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13. The bisurea gelling agents were prepared by esterification of *N*-butoxycarbonyl (BOC)-aspartic acid in dichloromethane with 1-[3-(dimethylamino)propyl]-3-ethylcarbondiimide hydrochloride (EDCI), 4-(dimethylamino)pyridine (DMAP), and 1*H*,1*H*,2*H*,2*H*-perfluorodecanol followed by deprotection with trifluoroacetic acid/CH_2Cl_2 (50:50) and reaction with the appropriate mono- or bis-isocyanates in CH_2Cl_2 with excess triethylamine. The resultant bisureas were filtered off and washed with CH_2Cl_2, 1% aqueous HCl, water, and more CH_2Cl_2. All compounds gave spectroscopic characteristics consistent with their structure and were shown to be >95% pure. For more details of the synthesis of fluorinated aspartate bisureas and ureas, see *Science* Online (www.sciencemag.org/feature/data/1044209.shl).
14. Foam samples were fractured, sputter-coated with gold, then analyzed by SEM as described [K. Parks and E. J. Beckman, *Polym. Eng. Sci.* **36**, 2417 (1996)]. Sizes given throughout this report are average diameters, as generated from these analyses of SEM images.
15. Monomers (styrene, *N*,*N*-dimethyl amino ethyl methacrylate, *n*-hexyl acrylate, 1*H*,1*H*,2*H*,2*H*-perfluorodecyl acrylate; Aldrich) were purified using conventional procedures (washing to remove inhibitors, drying, vacuum distillation as appropriate). Copolymers were prepared via bulk polymerization at 65°C using azobisisobutyronitrile (AIBN) (0.2 mol %, recrystallized from methanol). Copolymers were purified via dissolution in 1,1,2-trichloroethane or perfluoromethyl cyclohexane, followed by precipitation into methanol. Copolymer content was quantified using ^{1}H nuclear magnetic resonance. The aspartate methacrylate monomer was prepared using the scheme shown in (*13*) and 2-isocyanato ethyl methacrylate (Aldrich). Styrene-fluorinated acrylate copolymers were sulfonated using an SO_3/acetic anhydride complex (acetyl sulfate).
16. We are developing CO_2-philic hydrocarbons to form the building blocks for the next generation of such agents (E. J. Beckman, *Design of CO_2-Philic Hydrocarbons*, paper presented at the Engineering Foundation Conference on Supercritical Fluids in Materials Processing and Synthesis, Davos, Switzerland, September–October 1999).
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Reversible Molecular Adsorption Based on Multiple-Point Interaction by Shrinkable Gels

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A general approach is presented for creating polymer gels that can recognize and capture a target molecule by multiple-point interaction and that can reversibly change their affinity to the target by more than one order of magnitude. The polymers consist of majority monomers that make the gel reversibly swell and shrink and minority monomers that constitute multiple-point adsorption centers for the target molecule. Multiple-point interaction is experimentally proven by power laws found between the affinity and the concentration of the adsorbing monomers within the gels.

Many proteins can specifically recognize and reversibly bind small target molecules. The binding site contains contacts from several amino acids from different locations along the protein chain. Even a slight change in the backbone conformation at distant sites can alter the spatial arrangement of these contact points and change the binding constant. Most synthetic polymers contain only one or two different types of monomer units, which might suggest that a similar type of specific reversible adsorption would be difficult to achieve with these materials.

We present a general approach for creating polymer gels that can recognize and capture a target molecule by multiple-point interaction and that can reversibly change their affinity to the target by more than one order of magnitude. The polymers consist of two species of monomers, each having a different role. The majority monomer species control network density and make the gel reversibly swell and shrink in response to an environmental change such as temperature. The minority monomers come into sufficient proximity to each other when the supporting gel shrinks so that they can function as multigroup adsorption centers for the target molecules. This adsorption can be switched on and off by the reversible gel phase transition.

To demonstrate the general principle, we carefully selected the monomers for the gels and their targets. As target molecules, we chose pyranine-3 and pyranine-4 for two reasons. First, they have three or four charges, respectively, allowing multiple-point interactions through the Coulomb force, a simple physical interaction. It was convenient that there are two types of pyranine with a different number of charges that allowed us to test the dependence of adsorption on the number of contact points. Second, their strong fluorescence and clearly separated ultraviolet (UV) adsorption peaks allow an accurate determination of the degree of adsorption by the gels, even at very low concentrations.

As adsorbing molecules, we chose methacrylamidopropyltrimethylammonium chloride (MAPTAC), which carries one positive charge. We envisioned that three or four MAPTAC groups would capture one pyranine molecule. A small amount of MAPTAC was embedded by copolymerization within a thermosensitive polymer network of *N*-isopropylacrylamide (NIPA) in the monomer ratio of less than 1/30 (*1*, *2*). In pure water, the gels underwent a thermal phase transition from the low-temperature swollen phase to the high-temperature shrunken phase at ~33°C. In the synthesis, the monomers were dissolved in methylsulfoxide along with cross-linker, *N*,*N*′-methylenebisacrylamide (BIS). Free-radical polymerization was initiated with azobisisobutylonitrile. The chemical structures of the monomers are shown in Fig. 1.

The release of a captured pyranine molecule requires replacement with another negative ion. We chose chloride ions for this role. Sodium chloride at a concentration of 100 mM was used so that pyranine and chloride ions could rapidly replace each other upon swelling and shrinking; that is, their affinities for the gels were comparable at this concentration. The gels showed a discontinuous volume change in water, but the transition became continuous when the salt was

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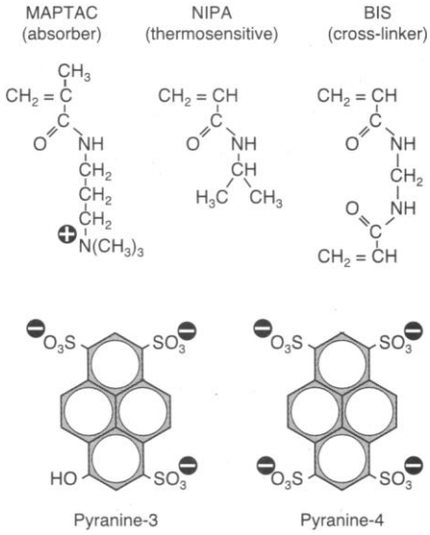
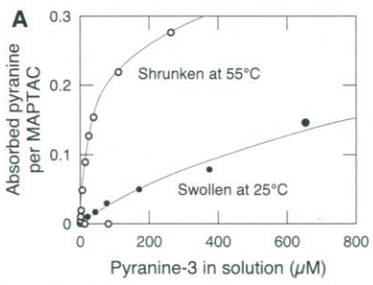


Fig. 1. The chemical structures of an adsorption site with a positive charge (MAPTAC), a thermosensitive monomer (NIPA), a cross-linker (BIS), and target molecules with three or four charges (pyranine-3 and pyranine-4, respectively). The recipe for synthesis was NIPA (6 M), MAPTAC (0.5 μM to 200 mM), and BIS (40 mM). They were dissolved in methylsulfoxide, degassed, and polymerized by free-radical polymerization initiated by azobisisobutylonitrile (7.3 mM) at 60°C.



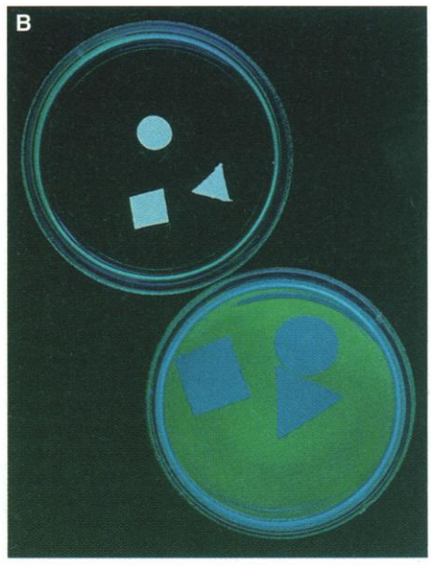


Fig. 2. (**A**) The adsorption of pyranine-3 per MAPTAC monomer as a function of pyranine-3 concentration in the swollen state at 25°C and in the shrunken state at 55°C. The MAPTAC concentration was 30 mM. (**B**) The shrunken gels at 55°C (upper dish) and the swollen gels at 25°C (lower dish) under illumination with UV. In the shrunken state, the gel adsorbed all of the pyranine molecules, but in the swollen state, the gel released them all as seen by their fluorescence. [Photograph by Felice Frankel, © 1999]

added because screening diminished the Donnan potential.

Cylindrical gels with a diameter of 300 μm were washed with water and placed in aqueous solutions of pyranine-3 or pyranine-4 at different concentrations (2.5 μM to 1 mM) at different temperatures. Using fluorescence or UV spectroscopy, we determined the pyranine concentration within the gel by directly measuring the fluorescence spectrum of the gel with pyranine and by measuring the decrease of pyranine concentrations in the outer solution. The equilibrium gel volume was measured under a microscope. From these measurements, we calculated the amount of pyranine adsorbed into the gel.

The adsorption of pyranine monomer per MAPTAC monomer as a function of pyranine concentration in the outer solution is shown in Fig. 2A. A photo of swollen gels at 25°C and shrunken gels at 55°C (Fig. 2B) shows that the shrunken gels adsorbed all of the pyranine (upper dish), but the swollen gels released pyranine (lower dish). The adsorption and release were reversible and reproducible.

To quantitatively analyze the result, we defined the affinity of the gel as the ratio of the molar concentration of adsorbed pyranine and that of pyranine in solution from the initial slope of the adsorption curve. The affinity is plotted in Fig. 3 as a function of temperature. It changed two orders of magnitude as the temperature was changed.

Figure 4 shows the affinity as a function of MAPTAC concentration at the time of polymerization within the gel. The log-log plot becomes a straight line with a slope of 3 for pyranine-3 and a line with a slope of 4 for pyranine-4 at higher MAPTAC concentrations in the shrunken state. Namely, affinity ≈ [MAPTAC]^3 for pyranine-3 and affinity ≈ [MAPTAC]^4 for pyranine-4. These power-law relations show that adsorption sites are formed when three adsorbing molecules (MAPTAC) gather to capture one pyranine-3 (three charges) and when four MAPTAC molecules are needed to capture pyranine-4 (four charges).

In the swollen state, the slope becomes 1, indicating that MAPTAC adsorbs pyranine with a single contact, which is reasonable because MAPTAC monomers are well separated from one another. The slope comes back to 3 or 4 after the gels shrink.

At a MAPTAC concentration of less than 10 mM, the adsorption by the major compo-

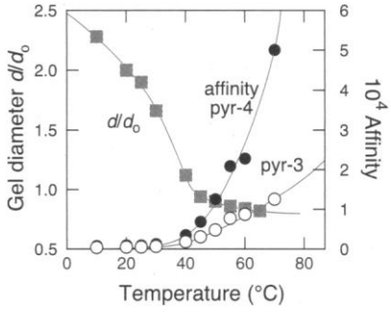


Fig. 3. The affinity of the gels to pyranine-3 and pyranine-4 as a function of temperature. The degree of swelling, d/d_o, of the gels is also shown, where d denotes the gel diameter in equilibrium and d_o is that upon synthesis.

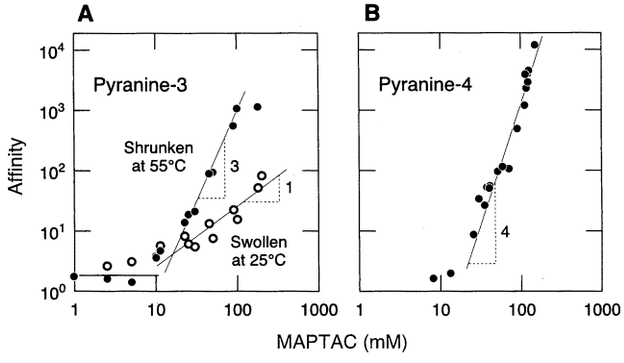


Fig. 4. (**A**) A log-log plot of the affinity of the gels as a function of MAPTAC concentration at the time of polymerization to pyranine-3 in the swollen state at 25°C and in the shrunken state at 55°C. The solid lines that best fit the data have a slope of 3 in the shrunken state and a slope of 1 in the swollen state. Thus, the gels adsorb the targets at three contact points in the shrunken state, whereas single-point adsorption occurs in the swollen state. (**B**) Similar data for pyranine-4 in the shrunken state. The slope of 4 indicates four-point adsorption. At low concentrations of MAPTAC, all of the curves have slopes of 0, indicating a small adsorption by NIPA monomers.

nent NIPA through hydrophobic interaction becomes more substantial than that by MAPTAC. The adsorption becomes independent of MAPTAC concentration and the power becomes 0.

The mechanism of multiple-point adsorption is different from that by charged gels through the nonspecific Donnan potential (*3*). Under our experimental conditions, where a high salt concentration (100 mM) was used, the Donnan potential was completely destroyed. Adsorption by the Donnan potential is estimated to be more than three orders of magnitude smaller than what we observed. Furthermore, dependence of the Donnan potential adsorption on MAPTAC should be much weaker (less than a power of 1) than the power of 3 or 4 as observed in our case.

Although we have not created the adsorber as specific as proteins, we have shown that, by varying polymer conformation and concentration, we can change the reversible affinity for target molecules by two or three orders of magnitude. In the compact state, in particular, the gel showed a dramatic change in affinity in response to a slight change in volume. In our experiments, the number of contact was three or four. If more contact points with more diverse interactions (such as hydrogen bonding and hydrophobic interaction) were used, it is possible that the gel-target interaction could be made more specific and the affinity might show a sharper response to change in polymer density (*4*).

In our experiments, we used temperature to trigger the adsorption and release. Similar gels can be, in principle, designed in which the reversal of affinity is triggered by other physical parameters such as solvent composition, pH, light, electric or magnetic field, and osmotic or hydrostatic pressure (*5*).

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4. There have been works on molecular adsorption, in particular, on its dependence on phase states of polymers and gels. These studies mostly used nonspecific hydrophobic interaction. The affinity changes in response to polymer density changes triggered by temperature. See, for example, M. Yamato *et al.*, *Connect. Tissue* **31**, 13 (1999).
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Pressure Effect on Hydrogen Isotope Fractionation Between Brucite and Water at Elevated Temperatures

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Experimental evidence for a pressure effect on isotopic partitioning at elevated temperatures demonstrates that equilibrium deuterium-protium fractionation between the mineral brucite [$Mg(OH)_2$] and pure water systematically increases by 12.4 per mil as pressure increases from 15 to 800 megapascals at 380°C. A linear relation is observed between the measured fractionation factor and the density of water (0.070 to 1.035 grams per cubic centimeter). The trend of the isotope pressure effect is the same as that of recent theoretical studies, but the magnitude is smaller. The pressure effect must be accounted for in the interpretation of isotopic data of geologic systems involving water (paleotemperature, source of fluids).

It has been commonly assumed in stable isotope geochemistry and cosmochemistry that temperature is the principal variable in determining equilibrium partitioning of the isotopes of light elements among different phases and chemical species and that pressure is of no importance. In classic statistical-mechanical calculations of reduced partition functions for geologically relevant materials, intermolecular forces and interactions of molecular species usually have been ignored. For solid phases, changes in molar volumes due to isotopic substitution are small except for hydrogen isotopes. Previous calculations indicate that pressure effects on isotopic partition function ratios of minerals are probably small (≤0.5 per mil in $^{18}O/^{16}O$) at pressures up to 1000 to 2000 MPa at elevated temperatures (*1, 2*). Pressure effects on isotopic fractionation between two minerals may even cancel each other as the potential change in partition function ratio of one of these minerals is similar in magnitude to that of the other mineral. Previous experimental investigations, primarily on oxygen isotope fractionation between minerals and aqueous fluids, have revealed no significant pressure effect (≤0.2 per mil) on isotopic partitioning at temperatures up to 700°C and pressures up to 2000 MPa (*3*).

Unlike minerals, which maintain a rigid structure with near-constant lattice parameters within a given temperature-pressure range, the structure and density of pure water change significantly with pressure, particularly in near-critical regions. Among the three normal modes of vibrations of water molecules, symmetric O-H and O-D stretching frequencies of H_2O and HDO, respectively, decrease significantly (red shift) with increasing pressure at a given temperature (*4*). Polyakov and Kharlashina (*2*) calculated, on the basis of thermodynamics, that the pressure effect on the reduced partition function ratio for D/H in pure water is substantial. More recently, Driesner (*5*) calculated from spectroscopic data that the reduced partition function ratio for D/H in pure water changes by as much as 20 per mil near the critical temperature of water (374°C) at low pressures (<100 MPa), whereas the pressure effect on the partition function ratio for $^{18}O/^{16}O$ in water would be small (on the order of 0.4 per mil) in the same temperature-pressure range. Partition function ratios for D/H in molecular water clusters in the vapor phase at elevated temperatures, calculated on the basis of molecular dynamics and ab initio methods, are significantly lower than those of isolated water molecules (*5*). On the basis of these calculations, Driesner (*5*) and Vennemann and O'Neil (*6*) argued that large discrepancies in experimental D/H fractionation factors between hydrous minerals and water could be ascribed to pressure differences in the experiments. The magnitude of the calculated pressure effect on the partition function ratio for D/H in water and the discrepancies in mineral water D/H partitioning in the literature (*6*) are too large to be ignored, and experimental verification is needed. Mineev and Grinenko (*7*) reported large pressure effects (26 to 55 per mil) in the system serpentine water at 100° to 200°C and 0.1 to 250 MPa, but details of their experiments and results are not available. Here, we report experimental results that confirm the pressure effect on D/H isotope partitioning between a hydrous mineral and water at elevated temperatures.

The isotope pressure effect in water is

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