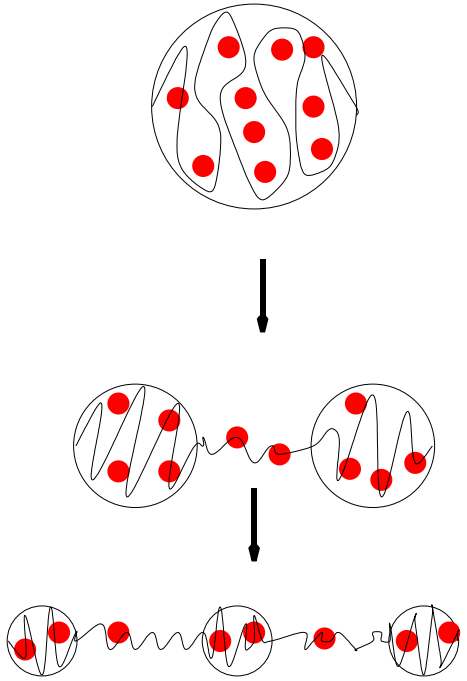
Part 2- Special Topics

- Polyelectrolytes in poor solvents
- Polyelectrolyte gels
- How to treat weak charges
- Polyelectrolyte brushes
- Phase behavior of polyelectrolyte complexes
- Intrinsically disordered proteins as polyampholytes

Topic: PE in Poor Solvents



Carbon backbone (oil) is poorly soluble in water!

Early cigar model (Khokhlov 1981)

Rayleigh instability (1882):
(charged oil drop)

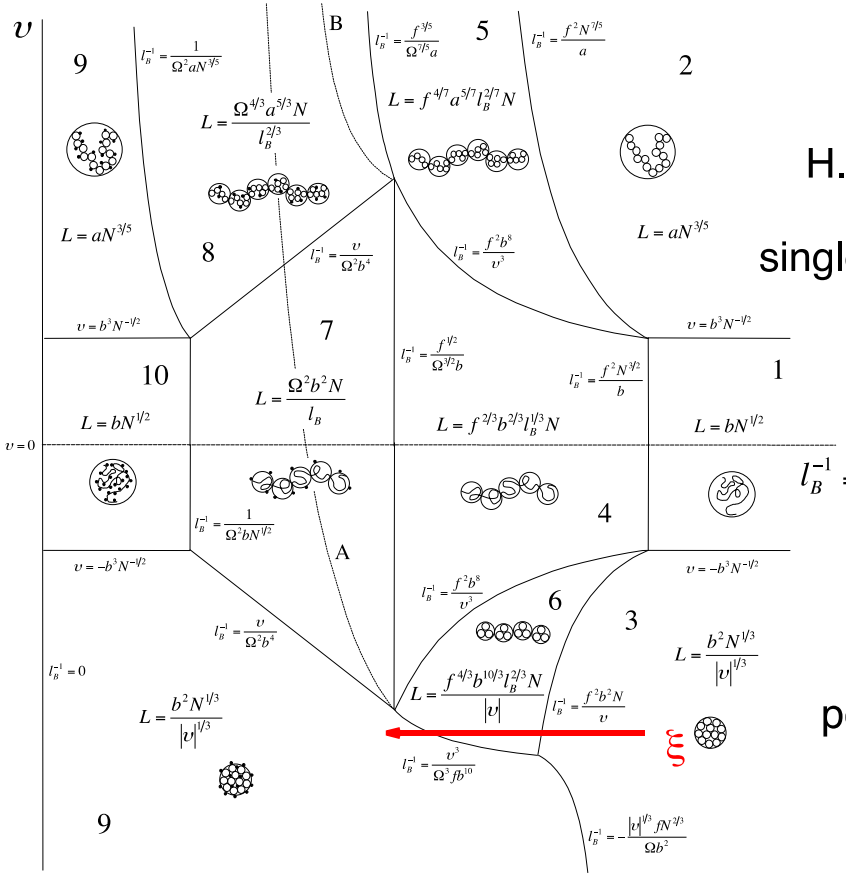
$$\frac{q^2}{4\pi\epsilon R} = \gamma R^2$$

pearl-necklace model

Kantor, Kardar - 1994: Polyampholyte

Dobrynin, Rubinstein, Obukhov - 1996: Polyelectrolytes

Single Chain PE Phase Diagram

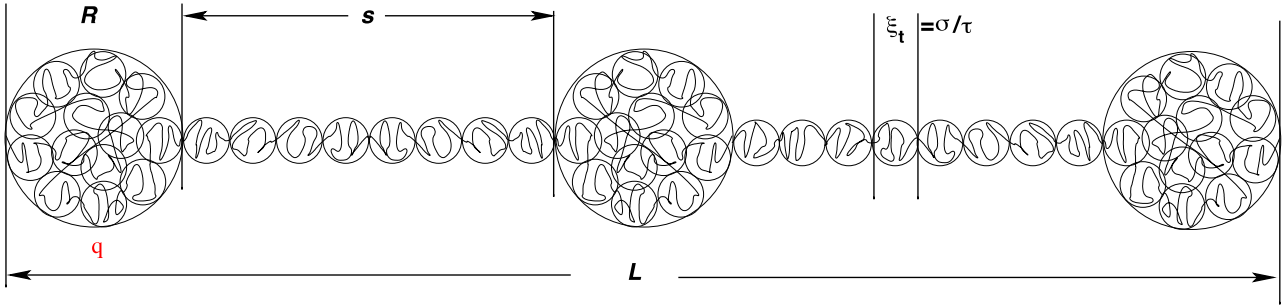


H. Schiessel, P. Pincus

single chain phase diagram

poor solvent

Scaling Picture for Weakly Charged PEs



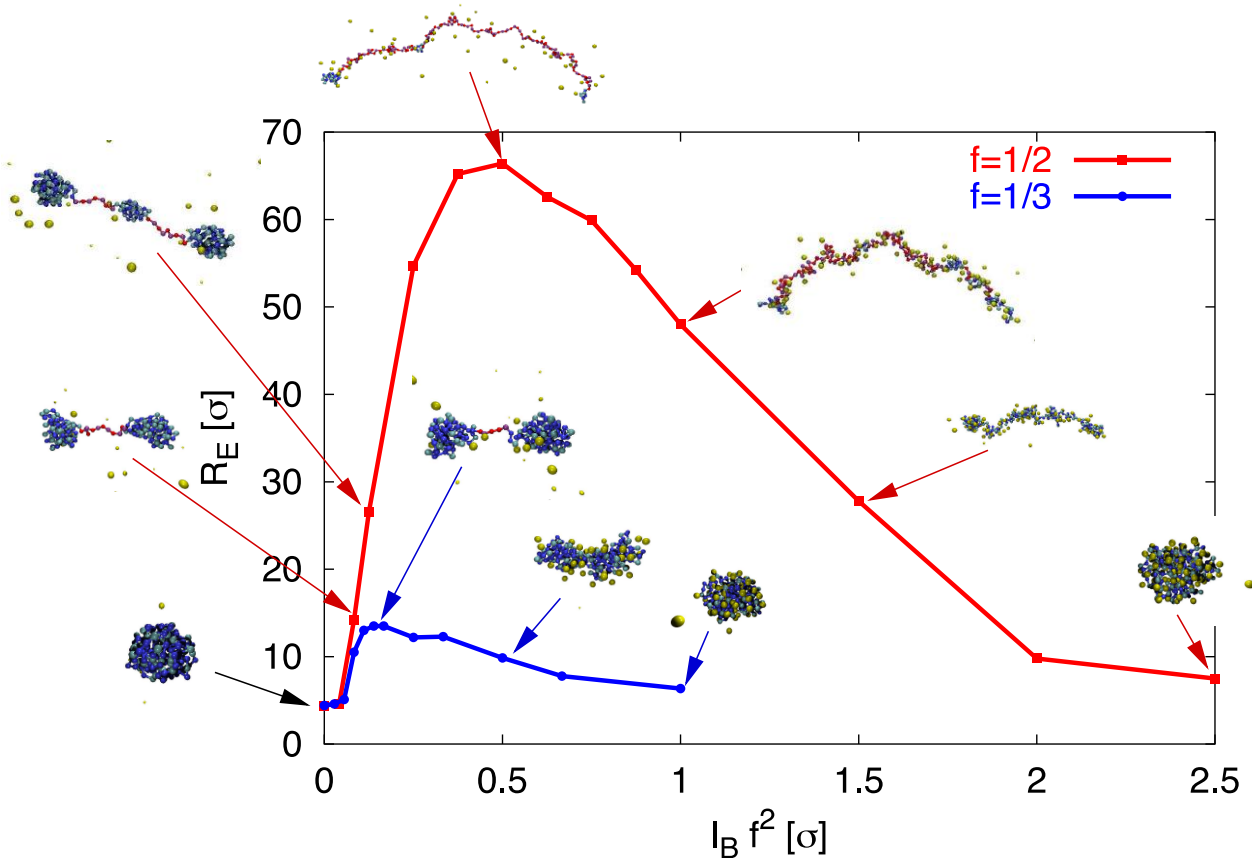
$$F/k_{\mathrm{B}}T = n_P\left(\frac{\ell_{\mathrm{B}}q^2}{R}+\gamma R^2\right)+(n_P-1)\,\gamma\xi_t s+\frac{\ell_{\mathrm{B}}Q^2}{L}$$

number of pearls: $n_P = Nf^2\ell_{\mathrm{B}}\frac{1}{\sigma\tau}$ necklace length: $L = N(\frac{f^2\ell_{\mathrm{B}}\sigma}{\tau})^{1/2}$

scaling variable: $f^2\ell_{\mathrm{B}}$ order parameter : $m = -k_BT\frac{\sigma N^{1/3}}{2R_H}$

Manning parameter: $\xi = \frac{f\ell_{\mathrm{B}}}{\sigma}$

Varying *f* and Validity of Scaling



Pearl-necklace fluctuations

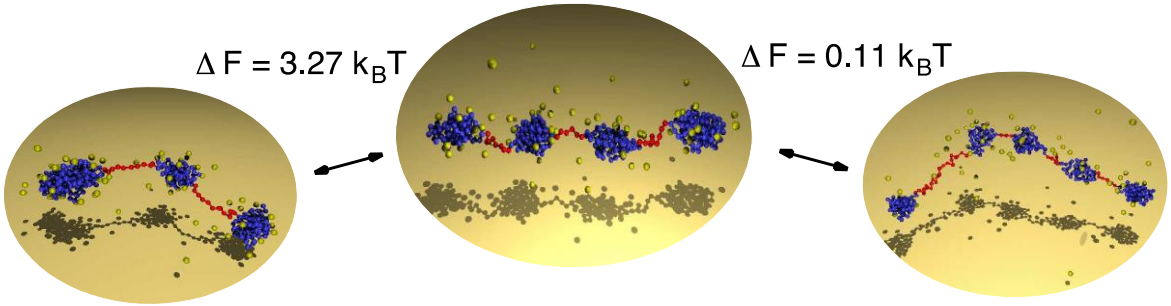
5 chains with

$N = 190, \quad f = 1/3$

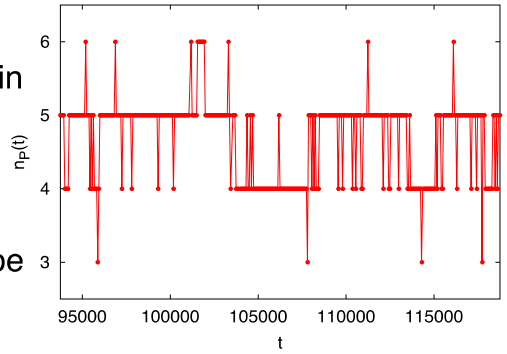
$\rho = 0.00002 \qquad \varepsilon = 1.75$

$l_B = 1.5 \quad \xi = 0.5$

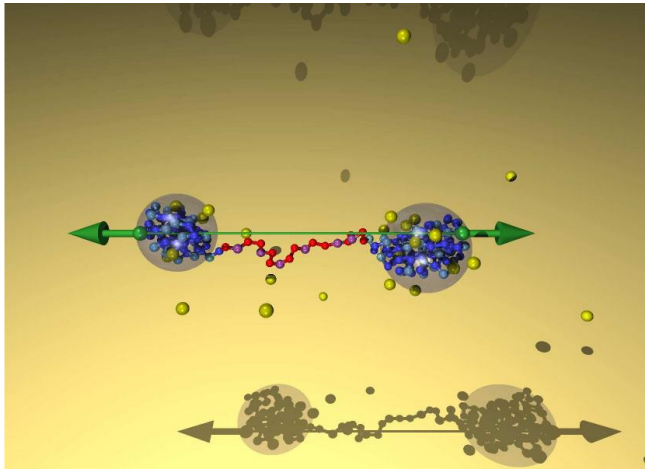
Fluctuations of pearl Structure

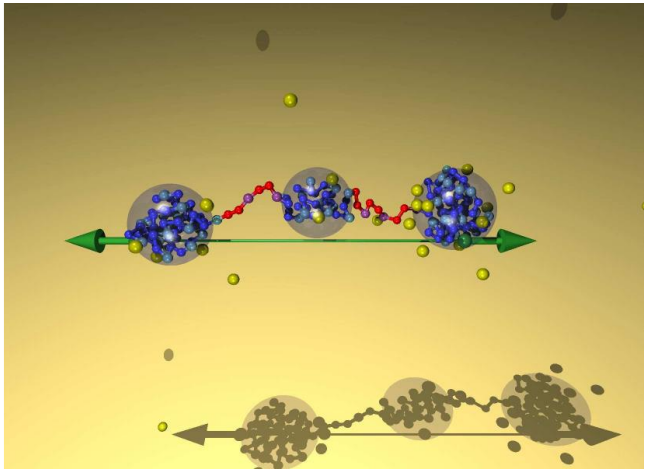


- structure type fluctuates for a single chain
- no frozen states
- large coexistence regime
- counterion distribution ⟷ structure type



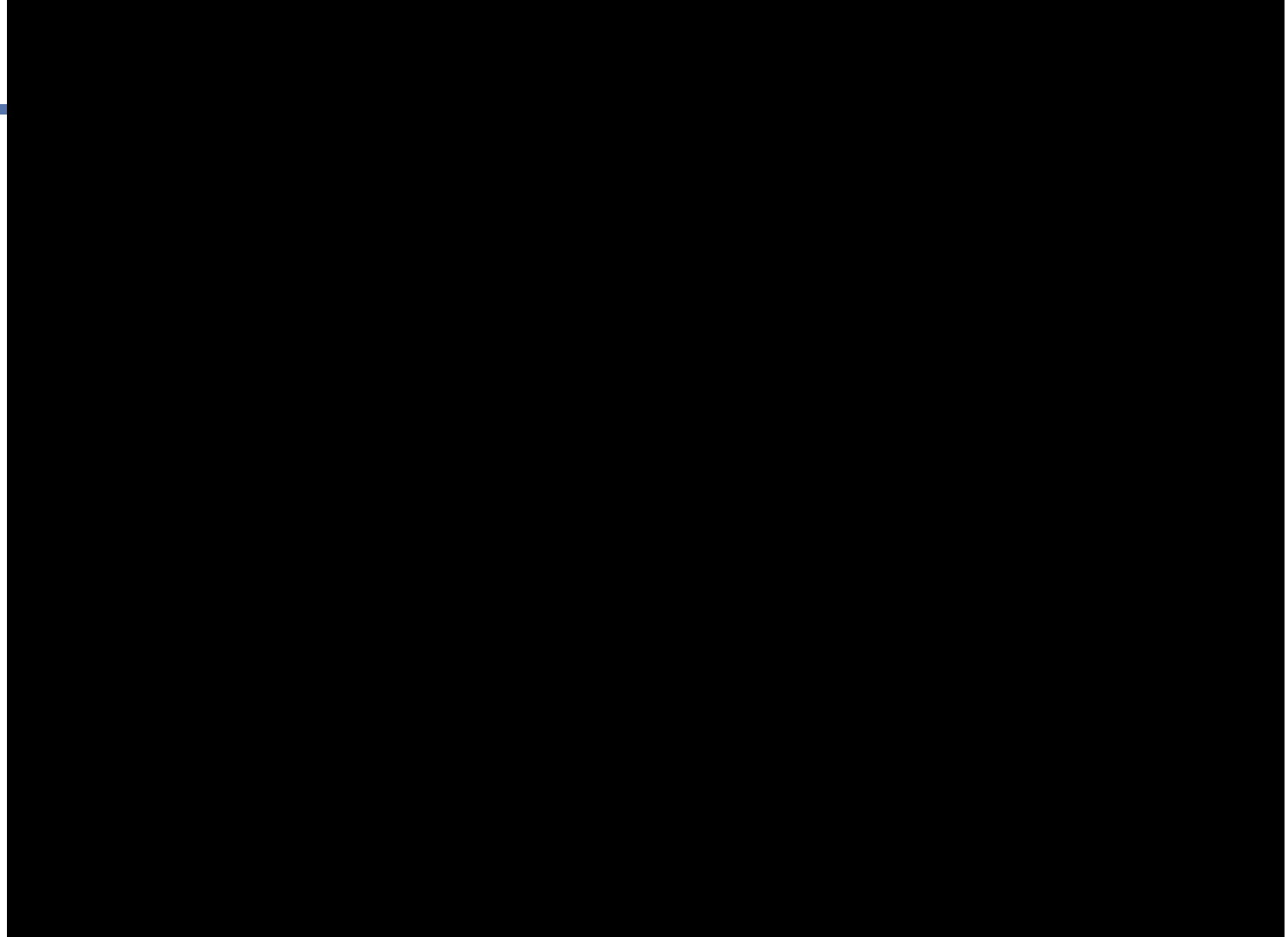
AFM Force Spectroscopy





Pulling statically along the main axis of gyration

Scaling theory (Tamashiro, Schiessel) predicts initial increase in pearl number $\longrightarrow$ confirmed! See Movie !



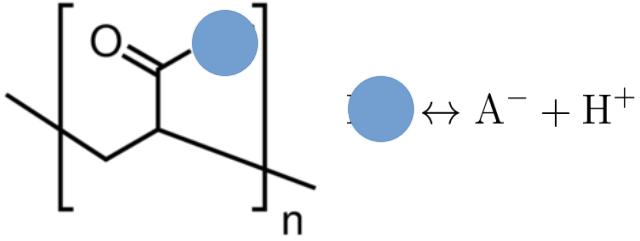
Conclusions Poor Solvent PEs

- Strong deviations from scaling theories in the strongly coupled regime
- Strong fluctuations make it difficult to experimentally observe pearl/necklace structures
- Coexisting pearl regimes

Hydrogels: Smart Funtional Materials

Outline

- Strong gels in contact with a reservoir salt solution
  - Periodic gel model (MD/MC)
  - Single chain cell-gel model (MD/MC)
  - Poisson-Boltzmann cell-gel model
- Weak gels
  - Algorithmic details MC/PB
  - pH dependent swelling
- (Applications)
  - Experiments
  - Desalination (with Katchalsky Model)
  - Huge pKa shift observed in brushes and explained simply by Donnan theory
  - Gelation of PE stars

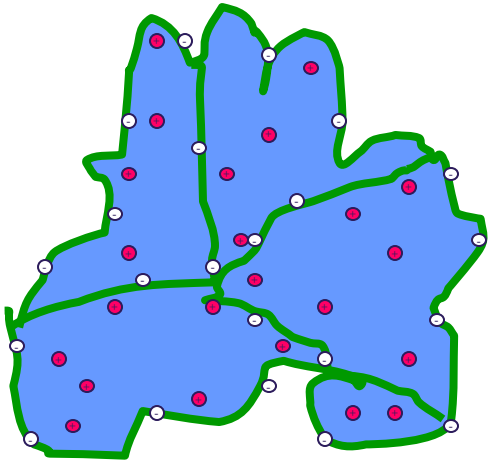


Why do Polyelectrolyte Gels Swell?

Poly-salt (dry)

neutral

Ions dissociate in H_2O

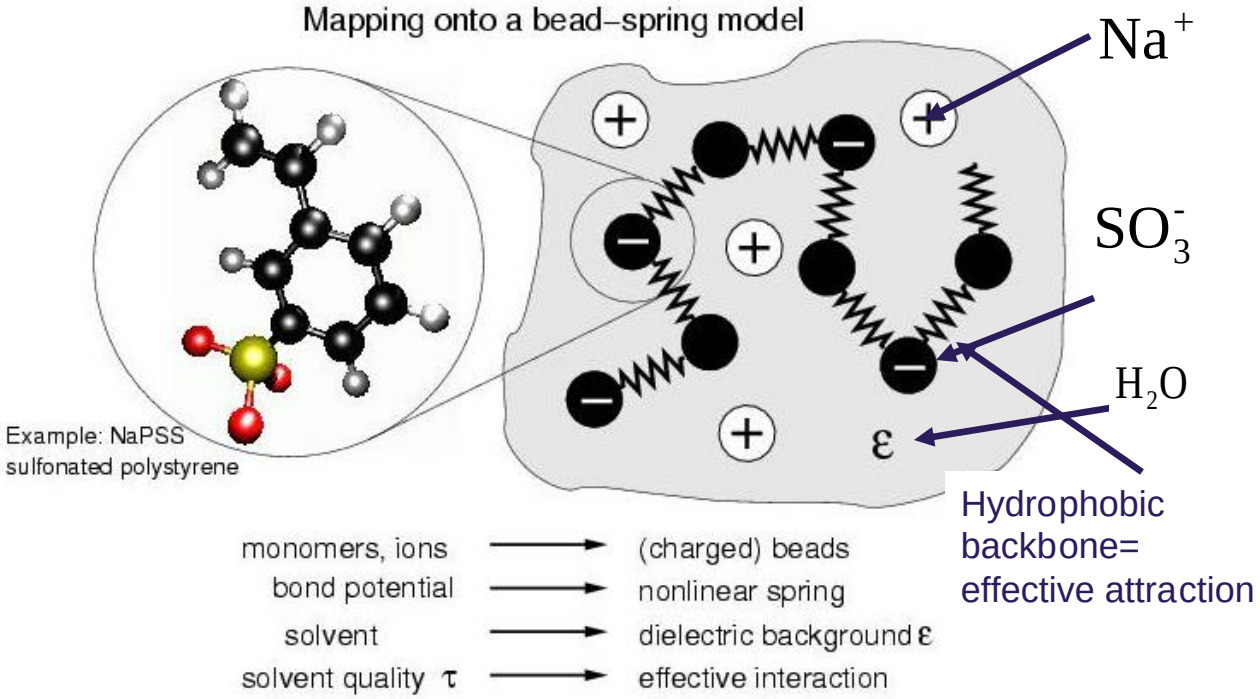


The free ions like space (entropy)
=> Osmotic pressure of counterions blows the gel up

The swelling proceeds until $P_{entropic} = P_{elastic}$

The gel can swell up to a few thousands times of its initial volume

Coarse-Graining Procedure

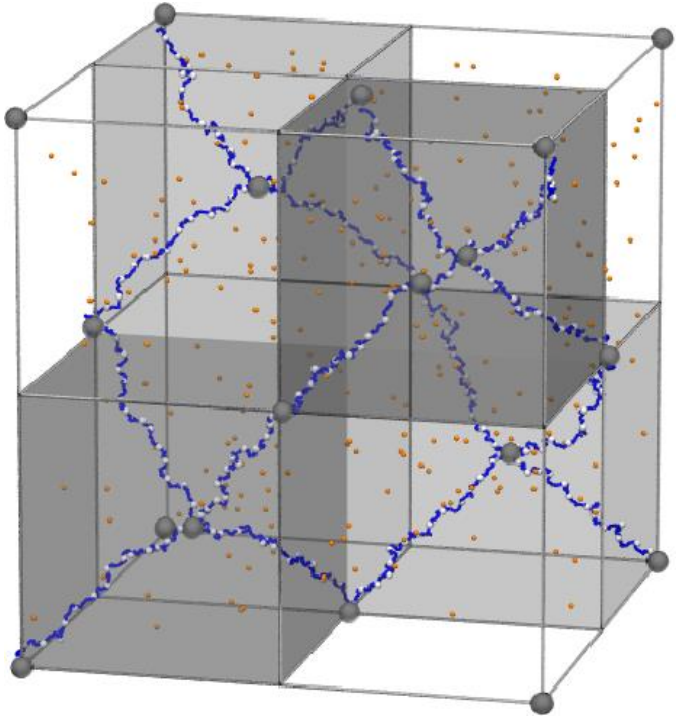


Polyelectrolyte Model Network

Parameters:

8 tetrafunctional nodes
N_P = 16 chains at N_m = 39 ,…, 259
f = 1/16 ,…, 1/1 $\Rightarrow$ N_{Cl} = 88 ,…,4152
($\Rightarrow$ charged particles 636 ,…, 8304)

- tune electrostatic interaction with Bjerrum length

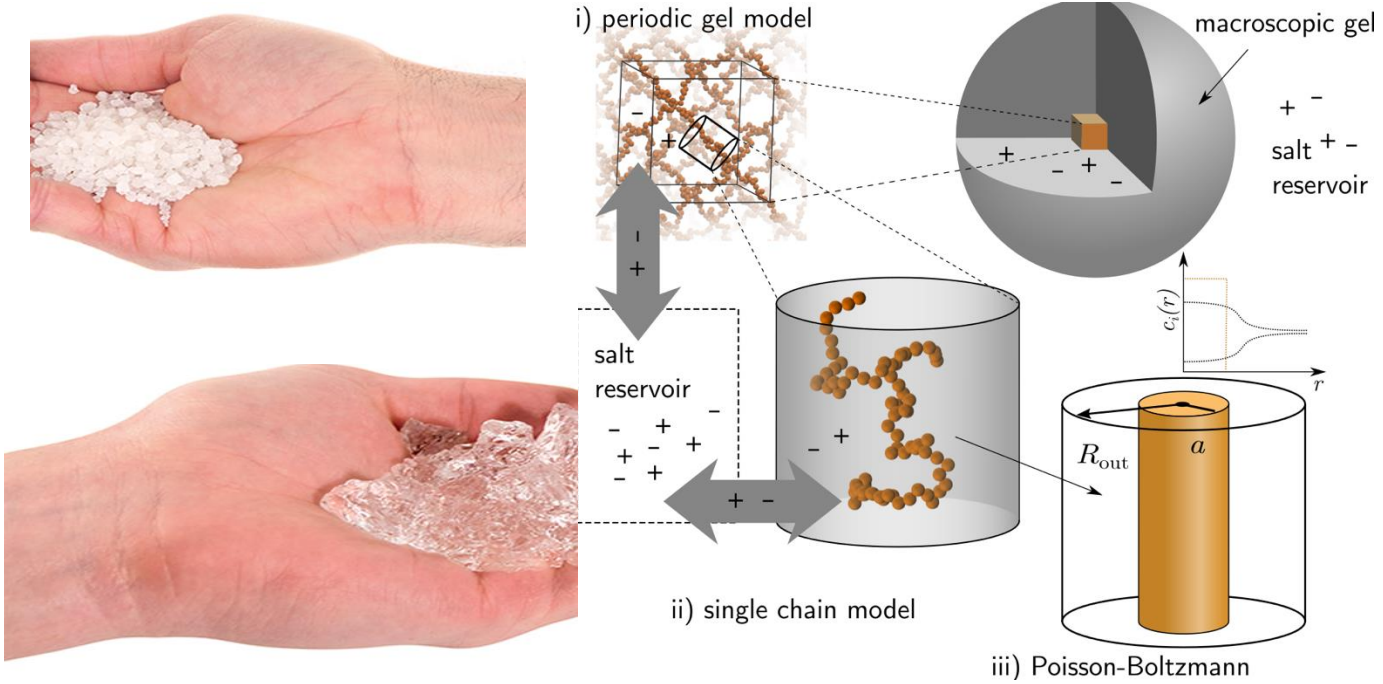


diamond-like topology

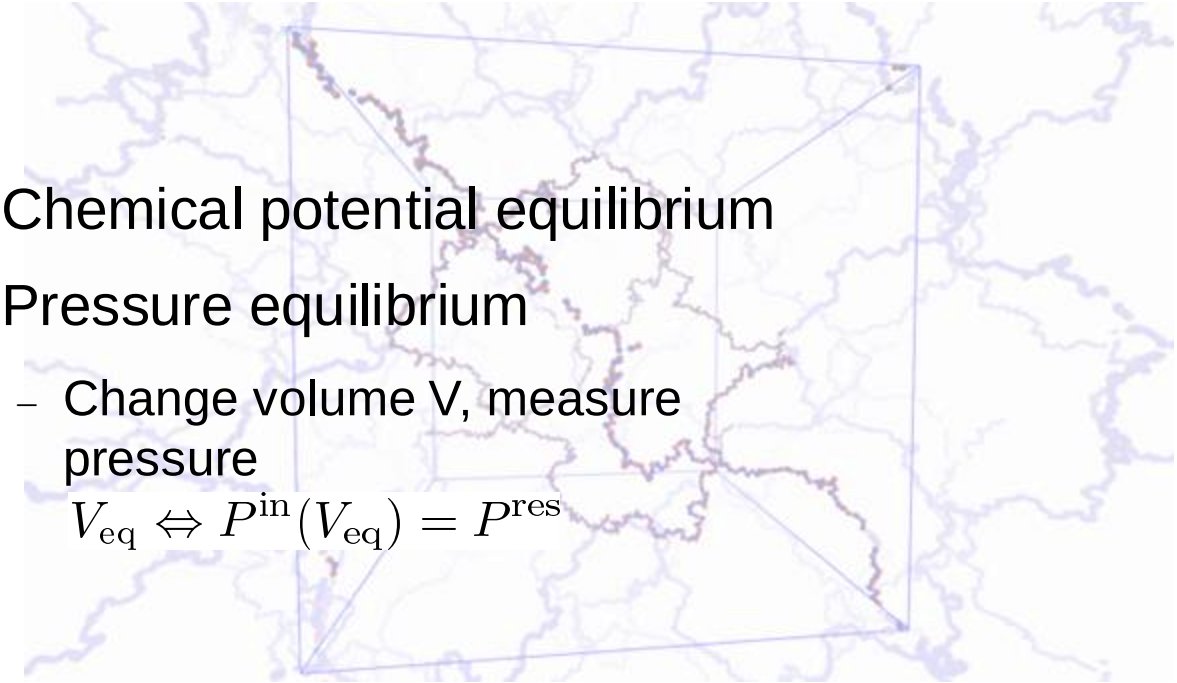
observables:

- chain's end-to-end distance $\langle R_E^2 \rangle$
- osmotic pressure Π_C of counterions
- elastic pressure Π_E of chains
- electrostatic pressure Π_{ℓ_B}

Modeling Approaches on Different Levels



Previous Work: Periodic Gel with MD



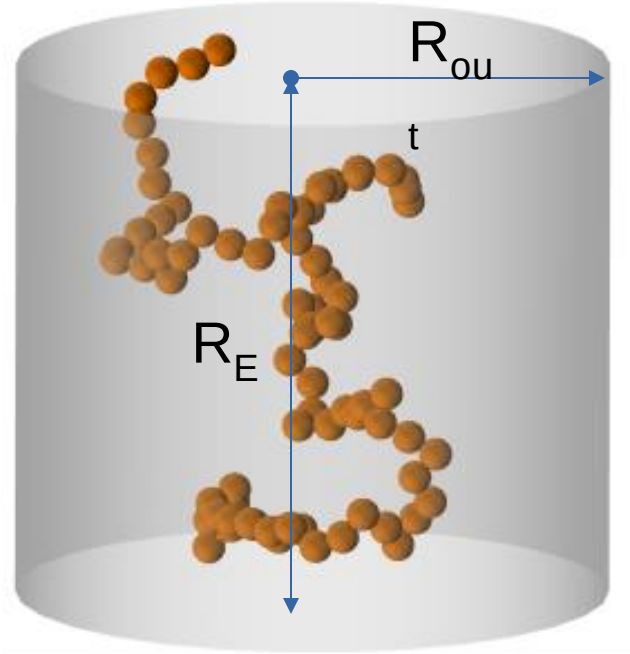
- Chemical potential equilibrium
- Pressure equilibrium
  - Change volume V, measure pressure

$$V_{\mathrm{eq}} \Leftrightarrow P^{\mathrm{in}}(V_{\mathrm{eq}}) = P^{\mathrm{res}}$$

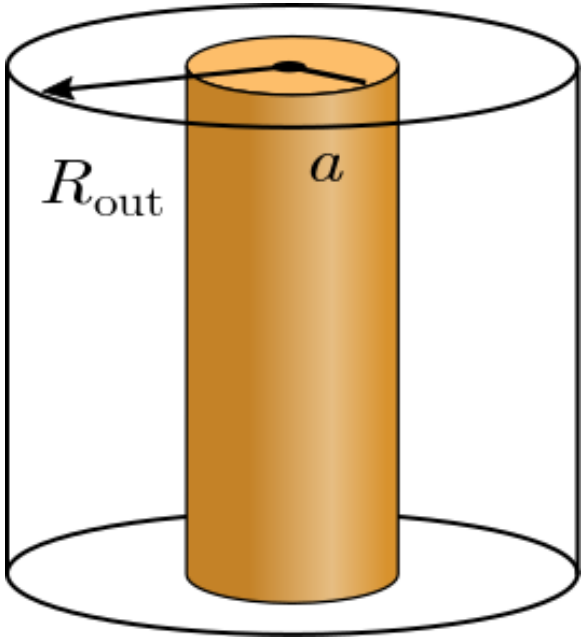
Kosovan, Richter, Holm, Macromolecules, 2015

Simplification: Cell-Gel Models (CGM)

$$V_{\text{chain}} = R_E^3/A = \pi R_{\text{out}}^2 R_E$$

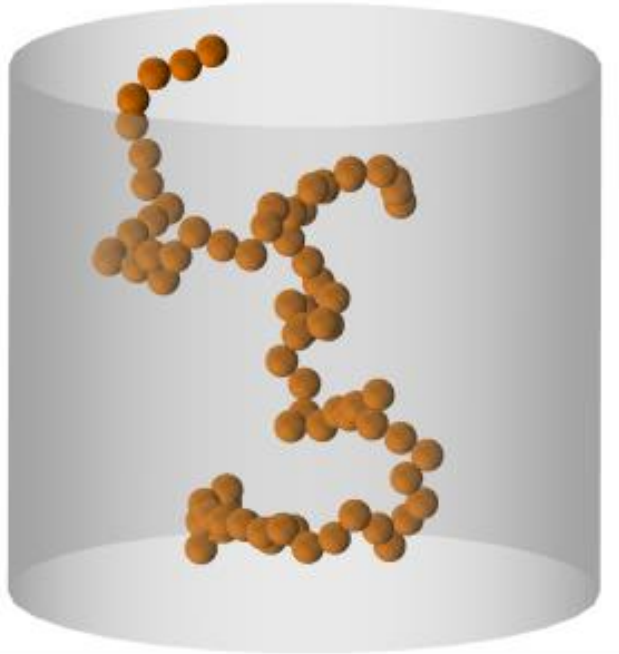


Particle-Based single chain CGM



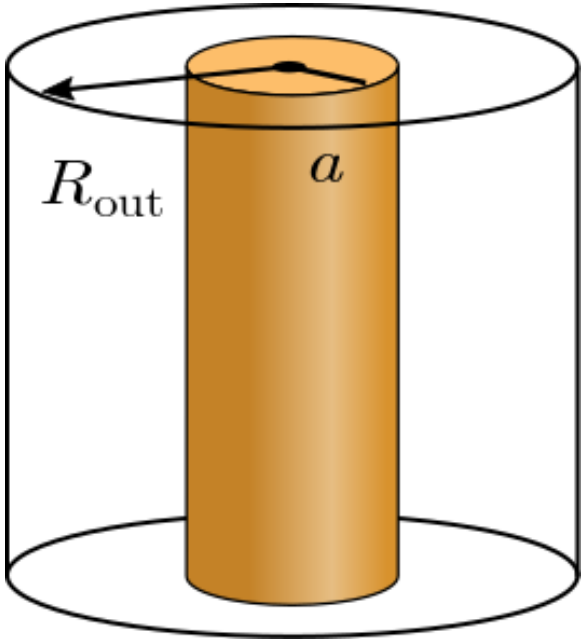
Poisson-Boltzmann CGM

Particle-Based Single Chain CGM



- MD simulation of single chain in periodically replicated cylinder
- P3M, WCA, FENE
- Langevin Thermostat
- Grand canonical particle insertions
- Measuring virial pressure and pressure on the walls

Simplification PB Model



- Match radius *a* such that charges have the same distance from the end-to-end axis as in MD ($\langle r \rangle_{MD}$)

Solve PB equation:

$$-\nabla^2\psi(\vec{r}) = \rho(\vec{r})/\epsilon$$

$$\rho(\vec{r}) = \rho_f(\vec{r}) + \sum_i c_i^b \exp\left(-\frac{z_i e_o \psi(\vec{r})}{k_B T}\right)$$

$$\rho_f(\vec{r}) = -N f e_0 p_a(\vec{r})$$

Boundary conditions: $E_r(0)=E_r(R_{out})=0$

$$P_{\text{cap}} = \underbrace{k_{\text{B}}T \sum_i \langle c_i \rangle_z}_{\text{kinetic}} + \underbrace{\frac{\epsilon_0 \epsilon_{\text{r}}}{2} \langle E_\rho^2 \rangle_z}_{\text{Maxwell}} - \underbrace{\frac{k_{\text{B}}T}{\pi R_{\text{out}}^2 b} \mathcal{L}^{-1}\left(\frac{R_{\text{e}}}{R_{\max}}\right)}_{\text{stretching}}$$

$$+ \underbrace{\frac{k_{\text{B}}T}{\pi R_{\text{out}}^2 b} \times \frac{\sqrt{\langle R_{\text{e,free}}^2 \rangle}^3}{R_{\text{e}}^3} \mathcal{L}^{-1}\left(\frac{\sqrt{\langle R_{\text{e,free}}^2 \rangle}}{R_{\max}}\right)}_{\text{confinement}}$$

$$P_{\text{side}} = k_{\text{B}}T \sum_i c_i(R_{\text{out}})$$

$$P^{\text{gel}} = \frac{1}{3}P_{\text{cap}} + \frac{2}{3}P_{\text{side}}$$

Katchalsky-Michaeli Model

A. Katchalsky, I. Michaeli, J. Polym. Sci. **15** 69 (1955).

Flory-Rehner type Ansatz $P_{ext} = P_{el} + P_{osm} + P_{str}$

$P_{el} = -k_B T \frac{c_{pol}}{N} \frac{(\alpha N)^2 \lambda_B}{3R_e} \left[\frac{2.5\xi}{(1+\xi)} - \ln(1+\xi)\right]$, Free energy for a stretched macromolecule with $\xi = \frac{6}{\kappa R_0}\left(\frac{V}{V_0}\right)^{\frac{1}{3}}$.

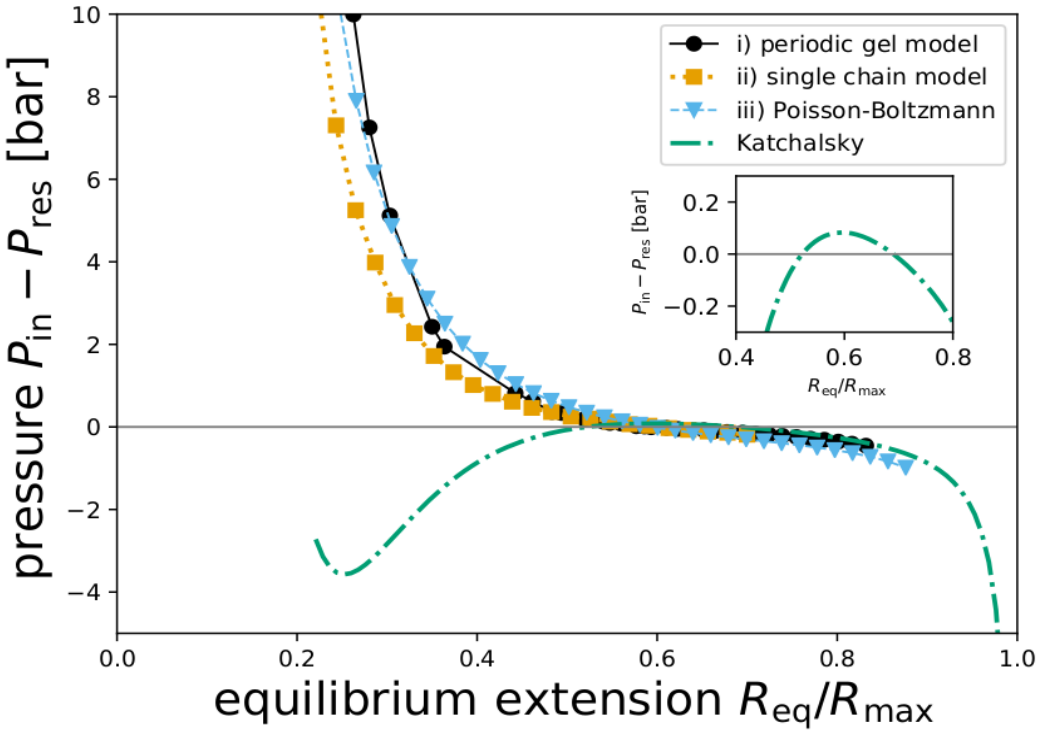
$P_{str}(R_e) = -k_B T \frac{c_{pol}}{3bN} R_e \left(\mathcal{L}^{-1}\left(\frac{R_e}{bN}\right) - \mathcal{L}^{-1}\left(\frac{R_0}{bN}\right)\right)$, where $\mathcal{L}^{-1}$ denotes the Langevin function for the polymer elasticity

For chemical and mechanical equilibrium we need to satisfy two coupled equations

$P_{str} + P_{el} = P_{ext} - P_{osm} = P_{ext} - k_B T\left(2c_s^g + \alpha c_{pol} - 2c_s^b\right)$ and $c_s^g = \left(\left(\frac{\alpha c_{pol}}{2}\right)^2 + \left(c_s^b\right)^2 C\right)^{1/2} - \frac{\alpha c_{pol}}{2}$,

with $C = \exp\left(-\frac{c_{pol}}{2c_s^g + \alpha c_{pol}} \frac{6\alpha^2 N \lambda_B}{\kappa R_0^2 (1+\xi)}\right)$.

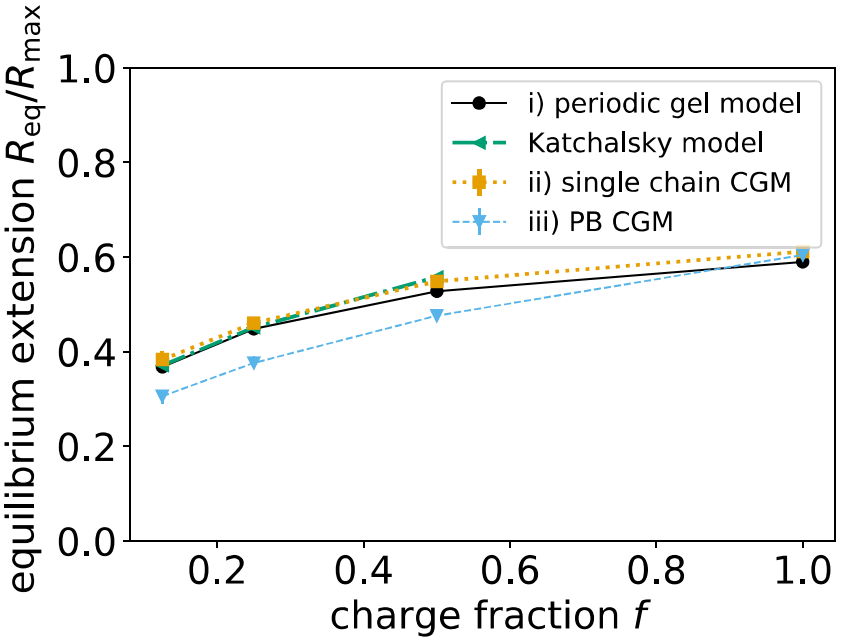
How to determine the Swelling Equilibrium

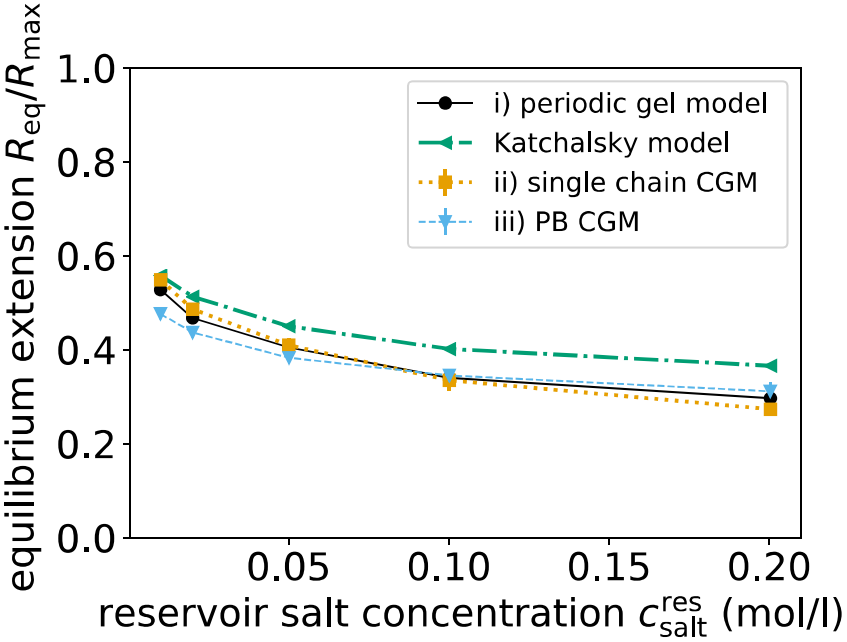


N=64, c_s=0.01 mol/l, f=1

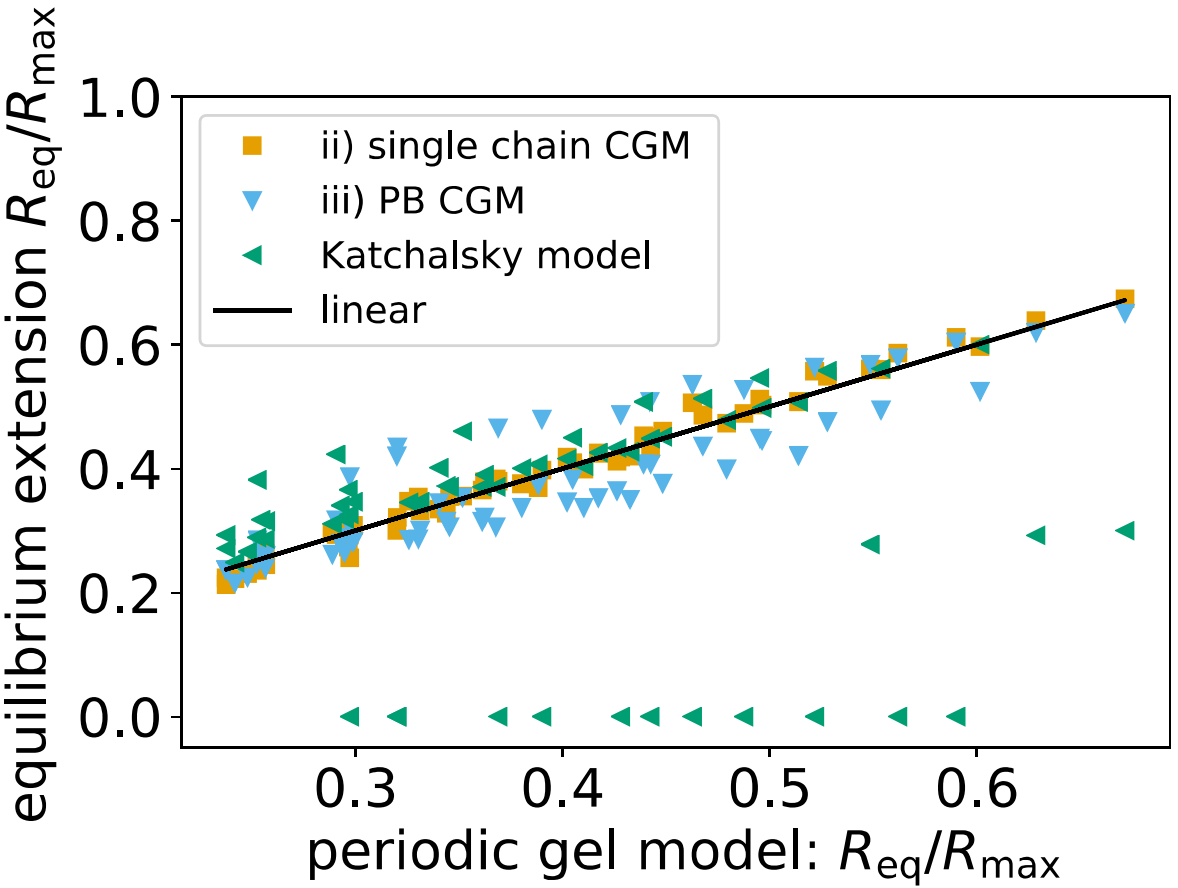
$$V_{\mathrm{eq}} \Leftrightarrow P^{\mathrm{in}}(V_{\mathrm{eq}}) - P^{\mathrm{res}} = 0$$

Results for the Equilibrium Extension





Comparison of all Models to Periodic Gel Model



Intermediate Conclusion

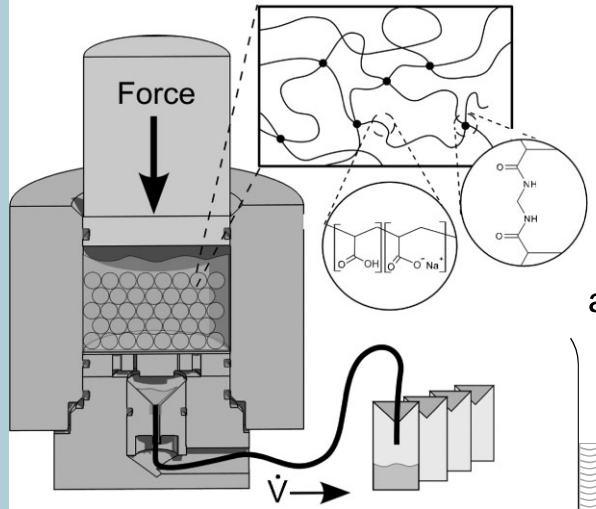
Complexity reduction is possible in various ways weeks->days->minutes

Single chain model optimal for best accuracy-time balance

Simple and old Katchalsky model works well for Manning parameters <1

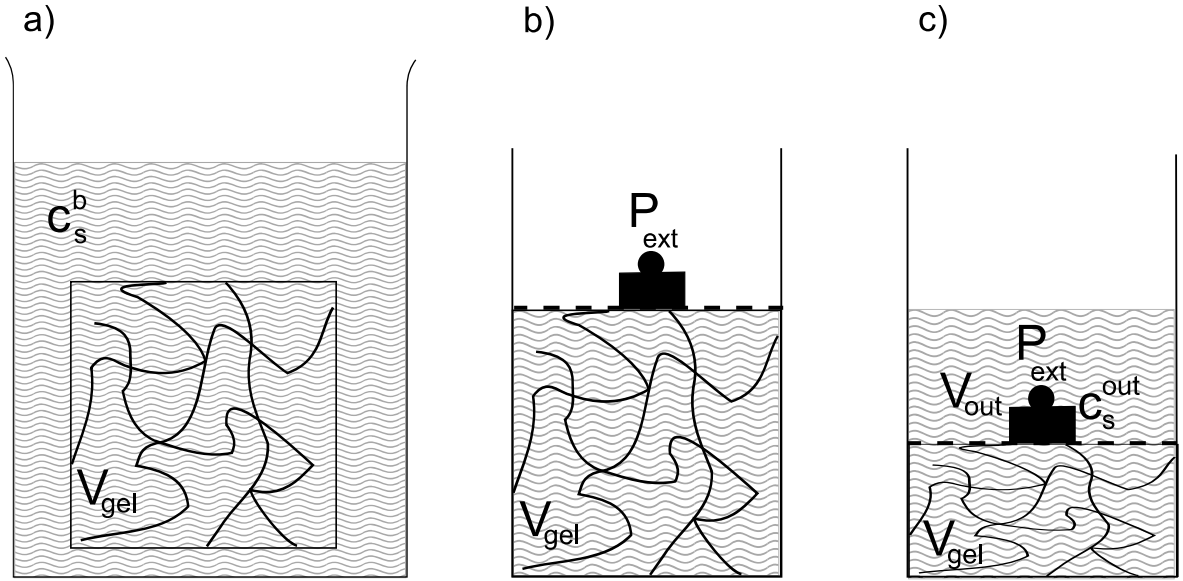
- J. Landsgesell et al., *Cell Model Approaches for Predicting the Swelling and Mechanical Properties of Polyelectrolyte Gels*, Macromolecules **52,** 9341-9353 (2019).
- J. Landsgesell et al., *Modeling Gel Swelling Equilibrium in the Mean Field: From Explicit to Poisson-Boltzmann Models*, Physical Review Letters **122,** 208002 (2019).

Desalination with Hydrogels



J. Höpfner, C. Klein, M. Wilhelm Macromol. Rapid Commun. **31** 1337–1340 (2010)

Need several pressure- desalination cycles until potable water level is reached

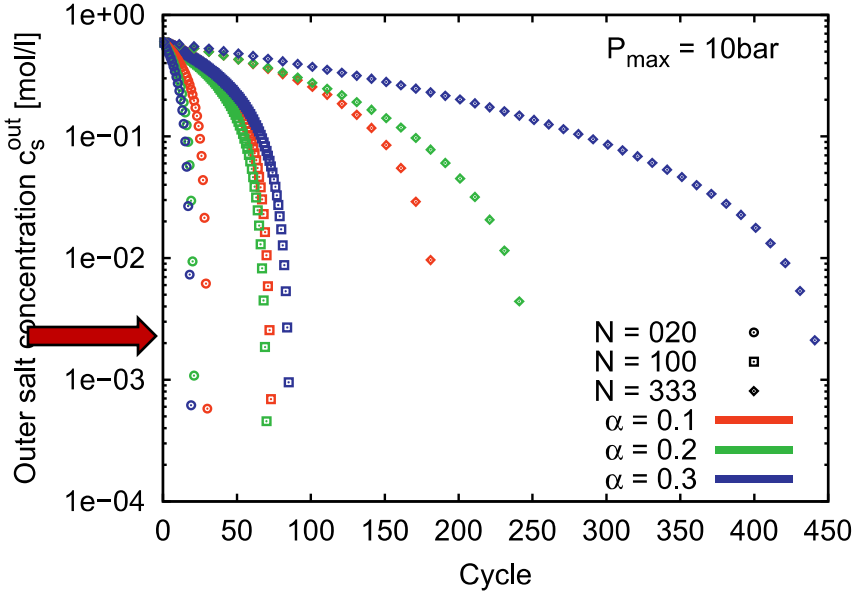


Theoretical Analysis Using the Simplest Model

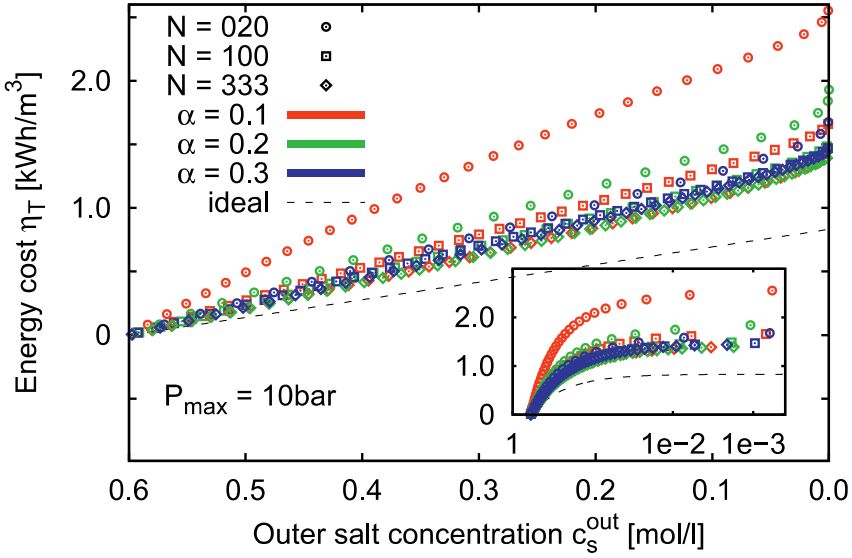
Based on the Katchalsky model:

A. Katchalsky, I. Michaeli, J. Polym. Sci. **15** 69 (1955) .

T. Richter et al., Desalination **414** 28–34 (2017)



Development of the outer salt concentration c^{out} for a set of gels that were compressed until P_{max} = 10 bar.



Cumulative energy cost per cubic meter η_T of desalinated water as a function the outer salt concentration cout .

Mini-Conclusion

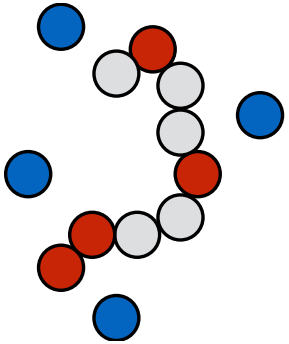
Analytical calculations are feasible for desalination efficiencies, etc.

But.. most PE hydrogels carry weak groups…..

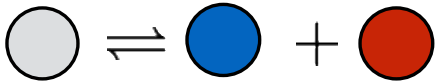
Conclusion

- Hydrogels swell due to pressure of couterions
- Simulations and theory on model networks can provide microscopic insights on different level of resolutions
- Adapt method to your question
- Gain insights into swelling, mechanical moduli, ion distributions and partitioning
- PE networks in poor solvent show necklaces
- Similarities to single chain poor solvent PE conformational behavior is found

Weak Group Dissociation Behavior



$$HA \rightleftharpoons H^+ + A^-$$



Reaction Constant
(units of mols)

$$K = \frac{[H^+][A^-]}{[HA]}$$

acidity constant
dissociation constant
equilibrium constant

Dissociated fraction

$$\langle \alpha \rangle = \frac{[A^-]}{([A^-] + [HA])}$$

degree of ionization

for polyelectrolyte monomers: charge is not just a fixed unit!

What Can We Do

- Equilibrium of a general chemical reaction

$$\nu_{\mathrm{A}}\,\mathrm{A} + \nu_{\mathrm{B}}\,\mathrm{B} + \ldots \rightleftharpoons \nu_{\mathrm{X}}\,\mathrm{X} + \nu_{\mathrm{Y}}\,\mathrm{Y} + \ldots$$

- ν_i is the stoichiometric coefficient of species i
- Conservation of mass: atoms can be re-groupped but not created or destroyed in a chemical reaction
- Predict *equlibrium composition* from the given *initial composition* and external conditions (temperature, pressure, composition of a reservoir)
- Time evolution is our adjustable parameter because of using MC algorithms

What can we not do

- Chemical kinetics – time-evolution of the composition
- Studying kinetics requires knowing or **postulating** the reaction mechanism

Ideal Dissociation of Weak Acids

- Schematic dissociation reaction of a weak acid HA

$$\mathrm{HA} \leftrightharpoons \mathrm{A^-} + \mathrm{H^+}$$

- General condition of chemical equilibrium (fixed T, p)

$$0 = \sum_i \nu_i \left(\frac{\partial G}{\partial N_i} \right) = \sum_i \nu_i \mu_i = \mu_{\mathrm{A^-}} + \mu_{\mathrm{H^+}} - \mu_{\mathrm{HA}}$$

- Ideal chemical potential

$$\mu_i^{\mathrm{id}} = \mu_i - \mu_i^{\ominus} = k_{\mathrm{B}} T \ln \left(\frac{c_i}{c^{\ominus}} \right)$$

- Ideal acidity constant

$$K_{\mathrm{A}} = \exp\left(-\frac{1}{k_{\mathrm{B}} T} \sum_i \nu_i \mu_i^{\ominus} \right) \overset{\text{ideal}}{=} \frac{c_{\mathrm{H^+}} c_{\mathrm{A^-}}}{c^{\ominus} c_{\mathrm{HA}}} \qquad \mathrm{p}K_{\mathrm{A}} \equiv -\log_{10} K_{\mathrm{A}}$$

- Corrections for non-ideal behaviour arise due to interactions

Henderson-Hasselbalch Equation

- Degree of ionization = probability that group HA is ionized

$$\alpha \equiv \left\langle \frac{N_{\mathrm{A}^-}}{N_{\mathrm{HA}} + N_{\mathrm{A}^-}} \right\rangle = \frac{c_{\mathrm{A}^-}}{c_{\mathrm{HA}} + c_{\mathrm{A}^-}}, \qquad c_{\mathrm{A}^-} = \alpha c_{\mathrm{A}}, \quad c_{\mathrm{HA}} = (1-\alpha) c_{\mathrm{A}}$$

- Ideal acidity constant in terms of α

$$K_{\mathrm{A}} \overset{\text{ideal}}{=} \frac{c_{\mathrm{H}^+} c_{\mathrm{A}^-}}{c^{\ominus} c_{\mathrm{HA}}} = \frac{c_{\mathrm{H}^+}}{c^{\ominus}} \frac{\alpha}{(1-\alpha)}$$

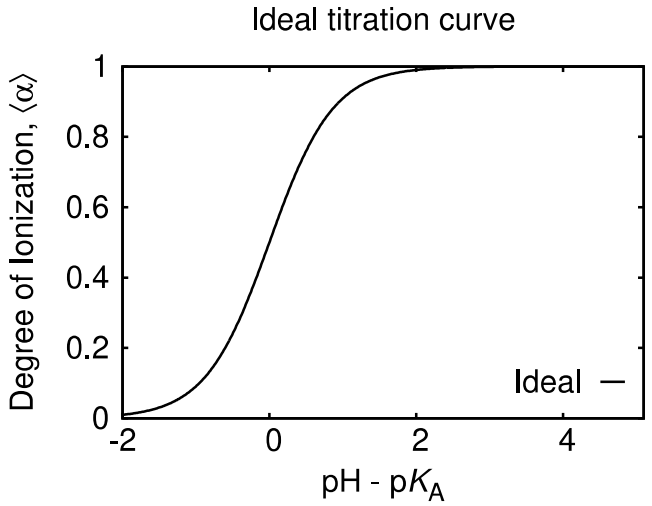
- Henderson-Hasselbalch equation

$$1/\alpha \overset{\text{ideal}}{=} 1 + 10^{\mathrm{p}K_{\mathrm{A}} - \mathrm{pH}}$$

$$\mathrm{pH} \overset{\text{ideal}}{=} -\log_{10}(c_{\mathrm{H}^+}/c^{\ominus})$$

- Rule of thumb:

$$\alpha \approx 0 \quad \text{at} \quad \mathrm{pH} - \mathrm{p}K_{\mathrm{A}} \lesssim -1$$
$$\alpha = 1/2 \quad \text{at} \quad \mathrm{pH} - \mathrm{p}K_{\mathrm{A}} = 0$$
$$\alpha \approx 1 \quad \text{at} \quad \mathrm{pH} - \mathrm{p}K_{\mathrm{A}} \gtrsim 1$$



Reactions in Poisson-Boltzmann Theories

- Charge regulation can be included into the PB model via enforcing local chemical equilibrium

$$\alpha(\vec{r}) = \frac{c_{A^-}(\vec{r})}{c_0(\vec{r})} = \frac{K c^o}{c^{res}_{H^+} \exp(-e_0 \psi(\vec{r})/(k_B T)) + K c^o}$$

c_0 is in this equation the concentration of titrable units

*Similar to Ninham, Parsegian, Journal of Theoretical Biology, 1971, see Landsgesell et al., PRL, **122**, 208002 (2019)*

The Grand-Reaction MC (G-RxMC)

- Chemical reactions (all equivalent)

$$\mathrm{HA} \rightleftharpoons \mathrm{A^-} + \mathrm{H^+}$$
$$\mathrm{HA} + \mathrm{OH^-} \rightleftharpoons \mathrm{A^-}$$
$$\mathrm{HA} \rightleftharpoons \mathrm{A^-} + \mathrm{Na^+}$$
$$\mathrm{HA} + \mathrm{Cl^-} \rightleftharpoons \mathrm{A^-}$$

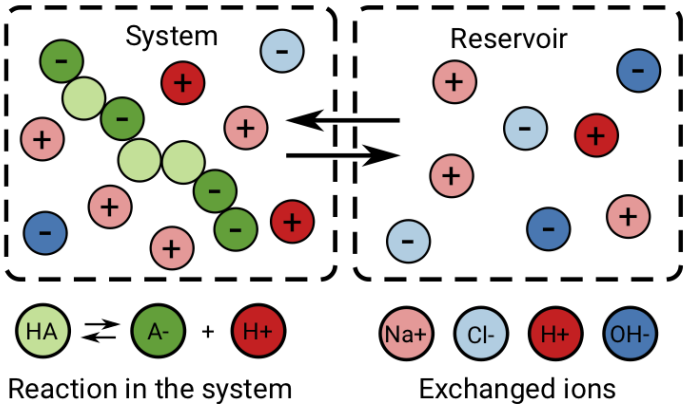
- Exchange of ion pairs

$$\emptyset \rightleftharpoons \mathrm{Na^+} + \mathrm{Cl^-}$$
$$\emptyset \rightleftharpoons \mathrm{H^+} + \mathrm{Cl^-}$$
$$\emptyset \rightleftharpoons \mathrm{Na^+} + \mathrm{OH^-}$$
$$\emptyset \rightleftharpoons \mathrm{H^+} + \mathrm{OH^-}$$

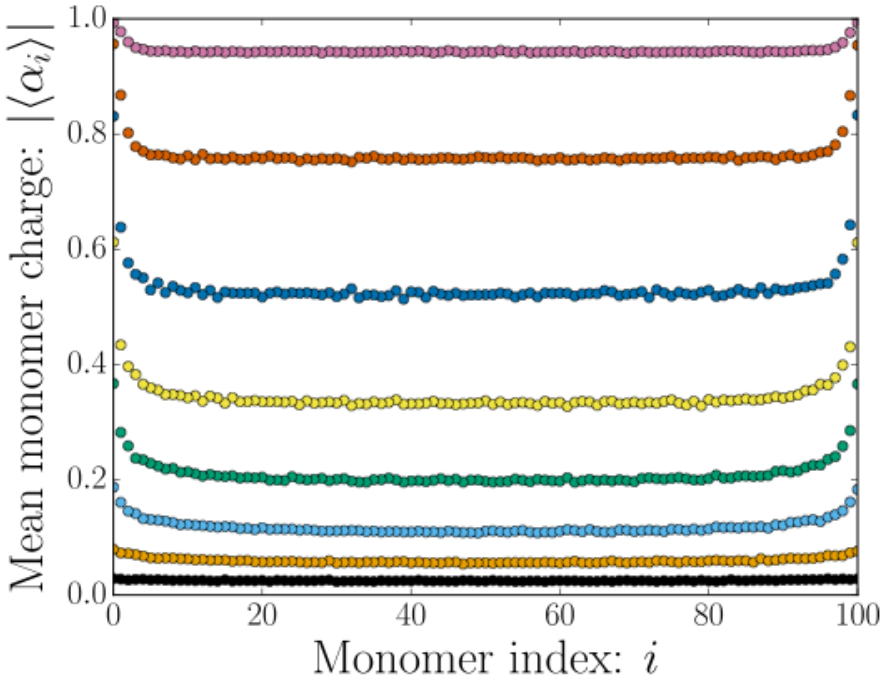
- Identity exchange of ions:

$$\mathrm{H^+} \rightleftharpoons \mathrm{Na^+} \qquad \mathrm{OH^-} \rightleftharpoons \mathrm{Cl^-}$$

Landsgesell et al., Macromolecules **53**, 3007 (2020)



Known Case: Linear PE



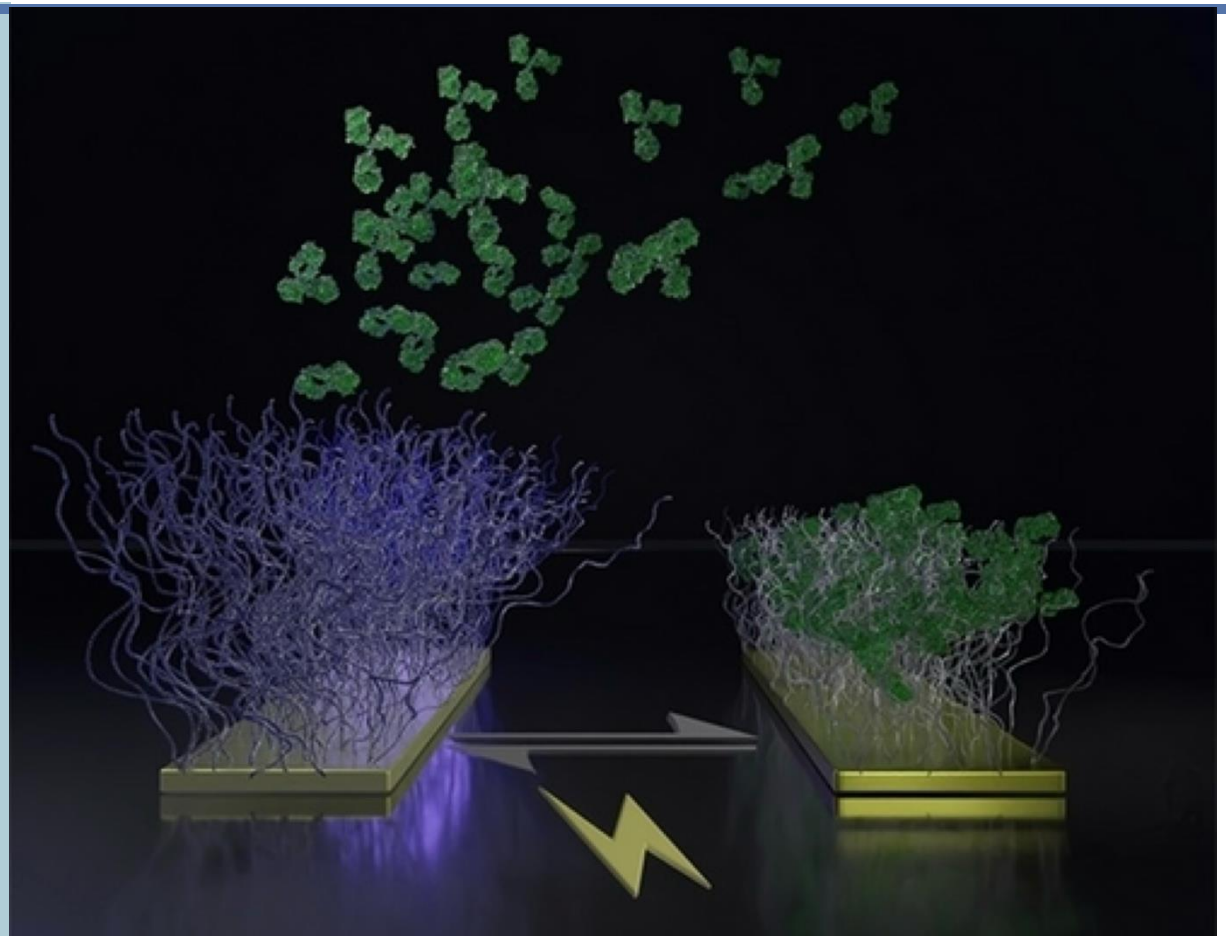
Increasing K_a

Position-dependent dissociation, similar as in microgels

„End Effect“

Ullner et al. JCP **104**, 3048 (1996)
Košovan *et al.* Soft Matter **6** 1872 (2010)
Castelnovo *et al.* EPJE **1,** 115 (2000)

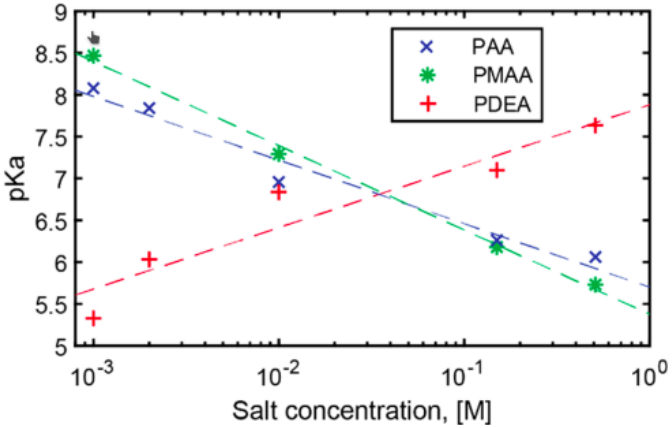
Protein Uptake into pH-responsive Brushes

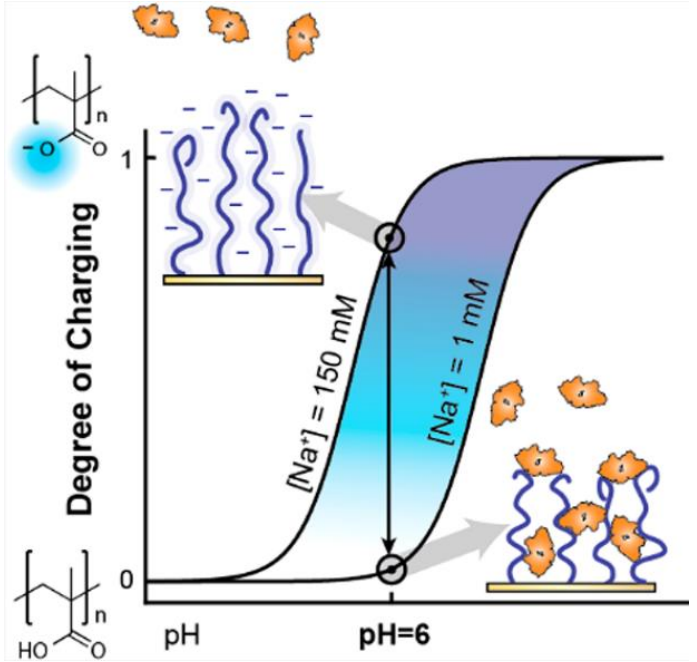


[1] del Castillo, Gustav Ferrand-Drake, et al. Angewandte Chemie International Edition, **61**(22), e202115745.

Giant pKa-Shifts in Weak Polyelectrolyte Brushes

- experiments: Ferrand-Drake et al.[1]
- titration measurements of grafted weak polyelectrolyte brushes
- observed effect: strong shift of titration curves, $pK_A^{eff} \equiv pH^{bulk}\ (\alpha = \frac{1}{2})$ scales linearly with $\log_{10} c_{salt}^{bulk}$



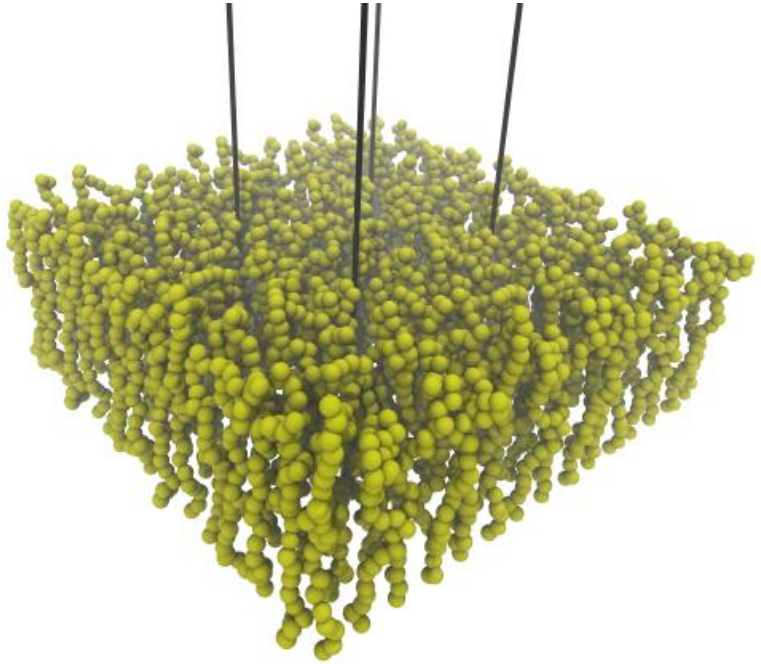


↪ Ferrand-Drake et al.

Ferrand-Drake et al, J. Phys. Chem. Lett. **11**, 5212−5218 (2020)

Giant pKa-Shifts in Weak Polyelectrolyte Brushes

- Kremer-Grest polymer model with explicit ions
- 5 → 5 chains of length 25 grafted to wall
- uniform grafting density $\Gamma = 0.1/\sigma^2$
- PBC in *x*- and *y*-direction
- P^3M with ELC for electrostatics
- coupled to bulk at constant pH, c_{salt}^{bulk} via G-RxMC

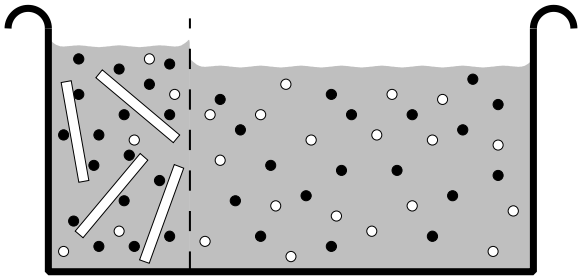


Ideal Titration plus Donnan Theory

Henderson-Hasselbalch Equation

$$\alpha = \frac{1}{1 + 10^{pK_A - pH^{brush}}}.$$

Donnan Equilibrium

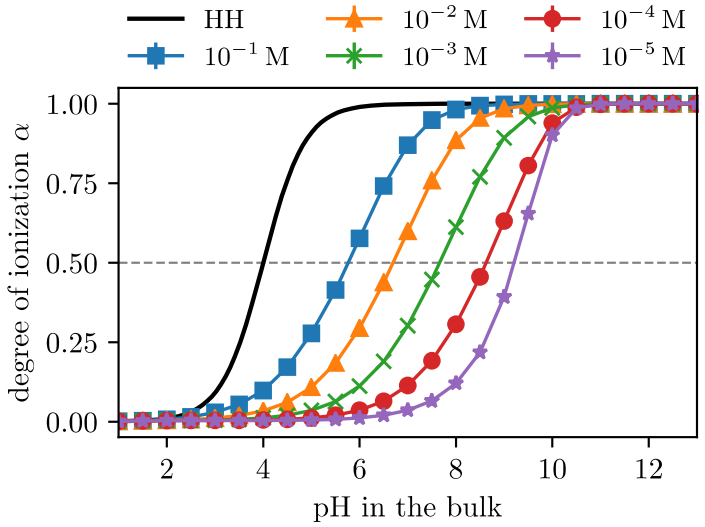


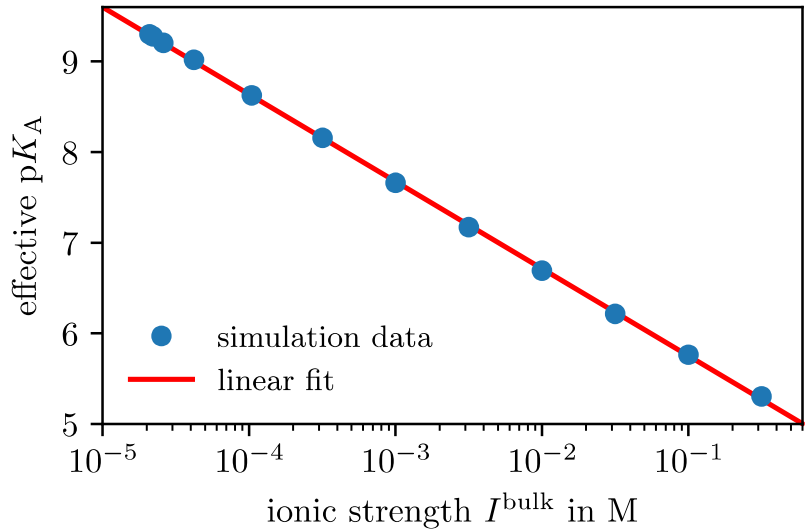
$$-\Delta^{Don}pH^{brush} - pH^{bulk} = -\log_{10}\left(\exp\left(-\beta e \Psi^{Don}\right)\right)$$

$$= -\log_{10}\left(\frac{c_{A^-}^{brush}}{2I^{bulk}} + \sqrt{\left(\frac{c_{A^-}^{brush}}{2I^{bulk}}\right)^2 + 1}\right) - \left(-\log_{10}\left(\frac{c_{A^-}^{brush}}{I^{bulk}}\right)\right).$$

$$\Delta^{Don}pH^{brush} \approx \log_{10}\left(\frac{c_{A^-}^{brush}}{I^{bulk}}\right).$$

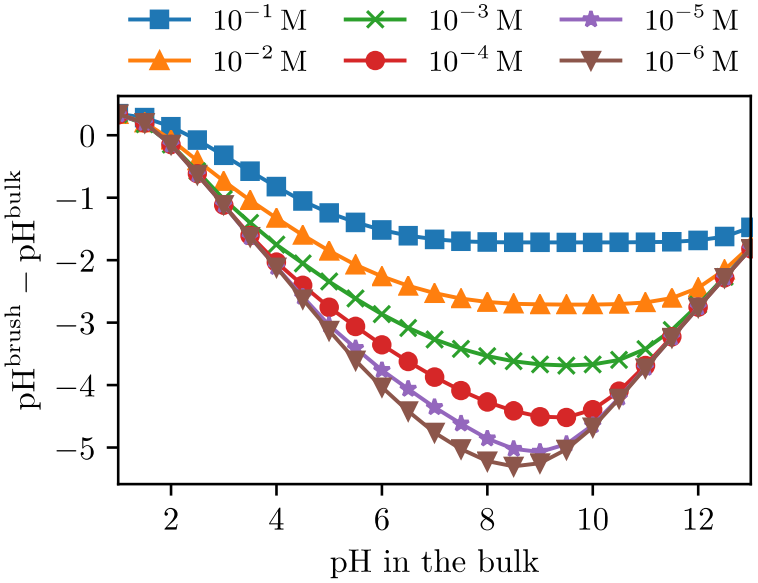
Results of GRx-MC Simulations





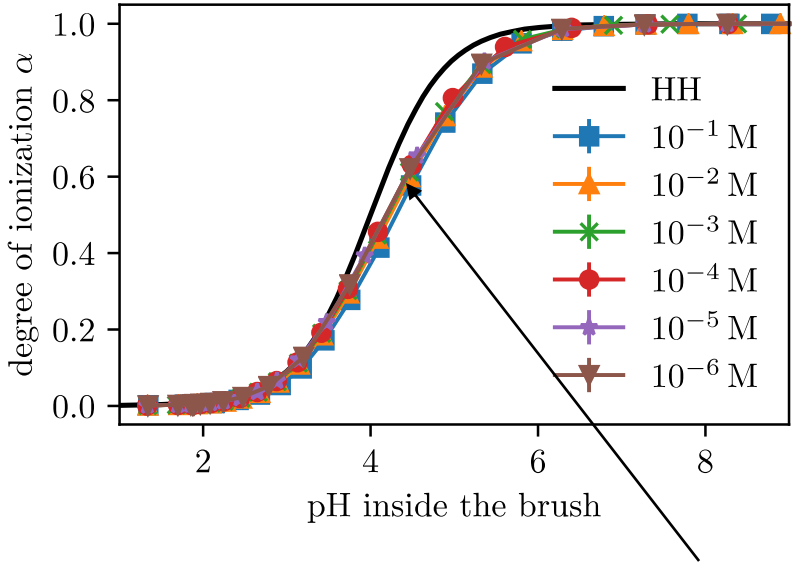
- Huge shift also observed in simulations
- Saturation at very low bulk salt concentrations because ionic strength becomes dominated by H^+
- linear scaling with $\log_{10} I^{bulk}$ is reproduced, slope -0.96 (vs. 1.0 for theory)

There is almost no shift in PKa



- pH can differ by up to 5 units between bulk solution and brush!

- Plotting the degree of ionization α vs. $\mathrm{pH^{brush}}$ removes most of the shift



Polyelectrolyte effect, almost independent of c_s

Mini-Conclusion

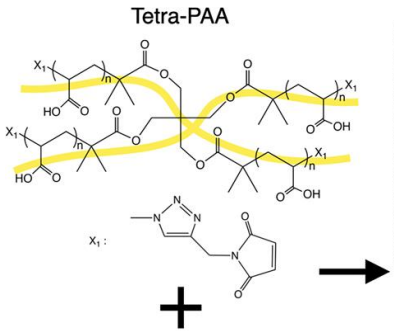
- The huge pKa shift of the proteins in the brush is only apparent

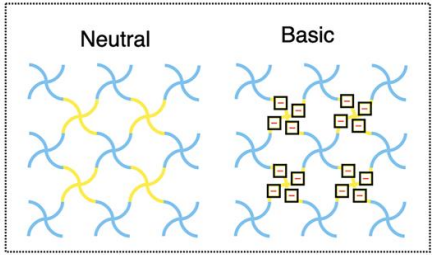
- Simple explanation in terms of Donnan theory:

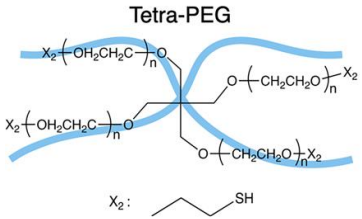
It is a consequence of the Donnan partitioning of ions between the bulk solution and the brush.

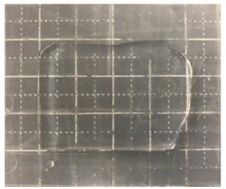
pH dependant Swelling of Tetra-PAA-PEG Gels

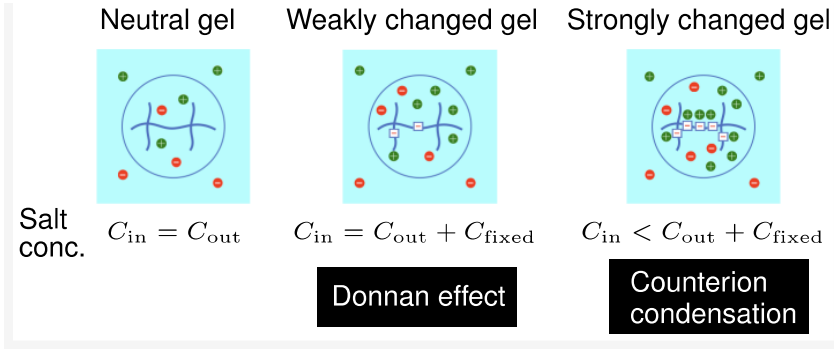
Tang et al., Macromolecules, **53**, 8244 (2020)





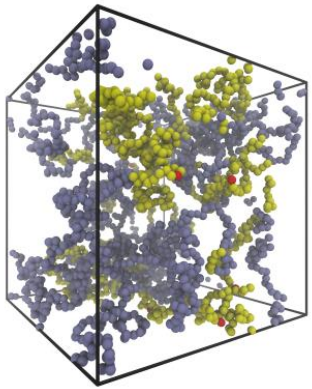




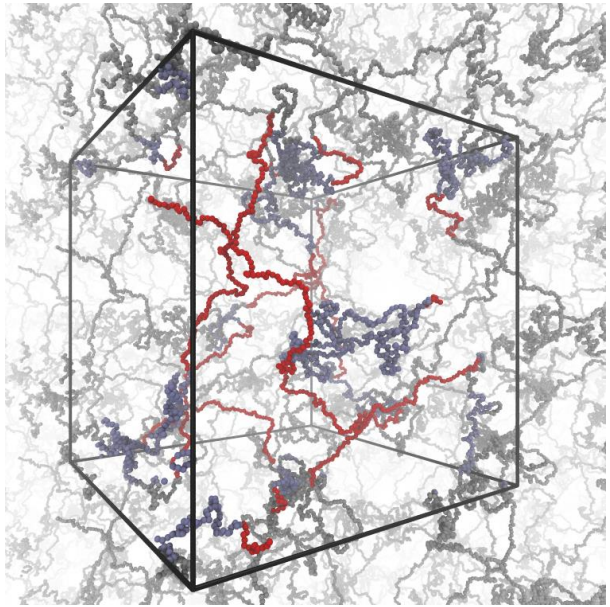


Covalently bound pH-dependent tetrafunctional gels

Structure of the Gel



a) c_{NaCl}^{res} = 10 mM, pH^{res} = 2, ↵ ↑ 0

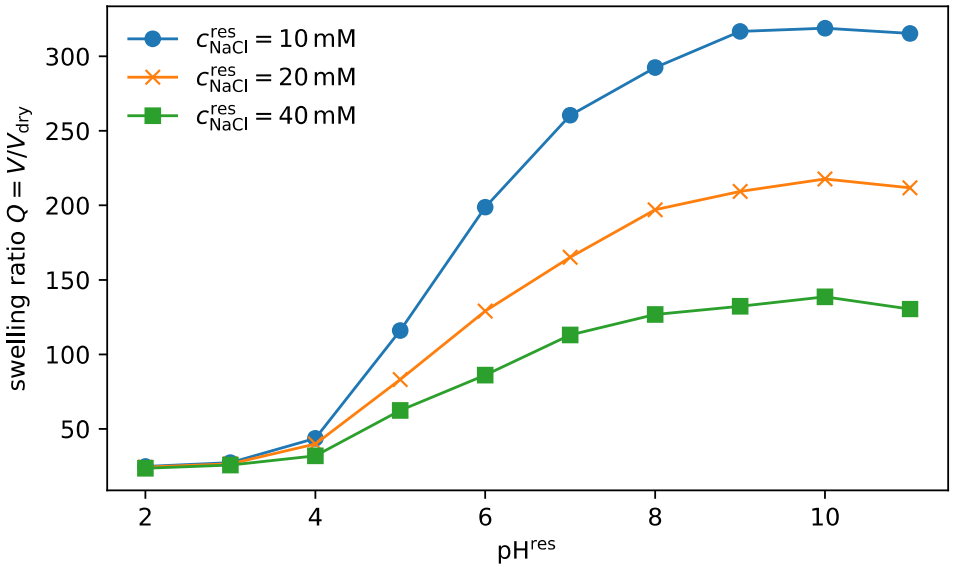


b) c_{NaCl}^{res} = 10 mM, pH^{res} = 11, ↵ ↑ 1

PAA (neutral) PAA (ionized) PEG periodic image

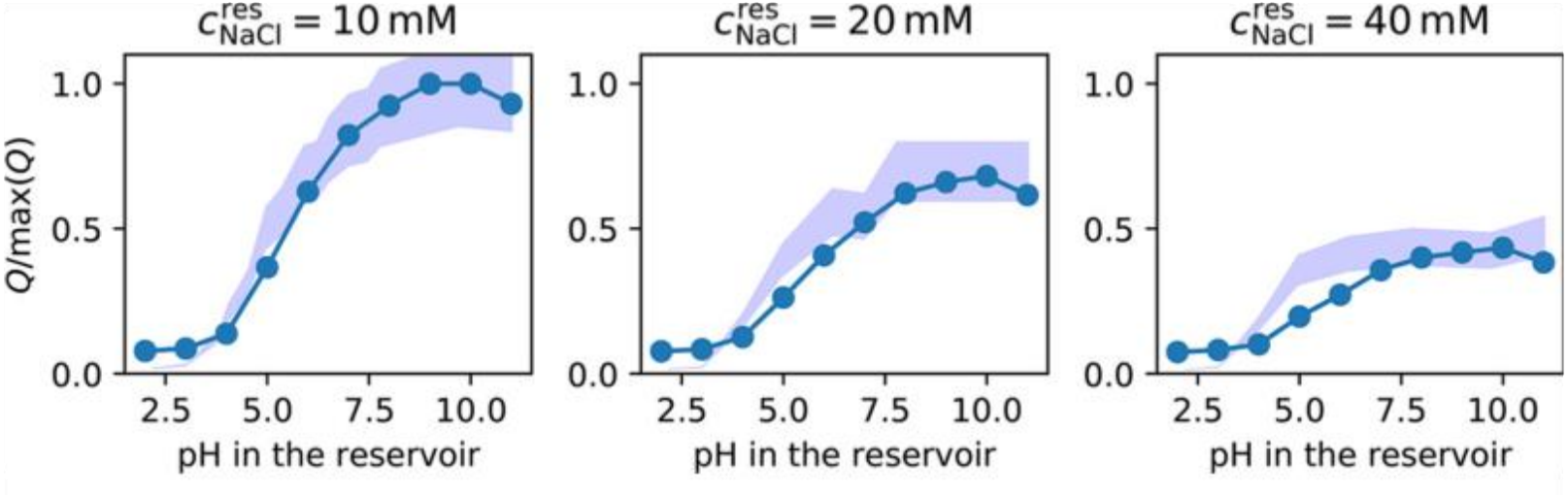
Simulation snapshot of the gel at c^{res}= 10 mM in the non-ionized state (a) and fully ionized state (b)

Simulated Swelling Behavior



Volume-based swelling ratio as function of the pH in the reservoir

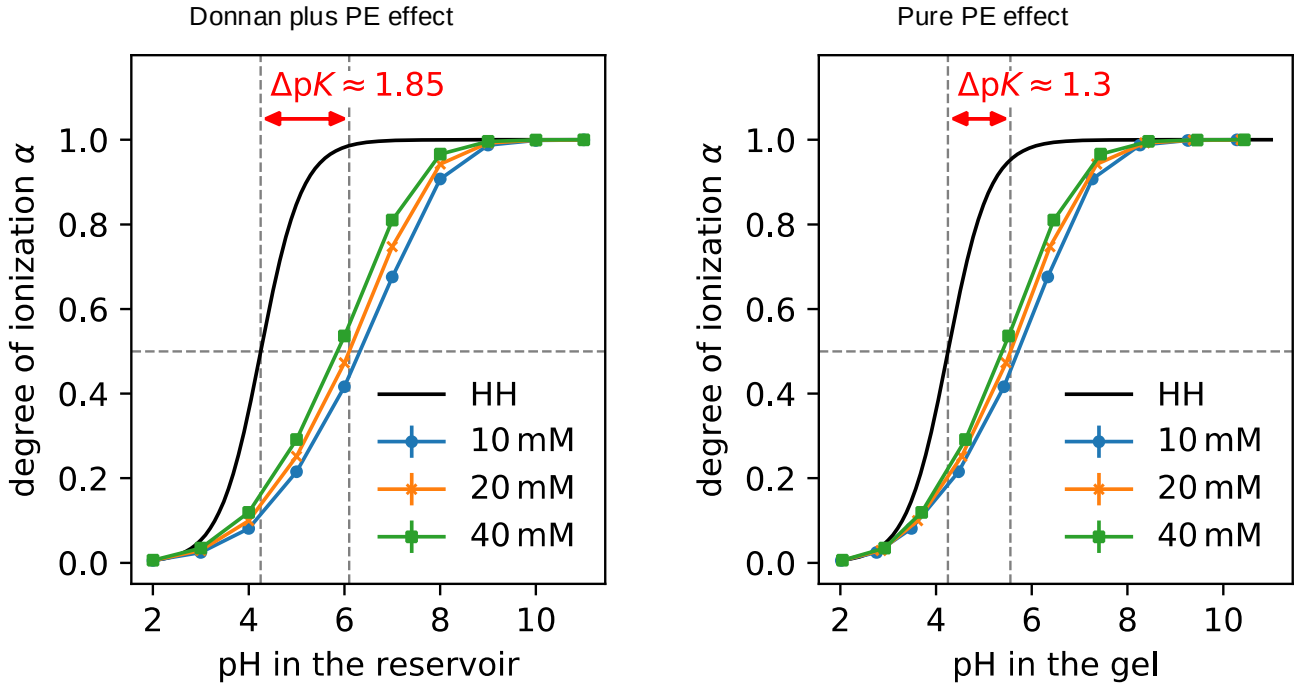
Experiment vs Simulations



Comparison of the volume-based swelling ratio against experimental data from Tang et al. (shaded area)

$Q \equiv V/V_{\mathrm{ref}}$ where we have chose as refererence state V_{ref} for $c_{\mathrm{NaCl}}^{\mathrm{res}} = 10\,\mathrm{mM}$ and $\mathrm{pH}^{\mathrm{res}} = 11$,

Experiment vs Simulations



$$\mathrm{pH}^{\mathrm{gel}} \approx \mathrm{pH}^{\mathrm{res}} - \log_{10}(c^{\mathrm{gel}}_{\mathrm{H}^+}/c^{\mathrm{res}}_{\mathrm{H}^+}) = \mathrm{pH}^{\mathrm{res}} - \log_{10}(c^{\mathrm{gel}}_{\mathrm{Na}^+}/c^{\mathrm{res}}_{\mathrm{Na}^+}).$$

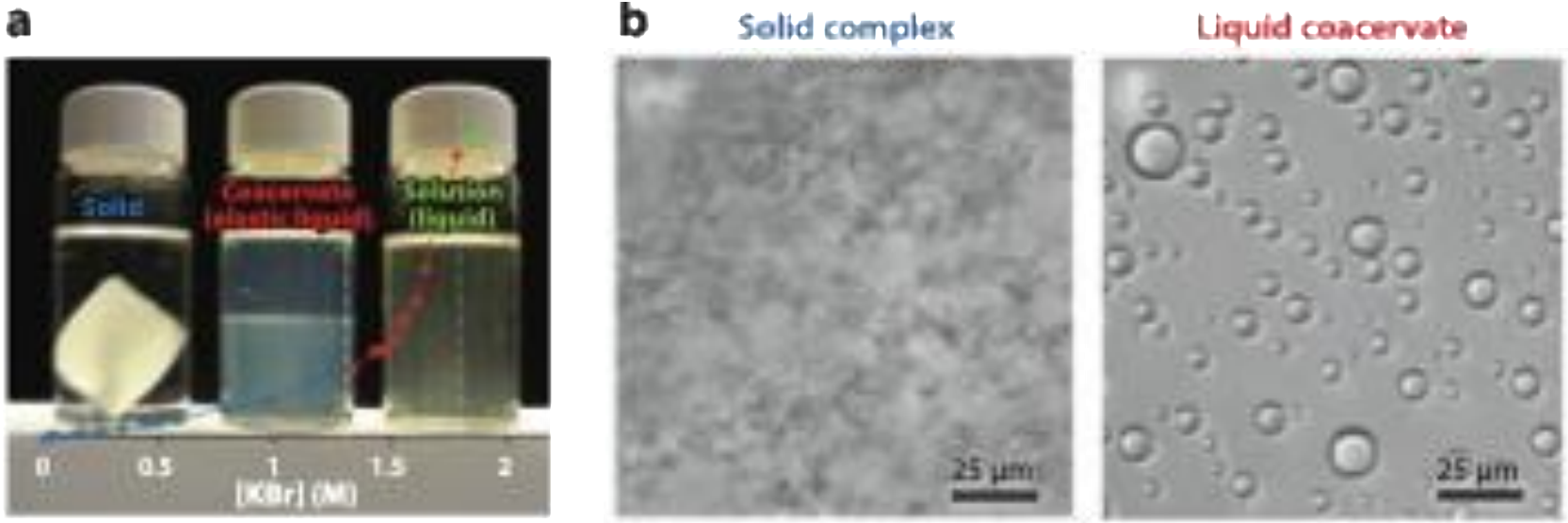
Ionization degree of the gels at various values of the reservoir salt concentration c^{res} : (a): as a function of the pH in the reservoir; (b): as a function of the pH inside the gel.

Intermediate Conclusion Tetra-PEG

- ionization of the gel as a function of pH is strongly suppressed when compared to the ideal Henderson–Hasselbalch result, hence the effective pK_A of the hydrogel is shifted to higher pH values by almost 2 units.
- One part is due to the Donnan effect due to the Donnan partitioning of ions, which makes pH in the gel lower than pH in the reservoir
- The other one is the polyelectrolyte effect due to electrostatic repulsion between ionized monomers in the gel
- the shift in the pK_A is predominantly caused by the polyelectrolyte effect, whereas the Donnan effect is much weaker in this system.

- Beyer, D., Kosovan, P., & Holm, C. (2022). Simulations Explain the Swelling Behavior of Hydrogels with Alternating Neutral and Weakly Acidic Blocks. *Macromolecules*, *55*(23), Article 23. https://doi.org/10.1021/acs.macromol.2c01916

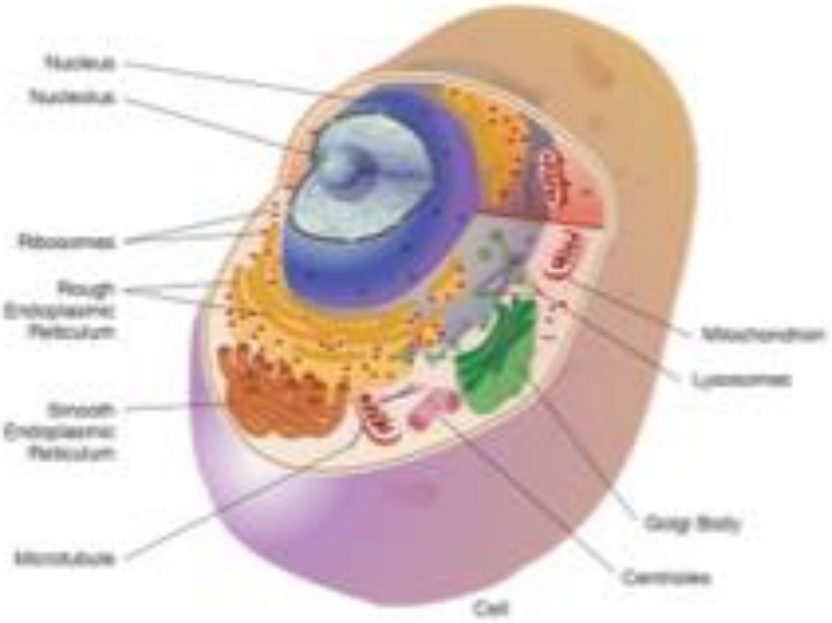
Phase Behavior of Polyelectrolytes



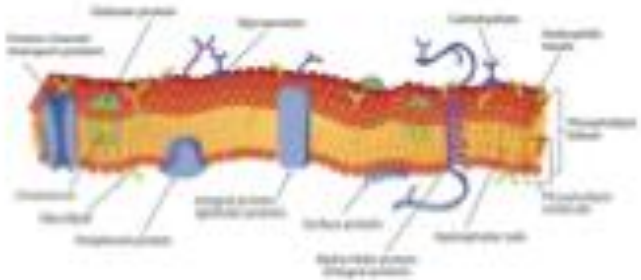
(a) Phase separation in the solution of oppositely charged polyelectrolytes leads to the formation of either solid precipitants or liquid coacervates. At high salt concentrations, the solution is uniphase.

(b) Microscopy images of solid complexes and liquid coacervates formed from oppositely charged polypeptides.

Biological Cells Are Highly Compartmentalized



www.genome.gov



www.chem.libretexts.org

Biomolecular Condensates

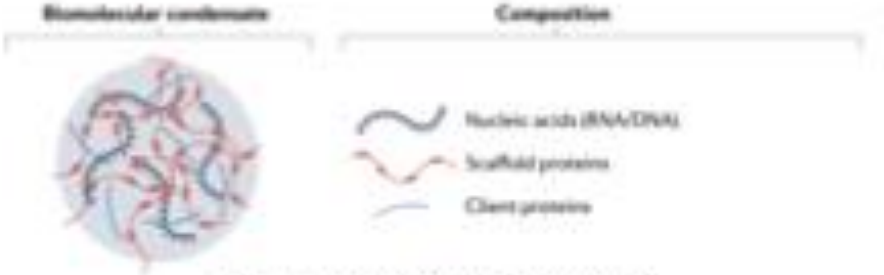
Biological cells contain "membraneless organelles" (MLOs):

Banani et al., Nat. Rev. Mol. Cell Biol. (2017)

MLOs are often liquid-like:

Brangwynne et al., Science (2009)

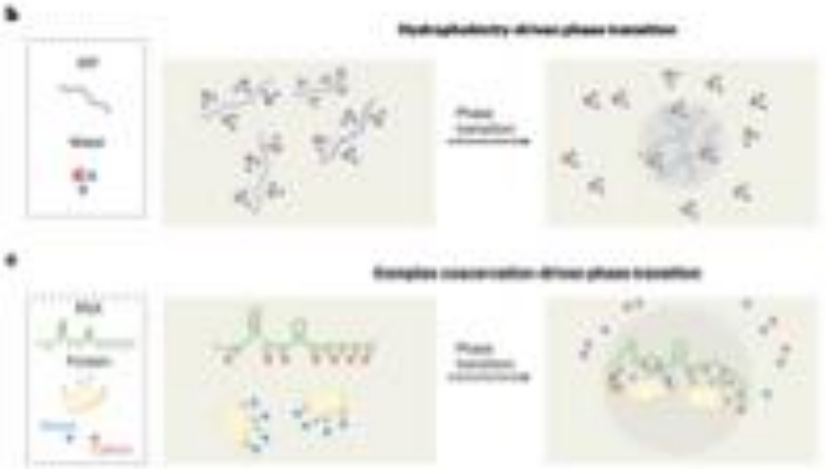
MLOs form by liquid-liquid phase separation of IDPs and other biomolecules:



Mitrea et al., Nat. Rev. Drug Discov. (2022)

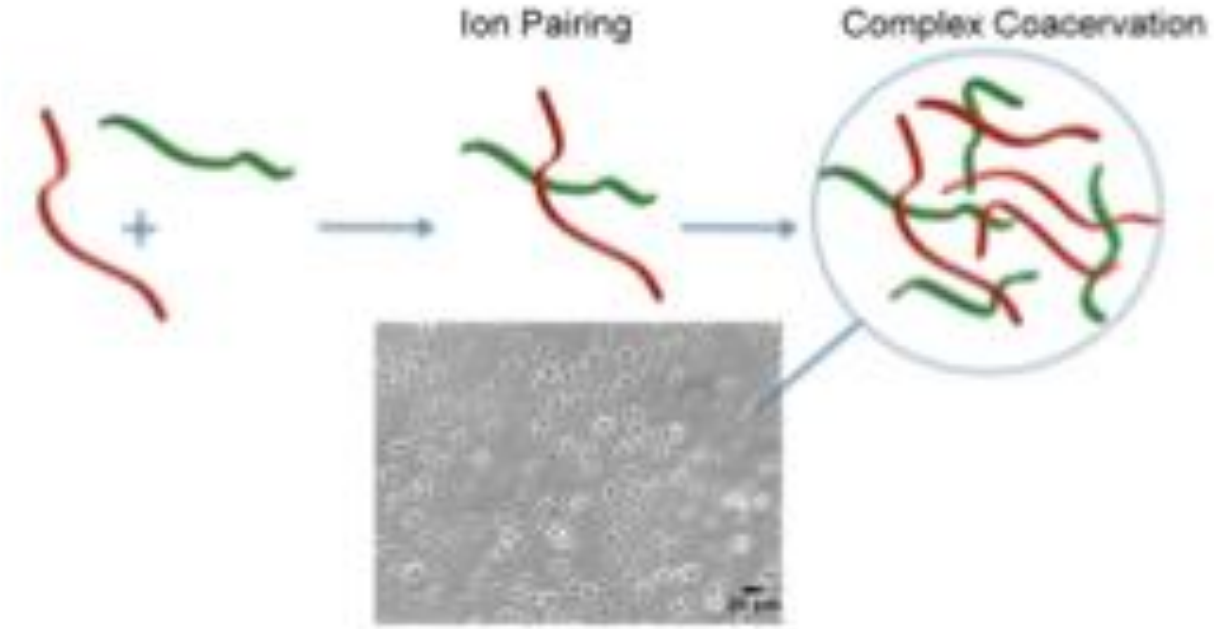
Membraneless Organelles are Biomolecular Condensates

Mitrea et al., Nat. Rev. Drug Discov. (2022)



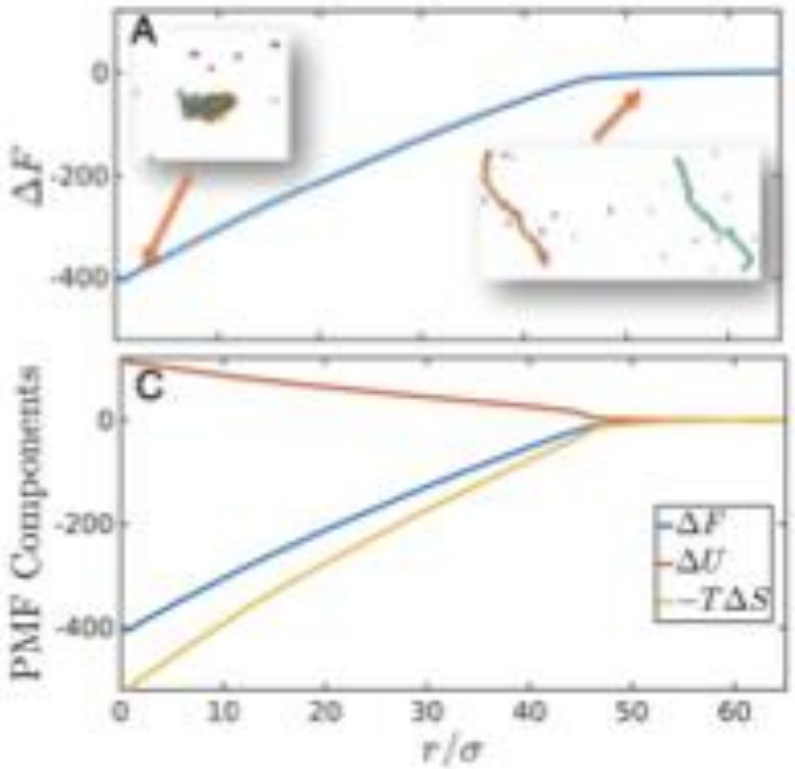
Dai et al., Nat. Chem. Biol. (2024)

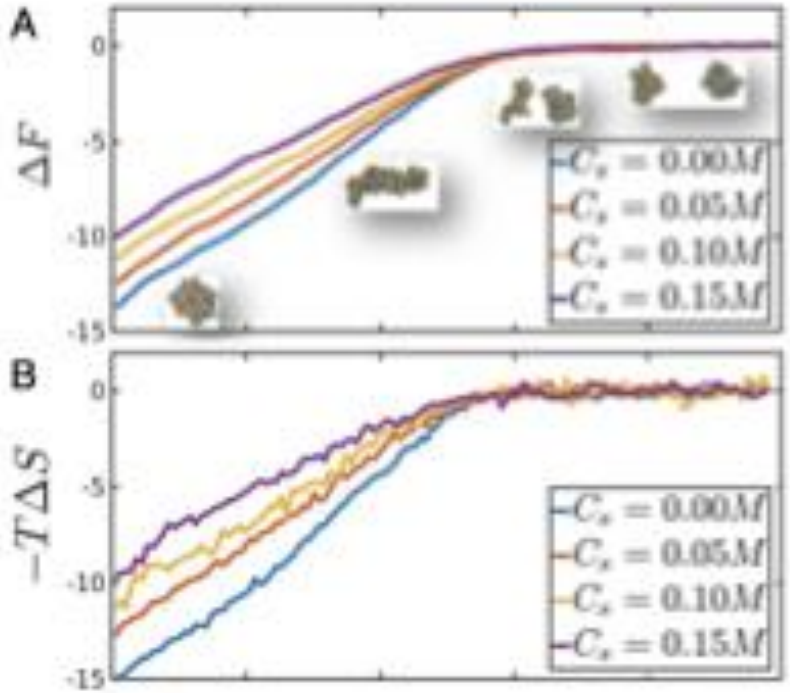
Polyelectrolyte Complex Coacervation



Priftis et al., Langmuir (2012)

Complex Coacervation is Entropically Driven

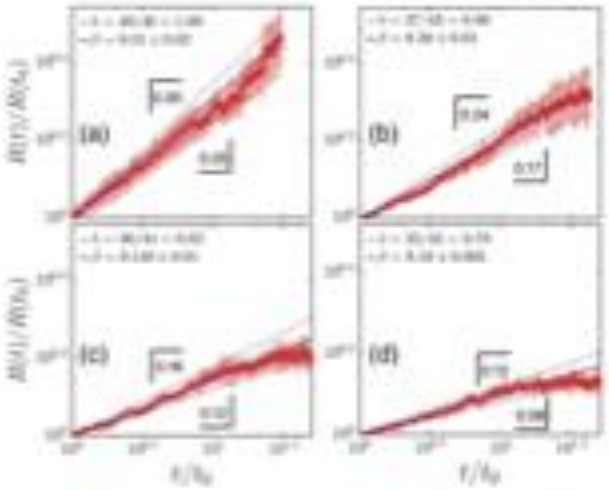




Chen and Wang, PNAS (2022)

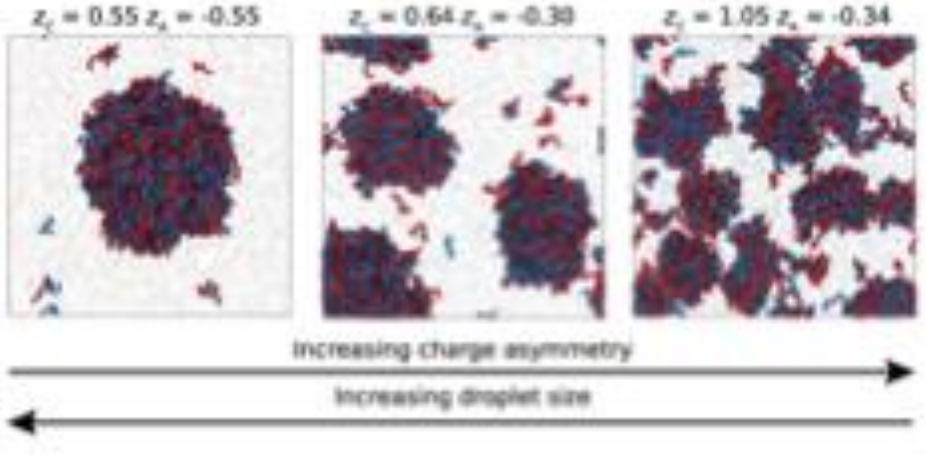
Effects of Charge Asymmetry

Charge asymmetry suppresses coarsening dynamics



Chen and Wang, PRL (2023)

Charge asymmetry controls droplet size

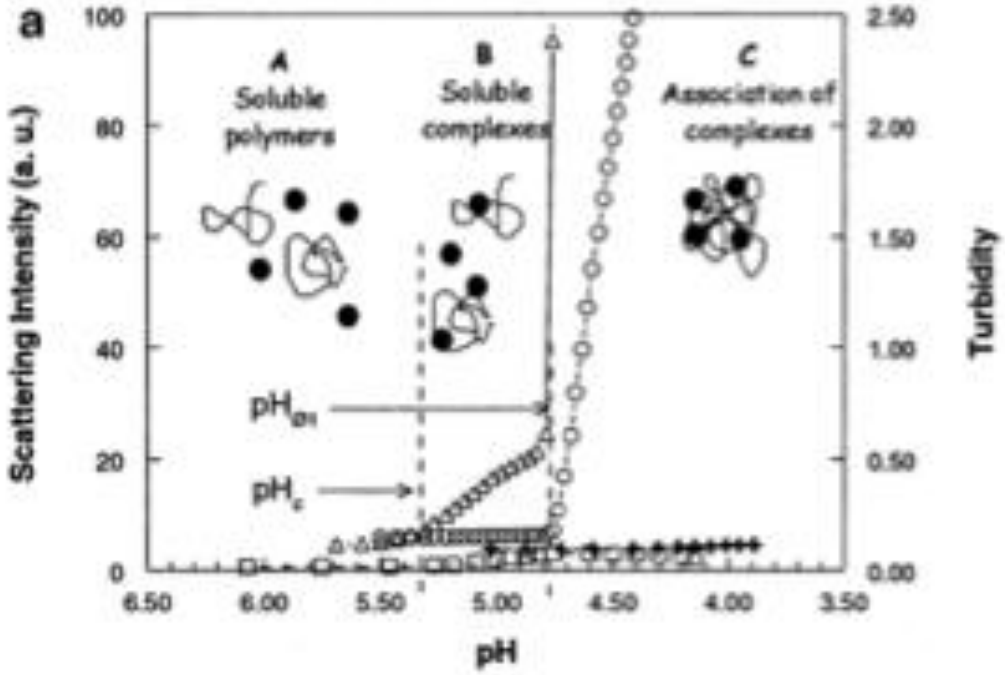


Luo et al., arXiv (2024)

pH-controlled Coacervation

System consists of Gum Arabic and Whey Proteins

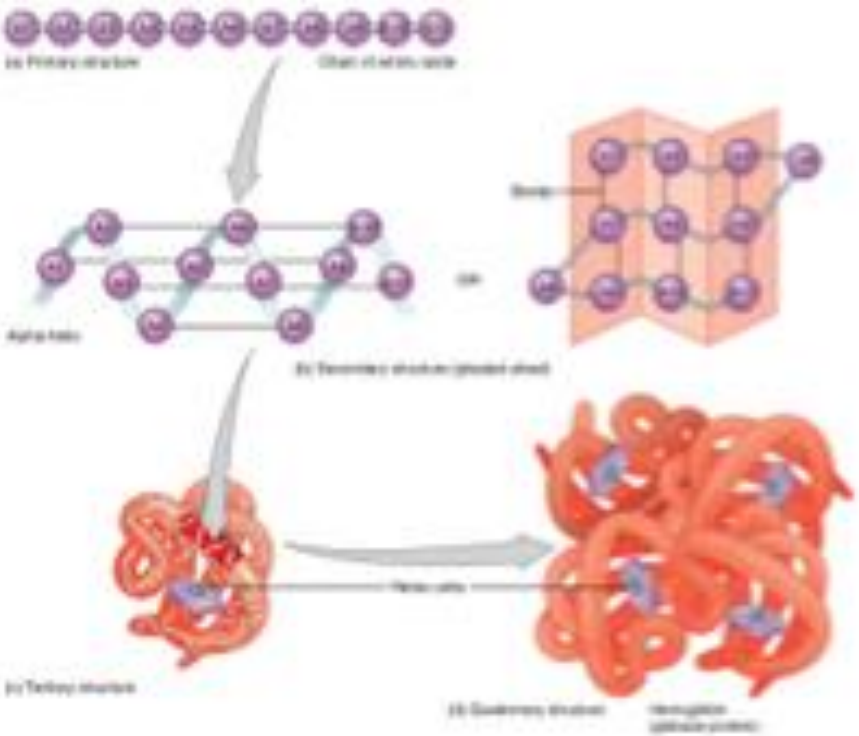
The polyelectrolyte and the protein are oppositely charged at low pH values, at high pH values they have the same sign



Weinbreck et al., Biomacromolecules (2003)

Sequence-Structure Relationship in Proteins

Classical view: amino acid sequence determines three-dimensional protein structure

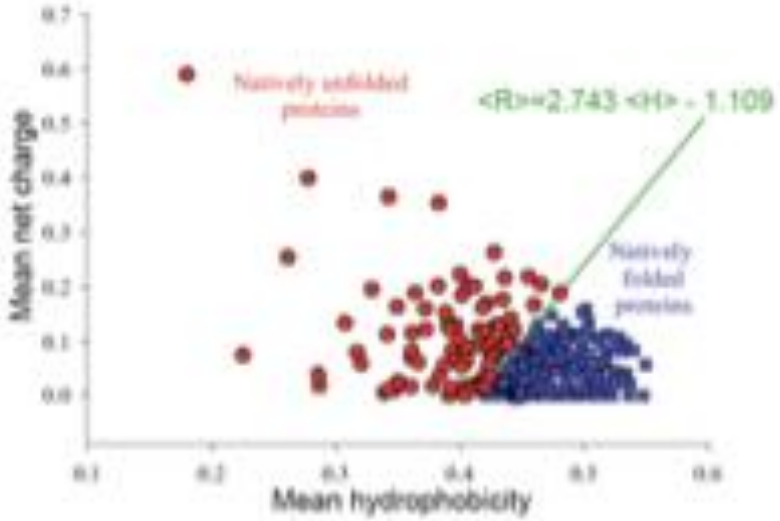


wikipedia.org

Intrinsically Disordered Proteins (IDPs)

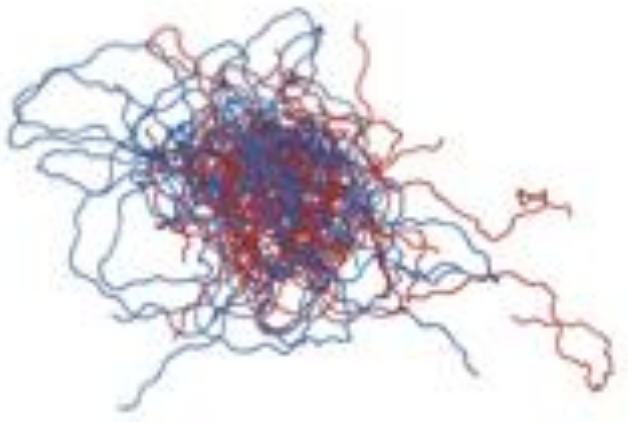
Research in the last ~ 25 years shows: many proteins do NOT fold into well-defined structures, they are **intrinsically disordered** and exhibit an **ensemble of conformations**

Low hydrophobicity, high net charge:



Dunker et al. BMC Genomics (2008)

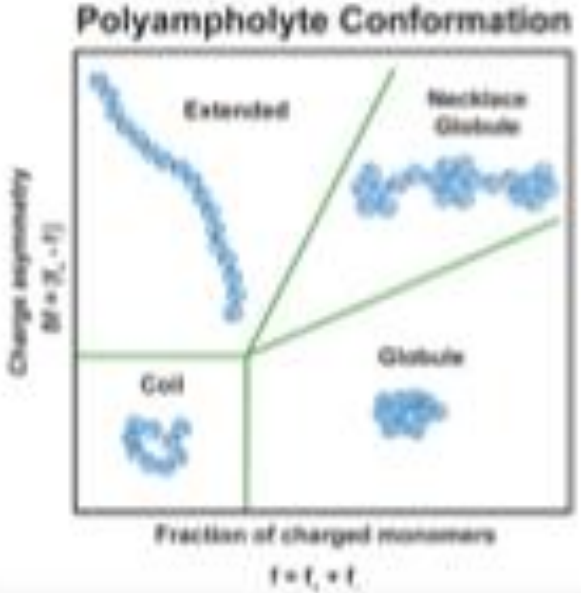
Conformational ensemble of an IDP complex:



Chowdhury et al., Annu. Rev. Biophys. (2023)

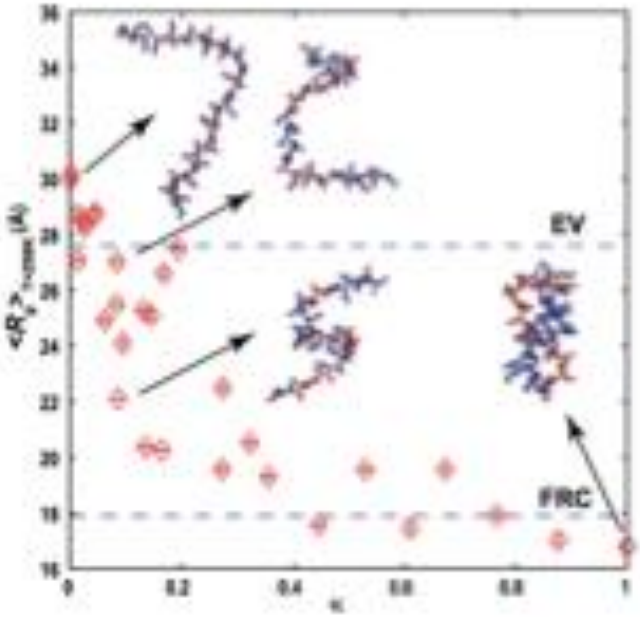
IDPs as Polyampholytes

IDPs are governed by polyampholyte physics:



Dinic et al., Curr. Opin. Colloid Interface Sci. (2021)

Specific sequence also contributes:



Das and Pappu, PNAS (2013)