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Conformation of Polymer Brushes at Aqueous Surfaces Determined with X-ray and Neutron Reflectometry. 1. Novel Data Evaluation Procedure for Polymers at Interfaces

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ABSTRACT: We present a new data refinement technique for the evaluation of X-ray and neutron reflectometry measurements of interface layers comprising linear molecules. The new method is particularly well-suited—but not limited to—modeling the structure of surface-grafted linear polymers organized in "polymer brushes". In this paper, we discuss technical details of the data inversion technique and demonstrate its capabilities by recovering the structure of a simulated molecular ensemble for which synthetic data sets have been constructed. In the following paper, we utilize this machinery to reveal the nature of a phase transition pertinent to surface-anchored lipopolymers at high molecular densities.

1. Introduction

Polymers are widely used to vary the physicochemical properties of interfaces in a controlled way. Chemical synthesis, theory, and experimental characterization collaborate closely to comprehend the effects due to polymer association with interfaces on the molecular level. One prominent example for an application is the stabilization of liposomes, used as drug carriers, where grafted polymers are employed to extend the circulation time in the bloodstream considerably.[1] Other similarly important examples in materials and life sciences include the grafting of polymers at solid-state interfaces, the compatibilization of polymer/polymer interfaces, or the association of DNA with model membranes for transfection processes in gene therapy.

The conformational and phase behavior of lipopolymers—amphiphilic molecules with one hydrophobic end to which a hydrophilic polymer is attached—organized in aqueous surface monolayers has recently received considerable attention.[2−6] The preparation of such monolayers in a Langmuir film balance facilitates control of the molecular surface density, the temperature of the adjacent aqueous subphase, and its chemical composition (ionic strength, pH, etc.). In other words, such an experiment enables the control of many environmental parameters that affect directly the organization of the surface-associated polymer on the molecular level.

In correspondence, powerful experimental characterization methods have been recently developed that probe the molecular organization of macromolecular interface films, such as surface-sensitive scattering[7] and spectroscopic[8] techniques. While such techniques have primarily been used to determine the molecular organization of alkyl chains in molecular films, the investigation of hydrophilic polymers immersed into the aqueous subphase calls for the extension of the established concepts.

In two closely related papers, we develop a novel inversion method for reflectometry data which we subsequently use to investigate the molecular organization of lipopolymer brushes at the air/water interface using X-ray and neutron reflectometry. In particular, we are interested in the nature of a phase transition that occurs in lipopolymer monolayers at high surface density. This is extensively discussed in the subsequent contribution which is a paper in its own right.

If one uses scattering techniques to determine interface structures, the loss of phase information enforces the use of indirect, i.e. model-based, data inversion techniques. While Majewski and co-workers have demonstrated that reflectometry is an adequate technique to investigate the structural behavior of lipopolymers at interfaces,[2,3] their data inversion strategy has been limited to the conventional approach in which the scattering length distribution is parametrized in terms of a stratified surface structure, i.e., in terms of a (relatively small) number of homogeneous slabs. Although this reveals a good deal of qualitative insight into the surface-associated structure,[3,6] if looked upon at day light, such a parametrization is clearly inadequate for a refined description of polymer brushes. We therefore use a more powerful and at the same time more intuitive data evaluation technique, developed by one of us,[9] that is particularly well-suited to determine from reflectometric measurements the molecular organization of linear polymers at interfaces. This data evaluation procedure—which is equally well-suited to investigate a host of similar systems—is introduced in this paper. In succession, a second paper describes its application to the investigation of a particular lipopolymer, a dialkylpolyoxazoline, in which the nature of the phase transition under study is revealed.[10] Since a similar phase transition has been observed with different lipopolymers in aqueous surface monolayers, it is then argued that the mechanism, a polymer-induced ordering of the hydrophobic chains, may be a general feature of lipopolymers associated with interfaces.

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2. Surface-Sensitive Scattering and the Problem of Data Inversion

X-ray and neutron reflectometry has been comprehensively dealt with in the literature.[11−14] In the kinematic approximation,[11] the reflectivity R of a laterally homogeneous, surface-associated structure as a function of the momentum transfer, Q_z, is related to the scattering length density (SLD), i.e., the electron density or neutron SLD, via

$$\frac{R(Q_z)}{R_F(Q_z)} = \frac{1}{\rho_0^2}\left|\int \frac{d\rho(z)}{dz} e^{-iQ_z z} dz\right|^2 \qquad (1)$$

where z denotes the distance from the interface and R_F and ρ_0 are the Fresnel reflectivity and the SLD of the substrate. Molecular interface films, such as (phospho)-lipid monolayers,[15] lipopolymer surface layers,[2,3,6] or polyelectrolyte multilayer films,[16,17] have been frequently interpreted as stratified structures and parametrized in terms of uniform slabs, in analogy to strip-function models, whose reflectivity was then evaluated in a more rigorous way than the kinematic approximation, often using Parratt's recursion method.[18] In such a slab (or "box") model, the SLD profile is assumed to be discontinuous at a number of interfaces along z and constant elsewhere, such that a box structure results. To account for blurring due to thermally excited capillary waves,[19] the step functions describing the stratified interface structure are convoluted with a Gaussian function of variance σ^2 where σ is proportional to the amplitude of the capillary waves.

More recently, it has been demonstrated that such slab models are inadequate to even describe the submolecular structure of such "simple" systems as phospholipids if looked upon at high resolution, and a more appropriate data modeling technique has been developed.[20,21] As will be shown in more detail in the subsequent paper,[10] slab models are quite inadequate to describe the structural details of lipopolymer surface monolayers, even if roughness parameters σ_i are introduced that may differ at the various (internal) interfaces i in a complex box model and are allowed to be much larger than the thermal roughness. We use thus a novel, structure-oriented data inversion method[9,22] that treats the film explicitly as an ensemble of interface-associated polymer (quasi-)molecules whose threadlike chemical structure is reflected in the parametrization, incorporating flexible joints at distances comparable with experimental resolution. Such an ensemble may thus obtain an (almost) infinite number of configurations. In addition, each molecule within an ensemble may be displaced along the z direction such that the hydrophobic/hydrophilic division within a molecule need not exactly coincide with the water surface, located at $z = 0$, and staggered arrangements may be formed. From all possible ensemble configurations, such ones are selected using an evolution strategy that are consistent with the experimental results, complying simultaneously with X-ray and neutron reflection data from various contrasts, and obey space filling in the aqueous compartment. While it is clear that in such an approach there is not *one particular* solution in parameter space that is best—or even exclusively—suited to describe the surface structure, the analysis of representative results leads to a quite realistic appreciation of the system, as we will show in the subsequent paper,[10] and permits a quantitative comparison with predictions from theory.

3. *String Fit*, a Quasi-Molecular Approach to Reflectometric Data Evaluation for Chainlike Molecules at Interfaces

To solve the optimization problem, we utilize an evolution strategy (ES).[23−25] In this context, one may use the terms "genotype" (the genetic information that is coded in a chromosome) and "phenotype" (the appearance of an individual, here a molecular ensemble or its reflectivity under well-defined constraints) in analogy to their definitions in biological evolution. A chromosome consists of a sequence of information units ("genes") that are represented by an n-dimensional vector (of real-type numbers). In the implementation of such an approach in the current work, a chromosome corresponds to the genotype of a certain molecular ensemble. The "fitness" of the individual that is used as a selection criterion in the ES is a numerical value and derives from the correspondence between the reflectivity computed for the molecular density distribution of the molecular ensemble across the interface and the experimentally observed data. To mimic biological evolution processes, individuals may be grouped. Such groups are then called "populations".

In technical terms, a multimembered (μ, λ) ES[23−25] is implemented in the *String Fit* algorithm that acts on ensemble conformations of the polymer.[9,22] The genuine ES algorithm may be formulated as follows:

Step 0: *Initialization*. An initial population of μ individuals is chosen at random. Each individual is characterized by its genotype (of a chromosome consisting of n "alleles") that unambiguously determines its fitness, ϕ.

Step 1: *Mutation*. μ individuals produce λ ($\lambda \geq \mu$) descendants by adding random n-component vectors whose components follow narrow Gaussian distributions around zero to the values of the parent chromosomes. The variances of these distributions may differ in functionally different sections of the chromosomes. Thus, most descendants differ only slightly from their parents. In addition, chromosome sections of different parents are exchanged with a small probability ("recombination" or "crossover").

Step 2: *Selection*. Only the best descendants are selected parents of the next generation.

Steps 1 and 2 are sequentially repeated until a termination criterion is fulfilled, e.g., either ϕ or the number of generations reaches preset values. An algorithm that consists strictly of these three steps can determine conformations of small molecular ensembles. For the investigation of large ensembles and to speed up the optimization process, more sophisticated operators are used. Full details of the algorithm implemented in *String Fit* are given elsewhere.[9]

In the implementation used to solve the problem at hand, the chemical structure of the lipopolymer (Figure 1a, top) is treated as a sequence of cylindrical segments, representing the hydrophobic alkyl anchor, ether linker, and hydrogenated or deuterated polymer chains (Figure 1a, bottom). Each of the segments is divided into subsegments of equal length that are characterized by effective SLDs per unit length, deriving from the scattering lengths and the molecular cross sections. The latter may be estimated either from bulk data of the monomers, from molecular simulations,[26,27] or from Connolly surfaces[28] of static molecular configurations.[17] As the chemical composition in the various segments

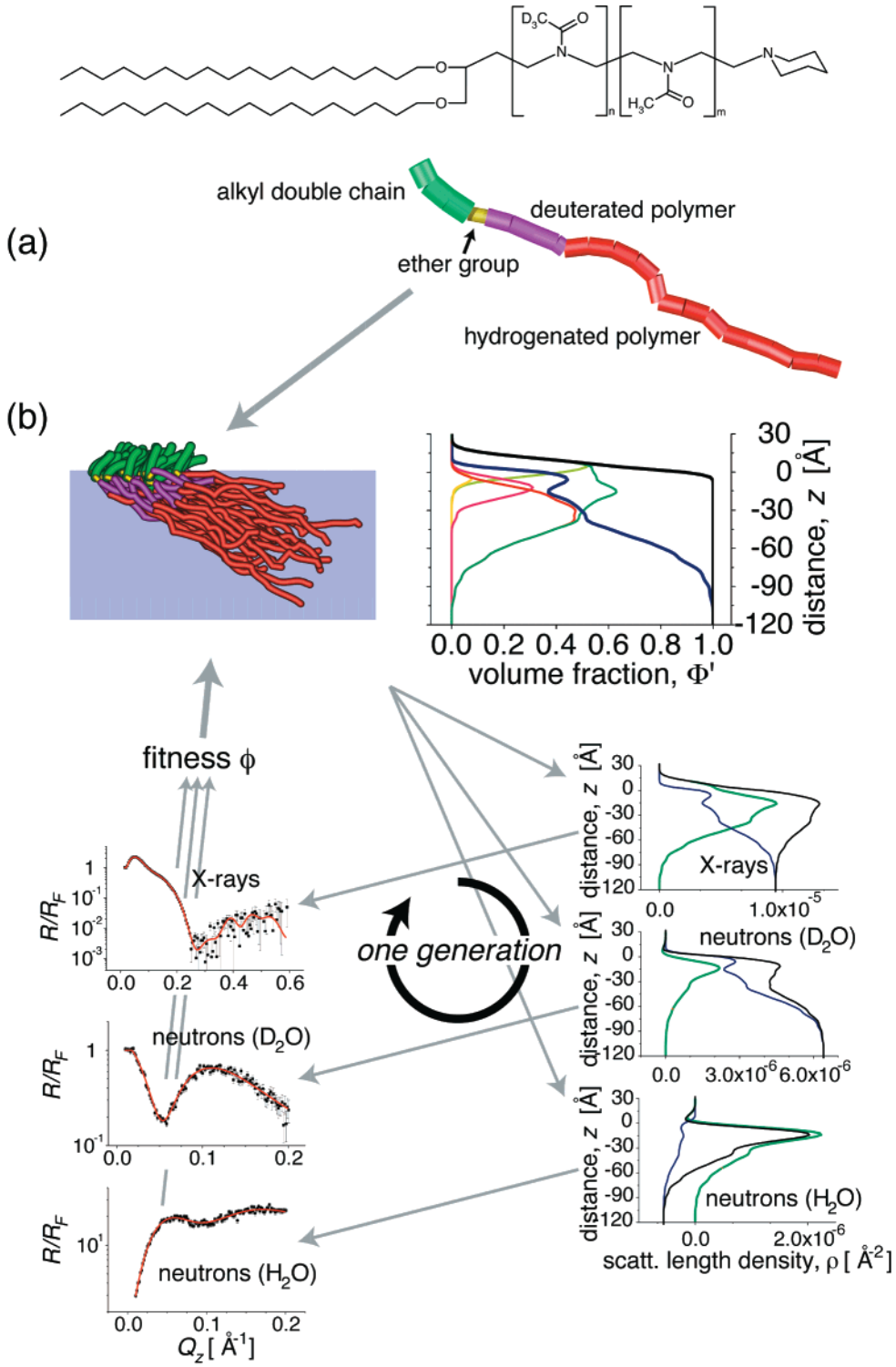

Figure 1. (a) Chemical structure of a poly(methyloxazoline) lipopolymer and its quasi-molecular representation within the data inversion algorithm. The partial volumes and the SLDs per unit length of the linear molecule are determined from a molecular model and its chemical composition. (b) Schematic representation of the composition−space refinement procedure used in connection with an ES approach to determine relevant ensemble configurations of the quasi-molecules at the interface. A number of quasi-molecules at the aqueous surface represent the "individual" in the ES algorithm (upper left). Because of the cylindrical symmetry of the problem, only *one* angle at each joint along the polymer chains determines the chain configuration. We have chosen to display all horizontal displacements of the chains to occur in one azimuthal direction, to the right, as the chain propagates toward the bulk of the subphase, since such a representation separates visually such conformations that are preferentially aligned with the interface from those that are pointing more straight toward the subphase. The explicit configuration of the molecular ensemble corresponds to a volume density distribution (upper right) from which the various relevant SLD distributions (lower right) are determined. Colors of the various traces correspond to the colors of the lipopolymer segments. Contributions of the entire lipopolymer are shown in dark green and those of water molecules in blue. By virtue of their correspondence with the experimental data, the reflectivities (lower left) corresponding to these SLD distributions in turn determine the fitness ϕ (cf. eq 2) used in the ES algorithm to select relevant ensemble configurations from an (almost) infinite configuration space (for details, see text).

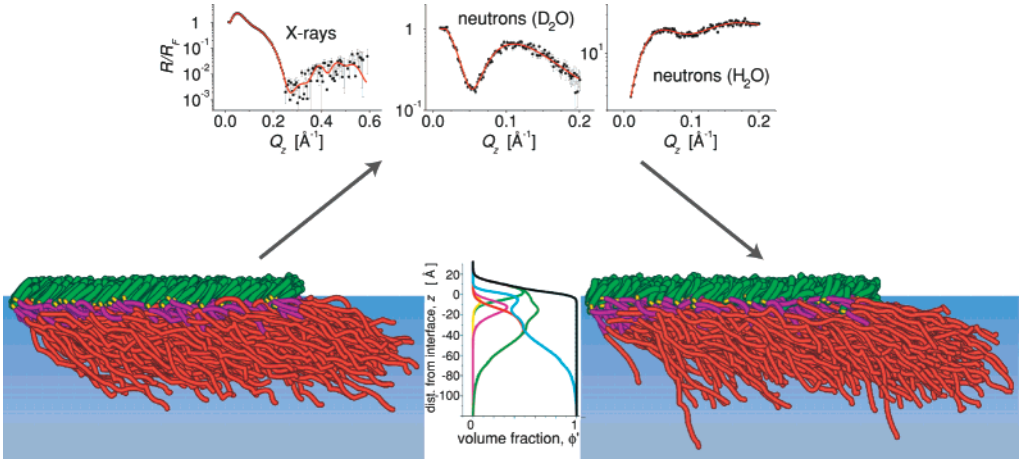

Figure 2. Testing of the implemented data inversion procedure by application to a "mock" data set. An ensemble of 640 quasi-molecules has been generated by applying a random walk to their polymer chains while fixing the chain ends at distances subject to a specific distribution (lower left), and reflectivity data have been determined that are inflicted with realistic experimental errors (see text). The lower right shows a ensemble configuration recovered in 16 independent runs with 40 quasi-molecules each. The corresponding volume density distribution is given in the center. Color code is the same as in Figure 1.

of a lipopolymer changes along its contour line, so does the representation of the molecule in terms of its SLD per unit length and volumetric cross section. Segments and subsegments are connected via flexible joints. One angle between each pair of neighboring (sub)segments is sufficient to determine the density distribution of a molecule along z. Thus, a sequence of orientation angles φ_i is used to describe the molecular conformation of an individual molecule. As the algorithm parametrizes the molecular configurations, it enables composition-space refinement[15,29] and may thus be used for the simultaneous fitting to various data sets from isotopically distinct samples or to neutron and X-ray data obtained under similar experimental conditions. This is schematically shown in Figure 1b and yields an "effective resolution" that is significantly better than the canonical resolution given by the sampling theorem.[21]

In the application of the described algorithm to the structural characterization of polyoxazoline lipopolymers as described in the subsequent paper,[10] an ensemble of $N = 40$ individual molecules is parametrized in terms of the angles $\varphi_{i,k}$ ($k = 1, ..., N$) between the (sub)segments on each molecule. The length distribution of the molecules within an ensemble accounts for the polydispersity of the lipopolymer sample. Thus, i runs up to different maximum values for different molecules k. Such an *ensemble* of molecules represents the individual in the ES algorithm. The scattering lengths of the (sub)segments per unit length were determined from their chemical structure. The angles $\varphi_{i,k}$ are the main constituents of the chromosome. Other alleles contain the distance, ζ_k, of the hydrophobic/hydrophilic interface within a molecule from the aqueous surface at $z = 0$, the average area, A, per molecule, and the surface roughness parameter, σ, describing the collective roughening of the interface by capillary waves, such that the chromosome may be represented as ($\{\varphi_{i,k}\}$, $\{\zeta_k\}$, A, σ).

As in the original ES algorithm,[24] data modeling proceeds in three steps. In the mutation step, each parameter value on a chromosome is varied within a narrow Gaussian distribution (half-width σ_G) centered at zero. The mean deviation between parent and descendant genomes is zero. In addition, crossover, i.e., the recombination of genes from different parents, is allowed to occur with a small probability. Subsequently, the lipopolymer ensembles in the resulting molecular conformations are placed at the interface, volume filling is determined in narrow ($\Delta z = 2$ Å) horizontal slabs, and mutations that lead to overfilling in any of those slabs are rejected. At $z < 0$, void volume is filled with water molecules of the appropriate isotopic composition. [By definition, we assign negative z values to the aqueous subphase and positive z values to the air compartment.] SLDs are then determined for the 2 Å slabs, and reflectivities are computed[18] and compared with the experimental results. This comparison is quantified using the fitness

$$\phi = \left(\sum_m \sum_j \frac{(R^m_{\mathrm{exp},j}(Q_z) - R^m_{\mathrm{model}}(Q_z))^2}{\epsilon^m_j} \right)^{-1} \qquad (2)$$

of the individual which is close related to the definition of χ^2 in conventional minimization procedures. m indicates the various (X-ray or neutron) data sets, j indicates individual data points within a set m, and ϵ^m_j are the experimental error bars determined from counting statistics. σ_G, a parameter that critically influences the performance of the algorithm, is also included in the genome of the individuals and thus optimized in the course of evolution.[9]

4. Performance Test: Application to a Simulated Lipopolymer Ensemble

Since the configuration space of an ensemble of surface-grafted polymer molecules is overwhelmingly large, it is not a priori clear that a particular configuration which has been identified to yield reflectivities compatible with the observed experimental data is actually similar in its structural properties to the real system.

(i) It has been demonstrated that a single—X-ray or neutron—data set is merely sufficient to identify the submolecularly resolved structure of a conventional phospholipid.[21,30] Revealing the resolved structure of a lipopolymer monolayer is clearly out of reach.

(ii) It has further been shown[31] that distinct SLD profiles which may be chemically plausible for a given system can lead to indistinguishable reflectivity data sets whose differing phases cannot be experimentally determined. A good way to avoid such a situation, however, is the co-refinement of data sets with different contrasts.

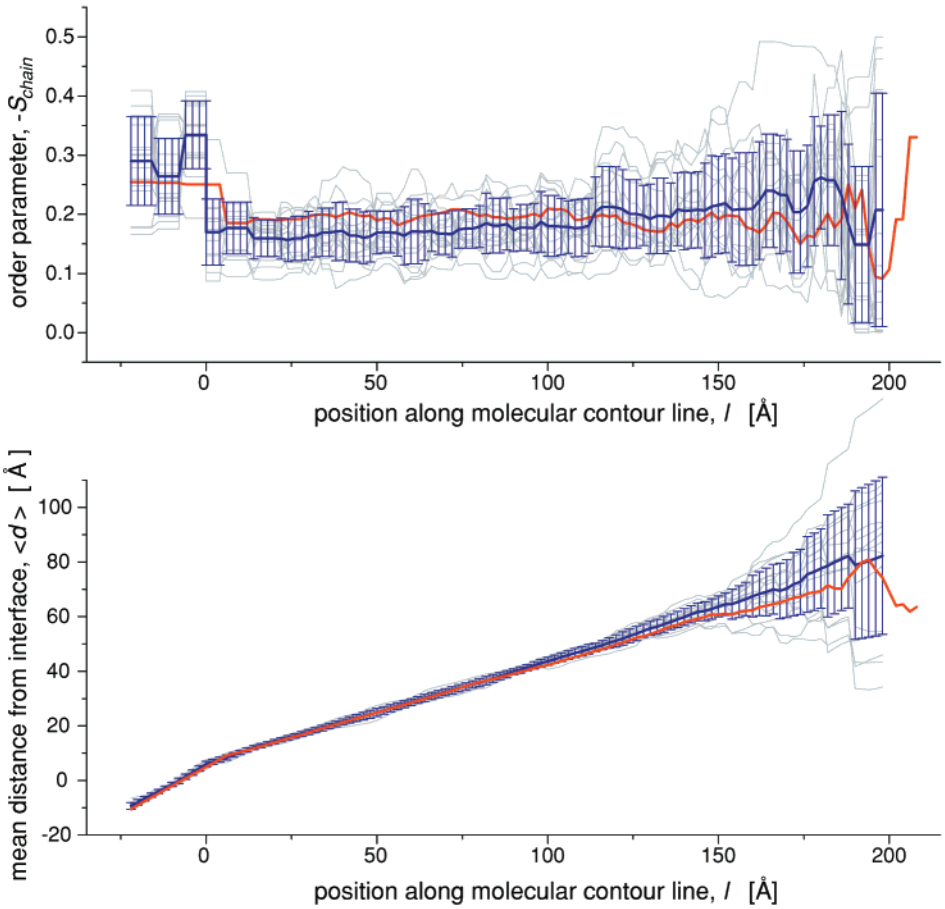

Figure 3. (a) Chain order parameter, S_{chain}, determined according to eq 4 and (b) mean distances, $\langle d \rangle$, from the aqueous surface of subsections located at distances l along the contour line of the polymer chains for the synthetic (red) and recovered (blue) configuration sets shown in Figure 2; negative l values correspond to the alkyl chains. Thin gray lines indicate data of individual data inversion runs. Error bars give standard deviations of 16 independent runs.

(iii) Finally, it is obvious that differing atomic configurations in space may lead to similar SLD distributions, such that there is not *one single* ensemble configuration that describes the real system best. By utilizing the connectivity of adjacent atoms within the molecules to largely constrain the results, the data inversion procedure introduced in this work selects those configurations that are reasonably compliant with the experimental data *and* chemically plausible.

In this section we investigate how closely a molecular ensemble configuration revealed from synthetic reflectivity data correlates with an input configuration that has been used to generate these data. Emphasis is put on examining under realistic conditions a situation that resembles closely the problem investigated in the subsequent paper[10] and on developing criteria that are suited to quantify the resemblance between the two configuration sets. For this purpose, we have prepared a synthetic ensemble of surface-grafted polymer quasi-molecules, similar in their nature to a lipopolyoxazoline, that consists of a hydrophobic anchor moiety linked to a water-soluble polymer chain with a large neutron SLD ("deuterated") in its upper portion and a low neutron SLD in its lower part (and constant electron density along its hydrophilic polymer chain) and have computed its (X-ray and neutron) reflectivities (see Figure 2). Absolute values of the SLDs and partial volumes in the polymer chain were chosen to resemble a methyloxazoline moiety.

To obtain a reasonable starting configuration, the polymer chains in an ensemble of 640 molecules were subject to a random walk, and the alkyl segments were inclined at an orientation subject to a Gaussian distribution around an average angle of 45° with a variance of 10°. For this synthetic sample, the X-ray and neutron (for H_2O and D_2O subphases) reflectivities were computed and subject to noise (proportional to Q_z^4 with an absolute value of 2% at $Q_z = 0.5$ Å^{-1} for X-ray data and of 5% at $Q_z = 0.2$ Å^{-1} for neutron data). Such reflectograms, terminated at $Q_z^{max} = 0.6/0.2$ Å^{-1} for X-ray/neutron data, served as a starting point for *String Fit* data inversion runs, operating on ensembles of $N = 40$ molecules. Sixteen such runs were performed and lumped together to resemble the simulated configuration set of 640 individual molecules. Figure 2 (upper row) shows the synthetic data sets together with the reflectivities (continuous lines) corresponding to the output configurations. In the lower part of Figure 2, the input (left) and output (right) configurations are shown together with the volume fraction (Φ') profile derived from the output configuration. In the configuration data, horizontal displacements of the chains are always depicted to occur to the right-hand side, such that chains within the ensemble that are preferentially oriented in the horizontal direction are visually separated from chains that are preferentially oriented in the normal direction. The strings of subsegments on the molecules are displayed as Bezier curves. A major difference between the input and output is that entropically unfavorable conformations occur in the latter in which single chains extend straight down into the subphase compartment. Such extended chains are not contained

in the input configuration. They occur in the output because the reflectivity is determined by the *gradients* of the SLDs (cf. eq 1), and the algorithm does not implement thermodynamic constraints. Other than that, the two configurations have the same general appearance, and the distributions of the various molecular moieties are virtually indistinguishable from each other in the input and output data. In view of a major conclusion drawn from the modeling of real experimental data in the subsequent paper,[10] we emphasize that the lipopolymer molecules in the output configuration are similarly well confined to the interface as they are in the input data although they were allowed to immerse into the subphase in the ES algorithm (see previous section).

We have chosen two criteria to scale the macroscopically averaged configurations of the input and output against each other: (i) The chain order parameter $S_{chain} = S_{chain}(l)$ defined in analogy to NMR order parameters[32] which is evaluated as a function of the location l along the contour line of the polymer chain and (ii) the average distance $\langle d \rangle = \langle d \rangle(l)$ of a polymer section from the hydrophobic/hydrophilic interface at $z = 0$. Generally, S_{ij} is defined in terms of the orientations Θ of two molecular axes i and j with respect to the surface normal, z:

$$S_{ij} = \frac{1}{2}\langle 3 \cos \Theta_i \cos \Theta_j - \delta_{ij} \rangle \qquad (3)$$

An order parameter defined in analogy to the carbon−deuterium order parameter in ^{2}H NMR on methylene chains is

$$S_{chain} = \frac{1}{2}(\langle \sin^2 \varphi_i \rangle - 1) \qquad (4)$$

[The notation S_{CD} so widely used in NMR literature is in perfect analogy to the parameter S_{chain} used in this work.] In Figure 3a, S_{chain} are compared for the input and output configurations. It is obvious that the general features as well as the absolute values of S_{chain} are well reproduced by the ES algorithm. Similarly, the mean distances $\langle d \rangle$ (Figure 3b) are well conserved in the output configuration. Only at the outermost polymer sections are differences observed that are beyond statistical error. These correspond to locations on the chains that extend artificially deep into the subphase due to the lack of thermodynamic constrains in the data inversion procedure.

5. Conclusions

We have developed a novel tool for the inversion of reflectometry data that is particularly well suited to reveal the structure of monolayers comprising linear polymers. Implementing an evolution strategy, the technique is capable of identifying such ensemble conformations in an overwhelmingly large configuration space that are simultaneously consistent with experimental X-ray and neutron reflection data of different contrasts and at the same time space-filling as well as compliant with the chemical structure. This technique may also be useful for the investigation of conformations of other linear molecules at interfaces, such as DNA (Politsch, Huebner, and Cevc, manuscript in preparation). For a synthetic example, we have shown that this confinement of the results in configuration space yields reasonable agreement between an input and output configuration in that the latter captures the essential features of the former. In particular, we note that the confinement of the lipopolymer quasi-molecules to the interface has been well preserved in the synthetic example. In the subsequent paper we will apply the developed tools to a real problem—the structure determination of a lipopolyoxazoline brush at aqueous surfaces as a function of the applied surface pressure.

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References and Notes

(1) Lasic, D.; Martin, D. *Stealth Liposomes*; CRC Press: Boca Raton, FL, 1995.
(2) Majewski, J.; Popovitz-Biro, R.; Bouwman, W. G.; Kjaer, K.; Als-Nielsen, J.; Lahav, M.; Leiserowitz, L. *Chem. Eur. J.* **1995**, *1*, 304−311.
(3) Majewski, J.; Kuhl, T. L.; Gerstenberg, M. C.; Israelachvili, J. N.; Smith, G. S. *J. Phys. Chem. B* **1997**, *101*, 3122−3129.
(4) Baekmark, T. R.; Wiesenthal, T.; Kuhn, P.; Bayerl, T. M.; Nuyken, O.; Merkel, R. *Langmuir* **1997**, *13*, 5521−5523.
(5) Baekmark, T. R.; Wiesenthal, T.; Kuhn, P.; Albersdörfer, A.; Nuyken, O.; Merkel, R. *Langmuir* **1999**, *15*, 3616−3626.
(6) Wurlitzer, A.; Politsch, E.; Cevc, G.; Gutberlet, T.; Kjaer, K.; Lösche, M. *Physica B* **2000**, *276−278*, 343−344.
(7) Als-Nielsen, J.; Jacquemain, D.; Kjaer, K.; Lahav, M.; Leveiller, F.; Leiserowitz, L. *Phys. Rep.* **1994**, *246*, 251−313.
(8) Mendelsohn, R.; Brauner, J. W.; Gericke, A. *Annu. Rev. Phys. Chem.* **1995**, *46*, 305−334.
(9) Politsch, E. *J. Appl. Crystallogr.*, submitted.
(10) Wurlitzer, A.; Politsch, E.; Krüger, P.; Weygand, M.; Kjaer, K.; Cevc, G.; Lösche, M. *Macromolecules* **2001**, *34*, 1334.
(11) Als-Nielsen, J.; Kjaer, K. In *Phase Transitions in Soft Condensed Matter*; Riste, T., Sherrington, D., Eds.; Plenum Press: New York, 1989; p 113−138.
(12) Russell, T. P. *Mater. Sci. Rep.* **1990**, *5*, 171−271.
(13) Penfold, J.; Thomas, R. K. *J. Phys.: Condens. Matter* **1990**, *2*, 1369−1412.
(14) Als-Nielsen, J.; Möhwald, H. In *Handbook on Synchrotron Radiation*; Ebashi, S., Koch, M., Rubinstein, E., Eds.; Elsevier North-Holland: Amsterdam, 1991; Vol. 4, pp. 1−53.
(15) Vaknin, D.; Kjaer, K.; Als-Nielsen, J.; Lösche, M. *Biophys. J.* **1991**, *59*, 1325−1332.
(16) Schmitt, J.; Grünewald, T.; Decher, G.; Pershan, P. S.; Kjaer, K.; Lösche, M. *Macromolecules* **1993**, *26*, 7058−7063.
(17) Lösche, M.; Schmitt, J.; Decher, G.; Bouwman, W. G.; Kjaer, K. *Macromolecules* **1998**, *31*, 8893−8906.
(18) Parratt, L. G. *Phys. Rev.* **1954**, *95*, 359−369.
(19) Pershan, P. S. *Faraday Discuss. Chem. Soc.* **1990**, *89*, 231−245.
(20) Schalke, M.; Krüger, P.; Weygand, M.; Lösche, M. *Biochim. Biophys. Acta* **2000**, *1464*, 113−126.
(21) Schalke, M.; Lösche, M. *Adv. Colloid Interface Sci.* **2000**, *88*, 243−274.
(22) Politsch, E.; Cevc, G. *Physica B* **2000**, *276*, 390−391.
(23) Rechenberg, I. *Evolutionsstrategie '94*; Frommann-Holzboog: Stuttgart, 1994.
(24) Schwefel, H.-P. *Evolution and Optimum Seeking*; J. Wiley & Sons: New York, 1995.
(25) Bäck, T. *Evolutionary Algorithms in Theory and Practice*; Oxford University Press: Oxford, 1996.
(26) Petrache, H. I.; Feller, S. E.; Nagle, J. F. *Biophys. J.* **1997**, *70*, 2237−2242.
(27) Armen, R. S.; Uitto, O. D.; Feller, S. E. *Biophys. J.* **1998**, *75*, 734−744.
(28) Connolly, M. L. *Appl. Crystallogr.* **1983**, *16*, 548−558.
(29) Wiener, M. C.; White, S. H. *Biophys. J.* **1991**, *59*, 174−185.
(30) Schalke, M. Ph.D. Thesis, Leipzig University, 2000.
(31) Vaknin, D.; Als-Nielsen, J.; Piepenstock, M.; Lösche, M. *Biophys. J.* **1991**, *60*, 1545−1552.
(32) Bloom, M.; Evans, E.; Mouritsen, O. G. *Q. Rev. Biophys.* **1991**, *24*, 293−397.

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