Co-fund DGA Thesis

Armaments Procurement Agency

Title: New methods of Raman spectroscopy for biological agent analysis

Full description

In many situations, one would like to be able to detect in real time the presence of some microorganisms of interest in a given sample. For armed forces for instance, it may be crucial to swiftly detect the occurrence of highly pathogenic germs aerosolized by the enemy. Though exquisitely selective and sensitive, molecular biology based assays are too slow to fulfil this requirement whereas spectroscopic techniques used in the currently available sensors intrinsically suffer from lack of selectivity and/or sensitivity.

Numerous reports suggest that it may be feasible to extract robust signatures of bacteria species from their Raman spectra, and that these signatures may be used to identify them at the species level. A promising avenue therefore consists in the integration of a Raman scattering based spectrometer into a flow cytometer. In order for such a device to achieve a limit of detection consistent with the operational needs, it should be able to reach a throughput in the range of several thousands of particles per second. Its selectivity will depend in turn on the quality of the spectra acquired at this rate. However, the acquisition duration that is currently needed to yield spectra with the required quality is incompatible with that rate.

The goal of the this PhD thesis is to develop new methods of non-linear Raman spectroscopy, compatible with the requirements of high throughput flow cytometry, and allowing at the same time the acquisition of Raman spectra of biological agents at a rate in the range of several thousands per second, a signal-to-noise ratio, and a spectral resolution consistent with their classification at the species level.

Using an original physical approach, the PhD student will first try to suppress the non resonant background that is currently one of the main obstacles to the integration of multiplex coherent anti-Stokes Raman scattering (M-CARS) spectroscopy into a high throughput flow cytometer. In parallel, he/she will develop a new method of multiplex stimulated Raman scattering (M-SRS) based spectroscopy consisting in the combination of a monochromatic pump and a supercontinuum Stokes beam.

With the aim of increasing the species-specific information content of the spectra of the biological agents used in this project, he/she will then develop a new multimodal Raman spectroscopy in order to acquire multidimensional Raman spectra.

In cooperation with a laboratory spin-off company, he/she will also be involved in the development of a new robust and cheap setup and laser compact source for this project.

Finally, he/she will assess the added value of these new methods by applying them to the classification at the species level of the biological agents used in this project. Using multivariate analysis tools, he/she will compare his/her results with the state-of-the-art. The PhD student will conclude this project by proposing technical requirements that a Raman activated cell sorter used for biosurveillance should fulfil.

Keywords: Raman spectroscopy, Coherent anti-Stokes Raman scattering, Stimulated Raman Scattering, Biodetection, Bacteria identification, biological agents identification

Funding: DGA (Direction générale de l'armement - Armaments Procurement Agency)

Conditions of access:

- Citizen of the European Union or Switzerland;
- Not having started their professional career;
- In preparation of a Master degree in the year of submission of the application;
- Or hold a Master or equivalent allowing them to enroll in thesis;

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