# Developmental Dynamics in Real Time

Stephen W. Carmichael,[1] Mayo Clinic

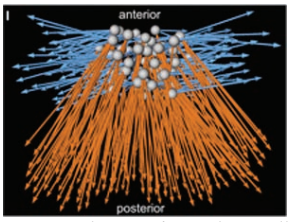
Embryologic development is a dynamic process that has been previously studied by examining static (usually chemically-fixed) specimens at different time periods and then extrapolating results by assembling a series of static images. Recently, Amy McMahon, Willy Supatto, Scott Fraser, and Angelike Stathopoulos have developed new methods to look at developmental migration patterns in real time.[2] They used an optimized imaging approach and quantitative methods to analyze a two hour period during which gastrulation occurred in the embryos of fruitflies (*Drosophila*). Specifically, they characterized the complex interactions between cells of the ectoderm and mesoderm by tracking the movements of over 1,500 cells, which involved the analysis of over 100,000 cell positions for each embryo!

The spreading of mesoderm cells in these embryos involves fast movement (up to 10μm/min) at a depth of up to 80 μm. For several technical reasons, such movements are difficult to track without comprising the viability of the organism. McMahon, Supatto, *et al.* used 2-photon excited fluorescence microscopy, but still this required optimization of each imaging parameter. All cells were engineered to express nuclear green fluorescent protein (GFP). Special optics were used, most notably a high numerical aperture objective lens of low magnification to optimize the light collection when imaging scattering cells deep inside an embryo. They customized software to extract quantitative information from the cell trajectories and to describe the details of the dynamic behavior of the cells. They redefined the positions of cells according to a cylindrical coordinate system (radial, angular, and longitudinal) rather than using the Cartesian system (*x*, *y*, and *z*) which better describes cubic structures.

McMahon, Supatto, *et al.* found that the trajectories of mesoderm and ectoderm cells correlated highly in the longitudinal axis, but not in the radial or angular directions. Further analyses suggested that the mesoderm cells are carried by the strong movement of the ectoderm during germ-band movement in the longitudinal direction. The mesoderm cells move independently of the ectoderm in the angular and radial directions. In the angular direction, mesoderm cell movement was symmetrical with respect to the ventral midline of the embryo.

During the time period of the study, each mesoderm cell divided twice, and these divisions were ordered in space and time. Cells nearest the ectoderm divided first and this was also true during the second division cycle. Tracking data revealed that the orientation of cell divisions within the mesoderm was random indicating it is unlikely that organized cell division plays a role in mesoderm spreading.

Earlier studies have suggested that fibroblast growth factor (FGF) is involved in regulating mesoderm cell migration. To study the function of the FGF signaling pathway, McMahon, Supatto, *et al.* used their methodology to examine the regulation of gastrulation by analyzing mutants (*heartless*) lacking a FGF receptor. They separated the basic elements of the cell movements within the mutant embryos along the three coordinates. The ectoderm-coupled movements of mesoderm cells were unaffected in the longitudinal direction in the mutants. However, mutant embryos displayed mesoderm cells defects that affected their movements in the radial and angular directions. Whereas these and other results demonstrated an important role for FGF in determining cell migration during development, there are other as-yet unidentified signals involved.




*Dorsal view of mesoderm cell displacement before (orange) and after (blue) subtraction of local ectoderm cell movements. Figure 2 from ref. 2. Reprinted with permission from AAAS.*

The study of McMahon, Supatto, *et al.* demonstrates that stereotypical morphogenetic events during embryonic development can be systematically quantified, analyzed, and compared between normal (wild-type) and mutant embryos by imaging large groups of cells. Future developments in imaging and cell tracking hold much promise for understanding embryonic development from the molecular level to that of the entire organism.

1. The author gratefully acknowledges Dr. Angelike Stathopoulos for reviewing this article.

2. McMahon, A., W. Supatto, S.E. Fraser, and A. Stathopoulos, Dynamic analyses of *Drosophila* gastrulation provide insights into collective cell migration, *Science* **322**:1546-1550, 2008.

## INDEX OF ARTICLES



## ABOUT THE COVER

The subject of this picture is a cross section of Tilia stem. It was taken through a Zeiss Universal microscope using a Nikon planapochromatic 4x objective and a Leitz Periplan 10x eyepiece. The camera used was a Nikon Coolpix 4500. The vivid colour results from the use of polarized light. Ron Neumeyer, ron@microimaging.ca

## COMING EVENTS

**2009**

- ✓ **Lehigh Microscopy School (Multiple Courses)**
  June 1-13, 2009, Bethlehem, PA
  www.lehigh.edu/microscopy/
- ✓ **3rd Advanced Materials Characterization Workshop 2009**
  June 3-4, 2009, University of Illinois, Urbana-Champaign, IL
  cmm.mrl.uiuc.edu/workshop2009/
- ✓ **AFM in Biology**
  June 3-5, 2009, Santa Barbara, CA
  www.asylumresearch/News/BioClassRegistration6-09.pdf
- ✓ **Frontiers in Polymer Science**
  June 7-9, 2009, Mainz, Germany
  www.frontiersinpolymerscience.com
- ✓ **Yale Microscopy Workshop**
  June 9-11th, 2009, New Haven, CT
  microscopy.med.yale.edu
- ✓ **14th Short Course on 3D Microscopy of Living Cells**
  June 13-25, 2009, Vancouver, BC, Canada
  www.3dcourse.ubc.ca/
- ✓ **Basic Confocal Microscopy Workshop**
  June 15-19, 2009, Columbia, SC
  dba.med.sc.edu/irf/price/irf/irf.htm
- ✓ **36th MSC Annual Meeting**
  June 17-19, 2009, Winnipeg, Canada
  msc.rsvs.ulaval.ca
- ✓ **Piezoresponse Force Microscopy**
  June 23-27, 2009, Aveiro (Portugal)
  pfm4.web.ua.pt
- ✓ **Inter/Micro Conference**
  July 6-10, 2009, Chicago, IL
  www.mcri.org
- ✓ **SEMICON West**
  July 14-16, 2009, San Francisco, CA
  www.semiconwest.org
- ✓ **Microscopy and Microanalysis 2009**
  July 26-30, 2009, Richmond, VA
  www.msa.microscopy.org
- ✓ **Microscocpy Conference 2009**
  August 30-September 4, 2009, Graz, Austria
  www.microscopy09.tugraz.at/welcome_mc09.html
- ✓ **EMAG 2009**
  August 30-September 4, 2009, Sheffield, UK
  www.emag2009.org
- ✓ **Neuroscience 2009**
  October 17-21, 2009, Chicago, IL
  www.sfn.org
- ✓ **CIASEM 2009**
  October 25-28-2009, Rosario City, Argentina
  www.cab.cnea.gov.ar/ciasem2009

**2010**

- ✓ **Microscopy and Microanalysis 2010**
  August 1-5, 2010, Portland, OR

**2011**

- ✓ **Microscopy and Microanalysis 2011**
  August 7-11, 2011, Nashville, TN

**2012**

- ✓ **Microscopy and Microanalysis 2012**
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*Please check the "Calendar of Meetings and Courses" in the MSA journal "Microscopy and Microanalysis" for more details and a much larger listing of meetings and courses.*

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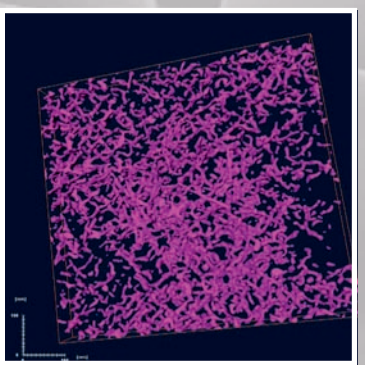

Electron tomography enables 3D visualization of nanonetworks.

Courtesy of
Dr. Joachim Loos, Eindhoven University of Technology, Netherlands.

## *In Situ* NanoProcesses
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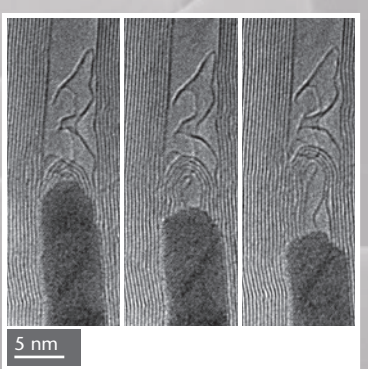
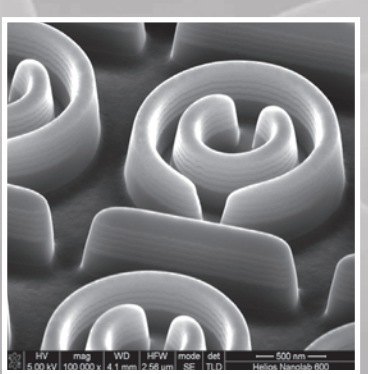



Materials confined within nanotubes potentially provide an in situ atomic scale chemical reaction chamber in the TEM.

Courtesy of
Julio A. Rodriguez-Mano, Florian Banhart and Mauricio Terrones, IPICyT, Mexico.

## 3D NanoPrototyping
**create down to the nanoscale**



Split-ring resonator array with a critical dimension of 120nm, prepared by FIB direct.

Background image: Split-ring resonator array with a critical dimension of 120nm, prepared by FIB direct. Image is darkened for artistic impression.