Integrating resistive pulse sensing with Raman microspectroscopy

An internship position is available at the Biomedical Engineering and Physics department of the Academic Medical Center (AMC). In our group, new treatment and diagnostic procedures based on innovative physical techniques are developed. Research is performed by a multidisciplinary team that includes physicists, engineers, mathematicians, medical doctors, biologists, and chemists.

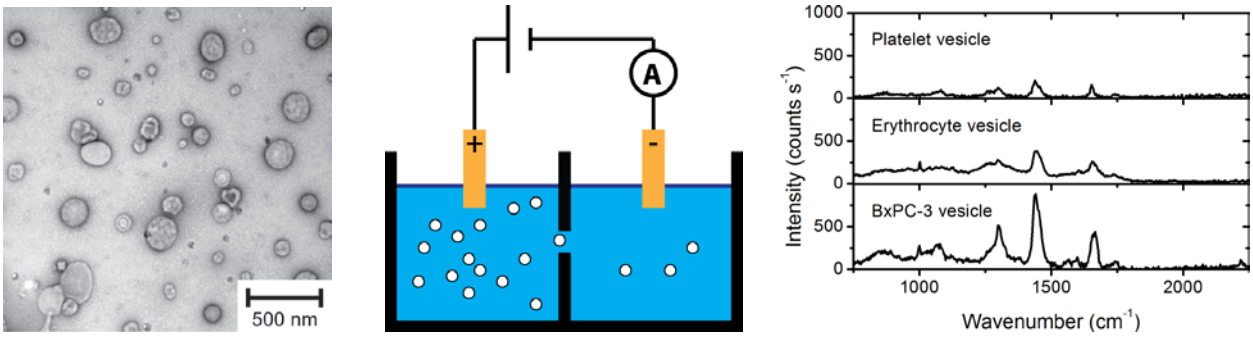
Background

Blood contains heterogeneous populations of spherical vesicles (Fig. 1A) that are released by cells and contribute to homeostatic processes, e.g. intercellular communication and transport[1]. Since the size, concentration, and composition of these vesicles is disease dependent, they are a potential biomarker for the presence of diseases. However, due to the extremely small size (30 nm – 1 μm) of vesicles, their detection is a major challenge[2]. Nowadays, the gold standards to detect vesicles either lack sensitivity[3] (e.g. flow cytometry) or are too laborious for routine application (e.g. transmission electron microscopy)[4]. Consequently, no instrument is available capable of determining the size, concentration, and composition of single vesicles in solution at high throughput.

Recent developments

Recently, we have utilized resistive pulse sensing to determine the size and concentration of vesicles. Resistive pulse sensing consists of two chambers divided by an insulating membrane containing a single nanopore (Fig. 1B). In each chamber, an electrode is immersed to drive an ionic current through the pore. Resistance peaks caused by vesicles moving through the pore provide information on the size and concentration of vesicles.

In parallel, at the University of Twente, we have applied Raman microspectroscopy to, for the first time, distinguish vesicles from different cell types (Fig. 1C) without the need of fluorescent antibody labeling. Fluorescent antibody labeling involves many practical problems.



(A) *(B)* *(C)*

Figure 1 (A) Transmission electron microscopy image of urinary vesicles. (B) Schematic representation of resistive pulse sensing. (C) Raman spectra of vesicles from different cell types.

Research description

In this project you will:

1. develop and test a custom-build Raman microspectroscopy setup
2. extent the Raman microspectroscopy setup with a resistive pulse sensor
3. as a proof of principle, test the hybrid setup with beads of known properties
4. apply the hybrid setup to detect vesicles from clinical samples

The combination of Raman microspectroscopy with resistive pulse sensing is entirely new and facilitates the detection of size, concentration, and chemical composition of single vesicles. All components to develop the setup are available and the Raman setup is currently in development.

Requirements

We are looking for a Master student in experimental physics or physical sciences. Experience with advanced optics, engineering, and programming is preferred.

Learning outcome

The student will gain knowledge in the field of biomedical optics and develop technical skills, general laboratory skills, and data analysis skills. Being part of an interdisciplinary and international research group the student will acquire competences including: (1) collaboration, (2) scientific writing, and (3) presentations.

References

1. van der Pol E, Böing AN, Harrison P, Sturk A, Nieuwland R. Classification, functions and clinical relevance of extracellular vesicles. *Pharmacol Rev* 2012; **64**:
2. van der Pol E, Hoekstra AG, Sturk A, Otto C, van Leeuwen TG, Nieuwland R. Optical and non-optical methods for detection and characterization of microparticles and exosomes. *J Thromb Haemost* 2010; **8**: 2596-607.2012
3. van der Pol E, van Gemert MJC, Sturk A, Nieuwland R, van Leeuwen TG. Single versus swarm detection of microparticles and exosomes by flow cytometry. *J Thromb Haemost* 2012; **10**: 919-30.
4. van der Pol E, Coumans F, Varga Z, Krumrey M, Nieuwland R. Innovation in detection of microparticles and exosomes. *J Thromb Haemost* 2013; **11**: 36-45.

Contact

Name: Edwin van der Pol

Email address: e.vanderpol@amc.uva.nl

Websites: http://www.amc.nl/bmep and http://www.edwinvanderpol.com