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An Overview of the Zeta Potential

Introduction

This Technical Brief provides a general overview of the concept of the zeta potential (ZP). We will discuss the two parameters that control the nature and behavior of every system in which one phase is dispersed in another phase. The phases are the disperse phase (for the phase forming the particles) and the dispersion medium (for the fluid in which the particles are distributed). The two parameters are the extent of the interface and the interfacial chemistry of the disperse phase. The physical nature of any dispersion depends on the respective roles of the constituent phases. There are numerous examples of dispersed systems, including foams (gas-in-liquid), emulsions (liquid-in-liquid), and aerosols (solid- or liquid-in-gas), that have found application in pharmaceutics. We will focus on the most widely-formulated type of dispersion, *viz* suspensions (solid-in-liquid). The physicomechanical and physicochemical characteristics that constitute the two respective fundamental parameters are summarized in Table 1. The interfacial chemistry is often a neglected parameter in pharmaceutical applications even though in formulation of suspensions, it is as or more important than the interfacial extent.

The ZP (symbol ζ) is related to the surface charge, a property that all materials possess, or acquire, when suspended in a fluid. The sign and magnitude of ZP affects process control, quality control, and product specification. At the simplest level, it can help maintain a more consistent product and at a complex level, it can improve product quality and performance. At the very least its measurement answers the question: Is the electrical charge on the material particle positive or negative? This information is often sufficient to guide formulation or processing. The next higher level of inquiry has to do with

Table 1

Fundamental Parameters that Control the Nature and Behavior of all Particulate Suspensions

Interfacial Extent	Interfacial Chemistry
Particle Size and Distribution	Surface Charge
Particle Shape/Morphology	Nature/Type of Group(s)
Surface Area (External/Internal)	Number and Distribution
Porosity	Dissociation
	Preferential Adsorption
	Hydrophobic/Hydrophilic Balance
	Surface (Interfacial) Tension
	Contact Angle

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quality control: Has the product sufficient electrostatic repulsion to maintain its stability?

The Origin of Charge in Polar Media

All materials will spontaneously acquire a surface electrical charge when brought into contact with a polar medium (i.e., water)[1]. Generally an interface in deionized water is negatively charged, but there are materials that can be positively charged[2]. The various charging mechanisms are:

1. Electron affinity differences of two phases
2. Ionization of surface groups
3. Differential ion adsorption from electrolyte solution
4. Differential ion dissolution from a crystal lattice
5. Surface anisotropy
6. Isomorphous substitution

Mechanism 1 is responsible for the development of the contact potential between dissimilar metals and is important in corrosion and thermoelectric effects[3]. This mechanism is a dominant process in initially determining the surface charge at the metal-solution interface. Nanoparticulate metal sols are being studied in wide variety of applications be-cause they offer greatly enhanced performance; their inherent surface charge is critical to any further processing or use.

Mechanism 2 is observed with all metal oxide surfaces (M-OH) as well as materials that contain carboxyl and/or amino groups. This latter category includes proteins, ionic polymers, and polyelectrolytes, many of which are widely utilized in pharmaceutical formulations. The ionization and/or dissociation of these groups (degree of charge development) and the net molecular charge (and thus sign, either positive or negative) depends strongly on the pH of the dispersion media.

In **Mechanism 3**, a net surface charge arises through the process of unequal adsorption of oppositely charged ions and may result in either a net positive or net negative surface. Many lyophobic material suspensions (i.e., polymer latexes and APIs) fall into this category. If surfactant ions are present, their adsorption will tend to determine the net surface charge.

Ionic solids, such as calcite ($CaCO_3$), hydroxyapatite [$Ca_5(PO_4)_3(OH)$] and barite ($BaSO_4$) can acquire a surface charge via **Mechanism 4** by unequal dissolution of the opposite-ly charged ions. Addition of small concentrations (ca 10^{-3} M) of Ca^{2+} ions (by using, for example, $CaCl_2$) can be used to adjust the net charge of a suspension of $CaCO_3$; the hardness of water becomes a factor that must be considered.

Mechanism 5 arises from the anisotropy of most crystal lattices. Charge development occurs because of n and p defects in the crystal. For mineral oxides, this results in amphoteric hydroxyl groups that can undergo reaction with either H^+ or OH^-. One pharmaceutically useful material in this group is the silicas[4]; the surface charge is negative because the silanol groups (-SiOH) are weakly acidic.

The oxides of most di- and trivalent metals (e.g., MgO and Al_2O_3, respectively) are amphoteric; any dissolution tends to be in the form of the hydroxide. Swings in solution pH must be avoided because it can cause re-precipitation back onto the oxide surface in a different chemical form thus altering the surface chemistry and hence charge.

Mechanism 6, isomorphous substitution, is a more extreme case of Mechanism 5. It occurs in clay materials (i.e., montmorillonite and vermiculite), where a large negative charge arises because of the difference in valence between the Al^{3+} and the Si^{4+} ions in the alumino-silicate crystal structure[5]; varying proportions of minor elements leads to a dizzying variety and complexity of minerals[6]. The net surface charge of any clay depends on the clays' prehistory; it may not be possible to substitute clay from a given manufacturer with that from another.

Electrical Properties in Non-aqueous Media

In solvents with moderate di-electric constants (>10 compared with ~80 for water) some degree of ionization is possible; charging mechanisms parallel to those in water can occur. Examples include low MW alcohols, amines,

aldehydes and ketones; ionic surfactants (i.e., Aerosol OT) and some simple ionic salts (i.e., LiCl) can dissociate to some extent in such media.
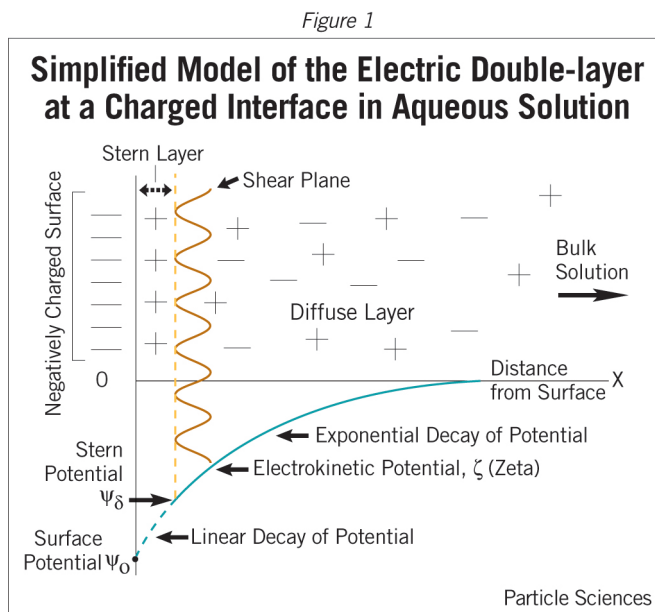
Although electrolytes cannot ionize in fully nonpolar media (solvents of very low dielectric, ~2, such as alkanes) particles dispersed in such a medium can acquire charge and electrostatic forces are important and do play a key role in stabilizing non-aqueous suspensions[7] but the charging mechanism is not the same as in aqueous dispersions. It arises because of acid-base (or electron donor-acceptor) interactions between the particle surface and the dispersing agent[8]. This is why acidic (i.e., polyvinylchloride) or basic (i.e., polymethylmethacrylate) polymers are very effective suspendants of particles in non-aqueous media.

The Electric Double-Layer

A particle dispersed in a liquid is solvated and the extent of the solvated layer is influenced by the solution conditions such as composition (i.e., pH, ionic strength), temperature and pressure[9]. The boundary between the edge of this solvated layer and bulk liquid is termed the shear plane.

Regardless of how charge separation is generated, the distribution of electrical charges at the interface is different from that in the bulk liquid phase. A "structure", called the electric double-layer (EDL) will be developed such that the particle surface charge is neutralized by an adjacent layer in solution containing an excess of ions of opposite charge to that of the surface, i.e., counterions; ions of the same charge as the surface are termed coions. The theory of the electric double-layer, (EDL) is extremely complex[10] and beyond the scope of this overview.

The EDL can be regarded as consisting of two regions or layers (hence the term electric double-layer; Figure 2): a region closest to the surface (the Stern layer) that is considered immobile (and it may include adsorbed ions) and an outer region (the diffuse layer) that allows diffusion of ions

Figure 1

Simplified Model of the Electric Double-layer at a Charged Interface in Aqueous Solution

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that are distributed according to the influence of electrical forces and random thermal motion.

The electric potential decreases linearly from ψ_0 (the actual thermodynamic surface potential) to the Stern potential, ψ_d and then it decays exponentially to zero in the diffuse layer. This is described by:

$$\psi = \psi_d \exp[-\kappa x]$$

where, x is the distance from the material surface and κ, called the Debye-Hückel parameter, is defined as:

$$\kappa = [2e^2 N_A c z^2 / \varepsilon \varepsilon_0 k_b T]^{\frac{1}{2}}$$

where, e is the protonic charge, N_A is Avogadro's constant, c is the concentration of electrolyte of valence z, ε is the dielectric constant, ε_0 is the permittivity of free space and k_b is the Boltzmann constant.

Hence, it can be seen that the electric potential depends (through κ) on the ionic composition of the medium. If κ is increased (the electric double layer is "compressed") then the potential must decrease.

Unfortunately, the fundamental interfacial property (ψ_0) is inaccessible[11]. What can be derived (and measured) is an electrokinetic potential – termed the zeta potential ζ. This quantity, defined as the potential at the shear plane, has become a very useful experimental parameter to monitor electrokinet-

ic behavior of suspensions, especially changes in such behavior[2].

The Relation between Zeta Potential and Surface Charge

Although ζ is not the actual thermodynamic (or surface) potential, in theoretical calculations, ζ is frequently taken to be identical with the Stern potential, ψ_d.

When specific adsorption of charged moieties occurs at a surface, counterion adsorption usually predominates over coion adsorption. With polyvalent and surface-active counterions, it is possible for a reversal of charge to take place within the Stern player – i.e., for ψ_0 and ψ_d (and, hence ζ) to have opposite signs. The adsorption of nonionic (i.e., polyoxyethylene-based) surfactants would result in a ζ being close to zero. As the MW of any macromolecular species increases it results in the shear plane being located at a larger distance from the Stern plane. All these types of "charge modifying agents" are used extensively in formulations of suspensions.

Thus, it is possible that a surface can have an inherent (thermodynamic) charge but have no measurable ZP and vice-versa[12]. This does not mean to imply that the ZP measurement is not useful. On the contrary, ζ is, in the

practical sense, the effectiveness of the particle surface charge in solution. While ζ may derive, initially, from the fundamental number of surface sites, (how many, what type, etc.), more importantly, from a practical application, are the solution conditions themselves because they control the resulting final sign and magnitude of ζ. The consequence of this to the process of dispersing particles is critical. And importantly, it is useless to quote a measured ζ value without specifying the suspension conditions under which the measurement was made.

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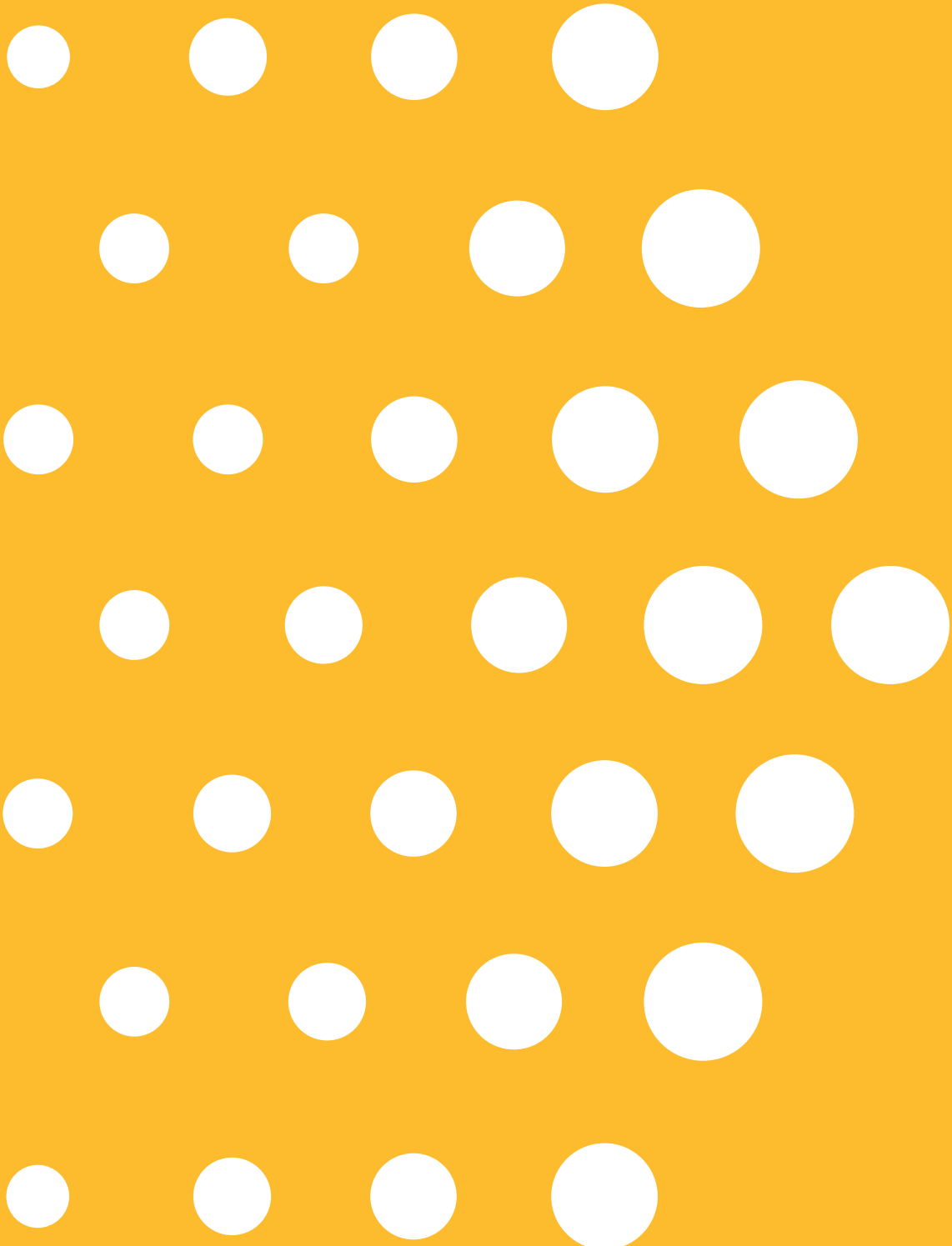
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