Development of High Content Screening Confocal Microscope Connected to Detection Components with Multi-mode Fiber

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A new approach to early drug discovery was introduced with the launch of High Content Screening (HCS) around the initial ArrayScan (Cellomics, Pittsburgh, PA) instrument in 1997 [1]. HCS is a technology platform designed to define the temporal and spatial activities of genes, proteins, and other cellular constituents in living cells [2]. To define the temporal and spatial activities of cells, high speed and high resolution optical microscope is needed. The confocal fluorescence microscope has the capability to acquire real-time high resolved fluorescence image and three-dimensional reconstructed image from two-dimensional sectioning images.

We develop a new HCS confocal microscope system. We use RGB lasers (488 nm, 543 nm, 633 nm wavelength) for excitation lasers and utilize acousto-optical tunable filter (AOTF) for the fluorescence spectral detection. For screening cell cultures on many wells, HCS confocal microscope should be loaded on high precision X-Y stage. Therefore, the confocal microscope system should not be bulky or heavy. In addition, it should be very robust against the vibration generated from X-Y stage motion. For robust system against the vibration, we propose a new design that the microscope body part and the detection body part are mechanically separated. Two body parts are connected with the optical fiber. The single-mode fiber has a capability that maintains the beam quality such as the intensity profile of laser beam. However, the single-mode fiber has much bigger light loss than that of multi-mode fiber. In general, the fluorescence signal from stained cells has very weak intensity. It is very important to minimize the loss of fluorescence signal. Therefore, we use the multi-mode fiber for connecting microscope body part with detection body part. RGB lasers generate the light loss due to the chromatic aberration in fiber collimator and fiber focuser. We design the aberration-corrected fiber collimator and focuser. Finally, we acquire confocal fluorescence images of stained cells and estimate the performance of proposed confocal microscope system.

References