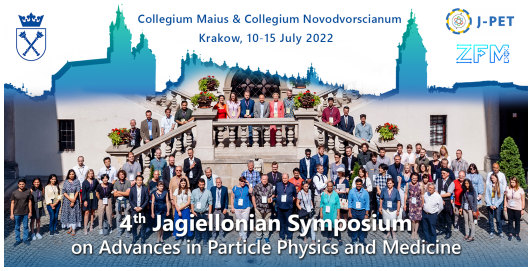

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A mid-IR fluidic-plasmonic biosensor for extracellular vesicles detection and molecular profiling

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Extracellular Vesicles (EVs) are considered a promising source of cancer biomarkers. Despite this potential, the EV translational process in diagnostics is still at its birth, and the development of novel approaches for their label-free characterization is highly demanded [1,2]. In this work, we present the proof-of-concept of a lab-on-chip platform for EV characterization with application in cancer diagnostics. The device combines three advanced biophysical technologies: i) a SEIRA metasurface for the biochemical characterization of EVs, ii) an SPR sensor for mass quantification, and iii) a hydrophobicity-driven wet sample holder that enables IR measurements in a liquid phase.The metasurface was fabricated in gold on CaF2 using EBL and, subsequently, functionalized with Anti-CD63 for EV immunocapture. The fluidic holder was realized in PLA with 3D printing. EVs extracted from human cancer cells were used as a model system, after extensive ultrastructural characterization. IR measurements were carried out with an FTIR spectro-microscope. The proposed sensor is endowed with chemical sensitivity, being tunable on the specific absorption bands of biomolecules within EVs, namely the Amide I-II (1700-1500 cm-1) and lipid (3000-2750 cm-1) bands. The 3D-printed holder enables IR measurements in liquid using a 10 µl droplet. The device allows real-time monitoring of the metasurface functionalization with antibodies and the subsequent EV immunocapture. A protein sensitivity down to the zeptomoles range is demonstrated. Most importantly, the sensor allows for measuring the specific IR spectral fingerprint of EVs in the Amide-I and II regions.
Thanks to the high protein sensitivity and the possibility to work with small sample volumes - two key features for ultrasensitive EV detection - our lab-on-chip can positively impact the development of novel liquid biopsy approaches for cancer diagnosis based on the label-free characterization of EVs.

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References

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