

Context: Flow Cytometry and EV Detection

Flow cytometry is a powerful analytical technique used to study the physical and chemical properties of particles suspended in a fluid stream as they pass through a focused beam of light. It is widely applied in various fields, including immunology, cell biology, and clinical diagnostics. One of its critical applications is in the detection and characterization of extracellular vesicles (EVs), small lipid-bound particles released by cells that play crucial roles in intercellular communication. EVs are of significant interest in research due to their potential as biomarkers for diseases such as cancer and neurodegenerative disorders.

Detecting EVs poses unique challenges because of their small size, heterogeneity, and often low refractive index. These factors make distinguishing them from background noise and other particles difficult. Traditional flow cytometers often rely on forward scatter (FSC) and side scatter (SSC) signals to detect and classify particles. However, the resolution and sensitivity required to study EVs demand advanced systems and methods, including robust calibration to better understand and improve detection processes.

About FlowCyPy

FlowCyPy is a currently-developed simulation tool designed to create a digital twin of flow cytometry systems. By combining computational physics, optics, and signal processing, FlowCyPy offers a detailed virtual representation of the key processes within a flow cytometer. This includes modeling how light interacts with particles, the behavior of optical detectors, and the generation of electronic signals. FlowCyPy leverages **PyMieSim**, a computational library for simulating Mie scattering, to replicate forward scatter (FSC) and side scatter (SSC) signals with high accuracy.

One of FlowCyPy's distinguishing features is its ability to incorporate realistic noise models, such as shot noise, thermal noise, and detector saturation effects. Additionally, the software accounts for baseline shifts and digitization, enabling it to mimic the nuances of real-world experiments. These capabilities make FlowCyPy a vital tool for understanding the limitations and performance of flow cytometers, especially for challenging applications like EV detection.

The Role of Digital Twins in Flow Cytometry

FlowCyPy operates within the framework of digital twins, an approach in scientific research and engineering. A digital twin is a virtual representation of a physical system that allows researchers to simulate, predict, and optimize its behavior under different conditions. By creating a digital twin of a flow cytometry system, FlowCyPy empowers researchers to explore experimental setups and test hypotheses without the need for costly and time-consuming physical experiments.

This virtual approach is particularly valuable in optimizing the detection of EVs, where fine-tuning parameters like particle size thresholds, scattering angles, and detector sensitivity is crucial. By simulating various configurations, FlowCyPy can guide the design of experiments that maximize EV detection while minimizing noise and false positives.

Internship Objectives with FlowCyPy

During this internship, you will play a critical role in validating FlowCyPy's outputs against experimental data, ensuring its simulations align with real-world observations. This involves comparing simulated FSC and SSC signals with those obtained from standard calibration beads and EV samples. Additionally, you will contribute to expanding the software's capabilities, such as refining noise models, enhancing peak detection algorithms, or exploring new scattering configurations.