Characterization of nanoparticles by continuous contrast variation in SAXS

Physikalisch-Technische Bundesanstalt

Raul Garcia Diez

March 5, 2016

Contents

Chapter 1

Introduction: Nanoparticles in medicine and biology

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper. [1]

1.1 Polymeric colloids

1.1.1 Functionalization for protein binding

1.1.2 Polymerization consequences

initiator, co-monomer, surfactants

1.2 Liposomal nanocarriers

formation from amphiphilic lipids

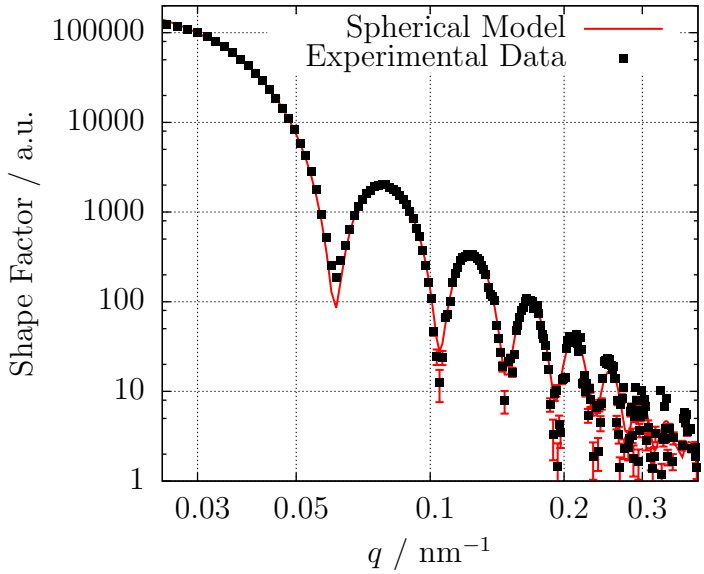

Figure 1.1: Figure test

1.2.1 Phospholipid bilayer

typical lipid HSPC, DPPC, cholesterol, PEG

1.2.2 polydispersity control

extrusion, paper with zoltan about scattering in SSLs

1.2.3 Drug carrier and SSLs

stealth function, bilayer stability, filling with pH gradient

1.3 Physicochemical characterization

1.3.1 Dimensional metrology and traceability

1.3.2 Characterization tools

Single-particle method

AFM, TEM, SEM, TSEM

Ensemble methods

DLS, DCS, SAXS

Chapter 2

Theoretical Background

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper. [3]

2.1 Interaction of light and matter

2.1.1 X-ray cross sections

2.1.2 Rayleight and Mie scattering

2.2 Small-angle X-ray scattering

2.2.1 Physical process

2.2.2 Evaluation of the scattering intensity

Form factor * S(q) Electron density Number of colloids

What is q?

Modelling of the scattering curve

What about size distributions? Log-normal, gaussian, Monte-carlo free number of sizes (Pauw)

Sphere	Gudrun polymeric colloids???
Core-shell	Interface effects???
Onion model	It can be used for single-SAXS experiment maybe
Vesicle	5 gaussian????
nclusion of background	a+b*q-4

Guinier approximation

deviation when using too few point Polydispersity effects

2.3 Contrast variation

Solvent variation ASAXS

2.3.1 Isoscattering point

Possible deviations

Polydispersity and ellipticity smearing (simulation, calculation)

2.3.2 Basic functions approach

Shape factor

Guinier law

Gyration radius

$I(0)$

what happens in polydisperse systems?

Chapter 3

Experimental setup for SAXS measurements

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper. [2]

3.1 BESSY II

3.2 FCM Beamline

3.2.1 Transmission measurements

calibrated diodes, SYRES II????

3.3 Small-angle X-ray scattering

3.3.1 Pilatus detector

high dynamic range noise free

3.3.2 HZB SAXS setup

distance calibration

10-4 uncertainty

3.3.3 Radial integration and error propagation

3.3.4 Absolute intensity calibration

Flux monitor

thin diode

Detector efficiceny

pilatus and thin diode

3.4 Continuous contrast variation

3.4.1 Filling of capilaries

galden at bottom, reference layer

Capillary homogeneity

Hilgenberg

3.4.2 Calibration of solvent density and finding of main axis

3.4.3 Limitations

Density range

sucrose, fructose, iodixanol

Challenges with different contrast agents

Background subtraction, induced aggregation by heavy salts

Comparison to other contrast variation scattering techinques

SANS (deuterated water) RSoXS in polymeric colloids (H.Abe 2006), Carbon K-edge

Chapter 4

Contrast variation in SAXS with the density gradient technique

helo, hello

4.1 Materials and Methods

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper.

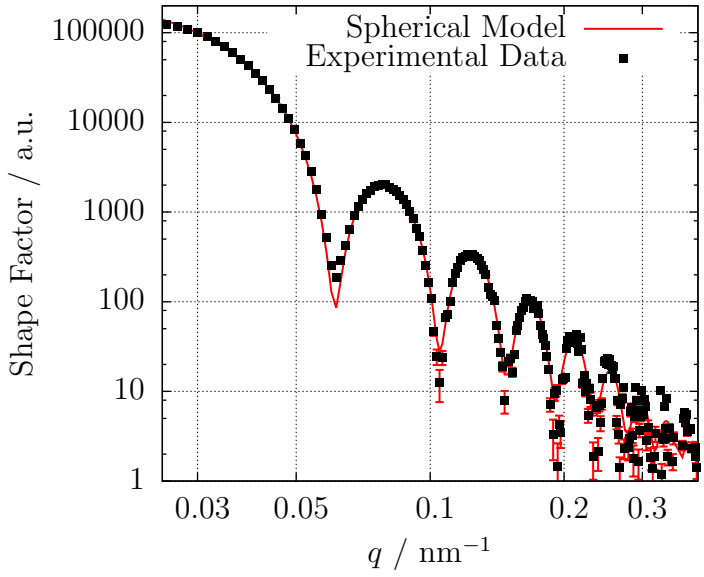

Figure 4.1: Figure test

4.1.1 Particles and chemicals

4.1.2 Diffusion time and calibration height

4.2 Continuous contrast variation in SAXS on PS-PMMA colloids

4.3 Model dependent evaluation

4.3.1 Core-shell form factor fit

4.4 Model-free approach to contrast variation data

4.4.1 Isoscattering point

Quantification: Relative standard deviation

4.4.2 Guinier region

Average electron density

First point Comparison of accuracy

Extrapolatio Using just the Guinier region or extrapolating from first minimum

4.5 Summary

Chapter 5

Simultaneous size and density determination of polymeric colloids

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper. [2]

5.1 Materials and methods

5.1.1 Particles and chemicals

5.1.2 Differential Centrifuge Sedimentation (DCS)

5.2 Technique validation for the determination of the particle size distribution

5.2.1 Inter-laboratory comparison of the mean particle size

5.2.2 Colloidal size distribution

5.3 Considerations about contrast variation data evaluation

5.3.1 Shape factor formalism

Simulation depending on number of curves

Advantages and disadvatages

5.3.2 Isoscattering point approach

Simulation depending on many things

Advantages and disadvatages

5.4 Determination of the particle physical density

5.4.1 Validation through comparison with DCS

Uncertainties

Physical density innacurracy, beam size

5.4.2 Use for homogenous polymeric colloids

PMMA-COOH

5.5 Summary

Chapter 6

Continuous contrast variation applied to relevant bio-materials

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper. [2]

6.1 Materials and methods

6.1.1 Caelyx: PEGylated liposomal doxorubicin

6.1.2 Iso-osmolar contrast agent: Iodixinol

6.1.3 Sterically Stabilized Liposomes (SSLs) of different sizes

6.1.4 Lipoproteins

HDL and LDL

6.2 Traceable size determination of a liposomal drug

6.2.1 Isoscattering point approach

6.2.2 Shape factor calculation

6.3 Osmotic effects in liposomes

6.3.1 Application to drug-stabilized liposomes

6.3.2 Size dependency of the osmotic activity

6.4 Application to blood plasma componenents

6.4.1 HDL

6.4.2 LDL

6.4.3 Literature comparison

6.5 Protein-coated low-density nanoparticles

6.5.1 Singe-contrast SAXS

Caterina Minelli Paper ECASIA

6.5.2 Contrast variation

Isopoint subtraction, as in BioSurf

6.6 Summary

Bibliography

[1] Araki, T., Ade, H., Stubbs, J. M., Sundberg, D. C., Mitchell, G. E., Kortright, J. B., and Kilcoyne, A. L. D. Resonant soft x-ray scattering from structured polymer nanoparticles. *Appl. Phys. Lett. 89* (2006), 124106.

[2] Ballauff, M. SAXS and SANS studies of polymer colloids. *Current Opinion in Colloid & Interface Science 6* (2001), 132–139.

[3] Banc, A., Genix, A.-C., Dupas, C., Sztucki, M., Schweins, R., Appavou, M.-S., and Oberdisse, J. Origin of Small-Angle Scattering from Contrast-Matched Nanoparticles: A Study of Chain and Filler Structure in Polymer Nanocomposites. *Macromolecules 48* (2015), 6596–6605.