Multiple-Contact Adsorption of Target Molecules by Heteropolymer Gels[†]

Kenji Ito,*[1] *Jeffrey Chuang*,[2] *Carmen Alvarez-Lorenzo*,[3] *Tsuyoshi Watanabe*,[4] *Nozomi Ando*,[5] *Alexander Yu. Grosberg*[6]

[1]National Institute of Advanced Industrial Science and Technology, Tsukuba, Ibaraki 305–8565, Japan; E-mail: k-ito@aist.go.jp

[2]Department of Biochemistry and Biophysics, University of California, San Francisco, California 94143, USA

[3]Departamento de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Santiago de Compostela, 15706-Santiago de Compostela, Spain

[4]Fundamental Research Laboratory, SUMITOMO BAKELITE Co., Ltd., Totsuka-ku, Yokohama-shi, Kanagawa 245–0052, Japan

[5]Department of Physics, Cornell University, Ithaca, New York 14853, USA

[6]Department of Physics, University of Minnesota, Minneapolis, Minnesota 55455, USA

Summary: We examined adsorption of target molecules through a multiple-contact interaction in a thermo-sensitive heteropolymer gel which can undergo a volume transition at 34 °C in water. Multi-valent anionic target molecules were adsorbed electrostatically by monovalent cationic adsorbing sites in the gel. The overall affinity (*SK*) between the gel and the target molecule was calculated from the initial slope of the Langmuir adsorption isotherm: $[T_{ads}] = KS[T_{sol}]/(1 + K[T_{sol}])$, where S, K, $[T_{sol}]$ and $[T_{ads}]$ represent the number of adsorption sites per unit volume of the gel, the effective binding constant, the equilibrium target concentration in the external solution, and the target concentration adsorbed in the gel, respectively. The affinity for the collapsed gel at 60 °C was studied in terms of the concentrations of three factors: the adsorber ([Ad]), the coexistent salt (replacement ion, [Re]), and the cross-linker ([Xl]). We found that the relationship between the affinity and these factors can be summarized by the following formula first suggested by T. Tanaka:

$$\text{Affinity, } SK \propto \left(\frac{[\text{Ad}]}{[\text{Re}]}\right)^{p} \exp\left[-c(p-1)\frac{[\text{Xl}]}{[\text{Ad}]^{2/3}}\right].$$

Here c is a constant and p is the number of the contact points between the adsorber units and the target molecule.

[†]This work was largely carried out in the Department of Physics and Center for Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139.

 DOI: 10.1002/masy.200450301

Introduction

Polymer gels belong to the privileged class of the most actively studied polymer systems. The main immediate motivation for most gel studies has been various technological applications. At the same time, T. Tanaka (1947–2000), as one of the leaders of the science of gels, wanted to look further. His ambitious goal was to mimic some properties of proteins using gels as a model system.

In some instances, gels do exhibit features of protein-like behavior. For example, in one experiment, a gel was created with a catalytic activity that could be switched on and off by an infinitesimal change in temperature or solvent composition.[1,2] The on-off behavior apparently resulted from the fact that several functional monomers were able to cluster into a catalytic center in the collapsed state of the gel, while they were unable to do so in the swollen state. In general, a key to the design of protein-like gels is to understand how functional monomers in the gel cluster and interact with substrate molecules. This realization led Tanaka to formulate the problem of multiple-point adsorption by a heteropolymer gel.

For the last few years, we performed an extensive study of the adsorption of such substrates, or 'target molecules,' into heteropolymer gels. In these systems, a main gel component monomer (e.g. *N*-isopropylacrylamide, NIPA) was polymerized with a small amount of monovalent functional monomer (e.g. methacrylamidopropyl trimethylammonium cation, $MAPTA^+$) and cross-linker (e.g. *N,N*-methylene-bis(acrylamide), BIS). Multivalent target molecules (e.g. 1,3,6,8-pyrene tetrasulfonate anion, Py^{4-}) with the opposite charge sign were then adsorbed into the gel. The experiments characterized whether adsorption of the targets was through multiple adsorber contacts, or by single adsorbers, and under what conditions the different types of adsorption would occur.

Recent investigations have confirmed that several adsorbers take part in the adsorption of one target molecule in the collapsed state of gels, while only a single monomer does in the swollen state.[3] Such conclusions can be drawn from the dependence of the affinity on the adsorber concentration in the gel. The affinity for the collapsed gel is much stronger than that for the swollen gel above certain adsorber concentrations. The results suggest that the binding sites in the gel behave like active sites on a protein, in

that they can catch and release target molecules. Tests of the affinity dependence on the coexistent salt concentration in the outer solution supported such a mechanism.[4]

The cross-linker dependence of the affinity can be used to characterize the binding sites in the gel as well. If a target molecule is adsorbed by several adsorber monomers, then the polymer chains in the gel will be constrained, and the system will suffer a loss of entropy. This entropy loss can be observed as a decrease of the affinity with an increase of the cross-linker concentration in the gel. The quantitative relationship between the affinity and cross-linker concentration can be used to relate the number of contact points to the microscopic properties of the gel.

In this paper, we establish a simple model, proposed by Prof. Tanaka, describing the adsorption of target molecules through a multiple-contact interaction. This model provides an expression for the affinity, which successfully explains the experimentally determined dependence of the affinity on several factors: the concentration of adsorber monomers in the gel, the concentration of replacement ions (the coexistent salt) in solution, and the concentration of cross-linker in the gel. These experiments are detailed in the sections that follow.

Tanaka equation

Here we provide a summary for what has been called the Tanaka equation, which relates the target molecule affinity of a random gel to several key experimental parameters. The Tanaka expression for the affinity of a gel to adsorb target molecules from a solution is

$$\text{Affinity} = \frac{[\text{Ad}]^p}{p[\text{Re}]^p} \exp\left(-\beta p \varepsilon\right) \exp\left[-c(p-1)\frac{[\text{Xl}]}{[\text{Ad}]^{2/3}}\right]. \qquad (1)$$

The concentration of adsorbing monomers in the gel is denoted by [Ad], and [Re] is the concentration of replacement molecules, i.e. salt molecules that each bind with a single site on the target molecule when it is not bound to adsorbing monomers. p is the number of bonds between separate adsorbing monomers and the target molecule. β is the Boltzmann factor $1/k_BT$, and ε is the difference in binding energy of a target molecule with a) an adsorbing monomer or b) a replacement molecule. [Xl] is the concentration of cross-linker (e.g. BIS). c is a constant which can be estimated from the persistence length and concentration of the main component of the gel chains (e.g. NIPA).

The Tanaka equation has done a good job of explaining how adsorber monomer concentration, salt concentration, and cross-linker concentration control the affinity. The main assumption in eq.(1) is that adsorption of target molecules is dominated by one value of p at a time. In general, the validity of this assumption depends on the concentrations of the various components of the gel and the target-monomer binding energy.

Langmuir adsorption expressed by

$$[T_{ads}] = S\frac{K[T_{sol}]}{K[T_{sol}]+1} \qquad (2)$$

has been used to interpret the binding affinity of a gel for a target molecule in the experiments described below. Here $[T_{ads}]$ is the concentration of target molecules adsorbed into the gel, $[T_{sol}]$ is the concentration of target molecules in solution, and S is the concentration of binding sites. K is the binding constant — it can be thought of as the affinity per binding site. SK is the overall affinity of all binding sites in the gel for the target molecule and is equivalent to the affinity mentioned in eq.(1).

The overall binding affinity SK can be determined from the partition function that sums over the different possible states of the target molecule — 0 adsorbers bound, 1 adsorber bound, ... p_{max} adsorbers bound. The partition function will be of the form $Z = Z_0 + Z_1 + Z_2 + ... + Z_{p_{max}}$, with Z_p indicating the term of the partition function in which a target molecule is bound by p adsorbing monomers. Z_0 corresponds to the case of the target molecule being completely unbound. From the equation of the Langmuir isotherm (eq.(2)), we can see that $SK[T_{sol}]$ is the concentration of bound target molecules, and SK should be the ratio of bound to unbound molecules. Therefore $SK = (Z_1 + Z_2 + ... + Z_{p_{max}})/Z_0$.

We now give a qualitative explanation of the various terms in the Tanaka equation. We first consider the power-law dependence of the affinity SK on [Ad]. For a target molecule to be adsorbed, there must be p adsorbing monomers clustered together to simultaneously bind it. The probability of such a cluster existing at a given point in a random gel is a product of the probabilities for each of the adsorbing monomers. Therefore the dependence goes as $[Ad]^p$. Each of these clusters requires p adsorbing monomers, hence SK is proportional to $1/p$.

The affinity is proportional to $[\mathrm{Re}]^{-p}$ because these replacement molecules (typically salt ions) act as competitors to the adsorbing monomers. In solution, a target molecule may either be adsorbed into the gel or bound by p replacement molecules. Binding to the replacement molecules prevents adsorption by the gel. In order for a target to be bound to p replacement molecules, the replacements must cluster around the target. This creates a power-law dependence similar to that for target molecule adsorption by adsorbing monomers, but with an opposite sign exponent. Note that we have assumed that each replacement molecule binds to one site on the target molecule, as do the adsorbing monomers. If the adsorber monomers and replacement molecules have different valences, these exponents should be modified.

The energetic attraction of a target molecule to p adsorbing monomers is encapsulated in the term $\exp(-\beta p\varepsilon)$. This is a Boltzmann probability based on a binding energy ε per adsorbing monomer.

The dependence of the affinity, *SK*, on the cross-links can be explained as follows. The adsorber units in the gel can move rather freely within a certain volume determined by the cross-link density. It has been established that, below a certain length scale associated with the cross-link density, the gel behaves like a liquid. Beyond that length scale, however, the gel behaves as an elastic solid body. The adsorber units cannot diffuse further than that length scale.

We therefore envision that each adsorber is at one end of a fictitious Gaussian chain with a length half the average polymer length between the nearest cross-links (Xl), $l = nb = ([\mathrm{NIPA}]/[\mathrm{Xl}]/2)a$. Here n is the number of monomer segments of persistent length b contained in the chain. If there are [NIPA]/2[Xl] monomers between the cross-link and an adsorbing monomer group, then $n = [\mathrm{NIPA}]/(2m[\mathrm{Xl}])$ and $b = ma$, where m is the number of monomers involved in the persistent length and a is the length of each monomer. At a concentration of [Ad] of adsorbing monomers, the average spatial distance between adsorbing monomers is $R = [\mathrm{Ad}]^{-1/3}$. For a molar concentration C_{ads} this corresponds to $R = 1\ \mathrm{cm}/(C_{\mathrm{ads}}N_{\mathrm{A}})^{1/3}$, where N_{A} is the Avogadro number. The fictitious Gaussian chain represents the restricted ability of the adsorber groups to diffuse within a certain volume in the gel.

We expect that the probability for two adsorber monomers to meet should be proportional to the Boltzmann factor of the entropy loss associated with the formation

of one pair of adsorbers, $P = P_0\exp(-R^2/nb^2) = P_0\exp(-c[\mathrm{Xl}]/[\mathrm{Ad}]^{2/3})$, where the quantity c is determined by the persistence length, the number of monomers in a persistence length, and the concentration of the main component of the chains through the relation $c = 2m/([\mathrm{NIPA}]b^2)$. Since the adsorption of a divalent target by two adsorbers brings together each end from two fictitious Gaussian polymers, the affinity should be proportional to this probability. If more than two contact points are expected, the equation can be generalized as

$$SK \propto \exp\left[-c(p-1)\frac{[\mathrm{Xl}]}{[\mathrm{Ad}]^{2/3}}\right], \qquad (3)$$

where p is the number of contact points. In other words, the cross-links will frustrate the formation of a target-binding site requiring multiple ($p > 1$) adsorber monomers, and the frustration will increase with p. On the other hand, if the target molecule adsorbs by a single point only ($p = 1$), SK should be independent of the cross-linker concentration.

Together these contributions make up the Tanaka equation eq.(1) for binding of a target molecule by p adsorber monomers. It can be shown by consideration of the relative weights of the terms Z_p, that for a given set of experimental parameters, the affinity SK will almost always be dominated by one value of p, either $p = 1$ or $p = p_{\max}$, depending on the parameters chosen. Therefore, the Tanaka equation is quite general, and one can ignore the contributions of different types of adsorption. At the gel volume phase transition, the concentrations of adsorber, cross-linker, and salt, as well as the temperature of the system may be altered. To make a gel in which p changes across the volume phase transition, one should choose components such that the difference in $Z_{p_{\max}}$ and Z_1 changes sign across the transition.

To conclude the theoretical section, we should discuss the important condition that salt concentration should be large enough. That is necessary for the applicability of the above theoretical considerations, because we have assumed everywhere that Coulomb interactions were effectively short ranged, which is only true if they are sufficiently Debye-Hückel screened. This requirement is safely met under the conditions of the experiments described below. However, as a matter of principle, it should be understood that at smaller salt concentration a completely new set of phenomena may arise, such as Coulomb correlation effects between target molecules (see the review article[5] and references therein). These effects comprise an interesting subject of future studies, but

we leave them outside the scope of the present paper following the idea that mainly the single particle behavior with respect to target molecules is of interest in the context of the attempts to mimic protein-style behavior.

Experimental verification of the Tanaka equation

Methods

Gel preparation The gels were prepared by free radical polymerization using 6 M *N*-isopropyl-acrylamide (NIPA, which was kindly supplied by Kohjin Co., Japan), 0–120 mM methacrylamidopropyl trimethylammonium chloride (MAPTAC, Mitsubishi Rayon Co. Ltd., Japan) and 5–200 mM cross-linker *N,N*-methylene-bis(acrylamide) (BIS, Polysciences Inc., PA). After the monomers were dissolved in dimethyl-sulfoxide (DMSO), 10 mM 2,2-azobisisobutyronitrile (AIBN, initiator) was added, and the solutions were immediately transferred to test tubes in which micropipettes of inner diameter of approximately 0.5 mm were placed. The solutions filled the micropipettes, and were then degassed under vacuum for a few seconds. The polymerization was carried out at 60 °C for 24 hours. After gelation was completed, the micropipettes were crushed. To remove unreacted chemicals, the gels were washed with large amounts of 100 mM hydrochloric acid (HCl) and sodium chloride (NaOH) aqueous solutions and

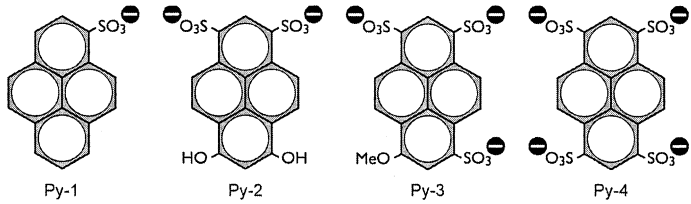

Figure 1: Chemical structure of targets.

then with deionized distilled water for ten days. Finally, the gels were removed from the solution and dried under vacuum for one week. The obtained gel can undergo a volume phase transition at 34 °C in water, and the gel is in the swollen state below that temperature, while is in the collapsed state above that.[6] Then we confirmed that a swelling ratio for all collapsed gels at 60 °C was 1, meaning the same as that at preparation, irrespective of the experimental conditions such as adsorber concentration

(0–120 mM), salt concentration (27–200 mM), and cross-linker concentration (5–200 mM).

Adsorption studies As target molecules, several different types of pyrene sulfonate derivatives were used: 1-pyrene sulfonic acid sodium salt (Py-1), 6,8-dihydroxy-pyrene-1,3-disulfonic acid disodium salt (Py-2), 8-methoxy pyrene-1,3,6-trisulfonic acid trisodium salt (Py-3), and 1,3,6,8-pyrene tetrasulfonic acid tetrasodium salt (Py-4), portraying in Figure 1. These chemicals present 1 (Py-1), 2 (Py-2), 3 (Py-3) or 4 (Py-4) anionic charges, which can interact electrostatically with a cationic charged site such as on $MAPTA^+$.

Pieces of cylindrical gel (5–20 mg dry weight) were placed in 1.5–4 mL target aqueous solution with the concentration of the targets ranged from 2 μM to 0.5 mM. The solutions also contained NaCl of a prescribed concentration to provide monovalent

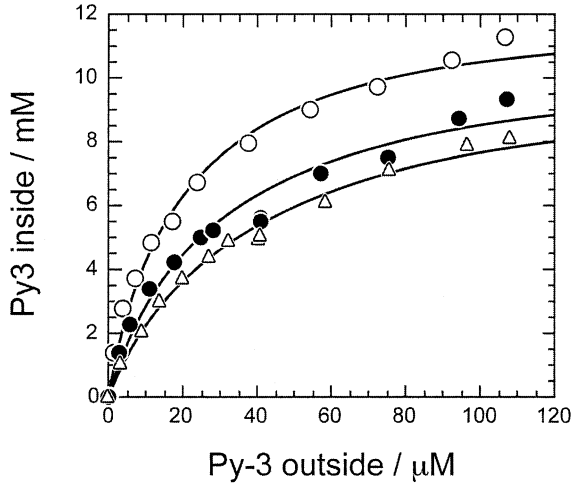

Figure 2: Typical adsorption isotherms of the collapsed gel at 60 °C for the adopted binding systems. The plot shows the isotherms for the gels with the following experimental conditions as: The target molecule is Py-3. The concentrations of the main monomer (NIPA), the adsorber (MAPTAC) and the replacement ion (NaCl) are 6 M, 60 mM and 80 mM, respectively. The BIS concentrations are 5 mM (open circle), 100 mM (closed circle) and 200 mM (triangle). All isotherms observed in the present work were well fit by the Langmuir equation eq.(2).

chloride ions to replace the target molecules. The samples were kept swollen (20 °C) or

shrunken (60 °C) for 48 hours. Equilibrium concentration of the target molecules in the medium was measured using UV spectrophotometer. The amount of the adsorbed target molecules was then evaluated as the difference between the initial and the final quantities in the outer solution. These amounts were then converted to units of moles of target molecule per volume of gel at the time of synthesis. The adsorption isotherms were analyzed in terms of the Langmuir equation, $[T_{ads}] = KS[T_{sol}]/(1 + K[T_{sol}])$. Once again, in this equation, $[T_{ads}]$ is the amount of target adsorbed per unit volume of gel in the shrunken state, $[T_{sol}]$ is the final equilibrium concentration in the solvent, S is the number of adsorbing sites per unit volume of gel, and K is the affinity of one adsorption site for a target molecule. From the slope and the intercept at zero $[T_{sol}]$, both S and K, and the overall affinity SK were deduced. Typical adsorption results are shown in Figure 2, which displays the adsorber dependence of the adsorption of Py-3 for a collapsed gel. All the adsorption isotherms were well fit by the Langmuir equation.

Adsorber dependence

The dependences of the affinity for Py-3 and Py-4 as a function of the MAPTAC concentration are shown in Figure 3. At MAPTAC concentrations below 10 mM, the absorption for the collapsed gels becomes independent of MAPTAC concentration, indicating that the gel major component NIPA contributes more to the absorption of

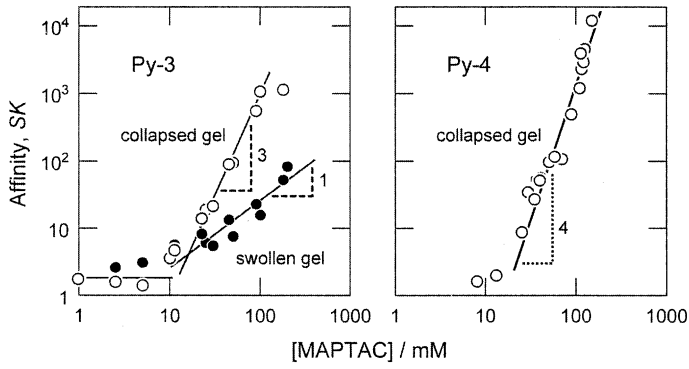

Figure 3: Adsorber dependence of affinity for Py-3 and -4 adsorptions. The data were quoted from Ref. [3].

pyranine (due to a hydrophobic interaction) than do the $MAPTA^+$ groups in that regime. Above these MAPTAC concentrations, both log-log plots show a straight line with slope three for Py-3 and with slope four for Py-4. In this experiment, the coexistent salt concentration of the system was kept at a constant (100 mM) so that the Donnan potential, which might cause a nonspecific adsorption of the target molecule, was swept out. Thus, it is concluded that the power-law relationships observed above the MAPTAC concentration (~10 mM) are due to three- and four-point absorptions, respectively. Absorption sites are formed when three (or four) equivalent adsorbing molecules ($MAPTA^+$) gather to capture one Py-3 (or Py-4) molecule. The obtained power laws are explained well by the Tanaka equation.

On the other hand, the log-log slope for the swollen gel is one, indicating that $MAPTA^+$ absorbs the target molecule with a single contact. Single-point absorption is favored because the $MAPTA^+$ monomers are well separated from one another. The slope returns to 3 or 4 upon shrinking, showing recovery of the multipoint binding sites.

These results suggest the following picture. In the gel's collapsed state, the adsorber monomer units can be clustered to form sites in which a target molecule can bind with several adsorber monomer units simultaneously. If the gel is made to swell, the adsorber groups separate, and it becomes entropically unfavorable for the multipoint adsorption complex to assemble.

Replacement ion dependence

Figure 4 shows the affinity *SK* of the collapsed gel for the various target molecules as a function of NaCl concentration. In the adopted system, concentrations of the adsorber ([MAPTAC]) and the cross-linker ([BIS]) were fixed at 40 mM and 10 mM, respectively. The affinities correlated very strongly with the NaCl concentration. For instance, in the case of Py-3, when the NaCl concentration was increased by a factor of three, the affinity decreased by more than two orders of magnitude. More importantly, the plots clearly show the linear relationships between ln([NaCl]) and ln(*SK*) for the different target molecules. In each case, the log-log plot has a slope of $-p_{max}$, where p_{max} is the number of charged groups on the target molecule Py-p_{max}. The evidence obtained here follows well our prediction described in the theory section, which means that the chloride ions of NaCl act as replacement ions for the charged groups on a target

molecule and they substitute for the target molecules in binding to the p_{max} adsorbers, preventing adsorption of some of the targets.

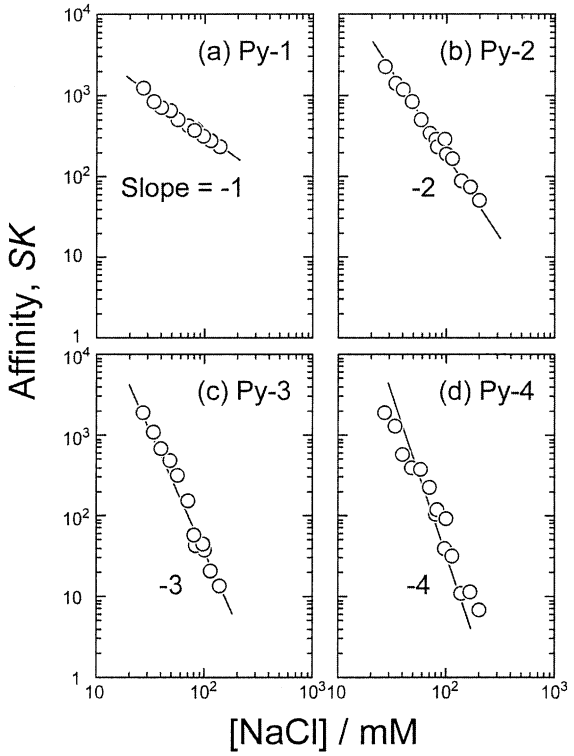

Figure 4: Replacement ion dependence of affinity for Py-1 to -4 adsorptions. The data were quoted from Ref. [4].

We also considered whether it is solely the ratio of adsorber to replacement concentration that determines the affinity, or whether the absolute value of the salt concentration plays some role. For example, it is conceivable that there is some sort of coulombic screening that does not follow the mass action law. To fix these expectations, we examined the dependence of the affinity for Py-3 and Py-4 on the ratio of the adsorber concentration [Ad] to the external salt concentration [Re] as shown Figure 5.

The two variables, [Ad] and [Re], were tested in separate experiments. In one, the replacement ion concentration [Re] = [NaCl] = 80 mM was fixed while [Ad] was varied. In the other, [Ad] = 40 mM was fixed while [Re] was varied. In both cases, [BIS] was fixed to 10 mM. The affinity curves from the two experiments are practically coincident.

This experimental evidence suggests that the affinity is universally determined by the ratio of adsorber to replacement concentration, that is, affinity $\propto$ $([Ad]/[Re])^p$. Here, it is confirmed that the power-law relationship followed the proposed model.

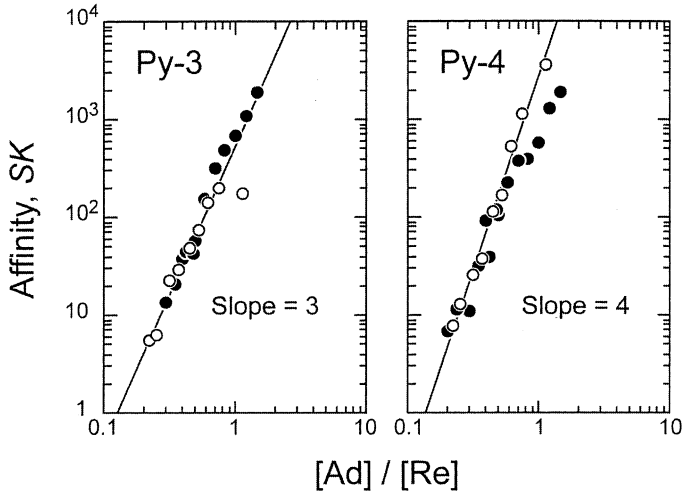

Figure 5: Dependence of the affinity on the ratio of the adsorber to the replacement ion for Py-3 and -4 adsorptions. Open and closed circles represent the variables of the adsorber and replacement ion, respectively.

Cross-linker dependence

Figure 6 shows the dependence of the affinity *SK* on the degree of cross-linking for several target molecules that can establish different numbers of contact points (*p*). For each target molecule, the affinities exponentially decrease as the cross-linker, BIS, is increased. This effect is especially significant for the cases of contact numbers above two. As can be seen, the slope for the target with $p = 1$ is almost negligible, while for increasing *p* the slope becomes larger. The initial slopes were well fit by an exponential function. This exponential nature can be understood by the discussion described above. Adsorption of the target molecules by multiple contacts is affected by the required entropy loss of the polymer chains.

Let us consider the situation more quantitatively from a microscopic point of view. Figure 7 shows a plot between the number of contact points and the exponential decay rate defined as

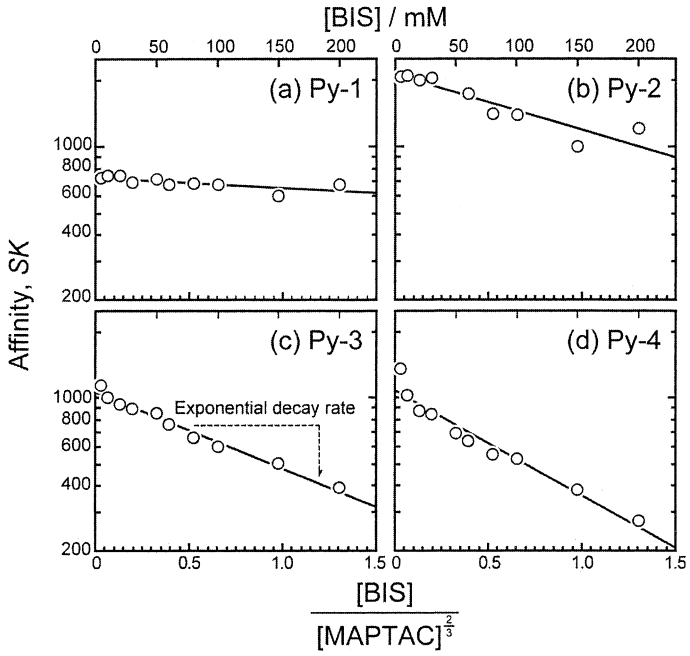

Figure 6: Series of semi-log plots for the affinity vs the BIS concentration for a collapsed gel at 60 °C. The concentrations of MAPTAC and NaCl are 60 mM and 80 mM, respectively. The lower horizontal label shows the ratio of BIS concentration to that of MAPTAC to the two-thirds power, while the upper label shows the corresponding BIS concentration.

$$\text{slope} = -\frac{\partial(\ln SK)}{\partial\left(\dfrac{[\text{BIS}]}{[\text{MAPTAC}]^{2/3}}\right)}, \qquad (4)$$

which is obtained from a fit of each plot in Figure 6 to eq.(3). The plot gives a linear relationship in which the slope is 0.32. Following the proposed model, the obtained slope should associate with the parameter c in eq.(1), though there is a correction factor because here the concentrations are reported in moles per liter, rather than particles per liter. This parameter c can be used to calculate the persistence length $b = ma$ for the polymer chains of the presented system. $b \sim 2.9$ nm is obtained with $c \sim 0.32$, which is within a reasonable range.[7]

To test the effect of the adsorber concentration on the frustration, we examined the dependence of the affinity on the degree of cross-linking at various adsorber

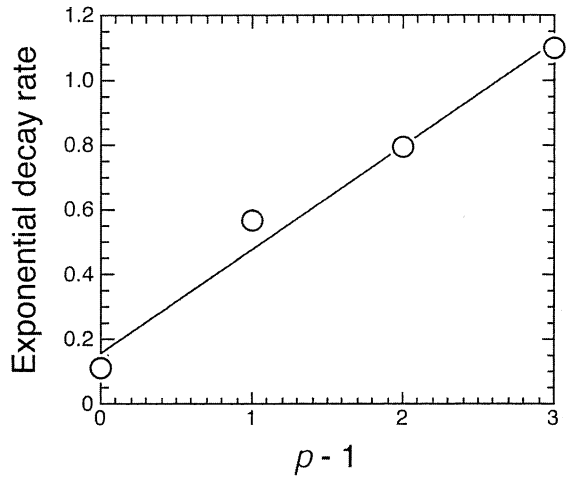

Figure 7: Plot of observed exponential decay rate vs $p - 1$, where p is the number of contact points on the target molecule. The decay rates were obtained through a curve fitting using eq.(3) on the data of Figure 6. The plot shows a good linearity, with a slope of 0.32.

concentrations ([MAPTAC] = 30–60 mM) and a NaCl concentration of 30 mM, for a target molecule (Py-4) that can establish four contact points (p = 4). The gels were prepared with 6 M NIPA. The results are shown in Figure 8. As was mentioned in a

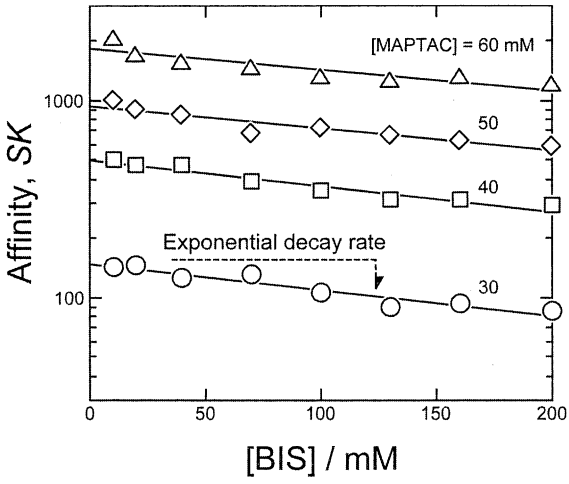

Figure 8: Dependence of the affinity on the degree of cross-linking at various adsorber concentrations, at a NaCl concentration of 30 mM for Py-4 adsorption by collapsed gels at 60 °C. The affinity decreases exponentially with cross-linker concentration, in accordance with eq.(1).

previous section, increasing the amount of adsorber groups increases *SK*, since the saturation capacity of the gel and the probability to accomplish the acquired number, i.e. p of the adsorbers per adsorbing site becomes larger. The slope of the cross-linker-affinity log-log plot should be affected by the adsorber concentration according to eq.(1), in which $[Ad]^p$ should lead stronger contribution to the affinity than the term, $\exp(-[MAPTAC]^{-2/3})$ in the given conditions. As the result, we obtained four apparently parallel curves showing the exponential decrease of *SK* with the cross-linking density for gels prepared at four different MAPTAC concentrations. However, $\partial(\ln SK)/\partial([BIS])$ decreases with ln([MAPTAC]) as shown in Figure 9. According to eq.(3), the quantity,

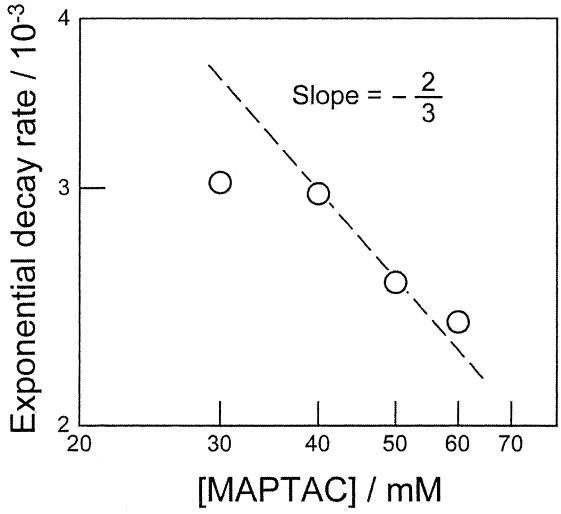

Figure 9: Double log plot of exponential decay rate versus the adsorber concentration.

$\partial(\ln SK)/\partial([BIS])$, should be proportional to a value $-3c[MAPTAC]^{-2/3}$ ($p = 4$). There is reasonable agreement with the predicted slope of –2/3, particularly above [MAPTAC] ≥ 40 mM. The negative deviation at [MAPTAC] = 30 mM may be caused by a non-specific interaction with the NIPA main-chain, which is more relevant at smaller values of *SK*.

Conclusion

In this work, we have formulated a theory for the adsorption of target molecules into a random heteropolymer gel and have verified the theory by a large series of experiments.

The gel has been modeled as a set of adsorbing monomers connected by Gaussian chains to fixed cross-linking points. The theory can be summarized by the Tanaka equation, which predicts power-law dependence of the gel affinity with regard to the adsorbing monomer concentration, salt concentration, and cross-linker concentration. Based on this model, we have established that for gels of the appropriate composition, adsorption occurs through multiple contacts in the collapsed state, but through single contacts in the swollen state. Thus the model allows us to quantify the affinity with respect to parameters such as composition of the gel, the number of contact points, and the target molecule chosen. Furthermore, the model provides the basis for understanding imprinted gels,[8] which, through control of the monomer sequence, can be designed to have even higher affinity and specificity for target molecules.[9] Such imprinted gels offer the promise of specific molecular recognition, and will hopefully lead to the development of true protein-like functionality in a synthetic polymer.

[1] T. Tanaka, T. Enoki, A. Y. Grosberg, S. Masamune, T. Oya, Y. Takeoka, K. Tanaka, C. Wang, and G. Wang, *Ber. Bunsenges. Phys. Chem.* **1998**, *102*, 1529.
[2] G. Wang, K. Kuroda, T. Enoki, A. Yu Grosberg, S. Masamune, T. Oya, Y. Takeoka, and T. Tanaka, *Proc. Natl. Acad. Sci.* **2000**, *97*, 9861.
[3] T. Oya, T. Enoki, A. Y. Grosberg, S. Masamune, T. Sakiyama, Y. Takeoka, K. Tanaka, G. Wang, Y. Yilmaz, M. S. Feld, R. Dasari, and T. Tanaka, *Science* **1999**, *286*, 1543.
[4] T. Watanabe, K. Ito, C. Alvarez-Lorenzo, A. Yu. Grosberg, and T. Tanaka, *J. Chem. Phys.* **2001**, *115*, 1596.
[5] A. Grosberg, T. Nguyen, and B. Shklovskii, *Rev. Mod. Phys.*, **2002**, *74*, 329.
[6] H. G. Schild, *Prog. Polym. Sci.* **1992**, *17*, 163.
[7] A. Yu. Grosberg and A. R. Khokhlov, "*Statistical Physics of Macromolecules*," AIP, New York 1994.
[8] T. Enoki, K. Tanaka, T. Watanabe, T. Oya, T. Sakiyama, Y. Takeoka, K. Ito, G. Wang, M. Annaka, K. Hara, R. Du, J. Chuang, K. Wasserman, A. Y. Grosberg, S. Masamune, and T. Tanaka, *Phys. Rev. Lett.* **2000**, *85*, 5000; C. Alvarez-Lorenzo, O. Guney, T. Oya, Y. Sakai, M. Kobayashi, T. Enoki, Y. Takeoka, T. Ishibashi, K. Kuroda, K. Tanaka, G. Wang, A. Y. Grosberg, S. Masamune, and T. Tanaka, *Macromolecules* **2000**, *33*, 8693; C. Alvarez-Lorenzo, O. Guney, T. Oya, Y. Sakai, M. Kobayashi, T. Enoki, Y. Takeoka, T. Ishibashi, K. Kuroda, K. Tanaka, G. Wang, A. Y. Grosberg, S. Masamune, and T. Tanaka, *J. Chem. Phys.* **2001**, *114*, 2812.
[9] The review including the presented work can be found in: K. Ito, J. Chuang, C. Alvarez-Lorenzo, T. Watanabe, N. Ando, and A. Yu. Grosberg, *Prog. Polym. Sci.* **2003**, *28*, 1489.