COAGULATION-RESISTANT SURFACES AND A MECHANISTIC MODEL OF ADSORPTION ON POLYMER SURFACES

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Upon the recommendation of the professor in charge of the thesis and of the chairman of the DEPARTMENT OF METALLURGY this thesis is hereby accepted in partial fulfillment of the requirements for the degree of

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Date

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And to Barb and Tonio, for they made it all meaningful, happy, exciting, and worthwhile.

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CHAPTER I

INTRODUCTION

The use of artificial materials in surgery has grown considerably in the past decade. Many successful surgical techniques are now dependent on devices constructed from "foreign" materials. Every one of these applications faces a fundamental problem: the material/biological interface. There is no way to isolate. There is always an interface, and little is known about the processes and reactions which may be occurring at such interfaces. Perhaps the most critical and also the most fundamental problem in the use of materials in biomedical applications is that we do not understand the interfacial processes which occur, and, perhaps more importantly, we are most likely largely unaware of the existence of many processes which are occurring.

It is well established that blood coagulation can be initiated by contact with a "foreign surface." The exact reason or purpose for such a mechanism is not known, though Vroman[1,2] believes it may be an evolutionary remnant, a more specialized form of the general coagulation of cytoplasm. There is growing evidence that adsorption at the foreign surface, particularly protein adsorption, plays a fundamental role in the initiation of blood coagulation. Protein adsorption processes may also be important in other tissues. Synovial fluid, where protein adsorption on artificial joints may play a role in friction and wear processes, is but one example. There is now a growing acceptance

of the importance of fundamental surface studies in elucidating the mechanism of "surface-induced" blood coagulation, particularly work on protein, lipid, and platelet adsorption.

There is relatively little work available on protein adsorption at the solid-liquid interface. The work that is available deals primarily with adsorption on high-energy surfaces. The statistical theories that have been developed for the adsorption of linear flexible polymers cannot be expected to hold for a rigidly structured protein molecule. Most adsorption theories are thermodymanic in nature.[3] Levine's[4] recent thermodynamic theory is an attempt to treat protein adsorption on a fundamental level.

Proteins adsorb. It can almost be said that all proteins adsorb on everything, though that may not be quite true. Concepts such as surface charge or surface energy are not generally applicable. Perhaps the most perturbing fact about protein-polymer interaction is that there <u>is</u> an interaction. One can understand the adsorption of proteins on glass or metal or other high energy surfaces as a decrease in the overall surface energy. This is manifested in the decreased wettability of the proteinated surface. However, when proteins adsorb on low energy polymer surfaces, the surface energy is increased. This can be demonstrated by a change in the surfaces' wetting properties.[5] Thermodynamically, this makes little sense, as nature does not tend to produce situations of higher energy, particularly when the entropy must decrease as well.

Protein adsorption is not well understood. This is due not only to the complex nature of proteins, but also to the lack of a general mechanistic model of adsorption. Before one can hope to understand protein adsorption, one must understand the adsorption of simple compounds on a molecular level.

The original objective of this work was to develop and characterize a blood coagulation-resistant surface for use in medical implant applications. This proved to be an enormous and unfinished, though not necessarily unsuccessful, task.

The author's attempts to develop coagulation-resistant surfaces, particularly that of proteinated polystyrene, are briefly discussed in the next chapter; following these is a discussion of the use of fluorescence microscopy to detect protein adsorption on a microscopic level. For those readers unfamiliar with these general areas, it would be helpful to read the sections on proteins and adsorption in Chapter III before reading Chapter II.

The objective of the major part of this work, however, is to develop a molecular model of adsorption on hydrophobic surfaces, with applications to proteins, in the hope of gaining a rudimentary understanding of the mechanism of adsorption. Intermolecular and interfacial forces must be taken into consideration, but before such forces can be applied, the nature and structure of the medium through which they act, water, must

be considered. One must also consider the nature of the solute molecule and the properties of the polymer surface. These considerations will permit the interpretation of solid-solute, solid-solvent, and solute-solvent interactions, in addition to solvent-solvent interactions. With this background a model of adsorption on polymer surfaces will be developed. The model will first treat very simple species in the vicinity of a surface, then it will treat albumin, gamma globulin and fibrinogen. The results of the model and the computer calculations derived from it will then be compared to data on the adsorption of simple compounds and proteins. The development will be both qualitative and quantitative for the adsorption of simple molecules. The adsorption of proteins will be discussed more qualitatively.

The model will attempt to show that adsorption on the molecular level is a natural consequence of the asymmetric force field in the vicinity of an interface. It will also show that a large part of the asymmetry of that force field is due to solute-solvent effects. It will further attempt to show that one need not postulate active sites or binding sites to explain adsorption, though they may aid it. It will then show that one may minimize adsorption of a particular species by proper choice of certain surface parameters.

The development of the model will require knowledge of the structure of water, the nature of the polymer surface, the nature of adsorption, and the nature of intermolecular forces. These subjects will

be discussed before the model is presented.

All calculations and values are given in c-g-s units, where charge is expressed in electrostatic units (esu). All energies are in ergs, and all forces in dynes. All distances are given in angstroms, though centimeter units must be used in all of the calculations.

CHAPTER II

PRELIMINARY EXPERIMENTAL WORK

A. Coagulation-Resistant Surfaces

1. Polyorganofluorophosphates:

The intrinsic blood coagulation mechanism is believed to be dependent on the modification of a plasma protein by surface denaturation and its subsequent reactions. In the classical Ratnoff and MacFarlane cascade theory[6,7] Factor XII (Hageman Factor) is surface-activated to XII*, an enzyme, which can then catalyze the reaction XI → XI*, and the cascade mechanism is initiated.

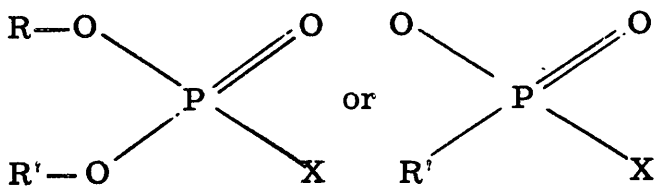
Though Factor XII has been isolated and purified, it is still a relatively uncharacterized protein, and controversy as to its role, and possibly even its existence, continues. It is generally accepted, however, that the intrinsic clotting mechanism is dependent on a modification of some plasma protein at a solid surface, be it Factor XII, Factor XI, or prothrombin.[8] Some very recent work casts doubt on the protein modification theory.[9]

If clotting is indeed due to the surface modification of some protein, the logical question is how to prevent that modification from occurring, and thus prevent the necessary activation. If one assumes that the denaturation process exposes certain reactive groups which are then capable of reacting with the next protein in the clotting sequence or

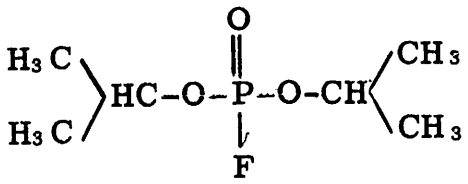
perhaps with other parts of the same molecule, the blocking of those reactive groups should prevent coagulation from occurring. This may be possible with enzyme inhibitors. The problem is that the active groups necessary for clotting have not been isolated, if indeed active groups are responsible at all. Most inhibitors tend to be effective in decreasing clotting activity in solution; the action of an inhibitor bound to a solid substrate is not known.

There are some clues as to the active site of prothrombin, but such information on Hageman Factor is virtually non-existent. Hageman Factor may be inhibited by diisopropylfluorophosphate[10] (DFP), an esterase inhibitor, but such a treatment may inhibit its esterase activity without inhibiting its clotting activity.[11] The work of Ray and Roy[12] and of Caldwell and Seegers[13] showed that disulphide and free amino groups are essential for prothrombin activity. Inhibition of these groups led to a loss in activity. The amino may be inhibited by dinitrofluorobenzene and phenylisocyanate; the sulfide can be inhibited by reducing agents.

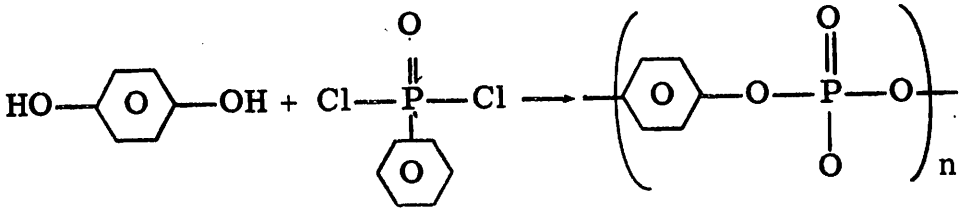
DFP is an extremely toxic and reactive member of a class of organophosphate compounds which irreversibly inhibit esterase enzymes. The general formula for these compounds is



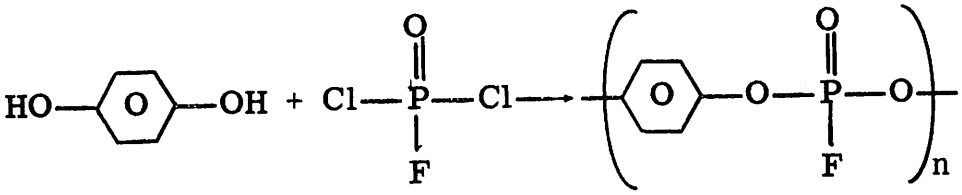
where X can be -F, -CN, or -O-  -NO_2. The formula for DFP is



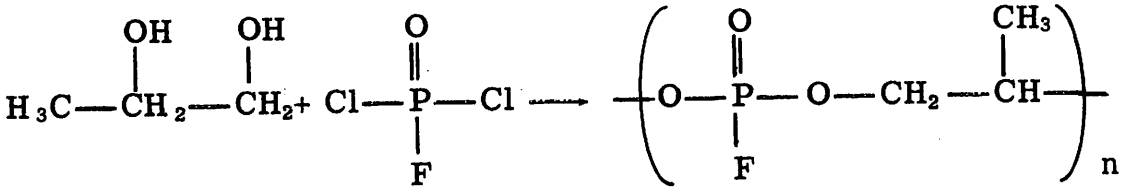
Sorenson's book on polymer chemistry[14] contains the reaction:



If this reaction is performed with phosphorousoxydichlorofluoride instead of with phenylphosphonyldichloride, one gets:



Such a polymer contains the reactive heart of the organofluorophosphate inhibitors. If now the polymerization is produced using propylene glycol instead of hydroquinone:



Such a polymer has a frightening resemblance to DFP. Molecular models of this polymer indicate that conformations exist wherein the P-F bond is directed up and out from the surface. Such a surface should have a very high reactivity for enzymes. By proper choice of the glycol, one can vary the R-groups on the organofluorophosphate, which should vary

its enzyme reactivity.

The synthesis and characterization of these polyorganofluorophosphates was performed by Mr. Herbert Yen and are described in his thesis.[15]

Shortly after beginning this work it became evident that a DFP-like polymer would probably bind other proteins long before it ever contacted Hageman Factor. Thus a polyorganofluorophosphate surface would tend to become rapidly and irreversibly proteinated as soon as it contacted blood. A proteinated surface could surely be produced by more direct means than synthesizing special, new, and possibly toxic polymers.

2. Albuminated Polystyrene:

Ten years ago Copley[16] showed that blood coagulation times in fibrin-coated test tubes were relatively long. Recent work on the blood compatability properties of collagen[17] "...suggest that the collagen surface is remarkably free of thrombogenic properties." It has also been clearly demonstrated that the first thing that happens to most materials when contacted with blood is the rapid formation of a film of adsorbed protein[18-20] (see also Chapter III). Such a film is not necessarily stable, however, as competitive adsorption is known to occur with proteins;[1,18] just as with synthetic polymers[21] (see also Chapter III); indeed, this is the basis for the adsorption chromatography of proteins. It has been well documented that heparinized surfaces adsorb proteins.[22,23] Adsorption on a heparinized surface is quite strong,[23] thus competitive adsorption may not occur. It seems, therefore that thrombo-

resistant surfaces may contain a layer of bound or complexed and relatively immobilized protein.

The above discussion leads naturally to the concept of surface proteination as a potential method of rendering surfaces non-thrombogenic.

Protein bonding to synthetic polymers has been extensively utilized in biochemistry; the methods and techniques were thoroughly reviewed recently.[24] Polystyrene was selected as a substrate for this experimental work because polystyrene and its derivatives have been widely used as insoluble supports for the binding of enzymes and other proteins.[24] Another reason for using polystyrene is that it is inexpensive and readily available in sheet and tube form.

The diazo coupling reaction can be used to couple proteins to supports containing amino groups. It is fairly well established[25] that the coupling of diazonium salts of $H_2N-Ph-X$ with proteins introduces $-N{=}{=}N-Ph-X$ groups to the imidazole and phenol residues, though epsilon-amino, guanidino, and imino groups may also be involved.[26] Polyaminostyrene can be prepared by nitration and then reducing to the amine; Falb's method[27] was used for this work. The polyaminostyrene surface was then diazotized and coupled to protein following the technique of Gyenes and Sehon.[28] The surface modifications and protein binding were detected by multiple attenuated total reflection (MATR) infra red spectroscopy; the MATR spectra were made by Mr. Fran Bonomo,

Chemistry Division, Denver Research Institute. The nitration, amination, and proteination steps were evident in some of the spectra. Generally, however, the reactions were not reproducible and were thus somewhat unreliable. A simpler and more reproducible reaction was sought.

Friedel-Crafts reactions in aqueous solutions are discussed briefly in Olah's treatise.[29] Jenny[30] prepared diphenylmethane by reacting benzene with benzyl chloride. The catalyst was zinc chloride in a saturated aqueous solution of hydrochloric acid. The reaction was carried out at the interface between the aqueous and organic solutions. The reaction conditions used (3 hours at 50 C) prompted the use of a similar technique for the proteination of polystyrene, where the reaction would take place at the interface between the polystyrene and the protein solution.

Polystyrene sheet (10 mil) and tubing ($\frac{1}{4}$ inch ID) were obtained locally.[31] The sheet was cut into 18 × 50 mm tabs for ease in MATR analysis; the tubing was machined into Gott vena cava rings[32,33] for the in vivo blood compatibility studies.

The polystyrene samples were washed in ethanol and then chloromethylated according to Falb's method.[38] The dry samples were immersed for 15 seconds at room temperature in a solution containing 5 grams of $AlCl_3$ and 3.6 ml of chloromethylmethyl ether (Aldrich Chemical Co.) in 100 ml of nitrobenzene. The salmon-pink samples were then plunged immediately into 100 per cent ethanol until a uniform white surface appeared; they were then thoroughly soaked and rinsed in 95 per cent

ethanol until no further trace of nitrobenzene was evident. MATR spectra of the tabs indicated extensive para substitution of the aromatic groups (Fig. 1). The differences between the MATR spectrum of polystyrene and chloromethylated polystyrene are evident from Figure 1.

The use of albumin for the chemical proteination of surfaces was first suggested by Dr. Leo Vroman.[35] Albumin is probably the best choice as it is a relatively innocuous protein whose primary biochemical function appears to be the maintenance of osmotic pressure. The other proteins in blood, e.g., fibrinogen and the gamma globulins, all have rather specialized functions in addition to their role in the osmotic balance.[36] Thus an albuminated surface may be an especially passive or inert surface for application in contact with blood.

About 0.7 gram of $ZnCl_2$ was added to 100 ml distilled water; the solution was slowly adjusted to pH 4 with 0.1 N HCl. One gram of albumin[37] was then added with stirring. The control solution was identical except that 0.9 grams of NaCl were substituted for the $ZnCl_2$. The chloromethylated samples were immersed in the albumination and control solutions at 40 C for at least 8 hours. The samples were then thoroughly washed and rinsed in 0.9 per cent saline until there was no evidence of protein remaining; this required many changes of the saline over a period of 2-3 days. MATR spectra of the control and albuminated surfaces are given in Figures 2a and 2b. Note that the control surface shows little evidence of protein (peptide bands) but that the peptide band is strong in

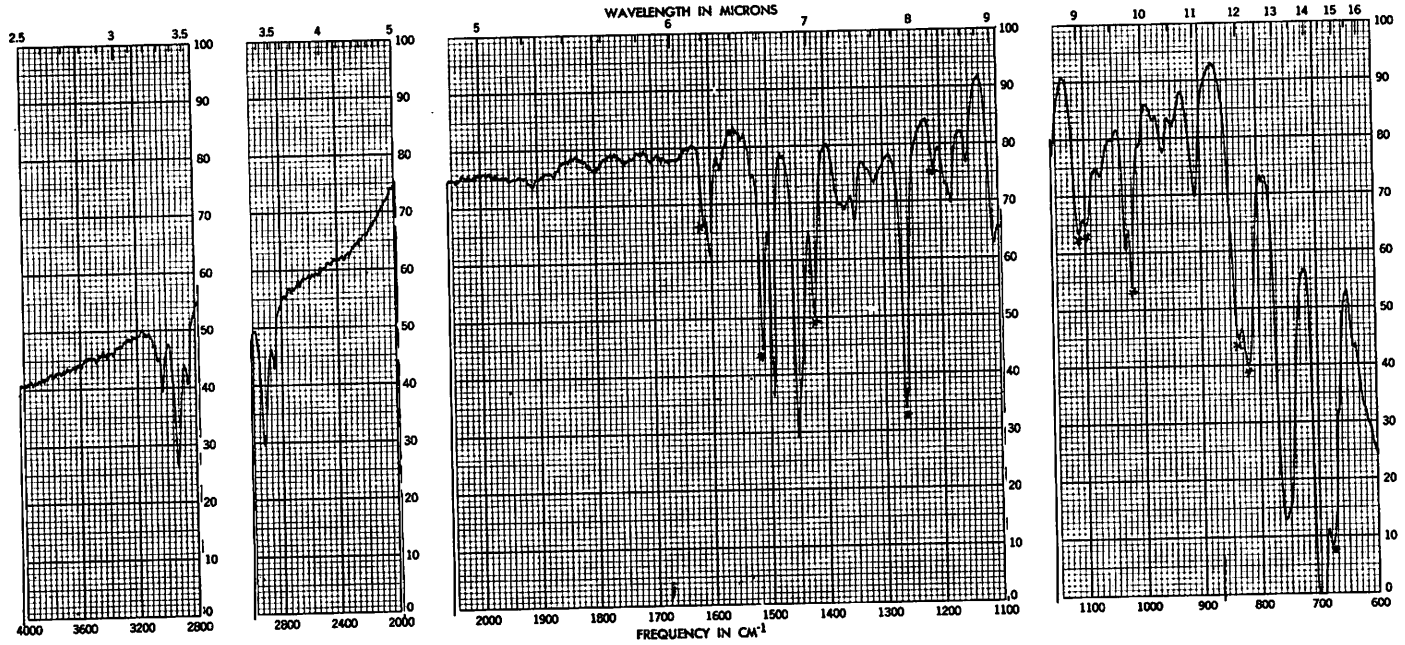


Figure 1. MATR Infra-Red Spectrum of Chloromethylated Polystyrene. Characteristic Chloromethyl Bands are Present. The Decrease in Intensity of Some of the Polystyrene Bands Indicates Para Substitution of the Aromatic Ring.

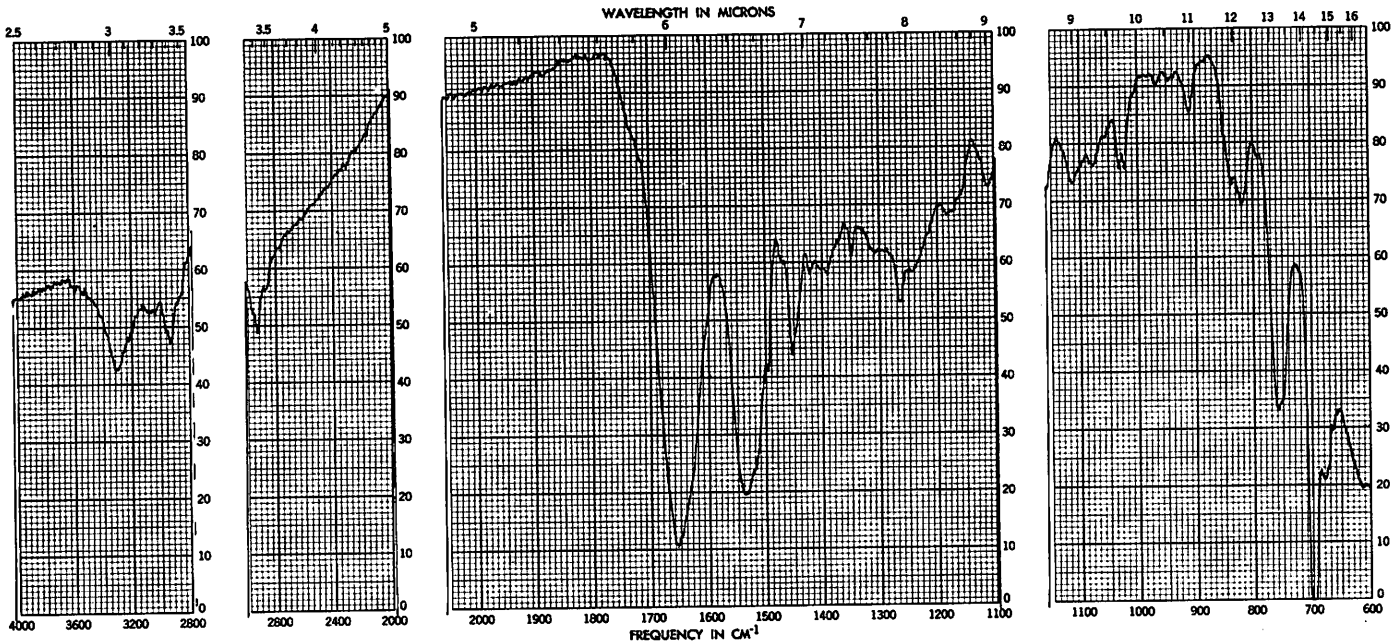


Figure 2a. MATR Infra-Red Spectrum of Albuninated Polystyrene. The Spectrum is Essentially That of Chloromethylated Polystyrene With Some Protein Bands Superimposed on it. The Peptide Absorption Band at About 1650 cm^{-1} is Particularly Evident.

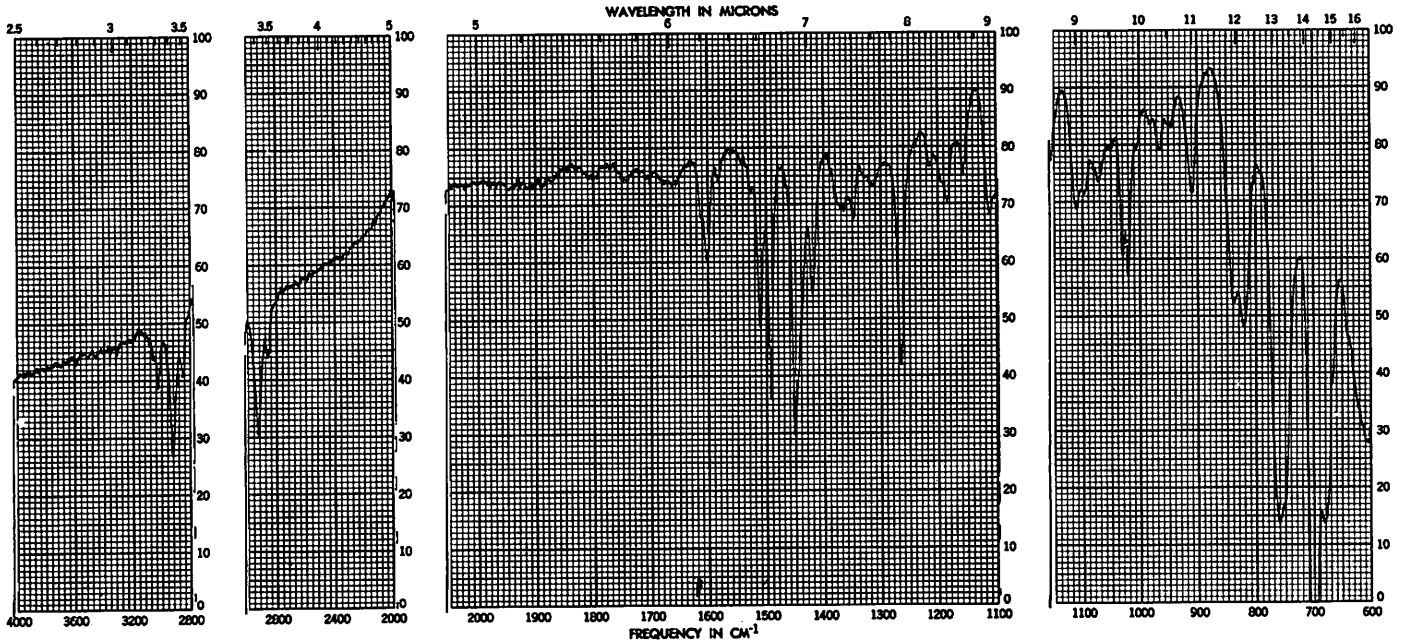


Figure 2b. MATR Infra-Red Spectrum of a Control Sample of Chloromethylated Polystyrene. This Sample was Treated in Exactly the Same Way as That in Figure 2a, Except that the $ZnCl_2$ Catalyst was Replaced by NaCl. There is no Evidence of Protein. The Spectrum is Essentially That of Chloromethylated Polystyrene (Fig. 1).

the treated samples. The treated samples also show a decrease in intensity of the C-Cl bands, indicating Cl^- displacement and protein bonding.

The reactions described above were performed on vena cava rings under sterile conditions and shipped to Dr. Vincent Gott in sterile saline. Control and treated rings were implanted in dogs[33] for acute (2 hour) and chronic (2 week) tests. The acute tests showed that the control rings were thrombosed; the treated rings were essentially free of thrombus. Of the four rings submitted for chronic testing, two were completely free of thrombus, and two "...had relatively minimal thrombus."[38] The non-thrombogenic behavior of this albuminated polystyrene thus appears to be about as effective as a heparinized surface.

In vitro tests were not performed. The problems and artifacts produced in conventional in vitro clotting tests, probably by the transfer of denatured protein monolayers to the test surfaces, make such tests unreliable, unless the air/blood interface is completely eliminated.[19]

The actual nature of the albuminated polystyrene surface described here is not known. It is a rough surface, as the nitrobenzene attacks the polystyrene surface during the chloromethylation reaction. The surface obviously contains a great deal of protein, as evidenced by the MATR spectra. Whether that protein is in its native form or not is not known; it may be complexed with zinc ions. The surface may even consist of protein fragments, though this is doubtful, as the reaction conditions are

not particularly severe. The biological half-life of such a surface is not known.

A mechanism for the non-thrombogenic behavior of the surface is not known. Perhaps it is due to the innocuous nature of albumin, discussed earlier. Lyman has shown[9] that surfaces precoated with a layer of undenatured protein do not adsorb platelets, while those containing a denatured layer do adsorb platelets. If the albuminated surface consists of undenatured albumin, then Lyman's results may explain the non-thrombogenic behavior of albuminated polystyrene.

Another possible explanation lies in the water-containing or gel-like nature of a proteinated surface. This mechanism is discussed in Chapter III, as it is dependent on the adsorption model developed in that chapter.

B. Protein Adsorption by Fluorescence Microscopy

The coagulation of blood has been discussed as a surface energy-dependent process.[39] If this is so, then microscopic changes in surface energy might have significant effects on the overall behavior of the materials. Both Lyman [39] and Merrill [23] have mentioned this possibility. Studies of polymer morphology have clearly shown striking differences in surface energies (see the discussion of the polymer surface in Chapter III). Therefore, it was of interest to look at protein adsorption on a microscopic level to see if there was any correlation between adsorp-

tion and surface morphology. Only two techniques appeared to be suitable to detect adsorption at the microscopic level with the sensitivity necessary to detect a monolayer: fluorescence microscopy [40, 41] and microautoradiography. [42] The former was chosen, largely because of convenience. It will be shown that the fluorescence microscopy method left much to be desired.

The study of protein adsorption on a microscopic level places severe limitations on the techniques which can be used. The microscopic requirements requires that the technique be compatible with microscopic observation. The low concentrations involved* require that extremely sensitive techniques be used. The concentrations* are at the limit of detectability of both fluorescence microscopy and microautoradiography. The microautoradiography method would require long exposure times, even with proteins of high specific activity. Also, radiolabeled proteins were not commercially available. Thus the fluorescence microscopy technique was selected. It was also felt that if the method proved successful, it might be used with specific fluorescent antibodies; thus studies of competitive adsorption of proteins could be undertaken.

* The projected areas of albumin for side-on and end-on orientations are about 4,600 A^2 and 1,700 A^2, respectively.[19] If one considers a monolayer of adsorbed albumin, a one micron square area of surface would contain about 6,000 molecules in the end-on orientation, which is 10^{-19} moles or 7×10^{-15} grams; in the side-on orientations, only 23,000 molecules could be accomodated, giving 4×10^{-20} moles or 3×10^{-14} grams.

The properties of a protein are relatively unchanged after conjugation with the highly fluorescent molecule, fluorescein isothiocyanate (FITC). Changes in solubility, net charge, stability, and molecular size and shape are slight, though there can be a 1 to 2 percent increase in molecular weight. FITC is not a small molecule, and there may be up to 10 FITC molecules conjugated to each molecule of protein,[40, 41] thus one might expect significant changes in surface properties. The results with fluorescent antibodies do not tend to bear out this suspicion, however. Antibodies conjugated with FITC and other fluorochromes retain their antigenic specificity. The interaction between a protein and its antibody is very subtle and sensitive. If fluorescent conjugation does not significantly affect such interactions, it can probably be assumed that solid surface interactions will also not be significantly affected, though the possibility must be kept in mind.

FITC-conjugated bovine albumin, gamma globulin, and fibrinogen were obtained from Mann Research Labs.[37] The material was conjugated by the Rinderknecht technique [43] in phosphate-buffered saline.[40] The buffer system may have been a poor choice as it is known to have a desorption effect on denatured albumin.[44] It is also quite probable that the rapid Rinderknecht method may yield a lower degree of conjugation than slower methods.

A drop of protein solution was placed on a freshly prepared polymer film in an inverted Petri dish. After adsorption times of $\frac{1}{2}$ to 2 hours the

drop was washed off with distilled water, quickly dried, and stored in a clean container until examined.

The filter system chosen was that recommended by Goldman.[45] The exciter filter was a UV-blue transmitting Schott BG-25 filter[46] coupled with a heat absorbing filter. The blue excitation light then excited fluorescence in the specimen. The barrier filter was a single piece of Kodak Wratten No. 12 gelatin, followed by a clear Wratten 2B to absorb the UV component which is transmitted by the No. 12 filter. The arrangement is given in Figure 3.

The optimum excitation system was found to be transmitted light dark-field illumination, which prevents most of the excitation light from entering the objective; the barrier filters need not be as absorbent, therefore, as for bright field illumination. The use of a reflected light excitation system was inferior to the above, largely because of absorption in the half-silvered mirror. At first a 150 watt xenon arc was used unsuccessfully; a 200 watt high pressure mercury arc proved somewhat better.

After proper alignment and adjustments, the sample was placed on the inverted microscope stage and an interesting morphological field was selected. The initial observation was performed with a Wratten No. 15 filter in the light path to prevent excitation of the sample. The No. 15 filter was then replaced with 3 mm of BG-25 and the fluorescence observed in a dark room under a photographer's cloth.

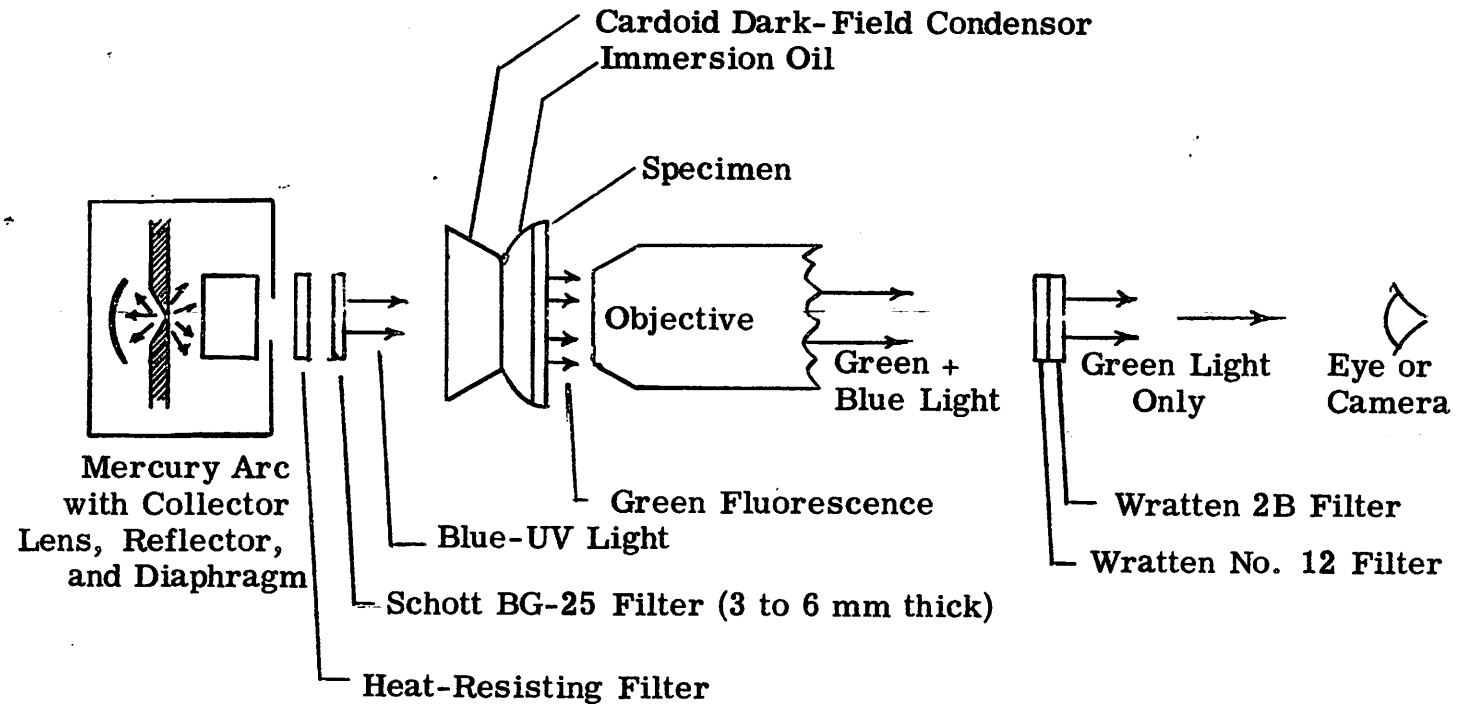


Figure 3. The Optical Arrangement for Excitation and Observation of Fluorescently Labeled Proteins.

Extensive evaluation tests were conducted with fast negative films and developer combinations—none was as satisfactory as Polaroid's "Polascope" film (ASA rated at about 10,000), not even Kodak 2475 and 2485 high-speed recording films, even with extensively forced development. The fast Kodak films are panchromatics and apparently could not respond as well to the green fluorescence (about 5250 A) as the Polaroid film could.

Unfortunately, even the Polaroid film could not successfully record the very faint fluorescent images which resulted. The images were barely observable by eye but not with sufficient clarity or resolution to relate the results to the morphology of the sample. An image intensification system might have made it possible to record the results, but the resources for such an expensive system were not available. A more important problem was that in many cases the polymer itself was fluorescent, probably due to commercial additives; in a few cases (a commercial polypropylene) the polymer fluorescence was so intense that it was literally blinding. Extraction of the polymer (in hexane, for example) succeeded in removing much of the fluorescence, but never all of it. In nearly all cases the fluorescence remaining was greater than the contribution from adsorbed protein. In addition to contamination with additives which may be fluorescent, polymers are known to adsorb organic compounds from the atmosphere; the behavior can result in highly fluorescent species on the surface.[47] In practically all cases these fluorescent

artifacts completely overwhelmed the contribution due to adsorbed protein.

It was thus clear that the fluorescence microscopy technique was an unsatisfactory choice, and the effort was abandoned.

CHAPTER III

A MECHANISTIC MODEL OF ADSORPTION ONTO APOLAR POLYMER SURFACES

A. Background

1. The Polymer Surface:

The clean polymer surface is generally considered to be a relatively homogeneous structure with quite reproducible surface properties. Detailed surface studies of the wetting properties of high polymers have justified this assumption;[48] but there is now a growing body of evidence to indicate that polymer surfaces may not be as homogeneous as previously suspected.[49]

The crystallinity of high polymers is now firmly established, and several monographs on the subject are available.[50, 51] The crystallinity of polymers can vary from 0 percent, as for atactic polystyrene, to in excess of 90 per cent, as for polytetrafluoroethylene. The degree of surface crystallinity of polymers has recently been shown to strikingly affect their surface properties.[52, 53]

The characteristic mode of growth of crystalline polymers from the melt and viscous solutions is spherulitic. The spherulite is considered to grow from some nucleus, possibly a tiny single crystal;[51] nucleated heterogeneously on particles or on a substrate. Because of viscosity effects and temperature gradients, the single crystal cannot continue to grow, and the growth degenerates into lamellar fibrils.

The lamellae tend to grow radially from the nucleus, producing a structure of spherical symmetry whose growth rate tends to be a linear function of time. The spherical symmetry results from non-crystallographic branching of fibrils (groups of adjacent lamellae) at an unstable growth interface.[54, 55]

Commercial crystalline polymers (polyethylene, polytetrafluoroethylene, polypropylene, cellulose, nylons, etc.) are normally composed of very small crystallites, generally unresolvable in the optical microscope. Nevertheless, though the surface of a crystalline polymer may appear homogeneous to a macroscopic contact angle drop, it certainly must appear heterogeneous to a microscopic protein or a simple compound. Amorphous polymers and elastomers may be relatively homogeneous, e.g., polystyrene, polymethylmethacrylate, etc.

Zisman[48] has related the surface energy of polymers to their chemical constitution by detailed studies of their wetting properties. He obtains a quantity called the "critical surface tension," γ_c, which is probably closely related to the surface free energy. The range for common polymer surfaces is from about 18 or 19 dynes/cm for polytetrafluoroethylene to 46 dynes/cm for 6/6 nylon.[48]

It is reasonable to expect that the different faces of a polymer single crystal or lamella will have different surface energies. Hoffmann[56] estimates that the lateral surface energy is about 10 ergs/cm^2

and the energy of a fold surface is 57 ± 5 ergs/cm^2 for polyethylene; Keller[57] believes that a significantly higher value is more accurate. The energy of a "typical" polyethylene surface is probably some average of the two, possibly close to Zisman's[48] γ_c value of 31 ergs/cm^2. Hoffman[56] also gives data for polychlorotrifluoroethylene, where the lateral energy is 4 ergs/cm^2 and the fold surface energy is 40 ergs/cm^2; Zisman's γ_c for this polymer is also 31. Thus the γ_c value does not necessarily shed light on the energies of the crystallites.

Polymer single crystals are microscopic and have not been grown in large enough sizes to allow one to use contact angle techniques for surface energy determination. Because of their lamellar nature, however, single crystals can be allowed to deposit from dilute solution to form an aggregate with the C-axis fairly well oriented perpendicular to the aggregate surface. Schornhorn and Ryan[58] have studied the wettability properties of polyethylene single crystal aggregates by contact angle measurements. The aggregates were highly crystalline. Their value for the surface of polyethylene single crystal aggregates is 53.6 dynes/cm^2. As the surface of an aggregate must be almost completely composed of fold surfaces, their results are in excellent agreement with Hoffman's[56] value of 57 ± 5. It is thus clear that the surface energy of a crystalline polymer is not only a function of its chemical nature but is also a function of how the molecules are oriented.

Polymers are usually cast or molded against low-energy surfaces

which tend to reduce sticking. As the polymers crystallize, the low molecular weight or impurity species are rejected from the growing crystal.[54,55] A polymer crystal thus tends to be surrounded by uncrystallized material, which is probably why γ_c and other surface properties are not particularly sensitive to crystallinity or bulk density.[58,59] If the polymer is cast against a high energy substrate, which can furnish many heterogeneous nucleation sites, its surface properties are different from those of conventionally formed polymers. This has been demonstrated by Schornhorn in several papers.[52,53] He studied the surface properties of both crystalline and non-crystallizable polymer surfaces prepared by melting on both high energy (gold) and low energy (nitrogen gas) substrates. A portion of his data is given in Table I.

TABLE I

SURFACE PROPERTIES OF POLYMERS

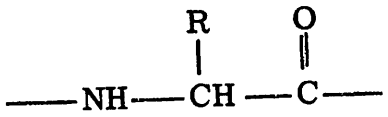
NUCLEATED AGAINST GOLD SUBSTRATES[53]

Polymer	Bulk Density	$(\gamma_c)_{N_2}$	$(\gamma_c)_{AU}$
1. Polyethylene	0.95	35	69.6
2. 6/6 Nylon	1.14	46	74.4
3. Polychlorotrifluoroethylene	2.12	31	58.9
4. Polypropylene (Isotactic)	0.90	29	39.5
5. Polypropylene (Atactic)	0.86	29	28.0

The surfaces of crystalline polymers are not necessarily homogeneous. The surfaces of a crystallite can have energies significantly different than the "amorphous" surface. An even greater energy difference exists between the lateral and fold surfaces of crystallites. The assumption will be made that a polymer surface consists of randomly arranged molecules, though the effect of different surface orientations will be qualitatively discussed.

2. Proteins:

A protein is a complex, highly structured, nylon-like copolymer to which many of the principles of polymer chain statistics are not applicable. A protein can contain up to about twenty different monomer units, called amino acids, each linked together by a peptide bond with its very prominent hydrogen-bond forming properties. The mer unit can be represented as



where R can be any of twenty different groups, some acidic, some basic, others hydrophobic. These are discussed in all biochemistry texts. The amino acid sequence of a protein is termed its primary structure. The alpha-helix conformation along many portions of the chain, resulting primarily from hydrogen bonding between the peptide linkages, is called the secondary structure. If one folds and fastens the protein back on

itself at several points, by disulfide linkages, hydrogen bonding, and hydrophobic interactions, a three-dimensional configuration of the chain is obtained. This is the tertiary structure. Finally, to further increase the complexity, most proteins are composed of two or more chains bound together into a complex quaternary structure.

The great variability of properties among different proteins and the phenomenal specificity exhibited by many of them is due largely to their fragile and complex tertiary and quaternary structures. The fragile structure can be stabilized or disrupted, depending on the ionic environment of the protein solution. The ionization tendencies of the various pendant groups depend on the pH of the medium. The pH of plasma is approximately 7.4. Buffer systems are employed in the body and in biochemical preparations to keep the pH constant. A very important property of a protein is its isoelectric point (IEP).

> The total charge on a protein molecule depends on the pH of the solution and the relative number of each kind of amino acid in the molecule. When the net charge density of the molecule is zero, that is, when total negative and positive charges effectively neutralize each other, the protein will not migrate in an electrical field, and that pH is its isoelectric point (IEP). At a pH alkaline to its IEP, the protein will carry a negative charge; at a pH acid to its IEF, the protein will carry a positive charge.
>
> Ref. 60, p. 41.

The fact that water tends to avoid apolar groups (discussed in the next section) while it is drawn to charged or polar groups leads to some important results. When a flexible molecule containing both hydrophobic

and hydrophilic groups is dissolved in water, the molecule assumes a stable configuration where its hydrophobic groups tend towards the center of the molecule (away from the water), while the hydrophilic groups are on the surface, nearest to the water. The hydrophobic groups can only interact with water by dispersion forces. These forces cannot compete with hydrogen bonding, and therefore water tends to "stay together" rather than interact with hydrocarbons. The situation is different at an interface, as now the force field is asymmetric and the London interactions are very significant.

The various side chains of amino acids have different ionization tendencies. Several of the groups have their isoelectric point around pH 7 and may be either charged or uncharged; acidic groups are negatively charged, basic ones positively charged. At pH 7 there are two amino acid residues which are negatively charged (acidic) and two that are positively charged (basic), in addition to the acid terminal of the peptide chain. The amino terminals may be either positively or negatively charged. The net charge and charge distribution of a protein molecule and its consequent dipole moment at pH 7 will be primarily dependent on the number and distribution of four different amino acids.[61] Amino acids capable of hydrophobic bond interactions are indicated by an AP notation in Table II. The other amino acids are assumed to be hydrophilic (P), except for glycine. For those amino acids which are charged at natural pH, the charge is given in parenthesis in Table II.

TABLE II

PROPERTIES OF SOME SELECTED PROTEINS[36, 68]

Amino Acid Composition (Moles/mole protein)	P or AP*	Albumin	Gamma Globulin	Fibrinogen	Ribonuclease
Lysine (+)	P	56	87	214	10
Arginine (+)	P	23	41	153	4
Aspartic Acid (-)	P	52	107	336	5
Glutamic Acid (-)	P	81	140	336	5
Amide NH_3	P	38	146	30	17
Glycine (*)	*	12	94	236	3
Alanine	AP	62	72	142	12
Valine	AP	41	131	119	9
Methionine	AP	5	10	59	4
Isoleucine	AP	8	30	125	3
Leucine	AP	60	102	184	2
Phenylalanine	AP	30	47	95	3
Histidine	P	15	27	57	4
Threonine	P	28	114	175	10
Serine	P	24	178	230	15
Proline	AP	25	100	169	4
½ Cystine	P	33	34	77	8
Tyrosine	P	16	62	104	6
Tryptophan	?	1	33	55	0
Total Carbonate		0.08%	2.9%	2.5%	---
N Terminals		Asp. Ala	Asp. Gly	Ala	Tyr Lys
C Terminals		Leu. Ala Val. Gly	Ser. Gly	-----	Val
Molecular Weight		69,000	160,000	340,000	14,000
Isoelectric Point (pI)		4.9	5.8 to 7.3**	5.8	9.4
P/AP Ratio*		1.58 (1.52)	1.58 (1.31)	1.92 (1.52)	2.27 (2.10)
Approximate Net Charge @ pH 7		-54	-119	-300	+4

* Glycine is often considered to be apolar, though steric effects would greatly inhibit its hydrophobic interactions. The P/AP value is calculated ignoring glycine; the value in parentheses considers glycine as apolar.

**The pI of the gamma globulins varies with the protein fraction tested. Many ionizable groups are no doubt immersed in the interior of the molecule for some configurations and thus cannot contact the solvent and ionize.

Table II presents data for ribonuclease and for the common plasma proteins albumin, gamma globulin, and fibrinogen. The structure of the plasma proteins is not known, nor are the exact amino acid sequences. The polar (P)/apolar (AP) ratios are also given in Table II. These ratios have been used by Ghosh[62] and Vroman[18] and may indicate the protein's tendency to adsorb by hydrophobic interactions. The P/AP ratio is determined by adding all the amino acids in the chain capable of polar interactions and dividing by the total number capable of only apolar (dispersion) interactions. The probable net charge at pH 7 is also given in the table.

The various properties of the plasma proteins have been succinctly reviewed by Putnam.[63]

Albumin is an ellipsoidal globular protein, usually considered to have an axial ratio of about 6:1. It is composed of a single polypeptide chain containing 16 to 18 disulfide bridges.[63] These bridges must all be intramolecular links tying and knotting the chain together; this accounts for albumin's stability. Albumin has a high concentration of acidic and basic amino acids and must therefore be quite polar, though its P/AP ratio indicates a significant number of hydrophobic residues. There is some evidence that albumin may have a somewhat hollow cylindrical shape.[64] It also has a strong tendency to dimerize,[63] which could indicate some type of mirror image charge distribution or structure.

The gamma globulins are a group of proteins which all have relatively similar solubility and electrophoretic properties. Their structure is commonly considered to be ellipsoidal and globular with a slightly greater axial ratio than albumin. "They have been considered to be a family of proteins, varying continuously, subtly, and ineluctably in their properties." (Ref. 63, p. 229). The gamma globulins have a relatively low alphahelix content, thus their structure is probably quite disorganized with respect to proteins of higher alphahelix content. Their folding into a compact configuration may be due to hydrophobic rather than hydrogen bonding.[63] The low alpha-helix content is in part due to the high proline concentration; proline cannot fit into an alpha helix. Gamma globulins also have an unusually large proportion of -OH containing residues (serine and threonine). Though they have over double the molecular weight of albumin, they have about the same number of disulfide bridges. Thus, the gamma globulins must have a structure which is capable of subtle changes in response to subtle influences. The structure is not encumbered by alpha-helices or by an excessive number of disulfide bridges, yet is is capable of extensive polar and dipolar bonding. The number of peptide chains in a typical gamma globulin is not well established,[63] but it is believed to consist of two small and two large polypeptide chains.[36]

Fibrinogen is a very large nodular or rod-like protein. The entire coagulation cascade appears to serve only to catalyze or modify fibrinogen so that it can polymerize with itself to form fibrin polymer, the network of a blood clot. It has been widely studied, mainly because of its importance in blood coagulation; an entire book is devoted to this one protein.[65] Fibrinogen appears to be composed of three pairs of polypeptide chains, each of molecular weights of about 50,000 to 65,000. Dipole moment measurements indicate "...a very high degree of charge symmetry with respect to the long axis of the molecule. The most likely arrangement, therefore, is mirror-image-like halves on both sides of the center of the molecule!" (Ref. 66, p. 69). Fibrinogen may have a very high water content, thus estimations of its shape vary greatly depending on the technique used and the assumptions made. The length of the molecule in solution is probably around 600 A;[66, 67] though electron microscope work gives a value of about 475 A for the dehydrated protein.[66] Electron microscope observations show a long needle-like structure with a nodule on each end and in the center; this structure is illustrated later in Figure 25. The nodules appear to be able to rotate, both perpendicular and parallel to the long axis. The structure can be summarized as "... Three nodular formations connected by loose, sponge-like segments" (Ref. 66, p. 84). About one-third of the chains are in the alpha-helix configuration. Fibrinogen is also known to dimerize.

3. Adsorption:

a. Introduction

A surface is a discontinuity. A surface is defined wherever a phase terminates. The phase may terminate in a vacuum or at the surface of another phase. The surface formed where two phases meet and terminate is an interface. The concept of a surface is, in most instances, really that of an interface. Perhaps the most complete and up-to-date treatment of surface science is given by Adamson.[69] Fowkes' comprehensive and recent review [70] and Davies' and Rideal's Interfacial Phenena[71] are also very useful. Treatments of interfacial energies and forces are more difficult to find: the American Chemical Society's Chemistry and Physics of Interfaces[72] is one of the most readable expositions, particularly the paper by Fowkes.[73] Good briefly deals with the subject in his review[74] and treats it in detail in his papers;[75-8] Fowkes' other papers also treat it.[79-82]

The attraction of the molecules in the surface layer of a liquid by the bulk phase results in a decrease in the number of molecules in the surface region, thus increasing the intermolecular distance on the surface; the result is a surface tension. Usually the surface tension or energy resides in the outermost layer, but in some systems there are contributions from the second and third layers. The forces responsible for the surface tension are the intermolecular forces which will be discussed. In the case of water, there are London dispersion and hydrogen-

bonding (dipole-dipole) attractions. Following the principle of additivity of intermolecular forces,[83] the interfacial tension, γ can be written as:[73]

$$\gamma_{water} = \gamma^{London}_{water} + \gamma^{hydrogen\text{-}bonding}_{water} \quad .$$

Consider the interaction between water and a saturated hydrocarbon. The only intermolecular force available for the interaction of hydrocarbons with themselves or other uncharged species is the dispersion force. The interface between water and a hydrocarbon can be considered to be composed of two adjacent interfacial regions; the sum of the surface tensions of the two regions gives the overall interfacial tension. The hydrocarbon molecules at the interface are not only attracted by their bulk phase, but they are also attracted by the dispersion interactions of the other phase. Therefore molecules at an interface between two different phases are in a different environment than those at the surface of a single phase. The molecules at the interface are not only involved in intermolecular interactions with their own kind, but they are also interacting with the molecules in the adjacent phase. The result is that the interfacial tension must be lower than the surface tension of water itself.

Adsorption is an interfacial process. It is generally defined as a surface excess of some component in or near an interface. The interfacial region can be treated as a separate phase with its own thermodynamic properties. This approach was pioneered by Gibbs (see Ref. 69)

and has been exhaustively developed.[3]

Interfaces can be divided into two general types: condensed-phase/vapor and condensed-phase/condensed-phase. Adsorption can also be divided into two classes: physical adsorption and chemisorption. Physical adsorption refers to interactions other than direct chemical bonds, while chemisorption is due to actual chemical bonds. There is a wide overlap between the two types; an excellent discussion is given in Chemisorption.[84]

Adsorption data is usually treated in terms of an adsorption isotherm, which is a plot of amount of material adsorbed against the concentration in solution; the data are taken at constant temperature and after equilibrium has been established.

The adsorption of gases on solids or liquids has been treated by a consideration of intermolecular interactions,[85,86] but adsorption from solution has been deprived of such mechanistic treatments and has had to depend on thermodynamic analyses. This is understandable, as a treatment of adsorption from solution in terms of inter-molecular interactions is complicated by solvent-solid and solute-solvent interactions. A more difficult problem is posed by considering adsorption from solution at the solution/air interface: how can intermolecular interactions account for such adsorption? The air certainly cannot significantly interact with the solute molecules. Thus one must resort to a consideration of solute-solvent interactions to attempt to explain the phenomenon.

This is the basis of the mechanistic model of adsorption from solution which will be presented and developed in the next chapter.

b. Simple Compounds

The surface tension of water is 73 dynes/cm. Addition of a second component to pure water usually results in a decrease in the surface tension. The decrease is due to solute adsorption at the air/water interface. Thus a measure of surface tension as a function of solute concentration is an indication of adsorption. Such surface tension isotherms are common in the literature. An example is given in Figure 4 for both surface-active and surface-inactive solutes. If the decrease in surface tension is due to the fact that some solute molecules are statistically in or near the interface at all times, thus affecting its properties, then the plot in Figure 4 should be a linear function of concentration (dotted lines). The surface tension should linearly decrease for a low-energy (surface-active) solute and should linearly increase for a high-energy (surface-inactive) solute. It is clear from Figure 4 that this is not the case. The surface tension drops very rapidly below the linear line (dotted) for the surface-active solute, indicating that a concentration of solute builds up at the surface or adsorption of solute occurs. For the surface-inactive solute, the line is below that expected for a linear increase, indicating that a surface deficiency of solute exists or negative adsorption occurs.

It has been suggested that adsorption at the water/air interface can be divided into two processes,[21] the diffusion of solute to the vicinity of

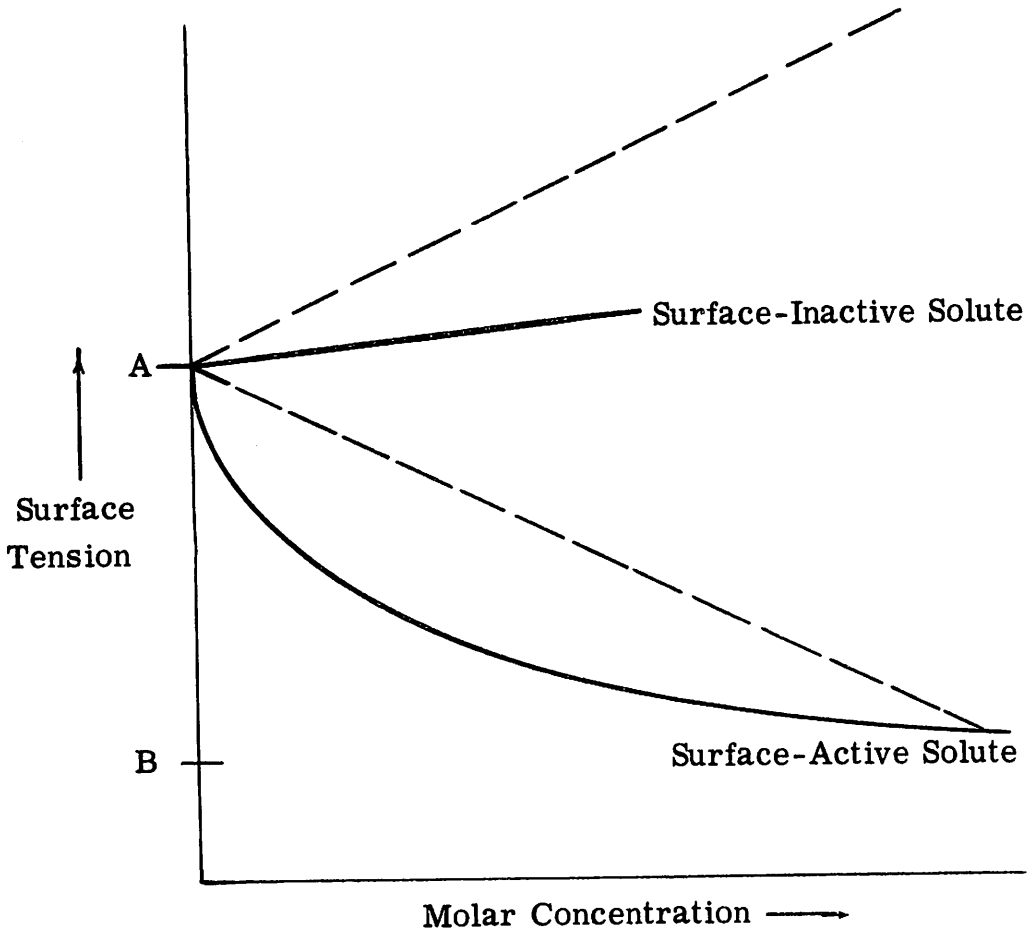


Figure 4. Hypothetical surface tension—concentration isotherms for surface-active (low energy) and surface-inactive (high energy) solutes (after Ref. 60, p. 211). A represents the surface tension of the solvent (73 dynes/cm. for water): B represents the surface tension of pure solute.

the interface, and the actual adsorption and orientation of the solute at the interface. The adsorption process tends to be very rapid for relatively small molecules, but becomes quite slow for larger molecules, probably due to the slower diffusion rates. Protein adsorption at the water/air interface often takes several hours or longer to equilibrate.

Though most of the adsorption occurs in a very short time, there is usually a small increase in adsorption for a long time before equilibrium is attained. One suggestion[21] is that the first molecules arrive at an empty surface and are free to orient and adsorb while later arrivals have more difficulty finding a place. Thus, the process should slow down rapidly when the surface is nearly completely covered, as observed. It is probable that adsorption at the liquid-air interface may continue to occur after an adsorbed layer has formed, particularly if the solute molecules can significantly interact with each other. Multiple layers are not, however, detectable by the more common techniques of change in surface tension or surface potential. If enough material is present it can form a second phase, as with oil films on water.

If the solute molecules are capable of extensive intermolecular interaction among themselves and with the water, as for stearic acid, the adsorbed molecules may form a stable, insoluble monomolecular film. Monomolecular films are very intriguing and have been studied a great deal.[87]

Unfortunately, there has been very little work or discussion of the relationships between adsorption processes at different interfaces. Kipling has attempted some discussion;[21] but could draw very few conclusions. Adsorption at the liquid/air interface does appear to be preferential for that component which most reduces the surface tension, though the same generalization is not necessarily true for adsorption at the liquid/solid

interface. The amount of material adsorbed at a liquid/solid interface is often greater than at a liquid/air interface.[21] Also, adsorption at the solid/liquid interface can be highly specific. Polar adsorbents preferentially adsorb polar compounds; apolar adsorbents preferentially adsorb apolar compounds. Solvent competition effects are also very important.

A detailed discussion of the adsorption of simple compounds will be given in Section C. 2.

c. Polymer Adsorption

The principles of polymer adsorption have been well summarized by Ullman and coworkers;[88] a recent review[89] is also available, as is a chapter in Kipling's book.[21] The general principles noted above for simple compounds also apply to polymers. Their large molecular weights tend to make interpretation of data more difficult.

Molecules of synthetic polymers in solution tend to assume a random-coil shape unless there are strong polymer-solvent interactions or strong interactions between portions of the polymer chain.

Polymer adsorption on solid surfaces tends to follow a Langmuir isotherm, implying monolayer formation. Data on the amount of polymer adsorbed clearly show that much more than a flat monolayer adsorbs, thus the monolayer must be composed of relatively random coils. The amount of polymer adsorbed is a function of molecular weight, increasing

with increasing molecular weight. Polymers are not homogeneous because of their molecular weight distribution. Thus, polymer adsorption produces a fractionating effect, because the higher molecular weight material is preferentially adsorbed. Polymer systems give good evidence of competitive adsorption. Kipling[21] cites data where low molecular weight species are adsorbed first, and then displaced by the more strongly interacting high molecular weight component.

Though initial polymer adsorption is relatively rapid, equilibrium is often not attained for weeks or months. Polymer adsorption is somewhat irreversible in that it is difficult to desorb polymers from a polymer surface. This is interpreted as due to the statistical improbability of breaking all of the many polymer-surface interactions simultaneously.

There has been little work on polymer adsorption from aqueous solutions due to the inherent insolubility of polymers in water. The adsorption of synthetic polyelectrolytes has been studied. Lauria's study[90] which included adsorption on polystyrene beads, utilizes the conventional techniques of high surface area adsorbent and solution concentration changes. His data seem "...to fit a type of Langmuir isotherm with repulsion between the adsorbed units." (Ref. 90, p. ix)

Polymer films at the liquid/air interface have been well studied and reviewed[87 91-2] If the polymers contain both polar and apolar groups, stable monomolecular films can be formed. Most of the work has dealt

with spread films rather than adsorbed films and is not applicable to our purposes.

Most of the various theories of polymer adsorption[89, 93] are concerned with the state of the polymer molecule at the interface, and not with how it got there. A very recent review of polymer adsorption theories has been given by Stromberg.[93]

d. Protein Adsorption

The adsorption of proteins has been reviewed by Cumper and Alexander[94] and by James and Augenstein.[95] The latter review is much more recent and is devoted primarily to enzyme adsorption. A wealth of information is available on protein monolayers at water/air interfaces.[87] Most of the data are given in terms of pressure-area isotherms, thus multi-layer adsorption is usually ignored. The adsorption studies at solid-water interfaces have usually been on adsorbents of high surface area using the conventional methods, which are questionable in the case of protein solutions because of their tendency to denature (see below) at air interfaces.

Proteins at an air/water interface are denatured, that is, their complex tertiary structure is disrupted. The polar regions interact strongly with the water, and the apolar regions are "rejected" by the water phase. Denatured proteins tend to be insoluble and to form monomolecular layers. Protein monofilms can yield much information about molecular weight, structure, activity, and other properties, and are

often purposefully prepared. Here the only concern is with adsorption from solution; films formed by gently depositing protein solutions onto a water surface will be ignored. Practically all the isotherms available for the air/water interface are film-pressure isotherms and are thus difficult to relate to other data.

When there is a relatively small amount of protein at the interface (less than 1 $mg./m^2$), the film is dilute[95] and essentially completely unfolded (denatured). In compressed films all of the molecules are not necessarily denatured, and some unfolded, intact proteins are usually present. The most reasonable model of protein films is the duplex model.[95] This states that the first molecules to arrive are probably denatured and a denatured monofilm is formed. Cumper and Alexander believe that "...surface denaturation of each molecule as it reaches a clean interface must be an almost instantaneous process," (Ref. 94 p. 134). As additional protein molecules arrive, they form undenatured multilayers. Other models are also available.[95] The tendency to form a monofilm is quite strong, as films can continue to form against an applied surface pressure.

Protein adsorption is always maximized when the solution pH is at the isoelectric point. At pH's away from the isoelectric point, adsorption is probably retarded by repulsive forces due to the charged protein molecules in the surface.[95] There is apparently a molecular weight effect as well, as the high molecular weight proteins form films less readily than smaller proteins.

There is evidence that only a small portion of a protein molecule need interact with a surface to enable denaturation to occur.[95] It is apparent that the formation of protein films is a slow process, as surface tension measurements do not approach a constant value until several hours after spreading. This is probably due to reorientation effects and more complete unfolding with time.

Denaturation at the oil/water interface is a function of the interfacial energy (about 73 ergs/cm^2 for the air/water interface). In systems where this energy is quite low, denaturation apparently does not occur. Adsorption does occur, however, but the molecules are probably in a more or less unmodified state. Adsorption at oil/water interfaces is more rapid than at air/water interfaces[95], but a satisfactory mechanism for this behavior has not been postulated.

There is a fundamental difference between solid/liquid and liquid/liquid interfaces. A liquid/liquid interface is relatively mobile, as both liquids are experiencing thermal motion, and their molecules are dynamic. Thus, it is relatively easy for an adsorbed molecule to orient at such an interface and even penetrate into one or both liquid phases. There is no such mobility at the solid/liquid interface. The methods of studying such an interface are also quite different, thus the results are not directly comparable.

Protein adsorption on solids tends to conform to the Langmuir isotherm, again implying monolayer adsorption of some type. Adsorption

from moderately concentrated solutions tends to produce films in which the proteins are not denatured and are probably in a relatively compact configuration. Adsorption from dilute solutions most likely produces a denatured film with an additional layer or two of weakly adhering intact molecules.[62,95]

Perhaps the surface most extensively studied is glass;[96] but the results are difficult to interpret. The variable nature of the surface of glass[97] is usually not considered in adsorption studies. Different surface treatments lead to strikingly different results.[95]

Much of the available work on protein adsorption stems from work on blood coagulation. It has long been known that blood coagulation occurs rapidly in glass containers but much more slowly on polymeric surfaces or paraffin-coated surfaces. This has led to the postulation of a surface-induced or surface-activated mechanism of blood coagulation, in addition to the intrinsic mechanism. These mechanisms are now fairly well established[6-8,98] though there is a great deal of controversy about the details within each mechanism. The two major theories are discussed by Vroman in a very readable little book;[1] in another work[99] they are synthesized by him in an adsorption model of coagulation as a sequence of protein-protein adsorption interactions. The activation role of the solid surface is believed to be due to the adsorption of a particularly surface-susceptible protein called Hageman Factor (after Mr. Hageman) and its resultant distortion.[100] This approach is not very satisfying, as Hageman Factor is present in

much lower concentrations in blood than many other readily adsorbable proteins. This puzzling situation has led to a great deal of effort to determine the true role of protein adsorption and surface-induced processes in blood coagulation. This work, and other more detailed adsorption studies, will be presented in Section C, where it will be compared against the model which will be developed in Section B of this chapter.

There are few studies where reliable and complete adsorption isotherms have been developed. The lack of a suitable model makes it difficult to put the available information in any sort of order or perspective.

4. Water:

The structure and properties of water play a fundamental and perhaps major role in protein-surface interactions? The most popular theory of water structure is the "flickering cluster" model first proposed by Frank and Wen in 1957 [101] and developed quantitatively by Nemethy and Scheraga.[102] The basis of the model is that hydrogen bond formation is a cooperative process, due to the acid-base nature of the bond.[101] When one bond forms, many tend to form; when one breaks, many break. Thus, small clusters are formed, constantly appearing and dissolving, whose lifetime is long enough to be physically meaningful. This model has been analyzed in depth, and its thermodynamic properties are

available.[102] The clusters are mixed with non-hydrogen bonded water molecules which are involved in dipole-dipole interactions. The Frank-Wen-Nemethy-Scheraga (FWNS) model accurately represents the known thermodynamic properties of water. It does not, however, account for the observed structural transitions in water.[103] One of these transitions occurs in the vicinity of body temperature and may eventually have a large significance in the understanding of body chemistry.

The other major theory of water structure is Pauling's model of water as a continuous clathrate or hydrate, though his model is not as popular as the FWNS theory. Pauling's model is visualized as a network of hydrogen bonded water cages, composed of 20 to 24 molecules and enclosing nearly spherical cavities in which a host molecule can be accomodated without disturbing the structure.[104] The host molecule does not collide with the cages and is in a symmetrical field, thus there is little hindrance to internal rotation. The host molecule may be a clathrate-forming atom, such as xenon, or it may be a water molecule.

Pauling has formulated a general theory of anesthesia[105] based on water-anesthetic interactions resulting in clathrate formation. The Pauling hydrate model has been thoroughly analyzed by Frank and Quist.[106] In their analysis the Pauling model is discussed in terms of flickering clusters of water cages.

The strong charge-dipole interactions between an ion and water dipoles produces a tightly bound and oriented hydration layer around an ion. The extent of this effect is dependent on the ion's polarizing power.[104] The hydration layer is rather rigid and at least one molecule thick. In addition to these relatively short-range effects, the electrostatic field of the ion can exert a torque on farther removed dipoles and thus interfere with structure-forming and structure-breaking. These effects are usually described in terms of the Frank and Wen[101, 107] multizone hydration hypothesis. In this model the ion is surrounded by two concentric zones: in the inner zone, the water molecules are oriented, immobilized, and compressed; in the outer zone, the water structure is disrupted and the molecules perhaps partially oriented. Outside these regions the water structure is relatively unaffected by the presence of an ion. Because of changes in the water structure, the dielectric constant near an ion is different then in the bulk. The value of the dielectric constant near the ion is not known, but it can be assumed that beyond eight angstroms it is essentially the bulk value.[104]

One might expect that the structure of water at an air/water interface would be well established. It is generally accepted that the surface of water is polar,[107-8] the oxygen portion pointing towards the surface and the hydrogens pointing toward the bulk. This arrangement is compatible with the high surface energy of water, but now there is evidence that the true arrangement might be just the opposite.[108]

It is well accepted that water tends to isolate apolar solutes, forming a more ordered structure around the foreign material, often called an "ice-berg." Such an arrangement minimizes the total energy of the system.[109] The tendency to reject or isolate apolar material has led to the concept of the hydrophobic bond.[102] Salem[110] has suggested that a more direct approach to an understanding of the hydrophobic bond may come from a consideration of intermolecular interactions. There is also evidence[107] that the water surface tends to exclude ions, as demonstrated earlier in Figure 4.

5. Intermolecular Forces:

The subject of intermolecular forces has been thoroughly treated in the book by Hirschfelder et al.[111] Shorter discussions have been given by Hildebrand and Scott;[83, 112] Margenau;[113] and Pitzer.[114] Several conference proceedings on intermolecular[115] and surface forces[116] are also available. Good's very recent review[74] neatly summarizes the subject and discusses some applications to solid polymers. Salem's papers[110, 116-119] review the nature of intermolecular forces and treat biological applications in a very lucid manner. Other discussions and reviews are also available[120,121]

Intermolecular forces can be artificially divided into short-range and long-range forces. The short-range forces are due to electron cloud overlap at very close separations, producing a repulsive force. Short-range forces are ignored here, as the separation distances which will be

considered will always be greater than several angstroms. The long-range forces can be divided into three major types: electrostatic, induction, and London dispersion forces. The electrostatic forces can be further divided into charge-dipole, dipole-dipole, and quadrupole interactions. Quadruple contributions will be ignored as they are usually negligible. [74] Intermolecular forces are responsible for deviations from ideal gas behavior and are, therefore, classed together under the general heading of Van der Waals forces, though often the term Van der Waals is used only in reference to London dispersion forces. These forces are not necessarily weak and may approach magnitudes of the order of chemical bonds.[74]

a. Electrostatic Interactions

The charge-dipole interaction energy, $U(Q - \mu)$, between two like particles is represented as:[111]

$$U(Q - \mu) = - (Q \cdot \frac{\mu}{r^2}) \cos \theta, \qquad (1)$$

where θ is the angle between r and the dipole axis, μ is the dipole moment, and Q is the charge. The expression for dipole-dipole interactions is more complex:[74]

$$U(\mu - \mu) = \frac{\mu_1 \mu_2}{r^2} [\, 2 \cos \theta_1 \cos \theta_2 - \sin \theta_1 \sin \theta_2 (\cos(\phi_1 - \phi_2))] \qquad (2)$$

where the angles are identified in Figure 5.

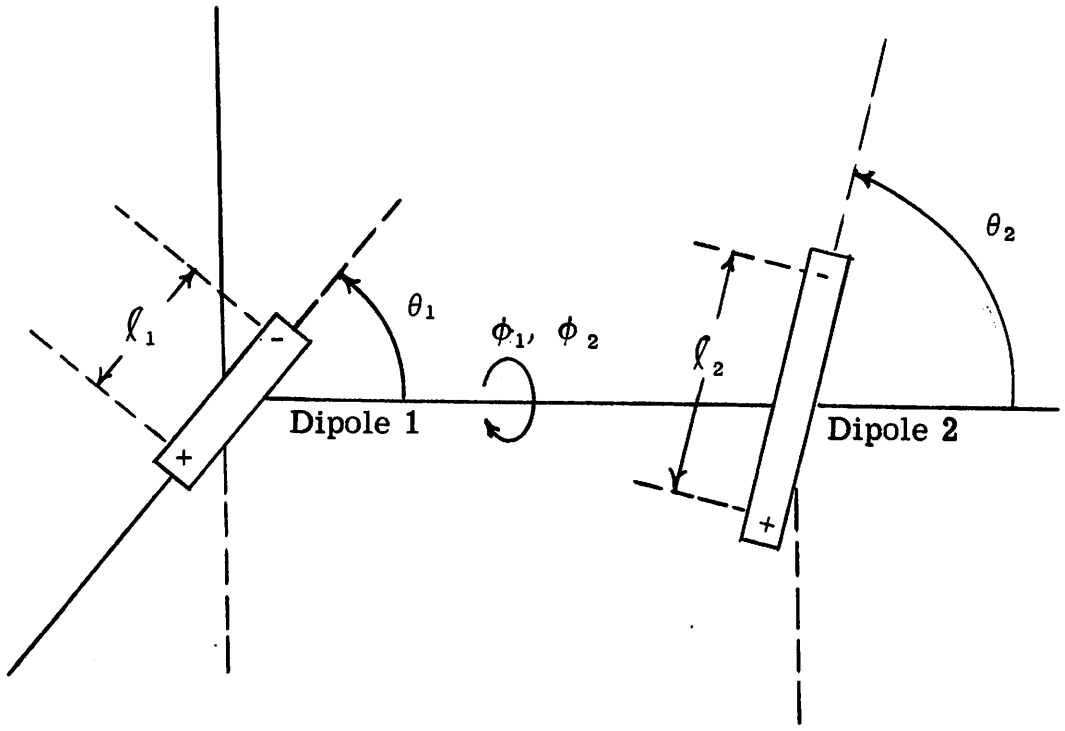


Figure 5. Orientation Relations Between Two Stationary Permanent Dipoles (After Ref. 74, p. 22).

If the two dipoles are free to rotate, they will assume the low energy head-to-tail configuration where all the angles go to zero, thus reducing equation (2) to:

$$U = -\frac{2\mu_1\mu_2}{r^3} \tag{3}$$

Equations (2) and (3) are obtained on the assumption that $\ell \ll r$. When this condition does not hold, the system cannot be treated as dipoles, and the interactions must be summed over the entire charge system. Hirschfelder[111] and Good[74] discuss the case where ℓ is not $\ll r$. When r/ℓ is less than 2.5, the expressions are in error by 25% or more.

The average distance of closest approach of two water molecules is estimated as 3.2 A.[102] The effective charge separation distance, ℓ, corresponds roughly to the C-H bond distance and can thus be estimated at about 1 A.[122] Thus r/ℓ is about 3.2 for water and r is sufficiently greater than ℓ to use the dipole expressions.

These expressions only apply to bi-molecular dilute gas phase interactions of molecules in fixed orientations. If the dipoles are free to rotate and the interaction energy is greater than the thermal energy of randomization, then there will exist a distribution of orientations with those of lowest energy predominating. The distributions are expressed by Boltzmann functions, and one obtains expressions for the average interaction energies; after expansion and simplification, the expressions reduce to[111,113]:

$$\overline{U}(Q - Q) = \frac{Q_1 Q_2}{r} \tag{4}$$

$$\overline{U}(Q - \mu) = \frac{1}{3kT} \frac{Q_1^2 \mu_2^2}{r^4} \tag{5}$$

$$\overline{U}(\mu - \mu) = \frac{-2}{3kT} \frac{\mu_1^2 \mu_2^2}{r^6} \tag{6}$$

where the $\overline{U}$ indicate time-average energies. Because of the requirements of the Boltzman expansion, equations (4-6) are only valid for relatively large separations, i.e., r must be greater than 3 A.

The hydrogen bond is often treated as a special type of inter-

molecular attraction,[74] but it is an unusually strong dipole-dipole interaction and can be treated in the same manner. For short hydrogen bonds, less than 2.5 A, there can be an appreciable covalent character to the bond (20 - 25%); this is usually negligible for bond distances greater than 2.8 A.[74] It will be treated as a strong dipole-dipole interaction.

b. Induction Interactions[111]

When a charge or permanent dipole interacts with a neutral molecule, a dipole moment is induced in the neutral molecule. The two species can then interact electrostatically:

$$U(Q - \text{ind. } \mu) = \frac{Q_1^2 \alpha_2}{2r^4} \quad , \tag{7}$$

where α_2 is the polarizability of molecule 2. For dipole-induced dipole interactions,

$$U(\mu - \text{ind. } \mu) = \frac{-\mu_1^2 \alpha_2}{2r^6} (3 \cos^2 \theta_1 + 1). \tag{8}$$

Averaging over the angles, Equation (8) becomes:

$$\overline{U}(\mu - \text{ind. } \mu) = \frac{-\mu_1^2 \alpha_2}{r^6} \tag{9}$$

Dipole-induced dipole forces are usually negligible[74] and will therefore be ignored, but charge-induced dipole contributions cannot be neglected.

c. London Interactions

London contributions to intermolecular and interfacial interactions may in many cases be greater than polar contributions, even in

polar molecules.[74] These will be discussed in some detail, as London forces are most likely the major contribution to protein-solid and water-solid interactions when the solid is a hydrophobic polymer.

The London force is explained by Hirschfelder et al.[111] in this way:

> At any instant the electrons in molecule a have a definite configuration, so that molecule a has an instantaneous dipole moment (even if it possesses no permanent electric moment). This instantaneous dipole in molecule a induces a dipole in molecule b. The interaction between these two dipoles results in a force of attraction between the two molecules. The dispersion force is then this instantaneous force of attraction averaged over all instantaneous configurations of the electrons in molecule a.

The London dispersion energy, U(d), is usually written as:

$$U(d) = -\frac{A}{r^6}, \tag{10}$$

where A is called the London constant and r is the distance between the interacting molecules. One of the well-known expressions for A is:

$$A = \frac{3}{2}\frac{\overline{C}_1\overline{C}_2}{\overline{C}_1+C_2}\alpha_1\alpha_2 \tag{11}$$

where $\overline{C}_1$ and $\overline{C}_2$ are average or effective excitation energies of 1 and 2 and α_1 and α_2 are static polarizabilities of 1 and 2. Other expressions for A are available;[117] using polarizabilities and number of electrons or using polarizabilities and diamagnetic susceptibilities, but equation (11) is the more generally used.

The terms $\bar{C}_1$ and $\bar{C}_2$ are often set equal to the first ionization energy, I, though Pitzer[114] suggests that $\bar{C} \simeq 2I$ is a more reasonable approximation for some simple molecules. Fortunately, Salem has carried out a rigorous analysis of the problem,[117] making fewer assumptions, and has calculated the interaction energy between two $-CH_2-$ groups:[118]

$$U(d) = -9.18 \times 10^{-11} \text{ erg/(d in A)}^6 = \frac{-3}{4} \bar{C} \alpha^2/d^6. \qquad (12)$$

If one uses a static polarizability value for $-CH_2-$ of[118] 1.84×10^{-24} cm^3 (see Table IV), equation (12) indicates that, for a $-CH_2-$ group, $\bar{C} \cong 2.16 I_{-CH_2-}$, in reasonable agreement with Pitzer's[114] suggestion. Using Salem's numbers[110] for water-water dispersion interactions, the $\bar{C} \simeq 2.2$ I approximation yields α- values for water within 7% of the commonly accepted value (Table IV). If the reasonable approximation, $C_i \simeq 2.2 I_i$, is used in equation (11) along with the generally accepted static polarizability and ionization potential values, dispersion interactions can be calculated. Equations (10) and (11) then become:

$$U(d) = \frac{3}{2}(2.2) \frac{I_1 I_2}{(I_1 + I_2)} \alpha_1 \alpha_2 / r^6 . \qquad (13)$$

This expression will be used for calculating dispersion interactions. Values of I and α are tabulated in Table IV for the groups and molecules to be considered. The quantities I, α, and μ are discussed in more detail later.

d. Multi-Molecular Interactions

The superposition principle of electrostatics [123] allows one to determine the force on any charge as a vector sum of the forces from each of the other charges.

Unless the orientation of each ion or dipole is exactly known, equations (1) and (2) cannot be employed. In liquid or solid media the molecules are usually not free to rotate, thus equations (4-6) are not valid. In the case of a solid polymeric surface each unit will be handled as a separate entity, or "bead", as suggested by Good,[74] and the appropriate group and bond dipole moments and polarizabilities (Table III) will be used.

London interactions are different from electrostatic effects in that the bi-molecular interaction is to a first approximation independent of the interaction with other atoms.[124] This is proved in Margenau's review.[113] Thus, the direct additivity of London forces is generally accepted.[69] Often the total contribution can be found by an integration. London interactions at large separation distances become complicated by a retardation effect, due to a phase difference between the fluctuating and induced dipoles. This has been treated[125] and is only important at large separations (of the order of 1000 A or greater); therefore it will be ignored.

The additivity of London forces in condensed media has been challenged.[126] The expressions are nevertheless valid if the medium

is accounted for[127-9] in the equations. Direct measurements of London attractions between solids have been made by Deryagin and his colleagues.[130] They found that the values obtained using the additivity concept agree with their results if the retardation correction is included (as they were working at distances greater than 1000 A). General theories of London forces in which retardation and media effects are included have been reviewed.[126, 131] Equations to calculate London interactions between atom distributions of different geometric shapes have been derived[124, 127, 132] and tabulated.[69] The appropriate expressions for the geometries to be considered here will be developed and discussed in Section B.

e. Determining α, μ, and I

The polarizability can be calculated from the expression[122, 133]

$$\alpha = \frac{3}{4\pi N_0} \left(\frac{\epsilon - 1}{\epsilon + 2}\right) \frac{M}{\rho}, \qquad (14a)$$

where ϵ is the high frequency dielectric constant, N_0 is Avogadro's number, ρ is the bulk density, and M is the molecular weight. Also, as $\epsilon = n^2$ (if ϵ and n are measured at the same frequency*) one can use

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* The dielectric constant is a function of frequency, as is the refractive index. At sufficiently low frequencies, the dielectric "constant" becomes a true constant, independent of frequency (see Ref. 134 for a lucid discussion). The value used for electrostatic problems is the constant value (78.3 for water at 25 C) but for dispersion interactions the high frequency value (1.76 for water) must be used, as the frequency of charge fluctuations responsible for dispersion forces is about 10^{15} sec.$^{-1}$.

the expression

$$\alpha = \frac{3}{4\pi N_0}\left(\frac{n^2 - 1}{n^2 + 2}\right)\frac{M}{\rho} \simeq 4 \times 10^{-25}\left(\frac{n^2 - 1}{n^2 + 2}\right)\frac{N}{\rho}, \qquad (14b)$$

when n is the refractive index, usually for the sodium D line.

These expressions yield a sub-microscopic polarizabilty from macroscopic data. The results are probably valid for isotropic substances or for anisotropic materials where ϵ or n was determined as a function of drawing or crystallographic direction. The polarizability would, of course, then also be direction-dependent. Values of ϵ or n in the literature[135] are not usually listed as function of direction, though such information is available for polyethylene.[136]

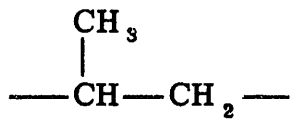
If directional polarizabilities are required, one may have to resort to bond polarizabilities. Values of $\alpha_{\parallel}$ and $\alpha_{\perp}$, the polarizabilities parallel and perpendicular to the bond direction, respectively, are available[111,137] (Table III). If the polarizing field is at some arbitrary angle, θ, to the bond direction, then:[111,137]

$$\alpha_\theta = \alpha_{\parallel} \cos^2 \theta + \alpha_{\perp} \sin^2 \theta. \qquad (15a)$$

If this expression is averaged over all angles, then

$$\alpha = \frac{1}{3}(\alpha_{\parallel} + 2\alpha_{\perp}). \qquad (15b)$$

Saturated polymer chains can be treated as "strings of beads".[74] For example, the $-CH_2-$ group can be selected as the representative segment in polyethylene, the



in polypropylene, the $-CH_2CHCl-$ in polyvinyl chloride, etc. The polarizability of the bead can then be calculated by equations (14a) to (15b). Unfortunately, equations (14a) and (14b) yield results different from equation (15b) in some cases. For benzene, the results are identical, but for polyethylene they are different. The $-CH_2-$ in polyethylene can be considered to have 2 C-H and 2 ($\frac{1}{2}$) C-C bonds. Equation (15b) then yields (see Table III for values) $\alpha = 1.94 \times 10^{-24}$ cm.^{3} Salem;[118] determining bond polarizabilities from molar refraction* data,[138] obtained an α-value of 1.84×10^{-24} cm.^{3} An average value of n^2 for high density ($\rho = 0.96$) polyethylene is 2.37 (Table IV). Putting these values in equation (14a), $\alpha = 1.82 \times 10^{-24}$ cm.^{3} Good[74] gives a value of 1.76×10^{24} for high-density polyethylene. The difference between the four results are quite significant, particularly when it is recalled that the London interaction energy (or force) is directly proportional to α.

When orientation is not a problem, α-values calculated from equations (14a-b) should be used, as they are dependent on macroscopic

*The molar refraction, R, is defined as

$$R = \left(\frac{n^2 - 1}{n^2 + 2}\right) \frac{M}{\rho} = \left(\frac{4}{3}\right) \pi N_0 \bar{\alpha},$$

where M = molecular weight and ρ = bulk density. See equation (14b) and Refs. 133 and 138.

properties. It is believed that polyethylene contains extraneous dipoles, possibly carbonyls.[139] They could produce a local field which would decrease the polarizability, in qualitative agreement with the results just calculated. Because of these impurities the polarizability of commercial polymers cannot be accounted for by only considering bond polarizabilities. However, if orientation effects are important, one must determine α from bond polarizability data (Table III).

The London expression also required ionization potential values. Tables of ionization potentials are available.[140-2] The ionization potential of the appropriate polymer segment can be deduced from values for "model" compounds. Most ionization potential data are determined in the gas phase. There is evidence that, because of the polarizability forces within a crystal, solid state ionization potentials are about 1 to 2eV lower than those in the gaseous state, especially for unsaturated organic solids.[143] Fortunately, this is already accounted for in equation (13). When the $\bar{C}$ is about 2.2 I approximation was made, it was using a conventional value of I, i.e., determined in the gas or in an apolar liquid. Thus, I values directly from the tables can be used (Table IV). Ionization potential for ions are not readily available and certain assumptions must be made to deduce values for charged groups.

Permanent dipole moments of molecules are well-known, and extensive tabulations are available.[61, 133, 144] In most cases, group dipole moments will be important, some of which are also tabulated.[74 133] Values for proteins and amino acids are listed in Cohn and Edsall's book.[134]

f. Medium Effects

The basic equations for the calculation of intermolecular forces between molecules separated by a vacuum have been presented. Now the expressions must be modified to account for the effect of the water medium. This is easily done for the electrostatic expressions by including the static dielectric constant of water in the Coulomb's Law expressions. The result is a D or D^2 term in the expression, depending on the type of interaction.[110, 121]

The modification of the London equation is a bit more subtle. As the London interactions are due to high frequency fluctuations, Setlow and Pollard[121] reasoned that one could use the $\epsilon \cong n^2$ approximations, which results in an n^4 term in the denominator (because the electrostatic analogy to the London forces, a dipole-induced dipole interaction, has a D^2 term in the denominator). This approach has been criticized,[145] as it leads to too great a decrease as compared to other more rigorous evaluations.

Fowkes[146] assumed one could use the high frequency dielectric

constant directly in the denominator ($\epsilon = n^2 = 1.76$ for water) and simply divided his expression by ϵ (as opposed to Setlow and Pollard's ϵ^2, above).

A rigorous analysis of this problem has been carried out.[128-9] Kestner and Sinanoglu[128, 145] concluded that the reduction between two polymer chains in water is 15 to 30%. Salem[110] has accepted their results and assumed a constant 30% reduction in water. Thus, the equations to be used later will include a 0.7 correction term. In addition, it will be assumed that the water medium correction is approximately the same as that for an apolar polymer medium, so the same corrected equation will be used for all calculations. This assumption is justified, as n^2 for water is 1.83, while n^2 for polyethylene is 2.4; any error resulting from such an assumption would easily lie withint the limits of error of the equations.

g. Additivity and Summary

When the dialectric constant is included, the important energy and force ($F = -dU/dr$) equations are:

$$\bar{U}\,(Q^2 - \mu) = -Q_1^2\,\mu_2^2\,/(3kT\,D^2\,r^4) \qquad (16a)$$

$$\bar{F}\,(Q - \mu) = -4Q_1^2\,\mu_2^2/(3kTD^2r^5) \qquad (16b)$$

$$\bar{U}\,(\mu - \mu) = -2\mu_1^2\,\mu_2^2\,/(3kTD^2\,r^6) \qquad (17a)$$

$$\bar{F}\,(\mu - \mu) = -4\mu_1^2\,\mu_2^2\,/(kT\,D^2\,r^7) \qquad (17b)$$

$$U(\mu - \mu) = -2\mu_1\mu_2/(D^2 r^3) \tag{18a}$$

for optimum orientation;

$$F(\mu - \mu) = -6\mu_1\mu_2/(D^2 r^4) \tag{18b}$$

for optimum orientation;

$$U(\text{Q-ind.}\ \mu) = -Q_1^2\alpha_2/(2r^4 D^2) \tag{19a}$$

$$F(\text{Q-ind.}\ \mu) = -2Q_1^2\alpha_2/(D^2 r^5)\cdot \tag{19b}$$

The final form of the London equation is:

$$U(d) = -(1.5)(2.2)(0.7)\, I_1 I_2 \alpha_1\alpha_2/[(I_1 + I_2) r^6] \tag{20a}$$

$$F(d) = -9(2.2)(0.7)\, I_1 I_2 \alpha_1\alpha_2/[I_1 + I_2) r^7], \tag{20b}$$

where the 2.2 is the ionization potential correction and the 0.7 is the water medium correction. All of the interactions are attractive (negative sign). The negative signs will be dropped for convenience, as attraction is understood.

Note that in the absence of charges, the two relevant expressions are functions of r^{-6} if random dipoles can be assumed. If one considers only the constant due to medium effects, i.e., $1/D^2$ in equation (17) and 0.7 in equation (20), then London forces have a 4500-fold advantage in water (as D^2 for water is about 6400). In the absence of water, such an advantage would not exist.

All the expressions necessary for calculating long-range inter-

actions between molecules and particles in water are now available. Using the general principle of additivity of intermolecular forces,[74,83,112] all the contributions can be summed to obtain the total effect.

Values of α and I are given in Table IV.

TABLE III

BOND POLARIZABILITIES AND BOND LENGTHS[111,137]

Bond	$\alpha_{\parallel} \times 0^{25}\,cm^{-3}$	$\alpha_{\perp} \times 10^{25}\,cm^{3}$	$\alpha_{\perp}/\alpha_{\parallel}$	Bond Length (Angstroms)
C-C (Aliphatic)	18.8	0.2	0.01	1.54
C-C (Aromatic)	22.5	4.8	0.21	1.39
C=C	28.6	10.6	0.37	1.34
C≡C	35.4	12.7	0.36	1.20
C-H	7.9	5.8	0.73	1.09
C=O	19.9	7.5	0.38	1.24
C-Cl	36.7	20.8	0.57	1.76
C-Br	50.4	28.8	0.57	1.90
C=S	75.7	27.7	0.37	1.62
C≡N	31	14	0.45	1.15
N-H	5.8	8.4	1.45	1.02
N≡N	24.3	14.3	0.59	1.09
Cl-Cl	66.0	36.2	0.55	1.98
H-H	6.8	8.9	1.31	0.74
H-Cl	31.3	23.9	0.76	1.27
H-Br	42.3	33.2	0.78	1.41
H-I	65.8	48.9	0.74	1.61
H-S	23.0	17.2	0.75	1.35

TABLE IV*

SELECTED PROPERTIES OF SOME GROUPS AND MOLECULES

Molecule or Group	α ($\times 10^{-24}$ cm^3)	I ($\times 10^{-11}$ erg)	ρ (gr/cc)	M	$n^2 = \epsilon$
$-CH_2-$	1.94 (a) 1.80 (b)	1.63 (c)	----	14	---
Ethane	4.54 (a)	1.87 [142]	----	30	---
n-Butane	8.42 (a)	1.70 [142]	----	58	---
n-Hexane	12.3 (a)	1.63 [142]	0.66 [150]	86	1.89 [150]
Polyethylene (High Density)	1.80 (b)	1.63 (c)	0.96 [149]	14	2.37 [150] **
Polypropylene	5.36 (b)	1.62 (d) [142]	0.90 [149]	42	2.22 [149]
Polystyrene	13.4 (b)	1.36 (e) [147]	1.05 [136]	104	2.54 [149] 2.46 (e)
Polytetrafluorethylene (PTFE)	2.00 (b, f)	2.4 (f) [148]	2.15 [149]	50	1.82 [149]
Water	1.48 [74]	2.02 [141]	1.0	18	1.77 (c)

* Parentheses refer to footnotes below

** 2.31 in α, β and 2.50 in γ crystallographic directions. [136]

a. Calculated from bond polarizabilty data (Table III and equation (15b).

b. Calculated from equation (14b).

c. Model compound: n-decane.

d. Model Compound: 3-methyl pentane.

e. Model compound: toluene.

f. Model compound: $CF_3(CF_2)_3CF_3$.

B. The Adsorption Model

1. Conceptual:

a. The Adsorption Force

The brief discussion of adsorption presented in the last chapter showed that, although many generalizations and thermodynamic treatments have been given, a general mechanistic model of adsorption is not available. The purpose of this chapter is to deduce such a model and then to place it on a physical foundation by considering intermolecular interactions. The general treatment must consider solute-water, water-water, water-surface, and solute-surface interactions. All of the discussions, derivations, and calculations will be for water as a solvent. The treatment can easily be generalized to consider other pure solvents if the appropriate physical constants are known.

The simplest example of adsorption from aqueous solution is the water/air interface. Figure 6a shows the forces on an apolar solute molecule in bulk water and the forces on an equivalent volume of water (the excluded volume). The superscript s indicates forces or energies due to interactions with the solute molecule, while the superscript w indicates interactions with the equivalent volumes of water. The subscript u (up) indicates that the interaction is with the finite water slab between the volume and the interface, while d (down) indicates that the interaction is with the infinite volume of bulk water. These notations

are merely for convenience. All of the forces are attractive, but a sign convention must be set up in order to consider directions and determine the net forces or energies. Thus, interactions in the direction toward the interface are negative, while those in the opposite direction are taken as positive.

The solute water forces are due to dispersion interactions only if the solute is a saturated hydrocarbon. The water-water forces are due to both dispersion and dipole-dipole (hydrogen-bonding) effects. In the vicinity of the surface (Figure 6b), there is an asymmetry of forces, since the finite slab of water cannot interact as strongly with both volumes as the infinite bulk water. If both volumes are on the surface (Figure 6c), there is only one force acting on each volume. This is the force responsible for the surface tension. The net force ($F_n = F_d - F_u$) or energy ($E_n = E_d - E_u$) due to water interactions is thus a maximum at the surface and rapidly approaches zero with increasing distance from the surface. A hypothetical plot of the energies as a function of distance is given in Figure 7a for water (the center curve), for a low energy solute (the lower curve), and for a high energy solute (the upper curve).

Consider a solute volume at a distance x_2 from the surface (Figure 7b) and an equivalent volume of water directly above it at a distance x_1 from the surface. Examine Figure 7a to see what energies are required to move the solute from x_2 to x_1 and simultaneously move the water volume

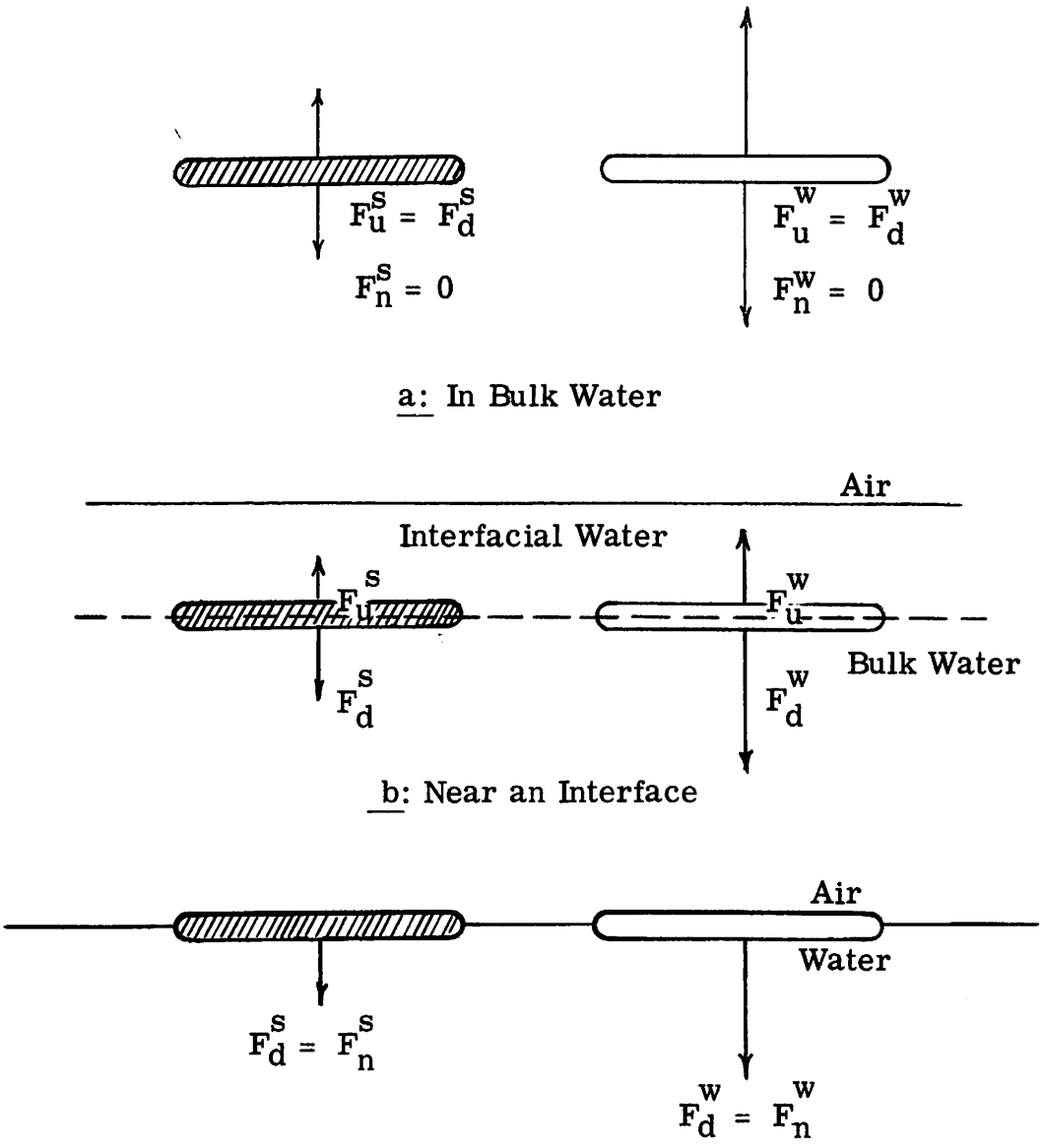
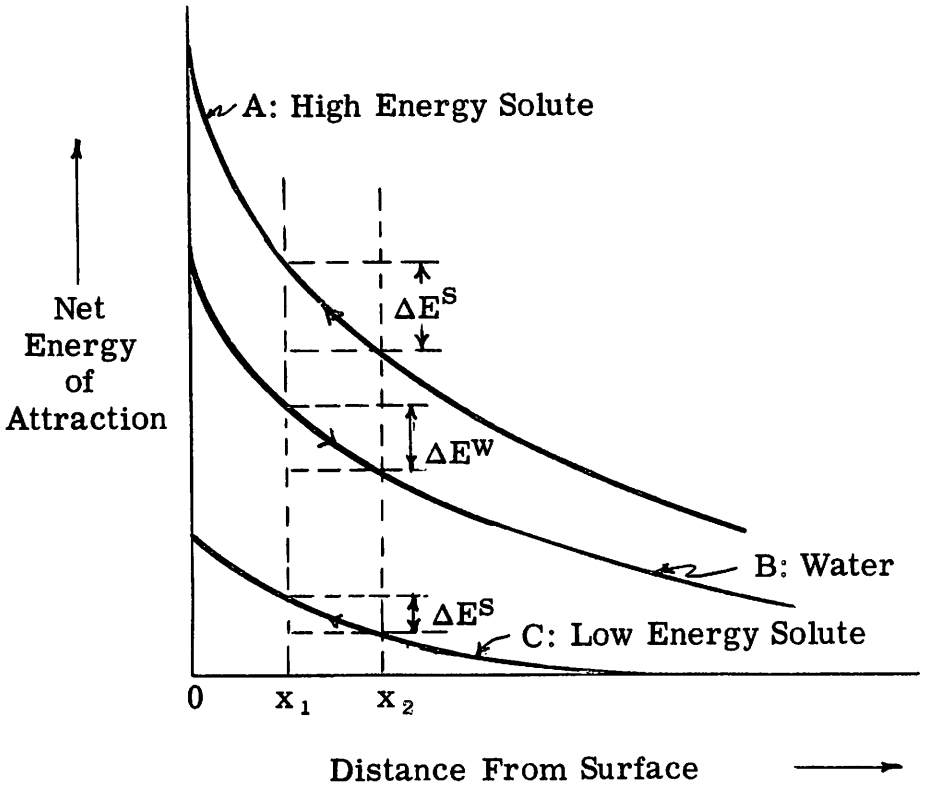
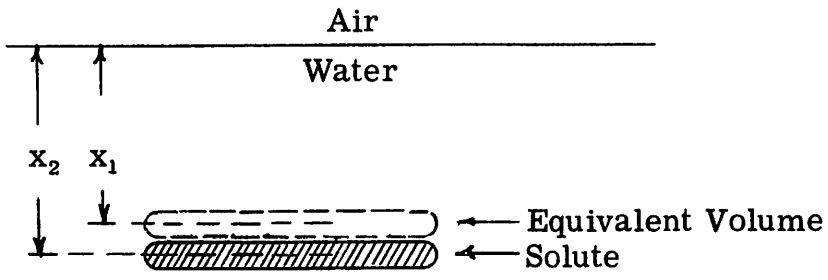


Figure 6. The Forces on a Solute Molecule and on the Equivalent Volume of Water Under Different Conditions: a. In Bulk Water; b. In the Vicinity of a Water/Air Interface; c. At the Water/Air Interface. The cross-hatched volume represents the solute molecule; the uncrosshatched volume is the equivalent volume of water. The notation is defined in the text.



a.



b.

Figure 7. a: Hypothetical Energy-Distance Curves for a High-Energy Solute, a Low-Energy Solute, and for an Equivalent Volume of Water.
b: The geometry corresponding to the arrows in a (see text).

from x_1 to x_2. These processes are indicated by the arrows in Figure 7a. To move the solute towards the interface required an expenditure of energy, ΔE^S, while the movement of the equivalent volume of water generates an amount of energy, ΔE^W. Clearly, $| \Delta E^W | > | \Delta E^S |$, and the process is favorable. The net energy difference can be considered as the driving force for adsorption. The result can be viewed as a virtual force acting on the system:

$$F^{virtual} \equiv \frac{| \Delta E^S | - | \Delta E^W |}{\Delta x} \equiv F^{ads} \quad . \qquad (21)$$

The virtual force is the force responsible for adsorption at the water/air interface. If $| \Delta E^S | > | \Delta E^W |$, then $F^{ads} > 0$ and adsorption cannot occur (curves A and B in Figure 7a). This is the case of negative adsorption, that is, there will be a deficiency of solute at the surface. If $| \Delta E^S | < | \Delta E^W |$, then $F^{ads} < 0$, and adsorption does occur (curves B and C in Figure 7a). These conclusions are in agreement with the results of Figure 4, discussed earlier. The same analysis will hold for any solvent if curve B is shifted appropriately. The high cohesive energy of water leads to greater adsorption tendencies than most common solvents.

The adsorption force is the difference between the net force on the solute and on the equivalent volume of water. It can be calculated by the expression

$$F^{ads} = | F_n{}^S | - | F_n{}^W |, \text{ where } F_n = F_d - F_u . \qquad (22)$$

If the solute molecule is apolar, as for a saturated hydrocarbon, then the solute-water interaction (F_n^S) can only be due to dispersion forces,[73] as dipole-induced dipole forces are negligible.[74] The dispersion force can be easily calculated with the London expression derived earlier; this will be done later. The calculation of the water-water interaction is less straight-forward, as there are large dipole-dipole as well as dispersion interactions. The calculation of dipole-dipole interactions requires that either the exact orientation be known, equations (2) and (3), or that random orientation can be assumed, equation (6) or (17). As the dipole-dipole interactions in water are certainly not random, and as the exact orientations are not known, the dipole-dipole interactions cannot be exactly calculated. They can, however, be estimated to a reasonable degree of accuracy using Fowkes' data.[73] The total surface energy of water at 20 C is about 73 ergs/cm^2 ; Fowkes has shown[73] that the dispersion force component of the surface energy of water is about 22 ergs/cm^2. Thus, the surface energy of water is to a good approximation equal to 3.3 times the dispersion energy. The force of adsorption at water/air interfaces is given by equation (22) where F_n is assumed to be 3.3 times the dispersion force.

The following assumptions are, therefore, important to the semi-quantitative development of the model which will follow:

1. The solute molecule can only interact with water by dispersion forces.

2. The total equivalent volume interaction is 3.3 times its dispersion interaction.

3. The polymer surface can only interact with water and with the solute molecule by dispersion interactions.

The first assumption limits the quantitative development to hydrocarbons, though polar and charged molecules will be discussed qualitatively.

The second assumption is only valid for water. In apolar solvents, the 3.3 term would net exist and F_n^w would be roughly of the same magnitude as F_n^s; adsorption tendencies would therefore be much lower than in a cohesive solvent.

The third assumption limits the analysis to apolar surfaces. If the solute is capable of dipole-dipole interactions, such as an alcohol or carboxylic acid, then F_n^s would be significantly greater and the net force of adsorption would be decreased. A polar compound would also be much more easily desorbed, as occasionally a cluster could form which might optimize the dipole-dipole interactions and return the molecule to the solution.

The case of a polymer/water interface is only slightly more complicated and is shown in Figure 8. In this case the polymer interaction forces, F_p^s and F_p^w, will modify the curves in Figure 7a. Curve B will start at a lower value, corresponding to the polymer-water interfacial energy; curve A will also be lower and will start at the polymer-solute

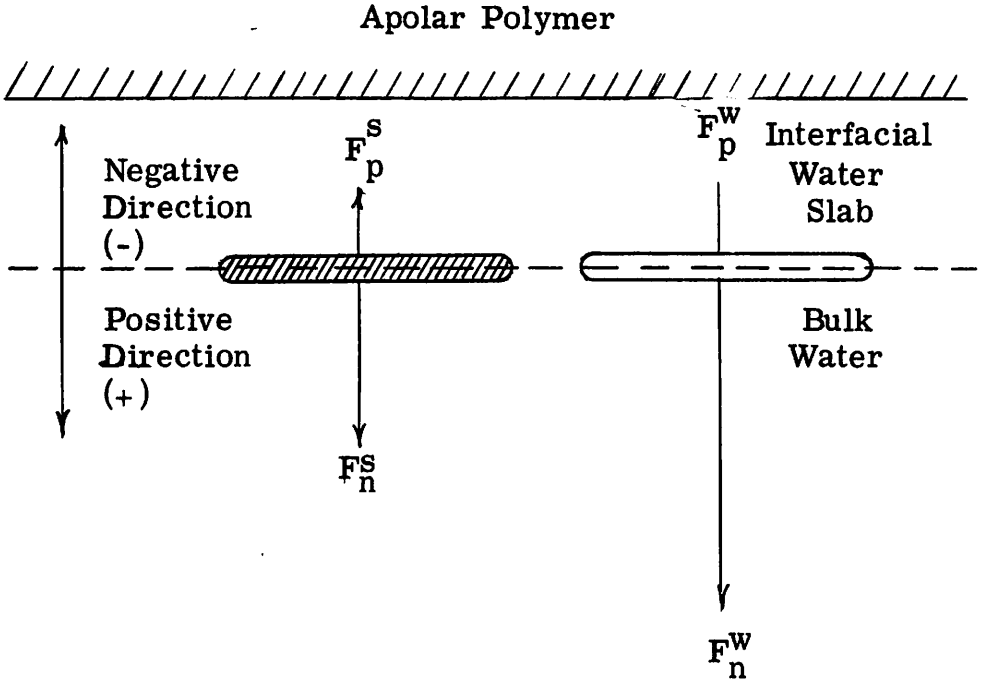


Figure 8. The Forces on a Solute Molecule and on the Equivalent Volume of Water in the Vicinity of a Water/Polymer Interface.

interfacial energy. The slopes will thus be decreased, resulting in lower ΔE values and in a lower value for the adsorption force. For the more general case of a polymer/water interface, the force of adsorption is:

$$F^{ads} = (F_n^s - F_p^s) - (F_n^w - F_p^w) \quad \text{or}$$
$$F^{ads} = (F_n^s - F_n^w) - (F_p^w - F_p^s). \qquad (23)$$

Only apolar polymers will be considered, thus, F_p^s and F_p^w can be calculated by dispersion equations. It is clear that the adsorption force may be lower at polymer/water than at air/water interfaces. If $F_p^s = F_p^w$, then the interactions with the polymer cancel out, and the adsorption

tendency is the same for air/water and polymer/water interfaces. If F_p^s is less than F_p^w, then water/polymer interactions are greater than solute/polymer interactions, and solute adsorption decreases. If F_p^s is greater than F_p^w, solute adsorption is greater than at the air/water interface.

It is evident that for apolar solutes and apolar polymers adsorption can not be prevented, though it can be maximized and minimized. This conclusion will be demonstrated later in the chapter when the calculations are performed and the results plotted. It will also be seen that different orientations of a solute molecule with respect to the interface will lead to very different adsorption tendencies, thus conclusions as to orientation of adsorbed species will be made. The orientation of the chains in the polymer surface, i.e., the crystallinity of the polymer surface, will also be discussed in relation to its effect on adsorption.

The above discussion provides a mechanism for adsorption from aqueous solution which is compatible with thermodynamic considerations and which will be used to explain several previously unexplainable phenomena in surface science.

In summary,

$$F^{ads} = (F_n^s - F_n^w) + (F_p^w - F_p^s), \qquad (24)$$

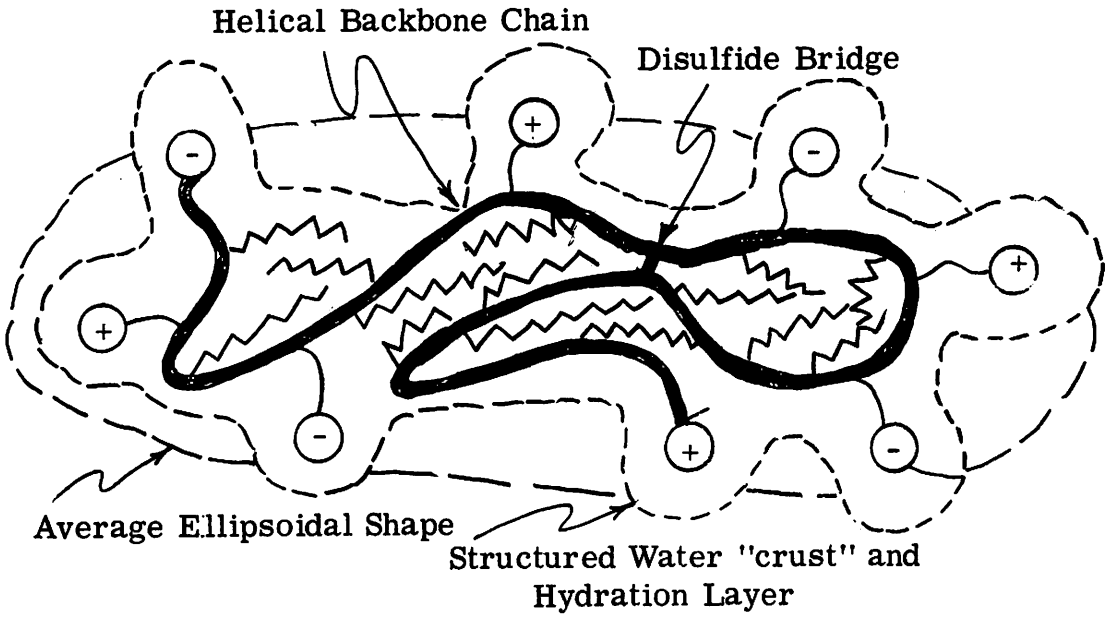
when F^{ads} is less than 0, adsorption occurs; when F^{ads} is greater than 0, negative adsorption occurs, i.e., a surface deficiency is produced. Forces are negative if they point towards the interface and positive if

they point away from the interface. The analogous expressions for the energy are straight-forward:

$$U^{ads} = (U_n^s - U_n^w) + (U_p^w - U_p^s). \qquad (25)$$

b. Protein Adsorption

Consider the hypothetical two-dimensional, ellipsoidal protein of Figure 9. Assume it has no net charge at pH 7; this is the case for some gamma globulins.[63] What happens when such a molecule approaches an interface? If the interface is charged or relatively polar, F_p^s can be treated in terms of electrical double layer theory,[4] at least for relatively large separations. At close separations the surface cannot see a net protein charge, but will feel the local charge and dipole distributions on the protein. If a protein has a locally charged region somewhere on its surface, which is not unreasonable as many proteins have large dipole moments;[133] then some of the proteins could be expected to adsorb in the manner sketched in Figure 10. A protein with a net negative or positive charge might be capable of adsorbing on both negatively and positively charged surfaces, if it contained a negatively charged region at one end of the molecule and a positive center at the other end. Albumin, which is highly negatively charged at pH 7, is known to neutralize both positive and negative ion-exchange resins by adsorption.[151] At large distances the net charges on the protein and the surface would probably interact, and,



Indicates Hydrophobic (Apolar) Side Chains

Indicates Negatively Charged Groups (COO^-)

Indicates Positively Charged Groups (NH_3^+)

Figure 9. A Hypothetical Two-Dimensional Protein With a Uniform Charge Distribution.

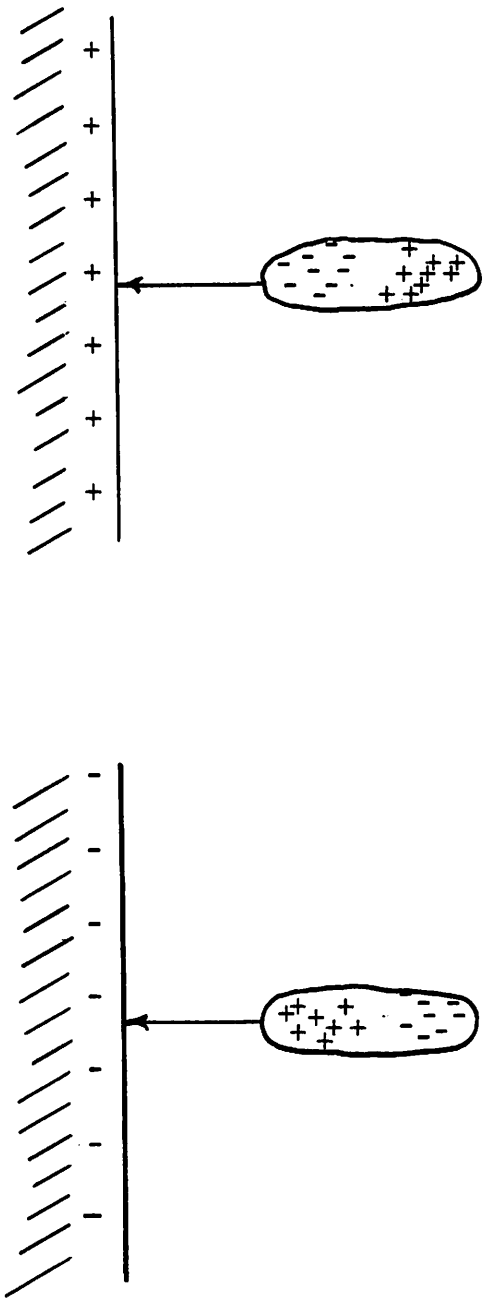


Figure 10. Neutral Proteins with Localized Charge Distributions Interacting with Charged of Highly Polar Surfaces.

if the interaction is strong enough, it could simply overwhelm the other interactions present.* Thus, the observations of Sawyer and his group[152] with metals are not necessarily in conflict with the negative surface charge concept voiced by Margolis.[100] Just as one cannot think of water as having a definite structure, one cannot naively assume that proteins can adsorb by only one mechanism. A protein is a macro molecule with a macroscopic surface of its own. It contains hydrophobic groups, dipoles, and charges, no doubt distributed and concentrated in various parts of the molecule (this will be shown later for ribonuclease), giving the particular protein its own unique properties. Thus, rather than expect all proteins to have the same adsorption properties, they should all be expected to adsorb differently, and to adsorb by different mechanisms on different surfaces.

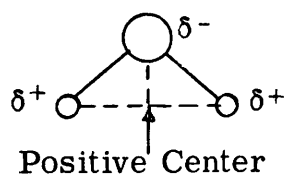
Electrostatic interactions may occur even if the surface is not polarized or charged. As a highly charged molecule such as albumin (net charge about -50 at pH 7) or fibrinogen (about -300 at pH 7) approaches a polymer surface, it can induce dipoles on the polymer surface; thus attraction is almost inevitable at small separation distances.

At large separations there is probably no protein-surface inter-

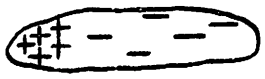
*This concept was suggested by Dr. James Bougas of Boston University in a lecture given to the Denver Conference on Biomedical Materials, Denver, Colorado, July, 1968.

action (F_p^s) unless the surface has a relatively high charge density. If it has a high charge density, then it will probably interact with the net charge on the protein, producing a repulsion or attraction. At nearer distances, the surface and proteins will interact by their own specific charge distributions. Proteins oriented so that attraction is maximized will tend to be adsorbed, while those oriented differently will not, though they, too, will eventually be adsorbed as electrical torques and thermal vibrations bring them into the necessary orientation. When the molecule is close to the polymer surface (of the order of 10 or 100 A), the interaction is due to dispersion forces as well. Finally, there may be dipoles induced in the polymer by charges on the protein, resulting in a net electrostatic interaction. Because of the increase in static dielectric constant with distance (to be discussed later), induced dipole effects will only be significant at very close separations (up to 5 A). These effects are aided by the ever-present adsorption force due to the cohesion forces of the water molecules themselves (equation (22)).

Figure 10 showed the proteins as having both negative and positive regions; this may be misleading. Such separations probably occur with some proteins, but they are not necessary to explain adsorption or dipole moments. Consider the water molecule:



The positive center of the dipole interacts less strongly than the negative seat as it is less concentrated. The same may be true in a protein; the protein below is neutral, yet it will interact much more efficiently with a negatively charged surface than with a positively charged one:



If these concepts of protein adsorption are accepted as valid, then the experimental results on many different types of surfaces begin to make some sense. If a surface is placed in blood, with its many protein constituents, it makes relatively little difference what its surface characteristics are (unless it has a gross charge on it), because sooner or later it will find proteins or other molecules with which in can interact. It is, therefore, no surprise that the zeta potential of most surfaces goes to zero when placed in contact with blood.[153]

It is also clear that adsorption need not stop after a monolayer is formed, though it will be shown later why this is often the case. The actual behavior will again depend on the surface-solute interactions, on the nature of the adsorbed layer, and on its interaction with both solute and solvent. A surface composed of an adsorbed monolayer may also have characteristic properties which could produce additional interactions, as so beautifully demonstrated by Vroman's model of coagulation as a series of hydrophilic-hydrophilic and hydrophobic-hydrophobic bonds.[1,99] If one molecule (A) has a greater interaction for a particular

surface than another (B), it is conceivable that A may displace B from the surface. Such competitive adsorption is the basis of adsorption chromatography.[154] Some of Vroman's work indicates that such a process may occur with Hageman Factor and adsorbed fibrinogen.[1] It was noted earlier that competitive adsorption occurs with synthetic polymers.

In the development that follows, only polymeric, hydrophobic, low-energy surfaces will be considered. For such surfaces, charge and dipole interactions will not be important, though charge-induced dipole interactions may be important at very close separations. The equations developed earlier, especially the dispersion expressions, will be used in an attempt to predict the magnitude of the forces responsible for adsorption. The expressions will be examined to see what surface characteristics are necessary to minimize those forces.

2. Preliminary Calculations

The various intermolecular forces and energies which may act on a body in the vicinity of an interface will now be estimated. The equations are listed below with the constants evaluated to two significant digits (using the sign convention of page 77):

$$\bar{U}\,(Q - \mu) = 8.0 \times 10^{13}\, Q^2 \mu^2 / (D^2 r^4) \qquad (26a)$$

$$\bar{F}\,(Q - \mu) = 3.2 \times 10^{13}\, Q^2 \mu^2 / (D^2 r^5) \qquad (26b)$$

$$\bar{U}\,(\mu - \mu) = 1.6 \times 10^{13}\, \mu_1^2 \mu_2^2 / (D^2 r^6) \qquad (27a)$$

$$\bar{F}\,(\mu - \mu) = \quad 9.7 \times 10^{13}\,\mu_1^2\mu_2^2/(D^2\,r^7) \qquad (27b)$$

$$U\,(\mu - \mu) = \quad 2.0\,\mu_1\,\mu_2/(D^2r^3) \qquad (28a)$$

for optimum orientation,

$$F\,(\mu - \mu) = \quad 6.0\;\mu_1\,\mu_2/(D^2r^4) \qquad (28b)$$

for optimum orientation,

$$U\,(Q\text{-ind }\mu) = \quad 0.5\,Q^2\alpha/(D^2\,r^4) \qquad (29a)$$

$$F\,(Q\text{-ind }\mu) = \quad 2.0\,Q^2\alpha/(D^2\,r^5) \qquad (29b)$$

$$U\,(d) = \quad 2.3\,A_0/r^6 \qquad (30a)$$

$$F(d) = \quad 14\,A_0/\,r^7,$$

where

$$A_0 = \frac{\alpha_1\alpha_2 I_1 I_2}{(I_1 + I_2)} \quad .$$

These equations yield the force in dynes and the energy in ergs when Q is expressed in esu units (statcoulombs), r in centimeters, I in ergs, α in cm^3, and μ in esu–cm. To get an approximate idea of the magnitudes involved, some values will be put in the equations (see Table IV):

Q = electron charge $\simeq 4.8 \times 10^{-10}$ esu

μ = water dipole moment $\simeq 1.8 \times 10^{-18}$ esu-cm

α = water polarizability $\simeq 1.5 \times 10^{-24}\ cm^3$

I = water ionization energy $\simeq 2.0 \times 10^{-11}$ erg.

Salem estimates[119] that the dielectric constant in water for a five angstrom separation distance is about fifteen. At ten angstroms it is most likely near the full value of 80, possibly 70. If two water molecules are interacting with no other molecules between them, then the dielectric constant is one; if the intervening medium is apolar, then a good approximation is two.[119] The results of the calculations are given in Table V for three different values of r and for the appropriate dielectric constants.

If one sums the $U(\mu-\mu)$ and U(d) energies at r = 3A, one gets a number for the hydrogen bond energy in water of about 5 kcal/mole, which is in agreement with the accepted values of 3.4 to 5.0 kcal/mole.[74] It is also clear that at three angstroms $U(d) \simeq 0.3$ U (total), in excellent agreement with Fowkes' results[73] that dispersion forces account for about 30% of the surface tension of water. It is clear that the dispersion term is very significant at close separations and becomes dominant at larger separations. The dipole-dipole energy will be negligible with respect to the dispersion energy at a distance of five angstroms or more. Therefore, making the good assumption that the total water interaction is about 3.3 times the dispersion interaction, one need only calculate dispersion forces for the case of hydrocarbons interacting with apolar polymers.

The interactions between two water molecules are only important at relatively close separations. At 10 A separations the dispersion

TABLE V

APPROXIMATE CALCULATIONS FOR THE FORCES AND ENERGIES BETWEEN TWO WATER MOLECULES AND BETWEEN WATER AND AN ELECTRON CHARGE

Quantity	r = 3A (D = 1)	r = 5A (D = 15)	r = 10A (D = 70)
$\bar{F}$ (Q - μ)	1.0×10^{-3}	3.6×10^{-7}	5.1×10^{-10}
F (Q-ind μ)	2.8×10^{-5}	9.7×10^{-9}	1.4×10^{-11}
$\bar{F}$ (μ - μ)	5.0×10^{-6}	6.3×10^{-10}	2.2×10^{-13}
F (μ - μ)	2.6×10^{-5}	1.5×10^{-8}	4.3×10^{-11}
optimum F (d)	2.0×10^{-5} *	5.7×10^{-7} *	3.1×10^{-9}
$\bar{U}$ (Q- μ)	7.9×10^{-12}	4.6×10^{-15}	1.3×10^{-17}
U (Q-ind μ)	2.1×10^{-13}	1.2×10^{-16}	3.5×10^{-19}
$\bar{U}$ (μ - μ)	2.5×10^{-14}	5.1×10^{-18}	3.7×10^{-21}
U (μ - μ)	2.5×10^{-13}	2.4×10^{-16}	1.0×10^{-18}
optimum U (d)	1.0×10^{-13} *	4.7×10^{-15} *	5.1×10^{-17}

kT energy is about 4.0×10^{-14} erg.

*These values do not include the 0.7 water medium correction as it is probably unnecessary at these separation distances.

energy is roughly 1/1000kT; such an energy is negligible. Energies (and the equivalent forces) which are of the order of 10^{-15} erg or less will be ignored. An energy 10^{-15} erg is about 2.5% of kT. When the interactions of thousands of groups with a single molecule are considered, the interaction energy becomes significant, even at 10 A and beyond.

3. Derivations and Calculations for Simple Models:

a. A Group Interacting with a Flat Plate

Consider a disc of radius ℓ and cross-sectional area of $d\ell dx$ in the slab of thickness δ (Figure 11a). The volume of the disc is

$$dV = 2\pi \ell \, d\ell dx$$

If R is greater than a few molecular diameters, it is said that the force can be computed by integrating.[124] If R is of the order of molecular dimensions, a summation must be used. Approximate summations are available[70, 155] which greatly simplify the computations. The expressions for both the energy and the force of interaction will now be developed. The starting equations are:

$$\begin{aligned} dU &= 2\pi N \ell \, d\ell dx \, f(r) \text{ and} \\ dF &= 2\pi N \ell \, d\ell dx \, f(r) \cos\theta, \end{aligned} \tag{31}$$

where f(r) is the appropriate interaction term and $\cos\theta$ gives the resultant force in the horizontal direction. For dispersion interactions equation (30) is used, and the appropriate expressions become:

$$U(d) = 4.6\pi\, NA_0 \int_0^{\delta} dx \int_0^{L} \ell\, d\ell \Big/ [(R + x)^2 + \ell^2]^3 \text{ and}$$

$$F(d) = 28\,\pi\; NA_0 \int_0^{L} \ell\, d\ell \int_0^{\delta} (R + x)dx \Big/ [(R + x)^2 + \ell^2]^4 \,. \tag{32}$$

The integrations are straight-forward when taken in the order given above. Letting L go to infinity, the terms in L go to zero; when δ is allowed to go to infinity, the expressions reduce to the simple forms:

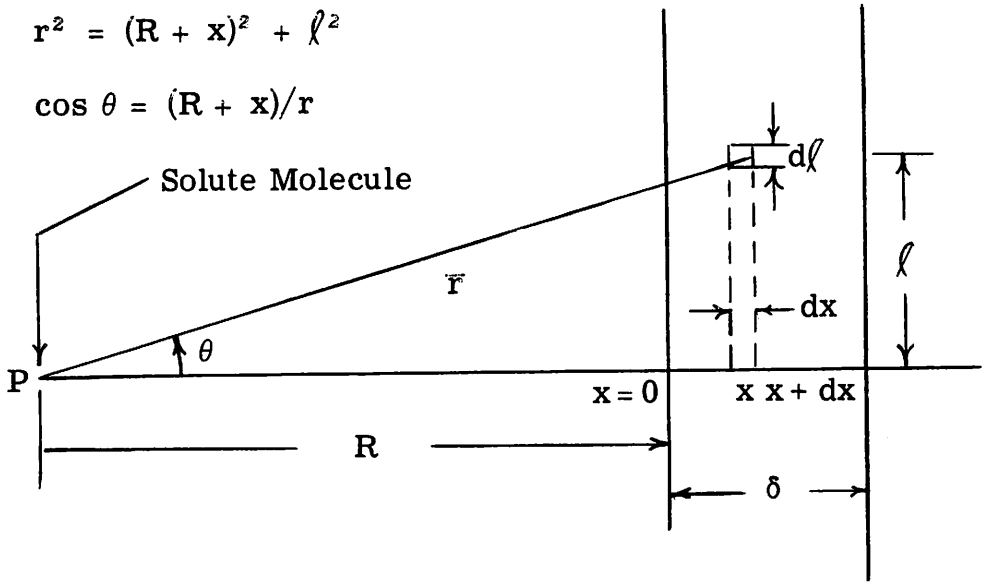
$$U(d) = 1.2\ N\ A_0/R^3 \text{ and}$$

$$F(d) = 3.7\ NA_0/R^4 \,. \tag{33}$$

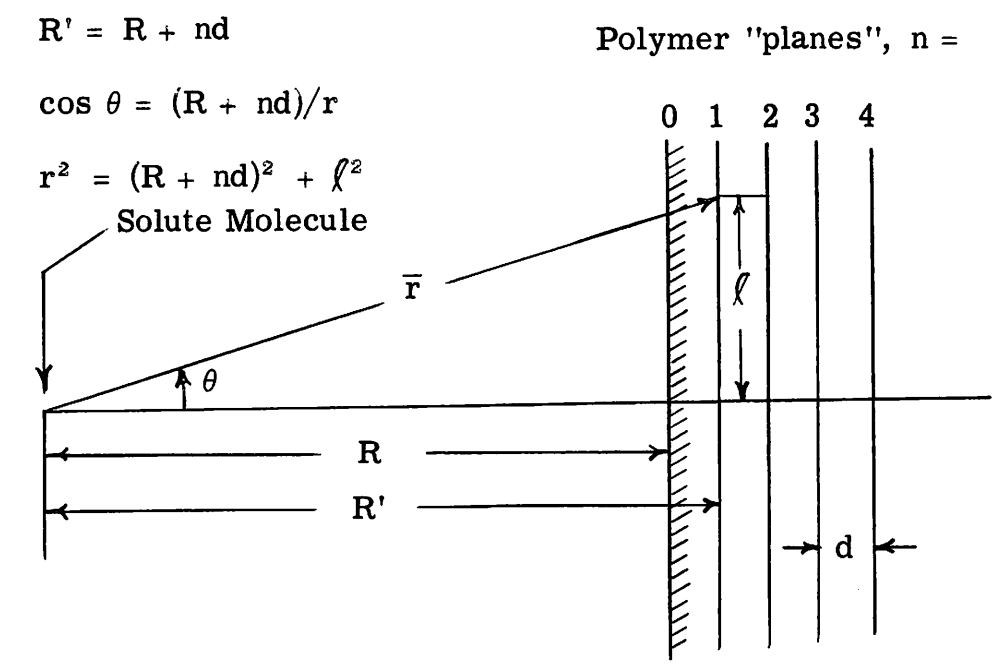
If the molecule is 10 A or farther from the surface, one may be justified in using equations (33) but for closer distances the triple integration is not valid and Crowell's summation method[155] will be used. It is assumed that the polymer units comprising the slab of Figure 11b are uniformly distributed on parallel planes a distance d apart. An integration over each plane is performed, and then a summation over the various planes. This technique has been used by Fowkes.[70] This means that the integration over x in equation (32) is replaced by a summation. The geometry is given in Figure 11b. The set-up and integrations are again straight-forward, giving

$$F(d) = 14.5\sigma A_0 \sum_{n=0}^{m} 1/(R + nd)^5 \text{ and} \tag{34a}$$

$$U(d) = 3.6\sigma A_0 \sum_{n=0}^{m} 1/(R + nd)^4 \,, \tag{34b}$$



a.



b.

Figure 11. The Geometries for a Molecule Interacting With a Flat Plate. a. For a Triple Integration; b. for Crowell's[155] summation method.

where σ is the number of groups per cm^2. The planar separation distance, d, is given as the cube edge of the average volume occupied by a group:

$$d = (M/N_0 \rho)^{0.33} = 1.18(M/\rho)^{0.33} \text{ A}, \qquad (35)$$

where M is the molecular weight and ρ is the density of the polymer. Values of d for several polymers and for water are given in Table VII.

Equations (33) and (34) were programmed and evaluated on the Burroughs 5500 computer at the University of Denver. The results (Table VI) clearly show that there is a significant difference in the forces calculated by equations (33) and (34), even when R is as large as 30 A. The same program also indicated that one need not consider more than ten polymer planes in the summation. In fact, considering only four to six planes is sufficient for an accuracy of three significant digits. It is also clear that forces beyond ten angstroms are probably not significant, as the interaction would be overwhelmed by kT energy.

Equation (34) is sufficient to calculate dispersion interactions between a molecule and a medium which can be approximated as flat planes. If only dispersion forces can act, then all the terms in equation (23) can be calculated using the assumption that F_n^W is about 3.3 times the dispersion interaction.

TABLE VI

THE DISPERSION FORCES CALCULATED BY INTEGRATION AND BY SUMMATION FOR A SINGLE WATER MOLECULE INTERACTING WITH A HIGH DENSITY POLYETHYLENE SURFACE

Force by Integration (Equation 33)	Force by Summation (Equation 34 for m = 5)	R, A
3.91×10^{-6}	15.4×10^{-6}	3.1
2.45×10^{-7}	5.57×10^{-7}	6.2
4.83×10^{-8}	8.65×10^{-8}	9.3
1.53×10^{-8}	2.39×10^{-8}	12.4
6.26×10^{-9}	8.98×10^{-9}	15.5
3.02×10^{-9}	4.07×10^{-9}	18.6
1.63×10^{-9}	2.09×10^{-9}	21.7
9.55×10^{-10}	1.18×10^{-9}	24.8
5.96×10^{-10}	7.08×10^{-10}	27.9
3.91×10^{-10}	4.50×10^{-10}	31.0
2.67×10^{-10}	2.99×10^{-10}	34.1

TABLE VII

DATA FOR THE EVALUATION OF

DISPERSION INTERACTIONS

Substance	α*	I**	d(A)	σ***
$-CH_2-$	1.80	1.63		
n-Ethane	4.54	1.875		
n-Butane	8.42	1.70		
n-Hexane	12.3	1.63		
Polyethylene (density = 0.96)	1.80	1.63	2.88	11.93
Polystyrene	13.4	1.36	5.45	3.33
Polytetrafluoroethylene	2.00	2.42	3.36	8.75
Polypropylene	5.36	1.62	4.24	5.50
Water	1.48	2.02	3.10	10.3

* $\times 10^{-24}$ cm^3.

** $\times 10^{-11}$ erg.

*** $\times 10^{14}$ Molecules/cm^2.

b. A Group Interacting with Its Environment Near a Flat Plate

Consider a volume of solute of water at Point P surrounded by water (Figure 12); the situation corresponds to Figure 6b. The force due to the infinite slab of water is F_d; the force due to the finite slab or water is F_u; and the force due to the infinite polymer slab is F_p. The water in the plane containing the molecule is ignored, as it produces an interaction which cancels out.

Using the sign conventions of Figure 8 and of equation (24) and the geometry of Figure 12, the expressions for F_u, F_d, and F_n become:

$$F_u = 14.5\ \sigma_w A_0 \sum_{m_1=1}^{m_1} (3.1m_1)^{-5}$$

$$F_d = 14.5\ \sigma_w A_0 \sum_{m=1}^{m} (3.1m)^{-5}$$

$$F_n = F_d - F_u = 14.5\ \sigma_w A_0 \sum_{m=m_1+1}^{m_1+5} (3.1m)^{-5}; \qquad (35)$$

while the expression for the polymer interaction is:

$$F_p = 14.5\ \sigma_p A_0 \sum_{n=}^{5} (R + nd)^{-5} \qquad (36)$$

where $R = 3.1\ (m_1 + 1)$.

The analogous expressions for the energies are:

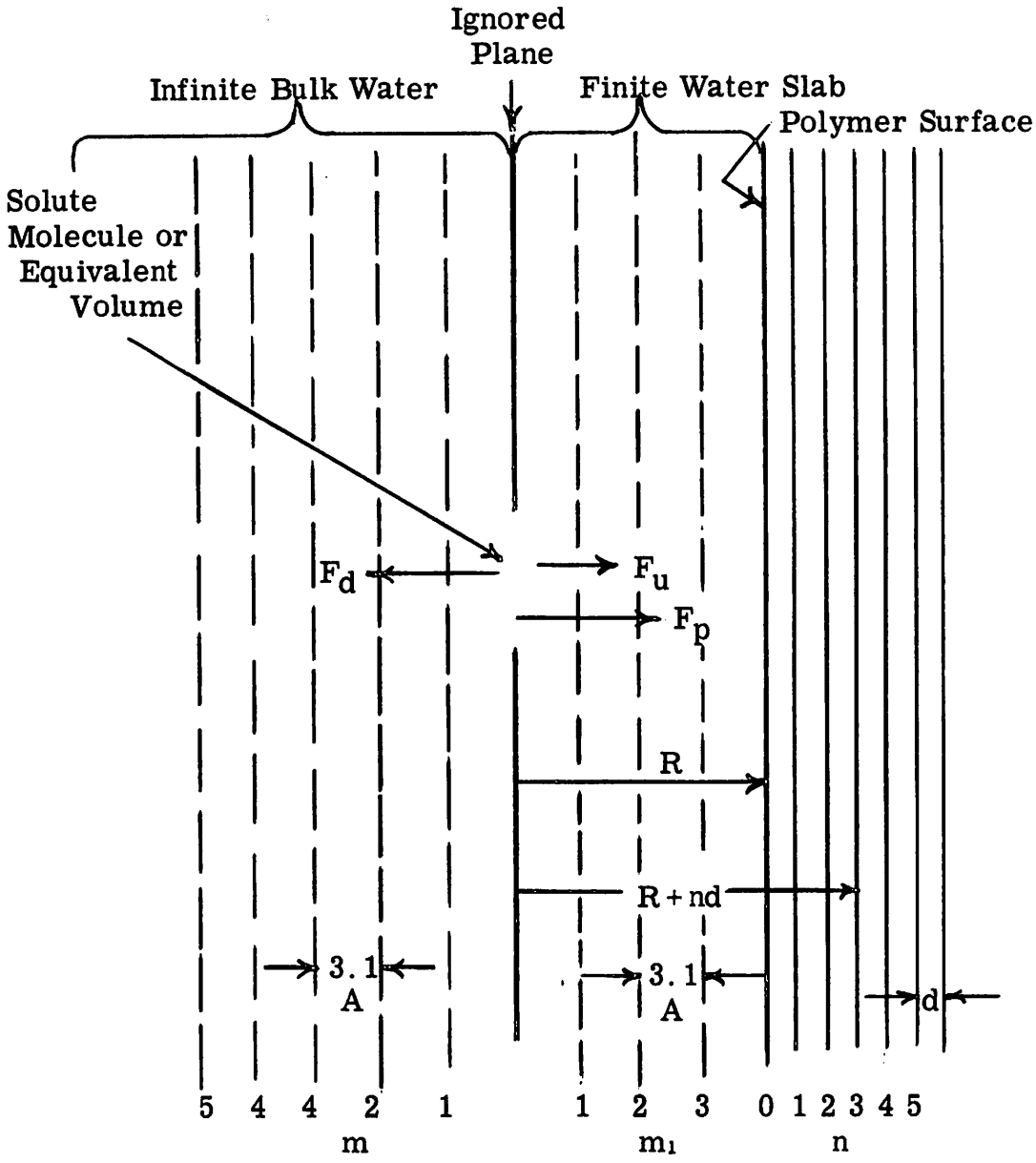


Figure 12. A Molecule Interacting with a Polymer Surface Through a Water Slab. See Figure 6 for Force Notations. The Separation of the Water Planes is 3.1 A (equation 35).

$$U_n = 3.6\,\sigma_w\,A_0 \sum_{m=m_1+1}^{m_1+5} (3.1\,m)^{-4} \quad \text{and} \tag{37}$$

$$U_p = 3.6\,\sigma_p\,A_0 \sum_{n=0}^{5} (R + nd)^{-4}\,. \tag{38}$$

The total force of adsorption is given by equation (24). Equation (35) will give both F_n^s and F_n^w; the only difference is that A_0 terms are different and that the expression for F_n^w must be multipled by 3.3. Equation (36) will give both F_p^w and F_p^s if the appropriate A_0 terms are used.

Though a $-CH_2-$ group and a water molecule are about the same size,[73] they do not occupy the same volume in solution. Water is a relatively loosely packed structure wherein each water molecule occupies a volume of about 30 A^3. If one examines scale molecular models of chains of $-CH_2-$ groups and allows for some vibration and rotation of the groups, the volume occupied by a $-CH_2-$ in an extended chain is about 20 A^3. If a long chain assumes a globular compact structure, the volume per $-CH_2-$ is closer to 30 A^3. The molecules to be considered here are all relatively small or short chains, thus the extended chain arrangement is more reasonable. The assumption is therefore made that a $-CH_2-$ group occupies about two-thirds the volume of a water molecule. Thus, the equivalent volume of water contains two-thirds the number of molecules contained in the solute volume. This can be

accounted for in the equations previously derived by incorporating an 0.67 X term in the A_0 expressions for excluded volume interactions, where X is the number of $-CH_2-$ groups in the solute molecule. Incorporating this correction, placing equations (35) and (36) in equation (24), and consolidating terms, the results are:

$$(F_n^S - F_n^W) = 14.5\,\sigma_W\,(A2 - 3.3\,A1)\sum_{m=m_1+1}^{m_1+5}(3.1m)^{-5} \qquad (39)$$

$$(F_p^W - F_p^S) = 14.5\;\sigma_p\,(A4 - A3)\sum_{n=0}^{5}(R + nd)^{-5} \qquad (40)$$

where A1 ≡ 0.67 X A_0, for water-water interactions;

A2 ≡ A_0, for water-solute interactions;

A3 ≡ A_0, for polymer-solute interactions;

A4 ≡ 0.67 X A_0, for polymer-water interactions;

$$A_0 \equiv \frac{\alpha_1 \alpha_2 I_1 I_2}{(I_1 + I_2)}\text{; and}$$

X = is the number of $-CH_2-$ groups in the solute. Values for α, I, σ, and d were given in Table VII. The sum of equations (39) and (40) gives the total force of adsorption.

Equations (39) and (40) and the analogous expression for the energies of adsorption were programmed and evaluated for the interaction

of a $-CH_2-$ group, ethane, butane, and hexane with some common polymers. The data for the $-CH_2-$ group are given in Table VIII and are plotted in Figure 13. The adsorption force in the absence of a polymer surface is given by equation (39) and is indicated in Figure 13. The adsorption forces due solely to the presence of the polymer phase are calculated by equation (40); the four lower curves in Figure 13 represent the various polymer contributions, decreasing in this order: polystyrene, polypropylene, polyethylene, and PTFE. The interaction roughly follows the trend in the values of the dispersion force component of the surface tension,[73] as expected. The total force of adsorption (equation 24) is given for the PTFE and polystyrene cases in Figure 13. These are the two upper curves in the figure and essentially give the range of interactions, as the curves for the other polymers fall between the two given. It is thus clear that for hydrophobic polymers, the difference in interactions between different polymers surfaces is minimal and never exceeds a spread of 7 to 10%.

The data for ethane, butane, and hexane are given in Tables IX, X, and XI, respectively. The trends are the same as for the $-CH_2-$ case. It is interesting to compare the interactions of the three solute molecules with the same polymer. This is done in Figure 14, where the net force of adsorption between all three alkanes and high density polyethylene is plotted. The differences between the three molecules is quite significant and roughly related to the size of the molecule.

TABLE VIII

THE ADSORPTION FORCES* AND ENERGIES*
BETWEEN A $-CH_2-$ GROUP AND SOME COMMON POLYMERS

R.A.	Water Force $F_n^S - F_n^W$	Water Energy $U_n^S - U_n^W$
3.1	$1.35\ 10^{-5}$	$1.08\ 10^{-13}$
6.2	$4.78\ 10^{-7}$	$8.11\ 10^{-15}$
9.3	$7.27\ 10^{-8}$	$1.90\ 10^{-15}$
12.4	$1.97\ 10^{-8}$	$6.94\ 10^{-16}$
15.5	$7.22\ 10^{-9}$	$3.18\ 10^{-16}$
18.6	$3.19\ 10^{-9}$	$1.68\ 10^{-16}$

R.A.	$F_p^W - F_p^S$	F^{ads}	$U_p^W - U_p^S$	U^{ads}
	High Density Polyethylene			
3.1	$0.65\ 10^{-5}$	$2.00\ 10^{-5}$	$0.53\ 10^{-13}$	$1.61\ 10^{-13}$
6.2	$2.36\ 10^{-7}$	$7.14\ 10^{-7}$	$4.04\ 10^{-15}$	$1.22\ 10^{-14}$
9.3	$3.64\ 10^{-8}$	$1.09\ 10^{-7}$	$0.96\ 10^{-15}$	$2.87\ 10^{-15}$
12.4	$1.00\ 10^{-8}$	$2.97\ 10^{-7}$	$3.56\ 10^{-16}$	$1.05\ 10^{-15}$
15.5	$3.69\ 10^{-9}$	$1.09\ 10^{-8}$	$1.65\ 10^{-16}$	$4.83\ 10^{-16}$
18.6	$1.64\ 10^{-9}$	$4.83\ 10^{-8}$	$0.88\ 10^{-16}$	$2.56\ 10^{-16}$
	Polystyrene			
3.1	$1.21\ 10^{-5}$	$2.56\ 10^{-5}$	$0.94\ 10^{-13}$	$2.02\ 10^{-13}$
6.2	$3.94\ 10^{-7}$	$8.74\ 10^{-7}$	$6.39\ 10^{-15}$	$1.45\ 10^{-14}$
9.3	$5.58\ 10^{-8}$	$1.29\ 10^{-7}$	$1.41\ 10^{-15}$	$3.31\ 10^{-15}$
12.4	$1.44\ 10^{-8}$	$3.41\ 10^{-8}$	$4.96\ 10^{-16}$	$1.19\ 10^{-15}$
15.5	$5.14\ 10^{-9}$	$1.24\ 10^{-8}$	$2.25\ 10^{-16}$	$5.43\ 10^{-16}$
18.6	$2.24\ 10^{-9}$	$5.43\ 10^{-9}$	$1.19\ 10^{-16}$	$2.87\ 10^{-16}$
	Polytetrafluoroethylene (PTFE)			
3.1	$0.61\ 10^{-5}$	$1.95\ 10^{-5}$	$0.48\ 10^{-13}$	$1.56\ 10^{-13}$
0.2	$2.12\ 10^{-7}$	$6.90\ 10^{-7}$	$3.59\ 10^{-15}$	$1.17\ 10^{-14}$
9.3	$3.21\ 10^{-8}$	$1.05\ 10^{-7}$	$0.84\ 10^{-15}$	$2.75\ 10^{-15}$
12.4	$0.87\ 10^{-8}$	$2.83\ 10^{-8}$	$3.08\ 10^{-16}$	$1.00\ 10^{-15}$
15.5	$3.19\ 10^{-9}$	$1.04\ 10^{-8}$	$1.42\ 10^{-16}$	$4.61\ 10^{-16}$
18.6	$1.42\ 10^{-9}$	$4.61\ 10^{-9}$	$0.76\ 10^{-16}$	$2.45\ 10^{-16}$
	Polypropylene			
3.1	$0.87\ 10^{-5}$	$2.22\ 10^{-5}$	$0.69\ 10^{-13}$	$1.77\ 10^{-13}$
6.2	$2.93\ 10^{-7}$	$7.71\ 10^{-7}$	$4.85\ 10^{-15}$	$1.30\ 10^{-14}$
9.3	$4.28\ 10^{-8}$	$1.16\ 10^{-7}$	$1.10\ 10^{-15}$	$3.01\ 10^{-15}$
12.4	$1.13\ 10^{-8}$	$3.10\ 10^{-8}$	$3.97\ 10^{-16}$	$1.09\ 10^{-15}$
15.5	$4.11\ 10^{-9}$	$1.13\ 10^{-8}$	$1.82\ 10^{-16}$	$5.01\ 10^{-16}$
18.6	$1.81\ 10^{-9}$	$5.00\ 10^{-9}$	$0.97\ 10^{-16}$	$2.66\ 10^{-16}$

*All forces and energies are negative, indicating adsorption.

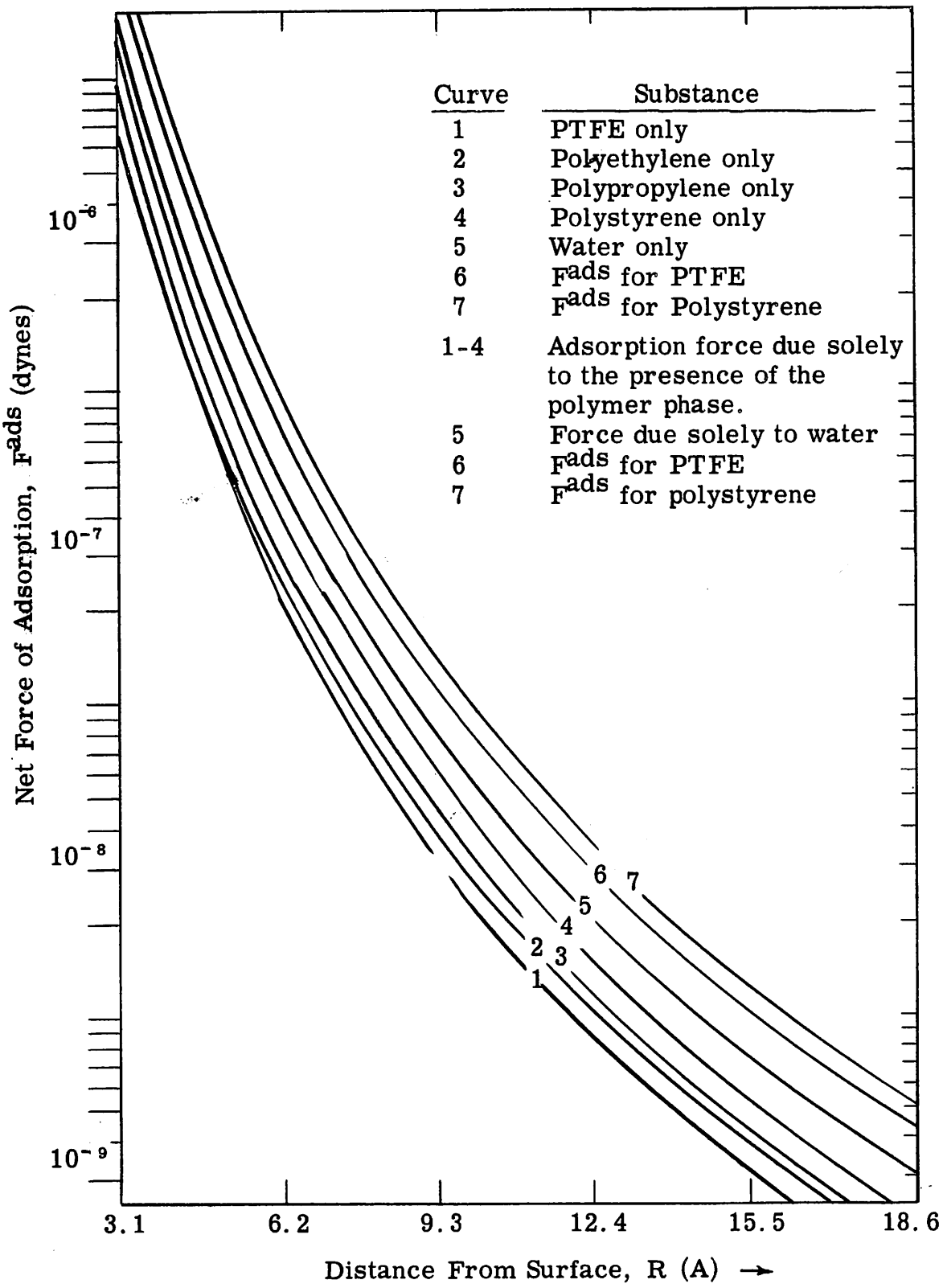


Figure 13. The Adsorption Forces Between a $-CH_2-$ Group and Some Common Polymers (see Text and Table VIII).

TABLE IX

THE ADSORPTION FORCES* AND ENERGIES* BETWEEN AN ETHANE MOLECULE AND SOME COMMON POLYMERS

R. A.	Water Force, $F_n^s - F_n^w$	Water Energy, $U_n^s - U_n^w$
3.1	$1.76\ 10^{-5}$	$1.41\ 10^{-13}$
6.2	$6.26\ 10^{-7}$	$1.06\ 10^{-14}$
9.2	$0.95\ 10^{-7}$	$2.49\ 10^{-15}$
12.4	$2.58\ 10^{-8}$	$0.91\ 10^{-15}$
15.5	$0.94\ 10^{-8}$	$4.17\ 10^{-16}$
18.6	$4.18\ 10^{-9}$	$2.20\ 10^{-16}$

R, A	$F_p^w - F_p^s$	F^{ads}	$U_p^w - U_p^s$	U^{ads}
		High Density Polyethylene		
3.1	$2.47\ 10^{-5}$	$4.23\ 10^{-5}$	$1.99\ 10^{-13}$	$3.41\ 10^{-13}$
6.1	$8.92\ 10^{-7}$	$1.52\ 10^{-6}$	$1.53\ 10^{-14}$	$2.59\ 10^{-14}$
9.3	$1.38\ 10^{-7}$	$2.33\ 10^{-7}$	$3.64\ 10^{-15}$	$6.14\ 10^{-15}$
12.4	$3.77\ 10^{-8}$	$6.34\ 10^{-8}$	$1.34\ 10^{-15}$	$2.25\ 10^{-15}$
15.5	$1.39\ 10^{-8}$	$2.34\ 10^{-8}$	$6.23\ 10^{-16}$	$1.04\ 10^{-15}$
18.6	$6.21\ 10^{-9}$	$1.04\ 10^{-8}$	$3.32\ 10^{-16}$	$5.53\ 10^{-16}$
		Polystyrene		
3.1	$4.49\ 10^{-5}$	$6.25\ 10^{-5}$	$3.50\ 10^{-13}$	$4.91\ 10^{-13}$
6.2	$1.46\ 10^{-6}$	$2.09\ 10^{-6}$	$2.37\ 10^{-14}$	$3.43\ 10^{-14}$
9.3	$2.07\ 10^{-7}$	$3.02\ 10^{-7}$	$5.22\ 10^{-15}$	$7.71\ 10^{-15}$
12.4	$5.35\ 10^{-8}$	$7.92\ 10^{-8}$	$1.84\ 10^{-15}$	$2.75\ 10^{-15}$
15.5	$1.91\ 10^{-8}$	$2.85\ 10^{-8}$	$8.35\ 10^{-16}$	$1.25\ 10^{-15}$
18.6	$8.31\ 10^{-9}$	$1.25\ 10^{-8}$	$4.41\ 10^{-16}$	$6.62\ 10^{-16}$
		Polytetrafluoroethylene (PTFE)		
3.1	$2.39\ 10^{-5}$	$4.15\ 10^{-5}$	$1.91\ 10^{-13}$	$3.32\ 10^{-13}$
6.2	$8.36\ 10^{-7}$	$1.46\ 10^{-6}$	$1.41\ 10^{-14}$	$2.48\ 10^{-14}$
9.3	$1.26\ 10^{-7}$	$2.21\ 10^{-7}$	$3.31\ 10^{-15}$	$5.81\ 10^{-15}$
12.4	$3.42\ 10^{-8}$	$5.99\ 10^{-8}$	$1.21\ 10^{-15}$	$2.12\ 10^{-15}$
15.5	$1.26\ 10^{-8}$	$2.20\ 10^{-8}$	$5.61\ 10^{-16}$	$9.78\ 10^{-16}$
18.6	$5.59\ 10^{-9}$	$9.76\ 10^{-9}$	$3.00\ 10^{-16}$	$5.20\ 10^{-16}$
		Polypropylene		
3.1	$3.29\ 10^{-5}$	$5.05\ 10^{-5}$	$2.59\ 10^{-13}$	$4.00\ 10^{-13}$
6.2	$1.11\ 10^{-6}$	$1.73\ 10^{-6}$	$1.83\ 10^{-14}$	$2.89\ 10^{-14}$
9.3	$1.62\ 10^{-7}$	$2.57\ 10^{-7}$	$4.16\ 10^{-15}$	$6.66\ 10^{-15}$
12.4	$4.28\ 10^{-8}$	$6.86\ 10^{-8}$	$1.50\ 10^{-15}$	$2.41\ 10^{-15}$
15.5	$1.55\ 10^{-8}$	$2.50\ 10^{-8}$	$6.90\ 10^{-16}$	$1.11\ 10^{-15}$
18.6	$6.86\ 10^{-9}$	$1.10\ 10^{-8}$	$3.67\ 10^{-16}$	$5.88\ 10^{-16}$

* All forces and energies are negative, indicating adsorption.

TABLE X

THE ADSORPTION FORCES* AND ENERGIES* BETWEEN A BUTANE MOLECULE AND SOME COMMON POLYMERS

R.A.	Water Force, $F_n^s - F_n^w$	Water Energy, $U_n^s - U_n^w$
3.1	$4.37\ 10^{-5}$	$3.50\ 10^{-13}$
6.2	$1.55\ 10^{-6}$	$2.63\ 10^{-14}$
9.3	$2.35\ 10^{-7}$	$6.18\ 10^{-15}$
12.4	$6.39\ 10^{-8}$	$2.25\ 10^{-15}$
15.5	$2.34\ 10^{-8}$	$1.03\ 10^{-15}$
18.6	$1.03\ 10^{-8}$	$5.46\ 10^{-16}$

R.A.	$F_p^w - F_p^s$	F^{ads}	$U_p^w - U_p^s$	U^{ads}
		High Density Polyethylene		
3.1	$3.91\ 10^{-5}$	$8.28\ 10^{-5}$	$3.15\ 10^{-13}$	$6.66\ 10^{-13}$
6.2	$1.41\ 10^{-6}$	$2.96\ 10^{-6}$	$2.42\ 10^{-14}$	$5.05\ 10^{-14}$
9.3	$2.18\ 10^{-7}$	$4.54\ 10^{-7}$	$5.76\ 10^{-15}$	$1.19\ 10^{-14}$
12.4	$5.96\ 10^{-8}$	$1.23\ 10^{-7}$	$2.13\ 10^{-15}$	$4.38\ 10^{-15}$
15.5	$2.20\ 10^{-8}$	$4.55\ 10^{-8}$	$9.85\ 10^{-16}$	$2.01\ 10^{-15}$
18.6	$9.82\ 10^{-9}$	$2.02\ 10^{-8}$	$5.26\ 10^{-16}$	$1.07\ 10^{-15}$
		Polystyrene		
3.1	$7.16\ 10^{-5}$	$1.15\ 10^{-4}$	$5.59\ 10^{-13}$	$9.09\ 10^{-13}$
6.2	$2.34\ 10^{-6}$	$3.89\ 10^{-6}$	$3.79\ 10^{-14}$	$6.42\ 10^{-14}$
9.3	$3.31\ 10^{-7}$	$5.6\ 10^{-7}$	$8.33\ 10^{-15}$	$1.45\ 10^{-14}$
12.4	$8.54\ 10^{-8}$	$1.49\ 10^{-7}$	$2.94\ 10^{-15}$	$5.19\ 10^{-15}$
15.5	$3.15\ 10^{-8}$	$5.39\ 10^{-8}$	$1.33\ 10^{-15}$	$2.37\ 10^{-15}$
18.6	$1.33\ 10^{-8}$	$2.36\ 10^{-8}$	$7.05\ 10^{-16}$	$1.25\ 10^{-15}$
		Polytetrafluoroethylene (PTFE)		
3.1	$3.70\ 10^{-5}$	$8.07\ 10^{-5}$	$2.95\ 10^{-13}$	$6.46\ 10^{-13}$
6.2	$1.29\ 10^{-6}$	$2.85\ 10^{-6}$	$2.19\ 10^{-14}$	$4.82\ 10^{-14}$
9.3	$1.96\ 10^{-7}$	$4.32\ 10^{-7}$	$5.13\ 10^{-15}$	$1.13\ 10^{-14}$
12.4	$5.29\ 10^{-8}$	$1.17\ 10^{-7}$	$1.88\ 10^{-15}$	$4.13\ 10^{-15}$
15.5	$1.95\ 10^{-8}$	$4.29\ 10^{-8}$	$8.69\ 10^{-16}$	$1.90\ 10^{-15}$
18.6	$8.65\ 10^{-9}$	$1.90\ 10^{-8}$	$4.64\ 10^{-16}$	$1.01\ 10^{-15}$
		Polypropylene		
3.1	$5.20\ 10^{-5}$	$9.57\ 10^{-5}$	$4.10\ 10^{-13}$	$7.60\ 10^{-13}$
6.2	$1.75\ 10^{-6}$	$3.30\ 10^{-6}$	$2.90\ 10^{-14}$	$5.53\ 10^{-14}$
9.3	$2.56\ 10^{-7}$	$4.92\ 10^{-7}$	$6.59\ 10^{-15}$	$1.28\ 10^{-14}$
12.4	$6.77\ 10^{-8}$	$1.32\ 10^{-7}$	$2.38\ 10^{-15}$	$4.63\ 10^{-15}$
15.5	$2.46\ 10^{-8}$	$4.80\ 10^{-8}$	$1.03\ 10^{-15}$	$2.12\ 10^{-15}$
18.5	$1.08\ 10^{-8}$	$2.12\ 10^{-8}$	$5.81\ 10^{-16}$	$1.13\ 10^{-15}$

*All forces and energies are negative, indicating adsorptions.

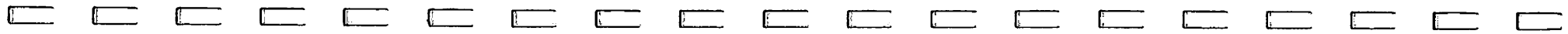


TABLE XI

THE ADSORPTION FORCES* AND ENERGIES* BETWEEN A HEXANE MOLECULE AND SOME COMMON POLYMERS

R, A	Water Force, $F_n^s - F_n^w$	Water Energy, $U_n^s - U_n^w$
3.1	$7.00\ 10^{-5}$	$5.62\ 10^{-13}$
6.2	$2.49\ 10^{-6}$	$4.22\ 10^{-14}$
9.3	$3.78\ 10^{-7}$	$9.90\ 10^{-15}$
12.4	$1.02\ 10^{-7}$	$3.61\ 10^{-15}$
15.5	$3.74\ 10^{-8}$	$1.66\ 10^{-15}$
18.6	$1.66\ 10^{-8}$	$8.76\ 10^{-16}$

R, A	$F_p^w - F_p^s$	F^{ads}	$U_p^w - U_p^s$	U^{ads}
	High Density Polyethylene			
3.1	$5.31\ 10^{-5}$	$1.23\ 10^{-4}$	$4.29\ 10^{-13}$	$9.90\ 10^{-13}$
6.2	$1.92\ 10^{-6}$	$4.40\ 10^{-6}$	$3.29\ 10^{-14}$	$7.50\ 10^{-14}$
9.3	$2.96\ 10^{-7}$	$6.74\ 10^{-7}$	$7.83\ 10^{-15}$	$1.77\ 10^{-14}$
12.4	$0.81\ 10^{-7}$	$1.83\ 10^{-7}$	$2.89\ 10^{-15}$	$6.50\ 10^{-15}$
15.5	$3.00\ 10^{-8}$	$6.75\ 10^{-8}$	$1.34\ 10^{-15}$	$2.99\ 10^{-15}$
18.6	$1.33\ 10^{-8}$	$2.99\ 10^{-8}$	$7.14\ 10^{-16}$	$1.59\ 10^{-15}$
	Polystyrene			
3.1	$9.78\ 10^{-5}$	$1.68\ 10^{-4}$	$7.63\ 10^{-13}$	$1.32\ 10^{-12}$
6.2	$3.19\ 10^{-6}$	$5.68\ 10^{-6}$	$5.17\ 10^{-14}$	$9.39\ 10^{-14}$
9.3	$4.51\ 10^{-7}$	$8.30\ 10^{-7}$	$1.14\ 10^{-14}$	$2.13\ 10^{-14}$
12.4	$1.17\ 10^{-7}$	$2.19\ 10^{-7}$	$4.02\ 10^{-15}$	$7.62\ 10^{-15}$
15.5	$4.16\ 10^{-8}$	$7.91\ 10^{-8}$	$1.82\ 10^{-15}$	$3.48\ 10^{-15}$
18.6	$1.81\ 10^{-8}$	$3.47\ 10^{-8}$	$9.62\ 10^{-16}$	$1.84\ 10^{-15}$
	Polytetrafluoroethylene (PTFE)			
3.1	$4.97\ 10^{-5}$	$1.20\ 10^{-4}$	$3.97\ 10^{-13}$	$9.57\ 10^{-13}$
6.2	$1.74\ 10^{-6}$	$4.23\ 10^{-6}$	$2.94\ 10^{-14}$	$7.16\ 10^{-14}$
9.3	$2.63\ 10^{-7}$	$6.41\ 10^{-7}$	$6.89\ 10^{-15}$	$1.68\ 10^{-14}$
12.4	$7.11\ 10^{-8}$	$1.73\ 10^{-7}$	$2.52\ 10^{-15}$	$6.13\ 10^{-15}$
15.5	$2.61\ 10^{-8}$	$6.37\ 10^{-8}$	$1.17\ 10^{-15}$	$2.82\ 10^{-15}$
18.6	$1.16\ 10^{-8}$	$2.82\ 10^{-8}$	$6.23\ 10^{-16}$	$1.50\ 10^{-15}$
	Polypropylene			
3.1	$7.07\ 10^{-5}$	$1.41\ 10^{-4}$	$5.57\ 10^{-13}$	$1.12\ 10^{-12}$
6.2	$2.38\ 10^{-6}$	$4.86\ 10^{-6}$	$3.94\ 10^{-14}$	$8.15\ 10^{-14}$
9.3	$3.48\ 10^{-7}$	$7.26\ 10^{-7}$	$8.95\ 10^{-15}$	$1.89\ 10^{-14}$
12.4	$9.20\ 10^{-8}$	$1.94\ 10^{-7}$	$3.23\ 10^{-15}$	$6.48\ 10^{-15}$
15.5	$3.34\ 10^{-8}$	$7.09\ 10^{-8}$	$1.48\ 10^{-15}$	$3.24\ 10^{-15}$
18.6	$1.47\ 10^{-8}$	$3.13\ 10^{-8}$	$7.89\ 10^{-16}$	$1.67\ 10^{-15}$

* All forces and energies are negative, indicating adsorption.

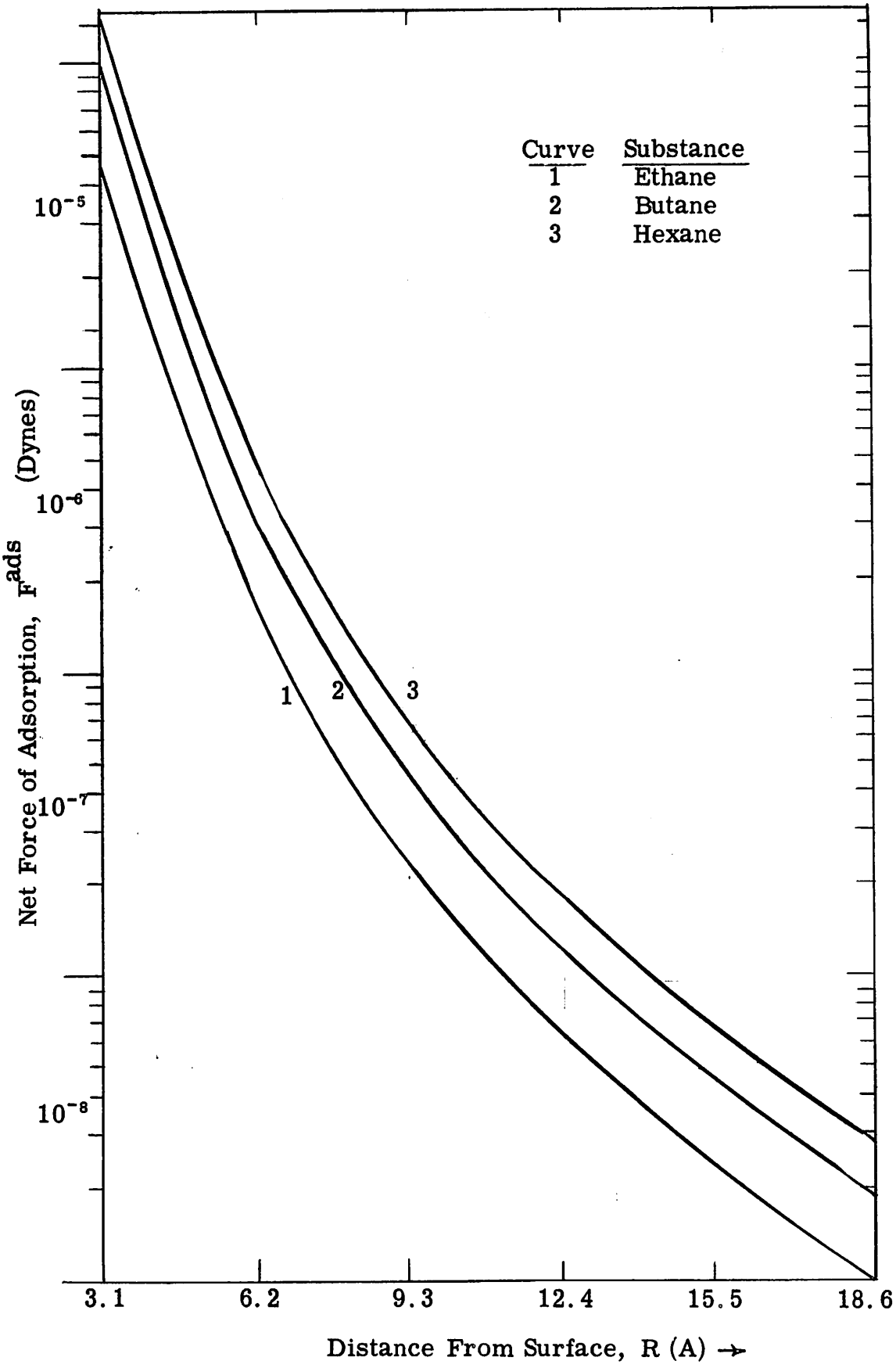


Figure 14. The Adsorption Force Between Some n-Alkanes and High Density Polyethylene.

Figure 13 shows that maximum interaction occurs with polystyrene and minimum interaction with polytetrofluoroethylene (PTFE). The data for polystyrene and PTFE are plotted in Figure 15 for the three alkanes and for a $-CH_2-$ group. The range of interactions for a given solute molecule does not overlap with those of the other solutes considered. If the odd alkanes, e.g., pentane, had also been considered, there would have been some overlap with the curves for the adjacent even-alkanes. It is, therefore, quite clear that the adsorption force is more dependent on the solute molecule than on the hydrophobic polymer surface.

These results all assume that the molecule can be located at a point and that the polarizability of the solute is a constant, independent of orientation. The case of orientation-dependent polarizability will be discussed later.

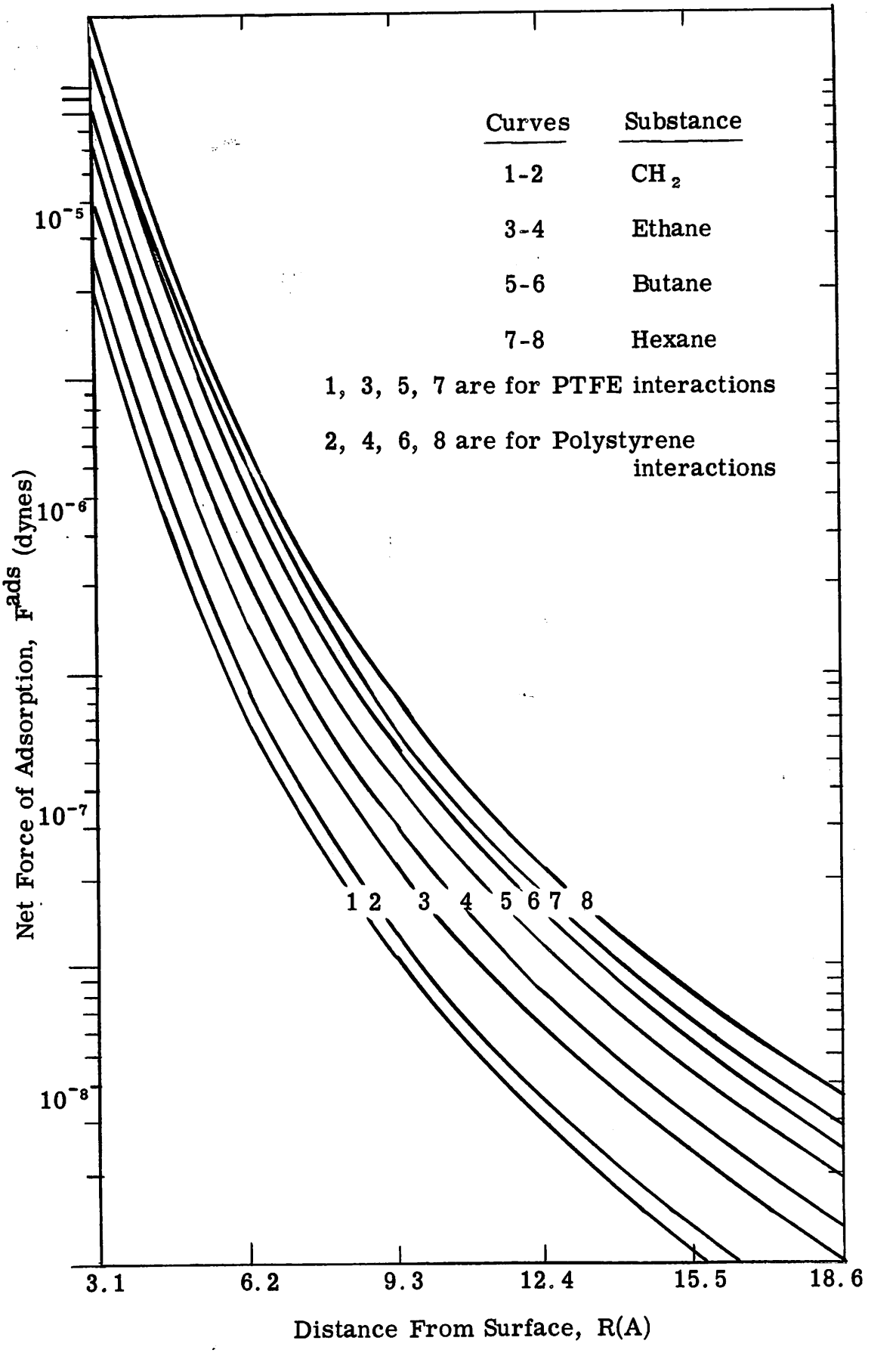


Figure 15. The Spread of Adsorption Forces for Some Alkanes Interacting With Some Common Polymers (see text).

c. Effect of Polymer Density and Water Content

The case where the polymer surface is porous and permeable to water will now be considered. This analysis and the calculations derived from it will be used in Section C to explain monolayer adsorption. The case where the polymer is impermeable (contains zero per cent water) has already been treated. The case where there is no polymer ("it" contains one hundred per cent water) corresponds to that of a solute molecule surrounded by bulk water, and the adsorption force must be zero. The case where the polymer density is variable, but it is impermeable to water, will also be treated. For this latter case, when the polymer density is zero, the situation must be the same as at an air/water interface.

Let the weight fraction of polymer be Y and the weight fraction of uniformly dispersed water be 1-Y. Only the case of high density (0.96) polyethylene will be treated. Thus, the polymer and water density are approximately the same, and the treatment is simplified. The effective polymer density is Y grams/cm^3 and the effective water density is (1-Y) grams/cm^3. The equivalent planar spacings of the water and polymer components can be calculated with equation (35). The value for polyethylene is

$$d_{PE} = 1.18\ (14/Y)^{0.33}\ A, \qquad (41)$$

and the value for dispersed water is

$$d_{dw} = 1.18\,[18/(1 - Y)]^{0.33}\,A. \tag{42}$$

The subscript PE denotes polyethylene and dw denotes "dispersed water." The number of molecules/cm^2, σ, is given by the equation,

$$\sigma = (\rho N_0/M)^{0.67},$$

where ρ is the density, N_0 is Avogadro's number, and M is the group molecular weight. The value for polyethylene is

$$\sigma_{PE} = (11.9 \times 10^{14})(Y)^{0.67}, \tag{43}$$

and the value for the dispersed water is

$$\sigma_{dw} = (10.3 \times 10^{14})(1 - Y)^{0.67}. \tag{44}$$

The polymer interaction, F_p (equation 36), is now composed of two terms. The first is due to the interaction with the actual polymer present, and the second is due to the interaction with the water dispersed in the polymer phase. Therefore, F_p becomes:

$$F_p = 14.5\left[\left(\sigma A_0 \sum_{n=0}^{5} (R + nd)^{-5}\right)_{PE} + \left(\sigma A_0 \sum_{n=0}^{5} (R + nd)^{-5}\right)_{dw}\right] \tag{45}$$

The adsorption force due to the presence of a water-permeable polymer now becomes:

$$F_p^w - F_p^s = 14.5\sigma_{PE}(A4 - A3) \sum_{n=0}^{5} (R + nd_{PE})^{-5} + 14.5\sigma_{dw}(3.3A1 - A2) \sum_{n=0}^{5} (R + nd_{dw})^{-5} \tag{46}$$

where σ and d terms are given by equations (41) to (44). Equation (39) is not affected by the presence of water in the polymer phase.

The case where the polymer density varies but no water is present in the polymer is also given by equations (39) and (46) if the second term in equation (46) is set equal to zero.

Equations (39) and (46) were programmed and evaluated for polymer densities varying from 0 to 1.0. The data are given in Table XII and plotted in Figures 16 and 17. The results are very interesting. Figure 16 clearly shows that the force of adsorption tends to zero as Y decreases (as the water content increases), as expected. If the polymer density decreases but the polymer is not allowed to take on water, the interaction force decreases with Y until at $Y = 0$ the force is the same as for an air/water interface (Figure 17).

TABLE XII

THE EFFECT OF POLYMER DENSITY AND WATER CONTENT ON DISPERSION INTERACTIONS BETWEEN A $-CH_2-$ GROUP AND POLYETHYLENE*

R, A	Water Force, $F_n^s - F_n^w$
3.1	$1.25\ 10^{-5}$
6.2	$4.42\ 10^{-7}$
9.3	$6.73\ 10^{-8}$
12.4	$1.82\ 10^{-8}$
15.5	$6.68\ 10^{-9}$
18.6	$2.95\ 10^{-9}$

Y	R, A	Impermeable Case $F_p^w - F_p^s$	Impermeable Case F^{ads}	Permeable Case $F_p^w - F_p^s$	Permeable Case F^{ads}
1.0	3.1	$7.79\ 10^{-6}$	$2.03\ 10^{-5}$	$7.79\ 10^{-6}$	$2.03\ 10^{-5}$
	6.2	$2.82\ 10^{-7}$	$7.25\ 10^{-7}$	$2.82\ 10^{-7}$	$7.25\ 10^{-7}$
	9.3	$4.37\ 10^{-8}$	$1.11\ 10^{-8}$	$4.37\ 10^{-8}$	$1.11\ 10^{-8}$
	12.4	$1.20\ 10^{-8}$	$3.02\ 10^{-8}$	$1.20\ 10^{-8}$	$3.02\ 10^{-8}$
	15.5	$4.44\ 10^{-9}$	$1.11\ 10^{-9}$	$4.44\ 10^{-9}$	$1.11\ 10^{-9}$
	18.6	$1.98\ 10^{-9}$	$4.93\ 10^{-9}$	$1.98\ 10^{-9}$	$4.93\ 10^{-9}$
0.8	3.1	$6.65\ 10^{-6}$	$1.91\ 10^{-5}$	$2.53\ 10^{-6}$	$1.50\ 10^{-5}$
	6.2	$2.38\ 10^{-7}$	$6.80\ 10^{-7}$	$1.02\ 10^{-7}$	$5.45\ 10^{-7}$
	9.3	$3.64\ 10^{-8}$	$1.04\ 10^{-7}$	$1.72\ 10^{-8}$	$8.45\ 10^{-8}$
	12.4	$9.92\ 10^{-9}$	$2.81\ 10^{-8}$	$4.94\ 10^{-9}$	$2.32\ 10^{-8}$
	15.5	$3.66\ 10^{-9}$	$1.02\ 10^{-8}$	$1.88\ 10^{-9}$	$8.56\ 10^{-9}$
	18.6	$1.63\ 10^{-9}$	$4.58\ 10^{-9}$	$8.53\ 10^{-10}$	$3.80\ 10^{-9}$
0.6	3.1	$5.44\ 10^{-6}$	$1.79\ 10^{-5}$	$1.17\ 10^{-6}$	$1.13\ 10^{-5}$
	6.3	$1.91\ 10^{-7}$	$6.33\ 10^{-7}$	$3.26\ 10^{-8}$	$4.10\ 10^{-7}$
	9.3	$2.89\ 10^{-8}$	$9.62\ 10^{-8}$	$3.92\ 10^{-9}$	$6.34\ 10^{-8}$
	12.4	$7.80\ 10^{-9}$	$2.60\ 10^{-8}$	$8.86\ 10^{-10}$	$1.73\ 10^{-8}$
	15.5	$2.87\ 10^{-9}$	$9.55\ 10^{-9}$	$2.88\ 10^{-10}$	$6.39\ 10^{-9}$
	18.6	$1.28\ 10^{-9}$	$4.23\ 10^{-9}$	$1.19\ 10^{-10}$	$2.83\ 10^{-9}$
0.4	3.1	$4.11\ 10^{-6}$	$1.66\ 10^{-5}$	$+4.63\ 10^{-6}$	$7.83\ 10^{-6}$
	6.2	$1.41\ 10^{-7}$	$5.83\ 10^{-7}$	$+1.61\ 10^{-7}$	$2.81\ 10^{-7}$
	9.3	$2.09\ 10^{-8}$	$8.82\ 10^{-8}$	$+2.43\ 10^{-8}$	$4.31\ 10^{-8}$
	12.4	$5.58\ 10^{-9}$	$2.38\ 10^{-8}$	$+6.53\ 10^{-9}$	$1.17\ 10^{-8}$
	15.5	$2.04\ 10^{-9}$	$8.72\ 10^{-9}$	$+2.40\ 10^{-9}$	$4.28\ 10^{-9}$
	18.6	$9.02\ 10^{-10}$	$3.85\ 10^{-9}$	$+1.07\ 10^{-9}$	$1.89\ 10^{-9}$

* All forces are negative, indicating adsorption, EXCEPT those specifically written with positive (+) signs.

Table Continued...

TABLE XII*

(Continued)

Y	R, A	$F_p^w - F_p^s$	F^{ads}	$F_p^w - F_p^s$	F^{ads}
		Impermeable Case		Permeable Case	
0.2	3.1	$2.56\ 10^{-6}$	$1.51\ 10^{-5}$	$+8.12\ 10^{-6}$	$4.34\ 10^{-6}$
	6.2	$8.46\ 10^{-8}$	$5.27\ 10^{-7}$	$+2.90\ 10^{-7}$	$1.52\ 10^{-7}$
	9.3	$1.22\ 10^{-8}$	$7.95\ 10^{-8}$	$+4.46\ 10^{-8}$	$2.27\ 10^{-8}$
	12.4	$3.18\ 10^{-9}$	$2.14\ 10^{-8}$	$+1.22\ 10^{-8}$	$6.02\ 10^{-9}$
	15.5	$1.15\ 10^{-9}$	$7.82\ 10^{-9}$	$+4.52\ 10^{-9}$	$2.16\ 10^{-9}$
	18.6	$5.03\ 10^{-10}$	$3.45\ 10^{-9}$	$+2.01\ 10^{-9}$	$9.38\ 10^{-10}$
0.1	3.1	$1.60\ 10^{-6}$	$1.41\ 10^{-5}$	$+1.00\ 10^{-5}$	$2.47\ 10^{-6}$
	6.2	$5.17\ 10^{-8}$	$4.94\ 10^{-7}$	$+3.58\ 10^{-7}$	$8.39\ 10^{-8}$
	9.3	$7.23\ 10^{-9}$	$7.46\ 10^{-8}$	$+5.52\ 10^{-8}$	$1.21\ 10^{-9}$
	12.4	$1.85\ 10^{-9}$	$2.01\ 10^{-8}$	$+1.51\ 10^{-8}$	$3.10\ 10^{-9}$
	15.5	$6.54\ 10^{-10}$	$7.33\ 10^{-9}$	$+5.60\ 10^{-9}$	$1.08\ 10^{-9}$
	18.6	$2.83\ 10^{-10}$	$3.24\ 10^{-9}$	$+2.50\ 10^{-9}$	$4.51\ 10^{-10}$
0.01	3.1	$2.30\ 10^{-7}$	$1.28\ 10^{-5}$	$+1.21\ 10^{-5}$	$4.12\ 10^{-7}$
	6.2	$1.07\ 10^{-8}$	$4.53\ 10^{-7}$	$+4.31\ 10^{-7}$	$1.18\ 10^{-8}$
	9.3	$1.42\ 10^{-9}$	$6.87\ 10^{-8}$	$+6.61\ 10^{-8}$	$1.25\ 10^{-9}$
	12.4	$3.43\ 10^{-10}$	$1.86\ 10^{-8}$	$+1.80\ 10^{-8}$	$1.81\ 10^{-10}$
	15.5	$1.15\ 10^{-10}$	$6.79\ 10^{-9}$	$+6.67\ 10^{-9}$	$7.90\ 10^{-11}$
	18.6	$4.77\ 10^{-11}$	$3.00\ 10^{-9}$	$+2.97\ 10^{-9}$	$2.16\ 10^{-11}$
0.001	3.1	$7.27\ 10^{-8}$	$1.25\ 10^{-5}$	$+1.24\ 10^{-5}$	$6.56\ 10^{-8}$
	6.2	$2.27\ 10^{-9}$	$4.46\ 10^{-7}$	$+4.42\ 10^{-7}$	$3.03\ 10^{-9}$
	9.3	$2.99\ 10^{-10}$	$6.76\ 10^{-8}$	$+6.76\ 10^{-8}$	$3.69\ 10^{-10}$
	12.4	$7.12\ 10^{-11}$	$1.83\ 10^{-8}$	$+1.85\ 10^{-8}$	$2.31\ 10^{-10}$
	15.5	$2.34\ 10^{-11}$	$6.70\ 10^{-9}$	$+6.82\ 10^{-9}$	$1.36\ 10^{-10}$
	18.6	$9.46\ 10^{-12}$	$2.96\ 10^{-9}$	$+3.03\ 10^{-9}$	$8.34\ 10^{-11}$
0	3.1	0	$1.25\ 10^{-5}$	$+1.25\ 10^{-5}$	$+1.59\ 10^{-8}$
	6.2	0	$4.42\ 10^{-7}$	$+4.45\ 10^{-7}$	$+2.31\ 10^{-9}$
	9.3	0	$6.73\ 10^{-8}$	$+6.80\ 10^{-8}$	$+7.24\ 10^{-10}$
	12.4	0	$1.82\ 10^{-8}$	$+1.85\ 10^{-8}$	$+3.18\ 10^{-10}$
	15.5	0	$6.68\ 10^{-9}$	$+6.84\ 10^{-9}$	$+1.66\ 10^{-10}$
	18.6	0	$2.95\ 10^{-9}$	$+3.05\ 10^{-9}$	$+9.55\ 10^{-11}$

*All forces are negative, indicating adsorption, EXCEPT those specifically written with positive (+) signs.

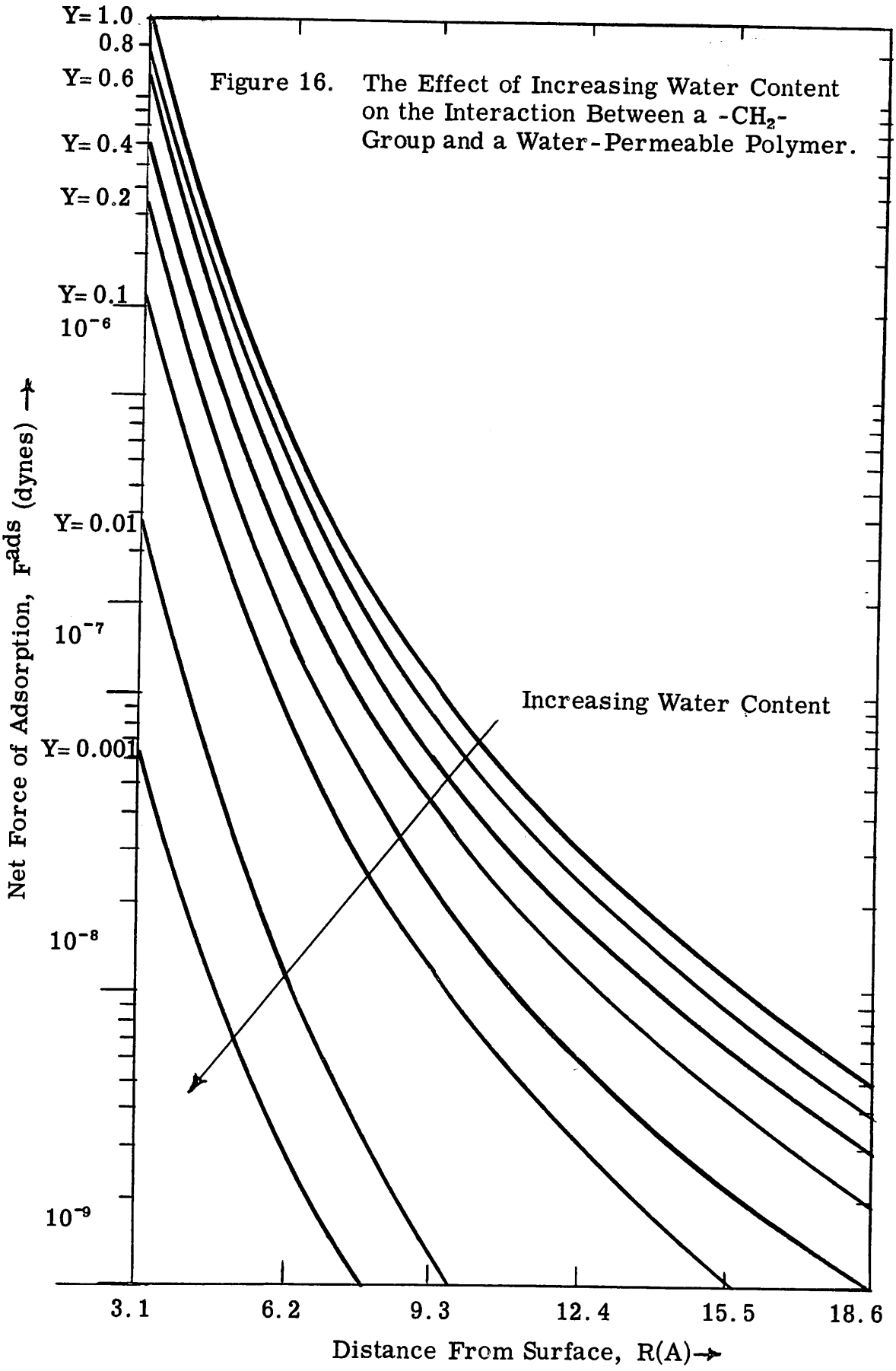


Figure 16. The Effect of Increasing Water Content on the Interaction Between a $-CH_2-$ Group and a Water-Permeable Polymer.

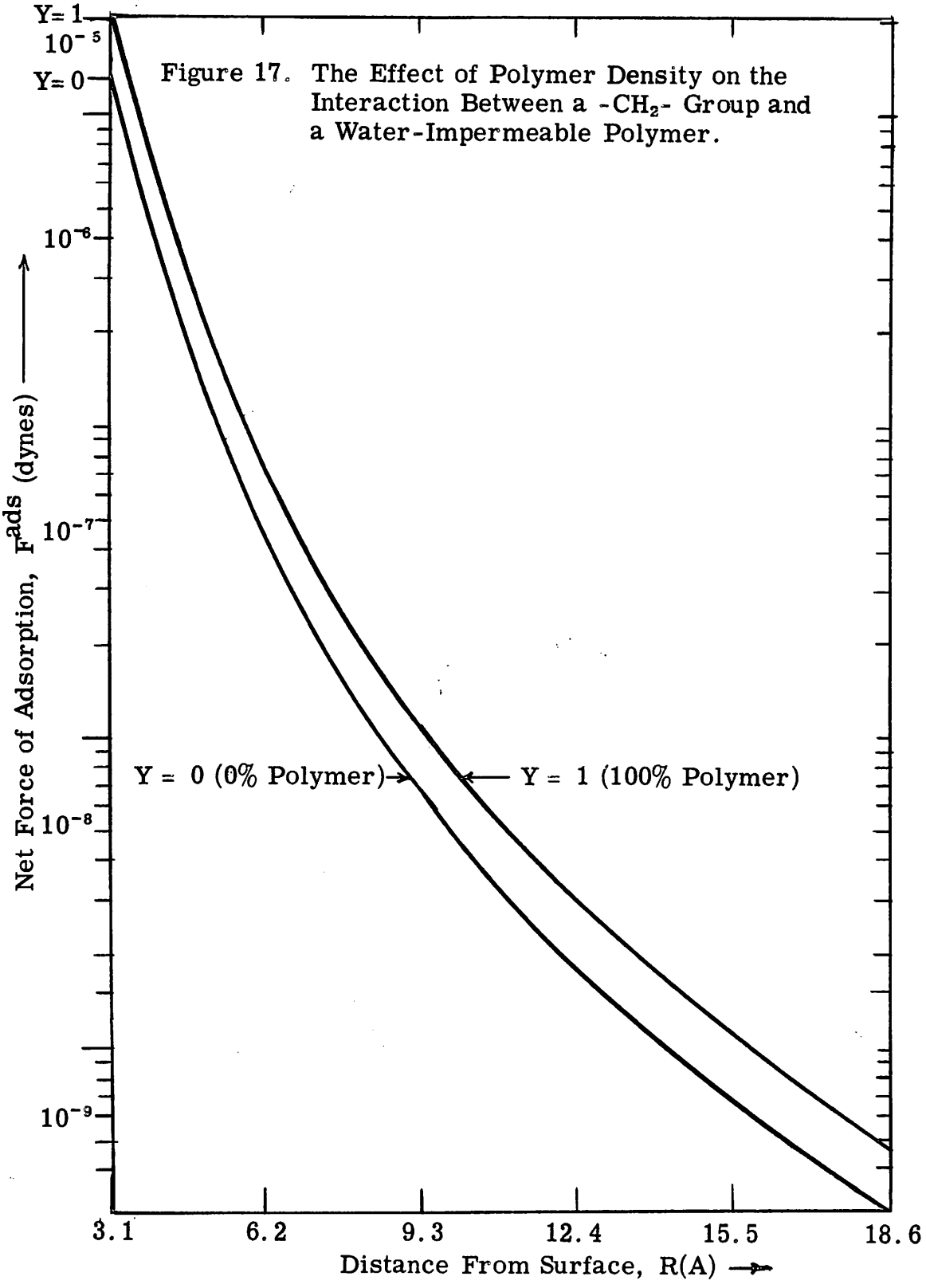


Figure 17. The Effect of Polymer Density on the Interaction Between a $-CH_2-$ Group and a Water-Impermeable Polymer.

d. Interactions Between a Flat Surface and Large Particles

The expressions derived and used up to now have been for a single molecule or group interacting with a flat plate. It is clear from Figure 11a that the interactions between two flat plates can be calculated by performing another triple integration. Fortunately, the expressions for the interactions between simple shapes are available in the literature[127,132] and have been tabulated.[69] All of the expressions contain the quantity π^2N^2A, which is called the Hamaker constant,[69] where N is the number of molecules/cm^3 in the particles and A is the London constant (equation 10). The values of the ionization potentials for many molecules and groups are all roughly the same (within a factor of two or three). The average bond polarizability values do not vary by more than an order of magnitude. The molecular or group density of most organic materials is also within an order of magnitude of 10^{22} molecules/cm^2. The net result is that the Hamaker constant is of the order of 10^{-13} erg. Thus, for the interactions of large particles, the factors governing the interaction are primarily the distance of separation and the dimensions of the particle.

Vold[132] has shown that for particles of colloidal dimensions the total attractive energy is of the same order as kT energy when the mean diameter is roughly equal to the particle separation, independent of the shape of the particles. The mean diameter is defined as the cube root of the particle volume. At smaller separations the interaction is greatest for plates and decreases in the order plates, rods, cylinders, and spheres, as ex-

pected. Thus, the greater the axial ratio of a protein, the greater its dispersion interactions.

The above generalizations will be used to qualitatively discuss protein adsorption later.

4. The Effect of Orientation Dependence of the Polarizability:

a. Orientation of the Solute

The expressions derived up to now have assumed that the polarizability, and that the solute molecule can be considered as a point. The polarizability assumption is probably valid at large distances, but at small distances one might expect the solute to align itself with the surface in the position of maximum interaction.

Because of the large asymmetry in the polarizability of the C-C bond, one expects that such a bond (in ethane, for example) would orient perpendicular to a surface. The perpendicular orientation would interact nearly two orders of magnitude stronger than the parallel orientation. The situation changes, however, when a longer hydrocarbon is examined. Consider the extended chain in Figure 18. The problem is greatly simplified if the polarizabilities of the C-C bonds are resolved along the chain axis. The results are:

$$\alpha'_{\parallel} = \alpha_{\parallel} \cos 34 \simeq 15.6 \times 10^{-25} \text{ cm}^3$$

and

$$\alpha'_{\perp} = \alpha_{\parallel} \cos 56 \simeq 10.5 \times 10^{-25} \text{ cm}^3;$$

it is assumed that $\alpha_{\perp}$ is negligible with respect to $\alpha_{\parallel}$. The primes

denote the resolved quantities. It is clear that there is not a significant difference between $\alpha'_{\parallel}$ and $\alpha'_{\perp}$.

Consider a hydrocrabon chain, some distance away from the interface, rotating about its center of gravity (Figure 19a). If R is measured to the center of the molecule, then any rotation or movement which brings a portion of the molecule closer to the surface will be energetically favorable. The molecule will thus tend to approach the interface in a perpendicular orientation. As the separation distance decreases, then the molecule will tend to assume a parallel orientation, which minimizes R and optimizes the interaction; this case is shown in Figure 19b.

An extended chain solute molecule tends to approach an interface in a perpendicular orientation, though it will assume a parallel orientation at small separation distances. If the non-aqueous phase is a liquid, then the solute may continue to approach and even penetrate in the perpendicular orientation.

b. Orientation of the Polymer Surface

The directional dependence of the bonds in the polymer surface may also influence solute-surface interactions. In crystalline polymers the orientation of the chains is different on a fold surface than on a lateral surface. It was shown earlier that this results in significantly different energies for the lateral and fold surfaces. The

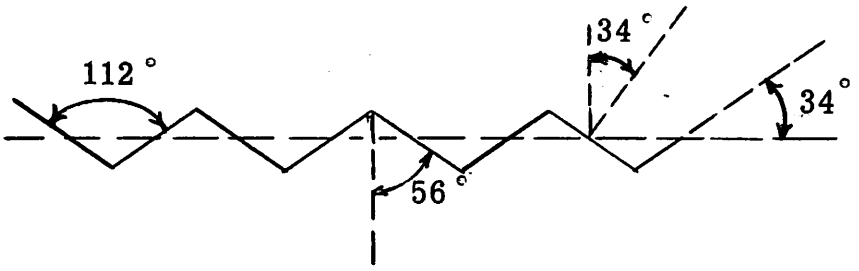


Figure 18. The Geometry of an Extended Hydrocarbon Chain.

a. At Large Separation Distances

b. At Small Separation Distances

Figure 19. Possible Orientations of a Solute Molecule Near an Interface.

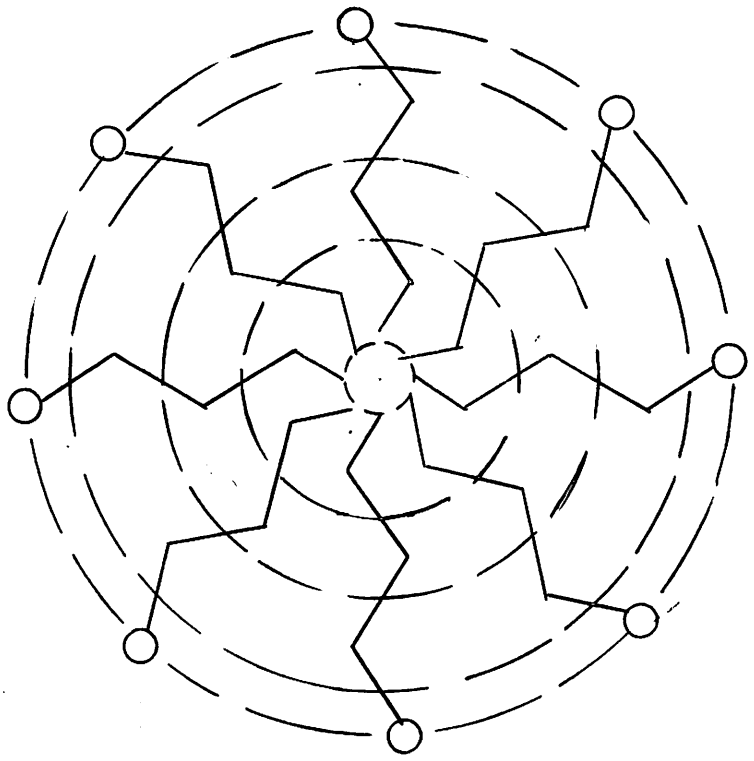
effect of the orientation is the same as that discussed for solute orientation. The chains making up a fold surface tend to be oriented perpendicular to the surface, while the lateral surfaces are composed of chains parallel to the surface. The bonds comprising a chain fold must be strained and distorted, so that conventional values of bond polarizabilities are probably not valid. Nevertheless, it is likely that the fold surfaces of polymer crystallites will interact more strongly than the lateral surfaces.

5. Complex Models:

a. Hypothetical Micelles

A very simple first approximation to the structure of a protein is a hypothetical micelle. A micelle is an aggregation of polar or charged molecules with long hydrocarbon chains. The intermolecular attraction leads to strong hydrophobic interactions among the apolar portions and strong dipole- or charge-solvent interactions with the polar portions. The result is often a structure of nearly spherical symmetry composed of an apolar interior and a polar exterior.

Consider the two-dimensional micelle of Figure 20a. This very idealized picture shows a symmetrical micelle composed of relatively small molecules and serves to illustrate micelle-surface interactions. The concentric circles in Figure 20a represent the areas occupied by the $-CH_2-$ groups as a function of radial distance. It is

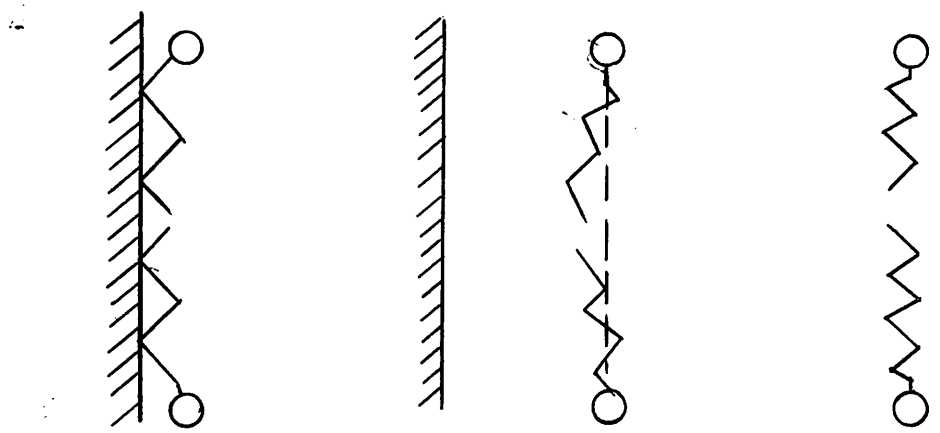


a.

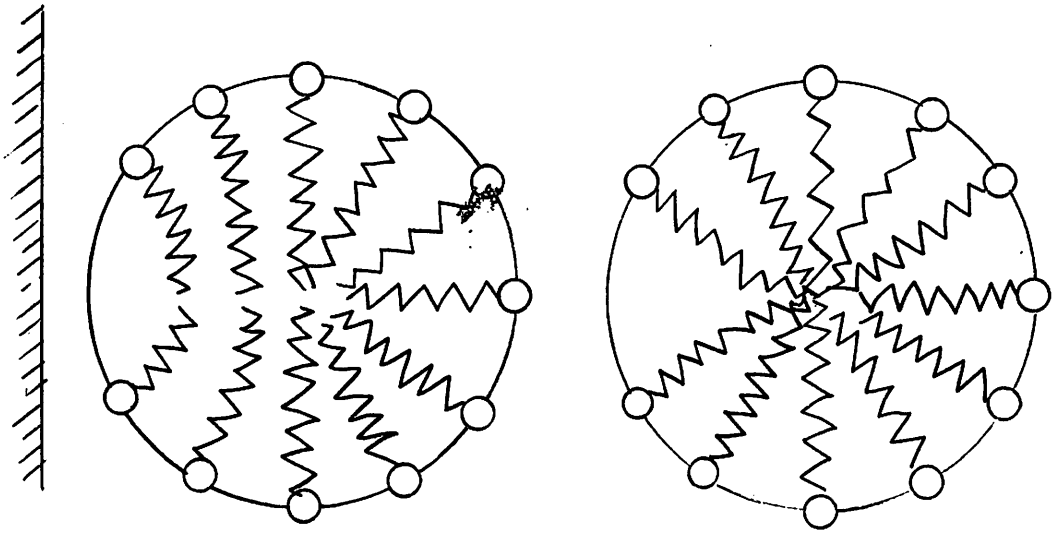
Figure 20. Views of Idealized Non-Ionic Micelles.

a. (Above) The Number of $-CH_2-$ Groups per Unit Area is Greater for the Inner Rings Than for the Outer Ones.

(See 20b and 20c next page.)



b.



c.

Figure 20. Views of Idealized Non-Ionic Micelles.

b. The Sketch on the Right Shows a Flat Micelle in Bulk Solution. The Center Sketch Shows it Undergoing a "Puckering" Distortion. The Left-most Sketch Shows its Probable Orientation on the Surface.

c. An "Unshielded" Nearly Spherical Micelle is Shown on the Right; a Possible Surface-Micelle Interaction Resulting in Distortion of the Micelle is Sketched on the Left.

assumed that because of steric hindrances, the center of the molecule is essentially empty. Each concentric ring contains the same number of $-CH_2-$ groups, but the area of each ring increases linearly with the radius. Thus, there would be a greater interaction force per unit area on the inner rings than on the outer rings if the micelle were oriented parallel to a surface. In such an orientation, each chain would be roughly parallel to the surface, which has already been shown to be an unfavorable orientation except at close separations. The net result would probably be a "puckering" of the micelle, as illustrated in Figure 20b, a side view of the two-dimensional micelle parallel to a surface. The puckering effect would produce an even greater interaction, as now the puckered groups would not only be closer to the surface, but would be more favorably oriented as well. The net result would tend to favor adsorption in the parallel configuration, but with the polar heads in the solvent and capable of extensive solvent-solute interactions.

Two-dimensional micelles probably do not exist. A three-dimensional micelle with perfect spherical symmetry would not tend to adsorb, as there would be extensive solvent-micelle interactions in all orientations. Thus, a spherical micelle would most likely never get close enough to a solid surface (10 to 20 A) for the interactions to be significant. If, however, one could have a micelle which is not truly spherical or well-shielded by the polar head groups, then certain orientations of the micelle might be favorable for interaction and even adsorption.

Such a micelle is sketched in Figure 20c, showing a slight puckering due to surface-micelle interactions. The micelle in Figure 20c is a reasonable approximation to the structure of some simple proteins; these will be discussed later.

Surface-solute interactions can be significant in distorting and reorienting structures to optimize the interactions and the consequent adsorption of solute. Such interaction and distortion can occur in spite of apparent shielding of the solute by polar-solvent interactions.

If the micelle is charged, then there would be even stronger interactions with the solvent, along with the increased complexity of counter ions. It is doubtful that a charged or even strongly polar micelle would adsorb from water solutions, as electrostatic interactions with the solvent would be much greater than the dispersion and induced-dipole interactions with the surface. For a very large micelle, e.g., a protein, the charge or dipole to surface area ratio would be much less, and the force of adsorption could be very significant.

b. Randomly Coiled Polymers

An apolar polymer probably could not exist in a random configuration in aqueous solution. Hydrophobic bonding would no doubt produce a relatively globular polymer configuration. This case is really no different from those treated earlier. As the polymer comes under the influence of the interface, certain "faces" of the globule could be

more energetically favorable for interaction than others; this will be evident later when ribonuclease is examined in detail. Rotations and distortions would occur to optimize the interaction. Once the polymer is at the interface, one might expect that the more mobile portions of the chain would tend to lie flat to further optimize the interaction. Certain bonds would no doubt be oriented for maximum interaction, perhaps on fold surfaces of crystallites, where both the C-C bonds of the surface and a C-C bond of the solute would be a parallel configuration, thus leading to extremely strong interactions. Such interactions may be irreversible and could be considered pinning points. An adsorbed polymer can, therefore, be visualized as a relatively globular (in aqueous solution) mass on the surface, with some portions of the chain oriented parallel to the surface, and with various groups optimally oriented, probably acting as pinning points.

Consider the effect after a monolayer of adsorbed polymer has formed. The structure of the monolayer is sketched in Figure 21 (see Ref. 89). Except possibly for extremely dilute solutions, one cannot expect the molecule to lie completely flat on the surface, though such a configuration might be the most energetically favorable. Thus the monolayer will have a thickness, d, probably related to the dimensions of the globule in solution. Because of the large number of fairly direct interactions, one would expect such an adsorbed layer to be irreversible, though the statistical fluctuations of flickering clusters and thermal

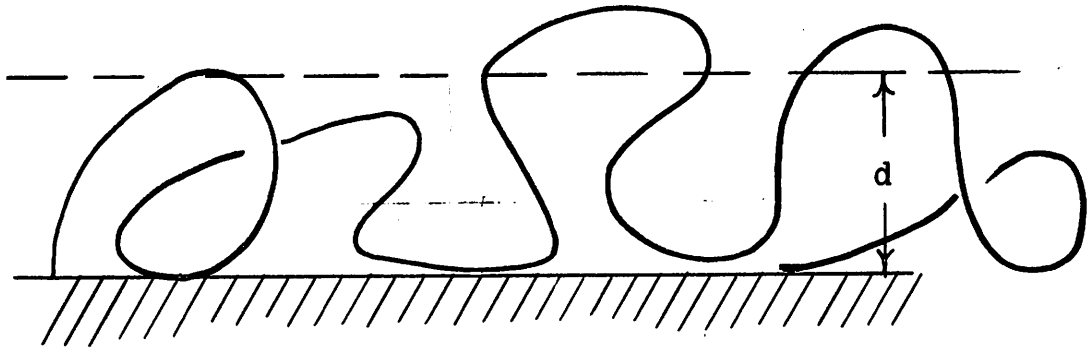


Figure 21. A Possible Structure for a Monolayer of Adsorbed Polymer (see Ref. 89).

energy would occasionally cause an adsorbed polymer to desorb; another one would most likely take its place. Eventually, the adsorbed polymers would be relatively fixed and permanent. The result of a fairly rigidly held and immobile monolayer is that a new surface is formed, roughly at a distance d from the original surface. The polymer density of the monolayer would be much lower than that of the polymer substrate, as it would contain trapped solvent molecules. It is reasonable to expect that d would be at least 10-15 A and probably greater. Thus, the substrate polymer would exert a negligible effect on additional solute interactions. The result is that the new surface exposed to the solution is composed of a low density polymer permeated by the solvent; this is the situation of Figure 16. The monolayer-solute interactions must be of smaller magnitude than the original substrate-solute interactions (Figure 16), due to the decreased density of the monolayer and its water content. Also, optimum binding sites, which

could have existed on the original polymer surface, are now absent. The net result is that adsorption on the monolayer must be relatively weak, though adsorption of the monolayer itself is quite strong. If adsorption on the monolayer does occur, it is probably reversible, as charge fluctuations would have a large effect on any species in the multilayers. The result of this discussion is that one must expect polymer adsorption to follow a monolayer isotherm, particularly in non-aqueous solutions, where the $F_n^S - F_n^W$ force could not be very significant. In aqueous solutions this force will be more important (because of the 3.3 term for water) and might lead to multilayer adsorption.

c. Amino Acids and Peptides

The adsorption of amino acids must be expected to be quite different from any solute considered so far. At neutral pH the carboxyl group is ionized, and the amino group may also be charged. Even though the net charge is zero at the isoelectric point, the dipole-water interractions would be very significant. In addition, the peptide bond is capable of strong dipole-dipole interactions. If these were the things to be considered, one would expect that amino acids could not be adsorbed from aqueous solution except possibly by highly charged surfaces. However, the effect of the highly variable side group leads to many possible surface interactions. It is at least conceptually pos-

sible that amino acids with long apolar side chains might interact with an apolar surface strongly enough to adsorb. Such adsorption would be transient, however, as cluster flickerings and thermal excitement could produce desorption very readily.

It is, therefore, possible that amino acids with strongly apolar side chains might adsorb from aqueous solutions, though such adsorption on apolar surfaces would probably be weak and hardly extensive. Amino acids without apolar side chains cannot be expected to adsorb from aqueous solutions onto apolar surfaces.

A peptide is a polymerized string of amino acids. Its adsorption properties should be similar to those of its constituent amino acids, though the charge-water and dipole-water interactions would not be as extensive as for an amino acid. A peptide will adsorb much more readily than its constituent amino acids, but again adsorption will be negligible unless it contains apolar side shains. A very long chain peptide can be considered a simple protein, if it is made up of many different kinds of amino acids.

d. Proteins

Detailed calculations of the dispersion interactions between proteins and a polymer surface will not be attempted. Such calculations are theoretically possible for those proteins whose structure is completely known, but the task would be immense. The polarizabilities

of C-N and N-H bonds are about the same as for C-C and C-H bonds, respectively. The polarizability of the carbonyl bond is also quite high ($\alpha_{\parallel}$ is about 20, $\alpha_{\perp}$ about 10). One must, therefore, expect significant dispersion contributions from the peptide linkages as well as from the apolar side chains. Order of magnitude estimates of the interaction energy can be made using the generalizations deduced by Vold [132] and previously discussed. Before doing this, it will be useful to closely examine a protein whose structure is completely known. Such information is only available for quite small proteins.

The volume and mean diameter of some proteins is given in Table XIII along with data on surface area and surface charge density (in square angstroms per net charge). Values of the net charges and polar-apolar ratios (P/AP) were given in Table II.

The properties of ribonuclease were given in Table II; its amino acid sequence is given in Figure 22, in which the disulfide bridges are shown and each cysteine is given a number (I to VIII). The numbers in Figure 22 are keyed to Figures 23a and 23b, which show Scheraga's schematic model of the structure of ribonuclease. The enzyme is composed of six helical sections, one helix at right angles to the other five. The detailed molecular model has been constructed and photographs of it are available.[156-7] Table XIV gives the amino acid sequence, net charge, and polar-apolar nature of the

TABLE XIII

PHYSICAL AND STRUCTURAL DATA FOR SOME PROTEINS

Protein	M	Semi-Major Axis, a, A	Semi-Minor Area, b, A	Surface Area, A^2 *	Volume A^3 **	Mean Diameter ***	Surface Area / Net Charge ****
Ribonuclease	14,000	25	12	3,160	15,000	11	790
Albumin	69,000	80	20	16,200	134,000	51	300
Gamma Globulin	156,000	120	25	30,600	315,000	68	≠
Fibrinogen: Ellipsoidal	340,000 to 400,000	325	32	102,000	1,400,000	110	340
Nodular	"	see Fig. 24	see Fig. 24	56,000	410,000	74	190

* The surface area of a prolate spheroid (formed by the rotation of an ellipse about its major axis, 2a) is:

Surface Area = $2\pi(b^2 + (ab/\epsilon)\sin^{-1}\epsilon)$, where ϵ = eccentricity of the ellipse = $\sqrt{a^2 - b^2}/a$ and $0<\epsilon<1$.

** The volume of a prolate spheroid is $V = 4\pi a b^2/3$.

*** The mean diameter is given by: $d = V^{0.33} = [4\pi ab^2/3]^{1/3}$.

****See Table II.

≠ If one assumes all side chains have access to the solvent, the value is about 260. However, this is a very poor assumption, as the pI data of Table II indicate. The variable structure of the gamma globulins prevents one from deducing a value for the surface charge density.

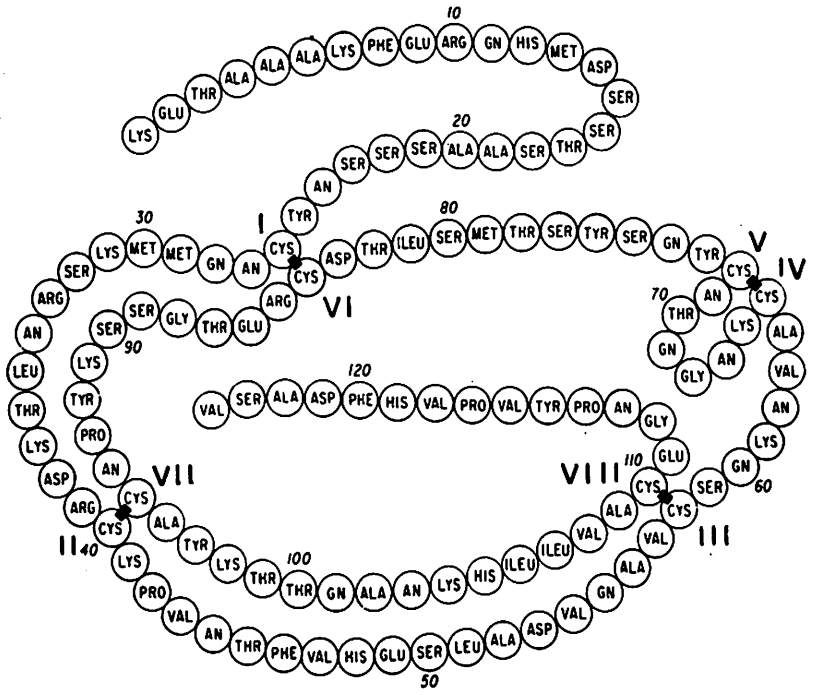
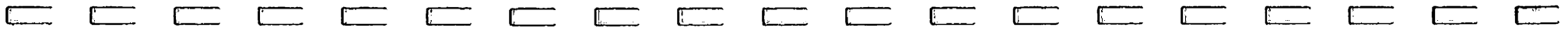


Figure 22. The Amino Acid Sequence of Ribonuclease. The Roman numerals Refer to the Disulfide Bridges in Figure 23. (After Ref. 36, p. 11.)



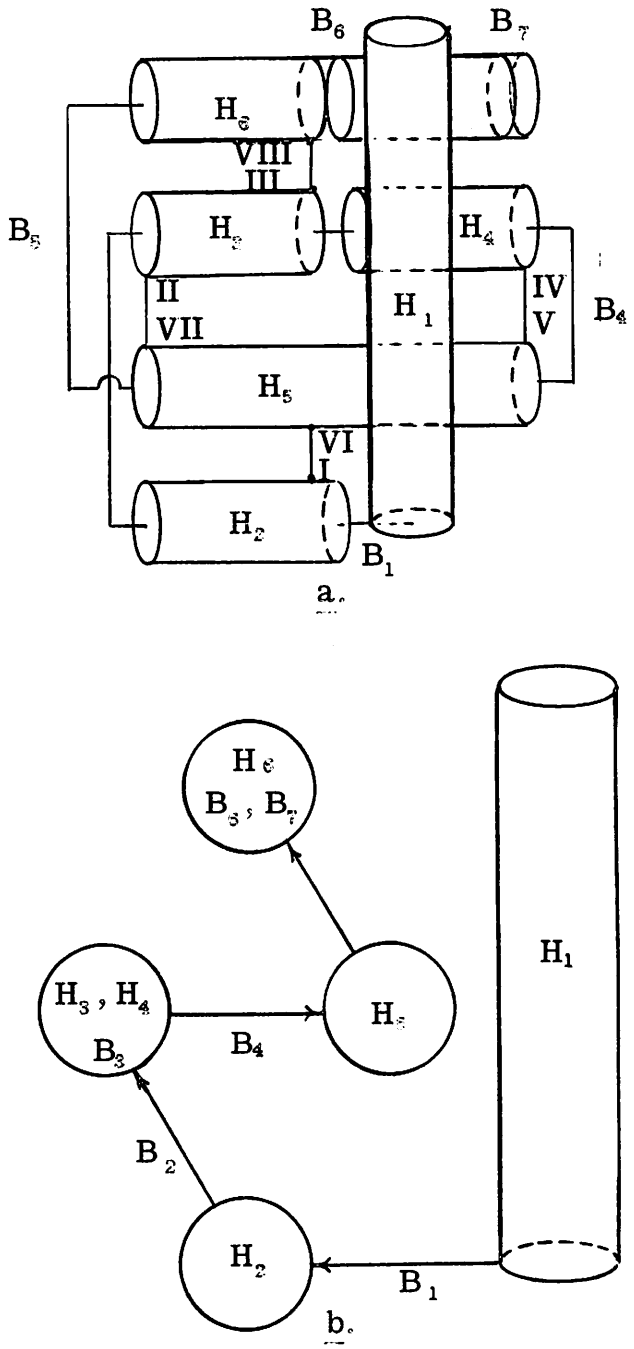


Figure 23. A Schematic Representation of the Structure of Ribonuclease (From Refs. 156, 157); a. Top View; b. Side View.

TABLE XIV

THE AMINO ACID CONTENT, NET CHARGE, AND P/AP RATIOS FOR THE HELICES OF RIBONUCLEASE*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
$NH_2 \oplus \rightarrow$	+	-	P	AP	AP	AP	+	AP	-	+	P	P	AP	-	P	P	P	P	AP	AP	P

Helix = H_1; P/AP = 2.0; Net Charge = 0

22																					37
P	P	P	P	P	P	P	AP	AP	+	P	+	P	AP	P	+						

Helix = H_2; P/AP = 4.3; Net Charge = +3

40																									65
P	+	AP	AP	P	P	AP	AP	P	-	P	AP	AP	-	AP	AP	P	P	P	+	P	+	P	AP	AP	P

Helix = H_3 - H_4; P/AP = 1.4; Net Charge = 0

72																									94
P	P	P	P	P	P	P	AP	P	AP	P	-	P	+	-	P	?	P	P	+	P	AP	P			

Helix = H_5; P/AP = 6.3; Net Charge = 0

98																												124	
+	P	P	P	AP	P	+	P	AP	AP	AP	AP	P	-	?	P	AP	P	AP	AP	AP	P	AP	-	AP	P	AP	⊖		

Helix = H_6; P/AP = 1.2; Net Charge = 0 COOH

*See also Figures 22 and 23. The N- and C- terminal groups were not counted in the P/AP ratio and net charge determinations.

different helices (helices 3 and 4 are combined in Table XIV). The non-helical portions of the molecule are not considered. It is obvious from Table XIV that the different helices have strikingly different polar-apolar natures. The short helix, H_2, is strongly polar and is the only helix with a net charge. Helix H_5, is very highly polar, but its net charge is zero. Thus, the characteristics and properties of ribonuclease certainly cannot be expected to be symmetrical, even though the shape of the molecule is roughly spherical. The interactions of ribonuclease with a surface will thus be strongly dependent on the orientation of the protein with respect to the interface. Helices H_1, H_3-H_4, and H_6 should be able to approach quite closely to a surface and interact strongly by dispersion forces; charge-induced dipole interactions would tend to cancel out, as the net charge on these helices is zero. The presence of charge- and dipole-bound water would hinder the approach to the surface, however. If the adsorbing surface is negatively charged, one might expect H_2 to be more energetically favorable, because of its net positive charge. For an apolar surface, only helices H_6 and H_3-H_4 can be expected to interact strongly, due to their greater apolar nature. The other helices would interact with water much more strongly, thus their approach to the surface would be hindered.

The consideration of the individual helices serves to indicate that the P/AP ratio of Table II may be highly misleading, at least

for the consideration of surface interactions. According to the ratio, ribonuclease is very polar, but from Table XIV it is clear that much of that polarity resides in helix H_5. Helix H_5 cannot be expected to interact directly with a surface, as it is essentially shielded or at least hindered by all of the other helices.

The interaction of H_3 -H_4 and H_8 may be aided by the puckering mechanism of Figure 20. The non-helical and non-hydrogen bonded regions, B_5 and B_8 (see Figure 23a), may be easily deformed, particularly at B_5, as it is somewhat apolar. Adsorption could, therefore, occur first at certain preferentially deformable sites; once these sites have tentatively affixed the molecule to the surface, other interactions would become important, as the separation distance would then be relatively small.

If one ignores the detailed structure of ribonuclease and simply considers it as an ellipsoidal organic particle, the interaction energy would only become significant at a distance of the order of 10-11 A from the surface (the value of the mean diameter, Table XIII).

The above discussion shows that one must expect a protein to be a very heterogeneous structure—capable of adsorbing by different mechanisms in different orientations on different surfaces. The heterogeneity of ribonuclease may be greater than in non-enzymatic proteins, as an enxymatically active site may require significant property differences among the participating helices. Ribonuclease is also peculiar

in that it is positively charged at neutral pH, while most plasma proteins are negatively charged. Also, the effect of non-helical regions has been ignored. These could be very important for both their own particular interacting behavior and the steric influences they might exert on the helix-surface interactions.

Albumin has been discussed and some of its properties were given in Tables II and XIII. As it is composed of a single polypeptide chain, the hypothetical protein of Figure 9 may be a reasonable approximation for the structure of albumin. Though the P/AP ratio for albumin is not particularly high (Table II), it is a very polar protein. Its polarity is indicated by its solubility properties, as well as by the relatively high surface charge density (about one net negative charge for every 300 A^2 of surface; Table XIII). If the protein is hollow[64] and the inner core contains water, then the charge density would be much lower.

As shown earlier, charge-induced dipole interactions are negligible until the molecule is very close to the surface; thus albumin must interact primarily by the adsorption forces discussed earlier. There could easily be relatively apolar portions of the molecule, as observed for ribonuclease. Again a puckering or distortion mechanism of initial adsorption could be acting.

Vold's mean diameter (Table XIII) criteria[132] indicate that the surface-albumin interaction becomes quite significant at a separation distance of about 50 A. Thus, albumin must be brought to the interface

by dispersion interactions; the interactions are optimized if the long axis of the molecule is parallel to the surface. Maximum interaction occurs when the long axis is flat on the surface, but the actual thickness of a monolayer must be somewhat greater than the minor axis, due to the non-efficient packing of an adsorbed layer. It is possible that short-range charge-induced dipole interactions would modify the orientation, but this is doubtful as the charges would be interacting strongly with the solvent and most of them would probably never come close enough to the surface to have a very significant effect.

It is unlikely that the adsorption process could produce a layer of efficient packing, thus the density of the adsorbed layer would probably be less than that of the substrate. Also, the adsorbed proteins would contain some bound and trapped water. This means that adsorption is expected to stop after the formation of a monolayer (see Figure 11). In addition to the density effect, the monolayer would now exhibit the net charge of the proteins within it. Thus there would be a tendency for the monolayer to repel similarly charged proteins. These two reasons for the absence of multilayer formation are not absolute, however. If the charge distributions are strongly localized, as discussed earlier, then multilayer formation could still occur.

The gamma globulins are much larger than albumin, though the overall shape seems to be about the same. Their mean diameter is 68 A, thus one would expect strong dispersion interactions out to

about 70 A. It is clear from the earlier discussion and the data of Table II that it is not possible to draw conclusions about the surface charge or structure of the gamma globulins. One might expect that their weak structure and resultant ability to respond structurally to subtle influences would make them easily denaturable. This same tendency would make them more susceptible to puckering distortions. As the isoelectric point of the gamma globulins can vary between 5.8 and 7.3 (Table II), depending on the fraction, some fractions can be uncharged at neutral pH, thus the argument of electrical repulsions between adsorbed solute molecules would not hold. Monolayer formation is still expected, however, due to packing, density, and permeability considerations.

It is reasonable to assume that the density of gamma globulin must be less than albumin, because the gamma globulins have proportionally a much lower alpha-helix content and fewer disulfide bridges than albumin. This assumption is not supported by the data of Table XIII, but this could be due to the ellipsoidal shapes of the molecules. The overall ellipsoidal shape of the molecule also includes its hydration layer, which can be a sizeable contribution to the total volume (Figure 9).

If gamma globulins are much less polar than albumin, as has been discussed, they would tend to have a much smaller hydration layer. Thus, the volumes given in Table XIII may be deceptive, as the volume

given for albumin may be significantly larger than the true volume. If this is the case, gamma globulin would indeed have a lower density than albumin, which would mean its dispersion interactions would not be as strong (per unit volume). One must not, therefore, expect gamma globulin to adsorb more strongly than albumin. A monolayer of gamma globulin would still be thicker than a monolayer of albumin because of the greater size of the molecule.

Fibrinogen cannot be considered as a globular or even ellipsoidal molecule. The data of Table XIII for the ellipsoidal model indicate that the density of fibrinogen (molecular weight per unit volume) is half that of albumin or gamma globulin, which is not reasonable. The dumbell-shaped structure sketched in Figure 24 will, therefore, be used for fibrinogen. This results in a surface area about twice that of gamma globulin but a volume not much greater than that for gamma globulin. The surface charge density is quite high, higher even than albumin. Part of this difference is because the dumbbell-shape dimensions are for the dry molecule and do not consider the volume of hydration. Thus the true area and volume in solution is probably a compromise between the two structures given in Table XIII. In any event, the net charge density will still be relatively high. The previous discussions indicated a lack of charge asymmetry along the long axis. The charge must, therefore, be evenly distributed.

Fibrinogen-surface dispersion interactions are probably significant out to between 70 and 100 A. The greatest interaction would be in the parallel orientation. One must expect fibrinogen to be a rather clumsy, unpredictable protein for adsorption considerations. As it contains large nodules, its orientation for adsorption is not necessarily as straight-forward as for albumin and gamma globulins. If a fibrinogen molecule "stumbles" into the vicinity of an interface in the perpendicular orientation of Figure 24, it will most likely continue to be adsorbed in that orientation if it is within 50 A of the surface (the mean diameter for a sphere 65 A in diameter is about 50 A*). It is probably not reasonable, therefore, to assume adsorbed fibrinogen to have a particular orientation. The majority of the molecules should be oriented parallel while many may have the perpendicular orientation, at least initially; after initial adsorption, close range interactions could pull a molecule from the perpendicular orientation into a more parallel position. This is not unreasonable, and is somewhat compatible with the structural properties of fibrinogen, i.e., that the nodules are connected by "...loose, sponge-like segments..." (see Ref 64).

Fibrinogen adsorption should result in a loosely packed layer of flat molecules entangled with bent or distorted molecules which were initially adsorbed in the perpendicular orientation. The thickness of such a layer should be somewhere between 70 and perhaps several

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*This curious result is due merely to the definition of mean diameter. The mean diameter is defined as the cube root of the volume.[132]

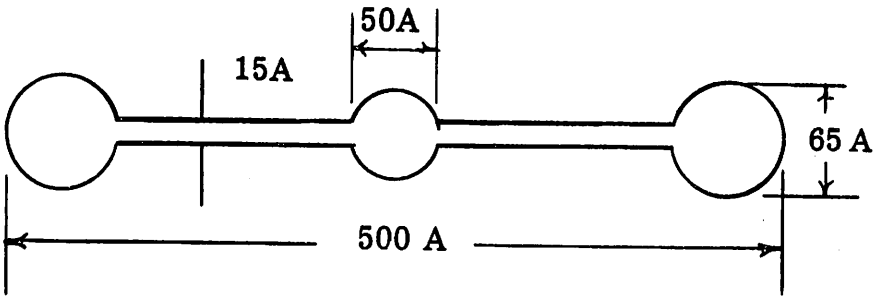

Figure 24. The Nodular Structure of Fibrinogen

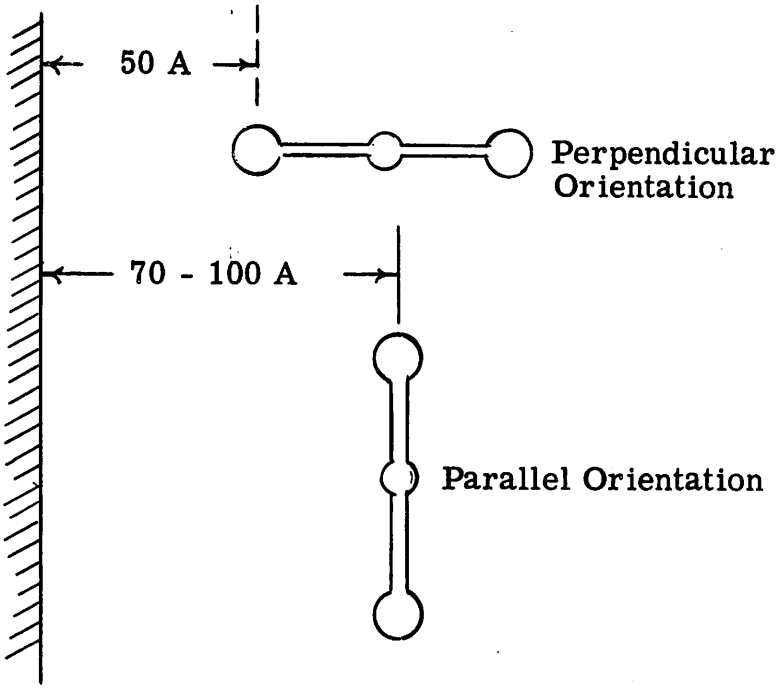

Figure 25. Two Limiting Orientations for a Fibrinogen Molecule in the Vicinity of an Interface.

hundred angstroms. Multilayer formation is not expected.

Fibrinogen will interact significantly with a surface by dispersion forces at greater distances than the other proteins considered. Thus, adsorption of fibrinogen can be expected to be more rapid than for the other proteins discussed. It is also possible that, because of its higher molecular weight and rod-like structure, it will interact more strongly with a surface than albumin or gamma globulin. This could result in competitive adsorption, where fibrinogen may successfully compete for occupied regions of the surface.

C. Comparison of the Model with Experiment

1. Simple Compounds:

The model predicts that apolar compounds should have relatively large adsorption forces acting on them, as the 3.3 term will dominate the other terms in equation (24); this will be the case at air/water and apolar polymer/water interfaces. The data of Tables IX to XI show that the forces and energies of adsorption must be significant at distances of 10 to 15 A, depending on the size of the molecule considered. Figure 14 clearly shows that the adsorption of large molecules is favored over smaller ones. It was demonstrated in Figure 15 that the differences between solute molecules result in significantly greater adsorption forces than differences among the apolar polymer surfaces. The solute molecule is also expected to approach the surface in a more or less perpendicular orientation, though it will tend to assume a parallel orientation if space and time are available for it to do so. Because of the relatively low polarizability of water (Table IV), F_p^s is usually greater than F_p^w, thus there is a slightly greater adsorption tendency at polymer/water than at air/water interfaces. This conclusion is evident from Figure 17, where the Y=0 curve is equivalent to that for an air/water interface, while the Y=1 curve represents the adsorption force at the polymer/water interface.

The model also predicts multilayer and monolayer adsorption, depending on the structure and nature of the first adsorbed layer. The

data of Table XII and Figure 16 clearly demonstrate that the adsorption forces decrease rapidly as the water content of the surface increases. An adsorbed layer which contains trapped or bound water molecules will, therefore, interact more weakly than the original surface. This has been discussed and was sketched in Figure 21 for random coil polymers, but the analysis is just as valid in the general case. If the adsorbed layer does not contain water, as might be expected of an adsorbed hydrocarbon, then the situation is given by Figure 17. Though the monolayer must have a lower density than the original surface, the force of adsorption is only slightly decreased. If the monolayer was of zero density and contained no water, adsorption would still occur, just as it does at the air/water interface.

The above predictions are in good agreement with experiment. Most of the generalizations and conclusions in Section A. 3. b (Adsorption of Simple Compounds) are in agreement with the predictions of the model. It was noted in that section that adsorption tends to be preferential for that component which most reduces the surface or interfacial tension; this conclusion is evident from Figure 7 and equation (24).

Perhaps the most complete study of adsorption of simple compounds at a polymer/water interface is that by Schneider et al.[158] They studied the adsorption of several hydrocarbons, alcohols, and organic acids from aqueous solution onto polystyrene beads. Their isotherms for ethane, propane, and n-butane are replotted in Figure 26; the

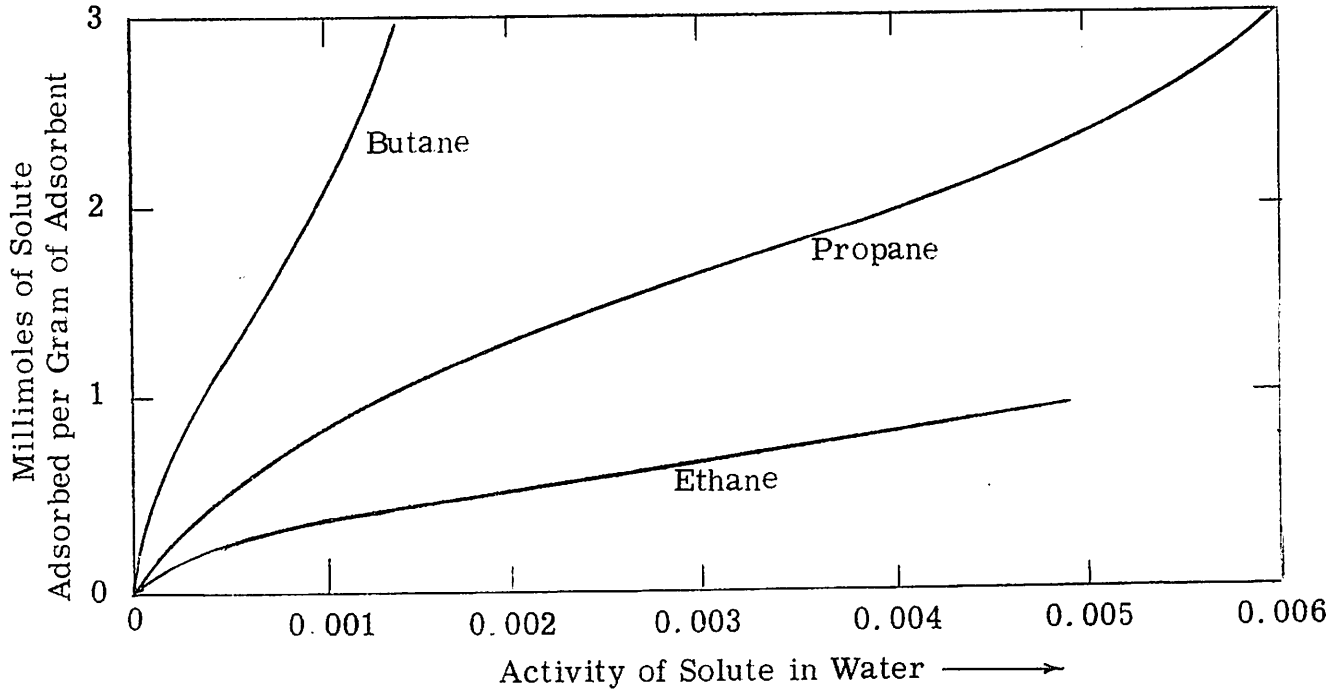

Figure 26. Adsorption Isotherms for the Adsorption of Simple n-Alkanes onto Polystyrene Beads (After Ref. 158).

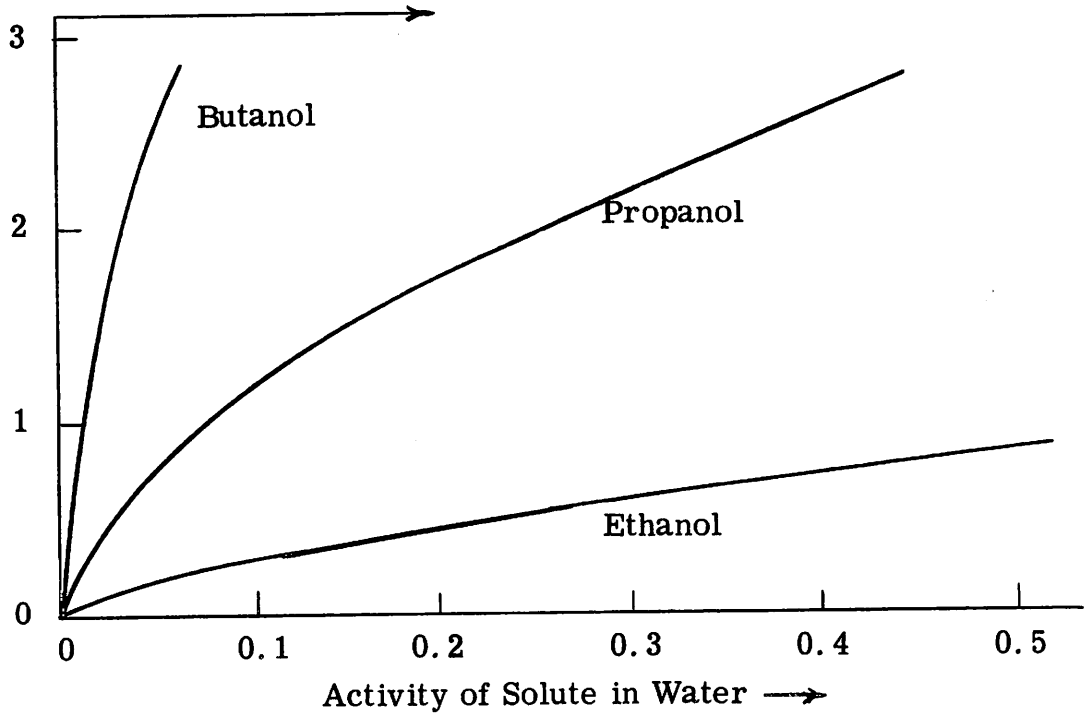

Figure 27. Adsorption Isotherms for the Adsorption of Simple n-Alkanols onto Polystyrene Beads. (After Rev. 158.)

isotherms for ethanol, propanol, and n-butanol are given in Figure 27. These isotherms (and most adsorption isotherms) are for equilibrium adsorption, thus one cannot obtain kinetic information from them. It is clear from the isotherms presented and from most isotherms in the literature that the degree of surface coverage or amount adsorbed is not merely a simple function of the size of the molecule. Propane would be expected to occupy roughly 50% more surface area than ethane, and butane twice as much area, yet the isotherms certainly do not show any such relationship. If adsorption is due to active sites, one would expect the number of moles of solute adsorbed per unit area of surface coverage to be independent of molecular size, as there is little reason to expect an active adsorption site for propane to differ from one for butane.

The extent of the isotherms presented is of course limited by the solubility of the solute in water. Ethanol is highly soluble, while butanol is much less soluble. There is some question about the hydrocarbon isotherms. In the case of butane and propane the isotherm indicates multilayer formation. It is possible, as pointed out by the authors,[158] that the adsorbed alkanes may diffuse into the polystyrene.

It is difficult to quantitatively examine Figures 26 and 27, as the surface area of the swollen polystyrene adsorbent is not known. It is clear, however, that the alkanes adsorb very readily from very dilute solutions; the alkanols require a hundred-fold greater concentration to produce the same amount of adsorption. The alkanols appear

to follow a monolayer (Langmuir) isotherm, while the alkanes seem to form multilayers.

The model predicts that alkanes should tend to produce multilayer isotherms, as discussed above. Small alkanes should not trap any water as they are adsorbed; in fact, the movement of the water between the solute and the interface is one of the major driving forces for adsorption (Figure 7). Therefore, one would expect a layer of adsorbed hydrocarbon to be relatively water free and probably less dense than the substrate. Thus adsorption of multilayers is expected to occur, though probably to a lesser extent than the original adsorption. These results are in good agreement with the isotherms of Figure 26.

The adsorption of small alkanols is expected to be relatively weak. The force of adsorption is now greatly decreased as compared to alkanes because of the extensive dipole-dipole interactions which must take place between the water solvent and the -OH group of the alcohols. Any adsorption which does occur would probably be quite reversible, as desorption must occur relatively easily whenever a water cluster forms nearby in an optimum interaction orientation. In order to obtain significant adsorption, Schneider et al.[158] had to use relatively high alcohol concentrations; this no doubt acted to eliminate some of the reversibility of adsorption.

Figures 26 and 27 are also in agreement with the conclusion

that large molecules are expected to interact more effectively than smaller ones. This conclusion is due to two effects; the greater force on a large molecule gives it an advantage in coming to the interface; once it is at the interface, it can interact strongly with each of its polarizable regions, which will tend to hinder desorption (the greater the number of strongly interacting sites, the less chance that desorption will occur). The net result is that larger molecules probably are adsorbed more rapidly than smaller molecules and, once adsorbed, they tend to stay there longer. The isotherms of Figures 26 and 27 are thus in qualitative agreement with the model.

The adsorption of polar compounds has been discussed qualitatively and some comparisons can be made. Data are available on the adsorption of some amino acids and peptides,[158] as well as on the alkanols just discussed. The following amino acids were studied[158] in solution at their isoelectric point: glycine (AP), alanine (AP), proline (AP), serine (P), glutamic acid (P), aspartic acid (P), tyrosine (p), and phenylalanine (AP). Only the latter two aromatic amino acids were adsorbed, but not to a significant degree. The adsorbent was polystyrene beads, thus the aromatic acids probably interacted directly with the pi-orbitals of the polystyrene. It is clear, however, that amino acids do not tend to adsorb. It would have been interesting if the study[158] had included leucine or isoleucine as well, as the long apolar side chain might have been more favorable for adsorption.

The same study did consider two peptides: gly-gly-gly-gly and leu-gly-gly. The former did not adsorb, supporting the contention made at the bottom of Table II, i.e., that though glycine can be considered to have an apolar side chain, steric effects must prevent it from interacting significantly. The leu-gly-gly peptide did adsorb (on polystyrene), showing that the leucine side chain can exert a considerable influence on the adsorption properties of a peptide or amino acid. Thus the results cited for amino acids and peptides are in agreement with the qualitative predictions made earlier.

2. Polymer Adsorption:

Polymer adsorption has not been widely studied and few generalizations are available. The model predicts that polymers adsorbed from solution onto polymer surfaces should form a relatively loosely packed and solvent permeated monolayer. Multilayer adsorption is not expected; the argument is the same as given above. Even though the molecule remains relatively globular and loosely packed on the surface, its very nature and size provides a large number of close-range interactions with the surface. As noted earlier, it is statistically improbable that all of these interactions could be disrupted simultaneously, thus polymer adsorption tends to be irreversible. Also, as noted above, the larger the molecule, the more stable it must be on the surface. Thus polymers of higher molecular weight must have

a longer surface lifetime than those of lower molecular weight; this is the basis of competitive adsorption. Equilibrium is thus difficult to achieve and requires a long time. The initial adsorption is expected to be very rapid, however, following the trend discussed above (the larger the molecule, the greater its adsorption tendency).

3. Protein Adsorption.

The detailed discussion of ribonuclease showed that protein adsorption must be extremely complex, as different portions of the same molecule may interact by very different mechanisms. Until the detailed structure of many more proteins is available, one must resort to qualitative discussions and extremely rough calculations. Using Vold's criteria[182] and applying it to protein-solid dispersion interactions, it was concluded that protein adsorption (to a first approximation) will be a function of the size and density of the molecule. Thus, it is expected that adsorption would increase in the order albumin, gamma globulin, and fibrinogen. Only monolayer adsorption should occur, with the monolayer thicknesses somewhat greater than the minor axis but significantly less than the major axis. The rod-like nature of fibrinogen will probably allow it to interact more strongly with a surface than the other proteins, thus, as discussed above, competitive adsorption should be expected.

Lyman et al.[19] have succeeded in determining protein adsorp-

sorption isotherms on plane polymer surfaces by means of total reflection infra-red spectroscopy. Their isotherm for gamma-globulin adsorption on polystyrene (at 37 C for two hours from distilled water) is given as Figure 28. They studied the adsorption of albumin, gamma globulin, and fibrinogen on commercial polystyrene, polyethylenes (low density), polydimethyl siloxane, and on a fluorinated ethylene-propylene copolymer (Teflon FEP). Except for gamma globulin on Teflon FEP, the behavior was analogous to Figure 28 for all combinations. Their results are given in Table XV; film thicknesses varied from 44 to 138 A (assuming a protein density of 1.3) but there was no adsorption of gamma globulin on the fluorocarbon. It is thus clear that the surface free energy concept[39] does not hold for protein adsorption since there is no trend of absorbed thickness with surface energy, though Lyman et al.[19] showed that such a trend does hold for platelet adsorption. The adsorbed proteins could not be desorbed over a wide pH range, thus Lyman et al.[19] concluded that "...adsorption in these systems is not reversible."

The above results are in qualitative agreement with the earlier discussion, though the values for polystyrene are lower than expected. The earlier calculations show polystyrene interacting more strongly than the other polymers. Lyman has also found[15 9] that adsorption increases in the order albumin, gamma globulin, fibrinogen. (See also Table XV).

TABLE XV

EQUILIBRIUM LAYER THICKNESSES FOR THE ADSORPTION OF PLASMA PROTEINS ON SEVERAL POLYMER SURFACES*

(After Ref. 19, p. 252)

Polymer	Layer Thickness, Angstroms		
	Albumin	Gamma Globulin	Fibrinogen
Polystyrene	44	54	130
Polyethylene (Low Density)	62	77	96
Polydimethyl siloxane	120	138	120
Fluorinated Ethylene-Propylene Copolymer (Teflon FEP)	62	0	108

*Adsorbed from distilled water at 37 C for 2 hours.

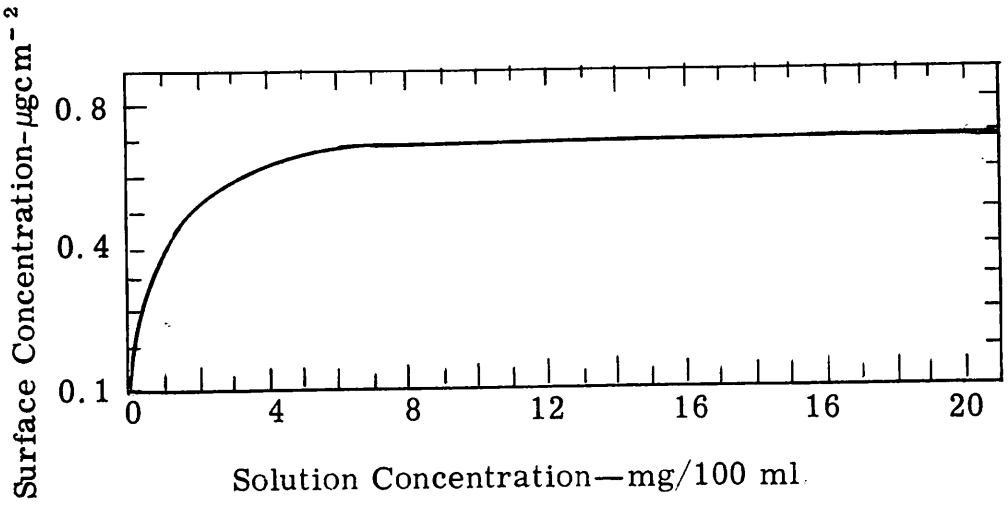

Figure 28. Adsorption of Gamma Globulin onto Polystyrene at 37 C. (From Lyman et al., Ref. 19, p. 251).

The layer thicknesses are quite large. They were interpreted as due to [19] "...the formation of a monolayer with the dimensionally intact globular molecules in closely packed array more or less end-on to the surface." This interpretation is compatible with the discussion of layer thicknesses given earlier.

Figure 13 showed that polyethylene and PTFE tend to interact to the same degree with solute molecules. This result is confirmed in Table XV by the data for polyethylene and Teflon FEP for albumin and fibrinogen. The result for gamma globulin is not explained; it is very interesting, but unpredictable by the criteria given here.

Vroman has studied the interaction of blood and blood proteins with surfaces using an ellipsometer. Much of his work and views on the role of surfaces in blood coagulation and protein adsorption are summarized in two recent reviews.[2,160] He has exhaustively surveyed and studied the role of hydrophobic surfaces in coagulation in an earlier paper.[18] The nature of the ellipsometric technique produces limitations on the selection of suitable substrates. Vroman usually uses tantalum oxide or silicon surfaces which are either wettable or non-wettable, depending on the surface treatments used (see Ref. 18). Thus the surfaces studied are certainly not polymeric but can be considered to consist of relatively loosely packed hydrocarbon chains for the non-wettable surfaces, as it is often prepared by rubbing on a monolayer of ferric stearate.

Ellipsometric studies are the only current source of information on adsorption dynamics. Vroman has found that "...all protein-containing solutes showed adsorption onto all four types of surfaces tested, at an initial rate of about 10-20 A per minute." (Ref. 2. p. 299). There was no difference in adsorption rates at room temperature on wettable or non-wettable surfaces,[18] which tends to indicate that the solute-solvent interactions dominate solute-surface interactions. After a few minutes the rate decreased abruptly for purified protein solutions and somewhat gradually for mixtures of proteins. This result tends to indicate monolayer formation of the purified proteins and continuing competitive adsorption of the protein mixture. Vroman has shown that multiple protein layers can be adsorbed under appropriate conditions.[160] Adsorption studies on hydrophobic powders have shown that many proteins (particularly certain coagulation factors) are preferentially adsorbed, including fibrinogen.[18,160] In the case of fibrinogen the preferential adsorption may be due to its great size and geometry; the coagulation factors which favor non-wettable surfaces may have relatively apolar "faces" as observed for ribonuclease. The film thicknesses Vroman gets are usually 30 to 40 A for most proteins and up to 80 A for fibrinogen.[18] These results are more in agreement with the discussion given earlier than those of Lyman.[19]

The conclusion that adsorption will not tend to occur on a surface containing a high water content (Figure 16) leads to some possibilities

for the preparation of adsorption-resistant surfaces. Such a surface probably results when a protein is chemically bonded to a polymer surface. The proteinated surface is probably similar to that of an adsorbed layer of protein, except that chemically bonded protein could not be desorbed; competitive adsorption thus could not occur. Such a surface has been prepared by binding albumin to chloromethylated polystyrene using an aqueous Friedel-Crafts alkylation reaction (See Chapter II). Attenuated total reflection infra-red data showed significant amounts of bound protein (Figures 1 and 2). Vena cava rings of this material were implanted in dogs by Dr. Vincent Gott of the Johns Hopkins University School of Medicine; initial results for chronic (two hour) and acute (two week) tests were very good, as no clots were found in the rings. The preliminary results of this severe test indicate that a proteinated surface may be a good coagulation-resistant material. Long-term tests, particularly on the stability and life-time of such a surface, are needed before definite conclusions can be made. The behavior of the surface is compatible with the model, if blood coagulation is truly a protein adsorption-dependent process.

Protein denaturation was not specifically discussed. It was noted that orientations of maximum interaction are favored. It is, therefore, reasonable to suspect that the forces of adsorption will continue to operate until the solute is flattened down on the surface and cannot be "pushed" farther. If the bonds responsible for the tertiary

structure in a protein are weaker than the adsorption force, those bonds may be disrupted, and denaturation will occur.

The discussions on protein adsorption given in Section B are thus in reasonable agreement with experiment. Much more adsorption data and further development of the model will be required, however, before a mechanistic model of protein adsorption can be produced.

D. Conclusions

1. The Role of the Surface in Adsorption from Solution:

Though the nature and magnitude of the charges or dipoles on polar surfaces may have significant effects on adsorption, the impermeable hydrophobic surface is probably not too important in adsorption from solution. The data presented showed that the spread of interactions on the different surfaces considered was not very great. Lyman et al.'s result[19] with Teflon FEP and gamma globulin is an exception to this conclusion. Vroman's results that the adsorption rate on wettable and non-wettable surfaces is about the same tends to agree with the above conclusion. The degree of crystallinity and orientation of crystallites in the surfaces of crystalline polymers might be important in adsorption; data on these surfaces will not be interpretable on a fundamental level until the nature of the fold and lateral surfaces of crystallites is better established.

A water-permeable polymer must experience much less adsorption than impermeable polymers (Table XII and Figure 16). A family of water-containing polymers, the non-ionic hydrogels, is available, though adsorption studies are not yet available on them. Their blood compatability properties are very impressive, however.[161-2] There is evidence (Chapter II. A) that a chemically proteinated surface behaves as predicted by the model. Thus, though a "conventional" polymer surface may be relatively unimportant in adsorption from aqueous

solutions, especially prepared surfaces, which can significantly intersect with water, may show promise as adsorption-resistant materials.

2. The Role of the Solute in Adsorption from Solution

In general, the larger the solute molecule, the greater its tendency to adsorb by dispersion interactions. This trend is clearly demonstrated in Figures 14 and 15, as well as by Vold's conclusions.[132] If the solute can compete for solvent interactions, then the force of adsorption will be decreased; this is evident in Figure 7. In some cases solute-solvent interactions may be greater than solvent-solvent interactions; the result in this case would be negative adsorption (Figures 4 and 7). Adsorption tends to become irreversible when the solute becomes quite large, as for a polymer or a protein.

A complex solute, such as a protein, probably adsorbs by different mechanisms, depending on the surface and on the orientation of approach of the solute. Certain regions of the molecule may interact in a particularly strong manner; if such regions are not tightly bound to other portions of the solute, distortion (puckering) effects may occur, which optimize the interactions.

3. The Role of the Solvent in Adsorption from Solution

Adsorption from aqueous solution is primarily dependent on the cohesiveness of water. The primary adsorption force is due to solvent-solvent interactions, influenced by solute-solvent effects.

Adsorption from other, less cohesive, solvents is expected to be much different, as then the B and C curves in Figure 7 would be much closer together; solvent competition effects would then be more important.

4. Critique and Limitations of the Model

The model is limited in that it considers only non-ionic aqueous solutions and apolar polymer surfaces. It is further limited in that only dispersion interactions are computed and that solute structuring effects are essentially ignored. Such structuring can be treated as an adsorbed layer; treatments of this type have been given by Vold.[163] The treatment of proteins has been very qualitative and there was no attempt to discuss the competitive adsorption of a number of different proteins. The greatest limitation, however, is the failure to specifically consider dipole-dipole and charge-dipole interactions between the solvent and the charged and polar groups on a protein molecule.

The model does provide a satisfying mechanistic picture of adsorption on the molecular level. It explains in a fairly satisfactory manner a phenomenon which was previously not explainable: monolayer adsorption of polymers and proteins. Perhaps its greatest contribution, however, will be that it can be used to design experiments which will lead to a better understanding of the mechanisms of adsorption.

5. Future Work

The model raises many questions and focuses attention on several areas of inquiry. The main conclusion is that the solvent plays a fundumental and probably major role in adsorption processes, particularly for polar solvents. This result can be tested by studies of adsorption from a series of solvents of varying cohesiveness.

Another major focus is the structure of the adsorbed layer and its role as a "new" surface. Suitable model systems can be prepared by chemically binding molecules to a surface and then studying the adsorption properties of the new surface.

The great bulk of data available on adsorption apparently resulted from many isolated experiments (see Ref. 21 for a discussion). There have been few studies designed to truly pin down a fundamental variable or concept. The work of Zisman[48] is one of the rare cases where detailed studies have been performed leading to basic, general conclusions.

The author intends to study adsorption of simple compounds from aqueous solutions by radioisotope methods as a function of ion content, pH, solute, and nature of the surface. The hope is that eventually it may be possible to formulate some general, fundamental conclusions. He also intends to study the role of surface morphology and crystallinity in the adsorption process by microautoradiographic methods.

CHAPTER IV

SUMMARY

The blood/materials interface is a crucial factor in the successful use of solid materials for blood-contact applications. The interactions which occur at such interfaces will not be understood until one thoroughly understands the mechanism of adsorption from aqueous solution, particularly onto polymer surfaces.

A mechanistic model of adsorption of apolar molecules from aqueous solution onto apolar polymer surfaces is presented. The nature of adsorption, the structure of water, and the forces which exist between molecules are all considered. The model shows that adsorption is a natural consequence of the asymmetric force field which exists in the vicinity of an interface. It shows that solvent-solvent and solvent-solute interactions are of particular importance, especially in aqueous systems. The solvent content of the adsorbate is considered, resulting in the conclusion that adsorption will not tend to occur on a solvent-loaded surface. The model predicts and provides a mechanistic explanation for monolayer and multilayer adsorption; it also discusses and predicts the orientations of adsorbed species. The role of polymer crystallinity effects and "active sites" is briefly examined; however, the role of the solid surface is shown to be minor with respect to solvent-solvent and solvent-solute effects. Calculations are presented

for a $-CH_2-$ group, ethane, butane, and hexane. Qualitative discussions are given for the adsorption of polar molecules and macromolecules, notably proteins. The structure of ribonuclease is examined; it is shown that different areas on the protein will have significantly different intermolecular interactions with the surrounding solvent or with a near-by adsorbate. The conclusion is that a protein must be expected to adsorb by different mechanisms on different surfaces. The surface-protein interactions may be highly dependent on the orientation of the protein with respect to the solid surface. The adsorption of albumin, gamma globulins and fibrinogen is also discussed. The model and its predictions are compared with available experimental data.

The rationale for the preparation of the potentially enzyme-inhibitory and non-thrombogenic polymers, the polyorganofluorophosphates, is briefly discussed. The rationale for preparing proteinated surfaces is also analyzed; the preparation of albuminated polystyrene is treated in detail and its non-thrombogenic behavior is discussed. A brief mention is given to the potential use of fluoroescence microscopy as a tool for studying protein adsorption on the microscopic level.

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ABSTRACT

The blood/materials interface is a crucial factor in the successful use of solid materials for blood-contact applications. The interactions which occur at such interfaces will not be understood until one thoroughly understands the mechanism of adsorption from aqueous solution, particularly onto polymer surfaces.

A mechanistic model of adsorption of apolar molecules from aqueous solution onto apolar polymer surfaces is presented. The nature of adsorption, the structure of water, and the forces which exist between molecules are all considered. The model shows that adsorption is a natural consequence of the asymmetric force field which exists in the vicinity of an interface. It shows that solvent-solvent and solvent-solute interactions are of particular importance, especially in aqueous systems. The solvent content of the adsorbate is considered, resulting in the conclusion that adsorption will not tend to occur on a solvent-loaded surface. The model predicts and provides a mechanistic explanation for monolayer and multilayer adsorption; it also discusses and predicts the orientations of adsorbed species. The role of polymer crystallinity effects and "active sites" is briefly examined; however, the role of the solid surface is shown to be minor with respect to solvent-solvent and solvent-solute effects. Calculations are presented for a $-CH_2-$ group, ethane, butane, and hex-

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The rationale for the preparation of potentially enzyme inhibitory and non-thrombogenic/polymers, the polyorganofluorophosphates, is briefly discussed. The rationale for preparing proteinated surfaces is also analyzed; the preparation of albuminated polystyrene is treated in detail and its non-thrombogenic behavior is discussed. A brief mention is given to the potential use of fluorescence microscopy as a tool for studying protein adsorption on the microscopic level.