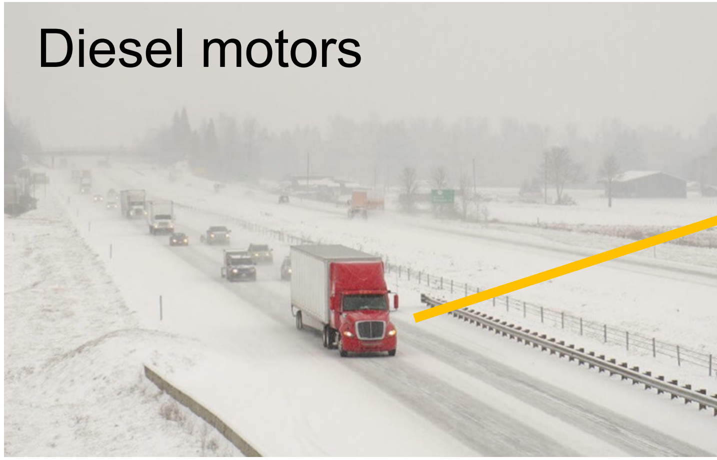
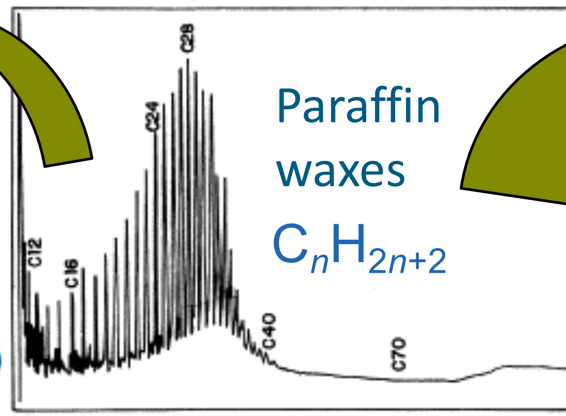
Soft-Matter and Biophysics Systems Studied with Small-Angle Neutron Scattering

Aurel Radulescu

Forschungszentrum Jülich GmbH, Jülich Centre for Neutron Science (JCNS) at Heinz Maier-Leibnitz Zentrum (MLZ), Garching, Germany

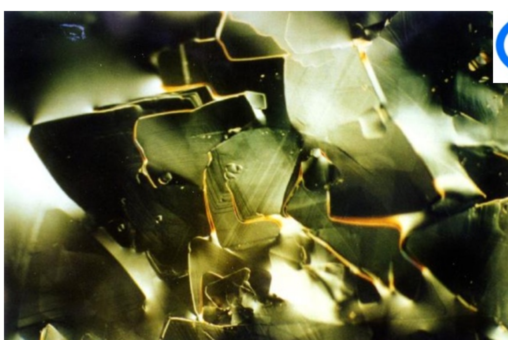


0°C → -20°C

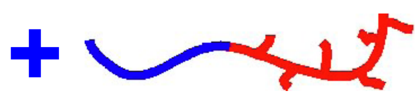


How?

untreated Diesel



treated Diesel

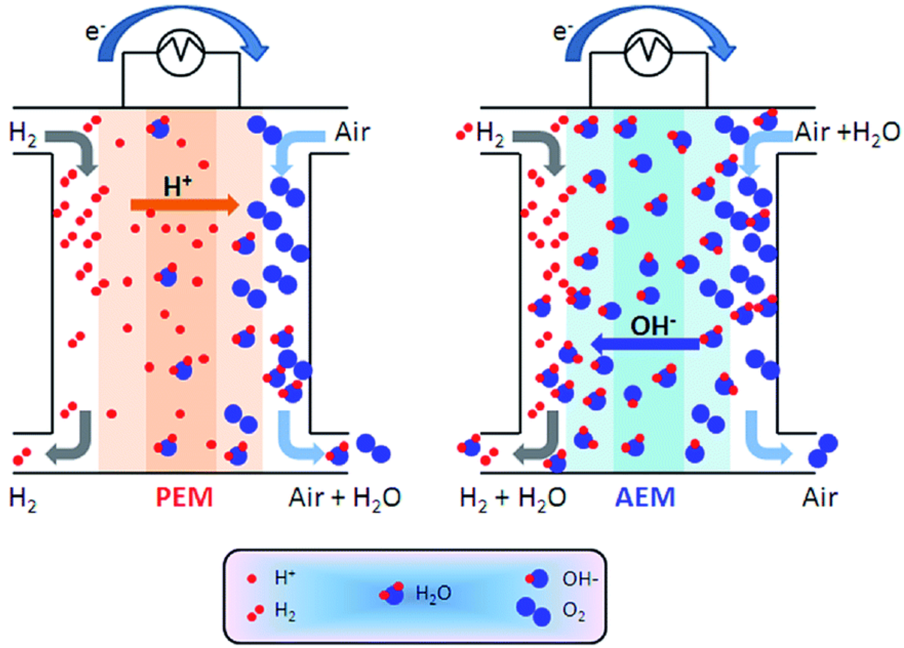


polymer additives

Energy Conversion via Fuel Cells

Fuel Cells (FC)

- convert chemical energy to electricity
- economical benefits (alternative to oil & coal)
- environmental benefits (less CO_2)
- proton-exchange membranes (PEM) or anion-exchange membranes (AEM) – polymers



Toyota

PEM FC (acidic medium)

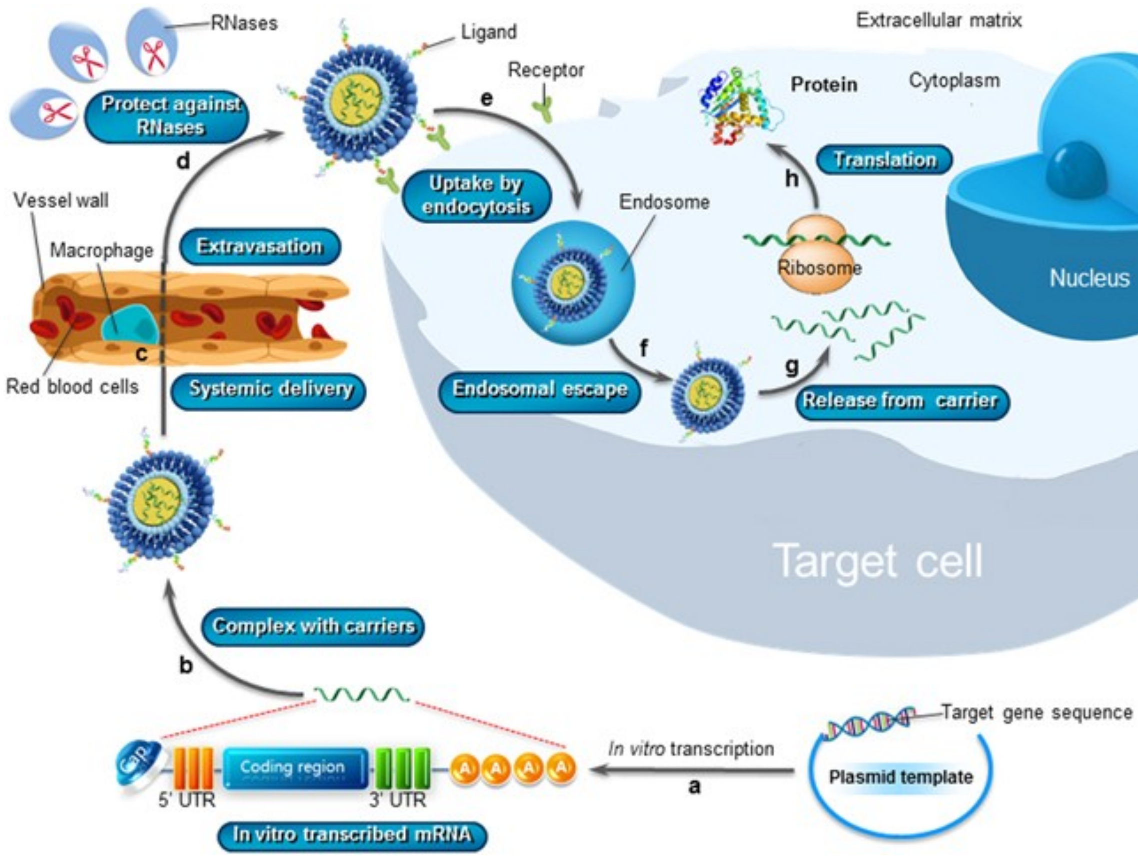
- in limited use
- but they need Platinum (Pt)

AEM FC (alkaline medium)

- do not need precious metals
- but the durability is still low

How to increase durability of AEM?

Nanocarriers for mRNA Therapies

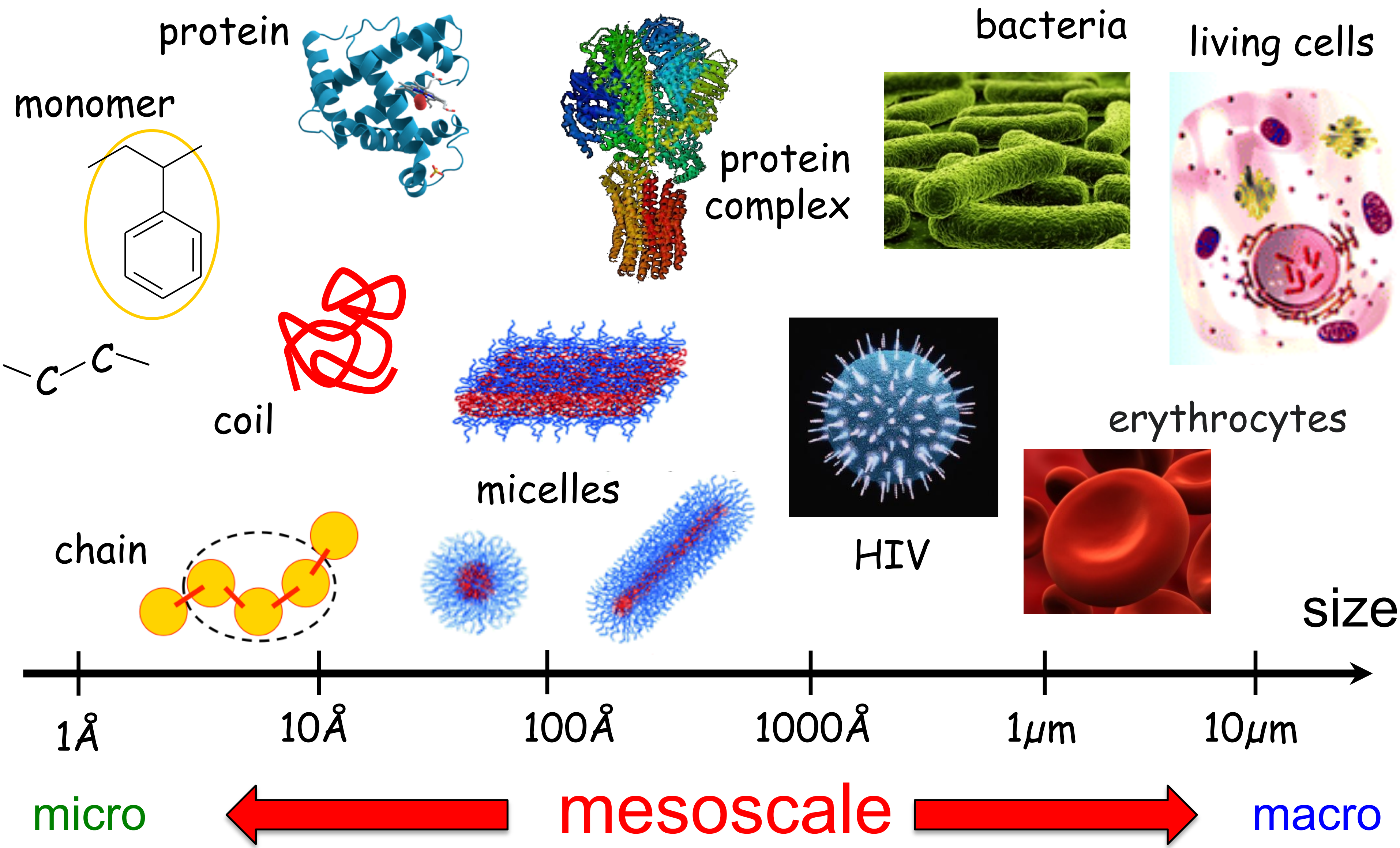


mRNA encodes a multitude of different proteins → in-vitro transcribed mRNA can regulate the aberrant or missing protein function

Lipid Nanoparticles (LNP) → since recently in clinical development to encapsulate, protect, carry and deposit the mRNA

How to optimize the composition of LNPs and increase the biological activity?

The Mesoscopic Lenght Scale

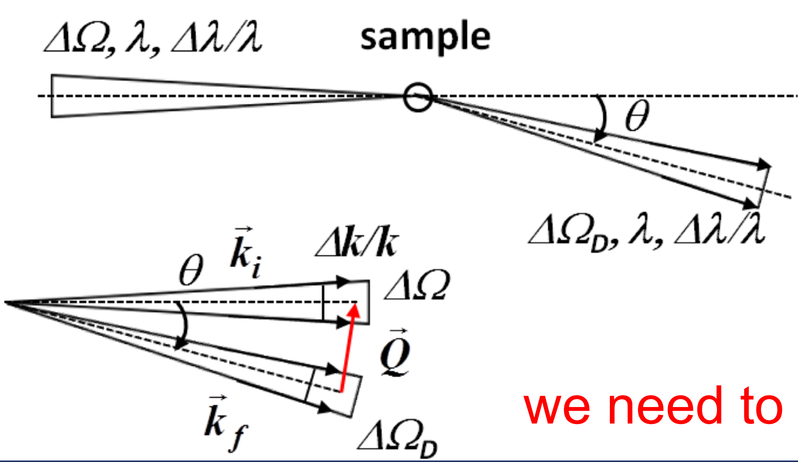


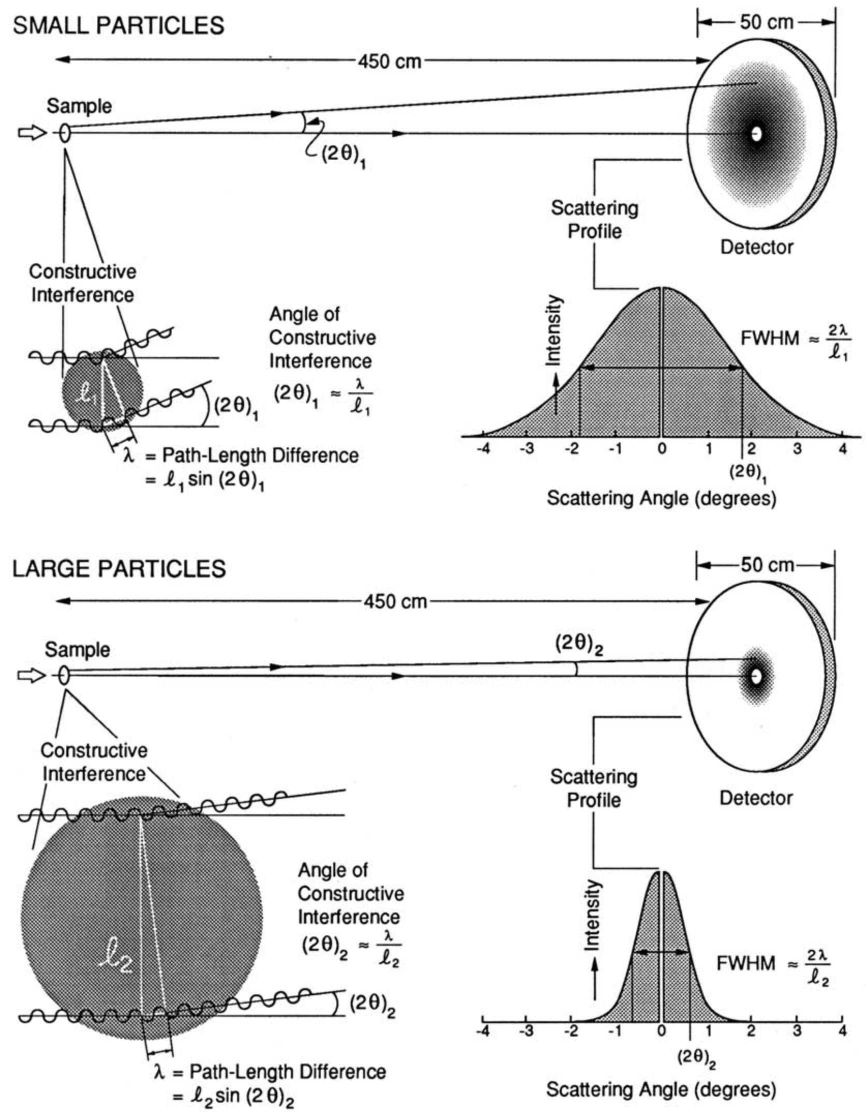
explore matter (structure) in reciprocal space

wave-vector transfer Q („scattering vector") – inverse yardstick

- large Q – small sizes – wide-angle neutron difraction (ND or WANS)
- small Q – large sizes – small-angle neutron scattering (SANS)

$$Q = |k_i - k_f| = 2k \sin\frac{\theta}{2} = \frac{4\pi}{\lambda}\sin\frac{\theta}{2}$$

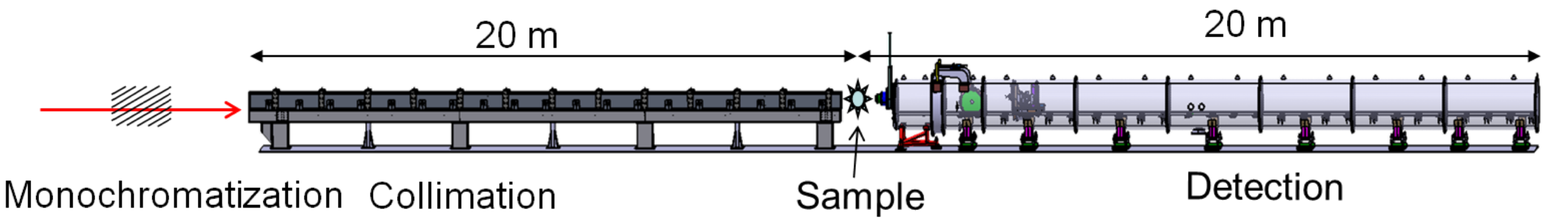




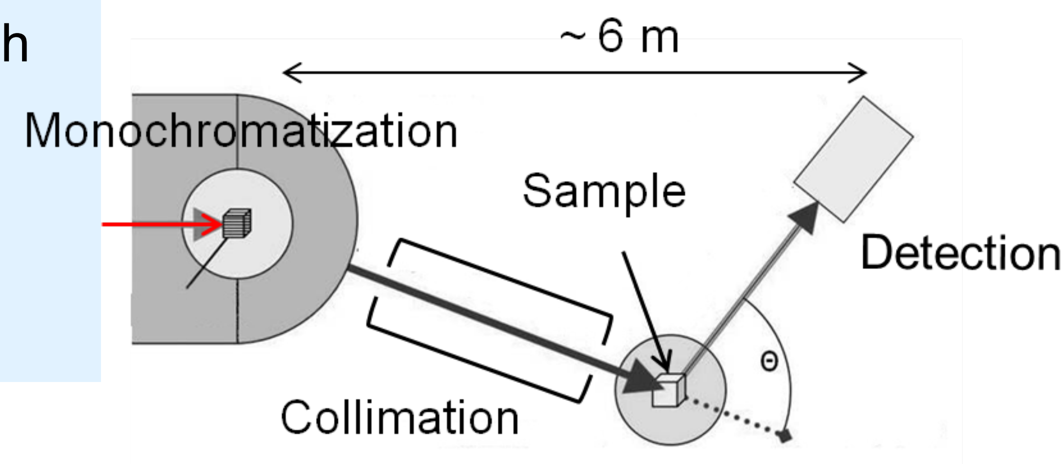
we need to know (define) λ - monochromatic beam

Neutron Diffractometers

SANS diffractometers – optimized for measurements at small angles
- long flight paths (collimated beam), typically 40m (D11 at ILL – 80m!)
- long wavelengths (λ > 4 Å), **cold neutrons!**
- aim at 10 Å – 1μm length scale

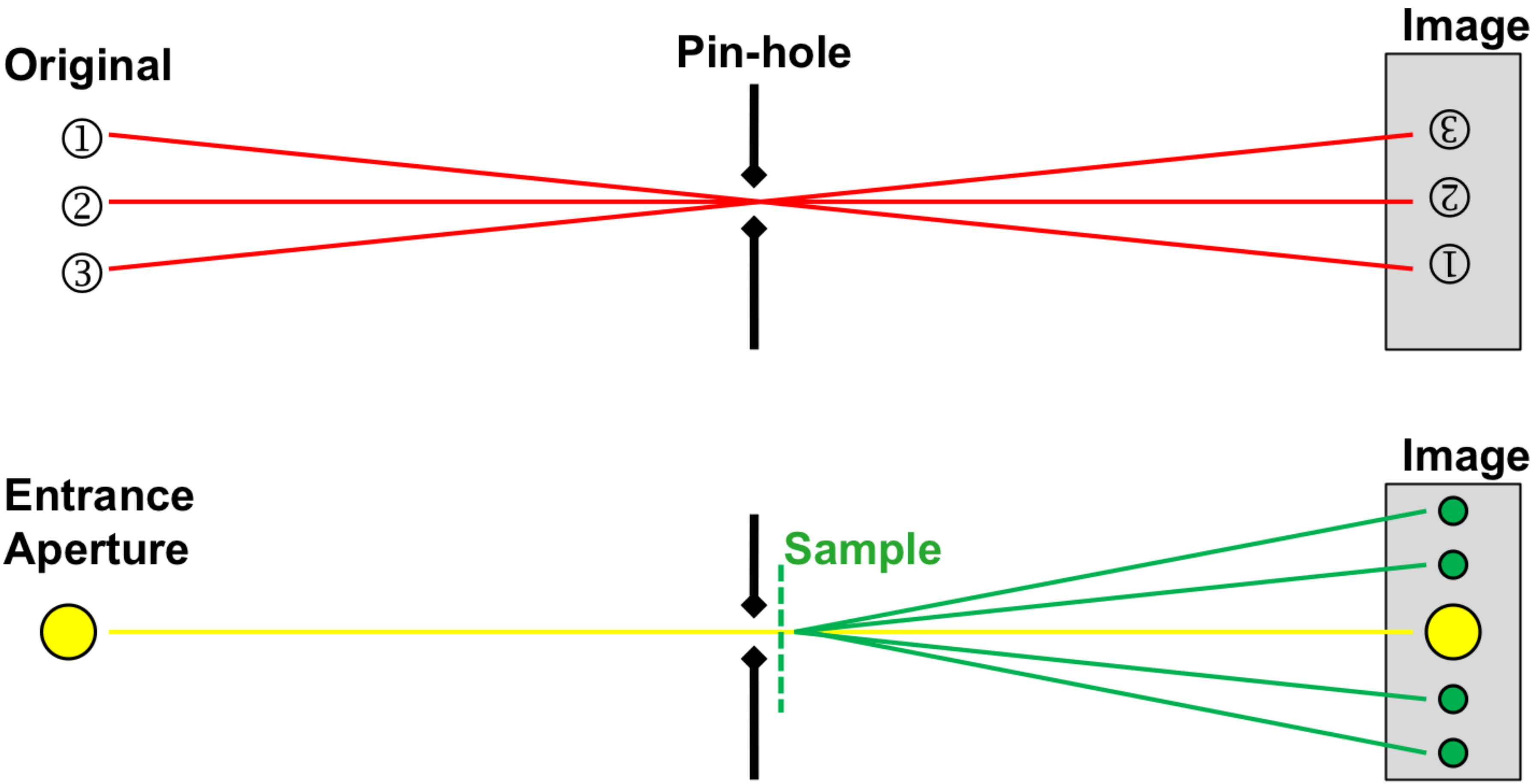


neutron diffractometers (WANS) – optimized for measurements at high angles
- compact instruments
- short wavelengths ($\lambda \sim$ 1-2Å), **thermal neutrons!**
- aim at 1-10 Å length scale

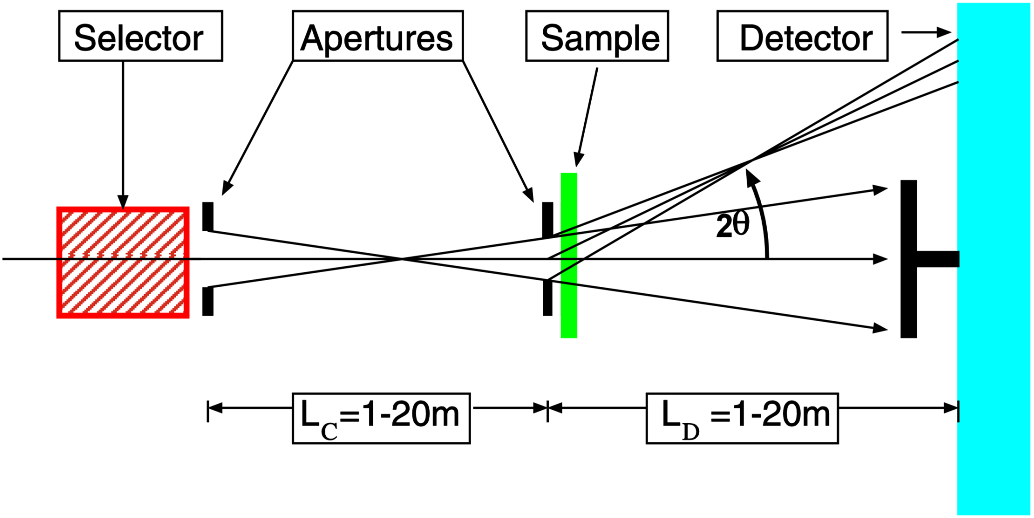


Pinhole Scattering Method

Magic of a pinhole camera for scattering

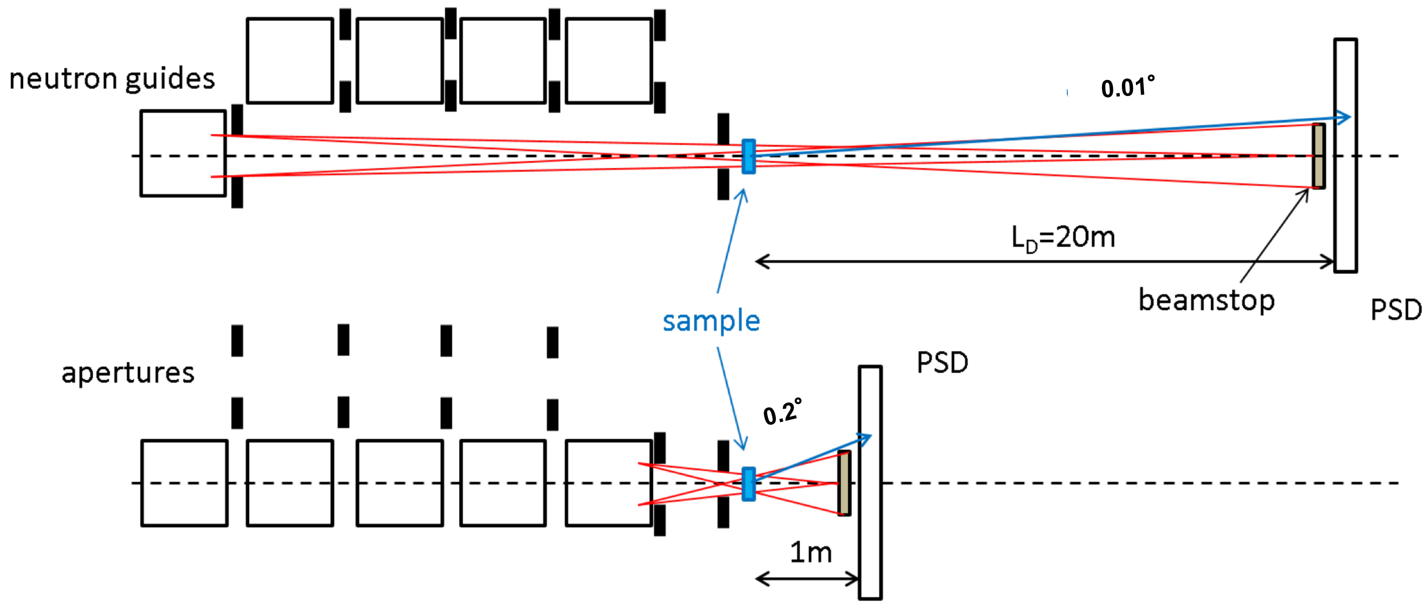


Pinhole Scattering Method



- $I(Q)$; $Q = 4\pi/\lambda \sin\theta/2$
- variable detection distance → wide angular range → wide Q-range
- typical Q-range pinhole SANS: $1\text{x}10^{-3}Å^{-1} \leq Q \leq 0.3Å^{-1}$
- use of several detection distances (typically, three) and one λ (typically, 5Å)

- L_D and λ – can be varied for reaching the scientific goal

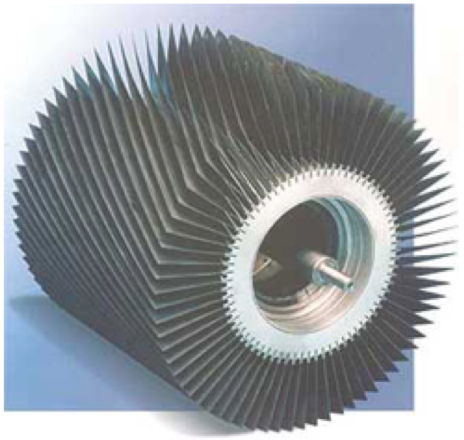


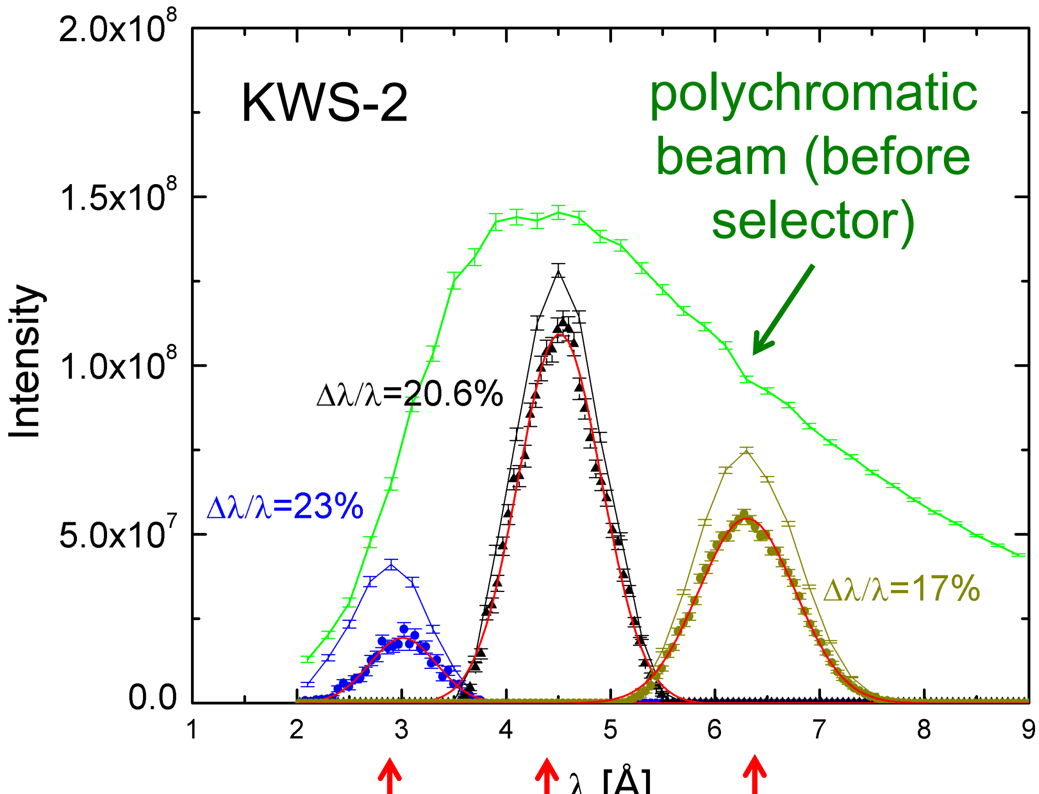
The SANS Monochromators

SANS – low resolution technique: high flux achieved by large $\Delta\lambda/\lambda$ → mechanical monocromators – velocity selectors (with twisted boronated lamellae)

n + ^{10}B → ^{7}Li* + ^{4}He → ^{7}Li + ^{4}He +2.31 MeV+ gamma

Astrium GmbH

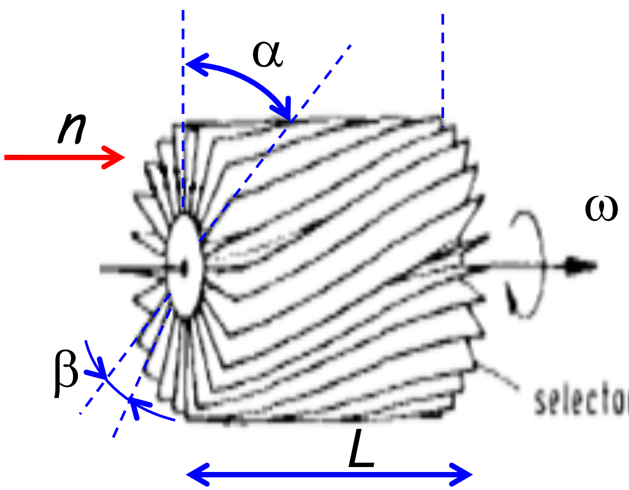




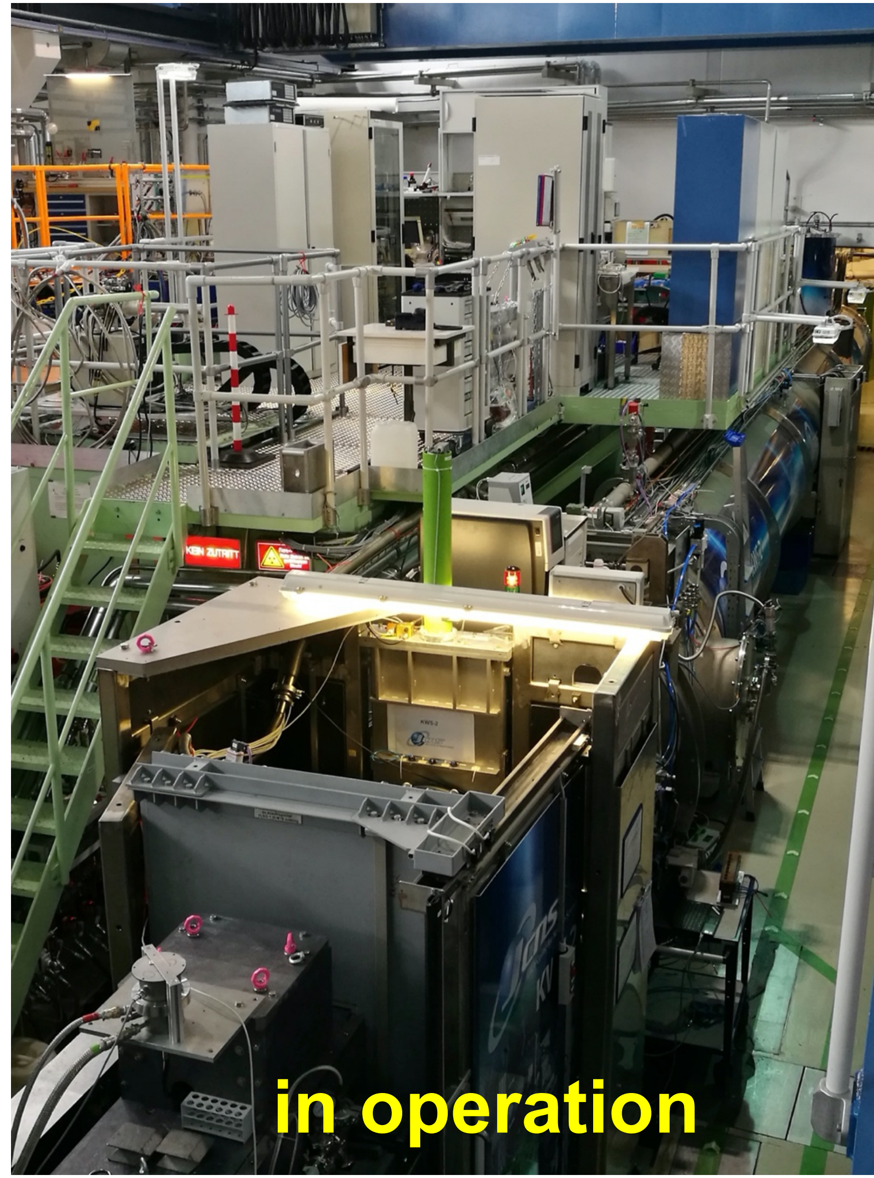
tilting angle -10° 0° +10°

λ & $\Delta\lambda/\lambda$ are defined by rotor parameters

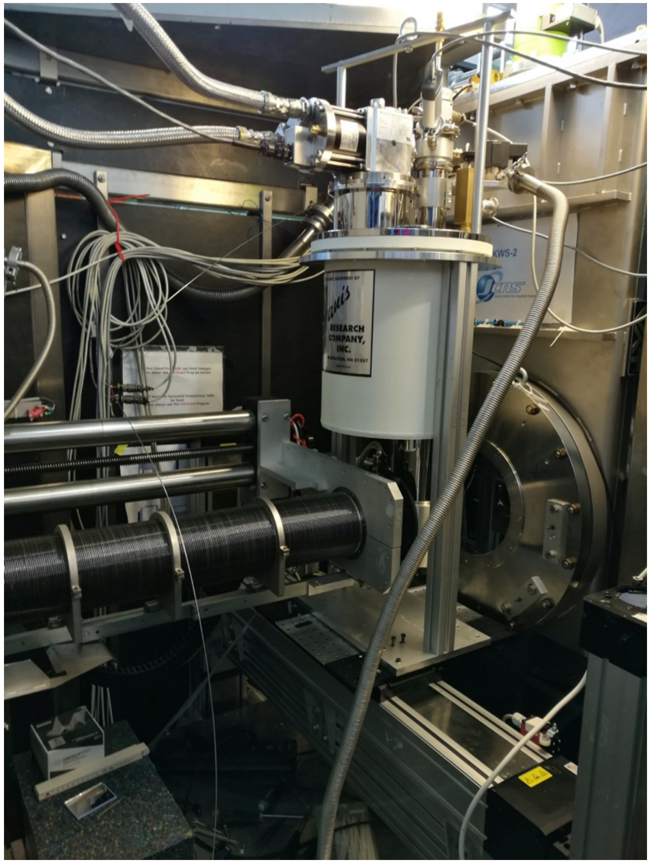
→ tilting to the beam axis → shift of λ, $\Delta\lambda/\lambda$



KWS-2 SANS @ MLZ, Garching, Germany

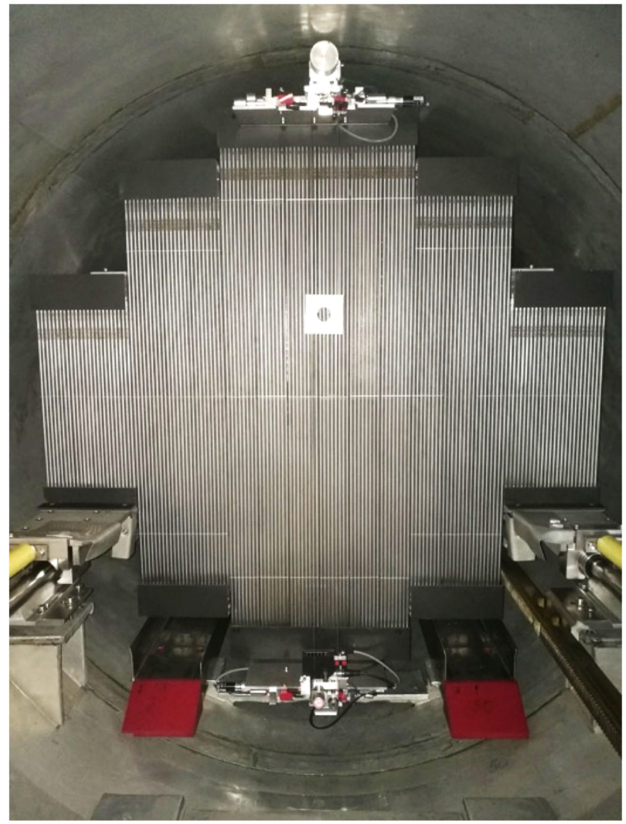


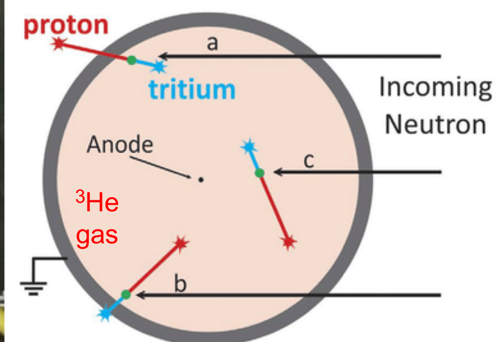
The Neutron Detector



sample position – space for large equipment (cryostats, magnets, etc.)

2D position sensitive detector – ^{3}He tubes array; movable between 1 m and 20 m after the sample; beam-stop in the middle (B_4C)

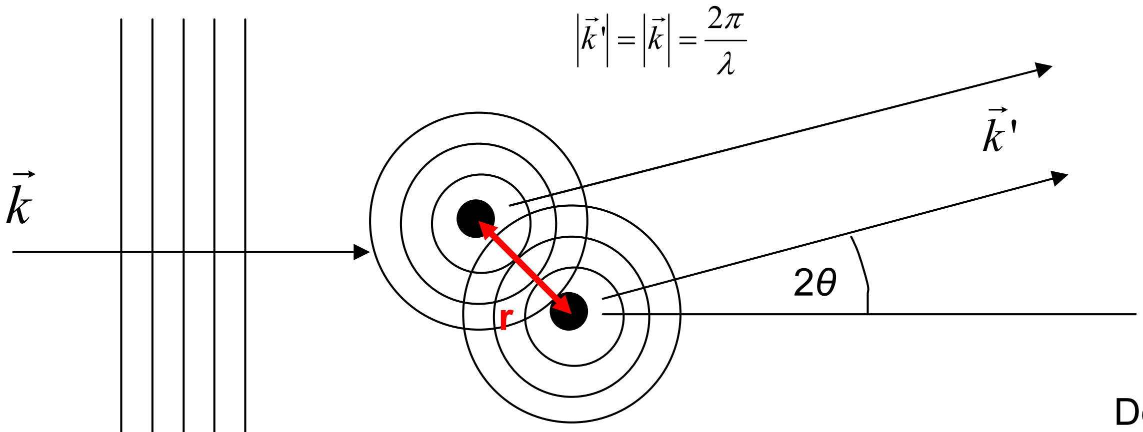




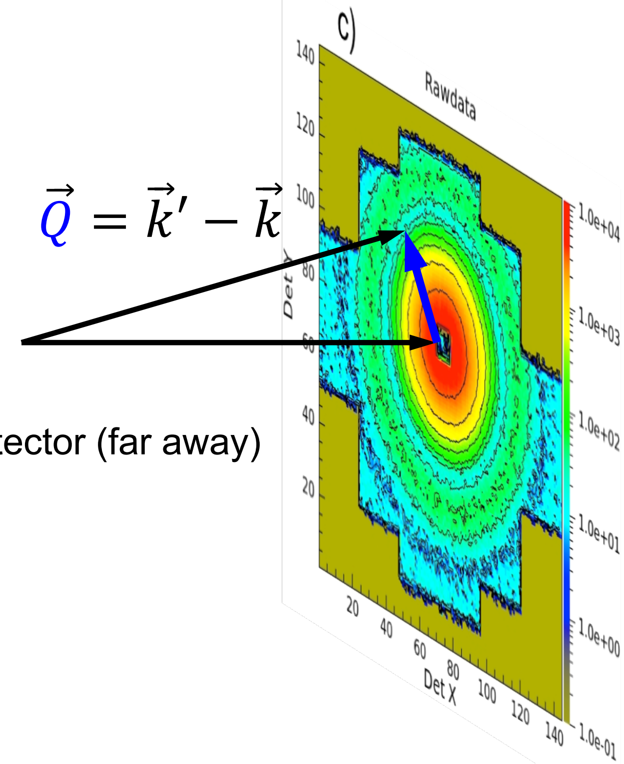
$$n + {}^{3}He \rightarrow {}^{3}H + {}^{1}H + 0.764\ \text{MeV}$$

Scattering Principle

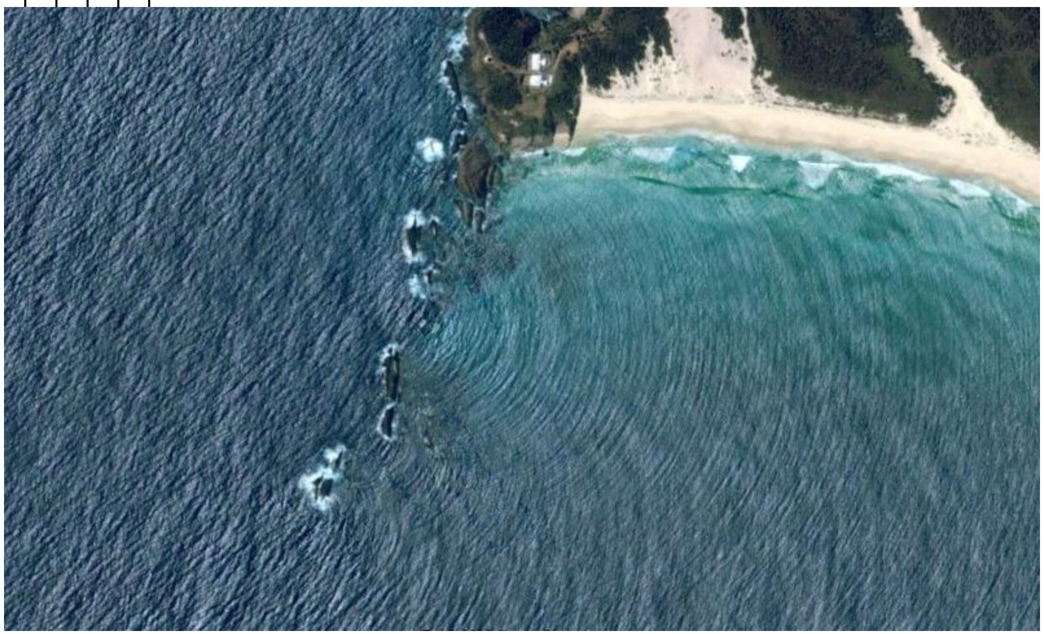
Diffraction – neutrons recorded only as a function of the wave-vector transfer $\vec{Q}$



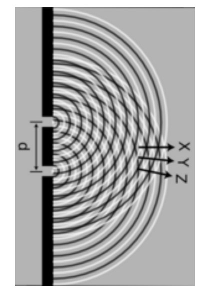
$\vec{Q} = \vec{k}' - \vec{k}$



Detector (far away)



Huygens-Fresnel principle



The Scattering Length Density

Fermi pseudopotential

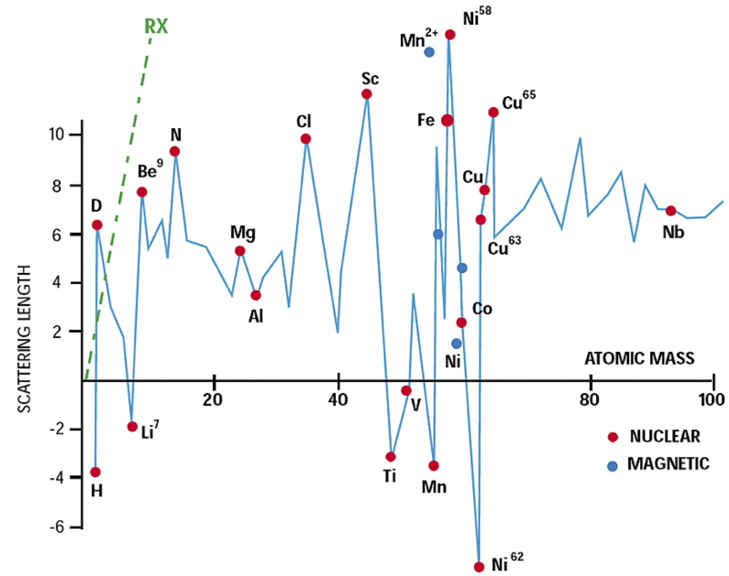
$$V(\vec{r}) = (2\pi \hbar^2)/m_n \; b\,\delta(\vec{r})$$

b – the scattering length

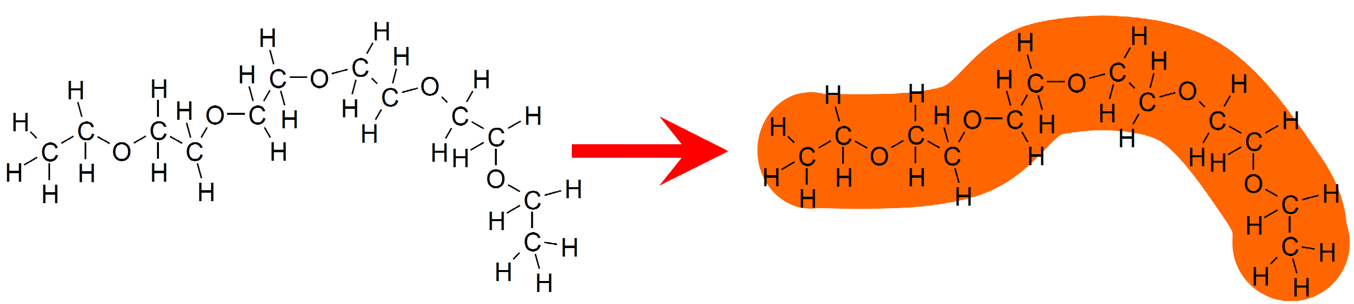
sum over all nuclei

$$\frac{d\sigma}{d\Omega}(\mathbf{q}) = \frac{1}{N}\left|\sum_{i}^{N} b_i e^{i\mathbf{q}\cdot\mathbf{r}}\right|^2$$

coherent term



When the length scales in question are much larger than atomic dimensions and it is easier to think in terms of material properties → the scattering length density $\rho(\vec{r})$



$$\rho_{\mathrm{mol}} = \frac{1}{V_{\mathrm{mol}}} \sum_{j \in \{\mathrm{mol}\}} b_j$$

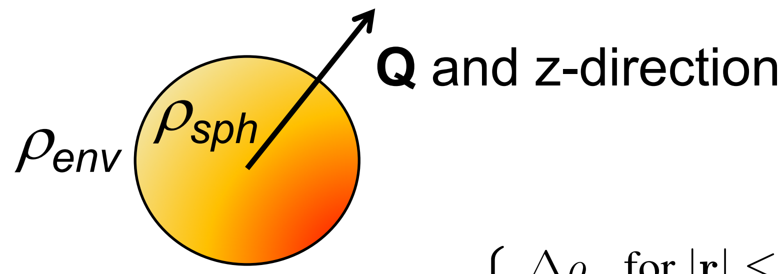
The Scattering from Single Particles

small angle scattering → inhomogeneities in scattering length density $\rho(\vec{r})$

$$\frac{d\Sigma}{d\Omega}(\mathbf{q}) = \frac{N}{V}\frac{d\sigma}{d\Omega}(\mathbf{q}) = \frac{1}{V}\left|\int_V \rho(\mathbf{r})e^{i\mathbf{q}\cdot\mathbf{r}}d\mathbf{r}\right|^2$$

$$\frac{d\Sigma}{d\Omega}(\mathbf{q}) = \frac{d\Sigma_{coh}}{d\Omega}(\mathbf{q}) + \frac{d\Sigma_{inc}}{d\Omega} + \frac{d\Sigma_{abs}}{d\Omega}$$

homogeneous particle



$$\rho_{\text{single}}(\mathbf{r}) = \begin{cases} \Delta\rho & \text{for } |\mathbf{r}| \le R \\ 0 & \text{for } |\mathbf{r}| > R \end{cases}$$

$$= \int_0^{2\pi} d\phi \int_0^{\pi} d\vartheta \ \sin\vartheta \int_0^{R} dr\ r^2\ \Delta\rho\ \exp\left(\mathrm{i}|\mathbf{Q}|\cdot|\mathbf{r}|\cos(\vartheta)\right)$$

$$= 2\pi\ \Delta\rho \int_0^{R} dr\ r^2 \left[\frac{1}{\mathrm{i}Qr}\exp\left(\mathrm{i}QrX\right)\right]_{X=-1}^{X=+1}$$

$$= 4\pi\ \Delta\rho \int_0^{R} dr\ r^2 \frac{\sin(Qr)}{Qr}$$

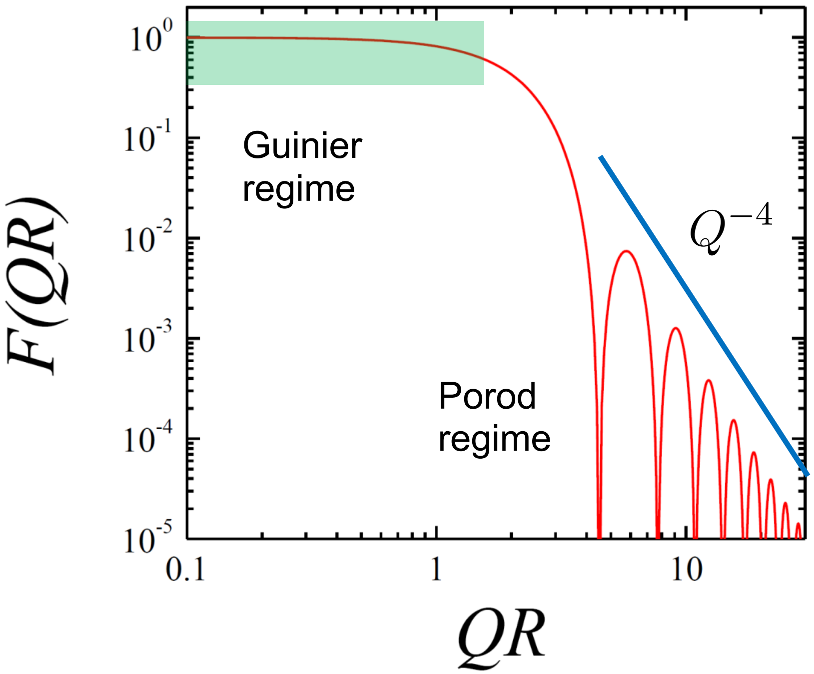
$$= \Delta\rho\ \frac{4\pi}{3}R^3 \left(3\frac{\sin(QR) - QR\cos(QR)}{(QR)^3}\right)$$

$$\frac{d\Sigma}{d\Omega}(\mathbf{Q}) = \frac{N}{V}\cdot\left|\rho_{\text{single}}(\mathbf{Q})\right|^2 =$$

$$= (\Delta\rho)^2\ \phi_{\text{spheres}}\ V_{\text{sphere}}\ F(\mathbf{Q})$$

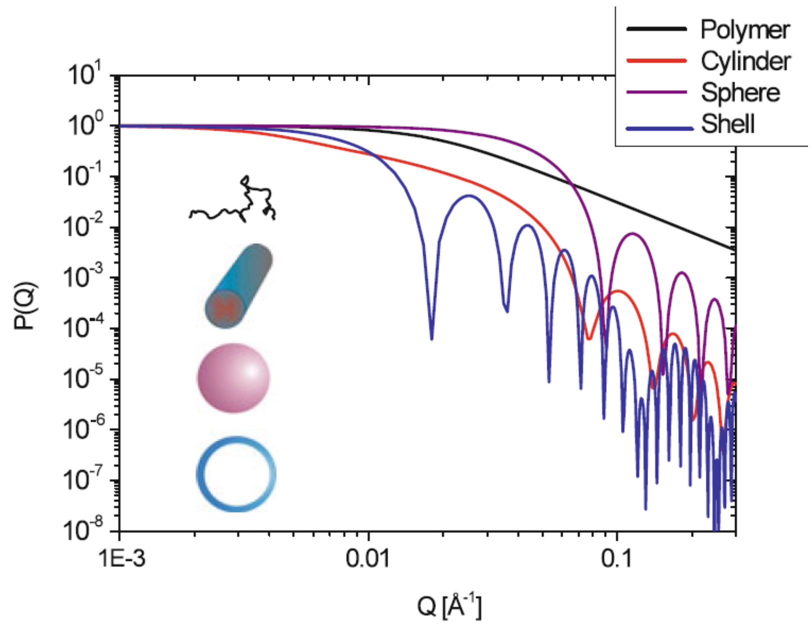
the form factor

The Form Factor F(Q)



Low-Q $\frac{d\Sigma}{d\Omega}(\mathbf{Q}\to 0) = \frac{d\Sigma}{d\Omega}(0)\cdot\exp\left(-\frac{1}{3}Q^2R_g^2\right)$

High-Q $\frac{d\Sigma}{d\Omega}(Q) = P\cdot Q^{-4}$ ➡ $2\pi(\Delta\rho)^2 S_{\mathrm{tot}}/V_{\mathrm{tot}}$

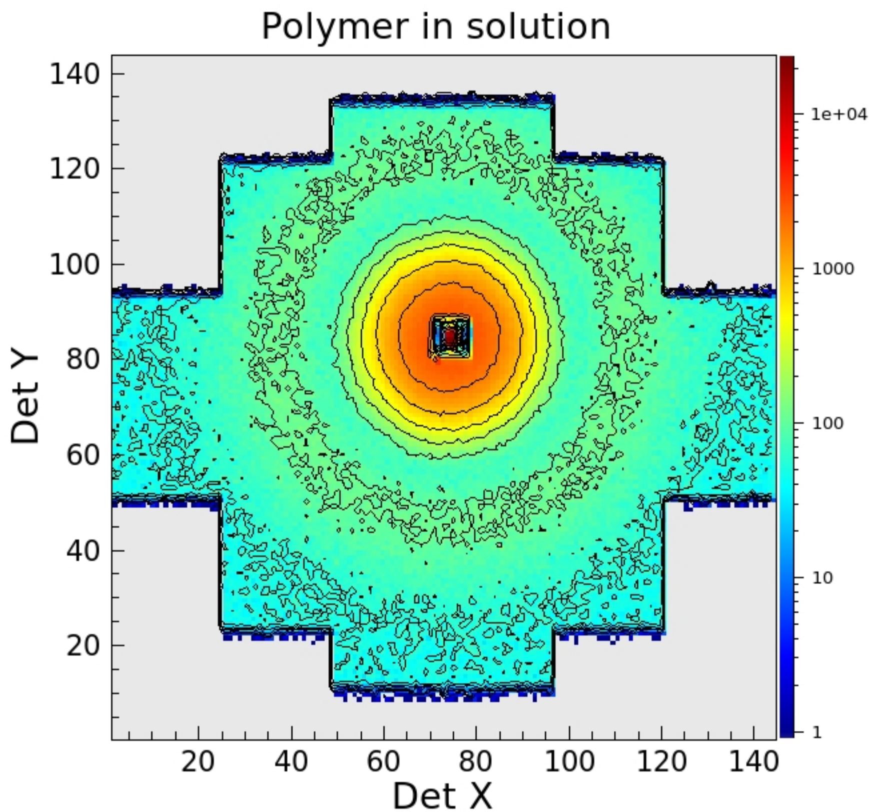


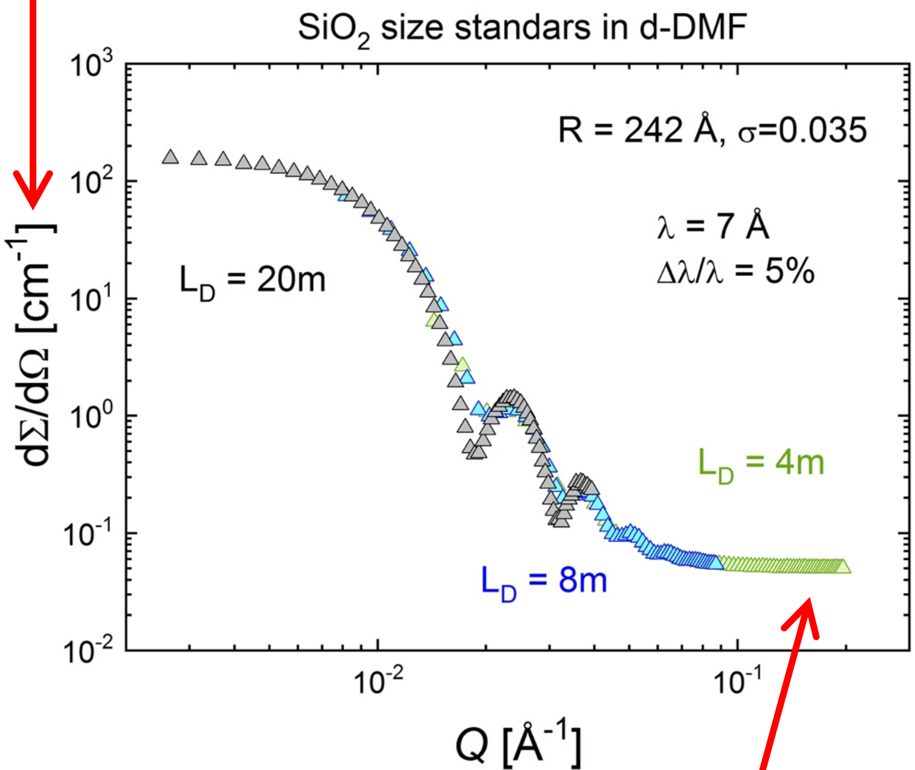
$$F(Q)=\begin{cases}\frac{2(\exp(-y)-1+y)}{y^2}, y=(QR_g)^2\\ (A_s(Q,R))^2, A_s(Q,R)=\frac{3(\sin(QR)-QR\cos(QR))}{(QR)^3}\\ \left(\frac{R_2^3A_s(Q,R_2)-R_1^3A_s(Q,R_1)}{R_2^3-R_1^3}\right)^2\\ \int_0^{\pi/2}\left(\frac{\sin(Q\cdot L\cos(\alpha)/2)}{Q\cdot L\cos(\alpha)/2}\frac{2J_1(Q\cdot R\sin(\alpha))}{Q\cdot R\sin(\alpha)}\right)^2\sin(\alpha)d\alpha\end{cases}$$

The SANS Experimental Results

$$\frac{d\Sigma}{d\Omega}(\mathbf{Q}) = \frac{N}{V}\cdot\left|\rho_{\mathrm{single}}(\mathbf{Q})\right|^2 = \boxed{(\Delta\rho)^2\ \phi_{\mathrm{spheres}}\ V_{\mathrm{sphere}}\ F(\mathbf{Q})}$$

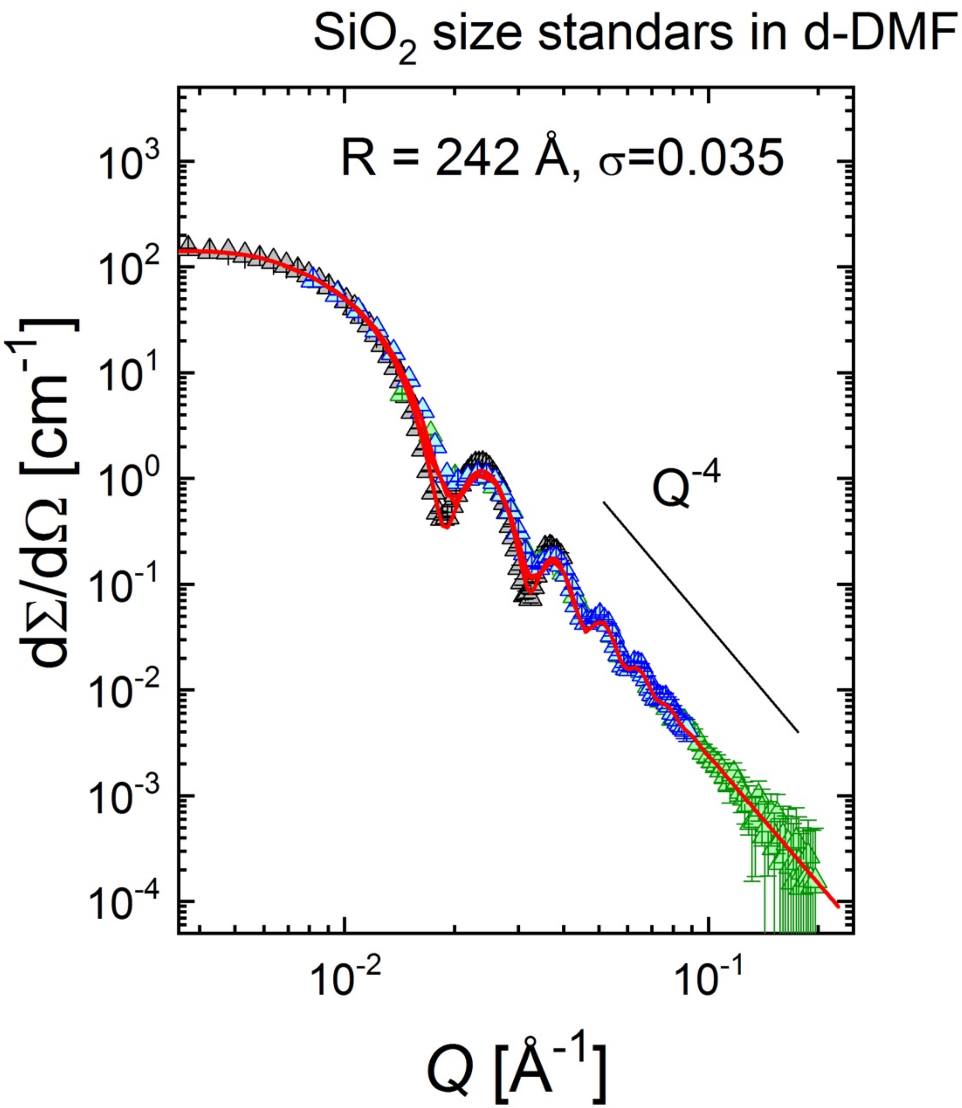
Units: $(m/m^3)^2$ 1 m^3 1





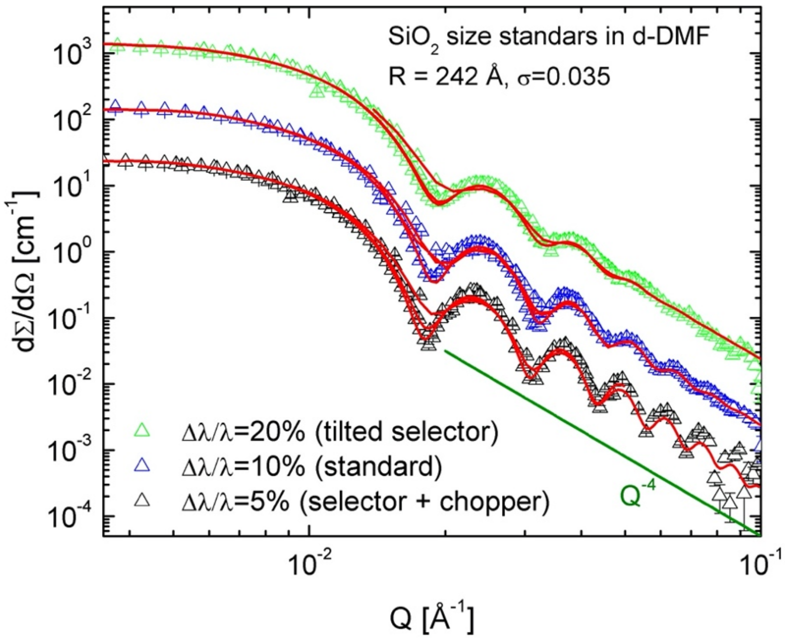
incoherent, solvent

The Instrumental Resolution



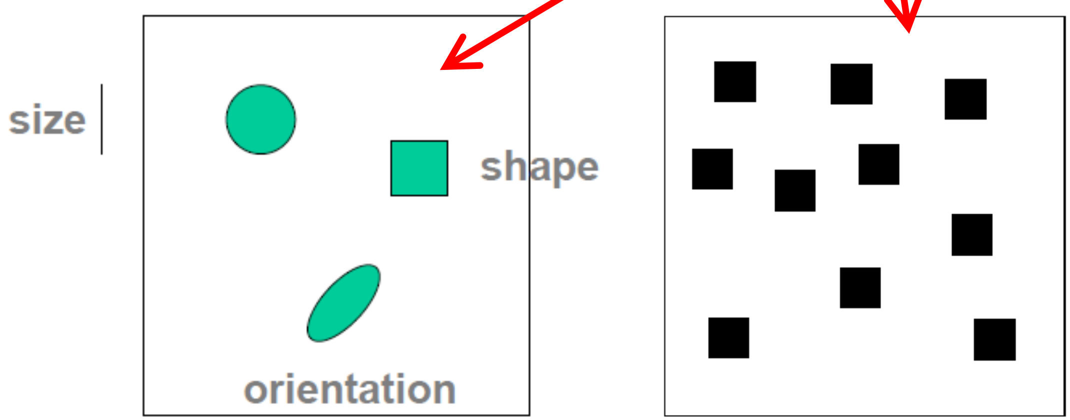
$$\left(\frac{\Delta Q}{Q}\right)^2 = \left(\frac{\Delta\lambda}{\lambda}\right)^2 + \left(\frac{2\Delta\theta}{2\theta}\right)^2$$

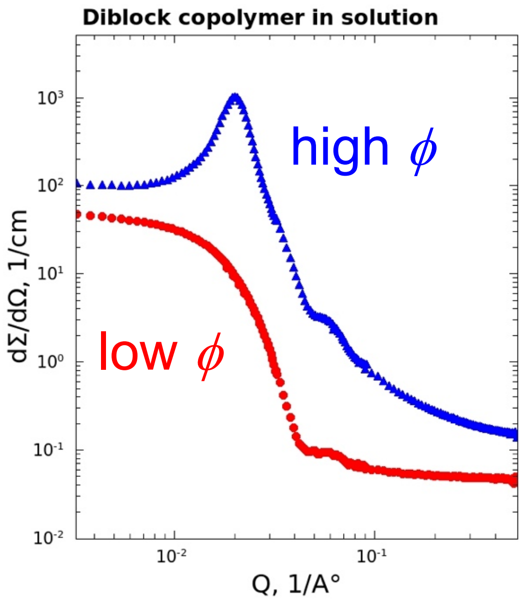
$$\left.\frac{d\Sigma(\bar{Q})}{d\Omega}\right|_{\text{meas}} = \int_0^\infty dQ\; R(Q-\bar{Q}) \cdot \left.\frac{d\Sigma(Q)}{d\Omega}\right|_{\text{theo}}$$

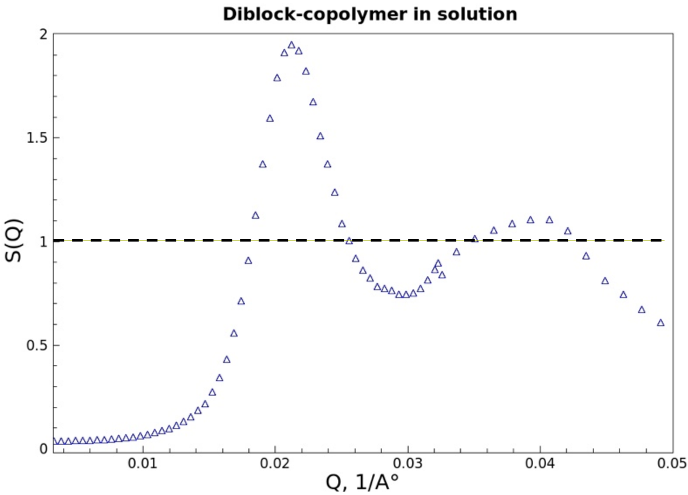


The Structure Factor S(Q)

$$I(Q) = \frac{d\Sigma_{coh}}{d\Omega}(Q) + B = \phi V_p \Delta\rho^2 P(Q) S(Q) + B$$





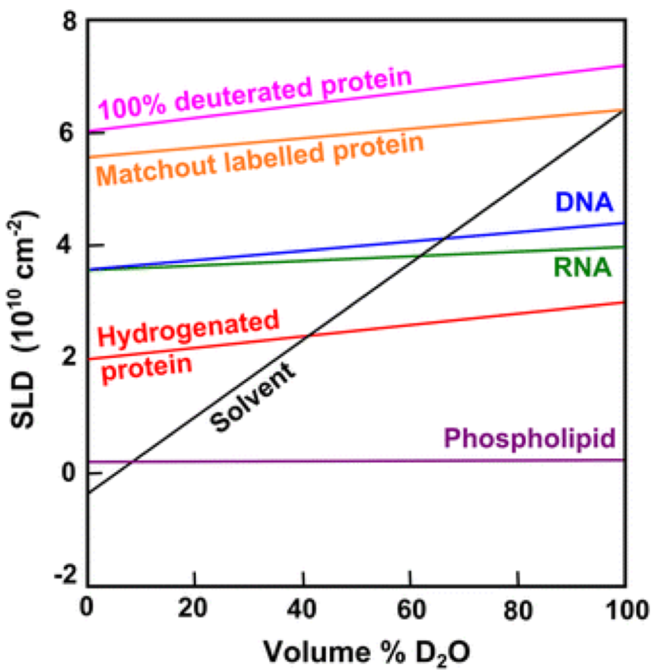


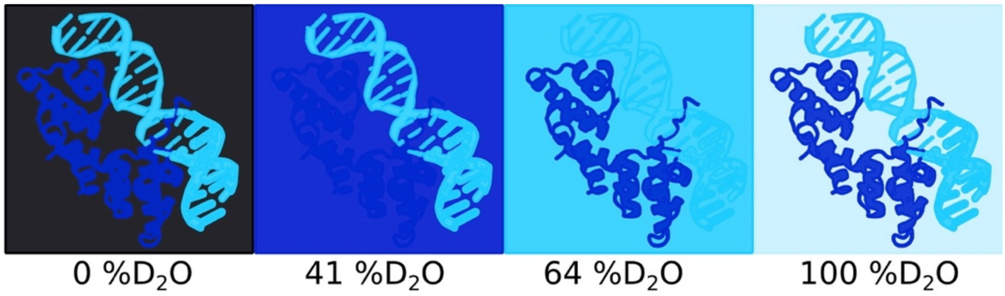
- $\Delta\rho^2$ – the contrast factor
- *P*(*Q*) – the form factor (single particle); *P*(*Q*)=F^2(*Q*), FT of real-space density distribution
- *S*(*Q*) – the structure factor (inter-particle, FT of *g*(r))
- *B* – the background (incoherent & matrix)

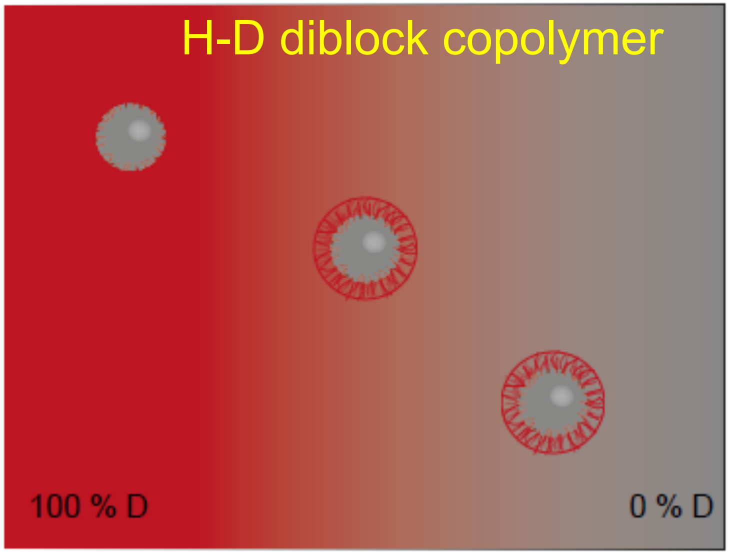
The Contrast Factor in Neutron Scattering

$$I(Q) = \frac{d\Sigma_{coh}}{d\Omega}(Q) + B = \phi V_p \Delta\rho^2 P(Q) S(Q) + B$$

contrast factor: $\Delta\rho = (\rho_{particle} - \rho_{matrix})$

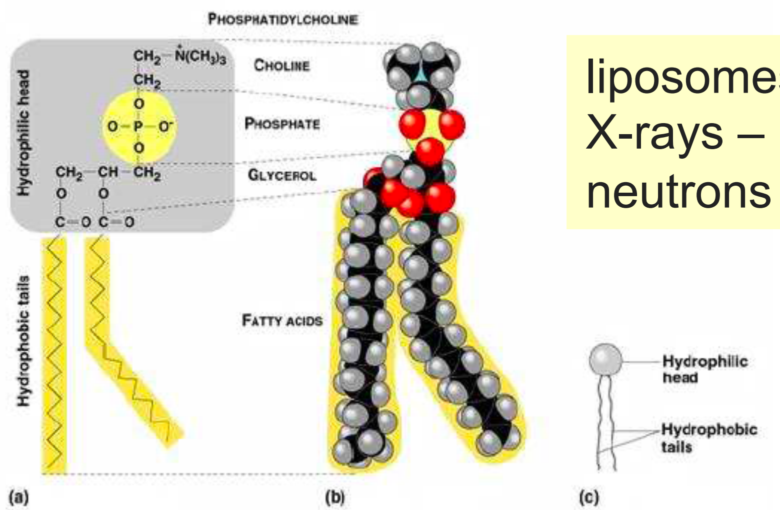






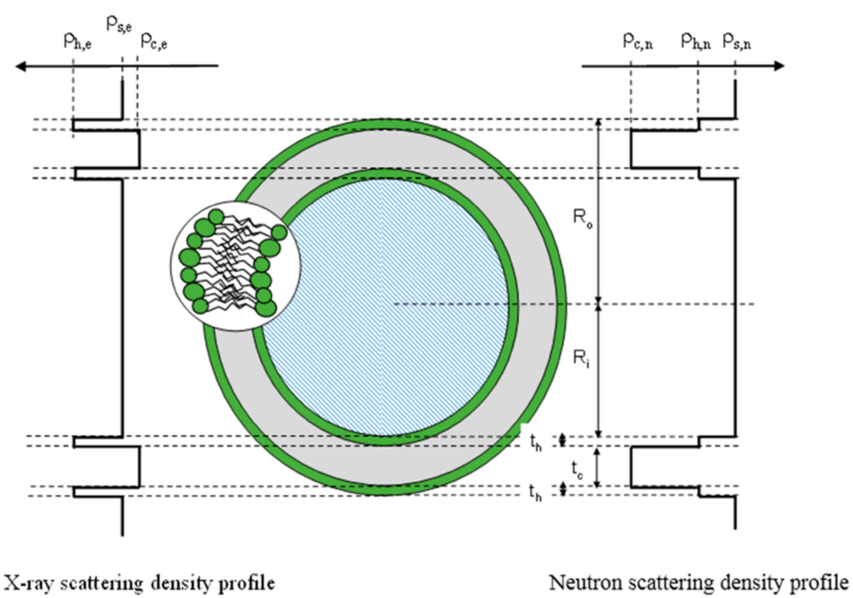
difference in scattering length between H (-3.74×10^{-15}m) and D (6.67×10^{-15} m)
→ unique advantage in case of multicomponent hydrocarbon systems: soft-matter & biophysics

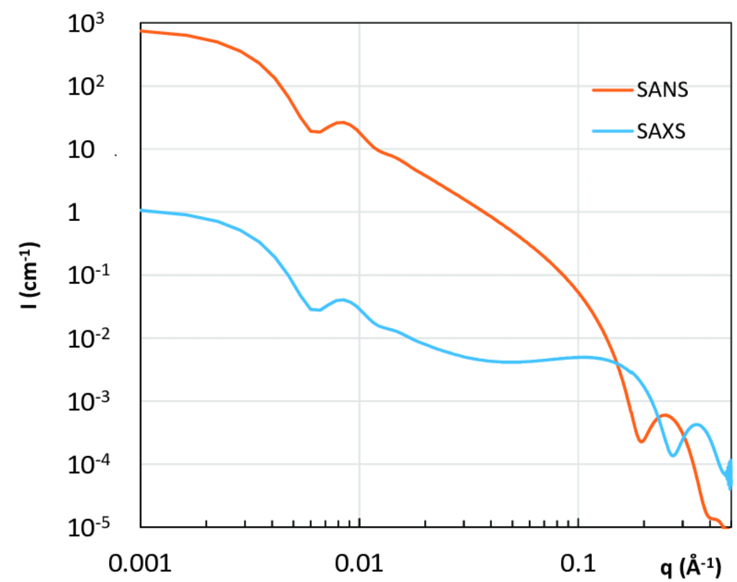
SANS vs. SAXS



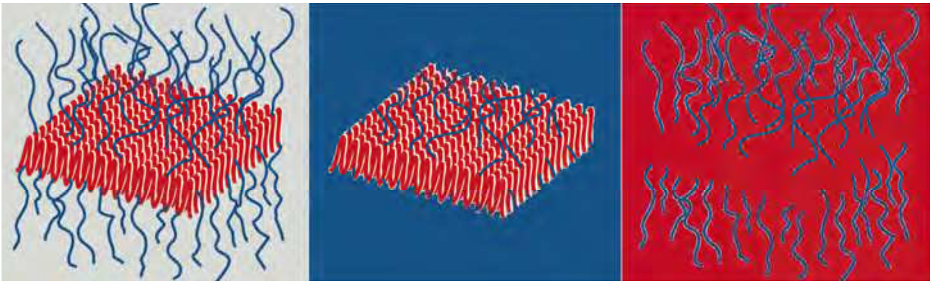
liposomes made of phospholipids in buffer solution:
X-rays – more sensitive to the polar layer (P, N)
neutrons – provide information on the hydrophobic layer

combining SAXS and SANS (contrast variation) → full characterization of complex materials

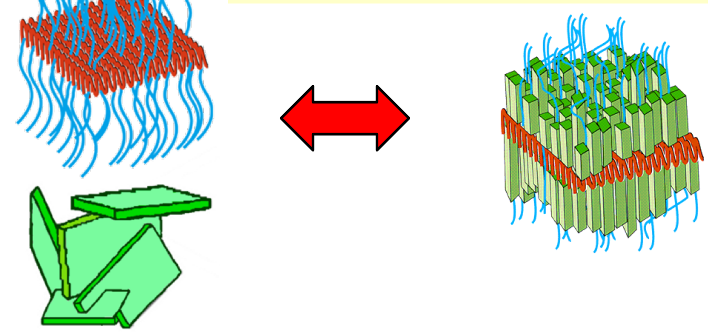




Polymer Additives for Diesels and Crude Oils

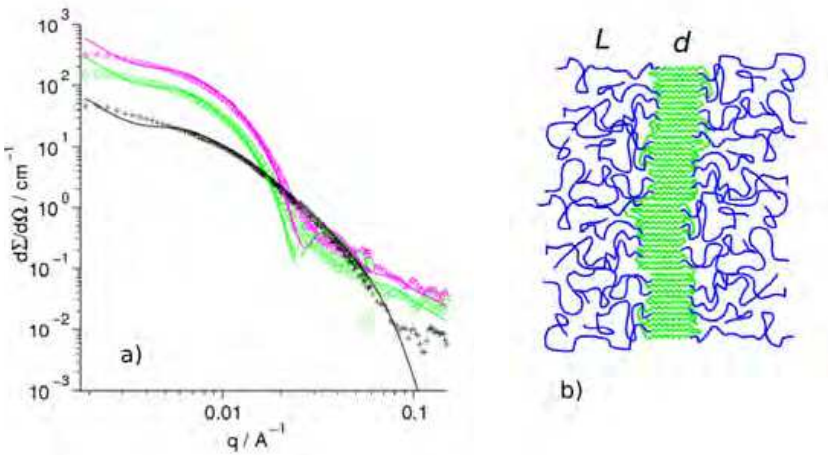


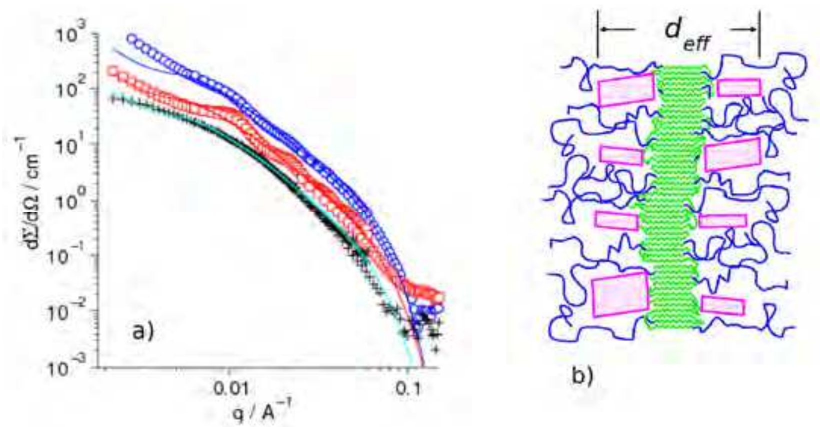
Infineum, Paraflow™



SANS with contrast matching on model ternary systems: polymer additive + wax + solvent

A. Radulescu et al., in *Crude Oil Emulsions* 2012





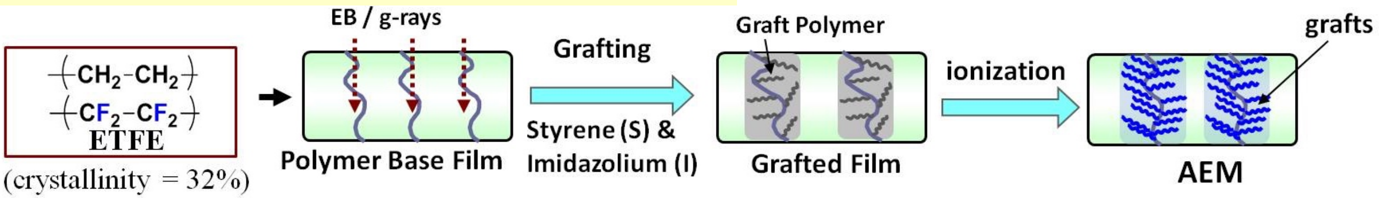
PE-PEP crystalline-amorphous copolymer: core-brush lamellar morphology

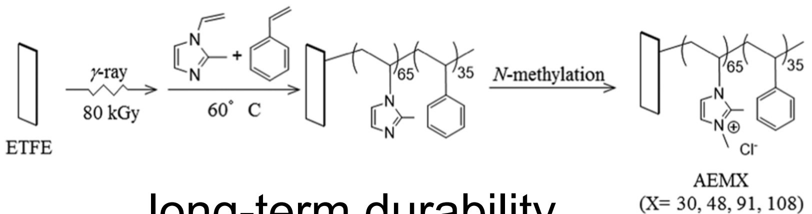
crystalline core – nucleation platform for wax crystallization at low temperature
amorphous brush – arrests the wax crystals growth

Anion-Echange Membranes for Fuel Cells

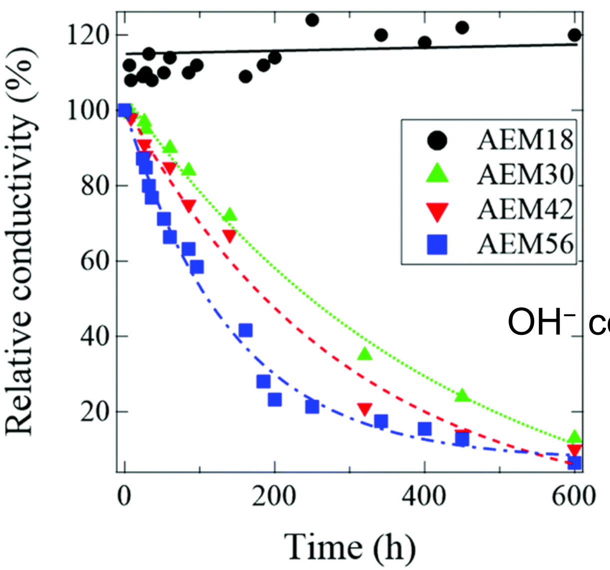
Department of Advanced Functional Materials Research, Takasaki Advanced Radiation Research Institute, Takasaki, Japan

fabrication of AEMs via radiation grafting technique





long-term durability

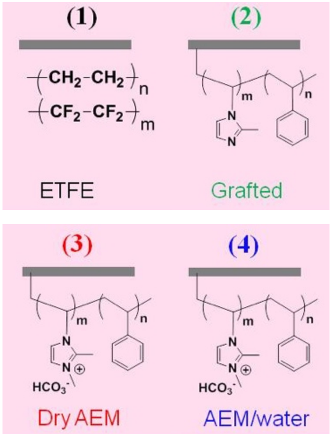


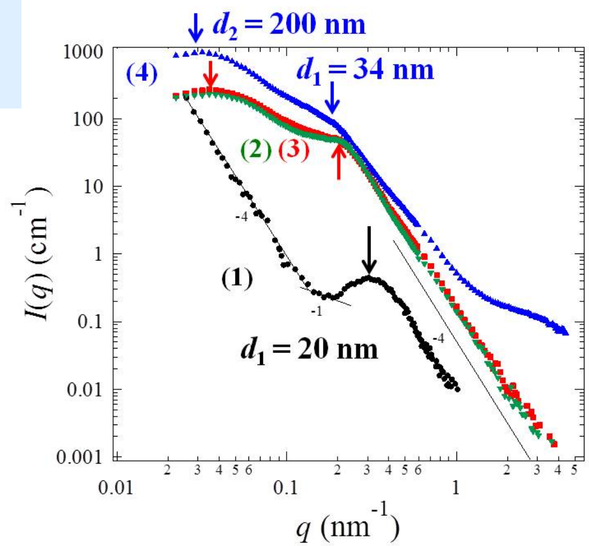
OH⁻ conductivity

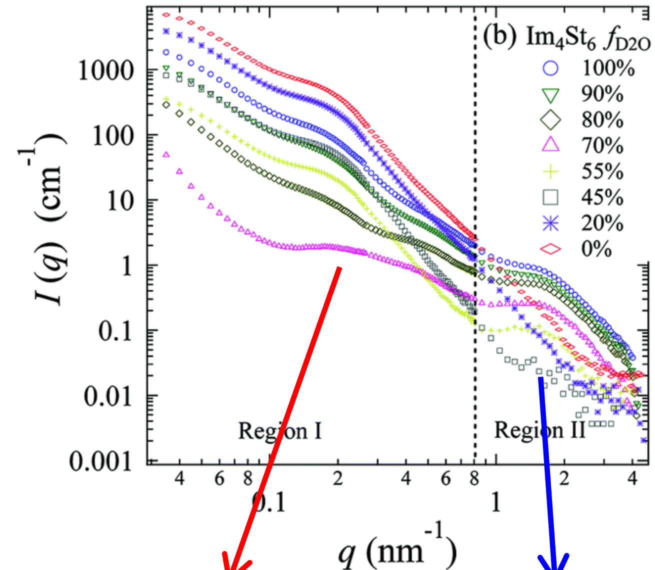
on the way to neutrons (Garching, Germany)

Anion-Echange Membranes for Fuel Cells

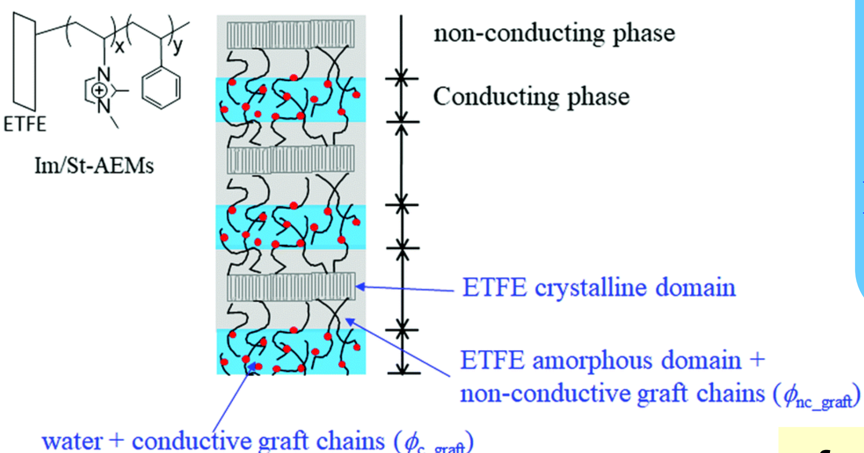
Y. Zhao, K. Yoshimura et al., in
Soft Matter 2021

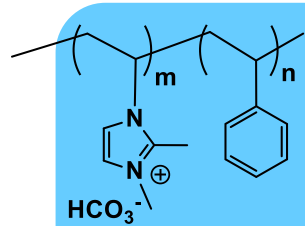




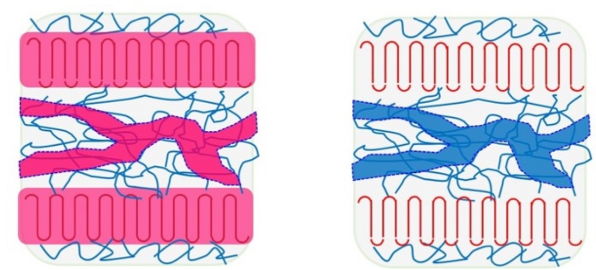


Conducting/non-conducting two phase system:





Hydrophilic phase:
grafts + water



matching of crystalline correlations

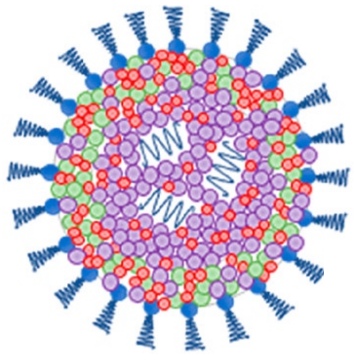
matching of amorphous hydropobic

feedback to chemistry, for improving fabrication

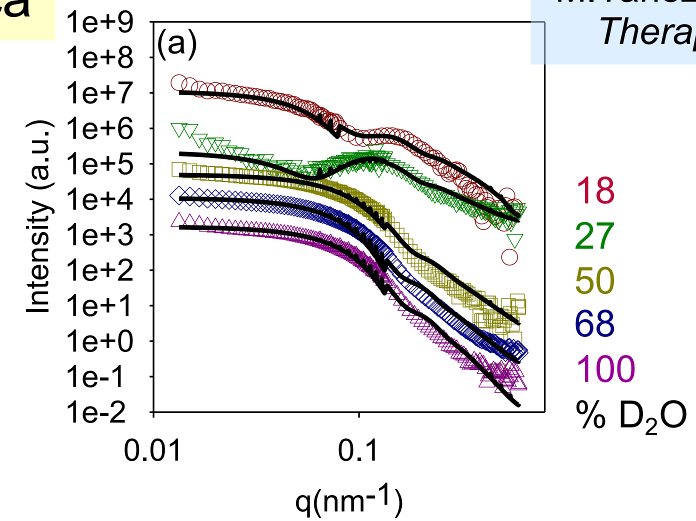
Lipid Nanoparticles for mRNA Therapy

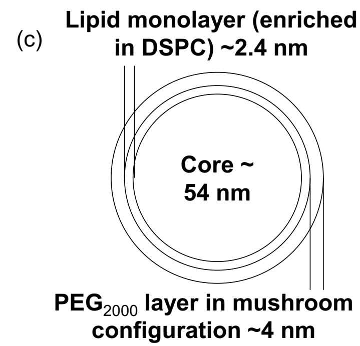
with AstraZeneca

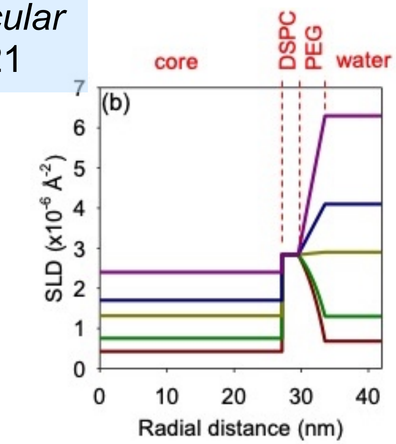
M.Yanez Arteta et al., in *Molecular Theraphy Nucleic Acids* 2021

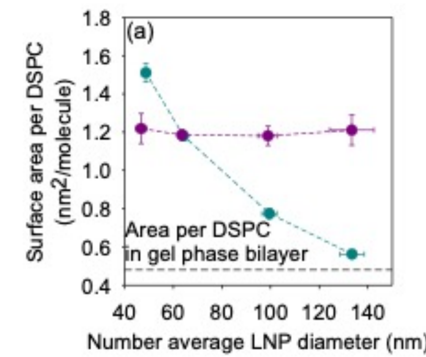


LNP + mRNA



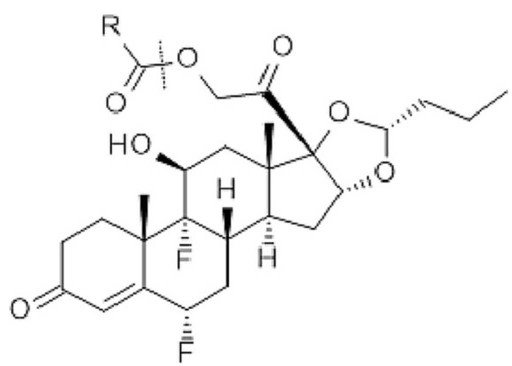


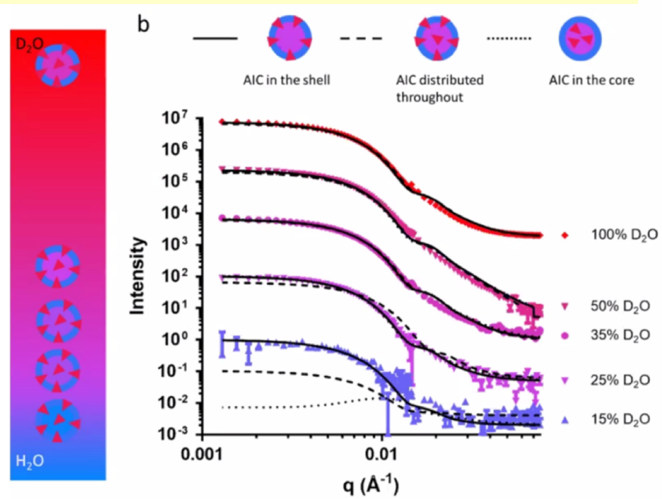


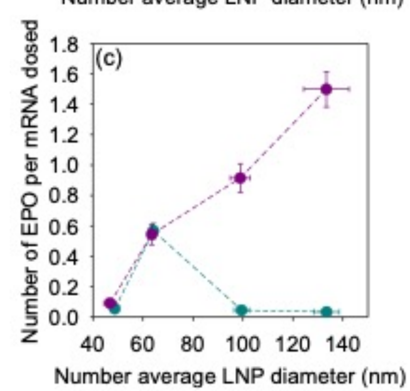


+ rofleponide-C14 prodrug
→ anti-inflammatory

SANS → information about the optimal composition







the anti-inflammatory drug is located at the edge → increased efficiency

Acknowledgement: KWS-2 Team

Thank you for your attention!