# Colloids as nucleons

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Finite-size equilibrium structures <-> macroscopic phase separation

Equilibrium clusters & periodic structures in systems with long-range repulsion and short-range attraction

Free energy of dispersed matter in capillary approximation:

Finite size –micro- *versus* macroscopic phase separation

$$F = F_0 + \gamma S$$

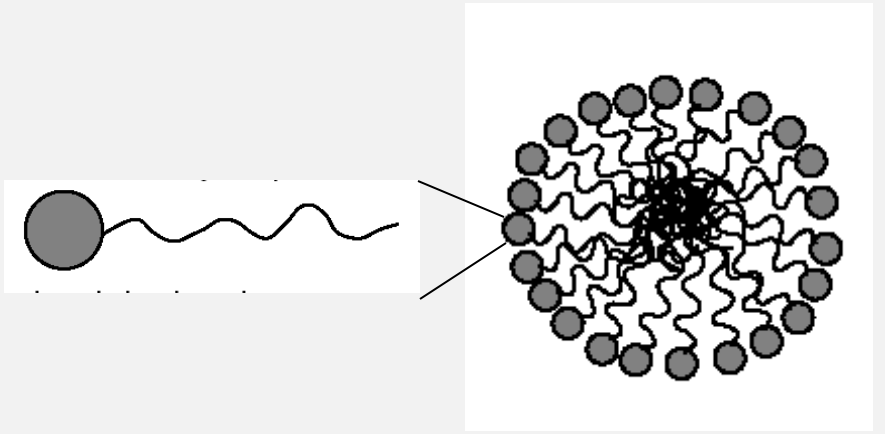
Bulk

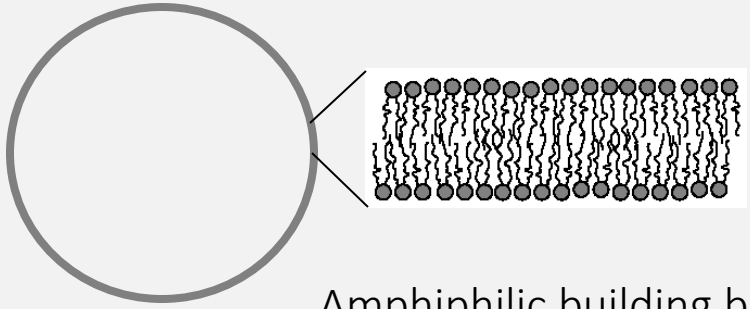
Surface

Minimize *F* by minimizing surface area *S* ⟶ macroscopic phase separation

**'Micro' phase separation: internal constraints**

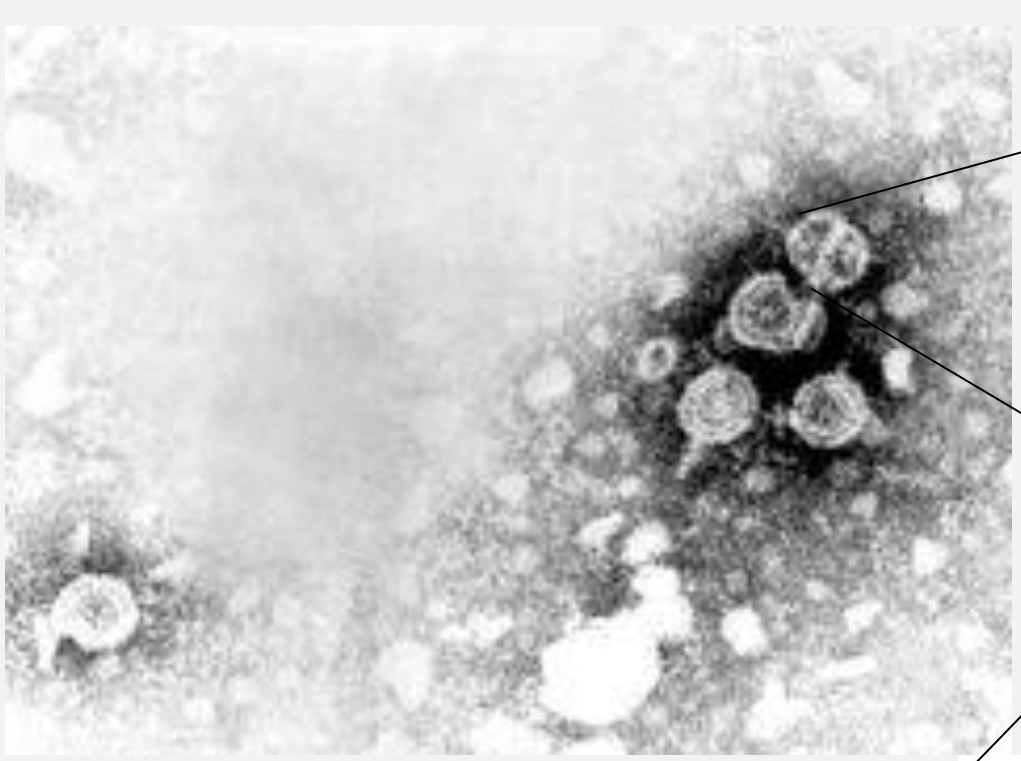
Micelles, microemulsions, vesicles, diblock copolymers…

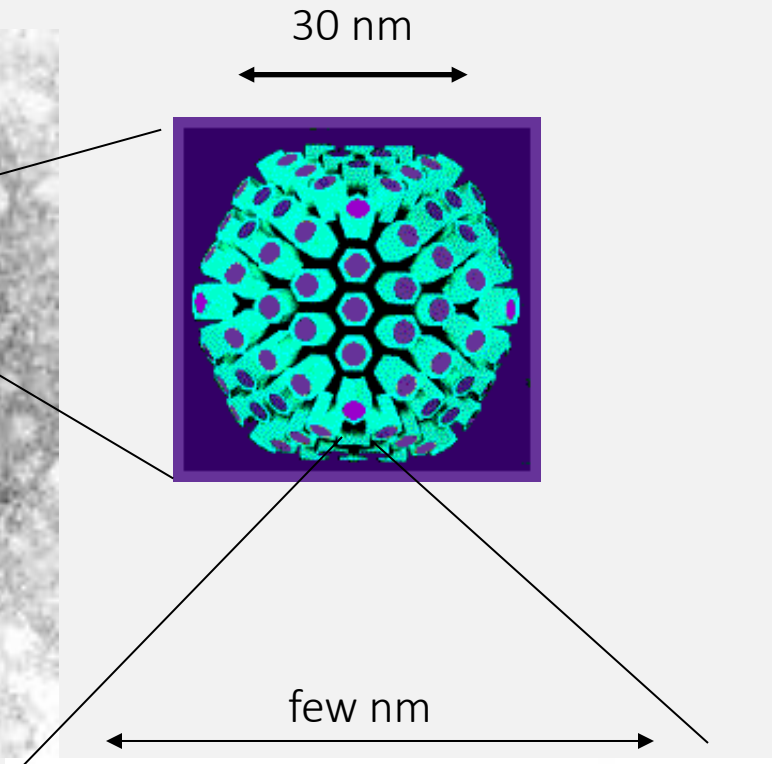




Amphiphilic building blocks

# ...virus capsids ~ 'coats' of viruses

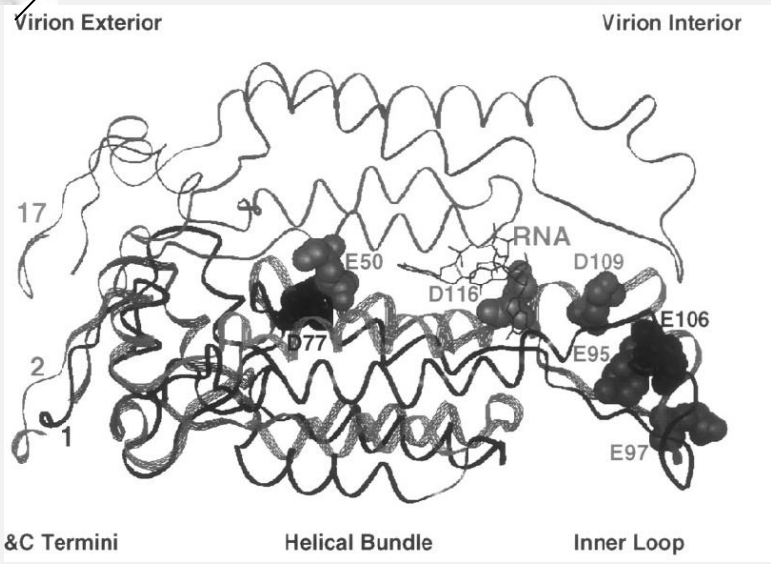





(Un)coating regulated by:
* Hydrophobic interactions between apolar **patches** on protein surface

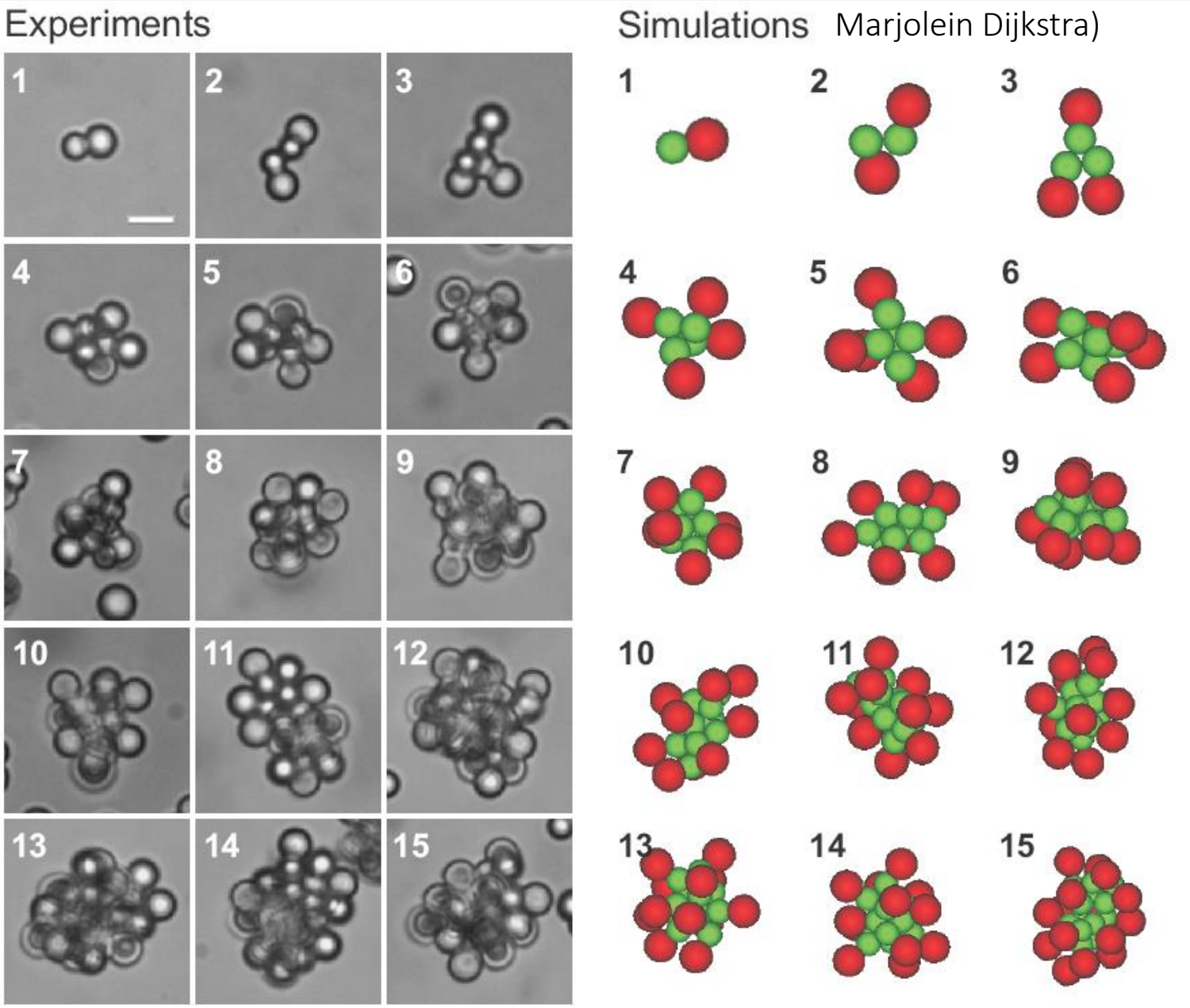
•Screened-Coulomb interactions

[WKK & P. vd Schoot, BPJ 2004; 2006]



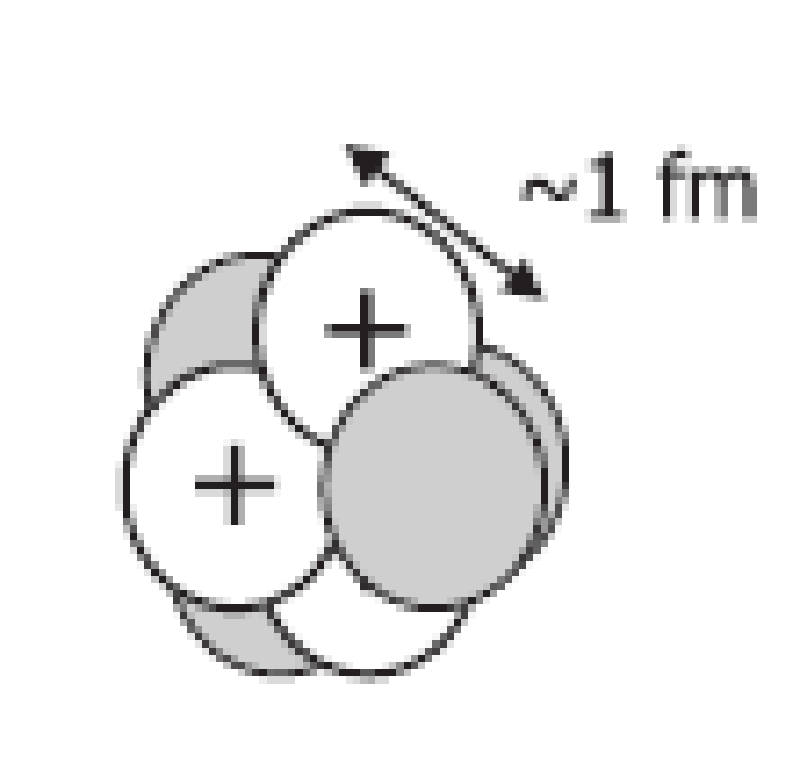
# Patchy ‘colloidal molecules’ [DJ Kraft ea, PNAS 2012]

(with Ran Ni, Frank Smallenburg, Marjolein Dijkstra)



Atomic nuclei –

internal constraint = long-range Coulomb repulsion

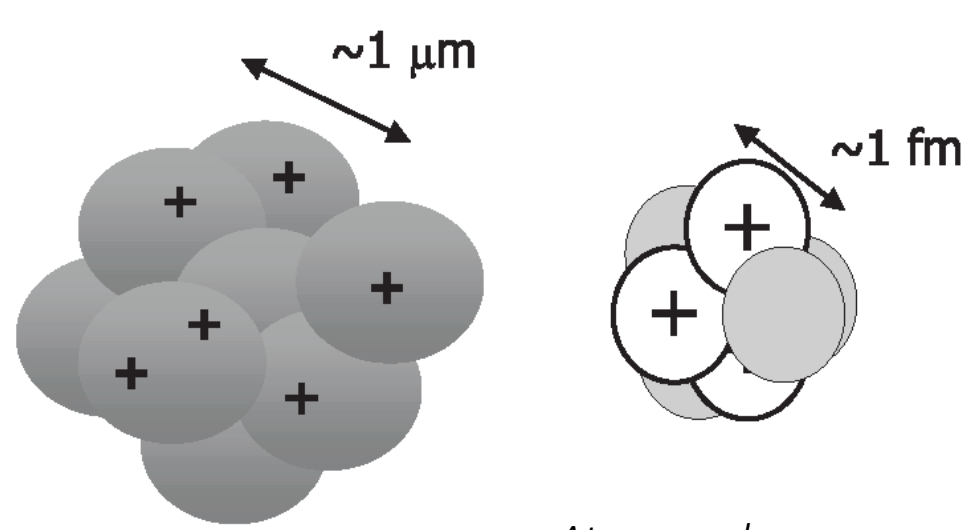


# Outline

- Weakly charged colloids, low screening: **colloids as nucleons** (High screening has been done: **DLVO**)
- Cluster phases in colloids & proteins – controversies
- Strong attraction : non-equilibrium clusters
- Higher densities – link with dense nuclear matter

# Colloids & nucleons

[J. Groenewold & WKK. *J. Phys. Chem. B* **105**, 11702 (2001); *J. Phys.: Condens. Matter* **16** S4877 (2004) ]




*Colloidal cluster*

*Atom nucleus*

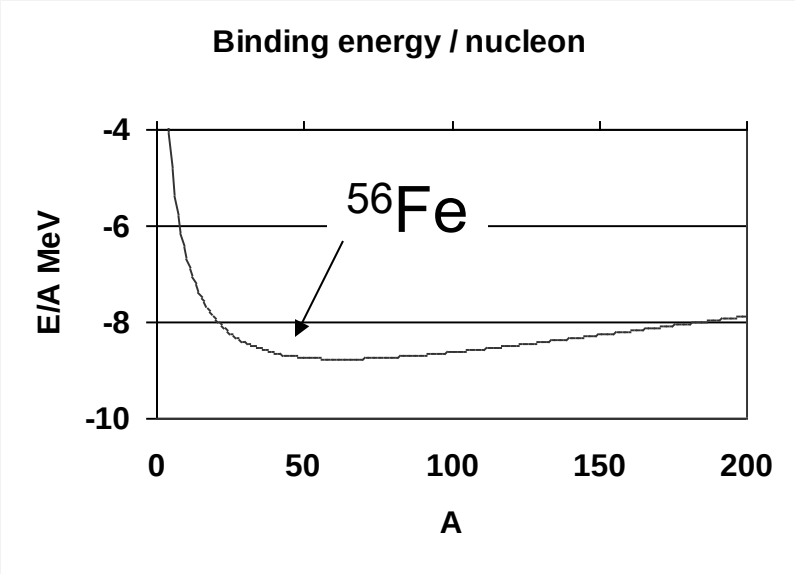
| | | |
|---|---|---|
| Short-range attraction<br>+<br>long-range repulsion | Van der Waals / depletion<br><br>(Screened) Coulomb | Strong nuclear force<br><br>Coulomb |

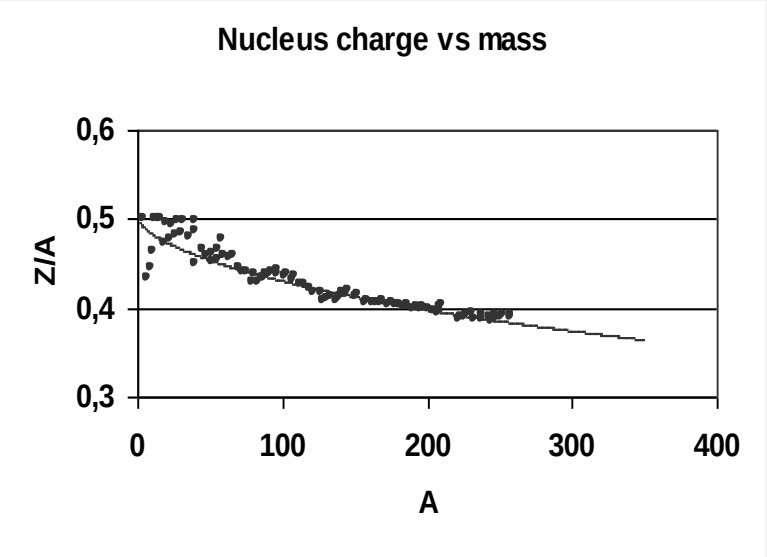
Mass formula (nuclei of atomic number A, nuclear charge Z):

$$F/A = -a_{vol} + a_{sym}\left(1-\frac{2Z}{A}\right)^2 + a_{surf}A^{-1/3} + a_{Coul}Z^2A^{-4/3}$$

$\sim A^{+2/3}$

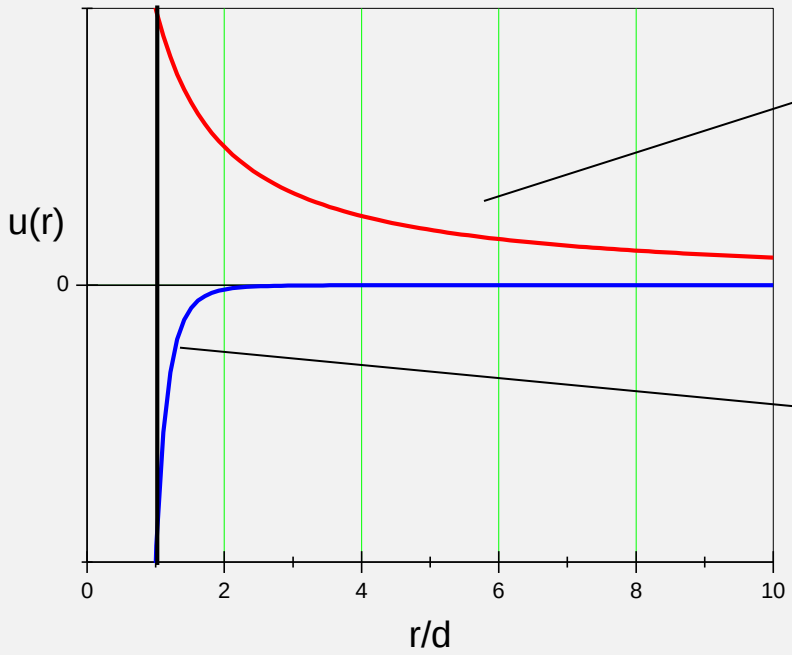
(neglect pairing term)




electron capture: $p + e^- \rightarrow n + \nu$

Colloidal equivalent:




Charged colloids in solvents with small dielectric constant: long-range repulsion (long screening length)

Attractive **potential of mean force** by (e.g.,) depletion of polymers

Quiz: equiv of charge generating term?

Ionic dissociation at low dielectric constants: dissociation energy $kT\lambda_B/b$ – ionization due to increased translational entropy of counter ions.

Bjerrum length

bond length

"ion capture": $C^{(n+1)+} + i^- \rightarrow C^{n+}$

Free energy density of spherical colloidal cluster of radius R:

$$f = f_0 + 3\gamma R^{-1} + \frac{4\pi}{5}\lambda_B\rho^2 R^2 + 2\rho\left(\ln(\rho/\rho_0) - 1\right)$$

Surface tension

Charges/ volume

Entropy (ions + combinatorial)

$$\rho_0^2 \approx \frac{e^{-\lambda_B/b}\sigma}{rb^3\phi}$$

# Intermezzo: site-binding model

Ions can be bound to colloid surface with energy $-\lambda_B / b$
or translate freely in bulk

*Free energy

$$F = -\ln Q = -\ln Q_{ads} Q_{bulk}$$

$$\lambda_B = \frac{e^2}{4\pi\varepsilon\varepsilon_0 kT}$$

$$Q_{ads} \approx \frac{Z_{\max}!}{Z!(Z_{\max} - Z)!}\left(e^{\lambda_B / b}\right)^{(Z_{\max} - Z)}$$

$$Q_{bulk} \approx \frac{V^Z}{Z! b^{3Z}}$$

Take $Z \ll Z_{max}$

$$\longrightarrow \quad f = \frac{F}{V_{cluster}} = 2\rho\left(\ln(\rho / \rho_0) - 1\right)$$

$$\sigma = Z_{\max} / 4\pi r^2$$

$$\phi = \frac{n v_{colloid}}{V}$$

$$\rho_0^2 \approx \frac{e^{-\lambda_B / b}\sigma}{r b^3 \phi}$$

*Minimum ρ *
(without Coulomb term)

r ≡ colloid radius

‘Entropic’ term ≡ charge - generating

Similar role as symmetry term in mass formula:

Expand around $\rho_0$:

$$2\rho\left(\ln(\rho/\rho_0)-1\right)\approx -2\rho_0+\frac{1}{\rho_0}(\rho_0-\rho)^2$$

Now cluster free energy *isomorphic* to ‘mass formula’ !

→ Map cluster free energy onto mass formula. Result:

$$A \to 4\pi R^3 / 3v$$

$$Z \to 4\pi R^3 \rho / 3v\rho_0$$

$$a_{vol} \to -f_0 v + 2\rho_0 v$$

$$a_{surf} \to 4.84\gamma v^{2/3}$$

$$a_{sym} \to kT\rho_0 v$$

$$a_{Coul} \to 0.48kT\lambda_B \rho_0^2 v^{5/3}$$

Numbers comparable for: ~1 μm colloids in solvent $\varepsilon \approx 10$
and sufficient charge density

…experimentally observed?

First indications:
Segre ea, PRL **86**, 6042, (2001)

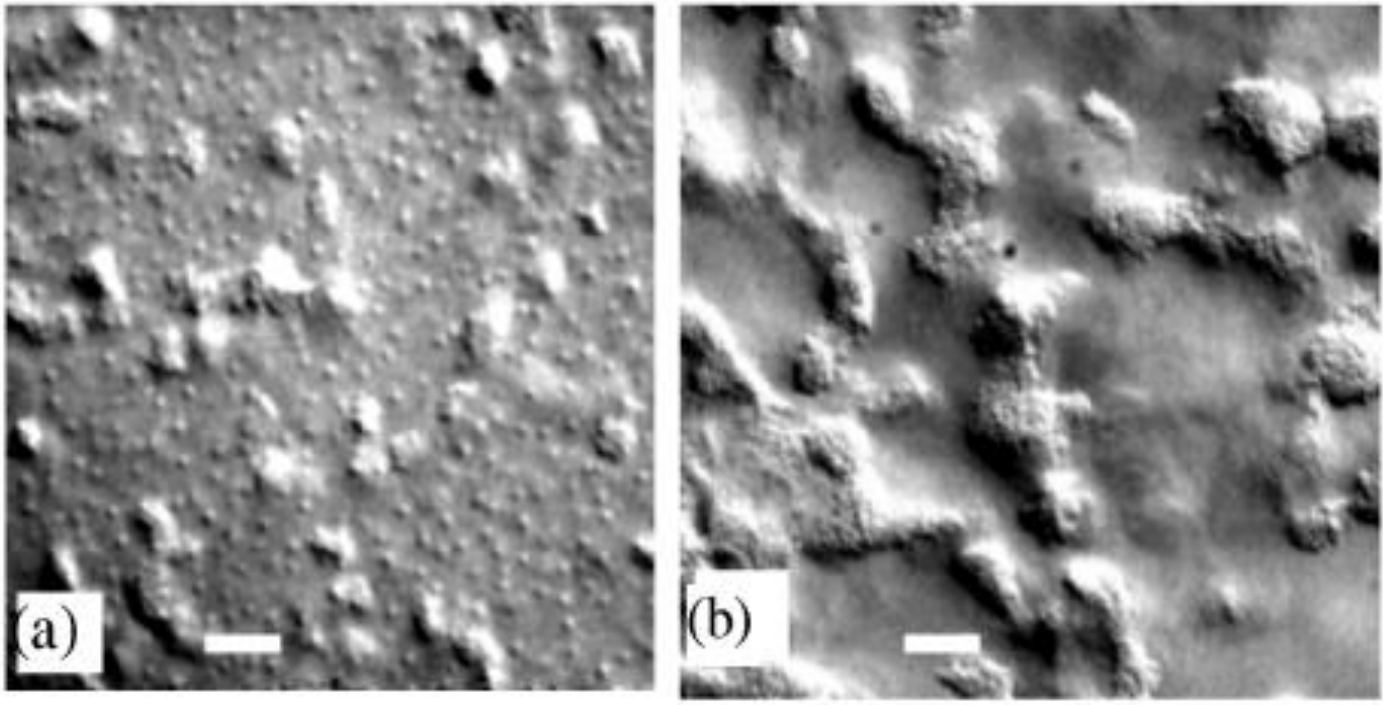
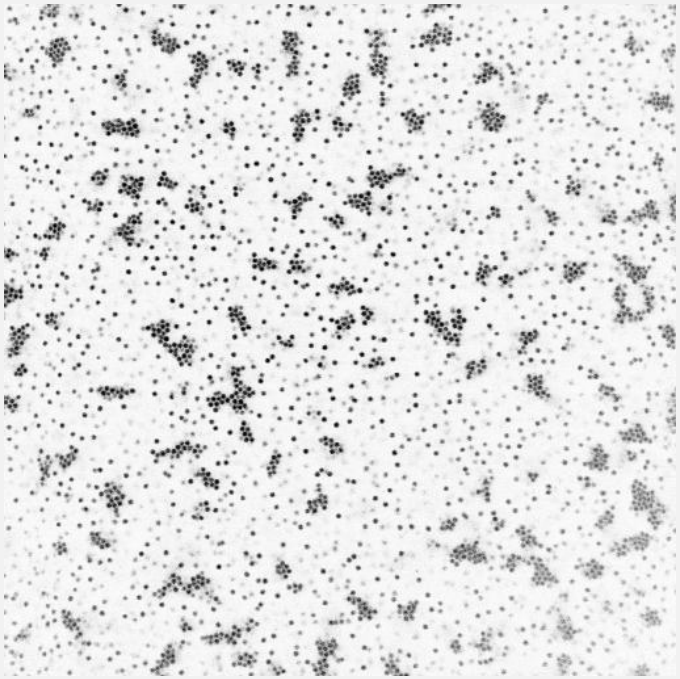
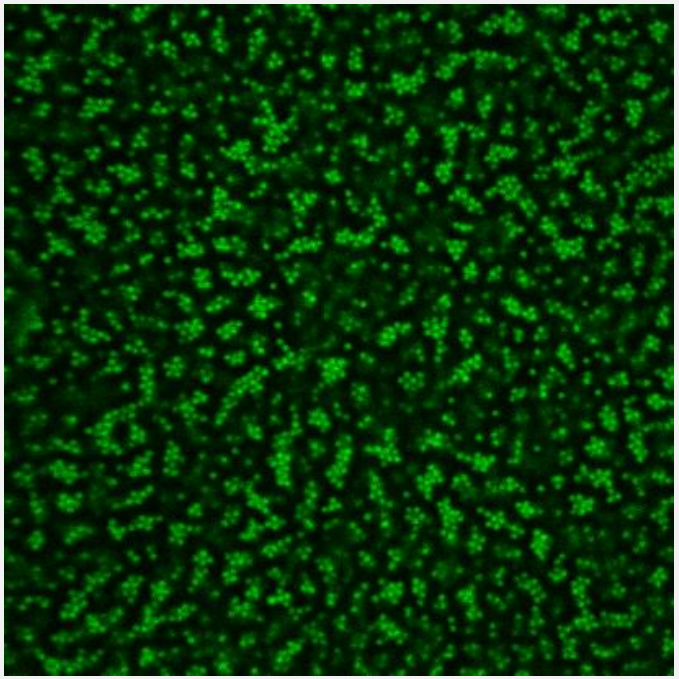



FIG. 2. DIC microscope images of (a) fluidlike and (b) solidlike phases. The attractive interactions are the same in both samples, $U \approx 4k_BT$, but the volume fractions are different, $\phi_a = 0.06$ and $\phi_b = 0.12$. The lines are 2.5 $\mu$m long.

[Segre ea, PRL **86**, 6042, (2001)]

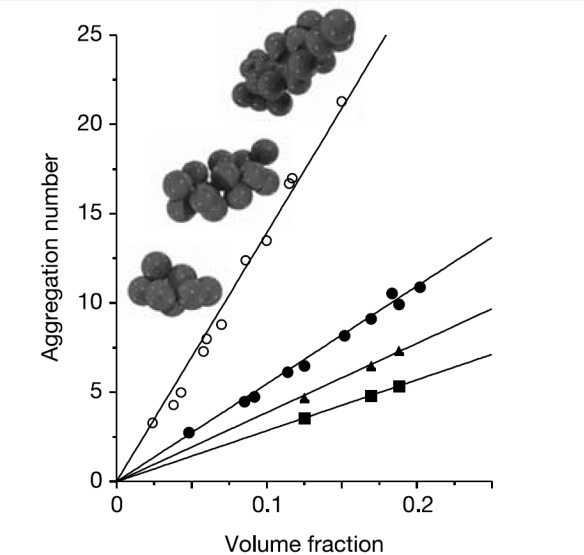


[Sedgwick ea , J. Phys.: Condens. Matt. **16**, S4913, (2004)
Stradner ea Nature **432**, 492, (2004)]



[M. van Schooneveld ea JPCB 2009]

Model prediction: optimum cluster radius $R_*^3 \propto \phi$

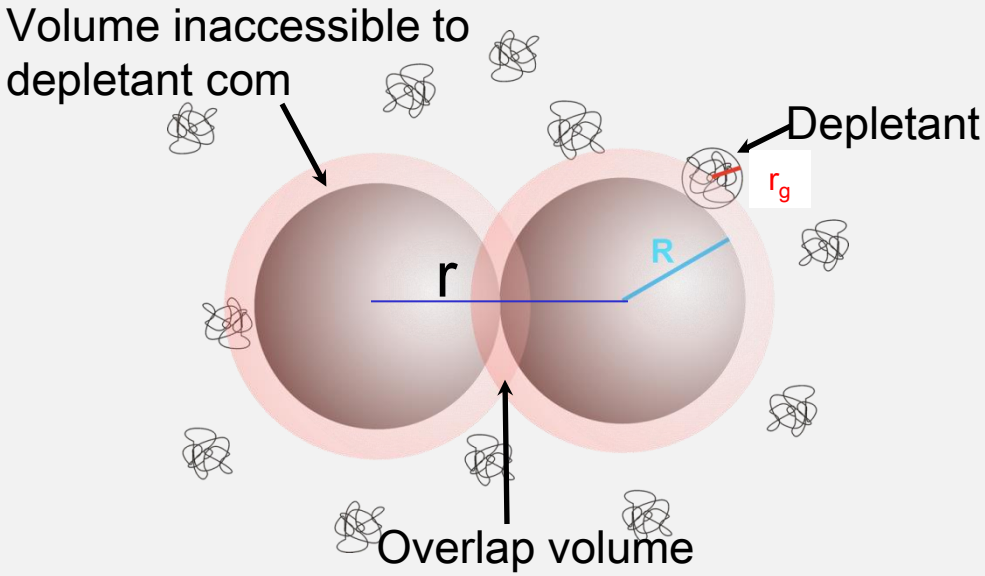



$$Aggr.\# \propto R_*^3 \propto \phi$$

[Stradner ea Nature **432**, 492, (2004)]

Other cluster shapes see, e.g, S. Mossa ea, Langmuir 2004

# Origin of attraction: depletion interaction




$$U = -\Pi \cdot V_{overlap}$$

Pairwise:

$$U = -kT\rho_p \frac{4\pi}{3}\sigma^3\left(1 - \frac{3}{4}\frac{r}{\sigma} + \frac{1}{16}\left(\frac{r}{\sigma}\right)^3\right)$$

(Asakura-Oosawa (AO) potential)

$$\sigma = R + r_g$$

Quiz:

Why $R_*^3 \propto \phi$

?

Why $R_*^3 \propto \phi$ ?

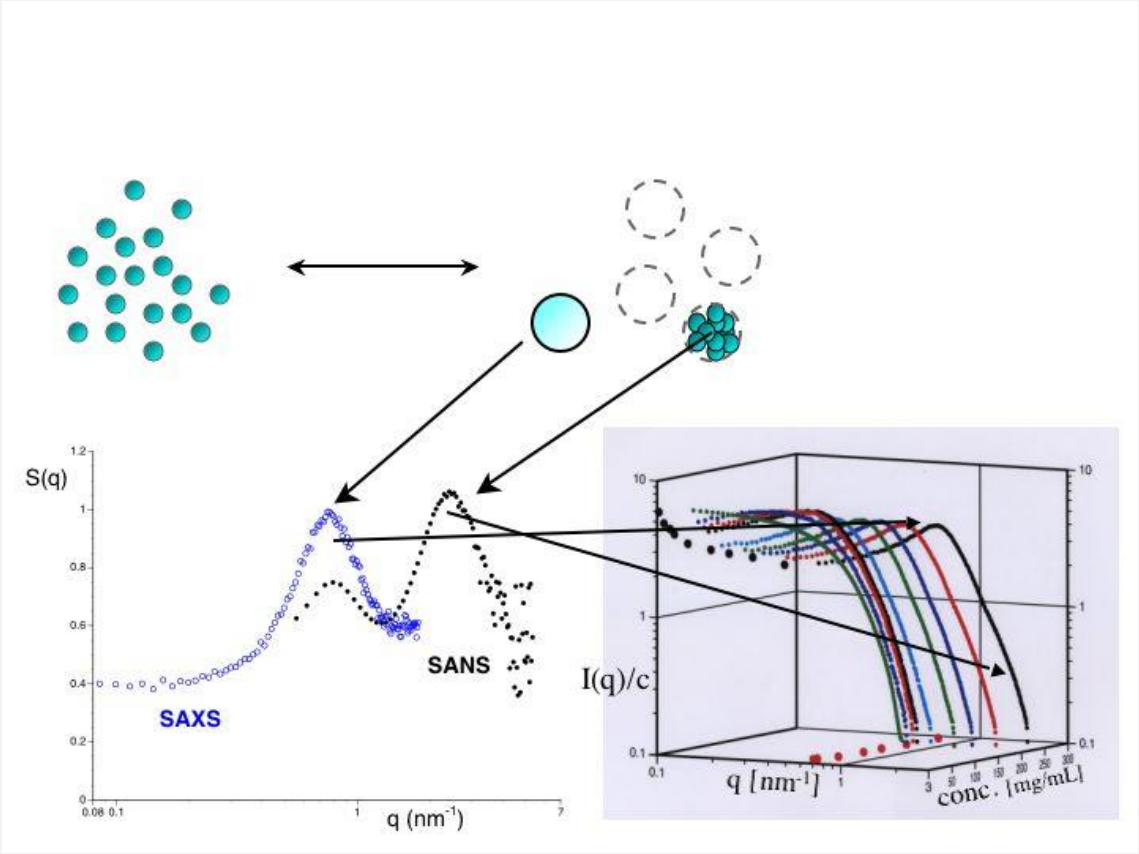
Minimize free energy density - result

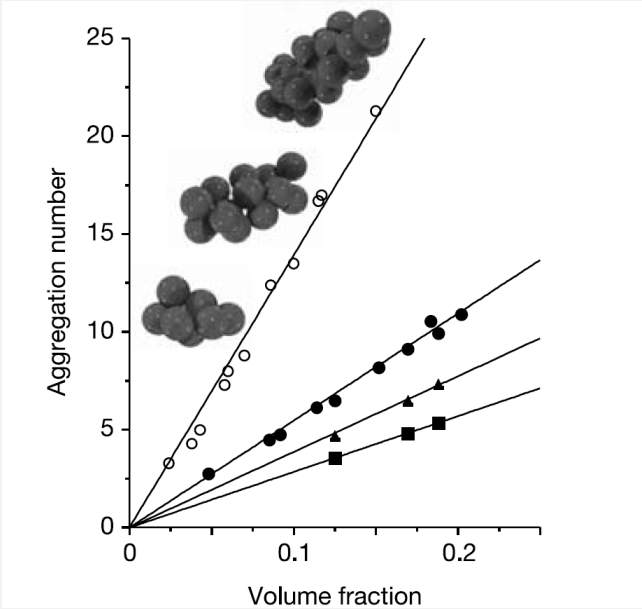
$$R_*^3 = \frac{15}{8\pi} \frac{\gamma}{\lambda_B \rho^2}$$

As long as $\rho \approx \rho_0$, and $\rho_0^2 \approx \frac{e^{-\lambda_B / b} \sigma}{r b^3 \phi}$

→ QED →

# Stable clusters also observed in aqueous protein solutions (without added salt)




$$Aggr.\# \propto R_*^3 \propto \phi$$

[Stradner ea Nature **432**, 492, (2004)]

Numbers (small R, large ε) make sense

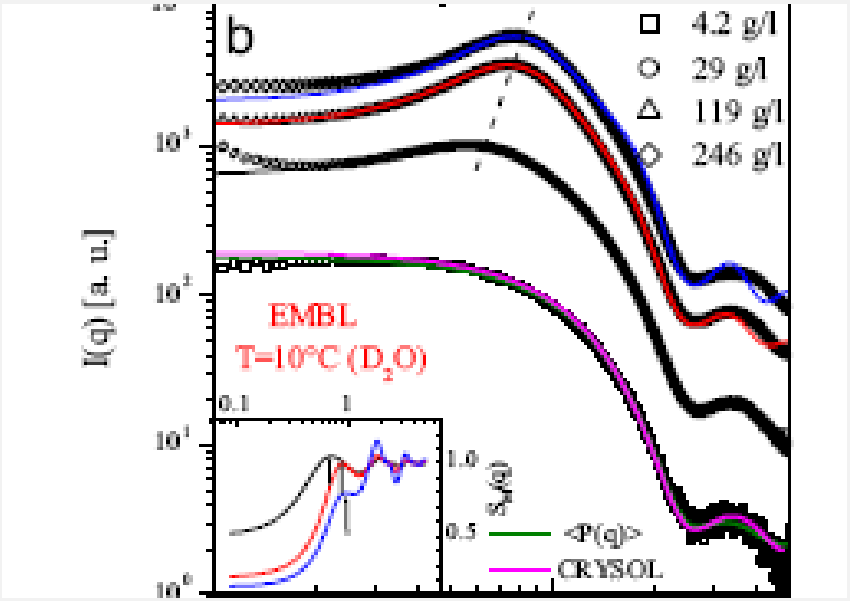
Cluster size cannot (much) exceed Debye length

# Controversy

## Absence of equilibrium cluster phase in concentrated lysozyme solutions

[PNAS **105**, 5075, (2008)]

Anuj Shukla*, Efstratios Mylonas†, Emanuela Di Cola*, Stephanie Finet*, Peter Timmins‡§, Theyencheri Narayanan*§, and Dmitri I. Svergun†§¶

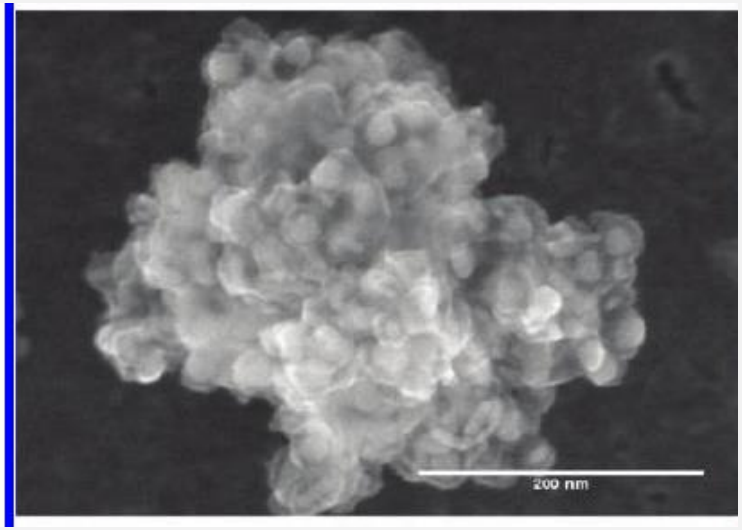


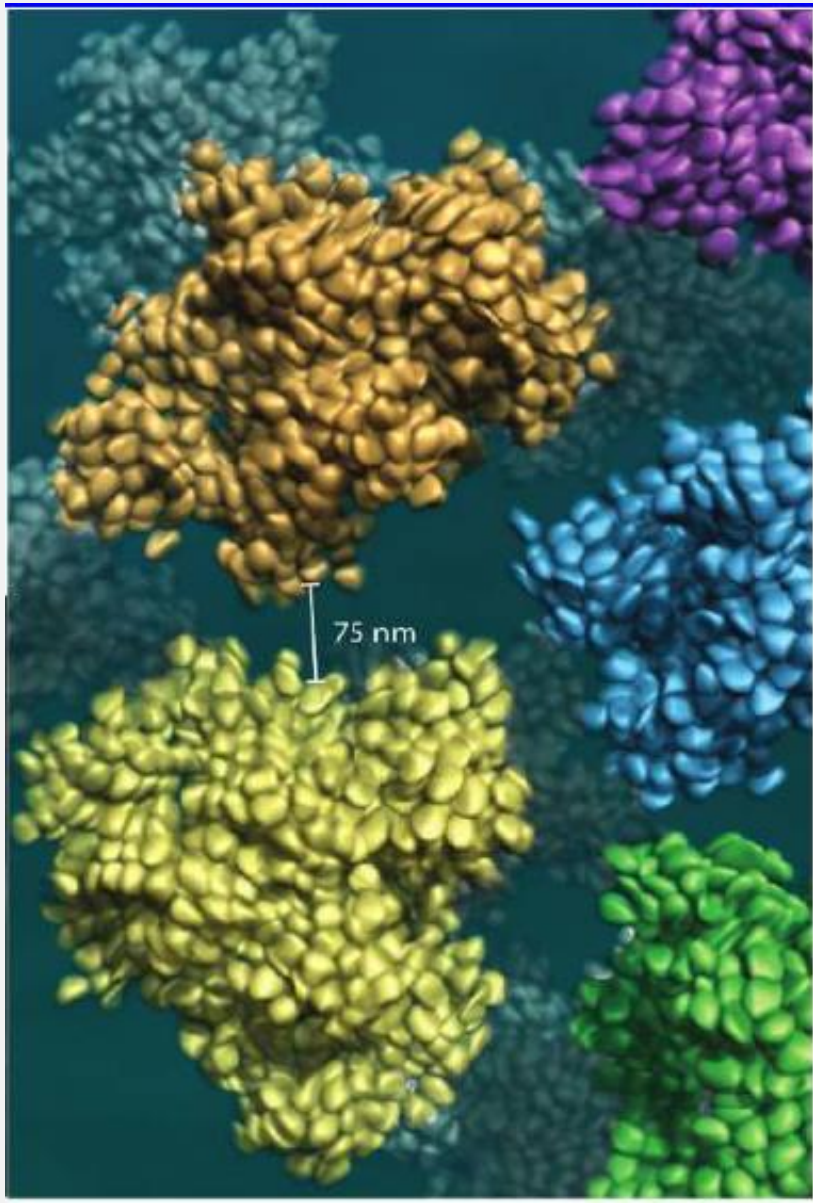

In case of clusters: expect *constant* peak with lysozyme concentration

…but ‘critical cluster concentration’ ≈ 200 g/l !

# Evidence for equilibium protein clusters *in vivo:*

[KP Johnston ea ACSNano 2012]




Cluster size >> Debye length

-> expect unstable to further growth

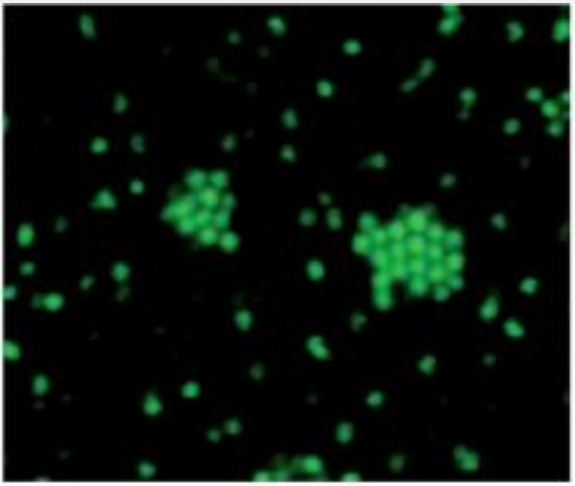
… but clusters hardly contain water

-> low local dielectric constant, ionic strength. Low screening.

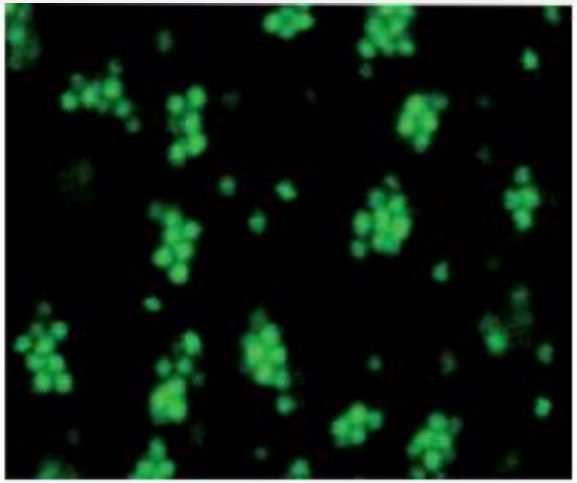
Cluster size versus attraction strength ε

$$R_*^3 = \frac{15}{8\pi}\frac{\gamma}{\lambda_B \rho^2} \qquad \rho_0^2 \approx \frac{e^{-\lambda_B/b}\sigma}{rb^3\phi} \qquad \gamma \approx \frac{|\varepsilon|}{4\pi r^2}$$

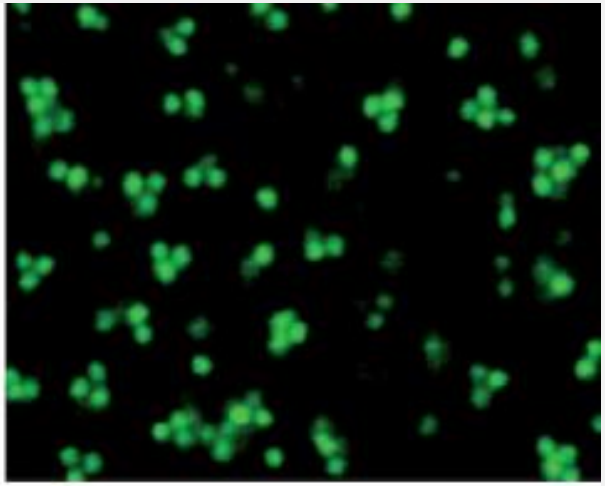
⟶ predict $R_*^3 \propto |\varepsilon|$



$| \epsilon | = 5.5\ kT$



$| \epsilon | = 8.8\ kT$



$| \epsilon | = 16.5\ kT$

... Opposite trend [Zhang ea Soft Matter2012]

Explain trend by classical nucleation theory:

Cluster formation free energy (out of colloidal gas state)

$$\Delta G(N) = N\Delta\mu + \gamma A_c + G_c$$

$$-kT\ln S$$

$$S = \phi_c/\phi_{coex}$$

$$\phi_{coex} \approx \frac{V_c}{\xi^3}\exp\left(\frac{6\epsilon}{kT}\right)$$

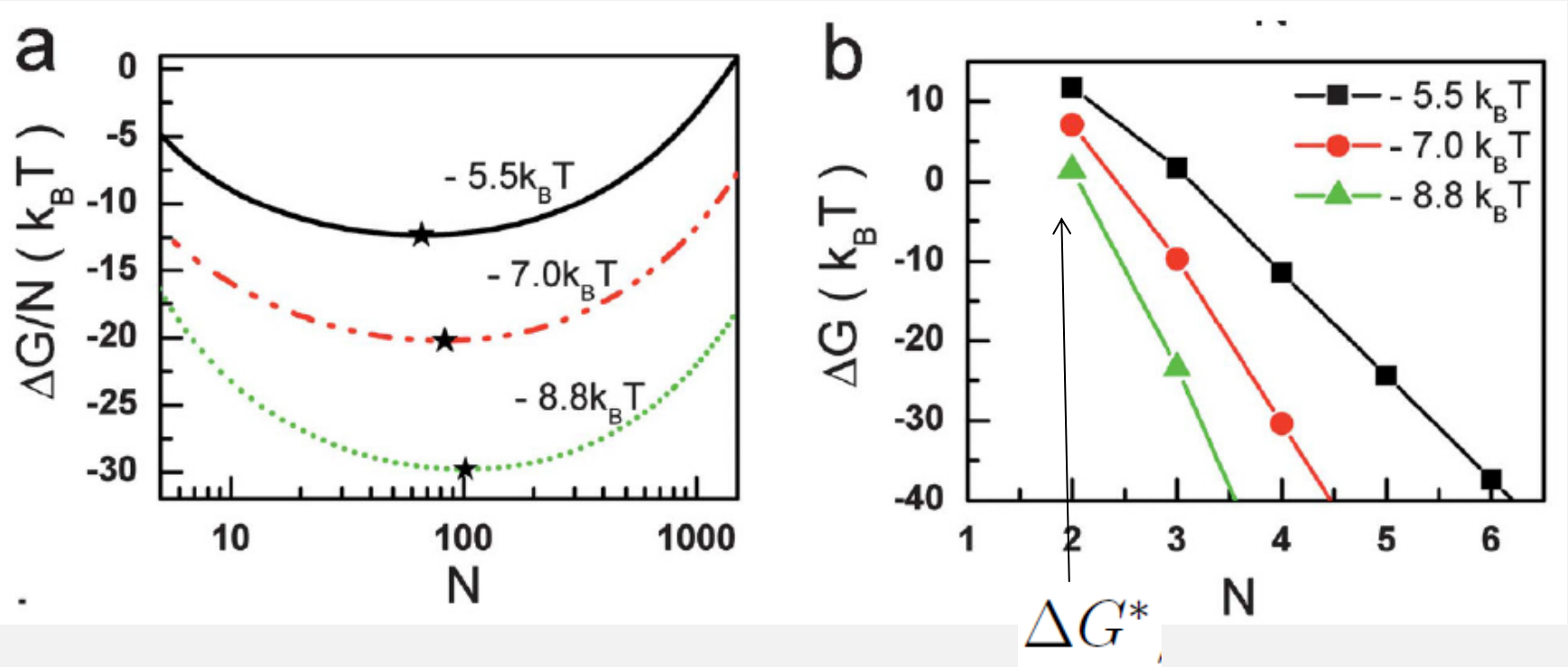
$$\frac{1}{2a}\lambda_B\rho^2 N^{5/3}$$

$$\approx c(N) \mid \epsilon \mid N^{2/3}$$

$$c(N) = 3 + 6/N \text{ for } N \geq 3$$

$$c(N) = 5.5 \text{ for } N = 2$$

# Result




Nucleation rate $J \propto \exp(-\Delta G^*/kT)$

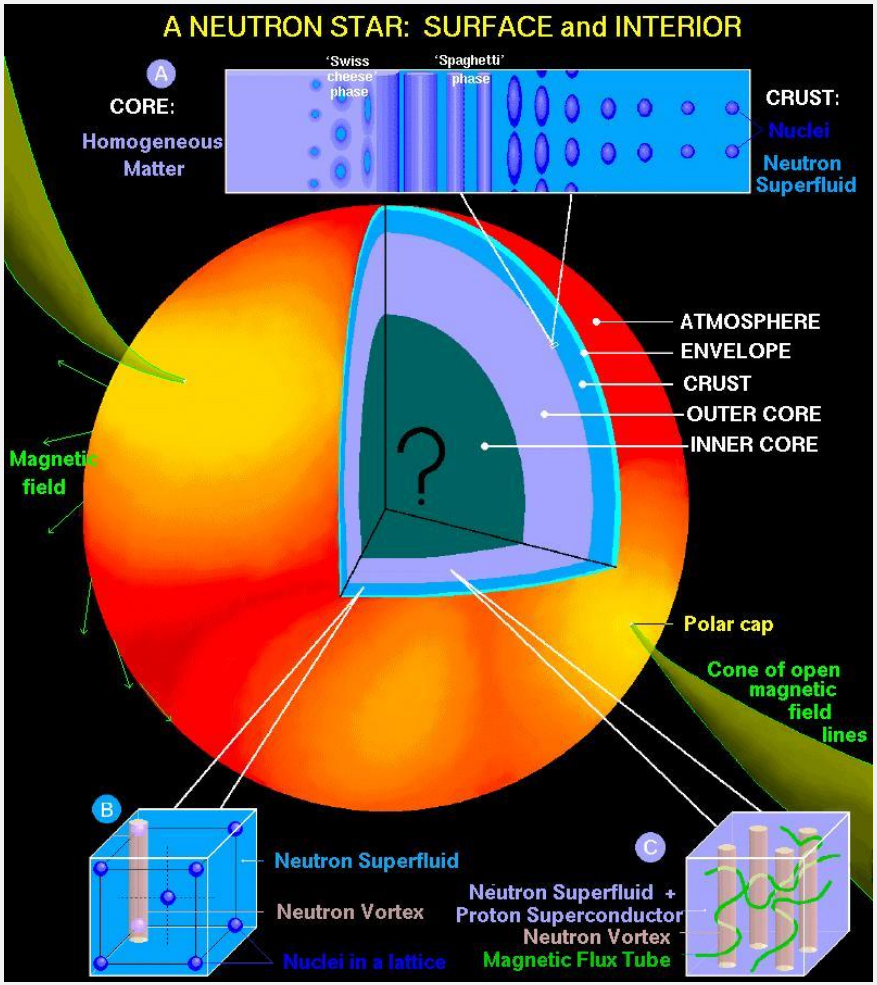
J (ε = -8.8 kT) ~ $10^4$ J (ε = -5.5 kT) ⟶

Initially more & smaller clusters with more attraction

# How far can we push the analogy with nuclear matter?

Large nuclear densities: neutron star interiors

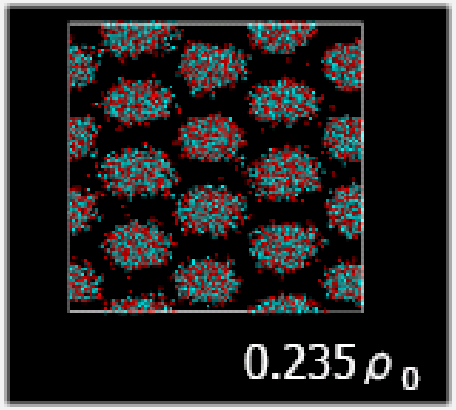
Several scenarios; first attempt: [Baym, Bethe & Pethick, Nucl. Phys. **A175**, 225, (1971)]



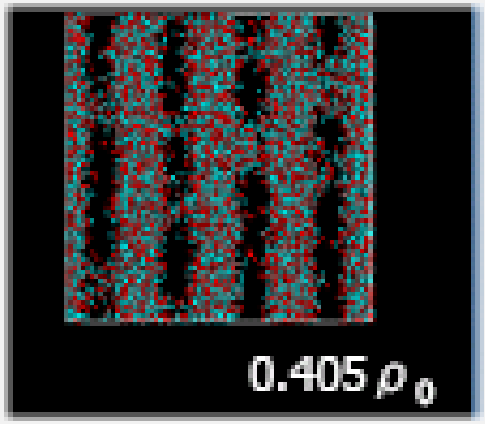

Core:
Density $10^{14}$ gcm$^{-3}$

# Nuclear matter at high density : several predictions, e.g.,

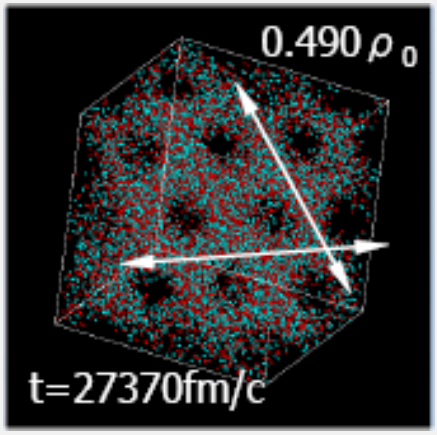
## nuclear “pasta”




“Spaghetti”




“Lasagna”




“anti – spaghetti”

[Watanabe, Sato, Yasuoka, Ebisuzaki, Phys. Rev. **C66**, 012801, (2002); **68**, 035806, (2003)]

# Periodic structures in MD simulation of MONODISPERSE ‘colloidal’ system

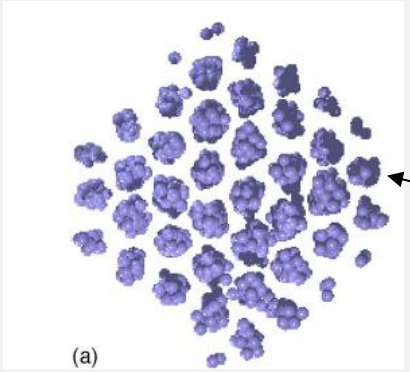
[A. De Candia ea, PRE **74**, 010403(R), (2006)]

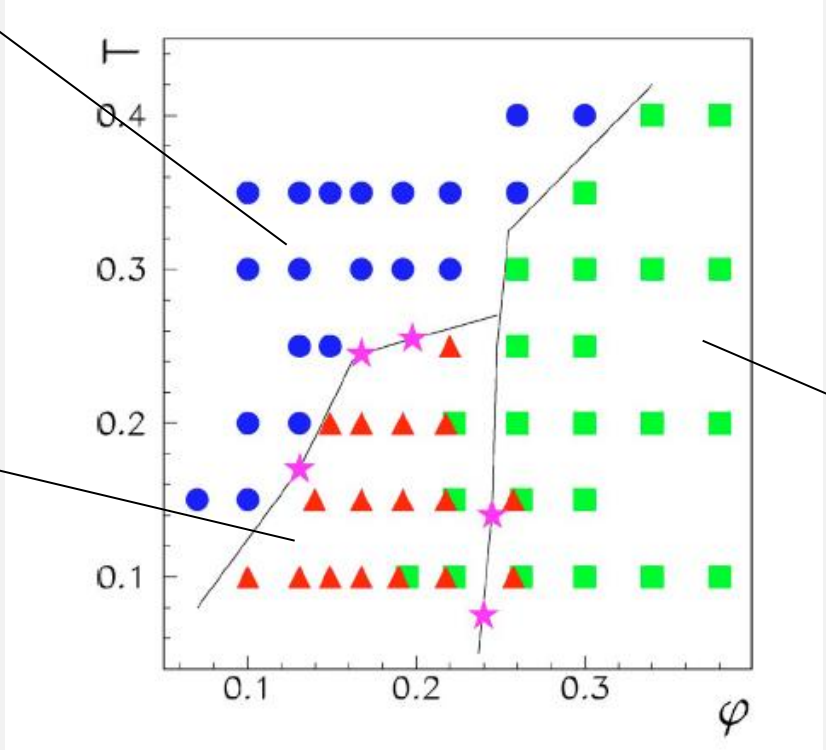
Model potential

$$V(r) = \epsilon\left[ a_1\left(\frac{\sigma}{r}\right)^{36} - a_2\left(\frac{\sigma}{r}\right)^{6} + a_3 e^{-\lambda(r/\sigma-1)} \right]$$

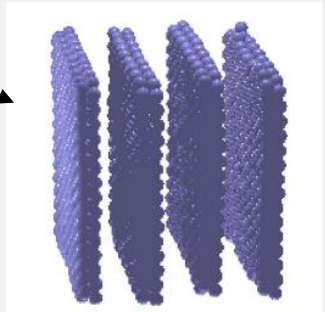
‘disordered’

columnar




lamellar

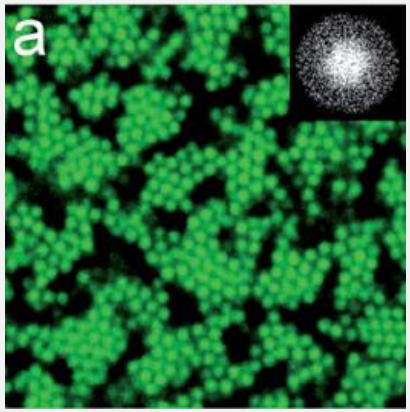


Experiments at higher colloid volume fractions : gelation.

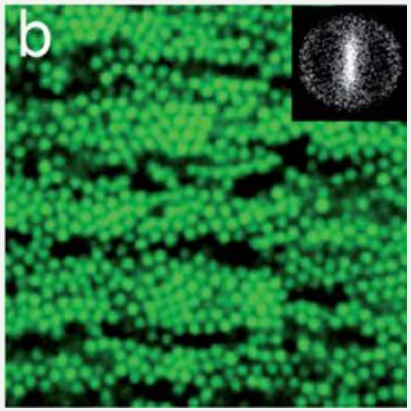
Force gel into columnar – like state by E-field and see what happens

[Zhang ea, Soft Matter 2015 ]

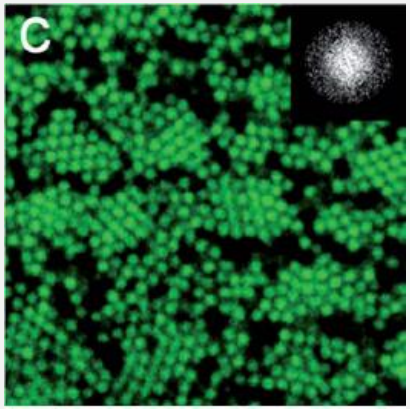
After preparation: gel



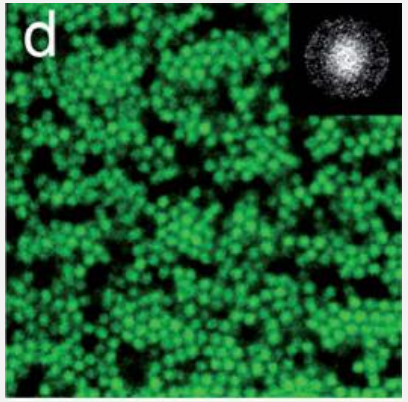

Field on : columnar




Field off – after 4 days




Field off – after 7 days




MD simulations of polydisperse systems: periodic structures unstable beyond 1% polydispersity [Zhang ea, Soft Matter 2015 ]

# Conclusions and further work

- Clusters are stable (colloidal) state of matter under conditions of long range repulsion (relative to the size of a colloid) and short-range attraction

- Non-equilibrium clusters appear at strong attractions

- At high colloid concentrations, colloidal gel is the stable state

Improve theory:

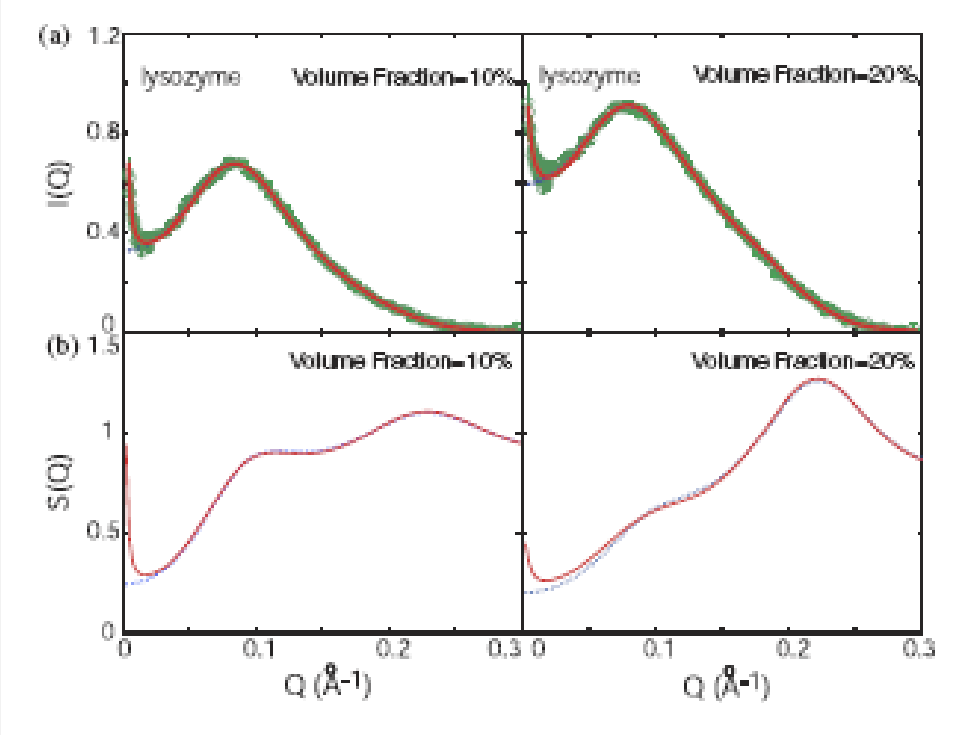
- beyond spherical clusters
- inhomogeneous charge distributions
- interactions between clusters
- allow for dielectric constant variation

Thank You!

# Controversies related to equilibrium protein clusters

- 1 Zero-Q peak: Long-range attraction in protein solutions

[Y. Liu, E. Fratini, P. Baglioni, R-R Chen, S.H. Chen, PRL **95**, 118102, (2005)]



Zero Q peak appears several days after sample preparation, related to impurities

[A. Stradner, F. Cardinaux, P. Schurtenberger, PRL **96**, 219801, (2006)]