Visions of the Future

A Day in the Life of a Scientist

Earlier this year *Science* asked readers to imagine what life would be like in the year 2050. Here, we present the final December installment of these fictional essays.

Address to the AAAS

by EDWARD McSWEEGAN

Thank you for the opportunity to address this session of the midcentury meeting of the American Association for the Advancement of Science. I regret not being able to attend this exciting gathering in person. I hope, however, that my digital persona is sufficiently imposing to hold your attention for the next few minutes. Certainly, this "virtual me" is more lively than the ancient, antiquated scientist who has been allowed to reminisce—or ramble—about the present state of science and his own life in science.

It is entirely appropriate that I attend this session in virtual form as so much of science and scientific gatherings has become virtual in nature. This is what many writers and futurists in the 20th century imagined would one day happen. Well, that day has come. Most of the younger members of today's AAAS have built their scientific careers within the computerized, networked Interspace that now exists between the messy physical world and the still-isolated mental world of the individual.

What began in the 20th century as the World Wide Web has today become the vast collection of intelligent databases and high-speed neural networks that support research through real-time simulation and modeling. Experiments in synthetic genetics, metabolic pathway redesign, pharmacokinetics, plasma engineering, urban ecology, artificial cell design, and multiuniverse cosmology are done routinely in virtual reality. Even clinical trials—nearly driven to extinction by their real-world complexity, billion-dollar costs, and decade-long life-spans—have been saved by our ability to simulate and model such complex phenomena as drug-drug interactions and pharmacogenomics. It is not yet true that "a hands-on experiment is a bad experiment," but that day is probably drawing closer as the size and power of Interspace continues to grow.

I know many of you have never seen the inside of a working laboratory, have never held a test tube, have never poured a gel, have never stayed up all night trying to clone a new gene. Many of you, in fact, disdain the "wet work" of research. But it is still the old-fashioned, hands-on bench work that validates in the physical world that which has been imagined and constructed in the virtual world.

It is likely, therefore, that the many commercial and academic contract labs we relied on, or work in, will continue to exist as critical adjuncts to virtual research. I hope so. I have found it refreshing to move between virtual research and actual hands-on experiments and demonstrations. It reassures me to know that I can do the work that I can imagine. It is, for me, a way of finding personal and professional validation in a world grown richer and more productive, yet somehow less tangible.

As I said, the university and private contract labs are the source of scientific validation. They are also important sources of employment and technical training for people wanting to do some science. And, of course, so much of our federal and foundation grant money goes to them in order to provide the real-world data, the working prototype, and the technical certification we all occasionally need to acquire. At the end of the last century, the size of the average National Institutes of Health grant was 100 times what it is today. Most of that early grant money went to pay for individual salaries and expensive laboratory equipment. Fifty years ago, there were huge research grants but not enough of them to go around. Fortunately, the concomitant rise of virtual research and robotic contract labs ended that trend. Today, a typical NIH investigator grant pays the meager costs of accessing on-line instrumentation and databases, and the occasional contract assistance of a robotic research facility. For someone as old as I am, it is startling to realize that the National Science Foundation budget now exceeds the NIH budget—partly because of the rise of on-line biomedical research and partly because of the cost of NSF's lunar- and Mars-based instrumentation.

As I mentioned, a large part of yesteryear's NIH grant money went to pay investigator salaries. But with the disappearance of so many independent academic depart-

ILLUSTRATION BY ADAM MCCAULEY

ments and research centers, the duplication of equipment and supply purchases ended. Tenure-track professor slots have also disappeared, and tenure is fast becoming a forgotten word. At my university, my old department is gone. The dorms are increasingly empty of campus-dwelling undergraduates. There are few freestanding degree programs still intact, and even fewer of the lengthy postgraduate, degree-granting programs I was nurtured in. The once-common university departments and schools are quickly giving way to the 2- and 3-year core programs in liberal arts, engineering, life sciences, etc. These, in turn, are feeding more and more students—of all ages and backgrounds—into a constantly changing number of technical and professional certification programs. This is perhaps the greatest change in the culture of science within my lifetime. I have lived to witness the decline of my own class—the professional, degreed scientist—and the rise of the amateur: the curious, interconnected, data-mining amateur.

The British coined the word "scientist" in 1833, and it seems to me that after little more than two centuries the word is likely to be replaced by a phrase that gave rise to it in the first place: "people of science." No longer is science the mysterious ritual of a singular class of professionals. It has been democratized. Inexpensive and powerful computers, interactive databases and simulators—all linked through Interspace—give everyone access to information and allow everyone to ask questions, test theories, and formulate new answers. The late technology editor Kevin Kelly—whose digital image, I am told, can still be seen late at night wandering the halls of the media lab at the Massachusetts Institute of Technology—called this nonprofessional, technology-driven science "nerd science." A less-than-dignified characterization, perhaps, but one that conveys the role of powerful technologies and nondegreed intelligence in shaping what we all still recognize as science—that is, the mixing of data and theory to generate new knowledge and new tools.

The academic and scientific mandarins balked at this loss of professional status. After all, what was the value of a Ph.D. if someone could take a few training courses, log on, and then start working on the same problems you were interested in? I have three old-fashioned university degrees, and I must confess to having taken a similar "attitude" with some of these amateur upstarts. Fortunately, that did not last too long. In an effort to keep up with my own field, I was forced to use new tools, to learn new techniques, and to take the advice and expertise of whoever had any to offer.

I remember the first distance-based learning program I enrolled in for certification: a postgraduate diploma in epidemiology from the London School of Hygiene and Tropical Medicine. I needed to learn some epidemiology, and I could not very well put aside family and work to go back to school full-time. The London school's early efforts at distance-based learning and certification were critical to my career. Since that first experiment in virtual study, I have taken certifications in biofilm engineering, clinical trials designs, virtual metabolism, and genomic vaccinology, to name a few. Those training certificates have come to mean more to me than my antiquated Ph.D. or my expensive, four-year bachelor's degree.

In some ways, today's practitioners of science have become like Thomas Edison. Edison loved to tinker and to build things, but he also knew he did not know everything. Occasionally, he would cross the Hudson River to Cooper Union where he would sit through classes on the latest theories and developments in chemistry and electricity. We do much the same today, although the commuting to classes usually takes place in the virtual environments of Interspace.

Has this decline in the status and numbers of professional, degreed scientists degraded the quality of scientific research and the scientific literature? Apparently not, judging from the real and virtual attendance at this meeting. More people than ever are engaged—either full-time or occasionally—in scientific pursuits. This is easily measured by examining access rates to on-line instrumentation, databases, artificial intelligence servers, and technical libraries. And, of course, by the number of grant applications submitted to the NSF, National Aeronautics and Space Administration, Department of Energy, NIH and other agencies for *in silico* research. More grants are going to more people to ask more questions about the world around them.

Nor has the quality of scientific literature suffered—although it is clearly very different from the "Dark Ages" literature I read as a graduate student. The decline of tenure-seeking professionals and the move to rapid electronic publishing killed off the static, stand-alone, hard-copy journal article. At the end of the last century, a European journal editor confessed that "80 to 90% of what is published is of little interest." The incentive to pump up one's résumé with forgettable publications is gone now. In the past, it was hard to measure the quality of a person's ideas or to appreciate the true impact of a particular publication. As a consequence, tenure committees and employers took to simply counting the number of published works to determine professional advancement.

ILLUSTRATION BY ADAM MCCAULEY

But numbers alone can be deceiving. Not so now. When a piece of work is posted to the Interspace BioMed database, reader hits are instantly registered. Additions and corrections are made to it by readers and by the authors, so that the work, in effect, becomes a dynamic document undergoing constant modifications. The database tracks the changes and graphs the subsequent publications that the original publication spawns. These branching publications give rise to other publications, and a three-dimensional representation of one's published "branch density" gives a visual measure of the interest and impact of one's work. My personal digital cyberarian regularly assures me that my own branch densities are as respectable as those of my elderly peers.

So science has survived and thrived. It is different now. Its practitioners are different. It is cheaper, faster, and more open to more people. It has become a dynamic enterprise linking the physical world, the virtual world, and the world of human imagination in ways that were only dimly perceived at the end of the last century.

Now at midcentury, we are faced with the rise of powerful artificial intelligence systems. These systems not only make possible much of our speculative scientific work, but some are beginning to formulate hypotheses of their own. The next 50 years for science and for the AAAS are likely to be spent making room within *in silico* research for *in silico* researchers. I happily leave that emotional and evolutionary challenge to you.

Thank you and good afternoon.

The author, a Maryland-based microbiologist who has abandoned the lab for the Internet, wonders whether H. G. Wells was right in asserting that "we are inclined to underestimate the certainties of the future." E. McSweegan, 1692 Barrister Court, Crofton, MD 21114-2602, USA. E-mail: edwardmc@qis.net

This essay is a work of fiction. Names, characters, places, and incidents either are the product of the author's imagination or are used fictitiously. Any resemblance to actual persons, living or dead, events, or locales is entirely coincidental.

Traditional and Cybernetic Sciences Combine to Combat Human Viruses

by CAURNEL MORGAN

Two researchers from different laboratories, with different scientific approaches, and from different eras are trying to demonstrate the strength of diversity in combating human disease.

Robert Jackson is a 108-year-old scientist with an M.D. in psychiatry and a Ph.D. in virology from the American Mental Health Research Institute (AMHRI). Dara Olu, of the American Biological Research Institute (ABRI), is a 23-year-old who has earned a Ph.D. in the emerging field of pixel biology from the ABRI, with an area of specialization in pixel genomics. She also has degrees in business and politics. Whereas Jackson runs a traditional brick-and-mortar laboratory at the AMHRI, Olu directs her independent laboratory in cyberspace. Together, Drs. Jackson and Olu head a team of scientists that is applying a novel approach to the treatment of viral infections.

A number of viruses have been successful in attacking humans because of their capacity for rapid mutation. The eradication of viruses that caused certain cancers, acquired immunodeficiency syndrome (AIDS), and other diseases were complicated by the viruses' ability to mutate in a relatively brief period of time after infecting humans. In the 20th century, the standard approach to studying human viruses was to isolate a viral culprit after an epidemic had occurred. When this approach was used, some viruses were well on the way to their second or third generation of mutations before effective therapeutics could be designed. However, the fight against viral infections was dramatically altered from the last decade of the 20th century into the first two decades of the 21st century. During this period, a number of DNA analogs with nonphosphodiester backbones were developed. These various forms of engineered nucleic acid (ENA) were used very effectively as antiviral agents (Jackson 2013).

Dr. Jackson pioneered the use of ENA antiviral technology. A number of DNA derivatives were designed in which the phosphodiester linkage has been replaced but the deoxyribose retained. However, only a few of these appear to be good structural DNA mimics. The first two successful attempts to replace the entire deoxyribose phosphate backbone resulted in morpholino derivatives and the polyamide nucleic acid (PNA), which contains a pseudopeptide backbone (for review, see Jackson 2007). These designs determined that the deoxyribose backbone is not essential for DNA mimics. ENAs have been demonstrated to form double and triple helices with themselves and natural nucleic acids (that is, DNA and RNA). The antiviral property lies in the ability of the ENA to bind to viral nucleic acid in a sequence-specific manner. This approach permitted Jackson and other virologists to target mutant forms of viruses as soon as their nucleic acid sequences could be determined (Jackson 2009).

Today, a large variety of engineered nucleic acid (ENA) is used to form sequence-specific double and triple helices with viral nucleic acid. Once formed, these complexes can halt the ability of the viral genes to serve as templates that direct the host cells to make viral proteins. One obstacle to applying ENA as an antiviral agent in vivo is that ENA entry into host cells typically occurs at a slow rate under normal conditions. However, the inclusion of a nuclear localization sequence (NLS) can dramatically increase the rate of sequence-specific ENA entry into cell nuclei. NLS-mediated ENA uptake occurs several times more efficiently than with ENA alone. Additionally, destruction of the