UNIVERSIDADE DO ESTADO DO RIO DE JANEIRO
INSTITUTO DE QUÍMICA – PPG-EQ

Ion-specific Effects on Biocolloidal Systems

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APS & ICTP-SAIFR Young Physicists Forum on Biological Physics: from Molecular to Macroscopic Scale (Bio2020)

Outline (Lecture 3)

- ✓ Applications to:
  - ✓ Protein adsorption;
  - ✓ Ions partitioning;
  - ✓ Electrostatic behavior of cell walls:
    - ➢ Classical charge regulation model;
    - ➢ Charged-regulated volume charge density.

Poisson-Boltzmann Equation in Bispherical Coordinates

✓ Hoskins & Levine (1956): nonlinear PBE was first solved in bispherical coordinates.

✓ Carnie *et al.* (1994): force between two similar spherical particles using bispherical coordinates and comparing with approximations.

✓ Stankovich & Carnie (1996): dissimilar spheres; a sphere and a plate.

Bispherical coordinates

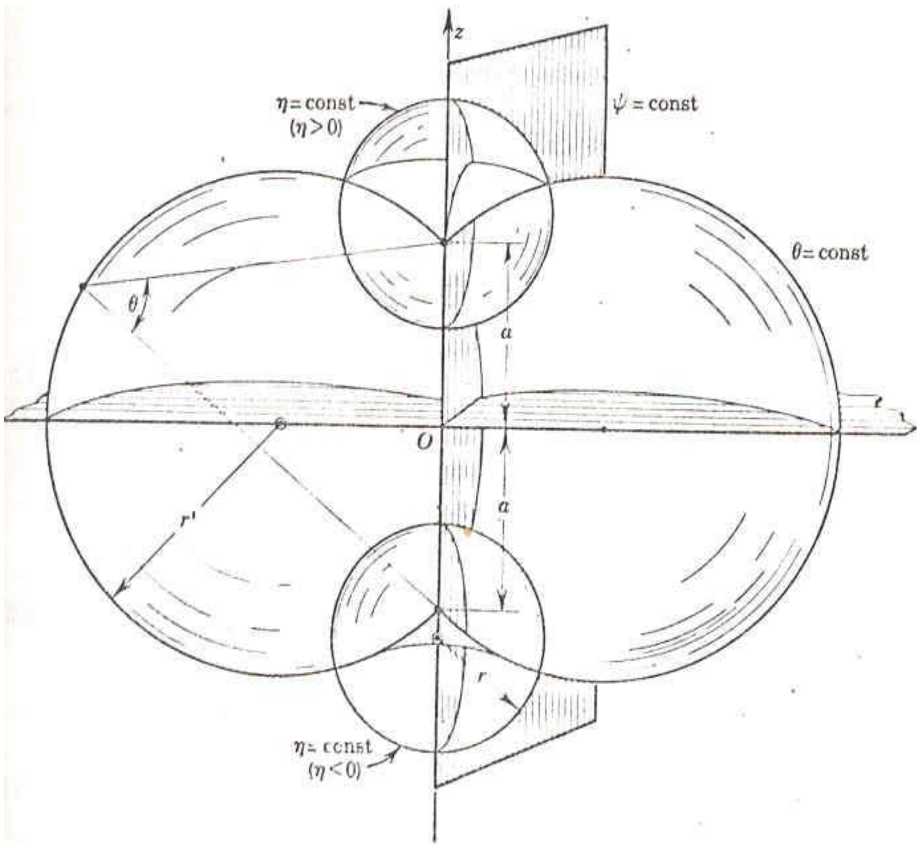
$$x = \frac{a \cdot \sin\theta}{\cosh\eta - \cos\theta} \qquad y = \frac{a \cdot \cos\theta}{\cosh\eta - \cos\theta} \qquad z = \frac{a \cdot \sinh\eta}{\cosh\eta - \cos\theta}$$

$$\nabla^2\psi = \frac{(\cosh\eta - \cos\theta)^3}{\beta^2 \sin\theta} \cdot \left[\frac{\partial}{\partial\theta}\left(\frac{\sin\theta}{\cosh\eta - \cos\theta} \cdot \frac{\partial\psi}{\partial\theta} \right) + \right.$$
$$\left. + \sin(\theta) \frac{\partial}{\partial\eta}\left(\frac{1}{\cosh\eta - \cos\theta} \frac{\partial\psi}{\partial\eta} \right) \right]$$

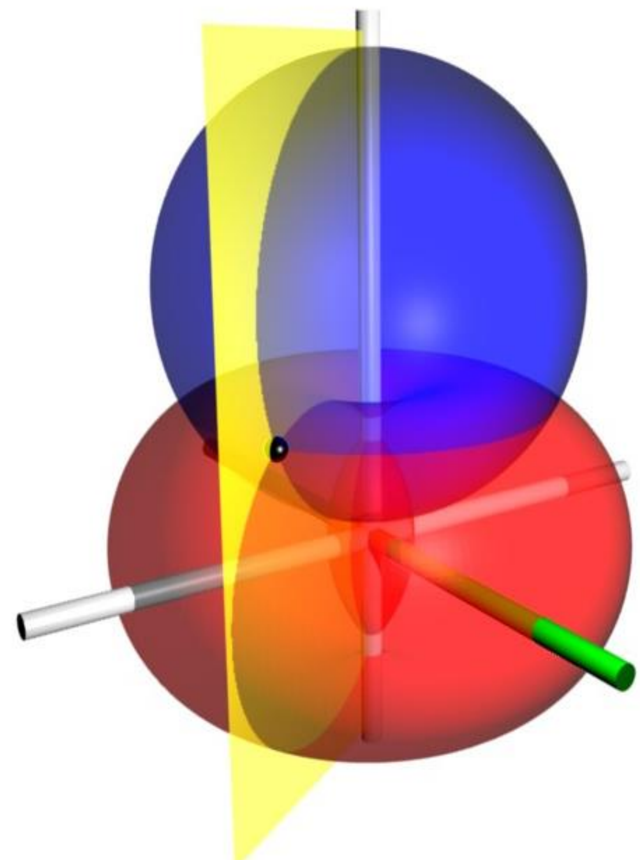
Bispherical Coordinates

$$0 \leq \theta \leq \pi$$

$$\eta_{01} \leq \eta \leq \eta_{02}$$

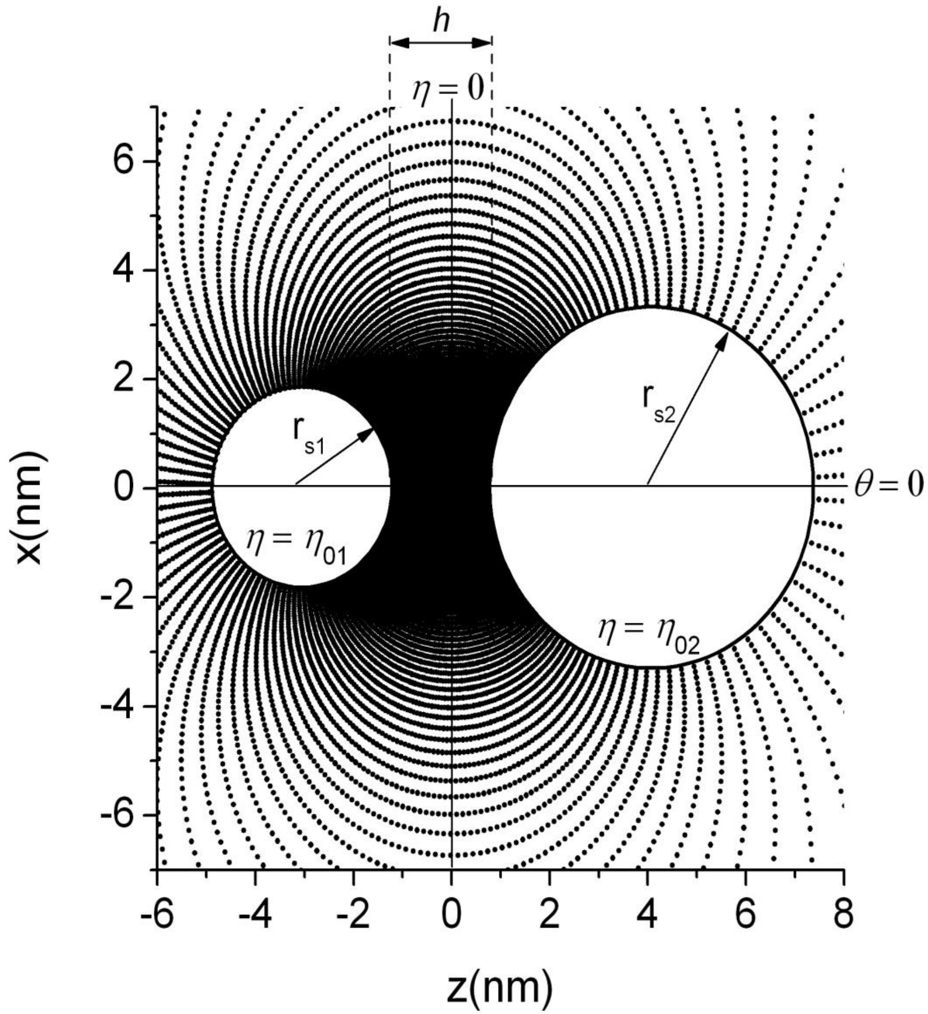


Moon & Spencer (1961)



Wikipedia (2008)

Bispherical Coordinates



Similar Spheres:

$$\cosh(\eta_0) = 1 + h/2r_s$$

$$a = \kappa r_s \sinh(\eta_0)$$

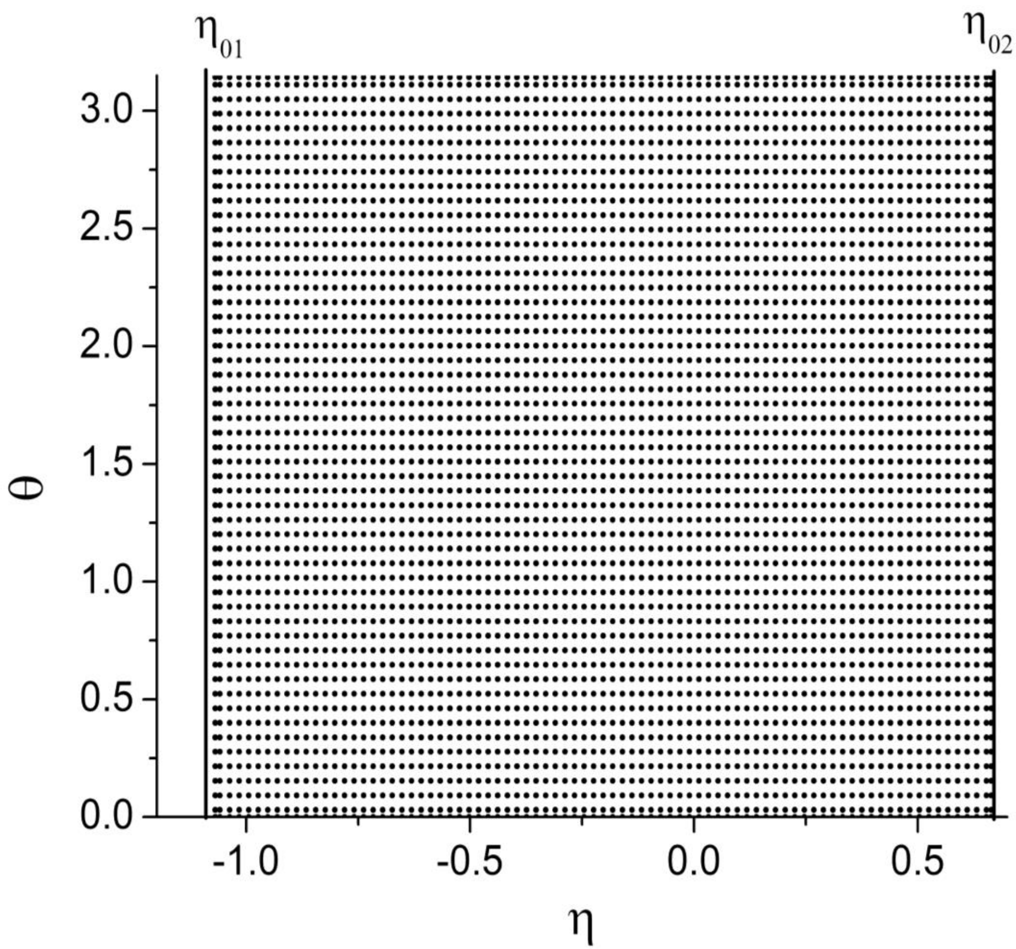
Dissimilar Spheres:

$$-\frac{a}{\sinh(\eta_{01})} = \kappa r_{S1}$$

$$\frac{a}{\sinh(\eta_{02})} = \kappa r_{S2}$$

$$\frac{a}{\tanh(\eta_{02})} - \frac{a}{\tanh(\eta_{01})} = \kappa r_{S1} + \kappa r_{S2} + \kappa h$$

Bispherical Coordinates



Similar Spheres:

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Dissimilar Spheres:

$$-\frac{a}{\sinh(\eta_{01})} = \kappa r_{S1}$$

$$\frac{a}{\sinh(\eta_{02})} = \kappa r_{S2}$$

$$\frac{a}{\tanh(\eta_{02})} - \frac{a}{\tanh(\eta_{01})} = \kappa r_{S1} + \kappa r_{S2} + \kappa h$$

Calculation of the Force between Particles

The dimensionless force between the two particles is given by integrating the stress tensor over a surface separating the two particles. Evaluating this integral over a surface of constant η we have

$$f = 2\pi \int_0^{\pi} \left\{ \left[\frac{a^2(\cosh(\psi)-1)}{(\cosh(\eta)-\cos(\theta))^2} + \frac{1}{2}\left(\left(\frac{\partial \psi}{\partial \theta}\right)^2 - \left(\frac{\partial \psi}{\partial \eta}\right)^2 \right) \right] \times [1-\cosh(\eta)\cos(\theta)] + \frac{\partial \psi}{\partial \theta}\frac{\partial \psi}{\partial \eta}\sinh(\eta)\sin(\theta) \right\} \frac{\sin(\theta)d\theta}{\cosh(\eta)-\cos(\theta)}$$

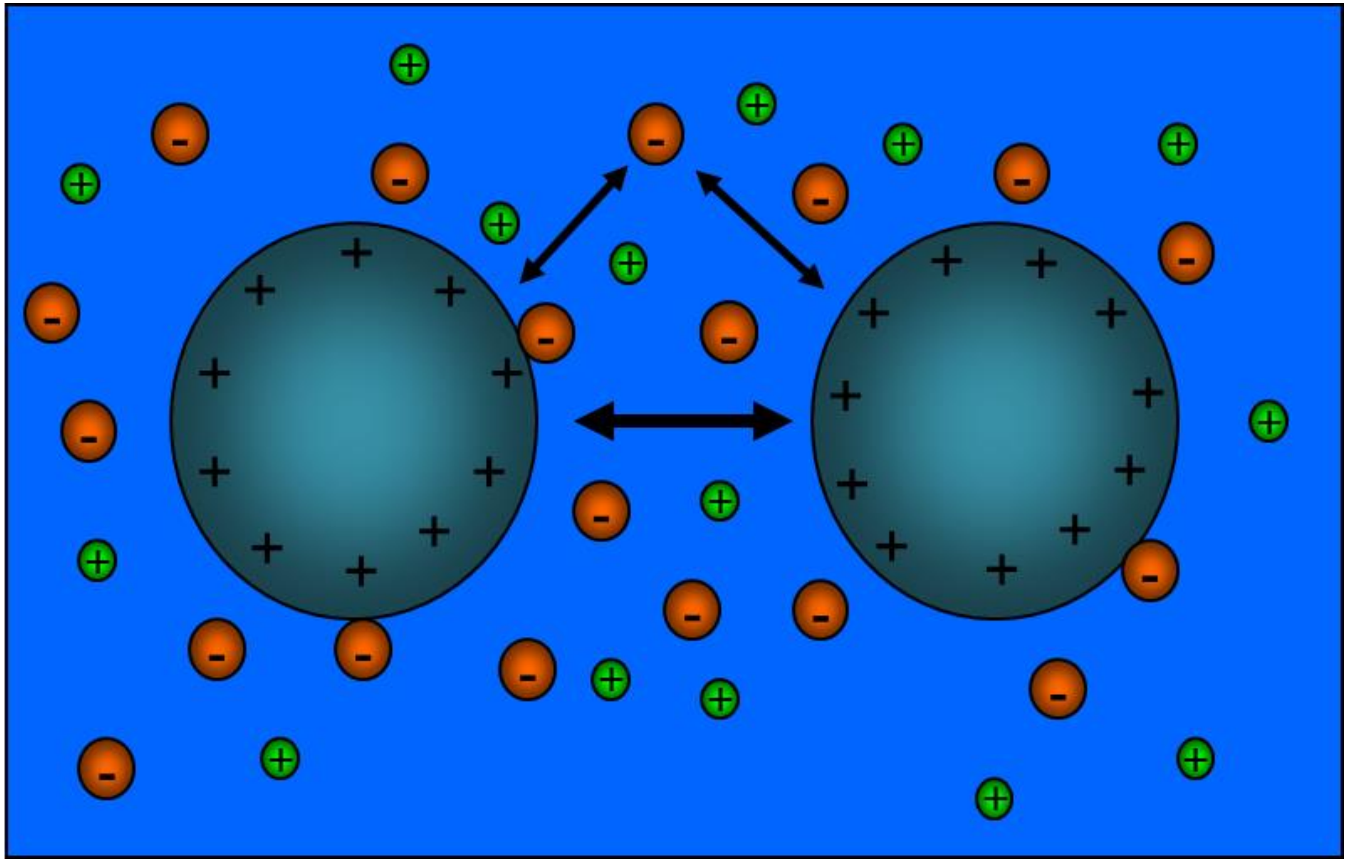
Sphere-plate: integral was evaluated over the surface $\eta = \eta_1/2$

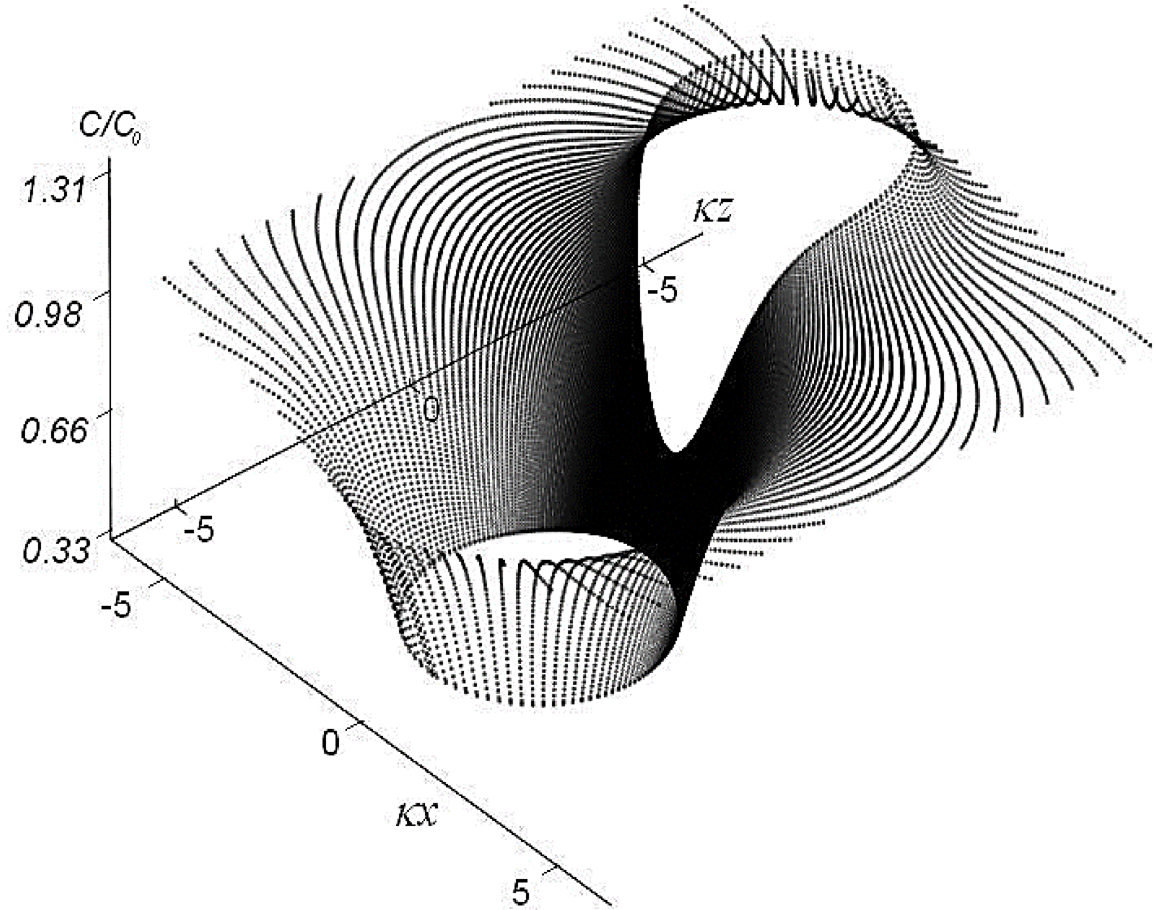
Sphere-sphere, it was evaluated over the surface $\eta = 0$

Lima et al., PCCP 9 (2007), 3174–3180;

Stankovich and Carnie, Langmuir12 (1996), 1453-1461.

Interactions between spherical colloidal particles



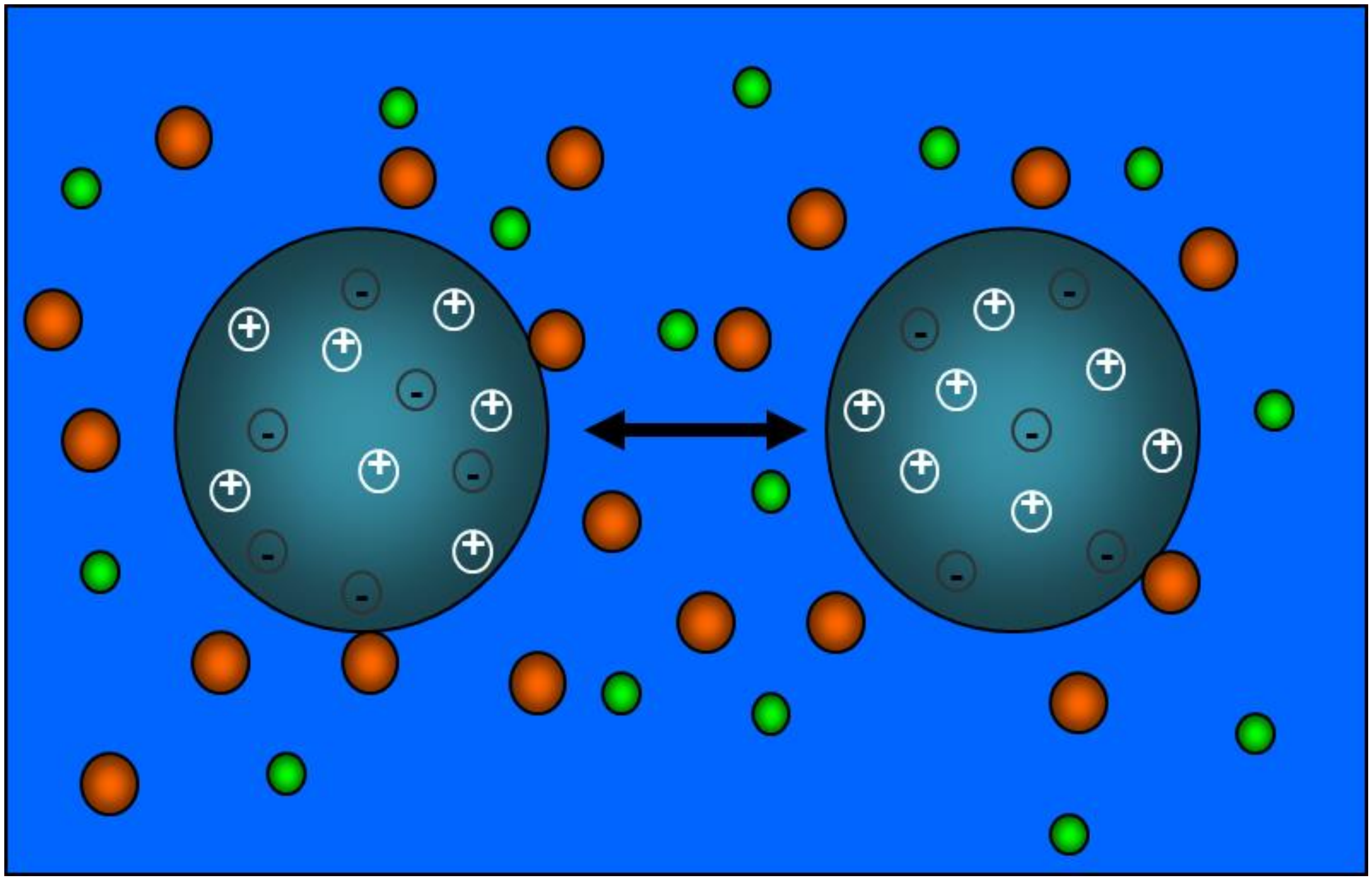


Concentration Profile of iodide ions

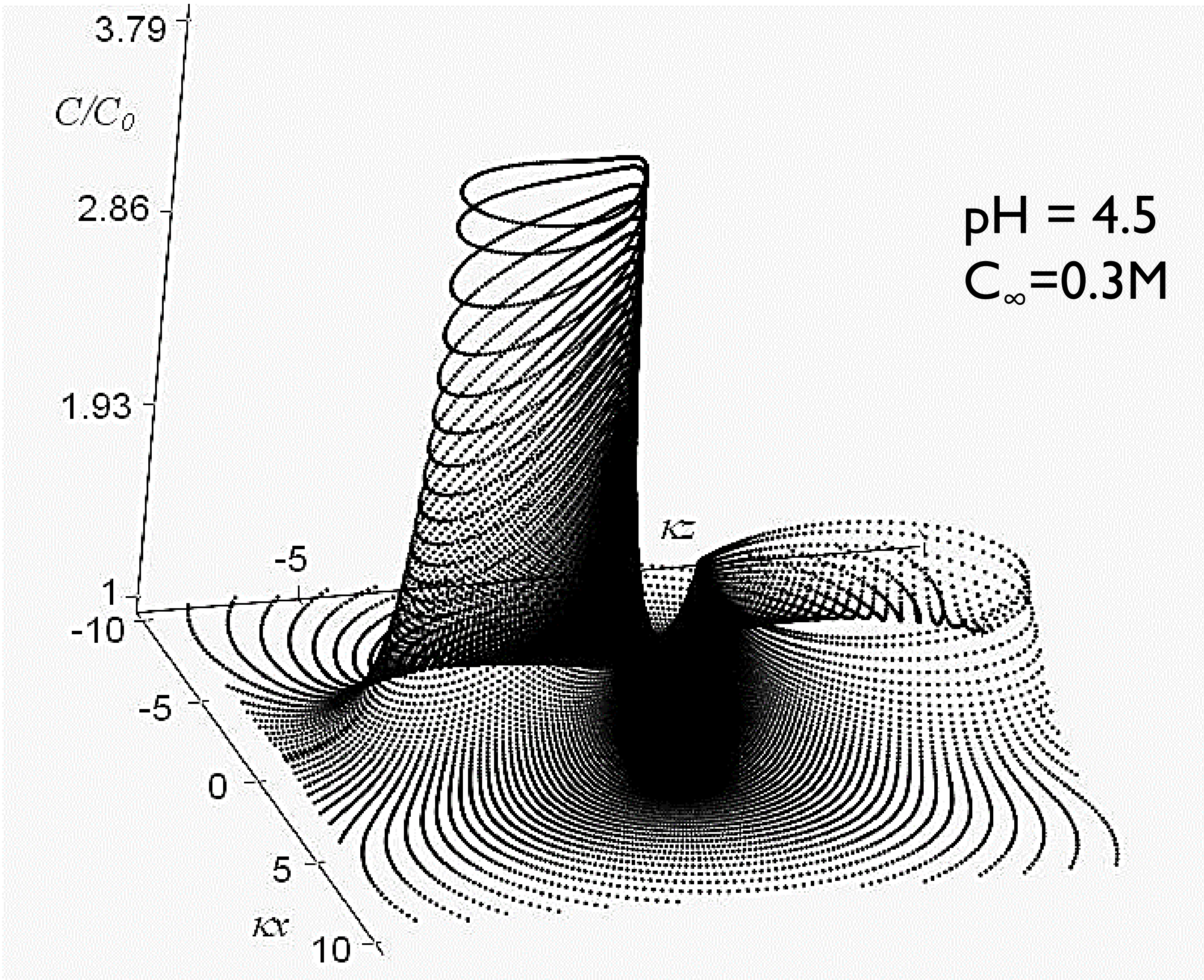
$\sigma_2 = 0.01 C/m^2$ $\sigma_1 = -0.03 C/m^2$

Lima et al. (2007), PCCP, 9, 3174

Interactions between globular proteins

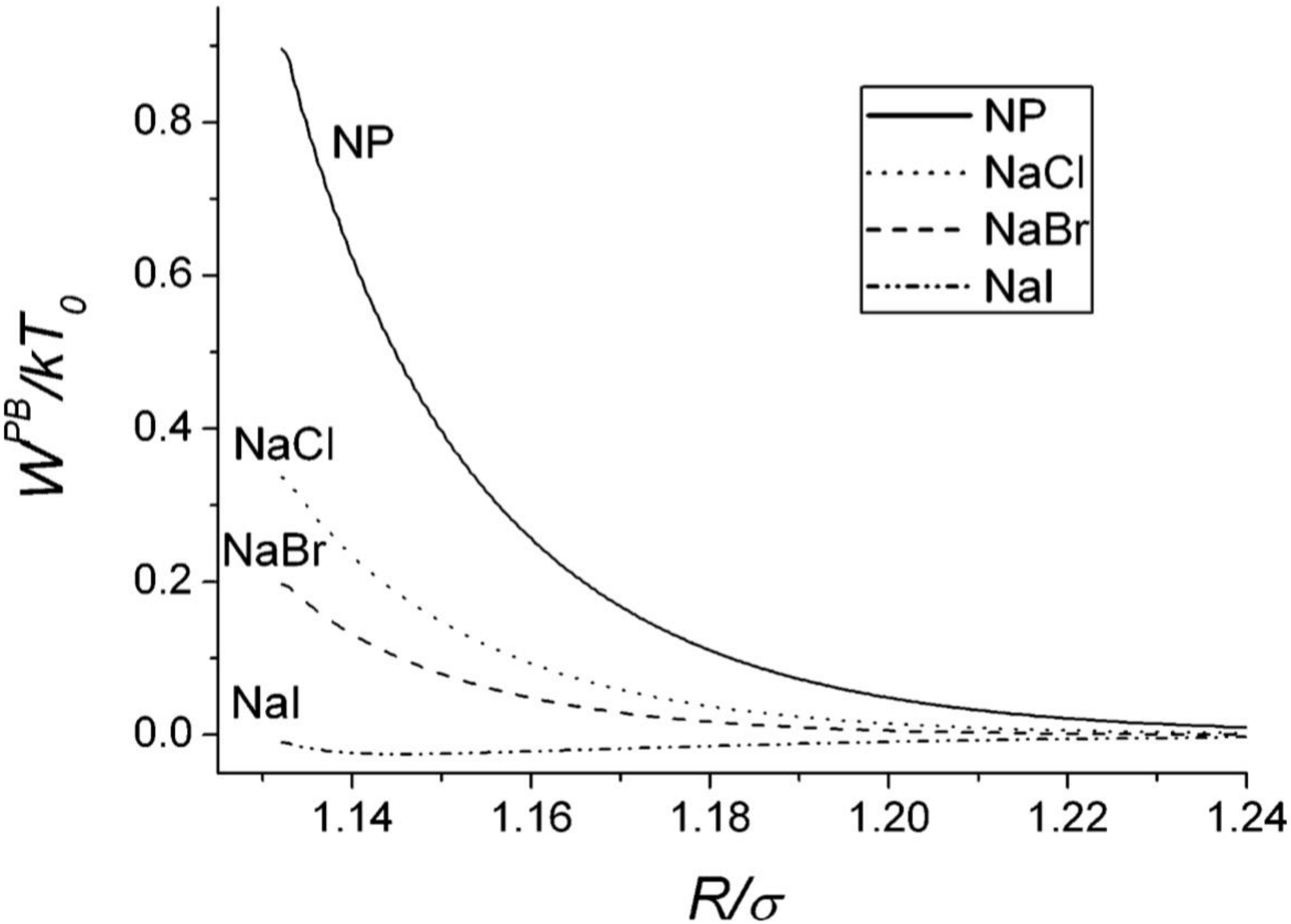


Iodide concentration around a lysozyme and a BSA



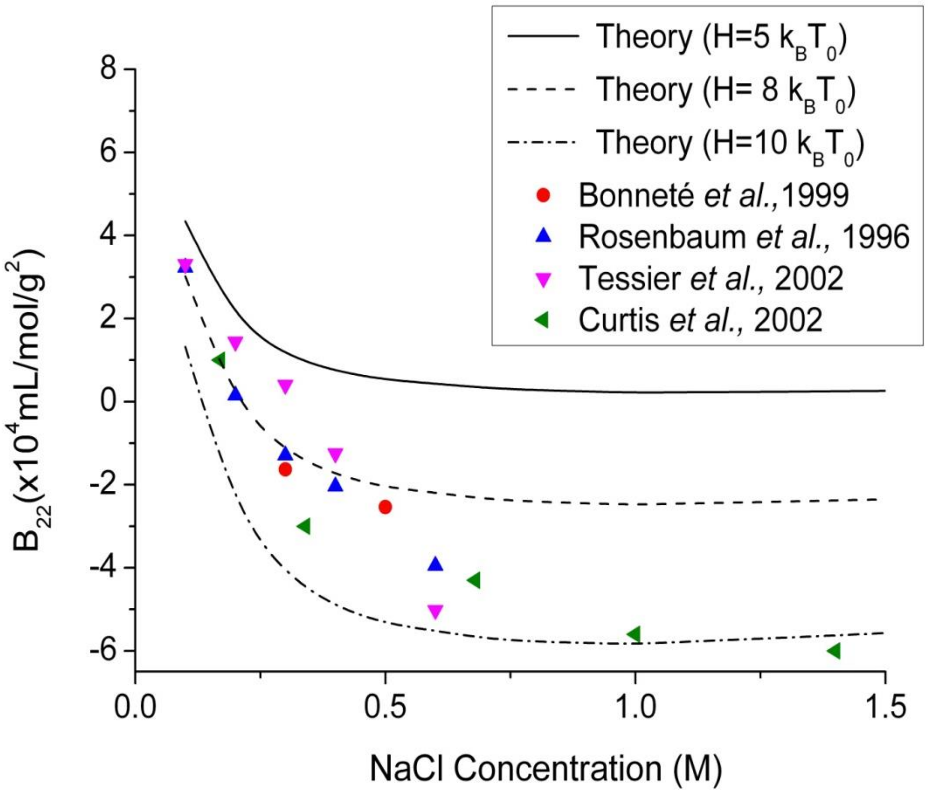
pH = 4.5
C_∞=0.3M

Modified Poisson-Boltzmann contribution to the Potential of Mean Force



Lysozyme in a 0.3M NaCl salt solution at pH = 4.5.

Osmotic second virial coefficient calculations



$$\frac{W^{PB}}{k_B T} = \frac{\varepsilon\varepsilon_0 k_B T \sigma}{e^2} \int_{\infty}^{r/\sigma} f \cdot d\left(\frac{r}{\sigma}\right)$$

$$W = W^{PB} + W^{Ham} + W^{hs}$$

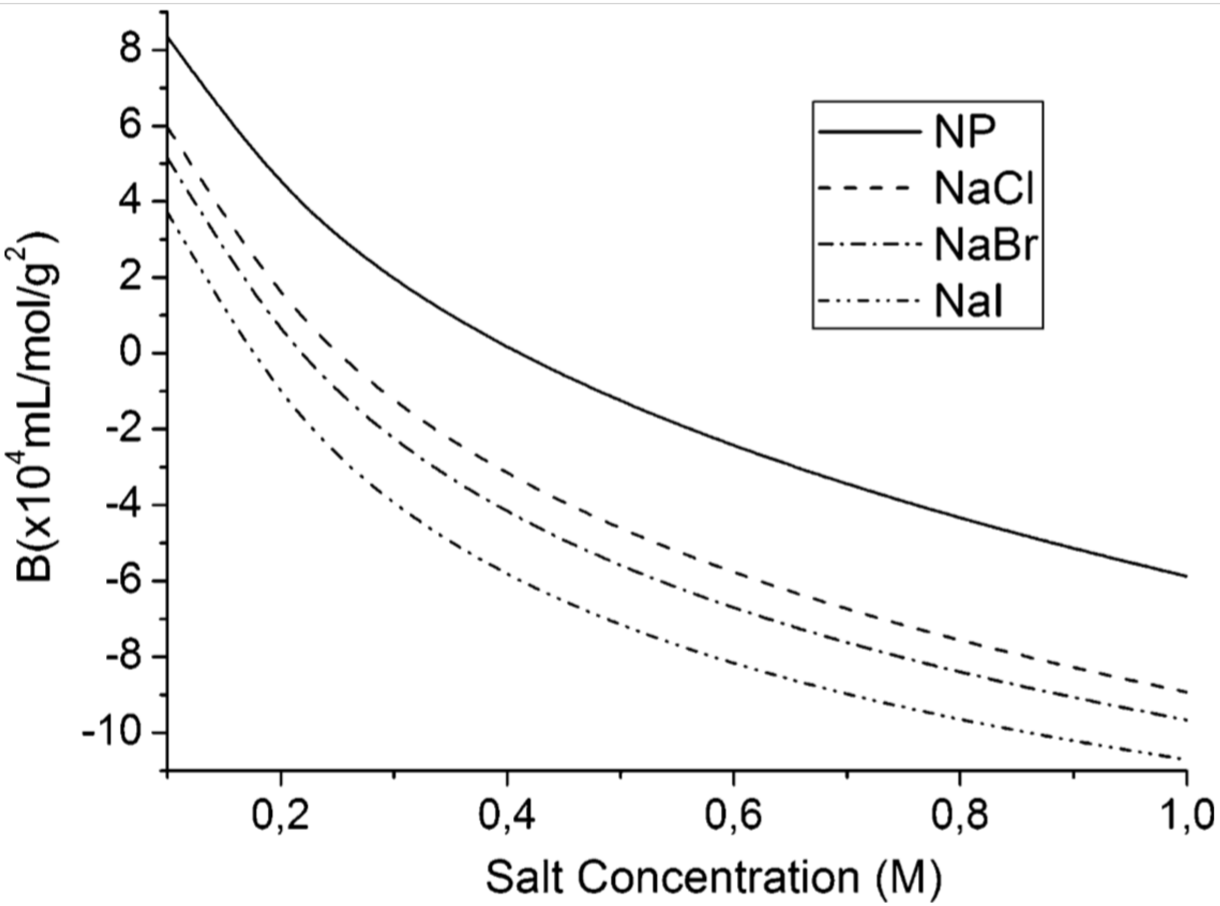
$$B_{22} = \frac{N_A}{2M^2} \int_0^{\infty} \left(1 - e^{-W(r)/k_B T}\right) 4\pi r^2 dr$$

OBS.: Predictive Model

Lysozyme in a 0.1M NaCl salt solution at pH = 4.5 and T = 298K.

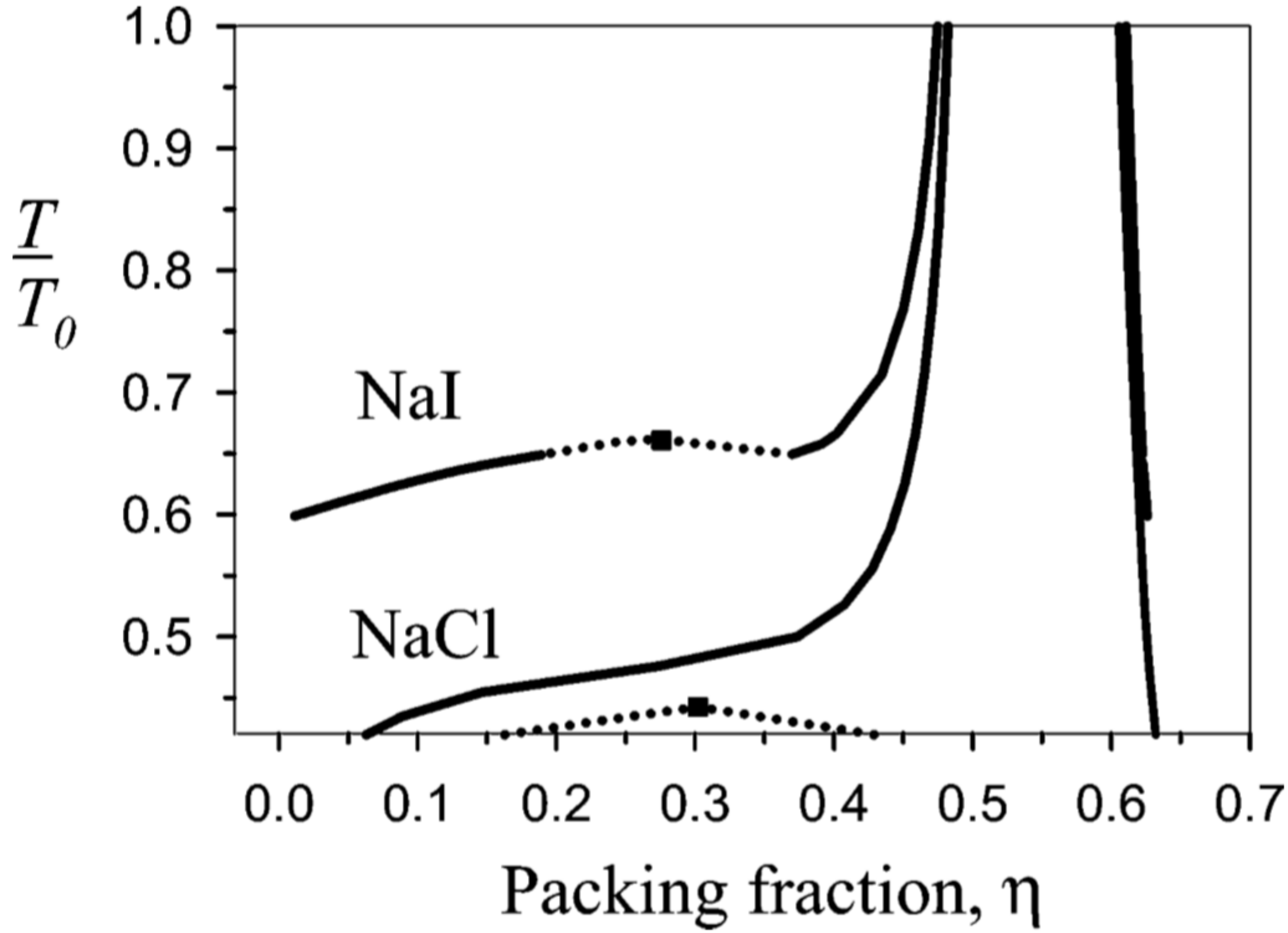
Lima et al. (2007), J. Phys. Chem.C, 111, 16055; 112, 8741.

Ion Specificity on Osmotic Second virial Coefficient



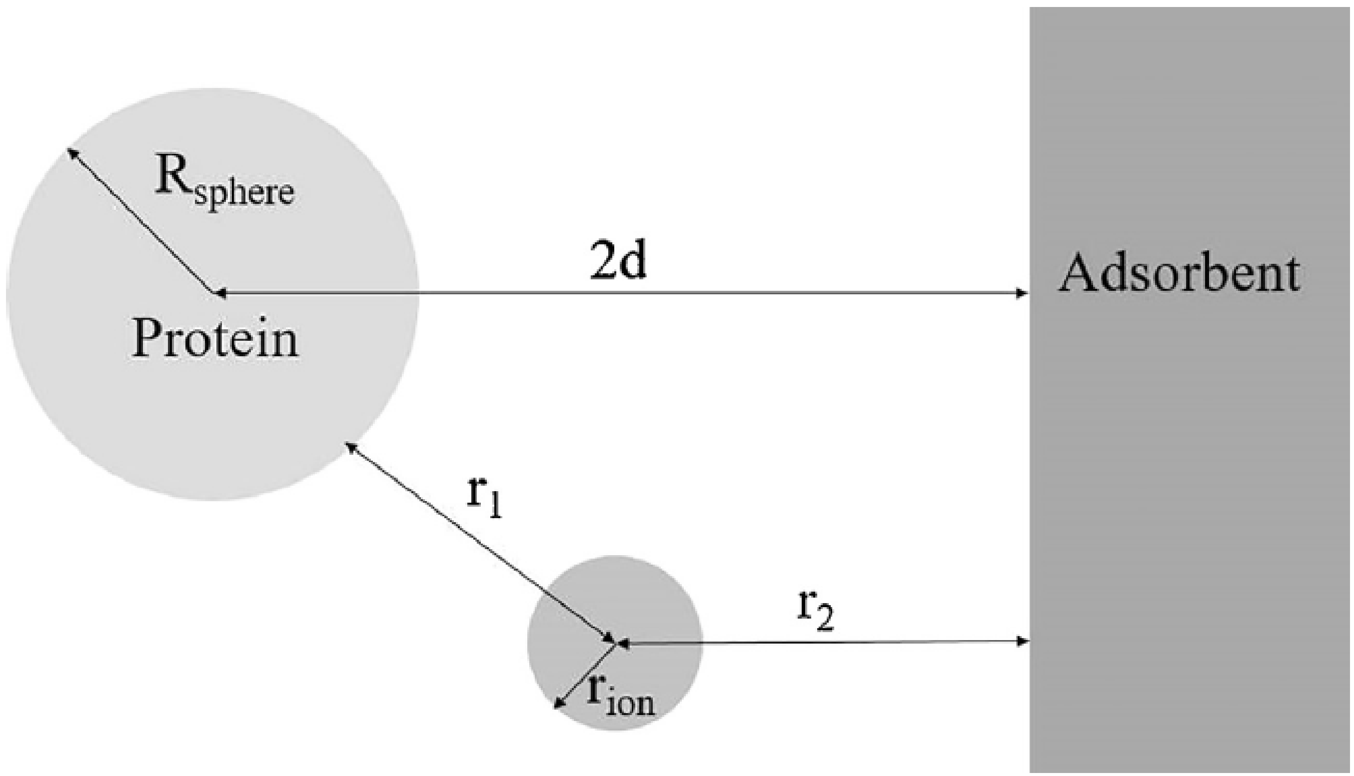
Lysozyme; pH = 4.5; T = 298K

Ion Specificity in Phase Diagrams



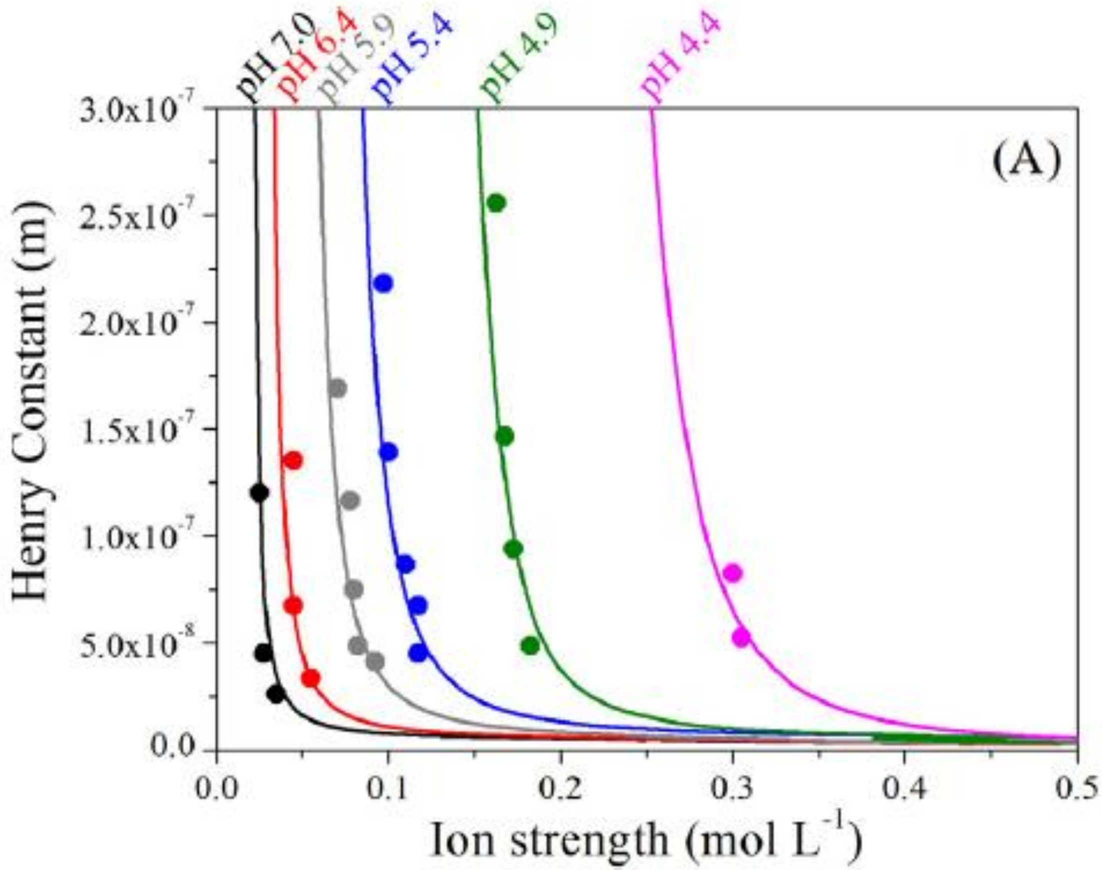
1[st] order perturbation theory; Lysozyme; C= 0.3 M; pH = 4.5; T = 298K

Chromatographic Purification of Proteins



Gama *et al. (2018),* Journal of Chromatography *A,* 1531, 74–82.

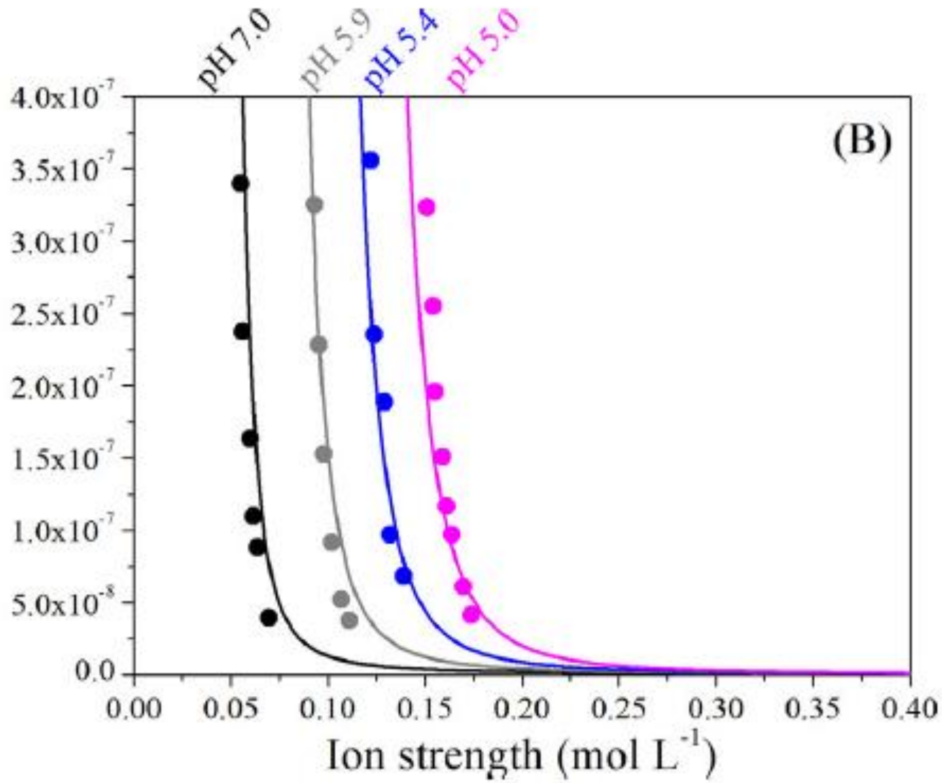
Protein Adsorption



Monoclonal antibody on Fractogel EMD SE HiCap

Gama *et al. (2018),* Journal of Chromatography *A,* 1531, 74–82.

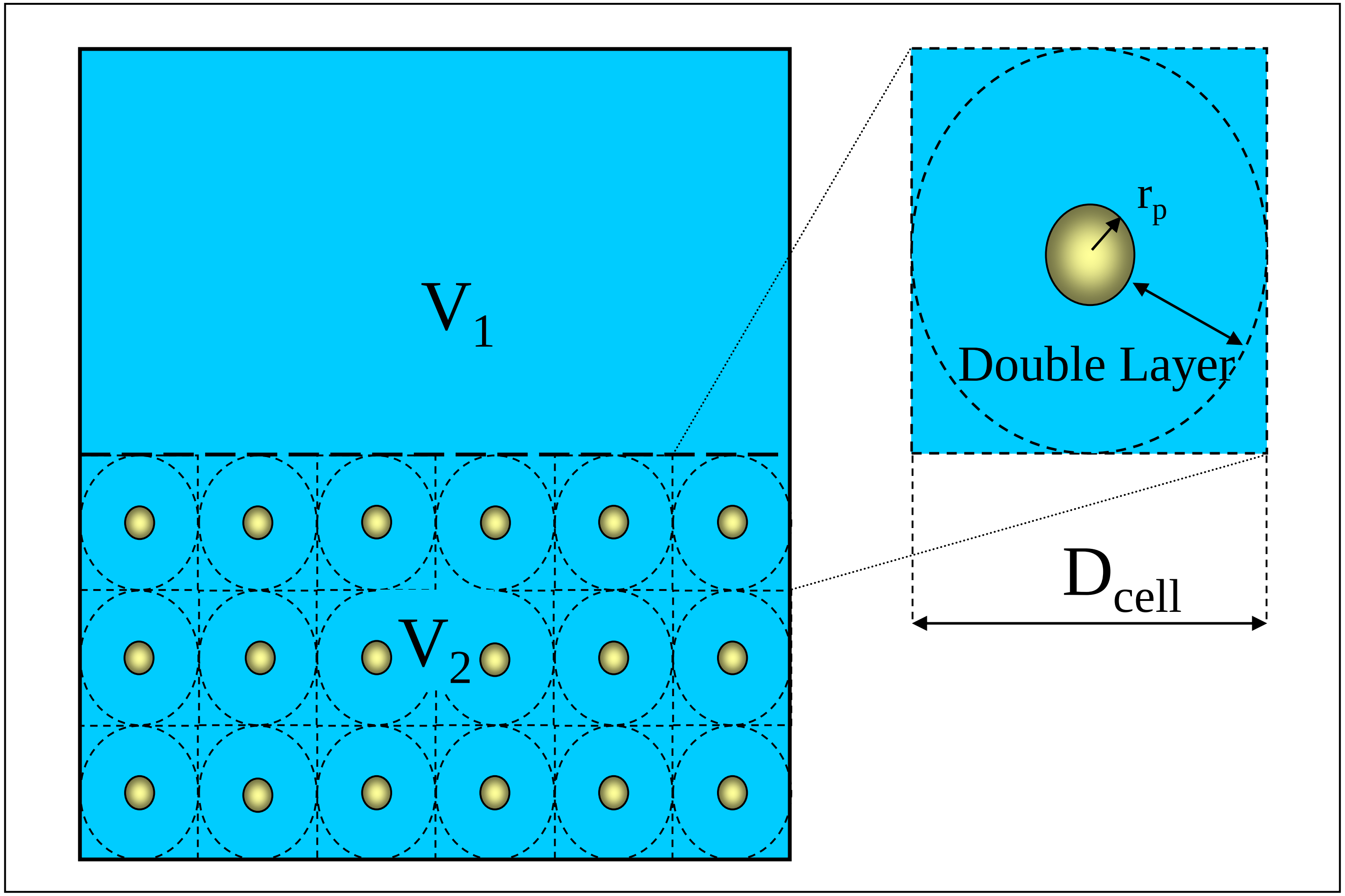
Protein Adsorption



Trastuzumab on YMC BioPro SP

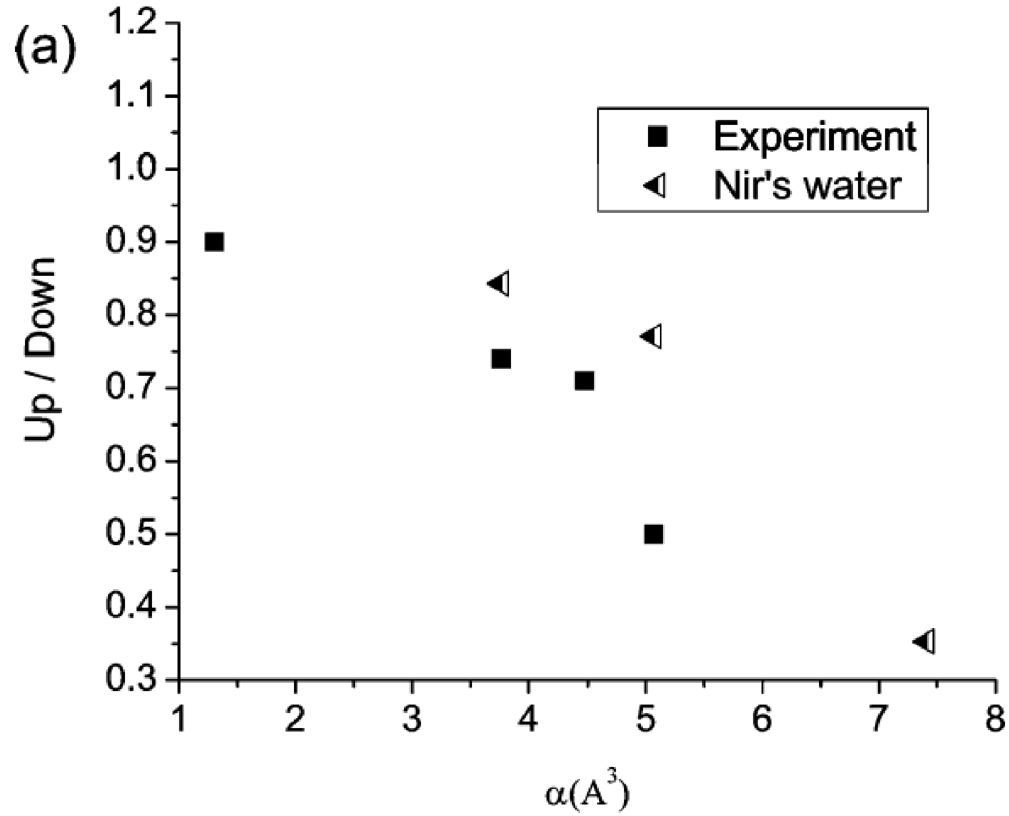
Gama *et al. (2018),* Journal of Chromatography *A,* 1531, 74–82.

Ions partitioning between two phases



Lima et al. (2009). JPBC, *113, 8124–8127*

Ion partitioning between two phases

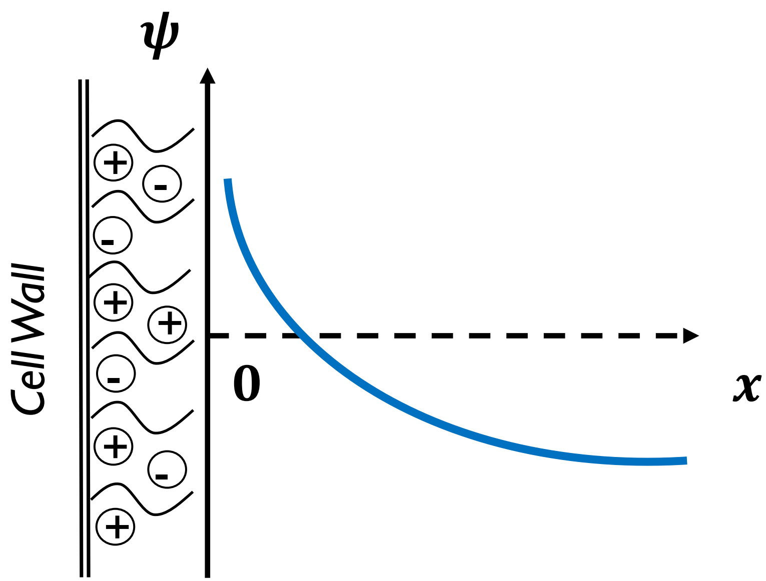


Lima et al. (2009). JPBC, *113, 8124–8127*
Experiments: Lagi *et al.*, 2007, JPCB, 111, 589.

Charge Regulation Model

$$\frac{d^2\psi}{dx^2} = -\frac{e}{\varepsilon_0\varepsilon}\sum_i z_i c_{i,0}\exp\left(\frac{-ez_i\psi}{k_BT}\right)$$

- Considering ε constant



Boundary Conditions:

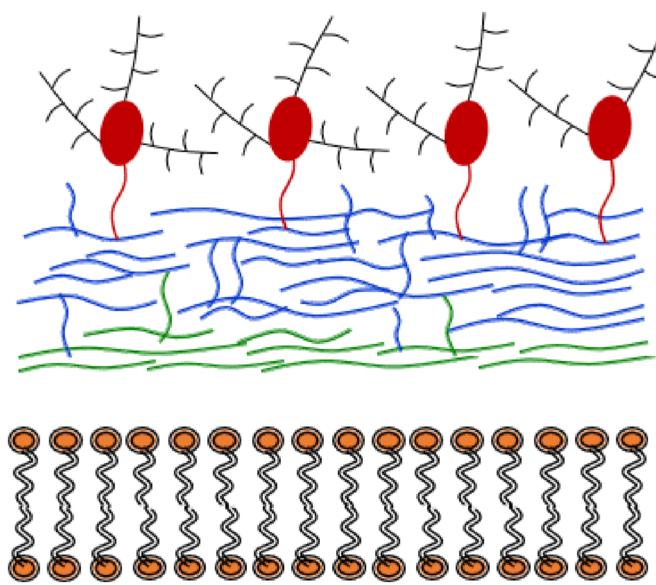
$$\left.\frac{d\psi}{dx}\right|_{x=0} = -\frac{\sigma(\psi)}{\varepsilon_0\varepsilon}$$

$$\left.\frac{d\psi}{dx}\right|_{x\to\infty} = 0$$

Hong and Brown 2008 DOI: 10.1021/la703564q

Charge Regulation Model

Yeast cell wall → Simplified *S. cerevisiae* yeast cell wall structure:



Glycoprotein → Surface charge

Chitin and β-glucan layer

Periplasmic space

Cytoplasmic membrane

S. cerevisiae's Functional Groups

- ✓ Two important parameters that characterize the surface groups are:
  - ➢ Number of groups
  - ➢ Dissociation constant

→ Potentiometric Titration Experiments

- ✓ Potentiometric titration
- ✓ Experimental results from Zhang et al. (2010)

Group:	pK_a	Site density (mmol/g)
(1) Carboxyl	3.52 – 5.34	0.45
(2) Phosphoryl	6.24 – 7.30	0.35
(3) Hydroxyl	9.47 – 10.13	0.25
(4) Amine	8.86 – 10.92	0.85

Zhang et al. 2010 DOI: 10.1016/j.jhazmat.2010.02.051

Charge Regulation Model

- **Yeast Surface Charge Function:**

Acid and basic groups equilibrium reactions:

$$> \mathrm{AH} \rightleftarrows\ > \mathrm{A}^- + \mathrm{H}^+ \qquad > \mathrm{BH}^+ \rightleftarrows\ > \mathrm{B} + \mathrm{H}^+$$

The total number of groups and their equilibrium constant can be written as following:

$$N_a = [AH] + [A^-] \qquad N_b = [BH^+] + [B]$$

$$K_a = \frac{[H^+]_s[A^-]}{[AH]} \qquad K_b = \frac{[H^+]_s[B]}{[BH^+]}$$

Hong and Brown 2008 DOI: 10.1021/la703564q

Charge Regulation Model

➢ **Yeast Surface Charge Function:**

- The total number of groups and their equilibrium equations can be rewritten to account for the charges present resulting in:

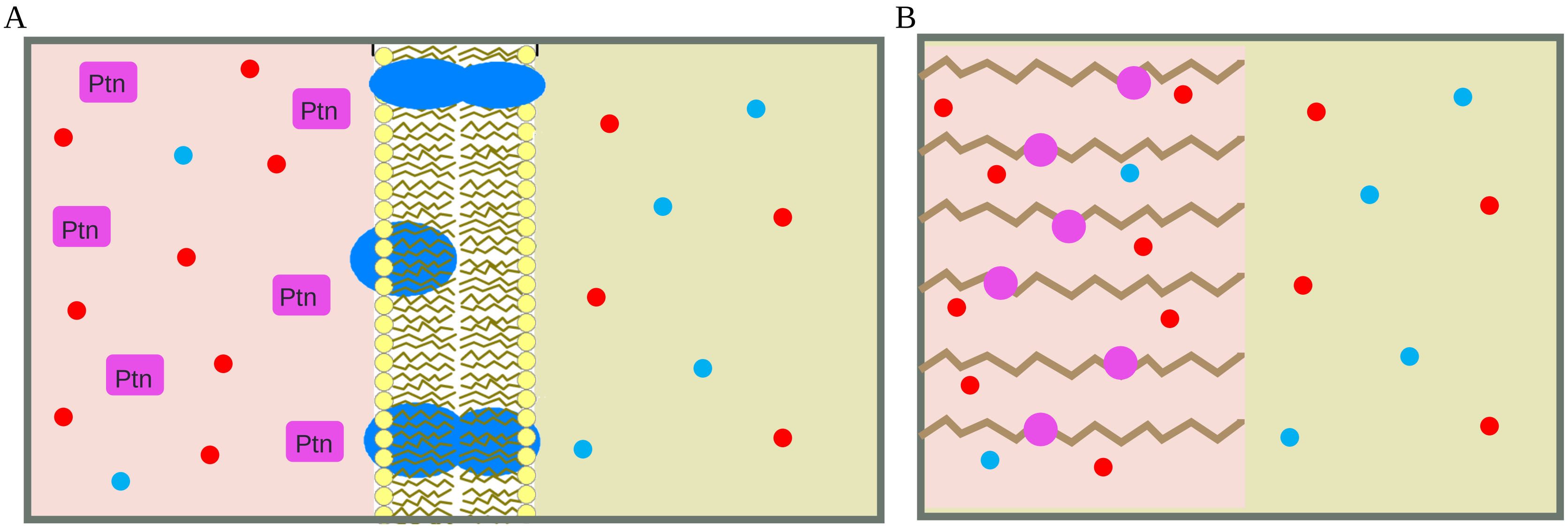
$$\sigma = \sum_k \frac{eN_{b,l}[H^+]_s}{[H^+]_s + K_{a\_bas,l}} - \sum_j \frac{eN_{a,k}K_{a\_ac,k}}{K_{a\_ac,k} + [H^+]_s}$$

- Local proton concentration $[H^+]_s$ on the surface is a function of the surface electrostatic potential.

$$[H^+]_s = [H^+]_{bulk} \exp\left(-\frac{e\psi_s}{k_B T}\right)$$

Hong and Brown 2008 DOI: 10.1021/la703564q

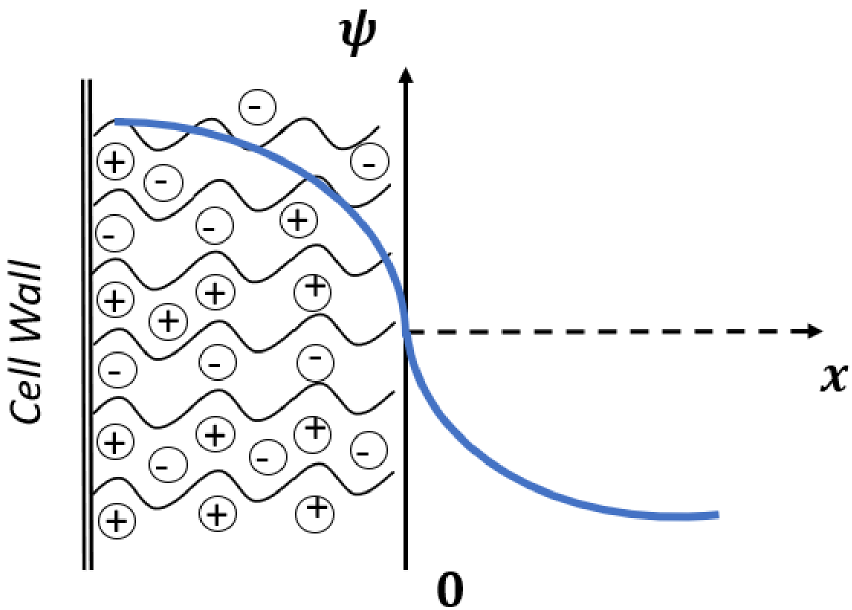
Donnan Potential



Charged-regulated volume charge density

$$\frac{d^2\psi}{dx^2} = -\frac{e}{\varepsilon_0\varepsilon}\sum_i z_i c_{i,0}\exp\left(\frac{-ez_i\psi}{k_BT}\right) - \rho_f$$

- Considering ε constant



Boundary Conditions:

$$\left.\frac{d\psi}{dx}\right|_{x\to-\infty} = 0$$

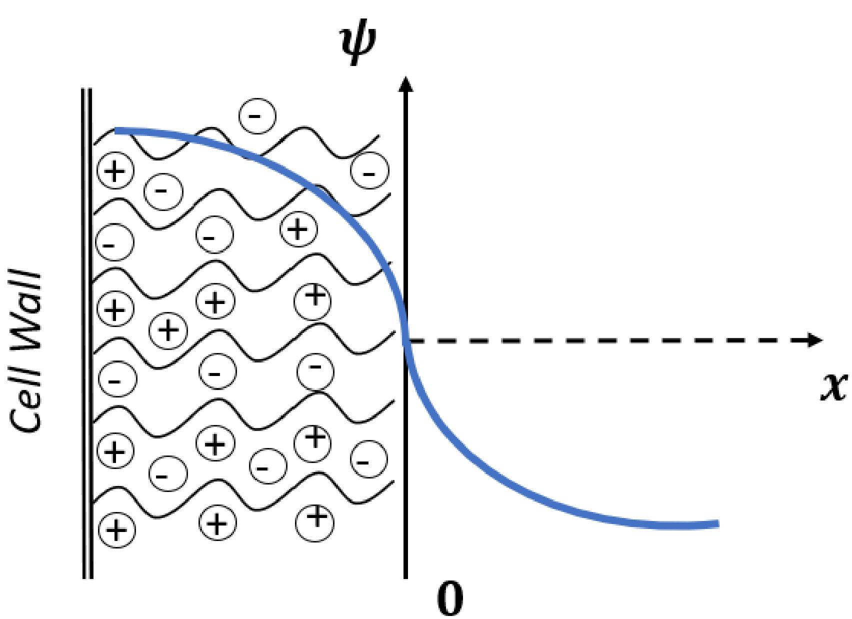
$$\left.\frac{d\psi}{dx}\right|_{x\to\infty} = 0$$

Barbosa, Lima, Tavares 2015 DOI: 10.1016/j.colsurfb.2015.06.066

Charged-regulated volume charge density

$$\frac{d^2\psi}{dx^2} = -\frac{e}{\varepsilon_0\varepsilon}\sum_i z_i c_{i,0}\exp\left(\frac{-ez_i\psi}{k_BT}\right) - \rho_f \rightarrow \sigma(\psi)$$

- Considering ε constant



Boundary Conditions:

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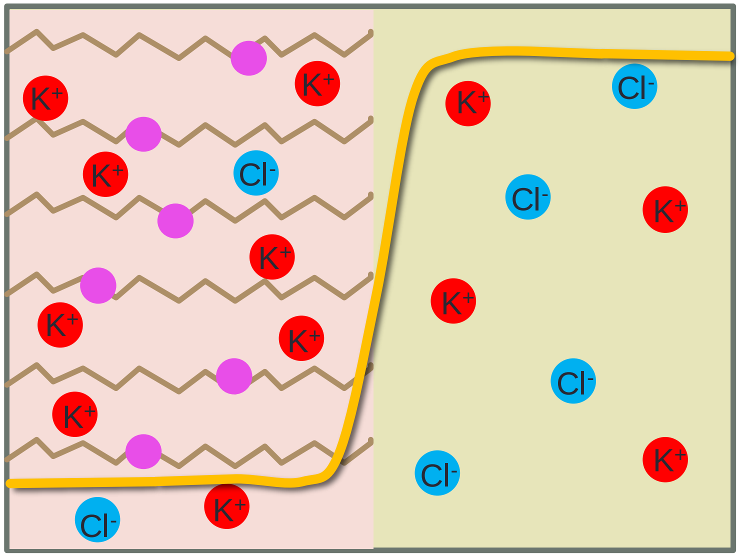
Smoothing Function



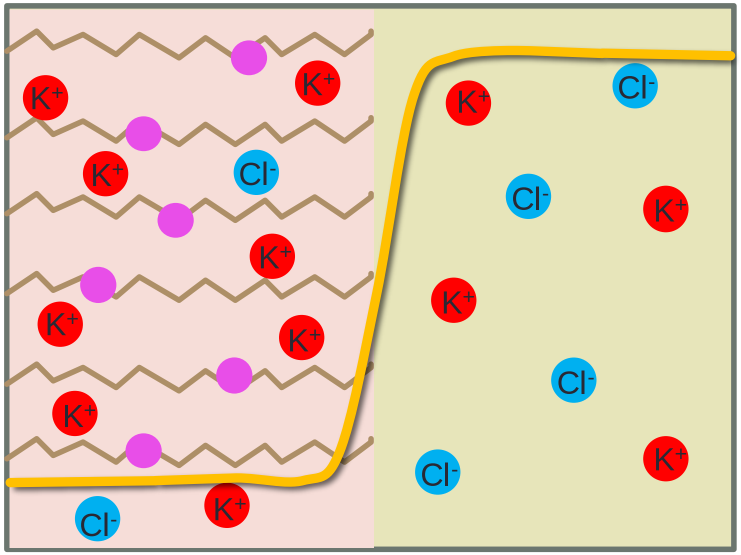
$$f(x) = \begin{cases} g(x), & \text{for } x \le x^* \\ h(x), & \text{for } x > x^* \end{cases}$$

$$F(x,\eta) = \nu(x,\eta)h(x) + [1 - \nu(x,\eta)]g(x)$$

$$\nu(x,\eta) = \frac{1 + \tanh\left(\frac{x - x^*}{\eta}\right)}{2}$$

Freitas; Quinto; Secchi; Biscaia. *An Efficient Adjoint-Free Dynamic Optimization Methodology for Batch Processing Using Pontryagin's Formulation*, 2012.
Barbosa; Lima, Boström,;Tavares. *J. Phys. Chem. B 119* (2015) 6379-88.

Smoothing Function



$$\rho_f(x,\eta) = \upsilon(x,\eta)\rho_{medium} + [1-\upsilon(x,\eta)]\ \rho_{cell\ wall}$$

$$\rho_f(x,\eta) = [1-\upsilon(x,\eta)]\ \rho_{cell\ wall}$$

Barbosa; Lima, Boström,;Tavares. *J. Phys. Chem. B 119* (2015) 6379-88.

Charged-regulated volume charge density

$$K_{aj} = \frac{c_{R_{aj}^-} c_{H^+}}{c_{R_{aj}H}} \qquad K_{bm} = \frac{c_{R_{bm}} c_{H^+}}{c_{R_{bm}H^+}}$$

$$R_{aj}H \leftrightarrow R_{aj}^- + H^+$$

$$R_{aj}H \leftrightarrow R_{aj}^- + H^+$$

+

$$c_{H^+} = c_{H^+,\infty} \exp\left(\frac{-ez_{H^+}\psi}{k_B T}\right)$$

+

$$N_{aj} = c_{R_{aj}^-} + c_{R_{aj}H}$$
$$N_{bm} = c_{R_{bm}} + c_{R_{bm}H^+}$$

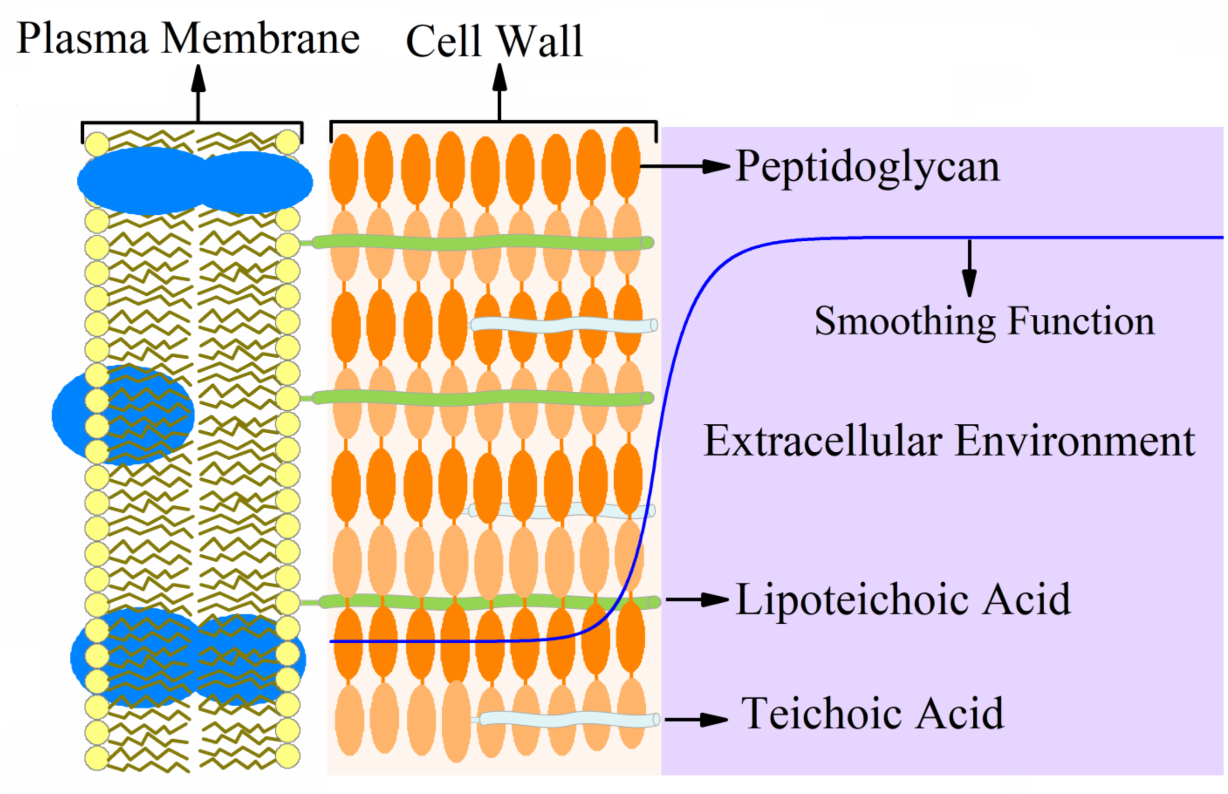
+

$$\frac{\rho_f(x)}{e} = [1 - \nu(x)]\left[\sum_m c_{R_{bm}H^+}(x) - \sum_j c_{R_{aj}^-}(x)\right]$$

$$\frac{\rho_f(x)}{e} = [1 - \nu(x)]\left[\sum_m \frac{10^{-pH_\infty} N_{bm}(x)}{10^{-pH_\infty} + K_{bm} exp\left(\frac{ez_{H^+}\psi(x)}{k_B T}\right)} - \sum_j \frac{K_{aj} N_{aj}(x)}{K_{aj} + 10^{-pH_\infty} exp\left(\frac{-ez_{H^+}\psi(x)}{k_B T}\right)}\right]$$

Charged-regulated volume charge density

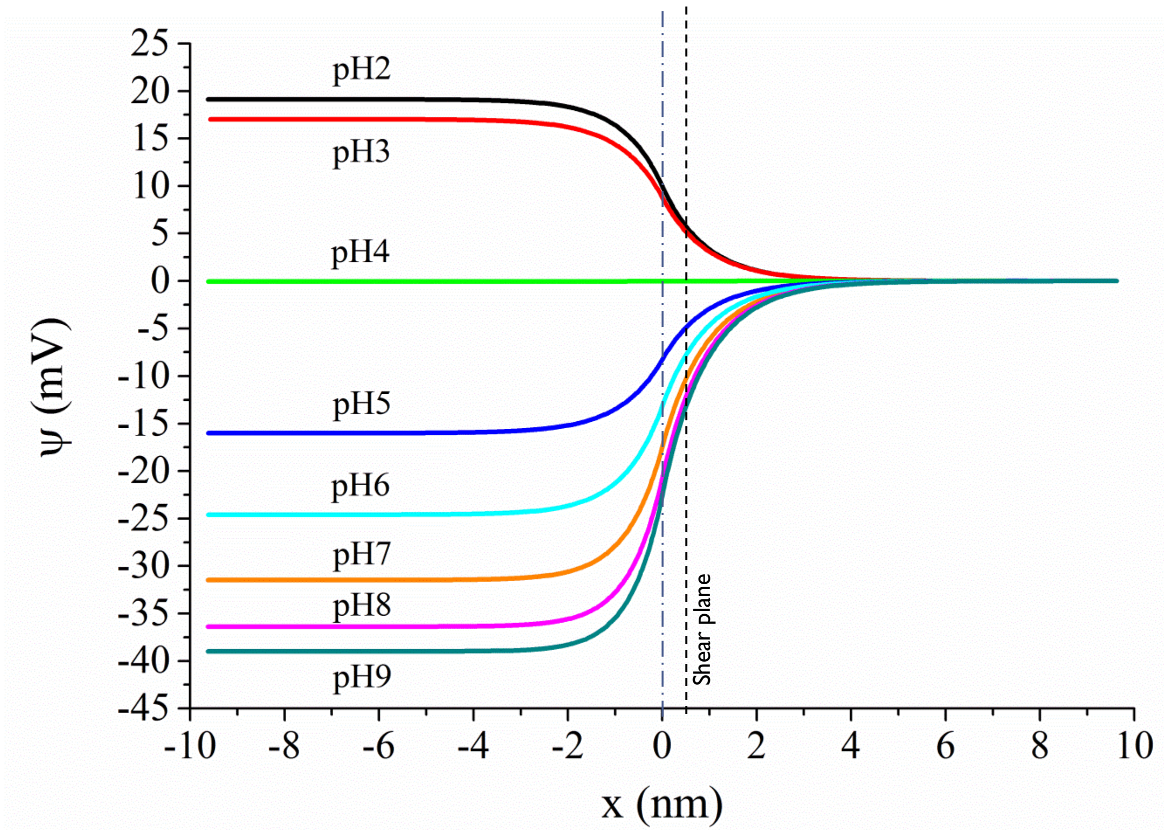
- Cell Wall of a Gram-positive bacteria:



Barbosa; Lima; Tavares. *Colloids Surf.*, v. 134, p. 447-452, 2015

Charged-regulated volume charge density

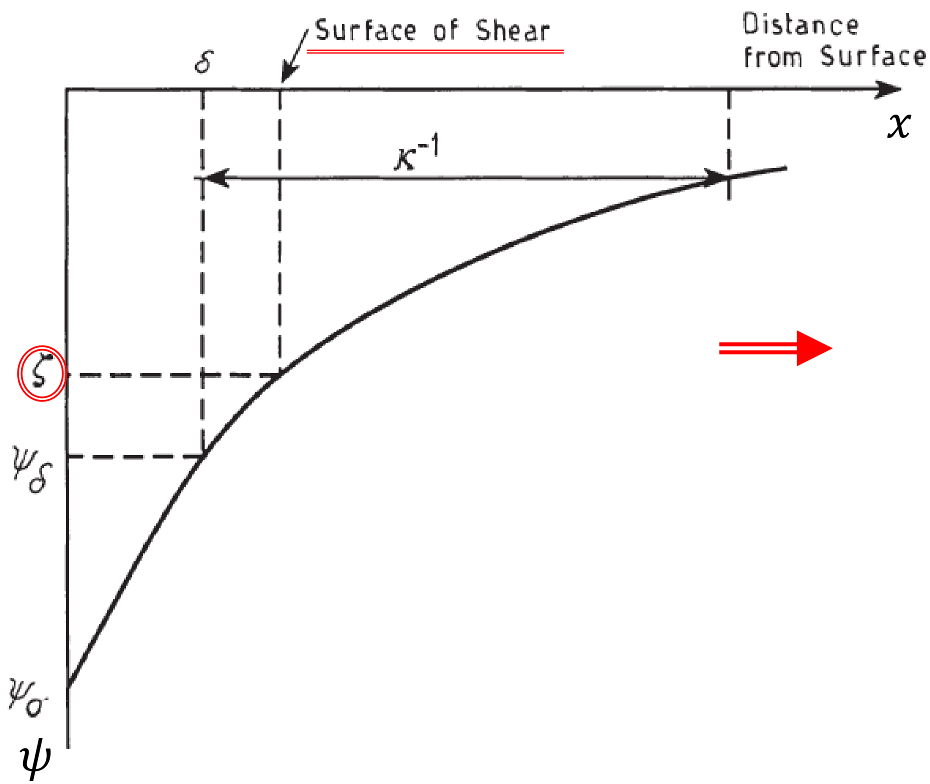
Electrostatic potential profiles in different bulk pH's:



Barbosa; Lima; Tavares. *Colloids Surf. B*, v. 134, p. 447-452, 2015

Zeta potential

➢ Distribution of electric potential (ψ) x distance (x):



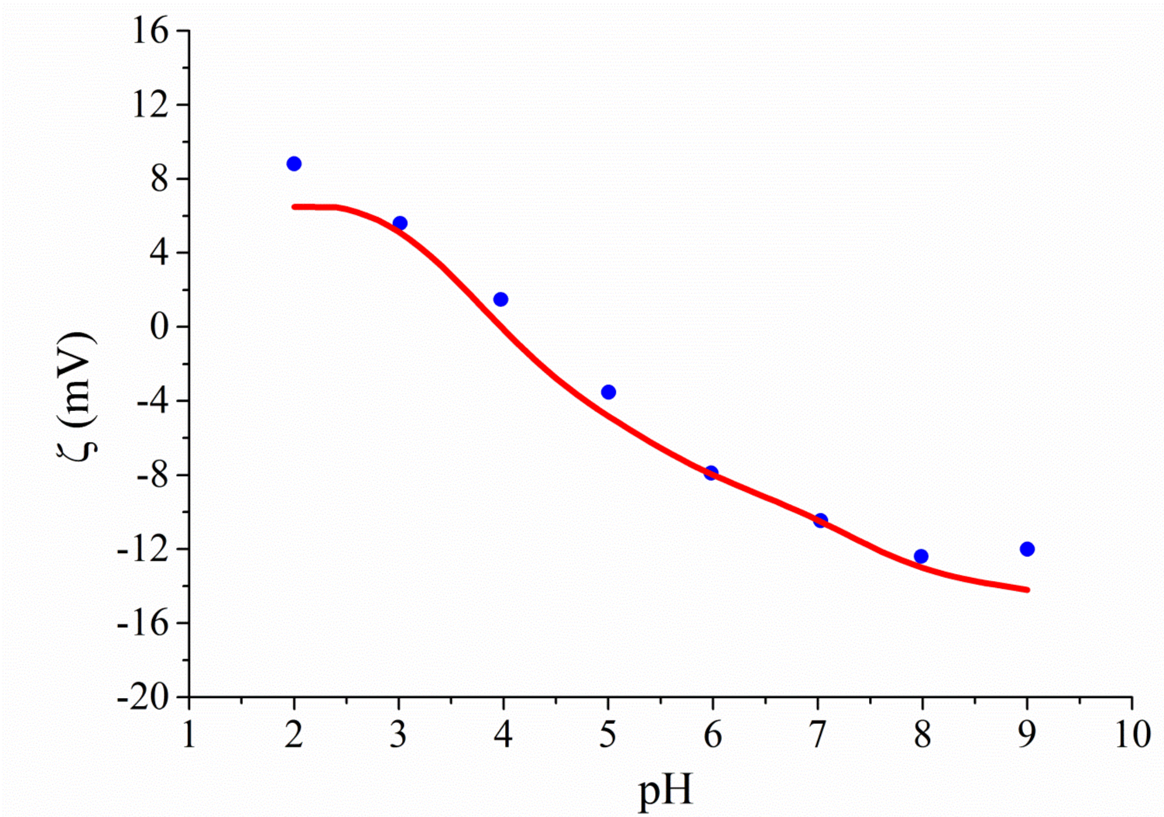
Estimate **zeta potential**

- Important parameter for indicating colloidal stability.
- It can be obtained experimentally.

Ohki, Ohshima 1995 DOI: 10.1007/978-3-0348-7318-5_4

Charged-regulated volume charge density

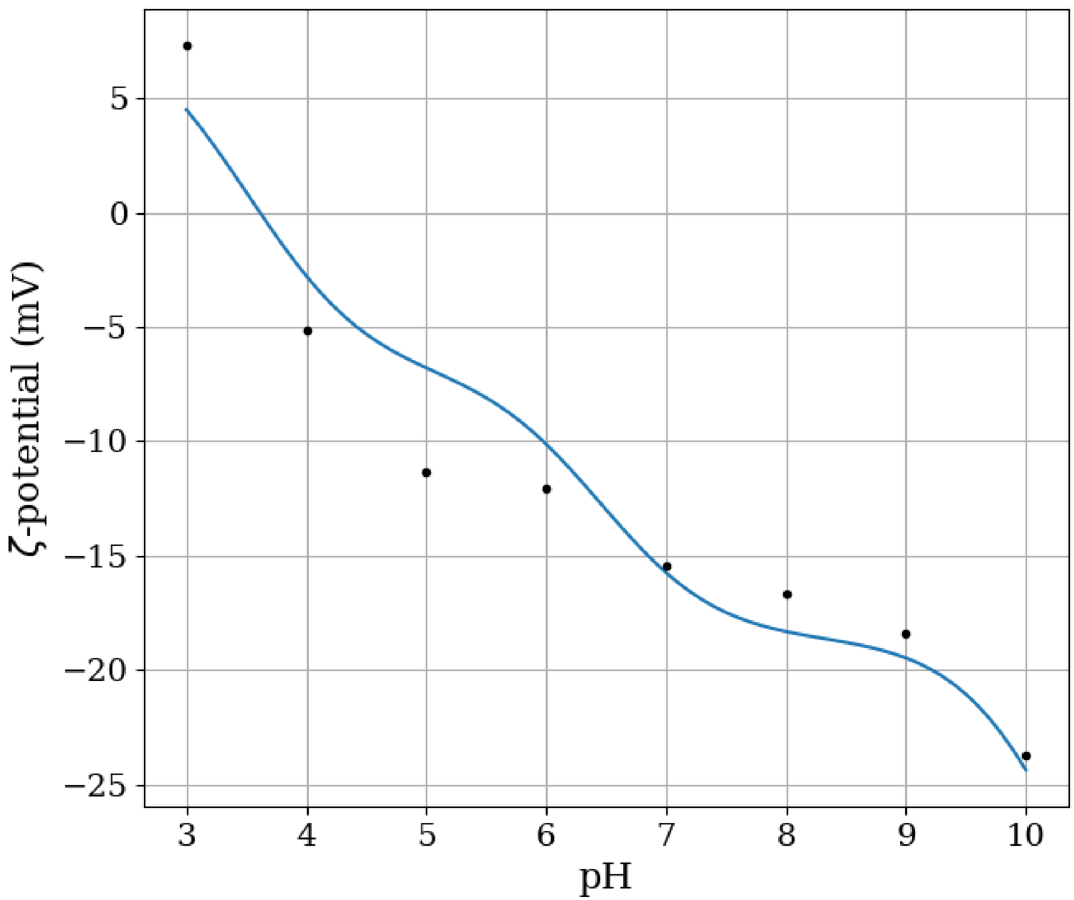
Bacillus brevis ζ potential as a function of pH:



Barbosa; Lima; Tavares. *Colloids Surf. B,* v. 134, p. 447-452, 2015

Charged-regulated volume charge density

S. cerevisiae ζ potential as a function of pH:



Calculated for:

$I = 10$ mM
$\lambda_{eff} = 3.34x10^{-4}$

Estimated pK_a:

pK_1	3.52
pK_2	6.24
pK_3	10.13
pK_4	10.92

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Thank you for your attention!!!