Title: Chemical and optical characterisation of nanomaterials in biological systems

Abstract

Many nanotechnologies take advantage of the fact that at the nanoscale materials have unique chemical and physical properties with the potential to interact with biological systems. Whilst the physical properties of these nanomaterials in their native state are often measured, a lack of suitable metrology for characterising their chemical and biological properties particularly in a post-manufactured state means their bio-chemical functionality is often unknown. Fluorescent nanoparticles (e.g. quantum dots) have a vast range of applications including biotechnology and biosensors. Compared to small molecule organic dyes fluorescent nanoparticles have many advantages including stability and spectral tenability, however the tools for characterising their optical properties have lagged behind user needs. A measurement framework is therefore required to support the chemical and biological characterisation of a range of commercially important nanomaterials.

Conformity with the Work Programme

This Call for JRPs conforms to the EMRP Outline 2008, section on "Grand Challenges" related to Health, New Technologies & Fundamental Metrology on pages 9 and 25.

Keywords

Nanomaterial, chemical, biological, characterisation, metrology, fluorescent nanoparticles; quantum dots; polymeric nanoparticles; single-particle imaging; intermittency; blinking; quantum yield; fluorescence spectroscopy

Background to the Metrological Challenges

Many nanotechnologies take advantage of the fact that at the nanoscale materials have different chemical and physical properties than materials on the micro and macro scale. In addition there is the potential for nanosized particles to be transported across biological barriers in ways that are different from their macroscale counterparts. However, these advantageous chemical and physical properties can change post-manufacture and it is becoming increasingly clear that current measurement methods are not sufficient for understanding the functionality of nanomaterials in commercial products. For example, the accurate measurement of metal oxides is usually performed in their dry manufactured state for size, surface area, charge and surface chemistry. However, these measurements do not account for how nanomaterials will change following manufacture or when they are incorporated into products or become exposed within biological systems. Indeed a lack of measurement techniques means the vast majority of nanoparticles have not been comprehensively assessed in regard to changes in their chemical and biological characteristics post manufacture and as such their functionality is not clear.

There are a number of methods that may be used to characterise the physical properties of nanomaterials in their native state for size, shape, concentration and composition. These measurement techniques are in various stages of development and their suitability for measuring nanomaterials in post-manufacture situations or biological interaction scenarios remains to be assessed. Some methods, for example dynamic light scattering (DLS) only provide robust measurements for monodispersed nanomaterials that have a spherical shape and is therefore not suitable for biological characterisation of size where the particles often become poly-dispersed due to protein-particle interactions and particle agglomeration.

The use of fluorescence in monitoring systems such as biosensors, diagnostic assays, and cellular imaging is widespread because of the high sensitivity and specificity that nearly background free detection offers, especially when compared to other optical methods such as absorbance. Also, the broad spectral bands of most organic dyes limit their utility for multiplexed detection applications, whereas some fluorescent nanoparticles such as quantum dots offer narrow emission peaks which are ideal for multiplexing applications. For these fluorescent nanoparticles to be widely adopted as tools within biotechnology and other industries, their optical properties, such as quantum efficiency (Φ_f), molar absorption coefficient (ε), photostability, spectral characteristics and intermittency (blinking) need to be determined. For example, the measurement of absolute quantum efficiency is difficult and therefore most measurements are made relative to a quantum yield standard. However, such standards are themselves often not traceable and if inappropriate standards or insufficiently rigorous measurement practices are followed, the measurements made are frequently inaccurate.

Scientific and Technological Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the JRP-Protocol.

The JRP shall focus on the development of chemical and biological characterisation to underpin bio-chemical functionality of nanomaterials and the characterisation of fluorescent nanoparticles with a focus on their use in biotechnological applications.

The specific objectives are to

1. Select reference nanomaterials for the chemical and biological characterisation
2. Select available and appropriate cell based models for biological characterisation
3. Validate physical measurement techniques for characterising nanomaterials based on properties such as size, charge, agglomeration state and concentration in biological systems.
4. Develop a method for simultaneous characterisation of size, shape and chemical composition of nanomaterials in biological systems and in dispersions
5. Develop methods for characterisation of fluorescent nanoparticles
6. Develop measurement techniques for biotechnology using fluorescent nanoparticles

The nano-objects under consideration should be selected and prioritised according to documented stakeholder needs. This JRP will require a close cooperation with experts from the relevant bio-medical area.

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes. To enhance the impact of the research, the involvement of the appropriate user community such as industry, and standardisation and regulatory bodies, is strongly recommended.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. The proposed JRP should clearly explain any relationship with existing results delivered from previous EMRP JRPs and demonstrate how it extends any relevant outputs from such JRPs.

The total eligible cost of any proposal received for this SRT is expected to be around the 2.7 M€ guideline for proposals in this call.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community. This may be through the inclusion of unfunded JRP partners or collaborators, or by including links to industrial/policy advisory committees, standards committees or other bodies. Evidence of support from the “end user” community (eg letters of support) is encouraged.

You should detail other impacts of your proposed JRP as detailed in the document “Guide 4: Writing a Joint Research Project”

You should detail how your JRP results are going to:

- feed into the development of urgent documentary standards through appropriate standards bodies eg CEN and ISO,
- transfer knowledge to the bio-medical and biotechnology sector,
- transfer knowledge to IUPAC and other professional organisations.

You should also detail how your approach to realising the objectives will further the aim of the EMRP to develop a coherent approach at the European level in the field of metrology. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards,
- the metrology capacity of Member States and countries associated with the Seventh Framework Programme whose metrology programmes are at an early stage of development to be increased,
- outside researchers & research organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.