Simultaneous size and density determination of polymeric colloids by continuous contrast variation in small angle X-ray scattering

Raul Garcia-Diez, Aneta Sikora, Christian Gollwitzer, Caterina Minelli, Michael Krumrey

PII: S0014-3057(16)30012-X
DOI: http://dx.doi.org/10.1016/j.eurpolymj.2016.01.012
Reference: EPJ 7204

To appear in: *European Polymer Journal*

Please cite this article as: Garcia-Diez, R., Sikora, A., Gollwitzer, C., Minelli, C., Krumrey, M., Simultaneous size and density determination of polymeric colloids by continuous contrast variation in small angle X-ray scattering, *European Polymer Journal* (2016), doi: http://dx.doi.org/10.1016/j.eurpolymj.2016.01.012

Simultaneous size and density determination of polymeric colloids by continuous contrast variation in small angle X-ray scattering

Raul Garcia-Diez[a,*], Aneta Sikora[b], Christian Gollwitzer[a], Caterina Minelli[b], Michael Krumrey[a]

[a] *Physikalisch-Technische Bundesanstalt (PTB), Abbestr. 2-12, 10587 Berlin, Germany*
[b] *Analytical Science, National Physical Laboratory, Hampton road, TW11 0LW Teddington, UK*

Abstract

Polymeric colloids are of growing importance in nanomedicine for drug or imaging agent delivery. Their characterisation is a crucial task but their traceable size determination is challenging, especially for particles with a complicated inner structure. This work describes the simultaneous determination of the size distribution and the density of polymeric particles by means of continuous contrast variation in small angle X-ray scattering (SAXS), which also reveals the inner structure of the colloids. The applicability of the technique has been evaluated by the comparison with other techniques, with focus on differential centrifugal sedimentation (DCS) in terms of the measured density. A novel approach to DCS is presented, which employs two centrifuge setups to enable the density and size determination of particles with physical densities close to water.

Keywords: polymeric particle, colloid, SAXS, DCS, characterisation, size, density

In the continuously growing world of nanotechnology, nanonoparticles have a preeminent position, employed as pharmaceutical or cosmetic products[1] and especially in the emerging field of nanomedicine. Indeed, nanoparticles open exciting new possibilities in this field as platforms for drug-delivery[2] or encapsulating imaging agents[3]. Nowadays, polymeric colloids and biodegradable nanocarriers are finding many research and medical applications[4] and are starting to undergo clinical trials[5–7].

The current advances in nanomaterial development for medical applications are focused towards tailoring polymeric nano-drug carriers with flexible surface functionalisation and controlled morphologies[8, 9]. Size and shape, combined with the choice of polymer and the mechanical properties, are fundamental and defining aspects of the particle functions, e.g. their *in-vivo* biodistribution[10–12] or their drug-delivery efficacy[13]. Therefore, a full and consistent characterisation of all properties of nanoparticles is of crucial importance and must be carefully adressed.

The characterisation of polymeric nanoparticles remains a challenge due to their typically complicate internal structure[14] and requires more than a single characterisation technique to detect these heterogenous compositions. For instance, electron microscopy is an effective tool for direct observation of the shape and size distribution of nanoparticles, although it cannot conclusively elucidate their internal morphology.

The use of an ensemble-average and non-destructive technique such as small-angle X-ray scattering (SAXS) arises as an appropiate alternative[15, 16]. SAXS can discern differences in the radial structure of polymeric colloids and offers advantages to other methods which require prior treatment of the sample and are not averaging[17, 18]. Despite being a highly informative method for the accurate characterisation of polymeric particles, the difficulties in the interpretation of the scattering curves demands complementary experimental information[19].

The contrast variation method in SAXS varies systematically the electron density of the suspending medium by adding a suitable contrast agent, e.g. sucrose, in order to resolve the different con-

*Corresponding author
Email address: raul.garciadiez@ptb.de (Raul Garcia-Diez)