



Cover, January, Healthcare, Technology

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## Debugging the Body







**The emerging ability to spot disease networks in humans - and reprogram them - will upturn the medical establishment and create new business opportunities**

If Leroy Hood is right - and, with his track record, you'd be unwise to bet against him - our current brand of medicine will change so radically in the next 10 to 15 years that all health care industries, even medical schools, will need to restructure almost every aspect of their operations. Not only will routine visits to your doctor resemble what Hood calls "Star Trek Medicine," but an array of today's most successful businesses will face a life-or-bankruptcy choice: Adapt to the needs and opportunities of the coming revolution, or blithely bet that their 20th-century ways will somehow let them ignore 21st-century developments in science, technology and diagnostics that will seem almost magical by today's treatment standards.

Hood's vision is "P4 Medicine," his term for a pioneering health care model that is Preventive, Personalized, Predictive and Participatory. Here's how this entrepreneurial scientist, who was personally lured to the Northwest by Bill Gates, and whom *Newsweek* recently named one of America's "Ten Hottest Nerds," envisions your medical checkup in 2018:

Instead of driving to your doctor's office, getting poked and prodded, answering a battery of questions and stopping by the lab afterward for a handful of blood tests or an X-ray, you'll be lounging on your living room couch. During the next commercial, you'll slide one finger into a device about the size of a cell phone. It will sample a drop of your blood, catalogue the 2,000 to 3,000 proteins suspended there, and then wirelessly transmit this protein "fingerprint" to a biotech laboratory, where sophisticated computer programs will analyze data about all of your body's organs and systems and assess their health. Both you and your physician will receive a comprehensive report via e-mail. You'll do this every six months or so.

"We'll be able to read those protein fingerprints and say, 'Your liver, your heart, your brain are

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[Leroy Hood's Bio on Wikipedia](#)  
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ADVERTISING

An advertisement for QuickBooks Payroll. It features a large "#1" in a gold box with "Small Business" next to it. Below that, "Payroll Solution" is written in green. A yellow banner in the top right corner says "\$50 OFF". A green box on the right shows the product packaging. A white button says "GET IT NOW" and below it, "60-DAY MONEY BACK GUARANTEE". At the bottom, "QuickBooks Payroll" is written in white on a green background.

just fine. But your kidney has a problem," Hood says. "I would say we would begin to see these instruments, in their early stages, in 10 years."

And this new relationship with your physician is just the beginning of the metamorphosis. "If you think about the consequences of this new medicine, I'd argue that it would change, in a very fundamental way, the business plan of every single sector of the health care industry: drug companies, insurance companies, HMOs, payers, medical instrumentation, IT health care and the like," Hood insists. "Over the next 10 years, the interesting question is: As this revolution manifests itself, how are these companies going to respond to these new kinds of opportunities? Will they be able to overcome their lumbering bureaucracies and their outmoded habits and succeed at a different game? Or will new, more agile companies seize these markets?"

If Leroy Hood were just another ivory tower academic, it might be safe to adopt a wait-and-see attitude about his sweeping, portentous predictions. But Hood, who helped create the Institute for Systems Biology in Seattle in 2000, invented the groundbreaking automated genome sequencer, a machine that made it possible to more efficiently map the unique genetic makeup of any person in the world. He helped start 14 biotechnology companies, including Amgen, now the world's largest, as well as Applied Biosystems, Systemix, Darwin and Rosetta. He is a medical doctor with a Ph.D. in biochemistry, and is one of only seven people (out of 6,000 living scientists) elected to membership in all three national academies - the National Academy of Science, the Institute of Medicine and the National Academy of Engineering.

"The guy's got a 40-year track record as a visionary," says Ed Lazowska, holder of the Bill & Melinda Gates Chair in Computer Science and Engineering at the University of Washington. "Lee's often been so far ahead of things that he garners his share of skeptics. But, so far, he's always been right."

What will it mean for business if Hood again is prophetic and P4 Medicine becomes reality as quickly as he says? It helps to first understand the four Ps. Yet to understand P4 Medicine, a look at some recent history of technology and computer science is essential.

Several developments have coalesced to propel P4 Medicine from the far-future doctoring practiced by Dr. McCoy on the Starship Enterprise into a magnet for the world's top scientific explorers. One, of course, was the invention of Hood's genome sequencer. This device, about the size of an office photocopier, made it possible to identify all 30,000 genes in each of us - genes for everything from red hair to specific kinds of breast cancer. A genome is in part an organism's complete catalogue of DNA, including all genetic material. Genes tell the organism what proteins to make - and these proteins perform most of life's functions and make up the majority of cellular structures.

New technologies that improve medical imaging procedures also are significant elements of P4 Medicine's coalescence, because these allow scientists to study "disease perturbations" at the cellular level. The evolution of biology from the practice of chasing butterflies with a net into an information science is crucial, as is the marriage of computer science with this new biology, a collaboration unimaginable half a century ago.

In 1962, James Watson and Francis Crick won the Nobel Prize for their description of DNA's double helix structure, a feat often called the most important biological discovery of the last 100 years. However, "Lee Hood has always said the big discovery of Watson and Crick is not the biochemical structure of DNA, but rather that the genome is a digital code," says Lazowska. "The fact that the genome is exactly like a computer code is very powerful. The power of biotechnology is that you can read and modify and rewrite that genetic code."

Indeed, the vast power of computers obtains from the ways zeros and ones get combined. Similarly, Lazowska explains, each digit in your genome has four possible values, represented by the letters A, C, G and T. "That's no different from having a computer code in which each digit is either written in zeros or ones."

In short, Hood's new health care digitizes medicine. By melding biology and computer science,

then improving computational methods that will allow your physician's laboratory to compare the protein fingerprint in your drop of blood with that of thousands of healthy people, physicians will not only discover illnesses at earlier stages but also determine the diseases to which you are susceptible - then intervene with therapies, drugs or lifestyle changes before you become sick. And someday, instead of sending you to the neurosurgeon for a messy craniotomy, your doctor may prescribe a computer code, so a pharmacist with a digital formulary can simply reprogram your genes to eliminate that brain tumor before it appears, or at least reduce its likelihood.

P4 MEDICINE IS SCIENCE FICTION FOR REAL. P4 IS ...

**Preventive:** Way beyond eating healthy food, getting exercise and quitting cigarettes. As P4 Medicine evolves, Hood says, it may well be able to create drugs that thwart or curtail cancer, alcoholism, diabetes or whatever else might eventually ail you. "So, say you're a woman that has an 80 percent chance of ovarian cancer by the time you're 60, but if you start taking these drugs when you're 40, that chance will reduce to 2 percent. That's what we mean," Hood says, "by preventive medicine."

**Personalized:** Now, when you get sick, you take off-the-shelf drugs or undergo therapies that have been reasonably proven on millions of others with similar health problems. You hope what's worked for them will help you as well. However, with P4 Medicine the promise is custom treatments, the opposite of a one-size-fits-all approach.

Because your doctor will have a detailed analysis of the proteins in your blood, which will be different from those of nearly everyone else in the world, tomorrow's pharmacists will use your individualized profile to design drugs precisely for your illness, with doses tailored to the severity of disease, your health history and also what your proteins indicate about future health challenges. By calibrating dosages to individual needs and tolerances, personalized therapies should be more effective, reduce drug side effects and perhaps lower costs.

In fact, medicine already is moving in this direction, developing medicines targeted at smaller populations. Scientists are identifying an increasing number of molecules that act as "biomarkers" for disease. For example, researchers at the University of Cincinnati have identified osteopontin-c as a reliable predictor of breast cancer. A device that can identify many such biomarkers from a single drop of blood is already close to development. But it has taken a visionary such as Hood to connect the dots, to see how and why these trends paint our future's health care picture.

**Predictive:** "In the history of medicine, we've been reacting to diseases," explains Dr. Joseph Gifford, senior medical director for Regence Blue Shield. "We learn of things *after* your heart artery is blocked, *after* your tumor is big, *after* you've got a big infection and a high fever. That's been the history of 20th century medicine." P4 Medicine, he says, will stand this on its head.

In the coming era, inexpensive genetic tests for multiple diseases, enhanced imaging technologies and proteomics - the study of proteins in your blood - will permit physicians to predict with accuracy all the diseases likely to kill or disable you. "We'll find diseases much more quickly," Gifford says, "before they get to be 'bad.' And we'll predict future disease states much sooner than we do now."

In the future, Gifford says, everyone will have a "future health record" that will list the probable risks to your life. P4 Medicine promises to identify the diseases programmed to harm you and help you defend against these with therapies and behavior modifications, or turn off the menacing genes so risks are reduced or eliminated.

**Participatory:** All of us will have our individual genomes mapped. Because of this, Hood says, "We'll know from our genome which particular diseases we're susceptible to. I really feel the role of the patient will be transformed by this new medicine. They'll be able to understand much of the information that comes to them, and they'll be able to help make more informed decisions about their own health care. This will change, in fundamental ways, the doctor-patient relationship."

YOU SAY YOU WANT A REVOLUTION? FOR P4 MEDICINE TO SPREAD WIDELY, HERE'S WHAT MUST

HAPPEN:

- Science must develop and refine new measurement technologies that can study thousands of blood proteins from extremely small amounts of material. Hood expects researchers to reach this goal within five years.

-Within five years, what Hood calls "nextgen" gene sequencing could well be in place, and it would allow for small but important segments of an individual's genome (about 1 percent) to be sequenced quickly for about \$1,000. He says the information gleaned in this process will be "clinically relevant" to the patient's medical care. And in 10 years, as the science evolves, Hood expects the cost of sequencing an entire genome to drop to an almost-affordable \$10,000.

- Simultaneously, new computational and mathematical techniques for handling massive amounts of data must also evolve quickly. Lazowska says techniques, known as data mining and machine learning (an automated way to discover facts from data, perhaps even machines that "think" on their own), are the keys to determining which aspects of your genome make you susceptible to illnesses.

- Once these elements are in place, those who would implement P4 models will need to study large segments of healthy populations and create baselines of healthy protein fingerprints. Then, by comparing your fingerprint with these normal models, doctors will be able to tell if your protein fingerprint indicates good health or specific diseases.

And then things get complicated. Both the pharmaceutical and insurance industries illustrate the kinds of problems businesses must cope with to succeed in the P4 paradigm.

"What I know is that the entire pharma model is built upon the idea that you want to develop one drug that is taken by lots of patients and, hopefully, chronically," says Carl Weissman, president and CEO of Accellerator Corp, a Seattle laboratory nurturing biotech start-up companies funded by venture capital. "This is why Lipitor is the biggest selling drug in the world. It doesn't cure anything, and people take it continually (26 million users, according to Pfizer's website).

"What personalized medicine is about is finding one drug that will cure one person, or just a small subset of people," Weissman points out. "So, it's an enormous problem, logistically, for the pharmaceutical companies to go from treating hundreds of thousands of patients to hundreds of patients. It's particularly difficult for the pharma companies to imagine, because it runs against their entire model."

Hood says the drug companies are spending more and more money and getting fewer drugs. "This new medicine offers completely new strategies, new ways for these companies to develop drugs," he says. "Will a drug company be able to adapt? Or will they sink into oblivion, pursuing drug discovery as they have done it in the past?" His hunch is that many won't succeed.

Health insurers face a similar challenge with a business model at odds with P4 Medicine's promise. "Preventive medicine is dramatically different than therapeutics medicine," explains David Galas, vice president and chief science officer for Biology and Life Sciences for Battelle Memorial Institute in Columbus, Ohio. He is also a faculty member at Hood's Institute for Systems Biology. He points out that insurance companies base their business on paying claims to people who are ill and need drugs or services. "So how do we provide health care services for people that are apparently healthy?" It will require new insurance models.

It also poses a serious privacy issue: What happens if your insurance company gets hold of your genome and decides to determine premiums or coverage based on your genetic flaws? The U.S. House of Representatives passed the Genetic Information Nondiscrimination Act of 2007, which, if passed by the Senate, would prohibit insurers and employers from discriminating on the basis of genetic information. But the possibilities for abuse are vast, which could make people wary of genetic testing and negate the benefits of P4 Medicine.

Putting aside these problems, Hood believes the new medicine will lower medical costs. "I think

that these technologies we're developing are going to lead to a digitalization in medicine - just like the digitalization in the communications industries and information technology industries. And this will decrease the costs in health care, just like it did in these other industries. That's the analogy," he says. "Medicine is going to go the same way."

Hood points out that early diagnosis of disease saves money, "and, ultimately, prevention will make things even less expensive." He believes P4 Medicine also should make the discovery of drugs less costly.

"At some point in the future there will be a stunning turnaround in the inflection point of ever-escalating costs of health care," Hood says. "And I think it will decrease to the point where we can export P4 Medicine to underdeveloped nations."

Yet Gifford isn't so sure. "This is a very complicated question," he says, explaining that healthier people, of course, will incur fewer costs, and that physicians, armed with their patients' genomic profiles, will be able to pinpoint those patients who will actually benefit from expensive, cutting-edge drugs. Doctors won't write pricey prescriptions for patients who lack the right genes to benefit, and this should save millions of dollars annually.

"But then there's the counterargument: In the history of medicine there has never been a new technology that has reduced costs," Gifford points out. "And, if we all live to be 100, society will be providing health care to a lot of people for a lot of years," another expensive side effect of improved medical care.

How quickly P4 Medicine actually becomes reality in your doctor's office will depend, Hood believes, on how much society is willing to contribute. "Right now, the billions spent on the Iraq War and the revenue lost to tax cuts has seriously curtailed funds for medical science and research. Relatively speaking, funding for medical science is at the lowest levels it's been at for a long, long time," Hood warns. "I don't see the money for doing this medicine coming from the government."

His prescription: an array of strategic partnerships to develop the necessary technological expertise - with universities, businesses, national laboratories and international collaborators. "What these partnerships must do is integrate all of these emerging technologies and computational tools around this focus of P4 Medicine," he says.

The Institute for Systems Biology already has begun exploring a P4 Medicine industrial consortium, attempting to persuade one company from each major sector of the health care industry to work with ISB on the multiple transformations that, ultimately, will remake medicine as well as these collaborators' business plans.

Partnerships and collaboration make sense because the problems and technological needs are simply too complex for individual scientists to go it alone. Financially, it seems smarter to share the risks. Hood says the key for business leaders seeking opportunities in the milieu of new medicine is more about collaboration than competition: "How can you become a part of the strategic partnerships that are going to catalyze these kinds of transformations?"

At the same time, he is eyeing international alliances because "when you create an international strategic partner, you open up completely new avenues of fundraising that don't exist at all when you stay within the boundaries of the continental United States. I'd like to see Seattle play a leading-edge role in catalyzing these international strategic partnerships," he emphasizes. "We're certainly poised to do so with Asia, and I've actually explored these with almost all the nations in Asia. I think there is an enormous enthusiasm there, and I think it's all very exciting."

And so, is Leroy Hood right again? Will *Star Trek* medicine remake the health care industry?

Place your bets. And quickly.

Those strategic partnerships already are coalescing.

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