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[Open Access Publishing - The Debate Continues](#)

Roy Auty (G6) and Stephanie Wai (G3)

"In the year 2003, the Public Library of Science made it possible for people all over the world to have access to the latest scientific discoveries. Shortly thereafter, things began to change."

- PLoS television spot

[The Two Towers: Harvard's New Research Buildings](#)

Sebastian Paige (G1)

Some of you may have heard of the "Not Ready Building" (NRB) or the "Never Complete Building" (NCB), but both the New Research Building (NRB) and the New Children's Building (NCB) are up and Harvard researchers have settled in. As with all new buildings, they have their benefits and disadvantages. Those who have moved in to either facility get to work in a shiny new building, but they also get the inevitable delays and annoyances associated with any move, hence the colorful nicknames. The Genetics and Pathology Departments have moved into the NRB along with other labs. The faculty members I spoke with in the NRB believe it is a beautiful building, but find fault with some things not being ready on time and some aspects of the

design. Professor Constance Cepko described the building as having a "...beautiful entryway and auditorium with excellent acoustics." She also found some of the unfinished electrical work to be inconvenient, and that many of the electrical problems are still unresolved. Both Dr. Cliff Tabin and Fred Winston, who moved to the NRB from the Warren Alpert building, thought that the greatest advantage of moving the Genetics department into the NRB was the opportunity it provided to hire new faculty. One new faculty member, Dr. Mitzi Kuroda, moved her lab to the NRB from Baylor College of Medicine, in Houston, Texas. She thinks that the new building is an excellent place to do science, but noted that designing such a building is difficult. She said that Baylor was a long building with skinny hallways that forced most researchers to pass the same areas, providing an opportunity to interact. Dr. Kuroda noted that the NRB is wider with more hallways, allowing people to take different routes and miss each other.

Faculty Profiles:

[David Knipe](#) | [Dyann Wirth](#) | [David Clapham](#)

[A Novel Thesis Proposal](#)

Mike Boyce (G5)

"The question of whether it is possible to automate the scientific process is of both great theoretical interest and increasing practical importance because, in many scientific areas, data are being generated faster than they can be effectively analysed. We describe a physically implemented robotic system that applies techniques from artificial intelligence.... In initial trials, using nine graduate computer scientists and biologists, we found that there was no significant difference between the robot and the best human performance... [This sort of automation in scientific discovery] is desirable because it frees scientists to make the high-level creative leaps at which they excel."

- King et al. Functional genomic hypothesis generation and

experimentation by a robot scientist. Nature 427, 247-251 (2004).

[A runner's guide to the sport of spectating.](#)

Aimee Shen (G3)

If you've never watched a marathon before, the Boston Marathon is one that you don't want to miss. It's the world's oldest annual marathon, and it's only a 15-20 min walk from the Longwood Medical Area. Not only will you be awed by the physical prowess of the elite runners, entertained by the inventive costumes of the more creative runners, shocked by the sight of bloodied nipples (it's true, despite the invention of band-aids), but you will be performing a great service to the participating runners and the tradition of the marathon itself.

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Recent BBS Student Publications:

Elias JE (G4), Gibbons FD, King OD, Roth FP*, Gygi SP*. Intensity-based protein identification by machine learning from a library of tandem mass spectra. Nature Biotechnology 22(2): 214-9.

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Bulletin Announcements

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*These authors contributed equally.

Announcements:

David Langenau (G4) married Brenna Hopkins in November 2003.

Nina Reiniger (G6) (vice-skip) and her curling team, Shelley Dropkin (skip), Phelicia Howland (second) and Dawn Gutro (lead) recently became the women's regional champions and will be playing in the US National Women's Curling Championships in Grand Forks, North Dakota at the end of February.

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David Clapham

Professor of Neurobiology
By Ray Shao (G4)

David Clapham

Research Interest: To understand how signal transduction regulates the function of ion channels and to understand the mechanism of intracellular calcium signaling.

Beginnings: Clapham was born in Monahans, Texas. When Clapham was fourteen, his family moved to Santa Cruz, Bolivia, because the oil company his father worked for began operations near the Amazon Basin. Clapham enjoyed his two years in Bolivia, where he was able to climb huge mango trees, go horseback riding, and fish in rivers in the middle of the rain forest. During that time, Clapham attended an English-speaking school, and took math and science correspondence courses with professors at the University of Nebraska. He would mail his algebra homework to his teachers and get the results back six weeks later. Clapham went to college at Georgia Tech in Atlanta for his undergraduate degree, where he studied electrical engineering and computer classes. He was also was on the

college gymnastics team.

Graduate School and Beyond: Clapham entered the M.D./Ph.D. program at Emory and did his thesis research with Lewis DeFelice, where he studied the biophysics of single ion channels in cardiac cells. During his residency at Brigham & Women's Hospital, Clapham went to Max Planck Institute at Göttingen and did a postdoc with Erwin Neher, who later shared the Nobel Prize with Bert Sakmann for inventing the patch-clamp technique. For his postdoctoral research, Clapham studied nicotinic and GABA_A channels and modeled the exocytosis and neuronal excitability of adrenal chromaffin cells. Clapham decided to pursue research rather than continuing with clinical medicine. He moved to Minnesota to direct the M.D./Ph.D. program at the Mayo Clinic and, ten years later, was recruited back to Harvard Medical School.

Outside Activities: In his free time, Clapham likes to spend time with his four daughters. He enjoys hiking, most recently at the Dover Reservation and in the Rocky Mountains. Clapham also enjoys fly fishing, particularly in Utah and Colorado, and sailing around Boston. His favorite outdoor adventure was a canoe trip along the Chatanooga River in Georgia, exactly where the movie *Deliverance* was filmed. He listens to all kinds of music (except for rap). His favorite musician is guitarist Eric Clapton. He loves almost any movie by Woody Allen. Clapham most admires Albert Einstein and Richard Feynman for their independent thinking.

Motto: Don't take yourself too seriously.

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David Knipe

Professor of Microbiology and Molecular Genetics
By: Dan (Phoebe) Zhang (G1)

David Knipe

Research Interests: Studying the replication and latency of herpes simplex virus (HSV) cells and exploring the use of mutant strains of HSV as a potential vaccine against the virus.

Beginnings: Knipe was born and raised on a farm in rural Ohio. As a child, Knipe was a member of the 4H Club, where he developed an interest in agriculture, animal science, and biology. He also discovered that he was much more interested in science than farming. While still in high school, Knipe participated in a research program at Michigan State. This experience further drew him into the field of science, leading him to major in biology for his undergraduate career at Case Western Reserve University outside of Cleveland. Initially, Knipe was interested in plant science research. However, during his junior year, Knipe's genetics professor who had been a postdoc at MIT told the story about how Drs. Baltimore and Temin had discovered reverse transcriptase, causing Knipe to become more

interested in molecular biology. To learn more about virology, Knipe went to MIT for graduate school.

Graduate School and Beyond: At MIT, Knipe worked as a joint student of David Baltimore and Harvey Lodish, where he studied the molecular biology of vesicular stomatitis virus (VSV). He then went to study the molecular genetics of herpes virus in Bernard Roizman's lab at the University of Chicago for his postdoc. In 1979, he joined the faculty at Harvard Medical School. Knipe has taught several courses at the medical school; he enjoys teaching as much as being a scientist. Knipe, along with Bob Kingston and Don Coen, helped to organize the BCMP200 course. Even though he is no longer the course director, he still gives lectures in a microbiology course for medical students.

Hobbies: Knipe loves to spend time with his wife and two daughters. In the summer, he likes to garden, though his wife takes care of the flowers. He also has enjoyed restoring his nineteenth-century Greek revival home in Newton with his family. He likes tearing down walls and his wife is a good carpenter. Knipe and his family's dog go running each morning and take walks during the weekend. In addition, Knipe loves all kinds of books and music. He is also a Red Sox fan.

Worst job experience: When he was still in college, he worked as a floor cleaner in a meat slaughterhouse. Factory work experience was a good motivation for him to stay in college.

If the office is on fire, the single item to save: His laptop, where has all of his figures and presentations saved.

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A Novel Thesis Proposal

Mike Boyce (G5)

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- King et al. Functional genomic hypothesis generation and experimentation by a robot scientist. Nature 427, 247-251 (2004).

TO: My TAC committee
FROM: Mike Boyce, G5
RE: My new thesis project proposal

As you know, in recent months I have become frustrated by the distinct lack of progress on my thesis project. My PI has

suggested that this is due to my "poor laboratory technique" and "appalling intellectual shortcomings," but I prefer to view it as a case of data being generated faster than they can be effectively analyzed, or, alternatively, because the Universe hates me. In any case, I feel that a change of project direction would be useful. Therefore, in this TAC meeting, I will outline my plan to build a Robot Scientist and have it perform the remainder of my thesis research for me.

Previously, Robot Scientists have been used successfully to tackle challenging problems in biology, such as re-discovering what is already known about aromatic amino acid synthesis and how to get your manuscript into Nature [see King et al. (2004) Nature 427 247-251]. Here, I propose to use a Robot Scientist to elucidate the pathways of mammalian apoptosis using a novel high-throughput chemico-genomic RNAi-mediated integrative systems biology computational silencing algorithm approach. As a control, my paper will also be published in Nature.

The first phase of this new thesis project will be the assembly of a customized Robot Scientist. The ad hoc construction of robots using readily available materials has been described elsewhere [see MacGyver et al. (1987) TV Guide 36 120] and will be adapted here. The physically implemented components of my Robot Scientist will be based on a twelve-channel automatic pipettor, steel solution basin and luminometer (Fisher Scientific), plus two Make Your Own Robot!™ play sets (Fisher Price). The artificial intelligence module, needed to plan, execute and evaluate experiments, will be built using my iPod, three Diet Coke cans and some duct tape. My Robot Scientist will be an improvement on previous work because it will perform several complex laboratory tasks such as tissue culture, pharmacological treatment and cell viability measurements. In addition, my Robot Scientist will feature a death ray. Also, it will make delicious fruit smoothies. It is especially important to incorporate these diverse laboratory capabilities into my Robot Scientist so that I can be left free to make the high-level creative leaps at which I excel, including updating my Friendster profile and eating cookies.

The second phase of this thesis project will consist of using

my Robot Scientist to perform original research. In keeping with the interests of our lab, my Robot Scientist will initially focus on questions in mammalian cell death that are amenable to robotic solution, such as what the synthesis of aromatic amino acids might have to do with apoptosis. Subsequently, my Robot Scientist will be used to solve knotty mysteries that have confounded scientists for decades, including the origin of life, locating weapons of mass destruction and the enduring popularity of Ben Affleck.

Finally, this new thesis project will enable me to answer outstanding questions in the Robot Scientist field itself. King et al. have shown that Robot Scientists can equal the performance of nine graduate students. My work will extend this finding by demonstrating that my Robot Scientist can outperform me in scientific discovery as it works in lab, doing my thesis research, while I go shoe shopping or stay home to watch Golden Girls re-runs. This project will also explore the crucial differences between Robot Scientists and graduate students. For example, it has long been known that both robots and graduate students can be made to perform repetitive, mindless laboratory drudgery in the absence of adequate financial compensation or the respect of children or the general public. However, it is not known whether the performance of a Robot Scientist could rival that of a graduate student in grant applications, thesis proposal writing, and other tasks that require exceptional communication skills and cogent, incisive thinking in order eloquently to communicate complex scientific concepts to other professionals. And stuff.

In conclusion, I ask you to approve this admittedly unorthodox request to change thesis projects during my fifth year. Hopefully, I have convinced you of the great novelty and significance of my Robot Scientist proposal, but if you require additional persuasion, please let me know and I will bring my Robot Scientist to your lab for a demonstration, perhaps of the death ray. I am confident that my Robot Scientist will make important contributions to science by demonstrating for the first time the power of machine automation in biological discovery. That would represent a significant improvement over my previous thesis project, which, anyway, was just scooped in PNAS by a toaster



oven.

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Open Access Publishing - The Debate Continues

Roy Auty (G6) and Stephanie Wai (G3)

"In the year 2003, the Public Library of Science made it possible for people all over the world to have access to the latest scientific discoveries. Shortly thereafter, things began to change."

- PLoS television spot

It was clear that something unusual was happening when a thirty-second television spot last summer heralded the launch of a new scientific journal. Although Medline has over 4600 indexed journals, they are not normally advertised on television, and they certainly do not claim to change the world. PLoS Biology was launched last October by the Public Library of Science and has become the so-called "poster child" of open access journals. Most others are published by BioMed Central (BMC), an exclusively open access publisher started in 1999 that now has a portfolio of over 100 journals.

Open access refers to a model of scientific publishing in which the author or institution pays for the editing, production, and distribution of a finished research article. For example, PLoS Biology charges authors \$1500 per edited article. Open access articles are then free for anyone to read in full, usually by downloading a .pdf file or viewing online. This is in contrast to conventional publishing, in

which only subscribers or members of a subscribing institution can read the complete article. In theory, conventional publications should be cheaper for scientists since they can access journals through libraries, which pick up the bill for distribution. However, scientists are often still responsible for page charges during publication. Also, institutional subscriptions tend to cost more than individual subscriptions - publishers want to recover any revenue lost when individuals cancel their own subscriptions in favor of accessing the journal through their library. Of course, taxpayers and charities are underwriting the whole bill, but with the conventional system, they must subscribe to journals or belong to a library to actually read the results of research they have funded.

Before we consider why scientists and the public should pay for access to the results of publicly-funded research, it is important to consider just how much the journals cost. Journal prices have become very expensive, and journals are often bundled to ensure that libraries do not select only the popular titles. The "Brain Research" institutional bundle goes for \$21,269 per year, which amounts to approximately \$160 per one printed issue - this is equivalent to a whole year's print subscription to PLoS Biology (and online access to PLoS Biology is, of course, free). Judith Messerle, Countway Librarian for the Harvard Medical and Boston Medical Libraries, notes that over the last 15 years Harvard has had to reduce by half the number of journals it carries, despite quadrupling its spending on journals to two million dollars annually over the same period. When premier institutions struggle to support their subscriptions, it is difficult to imagine how the general public, small institutions, and institutions in the developing world can afford to pay for access to important research relevant to their well-being and work.

Why are journals so expensive? One possible answer is that journals provide the valuable services of reproducing data, adding editorial input and disseminating the results. With time, publishing costs have increased along with inflation, the cost of materials, and the cost of managing an exponentially increasing amount of information. But the other possibility is that publishers have been taking

advantage of scientists, who are essentially "held hostage" in the absence of any alternative. Which answer you get depends on who you ask, as beautifully illustrated at the recent "Open Debate on Open Access Publishing," held in the New Research Building in December 2003.

In the debate, editors from the New England Journal of Medicine, Cell, Nature, and the Journal of Cell Biology discussed the open access issue with editors from BMC and PLoS. Marc Kirschner, head of the new Systems Biology department at HMS, also joined the open access half of the panel. The debate, organized by a committee led by Junying Yuan, allowed both sides to make their statements and rebut the opposite side's arguments. Theodora Bloom, Deputy Editorial Director of BMC, cited numerical data showing that publishing giant Elsevier had profit margins of more than 36%. Both Emilie Marcus, Editor of Cell (acquired by Elsevier), and Charles Jennings, Executive Editor of Nature, argued that publishers have helped increase access to research by placing materials online, thereby making materials available to more readers than ever before. However, when William Wells, News Editor of JCB, noted that JCB allows open access to articles more than six months old, Bloom countered by showing an ad (from Nature) that states, "A lot can happen in six months," and showed data supporting the fact that the most hits on journal web sites occur during the first month of publication.

Perhaps the strongest argument against open access is that the financial model remains untested. Jennings noted that, for open access journals, "... rejecting a paper is like throwing revenue away," which puts the interests of the publisher (making money) at odds with those of the editor (maintaining high standards). Traditional publishing models, however, align the interests of the publisher and editor because journals with the highest standards sell more copies. As the debate was closing, Vivian Siegel, the Editor of PLoS and a former Editor of Cell, stated her belief that scientists themselves would be responsible for the fate of PLoS and open access publishing. If the scientific community embraces and supports this movement, then open access can continue.

The gist is that scientists have now been empowered to change the status quo - but the question is, are you feeling empowered? It is easy to argue the benefits of open access publishing. But to actually publish in BMC or PLoS is a different issue entirely. A quick poll of BBS students yielded about 100 replies. Although 90 of those surveyed had heard of open access publications, only 30 belong to labs that considered publishing in one and only 10 of those had actually done so. As graduate students who must establish our reputation as scientists, most of us are hesitant to submit our precious papers to a journal that has only been in existence for a few months and may not exist at all by the end of the year. In fact, Siegel admits that PLoS was initially given enough money for about a year of operation. Whether or not PLoS Biology or BMC's Journal of Biology can ever compete with Cell/Science/Nature remains to be seen. Meanwhile, open access publishing has received approval from some of the world's largest scientific funding bodies, including the Howard Hughes Medical Institute, the Wellcome Trust and the Max Planck Institute. Also, a highly regarded investment firm has downgraded Elsevier to a riskier investment, citing open access journals as one of the factors in the decision. It seems that things are already beginning to change, but it will be up to each of us to choose our own course of action.

For more information:

PLoS <http://plos.org/>

BioMed Central <http://www.biomedcentral.com/>

Open Access Now <http://www.biomedcentral.com/openaccess/>

PubMed Central <http://www.pubmedcentral.gov/>

UC boycott of Cell Press <http://walterlab.ucsf.edu/cell.html>

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A runner's guide to the sport of spectating.

Aimee Shen (G3)

If you've never watched a marathon before, the Boston Marathon is one that you don't want to miss. It's the world's oldest annual marathon, and it's only a 15-20 min walk from the Longwood Medical Area. Not only will you be awed by the physical prowess of the elite runners, entertained by the inventive costumes of the more creative runners, shocked by the sight of bloodied nipples (it's true, despite the invention of band-aids), but you will be performing a great service to the participating runners and the tradition of the marathon itself.

Part of what makes the Boston Marathon such a great event is the sheer number and enthusiasm of the spectators that line the entire 26.2 miles of the course. In fact, I would argue that spectators make all the difference. Boston is a tough course. Deceptively enjoyable for the first 13 miles, a steady decline fools many a first-time Boston Marathon runner into thinking that they'll shatter their personal record. Okay, maybe not all Boston neophytes, but definitely this one. Despite being forewarned about starting off too fast, I "flew" through the first half of the race. Buoyed by the crowds and my faster-than-expected pace, I initially ignored the pangs in my legs after passing through the screaming wall of Wellesley College. However, as each subsequent mile passed slower than the first, each step I took sent sharp

stabs of pain in my quads, and I can safely say that the remaining 13 miles of the race was the most pain I've ever experienced. What would motivate me to continue running or hobbling? The friends that took a couple of hours out of their busy schedules to wish me good luck at Coolidge Corner. What kept me going after Coolidge Corner? It was the throngs of supportive people lining the streets. So if you have some time between experiments on Monday, April 19, 2004, walk out to Coolidge Corner or Kenmore Square and participate in this year's Boston Marathon. I know a number of runners who will definitely appreciate it!

A few tips (for more info, check out <http://www.bostonmarathon.org>):

- if you're looking for a particular runner, tell them in advance where you'll be standing (particularly which side of the road), and what both parties will be wearing: tired runners are not particularly perceptive
- avoid intersecting the path of oncoming runners when crossing the street (tired runners cannot steer)
- don't tell runners who are walking to start running - you might get dragged out onto the course
- bring some water, Gatorade, orange slices, and/or Vaseline (don't ask) to give people an extra boost
- eat some sinful, fattening food while watching athletes sweat it out - it tastes even better when they can't have any!

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The New Children's Building
(NCB)



The New Research Building
(NRB)

The Two Towers: Harvard's New Research Buildings

Sebastian Paige (G1)

Some of you may have heard of the "Not Ready Building" (NRB) or the "Never Complete Building" (NCB), but both the New Research Building (NRB) and the New Children's Building (NCB) are up and Harvard researchers have settled in. As with all new buildings, they have their benefits and disadvantages. Those who have moved in to either facility get to work in a shiny new building, but they also get the inevitable delays and annoyances associated with any move, hence the colorful nicknames. The Genetics and Pathology Departments have moved into the NRB along with other labs. The faculty members I spoke with in the NRB believe it is a beautiful building, but find fault with some things not being ready on time and some aspects of the design. Professor Constance Cepko described the building as having a "...beautiful entryway and auditorium with excellent acoustics." She also found some of the unfinished electrical work to be inconvenient, and that many of the electrical problems are still unresolved. Both Dr. Cliff Tabin and Fred Winston, who moved to the NRB from the Warren Alpert building, thought that the greatest advantage of moving the Genetics department into the NRB was the opportunity it provided to hire new faculty. One new faculty member, Dr. Mitzi Kuroda, moved her lab to the NRB from Baylor College of Medicine, in Houston, Texas. She thinks

The auditorium that is part of
the conference center at the
NRB



that the new building is an excellent place to do science, but noted that designing such a building is difficult. She said that Baylor was a long building with skinny hallways that forced most researchers to pass the same areas, providing an opportunity to interact. Dr. Kuroda noted that the NRB is wider with more hallways, allowing people to take different routes and miss each other.

Also in the medical center, The New Children's building has recently been completed and researchers are still moving in. NCB has allowed for the creation of six new programs split between the New Children's and Enders buildings. The New Children's Building houses Vascular Biology and Stem Cell/Developmental Biology and the Enders building houses Neuroscience, Genomics, Children's Hospital Informatics Program, and Tissue Engineering/Regenerative Medicine. Researchers in the NCB seem to have similar complaints as NRB scientists about the delays to their research and moving in before everything is completed, but were more upbeat about the opportunities to interact with other researchers. Ryan Murphey, a 4th year BBS student, liked working in the new building, but was unhappy with the delays to his research caused by the move and unfinished aspects of the building. Professor Leonard Zon said the building was "...wonderful and had the great advantage of large couches in a common gathering area on each floor." He also noted that the common space allowed for a coffee hour every Monday that fostered interaction between researchers. Overall the New Research Building and the New Children's Building have introduced some delays to the work of the scientists that have moved in, but they allow more researchers to join the medical center and contribute much to the work done here in the Longwood Medical Area.

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Faculty Profiles:

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Dyann Wirth

Professor of Infectious Diseases
By Yao Chen (G2)

Dyann Wirth

Research Interest: To understand parasite diversity in malaria and to gain insight into drug resistance.

Beginnings: Wirth was born in a small town in Wisconsin. As a child, she started doing science experiments in the family basement, where her lab consisted of some chemistry sets and a microscope. During high school, Wirth went to a National Science Foundation summer camp at the University of Indiana in Bloomington. There, she did experiments on animal physiology and had the opportunity to watch open heart surgery. The summer camp helped her to decide that she wanted to become a scientist. For her undergraduate degree, she went to the University of Wisconsin to study biochemistry and zoology. Wirth spent her junior year abroad at Freiberg University in Germany. There, she conducted research on cell cycle control, studied German literature, perfected her German, and met her future husband. She returned to Germany after graduating

from college on a Fulbright Scholarship.

Graduate School and Beyond: Wirth went to MIT, where she studied Sindbis virus glycoprotein maturation with in the labs of Phil Robbins and Harvey Lodish. She then did a postdoc with Wally Gilbert in the Molecular and Cellular Biology Department at Harvard, where she focused on mRNA processing. While a postdoc, she heard a talk about malaria at a departmental retreat. At that time, there were very few drugs against the disease and the molecular biology of the disease was still a mystery. Wirth began studying the molecular biology of malaria and co-taught a parasitology course at the Marine Biological Laboratory in Woods Hole with John David, who was the head of Tropical Public Health at Harvard. He learned of her interest in using molecular biology to study malaria and recruited her as a faculty member. She has been at Harvard ever since, with a great deal of overseas work in Latin America, South East Asia, and Africa.

Favorites: Wirth's favorite activity is snowboarding, which she took up about six years ago. She is currently learning to surf and looking forward to surfing at a meeting in Australia next year. Wirth's favorite author is Agatha Christie because she loves solving puzzles. Wirth enjoys classical music; her favorite composer is Beethoven. Wirth has spent a significant amount of time in Thailand due to her work; Thai food has become her favorite cuisine.

What Would You Take if Your Office Were on Fire? "My computer - it is part of my life."

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