Case Study

Application	*Medical*
Product	*M4i.2212-x8 Digitizer* *4 Channel 1.25 GS/s 8 Bit*

Fast Digitizer from Spectrum enables breakthrough in cell sorting

University of Toyko creates world's first high-throughput image-based cell sorter

Cell sorting plays a fundamental role in molecular biology, pathology, immunology and virology research. It requires the ability to rapidly search through and sort out cells based on their unique chemical features and shapes. Conventional methods are limited in uncovering these differences, or are too labor or time intensive, or have to tradeoff between speed and accuracy. The Department of Chemistry at the University of Tokyo has developed an intelligent Image-Activated Cell Sorter (IACS) with an ultra-fast Spectrum Instrumentation digitizer at the heart. This is the world's first, high-throughput, image-based cell-sorting technology that can process cells with unprecedented throughput and accuracy. The technology is highly versatile and expected to enable machine-based, scientific discovery in biological, pharmaceutical, and medical sciences and, in particular, cancer where it could sort for the slight differences between cancerous and non-cancerous cells.

Figure 1: Cell sorting plays a fundamental role in molecular biology, pathology, immunology and virology research

Real-Time machine intelligence sorting method

IACS uses real-time, machine intelligence technology to provide a radically new, data management infrastructure, allowing cells to be accurately sorted at an unprecedented rate. IACS combines high-throughput cell imaging, cell focusing, and cell sorting with a unique software-hardware data management infrastructure. It utilizes a number of different technologies including optics, micro fluids, electronics, mechanics and data processing. The system is flexible and scalable and also delivers real-time, automated operation for data acquisition, data processing, decision making and sort actuation. In fact, even when using complex learning algorithms, the complete process is performed in just 32 ms per cell!

Figure 2. The Spectrum M4i.2212-x8 digitizer simultaneously samples signals on 4 channels at sampling rates up to 1.25 GS/s and can transfer the acquired data over its fast PCIe bus at up to 3.4 GB/s

A crucial part of the IACS setup is the section dealing with image construction. Here a frequency-division-multiplexed (FDM) microscope, which was also developed at the University, is employed. The FDM microscope is important as it can produce continuous, high-speed, blur-free, sensitive bright-field and two-color fluorescence image acquisitions of cells flowing at 1 m/s. This is required to achieve the system's breakthrough processing rate of ~100 cells per second.

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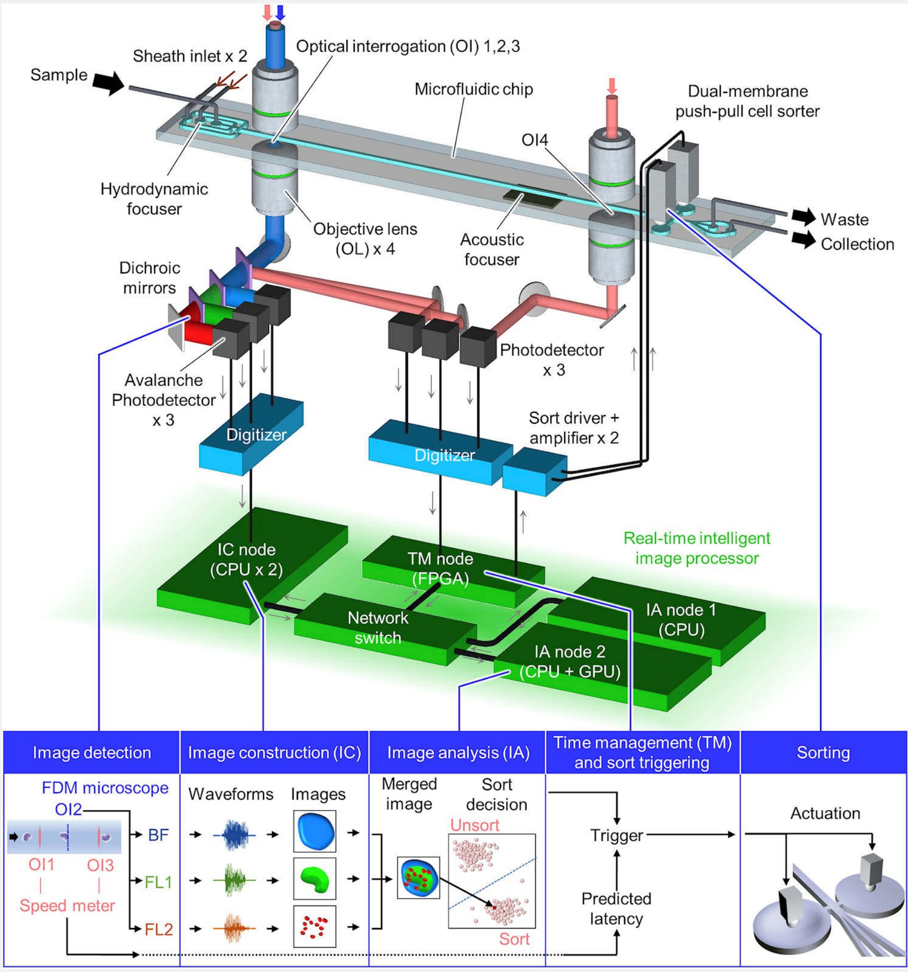
Acquisition of photodiode data from FDM

The other key to this ultra-fast cell sorting is to acquire the signals that come from avalanche photodiodes in the FDM. This is done by passing the signals to a Spectrum M4i.2212-x8 digitizer card (Figure 2) running at a sampling rate of 1.25 GS/s. The acquired data is then transferred over the card's high-speed PCIe bus to a PC where the spatial profiles, which are contained in the digitized waveforms, can be separated. The fast PCIe interface of the digitizer allows this process to run continuously with a high event rate. The separation process involves working in the frequency domain, by performing Fourier transforms, which reveal each signal's distinct modulation frequencies.

IACS cell sorting system

Once the image construction is complete, the results are transferred, using 10 Gb Ethernet, to the image analysis and time management stages of the IACS. Here a field-programmable gate array (FPGA), three central processing units (CPUs), a graphics processing unit (GPU), and a network switch, all combine to perform the necessary image processing and decision making using deep learning techniques on a neural network.

“This is an example of where our ultra-fast digitizer cards can play a critical role in enabling image recognitions systems to acquire and process images to meet the demands for increasingly faster and more accurate systems,” explained Oliver Rovini, CTO at Spectrum Instrumentation. “System designers want to create solutions that process images in real time and our ultra-fast digitizers can make that possible for applications such as this through to factory automation and process control.”



The complete IACS system is comprised of five key sections: Suspended cells injected into the IACS are focused by the hydrodynamic focuser into a single stream, imaged by the FDM microscope, analyzed by the real-time intelligent image processor, maintained in a single stream by the acoustic focuser during the computation, and sorted by the dual-membrane push-pull cell sorter triggered by decisions made by the image processor. The entire process is operated in a fully automated and real-time manner.

The Department of Chemistry at the University of Tokyo is part of a large consortium of institutes and organizations, from both Japan and the United States of America, which has undertaken fundamental research into the development of an intelligent cell search engine.

For a complete presentation of the IACS development, including details on the entire experimental setup and results, a journal article is available for download from Cell Press:

https://www.cell.com/cell/fulltext/S0092-8674(18)31044-4

There is also a video at

https://www.cell.com/cms/10.1016/j.cell.2018.08.028/attachment/376fe425-fe7a-44f2-87d7-73ab3cd3af3d/mmc1