

Part One
Fundamentals

1

Intermolecular Interactions

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1.1

Introduction

Nanotechnology may be broadly defined as the study, fabrication, and application of systems by manipulating structures or objects having nanoscale dimensions (say, between 1 nm and 100 nm). Of course, molecular scientists, in both chemistry and biology, have been dealing with nanoscopic (polymer) molecules and biological cell components for decades. So, what's new? New is that, with the advent in the 1980s of new instrumentation, in particular scanning probe microscopes – for example, atomic force microscopy (AFM) – *individual* nano-objects can be observed and manipulated (see Figure 1.1).

Using AFM, the positions of molecules and nanoparticles, relative to each other, may be rearranged in a controlled way. AFM furthermore allows the measurement of interaction forces between nanoparticles as well as between nanoparticles and macroscopic objects. Other recently developed devices, the so-called optical tweezers and magnetic tweezers, also enable the controlled motion of, and the determination of forces between, nanoparticles.

Manipulation on the nanoscale may be done in two “directions”, referred to as *top-down* and *bottom-up*. In the top-down approach, structures are made increasingly smaller by progressively removing matter, usually by etching. Perhaps the most well-known example of a top-down structure is the electronic chips present in various devices. Another example is the micro- or nano-sieve, a solid wafer punctured with equally sized micro- or nanopores. Nano-sieves are in particular relevant for food processing and water treatment. Because various agricultural and dairy products are of heterodisperse particulate nature, that is, emulsions, foams, and dispersions of solid particles, they may be fractionated using a series of sieves of varying pore size. The separate components thus obtained may be recombined to give newly composed products of superior quality. Also, nano-sieves could be used in (cold) sterilization by filtering out microbial cells.

In the agri-food sector, however, bottom-up nanostructures are more often encountered. Bottom-up implies that atoms or molecules are distributed and rearranged to build new, functional nano-objects. Nature itself is full of bottom-up

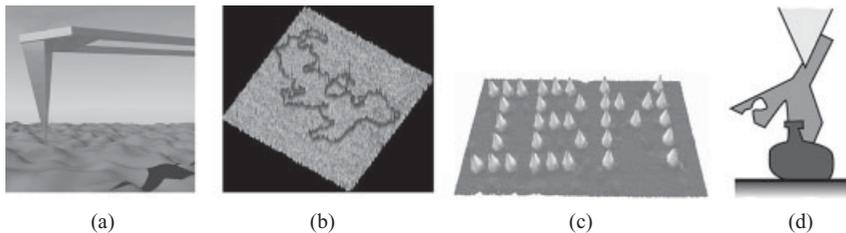


Figure 1.1 Atomic force microscopy. (a) The topography of a surface is scanned with subnanometer resolution, so that nano-sized objects can be (b) observed and (c)

manipulated. (d) Atomic force microscopy may also be applied to determine the interaction between two objects.

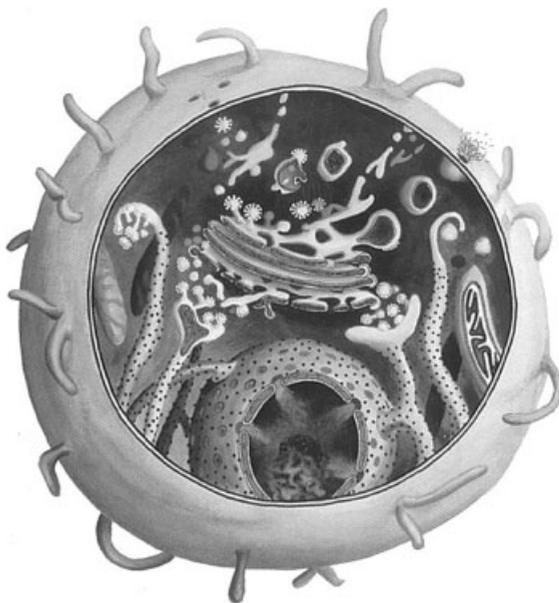


Figure 1.2 Cartoon of a biological cell showing a variety of nano-sized subcellular structures.

nanostructures, especially in living species. Think of viruses, where nucleic acids and proteins are arranged and interact such that viral activity results. Think of microbial, plant, and animal cells in which the various nano-sized organelles and membranes are complex bottom-up assemblies of precisely arranged building blocks (Figure 1.2).

Although nature is capable of making structures far more complicated and sophisticated than the ones that scientists can – for the time being – achieve in their laboratories, it may not be a surprise that nano-engineers are strongly inspired by nature. A few examples come to mind: in making addressable biocom-

patible nanoparticles to be used for the encapsulation and delivery of nutraceuticals and pharmaceuticals, nature provides clues as to how the surface of such particles should look; viruses may serve as a model in the design of particles carrying deoxyribonucleic acid (DNA) fragments to be used in gene therapy; non-fouling surfaces may be mimicked from the outer composition and structure of cell surfaces; and the texture of foodstuff may be optimized by imitating nanostructures as they occur in nature, for example, fibrillar protein aggregates in meat replacers and three-dimensional polymer networks in mousses.

To achieve the specific architectures related to the desired (biological) function of the nanostructure, the physicochemical interactions between the building blocks should be tuned with high accuracy. Needless to say, understanding the mechanisms underlying the various types of interaction is a prerequisite for successful tuning.

In this chapter an introduction to the main types of interactions that may play a role in bottom-up nanotechnology is given. These are physicochemical interactions more or less sensitive to changing environmental conditions and therefore result in the formation of annealed, responsive structures. The discussion here may not be the most rigorous one, as, in view of the scope of this book, the scientific language of chemistry and physics that involves formulas and equations will be avoided as much as possible.

In natural systems, including those of the agri-food sector, most nano-objects exist by virtue of their interaction with an aqueous environment. Not only their existence but also their shape and spatial structure are to a large extent determined by their interaction with water. It is, therefore, essential first to pay attention to some physicochemical properties of water.

1.2 Water

Water is one of the most abundantly occurring chemical compounds on Earth (although very unevenly distributed). Because of its ubiquity, we are inclined to think of water as a trivial, common, and normal liquid. However, from a physicochemical point of view, water is a highly extraordinary substance. By virtue of its unique properties, water is the medium in which life has evolved and is sustained. Which properties make water so special, and how can these properties be explained and understood at the molecular level?

Water, H_2O , has a molar mass of 18 g mol^{-1} . Under ambient conditions, water boils at 100°C . Among other components of comparable molar mass, this is an exceptionally high temperature. For instance, the boiling points of methane (14 g mol^{-1}) and ethane (30 g mol^{-1}) are -162°C and -88°C , respectively. Also, the heat of vaporization, which is essentially the energy required to separate the molecules when they go from the condensed liquid phase to the gas phase, is extremely high for water, 2255 J g^{-1} , whereas for methane and ethane this is a little more than 500 J g^{-1} . Another interesting property is the heat capacity, the amount of heat

needed to increase the temperature of a substance by one degree Celsius. For the sake of fairness, equal amounts of the substances should be compared and at the same temperature and pressure. While the heat capacity of water at 20°C and 1 atm amounts to $4.18 \text{ J K}^{-1} \text{ g}^{-1}$, the values for other liquids are much lower (cf. for chloroform it is $0.90 \text{ J K}^{-1} \text{ g}^{-1}$ and for ethanol $2.49 \text{ J K}^{-1} \text{ g}^{-1}$). These anomalously high values for the boiling point, heat of vaporization, and heat capacity (and, in this context, further extraordinary characteristics of water could be presented) originate from the phenomenon that water molecules attract each other. They attract each other so much that they strongly attach to one another. In scientific terms, water shows a strong internal coherence. Hence, to evaporate the liquid, favorable interactions between the water molecules have to be disrupted (which explains the large heat of vaporization), and this does not occur before the molecules have attained strong thermal motion (explaining the high boiling point). The large heat capacity reflects not only that heat is used for increasing thermal motion (corresponding to a one degree temperature rise) *per se*, but also that loosening of the internal coherence is necessary to increase thermal motion, which is the major energetic cost.

To understand the strong internal coherence, we zoom in on the molecular structure of water. Figure 1.3a shows a model of the molecular architecture of an H_2O molecule. The hydrogen (H) atoms are very small relative to the oxygen (O) atom. Hence, the H_2O molecule is nearly spherical, having a radius of about 0.14 nm. Atoms consist of a positively charged nucleus around which negatively charged electrons are orbiting. Hydrogen atoms have the tendency to donate their electrons for sharing with oxygen, which eagerly accepts that donation. Hydrogen is an electron donor and oxygen is an electron acceptor. Because of the positions of the H atoms relative to the O atom, the charge in the (overall electrically neutral) H_2O molecule is not evenly distributed. Positive charges ($+q$) are centered on each

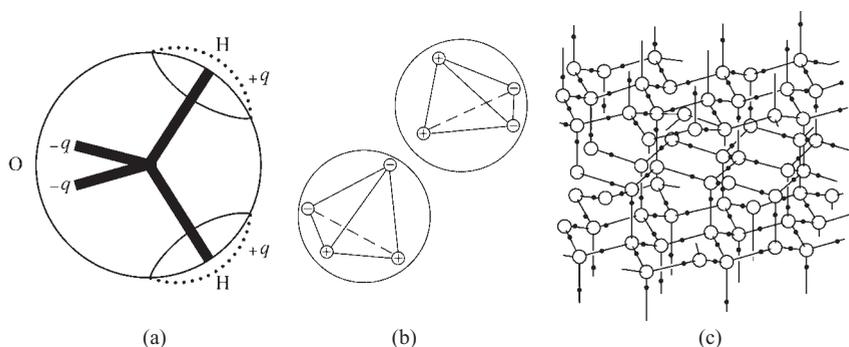


Figure 1.3 Water. (a) Model of a water, H_2O , molecule showing the positive charges $+q$ on the hydrogen atoms and the negative charges $-q$ on the oxygen atom. (b) Polar interaction occurs through so-called hydrogen bonds

between water molecules. (c) The three-dimensional structure of a water lattice in which all potential hydrogen bonds are realized (i.e., ice).

H atom, and compensating negative charges ($-q$) are on the opposite sides of the O atom.

Because of those positive and negative sides, H_2O is said to be a polar molecule. It is the polar character of the molecules that causes the strong internal coherence in water: the positive and negative poles attract each other (Figure 1.3b), so that each H_2O molecule tends to be connected to four other H_2O molecules via so-called hydrogen bonds. In its solid state, ice, the water molecules are in more or less fixed positions, with all four hydrogen bonds realized. Owing to the positions of the poles on the H_2O molecules this results in a relatively open structure (Figure 1.3c) with an H_2O volume density of 55%. When put under pressure some hydrogen bonds may become disrupted and the regular ice structure will be distorted: ice melts under pressure, and in the liquid state H_2O has a somewhat less open structure or, in other words, a higher density than in the solid state. This is another peculiarity of water. In the liquid state the H_2O molecules are still strongly associated in clusters and participate in about three out of the potential four bonds per molecule. Contrary to what one would expect for an associated liquid, the viscosity, that is, the fluidity, of water is not strikingly different from that of other, non-polar, liquids. The mobility of the individual water molecules in the clusters, underlying the macroscopic fluidity of the liquid, is retained, because the molecules readily rotate and hop about every 10^{-11} s from one partner to another, while having most, but not all (as in ice), hydrogen bonding potentialities satisfied.

Another property of water that deserves attention is the dielectric constant. Without going into detail, the dielectric constant is a measure of the ability to screen the electrostatic interaction between two charges at a given separation distance. Water has a high dielectric constant: in water, electrostatic interaction is 20 times weaker than in chloroform and about five times weaker than in ethanol. It is for this reason that salts in water dissociate into their oppositely charged ions. For the same reason, (bio)polymers, such as proteins, DNA, and polysaccharides, as well as synthetic polymers that contain ionizable groups, acquire charge in an aqueous medium. And so do the surfaces of (solid) materials when they are exposed to water.

Now, having gained some insight into some relevant characteristics of water, we may be able to understand the crucial role of water in shaping bottom-up nanostructures.

1.3 Hydrophobic and Hydrophilic Interactions

It has been illustrated and discussed in Section 1.2 that water is a strongly associated liquid because of favorable polar intermolecular interactions. Addition of another substance (referred to as “solute”) will disturb the coherence between the water molecules (Figure 1.4). If the solute molecules are also polar or have a net charge (ions), the polar water molecules interact favorably with the solute as well, just as they do with other water molecules. In that case the solute readily dissolves

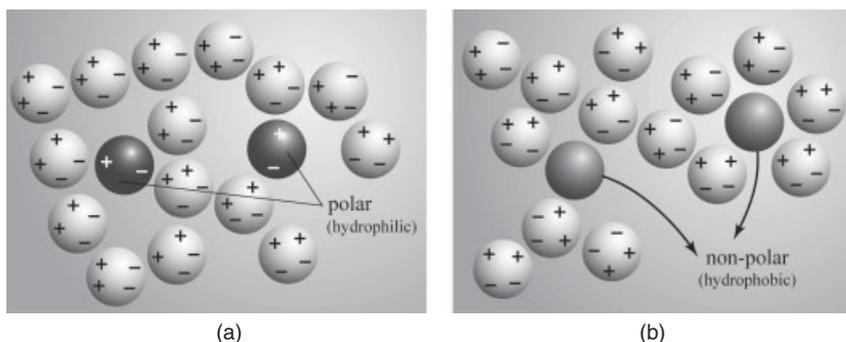


Figure 1.4 (a) Polar and (b) non-polar molecules immersed in water.

in water. The polar substance is called hydrophilic. Salts, sugar, and alcohol are examples of hydrophilic substances. However, if the solute is uncharged and non-polar (i.e., does not have an uneven charge distribution over its molecule), the water molecules prefer to stay attached to each other rather than to the non-polar solute molecules. This results in the non-polar molecules being expelled from the water and driven together to form a separate phase. Oils and fats therefore do not mix with water. For the same reason, the surfaces of plastics, Teflon, and so on, are poorly wetted by water. Such substances, disliked by water, are referred to as hydrophobic.

The description given above of water bordering other substances is highly simplified, especially in the case of non-polar, hydrophobic materials. There are still controversial issues to be solved. Nevertheless, theoretical and experimental studies indicate that, at hydrophobic surfaces, reorientation of water molecules imposes a higher degree of structural order in the adjacent water layer (the so-called hydration layer). Obviously, water molecules bordering non-polar surfaces tend to arrange themselves in a preferred orientation that allows them to form as many H bonds as possible with water molecules in the nearest-neighbor layer, and so on. As nature strives for disorder (in scientific terms, for maximum entropy), hydration of non-polar material is unfavorable and, consequently, the contact area between water and non-polar substances tends to be as small as possible. As a result, non-polar substances spontaneously associate in water because this leads to reduction of the contact area between water and the non-polar substance. Such association between non-polar, hydrophobic substances in an aqueous environment is known as *hydrophobic interaction*. Clearly, the hydrophobic interaction scales with the water-accessible surface area of the non-polar moieties involved. Hydrophobic interaction is one of the major types – if not *the* major type – of interaction occurring in biological systems. If interference by any other type of interaction does not occur, hydrophobic interaction leads to a featureless two-phase system: an “oil” (popular indication of non-polar) phase separates out from an aqueous phase. However, a different and more interesting pattern presents itself when solute molecules possess a non-polar and a polar part. Such molecules

are referred to as *amphiphilic*. They occur abundantly in nature, for instance in lipids and proteins.

A typical lipid molecule has a non-polar tail and a polar head-group, as depicted schematically in Figure 1.5a. In water, such molecules show dual behavior. The hydrophobic tails, rejected by the water, assemble together, but the polar heads are preferably hydrated. The exposure of the heads to the aqueous medium prevents phase separation on a macroscopic scale. Instead, microscopic or nanoscopic non-polar phases, surrounded by the polar, hydrated head-groups, are spontaneously formed. Depending on the dimensions of the tail and the head, relative to each other, the amphiphilic molecules aggregate in spherical, worm-like or bilayer structures that close to form spherical objects called vesicles or liposomes. Such structures that are spontaneously formed are named *self-assembled structures* (see Figure 1.5b–d).

Self-assembly plays an important role in shaping the spatial structure of proteins as well. Proteins may be viewed as hundreds of units (the amino acids) linked together to form a long chain, illustrated in Figure 1.6a. There are 22 different amino acids available and, therefore, an almost infinite number of sequences of amino acids along the chain is possible. Some amino acids are polar, others are non-polar. This makes the protein amphiphilic. In an aqueous environment, the chain will try to fold such that the non-polar groups are shielded from contact with water and the polar ones are exposed to water. Of course, other types of interaction, such as electrostatic ones (to be discussed in Section 1.5) may interfere with these tendencies. Still, globular proteins possess a relatively non-polar interior and a polar exterior (see Figure 1.6b). It may be clear that the exact folding pattern depends on the composition and, even more so, on the sequence of the various amino acids along the chain. Many different proteins are active in biological systems, each one having its own specific structure and function.

It should be emphasized that the lipid assemblies shown in Figure 1.5 and the folded protein structure in Figure 1.6 represent highly ordered structures. Their spontaneous formation demonstrates the constructive power of chaos: such ordered structures exist because of increased disorder in the water that is released from hydrophobic hydration.

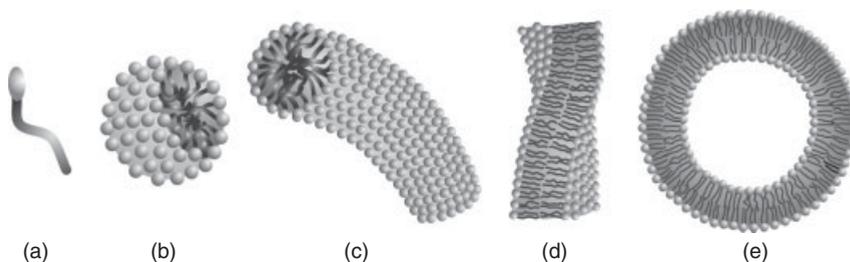


Figure 1.5 (a) The typical structure of an amphiphilic (= “lipid”) molecule consisting of a polar and a non-polar part. (b)–(d) In an aqueous environment, amphiphilic molecules aggregate to form supramolecular structures of various geometries.



Figure 1.6 Folding of (a) a poly(amino acid) chain, containing polar (black) and non-polar (gray) amino acids, into (b) a compactly structured globular protein molecule, where the non-polar amino acids prefer to reside in

the protein's interior, shielded from contact with water, and the polar amino acids prefer the periphery, exposed to the aqueous environment.

It is no surprise that (bio)nano-engineers are strongly inspired by the phenomenon of self-assembly. They design and synthesize tailor-made amphiphilic molecules to build their desired supramolecular assemblies and nano-objects.

1.4

Dispersion Interaction

Dispersion interaction is the most generic one among the different types of physical interactions. Wherever there is matter, irrespective of its properties, there are dispersion interactions.

The origin of dispersion interaction between two atoms may be understood as follows. In any atom, negatively charged electrons orbit around a positively charged nucleus. Although the time-average position of the electrons with respect to the nucleus may be concentric, at any point in time their positions deviate from that average, which gives rise to a small dipole moment. This instantaneous dipole generates an electric field, which, in turn, induces a dipole moment in a neighboring atom, and so on. Thus dispersion interactions are larger between atoms that have a larger polarizability. When the interaction occurs across a medium, the excess polarizabilities (i.e., the polarizability of the atoms in vacuum minus that of the atoms of the medium in vacuum) should be taken into account. Dispersion interaction across a medium is therefore strongly reduced, as compared to vacuum. Dispersion interaction between two atoms diminishes very strongly with separation distance (say, within 0.5 nm), but between particles, containing a large ensem-

ble of atoms, they are more long-ranged and may be effective over (tens of) nanometers.

The strength and the range of dispersion interaction between particles depend not only on the polarizability of the constituent atoms but also on the density (number of atoms per unit volume) and the size of the particles. Dispersion interactions may play significant roles in aggregation of particles, in coating of surfaces with particles, and in folding polymeric molecules into condensed structures, such as, for example, globular proteins. Because dispersion interactions are non-directional, do not require special properties of the interacting species, and occur always and everywhere, they hardly provide a handle to direct bottom-up fabrication of nanostructures.

1.5

Electrostatic Interactions

Electrostatic interactions occur between electric charges. We may distinguish between interactions involving (i) atoms and small molecules, and (ii) polymers, particles, and surfaces.

1.5.1

Atoms and Small Molecules

Atoms and small molecules interact electrostatically when they have a net charge (i.e., when they are ions), and also when they are uncharged but polar. Obviously, interaction between positive and negative charges is attractive, whereas charges having the same charge sign repel each other. In Section 1.2 it was mentioned that interaction between charges across a medium is inversely proportional to the dielectric constant of that medium. It was further pointed out that the dielectric constant is directly related to the polarity of the molecules of the medium.

Charged groups are almost always surrounded by water, but sometimes they reside in a non-aqueous environment. This occurs, for instance, when ionic amino acids become trapped in the interior of a globular protein molecule. In such a low-dielectric environment, ions can only exist when they form a pair: two oppositely charged ions close together, as depicted in Figure 1.7.

The question arises whether ion pairing would contribute to the folding of the protein molecule. An ion pair in the compact structure is electrostatically favored over a wider separation in the unfolded hydrated chain (where the dielectric constant is almost that of water), but the pairing goes at the expense of favorable hydration of the ions in the unfolded structure. These two effects more or less balance each other. Hence, ion pairing as a factor promoting either a compact or unfolded structure in an aqueous medium is highly uncertain. Yet, if ionic groups are forced into a non-aqueous, low-dielectric environment – for instance, due to hydrophobic bonding of adjacent non-polar moieties – pairing between ions of opposite sign is strongly promoted.

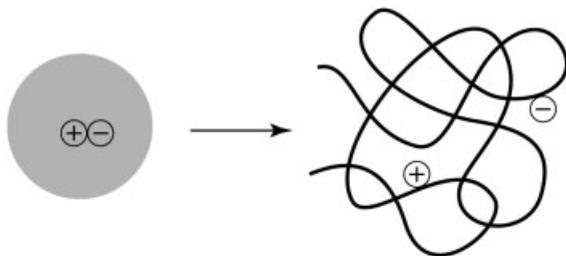


Figure 1.7 Ion-pair disruption in an unfolding protein molecule.

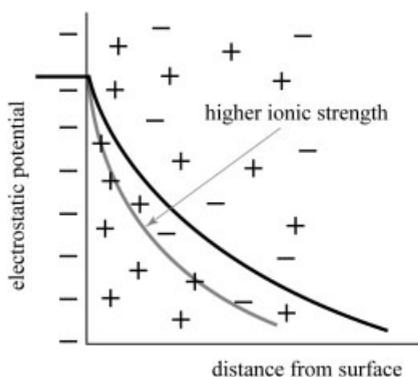


Figure 1.8 Electrostatic potential profile across an electrical double layer.

Similar reasoning applies to the weaker electrostatic interactions between an ion and a dipole, and to the even weaker dipole–dipole interaction.

Because of the relative strength of electrostatic interactions, inserting charged groups at selective locations in a polar and/or non-polar environment can help to direct construction of a desired nanostructure.

1.5.2

Polymers, Particles, and Surfaces

Polymers, particles, and (macroscopic) surfaces in an aqueous environment are often charged, in most cases due to groups that dissociate or associate with hydrogen ions. The charge is balanced by an uneven, diffuse distribution of counter-ions in the adjoining solution in a so-called electrical double layer (Figure 1.8). Electrostatic interactions involving polymers, particles, and surfaces are therefore referred to as *electrical double layer interactions*.

The diffuse distribution of ions in the electrical double layer gives rise to an electrostatic potential that drops off with increasing distance from the charged object. Without explaining the details here, it should be mentioned that the potential decays more steeply with increasing salt concentration in solution (= higher ionic strength) and the separation distance over which the two charged bodies

interact decreases correspondingly. For example, in tap water that distance would be about 15 nm, in milk 1.3 nm, in blood 0.8 nm, and in sea water 0.3 nm. For nano-engineers electrical double layer interactions are convenient to work with because of the possibility to modulate their magnitude by just varying easily adjustable parameters such as pH and ionic strength.

In bottom-up nanotechnology, charged soluble polymers, named polyelectrolytes, are essential building blocks. Natural polymers, such as proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and polysaccharides, are well-known examples, but synthetic polyelectrolytes are regularly used in nanotechnological applications as well. When the polyelectrolytes have the same charge sign, they repel and try to avoid each other; but when they are oppositely charged, interesting phenomena occur. Oppositely charged polyelectrolytes form complexes mainly because of the release of counter-ions from the electrical double layers, which implies increasing disorder and therefore a higher entropy in the system. Here, too, as described for amphiphilic molecules in Section 1.3, the formation of macroscopic aggregates is prevented if at least one of the two polyelectrolytes is linked to an uncharged hydrophilic polymer in a so-called block copolymer. During complexation of the two polyelectrolytes, the uncharged polymer block tends to remain dissolved in the surrounding water, thereby preventing the complexes from growing to macroscopic dimensions. This results in the formation of polyelectrolyte micelles, as shown in Figure 1.9, that are generally referred to as *polyion condensates* or *complex coacervate core micelles*. Recently these structures have attracted a lot of attention as potential nano-containers for the encapsulation and controlled release of pharmaceuticals and nutraceuticals, as well as for their application as nano-bioreactors.

Complexation between oppositely charged polyelectrolytes can also be used to regulate the consistency of certain foodstuffs. The texture of dairy products such as (drink) yogurts may be optimized by adding positively charged polysaccharides that associate with, for instance, negatively charged milk proteins.

Particles dispersed in water carry their charged groups exclusively at the aqueous periphery (except, perhaps, for a few ion pairs formed inside the non-aqueous

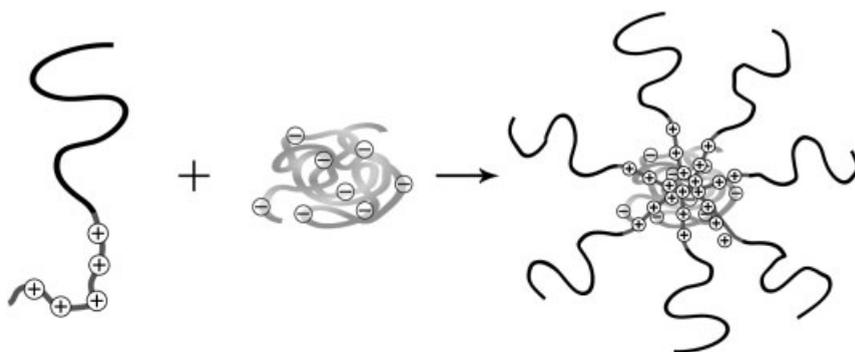


Figure 1.9 Formation of a polyelectrolyte micelle.

interior of the particle; see Section 1.3). When charged particles approach each other, the electrical double layers overlap, giving rise to repulsion between like-charged particles, and attraction if the particles are oppositely charged. A repulsive electrical double layer overlap helps to keep the particles apart and therefore contributes to the stabilization of the dispersion. Even when the particle surface is predominantly hydrophobic, at not too high ionic strength, electric double layer repulsion operating over a larger distance than attractive dispersion and hydrophobic interaction (see Sections 1.3 and 1.4) prevents the particles from aggregating. In media of higher salt concentration, typically beyond, say, 1% sodium chloride, electrical double layer repulsion is too short-ranged, and attractive dispersion interaction takes over and the like-charged particles aggregate. It goes without saying that oppositely charged particles readily aggregate under all conditions of ionic strength (see Figure 1.10).

The stability of nanoparticles against aggregation is a requirement in various food products, and in pharmaceutical and cosmetic formulations. Destabilization of particulate dispersions may be required when clearing, for example, wine or fruit juices and in (waste)water purification processes.

Electrostatic interactions between polymers and particles, between polymers and surfaces, and between particles and surfaces follow the same principles as described above for polymers and particles. Thus, attachment of polymers onto particles and planar surfaces, and of particles onto planar surfaces may be electrostatically favored or disfavored. As in nature, in nanotechnology, polymer–particle interactions often determine whether or not particles connect to each other. This will be further discussed in Section 1.6.

Surfaces can be covered by a layer of nanoparticles to provide the surface with special properties with respect to, for example, wetting or scratch resistance. Finally, polymers are applied at surfaces to render them resilient against (bio) fouling by suppressing the deposition of proteins, biological cells, and microbes. Non-fouling surfaces are a requirement for successful operation of equipment in food processing and water purification equipment, such as separation membranes, heat exchangers, and so on.

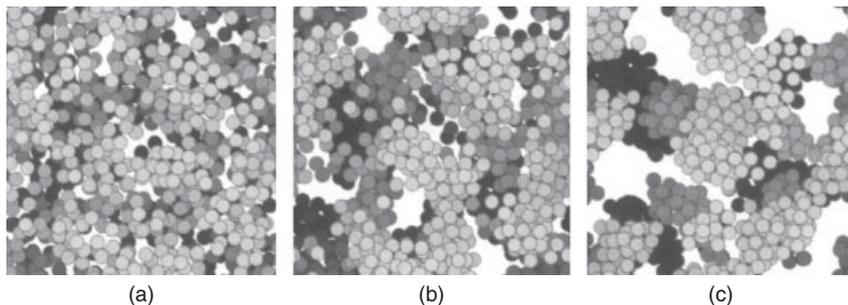


Figure 1.10 Different packing patterns of aggregated particles.

1.6 Steric Interactions Involving Soluble Polymers

In both naturally occurring and man-made nanoscopic constructs, polymers are present in solution and/or attached (= adsorbed) onto (particle) surfaces. The polymers could be uncharged or charged (polyelectrolytes), strongly hydrated or more compact. Polymers, either attached to a surface or not, influence the behavior of nanosystems through steric interactions. These interactions are intricate and delicate, and may change from attractive to repulsive by subtle variations of environmental conditions.

1.6.1 Depletion Aggregation of Particles by Non-adsorbing Polymers

The center of a non-adsorbing polymer molecule cannot approach a particle surface closer than its own radius. Hence, around each particle there is a zone where polymer molecules cannot be accommodated. When particles, by diffusion or otherwise, come closer than twice the radius of the polymer, the polymer will be moved aside and the gap between the particles will be depleted of polymer and just be filled with solvent. This situation is schematically illustrated in Figure 1.11. Because solvent and soluble polymers tend to mix homogeneously, solvent molecules flow from the gap into the solution, which drives the particles together. This type of aggregation induced by non-adsorbing polymers is referred to as depletion aggregation. Depletion aggregation is enhanced by increasing the concentration and the size of the polymer molecules.

1.6.2 Bridging Aggregation of Particles by Adsorbing Polymers

Most polymers tend to adsorb at surfaces. This may be due to binding of hydrophobic segments in the polymer chain (to escape from the hostile water), to hydrogen bonding with surface groups, or, in the case of polyelectrolytes and

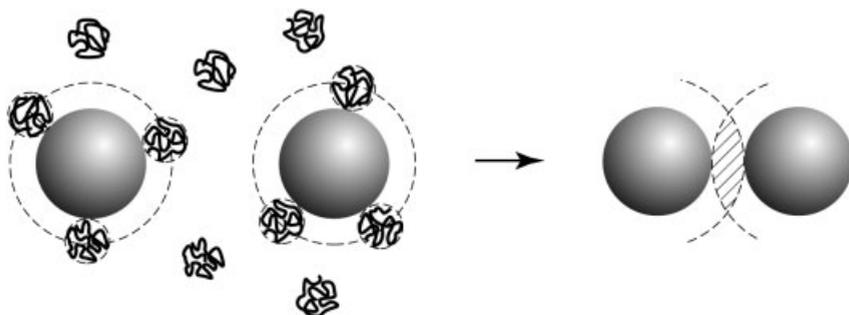


Figure 1.11 Aggregation of particles driven by overlapping polymer depletion zones.

charged surfaces, to favorable electrostatic interactions. When a polymer adsorbs onto a surface, it usually does not lie flat on that surface but adopts a “loopy” structure with loose tails at the terminal ends, as shown in Figure 1.12. If the particle surface is in excess of the polymer, the surface will only become partially covered by the polymer. This allows one and the same polymer molecule to bridge between different particles (see Figure 1.13). Similar bridging aggregation can occur if bare particles are added to particles that are covered with polymer molecules, fully or not.

Bridging aggregation requires that the polymer adsorbed on one particle extends into the surrounding solution far enough to reach another particle. When both particles are charged and repel each other electrostatically (Section 1.5), polymer bridging can only take place if the extension of the polymer exceeds the range over which electrostatic repulsion operates. For this reason, bridging aggregation is more likely to happen with longer polymers and at higher salt concentrations in solution, where the range of electrostatic interaction is reduced. The aggregates formed are loosely structured, with the particles not in direct contact with each other. Closer approach of the particles is detrimental, as it would impose unfavorable deformation of the polymer bridges between the particles.

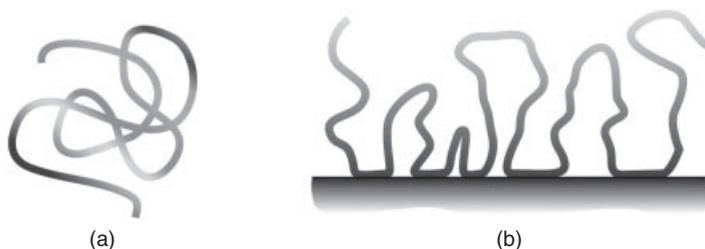


Figure 1.12 Structure of a coiled polymer (a) in solution and (b) adsorbed onto a surface.

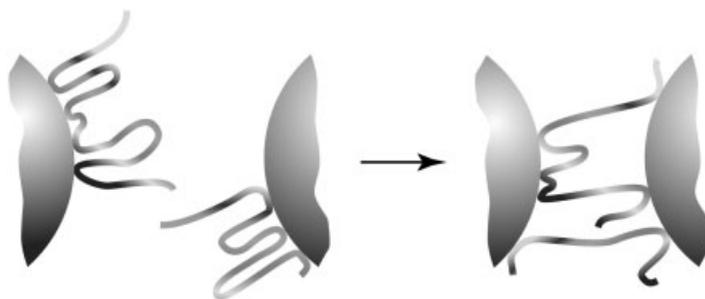


Figure 1.13 Particle aggregation by polymer bridging.

1.6.3

Stabilization of Dispersed Particles by Adsorbing Polymers

When there is an excess of polymers, each particle is saturated with a layer of adsorbed polymer. Then, upon approach of the particles, the outermost fringes of the loops and tails anchored to the respective particles begin to interpenetrate. This leads to unfavorable confinement of the polymer and, hence, to repulsion between the particles that is effective over roughly twice the thickness of the adsorbed polymer layer (Figure 1.14).

Such polymer coatings may be applied to stabilize dispersions under conditions where electrostatic repulsion is insufficiently strong to keep the particles apart, that is, in the case of oppositely charged and uncharged particles, but also of like-charged particles in media of high ionic strength (Section 1.5). To protect the particles from aggregation, the separation distance at which steric repulsion becomes effective (to be regulated by the thickness of the polymer coatings) should be large enough to suppress attractive dispersion interaction (Section 1.4).

Thus, the impact of polymers on interparticle interaction strongly responds to environmental conditions and can therefore readily be manipulated. For instance, by varying the quality of the solvent (e.g., by changing pH, ionic strength, temperature, additives, etc.), the polymer behavior may be adapted from adsorbing to non-adsorbing and vice versa. In this way, bridging may be eliminated, steric stabilization converted into depletion aggregation, and so on. When solvent quality is reduced to below the solubility of the polymer, steric repulsion between fully polymer-covered particles changes into attraction.

1.6.4

Polymer Brushes to Prevent Particle Aggregation and Particle Deposition at Surfaces

A very effective method of steric stabilization can be achieved by grafting polymers at one end onto a (particle) surface, leaving the rest of the molecule dangling in solution. This is best obtained by using diblock copolymers, of which one block has a strong affinity for the surface and the other for the solvent. The profile of

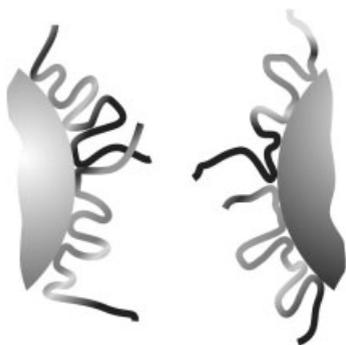


Figure 1.14 Steric stabilization of polymer-coated particles.

the polymer at the surface depends on the grafting density, as shown in Figure 1.15. Obviously, steric stabilization against particle aggregation or deposition improves with increasing grafting density, and is extremely effective when the polymer molecules are stretched out from the surface in a so-called polymer brush. The density of the brush prevents indwelling particles entering, and the strong hydration and high mobility of the polymer chains cause a strong resilience against compression. According to this principle, liposomes (see Section 1.3) used in drug delivery systems may be protected against removal by the immune system, allowing them a longer circulation time in the body. Similarly, the corona polymers of polyion micelles (see Figure 1.9) form a brush that stabilizes the micelles, possibly loaded with some functional ingredient, against external attack by, for example, enzymes or immunoproteins.

Polymer brushes may also be applied to planar surfaces to make them resistant to protein adsorption and microbial adhesion, which, in turn, suppress biofouling. An example is given in Figure 1.16. Besides use in various biomedical applications,

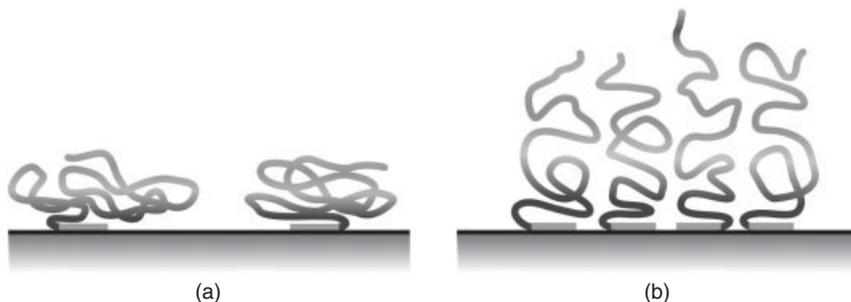


Figure 1.15 End-grafted polymers in (a) a mushroom and (b) a brush conformation.

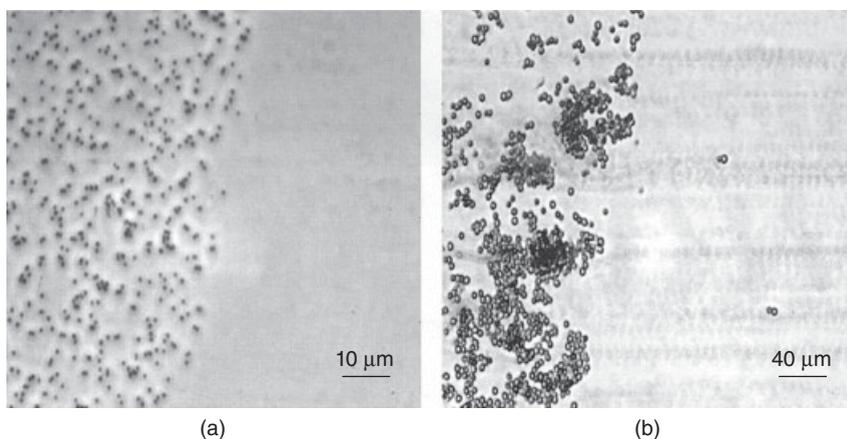


Figure 1.16 Effect of applying a polymer brush (right-hand side of each image) on the adhesion of micro-organisms: (a) *Staphylococcus epidermidis* and (b) *Candida albicans*.

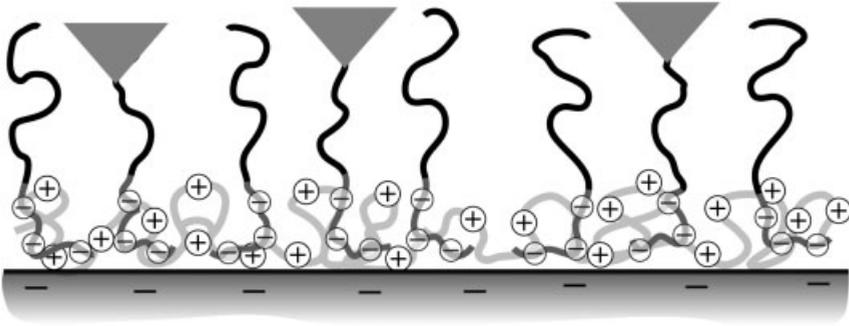


Figure 1.17 Cartoon of a functionalized bio-selective surface.

non-fouling surfaces are of the utmost importance in the food industry to avoid – or, at least, to retard – the formation of a biofilm that will reduce heat and mass transfer and increase frictional resistance and, moreover, may be a source of microbial contamination.

Nature uses its own polymers, usually polysaccharides, to keep cell surfaces clear of unwanted particles or molecules. Nature even goes a step further. At the far end of some polymer chains, receptor molecules may be attached that bind specific target molecules with high affinity. In this way, a bio-selective surface (Figure 1.17) is obtained that binds target molecules but prevents non-specific deposition of other species. Bio-nanoresearch is under way to mimic this principle for application in highly specific and sensitive biosensors and solid-state diagnostics. Such devices have great potential to be used for quality control in the agri-food sector.

1.7 Epilog

For (bio)nanostructures to be functional, they have to respond to an external trigger or signal. Internal bonds in such structures should therefore not be permanent but be sensitive to changing environmental conditions. The physical interactions discussed in this chapter provide such flexibility. For the sake of simplicity, the different types of interaction were presented separately. However, it should be realized that they rarely occur separately, but are usually interdependent. For instance, hydrophobic interaction may be accompanied by ion pairing in a non-polar environment. Conversely, like-charged ions may prevent hydrophobic interaction from occurring as in the case of stabilization of hydrophobic particles by electrical double layer interaction. Another example of interweaving interactions is the combination of electrostatic and steric effects induced by polyelectrolytes.

Hydrophobic, electrostatic, and steric interactions depend on different properties, that is, polarity, charge, solubility, and polymer adsorption behavior, whereas dispersion forces are less specific. Knowledge of the origin, characteristics, and

mutual dependence of the various types of interaction provides the nano-engineer with clues to design the building blocks to be used in bottom-up nanostructuring. If tailor-made building blocks are brought together in a well-defined, usually aqueous, medium, they may self-assemble to yield the desired nano-object. Isn't it miraculous? It is almost magic! It is like a car spontaneously emerging from the proper blend of its parts, screws, and bolts.

Further Reading

For more specific and detailed information the reader is referred to:

Norde, W. (2011) *Colloids and Interfaces in Life Sciences and Bionanotechnology*, 2nd edn, CRC Press, Boca Raton, FL (forthcoming).

Israelachvili, J.N. (2004) *Intermolecular and Surface Forces*, 3rd edn, Academic Press, New York.