Slide 1

Simulation Techniques for Soft Materials

1) What is a soft material?
2) Stability.
 – Double Layer → NVT MC
 – Effect of pH → Semi-Grand Canonical (**SGCMC**)
3) Flexible materials.
 – Conformational vs pH → Semi-Grand Canonical (**SGCMC**)
4) Water/Ion permeability
 – Effect of Charge/Ionic strength → Molecular Dynamics (**MD**)
5) Diffusion and Reactivity
 – Effect of crowding/aggregation → Brownian Dynamics (**BD**)

Slide 2

Colloids in Solution. What Theory says?

COLLOIDAL STABILIZATION: ELECTROSTATIC

$$\Delta G_{TOT} = \Delta G_{attr} + \Delta G_{rep}$$

VdW Attraction + Electrostatic Repulsion

DLVO Model
(Deryaguin, Landau, Verwey, Overbeek)
1940's

Function of surface charge, ionic strength

Function of material

Flocculation

Coagulation

ΔG_{rep} ΔG_{max} ΔG_{attr} ΔG_{TOT} **H**

Slide 3

Slide 4

COMPUTATIONAL MODELING OF MATERIALS SCHOOL
04-05 DECEMBER 2017
FACULTY OF CHEMISTRY AND PHARMACY
UNIVERSITY OF SOFIA

SIMULATION TECHNIQUES FOR SOFT MATERIALS

Sergio Madurga

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University of Barcelona
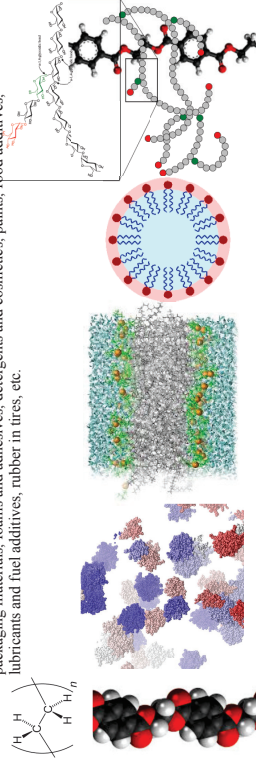
UNIVERSITAT DE BARCELONA

Horizon2020
Materials Networking

Slide 5

Soft Material

- These materials share an important common feature in that predominant physical behaviors occur at an **energy scale comparable with room temperature** thermal energy.

- Distinctive physics: **soft matter self-organizes** into mesoscopic physical structures that are much larger than the microscopic scale

- **Examples**: polymers (natural, synthetic), biological membranes, biomaterials, colloids, gels, microemulsions, proteins, surfactants,…

- **Applications**: wide range of technological applications. They may appear as structural and packaging materials, foams and adhesives, detergents and cosmetics, paints, food additives, lubricants and fuel additives, rubber in tires, etc.
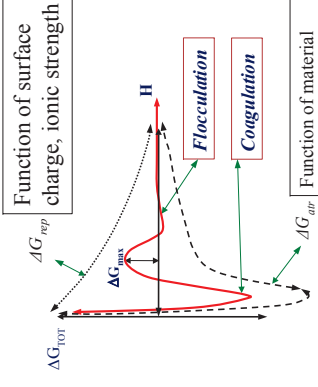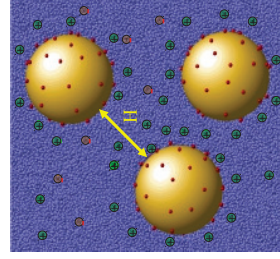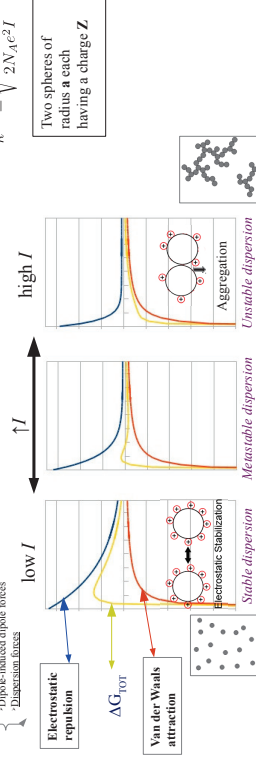
Slide 6

DLVO Model: Effect of the ionic strength

- Van der Waals attraction and the electrostatic repulsion due to the so called electric double layer (EDL) of counterions.
- The electrostatic part of the DLVO interaction is computed in the mean field approximation in the limit of low surface potentials

Electrostatic repulsion:
$$\beta U(r) = Z^2 \lambda_B \left(\frac{\exp(\kappa a)}{1 + \kappa a} \right)^2 \frac{\exp(-\kappa r)}{r}$$

Van der Waals attraction:
- Dipole-dipole forces
- Dipole-induced dipole forces
- Dispersion forces

$$\Delta G_{attr} = -\frac{A_H\, a}{12\, H} \qquad H = r - 2a \qquad A_H \text{ is the Hamaker constant}$$

λ_B is the Bjerrum length
κ^{-1} is the Debye-Hückel screening length

$$\lambda_B = \frac{e^2}{4\pi\varepsilon_0 \varepsilon_r\, k_B T}$$

$$\kappa^{-1} = \sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{2 N_A e^2 I}}$$

Two spheres of radius **a** each having a charge **Z**

low I $\uparrow I$ high I

Stable dispersion   Metastable dispersion   Unstable dispersion

Electrostatic Stabilization

Electrostatic repulsion ΔG_{TOT} Van der Waals attraction

Aggregation

DLVO
- Uniformly charged nanoparticles
- Mean field approximation for electrostatic interactions: no prediction of the overcharging phenomena
- Approximate prediction of the critical coagulation concentration (ccc)

Simulation Model

The electrical double layer (EDL) around charged colloids

The electrical double layer (EDL) is a key concept in physical chemistry referring to the ionic distribution formed by an electrolyte around a charged colloid

>Equilibrium and transport properties of colloidal systems are determined by the specific structure of the EDL. Related with experimental determined Zeta Potential.
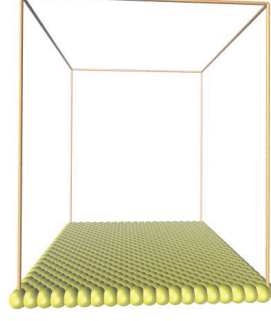
Selection of the Geometry of the simulation

Simulation of a fraction of the surface of the colloidal particle
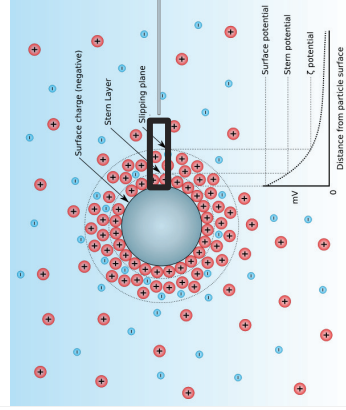
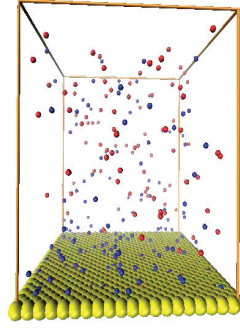Big colloid → Flat surface

Simulation Model

Coarse graining model of the charged surface of the colloid

$\sigma = 0.04\ C/m^2$

Coarse graining model of the charged surface of the colloid

$\sigma = 0.04\ C/m^2$
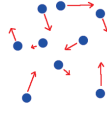
1:1 Electrolyte (NaCl) $c_s^* = 0.02$ M
a=3.6 Å

MC simulations: Canonical ensemble

1) MOVEMENT OF PARTICLES:
-Random selection of a Cation or an Anion.
-Small Random displacement.

2) CALCULATION OF ENERGY OF THE SYSTEM
-Coulombic interaction between all charges of the system (Ion-Ion, Ion-Surface).
-Volume exclude interactions between ions and charged surface.

3) ACCEPTANCE OF REJECTION OF THE MOVEMENT
- Metropolis algorithm: Configurations are sampled according to exp(-βΔE).
Accepted movement with probability:

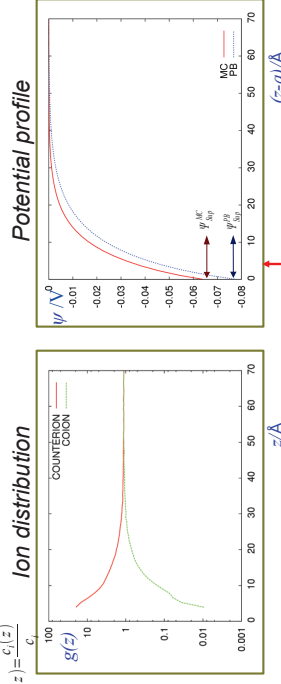$$p = \min\left(1, \exp\left(-\beta \Delta E\right)\right)$$

4) PROPERTIES
- Sampling averaging

$$\langle A \rangle = \sum_i p_i A_i = \frac{1}{N_{conf}} \sum_{i=1}^{N_{conf}} A_i$$

1:1 Electrolyte (NaCl)

$c_s^* = 0.1$ M
$\sigma = 0.08\ C/m^2$
a=3.6 Å

Ion distribution

$g_i(z) = \frac{c_i(z)}{c_i}$

Potential profile

Good agreement of the surface potential between PB and MC

2:1 Electrolyte (CaCl₂)

$c_s^* = 0.05$ M
$\sigma = -0.24\ C/m^2$
a=4.2 Å
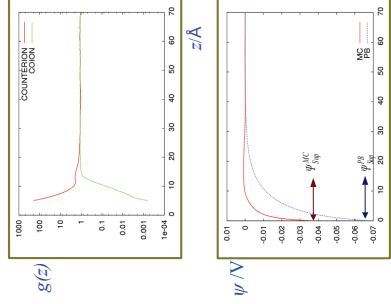
3:1 Electrolyte (LaCl₃)

$c_s^* = 0.1$ M
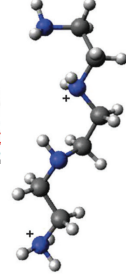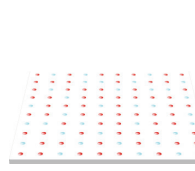$\sigma = -0.16\ C/m^2$
a=4.8 Å

Overcharging

Slide 1
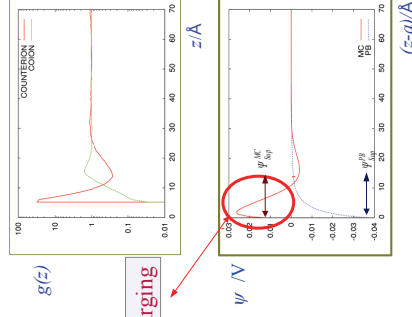
Semi-Grand Canonical Monte Carlo

- *Appropriated to study the effect of pH*
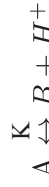- Appropriated to simulate systems with fixed number of sites.

For example:
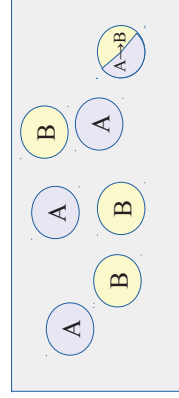
a) Surfaces of polyacids

b) Linear polyacids:

Slide 2

Semi-grand Canonical Ensemble

Ensemble to study mixtures (phase behaviour, interconversion reactions)

$$A \overset{K}{\leftrightarrow} B + H^+$$

$$n_A, n_B >> n_{H^+}$$

$$n_{Total} = n_A + n_B$$

- Fixed number of particles of the system
- The chemical potential of one component is fixed (H+)

Monte Carlo moves are attempted in which the identity of the molecules can be interchanged.

Slide 3

Semi-grand Canonical Ensemble

Ensemble to study mixtures (phase behaviour, interconversion reactions)

$$A \overset{K}{\leftrightarrow} B + H^+$$

$$n_A, n_B >> n_{H^+}$$

$$n_{Total} = n_A + n_B$$

$$\mu_i(P,T,x_i) = \mu_i^0(T) + k_BT ln(f_i)$$

Thermodynamic equilibrium:

$$\mu_A = \mu_B + \mu_{H^+}$$

- The chemical potential of one component is fixed (H+).
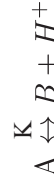- The chemical potential of other components (A,B) can be imposed by trial MC identity changes.

Slide 4

Each particle of the system

$$\mu_i(P,T,x_i) = \mu_i^0(T) + k_BT ln(f_i)$$

$$\xi_i = \frac{f_i}{\sum_{j=1}^n f_j}$$

fugacity fraction   fugacity

One of the N particles is selected at random and with equal probability assign it one of the n possible identities.

The probability of accepting a trial move is:

$$acc(\xi_i \to \xi_i') = min\{1, \frac{\xi_i'}{\xi_i} \exp[-\beta \Delta U(s^N)]\}$$

$\Delta U(s^N)$ Is the change in potential energy of the system if we change the identity of a randomly selected particle from i to i'.

Understanding Molecular Simulations. From algorithms to Applications. D. Frenkel & B. Smit

Slide 5

Acid/base in solution:

$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$$

Acid/base in surface:

```
--COOH
--COOH
--COO-
--COOH
--COO-
--COOH
--COOH
```

Effect of inert ions

Slide 6

$$pH = -log(a_H)$$

Solution....

$$K_a = \frac{a_{CH_3COO^-}\, a_{H^+}}{a_{CH_3COOH}}$$

$$K_C$$

$$-L + H^+ \Longleftrightarrow -LH$$

Proton coverage

$$K_C = \frac{c_{HL}}{c_L c_H} = \frac{1}{c_H}\left(\frac{\theta}{1-\theta}\right)$$

But, Kc is not constant!! Depend on concentration of ions

Slide 7

Accepted/Rejected trial movements with SGCMC:

Energy contributions for SGCMC
$$\begin{cases} \Delta F = \Delta U_{el} + k_BT(\ln 10)(pH - \log K_0) & \text{for protonation process} \\ \Delta F = \Delta U_{el} - k_BT(\ln 10)(pH - \log K_0) & \text{for deprotonation process} \end{cases}$$

Apply ΔF for Metropolis MC algorithm.
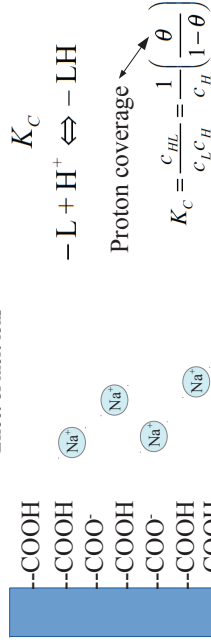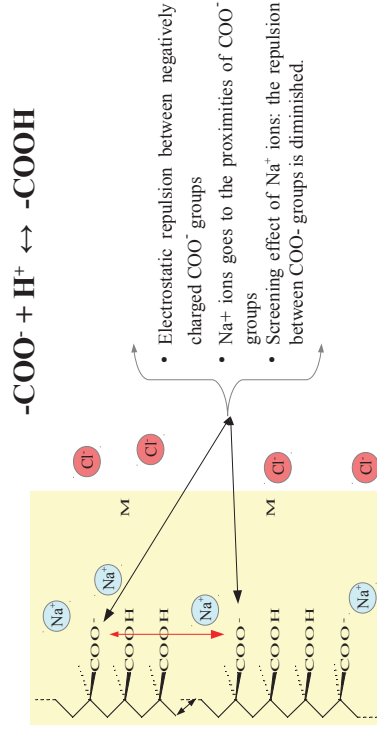Accepted movement with probability:

$$\min\{1, \exp(-\Delta F)\}$$

Polyelectrolytic effect
Effect of the ionic strength

Experimental titration curves of PAA in KNO$_3$

I = 0.005 M
I = 0.01 M
I = 0.02 M
I = 0.05 M
I = 0.1 M

Ionic strength

$I = 1/2 \sum_{i=1}^{n} c_i z_i^2$
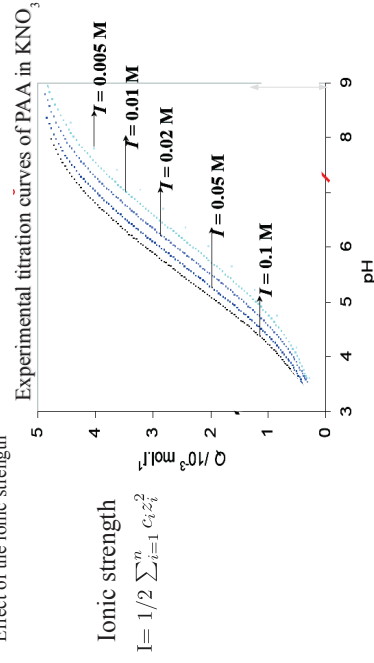
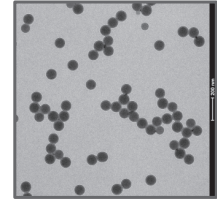At fixed pH, the increase of I makes a increase of the charge of the polyelectrolyte. Charge screening effect.

CARBOXYLATED LATEX PARTICLES

Transmision Electron Microscopy (TEM) of a dispersion of carboxylated latex particles

Behrens et al, Langmuir 16 (2000) 2566

Radius ≈ 155 nm

Surface Model: Planar geometry

$z=0$ CH$_2$-CH$_2$-COOH 3 Å r=1 Å
$z=1$ CH$_2$-CH$_2$-COO$^-$ 3 Å r=1 Å

Surface of Carboxylated Latex Particle

Simulation details

KCl Electrolyte:
c_{KCl} = 0.3–0.01M
σ_{max} = -0.098 C/m^2

Using hydrated to ionic radius of K$^+$ and Cl$^-$:
r_h(K$^+$) = r_h(Cl$^-$) = 3.3 Å
to
r_i(K$^+$) = 1.5 Å r_i(Cl$^-$) = 1.8 Å

Box dimensions
256 x 256 x 300 Å^3

400 COOH/COO- groups:
array of 20x20
Separation of 12.8 Å

Total number of ions:
238-2780 depending I and pH

hydrated radius
ionic radius
K$^+$

System: H$^+$ - PAA (polyacrilic acid)

-COO$^-$ + H$^+$ ↔ -COOH

- Electrostatic repulsion between negatively charged COO$^-$ groups
- Na$^+$ ions goes to the proximities of COO$^-$ groups
- Screening effect of Na$^+$ ions: the repulsion between COO-groups is diminished.

CARBOXYLATED LATEX PARTICLES: pH EFFECT

Experimental titration curves in 0.1M, 0.03M and 0.01M KCl

Exp 0.1M
Exp 0.03M
Exp 0.01M

Titration curves showing the dependence of the degree of dissociation, α, on the pH measured at different ionic strengths
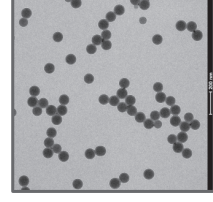
Behrens et al, Langmuir 16 (2000) 2566

Transmision Electron Microscopy (TEM) of a dispersion of carboxylated latex particles
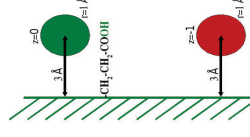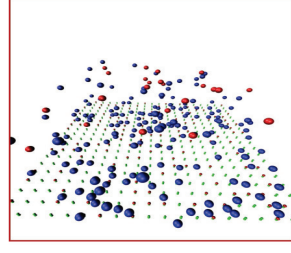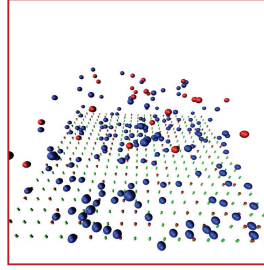
Radius ≈ 155 nm

Surface Model: Planar geometry

SEMI-GRAND CANONICAL MONTE CARLO SIMULATIONS

- Canonic Monte Carlo criterion is used to sample the configurations of salt solution.
- Macrocanonic Monte Carlo criterion is used to attempt for the ionization and deionization process of each ionizable group of the polyelectrolyte.
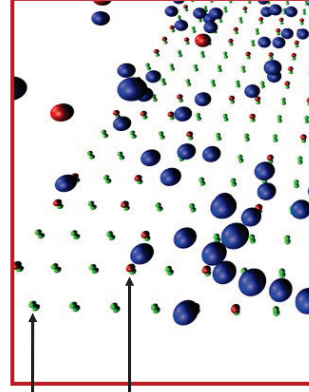
$$\Delta F^{SGC} = \Delta E_c \pm k_B T \ln 10 \left(pH\text{-}pK_0 \right)$$

$$\min \{1, \exp(-\Delta F)\}$$

-COOH
-COO$^-$

Snapshot for a solution of KCl 0.01M with a -0.098 Cm^{-2} charged polyelectrolyte surface.

Only counterions (blue) and coions (red) closer than a distance of 30 Å to the polyelectrolyte surface charges (green and red) are shown.
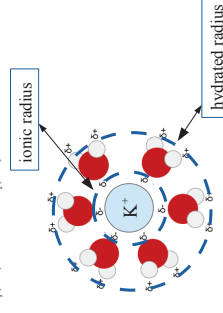
Slide 1 (top-left):

For 0.1 M and 0.01 M, a layer of hydrated K⁺ around charged and non-charged surface groups is observed.

COUNTERIONS (K⁺)

COIONS (Cl⁻)
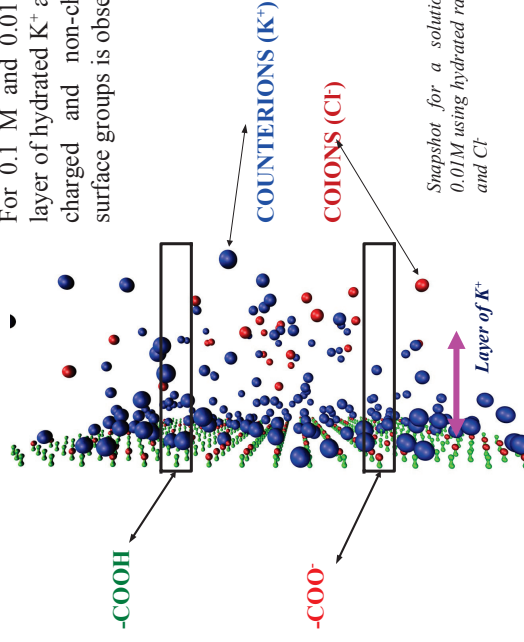
Snapshot for a solution of KCl 0.01M using hydrated radius for K⁺ and Cl⁻

Layer of K⁺
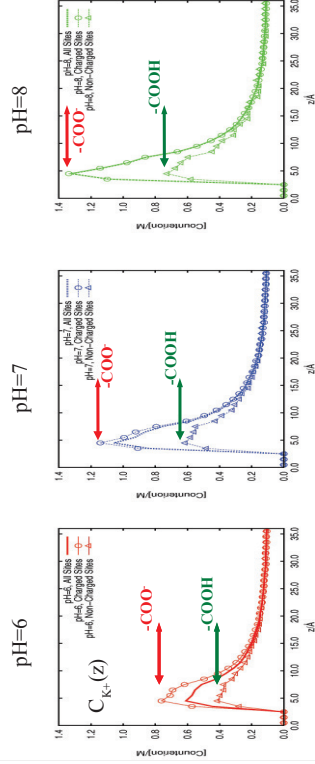
-COOH

-COO⁻

Slide 2 (top-middle):

Layering of Counterions around -COOH and -COO⁻

[K⁺] vs distance to -COOH or -COO⁻

KCl 0.01 M

pH=6   pH=7   pH=8

Slide 3 (top-right):

SGCMC for conformation and ionization

Case Study: conformational and ionization properties of linear poly(ethyl)enimine) (LPEI)

LPEI: $NH_2-(CH_2)_2-[NH-(CH_2)_2-]_{N2}-(CH_2)_2-NH_2$

a)

b) SBRIS

t g⁻ t t g⁺

t g⁻ t t g⁻ SBRIS
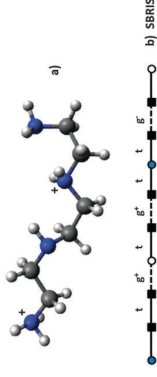
Description of a linear polymer:

• Site binding model (SB) with the rotational isomeric state (RIS): only three angles, those corresponding to energy minima of the bonds (i.e *trans, gauche+* and *gauche-*).

• Ionization state (charged/neutral) of the amine groups.

Slide 4 (bottom-left):

Degree of surface ionization (α) vs pH for a carboxylic functionalized surface in presence of inert salts

Surface-COO⁻ + H⁺ ↔ Surface-COOH

KCl Electrolyte:
c_{KCl} = 0.01M, 0.03M, 0.1M
σ_{max} = -0.098 C/m²

Titration profiles α vs pH are in good correspondence with the experimental profiles for the MC profiles for all c_{KCl} concentrations.

Exp 0.1M
Exp 0.03M
Exp 0.01M
MC 0.1M
MC 0.03M
MC 0.01M

α

pH

Titration curves showing the dependence of the degree of dissociation, α, on the pH were calculated using different radii values

---

Slide 5 (bottom-middle):

Layering of Counterions around -COOH and -COO⁻

[K⁺] vs distance to -COOH or -COO⁻

KCl 0.1 M

pH=6   pH=7   pH=8

$C_{K+}(z)$

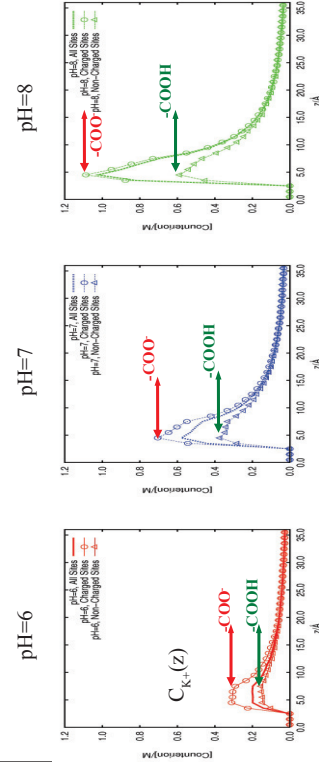-COO⁻   -COOH

Slide 6 (bottom-right):

Simulation Techniques for Soft Materials

1) What is a soft material?

2) Stability.
   – Double Layer → **NVT MC**
   – Effect of pH → Semi-Grand Canonical (**SGCMC**)

3) Flexible materials.
   – Conformational vs pH → Semi-Grand Canonical (**SGCMC**)

4) Water/Ion permeability
   – Effect of Charge/Ionic strenght → Molecular Dynamics (**MD**)

5) Diffusion and Reactivity
   – Effect of crowding/aggregation → Brownian Dynamics (**BD**)

Fundamental concepts

In general, internal angle rotation energy is similar to $k_B T$. As a consequence, macromolecules can easily change their conformational state (*i.e.* they are flexible).

Conformation as a result of two types of interactions:

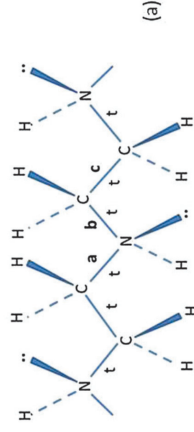- Short range interactions
- Long range interactions

Short range interactions (*e.g.* steric repulsion)

Long range interactions (*e.g.* excluded volume)
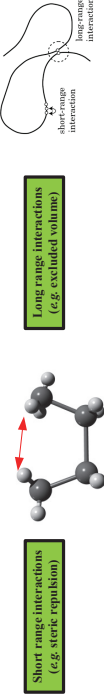
Conformational energy profile
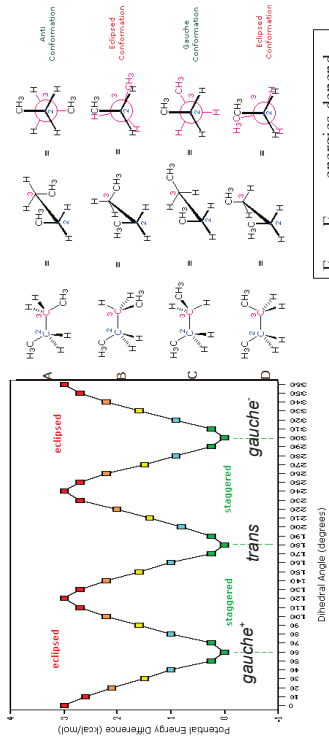
E_{trans}, E_{gauche} energies depend on each particular bond

Relevant conformations: trans, gauche⁺, gauche⁻

Site binding/rotational isomeric state (SBRIS) model

(a)

Three diferent dihedral angles:
a: C-C-N-C
b: C-N-C-C
c: N-C-C-N

Accurate description of the conformational properties requires different energetic parameters for *a*, *b* and *c* bonds.
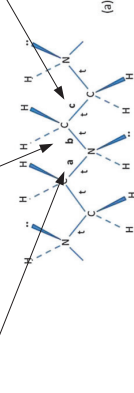

Different interaction parameters for each rotational angle: *a*, *b* and *c*

Transfer matrices for *a*, *b* and *c* of LPEI:

$$\Xi_{ref} = q U_{c,end}(U_{a,end} U_b U_c)(U_a U_b U_c)(U_a U_b U_c)...(U_a U_{b,end} U_{c,end})P^T$$

U_i: Correlation of two consecutive dihedral angles

$$\varphi_i = \quad \begin{array}{c c c} & \varphi_{i-1} = & \\ & t \quad g^+ \quad g^- \end{array}$$

$$\varphi_i = \begin{array}{c} t \\ g^+ \\ g^- \end{array}\begin{pmatrix} t-t & t-g^+ & t-g^- \\ g^+-t & g^+-g^+ & g^+-g^- \\ g^--t & g^--g^+ & g^--g^- \end{pmatrix}$$

$$U_a = \begin{pmatrix} 1 & \sigma & \sigma \\ 1 & \sigma\psi & \sigma\omega \\ 1 & \sigma\omega & \sigma\psi \end{pmatrix}$$

$$U_b = \begin{pmatrix} 1 & \sigma & \sigma \\ 1 & \sigma\psi' & \sigma\omega' \\ 1 & \sigma\omega' & \sigma\psi' \end{pmatrix}$$

$$U_c = \begin{pmatrix} 1 & \sigma' & \sigma' \\ 1 & \sigma'\psi & \sigma'\omega \\ 1 & \sigma'\omega & \sigma'\psi \end{pmatrix}$$

(a)
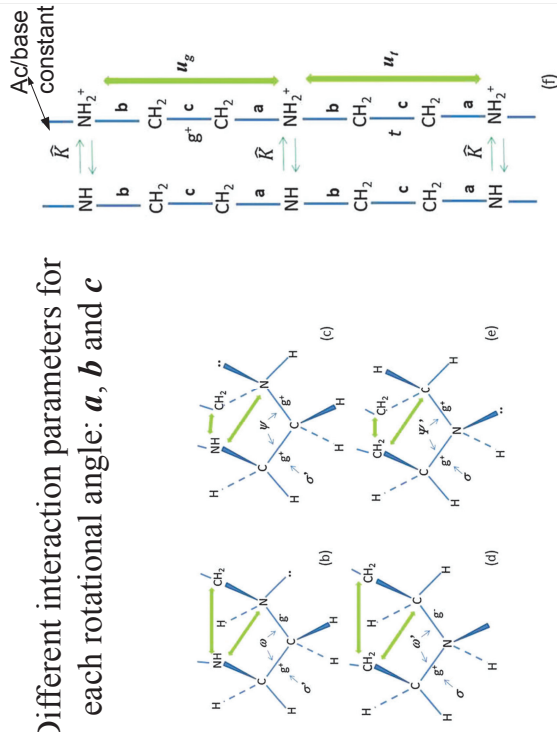
Long-range Interactions

- **Excluded Volume:**

  Each group has a hard-sphere radius:
  Amine group: 1.55 Å
  Methylene group: 1.70 Å

- **Electrostatic interactions:**

  The electrostatic interactions between distant amine groups are mediated by solvent and the ions in solution.

  Debye-Hückel potential:
  $$F_{DH} = \sum_{j>i+1} \frac{e^2}{4\pi\epsilon r_{ij}} \frac{exp(-\kappa r_{ij})}{r_{ij}}$$

  Debye length is: $\quad \kappa^{-1} = \left(\frac{k_B T\epsilon}{2N_A e^2 I}\right)^{1/2}$

  Ionic strength: $I = 1/2 \sum_{i=1}^{n} c_i z_i^2$

SGCMC of Polyamine

- Study of the conformational and ionization properties of linear polyamine

$NH_{2/3}-[CH_2-CH_2-NH_{1/2}]_{50}-$

N=50 monomer
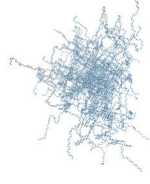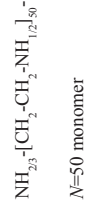
100 different polymer configurations

JL. Garcés, S. Madurga, M. Borkovec, *Phys.Chem.Chem.Phys.*, 2014, 16, 4626.

SGCMC steps

-Two configurational MC changes:

1) Rotational state of a bond.

— One bond is selected at random. The rotational change of a bond involves a ±120 degree rotation of its dihedral angle.

- …↔Gauche+ ↔ trans ↔ gauche-↔….

If some overlap takes place, the new configuration is rejected.

— Atoms of the polyamine has a hard sphere repulsion.

2) Binding state of amines

$$\begin{cases} \Delta F = \Delta U_{el} + k_B T(\ln 10)(pH - \log K_0) \\ \quad \text{for protonation process} \\ \Delta F = \Delta U_{el} - k_B T(\ln 10)(pH - \log K_0); \\ \quad \text{for deprotonation process} \end{cases}$$

Apply ΔF for Metropolis MC algorithm. Accepted movement with probability: $\min\{1, \exp(-\Delta F)\}$

SGCMC simulations.
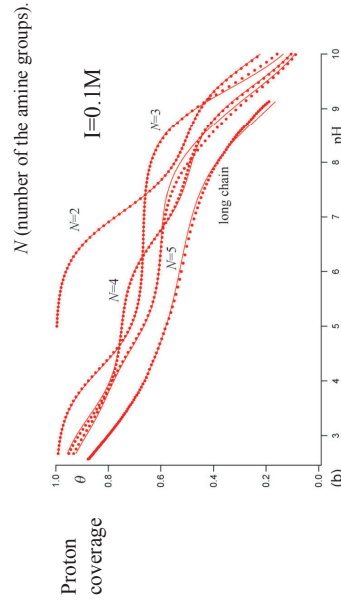
Equilibration: $2·10^8$ configurations
Sampling: $8·10^8$ configurations

Normalized radius of gyration

SGCMC conformations with long-range interactions are more extended

Long-range interactions have a significant **influence** on the **radius of gyration.**

$pH \uparrow \rightarrow q \rightarrow 0 \rightarrow Rg \downarrow$

Continuous lines: Simulation: SGCMC. (the excluded volume + long range electrostatic interactions).
Dotted lines: Theory (without long-range interactions).

JL. Garcés, S. Madurga, M. Borkovec, *Phys.Chem.Chem.Phys.*, 2014, 16, 4626.

Titration curves for different LPEI

N (number of the amine groups).
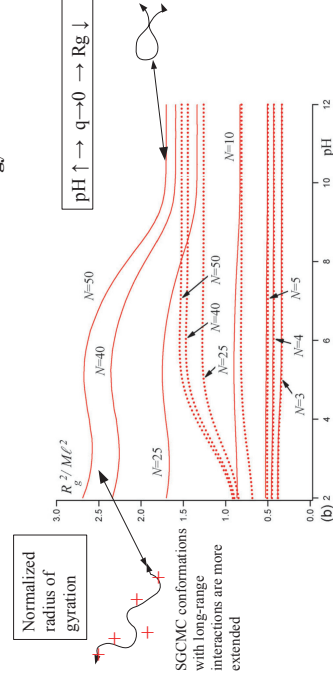
I=0.1M

Proton coverage

Dotted lines: Experimental binding curves.
Continuous lines: Simulation results.

JL. Garcés, S. Madurga, M. Borkovec, *Phys.Chem.Chem.Phys.*, 2014, 16, 4626.

Modeling the spherical colloid

- Hydrophobic core of the spherical colloid build with 942 fixed methane molecules.

- Dimensions: 6 nm

- Procedure: 6 concentric layers of methane molecules. Separation between layers of 0.5 nm

In the neutral state of the colloidal particle water molecules are not able to enter inside the particle.

6 concentric layers

6 nm

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Simulation Techniques for Soft Materials

1) What is a soft material?

2) Stability.

— Double Layer → **NVT MC**

— Effect of pH → Semi-Grand Canonical (**SGCMC**)

3) Flexible materials.

— Conformational vs pH → Semi-Grand Canonical (**SGCMC**)

4) Water/Ion permeability

— Effect of Charge/Ionic strenght → Molecular Dynamics (**MD**)

5) Diffusion and Reactivity

— Effect of crowding/aggregation → Brownian Dynamics (**BD**)

MD SIMULATIONS WITH MONOVALENT SALT

Na$^+$
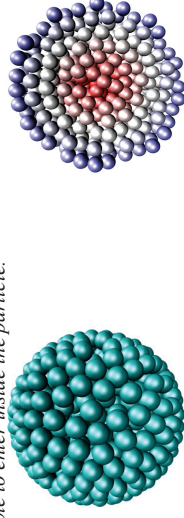
Modeling the spherical colloid
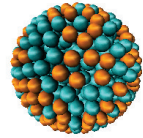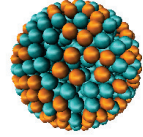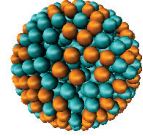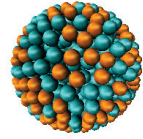
Charges:
25 -0.035 C m^{-2}
50 -0.07 C m^{-2}
100 -0.14 C m^{-2}
200 -0.28 C m^{-2}

Molecular dynamics simulations
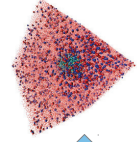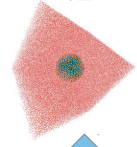
MD with Gromacs
NVT
10 ns
300 K

Na$^+$ and Cl$^-$,
or Ca^{+2} and Cl$^-$
for 0.1M to 1M

Simulation box:
16x16x16 nm^3
>10^5 H$_2$O

Density of Ions around the charged surface

[NaCl] = 1 M
Colloidal charge=200e

Colloidal surface

NaCl 1M

Na, 200q
Cl 200q

Ions inside
Ions outside

conc/M
distance to center/nm

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Density of Ions around the charged surface

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Na$^+$

Colloidal surface

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Ions inside
Ions outside

conc/M
distance to center/nm

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Density of Ions around the charged surface

[NaCl] = 1 M
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Na$^+$

Colloidal surface

NaCl 1M

Ions inside
Ions outside

conc/M
distance
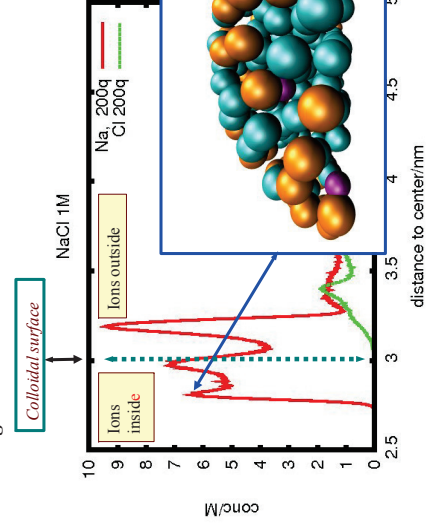
M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Density of Ions around the charged surface

[NaCl] = 1 M
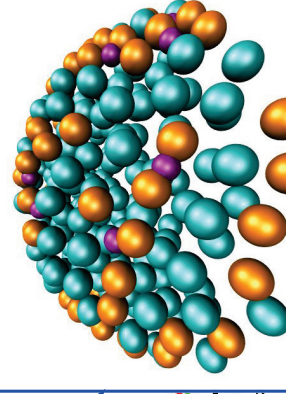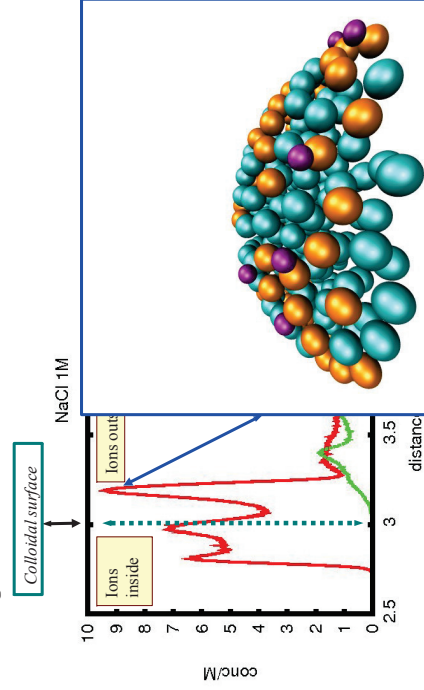Colloidal charge=200e

Na$^+$

Colloidal surface

NaCl 1M

Ions inside
Ions outside

conc/M
distance
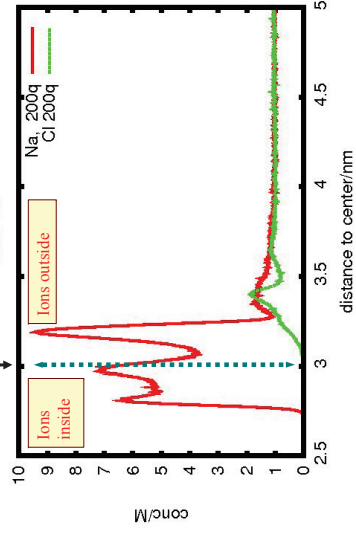
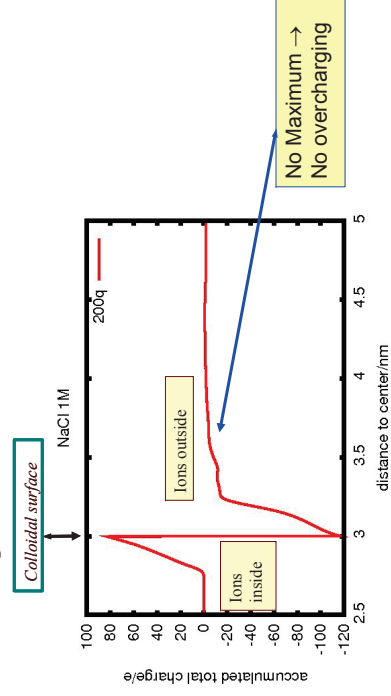M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Integrated total charge from the colloid center

[NaCl] = 1 M
Colloidal charge=200e

Na$^+$

Colloidal surface

NaCl 1M

200q

Ions inside
Ions outside

No Maximum →
No overcharging

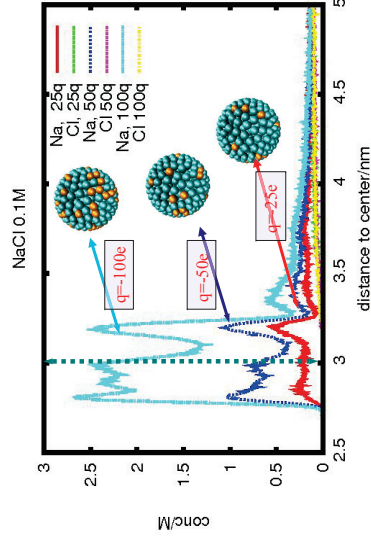accumulated total charge/e
distance to center/nm

No overcharging for a monovalent salt at 1M

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* 137 (2012) 174701

Comparison of different cases for Na at 0.1 M

- Greater amount of Na$^+$ are accumulated in the surface of the colloidal particle with the greater charge.
- Ions are accumulated between the two layers of methanes, between methanes of the last layer and outside the colloid.
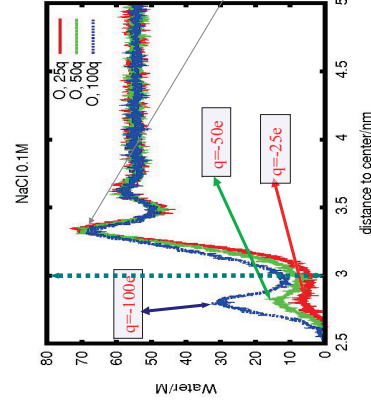
Na$^+$

NaCl 0.1M

Na, 25q
Cl, 25q
Na, 50q
Cl 50q
Na, 100q
Cl 100q

q=25e
q=50e
q=100e

conc/M — distance to center/nm

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* **137** (2012) 174701

Distribution of water molecules around the colloidal particle

Na$^+$

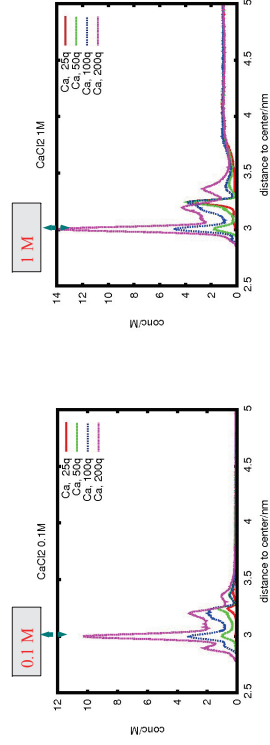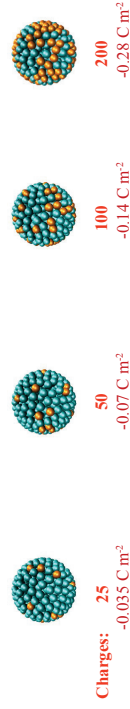*The highest content of water inside the particle corresponds to the highest charged colloid*

Waters close to the surface are more compacted.

NaCl 0.1M

O, 25q
O, 50q
O, 100q

q=-25e
q=-50e
q=-100e

Water/M — distance to center/nm

M. Nedyalkova, S. Madurga, et.al, *J. Chem. Phys.* **137** (2012) 174701

MD SIMULATIONS WITH DIVALENT SALT

Distribution of Ca^{2+} and Cl$^-$ ions at 0.1M and 1M

Ca^{2+}

Charges:
25 — -0.035 C m^{-2}
50 — -0.07 C m^{-2}
100 — -0.14 C m^{-2}
200 — -0.28 C m^{-2}

0.1 M

CaCl2 0.1M

Ca, 25q
Ca, 50q
Ca, 100q
Ca, 200q

conc/M — distance to center/nm

1 M

CaCl2 1M

Ca, 25q
Ca, 50q
Ca, 100q
Ca, 200q

conc/M — distance to center/nm

Integrated total charge from the colloid center

Ca^{2+}

[CaCl$_2$]= 0.1 and 1 M
Colloidal charge= -25, -50, -100 and -200e

0.1 M

CaCl2 0.1M

25q
50q
100q
200q

accumulated total charge/e — distance to center/nm

Colloidal surface

1 M

CaCl2 1M

25q
50q
100q
200q

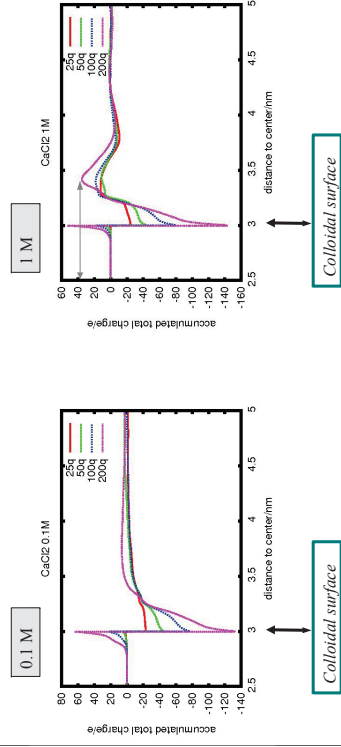accumulated total charge/e — distance to center/nm

Colloidal surface
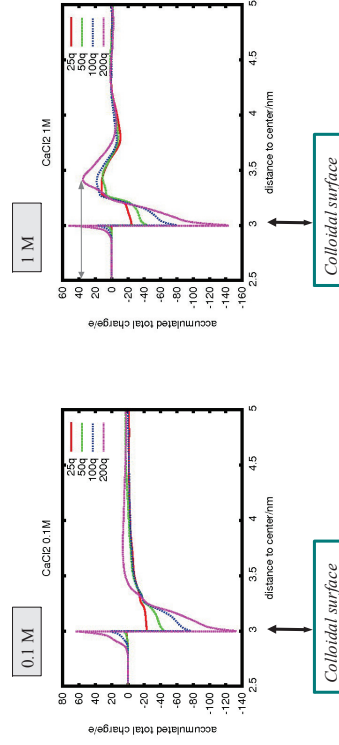
We obtain overcharging for Ca 1M

Integrated total charge from the colloid center

Ca^{2+}

[CaCl$_2$]= 0.1 and 1 M
Colloidal charge= -25, -50, -100 and -200e

0.1 M

CaCl2 0.1M

25q
50q
100q
200q

accumulated total charge/e — distance to center/nm

Colloidal surface

1 M

CaCl2 1M

25q
50q
100q
200q

accumulated total charge/e — distance to center/nm
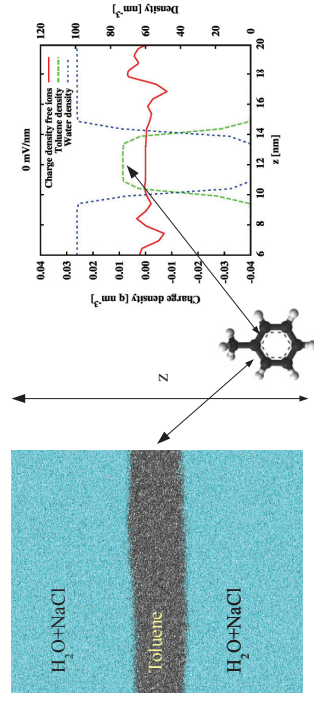
Colloidal surface

We obtain overcharging for Ca 1M

Layer of Toluene. Effect of Voltage

Electro-induced instability of a thin toluene emulsion film in contact with saline aqueous phase.

H$_2$O+NaCl — Toluene — H$_2$O+NaCl

Z

0 mV/nm

Charge density free ions
Toluene density
Water density

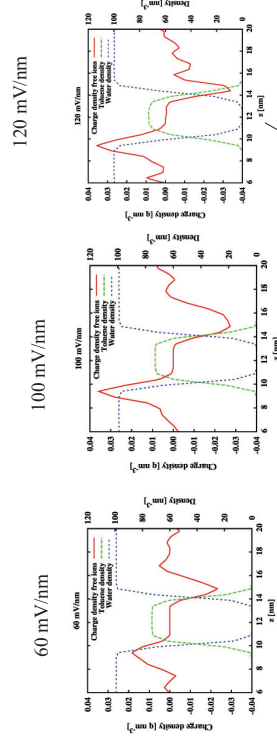Charge density [h nm^{-3}] — Density [nm^{-3}] — z [nm]

Then, external electric field applied perpendicularly to the toluene film

D. Diminova, S. Pisov, N. Panchev, M. Nedyalkova, S. Madurga, A. Proykova, *J. Chem. Phys.* **(2017)**

MD (NVT/NPT)+Voltage

120mV/nm external electric field

The film profile after 100 ps
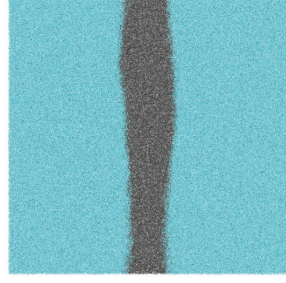
The film profile after 400 ps

Startup of rupturing of the thinnest part of the film - between 400 ps and 500 ps

---

Simulation Techniques for Soft Materials

1) What is a soft material?
2) Stability.
   – Double Layer → **NVT MC**
   – Effect of pH → Semi-Grand Canonical (**SGCMC**)
3) Flexible materials.
   – Conformational vs pH → Semi-Grand Canonical (**SGCMC**)
4) Water/Ion permeability
   – Effect of Charge/Ionic strenght → Molecular Dynamics (MD)
5) Diffusion and Reactivity
   – Effect of crowding/aggregation → Brownian Dynamics (**BD**)

What is macromolecular crowding?

→Enviroment of High concentration of macromolecules.

→ Crowding affect the properties (Diffusion & Reactivity).

Small Macromolecule   Big Macromolecule
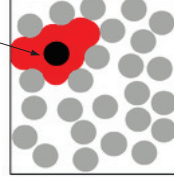
For example, crowding conditions occur routinely in living cells

The accessible volume (red) for two molecules of different sizes (black circles)

R.J. Ellis, *Trends Biochem. Sci.*, **26** (2001) 577

Effect of applied Voltage

Electro-induced instability of a thin toluene emulsion film in contact with saline aqueous phase.
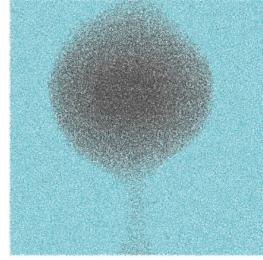
60 mV/nm   100 mV/nm   120 mV/nm

first 100 ps

Great accumulation of ions After 400-500 ps the film is

No ion penetration is observed within the toluene core until 120 mV/nm

---

MD (NVT/NPT)+Voltage

120mV/nm external electric field

Breakdown of the film and formation of a toluene drop at about 2000 ps

- When critical electric field is reached within a certain time after the field application, **electric discharge** occurs indicating the beginning of the rupturing process.
- Molecular dynamics simulations demonstrate the **role of charge accumulation** in the toluene-film rupture induced by a DC electric field.

Diffusion and Reactivity

Study effect of Movility and Reactivity in crowding media
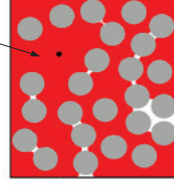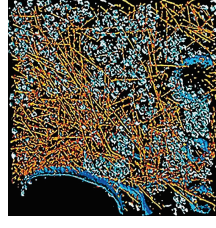
Brownian Dynamics (**BD**)

- **Introduction:**
  - **What is macromolecular crowding?**
  - **Diffusion in a crowded media**
  - **Brownian Dynamics (BD) simulations:**
    - **How to model Dextran?**
    - **Hydrodynamic Interactions (HI)**
    - **Reactivity**

Diffusion in a crowded media

Normal Diffusion:

Diffusion in a crowded media:

Einstein-Smoluchowski equation:
$$<r^2> = (2d)Dt$$

$$<r^2> = (2d)\Gamma t^\alpha$$

α ≡ Anomalous coefficient

α = 1 Normal Diffusion
α > 1 Superdiffusion
α < 1 Subdiffusion

Stokes-Einstein equation:
(spherical particles in a Newtonian fluid)
$$D = \frac{k_BT}{6\pi\eta R_H}$$

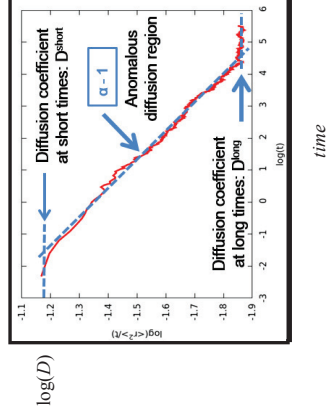$$D(t) = \frac{1}{2d}\Gamma t^{\alpha-1}$$

Diffusion

Diffusion in a crowded media

Off lattice simulations (Brownian Dynamics):

$\log(D)$

Diffusion coefficient at short times: D^{short}

α - 1

Anomalous diffusion region

Diffusion coefficient at long times: D^{long}

$\log(t)$
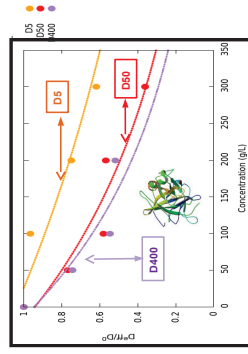
time

Vilaseca, E.; Isvoran. A.; Madurga, S.; Pastor, I.; Garcés, J.L.; Mas, F. Phys. Chem. Chem. Phys., 13 (2011) 7396

Experimental evidences: Diffusion studies in crowded media

Streptavidin protein (R_H = 4.9 nm, M_W = 52.8 kDa)
Fluorescence Correlation Spectroscopy (FCS)

α-Chymiotripsin protein (R_H = 2.33 nm, M_W = 25 kDa)
Fluorescence Recovery After Photobleaching (FRAP)

D5
D50
D400

Concentration (g/L)

Crowding agents

Dextran	M_w (kDa)	$R_{effective}$ (nm)
D5	5.2	1.23
D50	48.6	2.93
D400	409.8	6.69
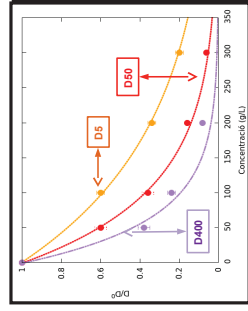
Banks, D.S. and Fradin, C. Biophys J. 89 (2005) 2960

Pastor, I.; Vilaseca, E. Madurga, S.; Garcés, J.L.; Cascante, M.; Mas, F. J.Phys.Chem.. 114 (2010) 4028.ibid 114 (2010) 12152.
Vilaseca, E.; Isvoran. A.; Madurga, S.; Pastor, I.; Garcés, J.L.; Mas, F. Phys. Chem. Chem. Phys. 13 (2011) 7396

Diffusion coefficient reduction depends not only on the obstacle concentration but on obstacle and protein size!

Brownian Dynamics simulations:

- The Langevin equation allows to simulate implicitly the solvent adding a stochastic force $F^R(t)$:

$$m\frac{dv(t)}{dt} = F_T(t) = F^D(t) + F^{fric}(t) + F^R(t)$$

- In the over-damped limit, this equation can be integrated. This gives the BD equation of motion:

$$r(t+\Delta t) = r(t) - \frac{\Delta t D \nabla V(r)}{K_BT} + \sqrt{2D\Delta t}\xi(t)$$

- In our model, a coarse-graining of macromolecules is done and each macromolecule is modeled as a single sphere

- An harmonic pairwise repulsion potential is used in order to avoid macromolecule overlapping:

$$V_{ij} = \begin{cases} \frac{1}{2}k(d_{ij}-R_C)^2 & d_{ij} < R_C \\ 0 & d_{ij} \geq R_C \end{cases} \qquad R_C = R_{c,i} + R_{c,j}$$
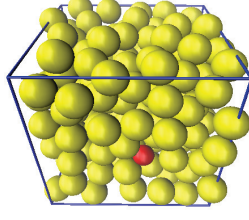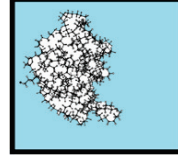
Simulation box of our BD code. A protein (in red) diffuses between Dextran obstacles (in yellow)

P. M. Blanco, M. Vía, J.L. Garcés,S. Madurga, F. Mas, *Entropy* 105 (2017)

Brownian Dynamics: Hydrodynamic Interactions

- Hydrodynamic Interactions (HI) emerge from the fact that Brownian motion of a particle generate solvent fluxes which disturb the other particles motion.

- Procedures to include HI:
  - Ermak and McCammon using the Diffusion tensor (precise but costly).

$$r(t+\Delta t) = r(t) - \frac{\Delta t}{K_BT}D\cdot F(r) + \sqrt{2\Delta t B}\cdot\xi(t)$$

3N x 3N Diffusion tensor

  - Tokuyama (mean field, fast procedure).

$$r(t+\Delta t) = r(t) - \frac{\Delta t D^{short}\nabla V(r)}{K_BT} + \sqrt{2D^{short}\Delta t}\xi(t)$$

$$D^{short}(\phi) = \frac{D_0}{[1+H(\phi)]}$$

$$H(\phi) = \frac{2b^2}{1-b} - \frac{c}{1+2c} - \frac{bc(2+c)}{(1+c)(1-b+c)}$$

D.L. Ermak and J. A. McCammon, J.Chem. Phys. 69 (1978) 1352.
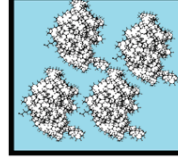

How to model Dextrans?

Experimental hydrodynamic radius:
Effective hydrated radius of a hard sphere that diffuses at the same rate as the macromolecule in dilute solution
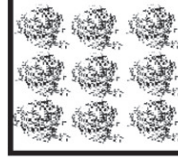
Effective radius:
Effective hydrated radius of a hard sphere that diffuses at the same rate as the macromolecule in concentrated solution

Compact radius:
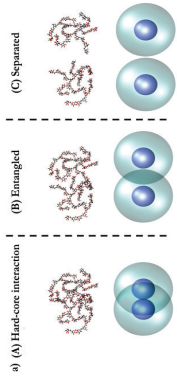*Radius that would have the macromolecule if it was in solid state*

Overestimation

Underestimation

Experimental hydrodynamics radius

Effective radius

Compact radius

BD Simulation

C=25 g/L   C=100 g/L

Concentration increase

(a)   (b)

Simulation box of two BD simulations of streptavidin protein (purple) diffusing among D50 dextran obstacles (blue).

As the concentration increases, steric compresion promotes macromolecules to become entangled.

Diffusion in a crowded media

Diffusion coefficient (D) versus time (t) in the logarithmic scale.

C=350 g/L

Diffusion at short times: $D = D^{short}$

Anomalous diffusion regime: $D(t) \propto t^{\alpha-1}$

Diffusion at long times: $D = D^{long}$

3000 BD simulations in a cubic simulation box with a side of 28.466 nm.
5 tracer particles (streptavidin) diffusing among 100 obstacle particles (D50 dextran).
Macromolecular crowding slows down the tracer diffusion coefficient from D^{short} to D^{long}

Reactivity – Brownian Dynamics

- Continuous 3D volume with periodic boundary conditions
- Solutes described explicitly
- Individual coarse-grained hard-spheres

Crowder ● Enzyme ● Complex ● Substrate ● Product ●

Transported via stochastic dynamics (Langevin equation)

$$R_i(t+\Delta t) = R_i(t) - \Delta t D \frac{\nabla V(R_i(t))}{k_B T} + \sqrt{2D\Delta t}\,\xi_i(t)$$
$$i = x,y,z$$

Harmonic pairwise repulsive potential

$$V_{ij}(\boldsymbol{R}_{ij}) = \begin{cases} \frac{1}{2}k_{pair}(d_{ij}-r_{ij})^2 & d_{ij} < r_{ij} \\ 0 & d_{ij} \geq r_{ij} \end{cases}$$

How to model Dextrans

Scheme of Chain Entanglement Soft-Core model.

a) (A) Hard-core interaction   (B) Entangled   (C) Separated

The particles effectively have two states, one extended and other compacted
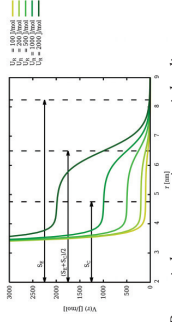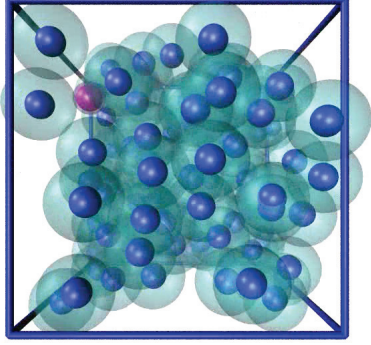
Potential energy vs inter-particle distance

- Macromolecules are modelled as spheres with two different shells.
- The outer shell (transparent blue) accounts for the soft-core repulsion between macromolecular branches.
- The inner shell (opaque blue) takes into account the hard-core steric repulsion due to the incrising steric repulsion.
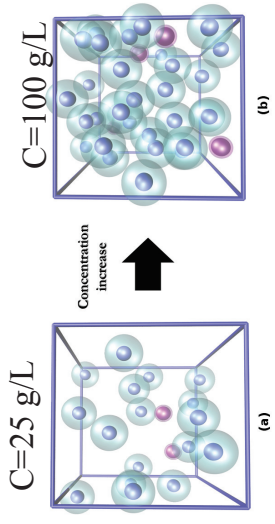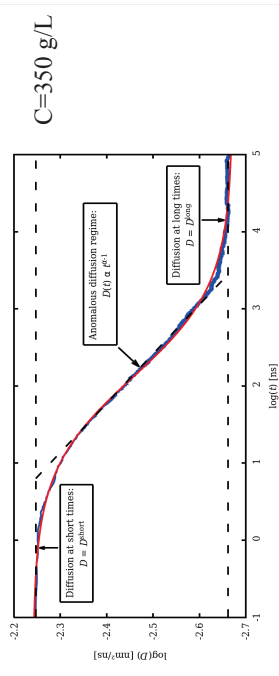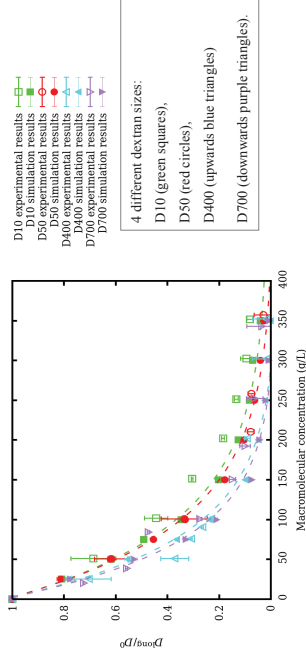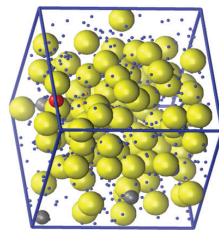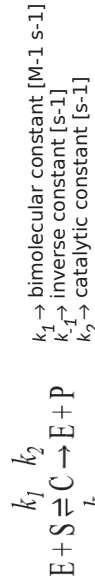

BD Simulation

C=100 g/L

Size: 43.2 nm
Enzymes: 5
Dextrans: 100
radii E. (Hidro/Compact): 3.04/2.45 nm
radii D. (Hidro/Compact): 5.2/2.3 nm

Effect of crowding

D^{long} for streptavidin versus macromolecular concentration.

D10 experimental results
D10 simulation results
D50 experimental results
D50 simulation results
D400 experimental results
D400 simulation results
D700 experimental results
D700 simulation results

4 different dextran sizes:
D10 (green squares),
D50 (red circles),
D400 (upwards blue triangles)
D700 (downwards purple triangles).

Results: Reactivity

Fast enzyme
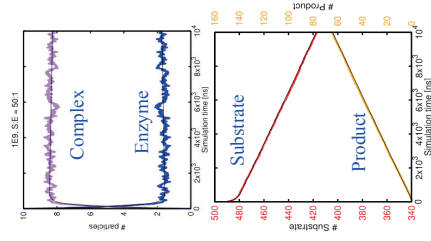
Slow Enzyme
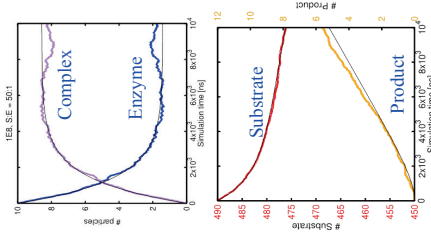
We obtain the temporal evolution of Enzyme, Complex, Substrate and Products.

Michaelis-Menten mechanism

<u>Reactivity</u>

Michaelis-Menten mechanism

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} E + P$$

$k_1 \rightarrow$ bimolecular constant [M-1 s-1]
$k_{-1} \rightarrow$ inverse constant [s-1]
$k_2 \rightarrow$ catalytic constant [s-1]

Probability of Reaction:

$$p_{react} = k_{micro} * \Delta t \qquad (0 < p_{react} < 1)$$

So we can use a Monte Carlo criterion

If random $> p_{react} \longrightarrow$ **no** reaction

If random $\leq p_{react} \longrightarrow$ **reaction**

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THANK YOU FOR YOUR ATTENTION

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