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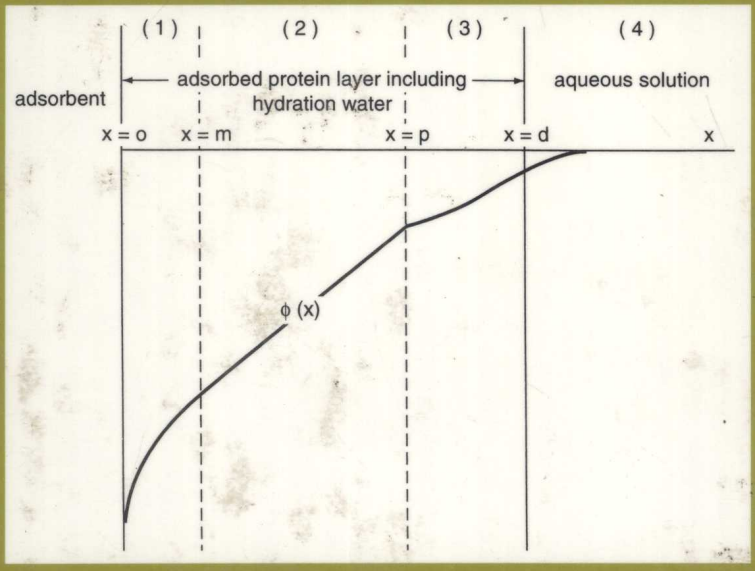
BIOPOLYMERS AT INTERFACES



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BIOPOLYMERS AT INTERFACES

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Preface

The interfacial behavior of biopolymers, and notably proteins, has attracted considerable attention during the last few decades. This is most likely due to the importance of protein adsorption for both biophysical and biochemical processes, including, for example, the initial steps of atherosclerosis and phagocytosis, as well as the applicability of these phenomena in a range of biomedical applications, such as solid phase diagnostics, drug delivery, extracorporeal therapy, and biosensors. In analogy to the interfacial behavior of simpler polymers, polyelectrolytes, and colloids, significant progress has been made regarding protein adsorption over the years, largely due to the development and application of high-performance analytical techniques, the increased use of protein mutants and variants with controlled variation in their amino acid composition for adsorption studies, and the parallel development in the understanding of the interfacial behavior of simpler polymer and colloidal systems.

Because of the high activity within the field of protein adsorption as well as its size—which spans from complex processes in biological systems such as blood to detailed physicochemical studies aiming at elucidating details in the structure of adsorbed protein layers—it is becoming increasingly difficult to obtain an overview of this area. Although to some extent this is the case for the entire area, it is particularly true regarding physicochemical aspects of protein interfacial behavior. This is unfortunate, since tremendous progress has been made over the last two decades regarding the interfacial behavior of polymers, polyelectrolytes, and colloids, and since much can be learned about protein adsorption from considerations of these simpler systems. This is not to say that proteins are simple polymers or colloids, but clearly they are also polymers and colloids.

This book was initiated in an attempt to fill some of the gaps in the literature concerning biopolymers at interfaces and to form a bridge between scientists working with more complex aspects of protein adsorption such as the acceptance and performance of extracorporeal devices and drug carriers on one hand and those concerned with the interfacial behavior of much simpler model systems on the other. Clearly, further progress in the field of biopolymers at interfaces can be made only by observing the similarities between biopolymers and simpler polymer and colloidal systems, and at the same time recognizing the significantly higher degree of complexity of biopolymer systems.

In order to try to achieve these objectives, several issues have been addressed. The first two chapters (by Cohen Stuart and Norde) deal explicitly with more general aspects of the physicochemical basis of protein and polymer adsorption. Chapter 3, by Basiuk, explores the adsorption of amino acids and peptides, and Chapter 4, by Roth and Lenhoff, covers modeling of protein adsorption. Each of the more fundamental chapters aims to discuss primarily one aspect of biopolymer interfacial behavior. Consequently, the book contains chapters extensively discussing adsorption kinetics (Ramsden), adsorbed layer structure (Chittur; Hlady and Buijs; Malmsten et al.; Billsten et al.) and dynamics (Tilton), interfacial orientation (Herron et al.), effects of self-assembly on protein adsorption (Nylander), interactions between biopolymer layers (Claesson), and interfacial exchange (Ball et al.; Wahlgren et al.). Finally, the volume focuses on general aspects of biopolymer interfacial behavior. Therefore, the number of chapters describing various applications of protein adsorption, for example, is limited, and the ones included (Holmberg and Quash; Malmsten; Belfort and Zydney) also treat in some detail the physicochemical basis of the respective applications.

I would like to take this opportunity to express my sincere gratitude to all participating authors for their support and involvement, which has made my job as editor an easy and enjoyable one.

Martin Malmsten

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Contents

1

Macromolecular Adsorption: A Brief Introduction

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I. BIOLOGICAL MACROMOLECULES

The primary structure of many biological macromolecules is simply that of a linear chain of monomers. In this respect, they do not differ from most synthetic polymers. Behind the chemical simplicity, however, rather complex and specific behavior may be hidden. For example, the secondary and tertiary structures of proteins often play an essential role in their specific biological function. For such molecules it may seem impossible to develop a universal description as is now well established for synthetic polymers.

However, one may wonder whether this has been attempted. Some of the concepts fruitfully introduced in polymer physics may be quite relevant for understanding the behavior of, say, globular proteins. It is the purpose of this chapter to discuss polymers at interfaces from a physical chemists' point of view, highlighting processes and central concepts rather than specific systems. Effects of conformational entropy, internal cohesion, electrostatic interactions, and intermolecular interactions on adsorbed layers will be considered, and processes like transport, attachment, unfolding and trapping will be discussed.

As said, most biological polymers are chemically more complex than homopolymers and have a copolymer character that cannot be ignored. However, considering the entire plenitude of phenomena that various classes of copolymers can display would by far exceed the limits of this introductory presentation. We will therefore not explicitly discuss copolymers.

II. MACROMOLECULES ARE SOFT PARTICLES

Around the bonds that connect the atoms in the main chain of a linear polymer, some rotation is usually possible. This gives the polymer a certain degree of flexibility, which is usually enough to allow the molecule to assume a large number of shapes or *conformations*. With this large number of conformations, a conformation entropy is associated. In the absence of external forces, the chain will wiggle because of thermal motion, and assume an average, approximately spherical *coil* shape with a characteristic size R dependent on the number of monomers N per chain (i.e., the length of the chain). This dependence can be generally expressed as a power law: $R \sim N^{\nu}$. The conformational entropy gives the coil a certain elastic resistance to deformations such as squeezing and stretching. This resilience is rather weak: the molecules can be considered "soft spheres."

The characteristic size R of the coil depends strongly on the solvent [1,2] but it can always be written as a power law of the chain length N: $R \sim N^{\alpha}$. *Good solvents* tend to keep the individual monomers separate. In such a solvent, most shapes permitted by bond rotation are energetically equivalent.

If the monomers would not occupy any volume (i.e., the chain is infinitely thin, this is called an *ideal chain* analogously to ideal gases) one could describe the chain in terms of a random walk (diffusion-like) process. However, because monomers do have a volume, walks that lead to overlap between monomers must be excluded. The proper description is therefore that of a *self-avoiding walk*. The characteristic size R of such a structure is known to scale as $N^{3/5}(\alpha = 3/5)$, and such molecules are denoted as *swollen coils*. The monomer-monomer repulsion also ensures that the molecules do not cluster but form a homogeneous solution. At higher concentration, however, this repulsion is not enough to keep the coils apart; as soon as they fill the entire solution volume, they begin to interpenetrate, thus forming a transient network. This situation is now commonly referred to as "semidilute" solution.

In less good solvents, there is, effectively, an attraction between the monomers. As long as this attraction is very weak, the coil may somewhat contract, but it remains swollen. At a certain point, the attraction becomes strong enough to compensate the effect of the excluded volume of the monomers. This is called the θ point or θ temperature. The behavior of the coil around the θ point is equivalent to that of an ideal chain, for which random walk statistics apply and one can prove the $R \sim N^{1/2}(\alpha = 1/2)$; this is called the Gaussian coil because the density of monomers inside the coil is a Gaussian function of the distance to the center [2].

Should the solvent become even worse, the entropy can no longer maintain the open, dilute structure of the coil and the molecule collapses to a compact *globule*. Inside this globule, the monomer density is essentially constant and therefore the mass must scale as R^3 so that $R \sim N^{1/3}(\upsilon = 1/3)$. Of course, monomer-monomer attraction will not only occur between monomers within the same chain, but also between monomers on different chains. Hence, in poor solvents there is a concentration where the molecules accumulate into a dense phase and we have phase separation.

As a parameter that describes the strength of the monomer interaction it is customary to use the so-called Flory-Huggins parameter χ, which is essentially an excess Gibbs energy of monomer-solvent contacts (with respect to monomer-monomer and solvent-solvent contacts) normalized by kT. In good solvents, χ is close to zero, at the θ point it equals 0.5, and for poor solvents, $\chi > 0.5$. In many texts, the parameter $\upsilon = 1 - 2\chi$ is used. It measures the strength of the monomer-monomer interaction relative to that at the θ point and is called the *excluded volume* parameter. Its value is zero at the θ point, positive in better solvents and negative in worse solvents (Fig. 1).

In poor solvents, where the molecules collapse into globules, deformation is not only counteracted by the conformational entropy, but also by the fact that the number of (unfavorable) monomer-solvent contacts increases at the