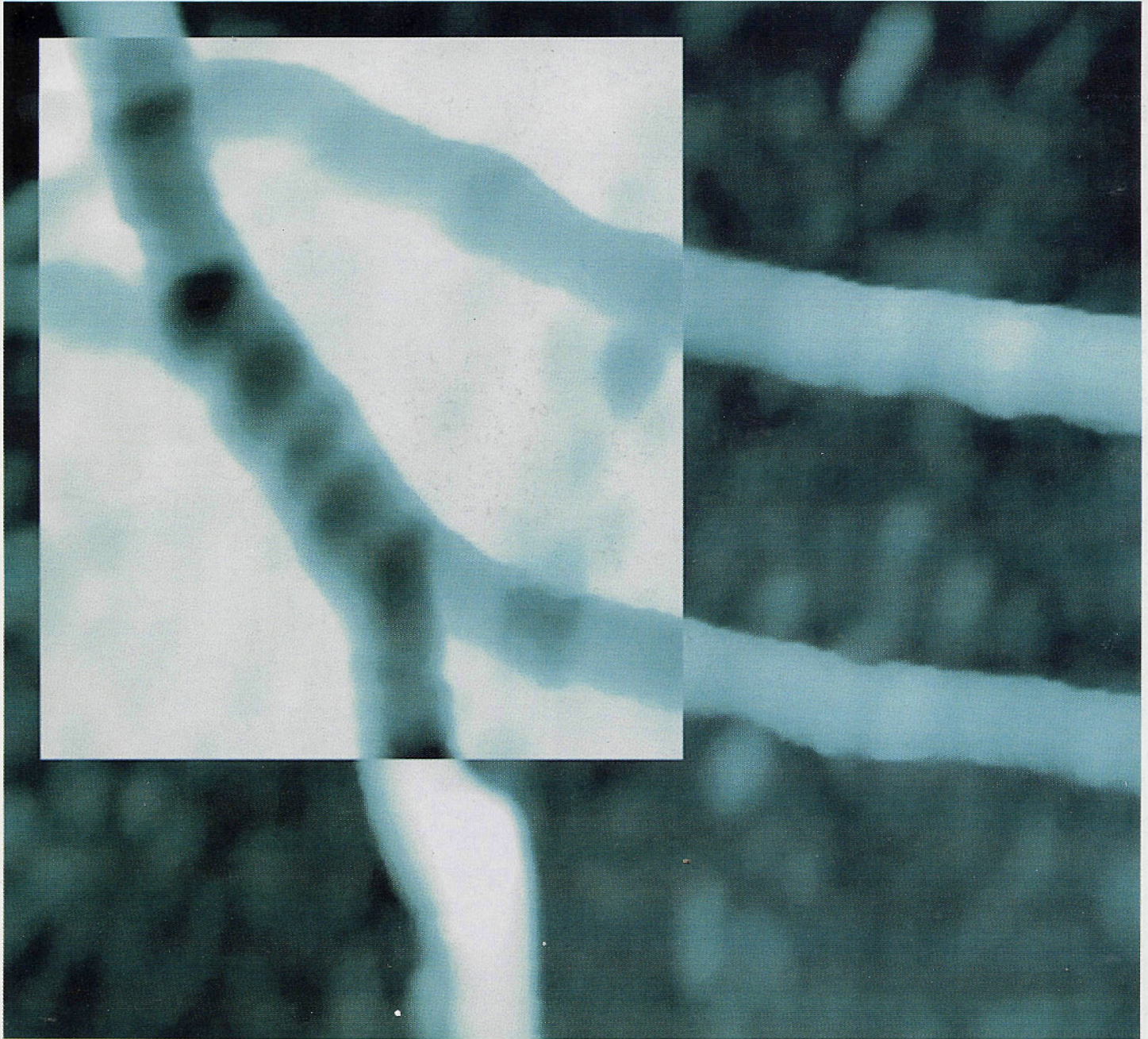


# MICROSCOPY TODAY

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## VIRTUAL EMBRYOLOGY

Stephen W. Carmichael,<sup>1</sup> Mayo Clinic

Old embryos are now being looked at in a new way. About a hundred years ago, an embryologist by the name of Franklyn Paine Mall devoted his career to collecting human embryos and fetuses (an embryo becomes a fetus after 2 months of gestation) from miscarriages and abortions. These specimens form the core of what is known today as the Carnegie Collection of Human Embryos, housed in the National Museum of Health and Medicine of the Armed Forces Institute of Pathology in Washington, D.C. Whereas this is a priceless national educational resource, how do we extract the information about our embryonic development from these specimens? Classic techniques involve slicing a specimen as thinly as possible on a microtome, then reconstructing the slices in a model large enough to study. The problem is the specimen is effectively destroyed in the process. What is needed is a technique that allows whole embryos to be examined, but not destroyed.

As shown in a stunning pictorial in a recent issue of *Scientific American*, Bradley Smith and his colleagues at the Center for In Vivo Microscopy at Duke University are using magnetic resonance microscopy (MRM) to display the Carnegie Collection in exquisite detail, without harming a specimen. Using the same physical principles behind magnetic resonance imaging (MRI), a stronger magnetic field is brought closer to the tiny specimens and stronger gradients are created. Protons in the water inside the specimen are brought sharply into alignment, then radio frequency energy is pulsed in to perturb the alignment. After this external energy is turned off, the protons come back into alignment, giving off some energy of their own in the process. This energy is detected and used to create a black and white image, at about one million times better resolution than conventional MRI. As with clinical MRI, MRM can be adjusted to detect different parameters of this emitted energy, creating what is known as a T<sub>1</sub> and T<sub>2</sub> images. In addition, diffusion imaging can also be used. These three modes of imaging take advantage of different

physical characteristics of the water molecules within the specimen, giving distinctly different images. Each modality displays certain structures to particular advantage. T<sub>1</sub>-weighted show major blood vessels, the heart, and the liver particularly well, T<sub>2</sub>-weighted images shows nonvascular tissues, and diffusion imaging is best for showing the central nervous system. Since neither the strong magnetic fields or the radio frequency energy harm the embryos, the specimens can be extensively examined and the priceless Collection remains intact.

Several tantalizing images are presented in *Scientific American*. Smith clearly demonstrates that one can zoom in or zoom out of the images that constitute the virtual embryos. Selected structures (the lungs are shown as an example) can be segmented and displayed separately. The virtual embryos can be sliced in any plane (but remember, the image is being sliced so the specimen is not damaged) or the gray scale of the image can be manipulated to introduce pseudocolor, highlighting structures of interest. But the most fascinating series of images allowed the viewer to approach the anterior neuropore, enter the neural tube, and "fly through" the developing central nervous system. This technology has exciting possibilities.

This is clearly a work in progress. A visit to the Multidimensional Human Embryo web site ([embryo.mc.duke.edu](http://embryo.mc.duke.edu)) will prove this to you. Several specimens from the Carnegie Collection are there for you to see, intact and in slices. Most are normal specimens, but abnormalities are noted in some specimens. Specimens from 22 days postconception through the first week of fetal development are being prepared for public display. Not all are ready yet, but they are promised to be available on your computer screen by June 2000. Virtual embryology is becoming a reality! ■

1. The author gratefully acknowledges Dr. Bradley Smith for reviewing this article.
2. Smith, B.R., Visualizing Human Embryos, *Scientific American* 280(3):76-81, (March) 1999.

### Front Cover Image

#### In-Situ Hot-Stage AFM Image of a PTFE Nanofibril

The 500 nm x 500 nm cover image of a poly(tetrafluoroethylene) nanofibril at 75 degrees Celsius was captured using a JEOL JSTM 4200D atomic force microscope (AFM). Contrast of the height image (z-range of 10 nm) clearly shows a shish-ka-bob like morphology of the fibril. Highly orientated poly(tetrafluoroethylene) (PTFE) was being investigated with AFM at temperatures ranging from ambient to 120 degrees Celsius with in-situ hot-stage AFM, when nanoscale fibrils perpendicular to the rubbing direction of the PTFE were found.

By D. N. Leonard, R. J. Spontak, P. E. Russell  
Materials Science and Engineering Dept., North Carolina State University, Raleigh, NC

## MICROSCOPY TODAY

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PO Box 620122, Middleton, WI 53562

Tel.: (608)836-1970 - Fax: (608)836-1969 - eMail: [MicroToday@aol.com](mailto:MicroToday@aol.com) - <http://www.microscopy-today.com>

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Don Grimes, Editor