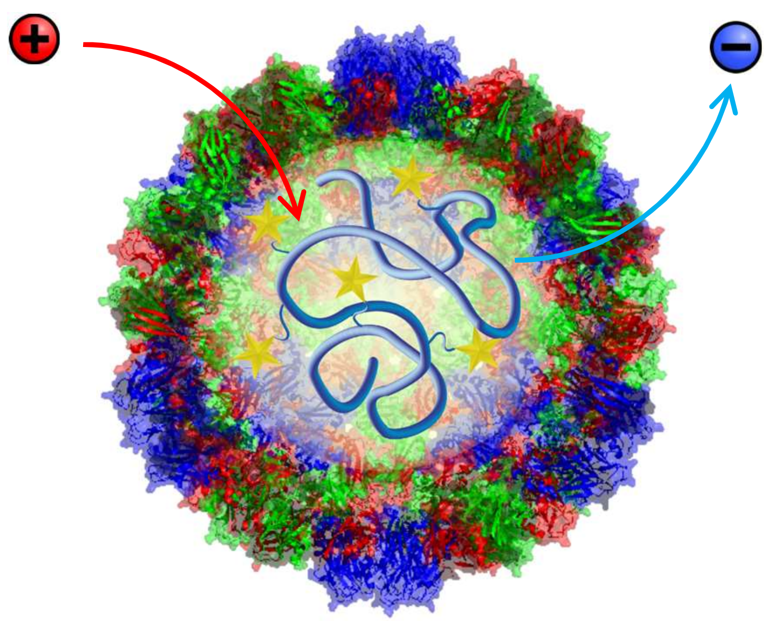
Solution pH in viruses, virus-like particles and other nanoshells

Donnan vs Poisson-Boltzmann theory



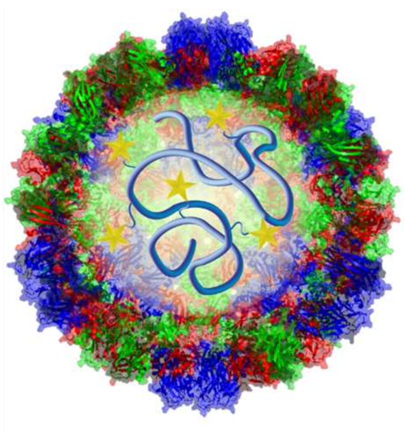
Paul van der Schoot

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

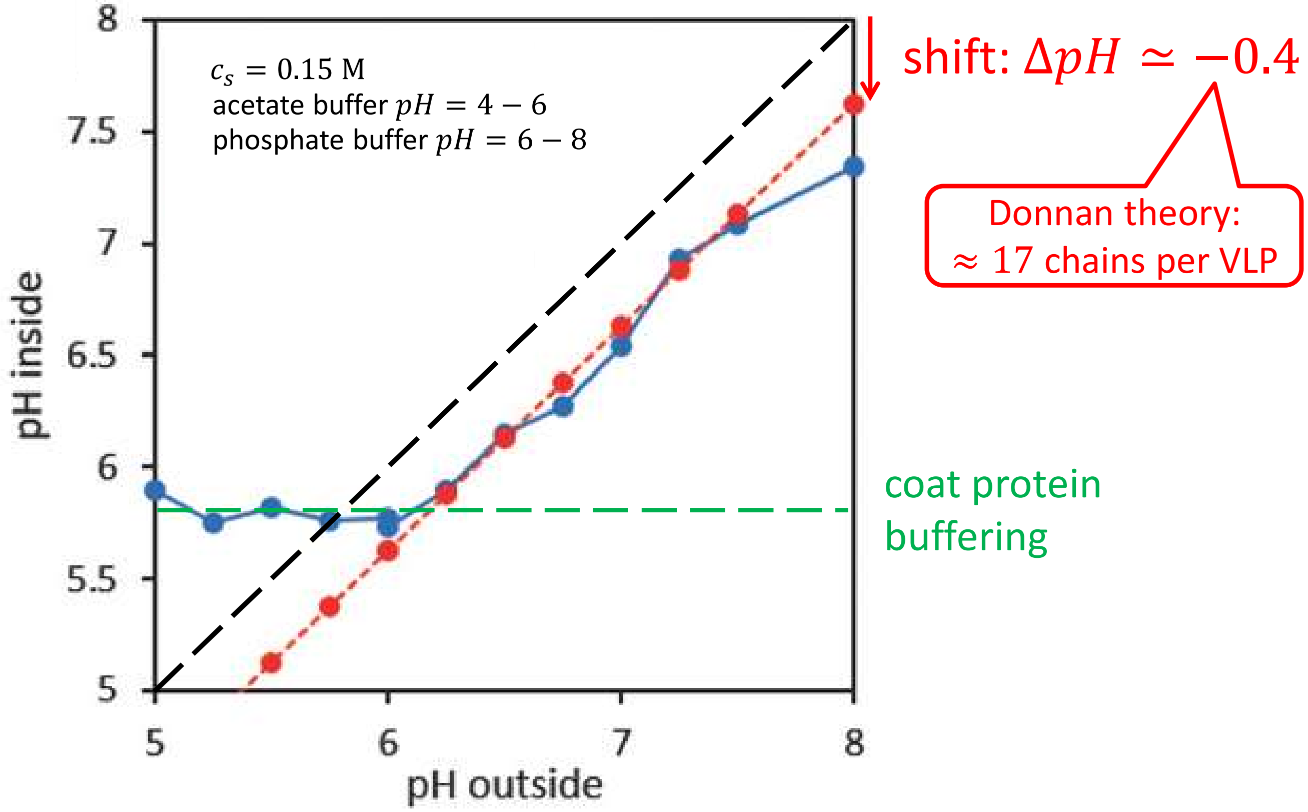
Muhren et al. *J. Phys. Chem. B* **127** (2023), 2160.

pHs inside and outside VLPs are not the same...

7.5 kDa random co-polymer
“FMA-PSS”

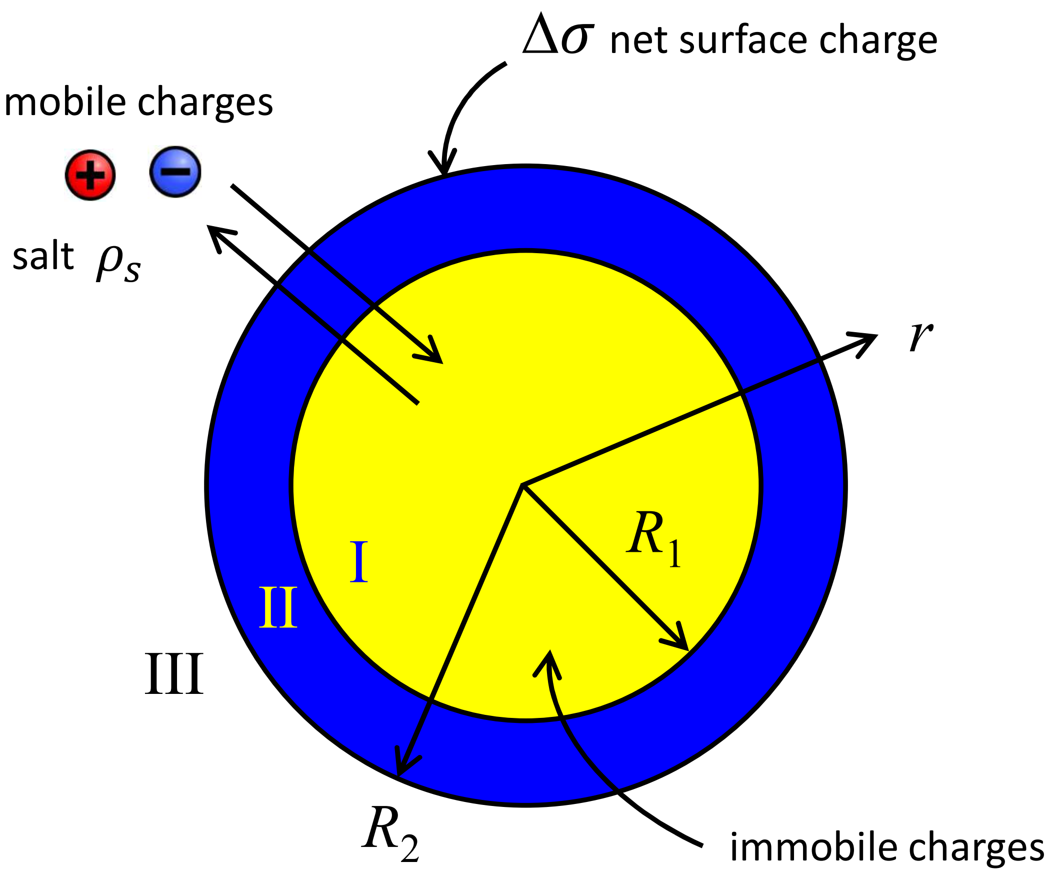


FMA-PSS + CCMV
T=1 virus-like particle



Maassen et al. *Small* **14** (2018), 1802081.

A simple electrostatic model...



$$\Gamma = (\rho_+ - \rho_-)/2\rho_s$$

"degree of overcharging"

Poisson-Boltzmann theory

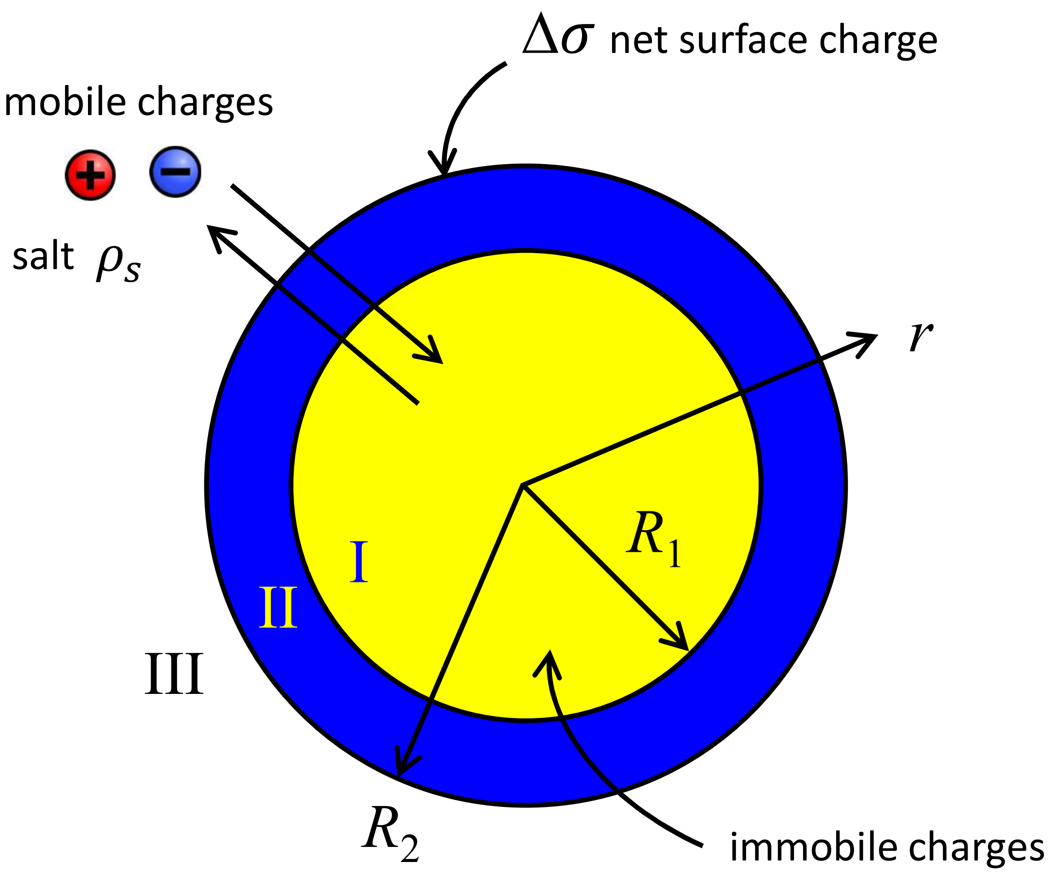
$$\begin{cases} \nabla^2\psi_I = \sinh\psi_I - \Gamma \\ \nabla^2\psi_{II} = 0 \\ \nabla^2\psi_{III} = \sinh\psi_{III} \end{cases}$$

boundary conditions

$$\begin{cases} \partial_r\psi_I(0) = 0 \\ \psi_I(R_1) = \psi_{II}(R_1) \\ \partial_r\psi_I(R_1) = \partial_r\psi_{II}(R_1) \\ \psi_{II}(R_2) = \psi_{III}(R_1) \\ \partial_r\psi_{II}(R_2) = \partial_r\psi_{III}(R_2) + 4\pi\Delta\sigma \\ \psi_{III}(\infty) = 0 \end{cases}$$

Muhren et al. *J. Phys. Chem. B* **127** (2023), 2160.

A simple electrostatic model...



$$\Gamma = (\rho_+ - \rho_-)/2\rho_s$$

"degree of overcharging"

Poisson-Boltzmann theory

$$\begin{cases} \nabla^2 \psi_I = \sinh \psi_I - \Gamma \\ \uparrow \\ \psi_I(r) = \phi + \Delta\psi_I(r) \end{cases}$$

$\downarrow$

Donnan potential $\quad \phi = \operatorname{arcsinh} \Gamma$

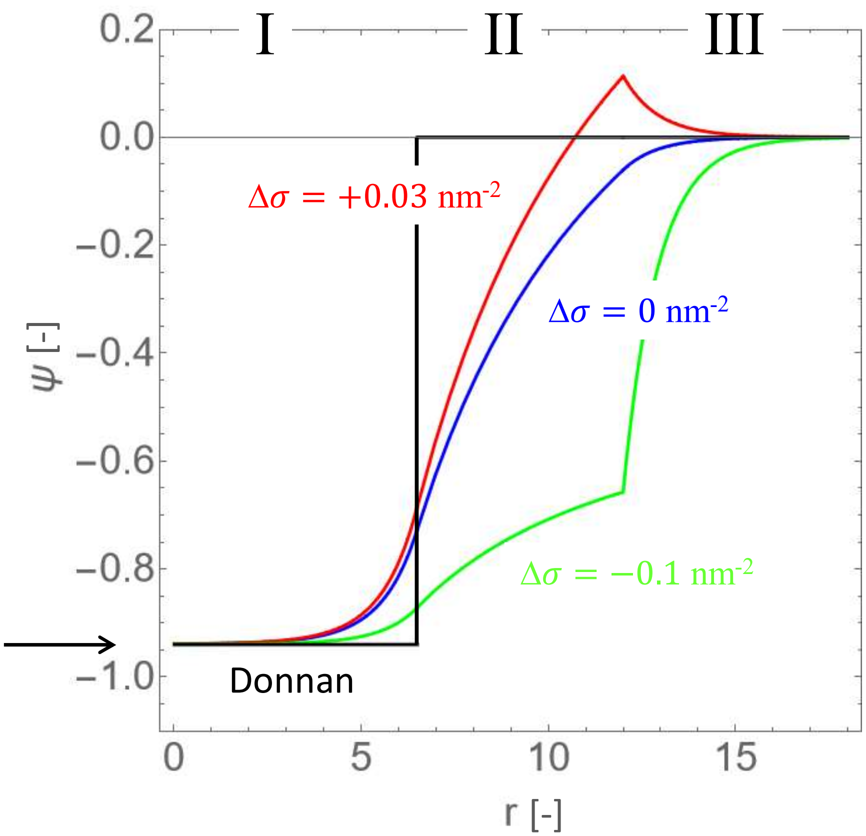
$\downarrow$

$$\begin{cases} \nabla^2 \Delta\psi_I = \sqrt{1+\Gamma^2} \times \Delta\psi_I + \cdots \\ \nabla^2 \psi_{II} = 0 \\ \nabla^2 \psi_{III} = \psi_{III} + \cdots \end{cases}$$

Lifson *J. Chem. Phys.* **27** (1957), 700.
Donnan *Z. Elektrochem. Angew. Phys. Chem.* **17** (1911), 572.
Muhren et al. *J. Phys. Chem. B* **127** (2023), 2160.

Donnan vs Poisson-Boltzmann theory…

$$\Delta pH = \frac{\psi}{\ln 10} = -0.4$$



CCMV $T = 1$

FMA-PSS 7.5 kDa

$R_1 = 5.0$ nm

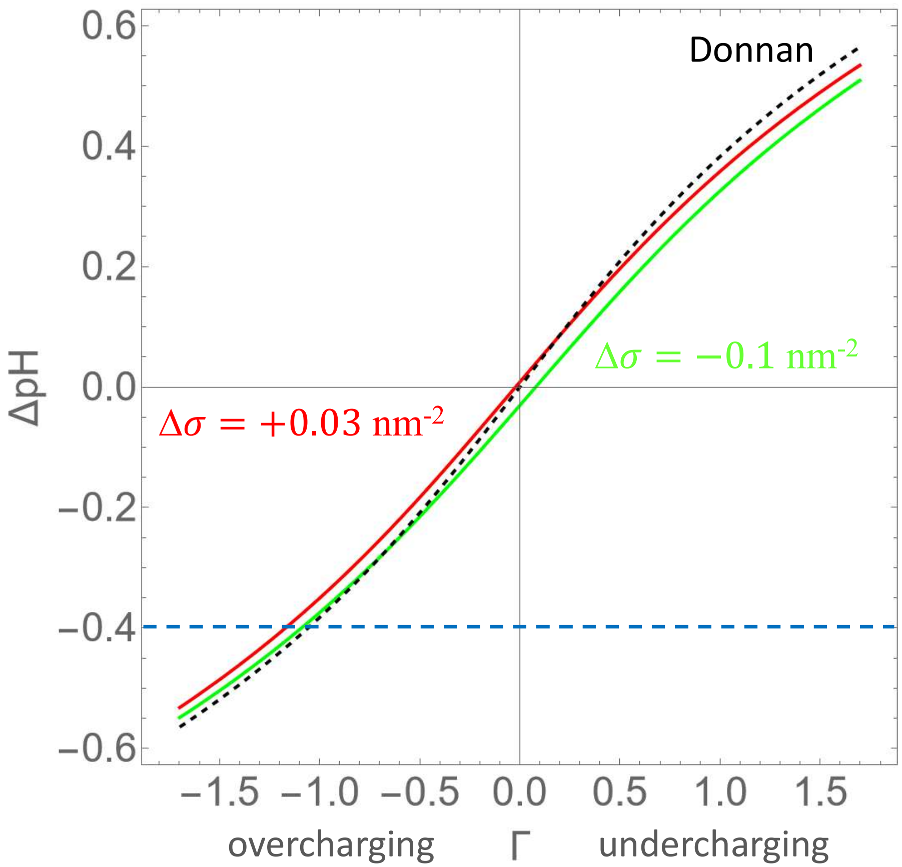
$R_2 = 9.5$ nm

$c_s = 0.15$ M

$pH = 6 - 8$

Maassen et al. *Small* **14** (2018), 1802081.
Vega-Acosta et al. *J. Phys. Chem. B* **118** (2014), 1984.
Muhren et al. *J. Phys. Chem. B* **127** (2023), 2160.

Donnan vs Poisson-Boltzmann theory…



CCMV $T = 1 \longrightarrow Q_+ = 600$

FMA-PSS 7.5 kDa

$R_1 = 5.0$ nm

$R_2 = 9.5$ nm

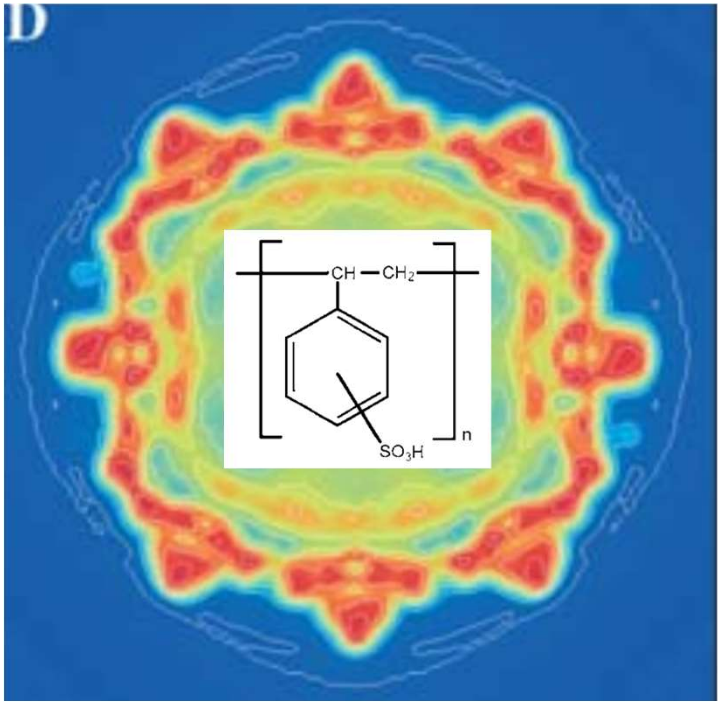
$c_s = 0.15$ M

$pH = 6 - 8$

$\approx 17 \rightarrow \approx 18$ chains per VLP

Maassen et al. *Small* **14** (2018), 1802081.
Vega-Acosta et al. *J. Phys. Chem. B* **118** (2014), 1984.
Muhren et al. *J. Phys. Chem. B* **127** (2023), 2160.

Donnan vs Poisson-Boltzmann theory…



Doan et al. *J. Struct. Biol.* **144** (2003), 253.

HCRSV $T = 3 \longrightarrow Q_+ = 2880$

PSA 990 kDa $\longrightarrow Q_- = 5400$

$pK_a = 1.0$

$pH = 5$

$R_1 = 9.0$ nm

$R_2 = 15$ nm

$c_s = 0.16$ M

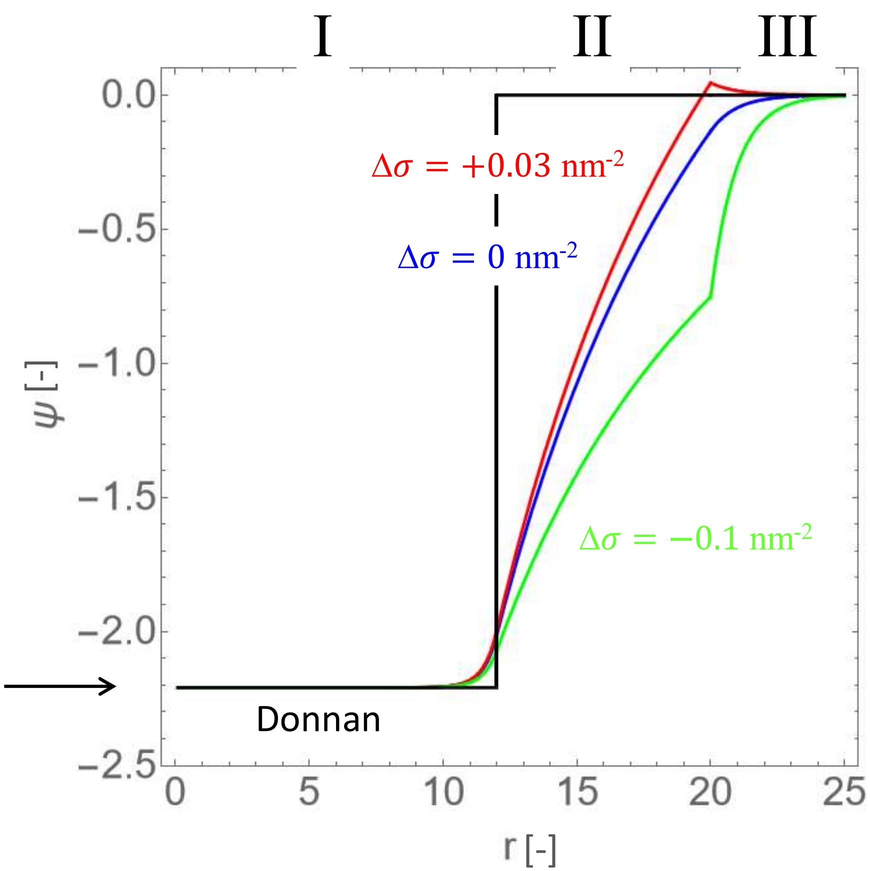
$\Delta\sigma = -0.01$ nm^{-2}

$$\Gamma = -4.3$$

$$\Delta pH = \frac{\psi}{\ln 10} = -0.9$$

Ren et al. *J. Gen. Virol.* **87** (2006), 2749.

Donnan vs Poisson-Boltzmann theory…



HCRSV $T = 3$ ⟶ $Q_+ = 2880$

PSA 990 kDa ⟶ $Q_- = 5400$

$pK_a = 1.0$

$pH = 5$

$R_1 = 9.0$ nm

$R_2 = 15$ nm

$c_s = 0.16$ M

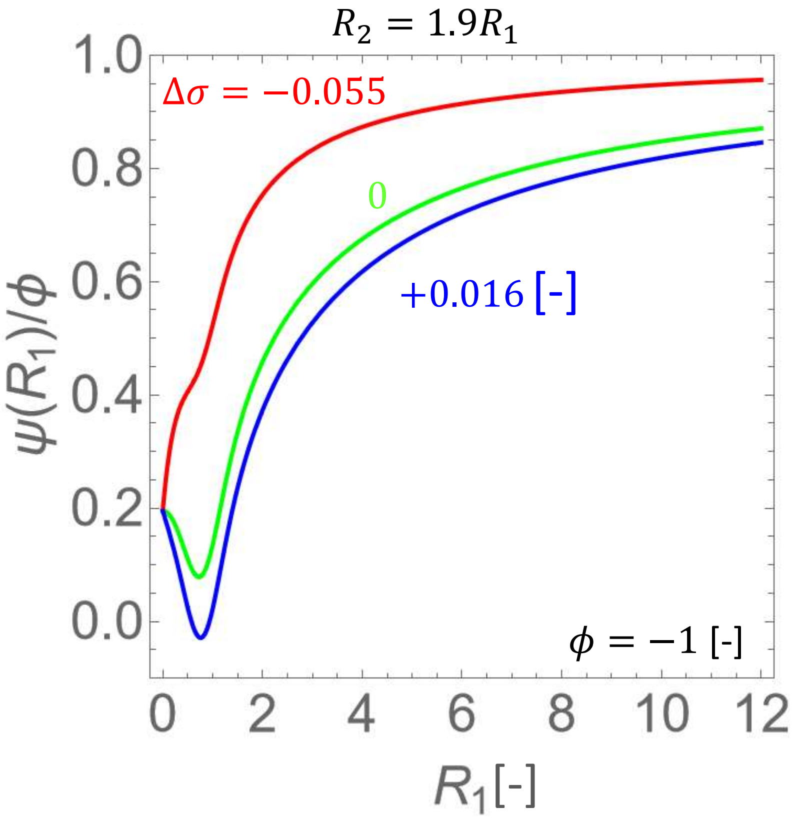
$\Delta\sigma = -0.01$ nm^{-2}

$$\Gamma = -4.3$$

$$\Delta pH = \frac{\psi}{\ln 10} = -0.9$$

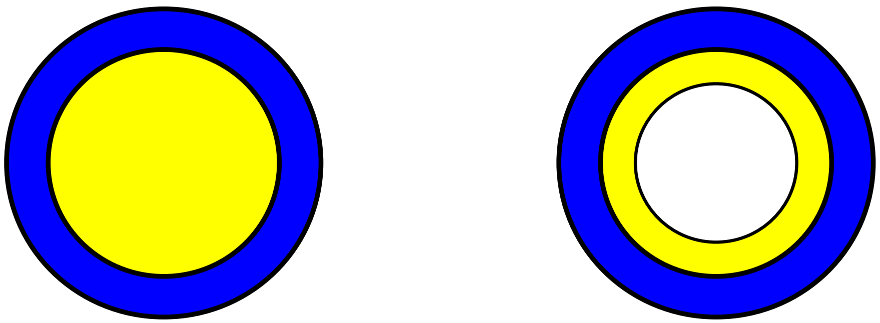
Ren et al. *J. Gen. Virol.* **87** (2006), 2749.

Breakdown of Donnan theory...



Take-home messages…

- The Donnan effect gives rise to pH differential across protein nanocages
- This differential can be as large as a full pH unit
- Donnan theory is consistent with Poisson-Boltzmann theory
- Donnan theory is simple yet under most practical conditions accurate
- Can be used to predict pH gradients or degrees of overcharging
- Assumption of uniform immobile charge distribution not strictly necessary



Odijk et al. *J. Phys. Chem. B* **107** (2003), 8074.
Gopmandal & Duval *Curr. Opin. Coll. Interface Sci.* **60** (2022), 101605.

Acknowledgments...

Thomas Muhren

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

Stan Maassen **Jeroen Cornelissen**

UNIVERSITY OF TWENTE.