Offsetting Diffusive Effects

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What is a colloid?

- Mixture of two (or more) substances where one is made up of insoluble particles dispersed throughout the other substance.
- A liquid with two phases: a microscopic droplet phase dispersed in a continuous phase. (usually H_2O)
- A *suspension* that does not settle down due to gravity. ✓
- Eg. Milk, paint, pigments, blood
- Can we consider cytoplasm to be a colloid?

Is the cell interior a colloid?

Colloidal stability of the living cell

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Cellular function is generally depicted at the level of functional pathways and detailed structural mechanisms, based on the identification of specific protein–protein interactions. For an individual protein searching for its partner, however, the perspective is quite different: The functional task is challenged by a dense crowd of nonpartners obstructing the way. Adding to the challenge, there is little information about how to navigate the search, since the encountered surrounding is composed of protein surfaces that are predominantly "nonconserved" or, at least, highly variable across organisms. In this study, we demonstrate from a colloidal standpoint that such a blindfolded intracellular search is indeed favored and has more fundamental impact on the cellular organization than previously anticipated. Basically, the unique

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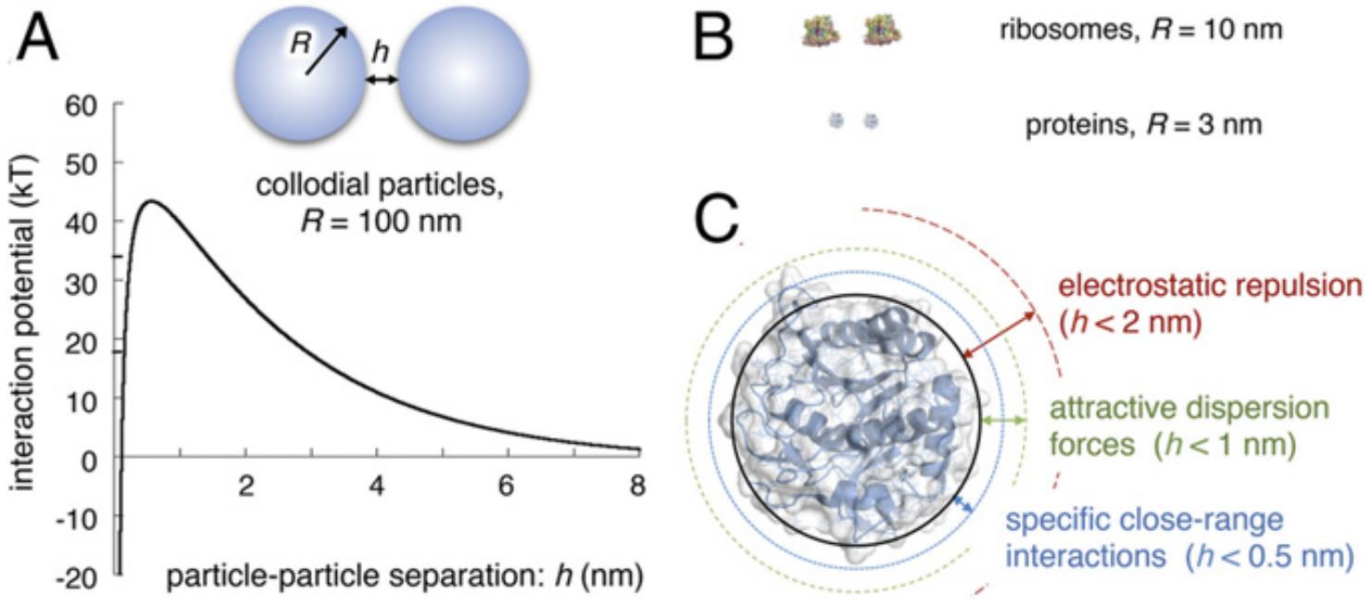
Is the cell interior a colloid?

BIOLOGICAL MILIEU



One must consider:
a) size,
b) strength of inter-particle interactions

Fig. 1. Dimensions and forces of biological macromolecules. (*A*) Colloidal description of particles (R ≥ 100 nm) yielding kinetic stability through a high repulsive association barrier. (*B*) Relative sizes of ribosomes and proteins, constituting the dominant fraction of soluble cytoplasmic components. (*C*) The separation distance (*h*) regimes of the balancing forces that modulate protein–protein interactions in vivo.

Is the cell interior a colloid?

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Dynamics of highly polydisperse colloidal suspensions as a model system for bacterial cytoplasm

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(Received 27 May 2016; published 30 August 2016)

There are various kinds of macromolecules in bacterial cell cytoplasm. The size polydispersity of the macromolecules is so significant that the crystallization and the phase separation could be suppressed, thus stabilizing the liquid state of bacterial cytoplasm. On the other hand, recent experiments suggested that the macromolecules in bacterial cytoplasm should exhibit glassy dynamics, which should be also affected significantly by the size polydispersity of the macromolecules. In this work, we investigate the anomalous and slow dynamics of highly polydisperse colloidal suspensions, of which size distribution is chosen to mimic *Escherichia coli* cytoplasm. We find from our Langevin dynamics simulations that the diffusion coefficient (D_{tot}) and the

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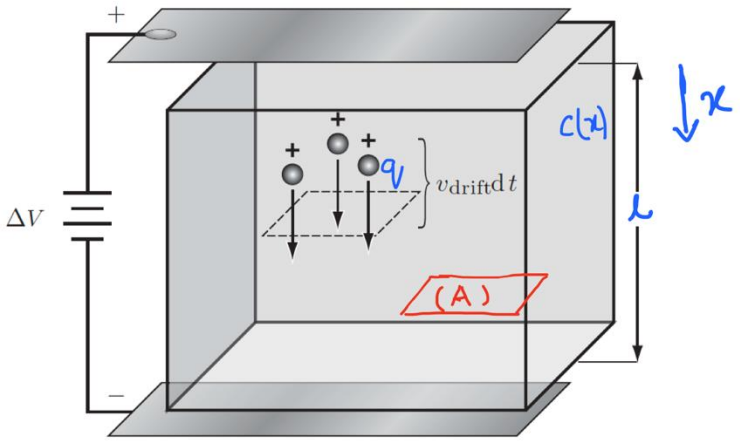
Offsetting Diffusive Effects:



Modified flux under the electric field,

NERNST-PLANCK FORMULA

$$j = D\left(-\frac{\partial c_{ion}}{\partial x} + \frac{q\xi\, c_{ion}}{k_B T}\right)$$

Generalizing:

$$\frac{\partial c}{\partial x} = \frac{q \cdot \xi(x) \cdot c}{k_B T}$$

$$\frac{dc}{c} = \frac{q\xi}{k_B T}\,dx \qquad \text{Force}$$

$$\int_{c_1}^{c_2} \frac{dc}{c} = \int \frac{(\text{force})(dx)}{(k_B T)}$$

$$\equiv \ln\left(\frac{c_2}{c_1}\right)$$

Offsetting Diffusive Effects:

With constant force, we may generalize to,

$$\ln\left(\frac{c_2}{c_1}\right) \equiv \frac{[\text{force}][\text{length}]}{(k_B T)}$$

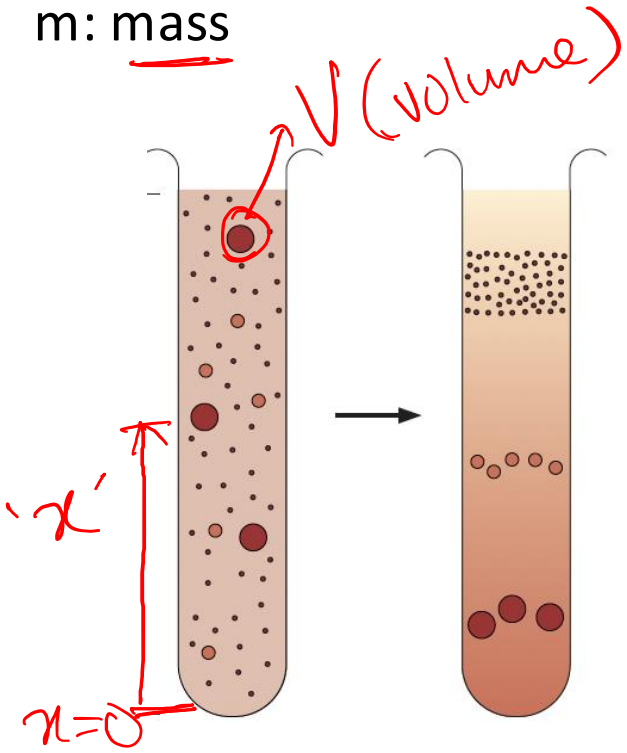
Offsetting Diffusive Effects:

2. Gravity: Sedimentation of heavy particles

ρ_W: density of "continuous phase" (usually water)

V: particle volume

m: mass



Offsetting Diffusive Effects:

Sedimentation equilibrium under gravitational force:

$$c(x) \propto e^{-(m - V\rho_w)gx/(k_B T)}$$

$m_{net} = m - V\rho_w$

Scale height:

$$x^* = (k_B T)/(m_{net} g)$$

Prob. Myoglobin (Mb) has a mass equivalent of 17 kDa, and a volume of 22.3 nm^3

a) Find the scale height (x*) of Mb at **300 K**

a) In a test-tube of Mb solution, find the *ratio* of the concentration at the bottom (C_0) to that at x = 4 cm from the bottom (C_x)

c) How does x* depend on *temperature* and m_{net}?

d) Compare x* at room temperature with that at the refrigerator temperature (276 K)

$$x^*_{300} = \frac{k_B T}{(m - V\rho_w)g}$$

$$x^* \approx 70\ m$$

$$\frac{c(x)}{c(0)} \sim \frac{1}{e}$$

At $x = 4\ cm$,

$$c(x) = c_0 \cdot e^{-0.04/70}$$

$$\sim c_0$$

$\rho_w = 10^3\ kg/m^3$

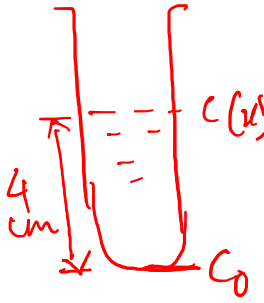
$m = \frac{17}{6.02 \times 10^{23}}\ kg$

$V = 22.3 \times 10^{-27}\ m^3$

$k_B = 1.38 \times 10^{-23}\ J\ K^{-1}$

$g = 9.8\ ms^{-2}$

$T = 300K$



Change from 300 K to refrigerator temperature (276 K):

$$x^*_{(276)} = x^*_{(300)} \times \frac{276}{300}$$

$$c(x)\Big|_{\substack{\text{at} \\ 276K, \\ x=4cm}} \approx C_0\Big|_{\substack{\text{corresponding} \\ \text{value}}}$$

Consider a large, 500 kDa protein (eg. yeat acetyl-CoA carboxylase) at 276 K:

R_{min} = 5.21 nm , Hence, $V_{min} = \frac{4}{3}\pi R_{min}^3$

At 300 K,

$$x^* = \frac{k_B T}{\left[m - \rho_w \times \left(\frac{4}{3}\pi R_{min}^3\right)\right] g}$$

Most protein solutions will remain “colloidal” even in the refrigerator!

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- A *suspension* that does not settle down due to gravity.

- Eg. Milk, paint, pigments, blood

- Can we consider cytoplasm to be a colloid?

Offsetting Diffusive Effects:

3. Centrifugal force for separation of components in a colloid:

At a distance *r*,

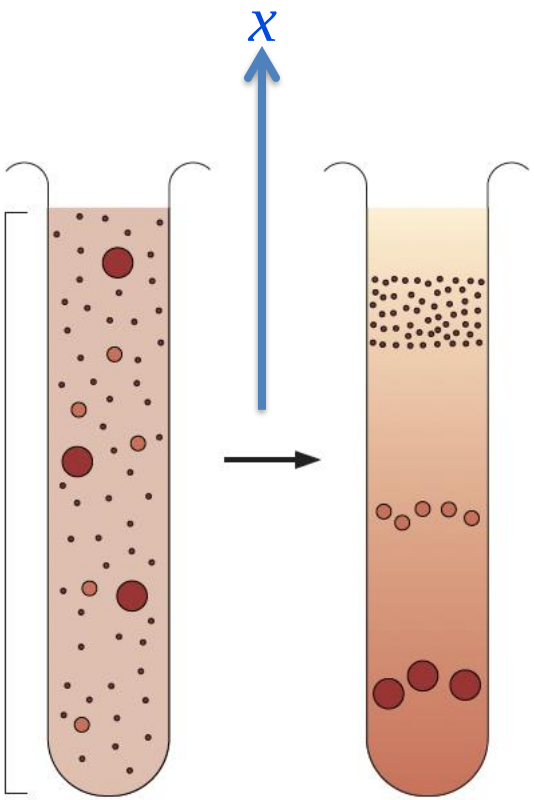
$$\ln\left(\frac{c_r}{c_0}\right) \equiv \frac{[m\omega^2 r][r]}{(k_B T)}$$

$$\equiv \left(\frac{1}{k_B T}\right) \times \frac{\left[4\pi^2 (r.p.m)^2 \times r^2\right](m)}{3600}$$

Angular velocity in rotations per minute

Centrifuge speeds ($\mathbf{g_c}$) are scaled in terms of **g**'

Centrifugation



Centrifuge speeds ($\mathbf{g_c}$) are scaled in terms of **g**'

Effective mechanical acceleration,

$$g_c >> g$$

When the effective drift force matches the centrifugal force,

$$\zeta v_{drift} = m_{net} g$$

$$\frac{m_{net}}{\zeta} = \frac{v_{drift}}{g}$$ → time scale

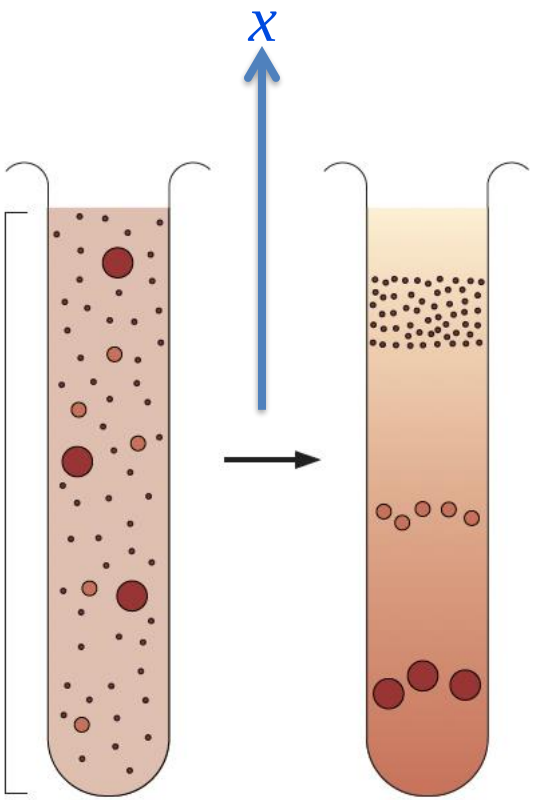
ζ: viscous friction coefficient

η: viscosity

For a spherical particle of radius 'a',

$$v_{drift} = \frac{m_{net} g}{(6\pi\eta a)}$$

Centrifugation



We get a centrifugation timescale from:

$$\frac{m_{net}}{\zeta} \quad \text{or} \quad \frac{m_{net}}{(6\,\pi\,\eta\,a)}$$

ζ: viscous friction coefficient

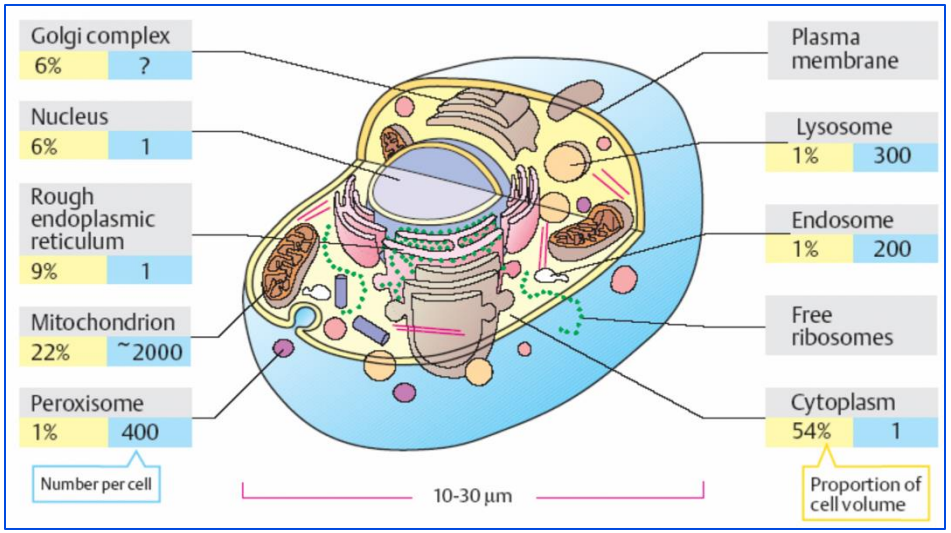
η: viscosity of medium (water)

For a typical protein,

$$\frac{m_{net}}{\zeta} \approx 10^{-13} \text{ seconds}$$

] Representative number.

Centrifugation

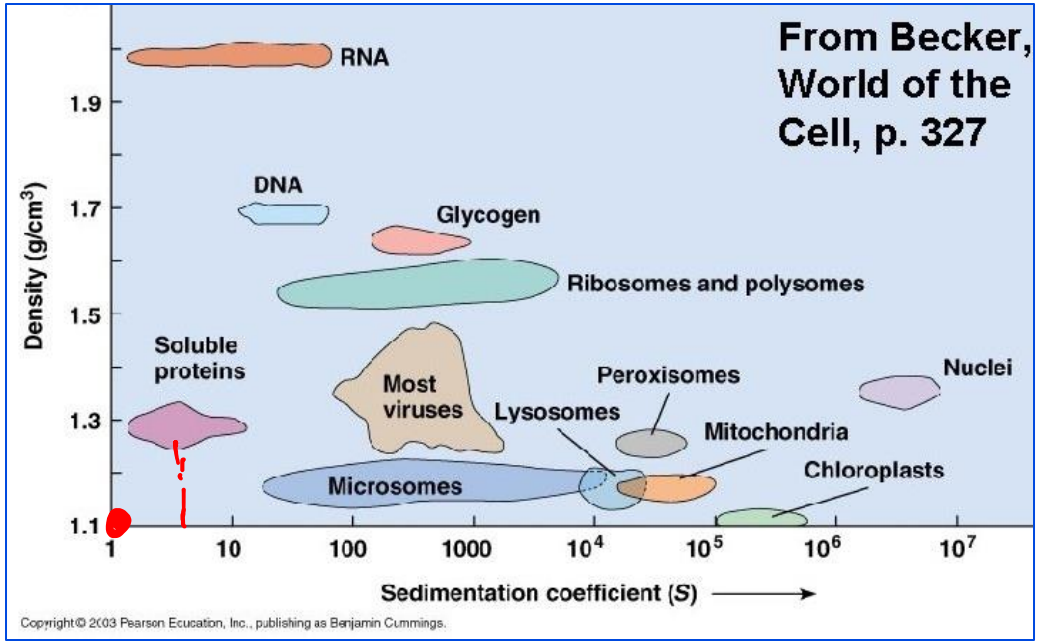


Sedimentation *time scale*,

$$t = \frac{m_{net}}{\zeta}$$

1 Svedberg (s) = 10^{-13} s

Material	Density (g/cm^3)
Microbial cells	1.05 - 1.15
Mammalian cells	1.04 - 1.10
Organelles	1.10 - 1.60
Proteins	1.30
DNA	1.70
RNA	2.00



Svedberg units are non-additive

Eg. Ribosome subunits