

# Fruitfly development, cell by cell

Multidirectional imaging of embryos allows researchers to track development of fruitflies in real time.

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In an advance that could transform our understanding of the complex cellular dynamics underlying development of animals, researchers have developed a method to track individual cells in a developing fly embryo in real time. Two papers published on the *Nature Methods* website today describe similar versions of the microscopic technique<sup>1,2</sup>.

Understanding how an embryo develops from two parental germ cells into an organism with an organized, communicating and interactive group of systems is a difficult task. To date, most studies have only been able to track pieces of that development in animals such as the zebrafish *Danio rerio* or the fruitfly *Drosophila melanogaster*. A more comprehensive understanding of the whole process and what drives it could inform research on diseases such as cancer, and help in the development of regenerative stem-cell therapies.

Current light-sheet microscopy techniques involve illuminating one side of the sample. Either one side of a developing organism is imaged continuously, or two sides are viewed alternately, with the resultant data reconstructed to form a three-dimensional view. However, viewing from one side at a time means that the cells cannot be tracked as they migrate from top to bottom, and rotating the sample to view both sides takes so much time that when the next image is taken the cells have changed, so that they no longer line up.

Simultaneous multi-view imaging solves this problem by taking images from opposing directions at the same time and piecing data together in real time. This required massive computing power; the data sets were as large as 11 terabytes (the amount of data on about 2500 DVDs) in one of the studies<sup>1</sup>. Now every cell in a *D. melanogaster* embryo can be visualized as the animal develops from a fertilized egg into hatching larva.

## Shining light

"Pretty much anyone who wants to study the development or function of biological systems will immediately benefit from this technique because it's the first time the process can be visualized," says Philipp Keller, co-author of one of the papers and a biophysicist at the Howard Hughes Medical Institute's Janelia Farm Research Campus in Ashburn, Virginia. "It's crucial to our understanding of developmental mechanisms that we actually see them in the first place."

The groups behind the two articles both chose *D.melanogaster* embryos to image. “We understand how the fly embryo works better than any other, and that comes from 100 years of genetic studies,” says Michael Levine, who studies developmental genomics at the University of California at Berkeley and was not involved in the research. “We have a basic blueprint of gene interaction, and this imaging technology should take the abstract blueprint and turn it into a living, breathing embryo.”

Keller says that the techniques allow researchers to see what is happening in an entire animal through every stage of development, and what goes wrong as a result of different mutations. “Until now, developmental biology was a qualitative field, describing different mutations and their effect during development. But we couldn’t see what individual cells were doing in an individual embryo,” he says. Keller and his colleagues are now using the technique to follow the growth and differentiation of neurons in the developing brain of *D.melanogaster* and other species.

Studying systems and genetic mutations in *D.melanogaster* could also provide insight in to human disease — a number of disease development mechanisms have been evolutionarily conserved from insects all the way up through mammals. “It will be extremely informative for human health and disease, as well as for basic knowledge, to use this technology to look at fly mutants,” Levine says. “This is really a wonderful time.”

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## References

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2. Krzic, U., Gunthur, S., Saunders, T. E., Streichan, S. J. & Hufnagel, L. *Nature Methods* <http://dx.doi.org/10.1038/nmeth.2064> (2012).