Future of Chemistry

Assumptions: Taking Chemistry in New Directions**

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"*When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong.*"
Arthur C. Clarke

The Temptations and Hazards of Predicting the Future

Speculating about the future of science seems to be genetically encoded in scientists. We all do it. We also take it as an article of faith that serious predictions are almost always wrong. Is thinking about the future an important thing to do, or just a diversion—like daydreaming, or gardening, or playing the lottery? Why do we spend our time guessing about matters we believe we cannot predict?

There are at least five reasons. The first is utilitarian: to plan our work. Thinking about the future is a part of choosing research problems. We who make our living in science tell ourselves that we work for the satisfaction of solving problems and for the thrill of discovery; sociologists, less charitably, suggest that we do so to make a living and to get ahead professionally. The truth is probably a mixture of the two. Finding good problems—problems that polish a new facet of reality and that change the way some part of the world works—is both satisfying intellectually and rewarding professionally.

The second reason is to feed our curiosity. We wonder about the world of the future. What neat widgets will make *that* world run? Which of our fantasies will grow into our grandchildren's realities?

The third is philosophical. Science and technology are major elements of the culture of our times. They, probably more than other elements (materialism, religious fundamentalism, capitalism, ...), will change the nature of individuals and of society. We wonder: What will the *big* changes be? How will science be involved?

The fourth is that society *expects* us to speculate. We are part of its early warning system for change.

The fifth is to answer an uncomfortable question: "Is there research that we should *not* do?" We scientists generally cohabit quite comfortably with an amoral curiosity. We should ask if there is research we can do now—research that is technically feasible and scientifically interesting—that we should forgo because it is ethically problematic. Are there questions we don't want to ask, because there are *no* circumstances in which we might want to know the answers?

The objective of science is to make a difference.

Science is a Mixture of the Ordinary and the Extraordinary

Surprises: Is the future of science really so unpredictable? The answer is both "no" and "yes". Science is a mixture of a lot of the relatively predictable "ordinary", and a little of the quite unpredictable "extraordinary". The part of science that is ordinary and business-as-usual—useful, important, familiar science—can often be extrapolated into the future with fair accuracy. It is the *extraordinary* science—the *surprises*—that we cannot predict, and it is this science that gives speculation about the future its well-deserved bad reputation. It is also the surprises that make science so intensely interesting, and that have the power, for better or worse, to turn the lives of our grandchildren upside down.

One of the many charms of science is that it provides an endless string of surprises. Some surprises grow slowly and incrementally, while some come, apparently, out of the blue. Each of us can make two lists of surprises: one of personal favorites, and one of surprises that have remade the world. These two lists are usually rather different. We have a particular affection for what we know, and find small quirks in familiar science endearing. Appreciation for big discoveries in unfamiliar fields requires more effort.

Since I am a chemist, I was immediately delighted—in fact, ecstatic—to learn that XeF_4 is a stable compound; because I knew less about biology, it took me years to assimilate the discovery of apoptosis, and to begin to appreciate how the cell chooses between life and death. Not all surprises are equal: xenon tetrafluoride clarified the chemical bond for chemists; apoptosis changed the understanding of "life" for all of science.

One unstated objective of science is to *make a difference*: to learn something,

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or make something, that changes the way people think or behave. Many of the biggest discoveries—the most important scientifically, and the most consequential socially—are surprises, and their consequences are unimaginable at the time they are made. Who would have predicted the changes in society that have come from classification of the elements into the periodic table, or from quantum mechanics, or the world wide web? Who could have guessed that the first NMR spectrum of ethanol would grow into the ability to watch the brain think?

The unpredictability of these big surprises makes us timid in our speculations: it is embarrassing to be publicly wrong, and big surprises make dunces of us all. But, avoiding speculation makes science dreary, and neglects our responsibility to society to warn of change, even as we cause it.

Picking Assumptions, Not Making Predictions

In speculating about the future, we—scientists and nonscientists—are really interested in knowing what the science and technology will be that will make a *big* difference, and in knowing whether that difference will be good, or bad, or both, or a matter of context, or circumstance, or personal opinion.

The process of starting with current science, extrapolating it into the future, and then guessing how society will use or abuse this future science is so uncertain it will probably fail. I suggest that a different and perhaps more direct approach to identifying where science might reshape society is to start by identifying areas where change would *matter*, and then ask if *imaginable* science might cause this change.

How are we to identify areas where society is vulnerable to change? Or where the push of a new idea or a new technology might topple established institutions? I propose that we begin by identifying the *assumptions* that our society makes, and then ask about the vulnerability of these assumptions in the face of plausible science.

An *assumption* is an idea that is taken for granted: it tacitly separates the imaginable from the unimaginable. If an assumption is vulnerable, then the probability that it will eventually fracture—for better or worse—under the blows of science is very high. Let me give an example. We assume, as an article of faith—a deeply held assumption—that we are the most intelligent entities on the planet. We would certainly be disconcerted to discover that science and technology had generated an entity more intelligent than we: a peer competitor (or perhaps a peer partner, although, as a species, we have never been good at "sharing"). How probable, technically, is it that science will do so? The answer to this question depends on whether you believe that intelligence is an oddity characteristic of highly evolved living organisms (humans, porpoises, whales, chimpanzees), or whether it is inevitable in (or perhaps can be engineered into) any information-processing system of sufficient complexity. So, will information science produce intelligent machines? (… and what is "intelligence" in a machine, anyway?) I don't know, but I (and others more knowledgeable than I) also don't know that it is impossible. Hence it is an area that we, and society, should watch carefully.

Society changes when it discards a major assumption.

Where, in the past, has science dissolved important assumptions with profound consequences for society? Failed assumptions are easy to identify in hindsight: they are the facts of daily life that we now accept as routine, but that would, at some earlier time, have provoked a reaction of "impossible!" If one had asked Frederick the Great or Sun Tsu if it would ever be possible utterly to destroy a city on the other side of the globe in a single stroke, their answer would have been "No!" They, and their societies, assumed this limitation to the art of war. We now accept as unremarkable a world in which science and technology—born as quantum mechanics and grown to be nuclear-tipped intercontinental ballistic missiles (ICBMs; or perhaps just a rental truck containing an amateur's fully functional fission bomb)—make this single stroke distressingly possible. The failure of this assumption has changed society.

We have discarded many other assumptions, with consequences both good and bad. At one time, knowledge could be passed on only through speech: the written word and moveable type gave our society a long-term memory. At one time it was impossible to talk to or to see others over long distances; the telephone, radio, TV, and the web are now among the threads that hold society together. Controlling human fertility fundamentally changed the relation of women to society. Society changes when it discards a major assumption.

Thinking about assumptions and working backward is not necessarily less fallible than thinking about science and working forwards, but it tends to focus more on big societal problems and less on small technological evolutions. Concentrating on assumptions might, therefore, provide better advance warning about issues that the scientific community (and society) should consider carefully than extrapolating from existing science. It would also accomplish four other ends. It would: 1) show that the dreary intellectual senescence suggested by John Horgan's stimulating book "The End of Science" is wrong-headed; 2) identify directions where science would unquestionably have large impact; 3) indicate especially interesting problems on which scientists might work; and 4) suggest new ways of doing business: big problems do not have disciplinary boundaries—academic departments do.

In what follows, I list nine assumptions that, I believe, are fundamental to western society, and that, I believe, are vulnerable to disproof by science. This list is entirely personal: others would make other lists. These assumptions are different in nature: some are conceptual, some are practical, and some are sociological.

Where Does Chemistry Fit In?

Chemistry has had a wonderful period of two centuries in which it revolutionized the understanding and manipulation of the physical world: it revealed the atomic and molecular structure of matter, and provided physical things—drugs, clothing, fuels, weapons, materials—that changed society. There is still much to be learned about molecules, bonds, and reactivity, but these subjects seem of a different character than aging, machine intelligence, and privacy—more evolutionary than revolutionary. Are the *revolutionary* discoveries now elsewhere, or are there still chemical discoveries as profound as the laws of thermodynamics, the nature of the chemical bond, and the molecular basis of inheritance waiting to be made?

Any answers to this question hinge on personal opinion, and on the definition of "chemistry". Is it profound to understand the origin of life, or the nature of sentience? It is, to me. Are these subjects "chemistry"? They are, to me. Is it profound to understand complexity (whatever "complexity" means), or to develop nonliving intelligence? Yes, and both have important chemical components. Is it profound to hybridize living and nonliving systems? Of course, and chemistry offers much to the effort.

This Essay is about the assumptions that our society accepts, and the potential of science to sweep aside these assumptions. It is not specifically about chemistry. However, I am a chemist, and I believe that chemistry can be *everywhere*, if chemists so choose, or that it can contract into an invisible part of the infrastructure of technology, if they don't. Chemistry, by its culture, has been almost blindly reductionist. I am repeatedly reminded that "Chemists work on molecules", as if to do anything else were suspect. Chemists *do* and *should* work on molecules, but also on the *uses* of molecules, and on problems of which molecules may be only a part of the solution. If chemists move beyond molecules to learn the *entire* problem—from design of surfactants, to synthesis of colloids, to MRI contrast agents, to the trajectories of cells in the embryo, to the applications of regenerative medicine—then the flow of ideas, problems, and solutions between chemistry and society will animate both.

As a technology, chemistry has built the foundation from which many of the discoveries of "biology", or "microelectronics", or "brain science" (or "planetary exploration", for that matter) have grown. There would be no genomics without chemical methods for separating fragments of DNA, and for synthesizing primers and probes, and for separating restriction endonucleases into pure activities. There would be no nuclear ICBMs without methods of refining plutonium and uranium, and making explosive lenses. There would be no drugs without synthesis and mass spectrometry. There would be no interplanetary probes without fuels, and carbon/carbon rocket throat nozzles, and silicon single crystals.

Those are the past. What about the future? Chemistry is, still, everywhere: It *must* be! It is the science of the real world. But, to remain a star in the play rather than a stagehand, it must open its eyes to new problems. It is impossible that the human life span will increase dramatically without manipulation of the molecules of the human organism, but understanding this problem will require more than manipulating molecules. Communication between the living and nonliving will also require engineering a molecular interface between them, but designing this interface will require understanding the nature of "information" in organisms and in computers, and how to translate between them. A society that uses information technology to interweave all its parts requires new systems for generating, distributing, and storing power, but batteries will be only one part of these systems.

Chemistry has always been the invisible hand that builds and operates the tools, and sustains the infrastructure. It can be more. We think of ourselves as experts in quarrying blocks from granite; we have not thought it our job to build cathedrals from them. Whether we choose to focus on the molecules, materials, and tools that are at the beginnings of discovery, or bring our particular, unique understanding of the world to bear on unraveling the problems at the end, is for us to decide.

I believe that everything from methane to sentience is chemistry, and that we should reexamine our own assumptions concerning the boundaries of our field. Examining the broader assumptions that follow may provide some stimulus to do so.

Assumptions

1. We Are Mortal

We assume we are mortal: we will die. We know that from experience, albeit the experience of others. But die of what? One hundred years ago, infectious disease was a major cause of death; now, it is a relatively minor problem. Most of us now alive will die of cardiovascular disease, cancer, Alzheimer's disease, diabetes, degenerative disease. Regardless of the details, we die of old age.

We know, however, that some cells age differently than others. Transformed cells are in some sense immortal (although they are not an organism); single-celled organisms that replicate by division have a kind of immortality. There are strategies that strongly prolong life: caloric deprivation does so in mice and fruit flies, and probably also does so in man. Inheritance certainly makes a difference.

Molecular biology has begun to illuminate each of our infirmities, and to suggest remedies. Cardiovascular (CV) disease is already following the path of infectious disease: the combination of medications that control blood pressure, and others (HMGA-CoA reductase inhibitors; aspirin) that control cholesterol concentrations and the clotting of blood is decreasing mortality as a result of CV disease; these benefits will increase when treatment begins earlier in life, before the damage is done. Understanding the role of free radicals in damage to tissues can help to limit injury after blockage to a blood supply. Infectious disease may also play an important role in the damage to the intima of the blood vessels, and help to initiate plaque formation. Changes in lifestyle—eating less fat and red meat, smoking fewer cigarettes—contribute to limiting injury. Many of the causes of CV disease seem understandable, and, in principle, controllable. Minimize these causes, and when these medical strategies finally fail, replace the dysfunctional organ with one from a pig engineered immunologically to resemble a human, or regenerate the organ entirely. There seems a realistic possibility that CV disease—now the largest single cause of death—may cease to be a significant contributor to mortality.

If CV disease were marginalized, other diseases would take center stage. Cancer is next in line, and is a much, much more difficult problem. The enormous advances in cancer biology have taught, if nothing else, how complicated cancer is. Cancer is fundamentally a cumulative derangement of the genome within a population of cells. By the time the disease is detectable, there is usually already extensive damage to genes and chromosomes. The growing, molecular-level understanding of the etiology of cancer explains why success in cancer therapy has been so halting.

While genomics has so far primarily been useful in understanding, rather than in treating, the disease, it offers many suggestions for the future. There are many genomic defects that are common among cancers: damage to the signaling pathways responsible for control of the cell cycle; breakdown in the processes that check for genetic damage, and guide the damaged cell to its own death through apoptosis; breakdown in the pathways that prevent cells from leaving their origin and colonizing other organs. Understanding the role of telomers—the chromosomal structures that count the age of cells by progressive shortening during each cell division—and resetting this internal clock may have important consequences. New approaches to cancer—especially blocking factors that are essential for metastasis; preventing vascularization of tumors; developing viruses that are specific to tumor cells—all suggest new strategies for control. Other strategies will certainly appear; some will certainly be useful. The nascent field of systems biology will help to coordinate these strategies.

For cancer (and perhaps for most diseases) prevention (or presymptomatic detection) may be more important than cure. Avoiding influences that cause genetic damage—most obviously, specific compounds in the environment or in foods (and especially in tobacco smoke) that react with DNA—and avoiding exposure to ultraviolet light or ionizing radiation may be the most cost-effective method of reducing this risk.

We certainly do not see an end to cancer, nor even, yet, a real beginning to its prevention and cure. We have, however, an enormously expanded molecular understanding of the disease, and ideas for therapies.

After cancer come the diseases of aging. The details of these diseases are even less-well understood than are those of cancer. For most, we have only hints of the importance of genetic susceptibility, infection, environmental exposure, and genomic programming. A flood of genetic information will, however, emerge from studies of multiple human and non-human genomes; we can control many infectious diseases and environmental exposures; we will be able to reset biological clocks and repair genetic dysfunction. We see the beginnings of broad *strategies* to combat the diseases of aging, although we have no idea of effective *tactics*.

These changes in the understanding of disease and aging, and of medical treatment, do not promise immortality. But, they are constructing, for the first time, a true molecular *science* of disease and of medicine. The change from empiricism to understanding, and from reaction to anticipation, forms the basis for a revolution in health care. As this revolution unfolds, it has the potential to transform society.

Immortality is not necessary to change the world; much less will do. How would our social institutions perform if the average life span were 200+ years? What would happen if the period of female fertility were 100 years? How would we behave if life expectancy could be extended by a factor of five, but only the very, very rich could afford the extension? How would the world change if the difference in life span between first and third world countries were a factor of ten?

Chemistry is at the core of changes in biomedicine. Chemistry makes drugs and vaccines. Chemistry makes the analytical systems that will enable detailed genomic analysis of individuals. Chemistry provides the understanding of the changes in molecules that accompany disease and aging. Chemistry identifies (and sometimes generates) the environmental factors that lead to biological damage. What chemistry does *not* do now is to integrate molecular-level characteristics with cellular and organismic behavior—to see the picture in the pointillist splatter of dots. Still, molecular chemistry, molecular biology, and medicine are fundamentally the same subject—the understanding of molecules important to life, and the application of that understanding to the improvement of human health.

2. Only Living Creatures Think; We Think Best

We are, at least in our own opinion, the crown of creation: the most intelligent and versatile of species, and renowned for our ability to subjugate other species. We assume that there is no threat to this position (barring the appearance of aliens, or some other incalculable improbability).

Will we continue to be unique? Is there another species that could become as intelligent as we are? It seems unlikely that other living creatures could emerge as superior intelligences: biological evolution is relatively slow, and we would probably not be kind or hospitable to a potential competitor. An alternative to the improbable emergence of another intelligent animal (or insect, or plant) species is that the next sentience on the planet might be silicon- rather than carbon-based.

Individual computers probably do not currently have the complexity necessary to be intelligent (or at least self-conscious) in the way that we are. As the global information network—the world wide web; high bandwidth communications systems; universal connectivity—is assembled (or, increasingly, as it self-assembles, to use the phrase from organic chemistry), there will be an opportunity (or perhaps even a certainty) for a complexity that rivals or exceeds that of each of us as individuals. A global, interconnected entity that operates at frequencies of petaflops will do things that we cannot begin to imagine. Why not think? Why not think about itself? Perhaps even think about us?

The probability of a new intelligence emerging by biological evolution is limited by the decades-long generational times of complex organisms, by the low rate at which new variants arise by mutation, and by the complexity and functional form of the central nervous system. Evolution and selection have taken millennia to jostle us into our present situation; I suspect it would require special circumstances for another to jostle us aside quickly. Our intelligence, adaptability, and self-awareness (aided by the chance development during evolution of an opposed thumb and an oddly positioned larynx) have enabled us to survive and out-reproduce many more voracious but less-intelligent and self-aware forms of life.

Computers operate by different rules, and without the constraints of biology. Computer cycles are much faster than the diffusion of neurotransmitters across synapses in the brain; change through evolutionary selection is much slower than change by adaptive reprogramming. With the Internet, computer interconnectivity will become very large, and communication among nodes very rapid.

Perhaps most importantly, the growth of complexity in the web is driven by us: a significant part of the creativity of the human race—perhaps hundreds of thousands of creative, energetic, purposeful people—is now devoted to the mission of making more competent components for the web, to enabling those components to communicate as efficiently as possible, and to encouraging the resulting systems to perform their tasks with little or no human supervision. As we develop software agents, applets, and autonomous systems, we seek local performance; what global connectivity among these local systems will bring remains for us to experience.

We could ask at least four interesting questions about the potential for sentience in computer networks. The first question concerns the connections between complexity, emergence, and intelligence. (The word "emergence" is taken to mean the appearance of properties in a complex system that we cannot predict from the properties of its individual components.) How complex must a system be to think? … to become sentient? Can we—scientists, and especially chemists, who generally are committed reductionists—predict complex behaviors based on knowledge of simple components? Understanding complexity has not been a strength of reductionist science. A second question concerns the basic requirements for "intelligence". Are complexity and density of connections enough, or is there something about the human brain that makes it uniquely capable of intelligence? I personally doubt that there is anything special about the wetware inside my skull other than its complexity, the three-dimensional density with which it is internally connected, and its ability to modify itself through experience; I doubt, but cannot disprove, that there are quantum subtleties to self-consciousness. A third question deals with the relationship between intelligence and self-awareness. Is there a correlation, or is self-awareness something different in character than intelligence? A fourth question touches on the delicate issue of the relation between life and intelligence. We speculate endlessly about evolution in living systems, and whether biological evolution leads inevitably to intelligence. What about intelligence *without* life? An intelligent web would certainly not be alive in any sense a biologist would recognize.

We have opinions about the potential of computer networks to support sentience, but not knowledge. Self-awareness is probably not unique to humans, and not all that is *Homo sapiens* is self-aware. A porpoise or a chimpanzee is probably self-aware. A human fetus is certainly not self-aware; a baby grows into self-awareness; an Alzheimer's patient grows out of it. Can we guarantee that a computer system would not grow to be self-aware? I doubt it.

Would we even know if some future version of the world wide web had developed self-awareness? I suspect that we would not, at least for a long time. Our ability to imagine existences not our own is profoundly limited. The ability of a silicon-based intelligence—one inhabiting a distributed web of cunningly doped crystals and giant magnetoresistive films, of optical fibers and satellite repeaters, and "thinking" through the flow of photons and electrons—to imagine a world of water, salt gradients, food, and sex seems equally improbable. If aqueous and silicon intelligences did become aware of one another, it is not clear what the outcome would be.

What does this have to do with chemistry? Probably everything. One of the great intellectual challenges humans face is to understand intelligence as a property that emerges from the interactions of molecules (which, whatever they are, are not intelligent). Chemistry is familiar with complexity, but has not yet embraced the task of understanding the forms of complex behavior that can emerge from large groups of molecules, or of systems (for example, cells) formed from molecules. In studying intelligence in a complex system, our own intelligence is probably the best example with which to begin. This effort is the best preparation we can presently imagine for an encounter with another intelligence, whether met on our own planet or encountered elsewhere.

Redrawing the Line between Living and Dead

3. Animals and Machines are Different

Humankind tends to categorize. Among the categories that have been separate in the past have been "living" and "nonliving", and "animal" and "machine". An animal is a biological entity made of tissue and bone. It is born of other animals, lives, and dies, and has characteristics that are what they are by virtue of evolution and genetic inheritance. In the past, we have not designed animals, although their performance may in a few cases have been optimized empirically through domestication and selective breeding to meet certain of our needs. Since we and animals are alive, we recognize various degrees of ethical responsibility toward them.

A machine is qualitatively different: an object of metal, ceramic, and plastic, which we design and build de novo. We now feel no ethical responsibilities toward machines.

This convenient distinction between animal and machine is beginning to fail at several levels. In the most biological sense, we are developing the ability to design animals. We are rapidly developing biological tools that will enable us to specify the characteristics of animals in a way similar to that in which we specify the characteristics of machines. We already use genetic engineering with animals for the same sorts of tasks as we use mechanical engineering with machines. We have chimeras that build components of one species into another; we can add or delete genes; we can re-engineer entire subsystems of one animal to resemble that of another. We are learning how to modify the surface antigens of one species to make its organs compatible with transfer into another species. We have taken the first steps in learning how to regenerate organs from stem cells, and perhaps to de-differentiate differentiated tissue, and then regrow it into regenerated parts. We are developing a toolkit that is making possible the machinelike design of animals using parts that can range from nucleotide sequences to whole organs.

Most of this work has, of course, been focused on objectives in biology and biomedicine. As the capabilities of biology extend, however, the idea of animals (or insects) for other uses quickly follows. Animals as sensors—that is, as "canaries"—is now plausible. Plants and microorganisms are unquestionably already alternatives to chemical reactors for carrying out some chemical transformations. We know that selective breeding can produce unusual plants and animals; applied biology can only increase our skills at "species engineering". We will ultimately consider—perhaps will *have* to consider—species-engineering for ourselves. Were we to embark on multigenerational space flight, would we be better off with artificial gravity and our current physical form, or with a physical form better adapted for low gravity, high radiation, and whatever other aspects of the environment the ship could best provide?

More radical, but much earlier in development, is work intended to fuse the world of man and machines. Current technology builds implantable sensors to control cardiac rhythm and glucose levels. Cochlear implants help the deaf to hear. The targets are becoming more ambitious: electrodes implanted in insects and rats that begin to control their motion or relay information about their environment; retinal chips to provide sight for the blind; systems that transduce thought directly into mechanical motion. For the more distant future, the goal is direct, efficient, communication between human brains and machines.

These efforts point toward an extraordinarily complex (and perhaps unachievable) future goal: the ability to connect brain and computer directly—that is, to allow information flowing in the nerves of an organism to shift directly into information flowing as electrons or photons in a computer. The technological barriers to this kind of fusion of animate and inanimate are immense, but do not violate any fundamental physical laws, and do not seem ultimately insurmountable. Progress in solving some of them—for example, in developing interfaces that are biocompatible—has been rapid; progress towards others—for example, learning how to transfer information between neural and silicon-based systems—has been slow. Given the unarguable fact that biology and information technology have been the scientific revolutions of the last half of the 20th century, it is almost certain that the 21st century will see their overlap and fusion.

What are the major technical problems? One must learn the code used in the brain and the nerves to convey, process, and interpret information; (we already know the code used in computers, since we *designed* it); one must learn how to build a physical interface between the two—perhaps between nerves and microelectrodes. One must learn how to convert between the currencies used by the neurons to transfer information—ion gradients across membranes and pulses of neurotransmitters in synapses—and the currencies used by silicon-based systems—electrons and photons. The goal of direct communication between human brain and computer also faces a serious problem of dimensional translation: computers are now intrinsically 2D in their architectures, and brains are 3D. We have no solution yet to the problem of making a sufficient number of the correct kinds of neural-to-computer connections. Perhaps growing specialized neural tissues to act as connectors—that is, genetic modification of the human to fit better to the computer—will be the final approach.

With a capability to build hybrid systems—systems containing not just two kinds of biological molecule or tissue, but systems containing some components that are biological and others that are silicon—the issue of whether computer networks might emerge as sentient entities capable of competing with humans could become moot: one could imagine wetware and silicon co-developing, and a blurring of the concepts of "animal" and "machine" and "alive" and "dead" in a way that is unimaginable now.

Many of the most important of these problems ultimately have components that are molecular. Although molecules may be only a part of the systems that transmit and interpret information in organisms, building interfaces between the living and nonliving, and designing translators to bridge the languages of ions and electrons, both depend intimately upon chemistry. The tools for genetic engineering of specialized neural tissues will require chemical manipulation of genetic materials. Biocompatibility is a molecular and materials problem.

The 21st century will almost certainly see us redraw the line between "living" and "dead," and many of the tools to do so must ultimately be molecular.

4. Human Life Is Invaluable

The idea of a long, healthy life fits neatly with the assumption of western civilizations that life is invaluable, and that prolonging it, when possible, is a moral obligation. This obligation is increasingly in conflict with the need to limit the costs of medical treatments, to balance the distribution of health benefits, and to stabilize population levels. We may be forced to confront the value of prolonging life on two fronts:

First, as we move toward the objective of a long, healthy life, we already see that there is an interval where life can be prolonged, but only at great expense, and not necessarily with high quality. If, for example, we can extend life through combinations of artificial devices (artificial joints and organs), xenotransplantation, immunosuppression, and organ regeneration, the cost to the patient may be a life of immunological crisis and constant flirtation with infection. We may be able to buy a longer life, but only an expensive and uncomfortable one. As biomedical science makes it possible to patch up (but not cure) many previously terminal conditions, a serious collision of interests seems inevitable.

Second, and more complicated, are the demographic consequences of reaching the technical goal of building a medical capability that greatly prolongs healthy life. Balancing prolongation of life span, birthrate, and population control requires arithmetically that something give: there must be either limitations on birthrates, or limitations on life spans. We may find that we have a choice: "New life or old?" Placing termination of life—killing a person—on the same footing as birth control—an everyday part of recreational sex—would mean a fundamental shift in values.

Sorting Humans

5. All Are Born Equal

An assumption in many western societies is equality at birth: equal rights under law, and equal access to opportunity. This assumption is respectful of the individual, and there have been no means—or no means that we have chosen to validate and adopt—of quantifying inequality. Genetics has the potential to change our convenient inability to measure innate capability; cognitive science and psychology will also contribute.

Pandora could not resist opening the box. Can we?

Genomic analysis of individuals is just dawning. The first complete maps of the human genome are still being refined, and the task of correlating and confirming the association of single genes and gene clusters with the characteristics of individuals has begun. It is the "Panama Canal" project of modern biology. Eventually there will be a highly profitable shipping trade between the genomic and phenotypic oceans, but now there is a lot of mud to move and many mosquitoes to swat. We do not know how complicated the task will be: it is possible that the characteristics that make us what we are will be determined by single proteins or relatively uncomplicated clusters of proteins, and that genomics will open a window directly onto behavior and capability; it is more probable that these characteristics reflect the behavior of complex biological systems, and will require many decades to decipher. In any event, even with dramatic improvements in the relevant technologies—both for the collection of the needed biological information and for its analysis—the task of correlating genetic constitution with the potential strengths and weaknesses of individuals will require decades (but probably not centuries) of work.

This enterprise—the mapping of genomic information onto an understanding of capabilities, weaknesses, and behaviors—has, of course, the potential for enormous good. It will be one foundation for medical science; it will help individuals to understand where they might be susceptible to damage through disease or environmental exposure; it will allow them the opportunity to identify and exercise their strongest capabilities.

It will also change society if used to *classify* individuals—especially children—according to these capabilities. If it is very *easy* to collect genomic information about individuals, will we be able to resist the temptation to use this information to understand as much about them as possible? Not just their susceptibility to emphysema from smoking, but their ability to handle the stresses of office work, combat, or marriage? Or their potential to be good parents? Or to pay traffic tickets on time? Or to have a sense of humor? We *are* incorrigibly curious and mischievous. Pandora could not resist opening the box; will we do any better?

For good or evil, chemistry is a central player in this project. The development of analytical systems that allow rapid, accurate, inexpensive analysis of the genome of individuals; the intimately linked areas of functional genomics and proteomics that will associate genes with proteins, and proteins with biological function; the correlation of environmental influences—from food components to stress, and from stress-induced chemicals to disease or dysfunction—will all depend centrally on chemistry to build the tools to study genomics, proteomics, and metabolism…

…and, eventually, to sort human beings according to their characteristics and potentials.

6. We Are Individuals, and Privacy is Important

We are accustomed to thinking of ourselves as individuals, and as such we value the accoutrements of individuality: freedom of choice, privacy, lack of control by others, self-determination. We are individuals in the sense that we choose our own paths; we keep our own secrets; we are unpredictable to others.

We are individuals partly by choice, and partly by accident: we are not able to read the thoughts of others, nor to control their thinking. Characteristic of the revolutions in information technology and in genetics is that they have the capability to provide information about individuals in such abundance and detail that privacy and unpredictability become moot. Many of us now have cellphones and other microelectronic assistants; these phones are a step toward a global technology in which everyone is able to communicate with anyone on the globe, at any time, using sound, sight, and data, by portable communications systems. The global positioning system (GPS) and related systems allow us to determine positions; with a simple transponder, it will allow others to determine our positions. Universal surveillance—by monitors inside buildings; from unpiloted, long-endurance vehicles outside buildings—will one day allow our actions to be monitored continuously. A history of our behaviors and actions can be stored in large databases. Genetic analysis has the potential to predict capabilities, susceptibilities, and patterns of behavior. Sociology and psychology, as they become sciences, will help to connect the dots between molecules and behaviors, and between individuals and crowds and societies.

It may be that it is still impossible to read our minds; but if it is possible to know our positions and circumstances, to watch and record our activities, to

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know our intrinsic capabilities, and to communicate with us at all times, it may be *unnecessary* actually to read our minds: all the information that is needed to predict our behaviors may already be available.

Many of the major technologies needed to begin to transform humankind from a society of individuals to a kind of hive-animal are, in practical fact, already available, albeit in the form of early prototypes: GPS, very high-density information storage; sensors for remote surveillance, systems for genetic testing. One essential technology that is not available is portable power. It is possible that we may develop methods of providing power wirelessly inside buildings and in cities as we now provide light; beyond enclosed spaces, devices for generation and storage of power will be required. To be in constant electronic communication requires that the individual carry devices that broadcast, but broadcasting requires power. The energy density of any battery that we can imagine will not fill this need: what is required is either a direct, low-temperature hydrocarbon fuel cell, or more exotic power sources: perhaps small nuclear power sources, or methods of extracting electrical energy from the metabolism of individuals. That extra cake for dessert might power more minutes of high-bandwidth communication!

The Democratization of Information and Expertise

7. Experts Know Best; Doctors Control the Medical System

We assume that specialized knowledge belongs to experts. I do not expect my auto mechanic—an expert in his own field—to do Diels–Alder reactions. We depend on experts, and on their ability to use their expert knowledge to our benefit.

We are, understandably, especially interested in the workings of the experts—doctors—in the medical system: we all become sick; we all age. The medical profession has been a prototypic guild—one controlled by highly trained individuals, who establish the standards that others must pass to join. Doctors also control most of the aspects of medicine: information about disease and treatment; approval of new drugs and new methods of treatment; and access to drugs. Although those who pay for medicine (in the US HMOs, or health maintenance organizations, and insurers) are challenging this system, doctors still largely run medicine. This system has many good features, and some bad ones as well.

An interesting consequence of the development of the world wide web is the ability of individuals with common interests to find and communicate with one another. There are few individuals who are as motivated as those who are sick (or who believe that they are sick) and who wish to be well. The development of web-based medicine allows these individuals to talk to one another, and to share opinion, gossip, and fact without formal medical supervision. They can often buy drugs that are not approved by the medical establishment, and they can experiment on themselves: the sales of "nontraditional" medicines is now claimed to be comparable to that of medicines that have regulatory approval. It is common for a physician to be faced with a patient carrying a thick folder of computer printouts describing the disease. In short, the medical profession is losing its control of the flow of authoritative medical information, and to an extent, of the course of medical treatment taken by patients.

Medicine is changing, and doctors must keep up with an enormous volume of information. Patients have as much access as doctors to much of the information, and often a more intense motivation to assimilate it. They may be better informed than their doctors, and collectively they can call on an extraordinary breadth of expertise. The Internet allows information—true, false, untested—to flow internationally without professional or peer supervision. Nontraditional and unapproved drugs are readily available.

The democratization of information and expertise that springs from the world wide web, and the power of groups of motivated amateurs to strike out on their own in technical subjects, is weakening the authority of "experts" in society. Travel agents are a disappearing breed—one can order tickets on the web. Accounting programs are replacing tax accountants. A free-form community of hackers and programmers developed the Linux operating system. Computers routinely land commercial airliners. The environmental and consumer advocacy groups that so bedevil technology (sometimes to excellent effect) are highly skilled in collective expertise and collective action. Doctors are losing their grip on their profession. Even universities are beginning to worry about their monopoly to certify expertise.

Of course, someone still has to hold the scalpel and the bedpan. Or some *thing*: the hand wielding the knife could well be a machine's.

The Globe

8. Earth Will Remain Habitable

Although discussions of the environment and global warming are endless, to much of the world the problems these phrases represent are still abstract. The first-world countries have not slashed their use of fossil fuels; the third-world countries continue to reduce forests to wastelands; and coal is the fuel of choice for some of the largest economies of this century.

There seems to be growing agreement that anthropogenic contributions—carbon dioxide, soot, methane, others—to the atmosphere are significant, and are increasing global temperatures relative to what they would be in the absence of these contributions. There is no agreement on the significance of this increase in temperature on society. The temperature of the Earth has gone through a set of sawtooth excursions over the last millennia: we are now in an exceptionally warm period in this normal climatic cycle in any event, and despite our mischievous efforts to achieve warming on a planetary scale, temperatures may again fall in the future.

But what happens if the assumption that the Earth will remain habitable (or at least as accommodating to mammalian life as it now is) proves wrong? Changes in the environment will probably be relatively slow; even if we melt the west Greenland ice sheet, it seems unlikely that we will tip the balance of the planet so that Earth becomes Venus (although we would submerge New York and Tokyo). We would adjust.

Other changes—for example, those resulting from all-out nuclear war or a large meteor strike—would probably give us much less time to adapt, and far fewer options.

How much of a technological insurance policy, and of what nature, should we have against events that might fundamentally change the habitability of earth? There are many possibilities to reduce carbon emissions significantly: replacing gasoline engines with efficient diesels, developing highly efficient fuel cells, developing solar and wind power optimally, and reintroducing nuclear power are four. Industrial solutions to pollution would proceed more rapidly if there were active investment in "green" technologies, and the rate of the investment is primarily a matter of regulation and public policy, albeit complicated by the fact that regulations apply locally within countries, but the problem is global.

Technical issues are less important than political ones in nuclear matters, and we have not begun to take the problem of a meteor strike seriously.

9. Nations Are the Most Powerful of Human Organizations

The world is now organized into nations—social and political entities with defined geographical boundaries. Nations made sense in a world in which wealth was based on natural resources, fertile land, water, and people. Wealthy nations were those that could lay claim to vast natural resources, and had access to trade routes; wealthy nations were also those that could afford to wage war.

It was easy to keep score with nations as central political entities. The ground has, however, shifted. It is more important now to be able to control and use information than to mine bauxite or diamonds. It is more important now to have a highly educated population than large reserves of coal. The fluidity of information, and the difficulty of owning and containing it, also opens opportunities for small groups of people. The Internet allows almost any group of people access to floods of useful information, and at almost no cost. The technology of information has redefined wealth—from material goods to information and services—and thus makes the centrality of nations—which control physical space but not information space—open to question.

As for war: The cold war was a period in which the two most powerful nations faced one another in a competition ostensibly organized along conventional lines: with armies and weapons. The armies were never used directly, although they were employed in surrogate conflicts in Korea, Vietnam, and Afghanistan. Ultimately, however, the conflict proved to be economic: the US won, in significant part because it outspent the Soviet Union.

As information, information systems, and people become central to wealth, large countries (especially those housing open societies) become more vulnerable to cyber attacks. The US and the Soviet Union also had a virtual monopoly on strategic nuclear systems for many years; they have no corresponding monopoly in terrorist weapons, especially those for biological weapons. Joshua Lederberg has said "biological weapons enable a single man to wage war," and biological and cyber attacks—plausibly originating in small countries or in nonstate entities such as criminal, religious, or ideological groups, or even, perhaps, corporations—now rank with nuclear attacks in the risk they hold for society.

Technology has started a shift away from nations as the central political entity to supranational entities: alliances, economic regions, multinational corporations, capitalist groupings, religions. It has posed risks to the developed countries, which value openness and capitalism, and which require relatively few barriers to the movement of people, information, and goods for efficient operation. This openness of western societies makes them difficult to defend. Developing new technologies to defend against these new threats—sensors, drugs, and defensive agents for use against biological threats; software agents and security systems to protect computer networks—are important problems, and all have central components in chemistry.

Deciding how much protection is "enough", and how much is "too much"—that is, deciding how to value security and privacy when the two are in conflict—is a broader question for society.

Not Everything is Built on Sand

Is there *nothing* that is secure, then? The answer is, of course, that we do not know, but a number of assumptions seem most unlikely to fall. We assume that it is impossible to read minds, or to teleport physical objects, or to move faster than the speed of light in vacuum. We assume that time can not be made to run in reverse, and that the major laws discovered by physical science over the last several centuries will continue to be true: water at room temperature will not spontaneously separate into steam and ice; objects will not spontaneously rise against gravity; we will not discover a source of energy for free. The second law of thermodynamics will continue to describe the world in which we live. Not everything is built on sand.

Are There Questions We Should Not Ask?

Is "big" science—science that changes the world—good for the world it changes? I am constitutionally an optimist, and would answer "Usually 'yes'". We (at least in the developed world) live longer than our forebears, devote less of our lives to personal survival; suffer less from disease; understand the world more fully; have more time to spend building society and appreciating existence. I *believe* that science has *generally* worked for the common good in the past, and will continue to do so in the future. Still, science and technology will unlock some doors we may not choose to open.

Science that changes the world inevitably brings ethical issues. Building a microfluidic system for analysis of the human genome may be no more or less challenging technically than building a better catalyst for the production of polyethylene, but it is more important for society.

We scientists *do* have something special to contribute to discussions of the outcomes of science. We know some things that *will* be done before they are done; we know some things that cannot be done at all; we can speculate about things that *might* be done. We can alert our neighbors to the possibility of change, and be a part of discussions and decisions that encourage the good, and avoid or forestall the bad. We can try to prevent fear of new ideas from blocking beneficial technology. In choosing to work on problems with the potential to change society, we should, ideally, accept an obligation to help society understand how it might benefit, and what it might pay, for that change.

We can suggest what doors can be opened, and what might wait in the rooms behind them. Our neighbors will decide for their own reasons whether they would like to open these doors and move in.

Finally: Is there science that must not be done? There are easy cases—I can see no redeeming virtue of publicly available research that develops strains of anthrax that are resistant to multiple antibiotics—but much of research is not easily classified as "good" or "bad".

Chemistry contributes broadly to the foundations of technology, and thus it is particularly difficult to guess its future impact: a new chemical reaction might be used to make a cancer therapeutic or a chemical weapon. Some of the opportunities that seem within the reach of investigation, if not within the reach of solution—technologies that might substantially prolong life, or develop new forms of life, or lead to sentient systems that rival us in intelligence—will do both good and harm. At the very minimum, those of us who pursue these problems should accept an obligation to explain to our fellow citizens fully and clearly what we are doing, and why, and (to the limited extent we can) with what possible outcomes.

Humankind will do what it will do, but at least everyone should understand—in so far as is possible—what the choices are, and what the consequences might be. Chemistry, if it takes more interest in (and responsibility for) the full scope of programs—from molecules, to applications, and to influence on society—may be able to use the very breadth of its connections to technology to help in this explanation.

After that, the surprises take over. The last, most realistic, assumption may be that the law of unintended consequences will ultimately apply.

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