provided grist for future meetings.

The last speaker, Rakesh Khurana, Bower professor of leadership development at the Business School (but, as master of Cabot House, a member of FAS), a scholar of organizational culture, returned to Jasanoff's introductory presentation. The issue for FAS was "How do we create an engaged community" that feels genuinely consulted? An uncertain era for higher education made such engagement more important than ever before. The faculty needed to "create a psychologically safe environment," Khurana said, where silence was not interpreted as agreement, where there was no pressure to create unanimity, and where people were not judged for raising ideas before they were fully formed. He suggested creating discussions to raise questions—and encouraging participants to do so—while deferring the presentation of solutions; and soliciting written feedback afterwards.

These may seem soft solutions to hard problems. Experiments like HarvardX and edX involve matters essential to professors' concerns, such as how they teach, at a time when everything about teaching is under question. A single MOOC—with videographers, computer programmers, and support services—may involve an investment of $250,000—and a much more centralized approach toward "producing" a course. And further centralization has occurred. The University libraries in effect are now led by professional managers, not by faculty members. The 2008-2009 financial crisis resulted in budget cuts and even more centralization of financial management to produce better controls. Funds from some faculty research centers continue to be tapped to shore up FAS's budget—a source of continued unhappiness.

Such factors have reshaped the context for faculty-administration relationships today, bringing discussion of governance to the fore within FAS once again. Khurana's remarks elicited applause, suggesting the faculty members' hunger for solutions to their current disquiet, and their enthusiasm for context-changing suggestions from someone they view as a colleague.

For a fuller account, see **http://harvardmag.com/governance-13**.

Systematic Drug Discovery

Midway through clinical trials for the experimental melanoma treatment PLX4032, researchers were convinced they had a miracle drug. Patients on PLX4032 had shown significant tumor shrinkage within weeks of beginning treatment, a radical change from the effective death sentence that is metastatic melanoma. And this was no ordinary treatment. PLX4032 was among the first apparent successes in the field of targeted therapy. The drug was directed to a specific, cancer-causing mutation present in more than half of all melanomas, and its success seemed to herald a new age of personalized medicine.

What followed was heartbreaking. The drug's early successes were followed by the sudden emergence of resistant tumors. One after another, patients relapsed. The drug that seemed to snatch them from the jaws of death wound up delaying disease progression by only an estimated six months. PLX4032 eventually received federal approval as the drug Vemurafenib, but its results fell far short of its initial promise.

"We need to reexamine the fundamental science behind drug therapy," says Peter Sorger, Krayer professor of systems pharmacology at Harvard Medical School (HMS) and head of the new Harvard Program in Therapeutic Science. The pathway to federal approval is littered with failed drugs, representing many years of labor and millions of dollars of investments; indeed, an estimated 70 percent to 75 percent of a successful drug's price reflects the cost of earlier losses during development. Even as science crafts increasingly sophisticated techniques for understanding chemical action at the level of molecules, the number of drugs approved by the Food and Drug Administration (FDA) has declined from approximately 100 to about 30 per year in recent decades.

To tackle this stark reality, the new HMS program aims to use multidisciplinary approaches from systems biology (a new discipline that uses quantitative and computational methods to study emergent behaviors of biological components; see "Seeing Biological Systems Whole," March-April 2005, page 67) to create a more rational basis for drug development. "We don't know why most drugs work," Sorger says. As the case of PLX4032 shows, drugs often have unpredictable side effects and remarkable variation in efficacy from one patient to another. Sorger, who has co-founded two companies himself, Merrimack Pharmaceuticals and Glencoe Software, sees research potential in the problems that plague pharmaceutical companies, regulators, and clinicians. "If you were to work closely with a pharmaceutical company," he says, "you'd continuously find these fantastically interesting biological questions spinning out. These questions are usually shelved in industry because timelines are tight, but they come back to haunt you over and over again."

Peter Sorger

Photograph by Channing Johnson/Harvard Medical School

"The Girls of HBS"

Harvard Business School (HBS) commemorated the entry of women into its M.B.A. program, half a century ago, with the W50 Summit in early April—complete with a survey of alumnae and the announcement of a new senior associate deanship for culture and community (see **http://harvardmag.com/hbs-13** for a full report). A related exhibit, *Building the Foundation: Business Education for Women at Harvard University,* at Baker Library|Bloomberg Center through September 22, documents that progress from Radcliffe College's one-year certificate program in 1937 to the residential integration of women at HBS in 1970.

A two-page, typewritten memorandum in the exhibit, to "The Women of the Class of 1971" on the subject of "Life at H.B.S.," composed by Robin Wigger, Class of 1970, gives a vivid sense of the world then, for women and men alike.

Written "in an attempt to answer some of the questions which I had last summer before beginning the MBA Program," it starts with the "vital" suggestion that "every woman have a fairly definite reply to the question: 'What's a nice girl like you doing in business school?'" Wigger explained the context:

> I do not wish to imply that you will be regarded as some sort of freak, for many times…this question is intended as a compliment. But I would like to warn you that the question will be a constant one, and it does help if you have a ready answer. Some of the first-year men appeared to assume that most of the single girls at HBS were there with the sole intent of finding rich husbands. Others really could not understand why any woman would want to learn about business and/or management.

From there, Wigger offered practical advice on "exactly what women were expected to wear to class." Most of her peers, she noted, chose "clothes appropriate to the suits and ties of the male students. We wore dresses or suits with low heels and hose." One consequence: "[I]f you just graduated from an all-women's college, you may find the switch in dress to be a bit of a shock to your clothes budget (especially the cost of nylons)."

After advising matriculating women to relax and be confident that they could adjust to the workload, to "classes in which there is a strong emphasis on discussion," and to "the frightening possibility of being called on to start a class," Wigger revealed her pioneering spirit. She and three other first-year women had participated in an "Experimental Residence Project" during the second half of the year, "to determine the adequacy of the facilities for women and also to discover whether there were any major problems for women living in the men's dorms." All four, she wrote, "deemed the experiment a great success and have chosen to live on campus again," in part to belong to study groups, use the library, and meet people. None suffered the imagined problem of "a possible loss of our (feminine) identity." The accommodations were far better than those of Radcliffe Graduate Center—although women who chose campus living must "provide your own iron and ironing board."

(A *Harvard Crimson* report of March 11, 1969, on "the only coed living plan at present in the University," quoted Colleen Burke, who petitioned with Wigger to live on campus, to the effect that the HBS administration had been "flexible and progressive despite its conservative image." They and "two other girls" drawn by lot, Peggy Jones and Dana Holzinger, inhabited McCulloch C-13 and -14, previously a lounge for female students. Wigger reported that "now guys can understand more why we're here. A lot of guys have found out that girls are absolutely normal." Men had apparently overcome initial misgivings, including, Burke said, complaints about "perfume wafting up the corridors.")

Wigger concluded, "I would not be providing you with an accurate picture if I stated that being a woman at HBS involves no additional problems or adjustments than those faced by the male students. However, the difficulties are not insurmountable and the personal experience and education" well worth it. Apparently so: she went on to be general manager, distribution and marketing, of IBM and, subsequently, a corporate director.

The exhibition materials come from the Baker Library Historical Collections and the Schlesinger Library on the History of Women in America (at the Radcliffe Institute). The website for the exhibition, with links to oral histories and research materials, is **www.library.hbs.edu/hc/wbe/exhibit_introduction.html**.

One among many: Harvard Business School pioneer Robin Wigger, suitably attired, in class among fellow M.B.A. students, circa 1970

Photograph courtesy of the Harvard Business School Archives Photograph Collection

Underlying the new initiative is the belief that drug discovery has been too focused on a reductionist approach. Historically, pharmacology has been focused on the idea of a magic bullet—a single drug for a single disease process, says Joseph Loscalzo, Hershey professor of the theory and practice of physic at HMS and chair of the department of medicine and physician-in-chief at Brigham and Women's Hospital (BWH), who is involved with the therapeutics initiative. Typical drug-discovery methods begin with high-throughput screens that identify single molecules that interact with a particular target—a protein or signal receptor that is known to go awry in disease. Increasingly sophisticated technologies can provide a detailed understanding of how the drug and its target interact at different dosage levels across time and cellular space, but Sorger nevertheless views this knowledge as insufficient. PLX4032, for instance, was derived from this highly targeted ap-

proach—a single drug for a single cancer with a single mutation—but the cancer cells' rapid resistance, as observed in the clinical trials, also shows how much remains to be learned. "In the case of Vemurafenib, we need a much more sophisticated understanding of the drug pathways," he says. "Most of that massive resistance is due to bypasses, where one pathway turns off and the next turns on."

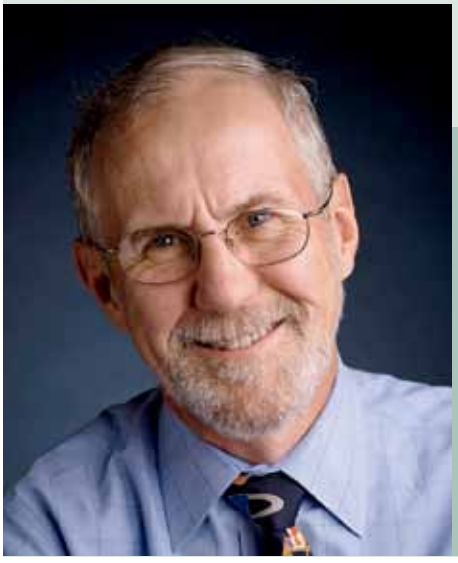
Sorger strongly advocates the use of more mathematical and computational methods to supplement biology's traditionally descriptive approach. When he taught at MIT, he co-founded its Computational and Systems Biology Initiative, and now his lab uses quantitative models to study the biological circuitry controlling decisions about programmed cell death, a process radically altered in cancer cells. "My interest in quantitative methods grew organically from being incredibly dissatisfied with this very anecdotal picture," he says. The new program in therapeutics will draw on MIT's position as a leader in computational biology, and Harvard's in systems biology (driven by the creation of the department of systems biology at HMS in 2003). "We need a radical rethink in the way that we organize and interpret biological data," he says. A more integrative research approach, based upon predictive models of cellular networks, will help explain and predict drug side effects and interactions. "Many drugs provoke paradoxical responses," he says. "These are effects that, once understood, could be applied in industry. It's time to rethink some of these underlying concepts." (For an initial outline of the new approach, see "A New Prescription for Drug Development," **http://harvardmag.com/pharmacology.**)

Such an integrative approach will require more interdisciplinary collaboration. A key component of the therapeutics initiative is a new Laboratory of Systems Pharmacology (LSP), a therapeutics research facility. Additionally, a therapeutics foundry will aim to develop methods and technologies for smarter drug design—for example, using known molecular parts to build proteins with desired functions. The LSP (construction is scheduled to finish in the spring) will eventually house an estimated 60 researchers from Harvard, MIT, and Tufts, and hospitals including Massachusetts General, BWH, and the Dana-Farber Cancer Institute. Researchers will have similarly varied backgrounds, ranging from experimental to computational biology, and from basic to translational to clinical research, all working in a single physical space. "Colocalization drives interdisciplinary science," says Sorger, praising the benefits of proximity among researchers. "No electronic technology we've discovered has been more than an aid." Loscalzo, whose own lab employs both experimental and computational approaches to medically relevant issues, hopes that by working alongside each other, researchers

University People

Peak Professors

Faculty of Arts and Sciences dean Michael D. Smith has named a new cohort of Harvard College Professors. The five-year professorships (five are conferred annually) recognize superb undergraduate teaching and advising. Honorands receive extra research funding and a semester of paid leave or summer salary. This year's cohort is: **Joseph D. Harris,** Higgins professor of mathematics; **Steven R. Levitsky,** professor of government; **Michael J. Puett,** Klein professor of Chinese history and chair of the committee on the study of religion; **Jennifer L. Roberts,** professor of history of art and architecture and chair of the committee on degrees in the history of American civilizations (read about her presentation at the May learning and teaching conference in "Talking about Teaching," page 48); and **Maryellen Ruvolo,** professor of human evolutionary biology.



INTERIM ED DEAN. Thompson professor of education and society Richard J. Murnane has been appointed Harvard Graduate School of Education's acting dean, effective July 1. He is the interim successor to Kathleen McCartney, who departs to become president of Smith College, as previously announced. Murnane, an economist, has examined changing demands for workers' skills in the evolving U.S. economy, and the effectiveness of education policies in responding to those changes. He also studies the effect of income inequality on educational opportunity. The search for a permanent dean continues.

Scientists at the Summit

Eight Harvard faculty members have been elected to the National Academy of Sciences: **Mitzi I. Kuroda,** professor of medicine and professor of genetics, Harvard Medical School (HMS); astronomer **Ramesh Narayan,** Cabot professor of the natural sciences, Faculty of Arts and Sciences (FAS); **Norbert Perrimon,** Stillman professor of developmental biology, HMS; **Daniel L. Schacter,** Kenan professor of psychology, FAS (see "The Social Life of Memory, page 10); **Beth A. Simmons,** Dillon professor of international affairs, FAS; **Gerhard Wagner,** Blout professor of biological chemistry and molecular pharmacology, HMS; **Fred M. Winston,** Andrus professor of genetics and tutor in biochemical sciences, HMS and FAS; and **Horng-Tzer Yau,** professor of mathematics, FAS.

Extraordinary Economist

The American Economic Association has conferred the 2013 John Bates Clark Medal on professor of economics **Raj Chetty,** who uses large data sets to examine taxation, employment, and education policy (see "Kindergarten Matters," November-December 2010, page 13). The medal recognizes the U.S. economist under the age of 40 judged to have made the most significant contribution to economic thought and theory. He was awarded a MacArthur Foundation Fellowship in 2012.

Photograph by Tom Kates

will gain a deep appreciation for the power of different research methods.

The new lab will explicitly tackle complex problems like neurodegenerative or inflammatory diseases, where traditional drug-discovery methods have made little progress. "I don't think these are intractable problems," says Loscalzo. "We have the data sets. We have the cellular and animal models, and we know the biochemical, molecular, and cellular underpinnings pretty well." Here, collaboration is crucial. He suggests that a better understanding of basic biology will enable clinicians to characterize disease profiles in terms of their underlying biology, rather than their large-scale, end-stage physiological effects. In many cases, Loscalzo says, "the therapies that have been used so far have been largely focused on the *end result* of a disease, not the *causes*." Exploring those causes could lead to novel therapeutic targets, as well as more effective diagnosis and treatment in a clinical setting.

The initiative also aims to foster a more collaborative relationship between academia and industry. The high cost of drug failures places a limit on how much companies are willing to risk. "You get stuck in a rut," says Sorger. "Research is too expensive, so you have to go with today's ideas, even if today's ideas aren't good enough." In contrast, he says, academia is better equipped to handle long-term, open-ended questions and to investigate principles that could lead to more rational drug design and usage. To that end, a graduate program in therapeutics will train students in the science behind drug discovery and regulation, while requiring internships at pharmaceutical companies to get a taste of industry. "Exposure to real-world problems will help students think about their own research projects," he says, by showing them what topics are best suited to each context. Nine students from existing HMS medical and doctoral programs are expected to enroll this fall in the new therapeutics certificate program.

Sorger also sees a role for academia in mediating the adversarial relationship between pharmaceutical companies and federal regulatory agencies. Regulatory science, he says, could be restructured to enable companies to alter and improve their treatment regimes during the trial process, and to continue monitoring after a drug reaches the market. "The FDA is complicit in the reductionist view of drug development, in that the approval process requires the pharmaceutical industry to identify a specific target for the drug candidate," adds Loscalzo. Yet infrequent toxicities and nontoxic side effects are also important components of how clinicians prescribe drugs. Furthermore, combination therapies may be the way forward for drugs like Vemurafenib (new drugs are already in development to combat the observed resistance), but the current lengthy approval process discourages collaboration between industry competitors on potentially powerful drug cocktails. Plans

PFOHO'S FIRST FAMILY. Anne Harrington, professor of the history of science—and acting chair and director of undergraduate studies for the department—and her husband, John Durant, have been appointed master and co-master of Pforzheimer House. Harrington's scholarship focuses on the mind-body connection and neuroscience; she has been a member of the faculty since 1988. Durant is director of the MIT Museum and an adjunct professor in that institution's science, technology, and society program. The couple have an eight-year-old son, Jamie. They succeed Nicholas Christakis and Erika Christakis, master and co-master since 2009, who are relocating to Yale.

Photograph by Kris Snibbe/Harvard News Office

Academy Academicians

Eleven faculty affiliates were elected members of the American Academy of Arts and Sciences: **David M. Altshuler,** professor of genetics; **Xandra O. Breakefield,** professor of neurology; **Paul A. Buttenwieser,** clinical instructor in psychiatry; **David W. Latham,** lecturer on astronomy; **Sara Lawrence-Lightfoot,** Fisher professor of education; **Joseph Loscalzo**, Hersey professor of the theory and practice of physic (see "Systematic Drug Discovery," page 54); **John F. Manning,** Bromley professor of law; **Richard J. Murnane,** Thompson professor of education and society (opposite); **Charles A. Nelson III,** professor of pediatrics; **William J. Poorvu,** M.B.A. Class of 1961 adjunct professor in entrepreneurship emeritus; and **Xiaowei Zhuang,** professor of chemistry and chemical biology and professor of physics (see "Shedding Light on Life," May-June 2008, page 40).

Science Funding Lows—and Highs

The Boston Globe's Robert Weisman reported in April that the city had for the eighteenth consecutive year led the nation in grants received from the National Institutes of Health ($1.78 billion in 2012), with Massachusetts General and Brigham and Women's hospitals (Harvard affiliates) and the Medical School (HMS) in the forefront. That such funding is being reined in is a source of worry and vulnerability for the school's research enterprise. So it was heartening that six of 27 investigator awards announced in May by the Howard Hughes Medical Institute went to Harvard scientists, four of whom are in medicine. The winners, whose salaries, benefits, and research are underwritten for five years, are: **Adam E. Cohen,** professor of chemistry and chemical biology and of physics, and **Hopi Hoekstra,** professor of organismic and evolutionary biology and of molecular and cellular biology, from the Faculty of Arts and Sciences; and professor of systems biology **Vamsi K. Mootha,** professor of genetics **David E. Reich,** professor of biological chemistry and molecular pharmacology **Johannes Walter,** and professor of neurobiology **Rachel I. Wilson**—all from HMS.

are under way for a partnership between the new therapeutics initiative and the FDA to add nuance to the current regulatory structure, and to implement a structure for failure analysis, as in engineering. Sorger also hopes to develop the science needed to test novel treatment methods; gene therapies, stem-cell therapies, and engineered proteins, for instance, are promising research frontiers that the current system is poorly designed to evaluate.

Ten-year costs for the therapeutics initiative are estimated at $200 million, with significant funding anticipated from private and philanthropic as well as federal sources; a $5-million grant from the Commonwealth's Massachusetts Life Sciences Center is funding the construction of the LSP. In the next decade, Sorger believes, the initiative will make significant advances in areas like toxicology and personalized therapy. Although federal budget cuts have drastically decreased funding of scientific research, Sorger is undeterred. "In crisis lies opportunity," he says, and institutions have been willing to consider more collaborative ways to organize research. The financial crisis and public debates on healthcare have imparted an additional sense of urgency to current research. "Given these tough economic times, people realize that we are fundamentally dependent on the success of the broader economy, and our economy is, in part, medical practice," he says. "The piece we can drive is innovation: innovation focused on improving patient outcomes and reducing costs." By promoting a more integrative view of drug development—from research through testing to regulation—the new therapeutic science team hopes to provide the needed change in the status quo. "We're trapped in a linear narrative here," says Loscalzo. "Genetics, genomics, and conventional wet-bench biology have evolved through linear, reductionist reasoning. It's not a feasible approach if you're thinking about systems and networks."

—KATHERINE XUE

Katherine Xue '13, a former Ledecky Undergraduate Fellow at the magazine, concentrated in chemical and physical biology and will be a freelance writer for the coming year before entering graduate school in systems biology. She recently won Harvard's Bowdoin Prize for Undergraduate Essays in the Natural Sciences for a manuscript adapted from her senior thesis.

THE UNDERGRADUATE

Harvard: The Mix Tape

by KATHRYN C. REED '13

A FRIEND in middle school used to make me mix tapes. He would find me by my locker after the last bell to hand me the cassette. I could barely make out the names of the songs, written in scratchy boy handwriting. Usually, they'd be rap.

The tracks ran into one another; sometimes they'd be cut off. I would have my favorite songs, but it was too hard to get the rewinding and fast-forwarding just right. I'd always end up in the middle, then go back too far. It was easier to listen straight through, anyway, in the order my friend wanted them to be heard.

They were all I had to listen to, until I bought a Walkman at the end of the year. I still kept the tapes after that, though we started burning CDs. You could fit more songs on the discs; it was easier to skip around. We'd sit on the bus wearing headphones—the big kind that wrap around your ears. At home, we'd upload to our computers, bring back more the next day.

Listening to the mix tapes ended in eighth grade. (We had continued to trade them occasionally, despite the convenience of CDs.) But the iPod had just come out, making the Walkman seem cumbersome in turn. Eventually I acquired a turquoise mini. (It, too, would seem cumbersome now.) I could carry thousands of songs with me; instead of mix tapes, we traded mp3s.

AT HARVARD in the fall of my freshman year, I went to the *Crimson*'s open house and signed up for every content board on the paper. Arts, Sports, News, Editorial, Fifteen Minutes—I thought I could do them all. "Most people only comp one," I was told. "Once you're on staff, though, you can write for any board you want." I went to each introductory meeting before deciding to drop to one.

A week earlier, my roommates and I had sat in our common room, searching through the course catalog, trying to decide what to shop. There were hundreds of options; for the next week, we could go to as many—or few—courses as we wanted. My friends made color-coded spreadsheets while I felt inundated by choices. I knew some who shopped more than 30

Illustrations by Zara Picken