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Establishing Mathematical and Physical Models for the Adsorption of Biomacromolecules

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Abstract

In this article, a series of mathematical and physical models for the adsorption of biomacromolecules are established. As shown, the adsorption of biomacromolecules is actually considerably complicated and often involves various interactions, such as electrostatic, hydrophobic, and hydrogen-bonding, etc. Considering this, these models show that if these interactions are heavily involved in the process, the plot of ln Q (or Q) vs ln C^* is normally expected to be a straight-line. Otherwise, if the linearity exists between C^*/Q vs C^*, the adsorption would be an ideal process without the intervention of them. Meanwhile, this article also presents corresponding relationships for the adsorption in multisited binding and multilayer forms. Other aspects including ion-exchange systems are also discussed (C^*, the equilibrium concentration of biomacromolecules; Q, the adsorbance).

Index Entries: Biomacromolecule; adsorption; theory; interaction; ion-exchange.

Introduction

There is considerable interest in the adsorption of biomacromolecules because of its importance in a wide range of biomedical applications, such as solid-phase immunoassay *(1)*, immobilized enzyme *(2)*, immunomagnetic cell separation *(3)*, drug delivery *(4)*, artificial tissue *(5)*, biosensor *(6)*, etc. As known, unlike the adsorption of small molecules, that of biomacromolecules is actually considerably complicated and often involves various interactions among themselves or biomacromolecules support.

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In regard to this, it is clear that the structure of biomacromolecules plays a crucial role. Biomacromolecules, such as proteins, consist of a series of amino-acid units, with some having side chains of carboxyl and amino groups. In the adsorption process, such structures can introduce a large number of interactions into the adsorbed molecules or those with support, such as electrostatic, hydrophobic, hydrogen-bonding interactions, etc. *(7,8)*. Furthermore, as the adsorption runs, the more molecules are adsorbed. The earlier adsorbed macromolecules will inevitably sterically hinder the latter adsorption. More recently, it is also found that some of macromolecular adsorptions can concern multisited binding and multilayers form *(9,10)*. Clearly, the practical process of macromolecular adsorption is much more complicated, in comparison with that of common small-molecules.

Historically, as noted, too much research has been done on this topic, and various mathematical and physical models have been proposed *(11–16)*. Unfortunately, as a result of the complexity of the practical process, most of these models are empirical or semi-empirical, presenting no distinct origin. Thus, the specific application of these models is actually limited. As also noted, currently almost no systematical work in this aspect is available. No doubt more works, especially the theoretical works, are necessary. As a supplement, a similar attempt is made in the present article. In order to aid the learning of the natural behavior of macromolecular adsorption, related theories are developed. The purpose is to reveal some information, particularly the intrinsic information, involved in the adsorption process of biomacromolecules.

Materials and Methods

Establishment of an Ideal Model

With respect to the adsorption of molecules, there is obviously a necessity of mentioning the Langmuir model, an ideal model (Fig. 1). It is well known that similar to the state equation of ideal gas in gas research, the Langmuir model, in adsorption, holds the dominative place, and is generally accepted as the fundamentality, whereas other models, more or less, are the derivatives. In the bulk phase, the solute, because of the interaction from the support, are absorbed onto the carrier, whereas over the surface, this adsorbate tends to escape from the surface because of heat movement. As a result, the total adsorptive-rate is determined by both adverse factors *(17,18)*:

$$\begin{aligned} v_t &= v_a - v_d \\ &= k_a N_t (1 - \theta) C - k_d N_t \theta \end{aligned} \tag{1}$$

Here v_a and v_d are respectively the rates for adsorption and desorption, k_a and k_d, the corresponding rate constants, C, the concentration of solute in the bulk phase, θ, the coverage degree of adsorbate over the surface, and N_t,

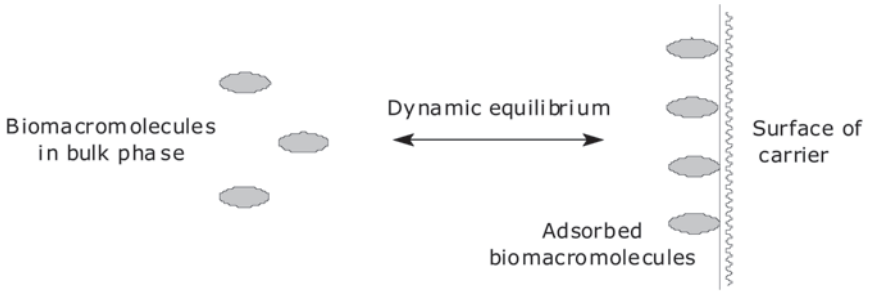

Fig. 1. Schematic profile of an ideal model.

the total number of combinable sites. In the beginning, the supreme *C* results in a maximal v_a. Subsequently, v_a decreases with declining *C*, whereas v_d increases with enhancing θ. This, with time running on, leads to a dynamic equilibrium. Clearly, in the equilibrium point, no macroscopical adsorption is actually achieved:

$$\begin{aligned} v_t &= v_a - v_d = 0 \\ &= k_a N_t (1-\theta) C^* - k_d N_t \theta \end{aligned} \tag{2}$$

Here the sign '*' characterizes the equilibrium. Solution to Eq. 2 gives:

$$\theta = \frac{K_L C^*}{1 + K_L C^*} \tag{3}$$

Now, substituting of $\theta = Q/Q_m$ into Eq. 3 will show:

$$\frac{Q}{Q_m} = \frac{K_L C^*}{1 + K_L C^*} \tag{4a}$$

or

$$\frac{C^*}{Q} = \frac{1}{K_L Q_m} + \frac{1}{Q_m} C^* \tag{4b}$$

Here K_L, coming from $K_L = k_a/k_d$, is the thermodynamic constant, *Q* and Q_m, the actual and maximal adsorbance. Clearly, according to this model, if no intermolecular interaction intervenes in progress, the plot of C^*/Q vs C^* is normally expected to be a straight line. Through the slope and intercept, the constant K_L, characterizing the affinity of biomacromolecules to support, can be achieved. As is widely shown, the applicability of the Langmuir model to small molecules cases is evidenced. However, for the adsorption of biomacromolecules, as already mentioned, there invariably is a certain degree of deviation as a result of the presence of various interactions. As a result, the specific example of the Langmuir-typed biomacromolecular-adsorption is actually quite limited *(19)*.

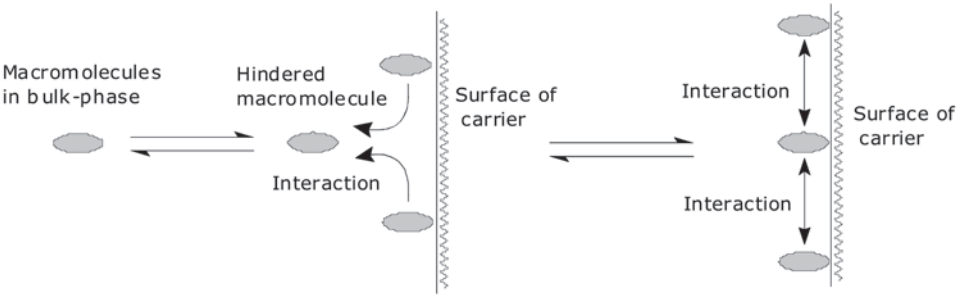

Fig. 2. Schematic profile of the adsorption with various interactions.

Modification of the Langmuir Model and Establishment of an Actual Model

As already explained, the adsorption of biomacromolecules can involve various interactions. Also the earlier adsorption can sterically hinder the latter adsorption. Hence, the rate of adsorption, as well as that of desorption, is actually a function of coverage degree in most occasions (Fig. 2) *(20,21)*:

$$\begin{aligned} v_t &= v_a - v_d \\ &= a e^{-E_a(\theta)/RT} N_t(1-\theta)\, C - b e^{-E_d(\theta)/RT} N_t \theta \end{aligned} \tag{5}$$

Here a, b are constants, $E_a(\theta)$, $E_d(\theta)$ are the activation energies of adsorption and desorption, and the rest are similar to Eq. 1. In the equilibrium point, there is:

$$v_t = 0 \tag{6a}$$

Thus this gives

$$\begin{aligned} \frac{\theta}{1-\theta} &= \frac{a}{b} e^{-\left(\frac{E_a(\theta) - E_d(\theta)}{RT}\right)} C^* \\ &= A \exp[\frac{q_m(\theta)}{RT}] C^* \end{aligned} \tag{6b}$$

Like a and b, here A is also a constant, and $q_m(\theta)$, the adsorption heat. As summarized *(18,21)*, in a practical case, the change of $q_m(\theta)$ vs θ can be in logarithmic or linear form:

$$q_m(\theta) = q_m^0 - \alpha \ln\theta \tag{7a}$$

$$q_m(\theta) = q_m^0 - \beta\theta \tag{7b}$$

Here α and β are constants, q_m^0, the original adsorption-heat. Now, substitution of Eq. 7a for 6b gives:

$$\theta^{\alpha/RT}\left(\frac{\theta}{1-\theta}\right) = A \exp\left(\frac{q_m^0}{RT}\right) C^* \tag{8}$$

On the left of Eq. 8, the change of θ in exponential form is much larger than that in fraction form. Hence, relating to the exponent, the effect of fraction moiety is actually minor. Clearly, as a reasonable approximation, Eq. 8 can be simplified into such form:

$$\theta = [A\exp(q_m^0/RT)C^*]^{RT/\alpha} = K_F(C^*)^{1/n} \tag{9}$$

Substituting of $\theta = Q/Q_m$ into Eq. 9 will give:

$$\frac{Q}{Q_m} = K_F(C^*)^{1/n} \tag{10a}$$

or

$$\ln Q = \frac{1}{n}\ln C^* + \ln K_F Q_m \tag{10b}$$

Here K_F and n are constants. Apparently, for practical adsorption, the linear relation can exist between $\ln Q$ and $\ln C^*$. Now, similar to Eq. 9, substitution of Eq. 7b for 6b gives:

$$\frac{\theta}{1-\theta} = A\exp\left(\frac{q_m^0}{RT}\right)\exp\left(-\frac{\beta\theta}{RT}\right)C^* = f\exp\left(-\frac{\beta\theta}{RT}\right)C^* \tag{11a}$$

Here f is also a constant. Placing of logarithmic forms in both sides of Eq. 11a will show:

$$\ln C^* = \frac{\beta}{RT}\theta - \ln f + \ln\left(\frac{\theta}{1-\theta}\right) \tag{11b}$$

In a middle coverage-degree, the value of $q/(1-q)$ is approximated to 1. This will lead to:

$$\ln C^* = \frac{\beta}{RT}\theta - \ln f \tag{12a}$$

or

$$\theta = \frac{RT}{\beta}\ln fC^* \tag{12b}$$

Substitution of $\theta = \frac{Q}{Q_m}$ to Eq. 13b gives:

$$Q = K_T \ln C^* + K_T \ln f \tag{13}$$

Like K_F, here K_T is also a constant. Clearly, similar to Eq. 10, Eq. 13 also describes the adsorption behavior in the presence of various interactions. In our previous works *(22,23)*, pepsin and BSA were adsorbed and immobilized onto the surface of modified PMMA microspheres. The result shows

that both Eqs. 10 and 13 can efficiently summarize this process. Under similar conditions, some researchers also presented the same results *(24,25)*. As noted, the provenance of Eq. 13 is based on the linear change of adsorption-heat vs coverage-degree, whereas Eq. 10 is derived from the logarithmic decrease. Thus, Eq. 13 actually describes a stronger interaction system, in comparison with Eq. 10.

Establishment of Multisited Binding Model

Multisited binding in biomacromolecular adsorptions has been reiteratively encountered *(26–28)*. However, most of the reported works are modal and qualitative, because of the difficulty in achieving an accurate binding profile. Biomacromolecules, such as protein, consist of a series of iterant units. In the adsorption process, the multireactivity of these unites and their iteration may lead to various interactions between the adsorbed molecules and the carrier. This thereby presents a convenience for the formation of multisited binding. Clearly, each adsorption or desorption of a specific biomacromolecule will concern the binding of several sites or release. Hence, the kinetic expression is expected normally to be an exponential form *(17,20)*:

$$\begin{aligned} v_t &= v_a - v_d \\ &= k_a[N_t\,(1-\theta)]^n\, C^* - k_d\,(N_t\theta)^n \end{aligned} \tag{14}$$

Here n is the number of sites involved by each adsorption and desorption. In the equilibrium point, Eq. 14 can be further sought into such form:

$$\begin{aligned} \theta &= \frac{(K_L C^*)^{1/n}}{1 + (K_L C^*)^{1/n}} \\ &= \frac{K_{LF}(C^*)^{1/n}}{1 + K_{LF}(C^*)^{1/n}} \end{aligned} \tag{15}$$

Here K_L and K_{LF} are constants. Now, substitution of $\theta = Q_/ Q_m$ to Eq. 15 gives:

$$\frac{Q}{Q_m} = \frac{K_{LF}(C^*)^{1/n}}{1 + K_{LF}(C^*)^{1/n}} \tag{16}$$

Clearly, Eq. 16 is the basic expression of the Langmuir-Freundlich model. Although derived originally from an empirical summarization, here whose profile of this model is evidenced. Now, considering various interactions, one can show:

$$\begin{aligned} v_t &= v_a - v_d \\ &= [N_t\,(1-\theta)]^n\, Ca\, e^{-E_a(\theta)/RT} - (N_t\theta)^n\, be^{-E_d/RT} \end{aligned} \tag{17}$$

In the equilibrium point, there is:

$$\left(\frac{\theta}{1-\theta}\right)^n = \frac{a}{b} e^{-\left[\frac{E_a(\theta) - E_d(\theta)}{RT}\right]} C^* \tag{18}$$

$$= A\exp\left[\frac{q_m(\theta)}{RT}\right]C^*$$

Substituting of Eq. 7a and 7b into Eq. 18 gives respectively:

$$\theta^{\alpha/RT}\left(\frac{\theta}{1-\theta}\right)^n = A\exp\left(\frac{q_m^0}{RT}\right)C^* \tag{19a}$$

$$\left(\frac{\theta}{1-\theta}\right)^n \exp\left(-\frac{\beta\theta}{RT}\right) = A\exp\left(\frac{q_m^0}{RT}\right)C^* \tag{19b}$$

In a middle coverage degree, Eq. 19a and 19b can be further sought into:

$$\theta = [A\exp(q_m^0/RT)C^*]^{RT/\alpha} = K(C^*)^{1/n} \tag{20a}$$

$$\theta = \frac{RT}{\beta}\ln[A\exp(q_m^0/RT)C^*] = \frac{RT}{\beta}\ln fC^* \tag{20b}$$

Apparently, in form, Eqs. 20a and 20b are the same as Eqs. 9 and 12b. This indicates that both equations can also describe the multisited binding in addition to monosited adsorption. This can also be observed in the examples of adsorbing histidine into copper *(29)* and coupling proteins to chromatographic support *(30)*.

Establishment of Multilayer Model

As aforementioned, the adsorption of biomacromolecules can involve a large number of intermolecular interactions. In progress, these interactions are likely to induce a multilayer form of adsorption *(31)*. As shown in Fig. 3, a series of adsorption in succession, resulting from the presence of electrostatic, hydrophobic, hydrogen-bonding interaction, and the like, are established on the surface of original adsorbed molecules. Obviously, the interaction subjected in the first layer is different from that in the other layers. Also the formation of successive adsorption does not require the completion of anterior adsorption. Assuming that S_0, S_1, S_2, ..., S_i, ... are respectively the surface area of covering 0,1,2, ..., *i*, ... layers of adsorbate. Clearly, in the equilibrium point, there is such relationship existing for the adsorption and desorption in the first layer:

$$a_1 C S_0 = b_1 S_1 e^{-q_1/RT} \tag{21}$$

Here a_1 and b_1 are constants, q_1, the adsorption heat of first layer. Similarly, for both layers, there is:

$$a_1 C S_0 + a_2 C S_1 = b_1 S_1 e^{-q_1/RT} + b_2 S_2 e^{-q_2/RT} \tag{22}$$

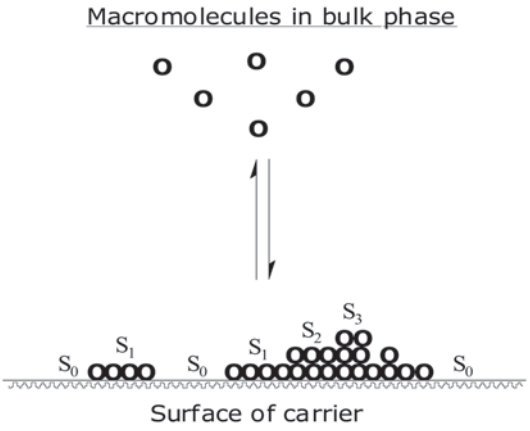

Fig. 3 Physical profile for multilayer adsorption.

Substitution of Eq. 21 for 22 will show:

$$a_2 C S_1 = b_2 S_2 e^{-q_2/RT} \tag{23}$$

Analogously, for the adsorption in more layers form, there are:

$$\begin{aligned} a_3 C S_2 &= b_3 S_3 e^{-q_3/RT} \\ &\cdots\cdots\cdots\cdots\cdots \\ a_i C S_{i-1} &= b_i S_i e^{-q_i/RT} \\ &\cdots\cdots\cdots\cdots\cdots \end{aligned} \tag{24}$$

Clearly, the total surface area for adsorption is

$$S_t = \sum_i S_i \tag{25}$$

and the adsorbance is

$$Q = Q_0 \sum_i i S_i \tag{26}$$

Here Q_0 is the adsorbance of forming monolayer adsorption in a unit of surface area. Now, correlating of Eq. 26 with 25 will give:

$$\frac{Q}{S_t Q_0} = \frac{Q}{Q_m} = \frac{\sum_i i S_i}{\sum_i S_i} \tag{27}$$

Here Q_m is the adsorbance of monolayer saturated-adsorption. As already explained, except for the first layer, the interactions subjected in other layers

are basically the same. Thus, as an approximation, one can expect such a relation existing among other layers:

$$\begin{aligned} q_2 &= q_3 = \cdots = q_i = \cdots = q_L \\ \frac{b_2}{a_2} &= \frac{b_3}{a_3} = \cdots = \frac{b_i}{a_i} = \cdots = g \end{aligned} \tag{28}$$

Under a specific condition, both q_L and g are constants. When further treating Eq. 27, there is obviously a necessity of correlating S_1, S_2, ..., S_i, ...with S_0. If assuming $(C/g)e^{q_L/RT} = x$ and $(a_1/b_1)Ce^{q_1/RT} = y$, then substituting of x and y into Eqs. 21, 23, and 24 will give:

$$\begin{aligned} &S_1 = yS_0 \\ &S_2 = xS_1 = xyS_0 \\ &S_3 = x^2yS_0 \\ &\cdots\cdots\cdots\cdots \\ &S_i = x^{i-1}yS_0 \\ &\cdots\cdots\cdots\cdots \end{aligned} \tag{29}$$

If assuming again $A_0 = \frac{y}{x} = \frac{a_1 g}{b_1} e^{(q_1 - q_L)RT}$, then S_i can be sought into such form:

$$S_i = A_0 x^i S_0 \tag{30}$$

Now, substitution of Eq. 30 for 27 gives:

$$\frac{Q}{Q_m} = \frac{A_0 S_0 \sum_{i=1} i x^i}{S_0[1 + A_0 \sum_{i=1} x^i]} \tag{31}$$

In the denominator, one can easily obtain:

$$\sum_{i=1} x^i = \frac{x}{1-x} \tag{32}$$

Similarly, the treatment of the numerator will give:

$$\sum_{i=1} i x^i = \frac{x \partial(\sum x^i)}{\partial x} = \frac{x}{(1-x)^2} \tag{33}$$

Substituting of Eqs. 32 and 33 into 32 will show:

$$\frac{Q}{Q_m} = \frac{A_0 x}{(1-x)\,(1-x+A_0 x)} \tag{34}$$

Because the adsorption is in a multilayer form, there may, in theory, be present an infinite adsorbance. Thus, in order to guarantee the achievement of $Q \to \infty$, the numerator must be kept as infinitesimal as possible. As a

result, the choice for x is left by 1 or $1/(1–A_0)$. As is often the case, the interaction subjected in the first layer is stronger than that in other layers. This leads to A_0 often bigger than 1 in most cases. Thus, such a value $1/(1–A_0)$ for x is almost meaningless. Clearly, in the point that $x = 1$, there presents

$$(C_0/g)e^{q_L/RT} = 1 \tag{35}$$

Here C_0 is the saturated concentration, corresponding to the saturate adsorption. Now, correlating of $x = (C/g)e^{q_L/RT}$ with Eq. 35 will show:

$$x = \frac{C}{C_0} \tag{36}$$

Substitution of Eq. 36 for 34 gives:

$$\frac{Q}{Q_m} = \frac{A_0 C}{(C_0 - C)\,[1 + (A_0 - 1)C/C_0]} \tag{37}$$

or

$$\frac{C}{Q(C_0 - C)} = \frac{1}{Q_m A_0} + \left(\frac{A_0 - 1}{Q_m A_0}\right)\frac{C}{C_0} \tag{38}$$

As apparent in equation 38, if the adsorption involves a multilayer form, the plot of $C/[Q(C_0 - C)]$ vs C is normally expected to be a straight line. Similarly, considerable endeavor, as noted, has recently been made by Gritti and his colleagues *(32–34)*. In their works, various isotherms of components were determined by liquid chromatography. Subsequently, based on frontal analysis, the pseudo-steady-state was used to treat the equilibrium. For the fraction θ_0, i.e., the free solid surface, kinetics showed:

$$\frac{\partial\theta_0}{\partial t} = 0 = k_s^d\theta_1 - k_S^a C(1 - \theta_1 - \theta_2 - \cdots - \theta_n) \tag{39}$$

This thus gave:

$$\theta_1 = b_S C(1 - \theta_1 - \theta_2 - \cdots - \theta_n) \tag{30}$$

For the first layer of adsorbate, the same kinetic constraint was expressed as follows:

$$\frac{\partial\theta_0}{\partial t} = 0 = k_s^a C(1 - \theta_1 - \theta_2 - \cdots) - k_s^d\theta_1 - k_L^q\theta_1 + k_L^d\theta_2 \tag{31}$$

$$= \frac{\partial\theta_1}{\partial t} - k_L^q\theta_1 + k_L^d\theta_2$$

The solution to Eq. 31 showed:

$$\theta_2 = b_L C\theta_2 \tag{32}$$

Here the subscripts '*S*' and '*L*' represented the first layer and subsequent layers, respectively. Analogously, for the successive layers, the same relations could be derived. Combining Eqs. 30, 32 with the relations of 33 would give also Eq. 37.

$$\theta_0 + \theta_1 + \theta_2 + \cdots + \theta_n = \sum_{i=0}^{i=n} \theta_i = 1 \tag{33}$$

In literature *(17,18,20,21,31)*, the correctness of this relationship in biomacromolecular adsorption has been confirmed. It is also necessary to point out that in most operations, the adsorption is conducted under a rapid mixing round. Thus, there is considerable difficulty on forming a stable multilayer-adsorption, especially the infinite-layer adsorption.

Establishment of Ion-Exchange Model

Adsorption of multicomponent protein over ion-exchange surfaces can be often involved under various chromatographic conditions. In these systems, a modulator, often a salt, is frequently added to the mobile phase in fairly high concentrations (up to 1 *M*) to modulate the protein retention. As a result, induced salt gradient phenomena are usually observed. As mentioned, protein molecules have complex three-dimensional structures, relatively high molecular masses, and pH-dependent surface charge characteristics. Enthalpy changes accompanying the adsorption process can be endothermic or exothermic, and may be dependent on the coverage. Therefore, in the light of the complexity, various models currently available are inadequate to describe the equilibrium behavior. For this, as noted, much endeavor has been made over latest years. It has been known that in the presence of salt, a competition of combinable sites between counterion (salt) and protein can take place in the adsorption process *(35,36)*:

$$C_i + v_i\overline{Q}_s \Leftrightarrow Q_i + v_i C_{\text{salt}}$$

Here Q_i and C_i are the component concentrations on the stationary and mobile phases, respectively, C_{salt}, the salt concentration in mobile phase, v_i, the characteristic charge of adsorbed component, and $\overline{Q}_s$, the concentration of sites on the stationary phase available for adsorption. Clearly, the equilibrium constant for the ion-exchange reaction is given by:

$$K_{\text{SMA}} = \left(\frac{Q_i}{C_i}\right)\left(\frac{C_{\text{salt}}}{\overline{Q}_s}\right)^{v_i} \tag{34}$$

The electro-neutrality of the stationary phase requires,

$$\Lambda = \overline{Q}_s + \sum_{i=1}^{n} (v_i + \sigma_i)Q_i \tag{35}$$

Here L is the total ionic capacity of the stationary phase and s_i is the number of sites shielded by a specific component. Now, for the specific component, substituting of Eq. 35 into 34 would give the isotherm:

$$C_i = \left(\frac{Q_i}{K_{\text{SMA}}}\right) \times \left(\frac{C_{\text{salt}}}{\Lambda - (\sigma_i + v_i)Q_i}\right)^{v_i} \tag{36}$$

Clearly, Eq. 36 is the expression of the steric mass action (SMA) model. Considering the displacement of counterions and shielding effect of protein, the efficiency of this model has been well confirmed in various ion-exchange processes. The SMA parameters, namely the characteristic charge (v), the equilibrium constant (K_{SMA}), and the steric factor (s), once determined, can be used to describe the adsorption of proteins at various ion-exchange conditions. Also, they can be used to investigate the thermodynamics of protein adsorption by evaluating the change in Gibbs free energy during ion exchange. By using the SMA model, the Gibbs free energy of adsorption of a protein at a particular salt concentration can be obtained from (37):

$$\Delta G^0_{\text{ads}} = -RT \ln\left(\frac{Q_i}{C_i}\right) = RT \ln\left[K_{\text{SMA}}\left(\frac{\Lambda}{C_{\text{salt}}}\right)^v\right] \tag{37}$$

Like this, some endeavors, as also noted, were made by Li and Pinto *(38)*. Basing on each ion-exchange reaction of a single component, their NISS model gives the equilibrium constant:

$$K_i = \frac{(C_n\gamma_n)^{Z_i}\,\gamma_i^s n_i^s}{(C_n^s\gamma_n^s)^{Z_i}\,C_i} \tag{38}$$

Here C_n and C_i are respectively the salt and component concentrations, g_n, g_i, the corresponding activity coefficients, and Z_i, the number of sites occupied by specific component.

Conclusion

Adsorption of biomacromolecules, owing to their significance in a wide range of biomedical applications, has been widely studied. It is clear that unlike adsorption of small molecules, biomacromolecular adsorption is much more complicated and often involves various interactions. Moreover, as the adsorption runs, the more molecules are adsorbed. The earlier adsorbed macromolecules can sterically hinder the latter adsorption. As a result, there invariably is a certain degree of deviation from classic law. Historically, as noted, too much endeavor has been made on this topic, and various mathematical and physical models have been proposed. However, as a result of the complexity of practical process, most of these models are empirical or semi-empirical. As a supplement, a similar attempt is made in the present article. As shown, if these interactions are heavily involved by the adsorption, the plot of $\ln Q$ (or Q) vs $\ln C^*$ is normally expected to be a

straight line. Otherwise, if the linearity exist between C^*/Q vs C^*, the adsorption will be an ideal process with no intervention of these interactions. Meanwhile, this article also presents corresponding relationships for the adsorption in multisited binding and multilayer forms. Other aspects including ion-exchange systems are also discussed (C^*, the equilibrium concentration of biomacromolecules; Q, the adsorbance). It is also necessary to point out that some opinions in this article are likely somewhat tentative; further work is necessary and is currently underway. Other aspects that have not, as yet, been addressed here are also expected to be significant.

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