Colloidal interactions and dynamics at liquid interfaces and lateral motion of proteins and lipids on live cell membrane

Penger Tong

Department of Physics
Hong Kong University of Science and Technology

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OUTLINE:

1. Physics at interfaces
2. Colloidal interactions at liquid interfaces
3. Brownian dynamics of interfacial particles
4. Lateral motion of membrane-bound proteins and lipids
5. Summary

Collaborators:

Wei Chen, Yuan Peng, Hao Song, Wei He (HKUST)

Tai-Kai Ng, Lin Geng, Ben Peng (HKUST)

Su-Sheng Tan, Warren Ford (OSU)

Thomas Fischer (U of Bayreuth)

David Weitz (Harvard U)

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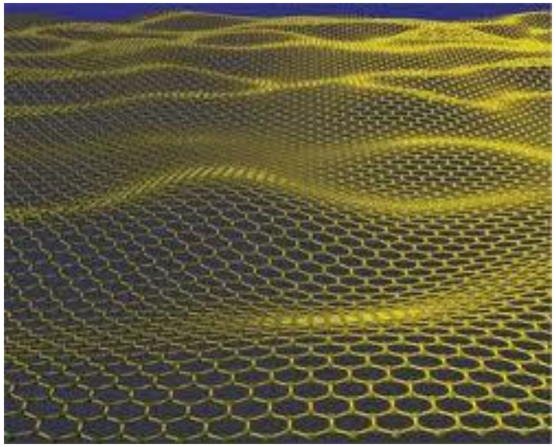
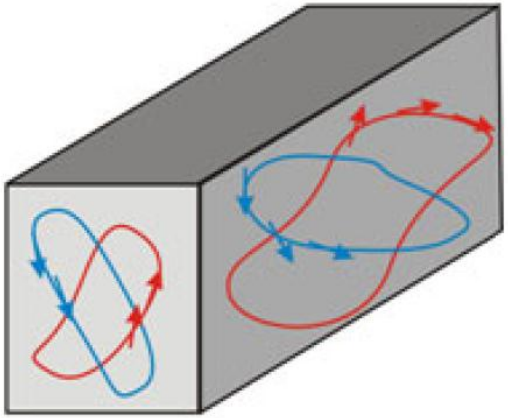
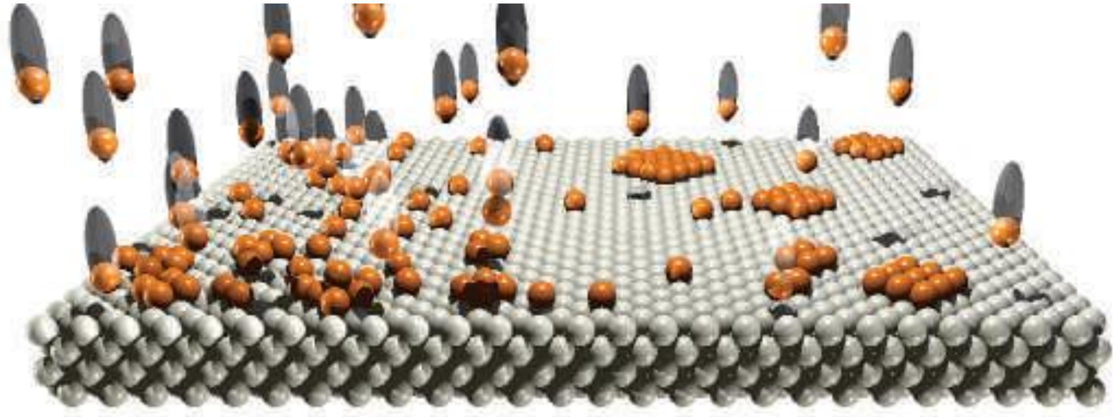
1. Physics at interfaces



Graphene



3D topological insulator



Surface @ P 🕓 0 atm and T 🕓 0K

Water drop on a super-hydrophobic surface (www.itg.uiuc.edu)

Water droplets on a non-wetted lotus leaf

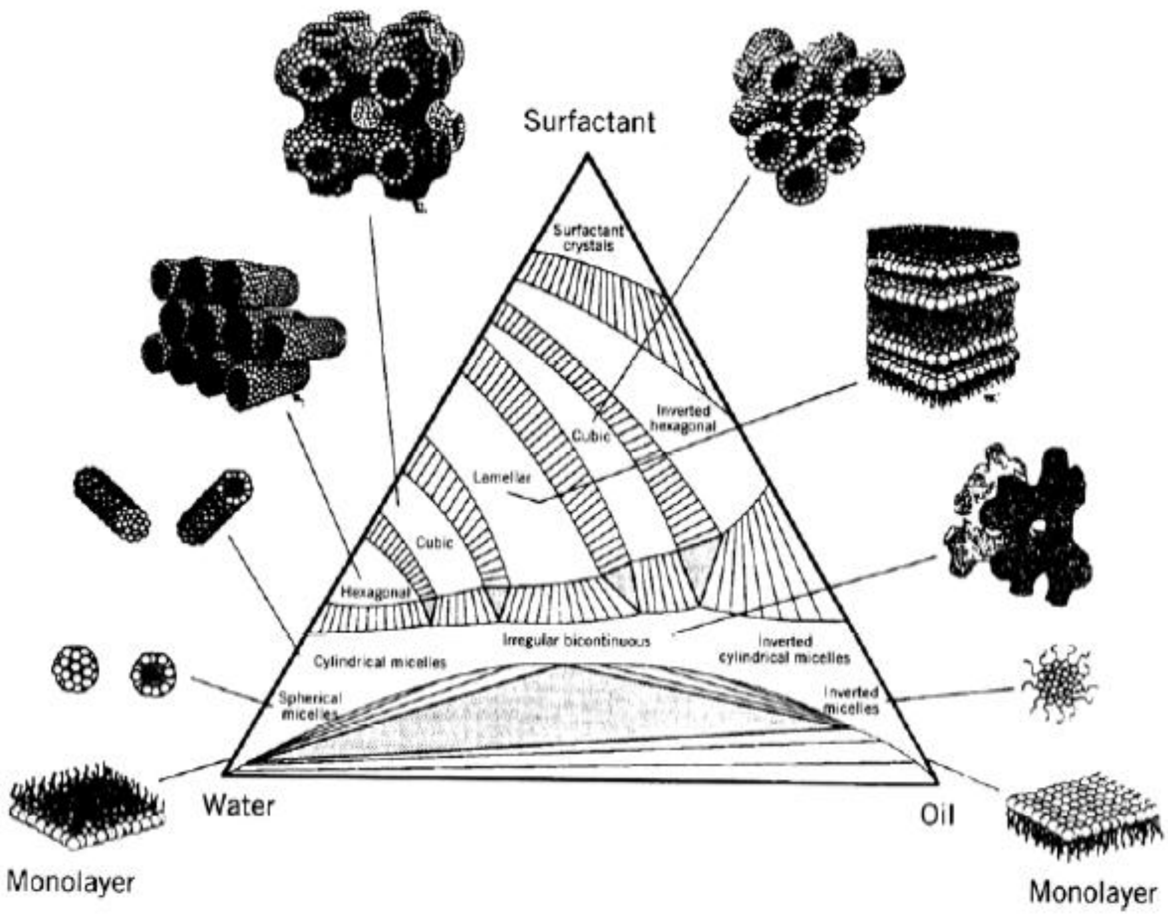
Spreading parameter:

$$S = \gamma_{sv} - \left(\gamma_{ls} + \gamma_{lv}\right)$$

$S > 0$, liquid likes the surface and a liquid film forms (complete wetting)

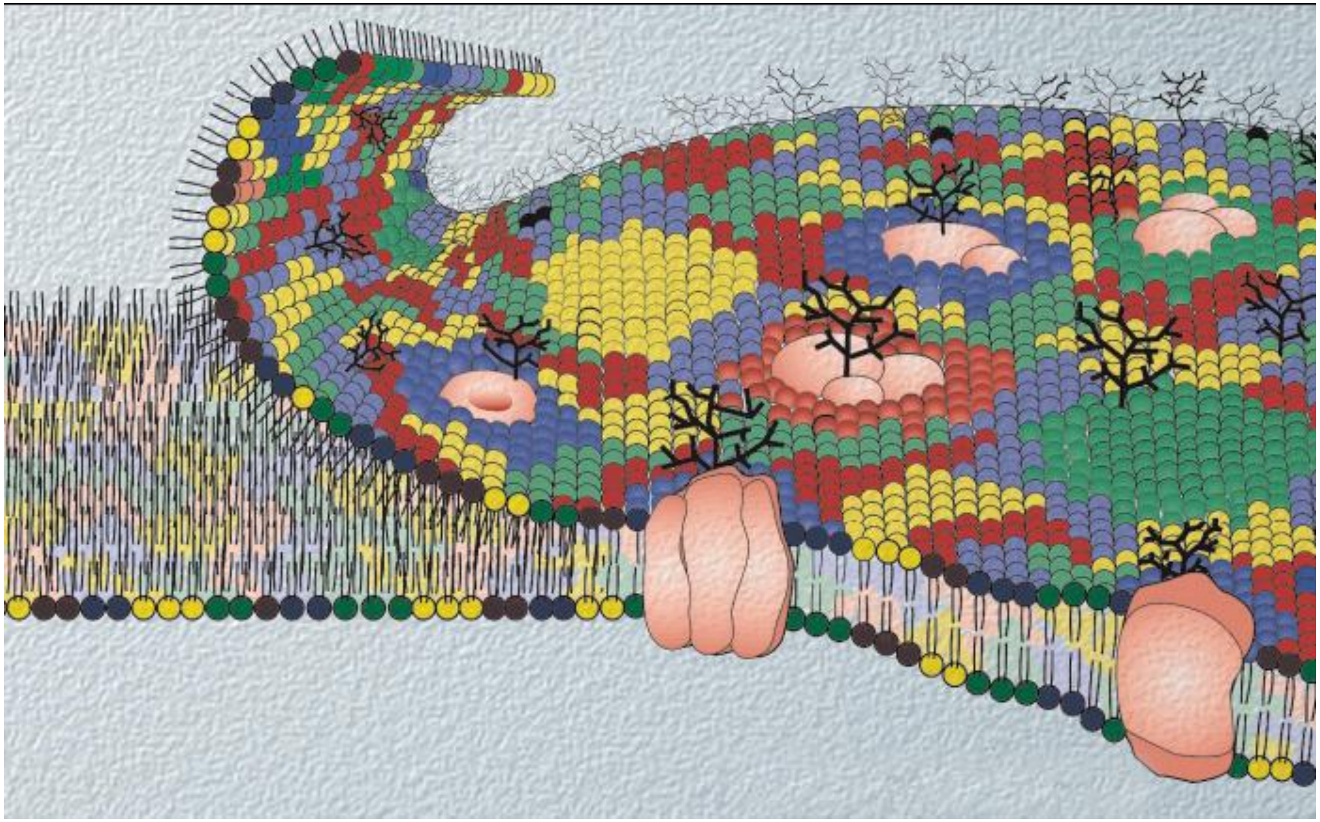
$S < 0$, liquid droplets form on solid surface (partial wetting)

Wetting properties of a fluid droplet on a solid surface represents a class of common natural phenomena. Understanding of these phenomena not only presents challenges to basic research but also leads to a variety of practical implications.



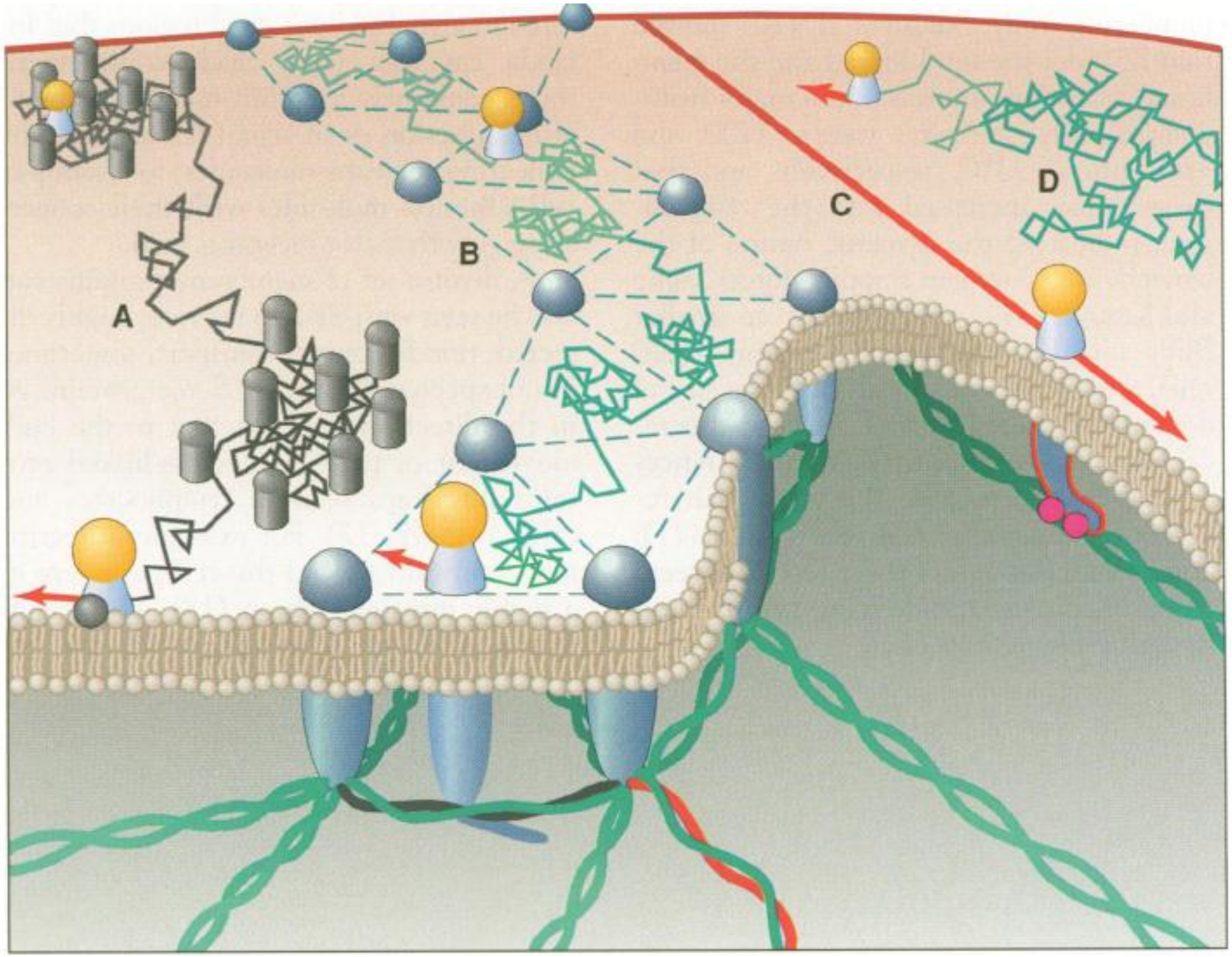
Schematic phase diagram of a surfactant/water/oil ternary solution

Liquid-liquid interfaces (e.g., water-air interface) covered by a monolayer of surfactant molecules



Fluid mosaic membrane of Singer and Nicholson (1972)

Revision on Fluid Mosaic Model (Jacobson *et al.*, *Science*, 1995)

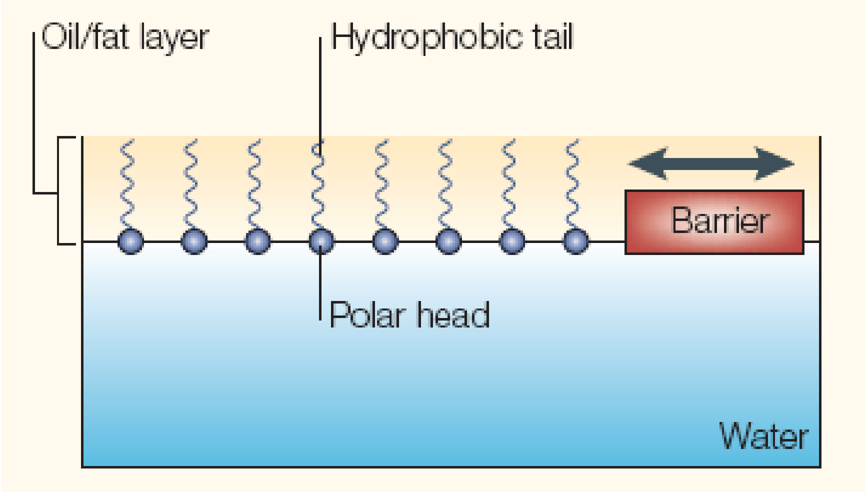


A: hindering by obstacle clusters

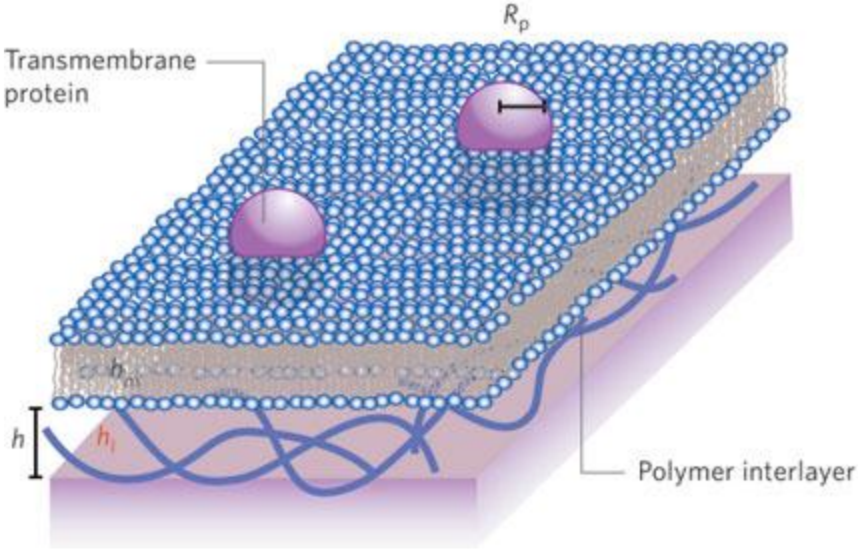
B: confinement by cytoskeleton traps (0.3-1 ❍m)

C: directed motion along microtubeles (motor driven?)

D: free diffusion

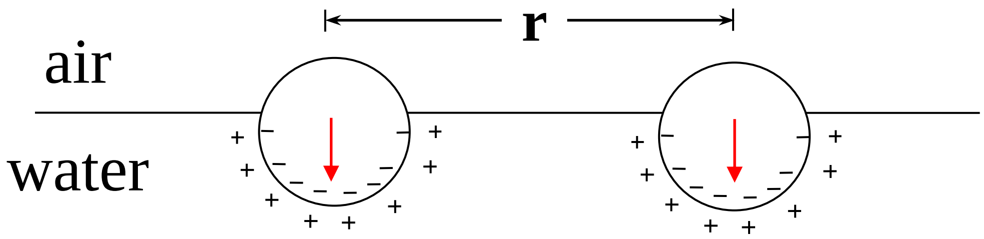


A monolayer of surfactant/lipid molecules at water-air interface

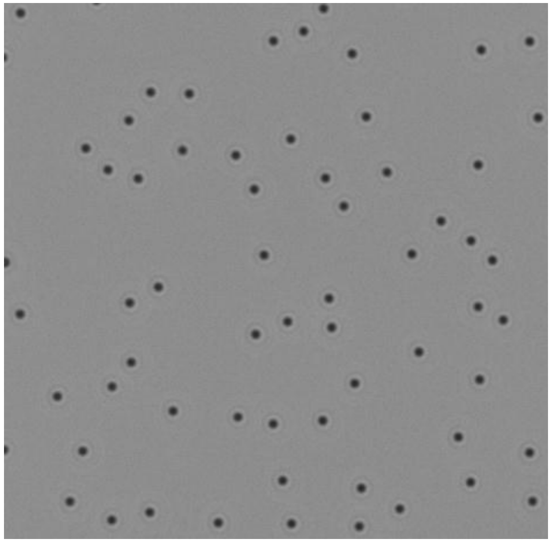


Polymer-supported membrane

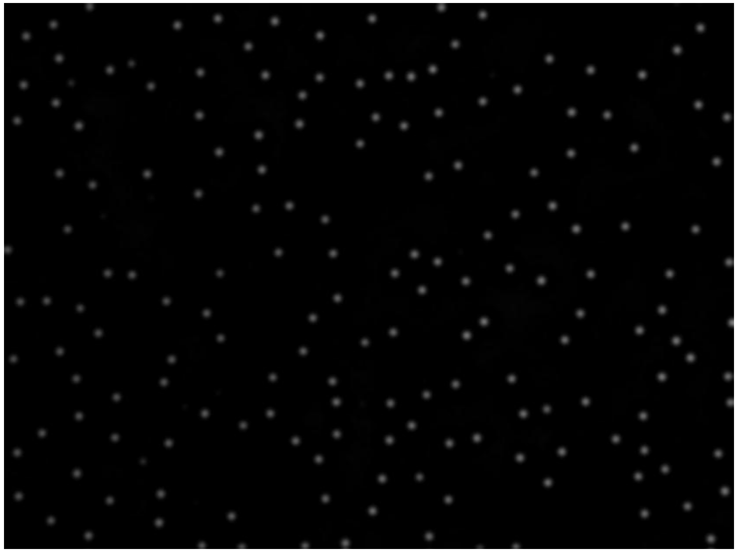
Colloids as surfactants (�1000): a model system to study interactions and dynamics at liquid interfaces



A 2D system without influence of gravity and clearly visible at any concentration without multiple scattering

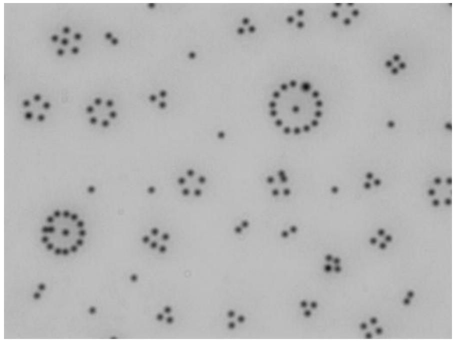


Charged latex spheres
at a water-air interface

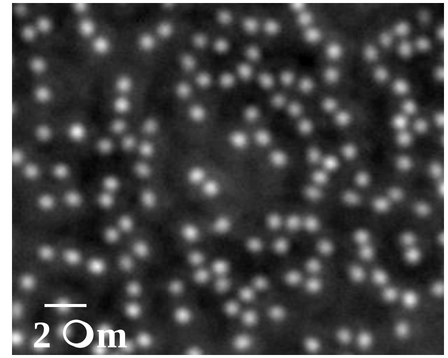


Nearly hard spheres (PMMA)
at a decalin-water interface

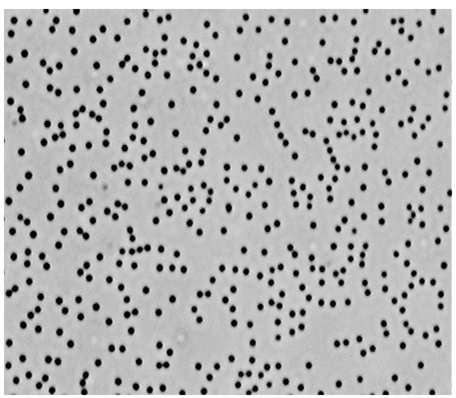
Our recent experiments on interfacial dynamics and interactions



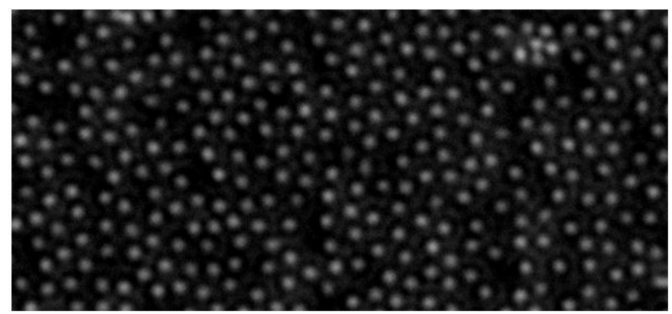
Interactions between strongly charged polystyrene spheres



Interactions between weakly charged silica spheres

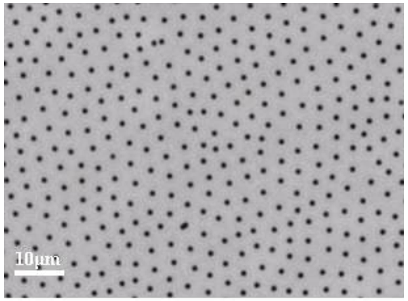


Short-time self-diffusion of nearly hard spheres (PMMA)

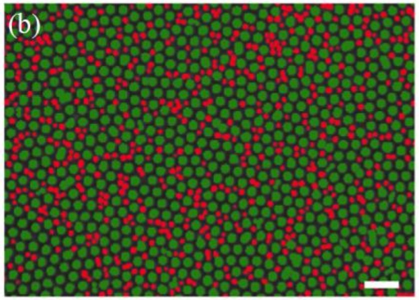


Short-time self-diffusion of weakly charged silica spheres

Current experiments on interfacial dynamics and interactions



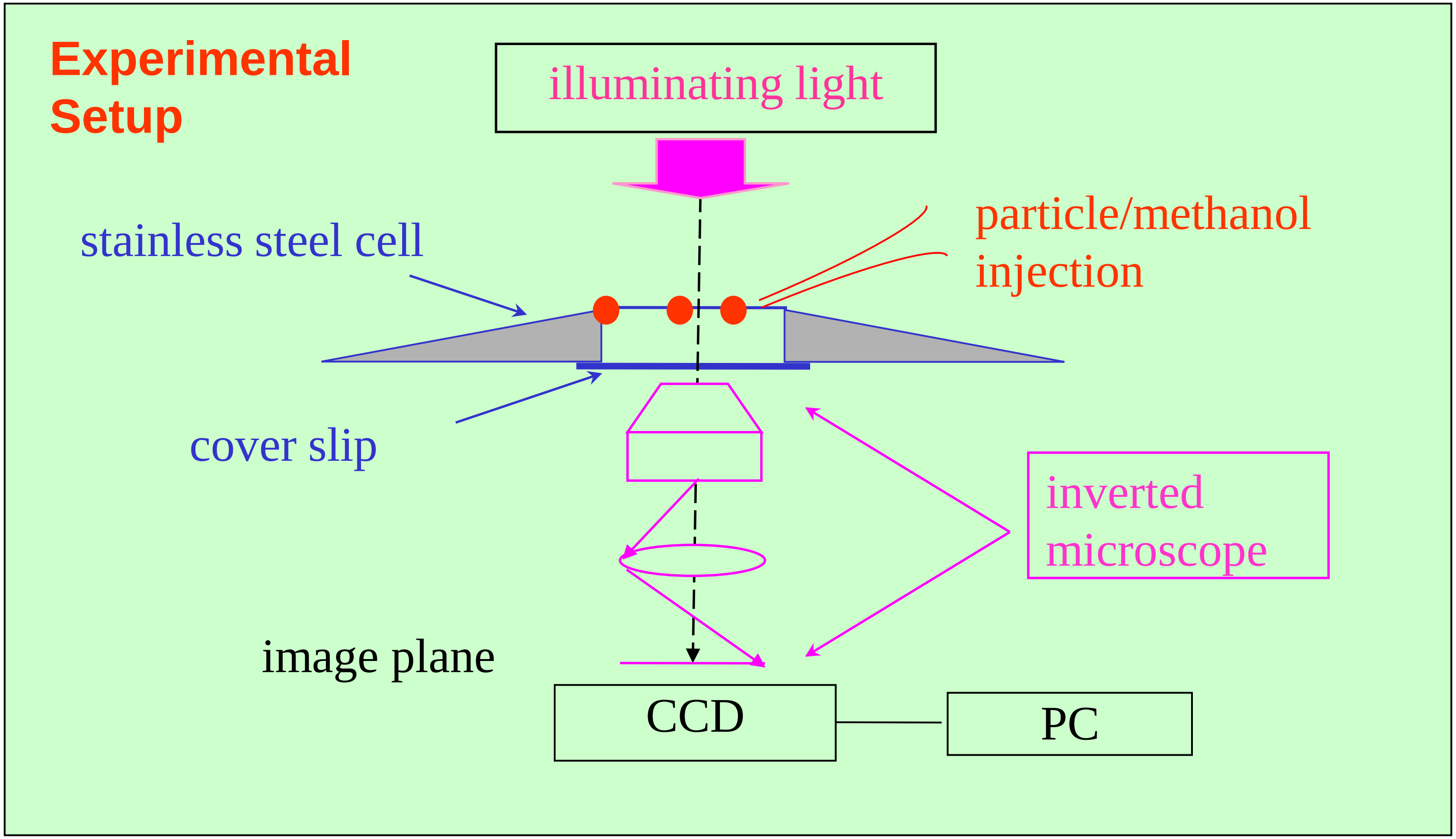
Self-diffusion of strongly charged polystyrene spheres



Glassy dynamics in monolayer suspension of bidisperse colloidal particles

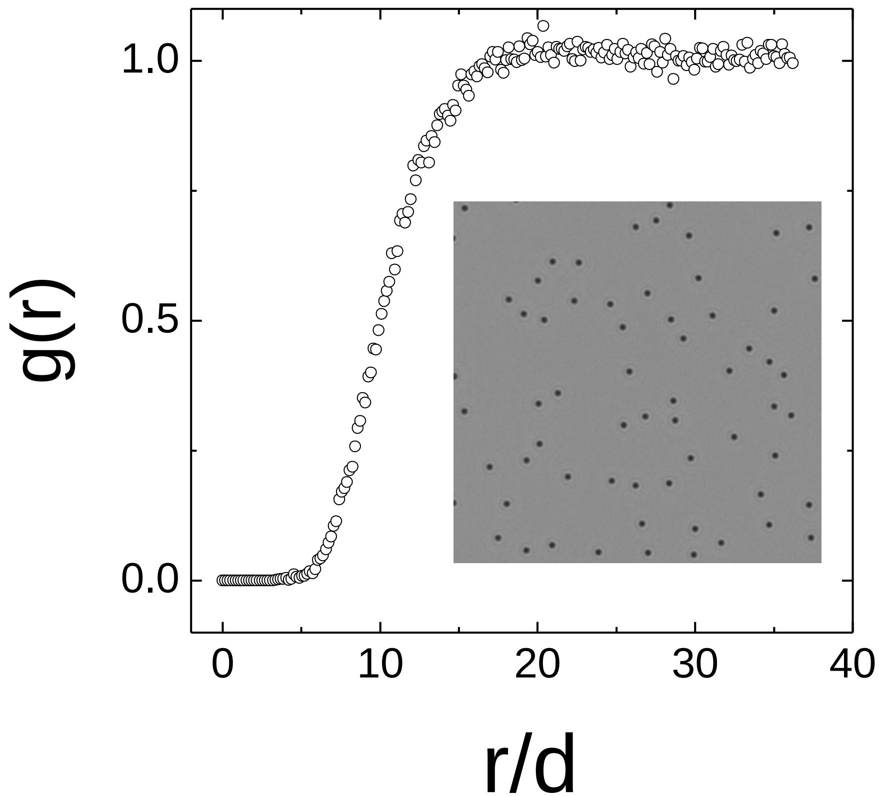
- W. Chen, S.-S. Tan, T. K. Ng, W. T. Ford, and P. Tong, *Phys. Rev. Lett.* **95**, 218301 (2005).
- W. Chen, S.-S. Tan, Z.-S. Huang, T. K. Ng, W. T. Ford, and P. Tong, *Phys. Rev. E* **74**, 021406 (2006).
- W. Chen and P. Tong, Europhys. Letters **84**, 28003 (2008).
- Y. Peng, W. Chen, Th. M. Fischer, D. A. Weitz, and P. Tong, J. Fluid Mech. **618**, 243 (2009).
- W. Chen, S.-S. Tan, Y. Zhou, T.-K. Ng, W. T. Ford, and P. Tong, *Phys. Rev. E* **79**, 041403 (2009).

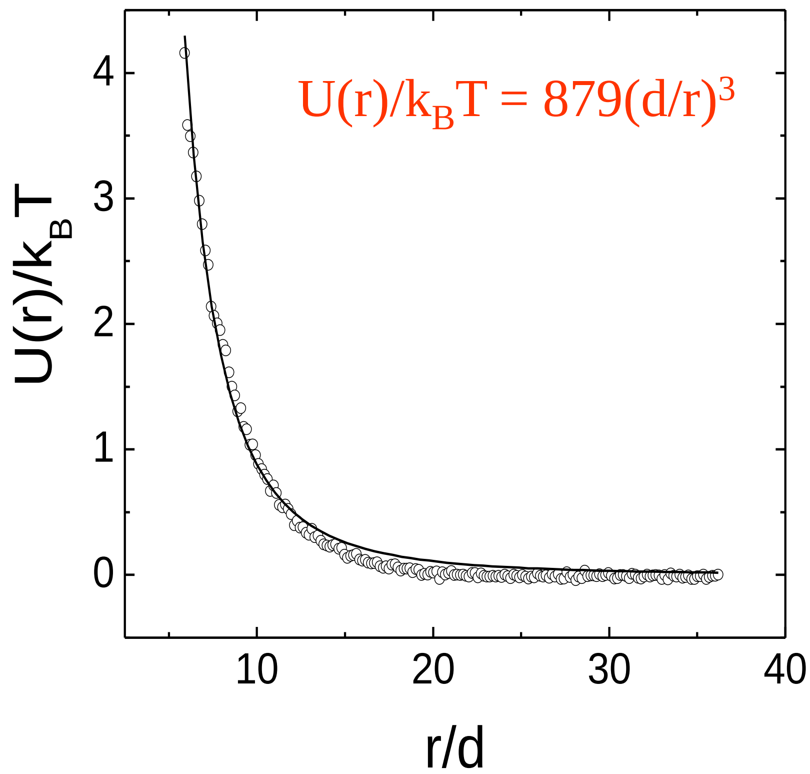
2. Colloidal interactions at liquid interfaces



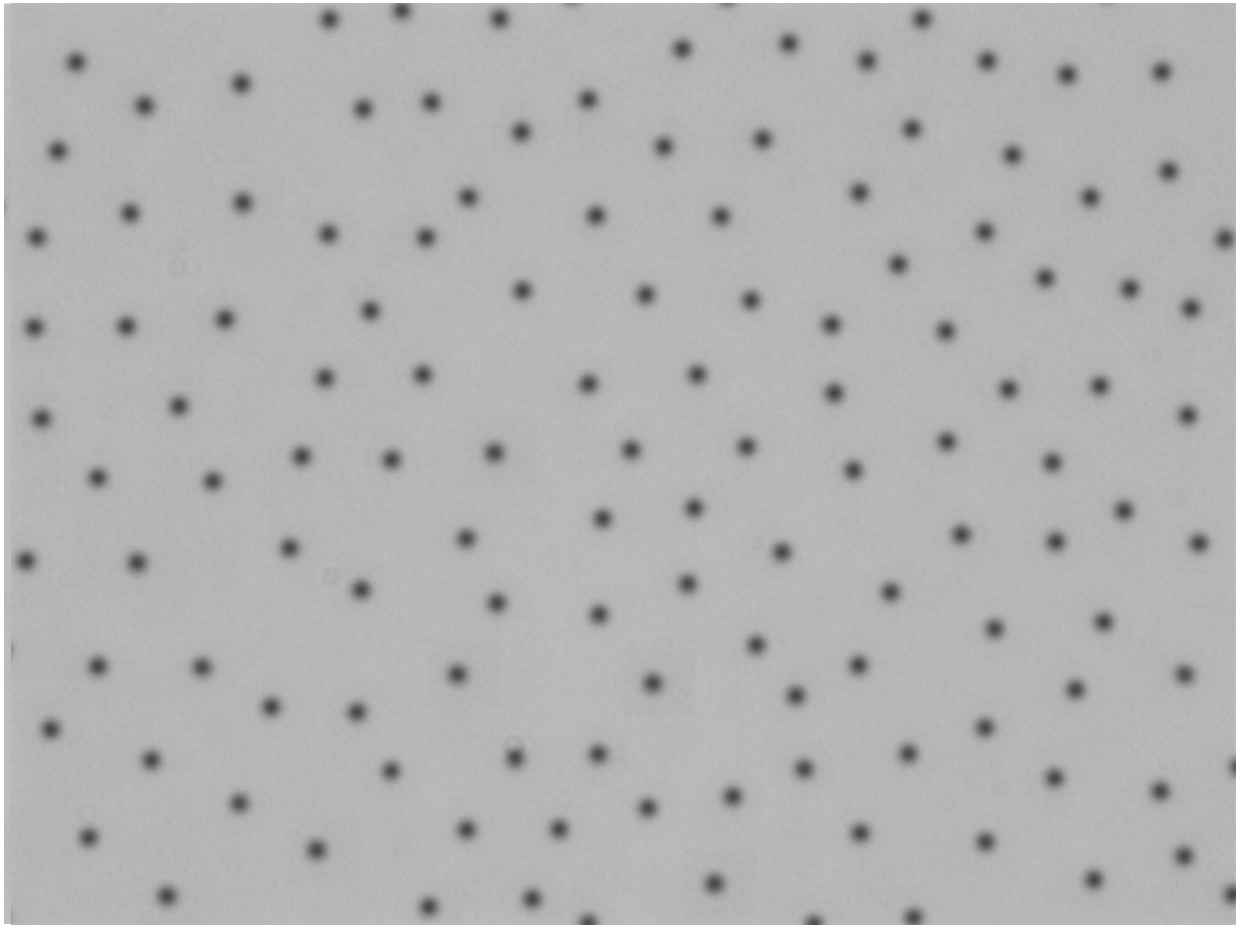
(i) Strongly charged polystyrene spheres (♦$_0$🕔12.5 μC/cm^2)

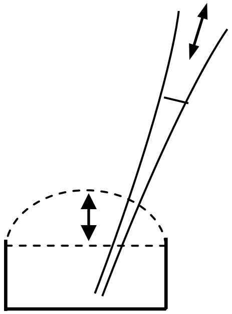
Measured g(r) at low surface coverage and the corresponding interaction potential $U(r)/k_BT$ 🕔 -ln[g(r)]





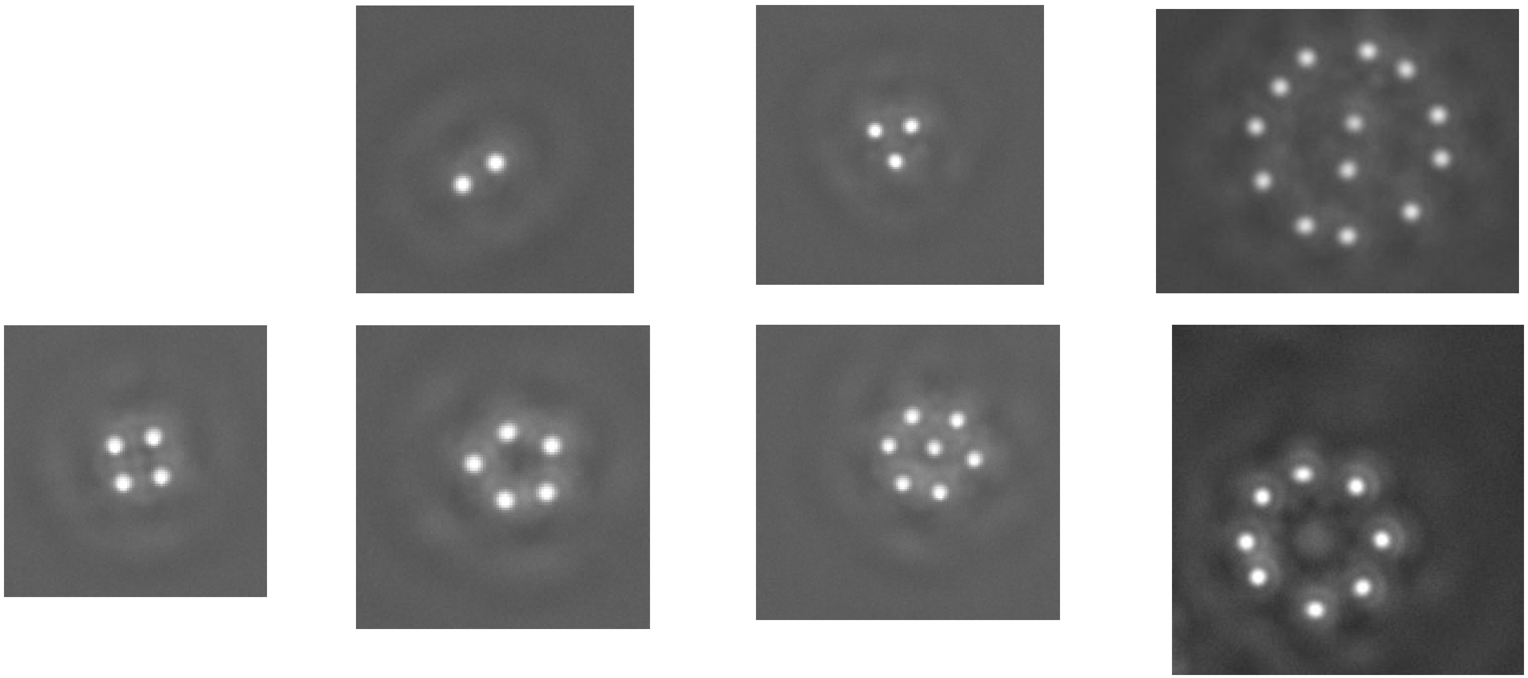
Formation of particle clusters by stirring the air-water interface





Periodic dilation of the interface provides kinetic energy $mv^2/2$ 🕔 $9k_BT$ to the interfacial particles to overcome an energy barrier.

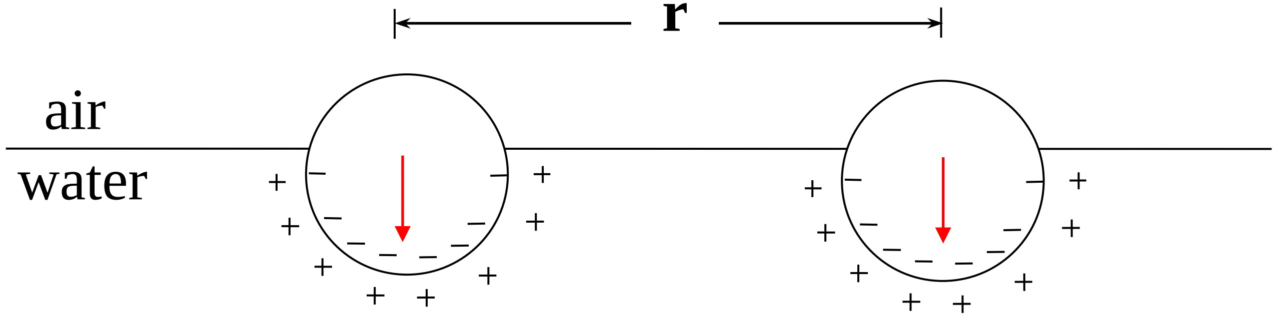
Particle clusters



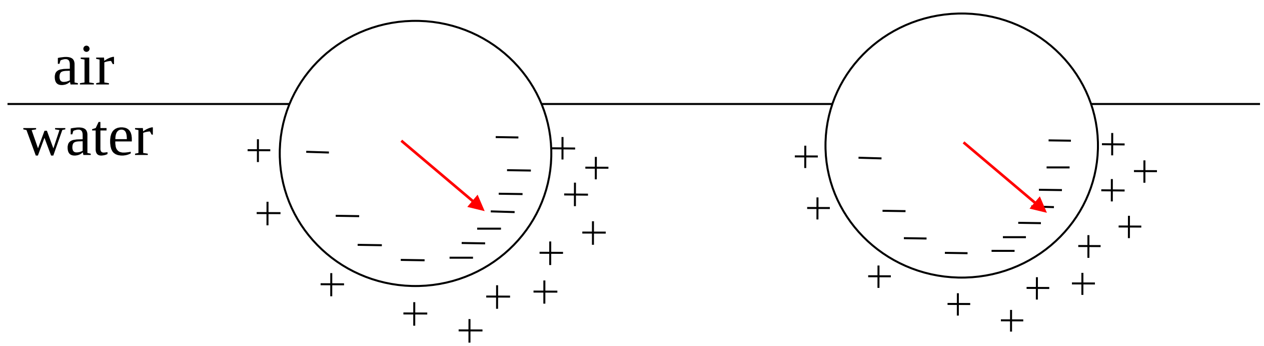
- “Coulombic molecules” result from a minimization of the total electrostatic energy of the entire cluster.

- Formation of circular chains is a hallmark of dipole-like attractions without an external field.

Where does attraction come from?

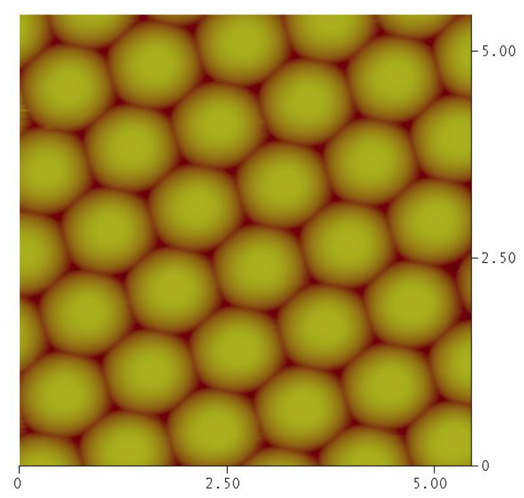


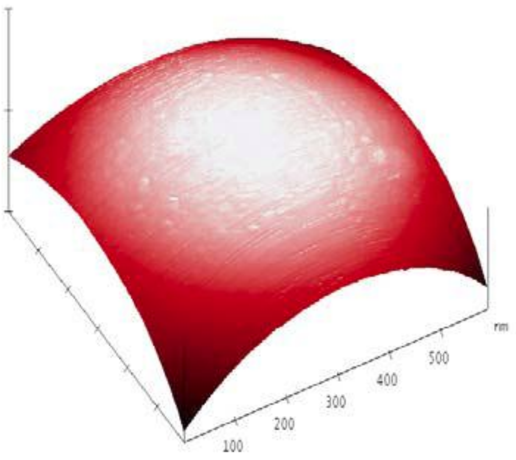
$$U(r) = A\frac{\exp(-r/\lambda_D)}{4\pi\varepsilon_0\varepsilon r} + \frac{P_z^2}{4\pi\varepsilon_0\varepsilon r^3} - \frac{P_{\parallel}^2\langle 3\cos\phi_1\cos\phi_2 - \cos(\phi_2 - \phi_2)\rangle}{4\pi\varepsilon_0\varepsilon r^3}$$



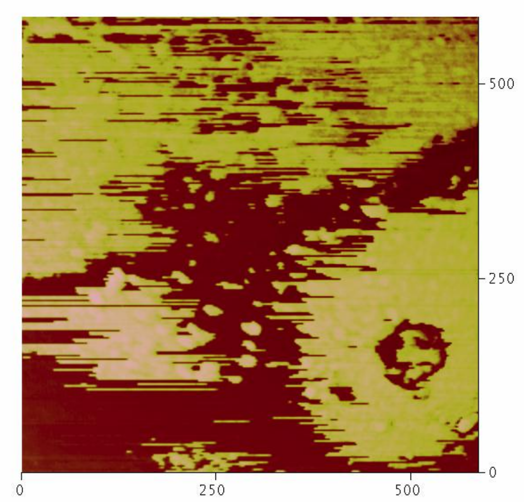
$$k_B T = \frac{2P_{\parallel}^2}{4\pi\varepsilon_0\varepsilon r_{\mathbf{N}}^{\mathbf{3}}}$$

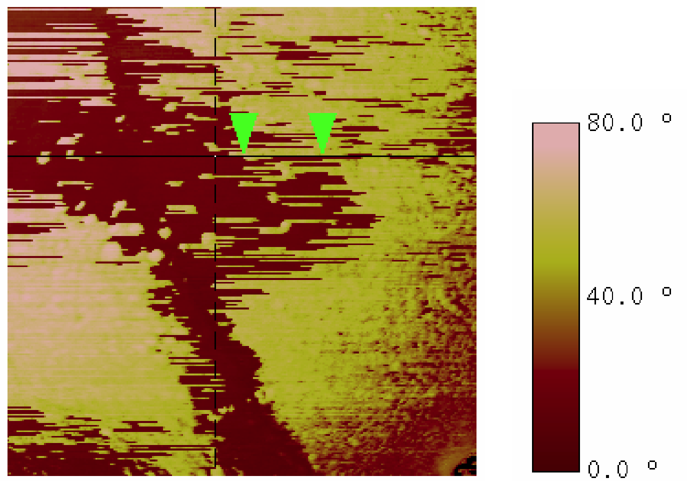
AFM images of the carboxyl polystyrene spheres





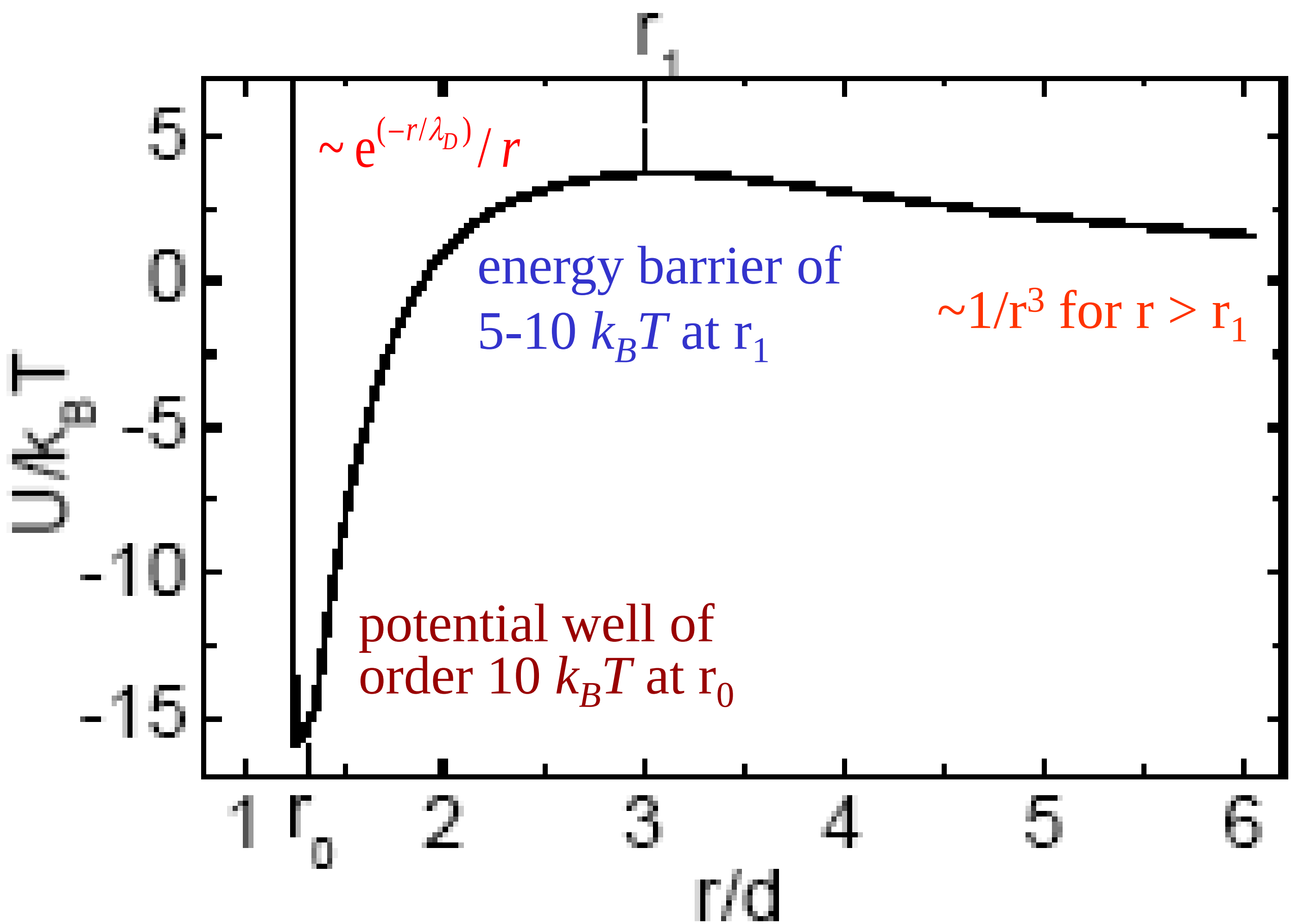
Topographic images of the particle surfaces



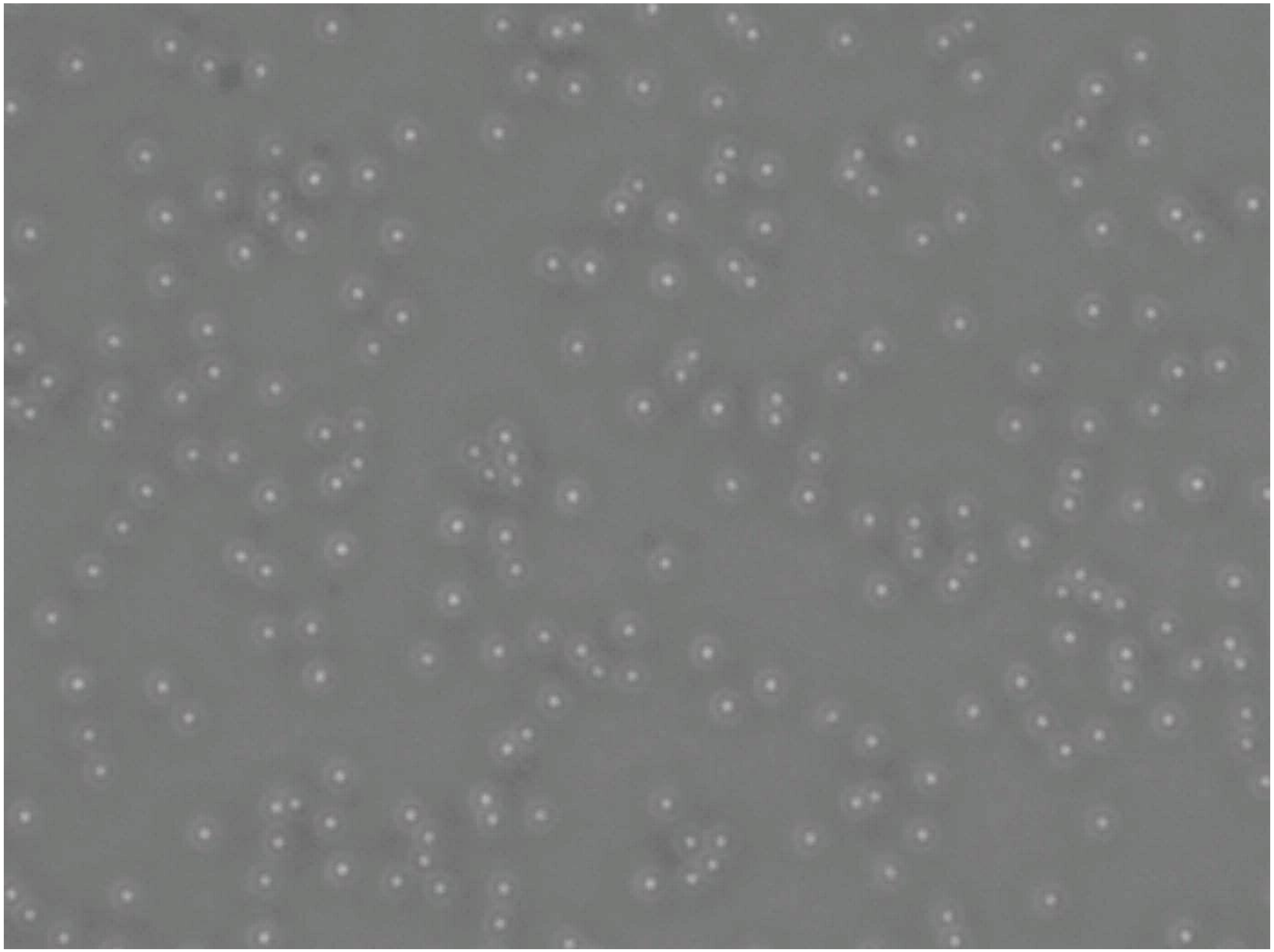


Phase images of the particle surfaces

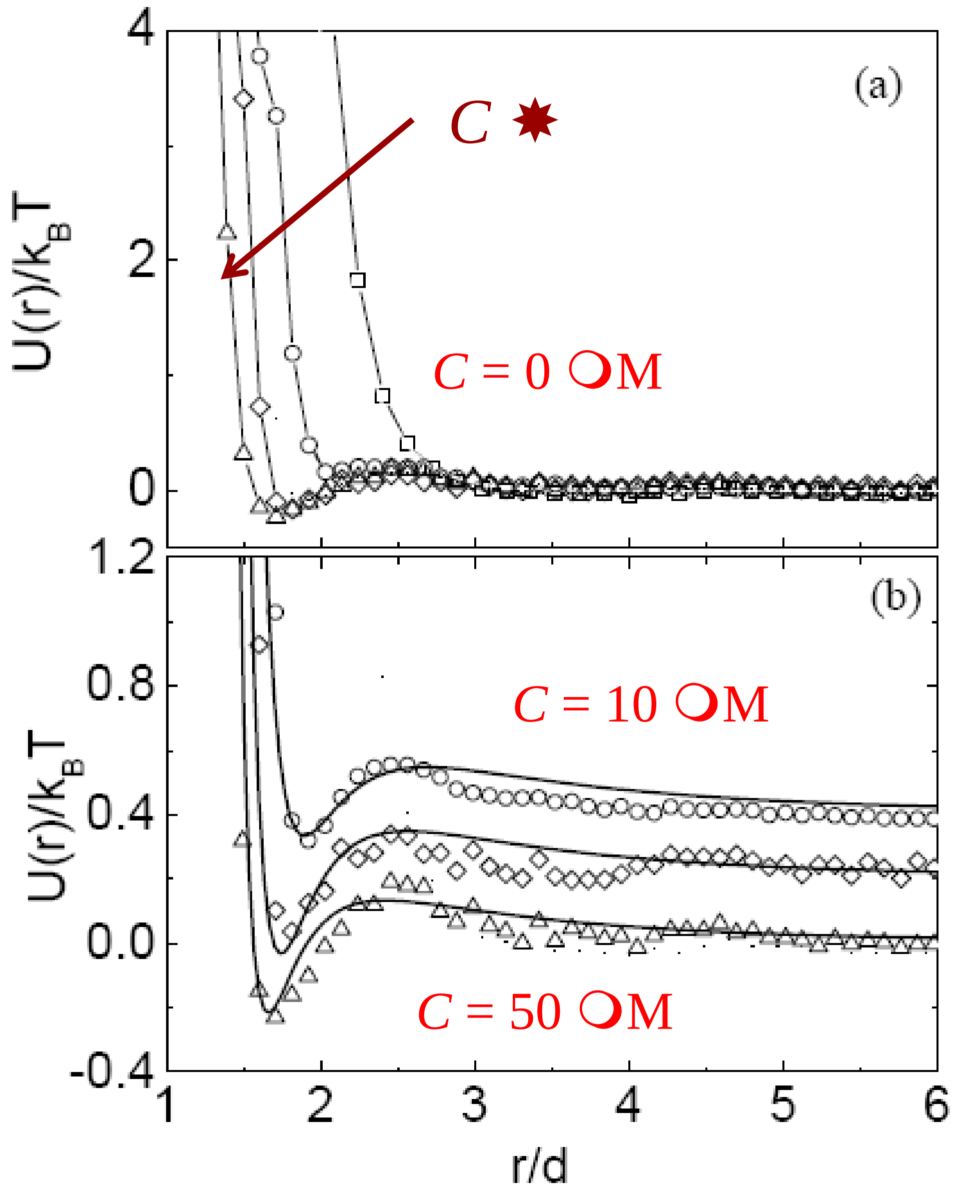
Characteristic features of the measured U(r)



(ii) Weakly charged silica spheres (♦$_0$ 🕔 1 � 10^{-2} μC/cm^2)



Effect of adding salt (NaCl)



Shortening of the screening range with increasing salt concentration C

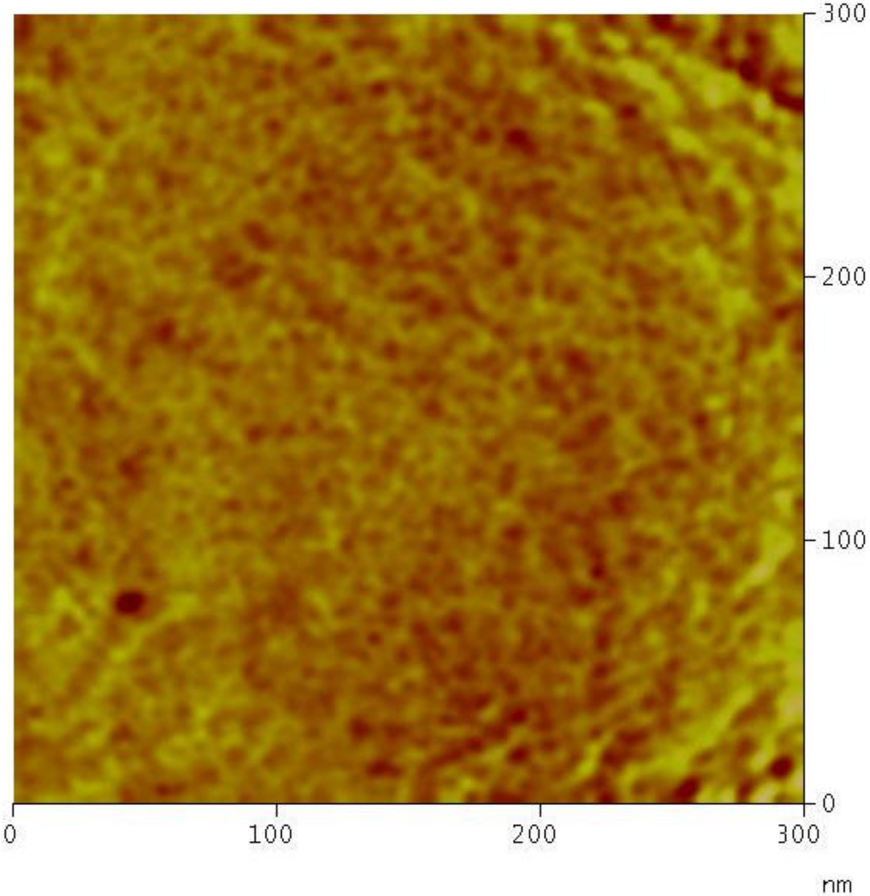
Gradual development of an attractive well of -0.3 k_BT

Gradual development of a repulsive barrier of ~0.15 k_BT

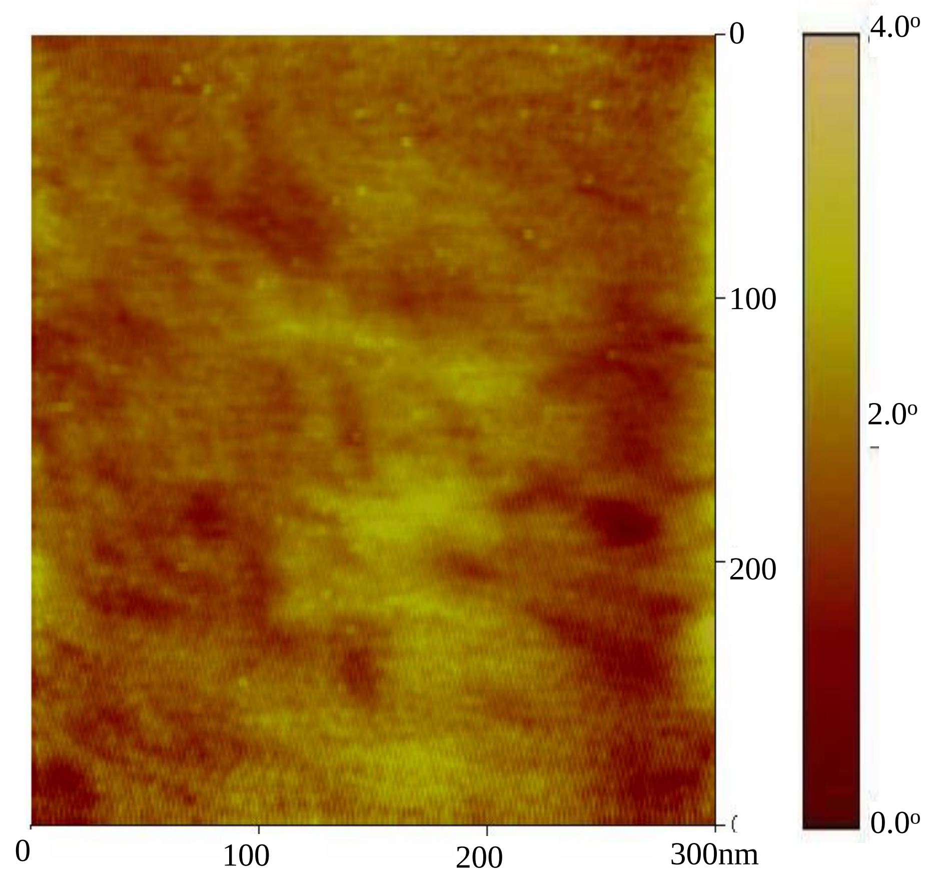
$$U(r) = U_C(r) + \beta \frac{1}{r^3} - \gamma \frac{1}{r^6}$$

Fitted value of γ suggests that there are N ≈ 50 charge patches randomly distributed on the particle surface with a mean separation s ≈ 130 nm

AFM phase images of the silica spheres

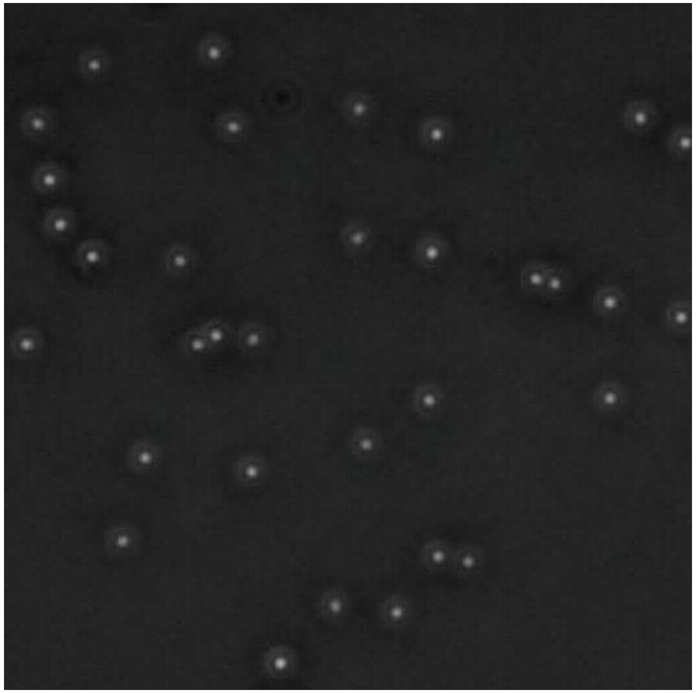


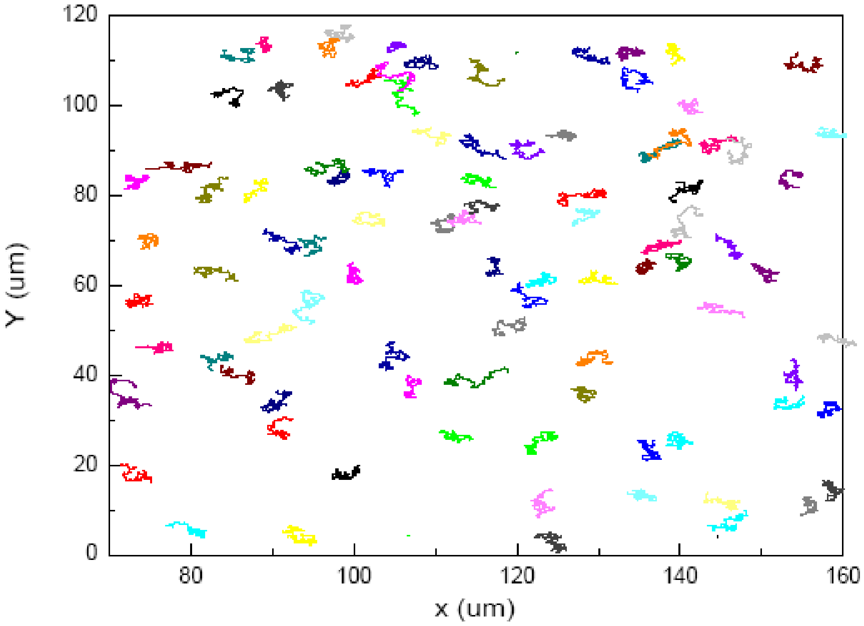
In air (no salt)



Fully immersed in a 1 mM NaCl solution; patch size ~100 nm

3. Brownian dynamics of interfacial particles





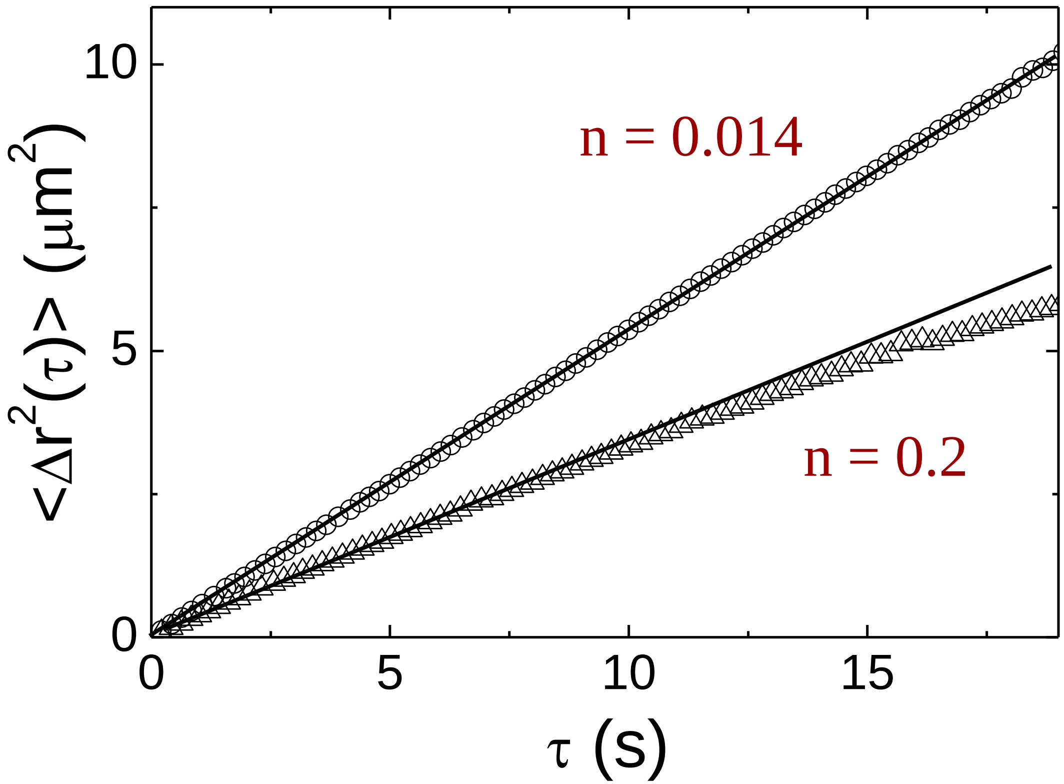
multi-particle tracking

- Monodisperse polymethylmethacrylate (PMMA) spheres at a decalin-water interface: d = 1.2 μm (PMMA1) and d = 0.7 μm (PMMA2)

- Silica sphere samples: S1: 0.73 ± 0.04 μm, S2: d = 1.57 ± 0.06 μm, S3: 0.97 ± 0.05 μm, ♦$_0$ 🕓 0.014 μC/cm^2.

- Strongly charged polystyrene sphere at a water-air interface: d = 1.1 μm.

PMMA1 (d = 1.2 ❍m)



Particle tracking

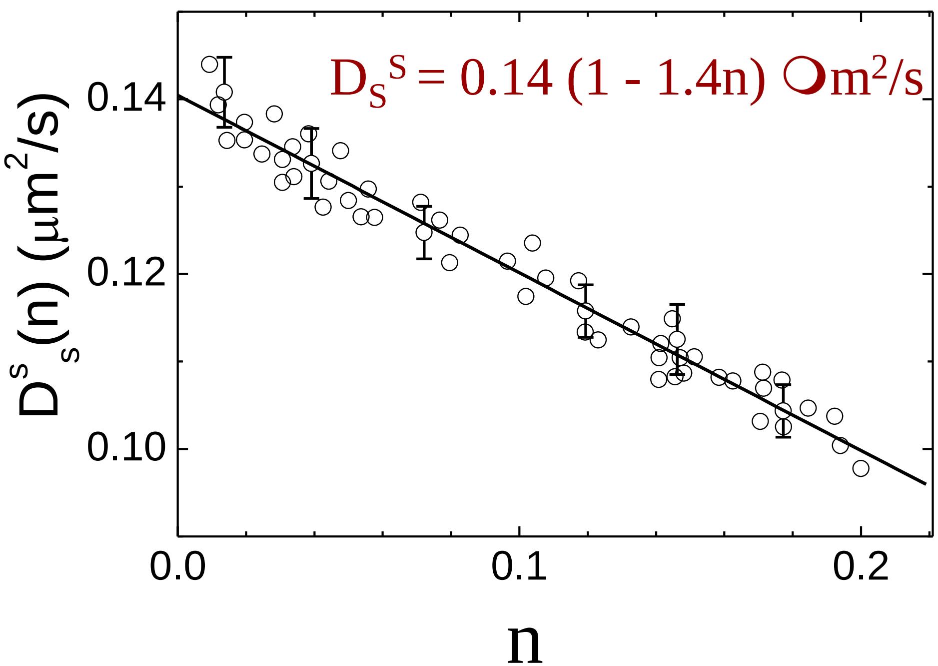
$$\Delta\mathbf{r}(\tau) = \mathbf{r}(t+\tau) - \mathbf{r}(t)$$

$$\langle \Delta\mathbf{r}^2(\tau)\rangle = 4D_S^S\tau$$

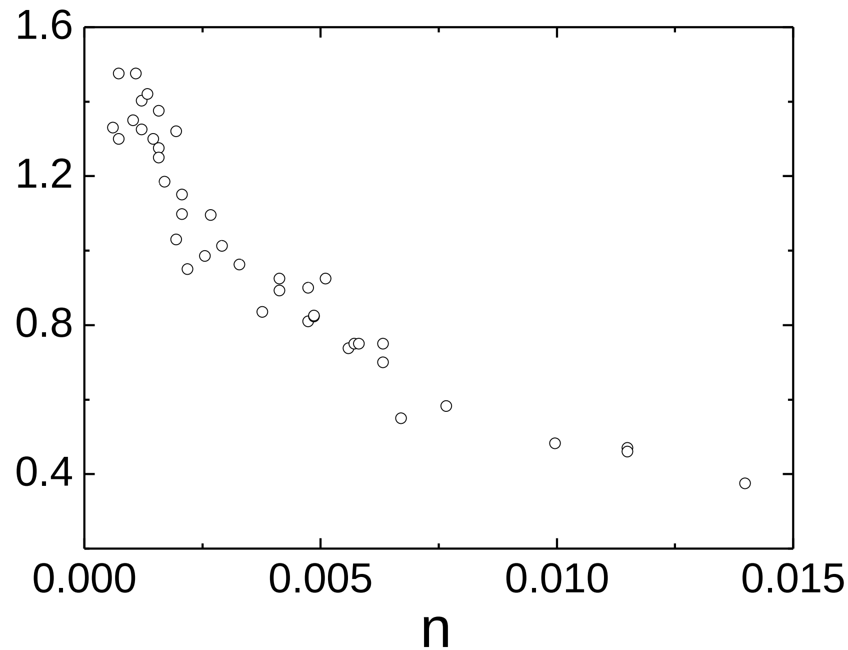
$$\ell = d\left(\frac{\pi}{4n}\right)^{1/2} \square\ 2d$$

$$t_0 = \frac{d^2}{D_0} \square\ 10s; \quad \mathrm{D}_0 = \frac{k_B T}{6\pi\eta_2 a} = 0.145\ \frac{\mu m^2}{s}$$

Particle diffusion is hindered by the surrounding spheres
Concentration dependence of the diffusion coefficient



PMMA spheres (d = 1.2 μm)



Highly charged polystyrene spheres (d = 1.1 μm)

$$D_S^S = \alpha D_0 (1 - \beta n)$$

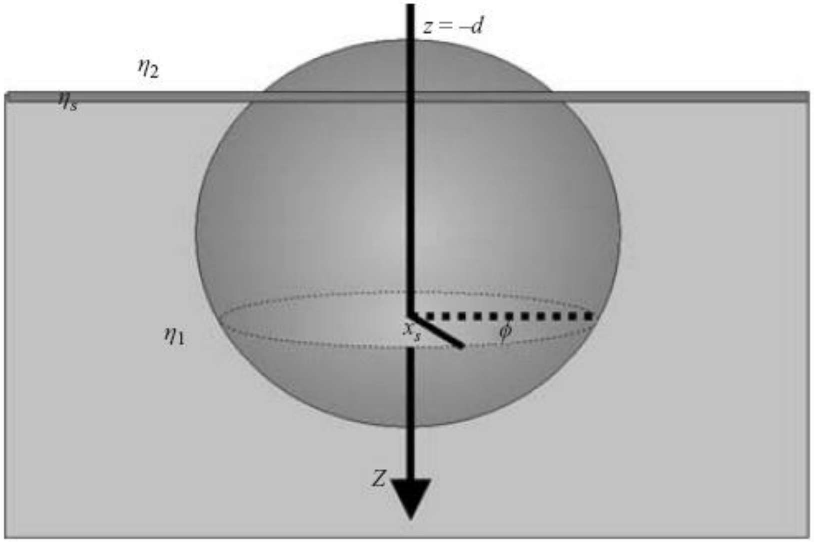
PMMA spheres at the decalin-water interface

Sample	d (μm) ($\pm 5\%$)	D_0 (μm^2/s)	α ($\pm 7\%$)	β ($\pm 10\%$)
PMMA1	1.2	0.145	0.97 (0.97)	1.4 (1.2)
PMMA2	0.7	0.26	1.04	2.8

Silica spheres at the water-air interface

Sample	d (μm)	α ($\pm 7\%$)	β ($\pm 10\%$)	Manufacturer
Si2	1.57 ± 0.06	1.19 (1.17)	1.6 (0.84)	Duke Scientific
Si3	0.97 ± 0.05	1.45 (1.45)	1.84 (1.53)	Bangs Laboratories
Si1	0.73 ± 0.04	1.18 (1.17)	2.89 (2.44)	Duke Scientific

Viscous drag for a sphere moving in a membrane



$$\xi = (\eta_1 a)\, f(z/a, B)$$

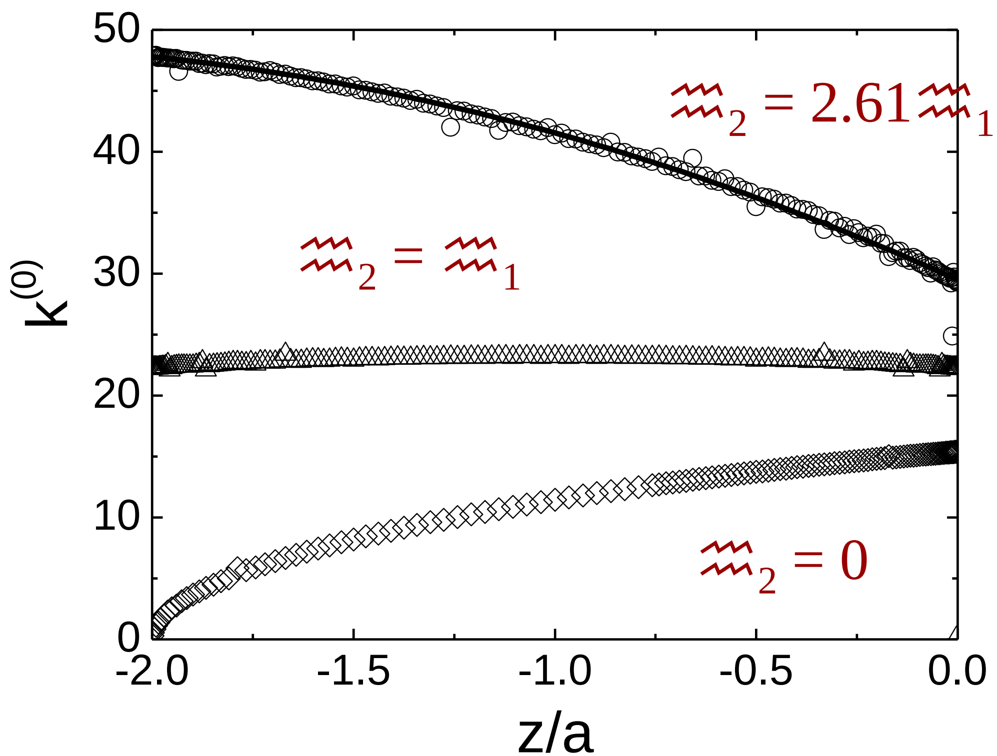
$$B = \frac{\eta_s}{(\eta_1 + \eta_2)a}$$

≈ 0

$$f(z/a, B) = k^{(0)}(z/a) + k^{(1)}(z/a)B$$

$$D_S^S = \frac{k_B T}{\xi} = \alpha \frac{k_B T}{6\pi\eta_2 a} \Rightarrow k^{(0)} \approx \frac{6\pi}{\alpha}\frac{\eta_2}{\eta_1}$$

incompressible surface

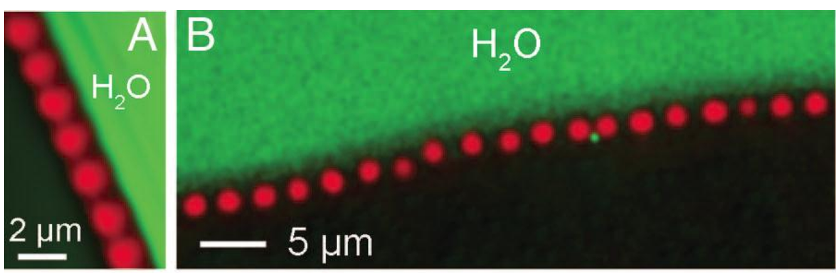


decalin-water interface

$$k^{(0)} = \frac{6\pi}{\alpha}\frac{\eta_2}{\eta_1} \square\ 47.28$$

♋ = 1.04
(PMMA2 & PMMA1)

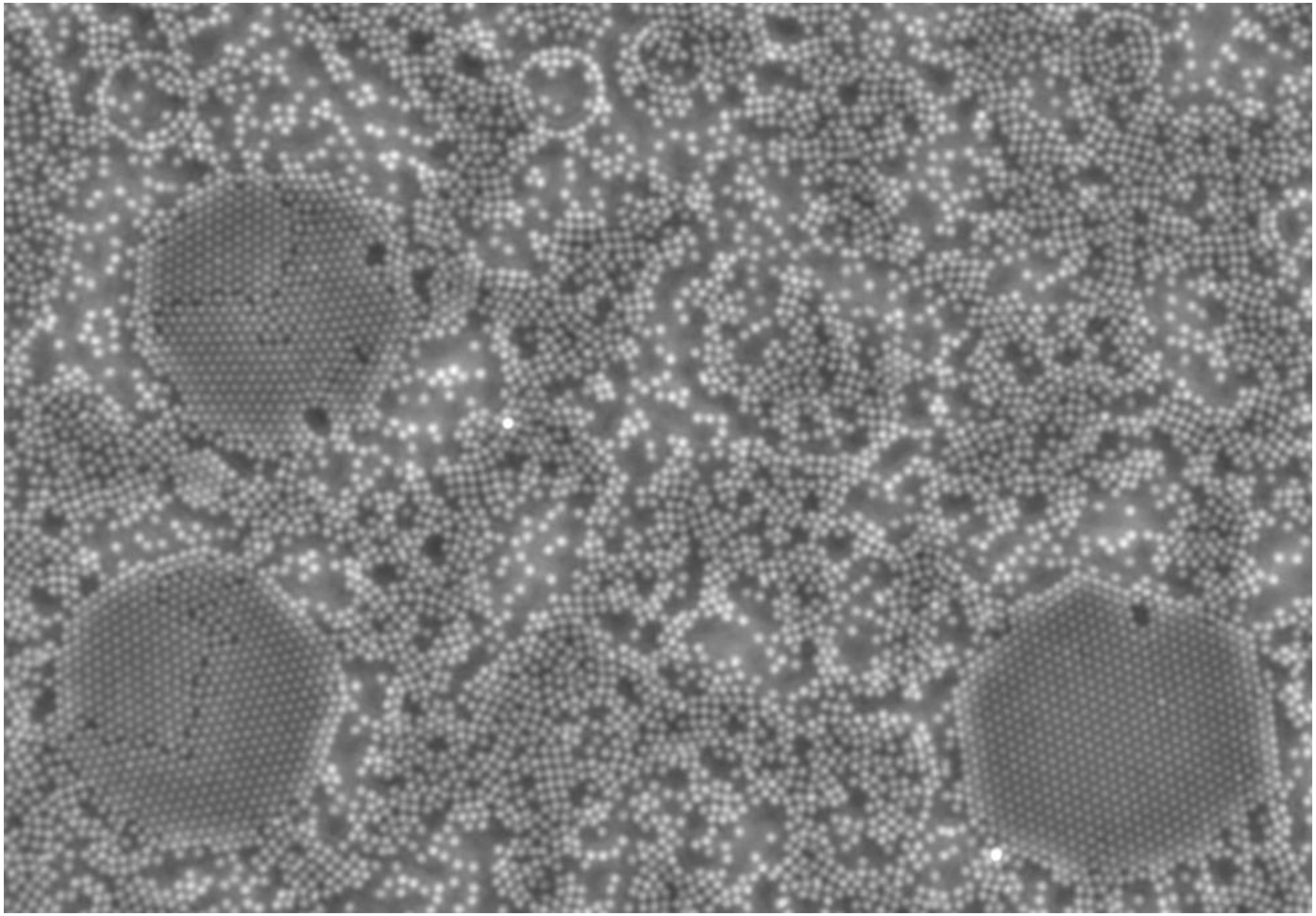
❾ z/a = -2 or ❑ 🕔 180^0



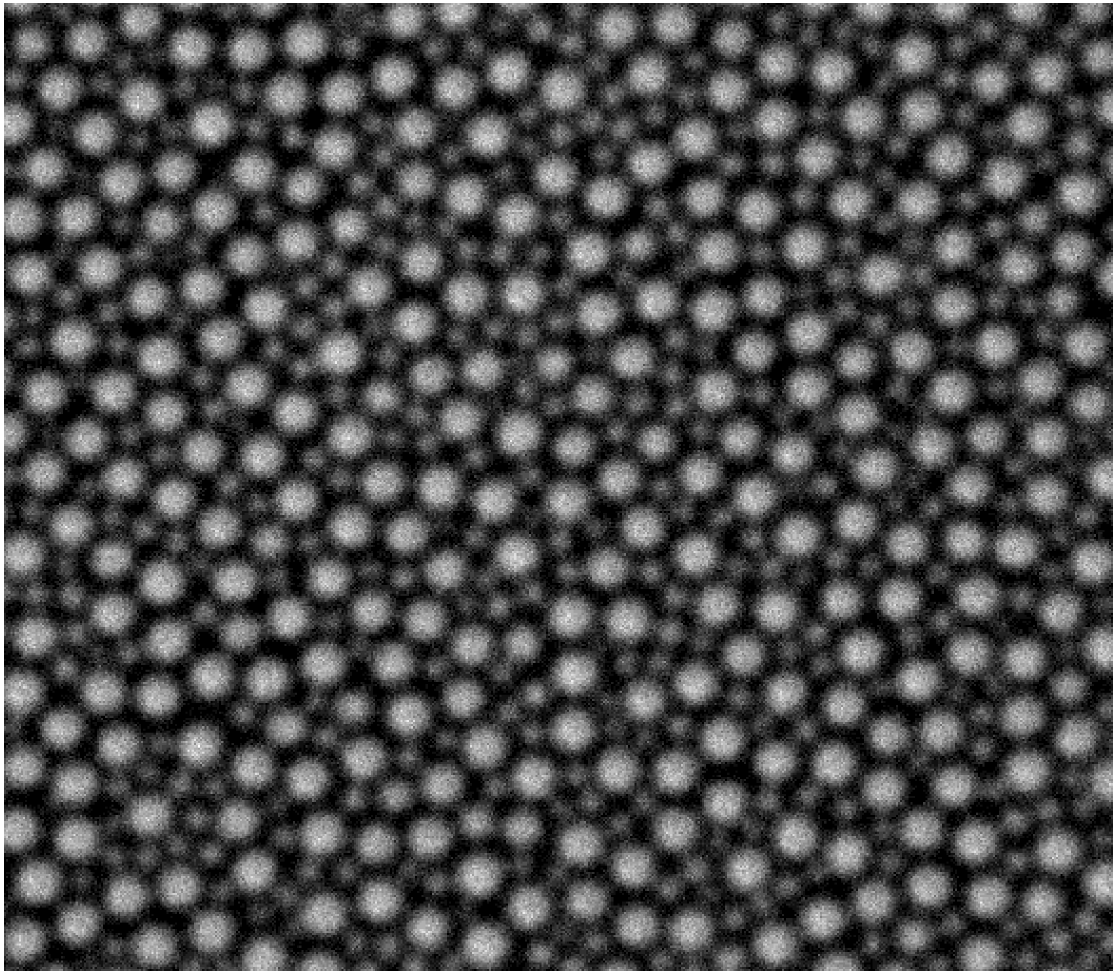
Leunissen et al. (PNAS, 2007): PMMA spheres sit at (from the decalin side) but not in the decalin-water interface

Dense colloids as a model system to study 2D phase transitions, nucleation, crystal growth and glass dynamics

(i) Dense silica spheres (short-range repulsion)

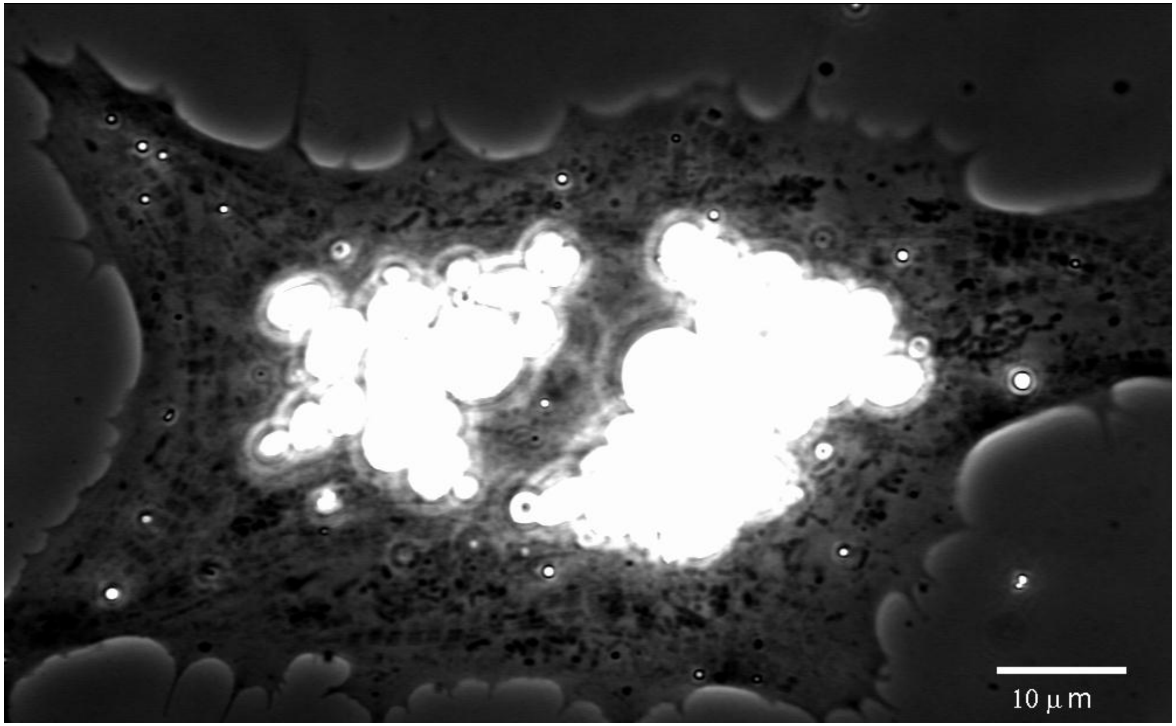


(ii) Glassy behavior in a binary mixture of hard spheres (PMMA)



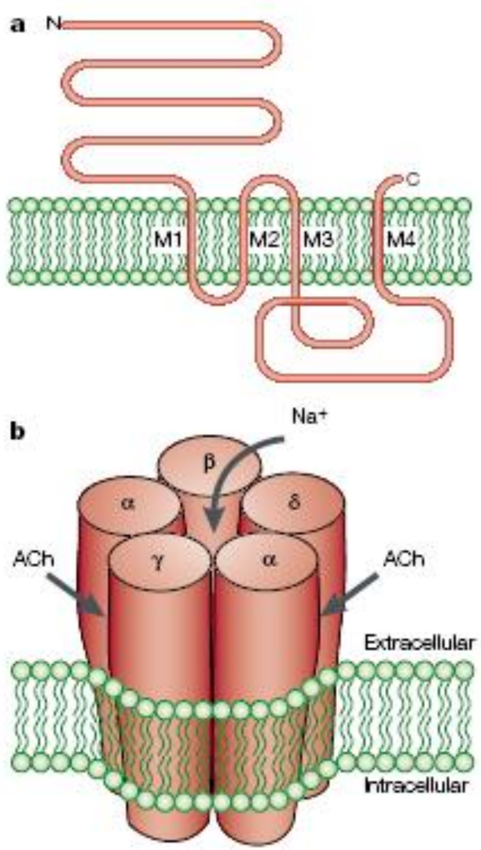
3. Lateral motion of membrane-bound proteins and lipids

Muscle cells cultured from Xenopus (African clawed frog) embryos, a model system to study the neuromuscular junction

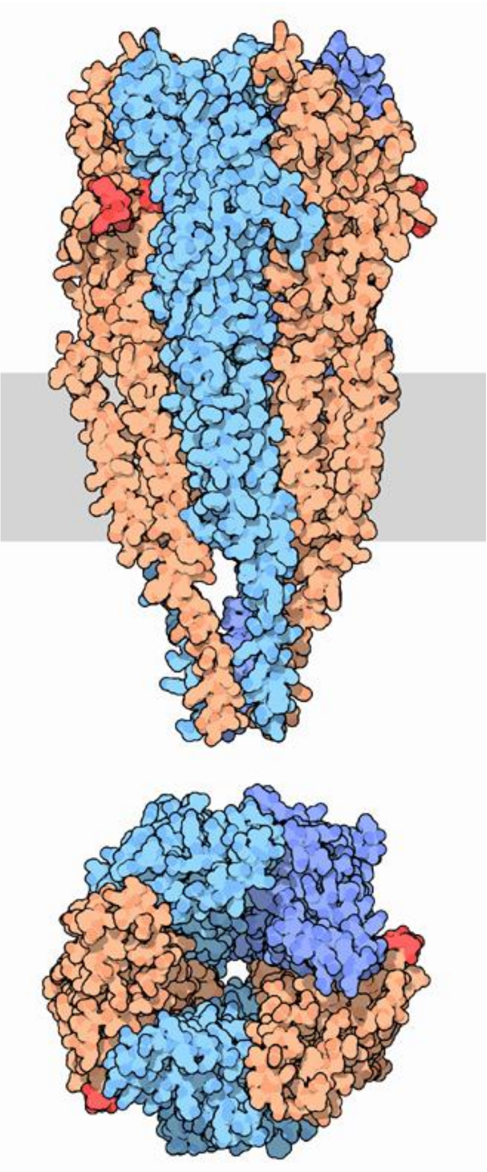


bright field image of a muscle cell (stage 22) with yolk in the center

(i) Lateral motion of the nicotinic acetylcholine receptors (AChR)



height: 20 nm
diameter: 7 nm

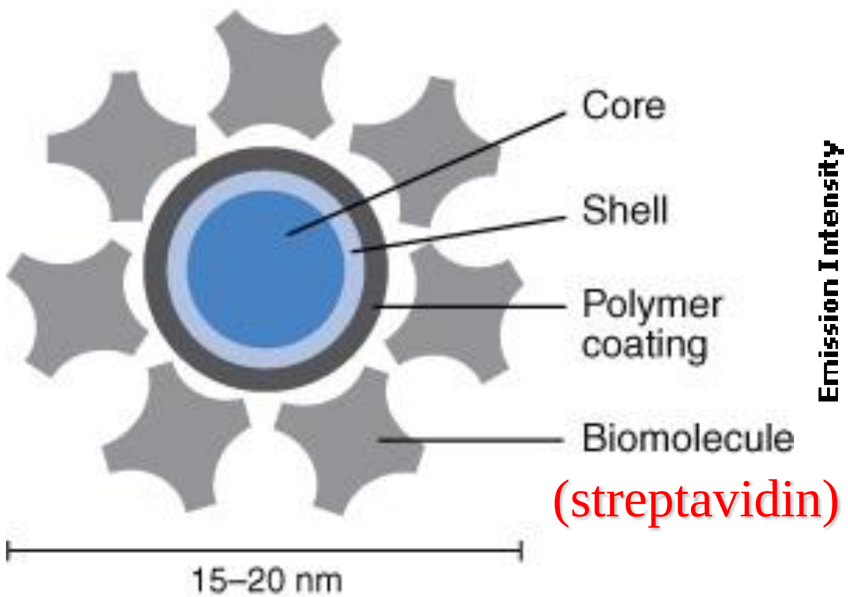


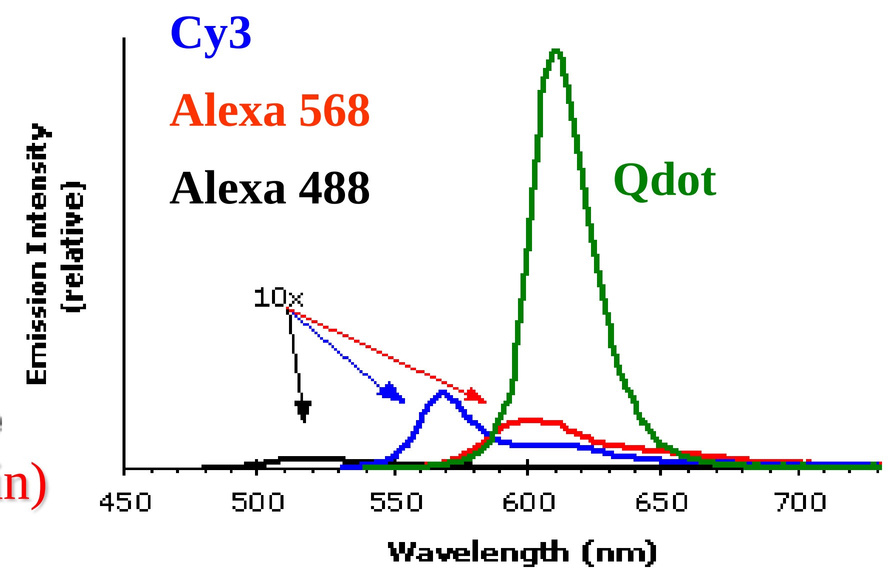
A cation selective, ligand-gated ion channel

Biolinkers: biotin-bungarotoxin-♋ subunits

Quantum Dots (Q-dots) for live cells and in vivo imaging

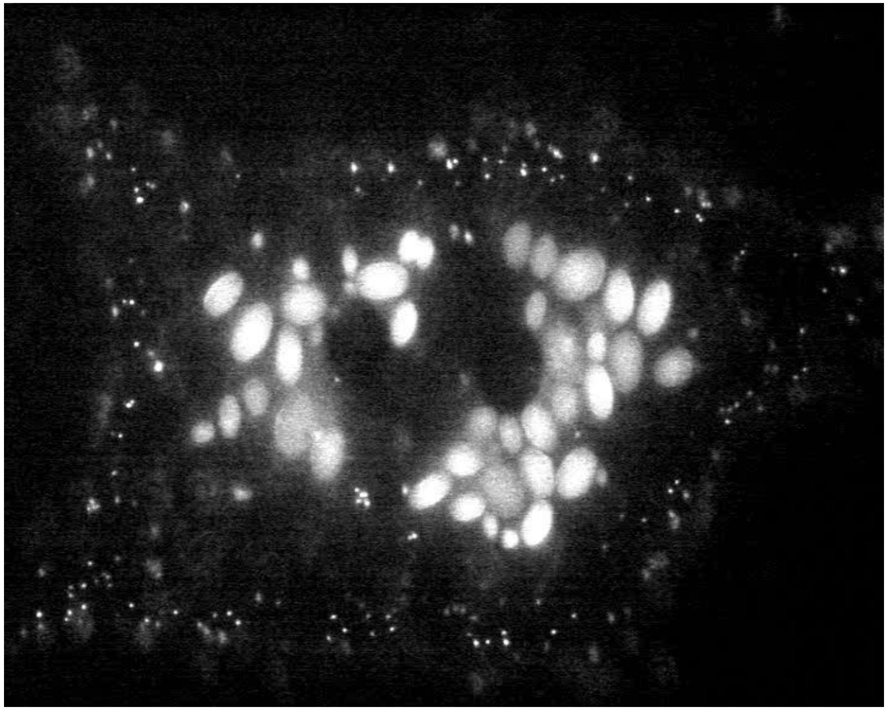
Advantages: brighter, longer fluorescence lifetime, and allows for single-molecule tracking



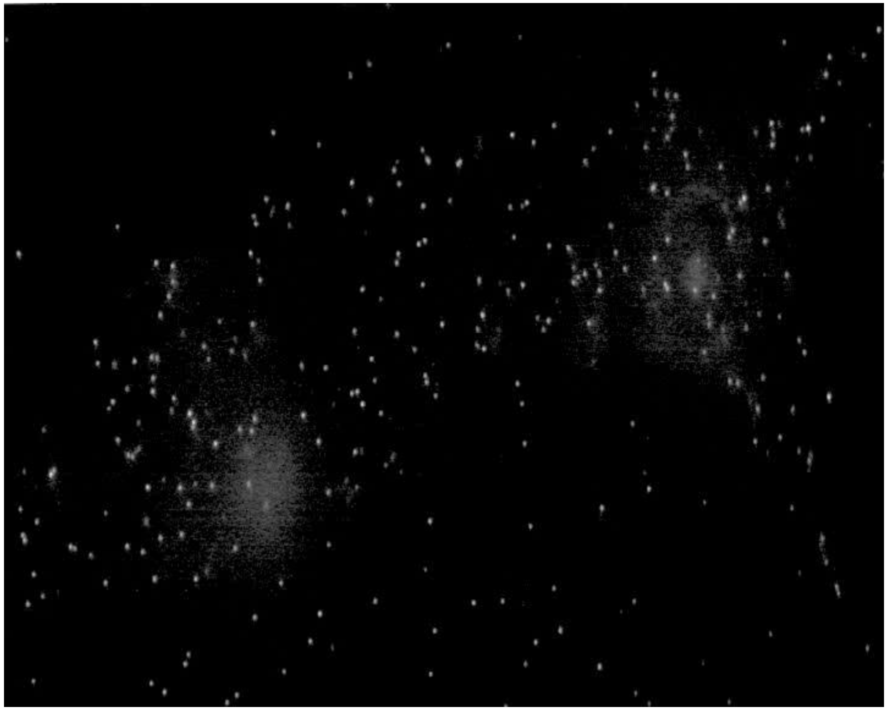


Experimental challenges: blinking, non-uniform intensity distribution among Q-dots, somewhat larger than typical protein molecules

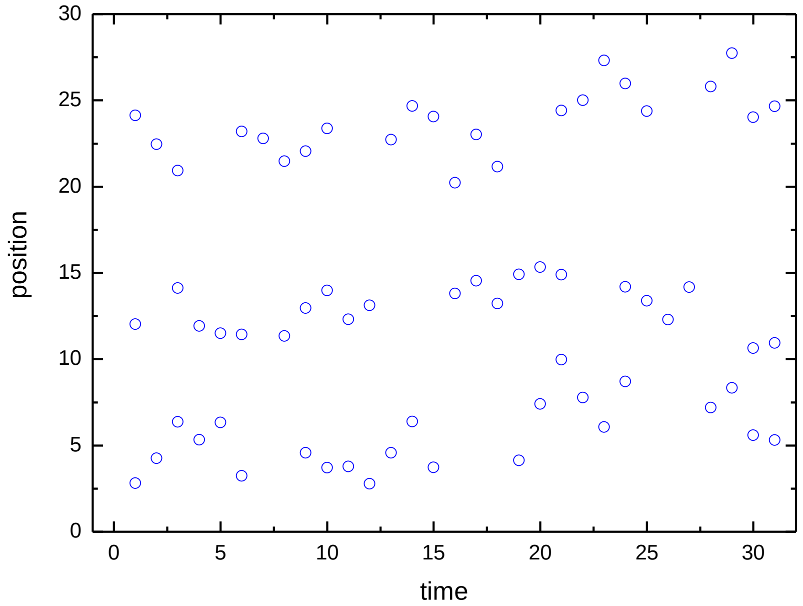
Fluorescent imaging of Q-dot labeled acetylcholine receptors



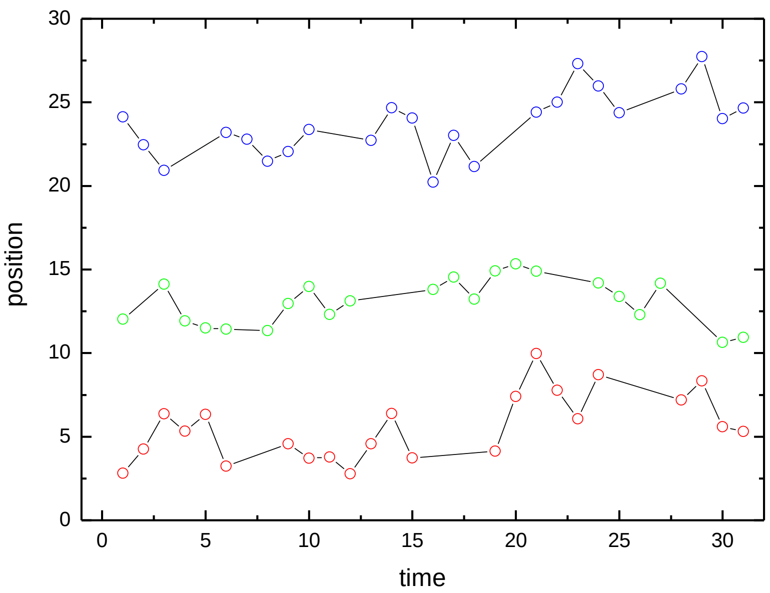
Focused at the middle plane of the cell



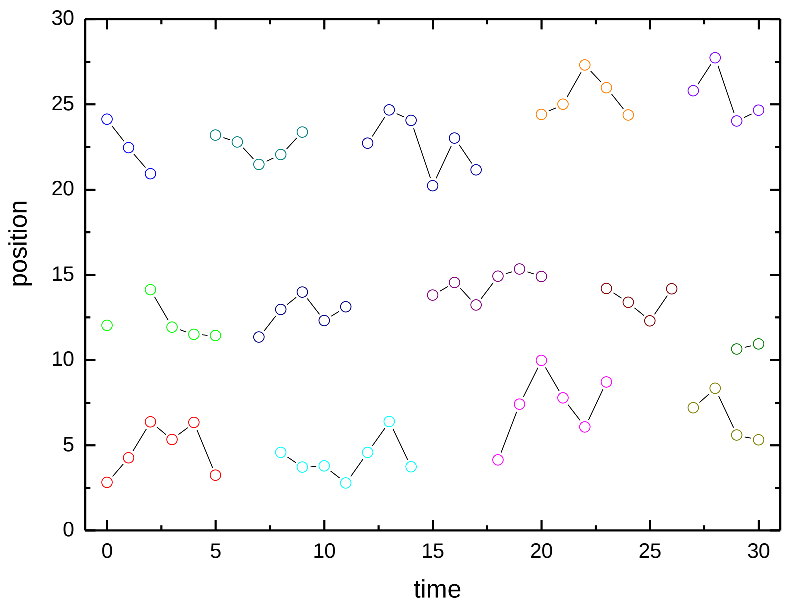
Focused at the bottom plane facing the substrate



Original positions

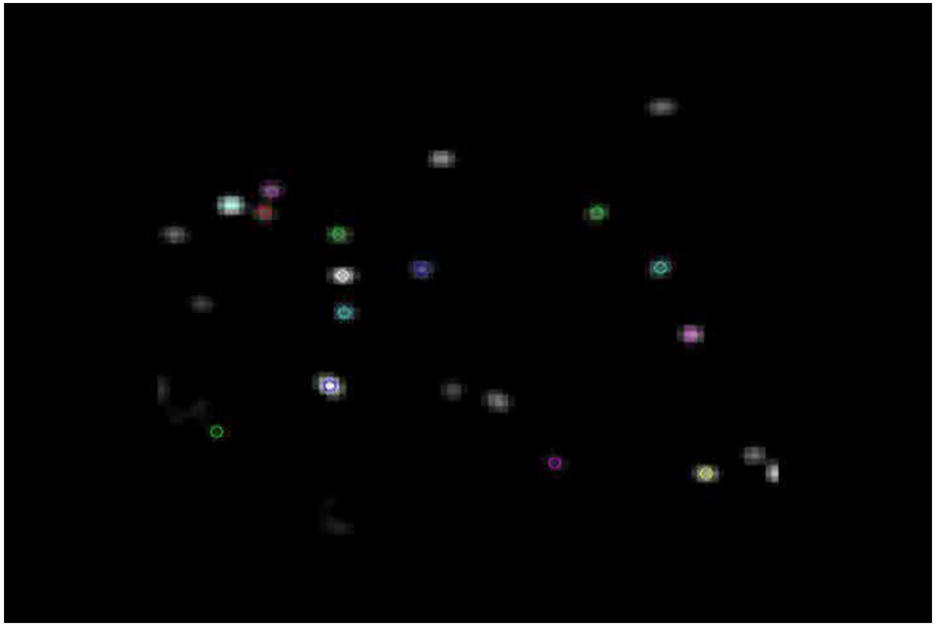


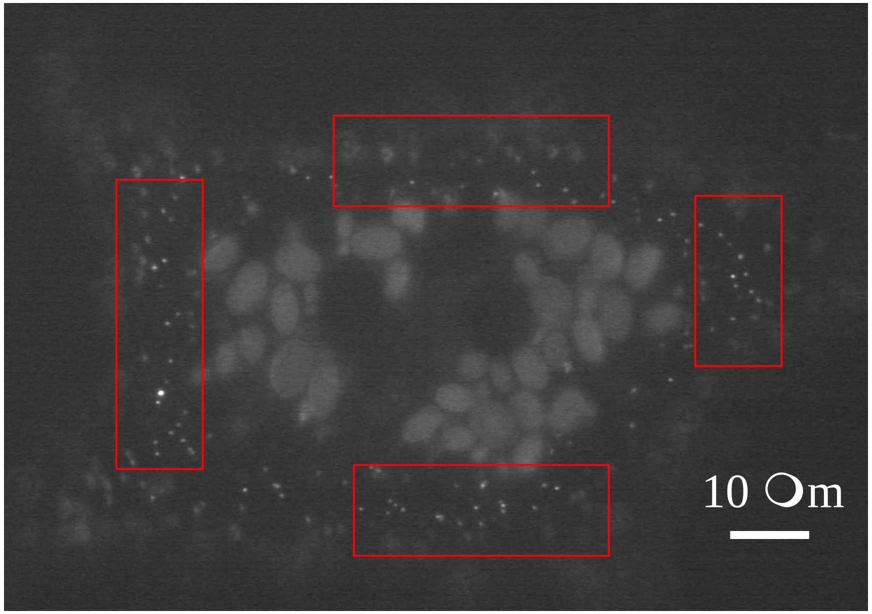
Final linked trajectories (60%)



broken trajectories due to Q-dot's blinking

Reconstructed real-time (5 fps) movie of Q-dot labeled AChRs (each Q-dot is coded with a different color)



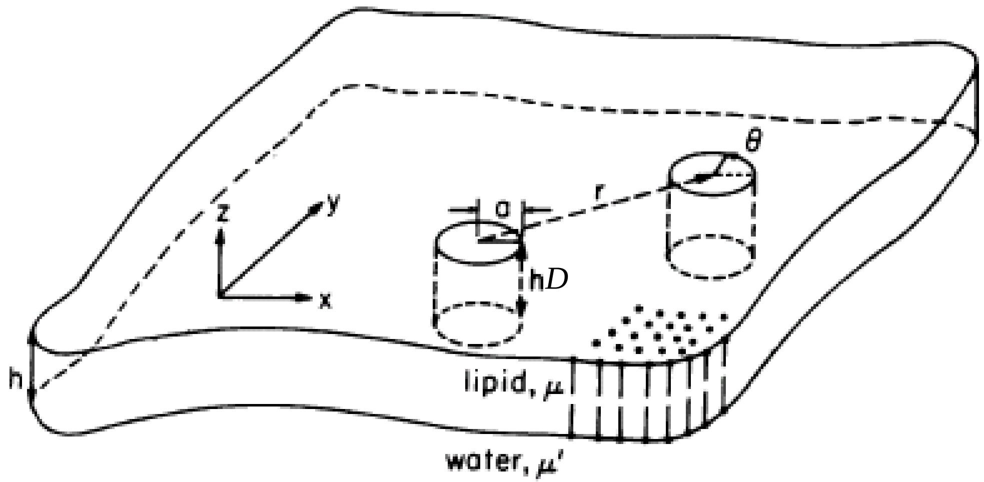


Typically, we take movies at 10-0.3 fps and ~400 frames per movie, each frame containing 50-150 Q-dots, and track 5-20 cells for each experiment. For each movie, we find ~640 (broken) trajectories and obtain ~360 linked trajectories.

Optimal sample/imaging conditions allow us to have accurate data with good statistics to study the single molecular motion in living cells.

Understanding of the lateral diffusion of membrane-bound proteins

Hydrodynamic model by Saffman and Delbrück (PNAS 1975)



A viscous layer bounded by aqueous phases on both sides

$$D_S = \frac{k_B T}{\xi} = \frac{k_B T}{4\pi\mu h}\left(\ln\frac{\mu h}{\mu' a} - 0.5772\right)$$

For h ≈ 8 nm, a ≈ 4 nm, and μ' = 1 cP (water), we have

$$\frac{\mu}{\mu'} \approx 7500, \quad \mu \approx 75 \text{ poise}$$

The viscosity of the cell membrane is far from being settled; the reported values varies from 1 poise up to 1000 poise.

Diffusion time over a protein diameter:

$$\tau_0 \approx \frac{d^2}{D_S} \approx \frac{(7 \text{ nm})^2}{0.05\ (\mu\text{m}^2/\text{s})} \approx 1 \text{ ms}$$

- Longest diffusion distance $r_1 \approx 6.3\ \mu m \approx 900d$; protein separation $r_2 \approx d[\pi/(4\times0.01)]^{1/2} \approx 10d \ll r_1$; long-time self-diffusion.
- Measured MSD is a linear function of delay tine Δt even for very large values of Δt, suggesting that the cell membrane is really fluid-like for trans-membrane proteins.

5. Summary

- Colloidal monolayers can serve as a model system to study interactions and dynamics at liquid interfaces.

- Optical observations of stable bonded particle clusters and the measured g(r) demonstrate that the attractive interaction between the interfacial particles is of dipole origin.

- AFM phase images reveal that surface heterogeneity is a general feature of the colloidal surface, which may develop either during the synthesis of the particles or during the ionization process in the aqueous phase.

- Such patchy charges introduce in-plane dipoles at the interface, leading to an attraction at intermediate inter-particle separations.

5. Summary (continued)

- Measured short-time self-diffusion coefficient has the form

$$D_S^S = \alpha D_0 (1 - \beta n)$$

- Obtained value of α is in good agreement with the numerical calculation for the drag coefficient of interfacial particles, assuming the interface is incompressible.

- Measured value of β differs from that of bulk suspensions and changes with the particle size, indicating that hydrodynamic interactions between the particles have interesting new features at the interface.

- Membrane-bound proteins show interesting dynamics different from that of Brownian motion. The lateral motion of proteins in cell membrane is constricted by a variety of constrains imposed by the soundings and may also be affected by the active processes inside the cell, such as protein motors. Further experimental and theoretical studies are needed.