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# NEWS AND NOTES 1993, VOL.4, NO.3

The Rockefeller University

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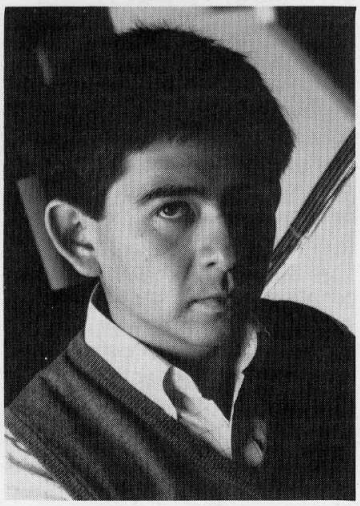
# news & notes

*September 24, 1993 Volume 4, Number 3* *The Rockefeller University*

**Graduate fellows Adrian Ferré-D'Amaré and Sabine Hilfiker-Rothenfluh have been selected as David Rockefeller Fellows.**

## RU names David Rockefeller fellows

Those who now work in the modern, 12-story John D. Rockefeller, Jr. and David Rockefeller Research Building are not the only ones still benefiting from the building's dedication one year ago. Two graduate fellows, Adrian Ferré-D'Amaré and Sabine Hilfiker-Rothenfluh, have been awarded newly created David Rockefeller Fellowships. These scholarships were established when the funds donated by friends of David Rockefeller to support the four-day dedication festivities exceeded actual expenses.

"Our graduate program is a vital part of the continuing mission of this university," said President Torsten Wiesel. "I am therefore pleased that the careful management of the dedication budget has meant that the generous gifts of David Rockefeller's friends are also supporting two fellowships."

The one-year fellowships will fund full scholarships for Ferré-D'Amaré and Hilfiker-Rothenfluh, who were selected on the basis of academic merit.

Ferré-D'Amaré, a fourth-year student, works in the Burley lab, determining the three-dimensional structure of DNA-binding proteins. Recently, he was instrumental in solving the structure and binding action of Max, a key transcription factor involved in cancer.

Hilfiker-Rothenfluh, technically a first-year student although she arrived at Rockefeller in January, works in the Greengard lab studying synaptic release. Currently, she is investigating the modulation of neurotransmitter release, focusing on a synaptic vesicle protein which is a putative receptor for synapsin.

"I'm very grateful to receive the David Rockefeller fellowship," Hilfiker-Rothenfluh said. "It is an honor to be selected. I hope that the work funded by this fellowship will be fruitful and productive."



## New courses enhance curriculum

Several new courses, including ones in cell and developmental biology, neuroscience and medical science, have been added to the roster of two dozen or so available this academic year.

"Rockefeller's graduate courses aim to give students a general background in particular sub-specialties of science as well as to teach them to approach papers and lectures in a critical manner," said Professor Peter Model, associate dean of curriculum. "This year's new courses offer students an opportunity to gain deeper insights into some areas of study."

One new course which began yesterday (Sept. 23) is Selected Issues in Development, taught by Associate Professors Steve DiNardo and Claude Desplan. Lecturers will include DiNardo, Desplan, Assistant Professor Ulrike Gaul, Assistant Professor Ali Hemmati-Brivanlou and two guest lecturers.

"I hope that students working in developmental biology labs will take our course, which fills an important gap in the curriculum," said DiNardo. "The course will be organized around issues in development, such as induction and cell signaling, formation of primary body axes, patterning along secondary axes and regionalization. We'll examine these issues in a variety of organisms to see what approaches have evolved to solve these problems."

Another new course being offered this fall is Disease "Du Jour," taught by Assistant Professor Naomi Fukagawa, Associate Professor Richard Galbraith and Professor Ralph Steinman. The lecturers, Rockefeller University faculty conducting disease-oriented research, will give an overview of the physiology and pathology of each disease and then lead "journal club" discussions of cutting-edge publications in the field.

"We wanted to offer a course on medicine available to all graduate students on campus," said Steinman. "For those in the M.D.-Ph.D., program, the course will provide a mechanism for keeping up on disease-related research. For those in the Ph.D. program, it will serve as an introduction to disease as a challenging scientific area."

In the spring, Mechanisms of Neural Development will make its debut, taught by Professors Mary Elizabeth Hatten and Nathaniel Heintz. Lectures and discussion will focus on the molecular and cellular mechanisms underlying the development of the mammalian nervous system. Topics will include induction of the nervous system, specification of neural cell fate, cell migration, axon guidance and establishment of neuronal connectivity.

This year, entrance requirements to many courses are more rigorous than in the past. Typically, students need to pass a take-home or oral exam testing basic knowledge of a subject before being admitted

*See* ***New Courses****, page 2*

## *Students share fascination with science*

For the 11 students who make up the entering class of Ph.D. candidates at The Rockefeller University, the fall of '93 will be remembered as a time of new beginnings: new labs, new course work, and, for many, a new city and country. While the students come from diverse backgrounds, they share a fascination with and commitment to scientific research.

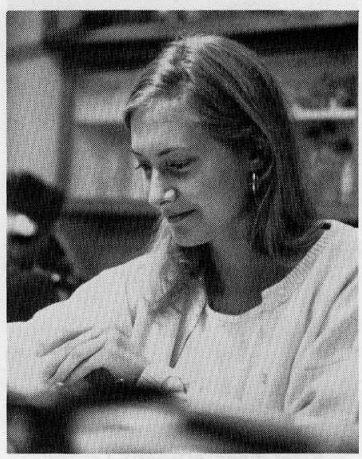
### Understanding fundamental aspects of disease

Kristi Levine, a native of Long Island and graduate of Cornell University, decided that research was her calling during her first years of medical school at Cornell University Medical College.

"I loved my medical courses," she said, "but the academic aspect of medicine interested me more than the clinical side. Understanding the fundamental aspects of disease is what really caught my interest—to conduct basic research with the ultimate goal of curing human disease."

After a year as a Howard Hughes Medical Institute medical research fellow at Memorial Sloan-Kettering Cancer Institute, Levine decided to take a leave of absence from

*See* ***Entering Students****, page 2*



**First-year student Kristi Levine hopes to conduct basic research on disease.**

# *Entering students share fascination with science*

*(continued from page 1)*

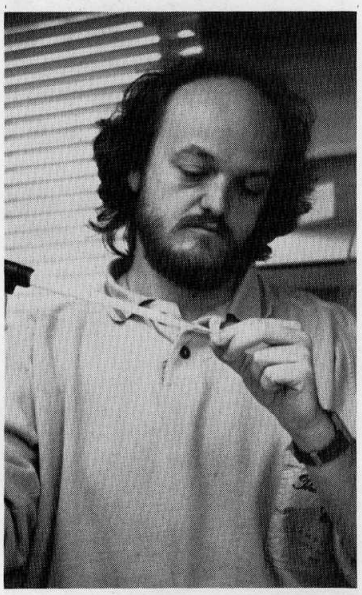
medical school to pursue Ph.D. work at Rockefeller. Working in Fred Cross's lab, Levine has begun preliminary work creating temperature-sensitive mutants in yeast cells. She hopes to learn diverse laboratory techniques in molecular biology that she can later apply to cancer research.

Levine spends time outside of the lab with her parents on Long Island, her twin sister Cindy (who, until this year had an identical transcript and scientific credentials), another sister Jill and friends. "My sister, who is doing Ph.D. research in biology at Cornell, has a kitchen and I don't, so I've been spending a lot of time there," Levine said with a smile.

### Putting together pieces of a puzzle

Goron Jovanovic, a native of Yugoslavia who graduated with a B.S. and master's degree from the University of Belgrade, went into science because of the challenge of solving problems, which he likens to putting together the pieces of a puzzle. "It is particularly rewarding when the pieces are your own," he said.

After working for a number of years at the Institute of Molecular Genetics and Genetic Engineering in Belgrade, he decided to study for a Ph.D. degree. He was drawn to Rockefeller by its flexible program, advanced courses and reputation for excellence in the biological sciences. In addition, he believes that training in the United States will help his career as a scientist.



**First-year student Goran Jovanovic is pursuing his interest in signal transduction in prokaryotic systems.**

Jovanovic has chosen to work in the Zinder-Model lab, pursuing his interest in signal transduction in prokaryotic systems. He has begun a project to find an activator gene of a phage shock protein operon. One aspect of Rockefeller he is enjoying greatly is the interaction with faculty, which he believes is very important in science.

Jovanovic is happy to live in New York City. "My wife, Lijiljana, is a painter," he said. "She is thriving on the art here. I love music, and I have been able to listen to jazz in the city."

Jovanovic's five-year-old daughter, Milica, is attending the university's Children's School.

### Fascination with living things

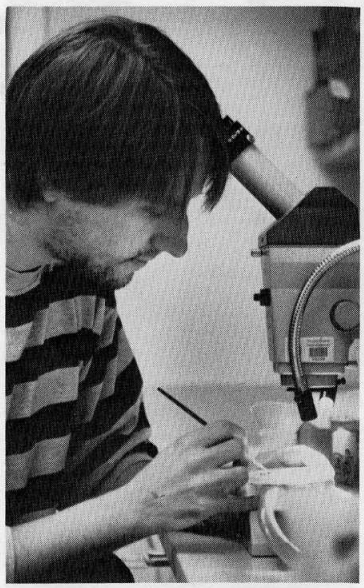
Like Jovanovic, Adrian Rothenfluh, who is Swiss, was attracted to science because he loves to solve problems, in his words, "to find different answers to a problem in different ways." When he was trying to decide on a career path at age 20, he was momentarily torn between disciplines.

"I also considered going into math," he said. "But there are so many interesting aspects to biology. I am fascinated by living things."

Rothenfluh, a graduate of the University of Basel, came to Rockefeller to work in the Young lab. Pursuing his interest in circadian rhythm, he is currently trying to characterize new circadian mutants in the fruit fly *Drosophila*.

When Rothenfluh was investigating Ph.D. programs in America, one prerequisite was that they be acceptable for both him and his wife, Sabine Hilfiker-Rothenfluh. Hilfiker-Rothenfluh is currently a student in the Greengard lab, studying synaptic release.

"Our decision to come to Rockefeller was a compromise,



**First-year student Adrian Rothenfluh is interested in circadian rhythm. He is now trying to characterize new circadian mutants in the fruit fly *Drosophila*.**

weighing the strengths of the labs in both our fields and the location," Rothenfluh said. "Taking these factors into account, Rockefeller was our first choice. So far, I have been impressed with the high level of expertise in a wide variety of fields here."

In his time outside of the lab, Rothenfluh likes to explore New York City. He also enjoys playing pool.

The other students in the entering class of Ph.D. candidates are: Alexander Akopian, Fiona Doetsch, Jian-nong Feng, Christo Houbaviy, Chi-Hon Lee, Jun Qin and Daniel Schwartz. Students in the entering class of M.D.-Ph.D. candidates are: Matthew Albert, Yu Chen, Toby Hohl, Lawrence Lum, Denise Marciano, Maurice Markus, Nori Okada, Michael Shiloh, Brian Wong and Monib Zirvi.

# Letter to the editor:

Like many people at Rockefeller, I was initially very impressed with the renovation of the cafeteria. The place looks great! But I wonder, isn't this a perfect example of the old adage—"If it ain't broken, don't fix it!"? What was so wrong with the old cafeteria? The service was great, the staff was congenial and the food was good.

I can live with paying ten cents more for my morning coffee. But did they have to take away my free refill? The "café" salad bar costs more per pound now than most deli salad bars. When a cafeteria starts to cost more than neighborhood delis and restaurants something is very wrong. Let's not lose sight of who and what we are. This is a university, not a corporation. Students and staff on limited incomes eat here. If trendy and chic is the aim, then we've succeeded. But if value and quality are still important let's rethink this "café" idea and come back to earth.

*Victoria Trahan*
*Administrative Assistant, Young lab*

# *New courses enhance graduate curriculum*

*(continued from page 1)*

to a course. According to Model, this will help raise the level at which courses are conducted and enable students to participate in them more actively. In most cases, entrance requirements are designed to encourage students to learn rather than to screen applicants.

In addition to completing a dissertation, students are required to prove proficiency in three areas of science, either by successfully completing course work or by passing an exam arranged with the faculty before qualifying for a Ph.D. degree. Subject areas for course work include: biochemistry, biophysics and physical chemistry, cell and developmental biology, endocrinology/pharmacology, genetics and molecular biology, immunology, medical sciences, microbiology, neuroscience, organic chemistry, virology, mathematics and physics. Support courses in electronics, computers and writing are also available.

Postdoctoral fellows and other members of the university community are often allowed to attend courses or the lecture sections of courses. Attendance of a single lecture in a series is discouraged.

For more information, contact the Deans' Office, x8086.

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# Electron crystallography shows shape of molecular heavyweights

*By Susan Blum*

It all depends on how you look at things. Take the case of the RNA polymerases, enzymes that are vital for transcription, the process by which the information in DNA is read out into RNA.

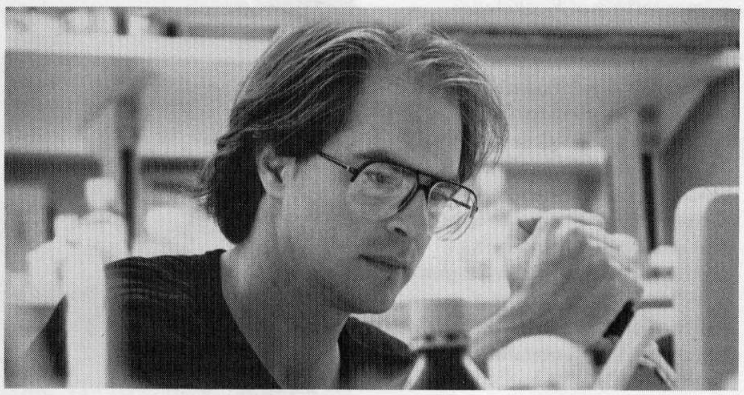
One molecule of an RNA polymerase weighs in at about 500 kilodaltons, roughly 500,000 times the mass of a single hydrogen atom. From the perspective of the everyday world—where even the largest single-celled creature is barely visible to the naked eye—such a molecule is almost unimaginably small. But on the subcellular level, when compared to many other molecules, RNA polymerases are real heavyweights.

Their heft is due to the fact that they are made up of many different protein subcomponents, which catalyze the various cellular events necessary for transcription. These events include the unwinding of double-stranded DNA, the synthesis of RNA and the motion of both DNA and RNA as transcription takes its course. With all their subcomponents combined together, polymerases acquire the characteristic three-dimensional shape whose peaks, valleys and tunnels endow it with the precise combination of chemical, mechanical and electrostatic forces necessary to accomplish their tasks.

## Large assemblies perform vital cell functions

Big as they are in their own right, functioning RNA polymerases form even larger "macromolecular assemblies" as they associate with DNA and RNA in the process of transcription. And transcription is not the only cellular process that involves such large molecular "machines." In fact, many of the central processes in the living cell are performed by assemblies of macromolecules that are arranged in functionally specialized units. Among these processes are the replication of DNA, the splicing of messenger RNA, the translation of messenger RNA into protein and the movement of newly created proteins to and across cellular membranes.

Large macromolecular assemblies pose a challenge for structural biologists, who aim to learn the shapes of molecules and to fathom how those shapes contribute to their functions. For a number of technical reasons, it is extremely difficult to determine the overall shape of large macromolecular assemblies using x-ray crystallography or nuclear magnetic resonance spectroscopy, two methods that are used to determine the shape of molecules (or regions of protein molecules known as "domains") on an atom-by-atom basis.



**Assistant Professor Seth Darst uses electron crystallography to study RNA polymerases.**

But another method, called electron microscopy and image processing (or "electron crystallography") can be used to gain a picture of the entire structure of a macromolecular assembly in one fell swoop—although not always at the high resolution that provides an atom-by-atom picture. One of the practitioners of this method is Assistant Professor Seth Darst, who joined the Rockefeller faculty last year. He is using the method to study RNA polymerases.

In principle, Darst explains, electron crystallography is similar to x-ray crystallography, in that a crystal is bombarded with a high-energy beam to obtain raw data (in the form of a "diffraction pattern") for structural analysis. X-ray crystallography uses x-ray beams, while electron crystallography uses beams of electrons.

But there are some significant differences between the two techniques. For instance, once the electron beam is diffracted off the crystal, it can be refocused by a physical lens—unlike a diffracted x-ray beam, which must be "refocused" by mathematics. Indeed, it is an aspect of this mathematical refocusing, known as the "phase problem," that contributes to the difficulty of analyzing large macromolecular structures by x-ray diffraction.

## Technique uses 2-D crystals

Another difference between the two methods is that x-ray crystallography uses three-dimensional crystals (which can be very difficult to grow) while electron crystallography uses two-dimensional ones. As their name implies, 2-D crystals are sheets of crystallized molecules that are hundreds or thousands of molecules long and wide, but only one molecule in depth. These vanishingly thin crystals are used, Darst explains, because "if you took a 3-D crystal and hit it with an electron beam, the beam would be scattered so strongly that it wouldn't even get through."

To minimize the impact of the electron beam, electron crystallographers use special microscopy methods including "low-dose" electron microscopy, which lowers the beam energy, and cryomicroscopy, which makes the proteins more resistant to damage by the beam. (A state-of-the-art electron microscope with these capabilities will round out the complement of Rockefeller's electron microscopes, all of which will be housed in the technology center in the John D. Rockefeller, Jr. and David Rockefeller Research Building.) Once the raw data is obtained by bombarding many different 2-D crystals of the macromolecule, each with a different orientation, complex computer-assisted computations make it possible to reconstruct a 3-D image of its shape.

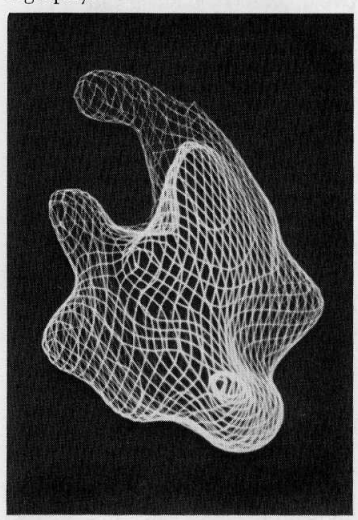
Electron crystallography has been used since the 1970s, but until recently its practitioners were limited to the study of proteins that naturally formed 2-D crystals, such as those found in the cell walls of bacteria and algae. Recently, though, methods have been developed that can prompt virtually any molecule—or macromolecular assembly—to form a 2-D crystal.

Darst was instrumental in developing these new techniques when he was a postdoctoral fellow in the Stanford University laboratory of Roger D. Kornberg. Using these methods, Darst, Kornberg and their colleagues obtained the 3-D structure of the RNA polymerase of the bacterium *E.coli* in 1989, and the 3-D structure of yeast RNA polymerase II in 1991. (Bacterial cells have only one RNA polymerase, while all nucleated cells, or eucaryotes, have three, each of which synthesizes different types of RNA.)

## Goal: catching polymerase in the act

Darst is now extending and developing this work at Rockefeller, concentrating on the *E.coli* polymerase. He and his colleagues want to refine the resolution of the structure already obtained in order to get an increasingly detailed picture, to elucidate the functions of its individual regions through "labeling studies," and to define the structure of the polymerase caught in the act of transcription, with the DNA and RNA in place.

For now, work in the lab is focused on the RNA polymerase alone. But elucidating its structure is just the first step in the researchers' search to understand the mechanisms and regulation of transcription. Ultimately, Darst says, "our goal is to define the physical interactions between the RNA polymerase, the DNA template, the nascent RNA and the accessory factors," such as transcription factors. To accomplish these goals, Darst will also employ x-ray crystallography. For, as he and Kornberg wrote in an paper on electron crystallography, "the best hope of revealing very large molecules at high resolution lies in solving the structures of component parts by x-ray diffraction and fitting the x-ray structures together with the aid of lower-resolution maps from electron crystallography."



**This 3-D structure of *E. coli* RNA polymerase shows a cleft on the surface of the enzyme that is just the right size and shape to accommodate double-stranded DNA. The image was derived through electron crystallography.**

# *Former nurse becomes computer expert*

*By Jennifer Horne King*

In her 13 years at The Rockefeller University, Rachael Kolb first cared for patients of the Hospital as a nurse practitioner. Now, in a dramatically different role, Kolb helps to demystify all aspects of computing to faculty and support staff alike as assistant director of Computing Services responsible for User Services.

"I know it sounds like a strange career change," said Kolb, "but after 25 years of nursing, I was ready for a change. What I like most about Rockefeller is that it gives people a chance to try their skills in new areas."

Kolb trained to become a nurse in her home state, Pennsylvania, and later took part in a two-year program to become a nurse practitioner at the Bronx Municipal Hospital Center. She went on to care for sick children in their homes in the Bronx area. "The work was intensive," recalls Kolb. "The children were very sick and, as a nurse practitioner, I had many responsibilities. After 10 years of this, I couldn't pass up the chance to use my nursing skills in the calmer setting of Rockefeller."

In the Ahrens lab at the Hospital, Kolb worked with both children and adults, many of whom were being studied for hypercholesterolemia, a condition resulting in an excess of cholesterol in the blood. "I liked clinical research," she recalled. "There was a sense that everyone on the team was involved for a common purpose."

It was during this time that Kolb first worked with computers. "As in most studies, we had a tremendous quantity of data to be collected and analyzed," said Kolb. "I got help from my co-workers and from Computing Services staff, but for the most part, I had to figure out how to use UNIX on my own. At times, it was very frustrating."

After six years of clinical research experience, Kolb left nursing altogether, and transferred to Computing Services. She explained: "Although I enjoyed nursing, I was ready to try my new-found skills in computing while continuing to work closely with people. I have always found that mastering something new is tremendously rewarding."

**Rachael Kolb *(right)*, once a nurse practitioner at The Rockefeller University Hospital, is now assistant director of Computing Services. Here, she helps student Fiona Doetsch.**

Recruited to help with Computing Services's outreach efforts, Kolb took part in university-wide computing instruction. With help from other members of the Computing Services team, hands-on workshops were introduced to replace what were formerly lectures.

"Thanks to university support, 69 workshops were held last year, drawing nearly 400 participants to the classroom of the new Users' Area," said Kolb, with excitement. "We haven't even started our workshops this year and already, our voice mail sign-up ran out the first day of registration. Wait lists are beginning to form."

"In an age when labs and departments are racing to keep up with technology, work demands and constant software upgrades, it's helpful to know that there are crash courses available nearby," continued Kolb. "I don't regret th change from nursing. I'm happy knowing that I can save people some of the frustration I encountered when I first learned how to use computers."

# Potpourri

### Tri-Institutional Noon Recital

The Winston String Quartet, a newly formed group of talented young musicians who have been associated with Juilliard, will play two quartets by Ludwig van Beethoven and Franz Schubert at the Tri-Institutional Noon Recital today (Sept. 24). The concert, to be held in Caspary Auditorium at noon, is free; all are welcome.

### Sunday film

*The Producers* (1968), directed by Mel Brooks, will kick off this season's film series in Caspary Auditorium at 7:30 P.M., Sun., Sept. 26. Admission is free.

### Conference

The Rockefeller University will host a conference on "Cancer Prevention and Early Detection: Practice Perspectives, Controversies and Future Directions," in Caspary Auditorium from 8:00 A.M. to 4:30 P.M., Wed., Sept. 29. Sponsored by the American Cancer Society and a number of other institutions, the conference will offer health care providers the most current recommendations for use in health practices. Subjects include tobacco control, nutrition and public education. There is a $40 registration fee which includes conference materials and a continental breakfast; lunch is not included. For additional information, registration, educational credit or student discounts, contact David Lehmann, 237-3824.

### Voter registration

Members of The Rockefeller University community are invited to register as voters in the Tower lobby in a drive conducted by the League of Women Voters, Fri., Oct. 1, 11:00 A.M. to 2:00 P.M. The next election will determine the mayor, comptroller, city council, public advocate, civil court judges and some borough presidents. (The registration deadline is Fri., Oct. 8.) U.S. citizens of 18 years or older who have resided at least 30 days at their current address are eligible. For more information, contact Mary Rivers, x8969.

### German classes

For more information on a beginner-level German course starting at the end of this month, call Piera Cicchetti, x8945.

### Luncheon service

Restaurant Associates is accepting reservations for luncheon service in Abby Aldrich Rockefeller Hall for two sittings: one at noon and one at 1:00 P.M. There is now a common table for those who have not made arrangements to join other guests. Call x8894 to make reservations. Walk-in guests will be seated if space is available.

### Computer workshops

The following computing workshops will be offered in the Computing Services Users' Area in Smith Hall A21, beginning Mon., Sept. 27:

- Macintosh Workshops: Introduction to the Macintosh (two hours); Microsoft Word 5.0, Parts I, II and III (each two hours);
- Macintosh and PC workshops: Introduction to Excel 4.0, Parts I and II (each two hours); Kermit for Macintosh and PCs (one hour);
- PC workshops: Introduction to Windows 3.1 (two hours); Introduction to Microsoft Word for Windows 2.0, Parts I, II and III (each two hours); WordPerfect 5.1, Parts I, II and III (each two hours);
- UNIX workshops: Introduction to UNIX and Electronic Mail (three hours); Introduction to the Vi Editor (two hours); UNIX for Sequencers, Parts I and II (each tw hours); and Electronic Mail (one hour).

To register, leave voice mail at x7768, giving full name, lab/depart ment, telephone number, box num ber, and the name and date of the workshop(s). A number of the workshops are filled. Future workshops will be scheduled using wait-listed names. All requests must be confirmed by Computing Services. Because space is limited please give prior notice of cancellations. For more information, call Computing Services, x8940.

### Software licensing agreement

The Digital Equipment Corporatio (DEC) has awarded The Rockefeller University a campus-wide software license grant. The grant provides, at no cost, licenses to use most DEC, VMS and ULTRIX software and various Alpha (OPEN/VMS and OSF) soft ware. The program is administered by Computing Services. Those interested in licenses should contac the consultant, x8940. In addition Computing Services will provide access to various VMS, ULTRIX and Alpha binary distribution media, as available.