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### Title

Lifetime-resolved flow cytometry for cell sorting and population heterogeneity using a heterodyning frequency-domain approach

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**Lifetime-resolved flow cytometry for cell sorting and population heterogeneity using a heterodyning frequency-domain approach.**

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**Abstract**

Flow cytometry is a widely used technique in many branches of biological science. The added capability of measuring fluorescence lifetimes in a conventional flow cytometer allows us to study lifetime distributions among cell populations very efficiently. Cell sorting based on lifetime differences improves accuracy. We have developed a time-resolved flow cytometer using a fast, frequency domain, heterodyning technique. In our experimental setup, an Argon ion laser is sinusoidally modulated through a Pockels-cell at about 100 MHz. The cross-correlation frequency is determined by the speed which a cell passes through the laser beam. For example, a flow of 1 m/s, the cell is under the laser beam for approximately 10 $\mu$ s. Typical cross-correlation frequencies applied at the detectors in our instrument are on the order of 400 kHz to 800 kHz, so that several periods of the cross correlation frequency can be acquired per cell. By referencing the phase signal from a second photomultiplier tube, the phase shift of the cell's fluorescence, relative to the light source, is obtained directly. There is no need to analyze nonfluorescence particles and to change filters for obtaining null phase information as performed in existing phase sensitive flow cytometers (Sailer et al., 1996, *Cytometry* 25:164-172). In our instrument, cell scattering, fluorescence intensity and lifetime information are obtained simultaneously. Data for fluorescent latex spheres and live cells labeled with fluorescence probes demonstrating various heterogeneities are presented. Supported by NIH RR03155 and UIUC/CRI Flow Cytometry grant.