

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. In a system, the first phase is called the disperse phase, or the phase forming the particles, and the second is the dispersion medium, or the fluid in which the particles are distributed. The two parameters we will focus on are the extent of the interface and the interfacial chemistry of the disperse phase. The physicochemical 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 some applications, it is as or more important than the interfacial extent.

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-in-gas or liquid-in-gas), that have found application in pharmaceuticals. We will focus on the most widely-formulated type of dispersion, which is suspensions (solid-in-liquid).

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

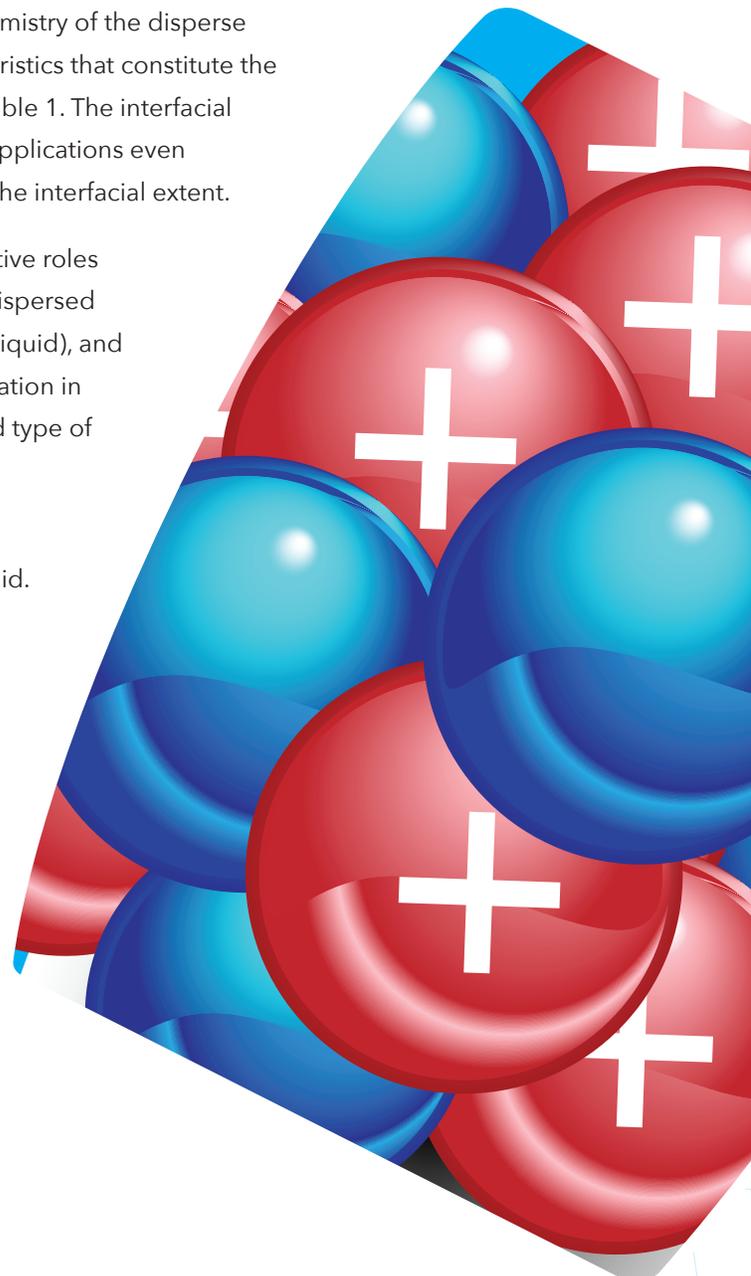


Table 1

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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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 positive². The various charging mechanisms are found below and will be considered in turn:

- Electron affinity differences of two phases
- Ionization of surface groups
- Differential ion adsorption from electrolyte solution
- Differential ion dissolution from a crystal lattice
- Surface anisotropy
- Isomorphous substitution

These operate by pumping the emulsion phases through the narrow gap between a perforated cylinder (the stator) and the blades of a rapidly rotating stirrer housed inside it (the rotor) where the forces are sufficient to make droplets as small as around 1 μm (Figure 2).

Electron affinity differences of two phases is responsible for the development of the contact potential between dissimilar metals and is important in corrosion and thermoelectric effects³. This mechanism is a dominant process in initially determining the surface charge at the metal-solution interface. Nanoparticulate metal solutions are being studied in a wide variety

of applications because they offer greatly enhanced performance. Their inherent surface charge is critical to any further processing or use.

Ionization of surface groups 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 poly-electrolytes, 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 **differential ion adsorption from electrolyte solution**, 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 active pharmaceutical ingredients (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 (CaCO₃), hydroxyapatite [Ca₅(PO₄)₃(OH)], and barite (BaSO₄), can acquire a surface charge via **differential ion dissolution from a crystal lattice** by unequal dissolution of the oppositely charged ions. Addition of small concentrations of Ca²⁺ ions (10⁻³ M) by using CaCl₂, for example, can adjust the net charge of a suspension of CaCO₃; the hardness of water becomes a factor that must be considered.

Surface anisotropy are defects in a crystal lattice that result in the development of negative and positive charges. For mineral oxides, this results in amphoteric hydroxyl groups that can undergo a reaction with either H⁺ or OH⁻. One pharmaceutically useful material in this group is the silicas⁴; the surface charge is negative because the silanol groups (-SiOH) are weakly acidic.

The oxides of most divalent and trivalent metals (e.g., MgO and Al₂O₃, 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.

Isomorphous substitution is a more extreme case of Isomorphous substitution. It occurs in clay materials (i.e.,

Unfortunately, the fundamental interfacial property (Ψ_0) is inaccessible¹¹. 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 electrokinetic behavior of suspensions, especially changes in such behavior².

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 co-ion 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.

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The adsorption of nonionic (i.e., polyoxyethylene-based) surfactants would result in a ζ being close to zero. As the molecular weight 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 the formulation of suspensions.

Thus, it is possible that a surface can have an inherent (thermodynamic) charge, but have no measurable ZP and vice-versa¹². This does not 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 important 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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