Characterization of Drug Delivery Nanoparticles by Light Transmission Spectroscopy (LTS)

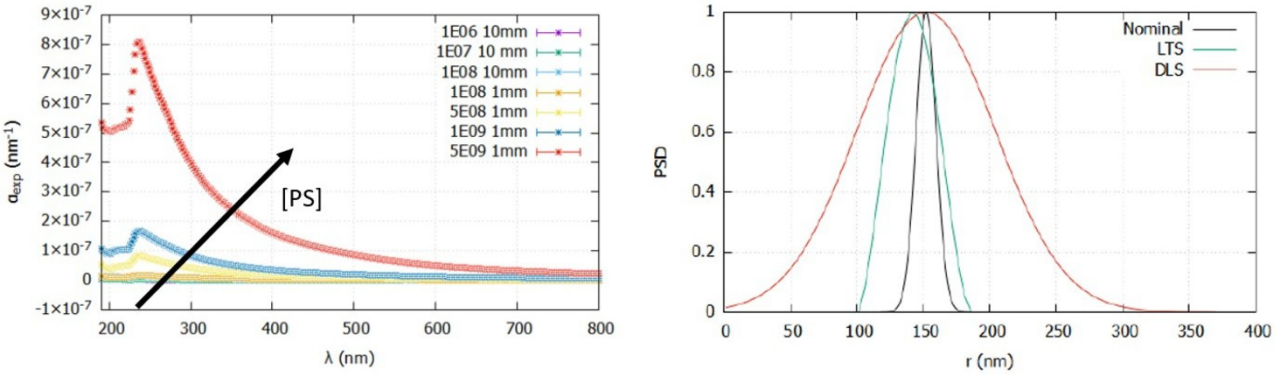
Gabriel Pérez-Romero [a,b], Claudia Fasolato [a], Federico Bordi [a], Angela Capocefalo [b], Simona Sennato [a,b]

[a] Consiglio Nazionale delle Ricerche, Institute for Complex Systems, Piazzale Aldo Moro 2, 00185 Rome
[b] Department of Physics, Sapienza University of Rome, Piazzale Aldo Moro 2, 00185 Rome

gabrielperezromero@cnr.it

In recent years, nanostructured drug delivery systems based on soft colloidal particles have attracted increasing interest due to their tunable properties, biocompatibility, and ability to improve drug stability and delivery efficiency. Among them, polymeric microgels, based on poly(N-isopropylacrylamide) (pNIPAM), are responsive colloids capable of entrap and release active molecules thanks to their stimuli-responsive reversible swelling and deswelling [1]. Solid polymeric nanoparticles based on Chitosan, derived from a non-toxic and biocompatible polysaccharide, represent another versatile drug delivery platform due to their mucoadhesive properties allowing sustained drug release through adhesion to biological membranes [2]. Soft lipid vesicles known as liposomes, consisting of a phospholipid bilayer and an aqueous core, also enables the efficient encapsulation and delivery of drugs or genetic material [3]. The characterization of such systems is commonly performed using scattering techniques, which provide particle size distributions (PSDs) but often lack access to absolute concentration. In detail, the hydrodynamic size obtained by Dynamic Light Scattering (DLS) differs from the true geometrical size, while complementary methods such as Small-Angle X-ray Scattering (SAXS) and Small-Angle Neutron Scattering (SANS) provide structural information.
Light Transmission Spectroscopy (LTS) is here presented as a powerful alternative to the above characterization techniques, enabling the simultaneous determination of both PSD and absolute particle concentration of colloidal dispersions[4]. LTS is based on the measurement of the wavelength-dependent extinction spectrum of a polychromatic light beam transmitted through the sample. The attenuation of light, arising from both scattering and absorption, is governed by the Beer–Lambert law and modelled using Mie scattering theory. By analysing the spectral dependence of the transmitted light and solving the associated inverse problem, LTS provides the number-based PSD and the average size. First, monodisperse polystyrene particles are employed as model systems to validate the methodology. Then LTS is applied to different soft nanostructured colloids used for drug delivery, to determine their particle concentration and the effect of the preparation protocol on the concentration of the final suspension.

Keywords:
Drug delivery, Light Scattering, Microgels, Liposomes, Chitosan, LTS, PSD, Absolute Concentration



Extinction spectra of PS nanoparticles (radius = 150 nm) at different concentrations and their corresponding particle size distributions (PSD) obtained by LTS, compared to DLS and the nominal size.

References:

[1] Plamper, F. A. et al., *Acc. Chem. Res.* , 50 (2017) 131–140.
[2] Brugnoli, B. et al., Carbohydr. Polym. Technol. Appl., 6 (2023) 100373.
[3] Torchilin, V. P., Nat. Rev. Drug Discov., 4 (2005) 145–160.
[4] Eneren, P. et al., J. Quant. Spectrosc. Radiat. Transf., 261 (2021) 107494.

Acknowledgements:
This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101169269.