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# Responsive and recognitive hydrogels using star polymers

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**Abstract:** Polymeric networks that have inherent capabilities to recognize different molecules and chemical changes in their environment are the next generation of materials that will aid in the diagnosis and treatment of diseases. We have prepared new networks based on star polymers that were designed to be responsive and recognitive. Using molecular imprinting with D-glucose and crosslinking with poly(ethylene glycol) dimethacrylate with an ethylene glycol chain of nominal molecular weight 600, we prepared star

polymer networks, which exhibited over 300% more uptake for D-glucose compared to D-fructose. Using copolymerization with methacrylic acid, we prepared star polymer networks with pH-sensitivity, which showed a sharp transition in swelling around a pH of 4.5. © 2004 Wiley Periodicals, Inc. *J Biomed Mater Res* 68A: 439-447, 2004

**Key words:** recognition; pH sensitive; molecular imprinting; modulated drug delivery

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## INTRODUCTION

Recent research in the biomedical field focuses on molecular design of polymeric materials to create efficient biomedical platforms that are able to perform the specific functions normally performed by biological entities.

Environmentally sensitive polymer networks, which have inherent capability to recognize chemical changes in their environment, are the next generation of materials in drug delivery and biosensing. Poly(ethylene glycol)-based materials containing methacrylic acid with low immunogenic and pH-sensitive characteristics have been shown to protect proteins and peptides against the harsh environment of the body and deliver them efficiently to the small intestine for oral delivery of proteins and peptides.<sup>1-3</sup>

The most promising area in environmentally sensitive polymer networks are recognitive polymer networks. Molecular imprinting of these polymer networks during polymerization forms interactions between the template molecule and the building

blocks of the polymer, stabilizing these interactions. This process renders the resulting network inherently able to recognize and bind a specific molecule in their environment, and distinguish between this molecule and structurally similar compounds<sup>4,5</sup> (Fig. 1).

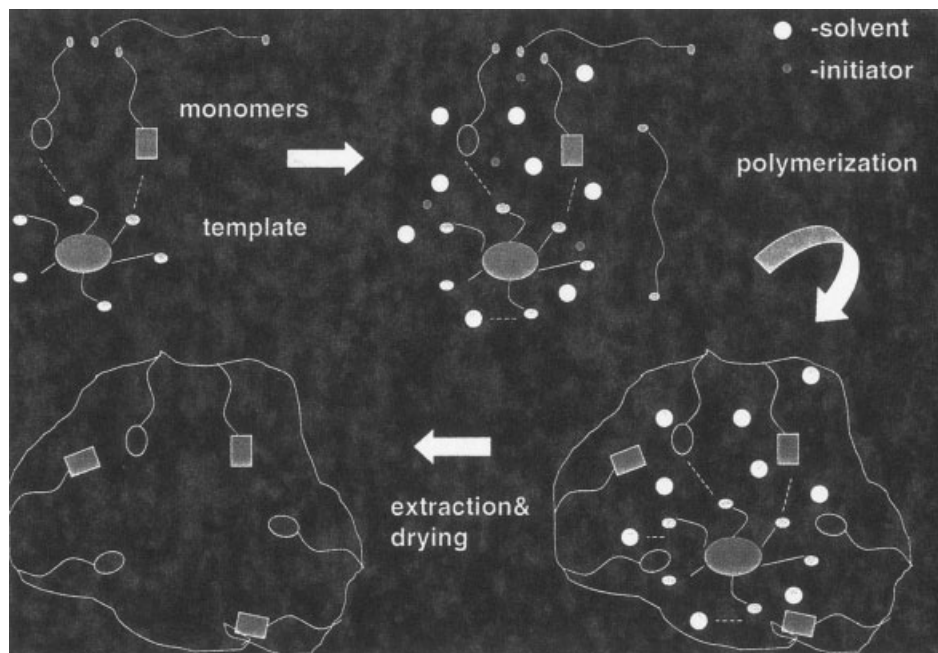
The important processes in creating a recognition-based polymer are (1) creating well-defined sites during the polymerization by the design of relevant interactions; (2) preserving the structure of imprinted sites intact; and (3) allowing for ease of diffusion of solutes into and out of the network.

The ideal imprinting effect would be one in which the imprinting creates an on/off switch such that only the template is bound and all other molecules are rejected. However, interactions for similar compounds are often the same, resulting in less selectivity and differentiation of similarly structured compounds. Moreover, the selectivity and differentiation between certain compounds are greatly affected by the application in which the imprinted polymers will be used. For instance, applications in analytical chemistry require distinction between molecules such as enantiomers. In drug delivery applications, however, the selectivity will be dictated by less similar compounds. Nevertheless, the major factors affecting the creation of specific sites are the interaction between the monomers and the template and having an increased number of point interactions. Our hypothesis was that by using monomers with a large number of available functional sites and increasing the probability of inter-

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**Figure 1.** Schematic diagram of molecular imprinting: polymerizable monomers and template are mixed, complexation occurs, and bonds are formed between different monomers and the template molecule; with the aid of a crosslinking agent and an initiator, polymerization takes place around the formed complex to freeze the interactions of the template in place; the template is extracted by washing and complementary sites are created in the network.

action between the template and monomer, we could create sites specifically for the template molecule. We are especially interested in this to create imprinted networks in water that would be based on noncovalent interactions between the template and monomers.

Star polymers are hyperbranched polymers with large number of arms emanating from a central core. The advantage of star polymers in creating responsive and cognitive networks is the presence of a large number of functional groups in a small volume. Although researched mostly for their rheological properties for a long time, star polymers and other dendritic structures are finding more and more applications such as tissue engineering and gene delivery.<sup>6-11</sup>

In this work, we investigated the use of star polymers as advanced materials for pH-sensitive and cognitive polymer networks. The success of these materials would lead to the development of synthetic networks with specifically designed molecular properties that can act as parts of modulated drug delivery devices that will sense compounds and deliver others at the same time.

## EXPERIMENTAL

### Materials

Poly(ethylene glycol) (PEG) star polymers were purchased from Shearwater, Inc. (Huntsville, AL)

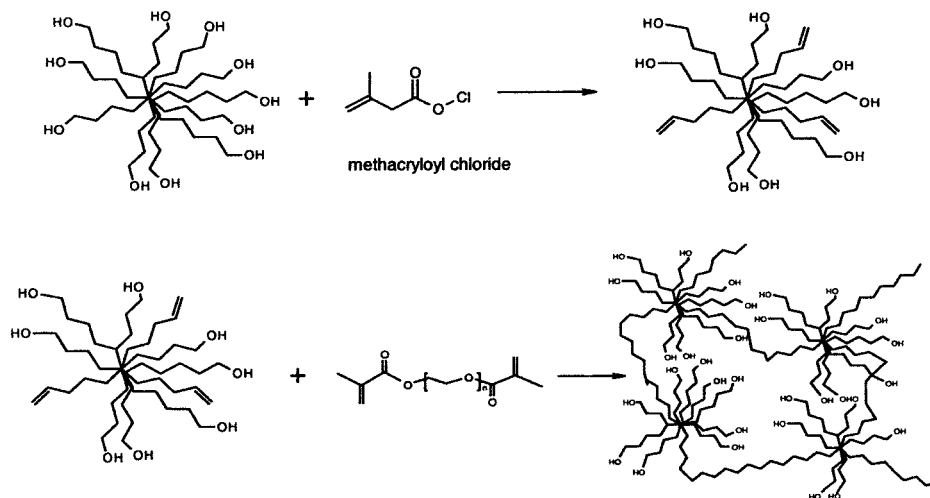
were treated as described in the next section. Methacrylic acid (MAA) (Polysciences, Inc., Warrington, PA) was vacuum distilled before use. Poly(ethylene glycol) dimethacrylate with a poly(ethylene glycol) chain of nominal molecular weight 600 (PEG600DMA) (Polysciences, Inc., Warrington, PA), D-glucose, D-galactose, D-fructose, (Sigma-Aldrich, St. Louis, MO), and Irgacure® 184 (Ciba Specialty Chemicals, Hawthorne, NY) were used as received.

### Synthesis of star polymer networks

Star polymer networks were synthesized by crosslinking polymerizable star polymer molecules in the presence of crosslinking agents and monomers. PEG star polymers with various number of arms and molecular weights were custom made by Shearwater, Inc. (Huntsville, AL). Properties of these polymers are listed in Table I. To make chain ends polymerizable,

**TABLE I**  
Properties of Poly(ethylene glycol) Star Polymers

Grade	Number of Arms	Molecular Weight per Arm, $M_n$ (g/mol)	Molecular Weight of Star Polymer, $M_n$ (g/mol)
Star-PEG 423	75	5970	450,000
Star-PEG 432	31	20,000	624,000



**Figure 2.** Schematic depiction of methacrylation and network formation of PEG star polymers.

star polymers were functionalized with methacrylate groups (Fig. 2).

Samples of 100 mL of tetrahydrofuran and 30 mL of toluene were poured into a 250-mL glass bottle. Approximately 1 g (all of the manufacturer's bottle labeled "1g") of PEG star polymer was dissolved in the mixture by ultrasonication for 30 min. After dissolution, the milky solution was mixed with 0.6 g of triethylamine and transferred to a 250-mL three-neck flask. Nitrogen gas was purged through the mixture for 20 min. A sample of 3 mL of methacryloyl chloride was placed in an ice bath and micropumped at a rate of approximately 100  $\mu\text{L}/\text{min}$ . The mixture was heated until 42°C and the reaction continued at  $42.8 \pm 1.9^\circ\text{C}$  for 16 h. The resulting mixture was vacuum filtered through a paper filter (#4, Whatman, Kent, UK). The white hygroscopic filtrate was dried in a vacuum oven at 36°C for 48 h.

#### Synthesis of pH-sensitive star polymers

Methacrylated 75 arm PEG star polymer (0.0592 g) was dissolved in a mixture of 0.3058 g of methacrylic acid (MAA), 2.7090 g of PEG600DMA, and 3.3658 g of deionized water. Irgacure<sup>®</sup>184 was added in the amount of 0.63 wt % of total solution.

The solution was purged with nitrogen in a closed environment with an air outlet for 17 min to remove oxygen. Then the solution was pipetted between two glass slides separated by a 0.7 mm thick Teflon<sup>®</sup> spacer. The solution was polymerized under a UV light of intensity 12.71 mW/cm<sup>2</sup> for 15 min.

The formed polymers were removed from the slides and washed in deionized water for 4 days until the unreacted monomers were removed. Then they were dried in a vacuum oven under 28 mmHg vacuum for 2 days.

#### Synthesis of cognitive star polymers

In a typical experiment, 0.1 g of methacrylated PEG star polymer was mixed with 1.5 g of PEG600DMA. 0.12 g of glucose was added to the mixture, which was then diluted with deionized water to contain 50 wt % water. Initiator Irgacure<sup>®</sup> 184 was added to comprise 1 wt % of solution.

The mixture of components was purged with nitrogen gas for approximately 20 min to remove oxygen, which acts as a free-radical scavenger. The degassed solution was pipetted between glass slides separated by 0.7 mm Teflon<sup>®</sup> spacers. The glass slides were placed under ultraviolet light (Acticure, Efos, Inc., Mississauga, ON) of intensity 10–15 mW/cm<sup>2</sup>. The polymerization reaction took place under a nitrogen environment for 15 min. Control polymers were also prepared without star polymers.

#### Methods for characterization of star polymer networks

The size and size distribution of the star polymer molecules were determined by photon correlation spectroscopy (PCS) using Coulter<sup>®</sup> N4 Plus Submicron Particle Sizer (Coulter, Miami, FL).

Unmodified PEG star polymer samples were dissolved in deionized water. The concentration was modified so that the intensity of the light was between  $5 \times 10^4$  and  $10^6$  counts per second. The incident light was at 90° with the sample.

#### Characterization of cognitive star polymer networks

To calculate the uptake of different compounds for imprinted and nonimprinted polymers, dry circular

discs were cut out of polymer films. These discs were approximately 1 cm in diameter and 0.7 mm thick. Samples of 0.5–1 g of polymer discs were placed in 10–30 mL of single or mixed sugar solutions in an amber bottle and placed on an orbital shaker. The shaker speed was carefully adjusted so that the polymer discs were not exposed to air and stayed in solution for the entire duration of the experiment, which was 24 h.

In dynamic experiments, a 0.5-mL sample was taken out of the sugar solution at constant time intervals. The samples taken from the binding experiments were then analyzed using high-pressure liquid chromatography (HPLC).

The permeability coefficients of glucose and other sugars were determined by using a side-by-side diffusion cell (Crown Glass Co., Fremont, MI). A thin membrane of crosslinked polymer gel that had been preswollen in deionized water was placed between the donor and receptor cells. The connection was sealed with a piece of Parafilm® (American National Can, Neenah, WI) and clamped together.

A concentrated solution of the desired compounds, typically 2500 mg/dL each, was placed in the donor compartment. Both compartments were thoroughly mixed for the duration of the experiment by a magnetic stirrer. A 1-mL sample was taken out of the receptor compartment at certain time intervals and replaced with deionized water. The samples were analyzed on the HPLC.

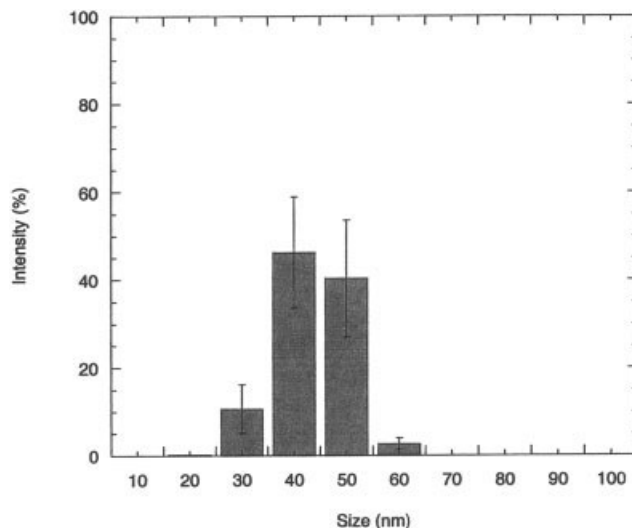
For detection on the HPLC, a 30 cm-long, 0.78-cm inner diameter column packed with 8% crosslinked sulfonated styrene divinyl benzene (Rezex RPM Monosaccharide Column, Phenomenex, Torrance, CA), was used.

#### Characterization of pH-sensitive star polymer networks

Solutions of different pH were prepared using citric acid buffer solutions at six different pH values between 2 and 8. Dry polymer films were cut in discs and each disc was weighed and placed in a solution with a different pH. At 18, 36, and 48 h, the discs were taken out of solution, patted on a piece of tissue paper to get rid of excess solution on the surface, and weighed. After the weight was recorded, the discs were placed back in solution. Dry samples and samples swollen to maximum weight were also weighed in a nonabsorbing solvent (heptane,  $\rho = 0.684 \text{ g/cm}^3$ ).

## RESULTS AND DISCUSSION

To estimate the area and volume available for interactions on each star polymer molecule, size distribu-



**Figure 3.** Size distribution of unmodified polyethylene glycol star polymers with 31 arms and molecular weight per arm of 20,000. The intensity of light scattered is measured as a function of size of particles. Data represent an average of  $n = 4 \pm$  standard deviation.

tion was obtained for unmodified star polymers. In Figure 3, the size and size distribution of PEG star polymers with 31 arms and  $M_n$  of 20,000 can be observed. Although some aggregation was observed at around 280–300 nm, dilution gave better results. For star polymers with longer arms, the average size was  $43.1 \pm 7.4 \text{ nm}$ .


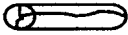


The formation of sites is dependent on proximity between various components of the system. The proximity is not determined by weight or molar ratios, but by the volume ratios of the components. The radius of star polymers in water was obtained by PCS. Star polymers and glucose were assumed spherical, the crosslinking agent and initiator were assumed cylindrical and water volume was calculated directly by using its density.

A set of values calculated for these systems is shown in Table II. It is clear that for star polymers, which are very large molecules, volumes should be taken into consideration when discussing imprinted properties. Although their weight percentage in the polymer was on the order of 2%, they occupied approximately 50% of the volume, which provided the high functional density required for the formation of highly specific sites.

Because these polymer networks are highly crosslinked, the mesh size of the polymer networks was a parameter that provided insight into the structure of the networks and the ease of diffusion of different sizes of molecules through them.

Gravimetric studies were also performed on both dry and swollen samples to determine the volume and volumetric expansion of gels in the presence of solvent.

**TABLE II**  
Calculated Volumes for Star Polymer Network Components for PEG Star Polymer with  $M_a = 20,000$  and  $N_a = 31$

Component	Shape	Radius (nm)	Length (nm)	Volume (cm <sup>3</sup> )	Volume Percentage (%)
Star Polymer ( $M_a = 20,000, N_a = 81$ )		20	—	3.2	50
PEG600DMA		0.15	3	0.7	11
Glucose		0.75	—	0.76	12
Irgacure®		0.15	0.5	0.0023	0.04
Water	—	—	—	1.7	27
Total				~6.36	

The volume and volume fraction of gels were calculated by:

$$V = \frac{W_a - W_h}{\rho_h} \quad (1)$$

where  $V$  is the volume of gel in cm<sup>3</sup>,  $W_a$  is the weight in air in grams,  $W_h$  is the weight in heptane in grams and  $\rho_h$  is the density of heptane (0.684 g/cm<sup>3</sup>).

By using the volume of the gel in different conditions, the volume fraction of polymer in solvent can be calculated.

$$v_{2,r} = \frac{V_d}{V_r} \quad v_{2,s} = \frac{V_d}{V_s} \quad (2)$$

where  $v_r$  is the polymer volume fraction in the relaxed state,  $V_d$  is the volume of polymer in the dry state,  $V_r$  is the volume of gel in the reacted state,  $v_{2,s}$  is the polymer volume fraction in the swollen state, and  $V_s$  is the volume of gel in the swollen state.

Molecular weight between crosslinks  $\bar{M}_c$  for a polymer prepared in the presence of a solvent is calculated from:

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{(\bar{v}/V_1)[\ln(1 - v_{2,s}) + v_{2,s} + \chi_1 v_{2,s}^2]}{v_{2,r} \left[ (v_{2,s}/v_{2,r})^{1/3} - \frac{1}{2}(v_{2,s}/v_{2,r}) \right]} \quad (3)$$

where  $\bar{v}$  is the specific volume of the polymer in the dry state,  $V_1$  is the molar volume of the solvent,  $\chi_1$  is the Flory interaction parameter for the polymer and solvent,  $\bar{M}_n$  is the hypothetical molecular weight that would be obtained in the case of a linear polymer under the same reaction conditions, and  $\bar{M}_c$  is the molecular weight between crosslinks.

The  $\chi_1$  factor used in this study was obtained from the empirical equation obtained for PHEMA by Bahar et al.:<sup>12</sup>

$$\chi_1 = 0.322 + 0.904v_{2,s} \quad (4)$$

The density of crosslinking in the structure was

indicated by the molecular weight between crosslinks. However, the mesh size of the network is an actual calculation of distance available within the network. The mesh size,  $\xi$ , is given by:

$$\xi = v_{2,s}^{-1/3}(r_0^{-2})^{1/2} = v_{2,s}^{-1/3}(C_n N \ell^2)^{1/2} \quad (5)$$

where  $C_n$  is the characteristic ratio (4.1 for poly(ethylene glycol)),  $N$  is the number of units,  $\ell$  is the distance between two backbone atoms (C–C; 1.54 Å). The number of units,  $N$ , is related to the molecular weight between crosslinks by:

$$N = \frac{2\bar{M}_c}{M_r} \quad (6)$$

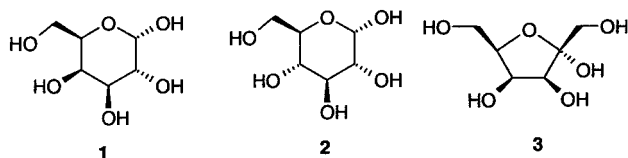
where  $M_r$  is the molecular weight of a single repeating unit.

The mesh size of glucose-imprinted P(PEG star-co-PEG600DMA) ( $M_a = 5970$ , 75 arms) polymer networks was determined to be 22.4 Å. This value was similar to the length of the crosslinking agent. Therefore, the volume within the network was determined largely by the crosslinking agent. Also, this mesh size is only slightly larger than the diameter of the diffusing small molecules (D-glucose: 15 Å).

### Recognitive star polymer networks

To assess the success of an imprinted polymer, several factors are important. The capacity of the polymers is important in identifying the difference between imprinted and nonimprinted polymers in binding of the template molecule. Also, the capacity of imprinted polymers for different molecules can be compared to calculate selectivity, which is the preference of the polymer to bind the template over structurally similar molecules.

The amount of sugar taken up by the polymer samples was calculated by the following material balance:



**Figure 4.** Chemical structures of template D-glucose (1) and structurally similar D-galactose (2) and D-fructose (3).

$$C_{si}V_{si} = C_{st}V_{st} + C_{pt}V_{pt} + \sum_{k=1}^1 C_{sk-1}\Delta V_{k-1} \quad (7)$$

Here,  $C_{si}$  is the initial concentration of sugar in the solution in mg/dL,  $V_{si}$  is the initial volume of solution in dL,  $C_{st}$  is the concentration of sugar at time  $t$ ,  $V_{st}$  is the volume of solution at time  $t$ ,  $C_{pt}$  is the concentration of sugar inside the polymer at time  $t$ ,  $V_{pt}$  is the volume of solution absorbed into the polymer at time  $t$ , and  $\Delta V$  is a constant volume of sample (0.5 mL) taken out for analysis.

The terms  $C_{si}$  and  $V_{si}$  were controlled precisely by weighing the solutions and sugars to the nearest tenth of a milligram. The term  $C_{st}$  was obtained from analysis on the HPLC, while  $V_{pt}$  was determined by dynamic swelling experiments by the following equation by incorporating the density of the sugar solution.<sup>13</sup>

$$V_{pt} = (W_s - W_d) \times 1.0175 \text{ ml/g} \quad (8)$$

The amount of solution at any time  $V_{st}$  was calculated from:

$$V_{st} = V_{si} - V_{pt} - \sum_{k=1}^t \Delta V_{k-1} \quad (9)$$

The product,  $C_{pt}V_{pt}$ , is the amount of uptake by the polymer. The capacity of the polymer was defined as:

$$\text{Capacity} = \frac{C_{pt}V_{pt}}{W_d} \quad (10)$$

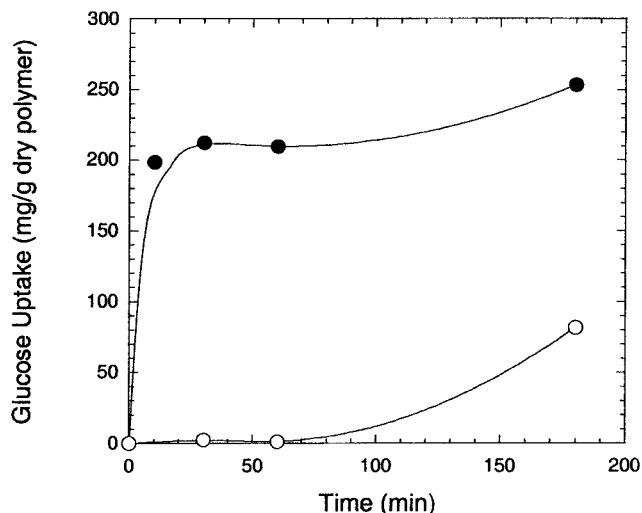
and was reported in mg/g dry polymer.

The selectivity of the star polymer networks was assessed by comparing the uptake of the template

**TABLE III**  
Capacity of Nonimprinted and Glucose-Imprinted Star Polymer Networks as a Function of Number and Molecular Weight of Arms

Polymer	Glucose Uptake (mg/g Dry Polymer)
Nonimprinted (31 arms, $M_a = 20,000$ )	118.7 ± 3.31
Imprinted (31 arms, $M_a = 20,000$ )	253.2 ± 1.24
Nonimprinted (75 arms, $M_a = 6,970$ )	197.5 ± 1.24
Imprinted (75 arms, $M_a = 6,970$ )	198.8 ± 1.78

Data represent average of  $n = 3 \pm$  standard deviation.



**Figure 5.** Selectivity of P(PEG star-co-PEG600DMA) ( $M_a = 20,000$ , 31 arms) imprinted with glucose. Data represent glucose (●) and fructose uptake (○).

molecule D-glucose and structurally similar sugars, D-galactose and D-fructose (Figs. 4 and 5).

The capacity of glucose-imprinted star polymer networks with 31-arm and 75-arm star polymers at 180 min are shown in Table III. The polymers reached swelling equilibrium on the order of 120–140 min. Binding equilibrium was reached within 180 min; however, imprinted polymers showed deviations from this time presumably due to sites with different affinity. The values reported here are the binding amounts at 180 min. The imprinted networks made with 75-arm star polymers showed similar capacity compared to the nonimprinted polymer, whereas the imprinted networks made with 31-arm star polymers showed a 213% increase over the nonimprinted polymer.

As networks based on hydrogen bonding, the capacity of these polymers correlated with an increase in selectivity. Glucose and fructose uptake of the glucose-imprinted system is shown in Figure 5 and Table IV. The ratio of glucose to fructose uptake for this polymer was  $3.13 \pm 0.44$ . The 75-arm materials that did not show differences in capacity between imprinted and nonimprinted polymers also did not show any selectivity between D-glucose and D-galactose.

Because the structure of the sugars that were tested

**TABLE IV**  
Selectivity of Glucose-Imprinted Star Polymer Networks ( $M_a = 20,000$ , 31 Arms)

	Glucose Uptake (mg/g dry polymer)	Selectivity Ratio
Glucose	253.2 ± 1.24	3.13 ± 0.44
Fructose	82.0 ± 9.9	—

Data represent average of  $n = 3 \pm$  standard deviation.

**TABLE V**  
Permeability Coefficients for Glucose in Imprinted and Nonimprinted P(PEG star-co-PEG600DMA) ( $M_n = 20,000$ , 31 Arms)

No. of Arms	Imprint Molecule	Percentage of Imprint Molecule in Initial Mixture (mol % without Solvent)	Permeability Coefficients for Glucose $\times 10^8$ (cm/s)
31	—	—	15.6
31	Glucose	24.5	20.6
31	Fructose	24.9	34.7

in this study were very similar, it is quite significant that such large selectivity was observed between them. The factors that were essential for this result were high crosslinking ratio, and large number of interactions between the template and monomers. What is even more significant was that the polymerization process was performed in water and selectivity was shown in water, which is a strong hydrogen-bonding solvent. This suggests that this type of imprinted polymers is highly promising for biomedical applications, where performance in aqueous environment is essential.

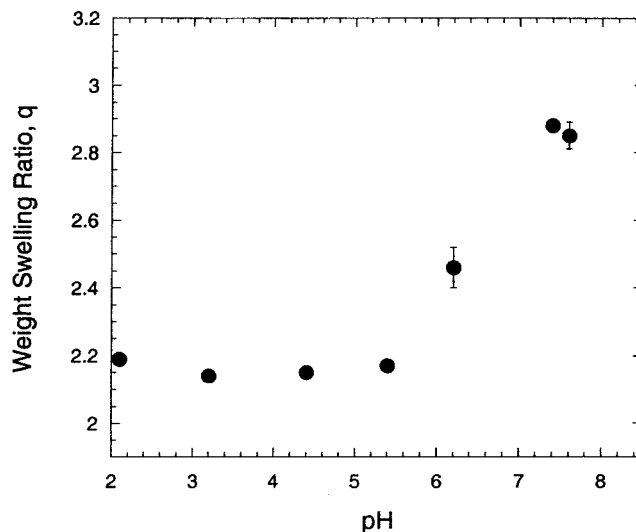
### pH-sensitive star polymer networks

Incorporating environmental sensitivity to the star polymer morphology is of great potential in the pharmaceutical and biomedical fields. Polymers with pH sensitivity have been used in the protection and delivery of drugs as well as sensing applications.<sup>14,15</sup> The advantage of using star polymers is the large number of groups that they contain, which can provide large changes in volume as a function of changes in the environment.

For detection of sensitivity in the change of the weight of polymer with respect to changes in pH, the weight swelling ratio,  $q$ , was used. By using the respective weights of the dry and swollen samples,  $q$  was calculated:

**TABLE VI**  
Permeability Coefficients for Fructose in Imprinted and Nonimprinted P(PEG star-co-PEG600DMA) ( $M_n = 20,000$ , 31 Arms)

No. of Arms	Imprint Molecule	Percentage of Imprint Molecule in Initial Mixture (mol % without Solvent)	Permeability Coefficients for Fructose $\times 10^8$ (cm/s)
31	—	—	11.9
31	glucose	24.5	17.0
31	fructose	24.9	25.2



**Figure 6.** Equilibrium swelling behavior as a function of pH of P(PEG star-co-MAA-co-PEG600DMA) polymers. Citric acid buffer was used to prepare the solutions used. Each datum represents an average of  $n = 3 \pm$  standard deviation.

$$q = \frac{W_s}{W_d} \quad (11)$$

where  $W_s$  is the weight of the swollen sample in grams, and  $W_d$  is the weight of the dry sample.

The pH sensitivity of the poly(polyethylene glycol star-co-methacrylic acid) [P(PEG star-co-MAA)] material can be observed in Figure 6. Below a pH value of 4.4, the swelling ratio of the polymer is constant around 2.15. Between the pH values of 4.4 and 7.4, the network opens up to swell to a ratio of 2.87. The reason for this behavior is twofold. First, at pH values below the  $pK_a$  of methacrylic acid ( $pH < 4.5$ ), the carboxylic acid groups of this moiety are protonated and neutral. When the pH exceeds 4.5, the carboxylic acids become deprotonated and strong charge repulsion occurs between these groups, which leads to the swelling of the network and uptake of more solvent. The second mechanism is the hydrogen bonding between the protonated carboxylic acid groups and the etheric oxygen on the polyethylene glycol chains at low pH.<sup>16</sup> This phenomenon has been studied thoroughly in our lab, and leads to an extra effect of swelling at higher pH, where the complexation is no longer active.

The exact placement of the methacrylic acid moieties are not known at this stage. According to the distribution of these groups and their relative position to one another, each of the above-mentioned mechanisms could be prevalent.

The high crosslinking ratio of these polymers did not allow for large changes in the swelling of the polymer networks as a function of changes in pH. Modification of the crosslinking will be essential in tuning the response of these materials.<sup>17</sup> However, the

swelling behavior shown by these polymers in the weight swelling ratio range of 2–2.9, was also consistent and sharp.

### Permeability of star polymer networks

Permeability of the compounds through imprinted and nonimprinted star polymer networks was determined in the following manner. First, a mass balance was set up for the compounds over both the donor and receptor cells of the diffusion apparatus:

$$VC_{a,n+1} + VC_{b,n+1} = VC_{a,n} + VC_{b,n}(1 - m) \quad (12)$$

where  $V$  is the volume of each of the cells in dL,  $C_a$  and  $C_{a,n}$  are the concentrations of solute in the donor cell at the beginning of the experiment and after a certain time period  $\Delta t$  where diffusion has taken place,  $C_b$  and  $C_{b,n}$  are the concentrations of the solute in the receptor cell in mg/dL, and  $m$  is the ratio of sample volume to cell volume. This ratio needs to be taken into account because the volumes of the samples (1 mL) are comparable to the volume of the cells (4 mL) and cannot be neglected.

The permeability of a membrane can be calculated from:

$$V \frac{dC_b}{dt} = AP(C_a - C_b) \quad (13)$$

where  $C_b$  is the concentration of solute in the receptor cell at time  $t$ ,  $A$  is the effective area of permeation, and  $P$  is the membrane permeability coefficient.

When Equation (12) is solved for  $C_{a'}$ , substituted into Equation (13), and integrated over  $t_n$  to  $t_{n+1}$ , the following equation results:

$$C_{b,n+1} = \frac{1}{2} \left\{ C_{a,n} + C_{b,n}(1 - m) - (C_{a,n} + C_{b,n}(1 - m)) \times \exp \left\{ \frac{-2AP}{V} (t_{n+1} - t_n) \right\} \right\} \quad (14)$$

The concentration and time data were fit to Equation (14).

The permeability coefficients for the imprinted polymers were slightly higher than for the nonimprinted polymers (Tables V and VI). However, the order of fastest to slowest diffusing sugars was not changed. Therefore, permeability order was governed by the general hydrophilicity/hydrophobicity of the solute.

The permeability coefficients for the imprinted membranes were similar to conventional polymer membranes. The fact that the permeability for the star polymers was similar while the uptake of the polymers was different reflects that the polymers were not limited by the diffusion of solutes. However, they also

have sites that have higher affinity for the imprint compound.

### CONCLUSIONS

In this work, responsive and cognitive polymeric networks based on PEG star polymers were prepared to respond to pH changes in their environment and to distinguish between D-glucose and similar sugars.

By using molecular imprinting the star polymer building blocks with the desired template, D-glucose, we were able to obtain polymeric networks that can distinguish between the template and a similar sugar; D-fructose. The large number of functional groups provided by the star polymers was essential to forming interactions between templates and the network during polymerization. Such networks that can work in aqueous environments are promising as sensing devices in biological environments.

Sensitivity to changes in the pH was obtained by copolymerization of star polymers with the ionizable methacrylic acid. Based on earlier studies, such systems have potential as oral drug delivery devices and actuators. Star polymers provide highly controllable and diverse systems for these materials.

These formulations constitute part of a new generation of materials that have been designed molecularly to meet the material and functional requirements for many emerging biomedical applications.

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