

DIRECTLY READING THE GENOME

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The code for the human genome is essentially complete, opening an expansive book about our biologic composition. But the problem is to read this book. The font size is very small. What you are reading now is 9 point font, and genetic information would correspond to approximately 10-50 point font, six orders of magnitude smaller. There are methods to derive genetic information, but recently Adam Woolley, Chantal Guillemette, Chin-Li Cheung, David Housman, and Charles Lieber have developed an elegant way to directly read genetic information with a microscope.² The microscope they used was an atomic force microscope (AFM) that employed a single-walled carbon nanotube as its probe. This very small tip provided resolution of about 3 nm, sufficient to reveal details of a DNA molecule.

But the real contribution of Woolley *et al.* was to develop a method to specifically label stretches along the DNA molecule that are of interest. This involved specific hybridization of labeled oligonucleotide probes to target sequences on the DNA. They used conditions that caused the probes to be annealed to their complementary target sequences, but not to sequences with a single-base mismatch. The real beauty of their technique is that they demonstrated the use of two different labels on different probes. They labeled single-stranded DNA molecules, then synthesized complementary strands, generating double-stranded DNA fragments that were then imaged with the AFM. Labels of different sizes at predictable positions were imaged. The labels were streptavidin and the fluorophore IRD800, which differed by more than a factor of two in size (1.7 nm and 0.7 nm, respectively).

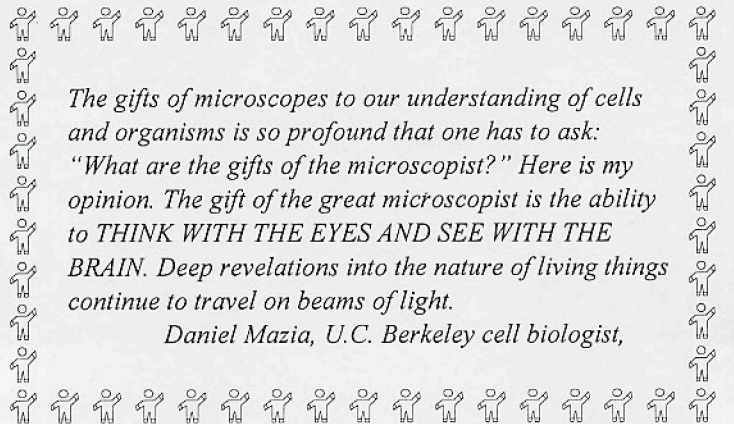
They specifically hybridized labeled oligonucleotides to complementary target sequences in template DNA, and the positions of the tagged sequences were detected by the AFM. They demonstrated the concept by directly imaging the position of the streptavidin and IRD800 probes at specific sequences in the plasmid M13mp18. They also applied the technique to determine haplotypes (the specific alleles associated with each

chromosome homolog) on the UGT1A7 gene.

This method promises to be able to read small but important variations in the genome that are termed single-nucleotide polymorphisms (SNPs, pronounced "snips"). SNPs are, in a sense, our genetic fingerprints. They represent the differences in the genetic code that make each individual unique. Most of the time, these differences are good (as when we resemble our parents), but SNPs can presage undesirable features, such as the likelihood for cancer, heart disease, and other underlying genetic predispositions. For example, the UGT1A7 gene is thought to be related to cancer.

This simple and elegant approach has the ability to be scaled up. Woolley *et al.* pointed out that the current throughput could be greater than 200 samples per day with a redundancy of 10 independent images per sample. By exploiting arrays that employ multiple AFM tips, they estimated that parallel processing could allow for haplotyping over 200,000 samples per day with a single instrument. This could be a valuable method for speed-reading a large and very important book! ■

- 1 The authors gratefully acknowledge Dr. Adam Woolley for reviewing this article.
- 2 Woolley, A.T., C. Guillemette, C.L. Cheung, D.E. Housman, and C.M. Lieber, Direct haplotyping of kilobase-size DNA using carbon nanotube probes, *Nature Biotechnology* 18:760-763, 2000.



The gifts of microscopes to our understanding of cells and organisms is so profound that one has to ask: "What are the gifts of the microscopist?" Here is my opinion. The gift of the great microscopist is the ability to THINK WITH THE EYES AND SEE WITH THE BRAIN. Deep revelations into the nature of living things continue to travel on beams of light.
 Daniel Mazia, U.C. Berkeley cell biologist,

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NEW AND/OR INTERESTING IN MICROSCOPY

➔ **VI Interamerican Congress on Electron Microscopy** will be held October 7/11, 2001 at the Hotel Emporio, Veracruz, Mexico. This is the official congress of the Committee of Inter-American Societies for Electron Microscopy (CIASEM).

The congress will take place at the Hotel Emporio, which has a fine location in the port of Veracruz. It is in the heart of the historic center. The tourist attractions of the port of Veracruz and surroundings range from a rich nightlife to sites of unmatched natural beauty. It was the home of the Olmeca culture and is where Hernan Cortez disembarked. There are wonderful beaches.

For information and reservations, contact: Dr. Jose Reyes-Gasga, email: jreyes@fenix.ifisicacu.unam.mx

➔ **Finding Reprint Authors' E-Mail Addresses**, as produced by Richard Gordon and Eric Cowdrey (Univ. of Manitoba), is a web site that makes it relatively easy to find the e-mail addresses of academic colleagues—for the purpose of requesting reprints. There are no advertisements or cost. If you use it, please let us know of omissions, corrections, or improvements you might suggest.

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Microscopy Highlights At PITTCON 2001

➔ An Atomic Force Microscopy Session, the fourth to be held at PITTCON, will take place on Monday afternoon, March 5, at 1:30 PM.

The symposium, chaired by Monte Heaton (Digital Instruments/Veeco Metrology), will focus on a variety of applications of AFM, including biology, materials science, and polymers. A special talk will be given explaining the advantages and complementary capabilities of AFM relative to other microscopies (SEM, TEM, etc.) and analytical techniques.

The program is recommended for anyone interested in, or performing, ultra-high resolution surface studies such as morphology (2-3 nm lateral resolution, sub-angstrom vertical resolution), monitoring of morphological and nanostructural changes during processing of materials, surface forces, and 3D compositional mapping of component concentrations, orientation, and distributions.

➔ Electron Microscopy & Microanalysis is a one-day short course that will be held on Sunday, March 4 at PITTCON 2001. The course is designed as an introduction to scanning electron microscopy, transmission electron microscopy and x-ray microanalysis for industrial analytical chemists. Numerous examples of the use of electron microscopy in materials analysis are presented. For further information contact the instructor, Dr. Mark Germani: tel.: 9630)325-8170, email: mgermani@micromaterials.research.com

➔ Applied Optical Microscopy, an ACS Short Course, is a three-day, hands-on course in light microscopy, including units on contrast techniques, becoming a better consumer, digital imaging, and quantitative polarize light. The course will be held at the Hyatt Regency Hotel on March 2-4. For tuition and other information, contact ACS at shortcourses@acs.org or (800)227-5558.

The Microbeam Analysis Society and its Tour Speaker Program

The Microbeam Analysis Society (MAS) is the world's premiere organization involved in the development and improvement of a wide variety of microbeam analysis techniques and instrumentation. Affiliated with MAS are almost two dozen Affiliated Regional Societies (ARS). Some members of these societies are MAS members who are involved in microbeam analysis. MAS provides its members with a number of benefits such as high quality microbeam analysis symposia at the national meetings held jointly with the Microscopy Society of America (MSA). However, MAS leadership recognizes that not all of the people who would benefit from the symposia are able to attend these meetings. Therefore, they long ago instituted a Tour Speaker program whereby MAS sponsors, free of cost, a tour speaker to each of the societies that request one. For the last decade or so, MAS has offered three speaker (topic) choices chosen by ARS representatives at a luncheon for this purpose during the national meeting. The speakers are chosen because they are at the leading edge of the science, they are developing a new technique, they are authorities on a particular topic, or they have a talk of particular interest to the analytical community. MAS leadership feels that there are a lot of people in the analytical field who don't know about this program, even within some of their affiliates. Therefore, I have decided to introduce the readers of "Microscopy Today" to the Tour Speaker program by publishing the abstracts of the current tour speakers, starting with my own (*Causes of Color in Minerals and Gemstones*, page 14). My hopes are that you will encourage your regional society (if affiliated) to request a speaker, to have your society consider affiliation (if not already affiliated), and your joining MAS to help support this wonderful program. Visit the MAS web pages to learn more about the society and the Tour Speaker Program. <http://www.microanalysis.org/> Application forms were published in the last issue of "Microscopy Today" and they can be found on the web pages.

Paul F. Hlava
MAS Director of the Affiliated Regional Societies

FRONT COVER IMAGE

HAPPY VALENTINES' DAY

Two "nanohearts" with apparent lateral sizes about 100 nm and one in-between "broken" nanoheart (it's happened sometimes even in a nanoworld) have been obtained by scanning tethered gold nanoparticles with a diameter of 10 nm with the damaged SPM tip.

Image size is 715 x 715 nm; Z scale is 19 nm. The image was obtained with Atomic Force Microscope, Tapping mode, by N. Fuchigami, V. Gorbunov and V. Tsukruk, Laboratory of Surface Engineering and Molecular Assemblies, Materials Science and Engineering Department, Iowa State University.

Call for Papers

❖ **Deadline – March 31, 2001** ❖

2001 Eastern Analytical Symposium Sept. 30 – Oct. 4, 2001 Atlantic City, NJ

The Eastern Analytical Symposium is the second largest meeting in the United States dedicated to the needs of analytical chemists and those in the allied sciences. Please help us to make the 2001 EAS the best ever—be a part of the program by contributing your own papers for inclusion in the oral or poster sessions.

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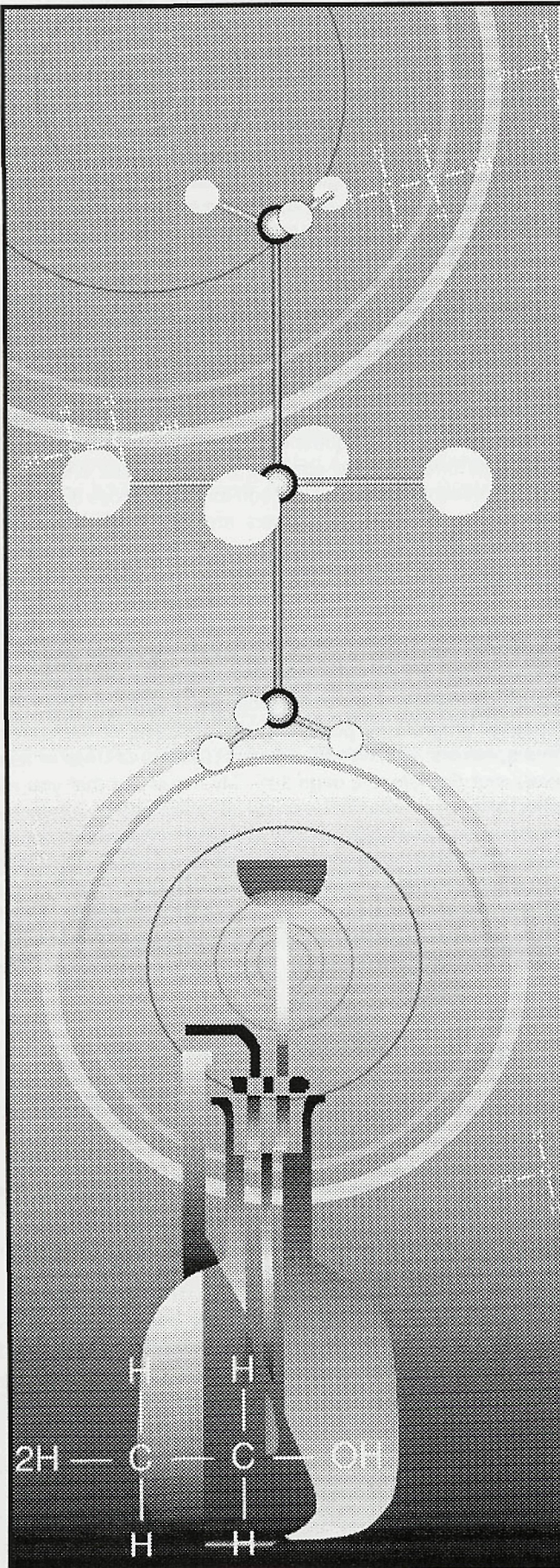
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COMING EVENTS

YEAR 2001 APPLIED OPTICAL MICROSCOPY CALENDAR Smithsonian Ctr for Materials Research & Educ. (Suitland, MD)

- ✓ April 9/13: Plant Anatomy and Morphology
 - ✓ May 14/18: Microscopy of Protective and Decorative Coatings
 - ✓ July 16/20: Polarized Light Microscopy—Fundamentals & Applications
 - ✓ Aug. 14/16: Interpretation of Archaeological metals
 - ✓ Aug. 20/24: Wood Anatomy and Identification
 - ✓ Sept 17/21: Microscopy of Protective and Decorative Coatings
- For further information: Ms. Francine Lewis: (301)238-3700 X102

YEAR 2001 McCRONE RESEARCH INSTITUTE SCHEDULE:

- ✓ April 9/13: Advanced FTIR Microscopy
 - ✓ April 16/20: Electronic Imaging
 - ✓ April 23/27: Scanning Electron Microscopy
 - ✓ May 30/June 1: Fluorescence Microscopy
 - ✓ Sept. 5/7: Microtomy
 - ✓ Sept. 10/14: Advanced FTIR Microscopy
 - ✓ Sept. 24/26: Caking of Crystals
 - ✓ Nov. 5/9: Particle Isolation, Manipulation and mounting for Additional Analysis
 - ✓ Nov. 12/16: Scanning Electron Microscopy
- For further information, contact Ms. Nancy Daerr: (312)842-7100, Fax: (312)842-1078, eMail: ndaerr@mcri.org

- ✓ February 25/28 '01: **Contact Mechanics in Adhesion Science** (The Adhesion Society) Williamsburg, VA, www.adhesionsociety.org/

- ✓ March 4/9 '01: **PITTCON 2001**, New Orleans, LA. www.pittcon.org

- ✓ March 25/29 '01: **12th International Conference on Microscopy of Semiconducting Materials** (Royal Microscopical Society) University of Oxford, UK, <http://www.rms.org.uk/currentevents2.htm#MSMXII>

- ✓ April 1/4 '01: **Focus On Microscopy 2001**, University of Amsterdam, The Netherlands. www.focusonmicroscopy.org/

- ✓ April 1/5 '01: **Inter- and Intra-Molecular Forces in Biological Sciences** (Amecical Chemical Society) San Diego CA, Prof. Jan Hoh: (410)614-3795

- ✓ May 5/7 '01: **SCANNING 2001**: (FAMS) New York City. Paula Pivnick : (201)818-1010, scanning@fams.org

- ✓ May 6/10 '01: **Modern Developments and Applications in Microbeam Analysis (EMAS)**, Tampere, Finland, www.emas.ac.uk/

- ✓ May 10/18 '01: **Analytical & Quantitative Light Microscopy** Marine Biological Laboratory) Woods Hole, MA. (508)289-7401

- ✓ May 13/16 '01: **Food Structure & Functionality Symposium 2001**, Minneapolis, MN. eMail: meeting@AOCS.org

- ✓ May 21/25 '01: **FE-SEM and Image Analysis Courses** Montreal, Canada. Dr. Pierre Hovington: (450)652-8125, eMail: hovington.pierre@ireq.ca

- ✓ May 22/29 '01: **Microinjection Techniques In Cell Biology** (Marine Biological Laboratory) Woods Hole, MA. (508)289-7401

- ✓ June 6/8 '01: **Microscopical Society of Canada Annual Meeting** Fredericton, New Brunswick, Canada, <http://www.unb.ca/msc2001>

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 - ✓ June 18/22 '01: Advanced Scanning Electron Microscopy Quantitative X-ray Microanalysis
 - ✓ June 18/21 '01: Analytical Transmission Electron Microscopy
 - ✓ June 19/21 '01: TEM Specimen Preparation
 - ✓ June 19/22 '01: Atomic Force Microscopy
- For further information, contact Ms. Sharon Coe at: tel.: (610)758-5133, fax: (610)758-4244, eMail: sharon.coe@lehigh.edu

- ✓ June 18/21 '01: **17th Annual Short Course on Molecular Microspectroscopy** (Miami University) Oxford OH. (513)529-2874

- ✓ July 2/6 '01: **16th International Conference on X-ray Optics and Microanalysis (ICXOM XVI)**, Vienna, Austria, www.icxom.at

- ✓ July 16/18 '01: **Summer WDS Short Course at MIT**: Cambridge, MA: e-probe-www@mit.edu

- ✓ August 5/9 '01: **Microscopy & Microanalysis 2001 (MSA/MAS)** Long Beach CA, Mary Rebedeau: msa@tradeshownet.com

- ✓ August 30/Sept 9 '01: **Practical Course on Electron Microscopy Immunocytochemistry and Stereology for Cell Biology (EMBL)** Heidelberg, Germany: www.EMBL-Heidelberg.DE/courses/ElectronMicroscopy01/

- ✓ Sept. 20/25 '01: **5th Multinational Congress On Electron Microscopy**. Lecce, Italy. Dr. Massimo Catalano, email: massimo.catalano@ime.le.cnr.it

- ✓ Sept.30/Oct.4 '01: **2001 Eastern Analytical Symposium**, Atlantic City, NJ, <http://www.eas.org>

- ✓ Oct. 7/11 '01: **VI Interamerican Congress on Electron Microscopy**, Veracruz, Mexico. Dr. Jose Reyes-Basga, email: jreyes@fenix.ifisicacu.unam.mx

- ✓ Oct. 10/19 '01: **Optical Microscopy & Imaging in the Biomedical Sciences** (Marine Biological Laboratory) Woods Hole, MA. (508)289-7401

- ✓ August 4/9 '02: **Microscopy & Microanalysis 2002 (MSA/MAS)** Quebec City, Canada. <http://msc.rsvs.ulaval.ca>

- ✓ September 1/6 '02: **15th International Congress on Electron Microscopy (ICEM-15)**. Durban, South Africa. www.icem15.com

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