves is sliced into ten 2D layers, which are cut with the cutting plotter, assembled and then bonded by thermocompression.[16] Fabricated chips are composed of ten layers of COP, 100 µm thickness each with a section of 1 $cm^2$ and 1 mm total thickness (Figure ESI-1). The valve chamber diameter is 4 mm, and depending on the number of layers, for inlet-outlet integration, the depth of the gap can be modified along with the valve volume. Valves with 6 and 7 µL volume were fabricated.

The ionogel was integrated in the modular microfluidic valve configuration as a proof of concept (Figure 1), whereby the valve dimensions were 4 mm in diameter, 600 µm in height and 7 µL in volume.

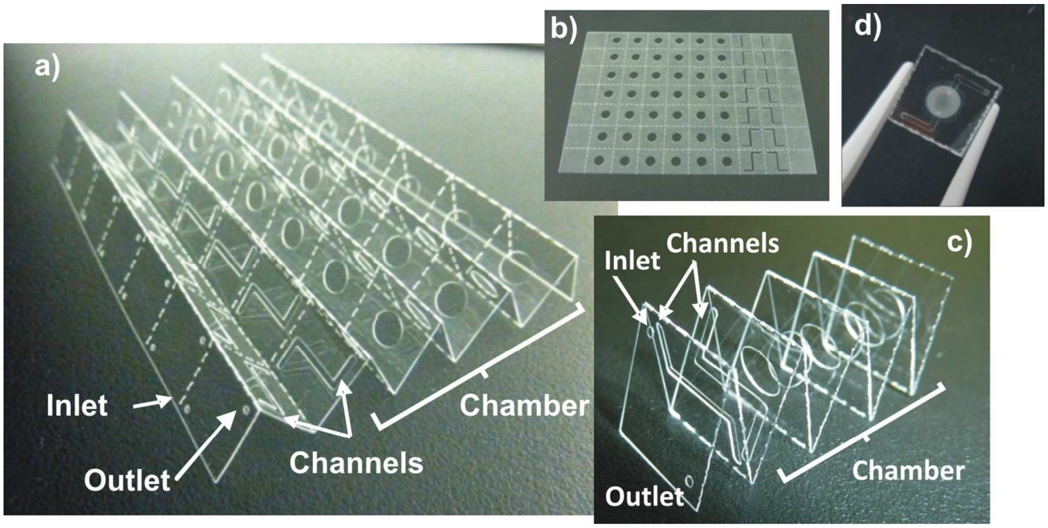

**Figure 1:** a) Set of valves after rapid prototyping fabrication and bending. b) COP layer with the valve features. c) Single valve before bonding. d) Picture of the modular microfluidic valve, suitable for many microfluidic configurations, incorporating the ionogel-based valve.

### Preparation of the thermoresponsive ionogel valves

A liquid prepolymer mixture was prepared by dissolving the NIPAAm monomer (2.0 mmol), the MBAAm (0.04 mmol) and the photo-initiator DMPA (0.02 mmol) into the ionic liquid (0.52 mmol) in a molar ratio of 100 : 2 : 1 in 1 mL of EMIES (5.3 mmol). The mixture was stirred and heated to 45 °C for approximately 10 min, until complete dissolution of the different reagents in the IL occurred.

7 µL of the solution was pipetted into the valve chamber of the open microfluidic device; the high viscosity of the solution prevents the liquid leaving the chamber and blocking the microchannels. Photopolymerisation was performed *in-situ* using the ultraviolet lamp UVP CL-1000L (Ultra-Violet Products Ltd., UK) at 365 nm (14.5 ± 0.5 µW $cm^{-2}$) for 7 min and 3 cm far from the gels. Then the ionogel valve was washed several times with deionised water (DI) and IPA, to remove any unpolymerised material and excess ionic liquid. Finally the valves were left to dry for 24 h at room temperature in the dark. The microfluidic valve was sealed by a PSA layer covering the top of the microfluidic device (see the microfluidic device fabrication section).

### Preparation of thermoresponsive ionogel and hydrogel discs

NIPAAm monomer (2.00 mmol), the MBAAm (0.04 mmol) and the photo-initiator DMPA (0.02 mmol) were mixed in a molar ratio of 100 : 2 : 1 in 1 mL of DI water in the case of the hydrogel (white and viscous solution) or in 1mL of IL in the case of the ionogel (transparent and viscous solution). The mixture was stirred and heated to 45 °C approximately for 10 min. The reaction mixture solution was pipetted into five different wells (100 µL in each well) of a transparent polystyrene 96-well microtitre plate (Greiner Bio-one, Germany) and the gels were UV polymerised at 365 nm (15.5 ± 0.5 µW $cm^{-2}$) for 7 min at 3 cm distant from the gels. The washing process followed the same procedure as for the ionogel valves.

## Characterisation of the thermoresponsive ionogel valves

### FTIR spectroscopy of the gels

The hydrogel, ionogel and EMIES ATR-FTIR spectra were collected with a Perkin-Elmer Spectrum 100 in the range of 650-4000 $cm^{-1}$ and were obtained from 16 scans with a resolution of 2 $cm^{-1}$. Before ATR-FTIR recording of the spectra, the samples were kept overnight in a vacuum oven at room temperature in order to extract adsorbed water from the samples. A background spectrum was also taken before the sample was loaded onto the ATR unit for measurement.

### Water holding capacity and degree of dehydration

In order to study the water holding capacity of both hydrogel and ionogel, structures fabricated using the same monomer concentration and volume of solvent (D.I. water or IL) samples were weighed before and after hydration and dehydration using a laboratory balance (Sartorius CPA 2235 with d = 0.0001 g, Spain). The degree of dehydration of the hydrogel and the ionogel at 23 °C and humidity of 62 % was measured from the decrease in gel weight over time. The degree of dehydration (α) is defined as:

$$\alpha = \frac{m_0 - m}{m_0 - m_f} \qquad \text{eq.1}$$

where $m_0$, $m$, and $m_f$ refer to the initial, actual, and final mass of the sample, respectively.[17]

The kinetic parameter (model rate constant ($k_m$)) was calculated using the same protocol proposed by Adnadjević *et al.*[17-18] using the equation:

$$\left[1 - (1 - \alpha)^{1/2}\right] = k_m \cdot t \qquad \text{eq.2}$$

being *t* the time.

**Disc volume changes**

Five different gels (ionogels and hydrogels) where placed in a thermostatic bath, either at 50 °C or 20 °C, with enough water to completely submerge the gels. To ensure a homogenous temperature within the gels, they were left to equilibrate for at least 30 min under these conditions.

Then, a picture of the gels was taken at both temperatures (Panasonic Lumix DMC-TZ7, CCD the 10.10 MP), and the diameter of the gel (swollen or shrunk) was measured from the picture by means of the image processing program (ImageJ, Java-based image processing program). This value was finally corrected using the diameter of a solid ring taken as a reference value (also present in the picture).

Figure 2 shows a top view picture of an ionogel and a hydrogel disc for size comparison after hydration in water at 23 °C for 20 minutes, and ambient humidity of 62 % (extracted from the water bath). In both cases, the initial diameter was 6.28 mm, which is the internal diameter of the microtitre well plate in which the polymerisation took place.

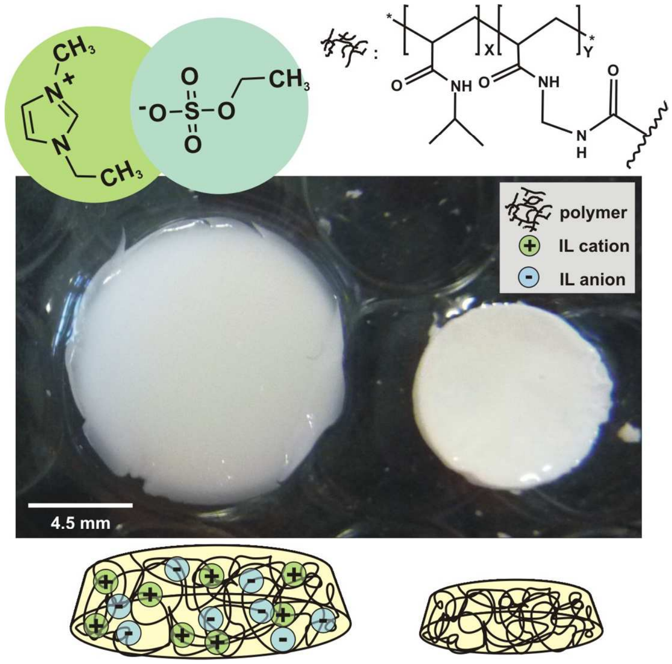

**Figure 2:** Top: Chemical structure of the polymer matrix, hydrogel, and the ionic liquid used for the fabrication of the ionogel. Middle: Picture of swollen EMIES-based ionogel (left) and swollen hydrogel (right) disc structures after 20 min

hydration in DI water at room temperature (RT). Bottom: Representation of ionogel and hydrogel components.

### LCST calculation

A similar protocol to the one presented above was employed for the determination of the LCST value of the ionogel and hydrogel, by looking at the change in the diameter dimensions of the gels as a function of temperature. In this case three different sets of hydrogels/ionogel discs were used and their change in diameter tracked with increasing temperature. The thermostatic bath was set at 15.0; 20.3; 22.1; 25.4; 27.1; 28.7; 30.0; 32.9: 34.9; 40.7; 45.0; 49.7 ± 0.3 °C and gel diameters were measured at each temperature. The LCST was determined by obtaining a first derivative plot of the diameter *versus* temperature. The first derivative of the size with respect to temperature is given by: D'(T) = dD/dT. The first derivatives have been calculated using the mean of the diameter at each temperature value (see supporting information). All calculations have been performed in triplicate using Excel 2007.

### Valve actuation characterisation

The modular microfluidic valve was placed in a homemade holder (Microliquid, Spain) that contains the heater (at the bottom) and the connectors (at the sides). The holder tightly constrains the microfluidic device and avoids leakages during valve actuation. A detailed fabrication and characterisation information of the holder can be found in the work presented previously by Verdoy *et al.*[19]

The heater provides a homogeneous heating rate of 7.4 °C $s^{-1}$ and a cooling rate of 2.4 °C $s^{-1}$ over the microfluidic device. The temperature of actuation was set between 50 °C to open the valve and 25 °C to close the valve. In addition, the holder and the microfluidic device were connected to a syringe pump (SP101IZ, WPI-Europe) for fluid control, placed at 40 cm distance from the holder, using flexible tubes of 2 mm I.D. and universal connectors. A constant flow of 1000 nL $min^{-1}$ is applied during duration of the experiments.

The flow rate passing through the valve was monitored using a flow microsensor (Sensirion CMOSens©, Switzerland) located after the holder and at 40 cm distance from the end of the holder. The microsensor reported an output of 1000 nL $min^{-1}$ when the valve was opened and 0 nL $min^{-1}$ when closed.

### Pressure resistance characterisation

A constant pressure increase of 100 mbar per minute was imposed across the device in order to characterise the valve pressure resistance. The set-up is similar to the one presented previously by Etxebarria *et al.*,[20] which includes a positive pressure flow controller that provides constant pressure over time (Fluigent MFCSTM FLEX, France), a flow microsensor to measure the flow rate passing through the valve and a pressure controller (EFD1500XL, USA), see Figure ESI-2. For pressures higher than 1000 mbar a Precision Fluid Dispenser (EFD 1500XL Liquid / Epoxy Adhesive Dispenser) was used. These elements are connected to the holder that houses the valve using commercially available connectors (Upchurch scientific, UK) and tubing (Anachem Ltd, Ireland) which allow for fast replacement of devices and leak-free operation.

## Results and Discussion

### Gels characterisation

#### a) Fourier transform infrared spectroscopy (FTIR)

The synthesis of both ionogel and hydrogel by co-polymerisation of NIPAAm in the presence of EMIES ionic liquid and water, respectively, to create hybrid materials for advanced functions is provided in the Experimental section. The two gels showed different physical properties after polymerisation, for instance, the ionogel is more flexible and transparent than the equivalent hydrogel. Apart from the advantage of the IL being non-volatile, another advantage of combining thermoresponsive gels with ILs over aqueous media is the possibility to tailor the properties of the resulting gels through the use of different pairs of anions and cations (polarity, viscosity, *etc*.). EMIES was chosen because it has halogen-free anion (less hazardous), it is stable at elevated temperatures, has great solution capacity for the NIPAAm monomers, it enhances water uptake/release, it shows greater thermal actuation behaviour, distinct solvatomorphology over its hydrogel equivalent[21] and biocompatibility, as demonstrated by us in a previous publication.[22] Moreover it is suitable for large-scale applications due to the reasonable price of this IL.[23]

Both gels were characterised by FTIR in order to prove that polymerisation of NIPAAm in the ionic environment of EMIES takes part similarly that the one in aqueous environment. Comparing the spectra for the hydrogel and ionogel in Fig. 3, the typical bands of NIPAAm are clearly visible. N-H stretching bands are present at

~3293 cm$^{-1}$ and ~3306 cm$^{-1}$ in the hydrogel and ionogel, respectively. The band at ~1640 cm$^{-1}$ for the hydrogel and ~1646 cm$^{-1}$ for the ionogel is assigned to the C=O stretching (amide I), while  for the amide II the N-H in-plane bending is given by the bands at ~1539 cm$^{-1}$ and ~1543 cm$^{-1}$ for the hydrogel and ionogel, respectively. Moreover, the symmetric vibrations of isopropyl methyls C-($CH_3$) are visible at ~1388 cm$^{-1}$ and ~1368 cm$^{-1}$ for the hydrogel and ~1392 cm$^{-1}$ and ~1368 cm$^{-1}$ for the ionogel.

Additionally, in order to ascertain the presence of EMIES ionic liquid inside the gel structure after the washing steps described in the experimental section, FTIR spectra comparison between the ionogel and pure EMIES was also performed. The two spectra clearly overlap on the band given by the C-H stretching vibrations of the imidazolium ring. In particular the carbons in position 4 and 5 give a band at ~3155 cm$^{-1}$ for EMIES and ~3157 cm$^{-1}$ for the ionogel, while the carbon in position 2 contributes for the band at ~3108 cm$^{-1}$ and 3110 cm$^{-1}$ for EMIES and ionogel, respectively. In addition, the C=N stretching vibrations band from the cationic ring is located for the pure EMIES at 1574 cm$^{-1}$, while for the ionogel the band is shifted to ~1570 cm$^{-1}$ as a small shoulder within the N-H in-plane bending (amide II) band of the polymer. Finally, the symmetric and asymmetric stretching vibrations bands from the -$SO_3$ moiety of the anion are also appearing in both spectra at 1217 cm$^{-1}$ and 1015 cm$^{-1}$ for EMIES and 1219 cm$^{-1}$ and 1018 cm$^{-1}$ for the ionogel, respectively.

This structural characterisation of the ionogel confirms both the successful polymerisation of poly(*N*-isopropylacrylamide) when using EMIES ionic liquid as solvent and, most importantly, the stable immobilisation of the EMIES inside the polymeric network, therefore its contribution to the actuation of the generated valves. The following sections will give more details about the thermoresponsive characteristics of the ionogel.

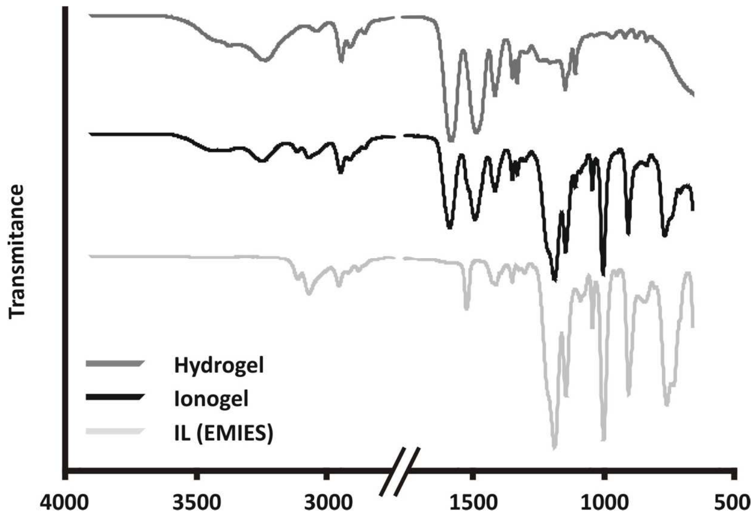

**Figure 3:** ATR-FTIR spectra of the hydrogel (blue), ionogel (red) and EMIES IL (black) from 4000 cm$^{-1}$ to 650 cm$^{-1}$.

### b) LCST values

Similar to chemical modifications of the polymeric backbone, the ionogel LCST can be considerably affected by the presence of the IL. In this case, the ionogel LCST was calculated to be 25.5 °C while the LCST of the hydrogel was 30.0 °C, see Figure ESI-3. These results are in agreement with the DSC temperature profiles obtained by Gallagher *et al.*[23], who reported LCST values of 26 °C and 31 °C for the ionogel and hydrogel, respectively.

### c) Degree of hydration

It was found that the water uptake of the ionogel is 3.8 times larger than the hydrogel. As can be seen in Figure 2, the ionogel increases its volume substantially more than the hydrogel when hydrated. As demonstrated by Gallagher *et al.*[23] since the ionogel is essentially anhydrous, the chemical potential drive for water absorption into the hydrophilic IL is very large, and therefore the ionogel swells considerably.

Figure 5 (left) shows the change in size of both hydrogel and ionogel discs with increasing-decreasing temperature. It can be seen that when using EMIES, the degree of swelling increased by 33.5 % with respect to the hydrogel while both structures reached the same shrinking volume after heating at 50 °C for 5 min. When comparing each gel separately before and after hydration, the hydrogel presents a large swelling effect, 35.5 %, which is nevertheless much smaller than the equivalent swelling of the ionogel, 57.6 %. On the other hand, under these experimental conditions, the shrinking effect of the hydrogel with temperature above its LCST is practically negligible, at *ca*. 2 %, which make this gel unsuitable for valve applications. The best performance was found for the ionogel, which shrinks by ca. 31 % of its original size at temperatures above its LCST.

### d) Degree of dehydration

Characterisation of the gel-based valve response is of high importance when the valve is integrated in a microfluidic device that is going to be used several times and/or after prolonged storage of the device prior to use.

One of the main drawbacks of using hydrogel valves is their rapid dehydration and disintegration over time when stored in the dry state. The use of ionogel gel-based valves prevents this occurring since ILs have a negligible vapour pressure so that a more robust gel can be obtained.[14] Figure 4 shows the degree of dehydration of the hydrogel and ionogel over time and their linear response (inset). These results demonstrate that valves fabricated using the EMIES ionogel dehydrate about three times slower than those based on the hydrogel. The calculated dehydration rate constants of the gels were found to be 5.8 x $10^{-3}$ $min^{-1}$ for the hydrogel and 2.3 x $10^{-3}$ $min^{-1}$ for the ionogel when using equation 2 in the linear range of $\alpha = 0 – 0.95$.

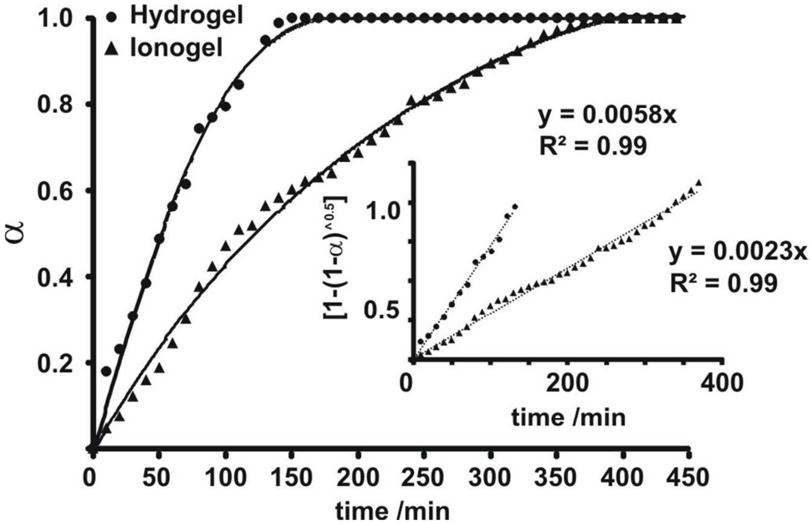

**Figure 4:** Dehydration curves of both hydrogel and ionogel at 23 °C as a function of time. Inset: It shows $[1-(1-\alpha)^{1/2}]$ *versus* time at the same conditions. Slope indicates dehydration rate constant of the gels.

Additionally, when comparing the dehydrated ionogel and dehydrated hydrogel, their physical characteristics are significantly different; with the hydrogel being hard and brittle (often cracking when dry), while the ionogel remains soft and with a homogeneous structure, since the EMIEM acts as plasticiser.

### e) Reversible swelling-shrinking behaviour

The difference in the swelling and shrinking mechanism between the hydrogel and ionogel can be attributed to the plasticising effect of the IL within the polymer network.[13] It is well known that lower crosslinking density results in increased water uptake, however this can result in a weaker mechanical stable gel. Therefore a compromise between physical–mechanical integrity (high degree of crosslinking) and extent of actuation (low degree of crosslinking) was established for this ionogel material in our previous publications.[23] [13] [5]

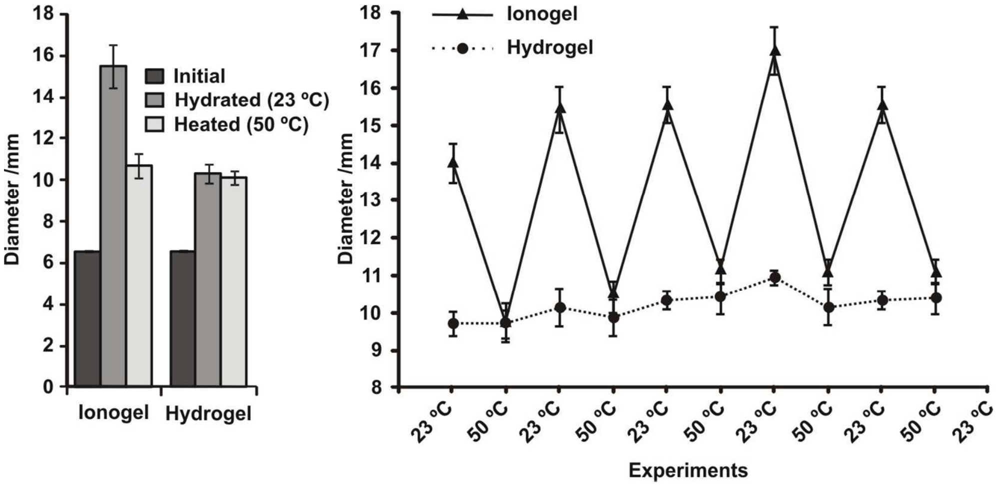

**Figure 5:** Diameter of ionogel and hydrogel at different conditions. Left: **Initial**: after polymerisation**; hydrated**: after 20 min in DI water at 23 ºC; and **heated**: after 5 min in DI water at 50 ºC. Right: actuation cycles of polymer discs, after 10 min swelling in DI water at 23 ºC and after 5 min shrinking in DI water at 50 ºC (n = 5).

Figure 5 (right) shows reversible actuation of the gels during up to five swelling and shrinking cycles. This experiment provides an estimation of the thermostability of the gels over time. In the case of the hydrogel the actuation is negligible with a substantial hysteresis. In the case of the ionogel the efficiency was found to be relatively constant with five different discs after five switching cycles. For example, the $\Delta D_{23\,^{\circ}C\rightarrow 50^{\circ}C}$ = 4.8 ± 0.7 mm (D = diameter) and the $\Delta D_{23\,^{\circ}C\rightarrow 50^{\circ}C}$ = 5.3 ± 0.6 mm have similar differences in dimension values, showing that these cycles are reproducible and repeatable, with little evidence of hysteresis. This result demonstrates that the ionogel material could be used at least five times, without significant thermodegradation. Therefore the valves fabricated with this material allow for the use of reversible, reproducible and cheap actuators by switching temperature below and above the LCST without losing performance over time.

The kinetic values of both swelling and shrinking mechanism were calculated to further investigate the feasibility of these materials as modular valves in microfluidic devices. During the swelling process, the ionogel has a $k_{sw} = 3.1 \pm 0.6 \times 10^{-3}$ $s^{-1}$, reaching the fully swollen structure after ~ 17 min, while the hydrogel has a faster kinetic value, $k_{sw} = 8.6 \pm 0.5 \times 10^{-3}$ $s^{-1}$, reaching complete swollen structure after ~ 3.5 min (Figure 6, top). These results demonstrate that the presence of EMIES IL in the gel interferes with the actuation mechanism of the gel. These differences can be explained considering the volume of water that each gel is able to accommodate. The hydrogel as presented in Figure 5 left (or Figure 6 top), hardly increases its volume when hydrated, reaching the thermostationary state very rapidly. In contrast, the ionogel is able to accommodate much bigger volumes of water, therefore increasing the time to reach the swollen steady state, and effectively decreasing the rate constant value. As demonstrated by Gallagher *et al.*[23] the highly porous morphology of the ionogel compared with the hydrogel (just poly-NIPAAm) has a significant effect on the hydration mechanism and therefore on the degree of swelling-shrinking.[24]

The shrinking process (50 °C) proved to be quite fast, with a complete actuation of the ionogel discs after 3.5 min. The shrinking rate constant was found to be $k_{sh} = 3.5 \pm 0.2 \times 10^{-3}$ $s^{-1}$ for the ionogel, while in the case of the hydrogel a slightly higher $k_{sh}$ was obtained $4.44 \pm 0.03 \times 10^{-3}$ $s^{-1}$, with a complete actuation after ~ 3 min (Figure 6, bottom). It has to be considered that in the case of the hydrogel this process is almost imperceptible, ~2 % (diameter change), as described above. It can be concluded that the addition of EMIES IL has no significant effect on the shrinking rate of the gels under these experimental conditions.

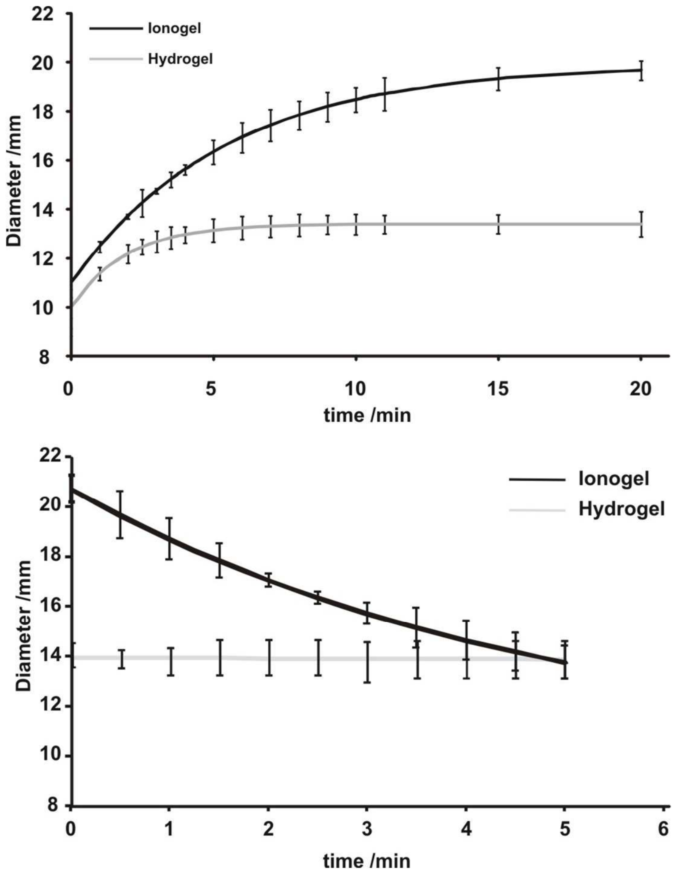

**Figure 6:** Top: Swelling kinetics of hydrogel and ionogel at 23 °C in D.I water after fully shrinking at 50 °C (n = 5). Bottom: Shrinking kinetics of hydrogel and ionogel discs at 50 °C in D.I water over time after fully hydration at 23 °C (n = 5). The model was fitted using the SOLVER function in MS Excel® 2011 and the exponential equation$f(t) = A(1 - e^{-kt}) + z$, where: $A$ is the pre-exponential factor, $k$ is the rate constant, $t$ is the time and the $z$ is the baseline offset.[25]

### Fabrication of the modular microfluidic valve

The three valves configurations were designed and fabricated as described in the Experimental section considering the two most efficient ways of incorporating the ionogel solution in the valve reservoir, filling in the channel or drop-casting, before photopolymerisation. Although the incorporation of the ionogel mixture is possible through the inlet of the channel and subsequent polymerisation through a mask, this process had some drawbacks (see the configuration of the valves "a" and "c", in the Figure ESI-1). In the valve "a", for instance, the outlet was blocked by the polymerised ionogel even after complete actuation of the valve, therefore, although the valve actuates, the polymerised gel in the channel make impossible for the liquid to flow through the channel. In the case of the valve “c”, since the inlet and outlet channels are connected to the valve chamber just through two small holes, those holes were often blocked by the ionogel and were not operative even after full actuation of the valve (< 5 % of the valves were operative after photopolymerisation). In the case of the valve “b”, since the inlet and outlet are connected through a channel that sits on top of the valve, more than 90 % of the valves were operative after photopolymerisation. The reason for that lies in the way the ionogel blocks the channel after hydration and in the effective opening of the channel after thermal actuation. Therefore the photopolymerisation of the ionogel solution in the valve chamber (i.e. a known volume of ionogel solution pipetted in the valve chamber) and subsequent closing of the valve gave much better results (see the configuration of the valve “b”, in the Figure ESI-1) and it was used for the characterisation of the modular microfluidic valve from now on.

### Characterisation of the thermoresponsive ionogel valves

After successful integration of the ionogel valve into the modular microfluidic valve (Figure 1) characterisation of the polymericvalve was carried out. Considering that the fabrication of the ionogels valves was performed manually by drop casting the monomer mixture, it is reassuring that the majority of the valves were operative after fabrication (> 90 %, n = 10). This percentage could be increased if the fabrication of the valves is automated by using other techniques like inkjet printing[26] [27]. The set-up described in the experimental section was used in order to investigate the failure pressure of the valve. The characterisation protocol is intended to identify the valve’s capabilities for flow blockage (*i.e.* pressure failure).

The failure pressure value, which is the minimum upstream pressure at which the valve will operate, gives information of the operability of the valve and therefore the microfluidic device module. When that pressure is reached the valve will no longer be completely effective.

Figure ESI-4 shows a typical result obtained using a modular microfluidic device incorporating an ionogel valve. The failure pressure was determined to be 1100 ± 100 mbar for four out of five of the investigated valves. This pressure is considered to be sufficient for most of the microfluidic applications.[28]

After valve failure, the thermoactuation process and associated swelling enabled the channel to be once again blocked, and the most of these valves could be reused, four out of five of the tested valves. Failure tests were repeated with these valves and the failure pressure values decreased substantially to 300 ± 100 mbar (n = 5) and their reproducibility was very low. Nevertheless, it was determined that an applied pressure of 200 mbar does not affect the performance of valves that had previously been exposed to extreme pressures (> 1100 mbar).

The actuation behaviour of the valves were characterised at a constant flow rate of 1000 nL min$^{-1}$, using the set-up described in Figure ESI-5. Four ionogel valves out of five operated satisfactorily and the one that was not operative was found to have a fabrication error (*i.e.* the inlet microchannel was blocked by the ionogel). Figure 7 presents the thermal reversibility of the ionogel-based modular microfluidic valve. Although the figure shows three full cycles, the valve was fully reversible for up to eight cycles with no significant decrease in performance.

When the valve was in the closed state, the flow sensor at the end of the system (see Figure ESI-5) reported a flow rate of 0 nL min$^{-1}$. After approximately 2 min, the heater was switched on and the temperature increased to > 50 °C, passing through the ionogel LCST (25.5 °C) in ~ 3.6 s. After that, the ionogel contracted, opening the valve in less than 4 ± 1 s, (n = 5). For full actuation of the valve, a longer time is obviously required, see Figure 6 bottom. The differences in actuation times with respect to the discs can be explained as follows: firstly, the heating efficiency of the holder containing integrated heaters is higher than using a traditional hot water bath to control the changes in temperature. Secondly, a faster response is expected for the ionogel-based valve since the amount of ionogel used is just 7 ± 1 µL compared with 100 µL used to make the discs for previous characterisation (*i.e.* the valves are considerably smaller features, with much shorter mean water diffusion pathlengths).

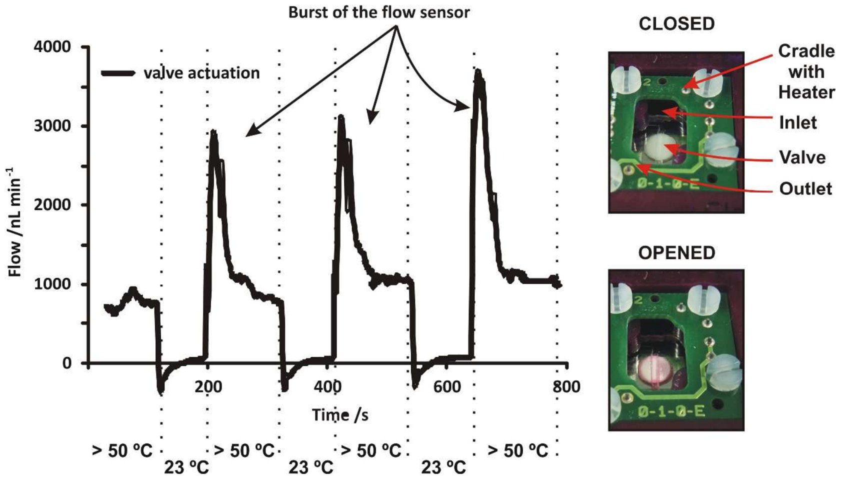

**Figure 7:** Top: picture of the ionogel valve (7 ± 1 μL) inserted in the holder with integrated heaters at the bottom. Bottom: open valve (flow at 1000 nL $\text{min}^{-1}$) and closed valve (flow at 0 nL $\text{min}^{-1}$) sequence for three full cycles. High flow spikes are due to the stabilisation of the microflow sensor after the opening of the valve.

Approximately 2 min after the actuation of the valve, the heater was switched off reaching the LCST of the ionogel in ~10 s. The valve recovery process was found to be very fast compared to the ionogel disc, with the channel becoming completely closed in 32 ± 2 s. In addition no substantial fatigue of the valve was observed through fast open and closing cycles (n = 10).

The thermocontrol of the valve actuation facilitates non-contact operation and therefore independent manipulation of liquids in multiple microfluidic channels within an integrated microfluidic manifold simply by positioning heating entities below the channels. It is clear that such thermoresponsive ionogel valves have the potential to greatly enhance the ease of fabrication and subsequent operation of multifunctional microfluidic devices.[29] [30] Moreover these ionogels valves are low cost to produce in terms of materials, and its *in-situ* fabrication via photo-polymerisation opens up the possibility of creating large arrays of valves in complex microfluidic structures.

## Conclusions

The swelling and shrinking mechanisms of a thermoresponsive imidazolium-based ionogel have been prepared, characterised and compared with an equivalent IL-free hydrogel. It was found that upon hydration of the gels, the ionogel swells 33.5 % more than the hydrogel in volume. After thermal heating, the ionogel decreases 31 % its volume as a consequence of the loss of water from the polymer matrix while the hydrogel volume change is negligible. Ionogel swelling and shrinking kinetics suggest that the ionic liquid entrapped within the polymer matrix has a significant influence on the actuation mechanism of the ionogel.

Modular microfluidic valve structures based on the ionogel were demonstrated to perform effectively within a microfluidic channel. The reusability of the whole platform was demonstrated through repeated channel open/close cycles of the ionogel valve. In its current configuration, the valve can be actuated up to 8 times without showing any sign of failure. Moreover, pressure tests performed on the polymeric valves demonstrated that four out of five valves resist pressures up to1100 mbar and it was concluded that all valves can be continuously operated at pressures above 200 mbar without failure.

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