

PICOSCOPIC MASS ANALYSIS OF MAMMALIAN CELLS PROGRESSING THROUGH THE CELL CYCLE

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The progression of cells through the cell cycle is a fundamental, physiological process (1). However, the interplay between the regulation of cell growth and mass and cell cycle awaits accurate physical quantification. Basic questions, such as to what extent the mass of adherent cells is regulated during different phases of the cell cycle, remain to be answered (2). To date, mass regulation in different states of the adherent cell (for example a cell cycle phase) could not be characterized, since only large population of cells that are not synchronized in their cycle state are commonly probed. To gain fundamental insights in cell mass regulation thus requires the mass characterization of single cells. We have recently developed a method to noninvasively measure the mass of single adherent mammalian cells at high mass and time resolution (3). This picobalance is based on a photothermally actuated microcantilever, which is mounted onto an inverted microscope and operates under incubator conditions. For mass measurements, a single cell is adhered to an microcantilever oscillating in the Ångstrom range. By determining the natural resonance frequency of the cantilever with and without an attached cell, the mass of a cell is measured.

(1) The regulation of cell size. *Cell* (2013) 154, 1194-1205.

(2) Live-cell mass profiling: an emerging approach in quantitative biophysics. *Nat Methods* (2014) 11, 1221-1228.

(3) Inertial picobalance reveals fast mass fluctuations in mammalian cells. *Nature* (2017) 550, 500-505.

In this PhD project, the student working together with outstanding nanotechnologists and cell biologists, will address how different adherent cells progressing through the cell cycle regulate growth and mass by applying and further developing our recently invented picobalance. Using the picoscopic device, in combination with time-lapse fluorescence microscopy, fluorescence cell state trackers, and biological and chemical perturbations will enable us to monitor and correlate cellular growth and mass with cell cycle phase and morphology.

We search for a highly motivated candidate to work in a multidisciplinary field that combines nanotechnology, biophysics, molecular and cell biology, and medicine. The candidate having a strong background in physics, biophysics and molecular and cell biology will work and be coached by a consortium of international experts such as needed to perform an excellent PhD project.