A multidimensional high content analysis system for studying cell-matrix interaction with GPU accelerated image processing

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Statement of Purpose: The interaction between cells and the extracellular matrix is fundamental in system morphogenesis, tissue engineering and developing new biomaterials. The extracellular niche determines the fate of stem cells and controls the cell phenotype. On the other hand, cells also remodel the surrounding extracellular matrix through enzymolysis, mechanical force and neomatrix protein secretion. There are many factors and signal pathways reported controlling the interactions between cells and extracellular matrix. Though great efforts have been made in the past decades, conventional single sample-based assays have not been capable of clarifying the complex relationship between cells and matrix. High content analysis (HCA) is an emerging technique which enables analyzing hundreds of factors simultaneously to understand mechanistic complexities. One bottleneck of HCA is the huge amount data needed to be processed, and current central processing unit (CPU), with only multi cores, based algorithms are not sufficient for high volume data processing. The graphic processing unit (GPU), which has hundreds of cores, has shown encouragingly faster capabilities in data processing. In the current project, we demonstrated a HCA system enabling high content automatic image acquisition and simultaneous high speed image processing using GPU computing for studying cell-matrix interactions.

Methods: GFP-actin transfected smooth muscle cells were mixed with type I collagen hydrogel and pipetted into the wells of glass bottom 96 well plates. After 16 to 24 hours of culture, all the samples were fixed and imaged with a 63X water immersion objective in a Leica SP5 confocal microscope. The image acquisition was programmed and performed as follows: multichannel stack mosaic scans were performed in each well, which kept the high resolution of 63X objective and expanded the visual field by stitching the images acquired from different adjacent positions. Reflection confocal microscopy was used to visualize collagen hydrogels to the level of each individual collagen fiber and the morphologies of the cell bodies were visualized through GFP-actin fibers. After the required images were acquired in one well, the motorized stage, which was controlled by the software, moved the adjacent well into the visual field for image acquisition repeating the same procedure as in the previous well.

The acquired images were simultaneously streamed to another computer for image processing. As a stitched image from one well contains dozens of cells, an individual cell was first identified by the software and a square window is drawn to segment each individual cell and the extracellular matrix surrounding it. Matrix density and alignment were evaluated by binaried image pixel counting and Fast Fourier Transform respectively. In terms of cell morphology, the 3D parameters were calculated, such as the cell volume and the aspect ratio of cell length, width and height. All the image processing was performed with an in house developed program using CUDA (NVIDIA) based GPU image processing algorithms.

Results: As shown in Figure 1, the whole system was highly automatic including image acquisition, cell identification, cell-matrix segmentation, FFT image processing and 3D parameter calculations. The accuracy of our software was equivalent to that performed manually. GPU based image processing was 7.2 times faster than CPU (Figure 2).

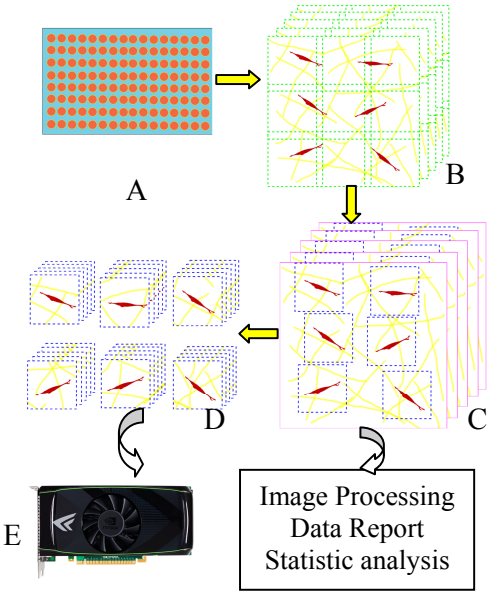

Fig. 1 The workflow of the multidimensional high content analysis system: A) SMCs and collagen hydrogel were prepared in 96 well plates. B) The scheme of multichannel mosaic stack image acquisition. SMCs are shown in red, collagen fibers are shown in yellow and the square dotted lines represent individual visual fields. C) Automatic cell identification. D) Segmented images of individual cell and collagen matrix. E) Image processing with GPU, data report and statistic analysis.

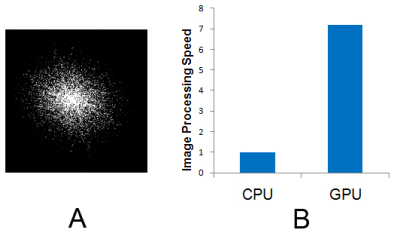

Fig. 2 A is a representative FFT spectrum image and B shows that FFT image processing with GPU is 7.2 times faster than CPU.

Conclusions: We demonstrated a highly automated HCA system for studying the interaction between cells and extracellular matrix. Our GPU based image processing accelerated the speed 7.2 times faster enable a simultaneous data analysis. The system will be a promising tool for biomaterial study and tissue engineering.

References: Power KA et al. Biomaterials. 2010, 31(26):6667-74