

Cells Connected by Tiny Tunnels

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Intracellular communication is imperative for multicellular organisms. Such devices as synapses and gap junctions have been recognized for decades. Now Amin Rustom, Rainer Saffrich, Ivanka Markovic, Paul Walther, and Hans-Hermann Gerdes have described a new model of cell-to-cell communication.²

While looking at PC12 (rat pheochromocytoma) cells in the presence of fluorescently labeled wheat germ agglutinin, Rustom *et al.* observed relatively long connections extending between cells. These structures were 50 to 200 nm in diameter and up to several cell diameters in length and were named tunneling nanotubes (TNTs). TNTs were subsequently found connecting cultured cells from other lines. They were consistently positioned along the smallest distance between the cells, did not contact the substrate, and occasionally were branched. TNTs immunostained positive for actin, but did not contain microtubules. Scanning and transmission electron microscopy definitively established that a TNT represented a seamless continuity of the plasma membrane from one cell to another.

Does a TNT represent a residual structure from cell division? No, rather they appear to form actively between unrelated cells. Over a period of minutes, a cell formed filopodia-like protrusions that appeared to be reaching out to another cell, like a blind person grasping for contact. Once one protrusion made contact, the other protrusions degenerated. A substance that depolymerizes F-actin

(latrunculin-B) eliminated the TNTs, suggesting that protrusions participate in TNT formation.

What is the purpose of a TNT? Interestingly, endosome-related particles could be seen to move in one direction along a TNT, at a rate of about 26 nm/second. However, smaller molecules, such as green fluorescent protein nor calcein (a small dye) did not appear to move between TNT-connected cells. So the TNT appears to be filled with F-actin that facilitates the transfer of relatively large structures between connected cells, but smaller molecules appear to be confined to their original cells. Several other experiments and observations were done by Rustom *et al.* that were consistent with this result.

TNTs appear to form as one of a few actin-driven protrusions that reach out to target cell(s), and once contact is made, the other protrusions disappear. Organelles, but not small molecules, can be unidirectionally transferred from the cell that presumably initiated the protrusion to the target cell. Although Rustom *et al.* pointed out that similar mechanisms have been documented in plants (at least in principle), this appears to represent a new means of communication between animal cells. It will be interesting to see if TNTs can be located in developing organisms or established animal tissues. This may open up an entirely new avenue of communication between cells, and this avenue is a tiny tube! ■

1. The author gratefully acknowledges Dr. Hans-Hermann Gerdes for reviewing this article.
2. Rustom, A., R. Saffrich, I. Markovic, P. Walther, and H.-H. Gerdes, Nanotubular highways for intercellular organelle transport, *Science* 303:1007-1010, 2004.

INDEX OF ARTICLES

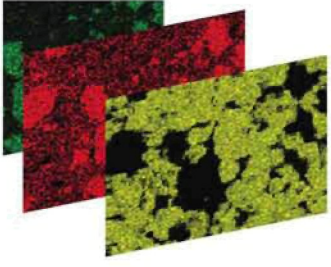
Cells Connected by Tiny Tunnels	3
<i>Stephen W. Carmichael, Mayo Clinic</i>	
Microscopy & Microanalytical Support for NASA's Microgravity Materials Science Programs	8
<i>Donald C. Gillies, NASA, Marshall Space Flight Center</i>	
High-Resolution Imaging with Atomic Force Microscopy	12
<i>Sergei Magonov Veeco Instruments Inc.</i>	
A Suspended Floor for High-Performance Electron Microscopy and Nanoscience	16
<i>Charles Eric Brown, Alan W. Nicholls, Thomas J. Royston, Waleed M. D'Keidek, University of Illinois at Chicago</i>	
RIMAPS and Variogram Analysis of Barley Leaf Surfaces	24
<i>Eduardo A. Favret and Néstor O. Fuentes Comisión Nacional de Energía Atómica, and Universidad Nacional de Gral. San Martín. Buenos Aires, Argentina</i>	
Preparation of Geological and Biological TEM Specimens by Embedding in Sulfur	28
<i>Richard C. Hugo and Sherry L. Cady, Portland State University</i>	
Artifacts from Rapid Microwave Processing of Trematode Tissues (Ascocotyle pachycystis and leighi)	32
<i>Mark H. Armitage, Liberty University, Thousand Oaks, CA</i>	
Principal Components Analysis of Multispectral Image Data	36
<i>Brent Neal* and John C. Russ**</i>	
<i>*Reindeer Graphics, Inc., & **North Carolina State University</i>	

Electron Microscopy Analysis of Multilamellar Vesicles Prepared from Synthetic Lipids: A Model System for Studying Membrane Structure in the Molecular Cell Biology Classroom and Laboratory	40
<i>Russell R. Camp,* Jungsoo Byun,* and Robert Jacob**, *Gordon College, Wenham, MA and **Elucida Research, LLC, Beverly, MA</i>	
Flicker Stereo: Digital 3D Viewing for PC & Presentation	46
<i>Nathan R. Greenhut and Victor A. Greenhut Rutgers University, Piscataway, NJ</i>	
New and Interesting at Microscopy & Microanalysis 2004	50
Industry News	53
NetNotes	58
Index of Advertisers	70

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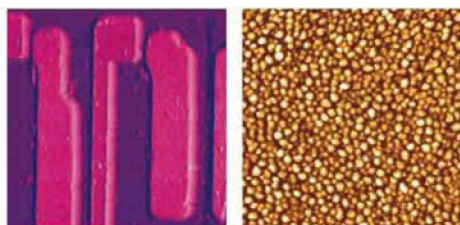
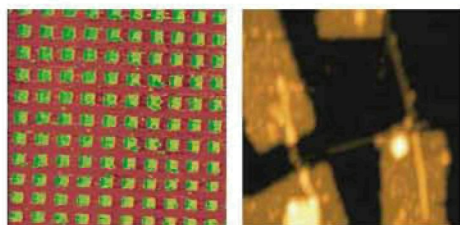
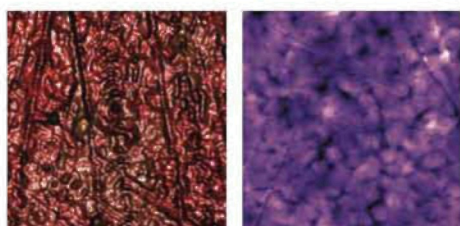
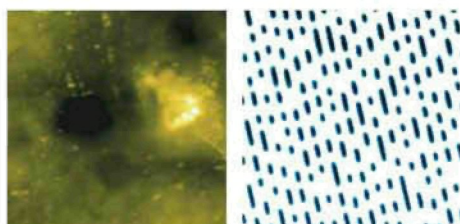
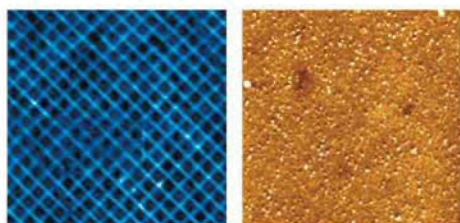
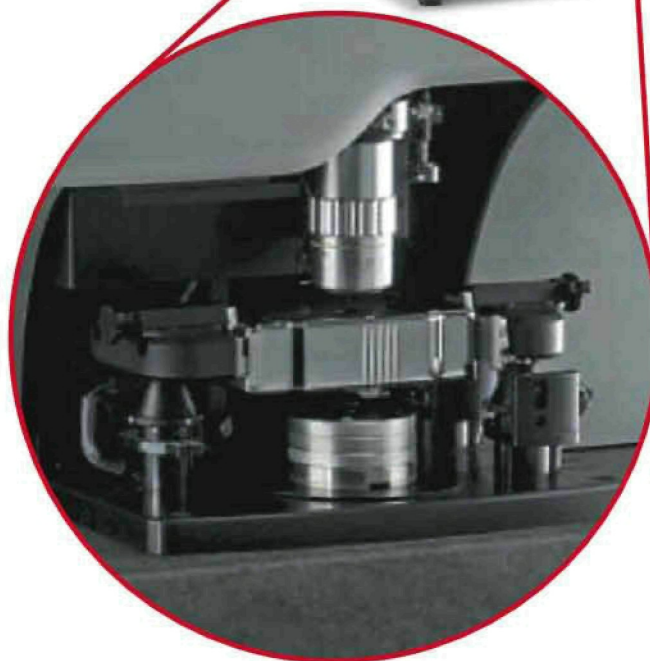
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