



20 Ideas That Will Rule Research in the Next 20 Years

On the edge of a brave new world.

By Matt Mahurin

As we head into the 21st century, knowledge is being created— and disseminated— far, far faster than ever before. Given this wealth of discovery, we invited some scientists to predict what questions or ethical issues will dominate their fields over the next 20 years. Their replies express not only excitement at the pace of discovery but also a broad concern about the use of new technologies and scientific information. Many noted the impact of the Human Genome Project— and the ethical problems that will attend screening patients' DNA for information about genetic vulnerabilities. Others remarked upon the parallel explosion of information— or, more precisely, surveillance— in cyberspace and how it, too, threatens individual privacy.

The business of science, so to speak, is knowledge. And knowledge is power. Deciding how to handle these new forms of knowledge will be just as important as— and probably far more problematic than— creating the knowledge itself.

Francis S. Collins, geneticist, director of the Human Genome Project

With the sequence of the human genome largely determined, laboratory research of human diseases will shift as researchers adopt a "genome attitude" toward solving problems. First, there will be increased emphasis on a systems approach.

Researchers will examine the integrated functions among many genes, gain insight into the web of coordinated interactions among cellular pathways, and determine the impact of external factors. The number of potential therapeutic targets will increase dramatically as a consequence.

Second, there will be a heavy emphasis on determining the hereditary contributions to common diseases. Among the insights with the greatest immediate consequence will be an understanding of individual variability in response to drugs.

Third, our increasing ability to predict the structure of proteins will accelerate our understanding of how individual proteins work and interact with other proteins

and/or DNA elements. This will also contribute to more rapid identification of potential therapeutic agents.

Fourth, human genetic and genomic research will become significantly more computational in approach. *In silico* will replace *in vitro* or even *in vivo* for many experiments.

Fifth, the debate about the ethical, legal, and social consequences of research in human genetics will intensify. While it is hoped that legislative solutions to the problems of genetic discrimination and breaches of privacy will be implemented in many countries, the challenge of educating health care providers to be practitioners of this new brand of genetic medicine will be considerable. Furious debates, not all of them grounded in the scientific facts, will rage about the limits of genetic intervention of our own species. To traverse these troubled waters successfully, we will need full and informed engagement by a diverse group of potential stakeholders.

Antonio Damasio, neuroscientist, University of Iowa College of Medicine

The near future of fundamental neuroscience will be dominated by the problem of consciousness. Curiously, the part of the problem that most thinkers consider difficult, perhaps impossible, to tackle is likely to be elucidated relatively soon. This is the problem of the self, which has to do with how the brain lets us know of our existence as individuals and of the amazing fact that each of us has a private mind that belongs to us and to no one else. But there is another part of the consciousness problem, the part that I describe in my book *The Feeling of What Happens*, as "the movie in the brain." A lot is already known about the molecules, neurons, and circuits with which the brain constructs the sensory patterns necessary to make a movie in the brain. Yet there is a gap in our understanding of how those sensory patterns, which do occur in well-specified circuits of this or that brain region, even become mental images. The challenge is to fill this gap.

But the developments in clinical neuroscience will be no less important. The remarkable success in identifying the genetic basis of single gene disorders, such as Huntington's disease, and in identifying the many genes that make individuals vulnerable to such disorders as Alzheimer's disease, suggests that the genetic contribution to several devastating neurological conditions will be discovered in just a few years. If neuroscience does its job properly, it will be possible to discover, for example, how the abnormal protein produced by a sick gene can lead to the death of nerve cells, thus opening a new universe of treatment possibilities before our eyes. We will be able to screen our own genome in the early part of our lives, and we will be able, by taking appropriate medications, to prevent the damage that a sick gene will cause, or repair it rapidly. However, this optimistic scenario is not without pitfalls. It will be argued that having one's genetic screening

made public could limit the choice of a career, preclude certain forms of employment, and make one uninsurable or perhaps insurable only at prohibitive cost. These dire scenarios can be preempted only by the development of effective treatments, much compassion, intense social awareness, and protective laws.

Ron Graham, professor of computer and information science, University of California at San Diego

It seems very likely that mathematics will become an increasingly essential component of almost all of the emerging sciences. These will range from physics (string theory and the subatomic "zoo"), biology (understanding the human genome and predicting protein folding), computing (creating effective Internet algorithms and guaranteeing security and privacy), chemistry (designing innovative methods for constructing new compounds), and economics (predicting the complex dynamics of the world economy), to name a few. As any science matures, its methods inevitably become more quantitative. So mathematics, as the language of science, is ideally suited for a deeper understanding of the science.

Bernardo Huberman, theoretical physicist, Xerox Parc, Palo Alto, California

One trend I see having a sizable impact will be our ability to access all kinds of information on a global scale, including genetic and private records of individuals. But we will also create legal and ethical problems around such access. Issues of privacy, ownership, and rights to information will become central to people all over the world, thus leading to the creation of novel mechanisms and international institutions. Twenty years ago, I thought that the most important trends would revolve around nonlinear dynamics and the increased sophistication of computers. But I did not envision the cheap global connectivity that the Internet would bring.

Mary-Claire King, professor of medicine and genetics, University of Washington

I think we will explore what it means to be human in new ways. How are we different from our closest relatives? What defines us as a species? What is the genetic basis of our definitive traits? At the genomic level, the answers will be learnable and probably ultimately pretty straightforward. But their philosophical meaning will be immense. Biologists and humanists will need to learn to talk together in ways we have only just begun to develop. I am glad I will still be working on these questions in 20 years.

Steven Pinker, professor of cognitive neuroscience, Massachusetts Institute of Technology

The biologist E. O. Wilson suggested a useful word for a trend in the human sciences that will accelerate in the next two decades: consilience, the unification of knowledge. The natural sciences will blend into the social sciences and humanities via an understanding of human nature provided by bridging disciplines, such as

cognitive neuroscience, evolutionary psychology, and behavioral genetics. This will stand in stark contrast to the two-cultures view in which biology and culture are sealed in parallel universes and it is politically dangerous for one to impinge on the other.

The humanities will be freed from sterile postmodernism and social determinism and be seen as being about products of human minds; they will thereby benefit from insights about perception, cognition, and emotion. Politics and history will be enriched by an understanding of the psychological roots of human aggression, cooperation, coalition formation, and conflict resolution, rather than invoking unanalyzed "social forces." Law will replace its folk theories of free will, deterrence, and "the reasonable person" with ones compatible with neuroscience, genetics, and evolution. Likewise, economics will augment its folk theory of "economic man" with research about human reasoning, decision-making, and passion.

Medicine will transcend its craftsman's understanding of disease and place itself on a theoretical foundation from evolutionary biology. Education will start with a better understanding of which skills develop instinctively in children and which require intensive instruction and hard work. These changes will not be unopposed. Professional insularity, lazy political arguments, and the ancient doctrine that the mind is a blank slate will slow them down. But the gains in insight will be too great to halt them for long.

Lee Smolin, professor of physics, Pennsylvania State University

During the next 20 years a revolution in physics that has been in progress since Einstein overthrew Newtonian physics will culminate in a new physical theory. It will combine all we have learned in the last century about relativity, quantum theory, elementary particle physics, and cosmology. The remainder of the time will be spent working out its implications. Dramatic progress in observational cosmology and experimental physics will also give rise to tests of the new theory. Then physicists and cosmologists will be able to attack questions on which progress was not previously possible, such as what happened before the Big Bang and why the universe is hospitable to life. The next 20 years also will be remembered as the time that real progress began to be made resolving the great problems of origins: the origin of life, the origin of galaxies, the origin of the human species, the origin of language and human social organization.

On the ethical side, the rapid growth of new opportunities outside the universities for people with scientific training will sooner or later give rise to a long overdue reform of the university system. Universities are among the most bureaucratic institutions in society; they will have to reform to compete for talent. The important

ethical question is the extent to which these reforms can be managed to foster the main values of the university: teaching, research, and scholarship. The question will be how to protect and foster these necessarily labor-intensive and fragile activities within new organizational structures that will resemble much more the horizontal structures of small technical companies than they do the present rigid and hierarchical university system.

Christopher Wills, professor of biology, University of California AT San Diego

Twenty years ago the Human Genome Project was not even a gleam in anybody's eye. Today the project is virtually complete. Much has been written about the project's impact on understanding cancer and aging and on the possibility of finding genes for intelligence and behavior. But another aspect of the project may be the most important of all. Our population is exploding, leading to widespread environmental damage, wars over shrinking resources, and famines. Our ability to take control over our reproduction has not kept pace with the problem. Condoms, the most widely used device for preventing conception, were employed by the ancient Egyptians in 1000 B.C. The Pill is a crude manipulation of female hormone levels that can have undesirable side effects.

Now, thanks to the Human Genome Project, we have the sequences of all the genes involved in human reproduction. This includes all the genes involved in the production of sperm, all the genes that govern the environment inside the uterus, all the genes involved in ovulation and implantation, and all the genes that code for neuropeptides and other hormones that influence sexual behavior. We do not yet know how most of these genes work, but the opportunities for finding cheap, safe, effective, and reversible ways to prevent conception are boundless. Let's find them before the next 20 years are up.