Applications of Electrospray - Differential Mobility Analysis (ES-DMA) to nano(bio)particles measurements in the health field

F. Gaie-Levrel[1], N. Clouet-Foraison[1], D. Brinet[2,3], M. Taverna[2], J. Kaffy[3], S. Ongeri[3], V. Delatour[1]

[1]Laboratoire National de Métrologie et d'Essais, LNE, Chemistry and Biology Division, 1, rue Gaston Boissier - 75724 Paris Cedex 15, France

[2]Proteins and Nanotechnologies in Analytical Science, Institut Galien de Paris Sud, UMR 8612, Univ. Paris-Sud, CNRS, Université Paris Saclay, 5 rue Jean-Baptiste Clément, 92296 Châtenay-Malabry Cedex, France

[3]Molécules Fluorées et Chimie Médicinale, BioCIS UMR 8076, Univ. Paris-Sud, CNRS, Université Paris Saclay, 5 rue Jean-Baptiste Clément, 92296 Châtenay-Malabry Cedex, France

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Presenting author email: francois.gaie-levrel@lne.fr

During the last decade, new analytical techniques have been developed for bio-nanoparticle characterization to answer the need generated by the explosive growth of bionanotechnologies.

In this context, LNE has implemented an experimental set-up composed of an electrospray source coupled to a Differential Mobility Analyzing system (ES-DMA) for nano(bio)particles measurements in the 3 - 40 nm range. Briefly, nanoparticles in aqueous solution are generated in the aerosol form using an electrospray. Resulting highly charged particles are then neutralized by a soft X-ray source, directly coupled to the ionization chamber, and are introduced into the mobility analyzer (DMA) in which they are separated according to their electrophoretic mobility. The selected particles are then enumerated by a condensation particle counter (CPC). During this presentation, two applications of ES-DMA to health sciences will be shown, and more specifically concerning Alzheimer's and cardiovascular diseases.

Alzheimer's disease (AD) and more specifically amyloidosis are pathologies characterized by the accumulation of extra or intracellular protein deposits named amyloids. AD, the most common form of late-life dementia (Mucke et al., 2009), is associated with the accumulation of intra-neuronal neurofibrillary tangles of hyper phosphorylated Tau proteins and extracellular plaques of insoluble fibrils mainly composed of the 42-residue amyloid-peptide ($A\beta_{1-42}$) (Goedert et al., 2006 ; Haass et al., 2007). In this study, ES-DMA was used to measure the time-dependent $A\beta_{1-42}$ oligomerization pattern (Brinet et al., 2016) which are supramolecular assemblies considered as nanoparticles. This technique was used to monitor the size distributions over time of the early, metastable and neurotoxic species. The ability of the ES-DMA method to monitor the activity of aggregation modulators on the early oligomerization process was demonstrated. The role of two compounds displaying opposite roles were studied as delayer and booster of the $A\beta_{1-42}$ aggregation process to respectively prevent the formation of small presumably toxic oligomers and boosts the fibrillar species formation by forming bigger and possibly less toxic species.

Cardiovascular diseases (CVD) are mainly caused by atherosclerosis, a pathology mostly induced and kept going by elevated LDL-cholesterol concentration (LDL-C). However, recent advances in the field of lipoprotein testing indicate that LDL particle number (LDL-P) is a better predicator of CVD risk than LDL-C and is a valuable adjunct target for therapy (Cole et al, 2013 ; Contois et al., 2009; Master et al., 2013) knowing that lipoprotein size is inversely proportional to CVD. In the case of CVD risk assessment, ES-DMA is a relevant tool for the analysis of lipoproteins, the bio-nanoparticles responsible for the transport of cholesterol and lipids in blood. Indeed, ES-DMA allows obtaining detailed information on the lipoprotein profile and measuring the concentration and size distribution of each lipoprotein sub-class in the aerosol phase. The link between aerosol and liquid phases particle counting was achieved by implementing a new electrospray nanofluidic injection system. This allowed controlling the liquid nano-flow injected in the electrospray using an on-line liquid nano-flowmeter. Absolute quantification of lipoprotein concentration in the liquid phase can thus be achieved thanks to this instrumental implementation and associated results will be presented in the context of the BioSITrace project.

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