

Development and Applications of Array Microscope Technology

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Abstract: The microscopy tradeoff between high-resolution and large-area imaging is eliminated by the use of an array microscope. We describe a system with 80 microscope objectives developed for scanning 30 microscope slides/hour at 54,045 dpi.

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1. Introduction

The tradeoff between field of view (FOV) and resolution is acutely apparent in medical or life-sciences microscopy systems, with which there is often a need to image relatively large areas of a microscope slide at high resolution. Conventional systems rely on tiled, pushbroom or whiskbroom scanning approaches.

An array-microscope approach offers a way around this tradeoff, using a large number of miniature microscopes to image large areas at high resolution [1]. Thanks to the benefits of parallel image acquisition and parallel processing, such a system can scan microscope slides at much higher speed than conventional systems and process digital data in real time.

2. Development Challenges

The first challenge is the fabrication of large numbers of identical lenses with characteristics that are sufficiently well-matched to allow simultaneous imaging of the object at the same conjugates and without variation of imaging performance across the array. The difficulties range from analysis of tolerances to fabrication of aspheric optics with sufficiently high accuracy and precision.

The image sensor presents the second challenge. To achieve the desired FOV and resolution, the array of objectives requires a large-format, small-pixel image sensor. Commercial sensors exhibit a correlation between physical size and pixel size. Our solution was to design a custom CMOS image sensor. The resultant image sensor captures data at 2,500 frames/second with 3.3- μm pixels and has ten parallel output channels. The current-generation array microscope (Model DX-40, see Figure 1) produces image data at a rate of 120 MB/sec. Custom hardware compresses the acquired image data in real time in order to reduce further the data rate sent to the host PC.

A final challenge is autofocus. An automated system for imaging histopathology slides, for instance, needs to locate tissue and select the best focus plane for a particular section of a microscope slide. To solve this problem in the case of an array of 80 microscope objectives, we suspended the array with the image sensor and relevant electronics on a triangular platform. This platform has the capability to change the optics-to-slide distance (z -direction), as is the case with conventional microscopes, but also pitch and roll. These added degrees of freedom allow the system to determine the optimum imaging position for each section of the scanned object. The result is a trajectory that the array-microscope optics follow across the microscope slide while imaging.

3. References

[1] R.S. Weinstein, *et al.*, "An array microscope for ultrarapid virtual slide processing and telepathology. Design, fabrication, and validation study." *Human Pathology*, **35**, No. 11, (November 2004) pp. 1303-1314.



Figure 1. The array-microscope microscope slide scanner.