FOSTERING COMMUNICATION AND COLLABORATION

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

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BUILDING 50: LABS FOR THE 21ST CENTURY

by Rebecca Kolberg

Almost everyone at NIH has heard about plans for an impressive new Clinical Research Center. But mention Building 50 and you'll probably draw a blank stare, unless you're talking to someone from one of the labs slated to move into the new multi-institute research facility.

If all goes according to schedule, ground will be broken next March and the 248,000-square-foot facility should be up and running by the fall of 2000—a full two years ahead of the Clinical Research Center's target opening date.

"What Building 50 does is replace Buildings 2, 3, and 7—the last lab buildings in the original round robin renovation process," says Steve Ficca, Director, Office of Research Services (ORS). Due to their historic nature, Buildings 2 and 3 will be preserved and converted into office space, while Building 7 is scheduled to be torn down in the last phase of the 20-year NIH Facilities Master Plan.

> "WE WANTED SCIENTISTS TO LOOK TOWARD THE COLLABORATIVE POTENTIAL OF A MULTI-INSTITUTE LABORATORY BUILDING"
> —*Cyrena Simons*

Parts of NHLBI, NIAID, NIAMS, NIDDK, and NCHGR will be moving into the new four- or five-story building, which will be located in what is now the parking lot just north of Building 12. About 300 parking spaces will be eliminated, but NIH officials

continued on page 6.

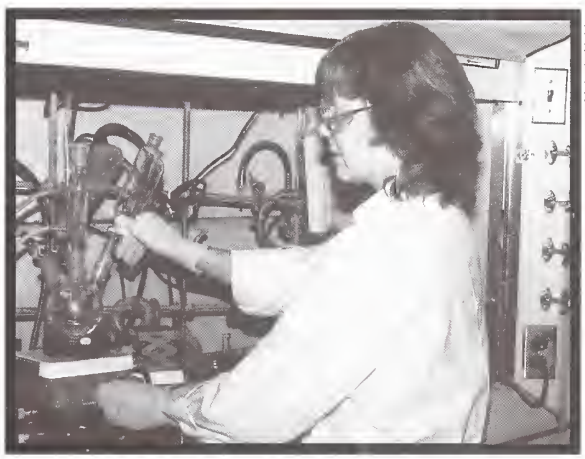
CHEMISTRY AND BIOLOGY, FINDING THE EQUILIBRIUM AT NIH

by Celia Hooper and Rebecca Kolberg

Maybe it's just part of the age-old scramble for scientific resources and respect. Maybe it's much ado about nothing. But then again, maybe it's a Kuhnian paradigm shift in which NIH scientists are increasingly turning to molecular biology, rather than pure organic chemistry, as the favored source of new raw materials, molecules, and ideas for their biomedical research.

Whatever is going on, one thing *is* certain: it's not easy being an organic or medicinal chemist at NIH these days. Some senior chemists report being squeezed out of lab space or finding themselves afraid to ask for funds to buy essential equipment. Younger chemists are fighting to convince their molecular biology colleagues—as well as tenure-review committees—that they are much more than simple craftspeople. And newly minted Ph.D.s in organic and medicinal chemistry are finding a dearth of post-doc slots in intramural labs.

On the basis of such concerns, the American Chemical Society (ACS) has repeatedly called on NIH over the past two years to strengthen organic and medicinal chemistry in the intramural program. In a 1995 letter to NIH, ACS President Ronald Breslow said he had looked into the situation of health-related organic chemistry in the intramural program "... and have been assured by some chemists at NIH that the situation is as bad as I had feared."



Melanie Holden

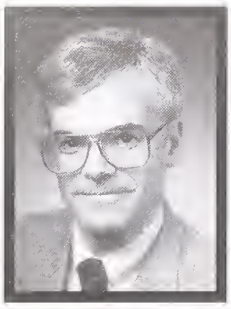
Amy Hauck Newman.
For more on chemists and their work, see pages 9-14.

In the same vein, a former ACS president, Ned Heindel, wrote to NIH in late 1994 to warn about the "weakening" of NIH's biological and medici-

continued on page 9.

CONTENTS

THE NIH INTRAMURAL SCIENTISTS DATABASE



Michael Gottesman

What do you do if you need to find an NIH scientist who routinely uses an instrument or technique that is not available in your lab? How can NIH respond quickly to a request from Congress for the newest intramural discoveries in a particular field or for the number of projects dealing with a rare disease? How many times per year are scientists bothered with administrative requests for information about their research and publications?

Our office is now joining forces with institute administrators, the Office of Human Resource Management, the Office of Equal Opportunity, the Office of Financial Management, and DCRT to develop a personnel database that uses modern tools for the electronic collection, cataloging, and distribution of data to answer these questions and others.

How will the NIH intramural database be assembled?

The goal of the NIH Intramural Scientists Database project is to have a comprehensive, easily accessible source of information for scientists, administrators, and the public while protecting the confidentiality of personnel information. The database will be physically located in DCRT computers, and information on all NIH scientists—including students, postdoctoral fellows, senior technical staff, staff scientists, visiting scientists, and tenure-track and tenured investigators—will be fed into the database from our personnel and financial records. Once a year, or as often as they please, scientists will update biographical information, annual reports, and bibliographies.

Currently, the best way to collect such data is through a questionnaire posted on the World Wide Web. Previously assembled information—from a bibliography or annual report, for example—can be electronically pasted into the appropriate field on the questionnaire. As it turns out, a Web site which satisfies most of our requirements already exists and is supported by the Community of Science (COS), housed at Johns Hopkins University. This easy-to-use site was created with a goal similar to ours, namely, to establish an international database of scientific expertise. With help from COS, this site is being adapted for our database. In the next few months, all NIH scientific staff will be asked to sign on to the NIH-COS site, answer some questions, and the annual task of providing data about your work will be almost complete. This year you will also have to supply an abstract of your research for the annual reports, but by next year, we hope to use the Web-based system to collect annual reports as well. Once collected, these data will be downloaded to the NIH central database and combined with administrative information needed for management of the intramural program. Training or service sites will be provided for scientists and support staff who are not already well-grounded in the use of the Internet.

What advantages will the NIH intramural database have for NIH scientists?

The new database should save time and money. Currently, NIH scientific staff are repeatedly asked to provide information on their research for, among other things, annual reports, annual bibliographies, and various catalogs of research activities. Scientists may also be queried about recent accomplishments, course work, and special expertise. Responses to each request may demand different formatting and hours of extra work, but once the new database is established, a yearly updating of a scientist's entry will suffice. Furthermore, thanks to the powerful search engines available for information on the World Wide Web, defined fields—such as scientists' bibliographies—can be searched easily and completely. This more useful, more up-to-date information will serve us better than our current catalogs in recruitment and in the enhancement of communication and collaboration with intramural and extramural colleagues.

How will the database be used as a management tool?

Institute and Scientific Directors and my office are charged with ensuring that NIH programs are effectively managed—for example, that postdoctoral fellows are given projects that result in publishable work, that pay is equitable, and that safety course work has been completed. The NIH Database Project will make it much easier to collect and analyze the management information we need.

How will we address security and confidentiality concerns?

One potential danger in establishing this large, central database is that confidential personnel information might be more easily accessible to individuals who do not have a legitimate need for it. Current security systems for databases create a "firewall" between public information—such as the annual abstracts now available via CRISP—and private personnel information, such as pay. Only individuals with appropriate access codes can obtain data behind the "firewalls." We will not release this database until we are satisfied that confidential information is adequately protected.

Are there any other benefits of the NIH intramural database?

Several. First, it will be simple to create catalogs that profile various subsets of scientists working at the NIH. These could be institute-based, discipline-based, special-interest-group-based, or even technique-oriented. In addition, we will be able to track students and postdoctoral fellows electronically once they leave the NIH. Fellows enrolled in our database could be asked automatically by e-mail to update their biographical information after they leave NIH. These data will help us determine the optimal size for our training program and provide trainees with accurate information about career prospects. Currently, lack of automated tracking puts these data beyond our reach. An added bonus of the database system is that requiring all members of NIH's scientific staff to be Web-savvy enough to retrieve and enter database information will help prepare scientists for the electronic commerce system, online journals, and "virtual" scientific meetings that are in our future.

At the outset, some staff may be reluctant to take the time to learn to use the Internet. I am confident, however, that the initial investment of time will be handsomely rewarded with future savings and new research and management tools. I welcome your ideas on creative ways to use the NIH Intramural Scientists Database and any concerns you may have about it. ■

Just Ask!

Dear Just Ask:
Why do we have both X numbers and *CAN numbers? Photography asks for an X number. Xeroxing asks for X and CAN. Other departments ask for just the CAN. Mysterious!*

—Anonymous

Dear Anonymous:
NIH's accounting system can indeed be mysterious. The use of the X, or universal number, is twofold: it is part of the mechanism that NIH uses to pay for certain frequently used Service and Supply Fund activities, *and* it allows for tracking of each use of shared facilities, such as the Copy Center or Medical Arts and Photography Branch (MAPB).

Each X number is affiliated with only one CAN, which is established by your institution's budget office to pay for a multitude of various services and personnel costs incurred by your organization. All services and personnel costs generally come out of one or more organizational CANs. Whereas the "status of funds system" (SFS) allows for tracking costs associated with one or more CANs, it does not allow for actual identification of charges against a specific X number. Copy Center and MAPB charges are identified by a particular X number, and the expenditures against a particular X number are tracked through the use of another NIH system called the "Administrative Data Base" (ADB). So, if each person within your organization has an assigned X number at the beginning of the fiscal year, all Copy Center and MAPB charges can be easily traced to the appropriate individual.


Rebecca Kolberg
Eugenie Lackey

If, on the other hand, your organization's CAN is used for all Copy Center and MAPB charges, there is no discernible way to tell who was spending what on Copy Center or MAPB services. It would be impossible to track individual expenditures because the same CAN is being used repeatedly by everyone.

I guess it all comes down to the intricate details of budgetary accountability and the checks and balances that have been set up to ensure that NIH's money is spent appropriately and efficiently. Mystery solved!

—Eugenie Gazdik Lackey, Administrative Officer, OIR

Catalytic Reactions

Below are comments that we received for topics that were raised in the July-August issue.

On charge cards coming to NIH:
This is long overdue. I have been at NIH since 1970 and have found the procurement procedures to be one of its worst features. I could write reams on the many nightmare situations I have experienced in the "black hole" of procurement.

—Peter H. Fishman, NINDS

Charge cards sound great. I'm eager to get one. I often need to order items that are relatively inexpensive but unusual for NIH scientists. These are practically impossible to get in a reasonable time frame under the current system.

—Robert Tycko, NIDDK

On campus parking problems:
My husband and I are both scientists at NIH. We carpool and have two small children at two different daycare facilities. It really irritates me when no spaces are available in front of the NIH preschool [Bldg. 35] when I am trying to drop my child off or pick her up because NIH employees, visitors, repairmen, delivery trucks, or construction workers are parked in spaces allotted for parents of NIH preschoolers. Then, I have difficulty finding a carpool space—even at 8:45 a.m. because general parking permit holders have parked in so many of the carpool spaces. [Carpool lots do not open to general permit parking until 9:30 a.m.] Employees with general permits should be more considerate of those who are carpooling. I realize that the NIH police can only ticket so many lots in a day; however, there are no penalties for repeat offenders. I believe such a penalty should exist, e.g. loss of parking privileges for several months after the tenth ticket in one year.

—Anonymous, NIH

One thing I'd like to know about the parking situation: There are so many carpool spaces on the campus, but I've never seen more than one person get out of or into a car parked in a carpool space—even cars with green stickers. How do these people get green stickers when they are obviously not really carpooling? And why are there so many spaces for them? ■

—Anonymous, NIH

RNA Symposium

On Oct. 22, 1996, the NIH RNA Interest Group will host the Mid-Atlantic Regional RNA Symposium, featuring talks by researchers from NIH and nearby universities, a poster session, and a keynote address by Tom Blumenthal, Indiana University, on "Operons in the Nematode Genome." Everyone interested in learning more about the RNA-related research going on in labs in the region is invited to attend. Anyone wanting to present a poster on an RNA-related topic must pre-register an abstract by September 23, 1996. There is no fee, but preregistration is essential to ensure that all posters can be accommodated. Information on how to preregister and submit abstracts, final schedule, updates, and more can be found on the RNA Interest Group's Home Page (http://www.nih.gov:80/sigs/rna/). For additional information, contact one of the organizers: Sue Haynes (phone: 496-0243; e-mail: sh4i@nih.gov), Brenda Peculis (phone: 402-8760; e-mail: brendap@bdg10.niddk.nih.gov), or Sarah Woodson (phone: 405-7956; e-mail: sw74@umail.umd.edu). ■

Ethics Forum: Intramural Seeing "Red" Over Peer Review Issues

by Joan P. Schwartz, Ph.D., NINDS

In the January-February issue of *The NIH Catalyst*, you may recall a box, entitled "Ethics in Peer Review: A Scenario to Consider." We invited readers to give their perspective on the following situation: A Dr. White reviewed the paper of a Dr. Red, despite the fact that White's lab was working on the same research problem. White shared the paper with colleagues in his lab, delayed publication by asking for revisions, and subsequently submitted a paper with results essentially identical to Red's, without citing Red's paper.

We received two thoughtful responses: one from Suzanne Epstein at CBER and one from William H. Goldwater, who retired in 1993 from the Office of Extramural Research.

Epstein writes: In my opinion, Dr. White had a clear conflict of interest and should not have reviewed the manuscript, since he was working on something too closely related. It is necessary to be competent in an area to review a paper in that area, but if one is actually working on the same thing, then one should be excluded as a reviewer.

Dr. White should have returned the paper without reading beyond the title. The journal could also have done better and prevented the problem. Dr. White should not have had the opportunity to read the manuscript. A journal I review for calls ahead with the title of a paper (and additional information if needed for a decision) to ask whether I can review it, and if there is a clear conflict of interest, the paper is not sent in the first place.

Goldwater writes: During the last years of my tenure in OER/OD, I developed and implemented many rules and regulations governing conflicts of interest and related topics for extramural operations (and pertinent likewise to intramural). This example shows many flaws in White's behavior, mostly in failing to communicate adequately with various other folks—contrary to NIH scientific peer-review standards for grants and contracts. These failures include

- failure to recognize that a conflict of interest (COI) question exists and to discuss it with the editor(s) running the review (the latter might or might not have changed the responsibility to another reviewer but should have, consistent with good standards to avoid COI);
- consequent failure to avoid review where there was a conflict;
- sharing the Red paper with his staff;
- failure to communicate to Red regarding the overlap of specific interests; and
- subsequent failure to cite Red's paper in his own publication.

Lorna Heartley

Joan Schwartz

Having committed these various breaches in the process, White should now, belatedly, communicate with Red and Journal L, where he published, regarding his failures of judgment. He should seek forgiveness and try to make amends. He certainly should have communicated earlier.

This situation is similar to one presented last summer in the AAAS on-line forum involving a half dozen or so scenarios concerning ethical problems in research.

During my communications with that AAAS forum last summer, I found that many persons and agencies do not hold to the same high standards as does NIH in avoiding conflicts of interest in peer reviews of grant/contract proposals. Some groups even allow a reviewer simply to inform the staff person running the review that he/she has a conflict, and then proceed to review the proposal as if nothing were wrong.

What actually happened: In fact, the scenario was based on the experience of an intramural scientist who suffered Red's fate. Conversations with "Dr. White" failed to elicit any satisfactory response and "Dr. Red" has now filed a complaint with the Office of Research Integrity. ■

Structural Biology Group to Host Colorful Workshop

The Structural Biology Interest Group is sponsoring a workshop on "The Importance of Global Membrane Organization in the Control and Function of Integral Membrane Proteins." The workshop will highlight recent findings in the laboratories of Richard Hendler, NHLBI; Ira Levin, NIDDK; and Burton Litman, NIAAA. In a collaborative study, Hendler and Levin have shown that lipids of the purple membrane of *Halobacterium halobium* directly influence the conformational structure of bacteriorhodopsin and control the kinetics, relaxation pathways, and regulation by actinic light of the photocycle intermediates of this integral membrane-protein proton pump. Litman's laboratory has demonstrated a direct effect of phospholipids on the photocycle of visual rhodopsin in native rod outer-segment disk membranes and liposomal vesicles. Visual rhodopsin is one of a family of G-protein-coupled receptors.

In addition to the NIH researchers, outside experts who will participate in the workshop are Walther Stoeckenius of the University of California at Santa Cruz and the Max Planck Institute, Frankfurt, Germany; Thomas Ebrey of the University of Illinois, Urbana; and Mostafa El-Sayed of the Georgia Institute of Technology, Atlanta. The one-day workshop will be held on Oct. 21, 1996, from 9:00 a.m. to 5:30 p.m. in the Lister Hill Auditorium. For more information on registration and further details contact Hendler (phone: 496-2610; fax: 402-1519; e-mail: rwh@hekix.nih.gov). ■

HHMI/NIH Training Earns Kudos

by Rebecca Kolberg

A new report from a panel of distinguished outside experts cites the joint NIH–Howard Hughes Medical Institute research training program for medical students as a program worth copying.

In a preliminary draft of the report which will be released in November, the NIH Director's Panel on Clinical Research, a 14-member committee charged with finding ways to revitalize U.S. clinical research, singles out the joint venture between the Howard Hughes Medical Institute (HHMI) and NIH as a paradigm for recruiting talented M.D.s into clinical research.

In the 11 years since its inception, the HHMI-NIH Research Scholars Program has brought 400 medical students from 89 U.S. medical schools to the Bethesda campus for a year of intensive basic research experience that adds a year to their regular medical training. According to the panel's report, 40 percent of participants in the first two years of the program now have full-time academic appointments. Over the past decade, HHMI research scholars have also published more than 250 research papers based on their work at NIH.

"It's a wonderful model," says David Nathan, president of the Dana-Farber Cancer Institute in Boston and chair of the panel. "We feel strongly that the making of a successful physician investigator usually begins in medical school." Nathan himself was drawn into research decades ago when, as a second-year medical student at Harvard, he pursued an independent research project that began as an effort to develop a model of hepatic coma and ended with a published paper describing a method to measure ammonia. "It was a huge thrill. It made me think, 'My god, I can do this!'... Without that experience, I'd probably be practicing medicine today in Cambridge."

Currently, HHMI-NIH scholars are recruited from the ranks of U.S. medical schools and work mainly in basic research labs at NIH. The draft report recommends that a similar research program be established at NIH's Clinical Research Center (CRC). Under that recommendation, as many as 30 medical students would select a preceptor who is a clinical researcher and would also participate in the CRC's formal training courses, called the core curriculum. "Total cost is estimated to be less than $1 million per year and [the CRC program] would serve as a model for other centers," the panel states.

Assistant Director for Intramural Affairs, Richard Wyatt, NIH's liaison for the HHMI-NIH Research Scholars Program, says that he is excited that the panel of outside advisors developed the idea of a clinically oriented scholars program. Wyatt adds that such a program "should also provide an opportunity for partnership in clinical research training with other private outside organizations, modeled after the valuable relationship between NIH and HHMI."

Barbara Ries

NIH Director Harold Varmus with HHMI-NIH Research Scholar

Other aspects of NIH's physician-researcher training program that particularly impressed the outside reviewers were the CRC's new core curriculum and NIH's loan repayment programs which pay off educational and medical school loans for clinical researchers from disadvantaged backgrounds and for researchers whose projects focus on acquired immune deficiency syndrome (AIDS).

Jean Wilson, professor of internal medicine at the University of Texas Southwestern Medical Center in Dallas and chair of the panel's training subcommittee, says the Clinical Center's core curriculum is a sterling example for other institutions to follow. "There is widespread sentiment that there needs to be more rigorous training for clinical investigators," Wilson says. "That should help to ensure the same quality of research in clinical investigation as in other types of biomedical research."

However, Wilson emphasizes that training is just half of the problem confronting clinical research today. The other half is recruiting top-quality candidates into the training programs. Unlike Ph.D.s and M.D.-Ph.D.s, most of whom graduate without a heavy debt burden, M.D.s are typically saddled with significant debt when they graduate. Financial constraints prevent many from even considering a research career, Wilson says. The subcommittee chair says he hopes that the loan-repayment programs now available to intramural NIH researchers—which pay up to $20,000 a year of a researchers' educational debt—can be expanded to improve M.D. recruitment at extramural research institutions.

Other recommendations included in the panel's draft are

- Enhance physician-researcher training programs by offering special degrees, such as an M.D. with honor or distinction or a special master's degree.
- Establish midcareer salary awards for clinical investigators and other special awards to relieve clinical investigators from clinical duties.
- Consider programs to provide clinically oriented training for Ph.D.s who do not have M.D.s.

Next, the panel will focus on other topics, including the current state of U.S. clinical trials, the role of the NIH Clinical Research Center in shaping the overall research landscape, and the impact of managed care on clinical research. ■

LABS FOR THE 21ST CENTURY
continued from page 1.

say the loss of those spaces will not affect on NIH's employee-to-parking-space ratio because staffing levels will be lower in the year 2000, and spaces that were planned for removal will be retained due to the construction. The architect chosen to design Building 50, Hansen Lind Meyer (HLM) of McLean, Va., along with GPR of White Plains, New York, a lab planning firm, and Ross Murphy Finkelstein (RMF) of Baltimore, a mechanical engineering firm, presented three design concepts to an NIH oversight committee in late June (see figures). The committee, which includes researchers and lab-safety experts, was slated to select in late summer one of the three concepts to be used as a basis for the final design development and construction.

Among the things that the designers took into account in drawing up their schematics were comments from interviews with the scientific directors and principal investigators whose labs will be in the building. In fact, ORS set up an electronic forum, or "listserv," to encourage the exchange of ideas among all the principal investigators who will move into Building 50, and it established a World Wide Web site where anyone from NIH can track the project's progress.

Square footage and bench space aren't the only topics of discussion. At "mixers" hosted by ORS, researchers from the various institutes got a chance to discuss the scientific projects with their neighbors-to-be. "We wanted scientists to look toward the collaborative potential of a multi-institute laboratory building," says Cyrena Simons, the facilities design liaison in the ORS Division of Engineering Services.

NIAID Scientific Director Thomas Kindt says the general reaction has been very enthusiastic. "Scientists like to be included in the overall design process. We aren't happy in a building that we haven't helped to design." Still, mixed in with the enthusiasm for a sparkling new facility are a few concerns about forsaking familiar confines. Kindt says that although Building 50 should offer an environment where it is easier and safer to conduct vaccine development and other projects involving infectious agents, some NIAID researchers are reluctant to move away from their "neighborhood" of Buildings 7 and 4. "It's the same kind of worries you might have when you move from a small town to New York City. You may miss the old place," says Kindt, who plans to move both his lab and the scientific director's office into the new facility.

Similar sentiments are present among many researchers now in Building 3, according to NHLBI Scientific Director Edward Korn. "We like the small building, the ability to get everywhere by running up and down steps ... the sense of 'family' that comes from knowing everyone," he says. "However, Building 3 has long been unable to serve the needs of contemporary research, and a move is both necessary and overdue." Korn adds that what will be lost by being in a larger building should be more than offset by the gains of being in close proximity with excellent scientists from other institutes who work in similar fields.

In a vision resembling the "layer-cake" plan for the Clinical Research Center, designers of Building 50 have physically separated lab areas from "interstitial" areas that house the mechanical, electrical, and venting systems for lab equipment. Such a design makes it cheaper and easier to perform routine maintenance and to make renovations without disturbing scientific research. However, Simons says designers are being careful not to repeat what happened in Building 37, where the placement of ventilation

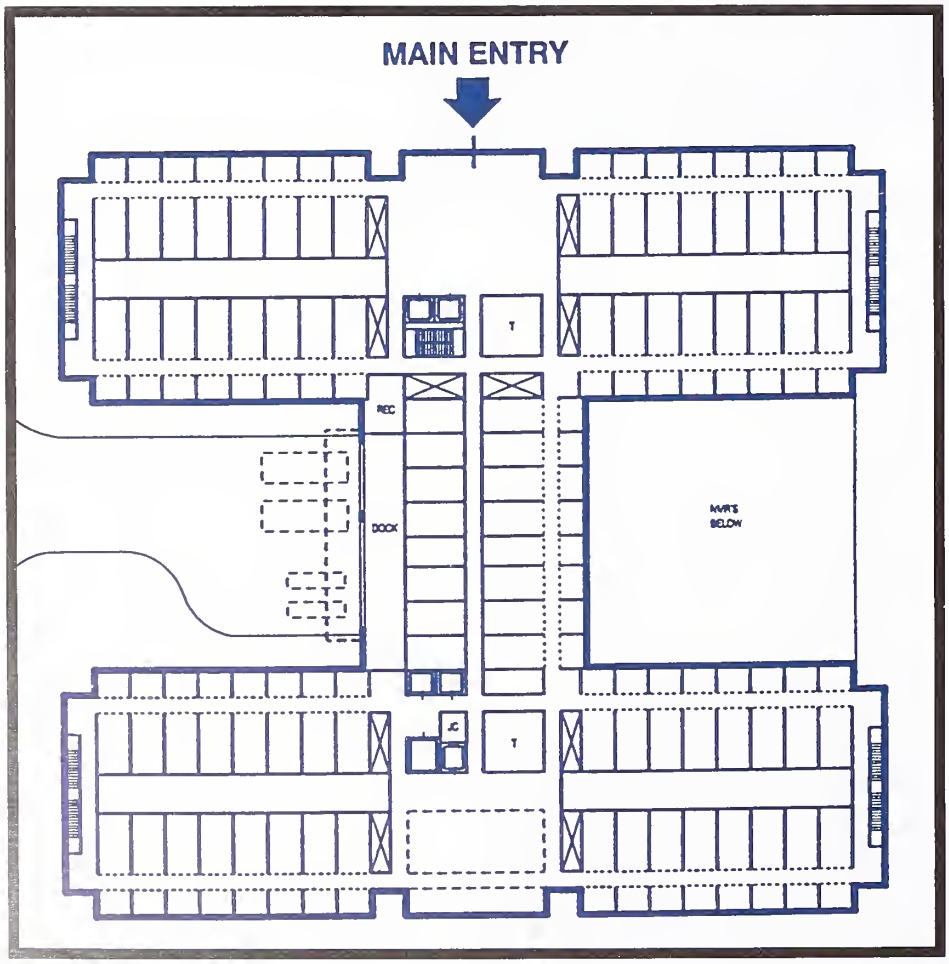


Figure 1. This is one of three plans for Building 50 that was under consideration in late summer.

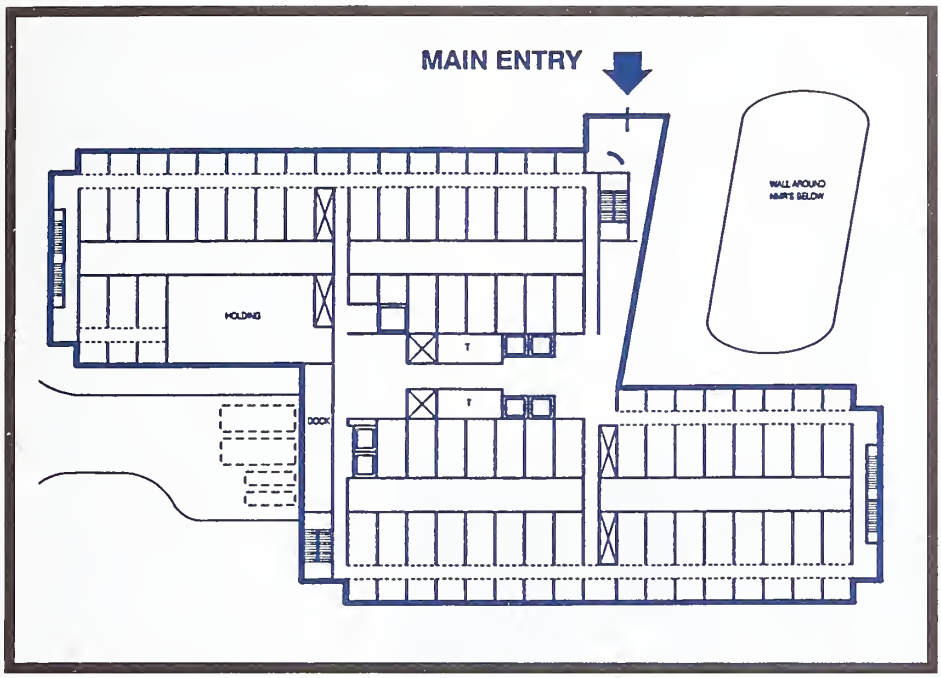


Figure 2. This is another plan also being considered for Building 50.

shafts created a floor plan that makes it difficult for scientists to get from one place to another.

One concept being debated in early summer was the creation of "linear equipment rooms," which would be used as a centralized area to house banks of shared equipment such as refrigerators and centrifuges. Another controversial concept is "ghost corridors," which would separate scientists' lab benches from their computer work stations. Some scientists feel strongly that removing work stations from the lab benches would lead to lost productivity, whereas others argue that the move would create more bench space and improve lab safety.

One unique aspect of Building 50's design is its basement. "You usually don't have much science going on in a basement. In this building, it is the area that is most oversubscribed," says Simons, noting that the underground space will be used to provide vibration-free space for sensitive instrumentation, such as high resolution electron microscopes and nuclear magnetic resonance (NMR) equipment, including a state-of-the-art gigahertz NMR machine.

From the vantage point of the building's project officer, Frank Kutlak, who is an architect with the ORS Division of Engineering Services, the biggest challenge in planning for Building 50 is anticipating what types of scientific questions its occupants will be addressing years from now. "Our design needs to be specific enough to meet the needs of current users but generic enough to easily adapt to change."

Serving a purpose similar to the Clinical Research Center's proposed balconies and alcoves, the Building 50 designs contain small break areas located adjacent to lab clusters in which researchers from multiple labs can chat informally or eat their lunches. "We want to maximize the science, but we also wanted to provide adequate 'people space,'" Kutlak says.

NIAMS Scientific Director Henry Metzger agrees, cautioning principal investigators to keep their staffing levels in sync with the spirit of the building. "We need to protect the decompression of overcrowded labs that this building will allow. It can be easily undermined by the overzealous hiring of as many bodies as can fit. That part of intramural behavior might best be left behind by the lucky new tenants of Building 50." ■

DDIR's Bulletin Board

All lab, branch, and section chiefs, along with all other interested NIH scientists, are urged to subscribe to the Deputy Director for Intramural Research's Bulletin Board. In addition to the regular bulletins distributed to subscribers following each scientific director's meeting, the list is used to send other messages that the DDIR needs to distribute quickly. To subscribe, send an e-mail message that reads "Subscribe DDIRBB-L Your Name" to the following e-mail address: listerv@list.nih.gov ■

Free Seminar Space

The FAES has announced that NIH seminars can be held free of charge at its Social and Academic Center between 10:00 a.m. and 4:00 p.m. on weekdays. The Center is located at the corner of Old Georgetown Road and West Cedar Lane across from the firehouse. The space may be booked for as long as two hours, and up to 40 people can be seated in a classroom arrangement in a room equipped with both carousel and overhead projectors, a screen, and a whiteboard. Food and beverages can be served. Call (301) 530-2194 to make reservations. ■

A Farewell and Thanks . . .

To Rebecca Kolberg, who served as managing editor of *The NIH Catalyst* for the past two years. Kolberg left to become the editor of Time-Life Medical's World Wide Web site. With a firm, skilled hand, Kolberg put *The Catalyst*'s publication schedule back on track and wrote numerous excellent articles. She launched new features, recruited new interns, and brought new life to the content and look of this newsletter. She will be missed. ■

Telemedicine at NIH

by David Ehrenstein, Ph.D., NIDCD

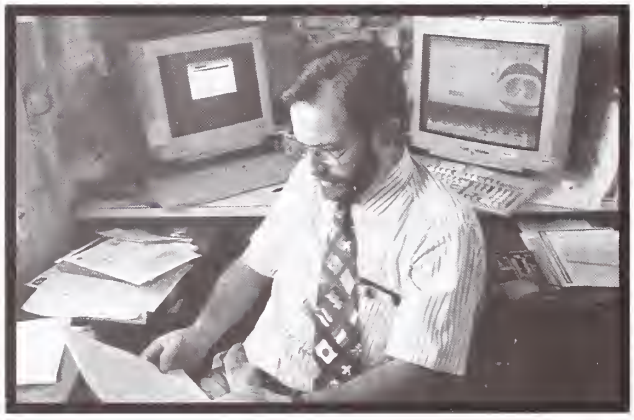
A doctor in a patient's room in the new NIH Clinical Center points to the computer monitor on the wall to review the patient's progress. She shows a summary of the treatment to date, along with X-rays, blood test results, and histopathology micrographs of the patient's diseased tissues over the course of the treatment regime. In response to a question about an X-ray, she calls the radiologist, who answers using a remotely activated pointer on the screen.

This scenario is now closer to fact than fantasy and may be commonplace when the new Clinical Center is built in a few years. "Telemedicine" is coming to NIH thanks in part to strong support from the head of the Clinical Center, John Gallin. "We would like the Clinical Center to be the pace-setter for using telemedicine in research," he says. According to David Henderson, the Clinical Center's deputy director for clinical care, telemedicine will "improve both the quality and efficiency" of care at NIH and "make better physicians of us all."

One element of telemedicine being developed at NIH is video conferencing. Gallin and Henderson foresee patients being interviewed for possible inclusion in NIH protocols via video link, reducing both travel costs and the hardships of travel on sick patients. Follow-up visits could also be reduced by video conference meetings with patients and collaborating doctors. Such telemedicine encounters will certainly be improved by the use of "virtual" exam tools, such as a stethoscope and an otoscope that will allow doctors at remote sites to see and hear right along with the physician doing the exam. Two telemedicine "suites," complete with such tools, are now under development at the Clinical Center.

Henderson and Gallin see these advances as especially appropriate for NIH, which draws patients from every state and many other countries. Previously unreachable patients, such as those in emergency rooms or too infectious to travel, could become subjects of NIH research. "When we conduct clinical trials, we'll be able to broaden the number of people who can be in the study—both patients and clinical collaborators," says Gallin.

Of course, clinical researchers at distant sites have been collaborating for many years, but one of their major difficulties has been sharing patient records. Steve Holland of NIAID is involved in a telemedicine project that should help in this area. Holland notes that keeping track of patient records and data and getting access to them can be challenging just within one hospital, but for collaborations between doctors across the country—as with Holland's work with collaborators at the National Jewish Hospital in Denver, with whom he is studying multidrug resistant tuberculosis (TB)—the recordkeeping is even more complicated.



David Ehrenstein

Steve Holland

The solution, developed by programmers at Los Alamos National Laboratory in New Mexico and doctors at National Jewish, is software that integrates the entire set of information on each patient into a single organized entity called the Graphical Patient Record (GPR). From his office in the Clinical Center, Holland can call up the GPR for a TB patient at National Jewish and view histories, lab test results, physician comments, X-rays, and any other data, all with the click of a mouse. Without this technology, there would be a lot more correspondence to keep track of, he says. "I would get X-rays in one pile, slides in another pile, records in another pile, and then it would be up to me to keep all that straight when each one came in."

This type of software should also allow patients and their doctors to view their records efficiently and in detail without leaving the hospital ward. Holland, who is troubleshooting the new software, says it is ideal for his research on multidrug-resistant TB because a detailed account of every drug used (and its effects) is essential for proper treatment of his study patients, who are located in both Bethesda and Denver. Along with the physician reports on each treatment, the GPR gives immediate access to test results, with one icon representing each type of analysis performed—from X-rays to sputum analysis. With all the data centralized, Holland can look at a CAT scan on his computer screen at the same moment as a Denver physician who is treating the patient and discuss the prognosis by phone. He hopes the software will thus put an end to the frustrating calls in which his opinion is sought based on an X-ray described over the phone.

In addition to making data more accessible, the GPR allows new kinds of analyses to be performed on the data. For example, looking at a specific patient's X-ray, a doctor can request all similar X-rays in the entire library of data from all patients. The images are then arranged in order of the degree to which they match the original X-ray, allowing direct comparison of a new patient's progress with outcomes from previous patients. "That's got enormous implications [for diagnosis]," says Holland. The software also allows many manipulations of CAT-scans, such as viewing of a particular slice of a patient's scans over the time course of his or her treatment.

Another benefit of these new methods is educational. A joint Telemedicine project between NIH, the National Naval Medical Center, and Walter Reed Army Hospital is primarily aimed at teaching and collaboration in the D.C. area, but it has the potential to benefit doctors nationwide. Rather than simply reading reports of NIH treatments of their patients, local doctors can be involved in their patients' treatments all along through telemedicine. "People at the NIH, in general, are experts [in specific fields], and the diseases we treat tend to be uncommon," says Holland. "So the chance for us to collaborate with local physicians in the care of their patients . . . has tremendous implications for improving the knowledge about some of these diseases and, therefore, improving knowledge about the things that we study overall."

Alan Graeff, chief of information systems for the Clinical Center, has been involved in the technical side of NIH telemedicine, including Holland's computer project and the development of the telemedicine suites. He cautions that, although the dreams of these technologies are certainly achievable, progress will be incremental. "We're not going to be jumping into virtual surgery overnight," he says. His office, the Clinical Center's Information Systems Office, is already helping several NIH researchers set up video links, however, and stands ready to support new telemedicine projects.

What difficulties lie in the path to telemedicine technologies? Video conferencing in its most basic form is well established from its use in the business community, but technical standards for telemedicine video links are needed, especially for virtual exam tools. Graeff is now working with consultants to develop these standards at NIH. Down the road, if telemedicine becomes widespread, a series of complex legal issues, such as liability, billing, and licensing, may need resolution.

There is also the issue of cost. Although the equipment requires major up-front investment, Holland thinks the money may be recovered in savings. "You may be able to save millions in the travel budget," he says, noting that both the state of Georgia and the Department of Defense have made major telemedicine investments in recent years partly for that reason. Also, certain specialists, such as radiologists (who read and interpret X-rays), may not be necessary at every hospital if they can work online. "I think that telemedicine and these sorts of interactive approaches will be necessary economies in the not very distant future," says Holland.

Gallin is enthusiastic about the opportunities that telemedicine offers for improving care and research at NIH and encourages clinical researchers to start giving serious thought to its applications. "My goal is to get people oriented so that when we move to the new hospital, we'll be ready for telemedicine." ■

CHEMISTRY AND BIOLOGY
continued from page 1.

nally related chemistry programs and to inform him that "the attractiveness of postdoctoral work at NIH for chemists has diminished."

Both Breslow and Heindel acknowledge that NIH has a proud tradition of organic and medicinal chemistry, represented by Bernhard Witkop, William Clark, Claude Hudson, and Lyndon Small, among others. However, they express concern that when luminaries such as these retire, they and many of their programs have not been replaced. To continue the intramural chemistry tradition, Breslow, a professor of chemistry at Columbia University in New York, is advocating that NIH recruit an organic or medicinal chemist of "international stature."


Peter Cutts Photography

Ronald Breslow

To get a bearing on whether NIH—especially its chemists—see the same problems and support the same solutions as the leaders of their professional society, *The NIH Catalyst* asked our readers and a variety of intramural chemists—from those just placed on the tenure track to long-time lab chiefs—for their opinions on the state of chemistry today, including the role for chemists in today's biomedical research environment and how they think NIH has treated the chemistry profession. In this issue, we present a sampling of the responses we received along with articles featuring insights from the chief of one of the largest chemistry labs at NIH, John Daly; one of the most-cited scientists in chemistry literature, Ad Bax; and a distinguished biologist and scientific administrator at the center of the storm, NIDDK Scientific Director Allen Spiegel.

WHAT THE CHEMISTS SAY

Louis Cohen, NIDDK: "As a science, chemistry can never die. It is the *practice* of chemistry that is dying, but only because the NIH administration and directors of the individual institutes have chosen to kill it. This choice is terribly misguided and short-sighted. The currently popular arts—molecular biology, genetic manipulation, immunology, virology—are all built on the basis of chemistry and will sooner or later hit a stone wall without the input and collaboration of chemistry and chemists."

Victor Marquez, NCI: "It is obvious that many of our friends in biology ignore the fact that everything in their biology is happening through chemistry. Chemistry is still regarded as a subservient science at NIH."

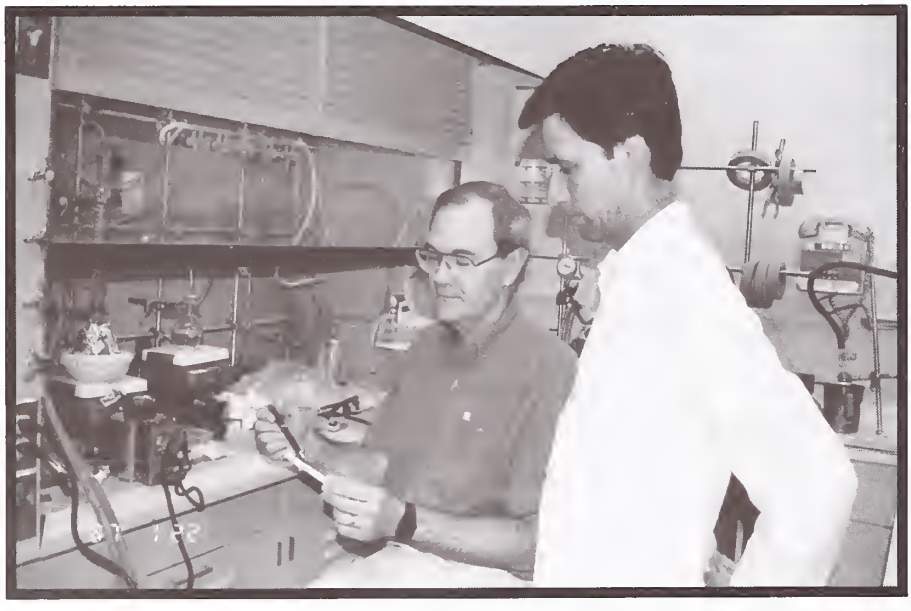
Thomas Spande, NIDDK: "The current research climate is not particularly supportive of chemistry, either medicinal or organic, as evidenced by these personal observations: three major natural products programs in NHLBI, NCI in Frederick, and NIDDK have been severely cut back; the long tradition of a biweekly seminar for organic chemists [has] died … there just were not enough participants; the Building 8 chemical stockroom is now the only one on the Bethesda campus (there were three previously); chemists have to periodically fend off proposals by the NIH library to discontinue even key chemical reference works, such as Beilstein; and chemically oriented NIH labs are lucky to find even one chemist (if so, usually an ad hoc addition) on panels of outside scientific counselors.

Jane Sayer, NIDDK: "In general, facilities and support services are designed to meet the needs of biological scientists rather than chemists. For

example, subscriptions to several major chemical journals and reference works are being discontinued by the NIH Library. ... In the design of our [Bldg. 8] hood system, no provision was made for conditioning or dehumidifying the incoming air, with the result that handling moisture-sensitive materials in these hoods presents a considerable challenge. ... The Building 8 chemical stockroom, the only such facility on campus, is in need of inventory and extensive reorganization."

Henry Fales, NHLBI: "While chemists themselves are accepted as useful, perhaps even necessary, professionals, chemistry is not recognized as a valid activity in its own right. There is indeed no encouragement to create or study molecules for the light they may shed on physical or chemical, as opposed to biological, processes."

Kenneth Kirk, NIDDK: "Chemistry is treated with respect and appreciation by most senior, practicing scientists, particularly those who have worked with chemists. However, administrators and policy makers sometimes give the impression that they think of chemists as slightly misguided scientists who don't quite understand what biomedical research is about."



Loma Heartley

Victor Marquez and Maqbool Siddiqui

Mark Sassaman, CC: "Sadly, the field of chemistry is a neglected discipline in the intramural program. The tremendous achievements at the interface of chemistry and biology are now to be found at institutions such as Scripps Research Institute (La Jolla, Calif.), which have reorganized their research programs to utilize the science and art of chemistry as the central focus in multidisciplinary surroundings. The consequence of such reorganization has led to an immense body of work, including the synthesis of taxol and other chemotherapeutic agents, the discovery of sleep-producing lipids in the brain, asymmetric syntheses of complex carbohydrates, self-assembling molecular cages, and the discovery of 'new' chemistry."

Paul Torrence, NIDDK: "There is little doubt that NIH and its hierarchy possess a diminished appreciation of chemistry—the central science. For instance, biomedical researchers have quickly forgotten the years of esoteric and mostly unheralded nucleic acid chemistry that now makes it possible for anyone who can read and count to use a DNA synthesizer.... Organic and medicinal chemistry are viewed as handmaidens or apothecaries to the medical sciences."

Kenneth Jacobson, NIDDK: "Researchers in industry know well that synthetic chemistry has *not* been superseded by molecular biology. There is an impression by some at NIH that the Human Genome Project and gene therapy will solve most medical problems in the future. As more protein targets are identified for therapeutic intervention, we will need small molecules to interact with these proteins. Structural biology is a major focus at NIH, but using this knowledge for therapeutic goals can generally benefit from a chemical synthetic approach."

Paul Kovac, NIDDK: "No matter whether some like it or not, everything around us is chemistry, including us, functioning or malfunctioning. Understanding any chemical phenomenon better can potentially help us understand complex phenomena in the life sciences. Therefore, any attempt to cut support of chemistry at NIH would be, putting it mildly, short-sighted."

On Changes Over the Past Decade

Spande: "Years ago, I collaborated in the probing of the binding site of one of Michael Potter's myeloma antibodies by synthesizing a heavy-atom-containing phosphorylcholine ester. This collaboration involved X-ray crystallographers, an M.D. (Potter), and biochemists, and it led us to one of the first visualizations of an antibody combining site by X-ray crystallography. I don't see this sort of collaboration occurring so readily now. I am uncertain of the reason, but it may have to do with the diminished visibility, due to declining numbers, of the chemical community at NIH. A lot of researchers may simply be unaware of our existence. Our numbers may be dropping below the threshold necessary to make waves or wield much clout."

Fales: "It seems unlikely that the contributions of the chemical community at NIH were better appreciated in the past, but due to easier sources of money and labor, we were better tolerated."

Kovac: "NIDDK's Laboratory of Chemistry was the oldest, one of the most successful, and, arguably, one of the most widely known and respected parts of NIH. That almost legendary institution no longer exists today as a structural unit."

Kirk: "I feel fortunate that I am not a young chemist at NIH because present-day postdocs in chemistry have virtually no opportunity to consider NIH as a career, no matter [how great] their talent. And I have very impressive postdocs."

Amy Hauck Newman, NIDA: "I have recently received over 50 applications for a postdoctoral position in my laboratory. Many of these applicants are coming from top-of-the-line laboratories and expect to have the opportunity to do cutting-edge research in medicinal chemistry. If chemistry is relegated to being a service and there isn't funding to conduct high-quality research, these young scientists will not be attracted to NIH."

On Criteria for Judging Chemists' Work

Marquez: "The impact that structural chemists have had in recent years on solving complex biological structures is beginning to be appreciated more fully. Sometimes, however, these people are not identified as chemists, but simply as X-ray crystallographers or NMR spectroscopists. The impact of synthetic organic chemistry is much less. If the molecular targets are too complex, the work is considered to be an esoteric exercise. If the molecules are simpler, after a few publications, the chemistry is gradually forgotten."

Jacobson: "It is rare that medicinal chemistry is accepted in the big-name journals; thus, this should be less of a criterion for judging chemists' merit. Biological relevance of the chemical work is essential at NIH."

James Silverton, NHLBI: "*Science* and *Nature* are very interesting journals, but do chemists and other physical scientists publish much there today? For myself, publications in the preeminent chemical journal, the *Journal of the American Chemical Society*, represent my highest achievements."

Medicinal Chemistry Award

One sign that all is not doom and gloom in NIH's chemistry community is the recent awarding of one of chemistry's most prestigious honors to an NIH chemist, Kenner Rice of NIDDK.

Rice received the 1996 American Chemical Society Division of Medicinal Chemistry Award in June for his research on neurotransmitters in the central nervous system, with an emphasis on drugs of abuse. Currently chief of NIDDK's Laboratory of Medicinal Chemistry, Rice earned his Ph.D. at Georgia Institute of Technology in Atlanta and came to NIH in 1972 after stints at Walter Reed Army Institute of Research in Washington, D.C., and Ciba-Geigy Corp. in Summit, N.J.

A process that Rice developed, called the "Rice process," is the only practical method for the large-scale production of medical opiates by total synthesis. In addition to giving the United States independence from foreign sources of opiates for use in medicine and research, Rice's work has furnished medicinal chemists with valuable new research tools and the potential for developing new nonnarcotic drugs. ■

Kirk: "One concrete step [toward improving the morale of NIH chemists] would be to allow us to be evaluated by a Board of Scientific Counselors that understands chemistry. This review committee is gaining increasing power over the fate of intramural researchers. It is discouraging—even frightening—to have one's research program evaluated and future career influenced by a panel of scientists who have such a bias toward their own approach to biomedical research—and who don't seem to understand either the problems or the promises of chemistry."

> "CHEMISTS ARE A DISEMPOWERED MINORITY THAT WILL CONTINUE TO DIMINISH IN STATURE AT NIH UNLESS IT FINDS A UNITED, POLITICAL VOICE."
> *—Paul Torrence, NIDDK*

C.P.J. Glaudemans, NIDDK: "Over the years, the [boards of scientific] counselors have been given power in lieu of their counseling role. I do not believe that the scientific directors hide behind the counselors to execute their own agenda. I do believe that the counselors can force the hand of the scientific directors by their own agenda. This is an executive tragedy and negates the responsibility of the scientific director, as well as the laboratory and section chiefs. ...We should abolish the practice of counselors altogether, or at least go back to the role of counselors as counselors, as in the past."

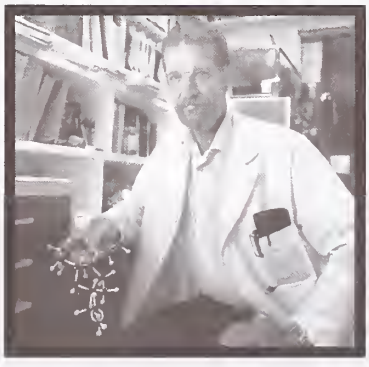
Fales: "My biological colleagues have always exhibited the deepest interest in my techniques and in my general welfare at NIH. Sure, they probably do regard me as a "craftsman." Why wouldn't they? I perform a valuable task in helping with a crucial part of their experiments, but the emphasis usually is on *part*. They also understand vaguely that I must have some other 'chemical' project that is my main interest. They would be universally shocked if I suggested that this was elucidating the pathway of oncogene regulation or something similar. On the other hand, in the board of scientific counselors' review, this is precisely the sort of activity in which I am expected to be engaged."

A Senior Chemist's Perspective

by John Daly, Ph.D., NIDDK

I came to NIH in 1958 as a postdoctoral chemist with Bernhard Witkop of NIAMD's Laboratory of Chemistry after receiving my Ph.D. in natural products chemistry at Stanford University in Palo Alto, Calif. Thirty-eight years later, I find myself chief of NIDDK's Laboratory of Bioorganic Chemistry, which, with nearly 50 scientists, is one of the largest—if not *the* largest—chemistry labs in the intramural program.

One could write a book on how important chemistry is to all other research conducted at NIH, including the currently emphasized molecular biology research aimed at gene therapy. Our discipline has designed and synthesized or isolated and elucidated structures of virtually all drugs used to treat human disease. Despite this overwhelming evidence of the value of chemical research in achieving biomedical goals, NIH today is suffering from an acute lack of appreciation for chemistry, a serious diminution of resources for chemistry, and a disturbing decline in the morale of its chemists.



Bill Branson

John Daly

In this era of fiscal restraint, NIH chemists often do not compete well for resources with the very costly field of molecular biology. At one time, my fellow chemists and I believed that our science was appreciated and fairly judged by the Board of Scientific Counselors, who used to have one chemist member rather than the current token, ad hoc chemist. Now, the counselors' reports usually state that our chemistry is good, but so what? If the biological aspects are not being pursued with brilliant success either by biologically oriented staff within the group or by strong collaborations outside the group, the program is judged a failure. If chemistry is a dying art at NIH, it is not dying because of the lack of excellent chemistry, but because of lack of money, positions, space, adequate review processes, and opportunities for collaboration.

Another difficulty facing chemists at NIH is the new two-pronged career path, which relatively early on classifies a promising postdoc as an independent "tenure-track scientist" or a more collaborative "staff scientist." During postdoc training, chemists develop insights into how chemical approaches can be applied to achieve biomedical objectives, for example, in pharmacology, drug design, and molecular biology. It is often easy to recognize an outstanding practitioner of the "art" of chemistry, but in most cases, only years will tell whether he or she will develop the all-important interface with biologically relevant programs. The tenure-track system does not serve chemistry well because most senior chemists at NIH have inadequate numbers of postdocs to pursue their own goals and hence are loathe to bring on a promising young chemist and provide him or her with two postdocs and complete independence for six years. If I were to do that, I would have no postdocs to pursue my own projects.

Unfortunately, chemistry now appears to be considered a science that NIH should, at best, keep at token levels. Consequently, the mindset of many intramural chemists has markedly changed for the worse over the years. Many biological scientists now seem to think that any chemistry needed at NIH could merely be contracted out. Somehow, strong, true collaborative links between biologists and chemists are now relatively rare at NIH, and chemists are often treated like "service providers." The development of such collaborations receives no apparent encouragement from the NIH leadership. I feel that NIH should increase or at least maintain support for chemistry, even if the good basic research does not have an obvious biomedical impact. No one can truly predict the direction and impact of basic research in chemistry—or in any other scientific discipline. At NIH, if there is not immediate biomedical gratification, chemistry receives poor marks.

Many other NIDDK chemists and I perceive, perhaps incorrectly, that the treatment of chemistry in our institute is designed to encourage us to leave, as well as to keep us from bringing on any young chemists to replace us. In fact, I have been told that my program will be abolished when I retire. I see in this decision a bittersweet recognition of my personal importance, and simultaneously, a failure to recognize the importance of natural products research to our institute and of chemistry to biomedical research as a whole. The programs of several other senior chemists also seem destined to be abolished when they retire. If no steps are taken to change the attitude toward chemistry at NIH, I fear that at some point, there will be no one left to continue NIH's once-proud tradition of chemistry. ■

CHEMISTRY AND BIOLOGY

continued from page 11.

On the Solutions

Torrence: "The very last thing NIH needs ... is a knight in shining armor of great repute brought in from the outside with his or her research clique. This would be a coup de grace to morale among those present at NIH... . Instead, resources could be allotted to the chemistry effort as a whole across campus. An outside individual could then be recruited as a 'chemistry chair' to further develop and implement a vision of chemistry in a biomedical environment, not for his or her personal aggrandizement but to establish a first-class department. ... This chair would report directly to the NIH director and be able to bring new investigators on board to suit his or her vision. With much good fortune, such an individual could help restore chemistry to its critical role in biomedical research at NIH."

Sayer: "Two measures that should be considered to support and revitalize chemistry at the NIH are 1) to change the way review groups are selected and organized, and 2) recruit one or two outstanding chemists who already have established programs and strong international reputations, either to set up new laboratories here or to take over the leadership of existing ones when laboratory chiefs retire."

Spande: "Acquiring some illustrious chemist from the outside would only make matters worse. ... It would be better, I think, to increase the number of chemists at NIH and add to the support staff. NIH does have a nucleus of outstanding chemists; what is needed is a pool of younger chemists to provide the next generation of leaders. NIH might also create a permanent lecture series ... inviting experts to present new techniques or topics of general interest to chemists. This would benefit not only NIH chemists, but the entire local chemical community."

Jacobson: "The synthesis of new molecules of biological interest could contribute to many projects ongoing at NIH. This does not mean starting programs devising new synthetic methods, i.e. 'chemistry for its own sake,' but rather using synthesis as a means of solving medical problems. If NIH is to recruit a well-known chemist, it should be someone who already works at the interface of chemistry and biology."

Sassaman: "The NIH infrastructure needs to be amended to take advantage of such an important resource. Ideally, this would include establishing a chemistry colloquium to allow for discussions, seminars, and collaborations within and across disciplines; expanding the chemical community; and encouraging research in chemistry, where goals are not narrowly defined by the mission of a particular institute, but by a broader sense of biomedical exploration."

Newman: "The lines of communication between chemists and scientists in other fields seem to have diminished to a point that the importance of our science to overall research at NIH has been forgotten. In many ways, the responsibility of enlightening our colleagues to the synergistic potential that we could provide by putting our heads together, is ours. With support (both in resources and morale), this responsibility would be more readily assumed."

Torrence: "Chemists are a disempowered minority that will continue to diminish in stature at NIH unless it finds a united, political voice. ... Simply put, in the present situation of multiple chemical fiefdoms, it is impossible to defend turf."

Cohen: "Unfortunately, too much damage has already been done, and repair may be extremely difficult and time-consuming. NIH has lost its international reputation as a Mecca for bioorganic-medicinal chemists because the word is out that these areas of research are receiving minimal support and recognition." ■

NIH's Most-Cited Chemist

Ad Bax, Chief of the Section on Biophysical NMR Spectroscopy, Laboratory of Chemical Physics, NIDDK, was listed as the most-cited chemist in the world by the Institute for Scientific Information in 1993 based on the average citation rate of his papers in the 1980s. He discussed his impressions of chemists and chemistry with The NIH Catalyst.

Q: Do you see yourself as a chemist?
Bax: I don't have a degree in chemistry—I'm a physicist by training—but the kind of work we do now is more related to chemistry and biochemistry.

Q: How did you get into chemistry?
Bax: I worked for my Ph.D. degree on the development of magnetic resonance techniques that are applied in chemistry. This required a little bit more physics than most normal chemistry-type experiments. A physics background is quite common among NMR spectroscopists. The postdocs in my lab have either a physics or chemistry background.

Ad Bax

Q: What do you consider your most significant achievement?
Bax: We've been able to develop a number of techniques in magnetic resonance that have become very useful to a lot of my colleagues for solving important problems. So, it's not one particular single achievement, it's a number of contributions that people are using widely now.

Q: How do you think the science of chemistry is regarded at NIH compared with other biomedical institutions?
Bax: I think there's a lot of respect for chemists, but then there's also possibly a feeling, particularly in the medical community, that a lot of the important questions are in areas such as molecular biology, structural biology, and cellular biology. As an institution, NIH seems to be quite supportive of chemists, as far as I've been able to tell.

Q: The American Chemical Society has called upon NIH leadership to recruit one or more chemists of international stature to replace the ones who've left recently.
Bax: I sympathize both with the ACS and the NIH leadership who would have problems, possibly, in making the commitments of space needed to hire a big name chemist, because it would be at the expense of something else.

Q: Chemistry papers generally don't get published in *Cell, Nature,* and *Science*. Do you think this handicaps tenure at NIH for chemists?
Bax: Possibly, if they were exclusively evaluated by people working in biology or medicine, because those are considered the top journals in those fields. In my experience, the tenure committees have been diversified enough that there always were people who could put it in perspective and evaluate the quality of science that is not always related to the journal in which it has been published. I can't speak for all of NIH, but I don't think that tenure decisions have adversely affected the quality of chemistry here.

Q: It seems as though chemistry journals don't get the same citation rates as the molecular biology journals.
Bax: That's true; they're typically lower. It's another order of magnitude lower in mathematics. It doesn't mean that the mathematical sciences are of a lower scientific level. One cannot directly equate the number of citations with the importance or quality of scientific work that people conduct.

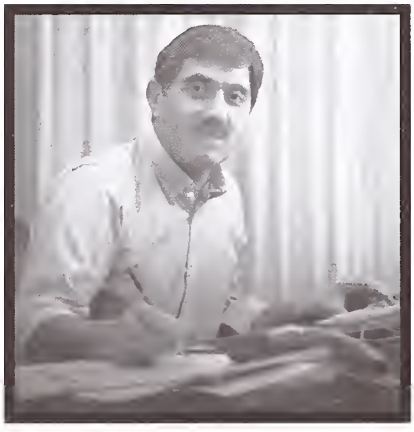
Q: How have you evolved as a chemist?
Bax: Maybe I've evolved into a chemist! I've evolved from working in small molecules to working on nucleic acids and proteins, and developing methods for studying them. NIH was a natural environment for me to start doing this, primarily stimulated by my colleagues. I've been extremely lucky that I was at NIH at the right time to apply the newest methodology to proteins, and that there were sufficient funds available for this type of expensive work. In academia it would have been very difficult for me to do this at the same kind of speed, because there's this enormous timelag while one applies for funds. At the time, the field was developing very rapidly, so this allowed us to stay ahead of the pack.

Q: Do you have any concrete suggestions for improving the status of chemistry and chemists here at NIH?
Bax: It is critical for NIH to keep a sharp eye on where in chemistry significant advances are anticipated and to take advantage of its ability to rapidly build up in such an area. ■

A Scientific Director's Views

by Allen M. Spiegel, Scientific Director, NIDDK

NIDDK's strong support of chemistry is the legacy of Bernhard Witkop and other key chemists from a previous generation, including John Daly and Kenner Rice (present lab chiefs) and their academic "progeny," including Don Jerina, Phil Skolnick, and Ken Jacobson. Notwithstanding the complaints that chemists are making now, this tradition of support continues. In addition to having two major chemistry labs (Daly's and Rice's) with substantial space, positions, and budgets, there is a service facility (Lab of Analytic Chemistry) with three staff scientists and expensive mass spectrometry and nuclear magnetic resonance imaging equipment devoted to the analysis of compounds made by our chemists as well as by those of other institutes, such as NCI. NIDDK Director Phil Gorden has only half-jokingly referred to NIDDK's intramural research program as "the Intramural Research Program of NIGMS," reflecting our strength in many of the basic sciences traditionally supported extramurally by that institute. NIDDK's intramural research program obviously supports "mission-oriented" research in diabetes and digestive and kidney diseases, but it also heavily supports fundamental research in areas such as structural biology (both X-ray crystallography and NMR spectroscopy) and molecular biology. In this context, NIDDK's support of chemistry research is not an anomaly. It is in keeping with our general commitment to outstanding basic science.



Bill Branson

Allen Spiegel

The key question is, Why should NIH's successful and well-supported chemists evince such low spirits now? I suspect that this stems from a feeling of being eclipsed by other, newer research approaches. Until the late '70s and early '80s, much of what now goes on at NIH and other biomedical research facilities (recombinant DNA, transgenic and knockout mice, novel cell-imaging techniques) didn't exist. It isn't difficult to imagine that chemists feel as if their time has passed when they see such powerful new approaches dominating the biomedical research scene.

I believe that what chemistry at NIH needs now is a sustained commitment to excellence in which we continue to recognize and support truly important chemistry research where it already exists and recruit its practitioners where needed. Stuart Schreiber at Harvard and Roger Tsien at the University of California at San Diego (UCSD) exemplify the types of chemists the intramural program would be more than happy to have working here. Rather than lament the eclipse of traditional chemistry by molecular and cell biology, these scientists have aggressively embraced new disciplines—not by abandoning synthetic chemistry but by combining the old and the new in creative, synergistic ways. Even if we lack the resources to attract established scientists such as Schreiber and Tsien, we may well be able to replace departing chemists with outstanding junior recruits.

There is no doubt that medicinal chemistry research still has a major role to play in biomedical research; despite the rise of biotechnology, most drugs that are useful for treating human disease still come from classic screening and/or synthesis programs. There is also little doubt that organic chemistry research has a major role to play in biomedical research. The recent development of combinatorial chemistry techniques is but one example. An important question here, however, is where such research is best and most appropriately done? Most medicinal chemistry has traditionally been done by drug companies that have the infrastructure to support all relevant aspects of the process.

For medicinal chemistry to be pursued successfully at NIH, it must be connected in some meaningful way to pharmacology and other biologic disciplines that can take a collection of molecules and determine where and how they act. Rice's program on opioids and other neuroactive drugs exemplifies how this can be done well. Compounds he has synthesized have been key in defining novel opiate receptor subtypes and have been used in PET scanning. The crucial point is that he always interacted with collaborators to study relevant biologic aspects. Jacobson's is another example of a successful program in which synthetic organic chemistry has been joined with molecular biology. His compounds were critical for labeling and purifying adenosine receptors. But synthetic organic chemistry cannot stand alone; in my view, it must be done in a biologic context. Daly embodies the effective joining of chemistry and pharmacology in a single individual and program. He has been able to identify novel and unique natural products and define both their structure and pharmacology. Many of these compounds have become important tools used by biochemists, physiologists, and pharmacologists. NIDDK will continue to support chemistry as long as it is outstanding and has the potential to have an impact on biomedical research.

I make no apologies with respect to our insistence—and the insistence of our board of scientific counselors (BSC)— that chemical work should have biological relevance, because we all interpret biologic relevance in the broadest sense. The work of Ad Bax, one of NIDDK's most outstanding "chemists," is not "biologic" in any strict sense—he works on fundamental aspects of NMR (see box). However, his work provides the basis for using NMR to solve the 3-D structure of biologically relevant macromolecules. As scientific director of NIDDK, I am delighted to support this type of fundamental research because it is absolutely outstanding and creative. We can readily see its biologic relevance.

Complaints about the evaluation of chemistry and the use of ad hoc counselors by the BSC are hardly unique to chemistry. NIDDK has a large and diverse intramural program. Even with a distinguished and broad BSC it is not possible for its members to represent every discipline and subdiscipline of those being evaluated. In part to meet that concern, NIDDK implemented an additional approach to the BSC review about a year and a half ago. We now obtain letters from scientists outside NIH evaluating everyone being reviewed (not just the people being promoted) before the BSC visit. These letters are obtained from individuals in the same discipline as those being reviewed. The BSC reads them after they have reviewed the written material and heard the labs' presentations, and the letters are subsequently incorporated in the BSC's written reports. Although not perfect, this approach helps ensure that there is input from individuals working in the same area as those being reviewed.

In response to reports from the BSC, I have closed branches and downsized labs, but the cuts have not fallen disproportionately on chemistry and have included areas such as cell biology and endocrinology. Harold Varmus and Michael Gottesman can't tout the rigor of intramural review to our external advisors and other oversight groups if the scientific directors do nothing in response to poor reviews. Inevitably, members of labs being "squeezed" will complain, but this cannot be viewed as an assault on chemistry as a discipline. As for the complaint that the programs of retiring chemists are not being continued, NIH has no entitlements or mandates that any specific scientific programs must continue in perpetuity, including when a principal investigator departs.

In this era of no-growth budgets, such hard-nosed scrutiny and reassessment of research priorities has become a fact of life in order to make room for new, cutting-edge science. I see important growth areas for NIDDK in revitalizing our clinical research effort. Toward this end, we have recruited a new liver disease section chief and are currently recruiting a thyroid investigator for our NIDDK-NICHD endocrine training program; bolstering the areas of transgenic and knockout mice, and continuing vigorous support of structural biology through tenure-track recruitments made in solid-state NMR and X-ray crystallography. ■

PRAT Fellowships Offer Special Opportunities and Benefits

by Doris Brody, NIGMS

More than 300 postdocs have graduated from the PRAT (Pharmacology Research Associate) Program since its inception over 30 years ago. Many of the former fellows of this small intramural research training program supported by NIGMS have now become leaders in academic and industrial research in pharmacology all over the country. One graduate, Alfred Gilman, M.D., Ph.D., who is at the University of Texas Southwestern Medical Center at Dallas, won the Nobel Prize in physiology or medicine in 1994. Several PRAT graduates currently head laboratories in the NIH intramural research program.

What distinguishes PRAT from other NIH postdoctoral fellowships, such as the standard IRTA (Intramural Research Training Award)? Rona Hu, M.D., a current PRAT fellow in the NIDDK Laboratory of Neuroscience, mentions the support that goes with the program and the considerable research independence permitted PRAT fellows.

Michael Rogawski, M.D., Ph.D., a former PRAT fellow (1981-83) who is chief of the Neuronal Excitability Section in the NINDS Epilepsy Research Branch, also cites the greater independence of PRAT fellows, saying, "the [financial] obligation is to the fellow, not the laboratory—the result is greater freedom."

Anita Roberts, Ph.D., deputy chief of the NCI Laboratory of Chemoprevention and a current member of the PRAT Advisory Committee, says PRAT differs "in that the applicant finds a sponsor and then, together with the sponsor, writes a research proposal. The applicant is chosen both on the appropriateness of the project and the lab in which the research will be carried out. . . .The PRAT fellow becomes a member of a group with an identity."

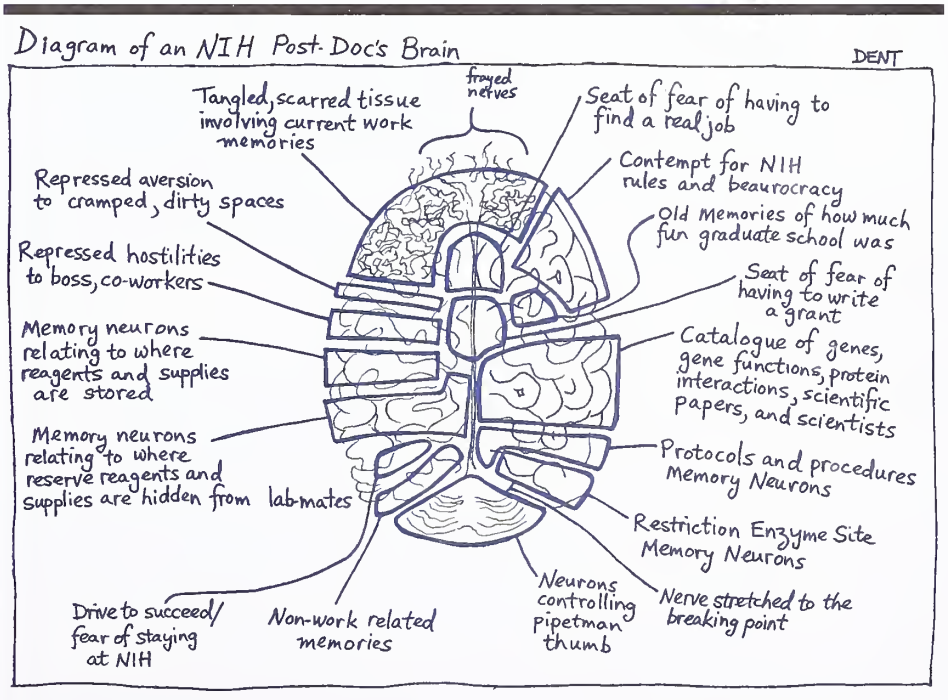
When the PRAT Program was created in 1965 at the request of then NIH Director James Shannon, M.D., the goal was to train researchers studying chemical-biological interactions in the environment and broad aspects of pharmacology and toxicology, including applied mathematics, biometrics, organic chemistry, biochemistry, physics, and instrumentation. Today, there is a heavy emphasis on molecular biology, biochemistry, signal-transduction mechanisms, cell biology, structural biology, and immunology—in addition to drug metabolism, chemistry, and drug design. PRAT Advisory Committee member Hynda Kleinman, Ph.D., chief of the Cell Biology Section of the NIDR Laboratory of Developmental Biology, says, "One really needs to be as knowledgeable as possible in as many of these areas as possible because of the nature of today's scientific research."

PRAT Co-directors Rochelle Long and Alison Cole note that "understanding mechanisms of drug action is just a beginning. Pharmacology can be an almost limitless field. In this era of rational drug design, the discipline encompasses the most basic to the most clinical sciences, from chemistry to cell biology to medicine. To predict target therapeutic sites, it is necessary to understand thoroughly how molecules, cells, tissues, and organisms function."

The goal of the PRAT Program is to attract and train the most promising future leaders in pharmacological research. In addition to fellowships, the program provides lectures, workshops, and career development and grantsmanship mentoring. A current PRAT fellow, Maria Rivera, Ph.D., who is in the NCI Laboratory of Drug Discovery Research and Development, believes that these elements are particularly important. Rivera is a former participant in another NIGMS training program, the Minority Access to Research Careers Program. Her goal is to become a faculty member at a university in her native Puerto Rico, where she would like to "motivate students to get involved in research."

The PRAT Program is seeking fellowship applicants and NIH preceptors for the next round of review, for which applications are due by Jan. 1, 1997. Applicants for the PRAT Program must have received a Ph.D. or a professional degree (M.D., D.D.S., D.O., D.V.M., or Pharm.D.) in a basic or clinical science within the past 5 years. They may not be conducting postdoctoral research at NIH or FDA at the time of application. Before submitting an application, they must identify a preceptor at NIH or FDA and contact him or her to develop a scientific plan. Potential PRAT preceptors must apply to become preceptors in the program and must have recent research productivity and experience in training postdocs.

To receive a PRAT fact sheet, contact the PRAT program assistant, Sandra Cain, at 594-3583 (e-mail: prat@gm1.nigms.nih.gov). ■



CATALYTIC REACTIONS

In this issue, we are asking for your reactions in four areas: chemistry at NIH, Building 50, Hot Methods Clinic, and parenthood vs. research. **Send your responses on these topics or your comments on other intramural research concerns to us via e-mail: catalyst@od1em1.od.nih.gov; fax: 402-4303; or mail: Building 1, Room 334.**

In Future Issues. . .

- Should NIH Start A Grad School?
- The Latest Trends In Image Processing
- Good Scientists and Good Parents?
- Biomedicine's Best "Bookmarks"

1) What do you see in the future for chemistry at NIH? Are chemists' complaints justified? What steps should NIH take now?

2) What are your general reactions to the design proposals for Building 50? What do you like? What should be different?

3) The Hot Methods Clinic will return soon. What updates can you provide on previous Hot Methods? What techniques would you like to see covered in the future?

4) We are considering an article about NIH researchers who are also parents. What does it take to be a good parent and a good scientist? How could NIH be more family friendly? What is the optimal timing of careers and kids? What are the problems and solutions?

The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 1, Room 334, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; e-mail: catalyst@od1em1.od.nih.gov

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