PURDUE UNIVERSITY

Weldon School of Biomedical Engineering

The Convergence of Differences, The Future of Excellence

BME 695N

Engineering Nanomedical Systems

Lecture 13

Assessing Zeta Potential

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I. Introduction – the importance of the zeta potential, which governs:

A. nanoparticle-nanoparticle interactions

B. nanoparticle-cell interactions

C. part of the initial nanomedical system-cell targeting process

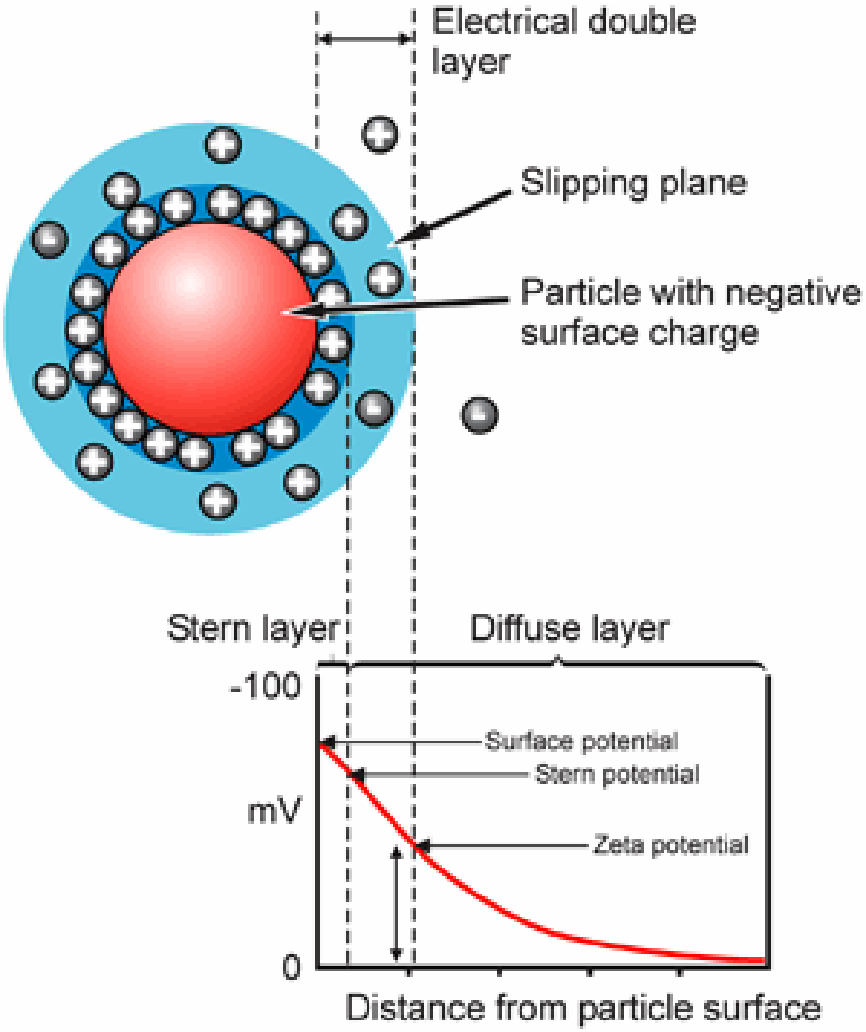
D. low zeta potential leads to low serum protein binding and potentially longer circulation, but can lead to particle agglomeration if particles are present at high enough concentration.

II. Zeta potential basics

A. What is the zeta potential

B. How is it measured?

Zeta Potential

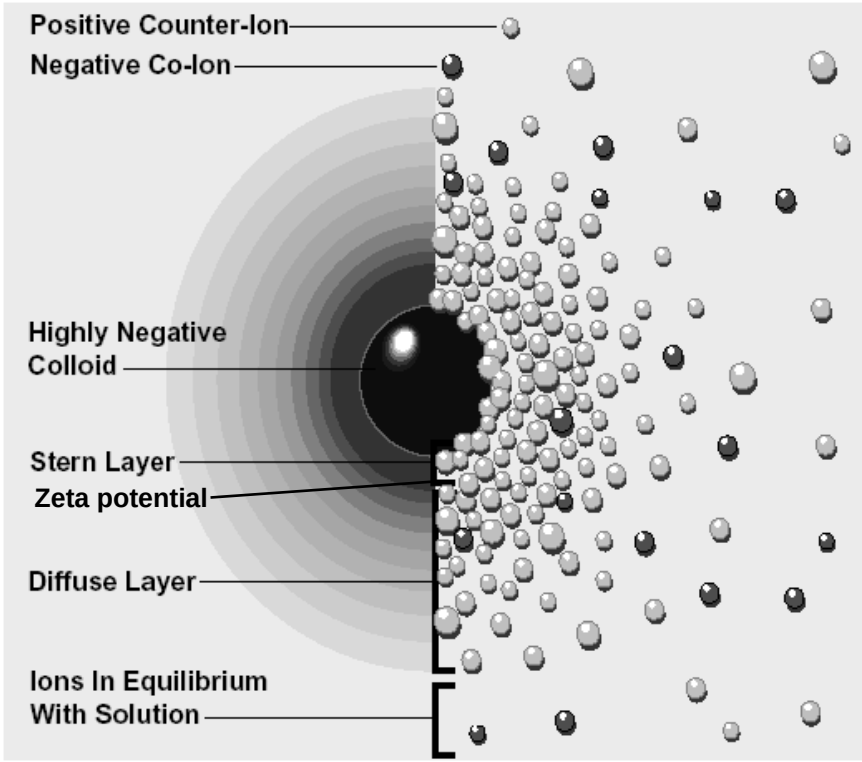


The liquid layer surrounding the particle exists as two parts; an inner region (Stern layer) where the ions are strongly bound and an outer (diffuse) region where they are less firmly associated. Within the diffuse layer there is a notional boundary inside which the ions and particles form a stable entity. When a particle moves (e.g. due to gravity), ions within the boundary move it. Those ions beyond the boundary stay with the bulk dispersant. The potential at this boundary (surface of hydrodynamic shear) is the zeta potential.

Source: "Zeta Potential: An Introduction in 30 minutes":
http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

Zeta Potential Properties of Nanoparticles

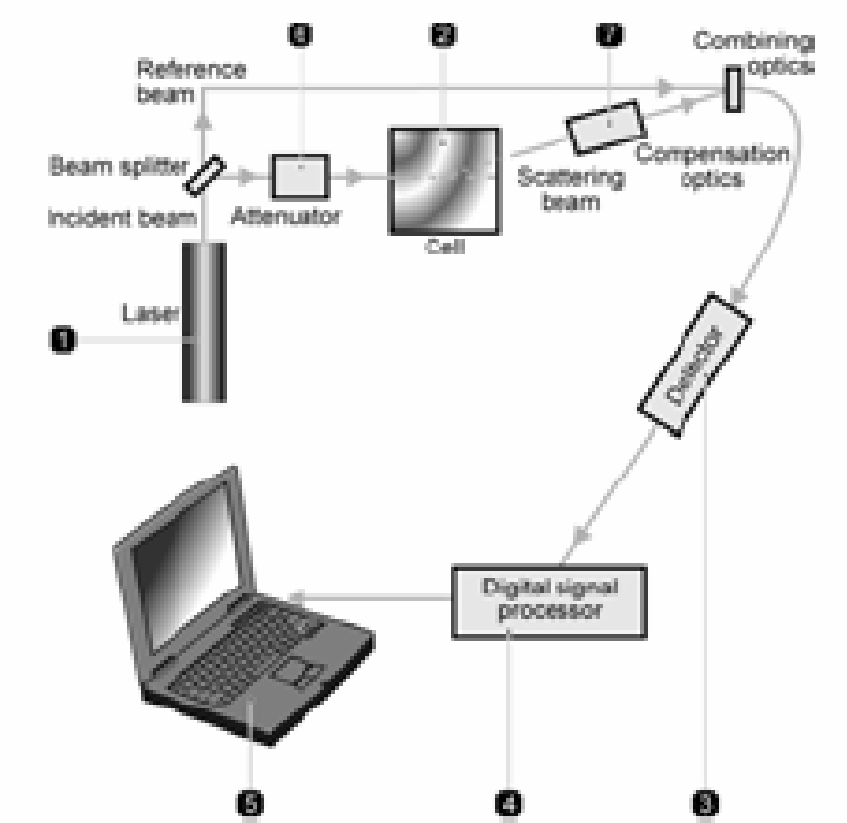
- The zeta potential is the electric potential at the shear plane, which is the boundary between the stern layer and the diffuse layer.
- This electrical property determines if a colloidal solution will agglomerate or remain a stable suspension.
- Zeta potential must be determined and controlled at each step in the construction of nanoparticles.
- Zeta potential of complete nanoparticle is important for controlling *in vivo* interactions.



Charge density and ion concentration surrounding a highly negatively charged nanoparticle.

Figure adapted from Zeta-Meter, Inc. Zeta-Potential: A Complete Course in 5 Minutes. Staunton: Zeta-Meter, Inc., 1997.

One Way to Measure Zeta Potential



Optical Configuration of a Zeta Potential Instrument
A zeta potential measurement system comprises of six main components (figure 10). Firstly, a laser 1 is used to provides a light source to illuminate the particles within the sample. For zeta potential measurements, this light source is split to provide an incident and reference beam. The incident laser beam passes through the centre of the sample cell 2, and the scattered light at an angle of about 13o is detected 3. When an electric field is applied to the cell, any particles moving through the measurement volume will cause the intensity of light detected to fluctuate with a frequency proportional to the particle speed and this information is passed to a digital signal processor 4 and then to a computer 5. The Zetasizer Nano software produces a frequency spectrum from which the electrophoretic mobility and hence zeta potential is calculated. The intensity of the detected, scattered light must be within a specific range for the detector to successfully measure it. This is achieved using an attenuator 6, which adjusts the intensity of the light reaching the sample and hence the intensity of the scattering. To correct for any differences in the cell wall thickness and dispersant refraction, compensation optics 7 are installed to maintain optimum alignment.

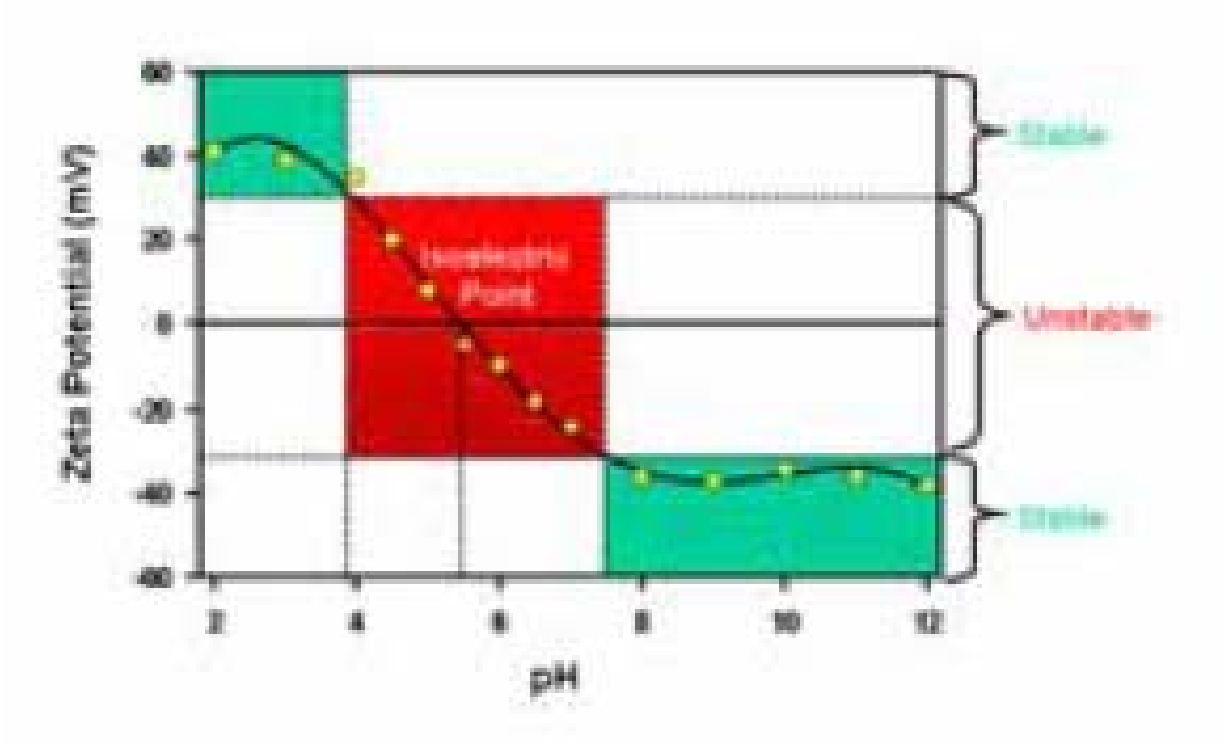
Source: Zeta Potential: An Introduction in 30 Minutes (Malvern Instruments)

III. Some factors affecting the zeta potential

A. pH

B. ionic strength

Zeta Potential and pH



Typical plot of zeta potential versus pH showing the position of the isoelectric point and the pH values where the dispersion would be expected to be stable

Source: "Zeta Potential: An Introduction in 30 minutes":
http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

By measuring the velocity of a nanoparticle in an electric field its zeta potential can be calculated

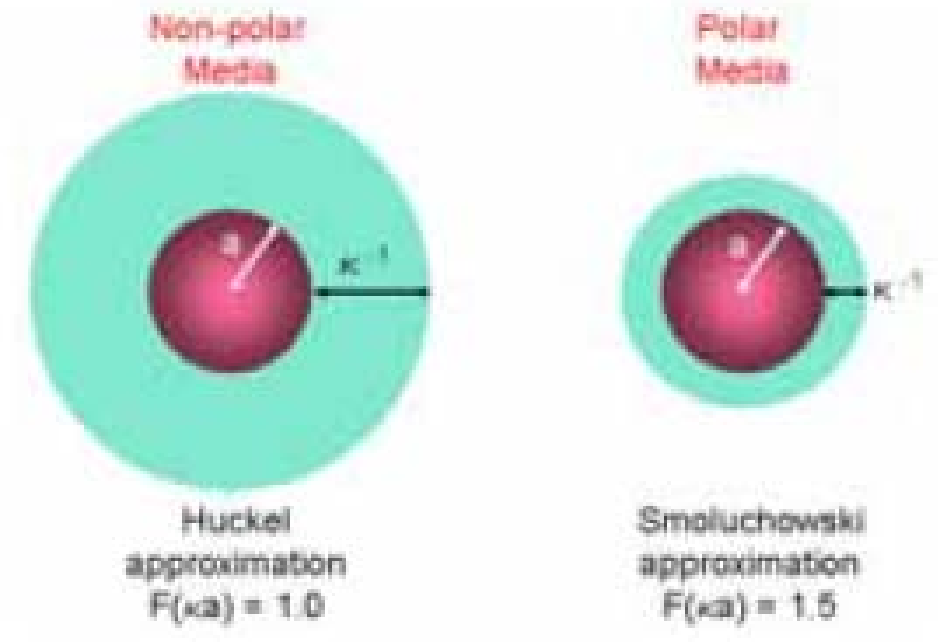
The velocity of a particle in a unit electric field is referred to as its electrophoretic mobility. Zeta potential is related to the electrophoretic mobility by the Henry equation:

$$U_E = \frac{2 \varepsilon z f(\kappa a)}{3\eta}$$

where UE = electrophoretic mobility, z= zeta potential, ε = dielectric constant, η = viscosity and f(κa) = Henry's function

Source: "Zeta Potential: An Introduction in 30 minutes": http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

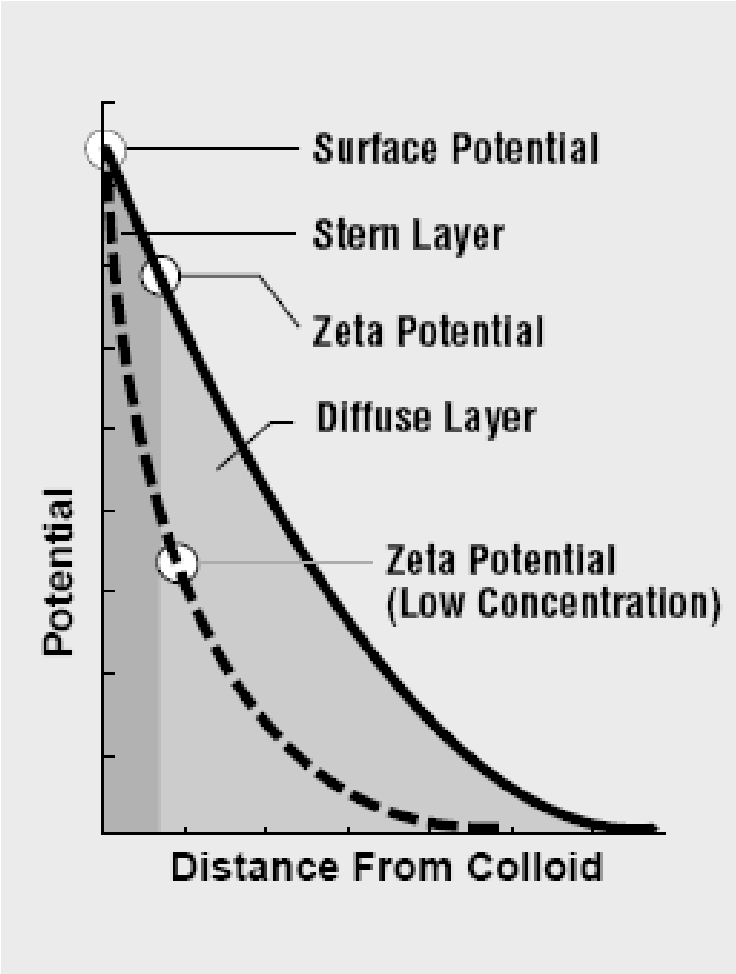
Assumptions about slip layer diameter when calculating zeta potential

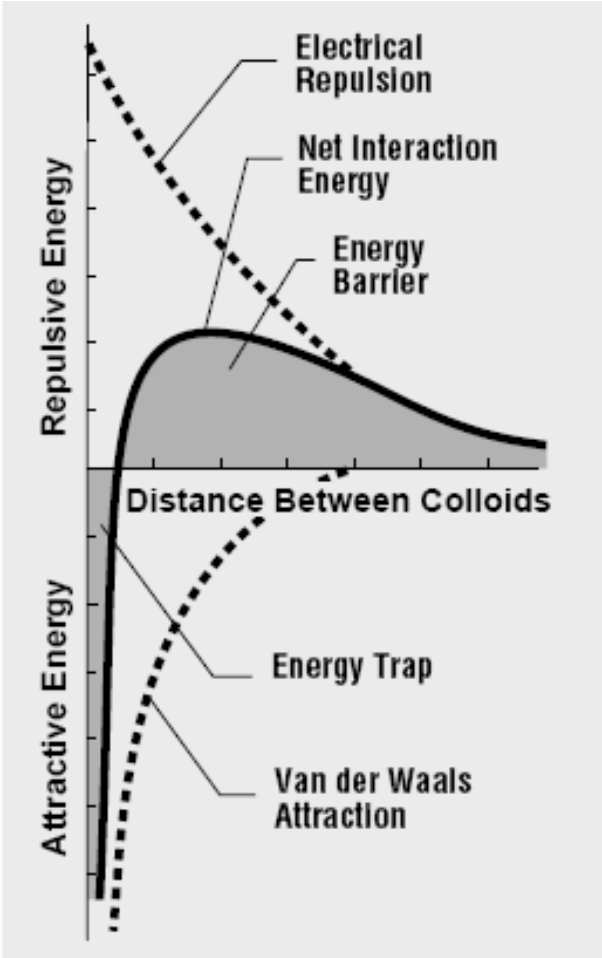


Schematic illustrating Huckel and Smoluchowski's approximations used for the conversion of electrophoretic mobility into zeta potential

Source: "Zeta Potential: An Introduction in 30 minutes":
http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

Zeta Potential: Effective Net Charge at a Distance





Zeta Potential vs. Surface Potential: The relationship between zeta potential and surface potential depends on the level of ions in the solution.

Interaction: The net interaction curve is formed by subtracting the attraction curve from the repulsion curve.

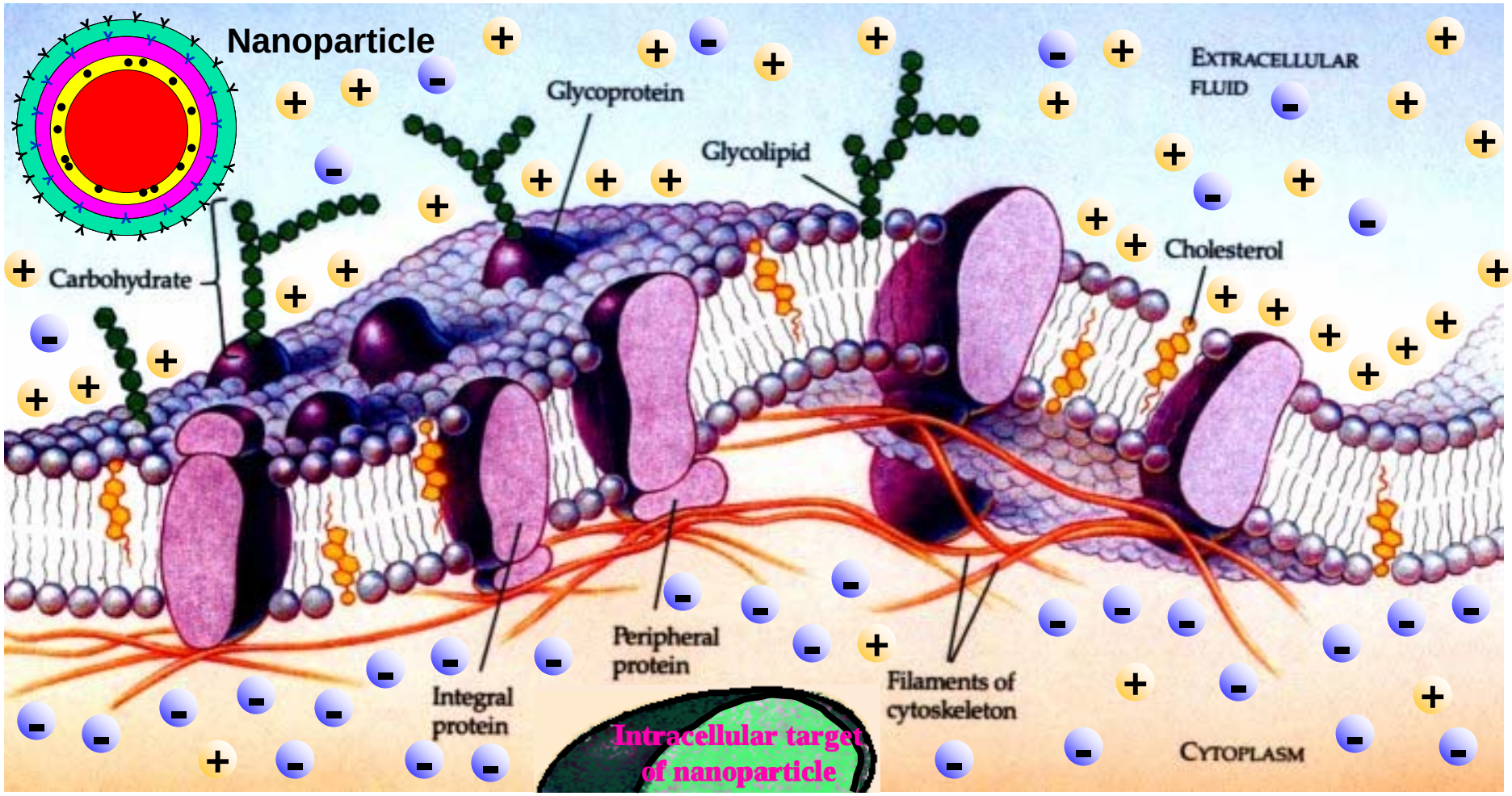
Source: "Zeta Potential: An Introduction in 30 minutes": http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

IV. Some zeta potential experiences

Following slides are from this reference:

Prow, T.W., Rose, W.A., Wang, N., Reece, L.M., Lvov, Y., Leary, J.F. "Biosensor-Controlled Gene Therapy/Drug Delivery with Nanoparticles for Nanomedicine" Proc. of SPIE 5692: 199 – 208, 2005.

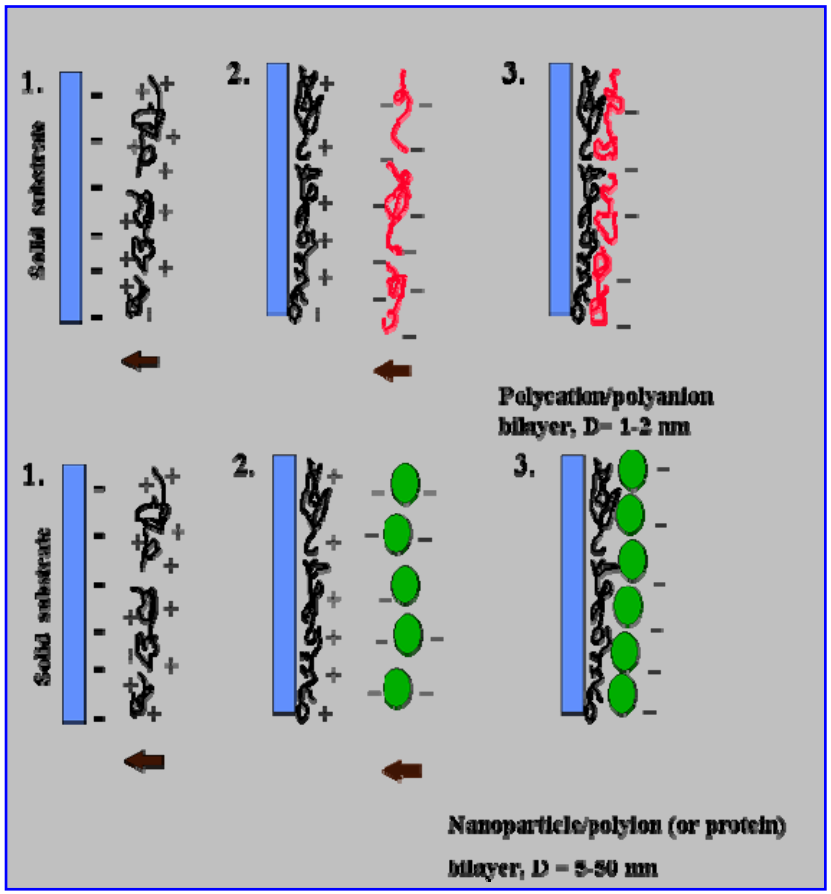
Interaction of Nanoparticles with the Cell Surface Based on Zeta Potential and Size



Adapted from Campbell, Neil A., and Jane B. Reece. Biology. 6th ed. San Francisco: Benjamin Cummings, 2002.

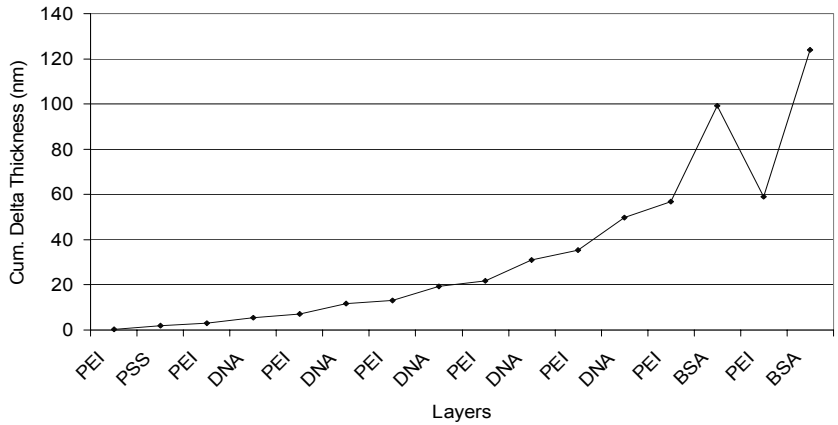
Size and Zeta Potential Changes During LBL Construction of Nanoparticles

Layer-by-layer (LBL) assembly of NP with charged polymers

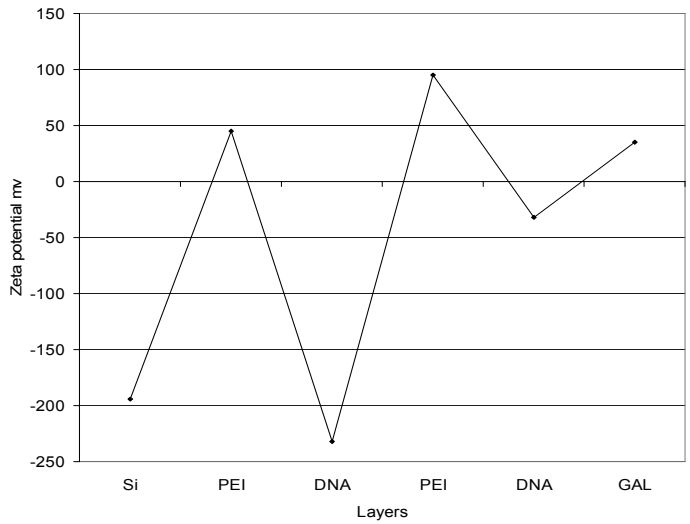


Ref: Prow et al., 2005

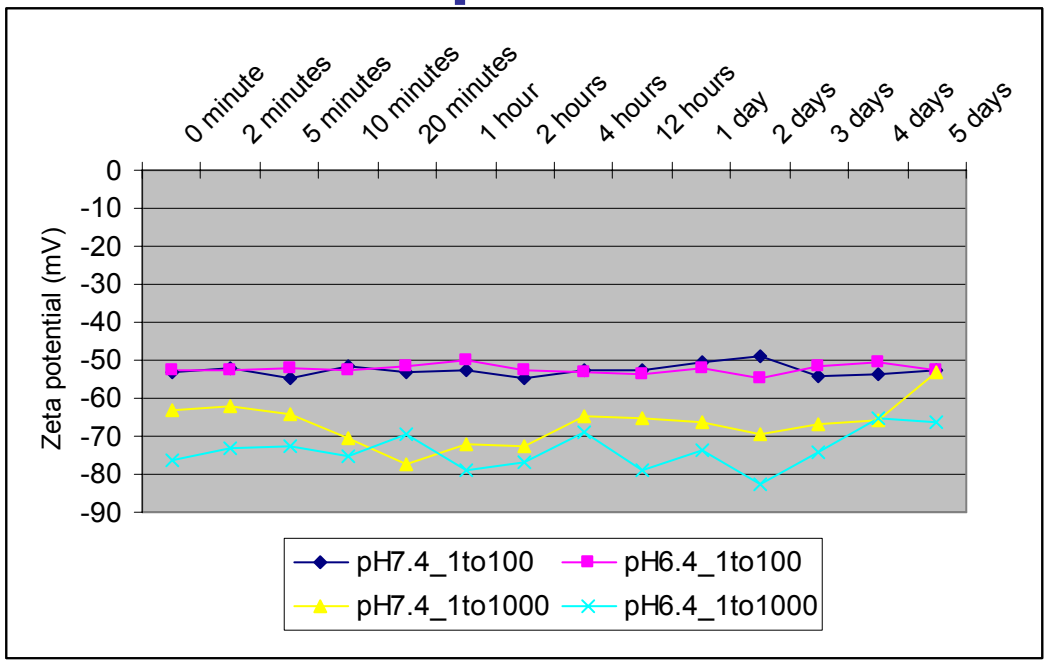
Increase in NP size with layers

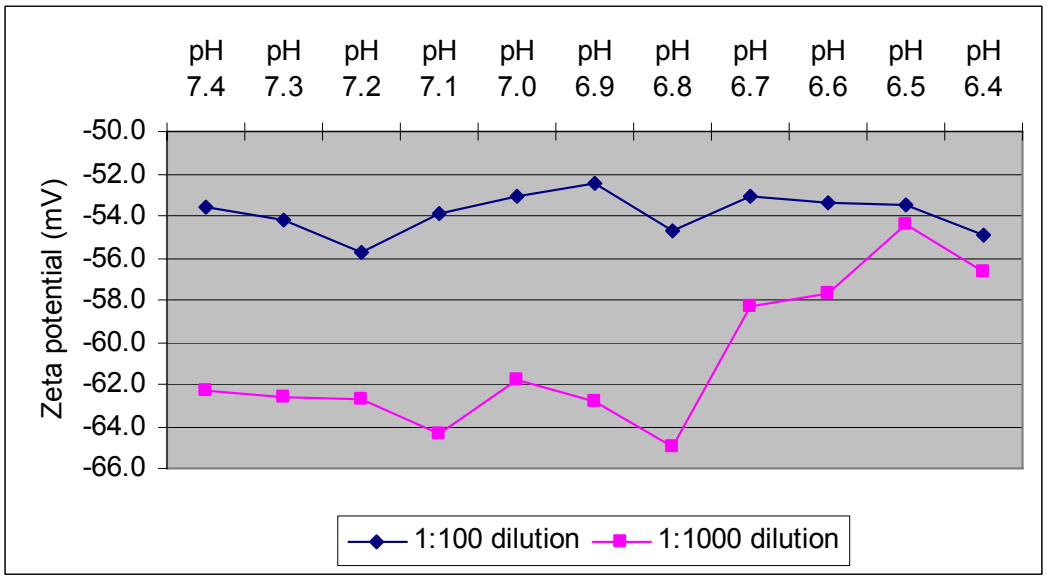


Change in NP zeta potential with additions of layers



Effects of pH and dilution on NP zeta potential

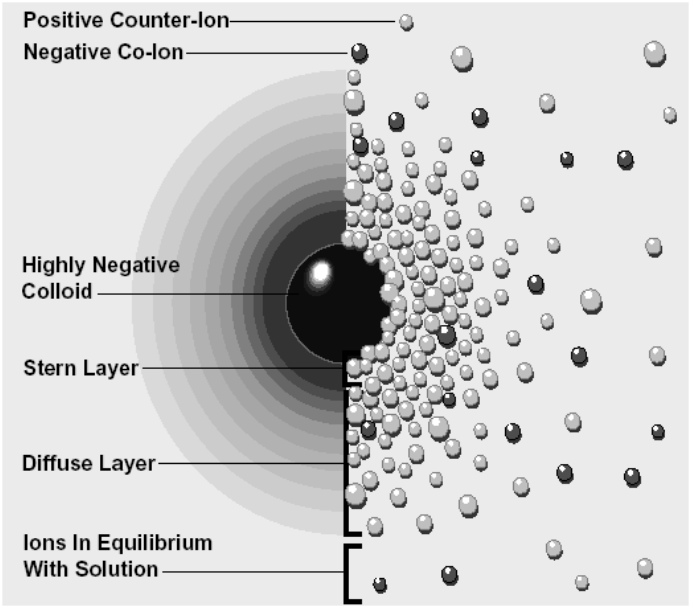


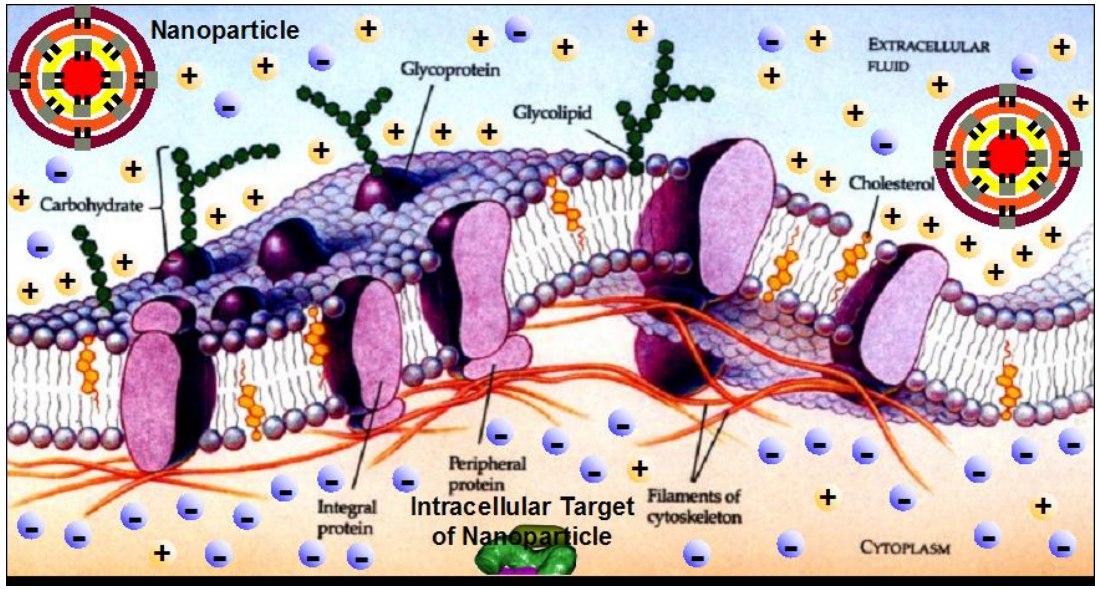


Zeta potential measurements of 40-50 nm silica particles tested over a 5 day time period at two different ph values and two different dilutions with distilled/ deionized water (affecting ionic strength)

Ref: Prow et al., 2005

Summary: Zeta Potential Properties of Nanoparticles





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References

"Zeta potential measurement using laser Doppler electrophoresis (LDE)": **http://www.malvern.co.uk/LabEng/technology/zeta_potential/zeta_potential_LDE.htm**

"Why Measure Zeta Potential?": http://www.malvern.co.uk/malvern/ondemand.nsf/id/67126

"Zeta Potential: An Introduction in 30 minutes": http://www.malvern.co.uk/malvern/kbase.nsf/0/26E2BC622DEE0CAC80256FBE00440C95/$file/MRK654-01%20An%20Introduction%20to%20Zeta%20Potential%20v3.pdf

Washington, C. "Zeta Potential in Pharmaceutical Formulation": http://www.malvern.co.uk/malvern/kbase.nsf/allbyno/KB000022/$file/Zeta_potential_in_pharmaceutical_formulation_MRK036-03-low_res.pdf

Using zeta potential to assess protein adsorption to surfactant coated latex: http://www.malvern.co.uk/malvern/kbase.nsf/0/AC284EC6076BF4D6802570D2005651E8/$file/MRK707-01%20Protein%20Adsorption%20to%20Surfactant%20Coated%20Latex.pdf

Prow, T.W., Rose, W.A., Wang, N., Reece, L.M., Lvov, Y., Leary, J.F. "Biosensor-Controlled Gene Therapy/Drug Delivery with Nanoparticles for Nanomedicine" Proc. of SPIE 5692: 199 – 208, 2005.