

Light Sheet Microscopy at the Harvard Center for Biological Imaging



We make it visible.

Light Sheet Microscopy at the Harvard Center for Biological Imaging

Author: Douglas Richardson, PhD
Director of Imaging
Harvard Center for Biological Imaging
Harvard University, Cambridge, MA

Date: July 2013

In the spring of 2013 the Harvard Center for Biological Imaging (HCBI) was able to demo, and eventually acquire, Lightsheet Z.1 microscope from ZEISS. A number of key users at the HCBI are involved in developmental research utilizing various model organisms and were excited to begin imaging their samples with light sheet microscopy after viewing the previously published studies by developers and early adopters.

We have now performed a number of long term embryonic development imaging experiments and the results have been impressive. Thus far we have imaged zebrafish, fly, worm, cricket, and salamander embryos in experiments ranging from 20 minutes to 36 hours.

Throughout these experiments, ZEISS Lightsheet Z.1 allowed us to acquire both fast dynamics and long-term changes during development.

Prior to our demo, we expected embryogenesis to be the primary application for ZEISS Lightsheet Z.1; however, we were quickly surprised by how versatile the system was.

We have also found it useful for imaging small aquatic organisms and various plant structures (Figure 1). However, the three greatest surprises for us were the rapid collection of large 3D volumes in fixed and live tissue explants, the ability to image various cells and organisms in suspension, and the flexibility in orienting samples that are traditionally difficult to mount on upright or inverted compound microscopes. Imaging fixed and live tissue explants (brain, kidney, GI tract) produced 3D images comparable in quality to those obtained by point scanning confocal microscopy (Figure 2).



Figure 1: Acorn Worm MIP

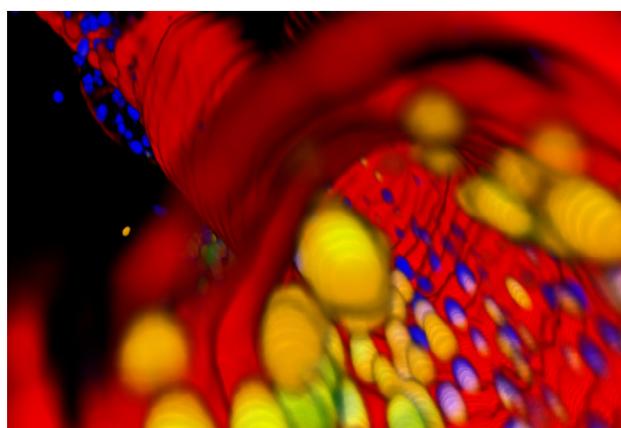


Figure 2: Drosophila GI tract 3D projection

We were excited to obtain imaging depths in the millimeter range depending on the opacity of the sample.

The rapid read-out of the dual CMOS cameras, in conjunction with a number of on-site developed sample mounting techniques, enabled us to capture images rapidly and track the movement of various mammalian, yeast, and algae cells over time in three dimensions. This opens an exciting new door for light microscopy as these cells no longer need to be tacked down to coverslips, a procedure that can be difficult and introduce artifacts.

Finally, we enjoyed the inherent sample mounting flexibility that comes with light sheet microscopy. The ability to rotate the sample in the microscope does away with the meticulous orientation procedure required when mounting samples such as zebrafish for traditional imaging.

Through a number of iterative steps that involved mounting samples in agarose at different angles, followed by imaging at a number of rotations within the microscope, we were able to excite and image structures that researchers told us were previously inaccessible via standard widefield or confocal mounting and imaging techniques.

Overall we are very pleased with ZEISS Lightsheet Z.1 microscope and are excited to be able to offer this technology to the users of our facility and researchers throughout the greater Boston region.



Carl Zeiss Microscopy GmbH
07745 Jena, Germany
BioSciences
microscopy@zeiss.com
www.zeiss.com/microscopy



We make it visible.