worth an extra look

Nostalgic about calculating statistical probabilities on a slide rule. Eager to immerse an avatar surgeon in a virtual operating room. More than two dozen JHSPH alumni share their visions from the nexus of technology and public health in personal essays and photos.

magazine.jhsph.edu/techessays

How do you protect the boys of Touba, Senegal and the rest of the country’s population from malaria? Defense may be the best offense against humanity’s perennial enemy. The Johns Hopkins Center for Communication Programs and its NetWorks project aim to cover every sleeping space in the country with a mosquito net.

next issue it takes a network

Don't Blink
Technology’s lightspeed transformation of public health
There’s no app for saving lives... yet.

Story / Christen Brownlee
Illustration / Dung Hoang
On a recent Friday, Alain Labrique opened his office door and noticed a new red and yellow DHL package waiting for him on his desk. It looked a little worse for wear. “What’s this?” he said to the visitor with him. He tore into the package’s rumpled overwrap. As he lifted the beige plastic box inside, the unmistakable tinkling of broken glass emanated. “That can’t be good,” mused Labrique, PhD ’07, MHS ’99, MS, an assistant professor in International Health. Cutting through the copious tape binding the box closed, Labrique flipped open its top. Enclosed were several glass slides with swipes of bacterial vaginosis, a disease that Labrique is well trained to diagnose, from women in rural Bangladesh. About half the slides were broken into tiny shards.

Immediately, he pulled out his phone and snapped a picture of the damage, sending it to his colleagues in Bangladesh—a technologically savvy image worth a thousand words on how not to package slides. “That’s mHealth 101 right there,” Labrique joked.

mHealth is short for mobile health, a growing field that takes advantage of mobile communications devices—mostly cell phones—to enhance access to health information, improve distribution of routine and emergency health services, or provide diagnostic services. With phones and other mobile technologies growing more ubiquitous by the minute, it was only a matter of time before public health researchers, practitioners and users took advantage of these media themselves. At the Bloomberg School, up and running mHealth projects range from saving the lives of pregnant women and babies in Bangladesh to assessing drug use patterns in inner city Baltimore.

But using phones to advance public health isn’t as simple as it seems. Researchers are grappling with complex questions that have already doomed hundreds of mHealth projects: How do you know whether mHealth projects are really working and worth the investment? How do you conquer the phenomenon known as “pilotitis,” and scale effective strategies into health systems that have regional or national impacts? And how do you make sure these projects are long-lasting additions, instead of the public health equivalent of a dropped call?

With a new University-wide project called the JHU Global mHealth Initiative (see sidebar on page 9), Labrique, his faculty colleagues and students from across Johns Hopkins are coming together to face these questions while building a new community—one that embraces this evolving technology as a game-changer with the potential of revolutionizing health.

mHealth projects are launching at an exponential rate.

An Evolving Landscape

The mHealth movement has taken hold of public health almost as fast as the exponential rise of cell phones themselves. As of early 2010, the number of cell phones in use worldwide had hit more than 4.6 billion, according to the International
Telecommunication Union, a UN agency. (To add some context, the world’s population hit 7 billion in late 2011.) A recent search of PubMed, the NIH biomedical research database, yielded hundreds of articles focused on the use of cell phones to improve health or gather health information, most added in the last three years.

Labrique recalls seeing the change himself over the past decade in rural Bangladesh. When he started work 11 years ago on the JiVitA project, a study designed to understand the effects of supplementing pregnant women’s diets with vitamin A, Labrique remembers the abysmal communication among members of the research team scattered throughout the rural countryside dotted with green rice paddies. The people were quick to offer a place to sit and a betel nut to chew, but were stunningly isolated.

“We couldn’t make a phone call to the next town,” Labrique says. The only reliable way to pass information among team members was to pay messengers to carry written memos by bus, so getting a simple answer to a question could be an all-day affair. “I joke when I lecture about this that we were seriously contemplating carrier pigeons,” he adds.

By 2004, the first cell phones started making their way through the area. With just a single tower nearby, it still wasn’t a useful way for Labrique and his colleagues to connect—it worked better as a landmark. His research team counseled visitors driving to their site to travel north until they saw that cell phone tower, then take a left to reach the field site.

But in a few short years, the landscape changed. As 30 new cell phone towers popped up around the JiVitA site, more and more of his local colleagues began using cell phones themselves—not just senior managers in the study, who could easily afford what started out as a luxury item, but, eventually, grassroots-level field workers as well.

“In the span of two years, these field workers—who usually have no more than an eighth-grade education—went from having no phones whatsoever, to almost every single one carrying a personal phone,” Labrique says.

Eventually, he and his colleagues started noticing that cell phones were infiltrating the narratives they were collecting from women and their families to describe obstetric crises and maternal or infant deaths. When they crunched the numbers, they found that about half the women in their study who’d experienced an obstetrical crisis had used a mobile phone to try to turn their situation around—by calling a provider, arranging transportation to a clinic, getting financial aid to pay providers or seeking out medical advice.

With access to cell phones skyrocketing in the area, either through direct ownership or access to a village phone, Labrique and his colleagues decided to start up a mobile phone–based labor and birth notification system. In a recent study, led by International Health Professor Parul Christian, when pregnant women went into labor, they or

How do we ensure they don’t become the public health equivalent of a dropped call?
their families called or sent text messages to a central number. This action dispatched nurse-midwife teams to the women’s homes, where 90 percent of births take place in rural Bangladesh. Results showed that about 89 percent of these births—which would normally have taken place without any medical care—were attended by highly skilled health care workers with the new system.

Empowered by this success, Labrique’s team will launch a new project this year called mCARE that takes these previous studies to a whole new level. Working closely with the Bangladeshi Ministry of Health and Family Welfare, complementing the government’s vision of a “Digital Bangladesh,” supported by the UBS Optimus Foundation, the researchers will be supplying cell phones to the community health workers who visit women periodically to get those who are pregnant into prenatal care as soon as possible. The phone is an inexpensive Chinese-made Android model—an operating system well suited to mHealth applications because its open-source nature makes it highly customizable to users’ needs.

On their regular pregnancy surveillance visits, these workers can use these phones to register their clients, possibly even snapping a quick picture so supervisors can verify who they’re talking with in subsequent visits. Guided by a customized app on the phone, the workers will then ask a series of questions incorporating lunar calendars and local events, to sort out when the woman’s last menstrual period took place. If it was more than five weeks ago, the app notifies the worker that this client is potentially pregnant.

That pivotal revelation will automatically trigger a series of other events. Based on the woman’s expected due date, the app schedules several prenatal appointments. It will send her reminders on her own phone, if she owns one, and to the community health worker, who will stop by a couple of days before appointments to emphasize the importance of each visit to the woman and her family. As with the previous study, each woman and her family will be encouraged to notify the study by text when they go into labor and if they need help, spurring a mobile health care team into action to attend the birth or facilitate a referral to clinical care. If labor appears premature according to the system’s records, it then signals a special alert to the health care team that they may be dealing with a preterm baby that may have more intense medical needs. Another text when the baby is born will trigger another series of visits one, three and five days later, to make sure that mother and baby are doing well.

“Each action here stimulates a reaction,” Labrique explains. “Rather than waiting
for a crisis to happen, we’re using mobile technology to respond to potential problems before they occur.”

The study’s impact on mortality is yet to be measured, but based on the pilot work with labor and birth notification systems and emergency dispatches of nurse-midwife teams, Labrique expects these efforts will pay off through better prenatal care for mothers, more attended births and targeted care for infants (especially high-risk, preterm babies)—ultimately saving the lives of mothers and their infants.

“The groundwork has been done to demonstrate that these systems can work in this challenging, resource-limited, remote context,” he says.

A Game Changer?

As Labrique and his astute colleagues noticed, cell phones are an ideal solution to connecting with low-resource populations. But mHealth isn’t just for the developing world, according to Betty Jordan, an assistant professor in the Johns Hopkins School of Nursing.

In 2009, when Jordan was serving on the board of directors at the National Healthy Mothers, Healthy Babies Coalition, she heard of a project that would send text messages with health advice to pregnant women three times a week. Then, once they gave birth, it would switch to health advice for newborns, all based on the due date that enrollees provide when they sign up for the service.

While many low-income women may not have computers or pregnancy books, the coalition reasoned, many of them do have phones—providing a way to deliver information that could have enormous impact on their health knowledge and behavior and the health of their babies.

“I thought it was a fabulous idea,” Jordan recalls. “A 16-year-old inner city pregnant teen may not be going to the library to read a pregnancy website or be able to afford childbirth classes, but she might be willing to read the message that comes across her phone.”

In early 2010, text4baby launched across the country. Since then, more than 260,000 have enrolled. But she and her colleagues wanted to make sure that text4baby was a success by other standards as well, so they built in measures to evaluate the program from the start.

According to Piers Bocock, project director for the Knowledge for Health Project, run by the Bloomberg School’s Center for Communication Programs (CCP), mHealth evaluation remains a huge hurdle. Governments and donors want to make sure that mHealth interventions can be measured so they can make the right decisions about funding comprehensive mHealth programs. “There are a lot of pilots out there,” says Bocock, “but not a lot at scale.”

CCP, which includes mHealth components in more than a dozen of its projects around the world, is constantly working to understand how mobile efforts are adding to the effectiveness of its programs.

“We all realize mHealth can be a game-changer, especially when it is part of other social and behavior change communication activities,” says Bocock. “The question

A New Vision for mHealth

In late 2010, Alain Labrique, Betty Jordan and other colleagues at Johns Hopkins came to the same realization: One way to move the mHealth field forward as a useful public health strategy would be to compare notes with as many people as possible. By learning from each other’s successes and failures, researchers could grow the evidence base for solid mHealth strategies. With that goal, the Johns Hopkins University Global mHealth Initiative (GmI) was born in mid-2011.

The team quickly found dozens of researchers across the schools of Public Health, Nursing, Medicine, and Engineering who were using cell phones in their work and invited them to join up.

Since then, he and other organizers have launched a speaker series and brought together Hopkins students and faculty members for transformative, interdisciplinary collaborations. They plan to develop a curriculum around mHealth, starting new courses and infusing existing ones with lectures on mobile technologies.

GmI also plans on offering guidance to outside organizations, Jordan says, serving as a thought leader in the same way that other Hopkins institutions have traditionally done. “Hopkins already has a footprint in the global community for lots of things—basic research, clinical research, health care,” she says. “We believe that we could be the go-to place for mHealth in the world.”

The EXACT Science of HIV Treatments

As antiretroviral therapies became more effective and available, Gregory Kirk and his colleagues found that some participants in the ALIVE (AIDS Linked to the Intravenous Experience) study could stick with their therapy and fend off AIDS, while others couldn’t.

Developing a good method to predict which drug users are likely to adhere to treatment and which ones will fail is the goal of the EXACT (EXposure Assessment in Current Time) study, a subset of the decades-old ALIVE study.

EXACT collects real-time information from drug users to develop predictive algorithms on what might cause them to use drugs, and ultimately, why they might not fully adhere to HIV treatments. Pilot studies using PalmPilots and wearable GPS devices yielded data multiple times a day from current or former intravenous drug users with HIV in the Baltimore-metro area.

After getting a prompt from their PalmPilots, 89 volunteers answered a series of questions on what they were up to and their stress levels, moods and drug use. The GPS recorded their location.

Ultimately, Kirk says, he and his team hope the study will help the health care team focus more time and resources on patients more likely to be nonadherent. Eventually, he adds, smartphones might help patients improve their health directly, alerting counselors such as peer navigators that patients need interventions.

—CB
Free phones and airtime for researchers and subjects have been the kiss of death for many mHealth pilot projects as they try to scale up to full-size programs.

we want to answer is how to quantify its effectiveness within the context of broader public health interventions.”

Garrett Mehl, PhD ’00, MHS ’94, a WHO scientist and a chair of its Health Data Forum Working Group on mHealth, notes that insufficient attention to the role of research has been the downfall of countless other mHealth projects.

“I think we can definitely say that there have been a considerable number of pilot mHealth projects, and a lot of them have failed in either their ability to demonstrate some health impact or in their ability to find a mechanism to sustain them,” he says. Mehl adds that in a joint project with a Bloomberg School intern that assessed the global state of evidence generation among mHealth projects, a considerable proportion of the projects were struggling with research—and donor support—needed to validate their efforts. Despite their presence in public databases, many mHealth projects were found to have already ended, suggesting their inability to transition from pilots to scaled-up programs. Often projects, Mehl notes, are driven by the pleas of donors to get implementations running quickly, without any forethought about how to judge success or pressure to plan for scale-up and sustainability.

“You begin to worry that a lot of investments are being made in this area, and if they fail, you worry that people won’t want to continue to invest,” he says. Fortunately, Mehl notes that donors are now beginning to pay more attention to evaluation and invest in mHealth evidence generation and synthesis.

To head off these problems, Jordan and her colleagues incorporated some unique evaluation methods into the fabric of text4baby. For example, to see whether the program is reaching its intended audience, researchers ask participants for their ZIP codes during registration. The result is a real-time map across the country that text4baby’s partners, including local health offices, can access and watch enrollment numbers change on a minute-by-minute basis. They can also instantly see whether ads to entice women to sign up have the desired effect. An ad for text4baby during the popular MTV program 16 and Pregnant, caused a huge spike in enrollment.

“It’s a huge strength of the program to see whether we’re hitting our intended audience,” Jordan says.

But demonstrating whether these texts are improving outcomes for mothers and babies is a much tougher problem to tackle, Jordan notes. “It’s easy to tell whether women are enrolling, find out whether they like the messages or see if the number of texts they get each week is acceptable,” she says. “It takes a lot more time, effort and evaluation.
strategies to demonstrate knowledge and behavior change.”

One step toward judging whether they’re achieving this goal, Jordan adds, is a series of interactive modules that the text4baby team recently began inserting into the typical texts that users receive. Around the end of October 2011, they sent their first interactive module: a questionnaire on whether users had received the flu shot, and if not, why. Within 48 hours, nearly a third of the 96,000 users who received the module responded, giving Jordan and other researchers involved with the project reassurance that users were engaged and interested in sharing information, as well as lending insight into their health behaviors.

Larry Cheskin, MD, an associate professor of Health, Behavior and Society, and director of the Johns Hopkins Weight Management Center, is hoping to get around the evaluation problem by incorporating mHealth into a randomized study—the gold standard for other health interventions.

He explains that the typical program at the Weight Management Center is a relatively time- and resource-intense affair. On their first visit, patients see a series of health care providers—a dietitian, psychologist, exercise expert and Cheskin himself—and come back frequently for follow-up. This care usually isn’t covered by insurance. Since those of low socioeconomic status are more likely to be obese in the U.S., it places the program out of reach for those who probably need it the most.

“It’s not translatable to the U.S. as a whole,” Cheskin notes.

Seeking a better way, he and his colleagues launched the TRIMM study—short for Tailored Rapid Interactive Mobile Messaging—in 2011. They’re recruiting 150 minority participants from inner city Baltimore who are interested in losing weight. All the participants will receive comprehensive counseling on diet and exercise, but half will receive customized text messages several times a day that address their self-identified problem areas. Cheskin and his colleagues plan to see how the two groups compare after six months—and then after another six months, when the text messages are shut off.

“It’s well known in this new field of mHealth that there’s not a lot of control data,” Cheskin says. “Doing a randomized controlled trial is a high quality way of seeing whether the outcome you’re hoping for is really there.”

Evaluation isn’t the only tough problem in mHealth—scalability and sustainability are issues that have doomed many other mHealth projects, notes Patricia Mechael, PhD ’98. She recently became the executive director of the mHealth Alliance, a Washington, D.C.-based organization hosted by the United Nations Foundation that serves as a convener of the mHealth community and provides guidance and support for those using mHealth tools. For example, giving out phones to researchers and subjects alike might be the kiss of death for many mHealth projects, according to Mechael. For a small pilot project, maintaining equipment and airtime might be manageable, but continuing to provide equipment and airtime for a full-scale project is oftentimes financially unsustainable. Unless a country’s government or private sector investor can invest in buying a phone and minutes for the target population, Mechael explains, that model simply won’t work for the long haul.

Similarly, Mechael says, multiple projects have failed because there is no standard for them to integrate with one another. For example, she explains, there’s a missed opportunity if one mHealth intervention evaluates patients for tuberculosis symptoms while another assesses HIV risk, but the two aren’t designed to easily combine their findings. Governments that are seeking a complete picture of these two diseases in the populations they serve will likely discard both programs.

From the outset, Mechael says, programs should examine how mobile technology can be leveraged to strengthen the health system as a whole and interact with other platforms, even if the initial funding is specifically targeting a particular health condition.

“mHealth is a lot more complicated than just giving out phones or developing apps,” Mechael explains. “Technology is only as good as the systems that it supports.”

“A public health preoccupation today seems to be the creation of ever-more-elaborate technologies that harvest hitherto unimaginable quantities of data. Never mind that the methodologies are ill-conceived or the questions inappropriate. Too often sidelined are the professionals who would translate the findings into action. Usually the best equipped to fulfill such roles are rare creatures called “public health epidemiologists.” In establishing the Epidemic Intelligence Service, the CDC’s Alex Langmuir, a former Hopkins faculty member, emphasized the importance of the “shoe leather epidemiologist,” who collected information in the field and devised solutions.

Better reporting systems are a priority. However, prospective solutions now focus on complex systems that minimize the need for human intervention. As one example, the U.S. now is planning to invest billions of dollars in two systems called BioWatch and BioSense—one to detect virulent particles in the air and a second to analyze daily data on clinic patients with complaints, like diarrhea or cold symptoms. The hope was that they would provide early warning of a developing epidemic. So far, BioWatch—when it has worked—has produced only false alarms; BioSense has detected influenza outbreaks about as quickly as elementary school teachers note higher absenteeism. Neither is expected to be of help in controlling an epidemic. Support for these vagaries has come at the expense of state and local programs. It seems to me that it would be far more effective to invest in the training and support of such professional staff. They are what we need to develop real solutions.

D.A. Henderson, MD, MPH ’60, Dean Emeritus, led the successful global smallpox eradication effort.
A Turtle to the Rescue

There’s water everywhere in Bangladesh where houses commonly are built on excavated mounds of earth and consequently surrounded by ditches and ponds. As a result, 17,000 kids drown here annually (46 every day) making it a leading cause of death in children ages 1 to 4.

The obvious solution—erecting barriers around the water—simply isn’t feasible. But perhaps the Safety Turtle is.

Marketed to swimming pool owners in the U.S. and Canada to protect pets and children, the Safety Turtle is a personal immersion alarm with a wireless base unit that blares a warning when the device (shaped like a small plastic turtle) hits water. The turtle can be affixed easily to a toddler’s wrist, says Adnan Ali Hyder, MD, PhD ’98, MPH ’93, an associate professor in International Health who directs the International Injury Research Unit.

He and Alain Labrique, PhD ’07, MHS ’99, MS, assistant professor in International Health, are pilot testing the device in the field—soggy as it is—to find out if it will work in a monsoon climate as well as be culturally appropriate and socially acceptable. The research is supported by a JHSPH Faculty Innovation Award to Labrique, who has worked in rural Bangladesh for more than a decade.

Although the $150 kit is prohibitively priced for use by most Bangladeshis, the researchers think one solution might be to divvy up the cost between a half-dozen families living together in a community; they could share a base unit connected to a dozen or more turtle devices, each of which would cost relatively little. “We’re targeting this as a supervision aid for parents of toddlers,” Hyder says. “If they are busy working and cooking and an alarm goes off, it will alert an entire community to look for the children and see who’s in the water.”

Driving Down Teen Collisions

Compelled by chilling crash statistics and inspired by watching his son play Grand Prix video games, David M. Bishai, MD, PhD, MPH, set out with a grant from the Center for Injury Research and Policy (CIRP) to improve something that’s largely been neglected for decades: driver’s education for teens.

“Hardly anyone’s examining what young drivers need to know to be safe,” says Bishai, a professor in Population, Family and Reproductive Health. While yawn-inspiring old-school driver’s ed may be of questionable value, he contends that an engaging program employing innovative software that emphasizes contemporary hazard-recognition content could, in fact, make a life-and-death difference in the same way that graduated licensing has. His aim: to create an interactive experience that teaches teens to anticipate road hazards.

With Hopkins colleague Sara Johnson, PhD ’05, MPH ’01, and Maria Schultheis, PhD, of Drexel University, Bishai is testing the validity of a Digital Mediaworks driving simulator. The team has tested 10 subjects so far, correlating measures of driving performance in the lab with measures of attention, risk-taking and intelligence.

Bishai’s goal now is to compare the performances of 100 16- to 18-year-old novices to more experienced drivers in the context of routine driving as well as with added stresses such as phones ringing.

As the simulator measures each subject’s specific competencies, it also gives researchers insight into the teen brain.

“If we show the simulator can differentiate between good and bad driving, and inexperienced and experienced drivers,” he says, “then we would have an ‘in virtuo’ model of the most lethal threat to teen health—driving.”
All Done with DUI

Imagine a smart steering wheel that could sense by the mere touch of a driver’s hand if he’s had one too many. This is the next generation of alcohol-sensing interlock technology: Automatically activated and pre-market installed, it would prevent a car from operating if a driver is beyond a pre-set limit, even if he (mistakenly) thinks he’s safe to hit the road.

A steering wheel capable of calculating a driver’s blood-alcohol concentration based on the chemical properties of his skin may seem futuristic. But it is one example of technology being applied to a new class of alcohol detection systems that are already in research and development by car manufacturers, says Shannon Frattaroli, PhD ’99, MPH ’94, an assistant professor of Health Policy and Management with CIRP.

“It’ll no longer be a matter of figuring out strategies to discourage people from drinking and driving,” she says. “Now, we can imagine a time when drinking and driving and all the deaths, injuries and mayhem associated with it will just not be possible.”

Injury prevention research has borne out the fact that passive interventions—those requiring no action on the part of users—are very effective, Frattaroli says. Think airbags, for instance.

What society decides to do with this technology once it’s available could have huge implications for public health. CIRP faculty members are monitoring the development of alcohol-sensing technologies and the policy options under consideration for advancing their application. “If we can end the devastation caused by drinking and driving—and it seems possible in the not-too-distant future—that’ll be an amazing advancement,” Frattaroli says.

Baby’s First Photos

Because gestational age is a critical indicator of newborn health, Parul Christian, DrPH ’96, MSc, MPH ’92, and colleagues enlisted 500 pregnant women in rural Bangladesh in a study that compared the gold standard for determining precisely how long a baby spends in the womb—ultrasound—with “last menstrual recall.”

The recall technique is shaky at best, particularly in the setting where Christian has spent a dozen years conducting research. It depends not only on whether a woman reliably recalls the first day of her last menstrual period—which may in turn depend on her level of literacy—but also whether her cycles are regular.

Neither assumptions nor the inherent uncertainty of memory bodes well for taking the critical first step in bringing about lifesaving policy changes: gathering good, accurate data.

“In public health we’re interested in trying to figure out the factors that lead to preterm birth, which is associated with a high risk of mortality and morbidity,” Christian says.

Having purchased a portable Sonosite Titan ultrasound device for $14,000, Christian and Alison Gernand, PhD ’11, MPH, RD, assembled a team in the JiVitA field site in rural Bangladesh, where 90 percent of women deliver at home.

Trained technicians assessed women who visited a study clinic, recording fetal crown-rump lengths on sonograms to estimate gestational age at birth. A sample of the sonograms and measurements were reviewed for quality control by collaborator Frank Witter, MD, of the Johns Hopkins School of Medicine.

“This is an important technology to use in populations where we don’t really know the burden of preterm birth, or may have only an inaccurate estimate of its magnitude,” Christian says.
Overload
The quest for knowledge in an era flooded with information

Story Jim Schnabel
Illustration Michael Gibbs
Every step you take, every move you make… Science can learn from you.

The tech revolution that has put iPhones in our pockets and a world of Google-able data at our fingertips has also been ushering in a golden age of health research. Take, for example, work being done by Thomas Glass, PhD, and Ciprian Crainiceanu, PhD, and their teams. They recently clipped accelerometers—smaller than iPhones—onto the hips of elderly research subjects. The devices can record people’s motions in detail, for indefinite periods and in real time if needed. The immediate aim, says Crainiceanu, a Biostatistics associate professor, is to devise a truer method of recording the physical activity of the elderly. But it’s the kind of approach that could turbocharge a lot of other health-related science. No more questionnaires, no more biased recollections, no more droopy-lidded grad students analyzing hours of grainy video. Just the cold, hard facts, folks. Just the data.

“In principle, we could take inputs from a wide variety of sensors—say, heat sensors, or portable heart monitors sending data by Wi-Fi or cell phones,” Crainiceanu says. “Our imagination is the limit.” And it’s not just portable gadgets that are making this possible. Brain imaging technology is still big and expensive, but its use is becoming more routine, and it now can deliver information on neural activity and density and connectivity at volumes on the order of a cubic millimeter. Next-gen genomics technologies can catalog DNA and gene-expression levels rapidly and with base-pair precision. Medical records are migrating to the digital and Web realms and containing ever more numeric and imagery-related detail. This gold rush of data gathering represents “an opportunity not just in terms of improving public health but also within biostatistics, for it gives us this tremendous new set of problems to work with,” says Karen Bandeen-Roche, PhD, MS, the Frank Hurley and Catharine Dorrier Professor and Chair of Biostatistics.

And the problems can be considerable. It’s not unusual for a public health study dataset nowadays to require a storage capacity on the order of 10 trillion bytes (10 terabytes)—the equivalent of tens of millions of 1970s-era floppy disks. Larger datasets are inherently better in the sense that they have greater statistical power to overcome random variations (known as noise) in data—just as 1,000 coin flips will be better than five coin flips at revealing the true 50/50 nature of a coin flip. In practice, though, large health-related datasets often contain a grab bag of information that isn’t always relevant and is distorted (biased) by hidden factors that may confound the savviest statistician. Moreover, traditional data collection, storage and analysis techniques can’t always be straightforwardly scaled up to terabyte levels.

“How to design data collection properly, how to avoid bias, how best to represent a population of interest—these sorts of challenges may be even greater for the ultra-large datasets than for the more manageable ones with which we’ve traditionally dealt,” says Bandeen-Roche.

For Crainiceanu and his team, the goal was to turn days of raw, wiggly, three-axis accelerometer voltage readouts into meaningful interpretations of human movements. Such a task essentially attempts to reproduce—with an artificial sensor system plus software processing—the ability of higher organisms like mice or people to recognize individual movements amid the vast, noisy streams of visual and somatosensory signals coming into their nervous systems. It’s a big-data-processing skill that took us mammals tens of millions of years to develop, and even in furry, small-brained ones it involves myriad wetware layers of filtering and logic.

Crainiceanu saw the parallels to neural processing right away, and chose speech perception as a guiding analogy. “Movement is essentially like speech,” he says. “It involves units like words, which combine into meaningful sequences that are like sentences and paragraphs. So we started by processing the accelerometer data into the smallest meaningful movement units, which we called movelets.”

Movelets represent short bursts of

### 5 STEPS TO TAMING BIG DATA

**Where does big data come from and how do researchers make sense of it all?**

Ciprian Crainiceanu walks us through one example, from collection to analysis.

1. **Accelerometers**—small, reliable recorders of movement—are affixed at hip level to seniors in a study.
2. Memory sticks in the devices record 30 observations per second—10 each in three directions.
3. Raw data amassed over hours, days or weeks are downloaded into a computer. (One hour yields 108,000 data points per person—2.6 million per day.)
4. To tame the oceans of information (think thousands of people monitored for a month), Crainiceanu’s statistical design team uses software to break long strings of data into meaningful indicators of motion called movelets.
5. Finally, movelets are stitched together into narratives that reveal the time and duration that subjects sat, stood, walked or lay down—creating a true guide to seniors’ daily activities.
motion data, roughly analogous to the phonemes that make up words. Breaking down the voltage readouts into movelets made manageable what would otherwise have been an ocean of data. “We sample the accelerometer data 10 times per second, so for three axes we’re gathering on the order of 30 observations per second,” says Crainiceanu. “And let’s say we want to monitor hundreds or thousands of people for a week, or a month, with their data continually being uploaded via the Web, for example.” His team’s movement-recognition algorithm essentially can crunch all these data—terabytes’ worth, for a large study—into relatively compact histories of distinct motions (now sitting … now getting up … now walking…), just as a speech recognition algorithm can condense a storage-hogging raw audio recording into a few pages of text.

Crainiceanu’s colleague Rafael Irizarry, PhD, a professor in Biostatistics, faces a similar challenge when he helps biologists sift through gene-sequencing data. “Modern gene sequencing technology is generating such enormous datasets now that biologists are having a hard time saving it on disks; NIH has even been having meetings with experts in the field to figure out how we’re going to store all these data or whether it would be more cost-effective just to generate it again whenever we need it.”

Genomic datasets also can be devilishly hard to analyze. Modern sequencing devices typically generate raw data that represent the color and intensity of fluorescent reporter molecules linked to short stretches of DNA; these intensity levels have to be interpreted into “reads” of the GATC genetic code.
One key to dealing with today’s ultra-large datasets is knowing what to leave out, says biostatistician Brian Caffo.

Each of these short, not necessarily error-free readouts of DNA then must be pattern-matched to the right location on a three-billion-base-pair reference genome—a bit like finding the right spot for a tiny piece in a football-field-sized jigsaw puzzle. “When I first got one of these datasets,” Irizarry says, “I wrote my own little software routine to handle it and I ran it and waited … and then realized that it was going to take six months to finish!” Irizarry soon hired a computer scientist, Ben Langmead, MS, who has expertise in solving this kind of problem quickly. Their group, working with Johns Hopkins Medicine geneticist Andrew Feinberg, MD, MPH ’81, has since been putting out a steady stream of high-profile papers on the genetics and epigenetics of tumor cells. (Epigenetics refers to reversible DNA-modifications that silence some genes and let others be active; derangements of the normal epigenetic patterns in cells may be as important as genetic mutations in promoting cancers.)

And then there is the uncertain value of some ultra-large datasets. “They often come with lots of complications and biases that don’t exist in smaller datasets,” says Scott L. Zeger, PhD, the former chair of Biostatistics who is now the University’s vice provost for Research. “A large observational study could be much less informative about the effects of a treatment than a smaller dataset from a placebo-controlled clinical trial, for example,” he says. Even among clinical trials, he adds, the traditional single-center study tends to be less noisy than the multi-center studies increase, are biostatisticians themselves. “The demand these days is always greater than the supply,” says Caffo. “In fact, statistics is often rebranded as something else—sabermetrics [baseball stat analysis] and Web analytics are two examples—in part because our field doesn’t produce enough people to fill the need.”

The intense math training needed, and the esoteric lingo—“Granger Causation,” “Markov models,” “Pearson’s Chi-squared test” and so forth—probably has something to do with it. “We’re also poorly branded,” Caffo says. “Biostatistics is actually one of the most exciting fields to go into right now.”

Get Dirty with Data
Clearly, number-crunching technology makes it possible to do studies that we could never have done before. However, it is very easy now to push a button and lose a lot of insight in the process.

The whole vitamin A–mortality connection... I wasn’t looking for that. I was looking for why some kids get eye disease. If I had asked a statistician to give me the associations for having vitamin A deficiency, I would have had associations with diet, pneumonia, measles... and published a nice paper about their correlation coefficients. Instead, I looked at the original data: 15 kids had night blindness on round-one, and on round-two, only four were still around. Hmmm. What happened to those kids? I looked, and the data told me that they were dead.

You’ve got to get into the raw data—and feel it, smell it, touch it and think about it and let it lead you, rather than going in with a preconceived notion and pushing a button. Click, done! Yes, you proved something or no, you didn’t. You may miss the really important thing which had nothing to do with the question you were originally asking, but is buried in the data.

Vitamin A is the perfect example: I’m sure I would have missed it if I hadn’t been so deep in the data. I’m absolutely confident things like that are missed every day, because people don’t get dirty with their data.

Dean Emeritus Alfred Sommer, MD, MHS ’73, discovered in 1985 that twice-yearly vitamin A supplements reduced the number of child deaths in Indonesia by 34 percent. This and subsequent findings have led to hundreds of thousands of lives being saved annually.

connections
Down in the basement of the Bloomberg School’s Wolfe Street building, past a wall of antiquated mailboxes, near dubious signage indicating the whereabouts of a fax, an incessant hum emanates from a secure room monitored by a surveillance camera.

Inside that room, cold air blasts from two 10-ton air conditioners, each the size of two old telephone booths and capable of cooling about 10 average-sized homes.

“Computers like it cool,” explains Fernando Pineda, PhD, director of the Department of Biostatistics’ High Performance Scientific Computing Core (HPSCC), half of which is now housed here since outgrowing a server room on the third floor.

Consuming more than 30 kilowatts of power, these machines generate lots of heat and depend on prodigious air conditioning to avoid meltdowns.

That the facility—which provides large-scale research computing and storage capabilities for Johns Hopkins researchers in biostatistics, statistical genetics, genomics, computational biology and bioinformatics—burst out of its original physical space not five years after it was established was no great surprise to Pineda, an associate professor in Molecular Microbiology and Immunology.

“Genomics is very computationally intensive,” Pineda says. “Our computing and storage capacity has doubled every year for the past six years, and there’s no end in sight. It’s a chronic problem; not a problem you solve, but a problem you manage.”

Some of the HPSCC’s best customers are genetic epidemiologists in the Department of Epidemiology. They analyze the 3 billion or so base pairs that constitute the human genome to identify and characterize genes that might be linked to complex diseases such as hypertension and cancer as well as schizophrenia and autism.

“Biologists used to rely on test tubes, Petri plates and lab notebooks,” Pineda observes. “Now they use next-generation sequencing machines that spew out massive data sets requiring complex analyses involving mammoth calculations.”

For instance, just one of the HPSCC’s prolific customers (Andy Feinberg’s lab in the Center for Epigenetics at the Johns Hopkins School of Medicine) can generate as much as one terabyte of data every week. That’s 10 to the 12th bytes. To put this amount of data in material-world terms, you can think of one terabyte as 50,000 trees made into paper and printed. Ten terabytes equals the entire printed collection of the U.S. Library of Congress. And the National Archives of Britain holds more than 900 years of written material, which amounts to about 60 terabytes of data.

“We currently have capacity for 95 terabytes on spinning disk and another 50 on tape,” Pineda says, indicating racks of storage devices, each of which someone has affectionately labeled with a name: There’s Fran and Stan, and Thumper I and II. Luckily, there’s room for the inevitable Fran II and Stan II, and Thumper III and IV.

“There’s always going to be more data,” Pineda says, explaining that sequencing costs soon are bound to drop below analysis and storage costs.

Surprisingly, computing and storage capacity isn’t the issue that keeps Pineda awake at night. It’s the cooling, he says: “The power and the cooling. And of those two, the cooling is the big headache.”

—Maryalice Yakutchik
Here are some things that David Sullivan knows how to do: He knows how to manage a modestly sized biological lab. He knows how to chemically test for proteins and other molecular markers of *Plasmodium*, the parasite that causes malaria. He knows how to build simple prototypes of diagnostic devices that can detect *Plasmodium* proteins in urine—a potentially enormous breakthrough because such devices could eliminate the expense and risk of malarial blood screenings. Those are the kinds of tasks to which Sullivan, MD, an associate professor in Molecular Microbiology and Immunology, has given the last 20 years of his life.

But here are a few things that Sullivan doesn’t know how to do: He doesn’t know how to organize and finance large-scale trials of his malaria diagnostics. He doesn’t know how to secure international patent protection for the devices. And he has no idea how to find factories that might manufacture them on a mass basis.

To fill in those gaps—and to increase the odds that his lab’s ingenuity will actually benefit people on the ground—Sullivan turned to the Johns Hopkins Technology Transfer Office.

In 2008, that office licensed Sullivan’s invention to Fyodor Biotechnologies, a small Baltimore company led by a former researcher from the Johns Hopkins School of Medicine. If all goes according to plan, Fyodor will conduct field trials of the urine diagnostic in Mali this spring. Hopes are running high, because an effective replacement for blood-based tests could have profound benefits in combating the disease that kills nearly 700,000 people annually. “We’ve been using a more than 100-year-old test, jabbing someone with a needle,” Sullivan says. “Our idea is to make malaria diagnostics more accessible to people in the home, almost like a pregnancy test. This may enable faster treatment and faster contact with health care personnel.”

Sullivan’s project is just one of several tech transfer ventures that have emerged from the Bloomberg School in recent years. Those efforts don’t always come easily or naturally to public health scholars. “The culture here has historically not been geared toward tech transfer,” says Shyam Biswal,
PhD, a professor in Environmental Health Sciences and one of the founders of Cureveda, a biotech venture that aims to create new therapies for inflammatory diseases. When you’re working on problems that afflict people in severe poverty, revenue streams are probably the last thing on your mind. For their part, tech transfer offices haven’t always known what to do with public health ideas that might not have a market in the U.S. Slowly but surely, however, both parties are learning how to make this marriage work. In certain circumstances, they have realized, the market might be the only way to ensure that a promising public health tool moves from the lab into the real world. “The tech transfer process can be frustrating because so many good ideas die on the vine,” Sullivan says. He is grateful that Hopkins’ tech transfer staff brokered his lab’s relationship with Fyodor. If the Mali trials go well, the company hopes to have the malaria diagnostics certified by the WHO, opening the door to potential large-scale purchases by The Global Fund. “In this day and age, if you just publish an idea, it probably won’t get done,” says Wesley D. Blakeslee, director of the Johns Hopkins Office of Technology Transfer. “I think there’s more of a recognition now that biotech companies can be partners with us. If you invent a cure for cancer and it only stays in the lab, doesn’t get out the door, then you haven’t had the impact.” Sullivan’s malaria diagnostic is just one among a diverse array of tech transfer ventures based at the Bloomberg School. They include a screening instrument for identifying aging adults at highest risk for intensive hospitalization; a set of prospective new therapies for chronic obstructive pulmonary disease; and a series of instructional videos designed to teach doctors how to candidly acknowledge and apologize for medical errors. Then there is the grandfather of Bloomberg School tech transfer efforts, which also happens to be the most lucrative in Johns Hopkins University history: the Adjusted Clinical Groups (ACG) System. The software package allows public health agencies, insurers and scholars to analyze and predict patterns of illness across large populations. More than two-thirds of gross royalties from ACG (which was
first made commercially available in 1992) have been poured back into the Bloomberg School’s research programs.

The tech transfer process begins when a scholar files a formal disclosure of invention to the University. If the idea seems at all promising, the University then files a provisional U.S. patent application—a relatively low-cost step that posts a claim on the concept for a 12-month period. Then the waiting game commences: If a company chooses to license the invention, that company usually assumes responsibility for pursuing permanent patent protection—a process that can involve hundreds of thousands of dollars in legal fees. But if no suitor emerges during the 12-month period, then the tech transfer office needs to decide whether to roll the dice and invest the University’s own money in permanent patent filings.

That was the dilemma that Sullivan’s urine-based malaria diagnostic faced in early 2006, 12 months after his preliminary patent application had been filed. In his case, the University decided to press forward with a permanent application, and the gamble paid off. Two years later, in 2008, Fyodor Biotechnologies licensed the technology—and agreed, as is typical in such cases, to reimburse the University for the money it had spent on patent fees.

That basic pattern is common, according to Blakeslee. Roughly 70 percent of the licenses that Hopkins signs are for inventions that had been developed at least three years earlier. In 2010, Hopkins spent more than $8 million on patent filings (that figure includes the staff time of the tech transfer office’s in-house attorneys), and received $3.79 million in patent fee reimbursements from licensees.

“We push our inventions continuously,” Blakeslee says. “Today the biggest part of our job is to engage with industry to find out their needs, and when we do, we examine our entire portfolio for a fit.”

But even if a three-year wait is typical, it was still disheartening for Sullivan, who says he has seen many good public health ideas founder because they don’t fit the profit-making imperatives of the pharmaceutical industry. “Timing is everything,” he says. “If a company is not ready to pick it up, then the idea just sits there.” He says that the Hopkins

“I’m hoping that we get the big blockbuster, for all the benefits that it would bring to our institution. We’ve come close a few times.”

—Wesley D. Blakeslee
tech transfer office seems to be stronger than many of its counterparts at other universities at breathing life into ideas aimed at the developing world.

Blake sees happily conceding he daydreams about lucrative pharmaceuticals with Western markets. “I’m hoping that we get the big blockbuster, for all the benefits that it would bring to our institution,” he says. “We’ve come close a few times.” But he says his office also uses a variety of strategies to support low-profit-margin ideas like Sullivan’s. Last year, his office brought together more than 80 scholars from across Hopkins at a meeting with representatives of GlaxoSmithKline’s “Open Lab” project, a nonprofit effort to develop new drugs to treat tuberculosis and other diseases of the developing world. The University has also made a low-cost licensing deal with the PATH Malaria Vaccine Initiative for a technology that was developed at the Bloomberg School.

One way for public health scholars to cope with economic constraints is to be more strategic about their research programs, according to Douglass B. Given, a biotechnology investor who serves on the Bloomberg School’s Health Advisory Board. Given believes that scholars at Hopkins and elsewhere should be more aggressive about finding venture capitalists and philanthropic partners to support the commercialization of new treatments for neglected diseases. The key, Given says, is to spot emerging waves of research financing—say, a new international anti-tuberculosis campaign, or surging interest in particular kinds of recombinant gene technology—and to concentrate an entire academic department’s resources on those themes. “You need to think about where the government funding is and where the school’s strengths lie,” says Given. “If you don’t use those kinds of strategies and screens when you hire faculty members, then you can wind up in a funding no-man’s-land.”

Biswal, the inflammatory disease researcher, says that the tech transfer climate at Johns Hopkins has “radically improved” since he first dipped his toes in the water seven years ago, but he believes much more can be done. One element that he does praise is the Bloomberg School’s program of seed grants for new tech transfer ventures. The School now awards up to three $50,000 grants each year for scholars who want to develop a business plan or to file patent applications. Biswal has won two of those grants, and he says that his Cureveda venture would have been impossible without that initial support. The grants allowed him and his colleagues to develop an infrastructure and to hire a chief executive officer, he says—and it was only after that foundation was in place that larger pharmaceutical companies began to knock on his door. (Cureveda now has a three-year research and development contract with GlaxoSmithKline.)

In the rare cases when university inventions lead to lucrative products and services, they can generate substantial streams of revenue. Under the terms of the Bayh-Dole Act of 1980, the federal law that established the modern day template for commercializing academic research, universities must reinvest their licensing payments and royalties in their research programs. At Johns Hopkins, those revenues are generally allocated as follows: 35 percent to the inventor, 15 percent to the inventor’s laboratory, 15 percent to the inventor’s department, 30 percent to the inventor’s school and 5 percent to the University as a whole.

ACG, for example, has brought revenue to the Department of Health Policy and Management—where one of its primary creators, Jonathan P. Weiner, DrPH ’81, MS, is based—and to the School. Most of this revenue comes from insurance companies and public health systems in more than a dozen nations—including the Medicaid programs of 15 U.S. states and systems in Canada, Spain, Taiwan and the United Kingdom—that use ACG’s software to analyze patterns of health care delivery and costs. But Weiner emphasizes that the system is also available to academic researchers at low or no cost. “We’ve developed a huge research and development program out of this,” he says. “It’s not just about industry.”

Weiner believes he and his colleagues struck the optimal balance: They kept

**Keep in Touch**

It is exciting and fascinating to experience the way science is unfolding at such a logarithmic rate. Technological innovations inspire a sense of wonder, especially for me as they are related to my original profession as a physician.

Although many types of technology were developed and then abandoned because they didn’t really accomplish what was anticipated, other kinds related to both diagnosis and treatment have grown and expanded in the most incredible ways. For collecting data or transmitting factual information, the latest technologies are of great value to humanity.

As a child, I remember visiting my father’s family farm in Iowa, where they relied on the party line telephone for communication. At that time, we could never have imagined that human-to-human communication would achieve the speed, convenience and worldwide reach that we now have available.

However, when communication goes beyond the cognitive, when it needs to serve a purpose other than the transmission of facts, that’s when I have concerns about our growing reliance on technology. Physical touch is very, very important. It has a deeply rooted biological basis. Human-to-human touch builds relationships; it’s a crucial bonding mechanism. To put one’s hand on a patient in distress, to hug a child—that kind of emotional communication depends on our basic biology. I would be very sad if our species, with all its emphasis on and fascination with technology, lost that.

Technologies are not the creations of gods. They are simply tools we have invented to facilitate meeting our needs. If all we needed was technology, then why do politicians still reach out to shake so many hands?

Edyth Schoenrich, MD, MPH ’71, a former senior associate dean at the School, is now director of the Part-time Professional Programs and associate chair of the MPH Program.
“What kind of biomedical scientist leaves the bench and goes around scrounging up funding and planning factories? But I actually see this as a continuation of my life’s work.”

—Eddy Agbo

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the ACG venture under the Hopkins roof rather than simply selling it to an external company. “Sometimes academics start a company or sell their patent,” he says, “but then that company is gobbled up seven times over and the project all but disappears.” By keeping ACG in-house, Weiner says, his team has been able to maintain the concept’s quality through nine or 10 iterations.

Quality control has also become crucial to Charles E. Boul t, MD, MPH, MBA, a professor of Health Policy and Management, who helped to develop Guided Care, a health care delivery model aimed at improving services for older adults with multiple chronic illnesses. In the Guided Care system, a single health care worker—typically a nurse—collaborates with several physicians to coordinate each patient’s care, ensuring that their needs are met and that various providers are not duplicating care or working at cross-purposes. A randomized trial found that the system improved the quality of patients’ care and tended to reduce the use of expensive services.

For the first two years of the model’s existence, Boul t and his colleagues simply released it into the public domain, with no intention of patenting, trademarking or licensing it. Then he began to hear from federal agencies that other people around the country were claiming to use “Guided Care” in their grant applications—but drastically watered-down versions of Boul t’s original model. “They were using ratios of one nurse to 500 patients, whereas the Guided Care model calls for ratios of 1 to 55,” Boul t says. “They were basically going to erode the system’s credibility … it was a far less intensive intervention than what had been developed and tested.”

So in early 2009, Boul t and his colleagues filed a disclosure with the Hopkins tech transfer office and began to secure their intellectual property. The process was a minor headache, he says, but his problem was solved. Whenever rogue versions of Guided Care emerge, the University’s tech transfer office sends a cease-and-desist letter.

At the same time, Boul t has insisted on keeping the licensing fees low. (Depending on how many Guided Care nurses are employed, health care systems pay between $1,000 and $50,000 for a three-year license.) “This model was developed with taxpayer money, and I feel an obligation to make it available to American taxpayers,” Boul t says. “If we’re licensing it in the United States, price should not be a barrier.”

Some activists at the Bloomberg School carry that sentiment further: They believe price shouldn’t be a barrier to Hopkins-generated innovations anywhere in the world. Kaci Hickox, who completed an MPH in December, has been a member of the Hopkins chapter of the University Alliance for Essential Medicines, an international campaign to ensure that medicines and medical devices are accessible in the developing world. “When I worked in Burma with Doctors Without Borders, I saw up close how important it is for people to have access to HIV medications,” Hick ox says.

For the near term, the Hopkins chapter’s goal is to persuade the University to sign on to the Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies, which was developed by the Association of University Technology Managers. Universities that sign the statement pledge to develop licenses that “align incentives among all stakeholders to promote broad access to health-related technologies in developing countries.” Duke, Harvard, Yale and 23 other institutions have signed the pledge—but many others have not.

In response, Blakeslee says: “Hopkins is fully committed to the ideals of assuring that essential medicines are widely available.”

Across town at the University of Maryland Biopark, Eddy Agbo, PhD, DVM, reflects on his latest venture in business and life. A Nigerian-born biomedical researcher who was a research fellow at Johns Hopkins School of Medicine, Agbo leads Fyodor (the small firm that is developing Sullivan’s urine-based malaria diagnostic).

“Ten years ago, this is something I never would have imagined myself doing,” says Agbo. “What kind of biomedical scientist leaves the bench and goes around scrounging up funding and planning factories? But I actually see this as a continuation of my life’s work. The only difference is that now, there’s a very targeted goal. We’re trying to bring some products to market and bring some tangible change to society.” Agbo hopes that someday these urine-based malarial diagnostics could be packaged together with small doses of medication, so that families could diagnose themselves at home and begin treatment promptly.

It has been a long road: Sullivan and his colleagues developed their diagnostic concept nearly a decade ago. “One thing I’ve learned is that you need to be patient,” says Sullivan. For now, he is doing what he knows best and sticking to his Hopkins lab. Among other things, he and his colleagues are combing through a huge library of drugs whose safety in humans has already been established, trying to learn if they might have effectiveness against rare diseases of the developing world.

If that research bears fruit, he will file a patent application—and steel himself for another decade of patience.