Hans Mollet, Arnold Grubenmann

Formulation Technology

Emulsions, Suspensions, Solid Forms

Translated by H. R. Payne

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What do we mean by the phrase "formulation technology"? The word "formulation" has long been established as a synonym for "recipe". For many people, this term suggests something of a black art rather than an exact scientific discipline. The source of the oldest formulations is probably pharmacy, in which the skills associated with the development and execution of recipes has grown into an independent discipline, galenics. In other fields of chemistry, particularly industrial chemistry, formulations are amongst a company's most closely guarded trade secrets on account of their often considerable economic value. With a few exceptions, such as for pigments, foodstuffs, cosmetics, and agrochemicals, there is no general work covering the whole area of formulation technology; formulation chemists are forced to rely on widely scattered, although admittedly numerous, references in the most varied journals.

A large proportion of chemical substances, whether inorganic or organic, natural or synthetic, must be refined and formulated before they can be used in medicine, industry, agriculture, foods, cosmetics, and so on. Often this is merely a question of grinding and mixing; pure dyes and pharmaceuticals must also be combined with suitable auxiliary substances simply to permit reasonable dosage. However, a recipe alone is not usually sufficient; in addition, knowledge of the necessary raw materials, of their preparation, and of the application is required. Most important of all is the processing of the formulation into its optimal form for trade and for use. Here we should mention freeflowing, dust-free powders of optimal particle size, agglomerates and granulates, stable concentrated solutions and suspensions, emulsions, microemulsions, instant products, slow-release preparations, microcapsules, liposomes, and so on.

It has long been recognized that the application properties of a substance to be formulated can be improved by suitable measures, such as an increase in solubility, solubilization, division of solids into a colloidal form, agglomeration of the substance to be formulated, above all the use of efficient tensides – all these create numerous effects, improvements, and new possibilities for use in the field of formulation. Often the competitiveness in the marketplace of a synthetic product that is excellent of itself is determined by its commercial formulation, as has been demonstrated by vitamins formulated to flow freely or dust-free dyestuffs.

The art of formulation is thus a scientific discipline, with a pronounced interdisciplinary character centered around physics, physical chemistry, colloid and interface chemistry, analysis, and not least process technology. Modern commercial forms and forms for application rely on many methods from process technology and on advanced modern analytical techniques. Thus the discipline of formulation has developed into formulation technology, which rests on solid scientific supports, and in which empiricism is increasingly being replaced by scientific criteria. This is not to say that creativity and inventiveness should lose their importance in the solution of problems and the creation of new or better commercial formulations.
A huge store of empirical knowledge is available to formulation chemists; this is useful, but not sufficient. The ability to diagnose current problems and, on the basis of accumulated knowledge, to relate them to solutions found earlier does indeed result in progress, but is not enough for a rapid and certain solution of problems of formulation. A more advanced method is the empirical deduction of relationships between the composition of a formulation and its properties and the expression of these in equations that correlate with the experimental data. Various computer-aided techniques common for correlation analysis are used for this purpose. Basically, these involve empirical trial-and-error schemes and regression methods. This methodology is very efficient if all the components of the formulation have already been selected by experiment or from practical requirements.

However, the soundest scientific approach is the understanding of the relationships between the components of a formulation and its properties (such as the stability of an emulsion or a suspension) in terms of molecular theory. Nowadays this is possible in simple cases, but not for complex systems. Simplifying assumptions have to be made, thus weakening the connection to the theory. So, for the time being, we cannot get by without empiricism. Nevertheless, awareness of the theoretical basis of colloid and surface chemistry, such as DLVO theory in the case of the stability of dispersions, may protect us from attempting solutions forbidden by theory. Whether formulation chemists are accustomed to approaching problems from a purely empirical angle or to seeking correlations between the components of a formulation and its application properties with the assistance of statistical computing methods, a knowledge of the physicochemical and technical basics relevant to formulation technology will be useful to them in making progress.

The present monograph is intended to fill the publication gap concerning the manufacture of optimized formulations, commercial forms, and forms for application. The aim of the book is a holistic treatment of the separate disciplines that play a role in the formulation of an active ingredient into its commercial form, in particular of colloid and surface chemistry and process technology, and the establishment of a coherent, interdisciplinary theory of formulation technology.

This general treatment of the subject, independent of individual products and of substance-specific formulation problems, makes up the heart of the book. Alongside it, the practical aspects of selected individual topics are summarized in order to provide an overview of the state of the art and the problems existing in these areas, such as pharmaceutical technology, dyestuffs and pigments, and cosmetics.

Finally, we wish to thank the many colleagues who have aided us in the realization of this project. First and foremost amongst these is Professor H.F. Eicke of Basel University, to whom we are indebted for his knowledgeable assistance and many suggestions and corrections. Amongst the many experts from industry who helped us with valuable contributions, we would like to single out Dr. U. Glor (Novartis), Dr. R. Jeanneret, Dr. E. Neuenschwander, and Dr. U. Strahm (Ciba SC), and Mr. A. Schrenk (Nestlé).
Thanks are also due to the publishers and authors who have allowed us to reproduce figures and tables. The references name the relevant sources and can be found in the literature sections of the individual chapters.

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1 Colloids, Phases, Interfaces

1.1 General Remarks

Colloid chemistry deals with systems that contain either large molecules or very small particles. With respect to particle size, they lie between solutions and coarse particulate matter; the size range is roughly 1–1000 nm, that is, 10 Å to 1 μm. This corresponds to $10^3$–$10^9$ atoms per molecule or particle.

Interface chemistry is concerned with the phenomena and processes of heterogeneous systems, in which surface phenomena play a major role. Examples include adsorption and desorption, precipitation, crystallization, dispersion, flocculation, coagulation, wetting, formation and disruption of emulsions and foams, cleaning, lubrication, and corrosion. The specific characteristics of the interfaces which are important in such phenomena are controlled by electrochemical properties (charges) or by the use of certain organic compounds called tensides (also known as detergents or surfactants), which contain both polar and nonpolar groups in each molecule.

Table 1.1. Examples of colloidal states (s = solid, l = liquid, g = gas).

<table>
<thead>
<tr>
<th>s/s</th>
<th>s/l</th>
<th>s/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>solid</td>
<td>dispersions</td>
<td>aerosols</td>
</tr>
<tr>
<td>pharmaceutical</td>
<td>suspensions, lime slurries</td>
<td>smoke</td>
</tr>
<tr>
<td>preparations</td>
<td>latex</td>
<td></td>
</tr>
<tr>
<td>reinforced plastics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>magnetic tape</td>
<td></td>
<td></td>
</tr>
<tr>
<td>l/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gel permeation chromatography separating gels</td>
<td>emulsions</td>
<td>aerosols</td>
</tr>
<tr>
<td>g/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>foam products</td>
<td></td>
<td></td>
</tr>
<tr>
<td>aerogels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>foamed concrete, meerschaum mineral</td>
<td>foam</td>
<td>fog</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>milk</td>
<td>spray</td>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>
| Examples of colloidal states are given in Table 1.1. This area of chemistry contrasts with the field of homogeneous-phase chemistry, which comprises the major part of synthetic chemistry. The usual training of a chemist concentrates on the homogeneous phase, and chemistry in the heterogeneous phase, interface chemistry, does not receive the attention that its great technical and biological importance merits. Exceptions that
attract notice at the level of an undergraduate course in chemistry are, for example, adsorption processes and surface tension. It is already 90 years since W. Ostwald described colloids as a "world of neglected dimensions". Very little has changed since then; colloid and interface chemistry remain neglected disciplines in education. We intend to reduce the level of such neglect with this book; we hope that the "art" of formulation, as it once was, can thus be developed into formulation technology, with a scientific basis and a pronounced interdisciplinary character, the emphasis being on chemistry, physical chemistry, especially interface chemistry, and process technology.

A leading interface chemist, Pradip K. Mookerjee, once wrote: "No school teaches about mixing things together so that they do what you want and don’t react with each other."

1.2 Physical Behavior of Atoms and Molecules inside Phases and at Interfaces and Surfaces

The three phases - gas, liquid, and solid - are depicted schematically in Figure 1.1.

![Figure 1.1](image)

Gas: The molecules are distant from one another; little or no attraction. High mobility results in elastic collisions.

Liquid: Molecules in constant motion. Cohesive forces between the molecules influence their motion. Only in special cases are these forces sufficient to form areas of local order.

Solid: Strong forces hold the molecules in a regular arrangement.

Figure 1.1. The three phases: gas, liquid, and solid.

For a solid or a liquid to hold together, there must be strong attractive forces between its atoms. An atom inside a phase is completely surrounded by other atoms and is in a state of dynamic equilibrium (Figure 1.2).
The atoms at the surface are in a very different situation. Because of the equilibrating forces in the outer sphere, they are in a state of surface tension. Molecules at the surface have fewer neighbors, that is, fewer intermolecular interactions compared with the molecules in the bulk of the liquid. This leads to an attractive force normal to the surface acting to pull the surface molecules into the liquid. The surface tension $\gamma$ is defined as the force necessary to counteract exactly this inward force, measured in mN (milliNewton) acting on a line of 1 m length parallel to the surface (formerly dyn acting on a line of 1 cm), and thus has the units mN/m.

$$\left[ \frac{mN}{m} \right] = \left[ \frac{dyn}{cm} \right]$$  \hspace{1cm} (1.1)

The free surface energy of a liquid is defined as the work necessary to increase the surface by 1 cm$^2$; units milliJoule/m$^2$.

$$\left[ \frac{mJ}{m^2} \right] = \left[ \frac{erg}{cm^2} \right]$$  \hspace{1cm} (dimensionally equivalent to: \(\left[ \frac{mN}{m} \right] = \left[ \frac{dyn}{cm} \right]\)) \hspace{1cm} (1.2)

(Note that m can stand for milli and for meter.)

The units of surface tension and free surface energy are therefore dimensionally equivalent! The surface energy is equal to the work that is required to bring atoms or molecules out of the interior of a liquid to the surface. Accordingly, the surface tends to contract; thus droplets form (smallest possible surface).

When two immiscible liquids are in contact, the forces of attraction acting on a molecule at the interface will be somewhat different than at a surface. There are interactions between the differing molecules at the interface (van der Waals forces; see below). Often, the interfacial tension $\gamma_{1|2}$ is somewhere between the surface tensions $\gamma_1$ and $\gamma_2$ of the two individual liquids (in contrast, the dispersion fraction $\gamma_0$ and the polar fraction $\gamma_p$ are always between the two individual contributions; see Section 1.7.2).
Example: The interfacial tension between hexane and water ($\gamma_{1\text{L}2}$) lies between the surface tension of hexane ($\gamma_2 = 18.43 \text{ mN/m}$) and that of water ($\gamma_1 = 72.79 \text{ mN/m}$): $\gamma_{1\text{L}2} = 51.10 \text{ mN/m}$.

**Table 1.2.** Surface tension and interfacial tension with water of liquids at $20^\circ \text{C}$ [mN/m]; water: $\gamma_1$ (from [1]).

<table>
<thead>
<tr>
<th>Liquid</th>
<th>$\gamma_2$</th>
<th>$\gamma_{1\text{L}2}$</th>
<th>Liquid</th>
<th>$\gamma_2$</th>
<th>$\gamma_{1\text{L}2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>72.75 (\gamma_1)</td>
<td>--</td>
<td>ethanol</td>
<td>22.3</td>
<td>--</td>
</tr>
<tr>
<td>benzene</td>
<td>28.88</td>
<td>5.0</td>
<td>$n$-octanol</td>
<td>27.5</td>
<td>8.5</td>
</tr>
<tr>
<td>acetone</td>
<td>27.6</td>
<td>--</td>
<td>$n$-hexane</td>
<td>18.4</td>
<td>51.1</td>
</tr>
<tr>
<td>acetic acid</td>
<td>23.7</td>
<td>--</td>
<td>$n$-octane</td>
<td>21.8</td>
<td>50.8</td>
</tr>
<tr>
<td>CCl$_4$</td>
<td>26.8</td>
<td>45.1</td>
<td>mercury</td>
<td>485</td>
<td>375</td>
</tr>
</tbody>
</table>

The attractive force between molecules in the bulk of the liquid is known as the **internal pressure** or the **cohesion energy** $\Delta E_v$. The cohesion energy density $\Delta E_v/V$ is an important quantity; it is defined in Equation 1.3:

$$\frac{\Delta E_v}{V} = \frac{\Delta H_v - RT}{V} = \delta^2$$  \hspace{1cm} (1.3)

$\Delta H_v$: enthalpy of vaporization [J mol$^{-1}$]  
$V$: molar volume [m$^3$ mol$^{-1}$]  
$R$: gas constant = 8.314 J K$^{-1}$ mol$^{-1}$  
$T$: absolute temperature [K]

A quantity of great practical use is the solubility parameter $\delta = \sqrt{\delta^2}$ (cf. Chapter 8, Solubility Parameters). The quantities necessary for its calculation, $\Delta H$ and $V$, are easily obtained from reference books. The mutual solubility of two components can be determined from $\delta$; the closer their $\delta$ values, the greater their mutual solubility.

**Example:**  
phenanthrene $\delta = 20.0$ MPa$^{1/2}$ \[1 \text{ MPa}^{1/2} = (10^6 \text{ N} \cdot \text{m}^{-2})^{1/2}\]  
carbon disulfide $\delta = 20.5$ MPa$^{1/2}$  
n-hexane $\delta = 14.9$ MPa$^{1/2}$

Phenanthrene is therefore more soluble in carbon disulfide than in n-hexane. This rule applies only to nonpolar substances; for polar substances, see for example references [2] and [3].
1.2.1 Disperse Systems

Simple colloidal dispersions are two-phase systems consisting of a disperse phase (for example a powder) finely distributed in a dispersion medium. Sols and emulsions are the most important types of colloidal dispersions. The fine distributions of solids in a liquid formerly known as sols (the expression sol was used to distinguish colloidal from macroscopic suspensions) are now called suspensions or simply dispersions. Unlike these, emulsions consist of liquid droplets distributed in an immiscible liquid dispersion medium.

The classification of dispersions created by W. Ostwald over 80 years ago is still valid today (Figure 1.3). In principal there is always an inner, disperse or discontinuous phase that is immiscible with an outer, continuous or homogeneous phase.

![Classification of Disperse Systems](image)

**Figure 1.3.** Classification of disperse systems according to W. Ostwald.

Table 1.3, which should be read as supplementary to Figure 1.3, lists a selection of typical colloidal systems.
Table 1.3. Some typical colloidal systems (from reference [4]).

<table>
<thead>
<tr>
<th>Examples</th>
<th>Class</th>
<th>Disperse phase</th>
<th>Continuous phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disperse systems</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fog, spray, vapor, tobacco smoke, aerosol sprays, flue gases</td>
<td>liquid or solid aerosols</td>
<td>liquid or solid</td>
<td>gas</td>
</tr>
<tr>
<td>milk, butter, mayonnaise, asphalt, cosmetic creams</td>
<td>emulsions</td>
<td>liquid</td>
<td>liquid</td>
</tr>
<tr>
<td>inorganic colloids (gold, silver iodide, sulfur, metallic hydroxides)</td>
<td>sols or colloidal suspensions</td>
<td>solid</td>
<td>liquid</td>
</tr>
<tr>
<td>clay, mud, toothpaste</td>
<td>slurry</td>
<td>solid</td>
<td>liquid</td>
</tr>
<tr>
<td>opal, pearls, colored glass, pigmented plastics</td>
<td>solid dispersions</td>
<td>solid</td>
<td>solid</td>
</tr>
<tr>
<td>foam</td>
<td>liquid foams</td>
<td>gas</td>
<td>liquid</td>
</tr>
<tr>
<td>meerschaum mineral, foamed plastics</td>
<td>solid foams</td>
<td>gas</td>
<td>solid</td>
</tr>
<tr>
<td><strong>Macromolecular colloids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>jelly, glue</td>
<td>gel</td>
<td>macromolecules</td>
<td>solvent</td>
</tr>
<tr>
<td><strong>Association colloids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>soap/water, detergent/water</td>
<td>–</td>
<td>micelles</td>
<td>solvent</td>
</tr>
<tr>
<td><strong>Biocolloids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>blood</td>
<td>–</td>
<td>cells</td>
<td>serum</td>
</tr>
<tr>
<td><strong>Triphasic colloidal systems</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oil-bearing rocks</td>
<td>porous stone</td>
<td>oil</td>
<td>water/stone</td>
</tr>
<tr>
<td>mineral flotation</td>
<td>mineral</td>
<td>water</td>
<td>air</td>
</tr>
<tr>
<td>double emulsions</td>
<td>–</td>
<td>aqueous phase</td>
<td>water</td>
</tr>
</tbody>
</table>

Table 1.4 distinguishes between particle sizes of the colloidal dispersion state on the one hand and those of smaller molecules and of coarse heterogeneous systems on the other. These size ranges are only guidelines; in some special cases, such as suspensions and emulsions, particles of diameter greater than 1 μm are generally present. The threshold at which colloidal behavior becomes the behavior of a molecular solution lies at about 1 nm.
Table 1.4. Distinction between size ranges of the colloidal state, smaller molecules, and coarse discontinuous states.

<table>
<thead>
<tr>
<th>area of defined size</th>
<th>heterogeneous systems; coarse discontinuities</th>
<th>colloids 1–1000 nm</th>
<th>homogeneous systems small molecules; ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>examples:</td>
<td>macroemulsions; dispersions</td>
<td>metal sols; biocolloids; macromolecules; micelles; microemulsions</td>
<td>water; dodecane Ca^{2+}</td>
</tr>
<tr>
<td>range of optical resolution:</td>
<td>magnifying glass → microscope → ultra-microscope → electron microscope</td>
<td>1 mm 100 μm 10 μm 1 μm 100 nm 10 nm 1 nm 1 Å</td>
<td></td>
</tr>
</tbody>
</table>

It is not necessary for all three dimensions of a colloid to be smaller than 1 μm. Colloidal behavior can also be observed for fibers, only two of whose three dimensions fall within the colloidal region; in the case of films, only one dimension does.

A cube can be divided into colloidal systems of various types (Figure 1.4): laminar, fibrillar, and corpuscular.

![Figure 1.4. Colloidal systems (from reference [5]).](image)

The increase in surface energy that results from this division explains the unique properties of the colloidal state.

Laminar: $1 \text{ cm}^3$ stretched into a film of 10 nm $\rightarrow$ total surface area $2 \times 10^6 \text{ cm}^2$.
Fibrillar: $1 \text{ cm}^3$ divided into fibers of 10 nm $\rightarrow$ total surface area $4 \times 10^6 \text{ cm}^2$.
Corpuscular: $1 \text{ cm}^3$ split into cubes of 10 nm $\rightarrow$ total surface area $6 \times 10^6 \text{ cm}^2$. 
1.2.2 The Importance of Surfaces and Interfaces

When a solid is crushed or ground, its surface area increases considerably, in relation to the degree of division. The technical importance of the process of division lies in the possibility of the manufacture of fine powders and dispersions with a very large surface area. The increase in surface area is measured in terms of the specific surface area \( S_w \), units:

\[
S_w = \left[ \frac{\text{cm}^2}{\text{g}} \right] \quad \text{or} \quad \left[ \frac{\text{m}^2}{\text{g}} \right] \quad \text{with respect to mass} \quad (1.4)
\]

\[
S_v = \left[ \frac{\text{cm}^2}{\text{cm}^3} \right] \quad \text{or} \quad \left[ \frac{\text{m}^2}{\text{cm}^3} \right] \quad \text{with respect to volume} \quad (1.5)
\]

Conversion from the diameter of spherical particles:

\[
S_w = \frac{6}{\rho \cdot d} \quad (1.6)
\]

\( \rho \): true density
\( d \): diameter [\( \mu \text{m} \)]

Conversion from the diameter of spherical particles:

\[
S_w = \frac{6}{\rho \cdot d} \quad (1.6)
\]

\( \rho \): true density
\( d \): diameter [\( \mu \text{m} \)]

**Figure 1.5.** Increase in surface area on division of a cube. Powder dispersed in 6 cm\(^3\) water. An interface of 8.6 m\(^2\) per cm\(^3\) of the dispersion is available (60 m\(^2\)/7 cm\(^3\)) [6].
1.2 Physical Behavior of Atoms and Molecules

The increase in surface area is shown by the following example (Figure 1.5): a cube of edge 1 cm is divided into cubes of edge 0.1 μm; this yields a surface area of 60 m² from an original area of 6 cm², that is, an increase by a factor of $10^5$. If this powder is dispersed in 6 cm³ of water, the result is an available interface of 8.6 m² per cm³. The more finely the solid is divided, the greater the interface between liquid and solid phases, and the more the properties of the interface determine the behavior of the resulting suspension.

The more finely a material is divided and its surface area increases, the greater the proportion of atoms/molecules found at the surface rather than in the bulk of the material. For a cube of edge 1 cm, only 2–3 molecules out of every ten million are found at the surface. When the cube has an edge of 1 μm, there is one molecule at the surface for every 450 molecules, and at 10 nm every fourth molecule is positioned at the surface; see Table 1.5. At dimensions less than 10 nm it is no longer possible to differentiate between surface and bulk molecules.

Table 1.5. Relationship of surface and bulk molecules.

<table>
<thead>
<tr>
<th>Specific surface area:</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_v = \text{surface area}/\text{volume}$ (with respect to volume)</td>
</tr>
<tr>
<td>$S_w = \text{surface area}/\text{mass} = S_v/\rho$ (with respect to mass); ( \rho = \text{density} )</td>
</tr>
</tbody>
</table>

spheres: \( \text{surface area} \pi d^2 \) \( \text{volume} \pi d^3/6 \) \( \rightarrow S_v = 6/d \)

cubes: \( \text{surface area} 6d^2 \) \( \text{volume} d^3 \) \( \rightarrow S_v = 6/d \)

Example: AgBr crystal

molecular volume \( 0.05 \text{ nm}^3 \)
distance between layers \( 0.37 \text{ nm} \)

In Figure 1.6, the variation in the number of surface molecules with the particle size is shown as a graph for this example. It is clear that when AgBr is divided into particles of 10 nm diameter, about 20% of the ion pairs are located in the surface layer, whereas for particles of 0.1 μm, this is the case for only 2% of ion pairs.

The chemical composition of the surface often differs from that of the bulk. Likewise, the arrangement of the atoms and the electronic structure at the surface are not the same as those inside the solid. The great importance of surfaces was recognized as a result of miniaturization in microelectronics. It has even been suggested that the surface region of a finely dispersed solid should be regarded as a new phase of matter.
1.3 Some Essential Concepts in Colloid Chemistry

*Monodisperse or isodisperse systems:* Systems in which all particles are approximately the same size.

*Polydisperse systems:* Systems containing particles of varying sizes.

*Lyophobic or hydrophobic colloids:* The particles are incompatible with the dispersion medium, which is organic in the case of lyophobic colloids, aqueous in the case of hydrophobic. Such systems demand special methods of manufacture, in particular dispersion accompanied by a reduction in size of the particles. The thermodynamic instability of such systems is visible in their tendency to clump, to aggregate, agglomerate, and flocculate.

*Lyophilic or hydrophilic colloids:* The particles are compatible with the medium. They interact with the dispersion medium. Unlike the lyophobes (hydrophobes), they form spontaneously and are thermodynamically stable. Examples: macromolecules, polyelectrolytes, association colloids.

*Amphiphilic colloids or association colloids:* The molecules have an affinity for both polar and nonpolar solvents. These form the large class of surface-active and related substances that includes micelles. They are thermodynamically stable.

### 1.3.1 Structure and Nomenclature of Particles

For a long time there was no uniformity in the nomenclature of particles; the DIN 53 206 standard, which has attained international recognition, has now remedied this unsatisfactory state of affairs (Figure 1.7).
### Primary particle or single particle

Can be recognized as individual particles by suitable physical means (e.g. light or electron microscopy).

Note: As a special case, a crystalline primary particle may be a single crystal or may consist of several coherently scattering lattice domains (crystallites) which may be distinguished with appropriate radiation (e.g. X-rays).

- blocks
- spheres
- rods
- irregular

Coherently scattering lattice domains (crystallites)

Primary particles

### Aggregate

Primary particles assembled face-to-face; their surface area is smaller than the sum of the surface area of the primary particles.

Aggregates

### Agglomerate

Primary particles and/or aggregates not permanently joined together but attached e.g. at edges and corners; their surface area does not differ markedly from the sum of that of the individual particles.

Agglomerates

### Flocculate

Agglomerate found in suspensions (e.g. in pigment–binder systems); can easily be separated by small shearing forces.

Flocculates

---

**Figure 1.7.** Structure and nomenclature of particles according to DIN 53206, with the addition of flocculate.
1.3.2 Analysis of Particle Size

Since colloidal systems occur over a large range of particle size, a number of different measuring techniques are required for size analysis. For particle sizes in the range 0.001 to 100 μm the methods shown in Figure 1.8 are suitable. The most important of these are represented schematically in Figure 1.9. The choice of a valid method of measurement for a collection of particles is of the utmost importance if one wishes to avoid completely false results. Figures 1.10 and 1.11 depict schematically some additional methods for the measurement of particle sizes.

![Diagram of particle size analysis methods and their ranges](image)

Figure 1.8. Methods of particle size analysis and their ranges. (SUV: small unilamellar vesicle; MLV: multilamellar vesicle.)
1.3 Some Essential Concepts in Colloid Chemistry

- **sedimentation analysis**
- **suspension methods**

- **measurement principle of the Coulter counter**

- **absorption**
- **diffraction**
- **scattering**

Range:
- $2 < x < 9000 \, \mu m$
- $1.5 < x < 500 \, \mu m$
- $0.3 < x < 50 \, \mu m$

Optical measurements

**Figure 1.9.** Analysis of particle size; methods from reference [7].
Sedimentation in a gravitational field

Rate of sedimentation of a sphere in water:
\[ v = \frac{g x^2 \Delta \rho}{18 \eta} \quad (x = \text{diameter}) \]
\( \eta_{H_2O} = 1.0 \times 10^{-3} \, \text{Ns/m}^2 \) (20°C)
g = 9.81 m/s²

for \( \Delta \rho = 0.5 \times 10^3 \, \text{kg/m}^3 \):

<table>
<thead>
<tr>
<th>( x ) (μm)</th>
<th>( v ) (mm/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>164</td>
</tr>
<tr>
<td>10</td>
<td>1.6</td>
</tr>
<tr>
<td>1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

(neglecting Brownian motion)

Sedimentation in a centrifugal field

Centrifugal velocity of a sphere in water:
\[ v = \frac{g r^2 \mu^2 \Delta \rho}{18 \eta} \quad (\omega = 2\pi f) \]

for \( \Delta \rho = 0.5 \times 10^3 \, \text{kg/m}^3 \)
\( r = 50 \, \text{mm} \)
f = 6000 r.p.m.

\[ \begin{array}{c|c|c}
\hline
\( x \) (μm) & \( v \) (mm/min) \\
\hline
100          & 164 \\
10           & 1.6 \\
1            & 0.1 \\
\hline
\end{array} \]

\[ \begin{array}{c|c|c}
\hline
\( x \) (μm) & \( v \) (mm/min) \\
\hline
10           & 55 \\
1            & 33 \\
100          & 20 \\
\hline
\end{array} \]

Sedimentation methods

1. Suspension method

2. Overlay method

Methods of mass measurement:
- scales (cumulative)
- manometer (cumulative)
- pipette (cumulative and incremental)
- photometer (incremental)
- X-ray (incremental)

Sieving analysis

Figure 1.10. Additional measuring techniques for particle sizes (reference [8]).

Optical methods should not be used unquestioningly for the analysis of particle size. Particle size and form and complex refractive indices, of the material of the particles and of the dispersion medium, must all be taken into consideration before a decision is made. Figure 1.11 classifies light scattering according to particle size.

The following optical methods exemplify those suitable for measurements on groups of particles:

- Methods:
  - diffraction of light (Fraunhofer diffraction)
  - quasi-elastic light scattering (QLS)
  - photorelation spectroscopy (PCS) or other designations.

- Advantages:
  - online measurement possible
  - measurement possible at high concentrations (up to approx. 1 %)
  - suitable for broad distributions
  - wide choice of dispersion media possible
  - user-friendly apparatus available

- Disadvantages:
  - limited resolution
  - working back to the values of the physical parameters:
    - size distribution by mathematically ill-defined problems
  - suitability for polydisperse systems problematic (in QLS)
1.3 Some Essential Concepts in Colloid Chemistry

1.3.3 Important Principles and Foundations of Interface Physics for Formulation Chemists

In order to describe the stability, formation, and decay of a colloidal system (a dispersion, an emulsion, ...), we need to know something about bond energies, surface and interface energies, and kinetic processes, amongst other things.

Two of the most important questions about colloidal dispersions and emulsions are:
1. Under what conditions is the disperse state stable?
2. Under what conditions does it flocculate or coagulate?

A fundamental principle of thermodynamics states that, at constant temperature, a system tends to alter spontaneously in such a way as to reduce its free energy.

The simple example of a weight under the influence of gravity will serve as a mechanical analogy: Figure 1.12.

![Diagram of free energy and stability](image)

Figure 1.12. Free energy and stability [4].
The energy of a gas, liquid, or solid that is available for performing useful work is known as the *free enthalpy* $G$ of the system:

$$G = H - TS$$  \hspace{1cm} (1.7)

$G$: free enthalpy (Gibbs free energy)

$H$: enthalpy

$S$: entropy

$T$: temperature

On account of the “disorder” of the molecules in the system, it is not possible to convert all the thermal energy it contains into mechanical energy. All systems tend to the greatest possible freedom of movement, to increased randomization or disorder, or, expressed in physical terms, to an increase in entropy. This is the second law of thermodynamics.

For a system to reach a stable state, its free surface energy tends to diminish. An increase in free surface energy $\Delta G$ in disperse systems is achieved by division of the particles and therefore by the increase $\Delta A$ in the total surface area $A$.

$$\Delta G = \gamma_{SL} \cdot \Delta A$$  \hspace{1cm} (1.8)

$\gamma_{SL}$: Interfacial tension between the liquid medium and the particles.

As $\Delta G$ of the system diminishes, the system becomes more stable; equilibrium is reached when $\Delta G = 0$. This can be achieved either by a reduction in $\gamma_{SL}$ or by a decrease in the area of the interface. The latter occurs through flocculation or coagulation. The interfacial tension can be reduced by addition of a tenside, but not to the extent that $\gamma_{SL} = 0$. Thus, the system remains unstable. It can be stabilized by the introduction of a repulsive force or a potential threshold, as described in Chapter 5 (for example, by the use of emulsifiers in emulsions). In brief: at constant temperature, the particles of a dispersion always tend to become coarser, to flocculate or to coagulate, if the system is not somehow stabilized. The more finely dispersed the particles, the less stable the system is unless it is protected, that is, unless there is a sufficiently high energy barrier resulting from an electrical double layer or steric protecting layer. This is the basic requirement for the manufacture of stable dispersions and emulsions. However, we use the word “stable” not in the thermodynamic sense, but in the practical sense to refer to behavior over a useful time period. Nevertheless, thermodynamically stable dispersions, the microemulsions, do exist (see Chapter 3).

### 1.4 Intermolecular Binding Forces

For the molecules in gases, liquids, and solids to form aggregates, they must be held together by intermolecular forces. These are manifested in *the cohesion of similar*
molecules and the adhesion of dissimilar molecules. A knowledge of these forces is necessary for the understanding not only of the properties of gases, liquids, and solids, but also of interface phenomena such as the stabilization of emulsions, flocculation in suspensions, the removal of dirt from surfaces, and so on.

1.4.1 Repulsive and Attractive Forces

When molecules meet, both attractive and repulsive forces come into play (Figure 1.13). Attraction occurs if, when two molecules approach one another, those sites bearing opposite charges coincide more nearly than those with the same charge. Molecules repel each other when their electron clouds interpenetrate. This force increases exponentially as the distance between the molecules decreases. At an equilibrium distance of 3–4 Å ($r_e$) the attractive and repulsive forces balance. At this point the potential energy of the two molecules is at its minimum; they are in a stable state. This holds true not only for atoms and molecules but also for larger entities such as colloidal particles and droplets in dispersions and emulsions.

![Diagram showing repulsion and attraction energies and their sum, potential energy ($E_p$), as a function of the distance between two particles. The energy minimum occurs at the equilibrium distance $r_e$.](image-url)

**Figure 1.13.** Repulsion and attraction energies and their sum, potential energy ($E_p$), as a function of the distance between two particles. The energy minimum occurs at the equilibrium distance $r_e$. 