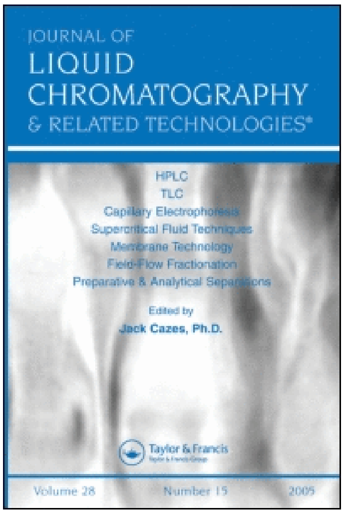

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THE MECHANISM OF COPOLYMER RETENTION IN INTERACTIVE POLYMER CHROMATOGRAPHY. I. CRITICAL POINT OF ADSORPTION FOR STATISTICAL COPOLYMERS

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ABSTRACT

A comprehensive analysis of interactive polymer chromatography is presented. Isocratic liquid chromatography of polymers at the critical eluent composition (the transition point where size-exclusion and adsorption interactions completely compensate each other) is currently used to separate functional oligomers and block copolymers. We have extended the concept of this critical elution chromatography to the cases of statistical copolymers as well as porous stationary phases with heterogeneous surfaces (viz., surfaces with both inert and active groups). The theory provides the quantitative condition for statistical copolymer chains to have a single adsorption-desorption transition point. The random copolymers with narrow chemical composition distribution (CCD) always posses such a point. For non-random copolymers this condition includes the comparison between the mean length of chain segments connecting the attractive walls of the pore and the chemical correlation segment characterizing the randomness of the copolymer microstructure or the surface of this pore.

If the critical transition point exists, then the copolymer chains behave as hypothetical homopolymer chains with a single energy of interaction between the effective monomer units and the active groups at the surface. The relationship between this energy and the microstructure of copolymer chains has been also analyzed. If copolymer has a broad CCD, each compositionally homogeneous fraction has its own adsorption-desorption threshold.

The partial transition points have been established for the copolymers with blocky or alternating microstructure. Only a portion of the copolymer chain effectively behaves as a homopolymer chain at these points. This property was used in the past for the separation of block copolymers according to the length of blocks comprised of the monomer units of a specific type.

INTRODUCTION

The chromatographic characterization of copolymers with molecular weight and chemical composition distributions (MWD and CCD, respectively) is generally a much more complex task than the chromatography of homopolymers. Thus, even the MWD of copolymers can not be measured accurately by a single size-exclusion separation because the size (i.e., hydrodynamic volume) of a macromolecule depends on both molecular weight and chemical composition. As a result, the true MWD of the copolymer can be broader or narrower than the apparent one measured by size-exclusion chromatography (SEC). The same is true for the CCD: even if different fractions eluted from the size-exclusion columns have nearly the same average composition, the overall copolymer CCD can still be significant.

The most obvious solution of this copolymer characterization problem could be a chromatographic approach to a cross-fractionation, when two chromatographic systems are coupled together so that the eluent from the first instrument, running in a semipreparative mode, flows through the injection valve of the second one. In this approach the fractions from one chromatographic system are transferred automatically or manually to another for further separation.[1] (This technique has been originally named *orthogonal chromatography*,[2] but the names *chromatographic cross-fractionation,*[3,4] *coupled column chromatography*,[5] and *two-dimensional chromatography*[6-9] are also used).

Two-dimensional (joint) distribution can be obtained if the first system separates the copolymer exclusively by one property, either molecular weight or chemical composition, and the following one separates each eluting fraction according to another property. To achieve this goal, many workers used conventional SEC as a first step in the two-dimensional separation, followed by the isocratic[1,2,5] or gradient[3,4,10,11] chromatography with mixed separation mechanism. But this method can be successful only if the copolymer has the homogeneous composition, i.e., its CCD is very narrow, or the chemical composition of macromolecules does not affect their size during the size-exclusion separation. If the retention volume in SEC depends on both variables (molecular weight and chemical composition), this first step does not result in the MWD of the copolymer.

Another approach to the chromatographic cross-fractionation is the use of interaction HPLC as a first step,[6-9,12-17] that implies weak non-steric interactions between a solute and a stationary phase.[18] Assuming these interactions differ for monomer units of different types in a copolymer, such chromatography can provide the separation based on chemical composition or other structural differences in macromolecules. The works of H. Pasch et al.[7-9,18,19] represent an elegant example of complete two-dimensional characterization of di- and triblock copolymers AB and ABA′ with a such approach. They have found the isocratic conditions when the chromatographic system separates macromolecules according to the size of one type of blocks, say B, while the size of A-blocks does not affect the retention. In the second step, another chromatographic system allows one to separate eluting fractions according to the A-blocks.

For example, the PMMA blocks in methyl methacrylate–styrene diblock copolymer are chromatographically "invisible" on a silica gel stationary phase at 70:30% by volume methylethylketone-cyclohexane eluent. At these conditions macromolecules elute exclusively with respect to the length of the polystyrene blocks, which have only steric interactions with the stationary phase. Accordingly, the MWD of the PS blocks in the copolymer can be calculated using the SEC column calibration based on narrow polystyrene standards. On the other hand, MWD of PMMA blocks can be obtained on the stationary phase Nucleosil RP-18 with the mobile phase of THF-acetonitrile 49:51% by volume, when the polystyrene blocks become "invisible", and the block copolymer is separated exclusively according to the length of the PMMA blocks.[9,19] Combination of these two chromatographic separations allows one to calculate both the MWD and CCD of corresponding diblock copolymers.[9,20]

Polyethylene oxide (PEO)–polypropylene oxide (PPO) triblock copolymers (PEO-PPO-PEO) were separated first on RP-18 columns using acetonitrile-water (43:57, v/v) as an eluent.[7] These conditions provide the separation exclusively with the respect to the inner PPO blocks, regardless of the length of the outer PEO blocks. The propylene oxide uniform fractions collected after this separation were subjected to the capillary supercritical fluid chromatography with the flame ionization detection, or conventional SEC,[7] or matrix-assisted laser desorption/ionization (MALDI) mass spectrometry.[21] In all cases, the complete structural characterization of the triblock copolymers was achieved.[9,18]

The possibility of such an unusual behavior of block copolymers in reverse or normal-phase isocratic separation, when one of the components does not affect the retention, was predicted by Skvortsov and Gorbunov.[22] They have showed theoretically that if at a certain mobile phase composition the size-exclusion and adsorption interactions for the blocks of one type A completely compensate each other, then retention occurs exclusively according to the remaining blocks B in macromolecules. That is, the blocks B only contribute to the retention of the block copolymer as a whole. In the case of homopolymers (single block systems), the entire macromolecules can remain "invisible" for the chromatographic system.[9] The eluent composition where this compensation phenomenon takes place, has been termed *critical point of adsorption (CPA)*,[9] *point of exclusion-adsorption transition*,[23] *critical conditions (of adsorption)*,[24,25] or *adsorption theta point*.[26]

At this transition point the repulsive polymer-surface steric (excluded volume) forces responsible for any change in the conformational entropy of a macromolecule, and short-range polymer-surface attractive forces with enthalpic nature, counterbalance each other. Such entropy-enthalpy compensation is well known in HPLC of low molecular weight compounds.[27] In the case of polymer chromatography, the important feature of this phenomenon is the independence of the CPA from the molecular weight of the entire macromolecule or its portion (e.g., block of a certain type), which offers opportunities for separating complex molecules.[18,24-26]

First experimental observation of the exclusion-adsorption transition was reported for polystyrene on silica by Belenkii et al. for a thin-layer chromatography[28] and by Tennikov et al. for HPLC.[29] Since then the critical conditions of adsorption were established for many other homopolymers and stationary phases,[30] including a capillary for the supercritical fluid chromatography.[31] Besides the aforementioned block copolymers, the isocratic HPLC at the CPA have been used for the separation of homopolymers according to the types of end-groups[32,16,33] and tacticity,[34] and the separation of polymer blends.[18]

The separation at the CPA is probably the only adequate approach for the isocratic interaction chromatography of polymers, except the adsorption chromatography of some low-molecular weight oligomers. The reason for that is a strong (usually exponential) polymer molecular weight dependence of retention volume, which makes the adsorption of macromolecules on an attractive surface of a stationary phase practically irreversible.

Because of this, the gradient HPLC is a much more powerful tool for the separation of copolymers with respect to chemical composition. The first separation of this kind was performed by Teramachi and co-workers.[35] They separated a mixture of three statistical poly (styrene-co-methyl methacrylate)s on silica gel through a carbon tetrachloride-methyl acetate gradient. Since that time the method has been applied to the compositional separation and determination of CCD of many statistical, block, and graft copolymers on both normal-phase and reverse phase columns (see recent review literature[4,11,18,36-38]).

The primary goal of gradient elution of copolymers is the separation based solely upon their chemical composition, i.e., independent of molecular weight. To achieve this goal, two different approaches have been developed. Glockner et al. (see[4] and refs. cited therein) employed gradient systems that were intentionally chosen to produce precipitation of the copolymer components on the top of a column. As the solvent strength of the mobile phase is gradually increased, the copolymer components redissolve and elute successively from the column according to their solubility. In this approach, which is usually referred to as *liquid precipitation chromatography,*[9] *liquid chromatography under limiting conditions of solubility*,[23] *precipitation-dissolution chromatography*[39] or *gradient polymer elution chromatography* (GPEC™),[40,41] the polymer solubility is a main factor in retention and the nature of stationary phase does not affect the separation significantly.[42] Because the solubility depends not only on chemical composition, but also on molecular weight and concentration of the polymer, this method seems to be of doubtful value in the reproducible separation of copolymers according to chemical composition. For example, in the case of homopolymers, this mechanism usually leads to a linear relationship between the elution volume of the polymer and the logarithm of its molecular weight.[39]

Another approach to gradient elution of copolymers utilizes conditions when copolymer fractions are adsorbed on the surface of the stationary phase and then elute successively as a content of a displacer component in the mobile phase increases (liquid adsorption chromatography[9]). The adsorption power of the stationary phase (both polar for normal phase and non-polar for reverse phase separations) plays a dominant role in retention.

Ideally, all of the components of the copolymer should be either in adsorbed or solvated state during the entire separation process. For example, Mourey[43] performed compositional separations of several acrylate and methacrylate ester homopolymers and statistical copolymers on silica in toluene–2-butanone solvent gradient. Mori et al.[17] used 1,2-dichloroethane–chloroform gradient to separate random styrene-methyl methacrylate copolymers according to chemical composition. All of these solvents are good solvents for these copolymers. Other examples are compositional separation of partially hydrolyzed poly (vinyl acetate) on reverse phase packing of polystyrene/divinylbenzene in water-THF gradient[44] and recently reported[45,46] separation of chlorinated polyethylenes on silica in n-hexane/chloroform gradient, which we describe in detail in the next paper. Both these polymers can be considered as statistical copolymers with vinyl acetate groups incorporated in poly (vinyl alcohol) or chloromethylene groups in polyethylene, respectively.

The situation when both components of the mobile phase are good solvents for all fractions of the copolymer is rather non-typical in gradient chromatography due to limited solubility of polymers. Thus, Mori et al.[10,47-50] used shallow gradient of non-solvent ethanol as a displacer in a compositional separation of styrene-acrylate and styrene-methacrylate statistical copolymers on silica. Due to low concentration of ethanol, the precipitation did not occur, and separation in full composition range took place according to the adsorption-desorption mechanism.

Shunk[12] separated methyl methacrylate-methacrylic acid statistical copolymers, including corresponding homopolymers, on silica using gradient of methanol (with or without 5% glacial acetic acid) as a displacer in toluene. Despite initial precipitation of higher mole % methacrylic acid copolymers, no elution was observed until well past the solubility limit. The precipitated fractions redissolved and absorbed on the silica surface far before they were eluted from columns. The elution in this case happens when the solvent reaches sufficient strength to displace the adsorptive interactions of retained macromolecules. In other words, the separation occurs according to adsorption-desorption, but not the solubility properties of polymer fractions. In any case, when a non-solvent is used in gradient elution of copolymers, the retention mechanism should be verified by comparison of the elution solvent concentration and solubility limit for corresponding fractions of copolymers, e.g., obtained by turbidimetric titration.[4,12,51,52] The effect of injected sample mass on retention and peak shape can also be used in elucidating the mechanism of separation.[12,53-55]

Usually, the independent of molecular weight compositional separation of statistical copolymers in gradient elution governed by the adsorption mechanism is achieved on narrow pore adsorbent for polymers with relatively high molecular weight.[10,12,43,17,47-51] The commonly accepted proposition is that the separation by chemical composition should not be superimposed by any size exclusion effects.[56,57] For this reason, the pore size for gradient elution should be either large enough for all solute macromolecules to penetrate into the pores, or so small that none of them can enter.[17]

This explanation has several flaws. First, under the conditions of adsorption interactions with the surface, flexible macromolecules can penetrate the pores, though they are completely excluded at SEC conditions.[24,58-60] The probability of penetration depends on the Gibbs free energy of the molecule inside the pore: the lower this energy, the higher the probability.[24] In the following section we will show that this probability increases when the pore diameter decreases.

Secondly, even if the separation occurs on the external surface of the particles (e.g., the particles are non-porous at all), the adsorption of macromolecules is always accompanied by steric interactions with the surface: the conformation entropy of a macromolecule changes when it is adsorbed by the surface.[59] And lastly, based merely upon adsorption interactions, the retention of macromolecules always exhibits strong dependence on molecular weight, which has been demonstrated in many experimental investigations of oligomer series.[61] The steric interactions, which are more pronounced for higher molecular weight macromolecules, attenuate this dependence[61] because of mentioned above counterbalancing between entropic and enthalpic effects. Only at critical conditions, the adsorption forces are completely compensated by the conformational entropy losses and the molecular weight dependence of retention disappears.

From the above reasoning it is clear that the true molecular weight-independent compositional separation of polymers in gradient elution can be achieved only if each polymer fraction has a CPA of its own, corresponding to a certain mobile phase composition, and elutes at this composition. Obviously, this approach can work for the gradient elution of blends comprising of homopolymers, if the CPA for each component is attained during the separation. The primary objective of the present work is to extend this approach to the gradient separation of copolymers.

In Part I of this work (present paper) we show how the theory of polymer solutions in a confined (e.g., porous) space furnishes the adsorption-desorption transition point for heterogeneous macromolecules (copolymers) and/or heterogeneous attractive surfaces, and how this point depends on microstructure of a macromolecule and a stationary phase. In Part II[62] we apply the concept of liquid chromatography at CPA to the theory of gradient elution of polymers, including polymer blends and copolymers. We demonstrate how available experimental data support the theory and discuss the feasibility of the method for the chemical composition separations of copolymers.

THEORY

Exclusion-Adsorption Transition in Interactive Chromatography of Homopolymers on Columns with a Homogeneous Pore Surface

Any chromatographic process is associated with selective distribution (partition) of an analyte between a stationary and a mobile phase, which is described by the corresponding distribution coefficient K, equal to the ratio of the analyte concentrations (partition functions) in these phases. Cassasa[63,64] has extended this general definition to the case of SEC: the interior of microporous adsorbent particles comprises the stationary phase having the total pore volume V_P, while the interstitial (exclusion) volume V_0 with the flowing solvent represents the mobile phase. Thus, the retention (elution) volume V of the system in SEC is:

$$V = V_0 + K\,V_P \qquad (1)$$

If the transverse pore dimension D (the width of a slit-like pore or the internal diameter of cylindrical or spherical pores) is comparable with mean dimensions of the polymer chain, e.g., its radius of gyration R_g, then there is an entropic cost for the macromolecule to enter the pores associated with a steric repulsive interaction between the polymer and the pore surface. Consequently, the conformational entropy of the macromolecule decreases when it enters the pore (confined space). In equilibrium, this decrease, caused by the spatial constraint, defines the distribution coefficient K_D for the pores of specific size D:

$$K_D = K_{D,SEC} = \exp\,(\Delta S/k_B) \qquad (2)$$

where ΔS is the difference in polymer conformation entropy (per macromolecule) between the confined and unconfined states, respectively, k_B is the Boltzmann's constant. Due to restriction of a macromolecule fluctuation motion inside pores, ΔS is always negative and decreases with the reduction in the pore size D, along with the distribution coefficient $K_{D,SEC} < 1$.

Usually, particles contain pores of various sizes D with corresponding volumes V_D (polydisperse sorbent), and the distribution coefficient K in equation (1) comprises the contributions from the pores of all possible sizes:

$$K\,V_P = \sum_D (K_D\,V_D) \qquad (3)$$

A rich variety of statistical models have been proposed to describe a polymer chain in a confined volume (see review in[65]). The best suited to the SEC application are random walk models (lattice and continuum), which allow one to calculate the partition coefficient K_D as a function of macromolecular and pore sizes, geometry of pore media, etc.[24,63-65] One most important result obtained by these models is that the distribution coefficient depends on molecule-to-pore dimension ratio R_g / D only, but not on these two sizes taken separately.[63] In the most important case, when pores and macromolecules are comparable in size, this dependence is universal in terms of both conformational properties of macromolecules (topology, rigidity, excluded volume effects) and pore geometry (slit-like, cylindrical, or spherical), including the case of polydisperse pore media.[65] This finding provides the theoretical basis for the universal calibration concept in SEC.[66]

In more general cases of interactive polymer chromatography (IPC), the electrostatic non-steric interactions between macromolecules and pore walls are superimposed on the size-exclusion (steric) effects of impenetrable surface. Depending on the polarity of stationary phase and chemical structure of an analyte, these interactions can be of the normal- or reverse phase types. But in both cases due to the size of polymer molecules, the adsorption is a primary mechanism of the retention in IPC, when monomer groups on polymer chains interact with polar groups of the surface (normal phase) or with solvated bonded moieties of the stationary phase for reverse phase chromatography.[36] Note that adsorption forces can be of different nature (Van der Waals interactions, hydrogen bonds, hydrophobic interactions, etc.).

The first theoretical analysis of IPC has been performed twenty years ago by Belenky et al.[28] From that time, the simple phenomenological model serves as a theoretical basis for almost every published isocratic chromatographic separation at CPA and is outlined in virtually all publications on this subject (see, for example, reviews in[4,18,36]). In the contest of this theory, the distribution coefficients in equations1 and 3 are subdivided into two parts,

$$K_{\mathrm{D}} = K_{\mathrm{D,SEC}} K_{\mathrm{D,INT}} \qquad (4)$$

where $K_{\mathrm{D,SEC}}$ is still given by equation (2), and $K_{\mathrm{D,INT}}$ is the additional contribution from non-steric interactions. This contribution is associated with the energy ΔE of interaction with the stationary phase:

$$K_{\mathrm{D,INT}} = \exp\left(-\Delta E/k_{\mathrm{B}}T\right) \qquad (5)$$

where T is absolute temperature. This energy represents a change in the free energy of the system (per macromolecule), related to the fact that a certain amount of monomer units of an absorbed polymer chain replace the solvent molecules near the surface and create reversible bonds with the adsorption (active) sites on this surface. If the resulting effective energy for one such bond (segment interaction energy) is ε, and the equilibrium fraction (per Dalton) of monomer units having temporary bonds with active sites on the surface is θ, then $\Delta E = M\theta\,\varepsilon$, where M is molecular weight of a polymer chain. Since only attractive interactions make sense in IPC, the quantities ΔE and ε are negative ($\varepsilon < 0$), and $K_{\mathrm{D,INT}} > 1$.

Note that the segment energy ε, thus defined, can also include some entropic effects associated with the solvent-sorbent active site-polymer group tertiary interactions,[67] which does not affect the conformation entropy of macromolecules.

In such a manner, the distribution coefficient K_{D} (4) is described by the Gibbs free energy change $\Delta G = \Delta E - T\Delta S$, due to both size-exclusion (entropic) and non-steric (enthalpic) interactions: $K_{\mathrm{D}} = \exp\left(-\Delta G/k_{\mathrm{B}}T\right)$. Equation (3) will continue in use to comprise the contribution from pores with different sizes D. But unlike the case of SEC, when $\Delta E = 0$, the sum in the right side of equation (3) should also include the term reflecting the possible adsorption of a polymer on the outer surface of the particles.[18] This term formally corresponds to $D \to \infty$ in equation (3). Such adsorption can affect the retention even for non-porous adsorbents.

The main assumption in the phenomenological approach developed by Belenky et al.[28] is the linear dependence of the thermodynamic functions ΔE and ΔS (and thus of ΔG) on the molecular weight M (or the number of repeating units) in the polymer homologue series. This assumption, known as the Martin equation, is well established in HPLC of oligomer series.[36] It furnishes very important conclusions for the IPC. Thus, in this case,

$$\frac{\partial K_D}{\partial M} = -\frac{\Delta G K_D}{M k_B T} \tag{6}$$

Equation (6) shows that the competition between the steric (repulsive) and non-steric (attractive) interactions play a crucial role in IPC. Thus, if the steric effects still predominate so that $-T\Delta S > -\Delta E$, then ΔG is positive, K_D is less than 1, and we have the order of elution, typical to the size-exclusion separation: $\partial K_D/\partial M < 0$, i.e., elution volume decreases as molecular weight of polymer homologues increases. In the opposite case of the adsorption mode of separation (adsorption prevails), $\Delta G = \Delta E - T\Delta S < 0$, K_D exceeds 1, and the retention increases with molecular weight: $\partial K_D/\partial M > 0$.

Lastly, the separation at CPA ("transition" mode) takes place when these two types of interactions completely compensate each other: $\Delta G = \Delta E - T\Delta S = 0$, $K_D = 1$, and $\partial K_D/\partial M = 0$, so that retention does not depend on molecular weight at all. The retention volume in this mode coincides with the total volume of the system: $V = V_T = V_0 + V_P$.

The important consequence from the linearity of ΔG as a function of M is that each of these three modes of chromatographic separation occurs for all polymer homologues simultaneously, because the sign of ΔG does not depend on M.

The best experimental verification of the foregoing phenomenological theory is the number of fan-shaped diagrams (so-called "critical" diagrams[33]) obtained for different homopolymers and representing the molecular weight calibration curves (logarithm of molecular weight versus retention volume) for isocratic separation of polymer homologous series at various mobile phase compositions or temperatures. The first diagrams of this kind were reported by Tennikov et al.[29] for isocratic separation of polystyrenes on silica gel (normal phase interactions) with chloroform-carbon tetrachloride as a mobile phase. The temperature and the mobile phase composition were two variables affecting the mode of chromatographic separation (i.e., the sign of ΔG). Figure 1 represents another example: the separation of polyethylene glycols on bonded silica (reverse phase interactions) in acetonitrile-water.[33] At 46% by volume of acetonitrile in the mobile phase, retention does not depend on molecular weight of the polymer, and corresponding mobile phase composition represents the CPA for this system.

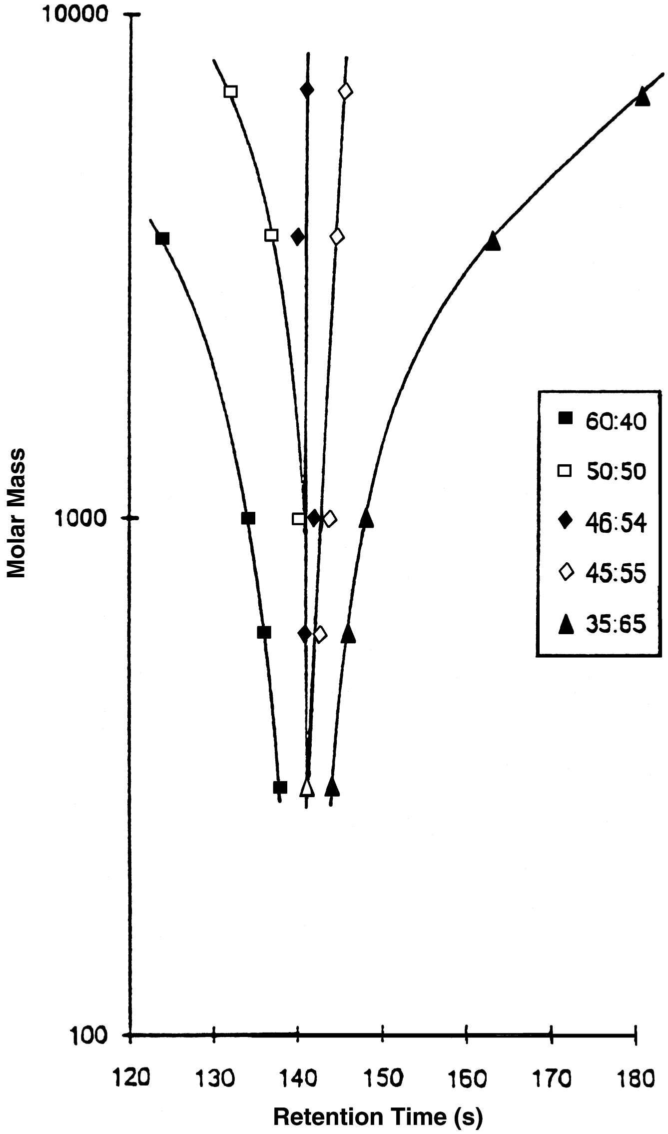

Figure 1. Critical diagram for isocratic separation of polyethylene glycols; stationary phase: Nucleosil RP-18, 60 × 4mm I.D., solvent: acetonitrile-water at various compositions (by volume) (Reprinted from Ref. 33).

In spite of a wealth of experimental evidence supporting the foregoing phenomenological approach to the IPC, this approach has serious limitations, which sometimes lead to confusion and misinterpreting the experimental results. Thus, the basic assumption about the linearity of free energy in isocratic elution has been the subject of much controversy when applied beyond the oligomer range of molecular weights.[36] For example, the Casassa's theory predicts the dependence $\Delta G = -T\ \Delta S \sim M^{1/2}$ for the size-exclusion separation of macromolecules comparable in size with the pore dimension, the most important range for SEC. Only for very narrow pores (close to the exclusion limit of the separation, when $R_g >> D$) this dependence becomes linear.[65]

For lack of possibility to provide the dependence of ΔS and ΔE on pore diameter D and effective interaction energy ε, the theory gives no way of estimating the distribution of macromolecules among the pores of different sizes in the case when the adsorption effects prevail. As a result, there is much speculation that large macromolecules can not penetrate into small pores even in the presence of adsorption interactions.[4] It is widely believed, also, that in the cases of a sorbent with very wide pores or a non-porous sorbent, the size-exclusion effects are absent at all ($\Delta S = 0$).[18] As a result, the use of packing material with very narrow ($D << R_g$) or very wide ($D >> R_g$) pores (ideally, non-porous at all) is considered as a way to avoid the overlap between size-exclusion and adsorption phenomena and to obtain normal- or reverse phase separations, which are independent of molecular weight of polymers.[4,36] Accordingly, the case, when $\Delta S = 0$, is called the ideal liquid adsorption chromatography (LAC) of polymers.[18]

In fact, the conformation entropy losses $|\ \Delta S\ |$ always increase with adsorption. This is true for the pores of any size, including the case of adsorption on the outer surface of a sorbent ($D \rightarrow \infty$), so that the ideal LAC for polymers can not exist even theoretically, as opposed to the ideal SEC. Intuition suggests that the number of available conformations (conformational mobility) and hence the conformational entropy of a macromolecule decreases with an increase in number of adsorption contacts with the surface of a sorbent.

What intuition cannot predict, is that at some threshold value of interaction energy $\varepsilon = \varepsilon_{cr}$, this decrease occurs abruptly as a sharp (phase) transition, when both thermodynamic functions ΔS and ΔE have discontinuities.

This and other results important for the IPC applications, follow from a molecular-statistical theory of chromatography of flexible-chain homopolymers, which has been developed mostly by Gorbunov and Skvortsov (see review[24] and refs. cited therein), and, recently, by Di Marzio et al.[26] This theory extends the Casassa's approach to the isocratic chromatographic separation of macromolecules on porous media with adsorption interactions.

Analogously to Casassa, Gorbunov, and Skvortsov use the continuous random walk model to describe an ideal (without excluded volume effects) flexible homopolymer chain inside a slit-like pore with attractive walls. This model allows one to obtain analytical solutions for the thermodynamic functions ΔS and ΔE, and thus the partition coefficient K_D for arbitrary values of macromolecule and pore sizes (R_g and D, respectively) and of segment interactive energy ε, including the "critical" (threshold) value $\varepsilon = \varepsilon_{cr}$, where the entropic and enthalpic effects mutually compensate each other. The existence of such a point in IPC is the reflection of more general phenomenon in polymer adsorption at a solid surface known as the adsorption-desorption transition point,[67] which in turn is the fundamental feature of the diluted polymer solutions: the conformational (coil – globule) phase transition of solvated macromolecules in the presence of an external field.[68]

The polymer adsorption has always been a "touchstone" problem for the statistical physics of polymers. This explains the unbelievably large number of publications devoted to this subject (see[24,26] for the comprehensive review). As in the case of a polymer chain confined in space with non-attractive impenetrable (solid) walls, the continuous or discrete lattice random walks were the most popular models of a polymer chain, while the standard techniques of the grand canonical ensemble (the method of generating functions) was most frequently used for the calculations of the thermodynamic functions for these models.[59,67,69]

Note that these two approaches (continuous and discrete) are fully equivalent to each other.[24] As a matter of fact, all results from a continual model can be obtained from the corresponding lattice model as an asymptotic limit for long polymer chains. But the continual model is more convenient in analyzing large-scale (global) conformational characteristics of macromolecules, independent of the structural details of a chain or an adsorbent surface, such as the existence of the critical energy ε_{cr}. This critical point indicates the adsorption-desorption transition, when the spatial distribution of the segment density of a polymer chain, confined between two attractive walls, experiences a dramatic change in the direction perpendicular to the surface of the walls. Such transition sometimes is called the collapse of the polymer chain.

On the other hand, the lattice model allows taking into account the local structure of macromolecules and porous media. Thus, the value ε_{cr} for the homopolymer chain adsorbed on the homogeneous surface, when each contact between the chain and the surface leads to the adsorption interaction, can be expressed in terms of the conformational partition functions, z and z_0, of chain units (monomers) in adsorbed and non-adsorbed states, respectively:[67]

$$X_{cr} = \exp(-\varepsilon_{cr}/k_B T) = 2z_0 / (z + z_0) \qquad (7)$$

The lattice model interprets the parameters z_0 and z as the coordination numbers of the space and surface lattices, respectively. These parameters depend on the geometry of the model lattices only. For a simple cubic lattice, $z_0 = 6$, $z = 4$, and $X_{cr} = 1.2$. Correspondingly, $X_{cr} = 1.334$ for a hexagonal lattice, 1.499 – for a face-centered lattice, and 2 – for body-centered lattice.

We now need to focus upon the theoretical results from the molecular-statistical theory, essential for the IPC applications and independent of specific model of a polymer chain.

When the energy of adsorption interactions ε is close to zero, so that $\varepsilon > \varepsilon_{cr}$ (recall that ε is always negative for attractive forces), the attractive forces are very weak and $|\Delta E| << T\ |\Delta S|$. The adsorption causes only slight perturbations of the conformational statistics of macromolecules in this case compared with that for the ideal SEC. These perturbations are effectively equivalent to a slight increase in a pore size.[24] Consequently, all relationships of the ideal SEC remain valid for this case, including the dependence $\Delta G \sim M^{1/2}$ when $R_g \leq D$. The distribution coefficient K_D decreases with the molecular weight M, and for very large macromolecules (theoretically, infinitely long), becomes zero, although the effective exclusion limit is shifted to higher values of M, compared to that of the case $\varepsilon = 0$. The important feature of this mode is that for any macromolecule, the value of K_D increases with the pore diameter D, that is a macromolecule "prefers" to penetrate wider pores, and avoid residing in narrower ones.

The situation changes dramatically when the energetic gains due to the chain adsorption become comparable with the losses of its conformational entropy. In this so-called "critical region,"[24] the free energy change ΔG gets a linear function of molecular weight, and at some point $\varepsilon = \varepsilon_{cr}$, $\Delta G = 0$, as has been predicted by the phenomenological theory. As we have mentioned above, this critical value ε_{cr} is independent of both the molecular size R_g (i.e., molecular weight M of a macromolecule) and the pore size D. Because the partition coefficient K_D is equal to 1 for any values of M and D, the macromolecules of every size are distributed evenly throughout all sterically available pores and the interstitial volume of the packing material.

If the absolute value of the energy ε continues to increase beyond the critical value ε_{cr}, so that $|\varepsilon| > |\varepsilon_{cr}|$, the chromatographic system switches to the adsorption mode, where $\Delta G < 0$, $K_D > 1$ and the retention increases with the molecular weight (size) of macromolecules. The important consequence from the theory[24] is that for pores of two different sizes D_1 and D_2, the ratio of logarithms of corresponding distribution coefficients is inverse to the ratio of these diameters. By this is meant that in adsorption mode, the narrow pores are thermodynamically preferable to the wide ones. For example, a macromolecule rather penetrates the narrow pore than adsorbs on the outer surface of the particles. Another important theoretical result is the exponential growth of the distribution coefficient K_D with the size of macromolecules, which is the direct consequence from the free energy-molecular weight linear relationship in the adsorption mode. This means that large macromolecules are retained by the stationary phase practically infinitely long time. With further increase of absolute value of the energy of adsorption interactions $|\varepsilon|$, the lower molecular weight macromolecules also exhibit practically infinite retention.

Thus, the gradual change of interaction energy from $\varepsilon > \varepsilon_{cr}$ to $\varepsilon < \varepsilon_{cr}$ causes the transition of chromatographic behavior of a macromolecule from the size-exclusion mode with the distribution coefficient $K_{D,SEC} < 1$ to the adsorption mode with multiple adsorption interactions, where $K_D \rightarrow \infty$, and the macromolecule is literally trapped by the stationary phase. The molecular-statistical theory leads to a very important estimation of the width of this transition through the critical value ε_{cr} in the energetic scale:

$$\Delta\varepsilon / k_B T \approx D\, a / R_g^2 \sim M^{-1} \qquad (8)$$

Here the quantity a is the width of thin monomolecular surface layer, where the adsorption interaction occurs (approximately, the size of a monomer unit, which for an ideal flexible chain equals the statistical (or Kuhn) segment length l).

This estimation conveniently demonstrates very sharp transition in chromatographic performance of large macromolecules in narrow pore adsorbent ($R_g >> D$), from non-retained state to infinitely strong retained state. Practically, the transition occurs at the single point $\varepsilon = \varepsilon_{cr}$. In other words, depending on the sign of the dimensionless difference, $\tau = (\varepsilon_{cr} - \varepsilon)/ k_B T$, high-molecular weight macromolecules in narrow pores can exist either in non-adsorbed state ($\tau < 0$, the fraction of adsorbed segments $\theta \rightarrow 0$), or adsorbed state ($\tau > 0$, $\theta \sim \tau$). Obviously, such chromatographic behavior is specific to the polymer molecules and does not have an analogy in liquid chromatography of low molecular weight compounds. On the contrary, relatively small macromolecules in wide pores ($R_g < D$) do not exhibit such an abrupt difference in the chromatographic performance when the interactive energy passes the critical value ε_{cr}, as it can be seen from equation 8.

These theoretical findings are pictorially illustrated by the experimental data similar to those shown at Figure 1: very small changes in the mobile phase composition, which determines the interaction energy ε, cause the dramatic difference in retention times for macromolecules with molecular weights 10^4 and higher. At the same time, the retention of macromolecules with more moderate molecular weights is not so sensitive to these changes.

The foregoing results for long macromolecules in narrow pores have useful interpretation in terms of the theory of phase transitions.[70] Any infinitely long chain ($M \rightarrow \infty$) can be considered as a macroscopic system, susceptible to the transition between two equilibrium states, i.e., phase transition. In the case of macromolecules distributed in equilibrium outside and inside pores with attractive walls, the first order phase transition occurs at the point $\varepsilon = \varepsilon_{cr}$; that is both energy ΔE and entropy ΔS change abruptly at this point. According to Gorbunov and Skvortsov,[24] in the case $R_g >> D$, the phase transition is associated with the dramatic change in the probability of a macromolecule to penetrate the pore at the critical point: in non-absorbed state (phase) $\varepsilon > \varepsilon_{cr}$, and this probability is zero (macromolecules stay in the mobile phase), while in adsorbed phase ($\varepsilon < \varepsilon_{cr}$) it tends to 1. By contrast, in the case of wide pores, this probability changes gradually with ε, and the phase transition does not occur. The phase transition analogy is important for interpretation of IPC results obtained in the vicinity of CPA.

The theory predicts that in the case of large, but finite value of the ratio R_g^2/aD, the system (macromolecule) can exhibit random "macroscopic" fluctuations, when one or another phase can exist in so-called metastable state. We consider the chromatographic consequences of this contention in the section, devoted to the experimental verification of the theory.[62]

Although most of the preceding has been formally obtained for an ideal (Gaussian) polymer chain at theta conditions, all important for IPC results, including the existence of the CPA and sharp transition in the vicinity of this point for the case of narrow pores, are valid also for other models, such as semi-rigid macromolecules,[71] or chains with excluded volume interactions.[72,24]

More serious limitation of the foregoing theory is the assumption about the homogeneity of the adsorbing surface. It suggests that any contact between the polymer unit and the surface approaching each other within short distance *a*, involves the adsorption interaction with energy ε. But this uniform surface is seldom the case for the most of the packing material used in IPC, especially for the normal phase separation. Usually, the adsorption interaction occurs only when the functional group of a polymer unit approaches the corresponding group on the surface.

For example, the phenyl groups of polystyrene or the carbonyl groups of poly (methyl methacrylate) interact only with the silanol groups of the silica surface.[73] All other contacts between polymer segments and the surface of the adsorbent contribute only in a steric-like reflection interaction, making the surface impenetrable.

For this kind of contact, the interaction energy $\varepsilon = 0$. In other words, the surface of pores in IPC should be considered as a heterogeneous one, comprised of "inert" areas with usually randomly distributed attractive segments. In the succeeding section we demonstrate that the situation with the random surface closely parallels that in adsorption of statistical copolymers.

Statistical Copolymers Near Attractive Surfaces. The Existence of a Single Adsorption-Desorption Transition Point for Random Copolymers

Only a few published papers have been devoted to the problem of polymer adsorption on chemically heterogeneous (or random) surfaces from a dilute solution.[74-76] Several theoretical attempts have focused on adsorption of statistical copolymers on uniform[77-80] and random[81] surfaces. Let us show that these two situations (random surfaces and statistical copolymers) are reduced to a single theoretical problem.

Copolymer macromolecules have two or more different energies of interaction with any surface: ε_A for segments A, ε_B for segments B, etc. In the case of chemically random surface, we have at least two different interaction energies even for a homopolymer chain adsorbed on this surface: $\varepsilon_A < 0$ for active groups (i.e., silanol groups in the case of silica), and $\varepsilon_B = 0$ for all other available sites on the surface.

Thus, if one considers a conformation of a homopolymer chain interacting with a heterogeneous surface, the type A can be assigned for all monomer units interacting with the active groups and B for all other segments. Obviously, the other equilibrium conformations of the same chain have different distributions of A and B units. This means that instead of a homopolymer we have an effective statistical copolymer with the reversible rearrangement of the primary structure of its chains. The average composition of this artificially constructed copolymer and the correlation between positions of its effective monomer groups A and B along the chain depend on the concentration of active groups on the surface and the randomness of their distribution on it. It is reasonable to assume that random distribution of active groups at the surface produces the random distribution of units A and B along the chains. Thus, the heterogeneity of the surface effectively increases the number of types of active groups in the polymer chain interacting with this surface. In the following we will consider adsorption of statistical copolymers on attractive walls with homogeneous surface, keeping in mind that the same model also describes the adsorption on the chemically random surfaces.

There are two issues of fundamental importance for the IPC: whether a statistical copolymer has a CPA, and if this is the case, how this point depends on the primary structure of the copolymer chains and the adsorption energies of various monomer units (segments).

The first question is not obvious. For example, the block copolymers do not have a single CPA, while its individual components (e.g., blocks of type A) can have one at appropriate conditions.[24] On the other hand, a strictly alternating copolymer AB is obviously equivalent to a homopolymer and thus may have a single CPA. The answer to this question, at least for the case of random copolymers (statistical copolymers with Bernoulli statistics of segments), is

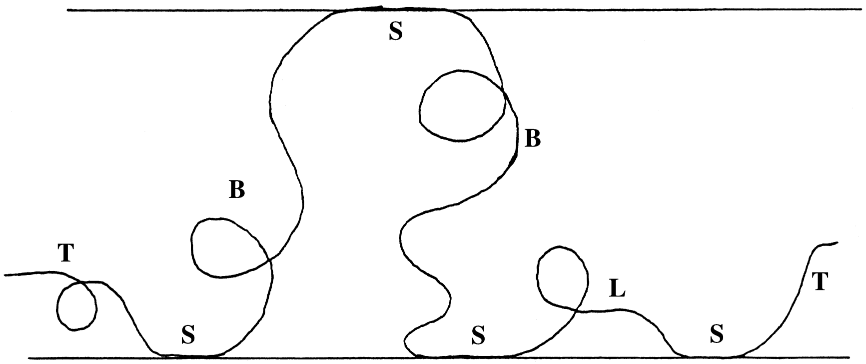

Figure 2. A schematic sketch of a polymer chain confined between two surfaces: T – tail, S – trail, B – bridge, L – loop.

evident from the work of Grosberg and Shakhnovich.[82] They used the renormalization group method[83] to analyze the coil-globule phase transition (collapse) of flexible random copolymer chains under the influence of external fields, which are different for the different types of units.

The mathematical problem was to find the solution to the dynamical renormalization equation for the Green function with non-commutative transition operators, which describes, in particular, the behavior of the random copolymer chain confined between two attractive surfaces. The fundamental result obtained was the renormalizability (or self-averaging[79]) of the system. It means that the random copolymer chains described by the Bernoulli statistics, behave as hypothetical homopolymer macromolecules with a single (effective) segment interaction energy ε_{eff}, which depends on the energies ε_A and ε_B of the individual units A and B and their relative amounts (probabilities) P(A) and P(B) in the copolymer. In particular, these chains have a single adsorption-desorption threshold, which coincides with the critical point for the corresponding homopolymer with $\varepsilon_{eff} = \varepsilon_{cr}$, where ε_{cr} is given, for example, by equation (7).

Let us provide some details concerning this result for random copolymers. Any polymer chain confined between two flat solid surfaces consists of loops (sequences of polymer segments whose ends are in contact with one plate and whose intermediate units do not touch the surfaces), bridges (the sequences of polymer units whose ends are in contact with different surfaces and whose intermediate segments lie between these surfaces without any contacts with them), trains (uninterrupted sequences of adsorbed units separated from each other by loops or bridges) and tails (the end pieces of the chain attached to the surface by one end only and dangling in free space) (Figure 2).

The bridges are lacking if the adsorption takes place at a single surface. The chain is in the adsorbed state if the trains comprise a finite portion of its units.

In coil-globule phase transition analogy, the adsorbed state corresponds to the globular state of the macromolecule with trains corresponding to a globular core, and bridges, loops and tails – to the fringes of the globule, i.e., to segments of the free (coil-like) chain, located in a large volume outside the external field region.[82]

The fundamental result derived many years ago[59] for the case of adsorption of a homopolymer is the statistical independence of different trains along the chain, which allows one to calculate the statistical weight of each macromolecular conformation (a microscopic state) as a product of statistical weights of individual segments.[84] This statistical independence is apparent from the property of coil-like fringes of the globule (loops and bridges), viz. their self-averaging nature,[82] which eliminates any correlations between neighboring trains, while an unstable dynamic behavior caused by non-commutation of transition operators takes place only for the globule core (trains). The direct consequence from this is the existence of the transition point (phase transition) between two different macroscopic states (thermodynamic phases) of macromolecules: coil-like state (solution) and globular-like state (adsorption).[67,69] In the case of random copolymer, the configurational statistics (the distribution of copolymer units along the chain) does not create any additional correlations (by the definition of the Bernoulli statistics), and the fundamental property of the statistical independence of the trains along the chain still stands.

A similar conclusion was made [74,76] for the case of homopolymer adsorption on chemically random surfaces. It was shown that the system had a single transition point and the transition temperature (which is equivalent to the effective segment energy ε_{eff}) is depressed by the amount proportional to the fraction of non-attractive sites on the surface.

The detailed analysis of adsorption-desorption phase transition in random A-B copolymer chains confined between two attractive solid surfaces or located near one plate, is presented by Gutman and Cakraborty.[79] Their consideration is based on the statistical field theoretical formulation of the propagator for the problem of interest. But unlike Grosberg and Shakhnovich, they employ a so-called replica trick to alleviate analytical difficulties which arise when considering averaging over the sequence distribution of A and B segments. This technique first has been applied to the spin glass theory[85] and now is very popular among polymer statistics scientists.[81] Gutman and Cakraborty extended the consideration of the conformational organization of polymers to include the potentials of the interaction forces between the different segments and surface with arbitrary different strength ε_A and ε_B, as well as the length scales.

The additional variables were the statistical segment length *l* (stiffness) of the chain and intersegment repulsion (excluded volume) interaction. The effect of all these parameters on the adsorption-desorption phase diagram was evaluated via an analytical route, as well as numerically.

Gutman and Cakraborty have confirmed the fundamental conclusion that any random copolymer has a single adsorption-desorption threshold and behaves near this threshold as a homopolymer with a single effective interactive energy ε_{eff}. The relative values of the potential length scales of the A and B segments mainly influence the conformational statistics of macromolecules far from the surface, while their strength determines the segment density profile in the interfacial region and hence has much more profound effect on the position of adsorption-desorption threshold.[79] An increase in the chain stiffness *l* shifts the position of the transition to the lower values of the adsorption segment-surface interaction energy, since stiff chains adsorb more strongly.[79] Interesting finding is the effect of excluded volume interaction. While this intersegment repulsion in a macromolecule repels it away from the surface and switches the adsorption-desorption threshold to higher values of the attractive energy necessary for this transition, the transition itself becomes sharper. Thus, this transition for the long polymer chain near a single attractive surface is a second-order phase transition at the theta-point, while in the case where excluded volume interaction prevails, the same transition is first-order.[79] This result is important for IPC, where the separation usually occurs in good solvents.

Statistical Copolymers Near Attractive Surfaces. The Case of Non-Random Statistics

As noted above, the continuous representation of the polymer chains is inconvenient to analyze the effects of chain structural details (microstructure). Probably for this reason Gutman and Cakraborty restricted the quantitative analysis to the simplest case of ideal random (Bernoulli) copolymers, although their initial intention was to consider more general model of random block copolymers.[86] This last model allows the chemical correlations between the monomer units along the chain through the length of the blocks (for the Bernoulli statistics any correlations of this kind are nil).

Nevertheless, one very important result involving the global (large-scale) conformational characteristics of macromolecules with non-random statistics follows immediately from the continuous approach. It provides necessary conditions for an existence of a single adsorption-desorption threshold for any non-random copolymer confined between two attractive solid surfaces (i.e., inside a slit-like pore). This result extends the fundamental property of random copolymers, when chains with different segment-surface interaction energies ε_A and ε_B are effectively equivalent to a homopolymer with a single interaction energy ε_{eff}, to non-random statistical copolymers.

As we have mentioned in the previous section, the necessary condition for the existence of transition point is the statistical independence of the adsorbed segments (trains) along the chain. In the cases of homopolymers and random copolymers, this independence is accomplished due to the free-coil segments (loops and bridges) that alternate with the trains. The non-random copolymer produces additional, "chemical" correlations caused by non-random distributions of the monomer units of different types along the chain. These correlations can disturb this independence if the corresponding scale (correlation length measured in number of monomer units) exceeds the length of loops and bridges (measured in the same units).

In other words, the statistical independence of trains requires attenuation of chemical correlations along the chain at the length much shorter than the average size of loops and bridges.

In the region close to the phase transition, the length of loops is comparable to that of entire chain,[59,69] while the bridges are restricted by the distance D between the surfaces (the pore diameter). It means that the relationship between the size of bridges and chemical correlation length only matters as soon as the length of chain exceeds the chemical correlation length. If these correlations attenuate at the distance much shorter than the mean length of the bridges, these latter have approximately identical chemical composition and microstructure, i.e., they are statistically equivalent (similar). Thus, the necessary condition can be stated qualitatively as follows: any long enough copolymer chain has a single adsorption-desorption transition point if the bridges are statistically equivalent.

In other words, the copolymer chain should be statistically homogeneous and bridges should be long enough to represent statistically the entire macromolecule. In a like manner, the entire copolymer sample has the single transition point if it is comprised of statistically similar macromolecules.

In what follows we formulate this result quantitatively using general statistical description of copolymer chains developed previously.[87] Thereafter we use the generating (partition) function method to determine the dependence of the effective interaction energy $\varepsilon_{\mathrm{eff}}$ on the chemical structure of random and non-random statistical copolymer chains.

The microstructure of any statistical copolymer can be described by the probabilities (molar fractions) P(U) of arbitrary sequences U of monomer units A and B in the chains. For example, P(A) and P(B) represent the probabilities of single units (monads) A and B (i.e., the average chemical composition of copolymer), and P(A) + P(B) = 1. The quantities P(AA), P(AB), P(BB) are the probabilities of diads AA, AB, and BB respectively, which characterizes the microstructure of copolymer, P(AA)+ 2 P(AB)+ P(BB) = 1, etc.

The sequence U may also include units located at non-adjacent positions of the chain. Thus, (AX^nA) $(n\geq 0)$ denotes an arbitrary sequence of the length n+2 flanked by the A units. For Bernoulli statistics the probabilities $P(AX^nA)$ do not depend on n, and so-called covariances[87,88]

$$\omega_n\,(A,A) = P(AX^nA) - P^2(A) \tag{9}$$

equal to 0 for any $n \geq 0$. For any other statistics these quantities differ from 0. For example, copolymers described by Markoff statistics[88] with transition probabilities $\nu_{AB} = P(AB)\,/\,P(A)$ and $\nu_{BA} = P(BA)\,/\,P(B)$, have[87]

$$\omega_n\,(A,A) = P(A)\,P(B)\,(1 - \nu_{AB} - \nu_{BA})^{n+1} \tag{10}$$

Recall that two independent parameters ν_{AB} and ν_{BA} completely describe the Markoff chain of first order.[88] For example, other transition probabilities can be calculated from the equations: $\nu_{AA} = P(AA)\,/\,P(A) = 1 - \nu_{AB}$, $\nu_{BB} = P(BB)\,/\,P(B) = 1 - \nu_{BA}$; $P(A) = \nu_{BA}\,/\,(\nu_{AB} + \nu_{BA})$.

Random copolymer is the specific case of Markoff statistics when $\nu_{AB} + \nu_{BA} = 1$, and, consequently, $\omega_n = 0$. The condition $\nu_{AB} + \nu_{BA} < 1$ means the tendency to the blockiness, while $\nu_{AB} + \nu_{BA} > 1$ reflects the more alternating microstructure of macromolecules compare with that of random chains. In the general case of Markoff statistics the sum $\nu_{AB} + \nu_{BA}$ (which is called heterogeneity index[87]) lies between two extreme cases: 0 for the blend of two homopolymers A and B, and 2 for strictly alternating copolymer AB, which formally can be considered as a homopolymer comprised from the monomer AB. The Markoff statistics describes the products of stepwise (condensation) copolymerization or addition copolymerization at low conversion of comonomers.[87]

In many cases, the correlations between the units along a chain of a statistical copolymer are damped out with n. It means that the absolute values $|\omega_n|$ become negligibly small when n exceeds some characteristic value n*. For instance, as can be seen from equation (10), the covariances decrease exponentially with n for Markoff copolymers, and the characteristic scale of this attenuation is given by equation

$$n^* = -\ln^{-1}|1 - \nu_{AB} - \nu_{BA}|. \tag{11}$$

The quantity n* determines the minimal portion of the chain statistically independent of other segments and can be called a “chemical correlation segment.” (The equivalent definition in conformation statistics of polymers is the Kuhn segment). The relative frequencies of individual monomer units A and B or any short continuous sequence U of these units (e.g., diads AA) encountered for this segment of length n* approach the respective probabilities P(U) for entire chain (the law of large numbers in the theory of stochastic processes[88]). If the copolymer has the tendency to the blockiness, the magnitude of n* is usually several times the biggest between mean lengths of the A or B blocks. Analogously, for alternating structures the value n* exceeds the mean length of alternating ABAB…. blocks.

In other words, any segment of length n* or higher represents statistically the microstructure of entire macromolecule. If the degree of polymerization L of the copolymer significantly exceeds its chemical correlation segment ($L >>$ n*), all macromolecules of this copolymer have closely related chemical composition and structure. For example, the CCD of such statistical copolymers is very narrow and described by normal law[87]

$$f(\xi) = (2\pi\sigma^2_L/L)^{-1/2} \exp\left[-L(\xi - <\xi>)^2/2\sigma^2_L\right] \qquad (12)$$

with the center $<\xi> = P(A)$ and variance σ^2_L/L. Here $f(\xi)$ is the molar fraction of macromolecules with fraction ξ of units A, $<\xi>$ is the average chemical composition of the copolymer. The parameter σ^2_L is given by equation

$$\sigma^2_L = P(A)\,P(B) + 2\sum_{n=0}^{L}\omega_n \qquad (13)$$

and practically does not depend on L for $L >>$ n* ($\sigma^2_L = \sigma^2_\infty$). The covariances ω_n are defined by equation (9) in general case of arbitrary copolymer chains or by equation (10) for Markoff chains. Since the variance of the distribution (12) tends to zero when $L \rightarrow \infty$, the differences in chemical composition (and microstructure) of macromolecules becomes negligibly small for $L >>$ n*.

This means that all macromolecules of the copolymer sample are statistically similar as soon as their length exceeds the chemical correlation segment.

We designated previously[87] the statistical copolymers described by equations (12) and (13) as ergodic copolymers, because the corresponding probabilities P(U) possess so called ergodic property.[88] All macromolecules of an ergodic copolymer have the same finite chemical correlation segment n*, and this copolymer compositionally and structurally homogeneous as soon as $L >>$ n*.

The necessary condition for the ergodicity of the statistical copolymer is the convergence of the series in the right side of equation (13), when $L \rightarrow \infty$. This means that the sequence $|\omega_n|$ should tend to zero faster than n^{-1}. This is valid, say, for Markoff copolymers or the products of some reactions of homopolymers with low molecular weight compounds, which do not conform to the Markoff statistics.[87]

Not all statistical copolymers are ergodic. Thus, the products of free-radical copolymerization at high conversion of monomers are devoid of ergodicity, and we call them non-ergodic.[87] It happens because the chemical composition and microstructure of each individual macromolecule depend on the monomer feed, which changes with the conversion of monomers. But each individual fraction of this copolymer generated at specific conversion of monomers represents the ergodic fraction referred to as an ergodic class.[87] Non-ergodic copolymers are comprised of ergodic fractions (or ergodic classes). Different classes of a non-ergodic copolymer usually have different chemical compositions, and such copolymer usually exhibits high composition heterogeneity (broad CCD), which does not depend on the degree of polymerization L.

Many block-copolymers are non-ergodic ones and have broad CCD. The blend of two homopolymers A and B can be considered as an extreme example of non-ergodic block-copolymer with two ergodic classes − homopolymers A and B. Another example is the mixture of two or more random copolymers with distinct chemical compositions.

Now we can formulate the condition when the non-random statistical copolymer confined between two attractive surfaces has a single transition adsorption-desorption point. First of all, the copolymer should be ergodic, e.g., possess the finite chemical correlation segment $n^* << L$. This is sufficient condition in the case of a single surface, or $L \leq D$.

If the chain length L significantly exceeds the distance D between walls (the diameter of slit-like pore), the number of monomer units in the bridges should also exceed the correlation segment n*, i.e., the biggest among the mean length of A-, B- and AB-blocks, respectively. In other words, the bridges between walls should be statistically similar to each other in the composition and microstructure. Thus, for a flexible macromolecule with the statistical Kuhn segment l, the average length of the bridge is D^2 / l, and the condition for a single transition point is $n^* << D^2 / la$, where a is the effective size of monomer units. This condition is necessary and sufficient for the ergodic copolymer to have a single transition point.

As we have mentioned above, the adsorption-desorption transition point for homopolymer chains near attractive surfaces corresponds to the CPA in isocratic chromatography of these polymers. The existence of the transition threshold for the ergodic statistical copolymers leads to the existence of the critical mobile phase composition, i.e., the CPA, for these copolymers also. This means that the retention of the copolymer at this point in isocratic mode is molecular weight independent.

In the case of non-ergodic copolymers, e.g., polymer blends, each of its ergodic fractions has its own CPA, which depends on the chemical composition and microstructure of macromolecules comprising the corresponding fraction.

This feature opens an opportunity of gradient separation of non-ergodic copolymers according to the chemical structure of their macromolecules, which is the subject of the following paper.[62]

Let us consider the ergodic copolymer with the blocks of at least one type exceeding in size the pore diameter D. In this case the chemical correlation segment n* exceeds the average size of bridges and a single transition point for the copolymer does not exist.

The chromatographic consequence of this situation was analyzed theoretically by Skvortsov and Gorbunov[22] for the case of multi-block AB copolymers in slit-like pores. They showed that if the size of inner blocks of one type, say, A-blocks, exceeds the pore diameter D, and the mobile phase composition corresponds to the CPA for the homopolymer A, the block-copolymer behaves chromatographically as a polymer comprised of B-blocks only and isocratic retention depends on their distribution along the chain. Similarly, if the size of blocks B exceeds D, we have the situation, when retention depends on A-block only at the CPA of the homopolymer B. Thus, the copolymer behaves as though it has two partial transition points, where the specific portion of the chain does not affect its retention. Note that both of these points are not the true adsorption-desorption transitions for the whole copolymer, and the retention at any one of them depends on molecular weight of the block-copolymer.

In a like manner, the statistical copolymers exhibiting sequencing (alternating) character can be considered. The correlation segment n* increases with the mean length of alternating blocks (see, as an example, equation (11) for Markoff copolymers when the sum $\nu_{AB} + \nu_{BA}$ is close to 2). This happens because the probabilities (and frequencies) of any segments with non-alternating fragments, i.e. diads AA or BB, decrease with the tendency to alternation, and the longer sequences of units are needed to gain the necessary statistics for the corresponding segments according to the law of large numbers. If the mean length of alternating blocks AB (or n*) exceeds the size of the bridges between pore walls, the chromatographic behavior of the copolymer changes abruptly at the CPA of the strictly alternating copolymer AB. The retention does not depend on the length of alternating blocks AB in this point and is affected by small non-alternating fragments like the diads AA and BB.

Note again, that this is not a true adsorption-desorption threshold since the retention depends, among other things, on the amount of alternating blocks in a macromolecule. We call these points as partial critical points of adsorption. Note that the isocratic elution at partial CPA is proved to be an excellent tool in chromatographic separation of block-copolymers.[7-9,18,19] We suggest that the separation of statistical copolymers with the tendency to sequencing at the corresponding partial CPA (i.e., at the CPA of strictly alternating copolymer AB) can also help in elucidating the microstructure of these macromolecules.

Statistical Copolymers Near Attractive Surfaces. The Dependence of Transition Point on Chemical Composition and Microstructure

The fundamental result concerning a prerequisite to the existence of a single adsorption-desorption threshold stated in the previous section provides the theoretical ground for the calculation of the critical point of the ergodic statistical copolymers with arbitrary microstructure. This result allows one to extend the use of self-consistent field models and well established in statistical mechanics computational techniques to this kind of polymers.

There are several techniques in statistical mechanics of polymers available to perform this kind of calculations. We prefer the generating function (or grand ensemble) technique,[67,69,84] which has certain advantages compare with the direct combinatorial enumeration[89] or transfer matrix methods.[26,59,71] In what follows we derive general analytical expressions which allow one to estimate quantitatively the effect of chain microstructure on the position of the critical point for statistical copolymers without regard to any specific lattice model of the polymer chains.

Consider the grand ensemble of adsorbed macromolecules, i.e., the ensemble of these macromolecules of every degree of polymerization *L*. Define the grand partition function of this ensemble as $\Xi_{ab}(\lambda)$. This is the generating function for the canonical partition function $Z_{ab}(L)$ of a chain with a fixed number *L* of monomer units[67]:

$$\Xi_{ab}(\lambda) = \sum_{L=1}^{\infty} Z_{ab}(L)\,\lambda^{-L} \tag{14}$$

In a similar manner trails, loops, bridges, and tails have their grand partition functions $\Xi_S(\lambda)$, $\Xi_L(\lambda)$, $\Xi_B(\lambda)$ and $\Xi_T(\lambda)$, respectively. The statistical independence of trains along the chain allows one to calculate $\Xi_{ab}(\lambda)$ by summation over all possible numbers of the trails separated by loops or bridges and flanked by the tails.[84] This leads to well known equation[69]:

$$\Xi_{ab}(\lambda) = \frac{2[\Xi_T(\lambda)]^2\ \Xi_S(\lambda)}{1 - \Xi_S(\lambda)\,[\,\Xi_L(\lambda) + \Xi_B(\lambda)]} \tag{15}$$

At critical point $\varepsilon = \varepsilon_{cr}$ the function $\Xi_{ab}(\lambda)$ diverges when λ equals to the conformational partition function of the monomer unit in the non-adsorbed state, z_0, i.e., $\Xi_S(z_0)[\Xi_L(z_0) + \Xi_B(z_0)] = 1$.[69]

On the other hand, $\Xi_L(z_0) + \Xi_B(z_0) = 1$ if the adsorption takes place at the surface, which at least in one dimension has the size comparable or larger than the size of the macromolecule.[67] Obviously, this condition is true for walls of any typical pores.

Thus, the general equation for the adsorption-desorption transition point has the form:

$$\Xi_S (z_0) = \sum_{L=1}^{\infty} [Z_S (\varepsilon_{cr}, L)\, z_0^{-L}] = 1, \tag{16}$$

where $Z_S (\varepsilon_{cr}, L)$ is the canonical function of the trail with L adsorbed units, i.e., its weight factor, at the critical point $\varepsilon = \varepsilon_{cr}$. For homopolymer chains

$$Z_S (\varepsilon, L) = z^{L-1} z' \exp (-\varepsilon L / k_B T) \tag{17}$$

where z is the conformational partition function of a monomer unit lying on the surface, z' is that of the monomer starting off the surface. Substituting this expression (17) at $\varepsilon = \varepsilon_{cr}$ into equation 16 gives[67]:

$$X_{cr} = \exp (-\varepsilon_{cr} / k_B T) = z_0 / (z + z') \tag{18}$$

For the lattice model $z' = (z_0 - z) / 2$, and equation (18) reduces to equation (7).

Now consider the case of statistical copolymers. The existence of the critical point for these polymers means that the transition occurs as soon as the effective segment interaction energy ε_{eff} reaches its critical value ε_{cr} given by equations (16), (18) or (7). Let us find the dependence of the effective energy ε_{eff} on the copolymer chemical composition and microstructure.

Consider again the binary ergodic copolymer with the interaction energies ε_A for segments A and ε_B for segments B. To describe the chain microstructure, we introduce two Ising-like random variables $\xi^A(i)$ and $\xi^B(i)$ for any sequence U of units at the chain: $\xi^A(i) = 1$ if the ith position in the sequence U is occupied by the A-unit, and $\xi^A(i) = 0$ otherwise.

The same manner $\xi^B(i)$ is defined by replacing A with B, so that $\xi^A(i) + \xi^B(i) = 1$. Due to the ergodicity of the copolymer, these functions do not depend on the position of the sequence U on the chain.

Consider a randomly selected trail of L adsorbed segments and assume (for simplicity) that the units A and B have the same conformational partition function z and differ only in the interaction energies ε_A and ε_B (any differences in conformational partition functions can be formally included in the segment energies ε_A and ε_B). Then the weight factor for this trail has the form:

$$Z_S (\varepsilon_A, \varepsilon_B, L) = z^{L-1} z' \prod_{i=1}^{L} [\xi^A(i) X_A + \xi^B(i) X_B] \tag{19}$$

$$X_A = \exp (-\varepsilon_A / k_B T), \quad X_B = \exp (-\varepsilon_B / k_B T)$$

The canonical partition function $\langle Z_S(\varepsilon_A, \varepsilon_B, L)\rangle$ for all trails of length L can be obtained from equation (19) by averaging $Z_S(\varepsilon_A, \varepsilon_B, L)$ over all possible sequences of units A and B. The details of this procedure one can find elsewhere.[87] The result of this averaging for an arbitrary binary ergodic copolymer can be written in the form:

$$\langle Z_S(\varepsilon_A, \varepsilon_B, L)\rangle = z^{L-1} z' \, W(L),$$

$$W(L) = \sum_{i,j=0}^{L} \{X_A^{\,i} X_B^{\,j} \sum_{i_k, j_k} P[A^{i1} B^{j1} A^{i2} B^{j2} \ldots A^{in} B^{jn}]\} \tag{20}$$

where the internal summation is over all non-negative integers i_k and j_k such as $i_1 + i_2 + \ldots + i_n = i$; $j_1 + j_2 + \ldots + j_n = j$.

The effective interaction energy ε_{eff} is obtained from equation

$$\langle Z_S(\varepsilon_A, \varepsilon_B, L)\rangle = Z_S(\varepsilon_{eff}, L) \,, \tag{21}$$

where $Z_S(\varepsilon_{eff}, L)$ is given by the right side of equation (17) at $\varepsilon = \varepsilon_{eff}$. The expression (20) at $L >> 1$ reduces to $W(L) = X_{eff}^{\,L}$ for any ergodic copolymer, so that finally

$$\exp(-\varepsilon_{eff} / k_B T) = X_{eff} \,, \tag{22}$$

where X_{eff} depends on microstructure of ergodic copolymer.

Thus, for the Bernoulli (random) copolymer

$$X_{eff} = X_{random} = P(A) X_A + P(B) X_B \tag{23}$$

Note that the same equations (22) and (23) at $X_B = 1$ ($\varepsilon_B = 0$) describe the adsorption of homopolymer with segment interaction energy $\varepsilon = \varepsilon_A$ on a random surface with the relative density of active groups P(A).

For more general case of Markoff copolymers X_{eff} is the root of equation

$$2X_{eff} = \nu_{AA} X_A + \nu_{BB} X_B + [(\nu_{AA} X_A - \nu_{BB} X_B)^2 + 4 X_A X_B \nu_{AB} \nu_{BA}]^{1/2}, \tag{24}$$

where ν_{AA}, ν_{BB}, ν_{AB} and ν_{BA} are the Markoff transition probabilities as before. This equation can be expressed also in the form

$$X_{eff}^{\,2} + X_A X_B (1 - \nu_{AB} - \nu_{BA}) = X_{eff} [X_A + X_B - (\nu_{AB} + \nu_{BA})(X_A P(B) + X_B P(A))] \tag{25}$$

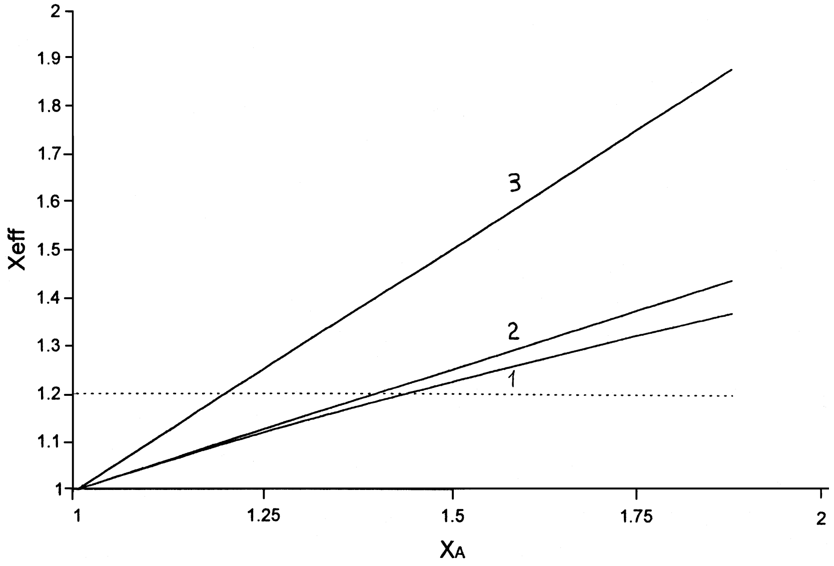

Figure 3. Effective segment energy as a function of the interaction energy of active groups. A for three types of copolymers: (1) – alternating, (2) – random, (3) – multi-block. For all cases, P(A) = P(B) =1/2, $\varepsilon_B = 0$. The dotted line is the critical threshold ($X_{eff} = 1.2$) for the cubic lattice.

which allows one to distinguish between the effects of chemical composition P(A) and microstructure $\nu_{AB} + \nu_{BA}$, respectively. The random statistics (23) results from equation (25) when $\nu_{AB} + \nu_{BA} = 1$. The two extreme cases of alternating and multi-block copolymers can also be easily obtained from this equation (25). Thus, for almost alternating copolymer $\nu_{AB} + \nu_{BA} \rightarrow 1$, P(A) =1/2 and from equation (25) we have $X_{eff} = X_{alt} = (X_A X_B)^{1/2}$, i.e., $\varepsilon_{eff} = (\varepsilon_A + \varepsilon_B)/2$. For multi-block copolymer, when the length of both A- and B-blocks significantly exceeds 1, $\nu_{AB} + \nu_{BA} \rightarrow 0$, and then $X_{eff} = X_{block} = \frac{1}{2}(X_A + X_B + |X_A - X_B|)$. Thus, the value of X_{block} equals to the greater value between X_A and X_B. This means that $\varepsilon_{eff} = \varepsilon_A$, if $|\varepsilon_A| > |\varepsilon_B|$, and $\varepsilon_{eff} = \varepsilon_B$ otherwise.

Figure 3 represents the comparison of the effective interaction energies ε_{eff} (or X_{eff}) calculated from equation (25) for three equimolar (P(A) = ½) copolymers with different microstructures and only one type A of the active groups ($\varepsilon_A < 0$, $\varepsilon_B = 0$). One can see that the alternating copolymer needs higher interaction energy $|\varepsilon_A|$ to achieve the transition into adsorbed state compare with the random or multi-block copolymers of the same chemical composition.

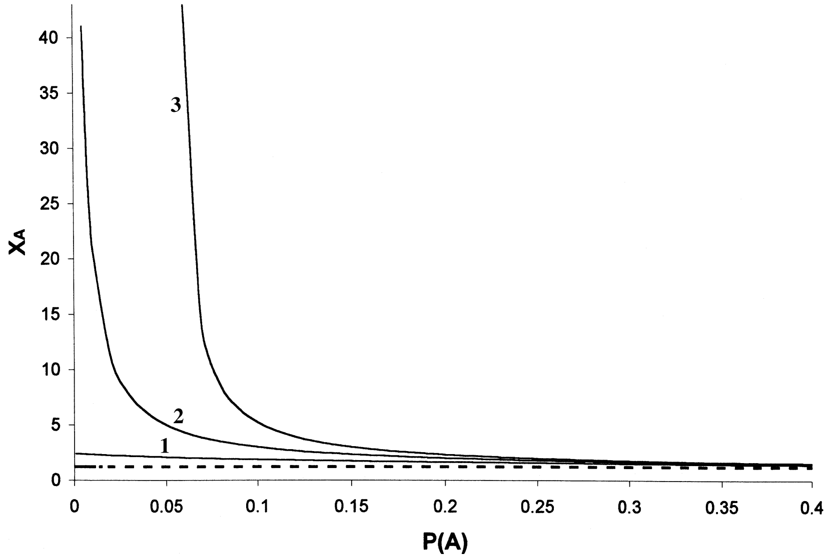

Figure 4. Dependence of the interaction energy of active groups A at the critical point $X_{ff} = X_{cr} = 1.2$ for the cubic lattice on the chemical composition of the Markoff copolymer with the inert B-group ($X_B = 1$), calculated from Eq.25 for the heterogeneity index $\nu_{AB} + \nu_{BA} = 0.5$ (1), 1 (2) and 1.5 (3). Dotted line represents the asymptotic value $X_A = 1.2$, which describes the homopolymer A (P(A) =1).

In other words, sequencing suppresses the ability for a macromolecule to the adsorption. Substituting the critical value $X_{eff} = X_{cr}$ from equation (7) into equations (24) or (25), one can analyze the effect of chemical composition (Figure 4) and microstructure (Figure 5) on the segment interaction energies of different monomer units at the threshold point, calculated for different lattice models.

Both Figures 4 and 5 demonstrate how the increase in the sequence heterogeneity affects the interaction energy of monomer units at the critical point. It can be seen that this influence is much more pronounced when the relative amount of the active units A decreases. In this region the effect of chemical composition becomes also very significant except for copolymers with the tendency to blockiness.

Recall that all these results refer only to the copolymers with chemical correlation segment n* << *L* (ergodic copolymers), i.e., chemically homogeneous copolymers with the mean length of blocks of all types (A, B, or AB) significantly less than the degree of polymerization *L*.

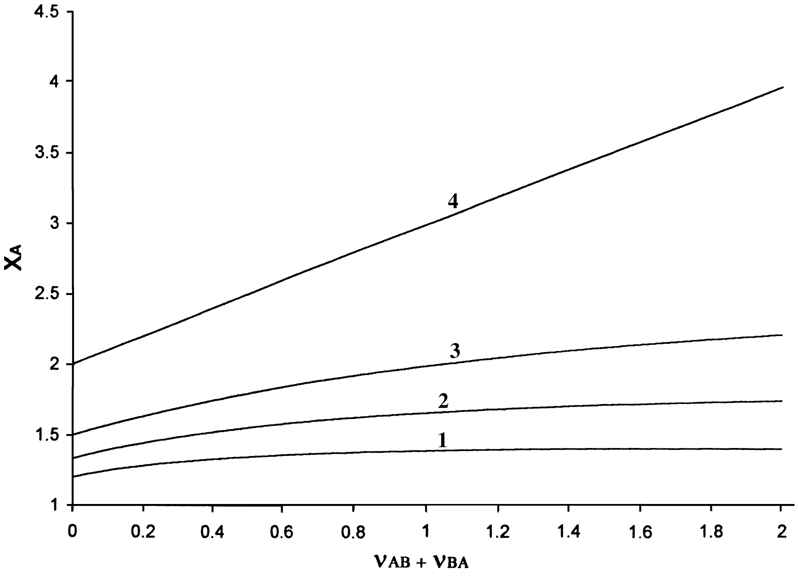

Figure 5. Dependence of the interaction energy of active groups A at the critical point $X_{eff} = X_{cr}$ on the heterogeneity index $\nu_{AB} + \nu_{BA}$ for equimolar Markoff copolymer (P(A) = ½) with the inert B-groups ($X_B = 1$), calculated from Eq.25 for cubic(1), hexagonal (2), face-centered (3) and body-centered (4) lattices.

If all these blocks are also exceeded in length by the bridges, the ergodic statistical copolymer has the single adsorption-desorption transition point, which is described by equations (22) – (25). Otherwise, this copolymer can have only partial thresholds, corresponding to the individual blocks of a specific type.

The foregoing theory developed for binary statistical copolymers can be easily extended to the case of multicomponent copolymers containing $m \geq 3$ types of monomer units A_i ($i = 1,2,\ldots,m$) with segment interaction energies ε_i.

Thus, the ergodicity of the copolymer is determined by the covariances[87,88]

$$\omega_n(A_i,A_j) = P(A_iX^nA_j) - P(A_i)P(A_j), \quad i,j \leq m \qquad (26)$$

which should tend to zero faster than n^{-1} for ergodic copolymers.[88] The CCD of ergodic multicomponent copolymers is described by the multidimensional Gaussian distribution (normal law).[87] The technical details about the statistical treatment of these copolymers can be found in the review.[87]

In the same way as in the case of binary copolymer, an ergodic multicomponent copolymer has a single adsorption-desorption threshold, if the average length of any of its blocks, including blocks of alternating units, is much less than the average length of bridges. In this case, the multicomponent copolymer is equivalent to some homopolymer with effective energy (22). For Markoff copolymers, the effective energy ε_{eff} (or X_{eff}) can be described in terms of corresponding transition probabilities $\nu_{ij} = P(A_iA_j)/ P(A_i)$ and X_i $(i,j \le m)$. We herein exemplify the case of multicomponent Bernoulli copolymers:

$$X_{eff} = X_{random} = \sum_{i=1}^{m} [P(A_i)\, X_i], \quad X_i = \exp(-\varepsilon_i / k_BT) \tag{27}$$

This equation also describes the adsorption of homo- or copolymers on the random surface, which has two or more different types of active groups. Note that each pair of the functional groups (one − from the surface, another − from the macromolecule) generates the corresponding interaction energy ε_i.

The effects of chain stiffness and excluded volume interaction should not change the preceding relationships between the effective interaction energy and chemical composition and microstructure of copolymers. The specific effects of local parking of monomer units near the surface may be of importance. A comprehensive description of these effects concerns a general problem of polymer globular state, when the concentration of chain units is high. One of the possible approaches to this problem is the representation of reference (ideal) state of a polymer chain as a chain of tangent hard spheres with a proper volume. This approach allows one to take into account the short-range (parking) effects. Different monomers can have different volumes, and if this difference is significant, the relationships found above can be affected. The quantitative description of such systems can be performed by the method developed previously.[90] This approach employs the approximation of disconnected monomer units for consideration of weak attractive interactions of any kind, including the interactions between monomer units and the solid surface.

CONCLUSIONS

The retention of macromolecules in IPC is a complex physicochemical process, which involves both steric and adsorption interactions between macromolecules and a stationary phase, as well as conformational transformations inside macromolecules attendant on their transitions from the solvated state into adsorbed state and back into solution. A fundamental understanding of this mechanism is possible only on the basis of contemporary molecular-statistical theory of polymer solutions. This theory has already helped to establish a novel mode of polymer chromatography: separation at CPA, which finds use in characterization of functional oligomers and block-copolymers.

In the present paper we have extended the concept of elution at CPA to the cases of statistical copolymers as well as of stationary phases with heterogeneous surface (which in actuality is inherent in most if not all of available sorbents).

The fundamental result obtained is the condition when the statistical copolymer with narrow CCD has a single adsorption-desorption threshold. This occurs if for any macromolecule inside a pore the segments of units connecting the opposite walls of this pore significantly exceed the average length of all blocks A, B, AB, etc., in the copolymer chain.

This is obviously true for random copolymers. The copolymer microstructure affects the position of adsorption-desorption transition. We analyzed this dependence by the example of Markoff copolymers, which can represent different types of non-randomness in the copolymer structure. The partial transition points have been established for copolymers with blocky or alternating microstructure.

The existence of the adsorption-desorption threshold leads to the existence of the critical mobile phase composition (CPA) at isocratic elution of such copolymers.

This opens an exciting opportunity for gradient separation of statistical copolymers with broad CCDs at critical eluent compositions corresponding to the chemical compositions of individual fractions.

The theoretical and experimental justification of this finding is presented in the following paper.[62]

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