Peering deep into the developing embryo with an oscillating sheet of light

During the earliest stages of a developing embryo, a steady stream of cells aggregate into primitive tissues which soon become the first stages in the formation of the backbone and nervous system, muscles, intestine and other organs and structures. Much on the minds of biologists is the choreography of cell and tissue movements where cells from different parts of the embryo congregate to form the tissues and organs. However, the migration of these cells, especially those deep in the embryo, has been difficult to photograph because the images rapidly fade with time and are also obscured by a background haze. SMART Research Scientist Dr. Dipanjan Bhattacharya, under the supervision of MIT Professor George Barbastathis and NUS Professor Paul Matsudaira, has developed a Digital Scanned Light Sheet Microscope that overcomes these limitations with innovations in hardware and software. With a "light sheet" the DSLM is capable of imaging a cubic millimeter (roughly the same size as a needle's head) of tissue within only a few seconds and with sub-cellular accuracy, *i.e.* better than 1/200 of a millimeter in each dimension. Also, the fading problem (due to an undesirable process called "photobleaching") becomes largely eliminated. To deal with the background haze, Dr. Bhattacharya in collaboration with MIT Professor Peter So and SMART Researchers Dr. Vijay Raj Singh and Chen Zhi, replaced the uniform light sheet with a "oscillating" light sheet (technically, a sinusoid) and then implemented an algorithm called "3D HiLo" that matches the perforations from two perpendicular directions to a mathematical model. The combination of the oscillating light sheet with HiLo eliminates most of the artifacts produced by the background light. As a result, biologists can follow the movements of cells deep in the embryo and start to deduce the forces and signals that coordinate these actions. This advance in imaging evolved about three years ago from an interest in the forces that mold the embryo by Prof. Matsudaira and Prof. Barbastathis' curiosity about light properties and the interaction of light with complex media (biological tissue qualifies as one of those.) Biophysicists Dr. Bhattacharya and Prof. So tackled the formidable challenge of bringing together the two disparate expertises. Amusingly, one formidable challenge still remains: each "3D movie" produced by the DSLM generates several Terabytes of data, so computer storage occupy a large footprint in the lab, not to mention strains the limit of the air-con units! The DSLM system is presently installed at the Centre for BioImaging Sciences (CBIS) and is studying not only embryo development but also the complex architecture of adult tissues and organs in live animals by researchers in the NUS Department of Biological Sciences (DBS) and the MechanoBiology Institute (MBI). Future work by Dr. Bhattacharya and his colleagues is targeted to further refinements in the instrument's operation, as well as biological studies more specifically targeted towards the health and life sciences, such as live embryonic development, finding stem cells in bone marrow or intestine, and other tissue studies of fish, mice and humans.

Reference:

"Three dimensional HiLo-based structured illumination for a digital scanned laser sheet microscopy (DSLM) in thick tissue imaging." D. Bhattacharya, V. R. Singh, C. Zhi, P. T. C. So, P. Matsudaira, and G. Barbastathis. Optics Express; 20(25), 27337-27347 (2012).