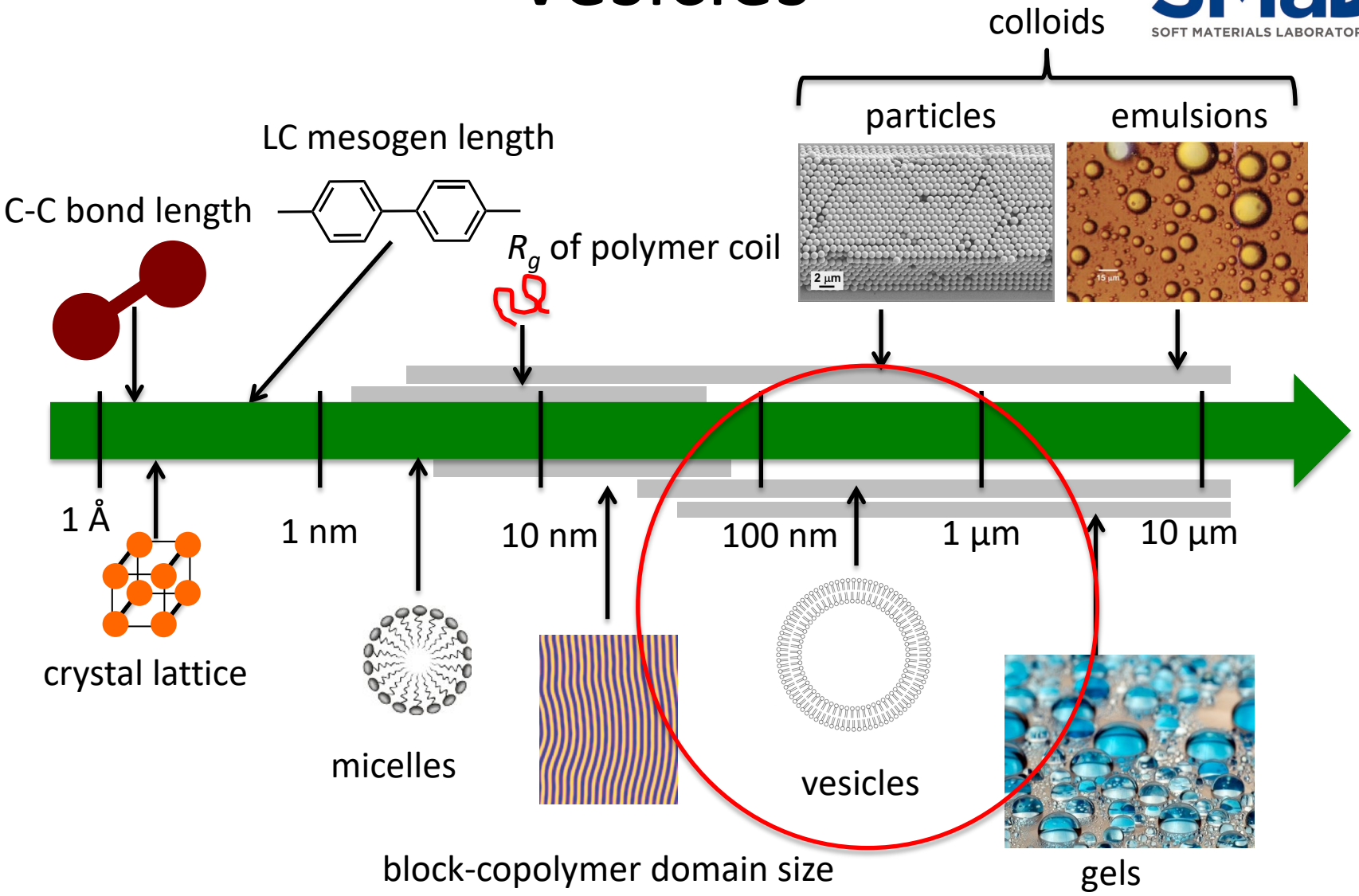
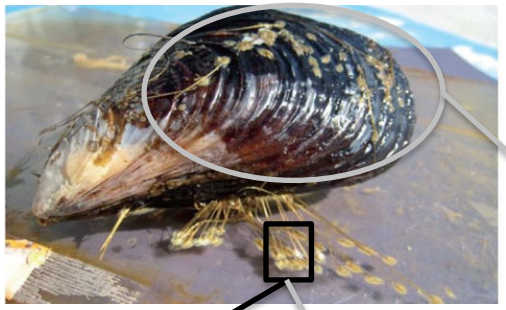
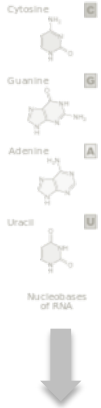
Vesicles


colloids
particles
emulsions
LC mesogen length
C-C bond length
R_g of polymer coil
2 µm
1 Å
1 nm
10 nm
100 nm
1 µm
10 µm
crystal lattice
micelles
vesicles
gels
block-copolymer domain size

Course outline

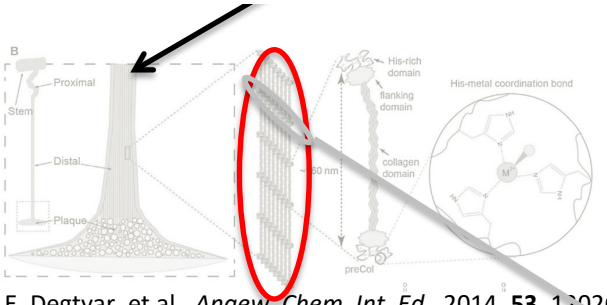


Introduction



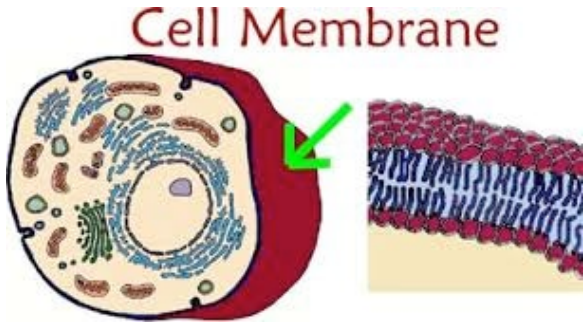
Ordered materials

Thermotropic liquid crystals



E. Degtyar, et al., *Angew. Chem. Int. Ed.*, 2014, **53**, 12026-12044

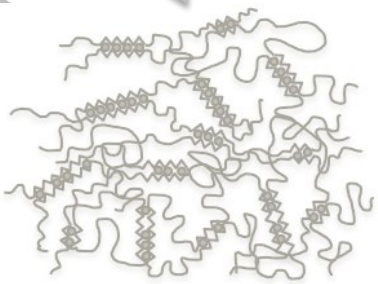
Lyotropic liquid crystals



Disordered materials

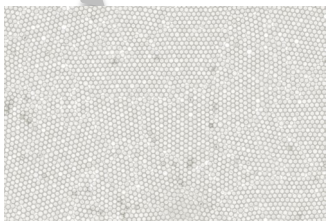
Polymers

Gels



Colloids

Nanoparticles



Emulsions

Outline

- Introduction: Vesicles
- Liposomes
- Polymersomes
- Vesicle production
- Characterization
- Applications

Outline

- Introduction: Vesicles
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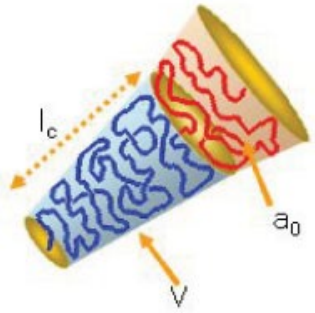
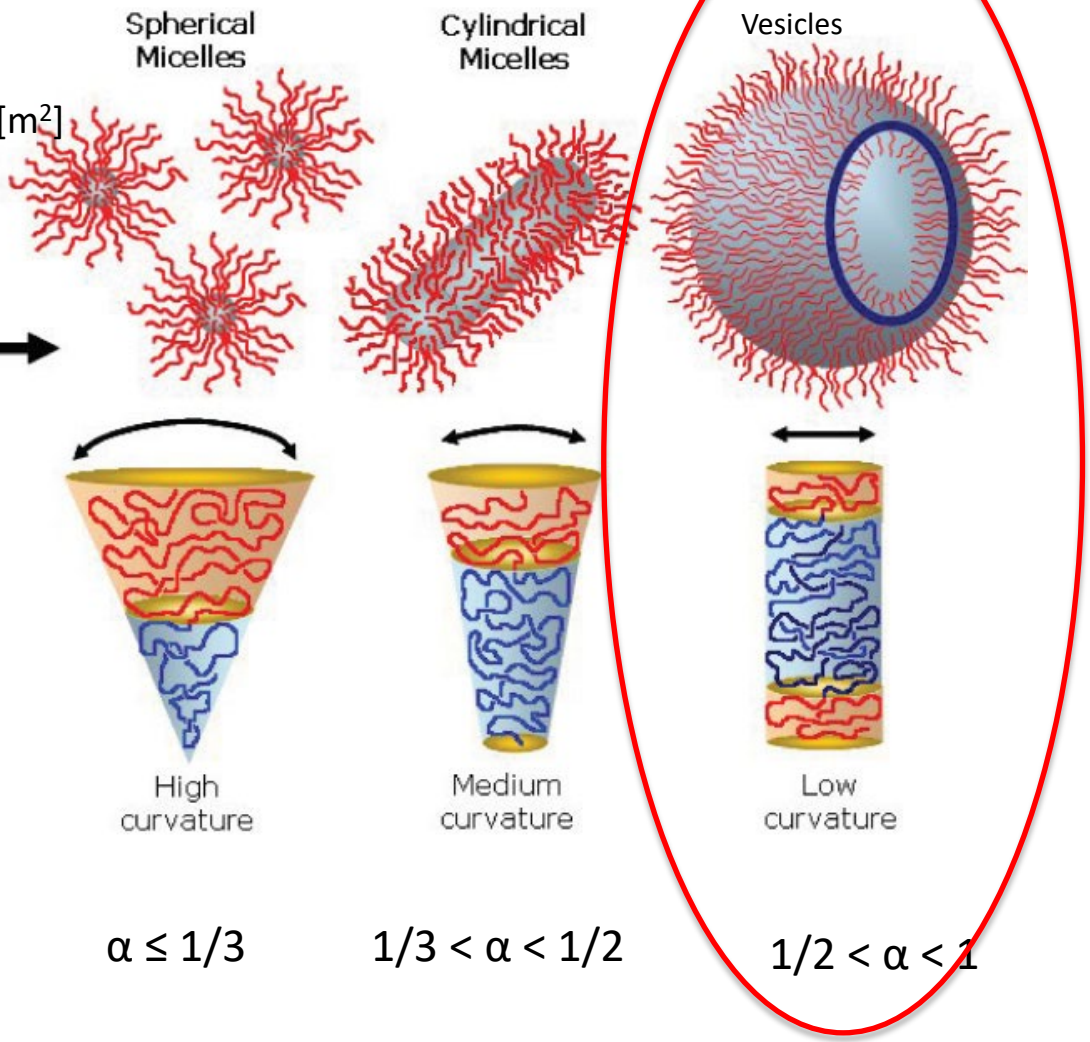
Vesicles

Vesicles are composed of bilayers made from amphiphilic molecules.

α: packing parameter [-]
v: volume of hydrocarbon chain [m^3]
a_0: optimal surface area of amphiphile [m^2]
l_c: critical chain length [m]





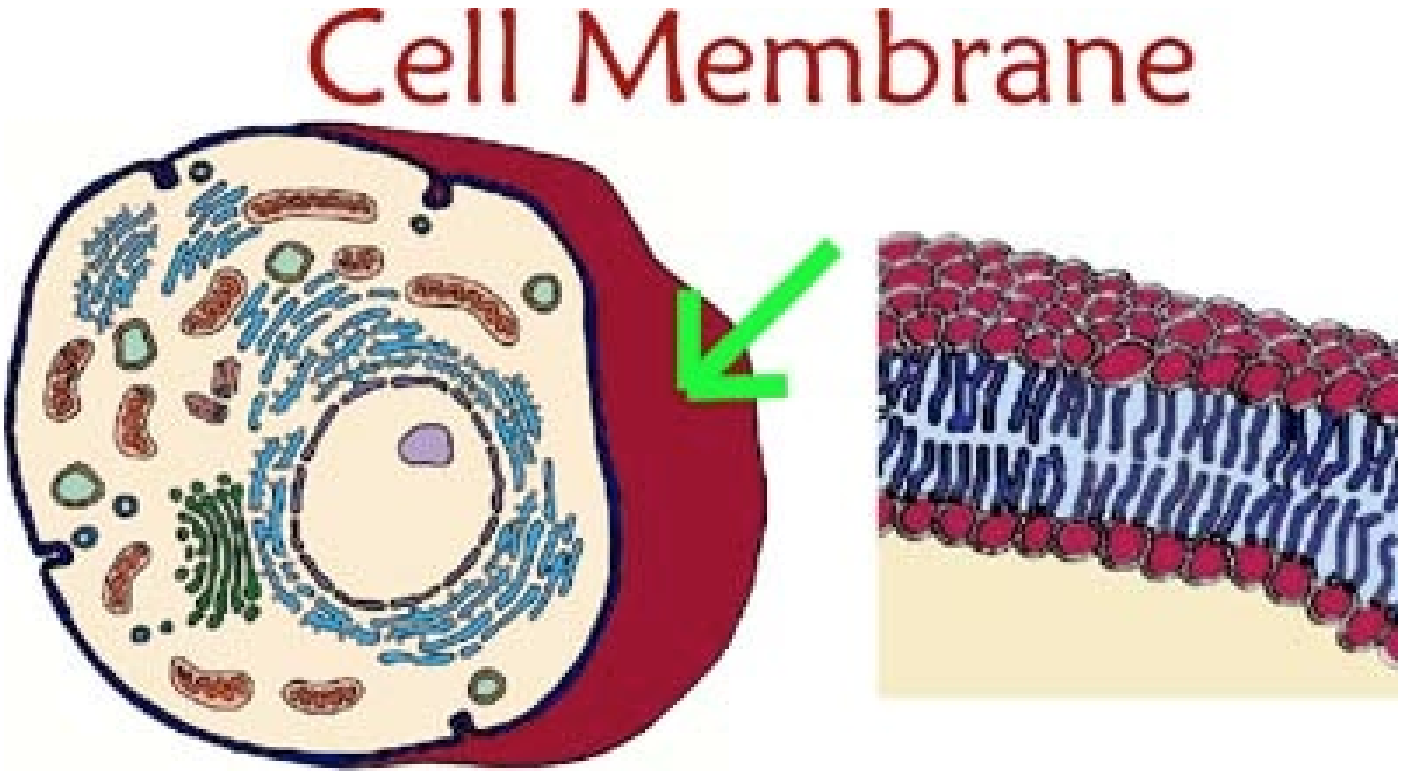
$$\alpha = \frac{v}{a_0 l_c}$$

α ≤ 1/3

1/3 < α < 1/2

1/2 < α < 1

Vesicles in nature



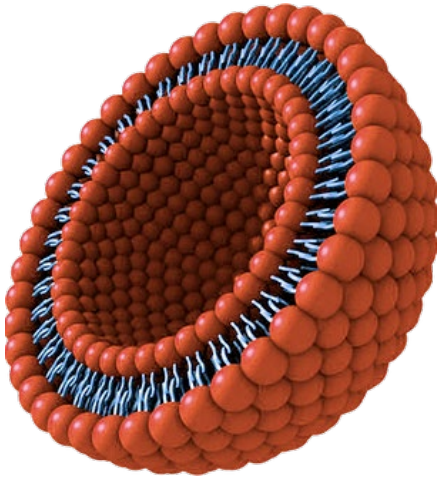
http://battleoftheorganelles.blogspot.ch/2013/10/the-celebratory-cell-membrane-cause-its.html

Outline

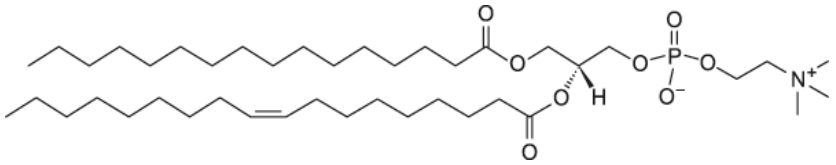
- Introduction: Vesicles
- Liposomes
- Polymersomes
- Vesicle production
- Characterization
- Applications

Vesicles

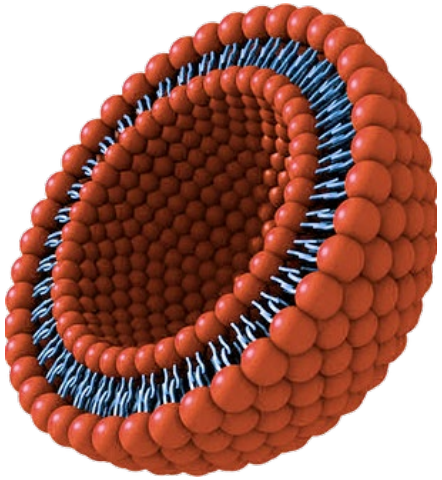
Liposomes are vesicles made from lipids.

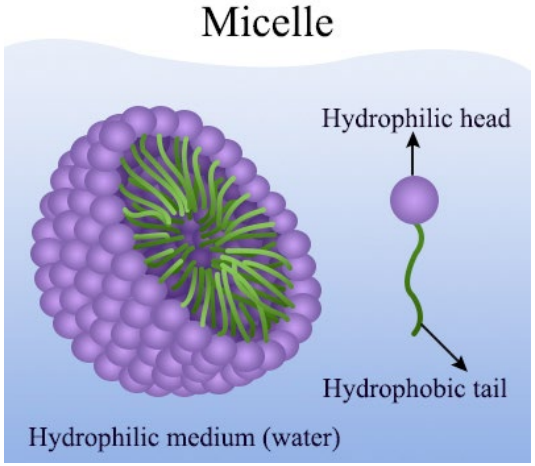


Example of a phospholipid:

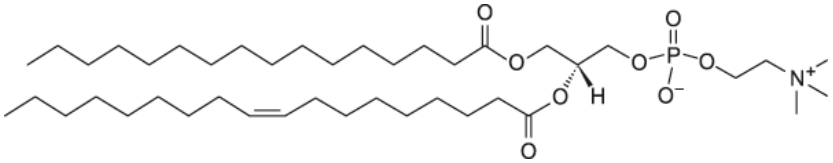


Vesicles vs. Micelles

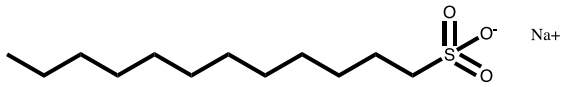




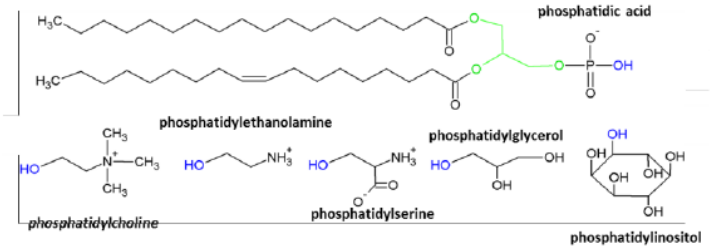
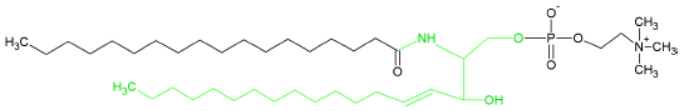
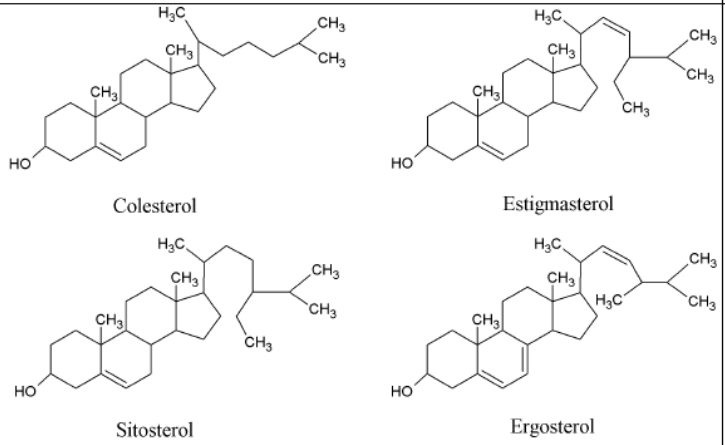
Example of a phospholipid:



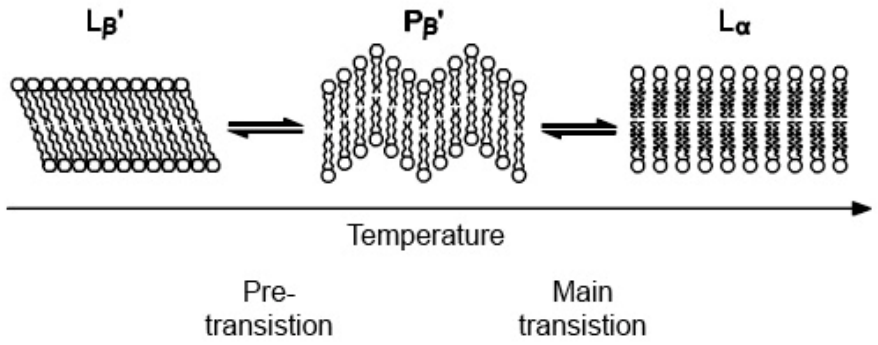
Example of an amphiphile that forms micelles:



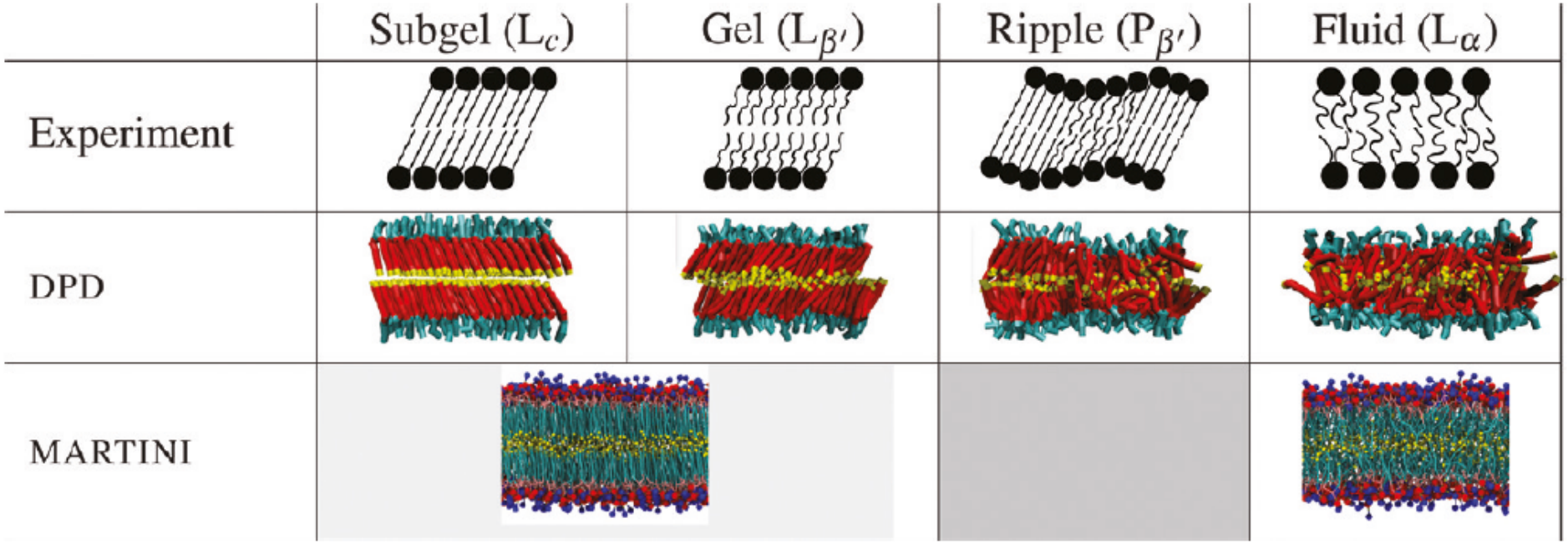
Liposomes consist of lipids

lipid type	chemical formula	examples
phospho-lipids		1,2-dipalmitoylphospho-choline (DPPC) 1-palmitoyl-2-oleylphospho-choline (POPC)
sphingo-lipids		sphingomyelins cerebrosides gangliosides
steroids		cholesterol estigmasterol sitosterol ergosterol phytosterols

Phase transition

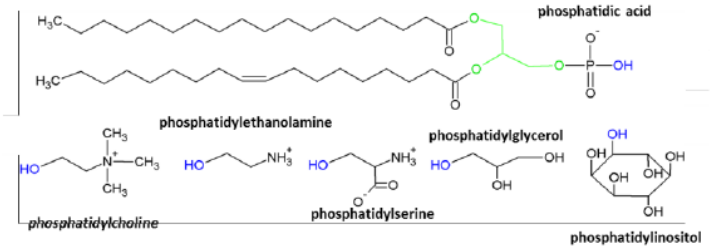
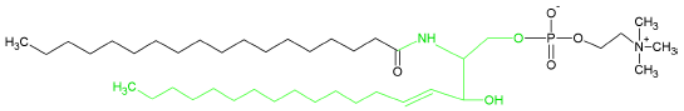
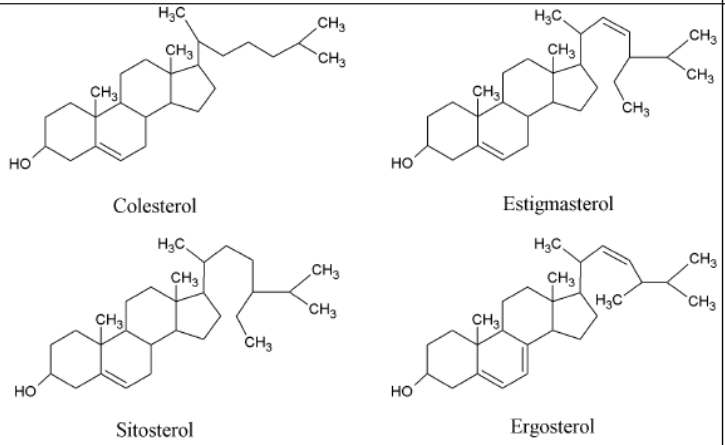


https://avantilipids.com/tech-support/physical-properties/phase-transition-temps/

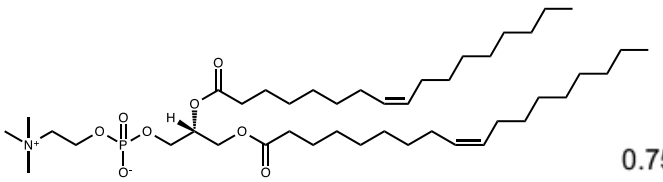


M. Rodgers, J. Sorensen, F. J. M. de Meyer, B. Schiott and B. Smit, *J. Phys. Chem. B*, 2012, **116**, 1551-1569

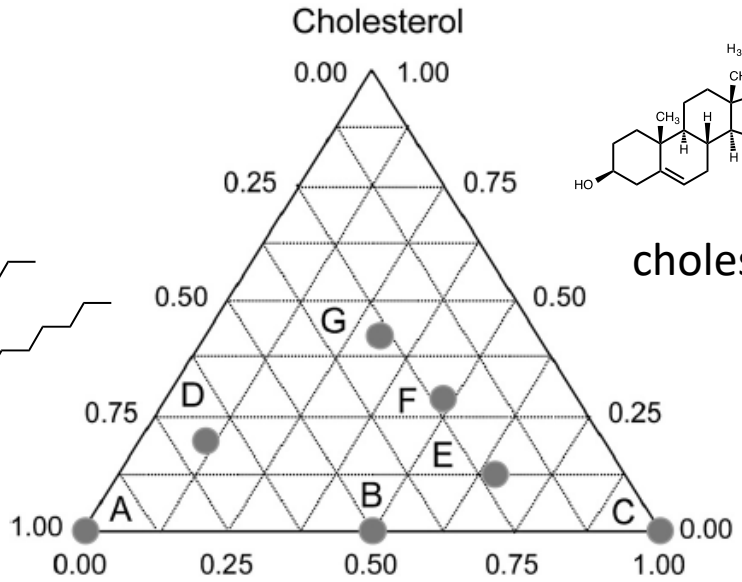
Liposomes consist of lipids

lipid type	chemical formula	examples
phospho-lipids		1,2-dipalmitoylphospho-choline (DPPC) 1-palmitoyl-2-oleylphospho-choline (POPC)
sphingo-lipids		sphingomyelins cerebrosides gangliosides
steroids		cholesterol estigmasterol sitosterol ergosterol phytosterols

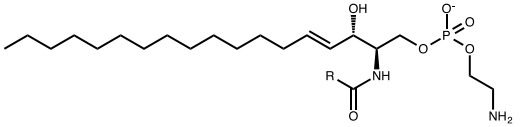
Liposomes made of mixtures of lipids



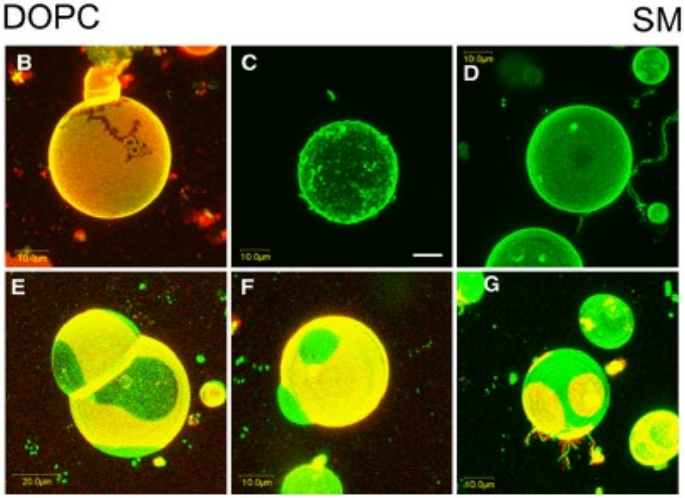
1,2 dioleoyl-sn-glycero-3-phosphocholine (DOPC)



cholesterol

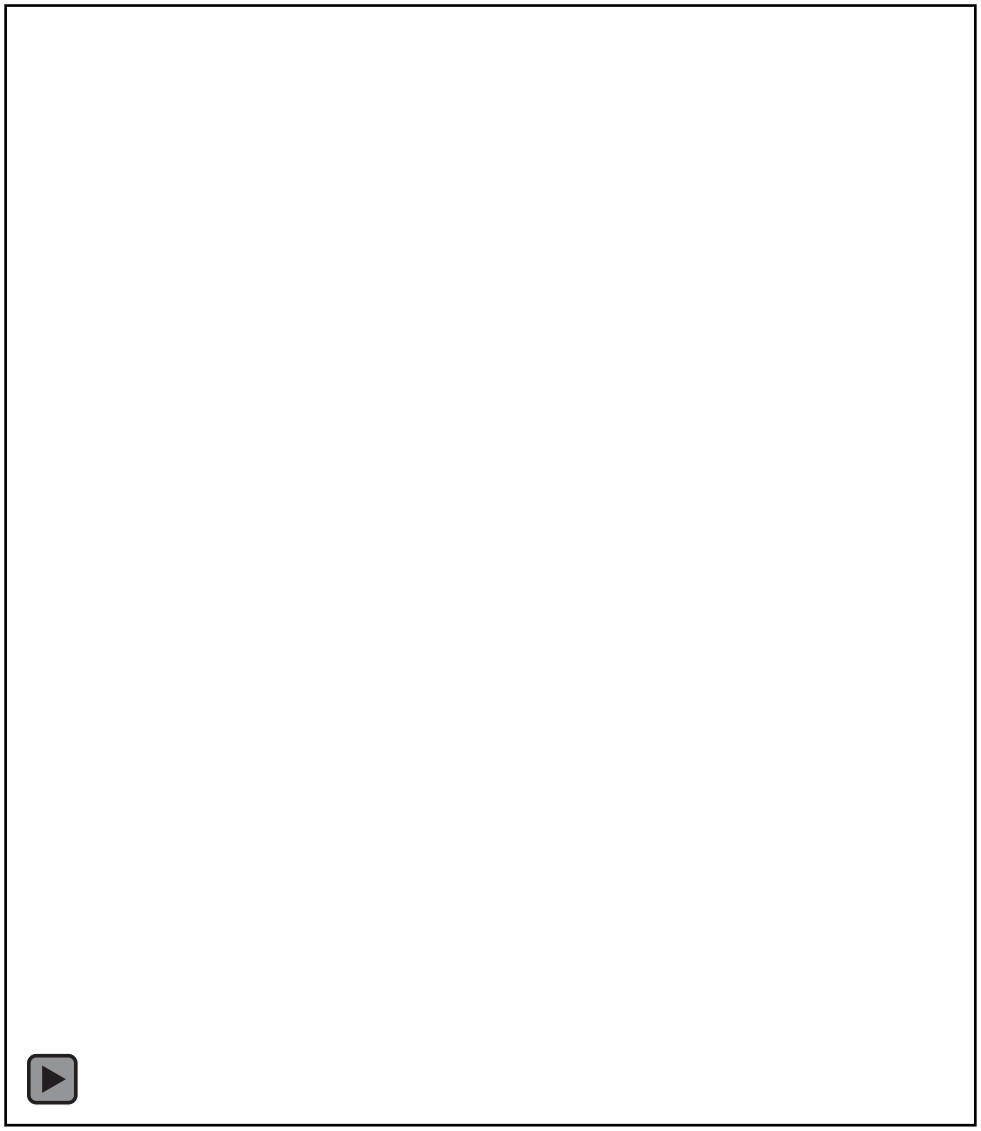


sphingomyelin (SM)



Ariola, F. S.; Li, Z.; Cornejo, C.; Bittman, R.; Heikal, A. A. *Biophysical Journal* **2009**, *96*, 2696

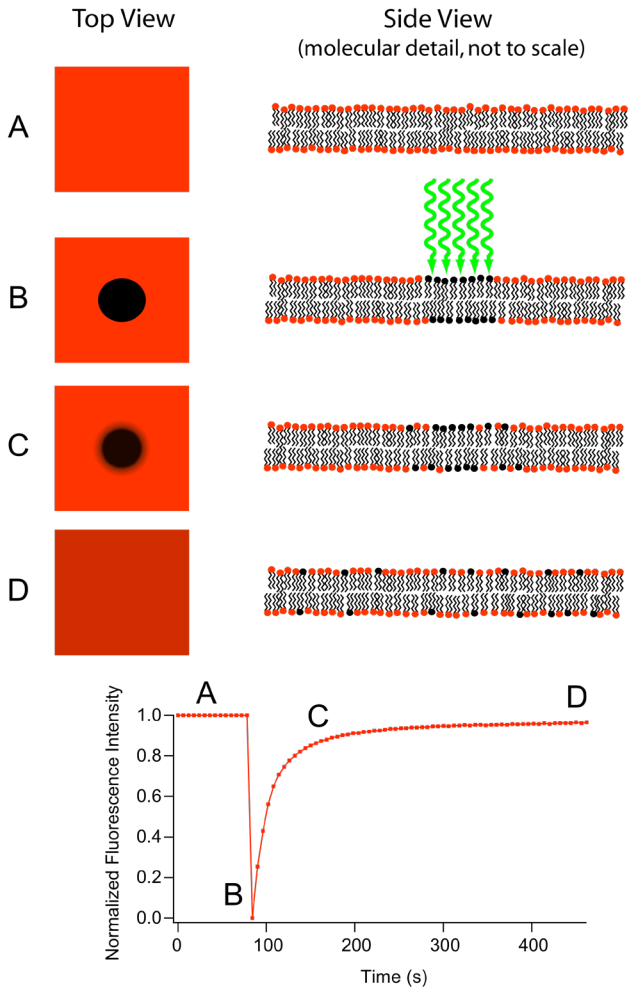
Mobility of phospholipids in bilayers



Oglecka, K.; Rangamani, P.; Liedberg, B.; Kraut, R. S.; Parikh, A. N. *Elife* **2014**, *3*

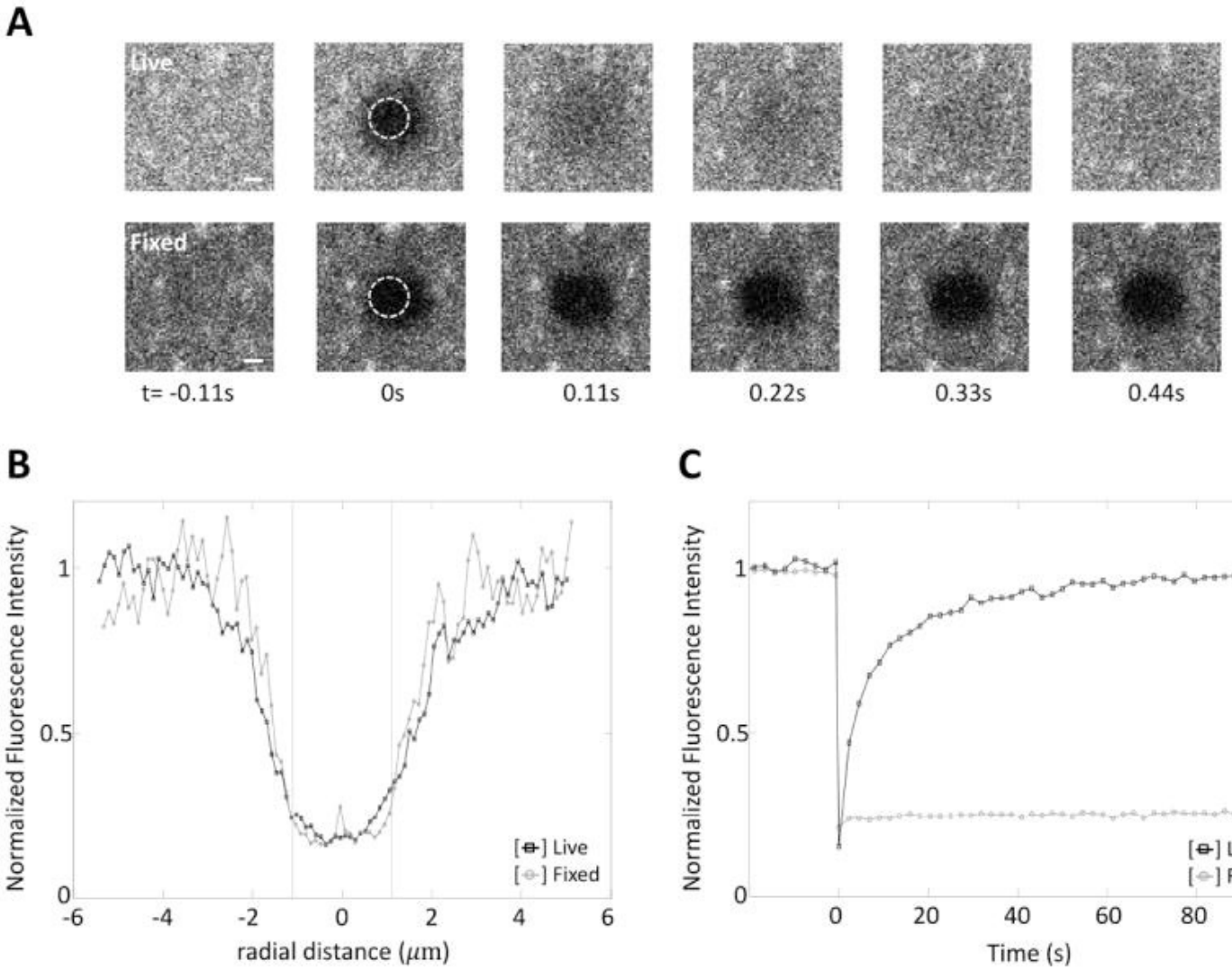
Diffusion coefficient

FRAP : fluorescence recovery after photobleaching



https://www.youtube.com/watch?v=CfRvmtBdZ9I

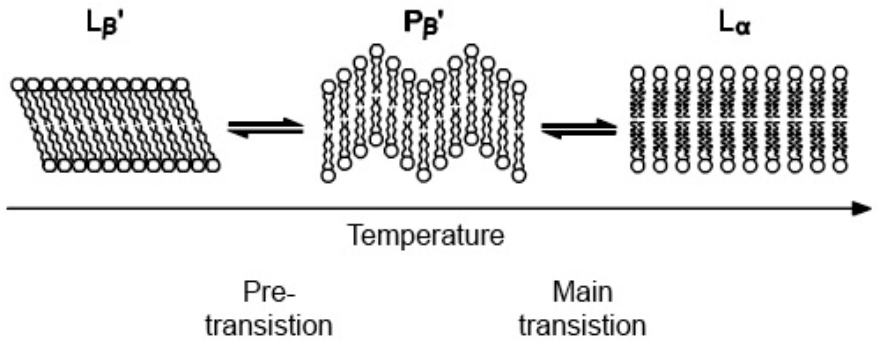
Quantification of the diffusion coefficient



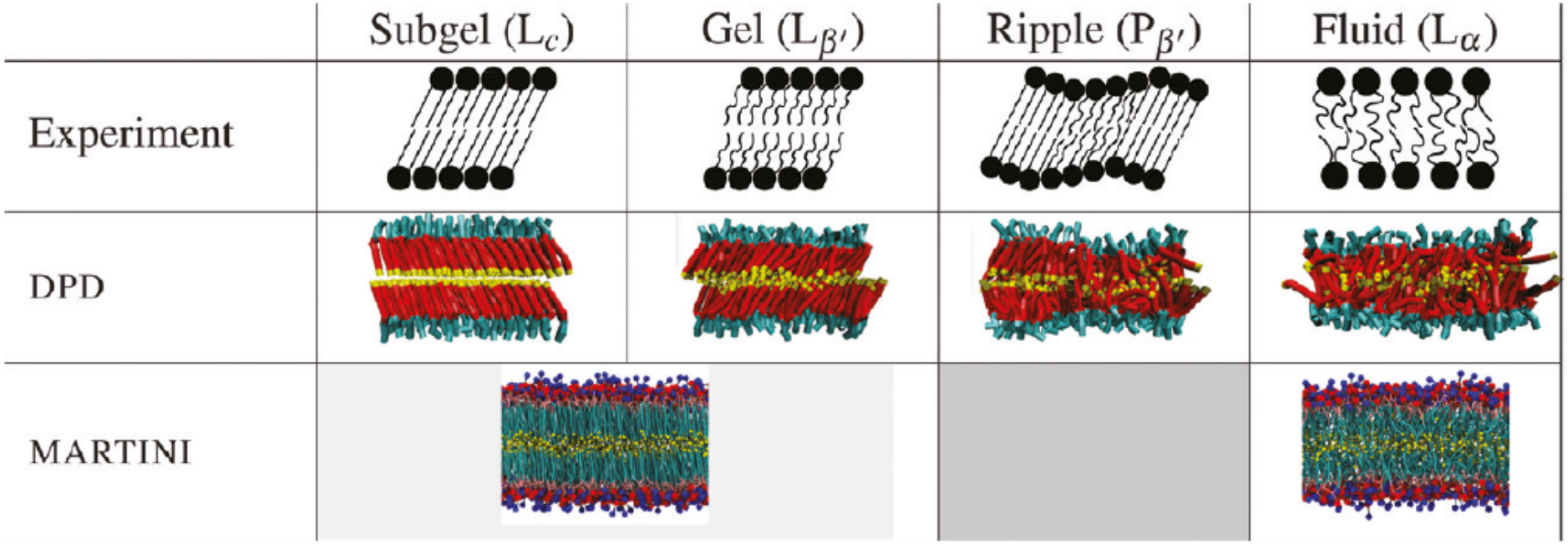
$$D_{r_n} = 0.224 \frac{r_n^2}{\tau_{1/2}}$$

Kang M, Day CA, Kenworthy AK, & DiBenedetto E (2012) *Traffic* 13(12):1589-1600

Phase transition

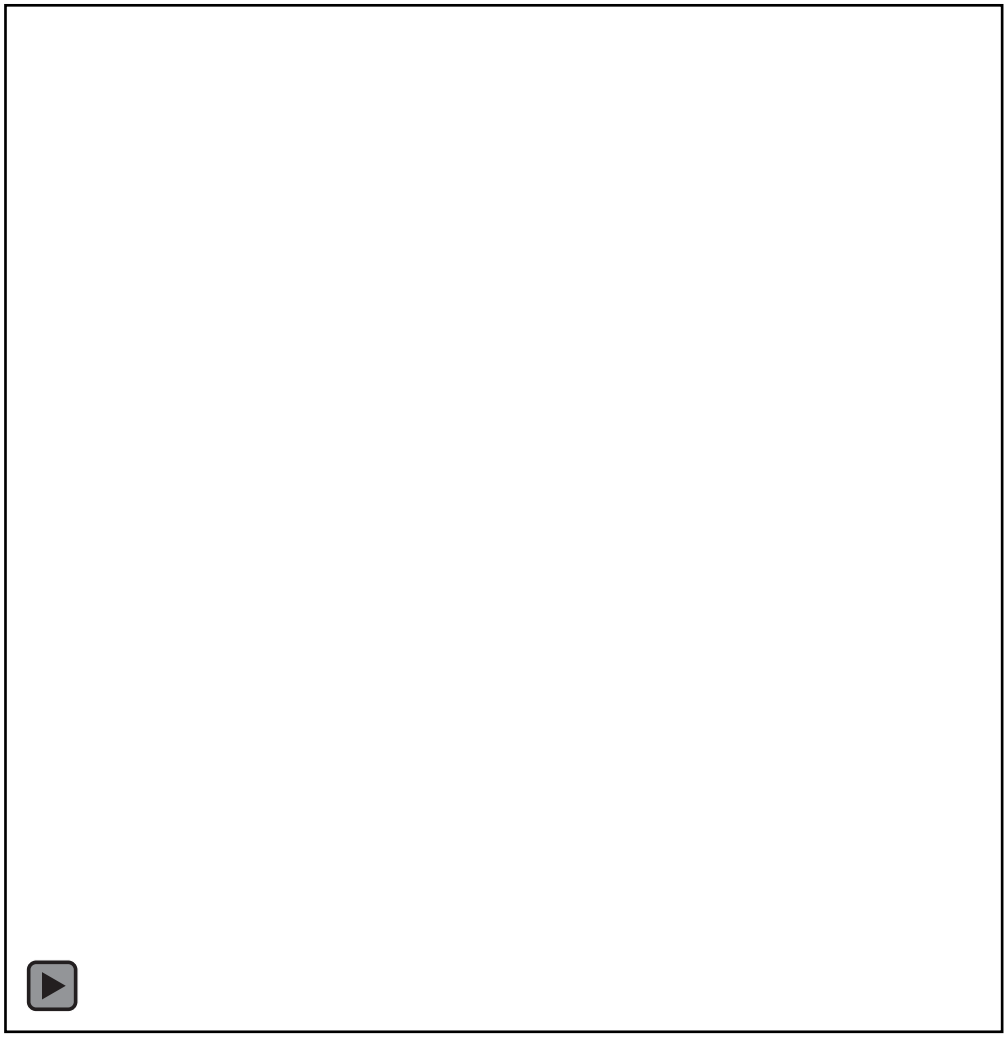


https://avantilipids.com/tech-support/physical-properties/phase-transition-temps/



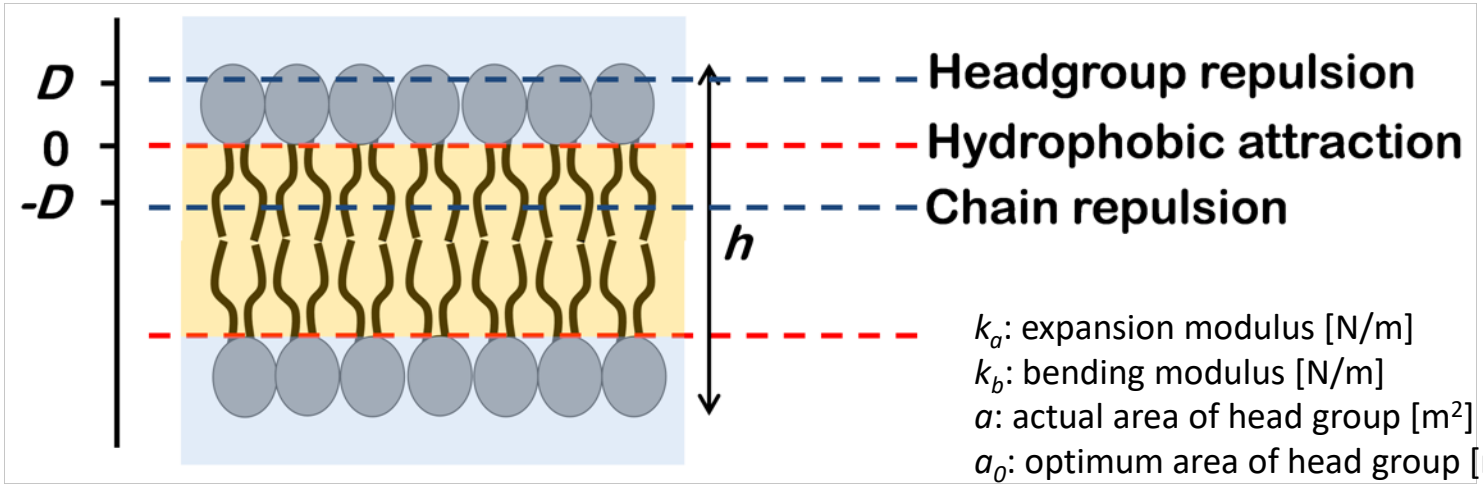
M. Rodgers, J. Sorensen, F. J. M. de Meyer, B. Schiott and B. Smit, *J. Phys. Chem. B*, 2012, **116**, 1551-1569

Vesicles can fluctuate



Oglecka, K.; Rangamani, P.; Liedberg, B.; Kraut, R. S.; Parikh, A. N. *Elife* **2014**, *3*

Mechanical properties of membranes



$$E_{comp} = \frac{1}{2} k_a \frac{(a - a_0)^2}{a^2} \qquad k_a \approx 4\gamma \approx \frac{4k}{a_0}$$

k_a: expansion modulus [N/m]
k_b: bending modulus [N/m]
a: actual area of head group [m^2]
a_0: optimum area of head group [m^2]
R: radius of vesicle [m]
D: distance from the center of the hydrophobic attraction forces to the plane of the repulsion forces [m]

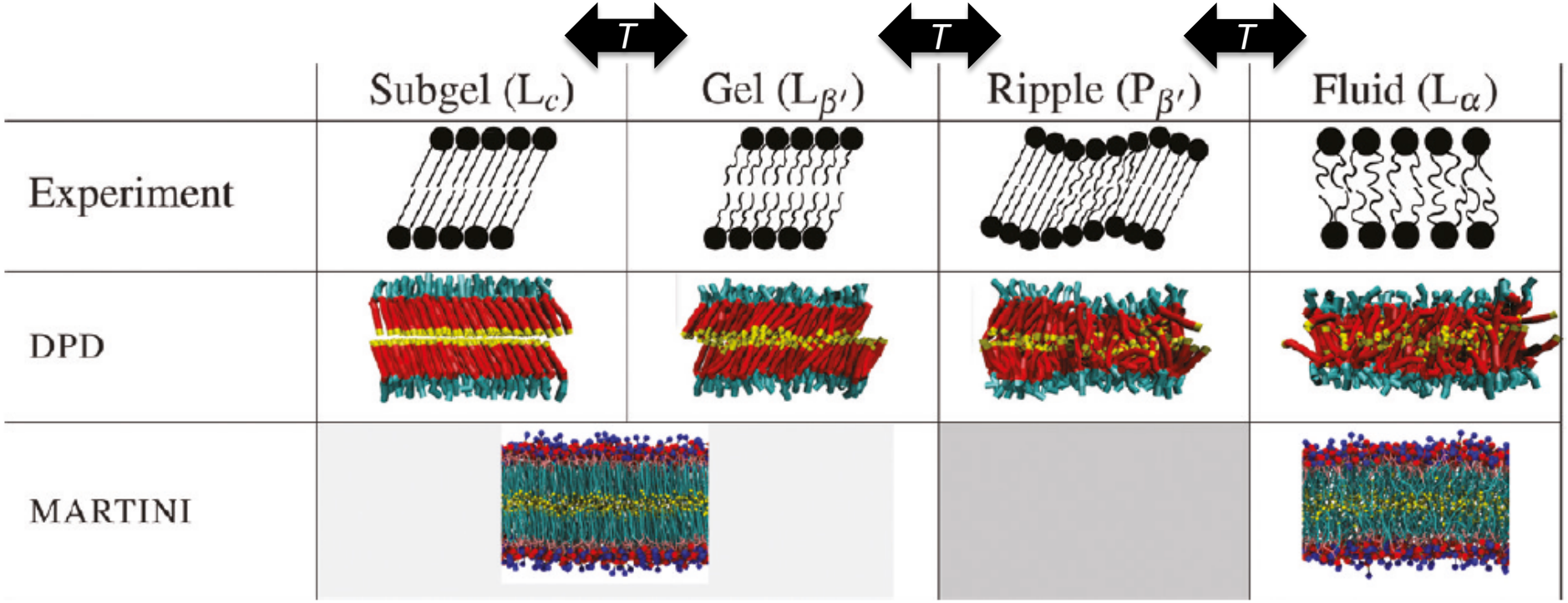
Assuming γ is between 20 and 50 mN/m, k_a ranges from 80 to 200 mN/m.

$$E_{bend} = \frac{1}{2} \frac{k_b}{R^2} \qquad k_b = -4\gamma h D$$

k_b is typically 1-20 $k_B T$

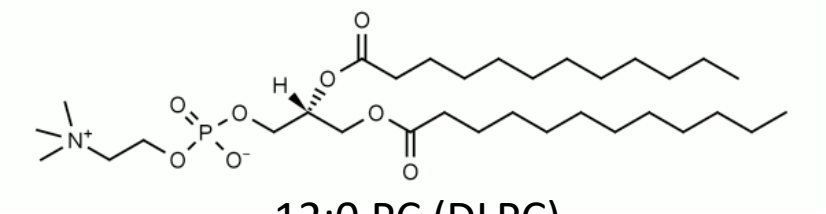
Amstad, E.; Arriaga, L. R. *Nanoparticle actuated vesicles*; Nova Science Publishers Inc.: Hauppauge, NY, 2013

Phases of lipids in liposomes



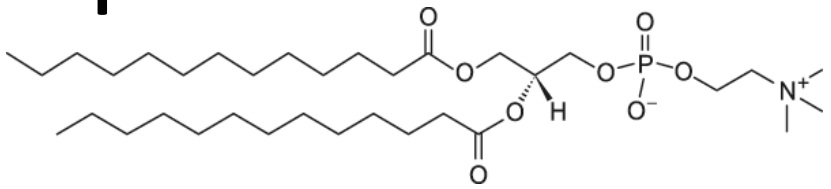
M. Rodgers, J. Sorensen, F. J. M. de Meyer, B. Schiott and B. Smit, *J. Phys. Chem. B*, 2012, **116**, 1551-1569

Phospholipids



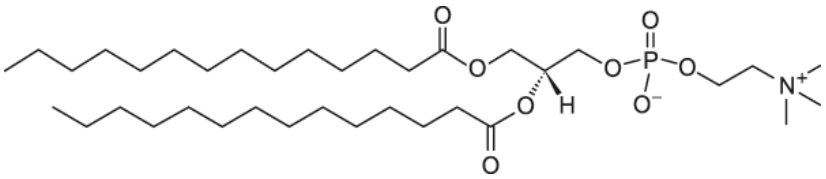
12:0 PC (DLPC)
1,2-dilauroyl-sn-glycero-3-phosphocholine

T_m ≈ -2 °C



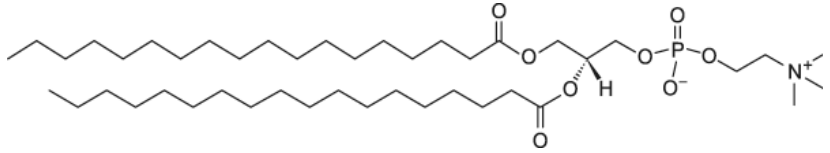
13:0 PC
1,2-ditridecanoyl-*sn*-glycero-3-phosphocholine

T_m ≈ 14 °C



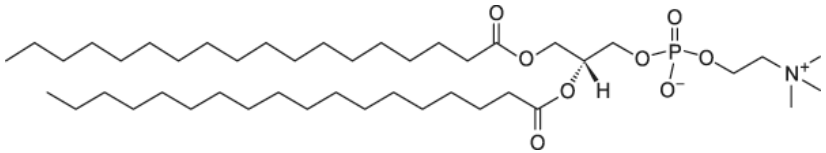
14:0 PC (DMPC)
1,2-dimyristoyl-*sn*-glycero-3-phosphocholine

T_m ≈ 24 °C



16:0 PC (DPPC)
1,2-distearoyl-*sn*-glycero-3-phosphocholine

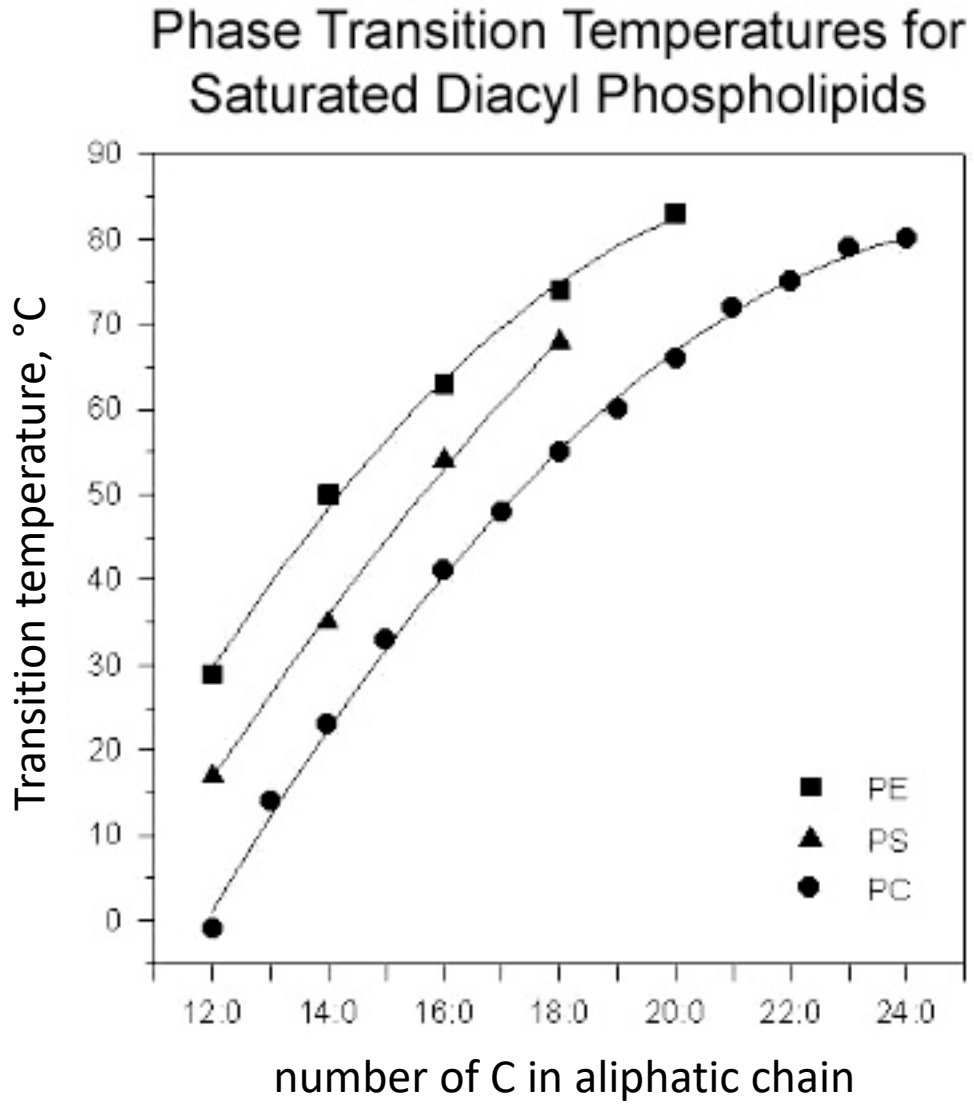
T_m ≈ 41 °C



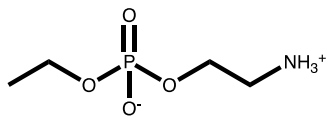
18:0 PC (DSPC)
1,2-distearoyl-*sn*-glycero-3-phosphocholine

T_m ≈ 55 °C

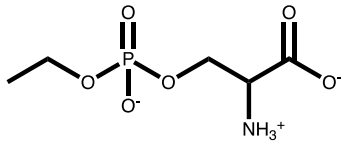
Transition temperatures



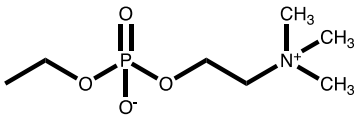
PE

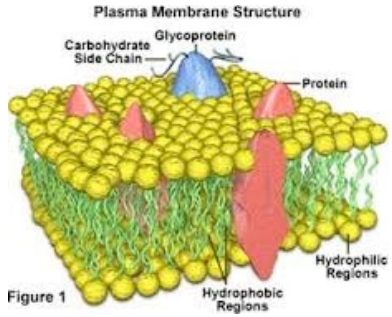


PS



PC

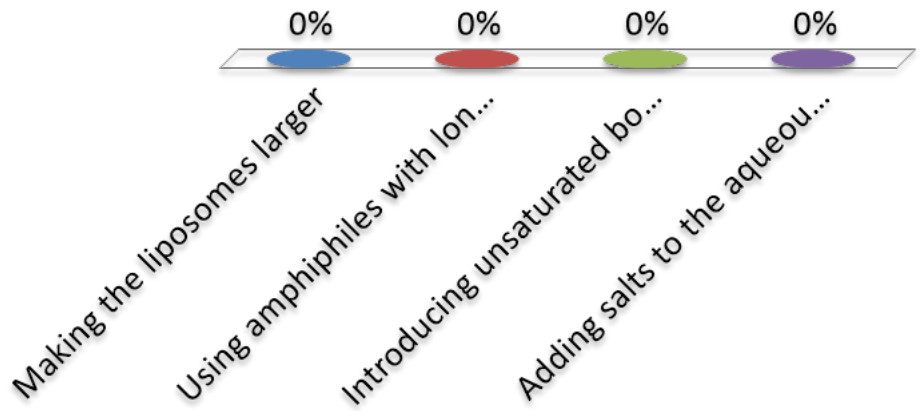




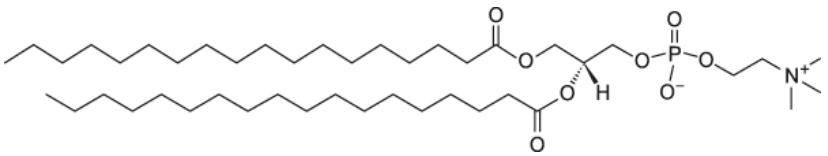
https://avantilipids.com/tech-support/physical-properties/phase-transition-temps/

How can the transition temperature of lipids contained in liposomes be lowered?

A. Making the liposomes larger
B. Using amphiphiles with longer hydrophobic chains
C. Introducing unsaturated bonds
D. Adding salts to the aqueous solution

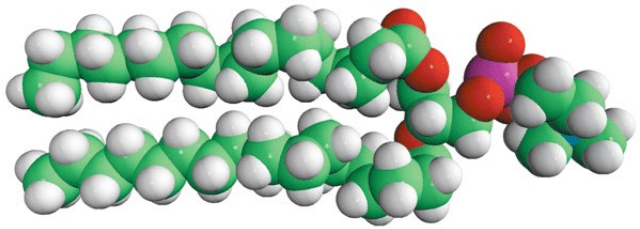


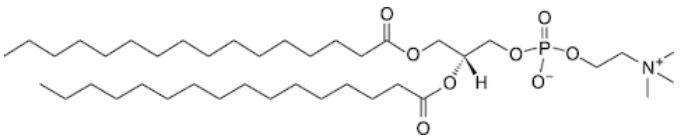
Phospholipids



18:0 PC (DSPC)
1,2-distearoyl-*sn*-glycero-3-phosphocholine

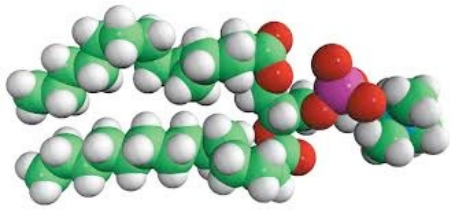
$T_m \approx 55$ °C

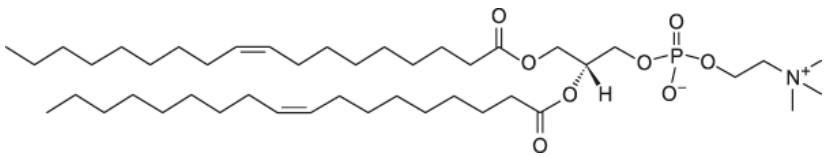




16:0 PC (DPPC)
dipalmitoylphosphatidylcholine

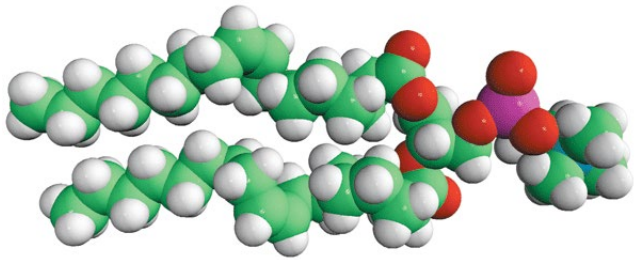
$T_m \approx 41$ °C

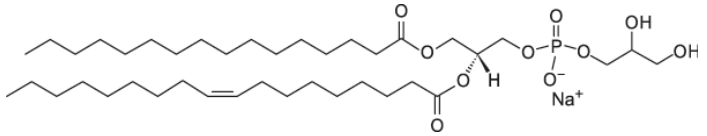




18:1 PC (DOPC)
1,2-dioleoyl-*sn*-glycero-3-phosphocholine

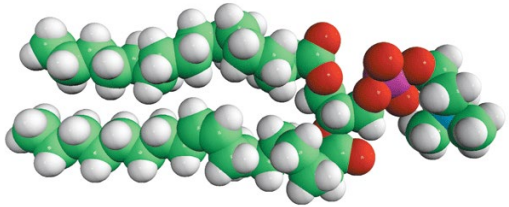
$T_m \approx -17$ °C



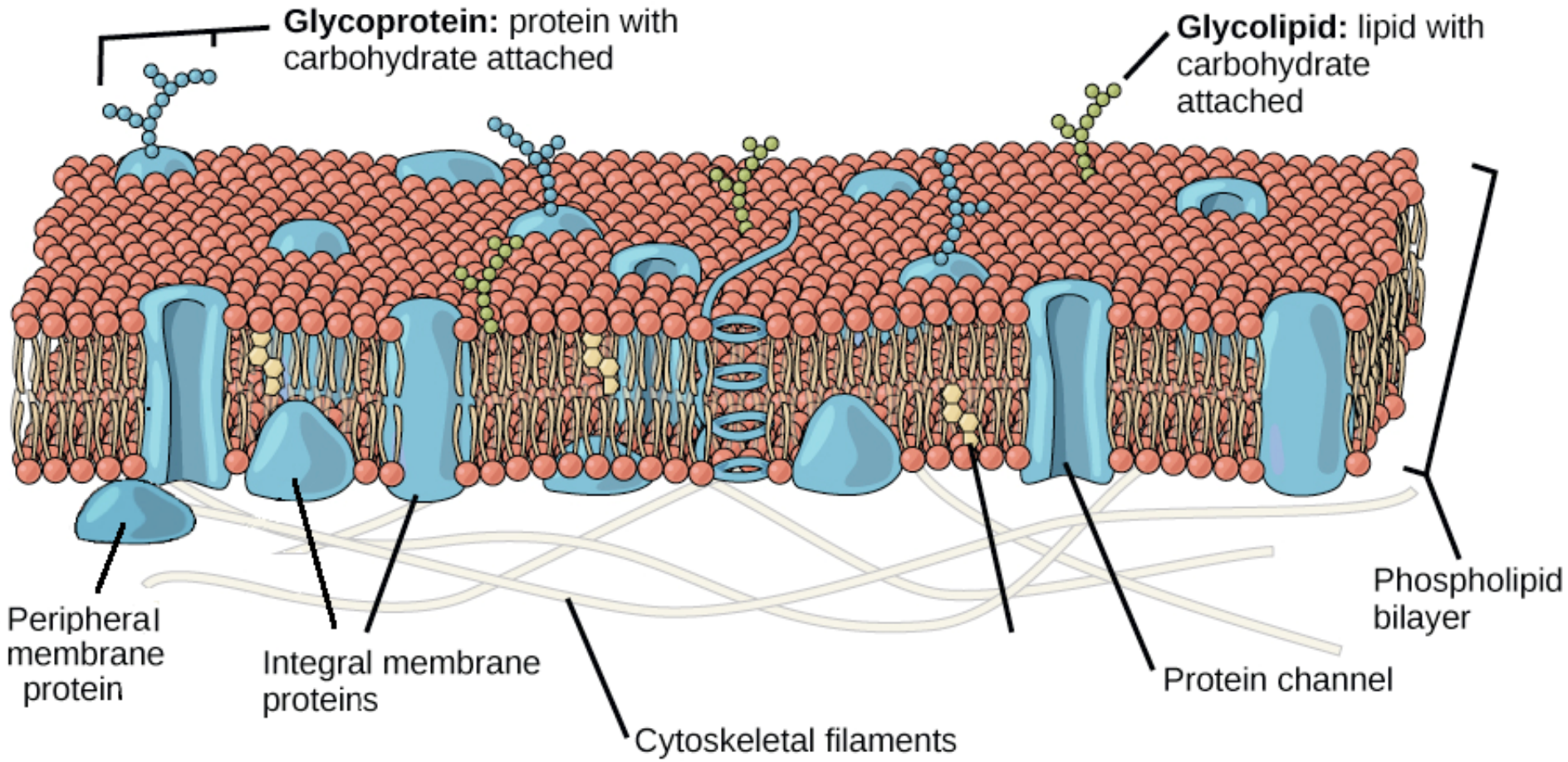


16:0-18:1 PC (POPC):
1-Palmitoyl-2-Oleoyl-sn-Glycero-3-Phosphocholine

$T_m \approx -2$ °C



Cell membranes



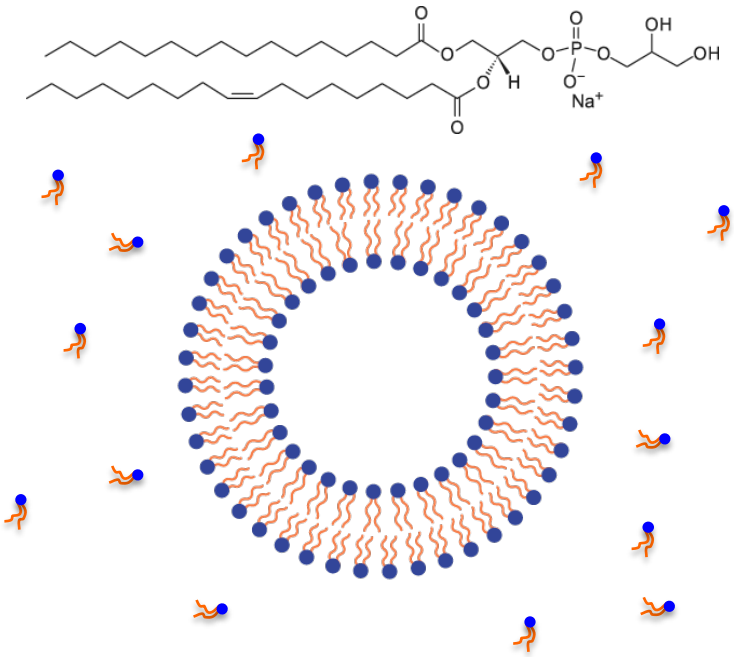
https://www.khanacademy.org/science/biology/membranes-and-transport/the-plasma-membrane/a/structure-of-the-plasma-membrane

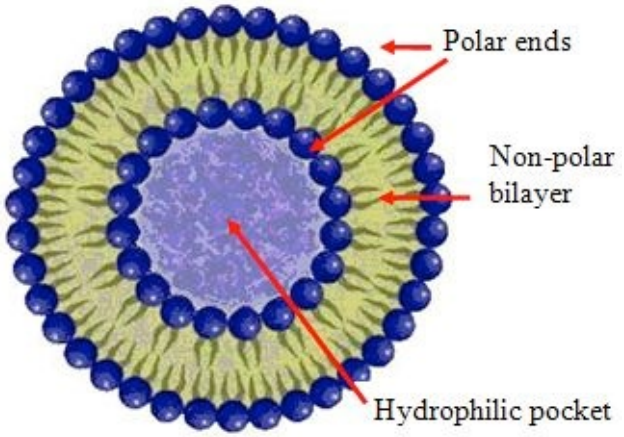
Stability of liposomes

Liposomes are often made from phospholipids.

Phospholipids have usually two hydrophobic chains connected to one head group.

$$\alpha = \frac{v}{a_0 l_c} \approx 1$$





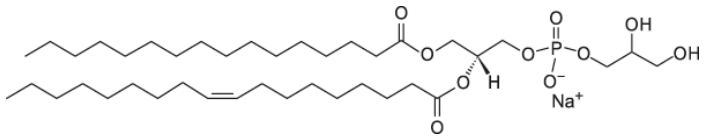
v: volume of hydrocarbon chain [m^3]
a_0: optimal surface area of amphiphile [m^2]
l_c: critical chain length [m]

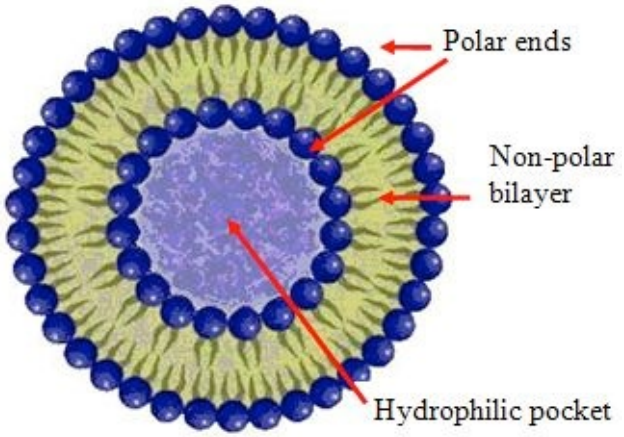
Stability of liposomes

Liposomes are often made from phospholipids.

Phospholipids have usually two hydrophobic chains connected to one head group.

$$\alpha = \frac{v}{a_0 l_c} \approx 1$$





$$CMC \approx exp\left[-\frac{\mu_1^0 - \mu_N^0}{k_B T}\right]$$

Phospholipids have a much lower CMC than molecules with only one hydrocarbon chain such that less free phospholipids are in solution.

The probability for a molecule to leave the bilayer $\propto e^{-\frac{\Delta E}{k_B T}}$

where $\Delta E = \mu_1^0 - \mu_N^0$

v: volume of hydrocarbon chain [m^3]
a_0: optimal surface area of amphiphile [m^2]
l_c: critical chain length [m]

Lifetime of molecule in aggregates

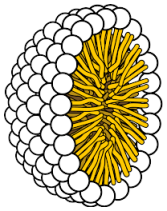
The mean lifetime of molecule in bilayer: $\tau_R = \frac{\tau_0}{e^{\frac{\Delta E}{k_B T}}}$

The probability that molecules that hit the interface will leave the bilayer.

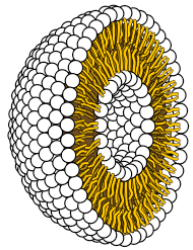
$$\tau_R = \frac{\tau_0}{e^{\frac{\mu_1^0 - \mu_N^0}{k_B T}}} \approx \frac{55\tau_0}{CMC}$$

τ_R: time for an exchange to take place [s]
τ_0: motional correlation time for amphiphiles in micelles or bilayers [s]
$\tau_0 \approx 10^{-9} - 10^{-7}\,s$
μ: chemical potential [J/molecule]
N: number of molecules contained in the aggregate [-]
P: constant that depends on the dimension of the aggregate [-]

For micelles $\tau_R \approx 10^{-4}\,s$



For vesicles $\tau_R \approx 10^{4}\,s$
$\tau_R \approx 3\ \ h$



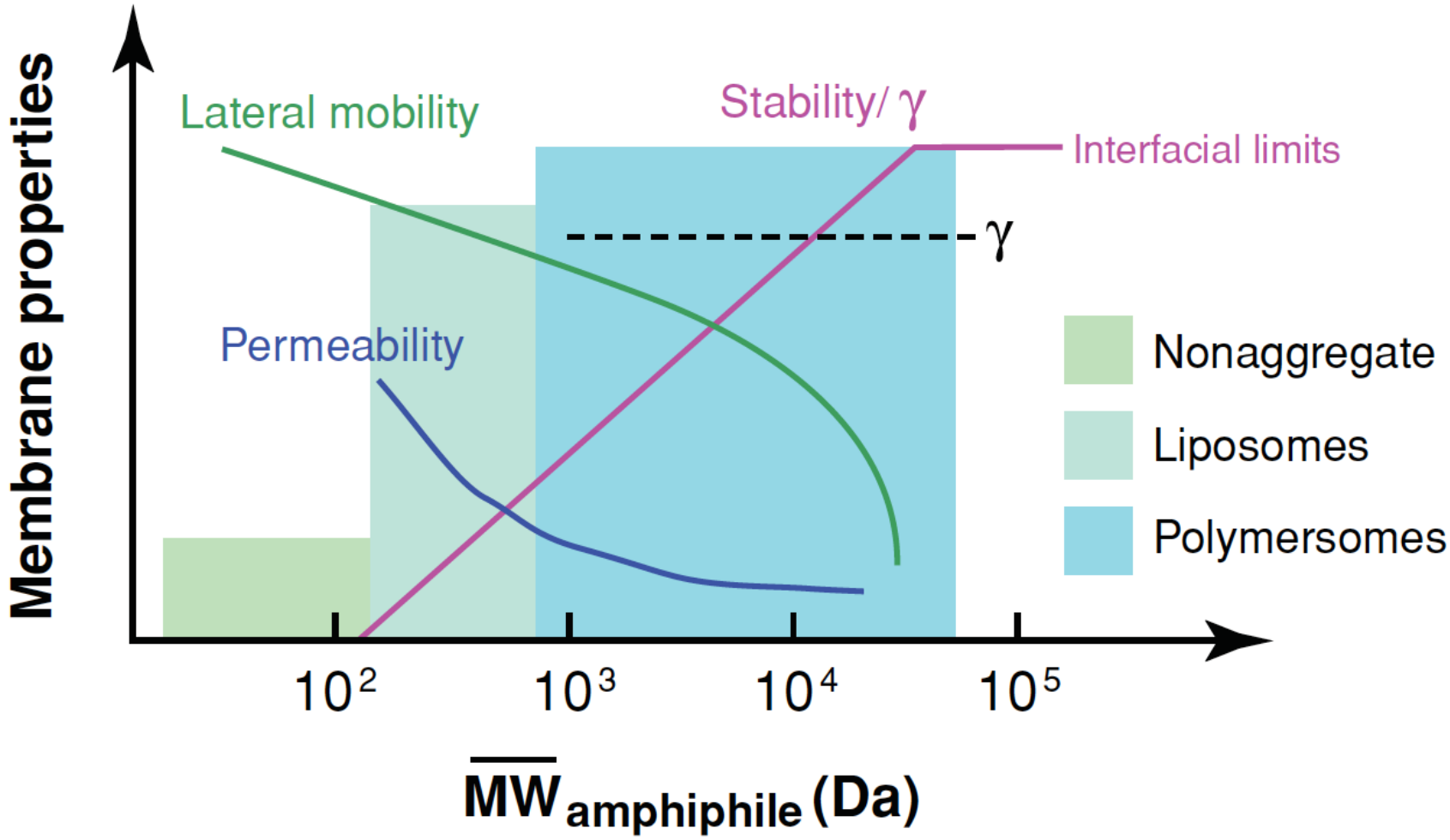
How much does the exchange rate decrease if one CH_2 group is added to the hydrophobic tail of amphiphiles containing 8 C atoms in its chain?

A. 10%
B. factor 2
C. factor 7
D. factor 10
E. factor 100

CMC of amphiphile with 8 C atoms: 2.2×10^{-7} M
$r \approx 0.2$ nm
CH_2-CH_2 bond length = 0.154 nm
angle between C-C bonds: 109°
$\gamma = 50$ mJ/m^2
$k_B = 1.38 \times 10^{-23}$ J/K
$T = 298$ K

$$CMC \approx e^{-\alpha} \approx e^{-\frac{2\Pi r l \gamma}{k_B T}}$$

Membrane properties



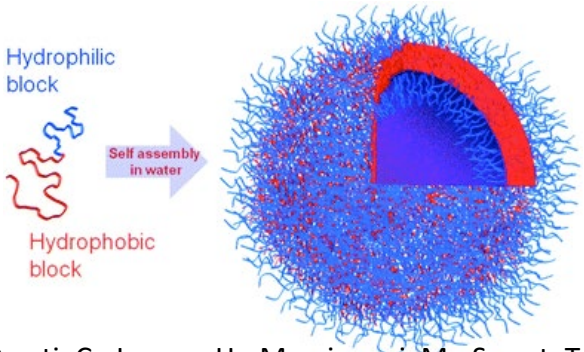
Discher, D. E.; Ahmed, F. Polymersomes. In *Annual Review of Biomedical Engineering*, 2006; Vol. 8, pp 323-341

Outline

- Introduction: Vesicles
- Liposomes
- Polymersomes
- Vesicle production
- Characterization
- Applications

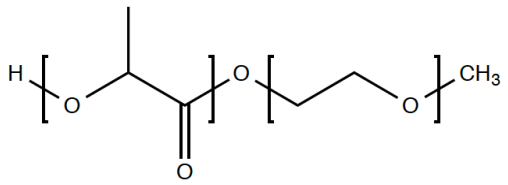
Polymersomes

Polymersomes are vesicles made from block-copolymers.



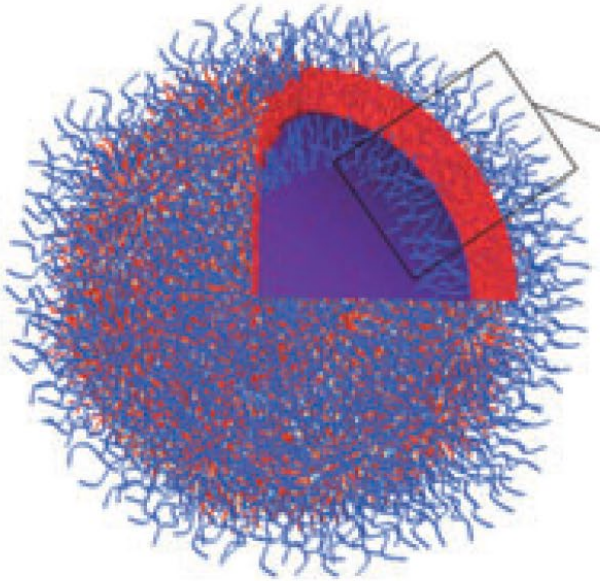
LoPresti, C.; Lomas, H.; Massignani, M.; Smart, T.; Battaglia, G. *Journal of Materials Chemistry* **2009,** *19* (22), 3576-3590.

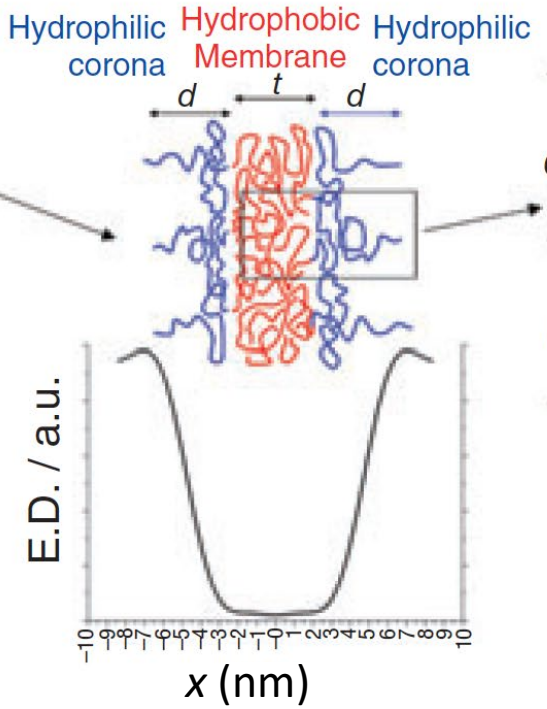
Example of a block-copolymer:

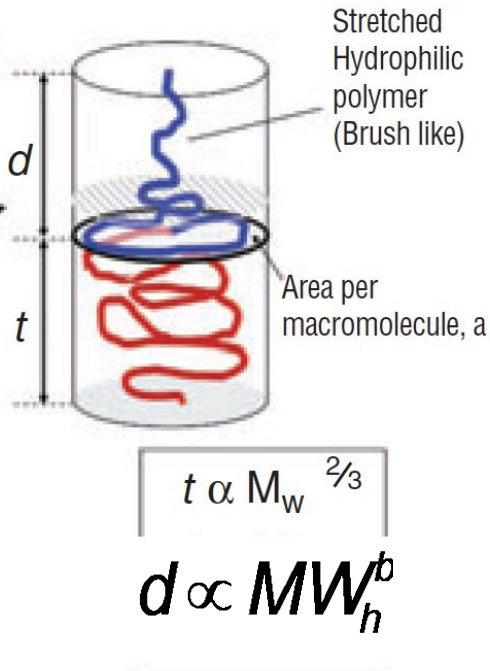


Polymersomes

Polymersomes are vesicles made of block-copolymers.







b = 0.5: random Gaussian coil
b = 1: fully stretched chain
b ≈ 0.55: experimentally determined value

Battaglia, G. *Nanomaterials for the Life Sciences Vol.10: Polymeric Nanomaterials*; WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, 2011.

$d_{membrane} \approx$ 5-18 nm

Block-copolymer mobility

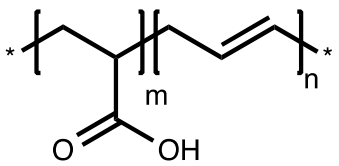
The mobility of block-copolymers in polymersome membranes is more than one order of magnitude lower than that of phospholipids in liposome membranes.

Comparison of diffusion coefficients in vesicles

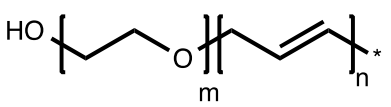
block-copolymers: $D \approx 0.1\ \mu m^2 s^{-1}$

phospholipids: $D \approx 1\ \mu m^2 s^{-1}$

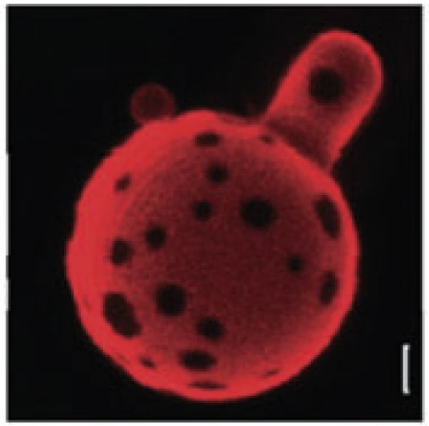
poly(acrylic acid)-poly(butadiene) (PAA-PBD)



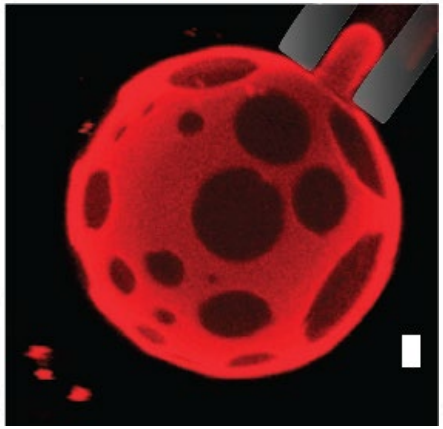
poly(ethylene oxide)-poly(butadiene) (PEO-PBD)



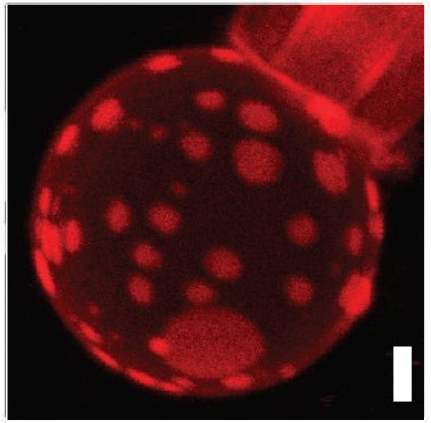
25% PAA-PBD 75% PEO-PBD



50% PAA-PBD 50% PEO-PBD



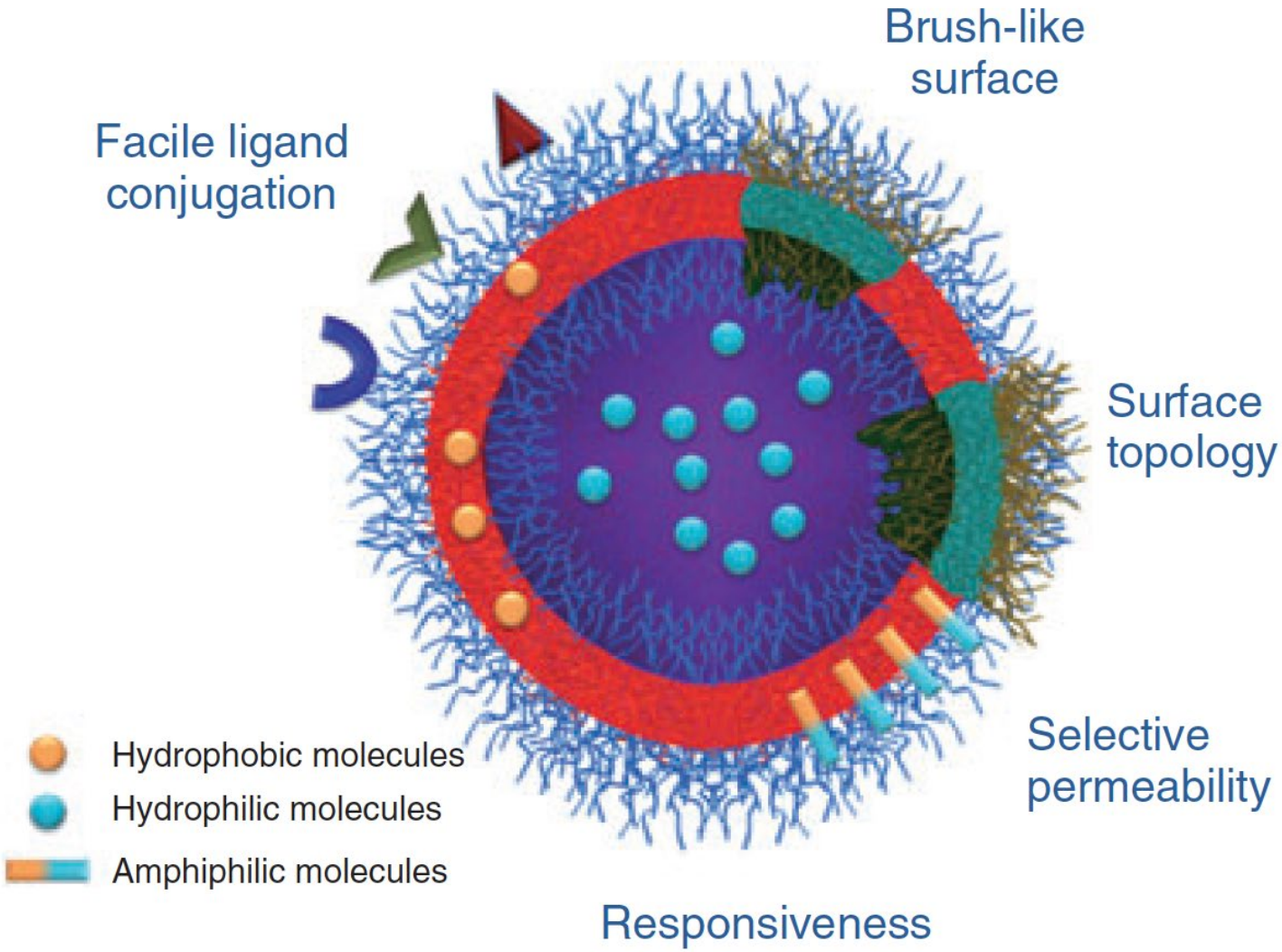
75% PAA-PBD 25% PEO-PBD



scale bars: 2 µm

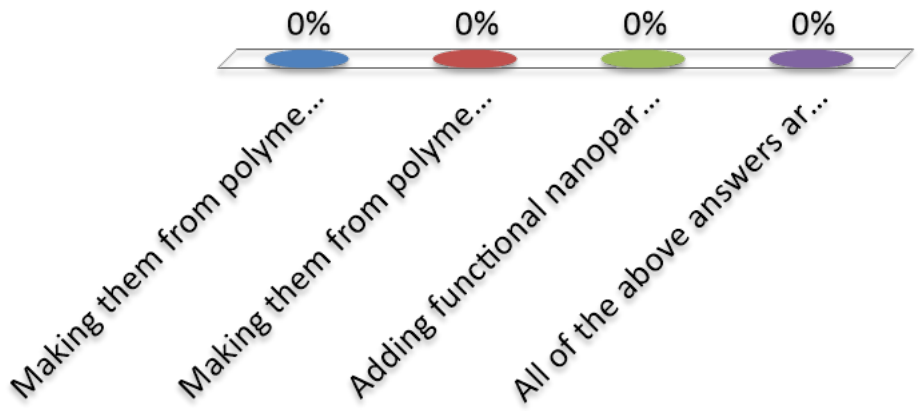
Christian, D. A.; et al. *Nature Materials* **2009,** *8* (10), 843-849.

Functionalization of Polymersomes



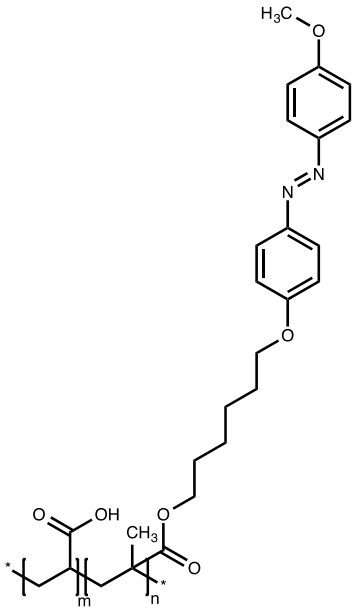
How can polymersomes be made responsive?

A. Making them from polymers that have responsive hydrophilic blocks.
B. Making them from polymers that have responsive hydrophobic blocks.
C. Adding functional nanoparticles into their membranes.
D. All of the above answers are correct.



UV-responsive polymersomes

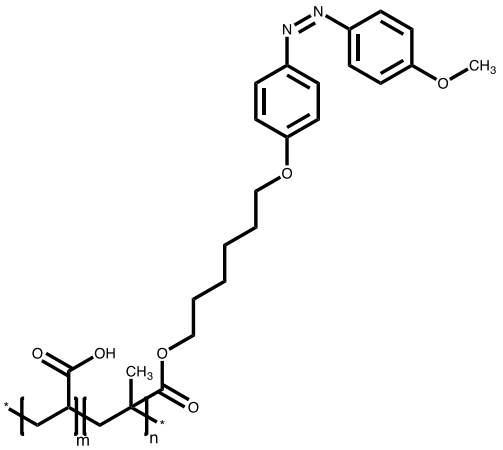
trans-configuration

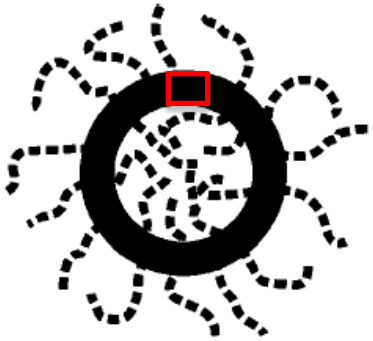


UV light

VIS light
or dark

cis-configuration

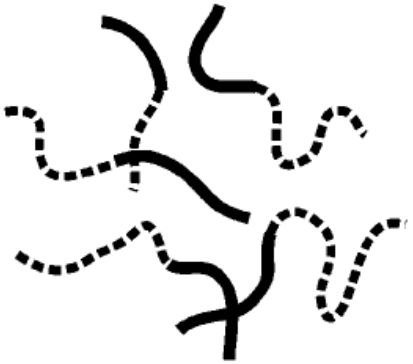




vesicle

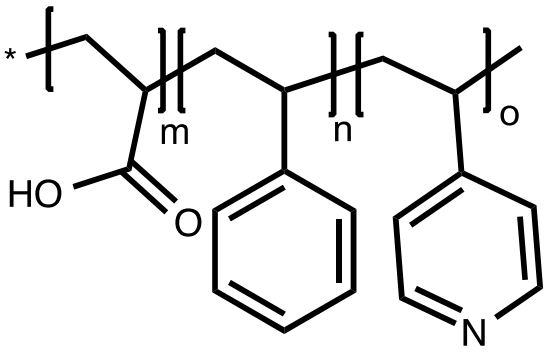
UV

Visible

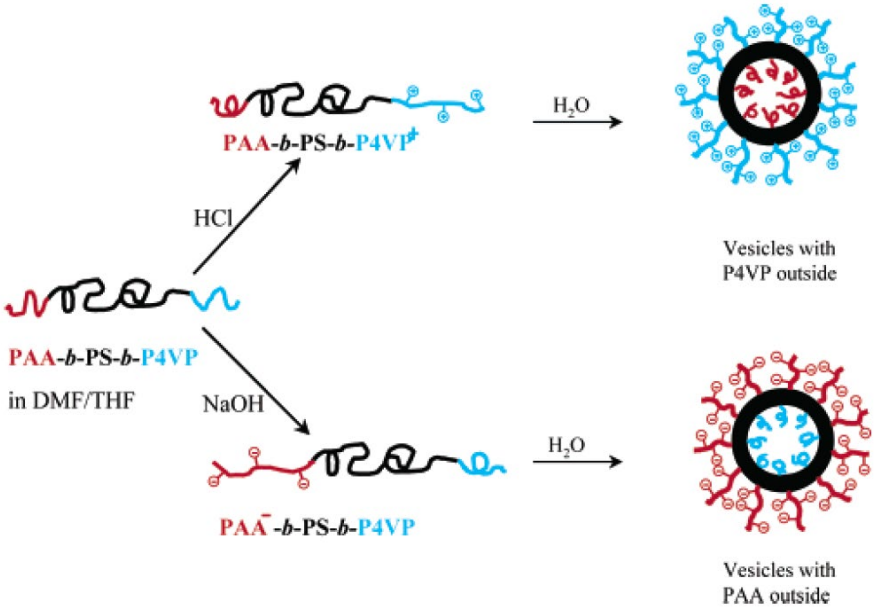


Wang, G.; Tong, X.; Zhao, Y. *Macromolecules* **2004,** *37* (24), 8911-8917.

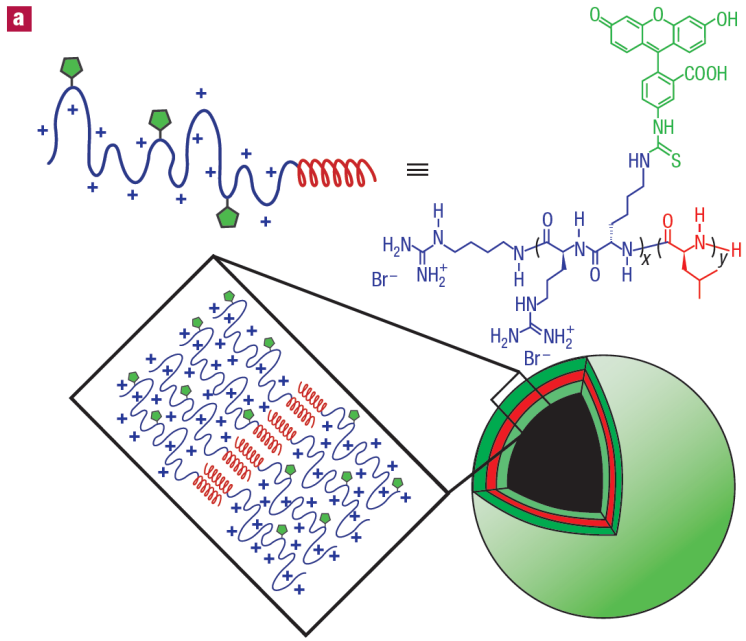
pH-Responsive polymersomes



poly(acrylic acid)-polystyrene-poly(4-vinyl pyridine)



Liu, F.; Eisenberg, A. *Journal of the American Chemical Society* **2003,** *125* (49), 15059-15064.

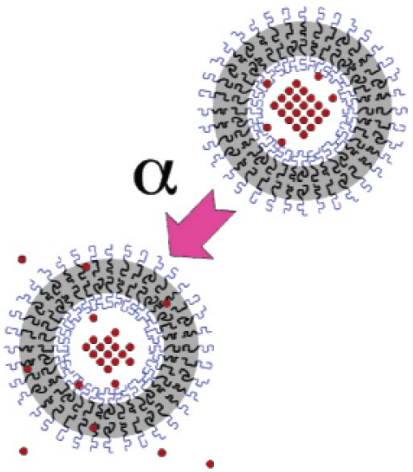


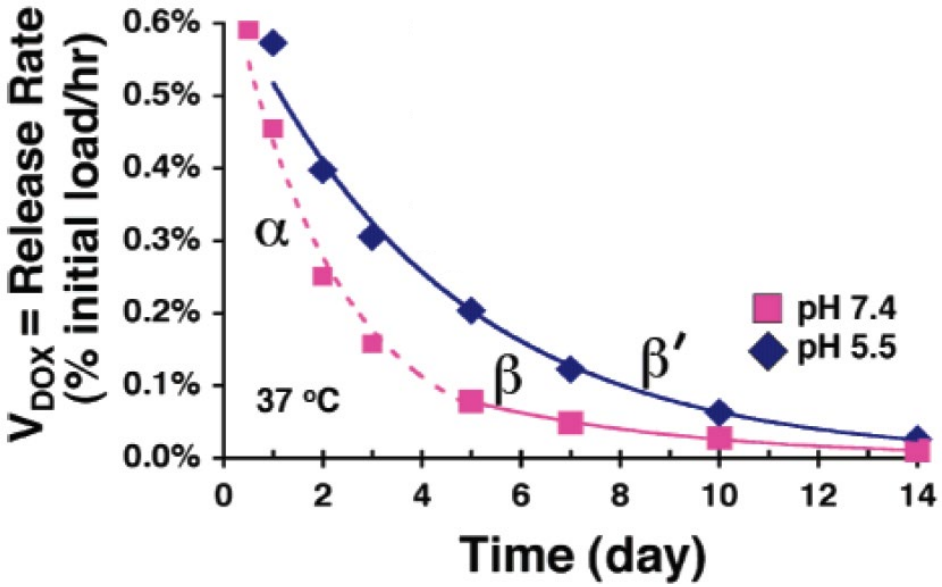
poly(arginine)-poly(L-leucine)

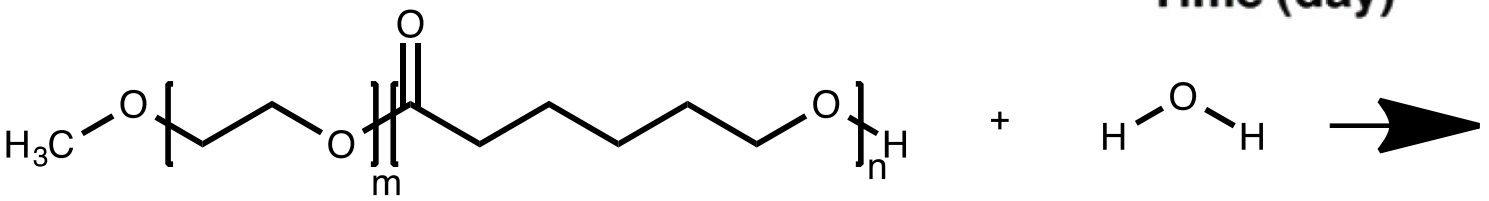
Holowka, E. P.; Sun, V. Z.; Kamei, D. T.; Deming, T. J. *Nat Mater* **2007,** *6* (1), 52-57

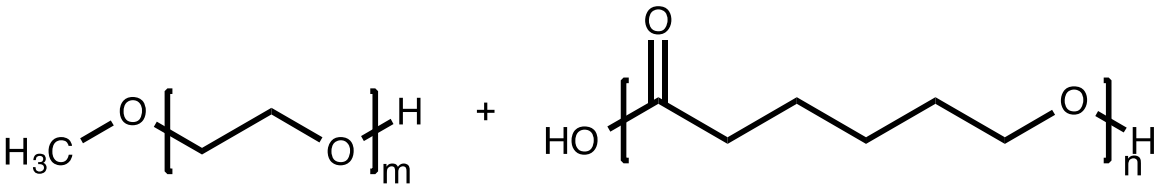
Polymersomes that can undergo hydrolysis

lower pH ➔ hydrolysis





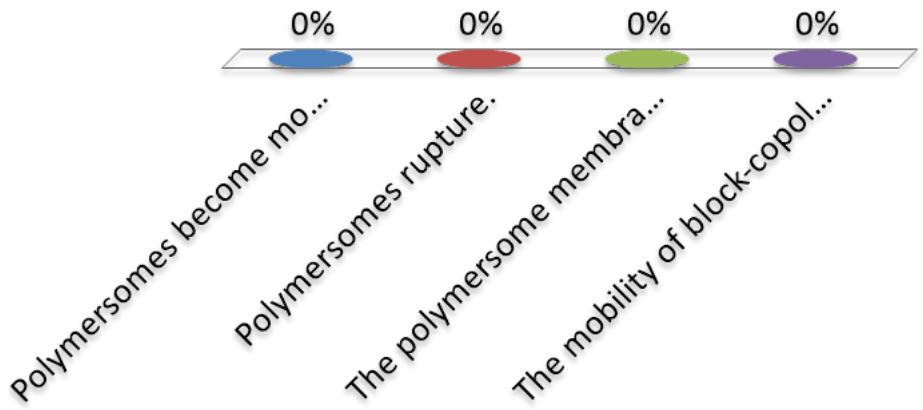




Ghoroghchian, P. P.; Li, G. Z.; Levine, D. H.; Davis, K. P.; Bates, F. S.; Hammer, D. A.; Therien, M. J. *Macromolecules* **2006,** *39* (5), 1673-1675.

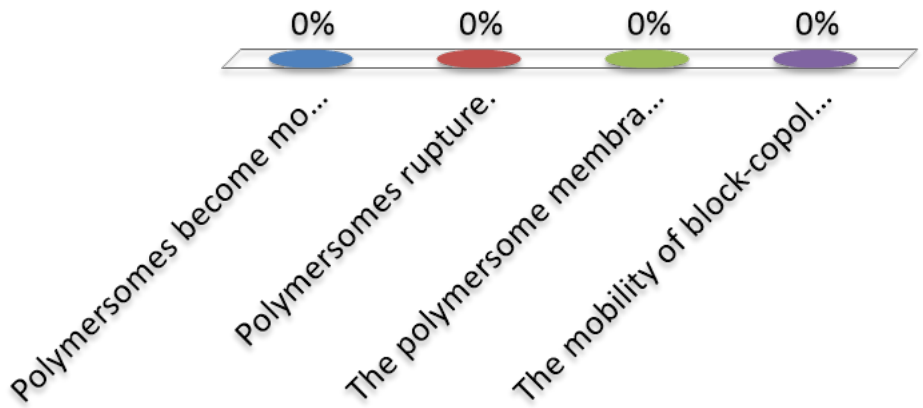
Polymersomes are made from block-copolymers whose hydrophilic block is temperature-responsive. What happens if the temperature is increased such that the hydrophilic block collapses?

A. Polymersomes become more permeable but remain intact.
B. Polymersomes rupture.
C. The polymersome membrane becomes more rigid.
D. The mobility of block-copolymers in the membrane increases.



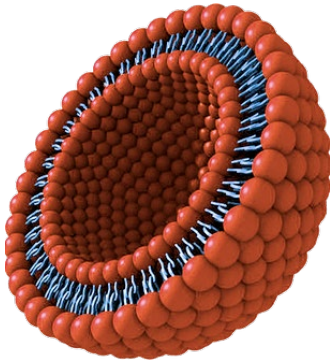
Polymersomes contain very small domains that are made of block-copolymers whose hydrophilic block is temperature-responsive. What happens if the temperature is increased such that the hydrophilic blocks contained in the small domains collapse?

A. Polymersomes become more permeable but remain intact.
B. Polymersomes rupture.
C. The polymersome membrane becomes more rigid.
D. The mobility of block-copolymers in the membrane increases.

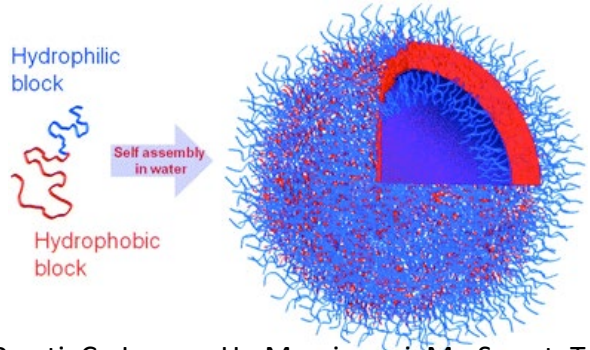


Vesicles

Liposomes are vesicles made from lipids.

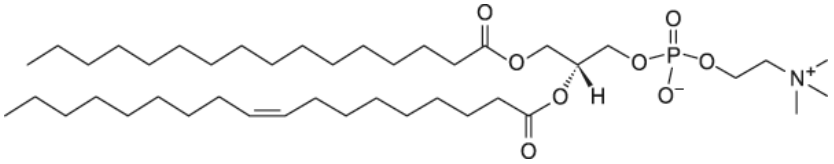


Polymersomes are vesicles made from block-copolymers.



LoPresti, C.; Lomas, H.; Massignani, M.; Smart, T.; Battaglia, G. *Journal of Materials Chemistry* **2009,** *19* (22), 3576-3590.

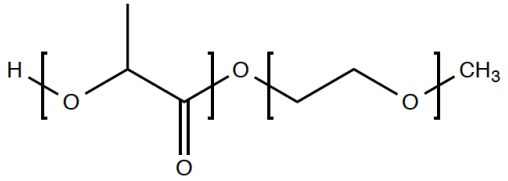
Example of a phospholipid:



Advantages:
- biocompatibility
- cell-membrane mimicking capsules

Disadvantage:
stability

Example of a block-copolymer:

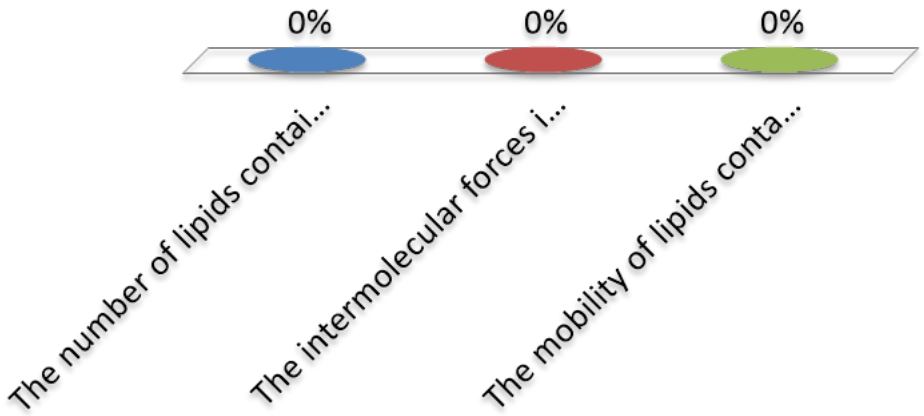


Advantages:
- versatility in the choice of the composition
- tunable membrane thickness
- tunable stability

Disadvantage:
more complex structure than liposomes

Liposomes can heal defects much faster than polymersomes can. Why?

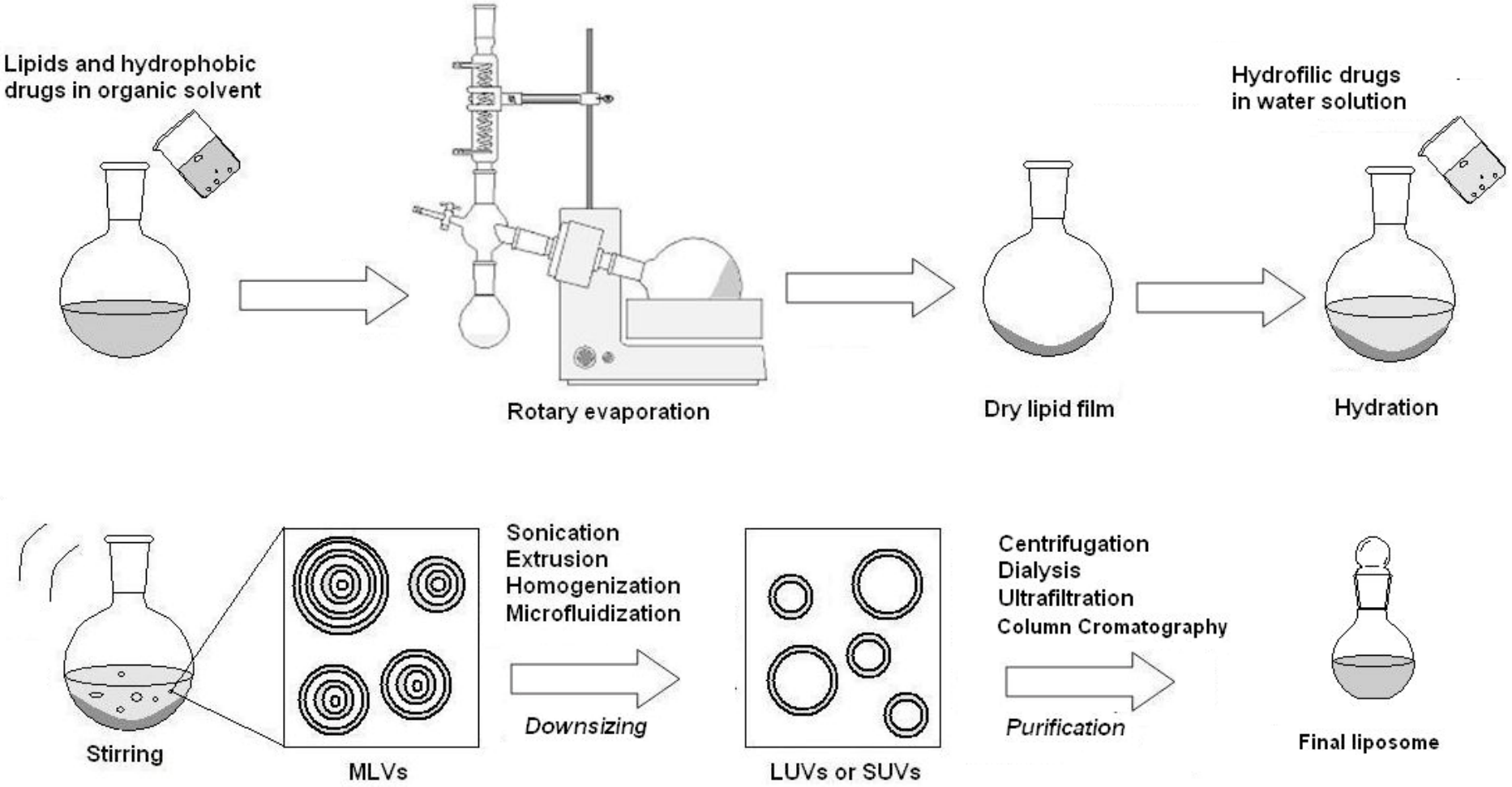
A. The number of lipids contained in liposomes is larger than the number of block-copolymers contained in polymersomes
B. The intermolecular forces in bilayers of liposomes are stronger than those in bilayers of polymersomes.
C. The mobility of lipids contained in bilayers is higher than that of polymers.



Outline

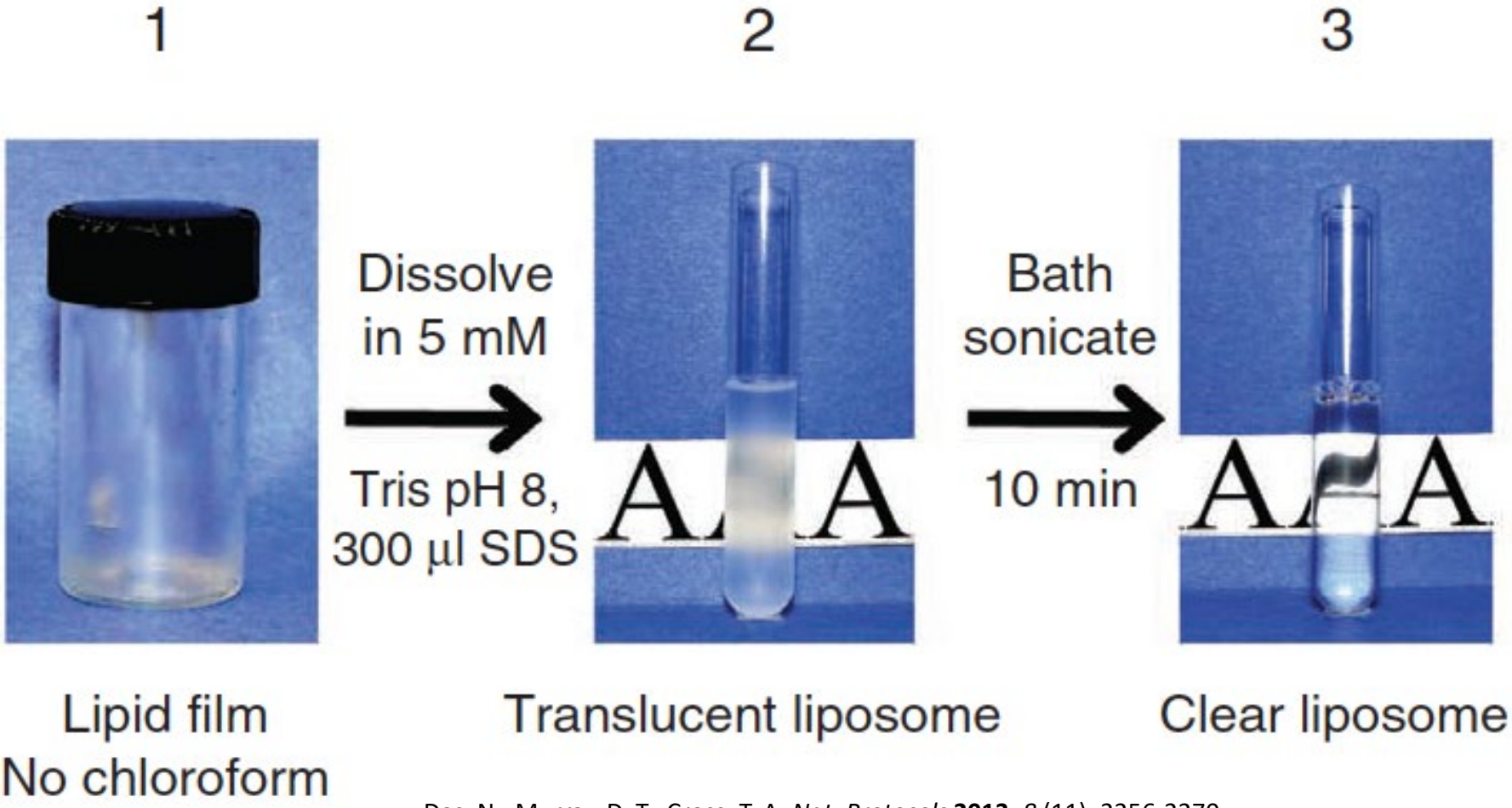
- Introduction: Vesicles
- Liposomes
- Polymersomes
- Vesicle production
- Characterization
- Applications

Vesicle formation: Rehydration



"Cancer Treatment – Conventional and Innovative Approaches", book edited by Letícia Rangel , ISBN 978-953-51-1098-9

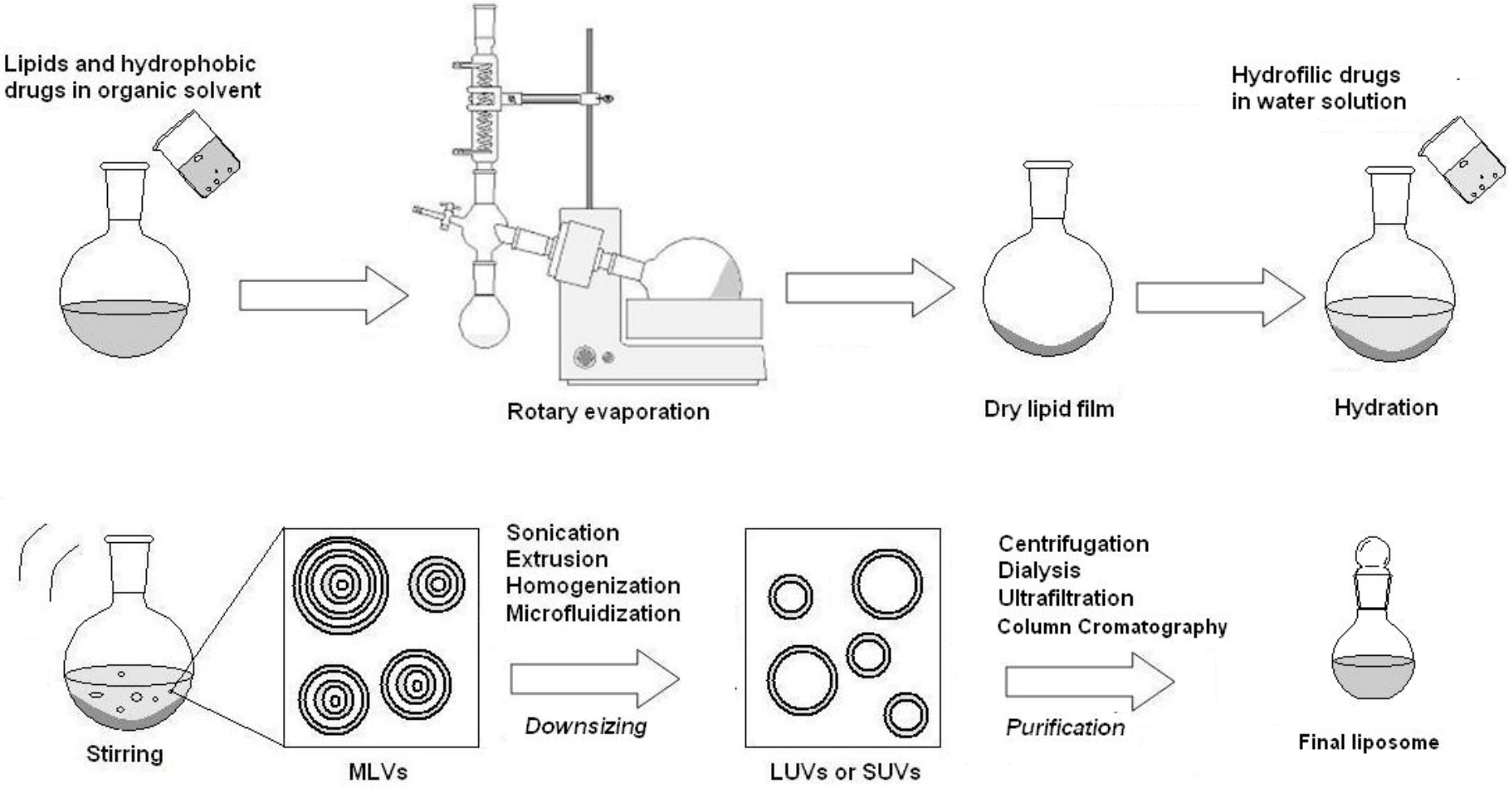
Sonication



Das, N.; Murray, D. T.; Cross, T. A. *Nat. Protocols* **2013,** *8* (11), 2256-2270.

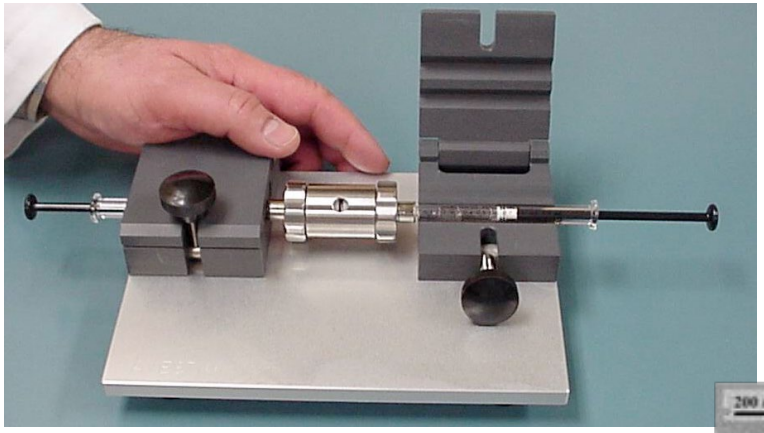
The vesicle diameter after sonication is between 50 nm and a few 100 nm.

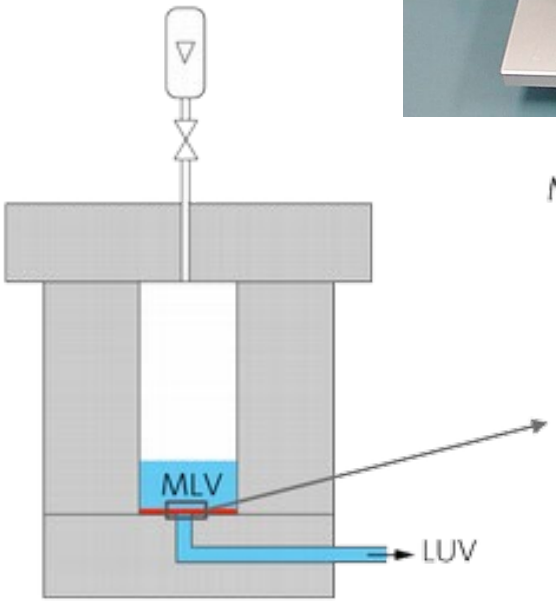
Vesicle formation: Rehydration

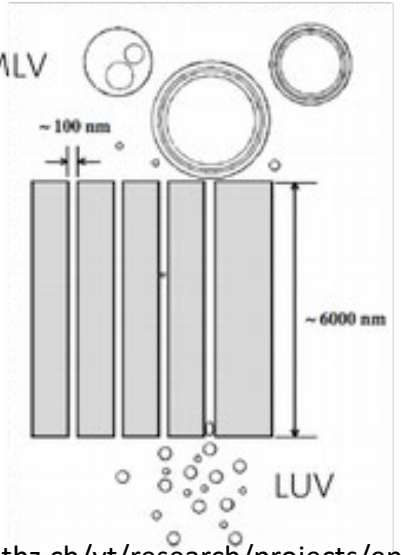


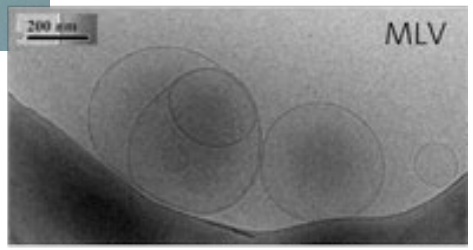
"Cancer Treatment – Conventional and Innovative Approaches", book edited by Letícia Rangel , ISBN 978-953-51-1098-9

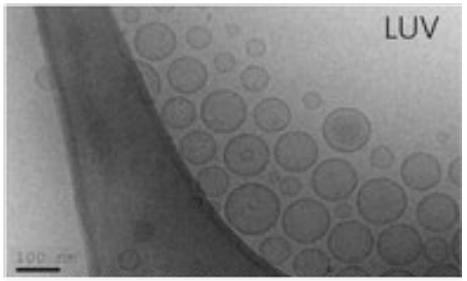
Extrusion







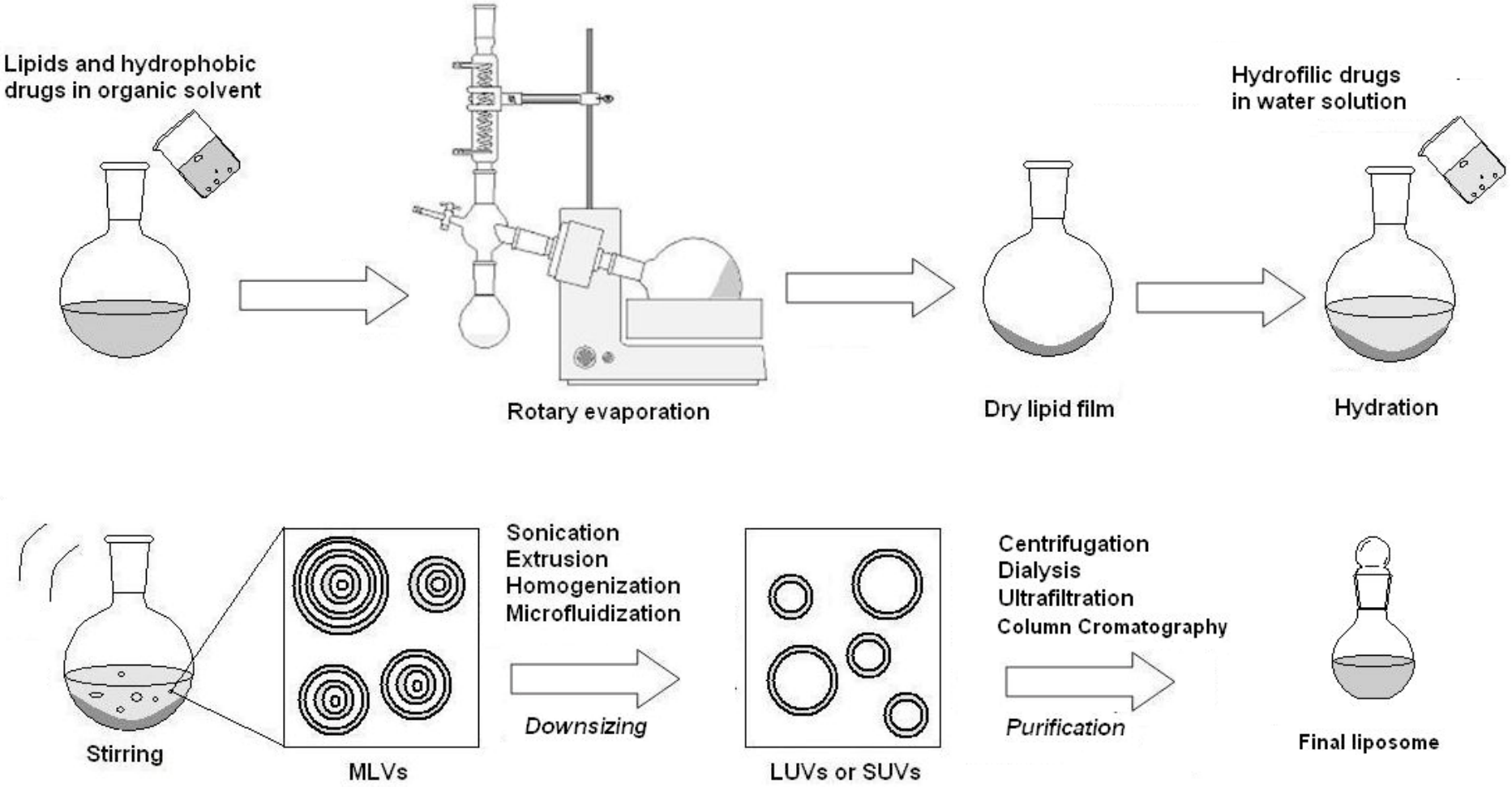




http://www.ifnh.ethz.ch/vt/research/projects/engelh

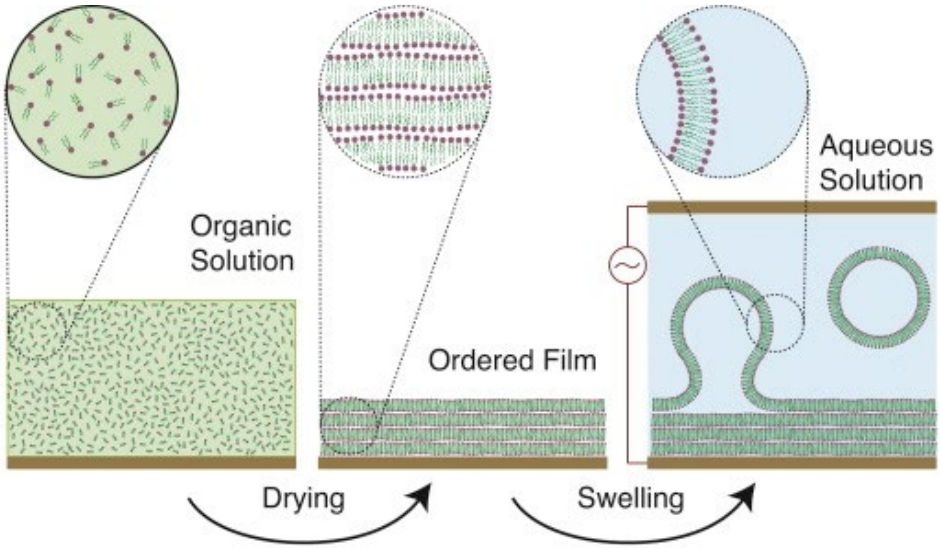
The vesicle diameter is similar to membrane pore size; it is usually between 50 nm to 500 nm.

Vesicle formation: Rehydration

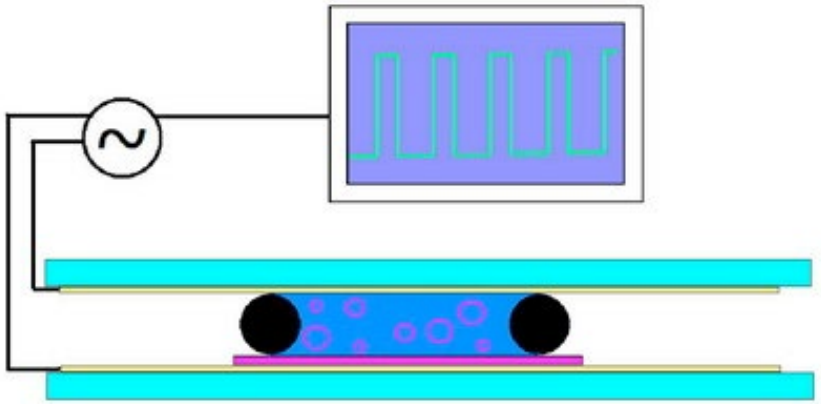


"Cancer Treatment – Conventional and Innovative Approaches", book edited by Letícia Rangel , ISBN 978-953-51-1098-9

Electroformation



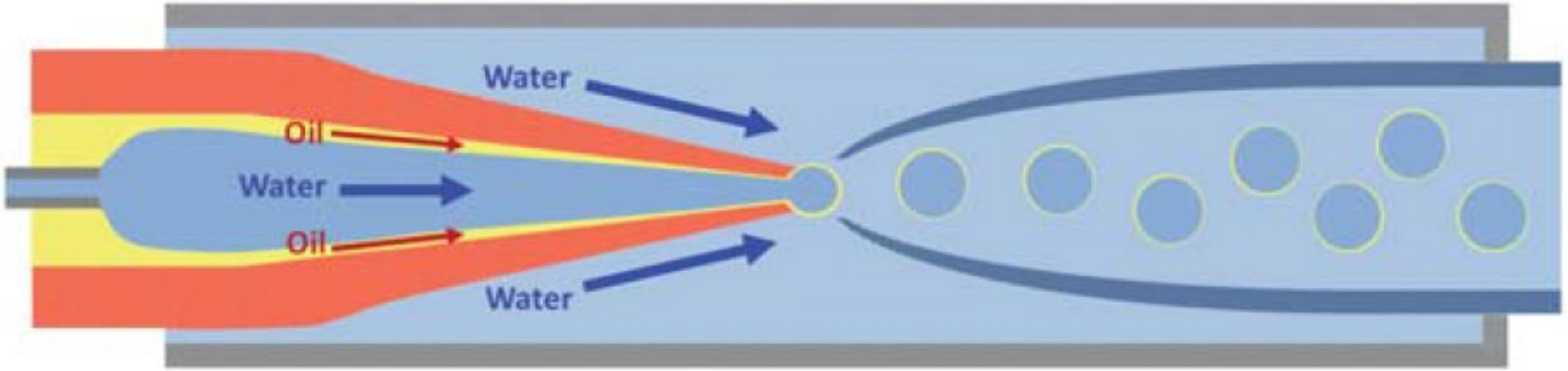
Mertins, O.; da Silveira, N. P.; Pohlmann, A. R.; Schroeder, A. P.; Marques, C. M. *Biophysical Journal* **2009,** *96* (7), 2719-2726.



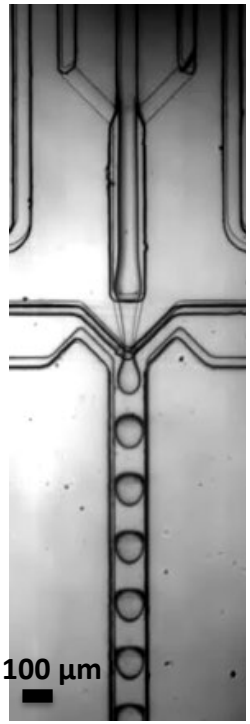
http://www.rpgroup.caltech.edu/courses/PBL/lipids.htm

The vesicle diameter ranges from a few up to a few 10s of µm.

Microfluidics

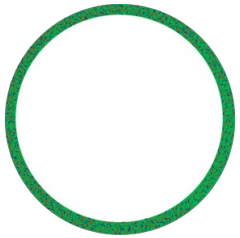


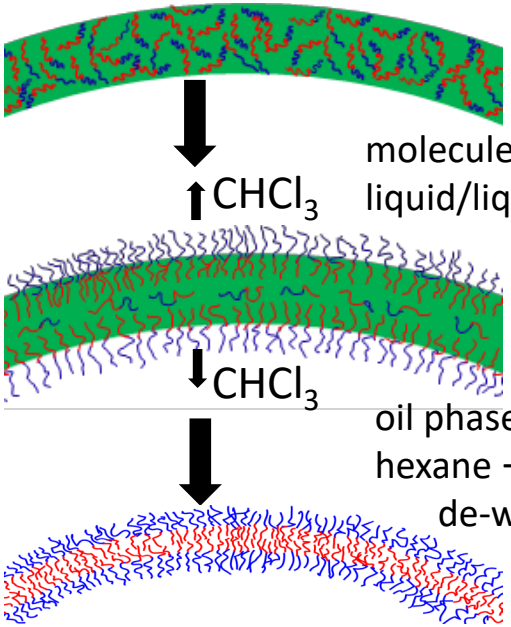
Kim, S.-H.; Kim, J. W.; Cho, J.-C.; Weitz, D. A. *Lab on a Chip* **2011,** *11* (18), 3162-3166.



Microfluidics

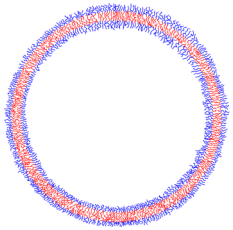
water/oil/water
double emulsion



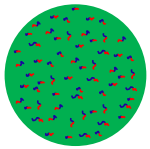


molecules assemble at
liquid/liquid interfaces

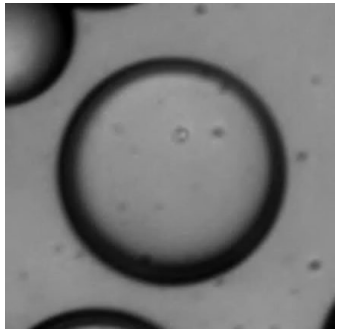
oil phase is enriched with
hexane →
de-wetting



vesicle



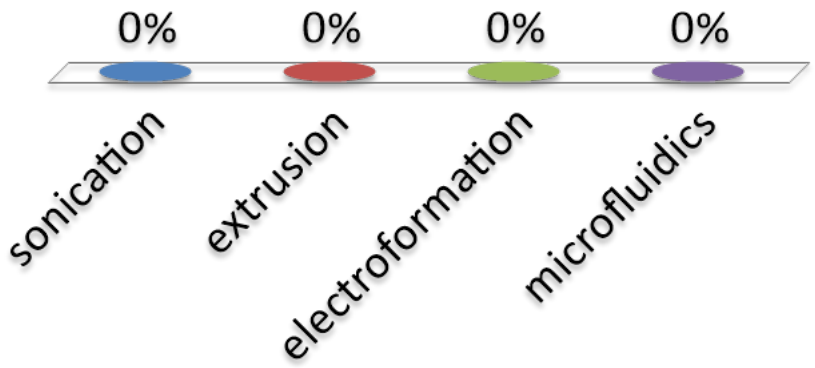
oil drop containing
excessive molecules



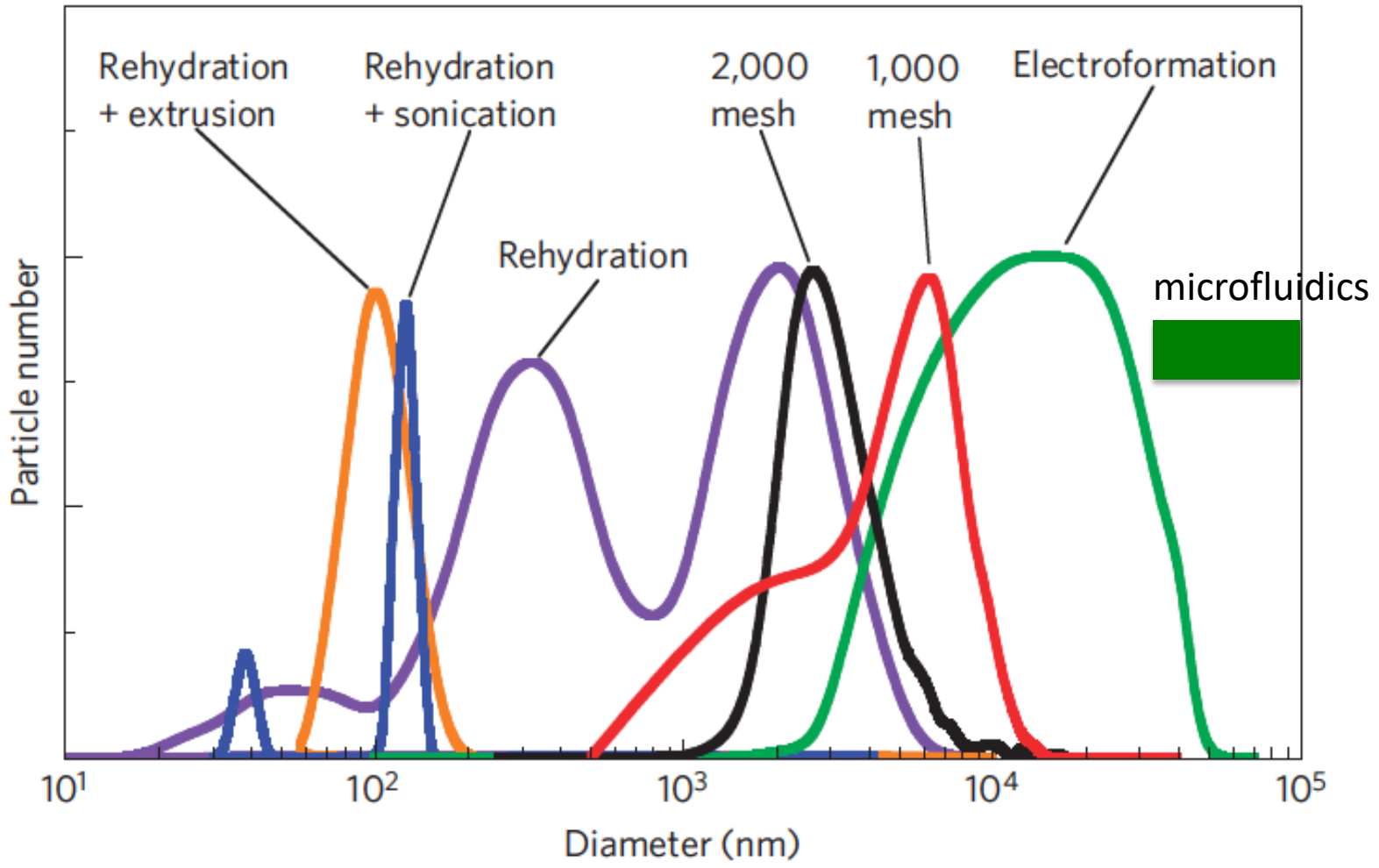
The vesicle diameter is similar to the diameter of double emulsion drops; it is usually between 50 µm and 200 µm.

You are asked to prepare vesicles with a diameter of 200 nm and an as narrow size distribution as possible. Which of these methods would you chose to prepare them?

A. sonication
B. extrusion
C. electroformation
D. microfluidics



Influence of production method on vesicle size

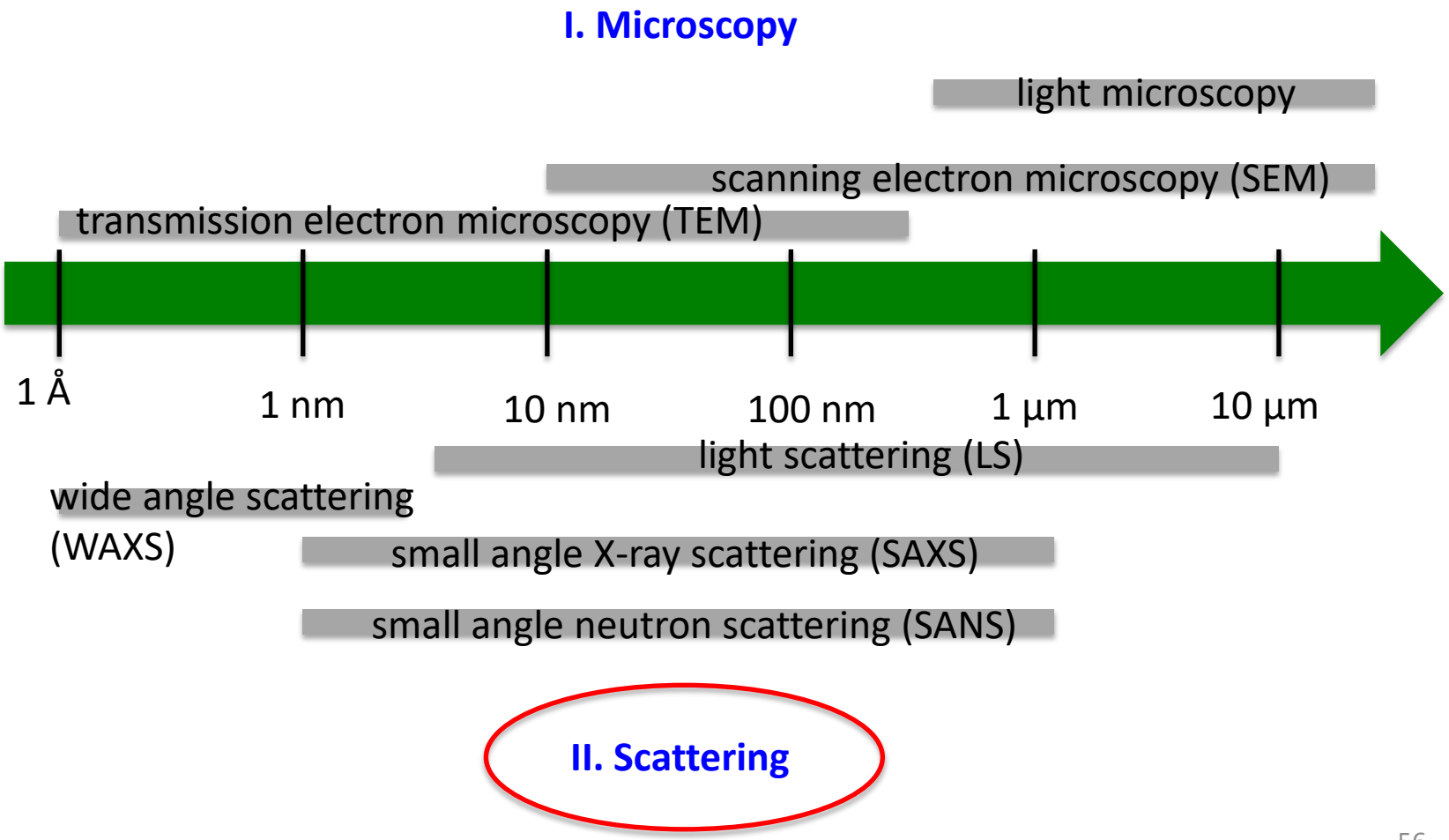


J. R. Howse *et al.*, *Nat Mater* **8**, 507 (2009).

Outline

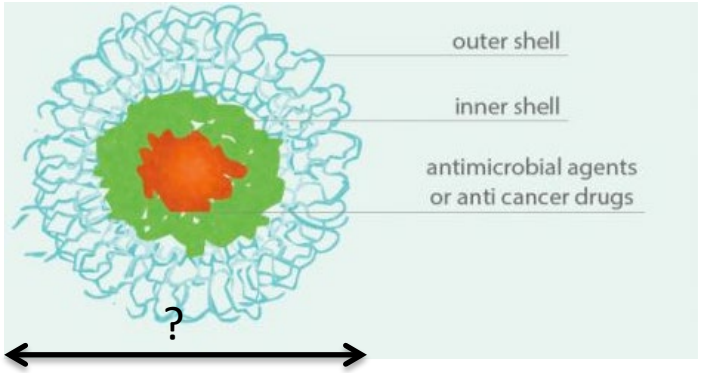
- Introduction
  - Vesicles
  - Vesicle production
- Liposomes
- Polymersomes
- Characterization
- Applications

Characterization of soft materials

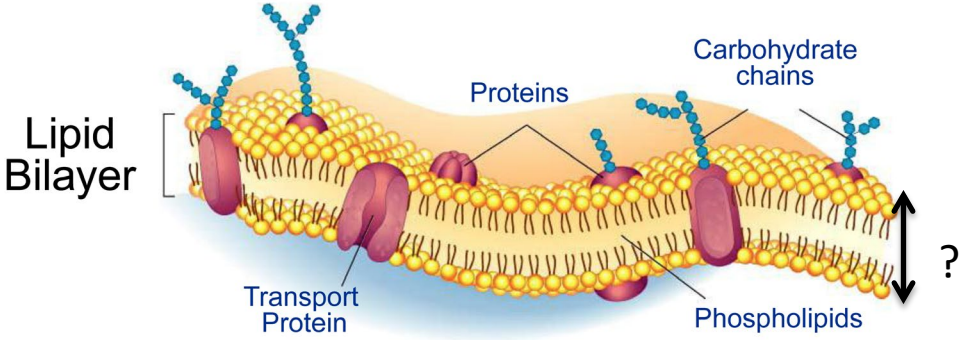


How would you characterize the dimensions of these samples?

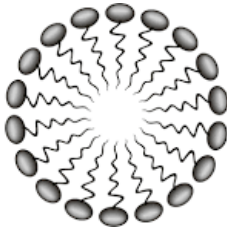
core-shell nanoparticles



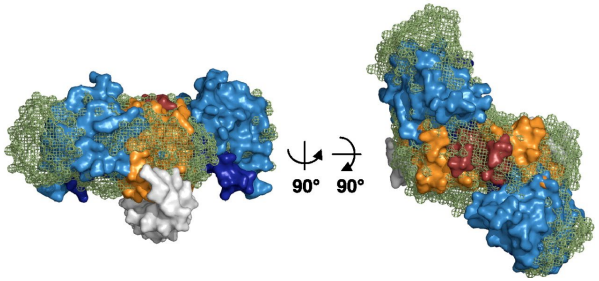
cell membrane



micelles

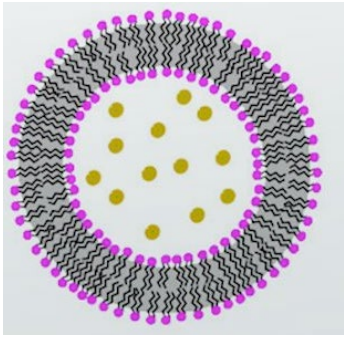


protein structure

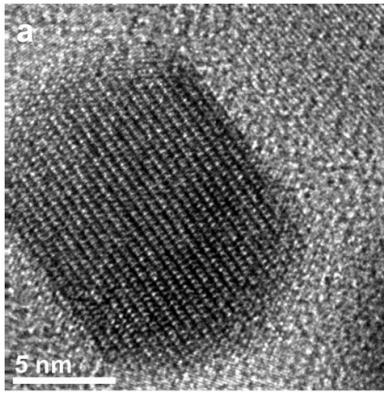


D. Strickland, K. Moffat and T. R. Sosnick, *PNAS,* 2008, **105**, 10709-10714.

vesicles

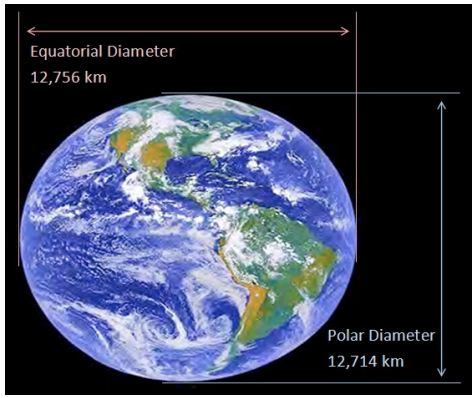


lattice spacing

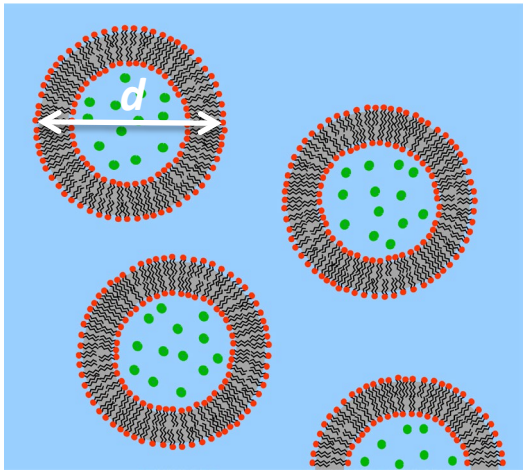


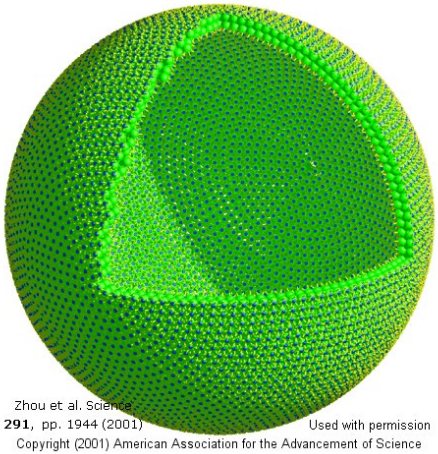
H.-M. Song, J. I. Zink and N. M. Khashab, *PCCP*, 2015, **17**, 18825-18833

Length scales

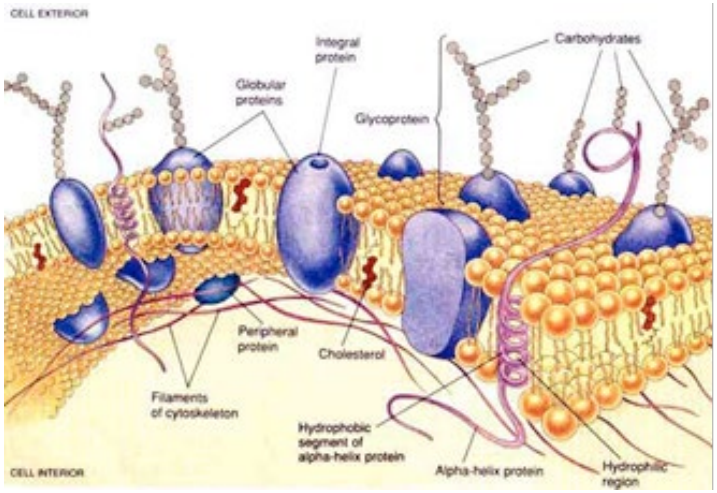


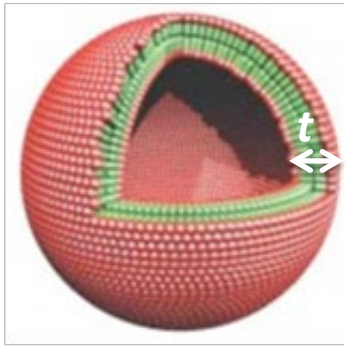
Scattering



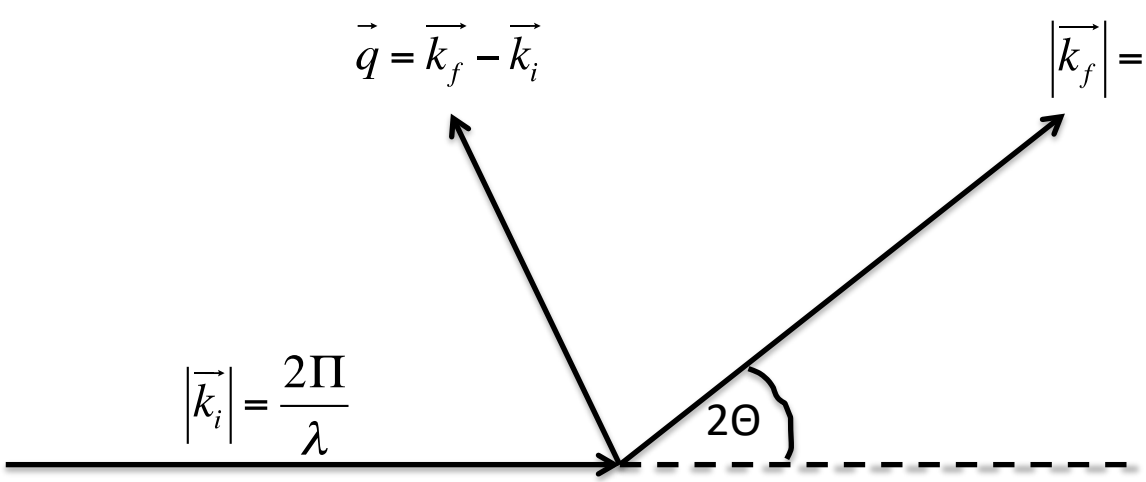


Zhou et al. Science **291**, pp. 1944 (2001)





Scattering

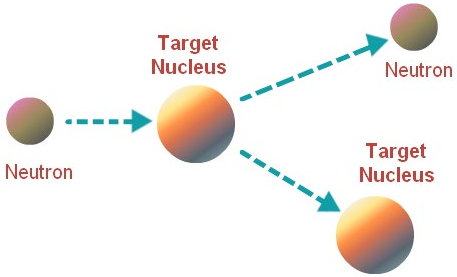


$$q = \left|\vec{q}\right| = \frac{4\Pi \sin\Theta}{\lambda}$$

k_i: wave vector of incident beam [m^{-1}]
k_f: wave vector of scattered beam [m^{-1}]
q: scattering wave vector [m^{-1}]
λ: wavelength [m]

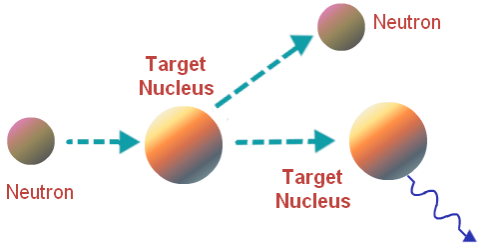
Elastic scattering

energy of incoming wave/object =
energy of outgoing wave/object



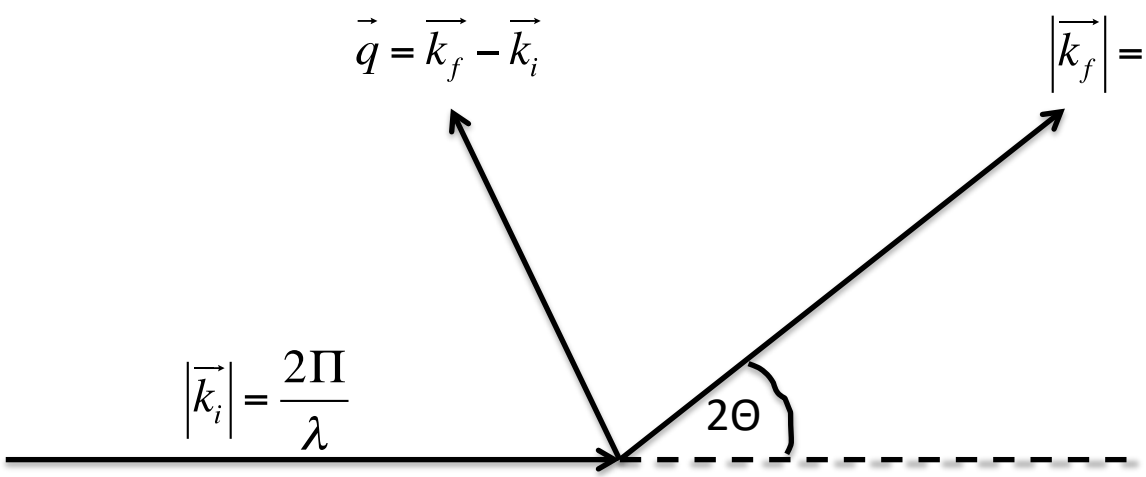
Inelastic scattering

energy of incoming wave/object >
energy of outgoing wave/object



http://chemistry.tutorvista.com/nuclear-chemistry/nuclear-chain-reaction.html

Scattering



$$q = \left|\vec{q}\right| = \frac{4\Pi \sin\Theta}{\lambda}$$

k_i: wave vector of incident beam [m^{-1}]
k_f: wave vector of scattered beam [m^{-1}]
q: scattering wave vector [m^{-1}]
λ: wavelength [m]

Light:
For the characterization of objects with sizes of a few nm up to approximately 10 µm.

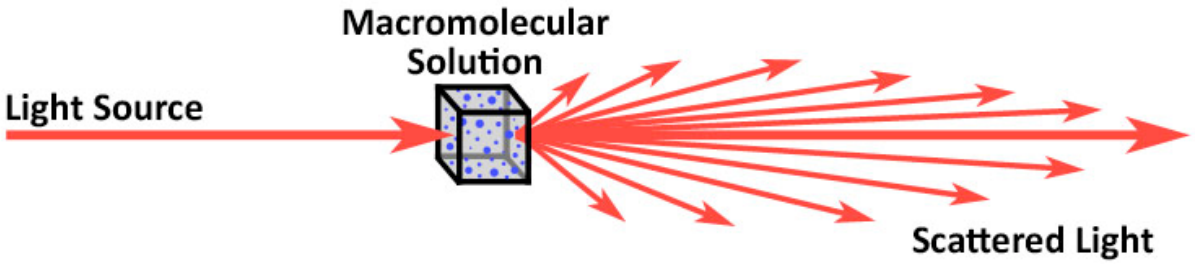
X-rays:
They interact with electrons and are good to visualize heavy atoms that give a strong response.

Neutrons:
They interact with atomic nuclei and

- are better suited to detect light atoms (H, O) than X-rays
- can easily distinguish atoms with similar atomic numbers
- can distinguish isotopes.

Light scattering

λ: 350 nm – 680 nm



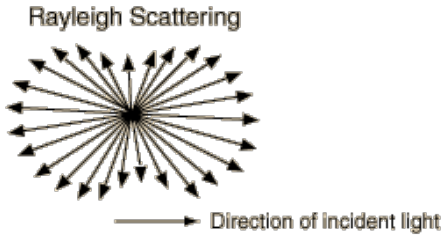
http://www.legendairy.com.au/dairy-foods/dairy-products/milk/how-milk-is-made

http://navanrfc.ie/blue-sky-desktop/

Light scattering

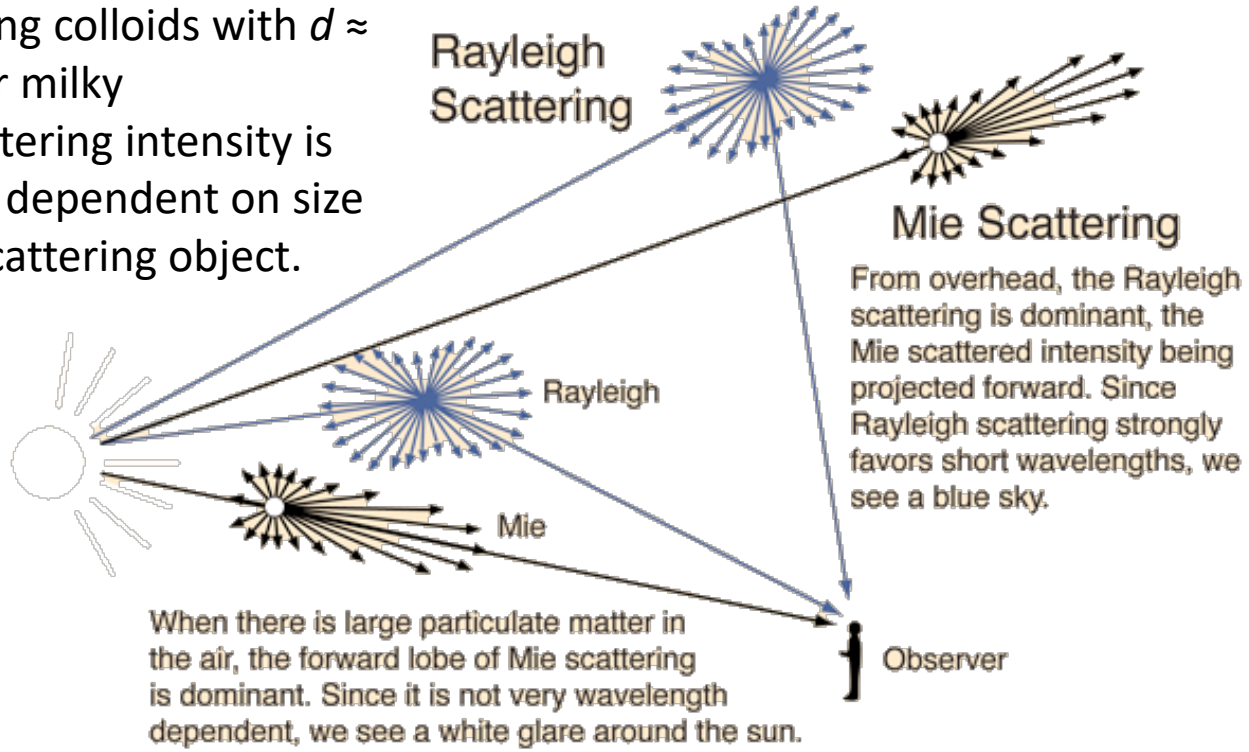
I: Scattering intensity [-]
d: diameter of particle [m]
λ: wavelength [m]

Rayleigh scattering: $d < 0.1\,\lambda$ $\quad I \propto \frac{1}{\lambda^4}$



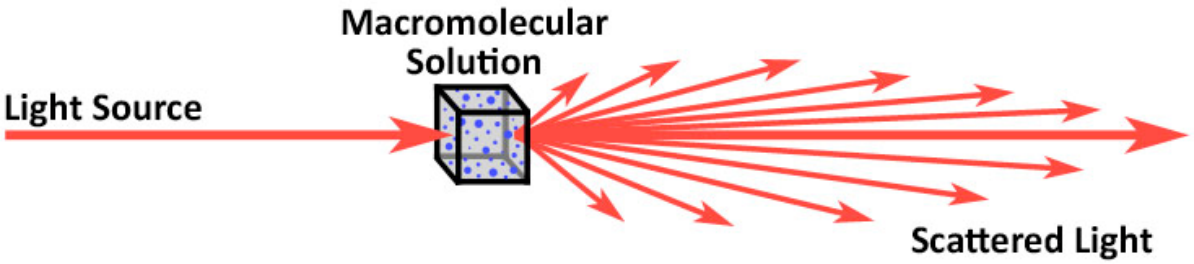
Mie scattering: $d \approx \lambda$

- The scattering intensity is only weakly dependent on λ such that dispersions containing colloids with $d \approx \lambda$ appear milky
- The scattering intensity is strongly dependent on size of the scattering object.

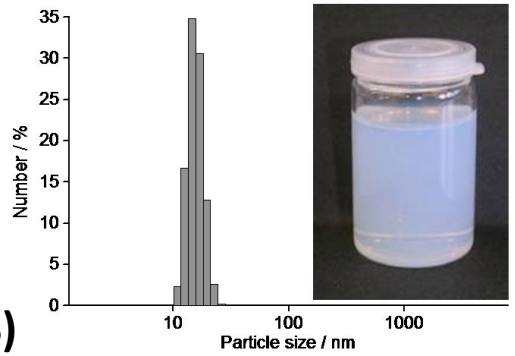


Light scattering

λ: 350 nm – 680 nm



example:



Dynamic light scattering (DLS)

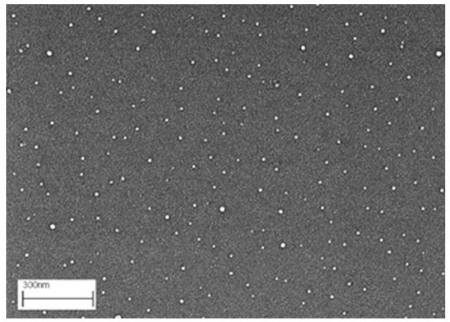
measures real-time intensities ➔ dynamic properties

- diffusion coefficient
- hydrodynamic diameter

Static light scattering (SLS)

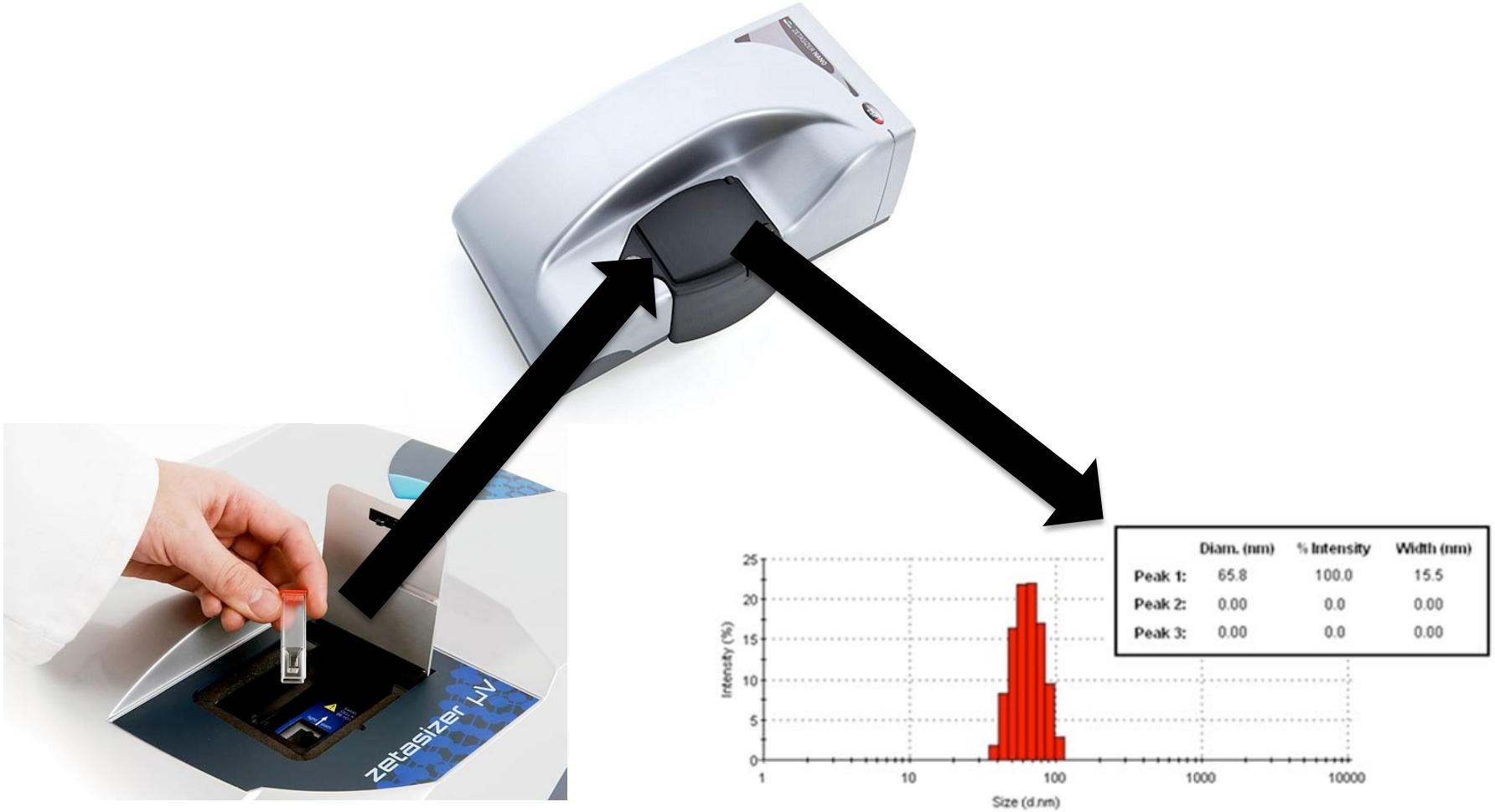
measures the time averaged scattering intensities

- particle morphology
- particle arrangement



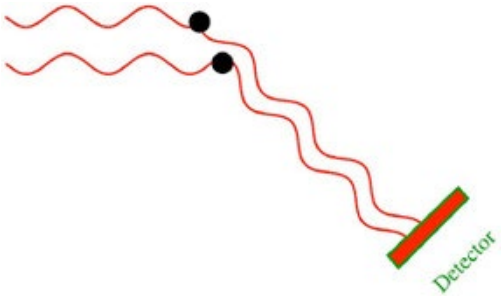
E. Hammarberg, *et al.*, J. Colloid Interface Sci. 2009, **334**, 29.

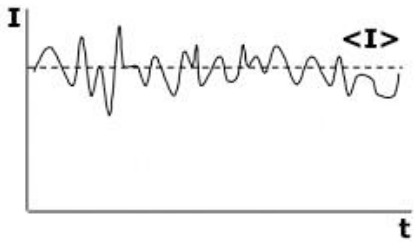
Dynamic light scattering



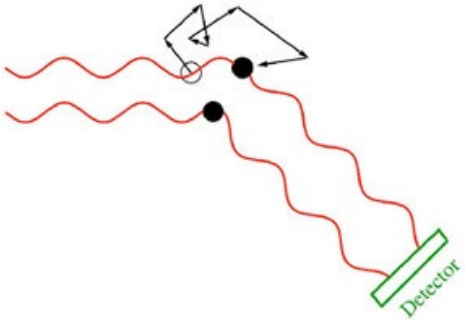
Dynamic light scattering (DLS)

constructive interference



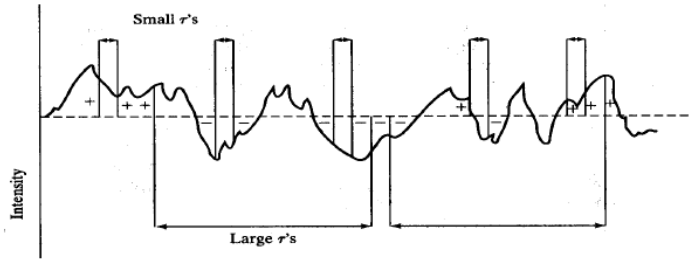


destructive interference



correlation function

$$G(\tau) = \sum I(t) I(t+\tau)$$



$$G(\tau) = G_0 e^{-Dq^2\tau}$$

plot ln ($G(\tau)$) vs. τ

slope: Dq^2

$$q = \frac{4\Pi \sin\Theta}{\lambda}$$

$$R_H = \frac{k_B T}{6\Pi\eta D}$$

Dynamic light scattering (DLS)

1. Raw data
correlation function

$$G(\tau) = G_0 e^{-Dq^2\tau}$$

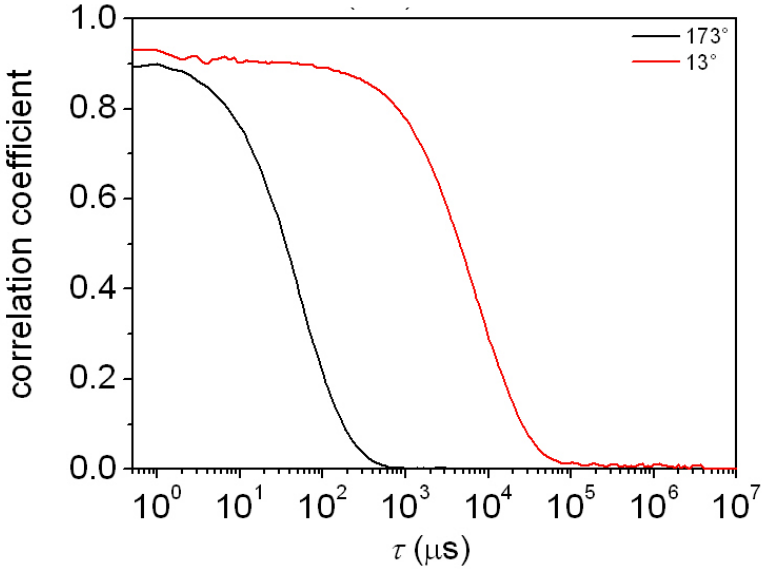
2. Fitting
deduce Dq^2

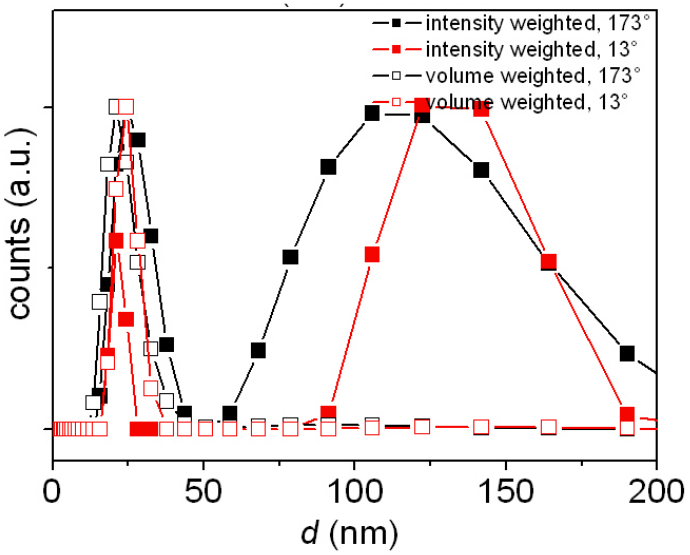
3. Calculation
determine D using the known q

$$q = \frac{4\pi n}{\lambda}\sin\Theta$$

4. Calculation
intensity weighted hydrodanymic radius

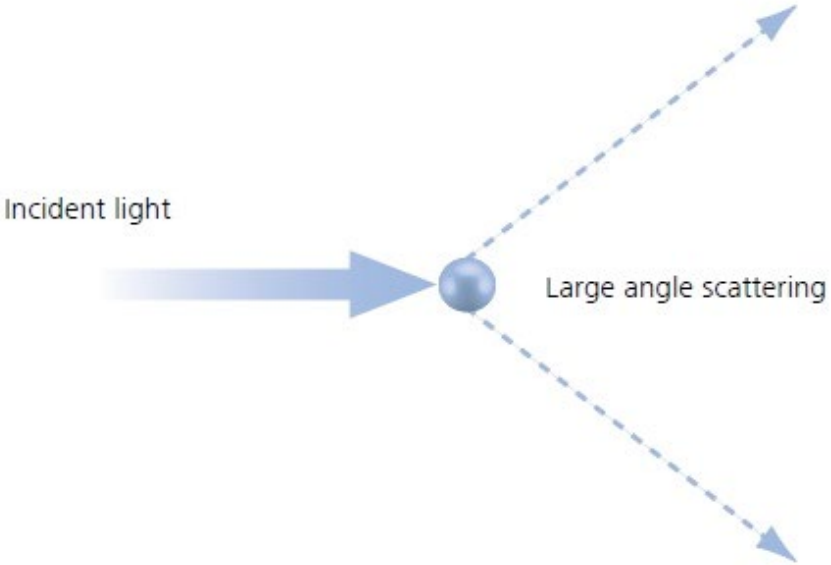
$$R_H = \frac{k_B T}{6\pi\eta D}$$





Influence of particle size

$$I \propto r^6$$



https://www.azom.com/article.aspx?ArticleID=9937

Dynamic light scattering (DLS)

1. Raw data
correlation function

$$G(\tau) = G_0 e^{-Dq^2\tau}$$

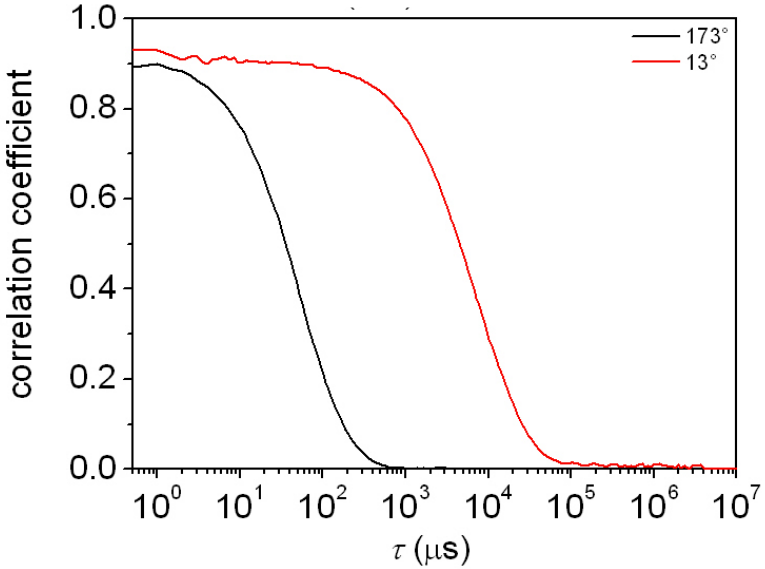
2. Fitting
deduce Dq^2

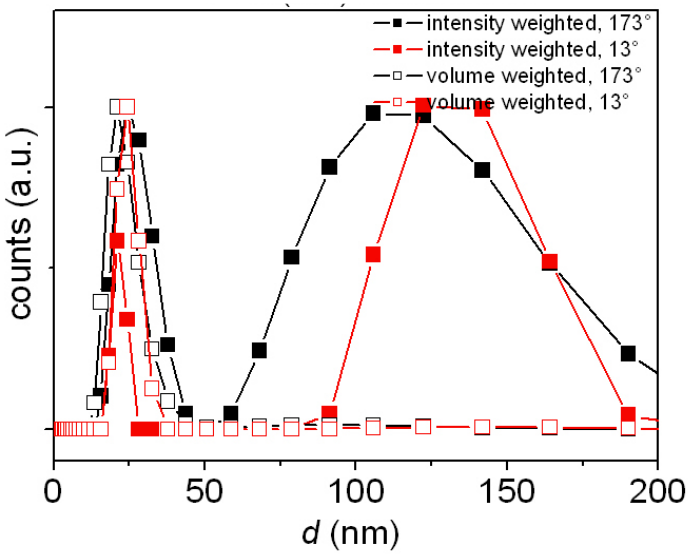
3. Calculation
determine D using the known q

$$q = \frac{4\pi n}{\lambda}\sin\Theta$$

4. Calculation
intensity weighted hydrodanymic radius

$$R_H = \frac{k_B T}{6\pi\eta D}$$

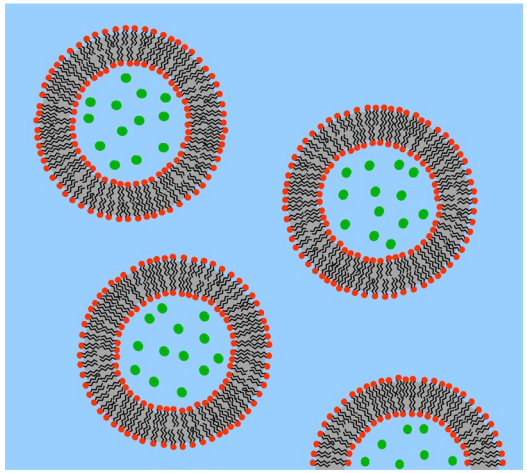


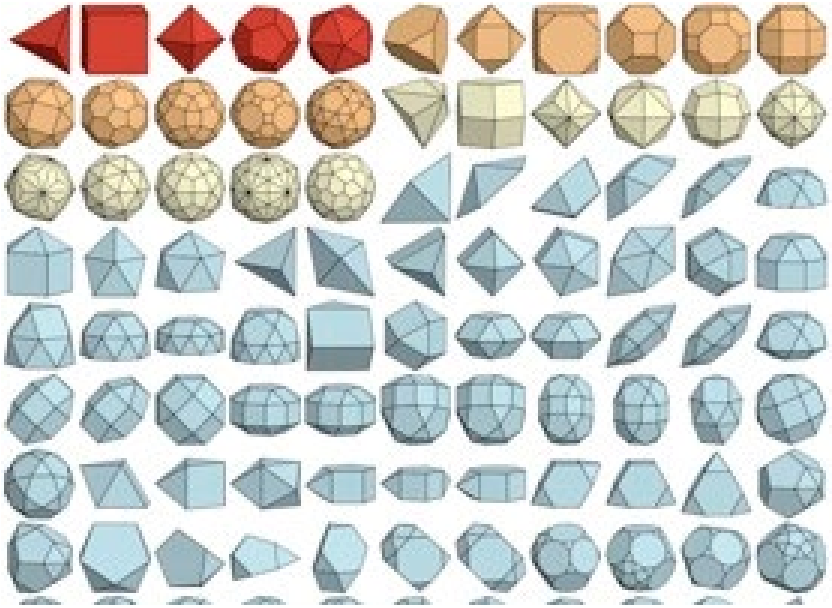


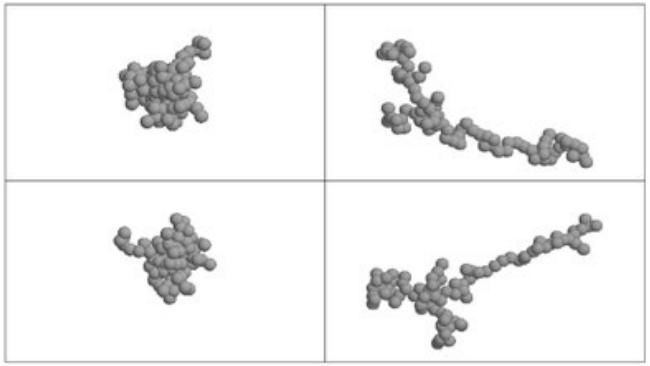
Assumptions:

1. spherical particles
2. homogeneous mass/density of particles
3. known real and imaginary refractive index

Scattering

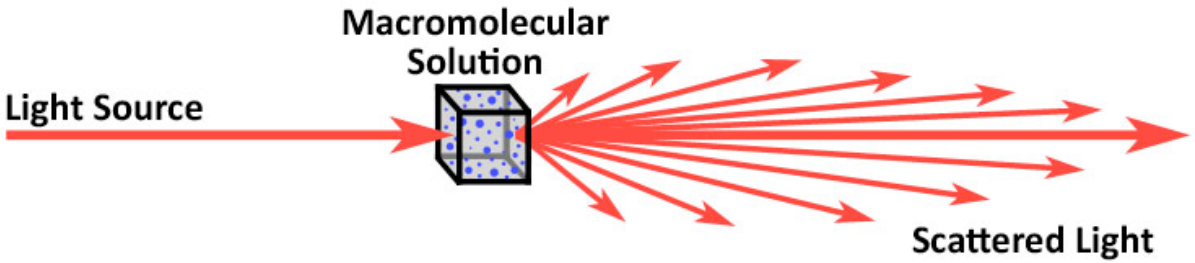






Light scattering

λ: 350 nm – 680 nm



Dynamic light scattering (DLS)

measures real-time intensities ➔ dynamic properties

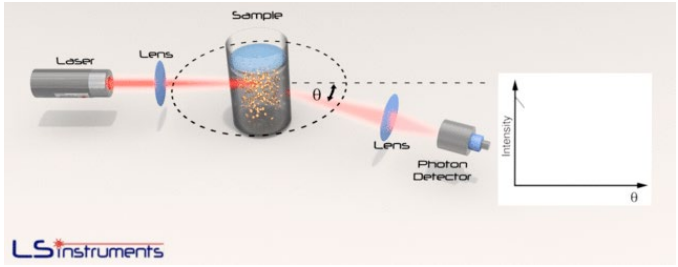
- diffusion coefficient
- hydrodynamic diameter

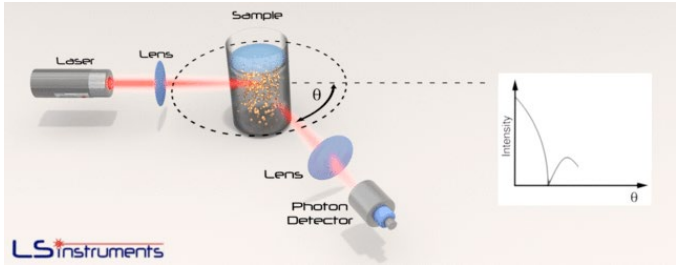
Static light scattering (SLS)

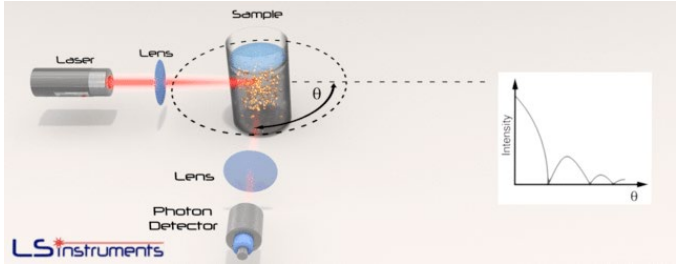
measures the time averaged scattering intensities

- particle morphology
- particle arrangement

Static light scattering (SLS)







$$I(\vec{q},c) = I_i \frac{f(\theta)}{R_0^2} c V_s \Delta\rho^2 V_p^2 P(\vec{q}) S(\vec{q},c)$$

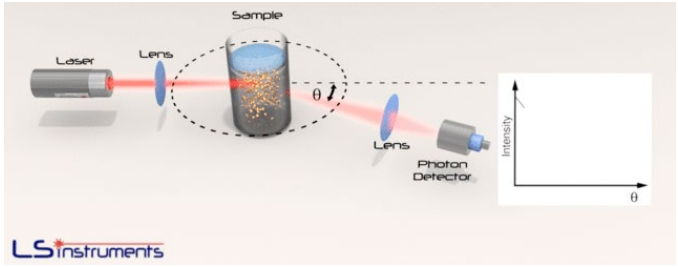
I: scattering intensity [-]
I_i: light intensity before impingement [-]
$f(\theta)$: geometrical factor accounting for polarization for incident and collected light [-]
R_0: distance between sample and detector [m]
P: form factor [-]
S: structure factor [-]
c: concentration [m^{-3}]
V_s: molecular volume solvent [m^3]
V_p: molecular volume particle [m^3]
$\Delta\rho$: difference in scattering length density [m^{-2}]

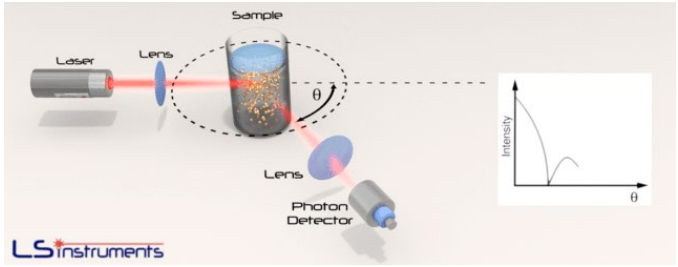
experimental parameters to be adjusted to get a sufficiently high scattering intensity

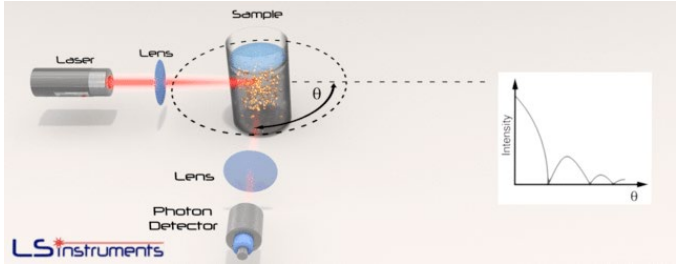
$$q = \left|\vec{q}\right| = \frac{4\Pi \sin\Theta}{\lambda}$$

http://www.lsinstruments.ch/technology/static_light_scattering_sls/

Static light scattering (SLS)







$$I(\vec{q},c) = I_i \frac{f(\theta)}{R_0^2} c V_s \Delta\rho^2 V_p^2 P(\vec{q}) S(\vec{q},c)$$

I: scattering intensity [-]
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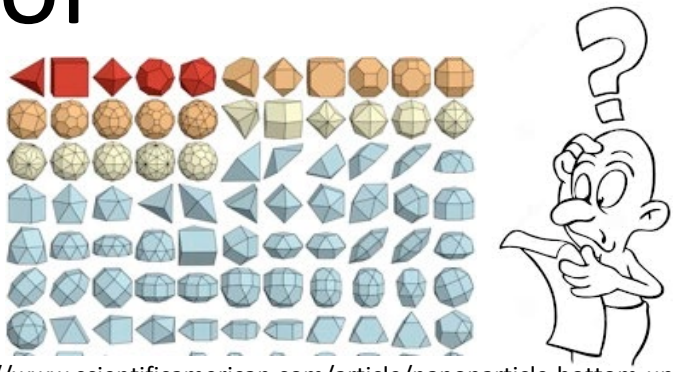
V_s: molecular volume solvent [m^3]
V_p: molecular volume particle [m^3]
$\Delta\rho$: difference in scattering length density [m^{-2}]

$$q = \left|\vec{q}\right| = \frac{4\Pi \sin\Theta}{\lambda}$$

http://www.lsinstruments.ch/technology/static_light_scattering_sls/

Form factor

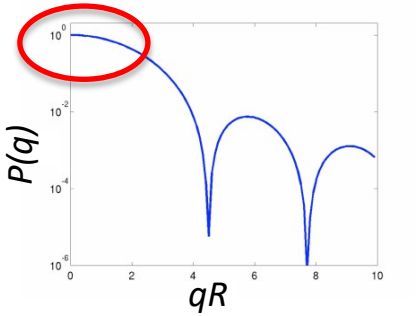
Tells us something about particle size and shape:



http://www.scientificamerican.com/article/nanoparticle-bottom-up/

For a sphere with radius *R*:

$$P(q)=\left[\frac{3}{(qr)^3}(\sin(qr)-qr\cos(qr))\right]^2$$



P: form factor [1]
r: position of particle time *t* [m]
g: pair correlation function [-]
q: scattering wave vector [m^{-1}]
R: radius of particle [m]
R_g: radius of gyration [m]

To obtain a simpler, general formula for the form factor, we introduce a pair correlation function *g*(*r*); it describes the probability to find two points, that belong to a particle at a distance *r*.

$$P(q)=\left[\int_0^\infty r^2 g(r)\frac{\sin(qr)}{qr}dr\right]^2$$

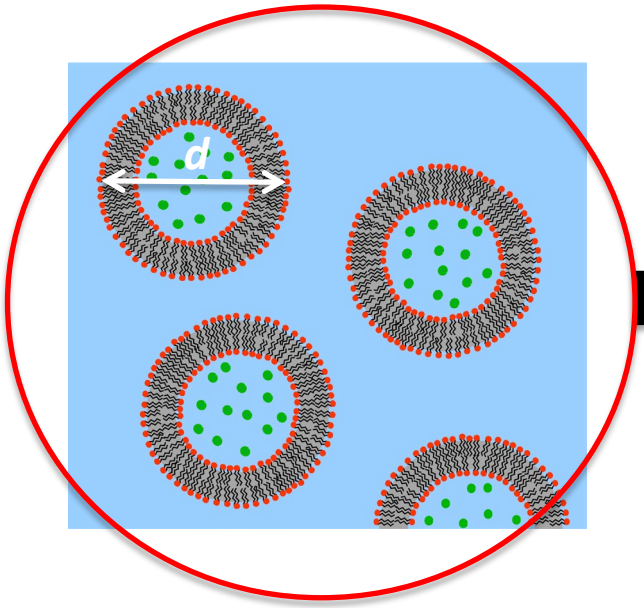
expanding $\frac{\sin(qr)}{qr}$

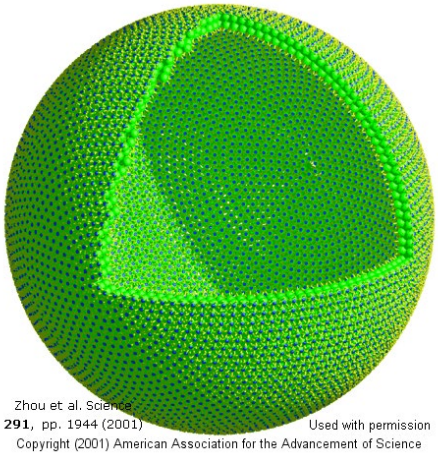
$$P(q)\approx 1-\frac{(qR_g)^2}{3}$$

with $R_g^2=\int_0^\infty r^2 g(r)dr$

http://www.lsinstruments.ch/technology/static_light_scattering_sls/form_factor/

Scattering





Zhou et al. Science
291, pp. 1944 (2001)
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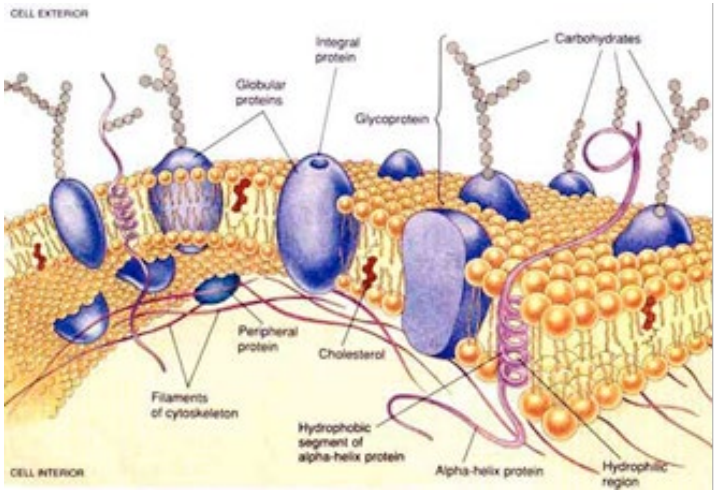
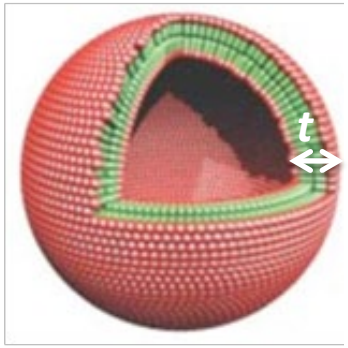
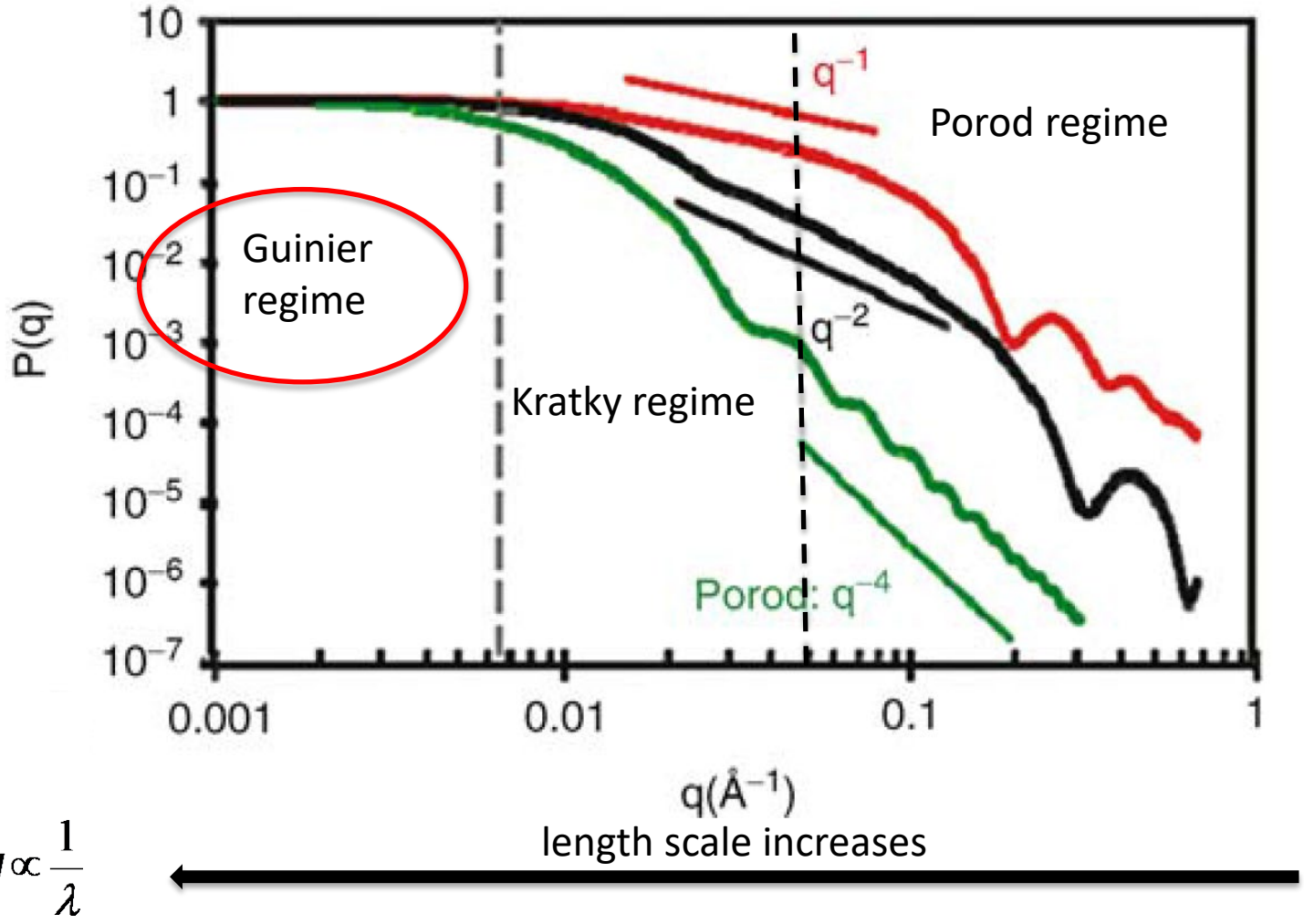




Small angle scattering data

Different regimes give information about the sample structure on different length scales.

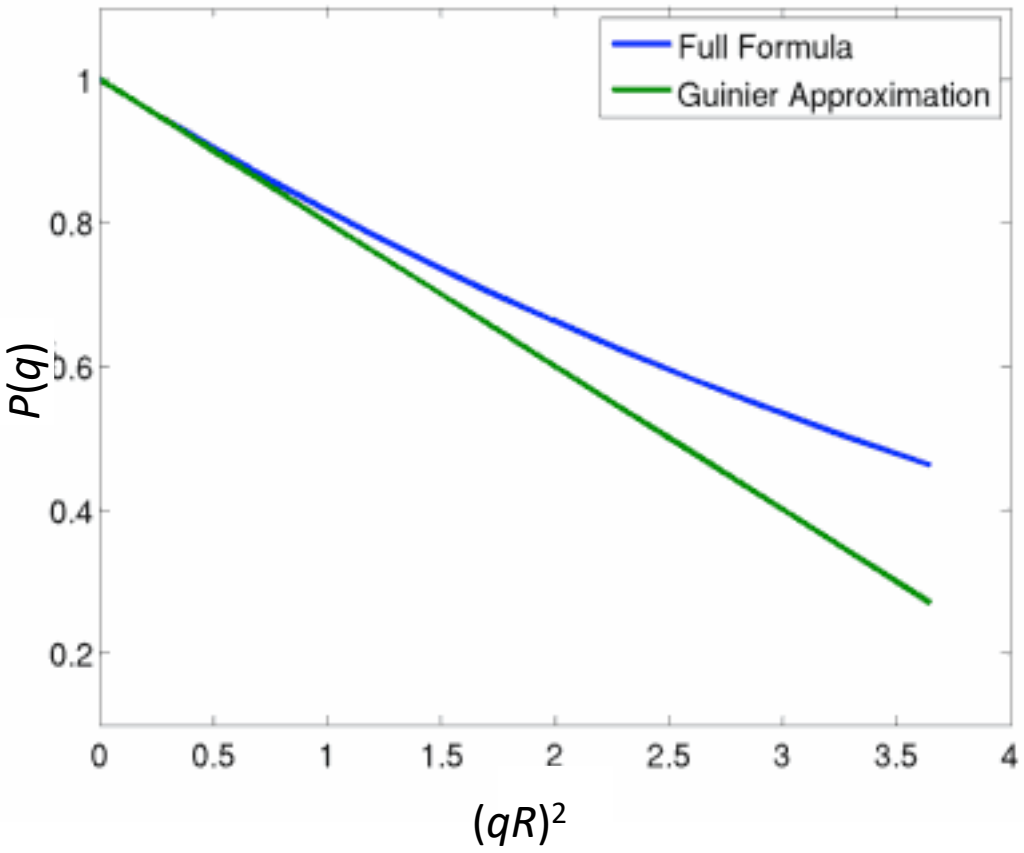


Grillo, I. *Soft Matter Characterization*; Springer Netherlands, 2008

Guinier approximation

For a sphere: $$P(q) \approx 1 - \frac{(qR_g)^2}{3}$$

P: form factor [-]
q: scattering wave vector [m^{-1}]
R: radius of particle [m]
R_g: radius of gyration [m]



The slope lets you determine the relation between *R* and R_g. In this case, $R_g = \sqrt{\frac{3}{5}}R$

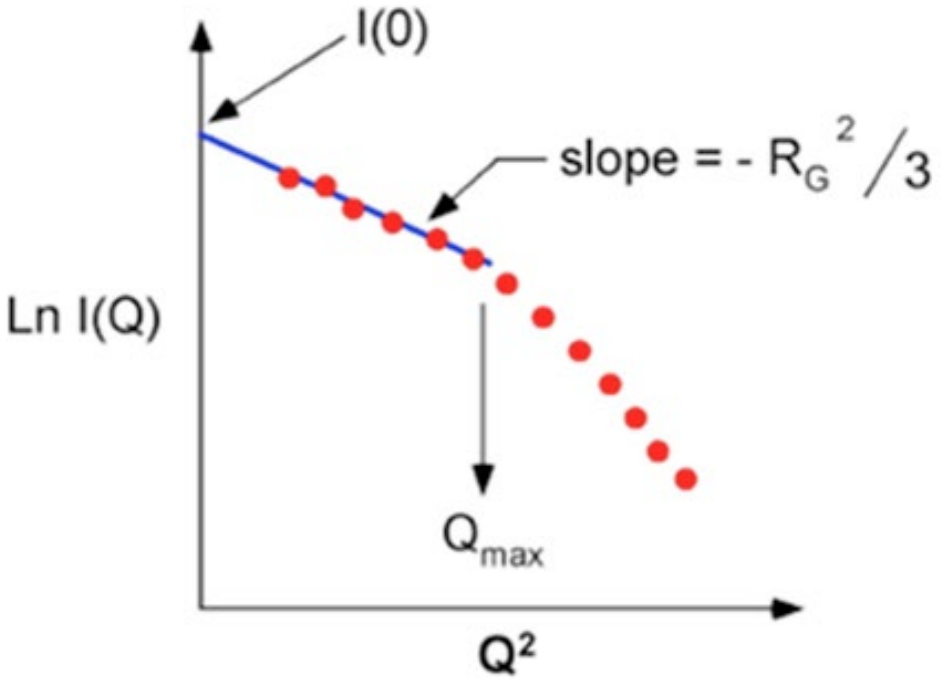
http://www.lsinstruments.ch/technology/static_light_scattering_sls/form_factor/

Guinier Region

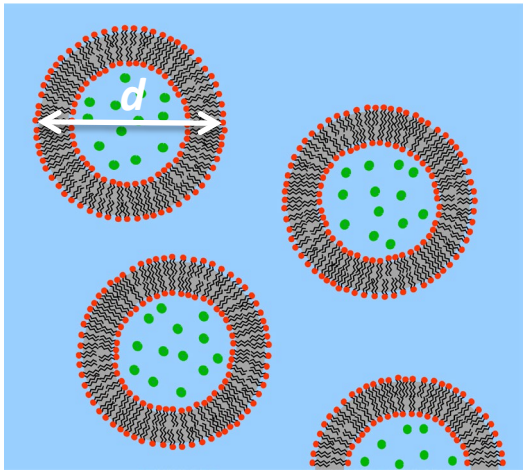
$q \rightarrow 0$

determine R_g

$$I(q) = I(0)e^{-\frac{(qR_g)^2}{3}} \qquad q = \frac{4\Pi\sin(\frac{\Theta}{2})}{\lambda}$$



Scattering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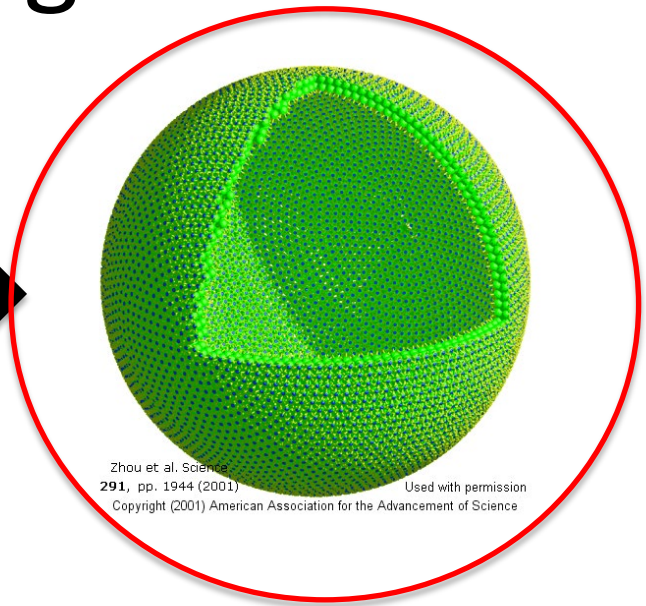
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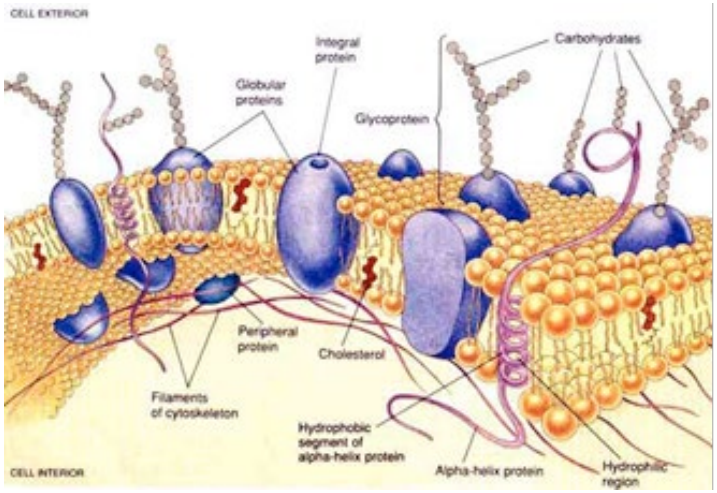
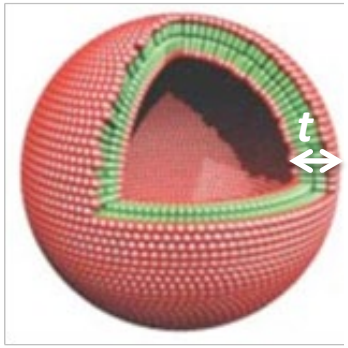
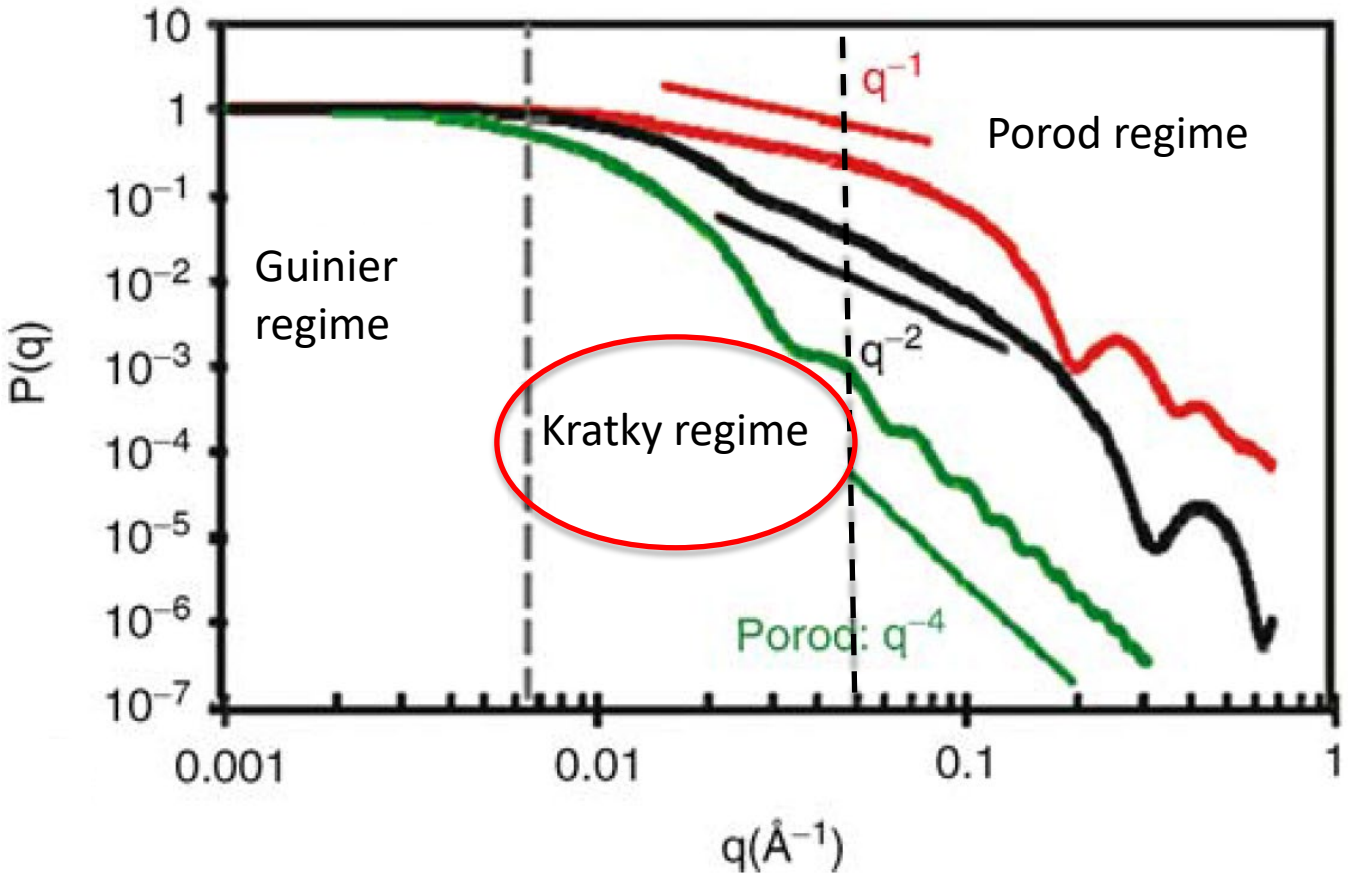

CELL EXTERIOR
Integral protein
Carbohydrates
Globular proteins
Glycoprotein
Peripheral protein
Cholesterol
Filaments of cytoskeleton
Hydrophobic segment of alpha-helix protein
Alpha-helix protein
Hydrophilic region
CELL INTERIOR


t

Kratky Region

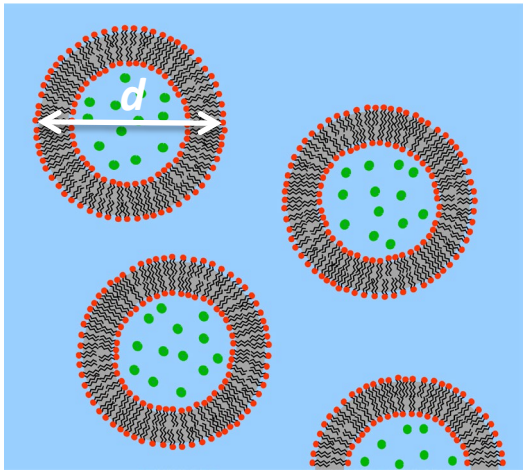
In certain *q*-ranges, the scattering behavior of polymers is like that of a Gaussian coil. This region has slopes typically between q^{-1} and q^{-3}.

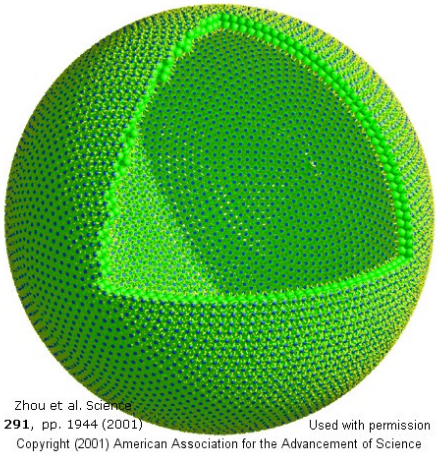


slope of q^{-1}: 1 D object e.g. rigid fiber

slope of q^{-2}: 2 D object or locally planar e.g. membrane

Scattering





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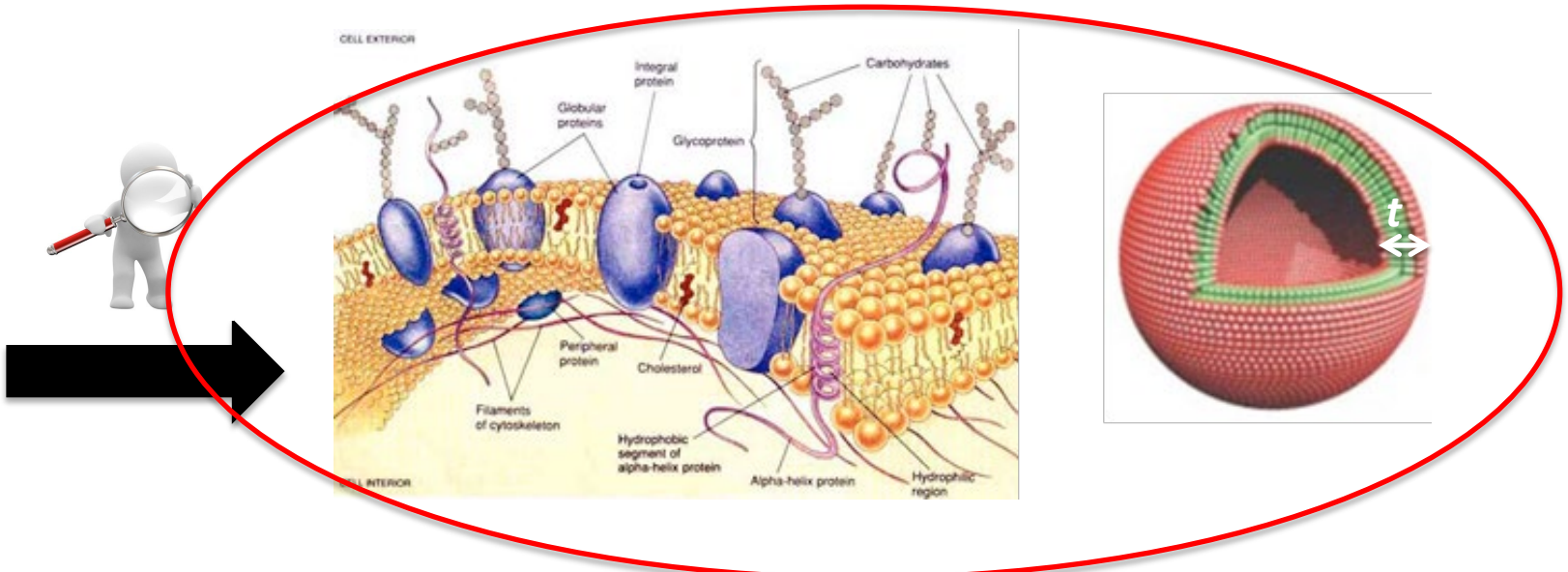
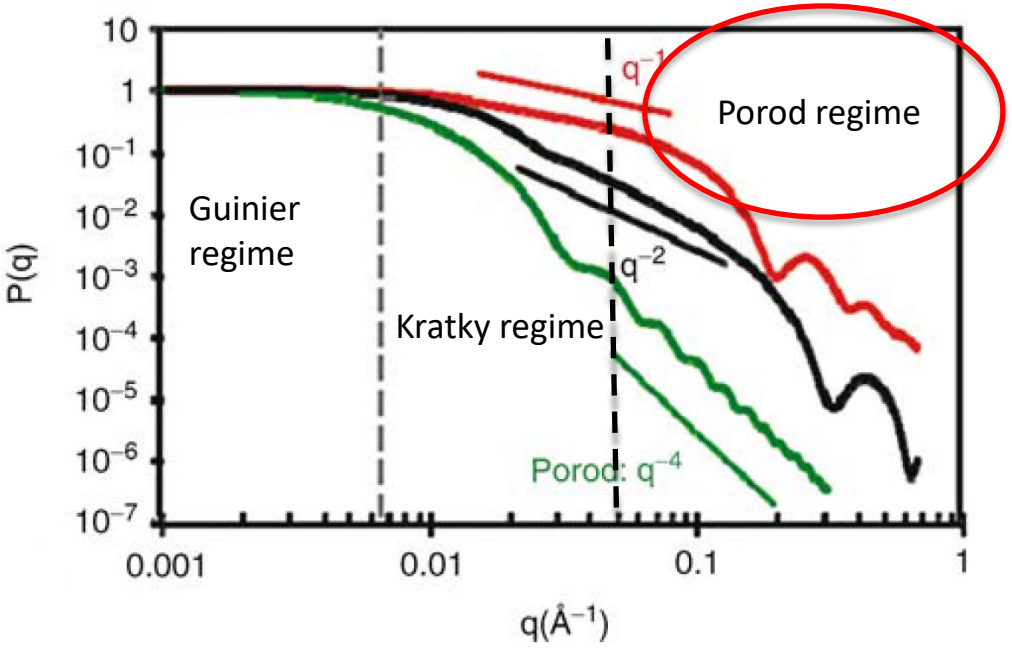


Porod Region

The minimum in $P(q)$ at highest q value is related to the smallest dimension of the object.



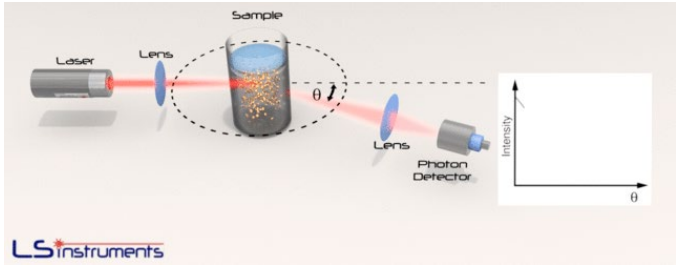
For sharp interfaces and large q's: $\sum = \frac{1}{2\Pi(\Delta\rho)^2} \lim_{q\to\infty} I(q)q^4$ $\sum$: specific surface area

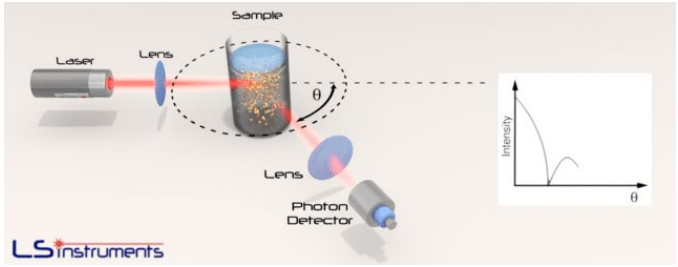
$$I \propto \frac{1}{q^{-4}}$$

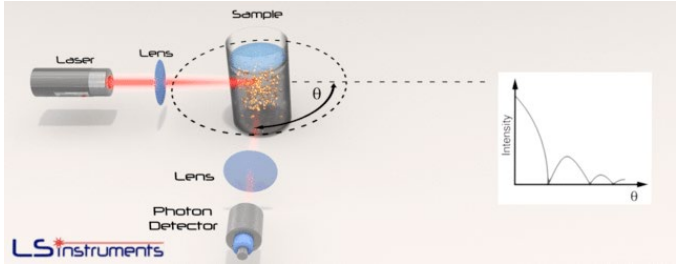
The Porod region can be used to

- determine shell thickness
- learn something about the surface roughness from the exact exponent of q

Static light scattering (SLS)







$$I(\vec{q},c) = I_i \frac{f(\theta)}{R_0^2} c V_s \Delta\rho^2 V_p^2 P(\vec{q}) S(\vec{q},c)$$

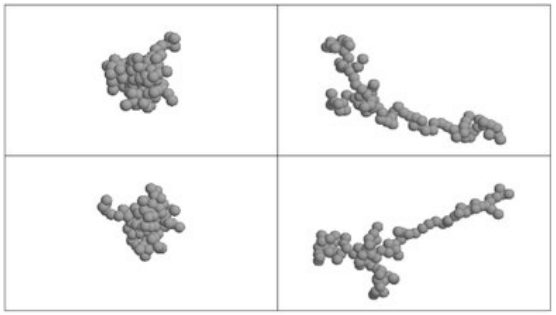
I: scattering intensity [-]
I_i: light intensity before impingement [-]
$f(\theta)$: geometrical factor accounting for polarization for incident and collected light [-]
R_0: distance between sample and detector [m]
P: form factor [-]
S: structure factor [-]
c: concentration [m^{-3}]
V_s: molecular volume solvent [m^3]
V_p: molecular volume particle [m^3]
$\Delta\rho$: difference in scattering length density [m^{-2}]

$$q = \left|\vec{q}\right| = \frac{4\Pi \sin\Theta}{\lambda}$$

http://www.lsinstruments.ch/technology/static_light_scattering_sls/

Structure factor

Tells us something about inter-particle interactions or particle arrangement within clusters.



$$S(\vec{q},c) = \frac{1}{N}\sum_{j,k}\left\langle \exp\left[-i\vec{q}(\vec{r}_j(t) - \vec{r}_k(t))\right]\right\rangle$$

phase shift between light scattered by particle *j* and *k*

S: structure factor [1]
N: number of scattering centers [1]
r_x: position of particle *x* to time *t* [m]

Structure factor

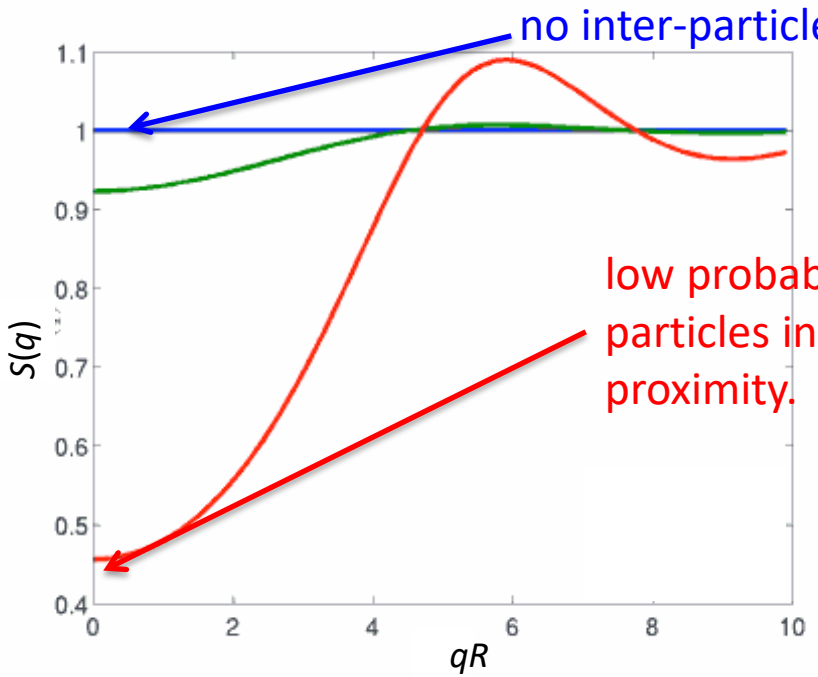
Introducing pair correlation function:

$$S(q) = 1 + c\int_0^{\infty} [g(r,c) - 1] \frac{\sin(qr)}{qr} 4\Pi r^2 dr$$

for c ➔ 0: S = 1

S: structure factor [1]
r_x: position of particle x to time t [m]
g: pair correlation function [1]
c: concentration [m^{-3}]

example: colloidal dispersion

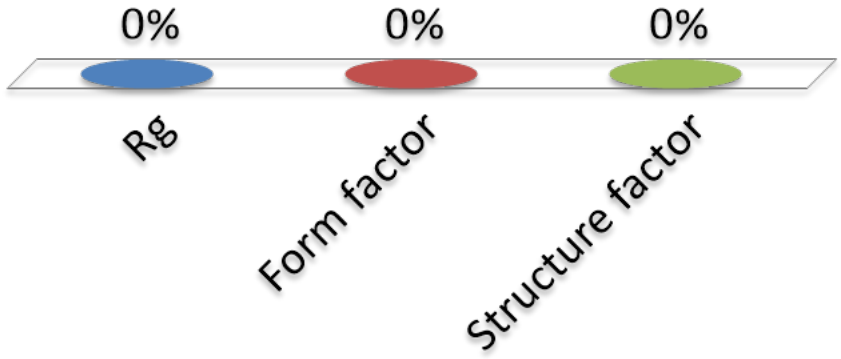


For particle dispersions and if measured at low (qR) values:
$S(q) < 1$: particles are repellant
$S(q) > 1$: particles are attractive

http://www.lsinstruments.ch/technology/static_light_scattering_sls/structure_factor/

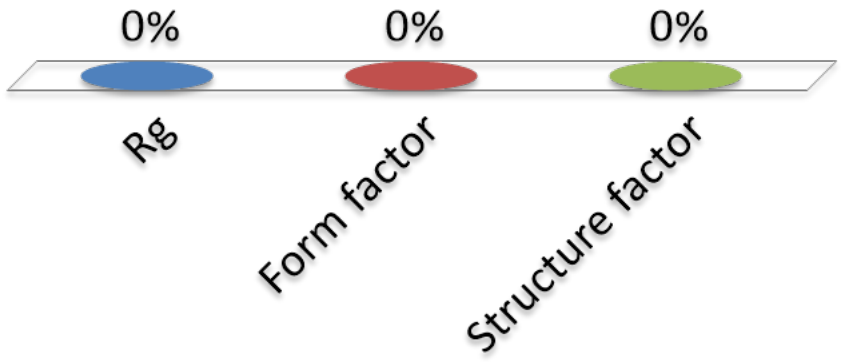
From what parameter can you extract information about the shape of a particle

A. R_g
B. Form factor
C. Structure factor



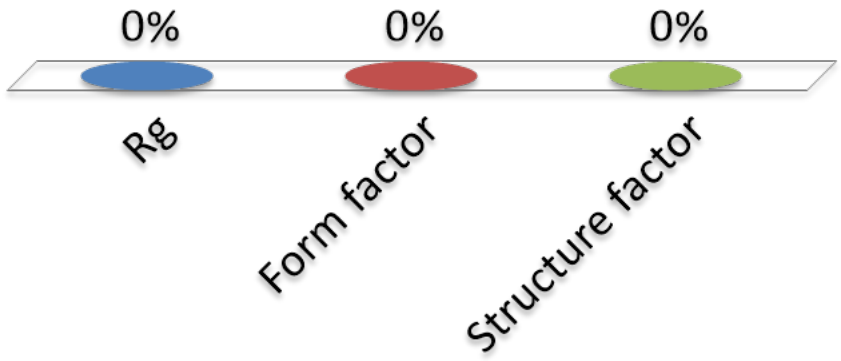
From what parameter can you extract information about the size of a particle

A. R_g
B. Form factor
C. Structure factor



From what parameter can you extract information about the aggregation state of a particle

A. R_g
B. Form factor
C. Structure factor

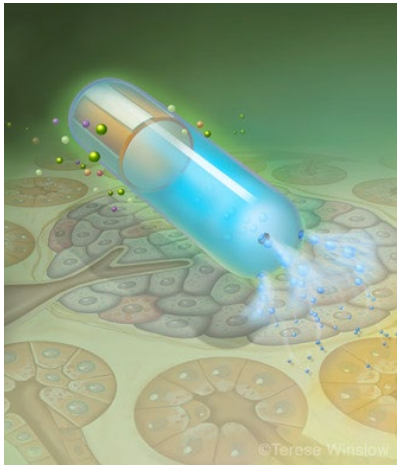


Outline

- Introduction
  - Vesicles
  - Vesicle production
- Liposomes
- Polymersomes
- Characterization
- Applications

Applications

drug delivery

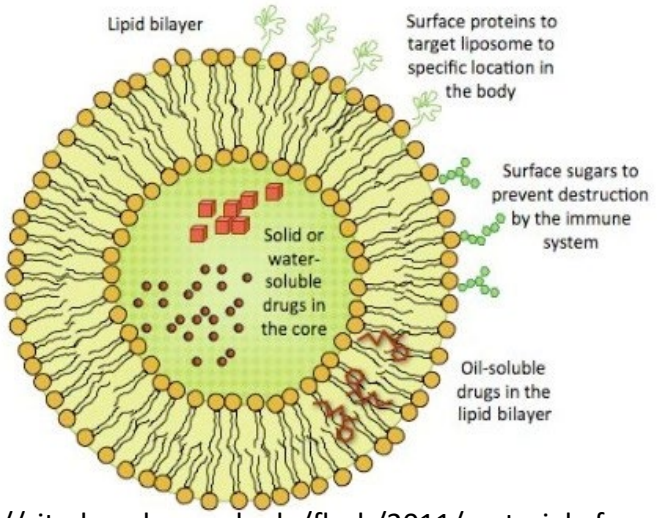


cosmetics

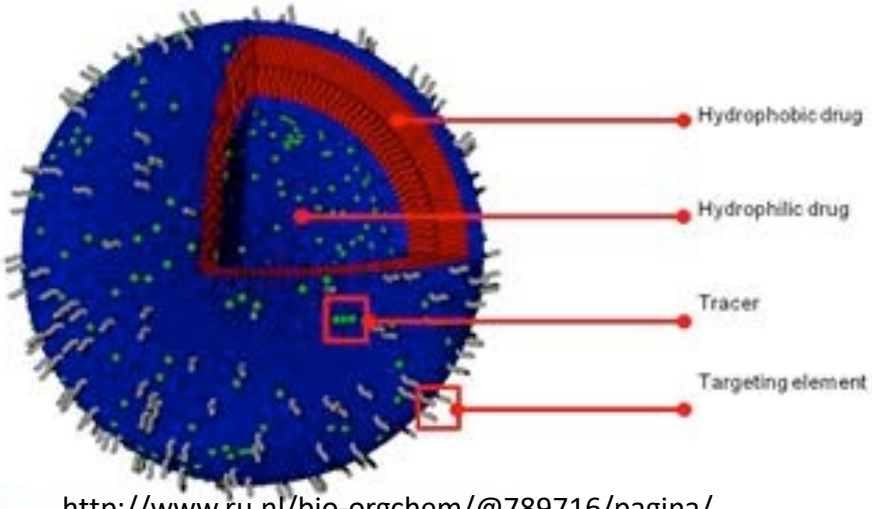
coatings

food

Vesicles as delivery vehicles

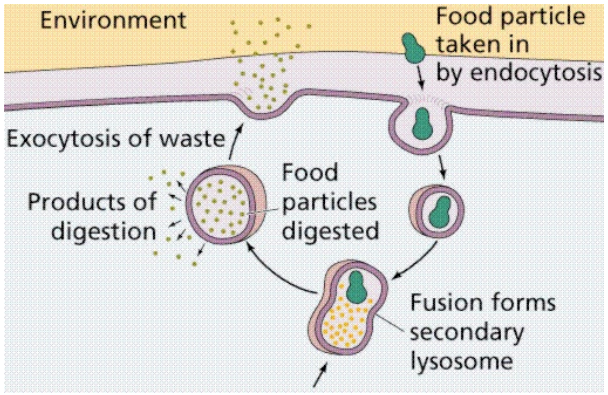


http://sitn.hms.harvard.edu/flash/2011/materials-for-drug-delivery/



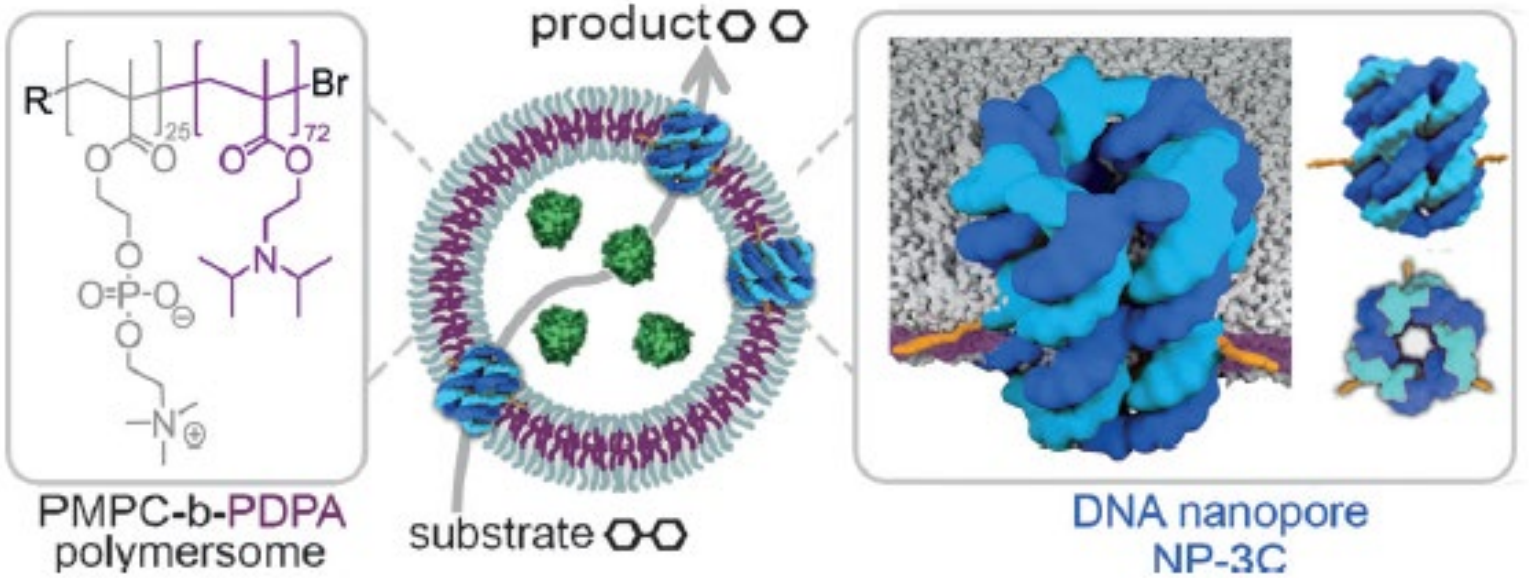
http://www.ru.nl/bio-orgchem/@789716/pagina/

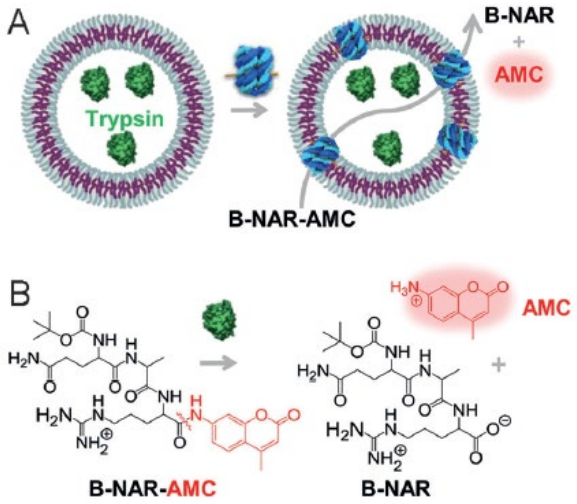
Vesicles in the body

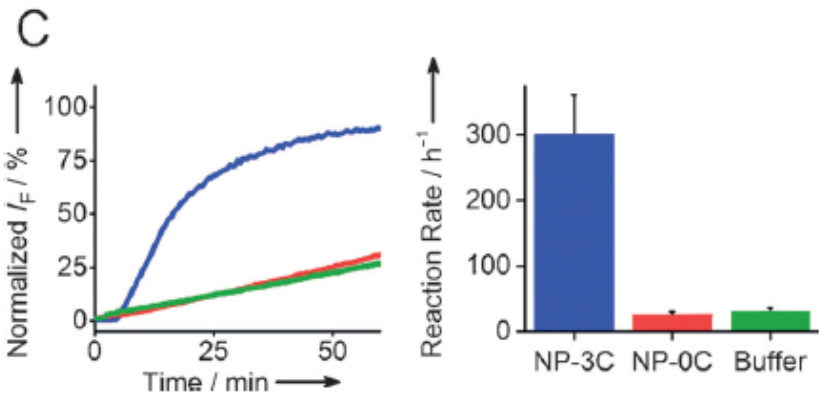


http://www2.estrellamountain.edu/faculty/farabee/BIOBK/BioBooktransp.html

Rendering polymersomes permeable







Messager *et al., Angewandte Chemie International Edition,* 2016, 55 (37), 11106-11109