The New York Review of Books

Our Biotech Future

JULY 19, 2007

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1.

It has become part of the accepted wisdom to say that the twentieth century was the century of physics and the twenty-first century will be the century of biology. Two facts about the coming century are agreed on by almost everyone. Biology is now bigger than physics, as measured by the size of budgets, by the size of the workforce, or by the output of major discoveries; and biology is likely to remain the biggest part of science through the twenty-first century. Biology is also more important than physics, as measured by its economic consequences, by its ethical implications, or by its effects on human welfare.

These facts raise an interesting question. Will the domestication of high technology, which we have seen marching from triumph to triumph with the advent of personal computers and GPS receivers and digital cameras, soon be extended from physical technology to biotechnology? I believe that the answer to this question is yes. Here I am bold enough to make a definite prediction. I predict that the domestication of biotechnology will dominate our lives during the next fifty years at least as much as the domestication of computers has dominated our lives during the previous fifty years.

I see a close analogy between John von Neumann's blinkered vision of computers as large centralized facilities and the public perception of genetic engineering today as an activity of large pharmaceutical and agribusiness corporations such as Monsanto. The public distrusts Monsanto because Monsanto likes to put genes for poisonous pesticides into food crops, just as we distrusted von Neumann because he liked to use his computer for designing hydrogen bombs secretly at midnight. It is likely that genetic engineering will remain unpopular and controversial so long as it remains a centralized activity in the hands of large corporations.

I see a bright future for the biotechnology industry when it follows the path of the computer industry, the path that von Neumann failed to foresee, becoming small and domesticated rather than big and centralized. The first step in this direction was already taken recently, when genetically modified tropical fish with new and brilliant colors appeared in pet stores. For biotechnology to become domesticated, the next step is to become user-friendly. I recently spent a happy day at the Philadelphia Flower Show, the biggest indoor flower show in the world, where flower breeders from all over the world show off the results of their efforts. I have also visited the Reptile Show in San Diego, an equally impressive show displaying the work of another set of breeders. Philadelphia excels in orchids and roses, San Diego excels in lizards and snakes. The main problem for a grandparent visiting the reptile show with a grandchild is to get the grandchild out of the building without actually buying a snake.

Every orchid or rose or lizard or snake is the work of a dedicated and skilled breeder. There are thousands of people, amateurs and professionals, who devote their lives to this business. Now imagine what will happen when the tools of genetic engineering become accessible to these people. There will be do-it-yourself kits for gardeners who will use genetic engineering to breed new varieties of roses and orchids. Also kits for lovers of pigeons and parrots and lizards and snakes to breed new varieties of pets. Breeders of dogs and cats will have their kits too.

Domesticated biotechnology, once it gets into the hands of housewives and children, will give us an explosion of diversity of new living creatures, rather than the monoculture crops that the big corporations prefer. New lineages will proliferate to replace those that monoculture farming and deforestation have destroyed. Designing genomes will be a personal thing, a new art form as creative as painting or sculpture.

Few of the new creations will be masterpieces, but a great many will bring joy to their creators and variety to our fauna and flora. The final step in the domestication of biotechnology will be biotech games, designed like computer games for children down to kindergarten age but played with real eggs and seeds rather than with images on a screen. Playing such games, kids will acquire an intimate feeling for the organisms that they are growing. The winner could be the kid whose seed grows the prickliest cactus, or the kid whose egg hatches the cutest dinosaur. These games will be messy and possibly dangerous. Rules and regulations will be needed to make sure that our kids do not endanger themselves and others. The dangers of biotechnology are real and serious.

If domestication of biotechnology is the wave of the future, five important questions need to be answered. First, can it be stopped? Second, ought it to be stopped? Third, if stopping it is either impossible or undesirable, what are the appropriate limits that our society must impose on it? Fourth, how should the limits be decided? Fifth, how should the limits be enforced, nationally and internationally? I do not attempt to answer these questions here. I leave it to our children and grandchildren to supply the answers.

2.

A New Biology for a New Century

Carl Woese is the world's greatest expert in the field of microbial taxonomy, the classification and understanding of microbes. He explored the ancestry of microbes by tracing the similarities and differences between their genomes. He discovered the large-scale structure of the tree of life, with all living creatures descended from three primordial branches. Before Woese, the tree of life had two main branches called prokaryotes and eukaryotes, the prokaryotes composed of cells without nuclei and the eukaryotes composed of cells with nuclei. All kinds of plants and animals, including humans, belonged to the eukaryote branch. The prokaryote branch contained only microbes. Woese discovered, by studying the anatomy of microbes in detail, that there are two fundamentally different kinds of prokaryotes, which he called bacteria and archea. So he constructed a new tree of life with three branches, bacteria, archea, and eukaryotes. Most of the well-known microbes are bacteria. The archea were at first supposed to be rare and confined to extreme environments such as hot springs, but they are now known to be abundant and widely distributed over the planet. Woese recently published two provocative and illuminating articles with the titles "A New Biology for a New Century" and (together with Nigel Goldenfeld) "Biology's Next Revolution."[*]

Woese's main theme is the obsolescence of reductionist biology as it has been practiced for the last hundred years, with its assumption that biological processes can be understood by studying genes and molecules. What is needed instead is a new synthetic biology based on emergent patterns of organization. Aside from his main theme, he raises another important question. When did Darwinian evolution begin? By Darwinian evolution he means evolution as Darwin understood it, based on the competition for survival of noninterbreeding species. He presents evidence that Darwinian evolution does not go back to the beginning of life. When we compare genomes of ancient lineages of living creatures, we find evidence of numerous transfers of genetic information from one lineage to another. In early times, horizontal gene transfer, the sharing of genes between unrelated species, was prevalent. It becomes more prevalent the further back you go in time.

Whatever Carl Woese writes, even in a speculative vein, needs to be taken seriously. In his “New Biology” article, he is postulating a golden age of pre-Darwinian life, when horizontal gene transfer was universal and separate species did not yet exist. Life was then a community of cells of various kinds, sharing their genetic information so that clever chemical tricks and catalytic processes invented by one creature could be inherited by all of them. Evolution was a communal affair, the whole community advancing in metabolic and reproductive efficiency as the genes of the most efficient cells were shared. Evolution could be rapid, as new chemical devices could be evolved simultaneously by cells of different kinds working in parallel and then reassembled in a single cell by horizontal gene transfer.

But then, one evil day, a cell resembling a primitive bacterium happened to find itself one jump ahead of its neighbors in efficiency. That cell, anticipating Bill Gates by three billion years, separated itself from the community and refused to share. Its offspring became the first species of bacteriaâ€”and the first species of any kindâ€”reserving their intellectual property for their own private use. With their superior efficiency, the bacteria continued to prosper and to evolve separately, while the rest of the community continued its communal life. Some millions of years later, another cell separated itself from the community and became the ancestor of the archea. Some time after that, a third cell separated itself and became the ancestor of the eukaryotes. And so it went on, until nothing was left of the community and all life was divided into species. The Darwinian interlude had begun.

The Darwinian interlude has lasted for two or three billion years. It probably slowed down the pace of evolution considerably. The basic biochemical machinery of life had evolved rapidly during the few hundreds of millions of years of the pre-Darwinian era, and changed very little in the next two billion years of microbial evolution. Darwinian evolution is slow because individual species, once established, evolve very little. With rare exceptions, Darwinian evolution requires established species to become extinct so that new species can replace them.

Now, after three billion years, the Darwinian interlude is over. It was an interlude between two periods of horizontal gene transfer. The epoch of Darwinian evolution based on competition between species ended about ten thousand years ago, when a single species, *Homo sapiens*, began to dominate and reorganize the biosphere. Since that time, cultural evolution has replaced biological evolution as the main driving force of change. Cultural evolution is not Darwinian. Cultures spread by horizontal transfer of ideas more than by genetic inheritance. Cultural evolution is running a thousand times faster than Darwinian evolution, taking us into a new era of cultural interdependence which we call globalization. And now, as *Homo sapiens* domesticates the new biotechnology, we are reviving the ancient pre-Darwinian practice of horizontal gene transfer, moving genes easily from microbes to plants and animals, blurring the boundaries between species. We are moving rapidly into the post-Darwinian era, when species other than our own will no longer exist, and the rules of Open Source sharing will be extended from the exchange of software to the exchange of genes. Then the evolution of life will once again be communal, as it was in the good old days before separate species and intellectual property were invented.

I would like to borrow Carl Woese's vision of the future of biology and extend it to the whole of science. Here is his metaphor for the future of science:

> Imagine a child playing in a woodland stream, poking a stick into an eddy in the flowing current, thereby disrupting it. But the eddy quickly reforms. The child disperses it again. Again it reforms, and the fascinating game goes on. There you have it! Organisms are resilient patterns in a turbulent flowâ€”patterns in an energy flow…. It is becoming increasingly clear that to understand living systems in any deep sense, we must come to see them not materialistically, as machines, but as stable, complex, dynamic organization.

This picture of living creatures, as patterns of organization rather than collections of molecules, applies not only to bees and bacteria, butterflies and rain forests, but also to sand dunes and snowflakes, thunderstorms and hurricanes. The nonliving universe is as diverse and as dynamic as the living universe, and is also dominated by patterns of organization that are not yet understood. The reductionist physics and the reductionist molecular biology of the twentieth century will continue to be important in the twenty-first century, but they will not be dominant. The big problems, the evolution of the universe as a whole, the origin of life, the nature of human consciousness, and the evolution of the earth's climate, cannot be understood by reducing them to elementary particles and molecules. New ways of thinking and new ways of organizing large databases will be needed.

3.

Green Technology

The domestication of biotechnology in everyday life may also be helpful in solving practical economic and environmental problems. Once a new generation of children has grown up, as familiar with biotech games as our grandchildren are now with computer games, biotechnology will no longer seem weird and alien. In the era of Open Source biology, the magic of genes will be available to anyone with the skill and imagination to use it. The way will be open for biotechnology to move into the mainstream of economic development, to help us solve some of our urgent social problems and ameliorate the human condition all over the earth. Open Source biology could be a powerful tool, giving us access to cheap and abundant solar energy.

A plant is a creature that uses the energy of sunlight to convert water and carbon dioxide and other simple chemicals into roots and leaves and flowers. To live, it needs to collect sunlight. But it uses sunlight with low efficiency. The most efficient crop plants, such as sugarcane or maize, convert about 1 percent of the sunlight that falls onto them into chemical energy. Artificial solar collectors made of silicon can do much better. Silicon solar cells can convert sunlight into electrical energy with 15 percent efficiency, and electrical energy can be converted into chemical energy without much loss. We can imagine that in the future, when we have mastered the art of genetically engineering plants, we may breed new crop plants that have leaves made of silicon, converting sunlight into chemical energy with ten times the efficiency of natural plants. These artificial crop plants would reduce the area of land needed for biomass production by a factor of ten. They would allow solar energy to be used on a massive scale without taking up too much land. They would look like natural plants except that their leaves would be black, the color of silicon, instead of green, the color of chlorophyll. The question I am asking is, how long will it take us to grow plants with silicon leaves?

If the natural evolution of plants had been driven by the need for high efficiency of utilization of sunlight, then the leaves of all plants would have been black. Black leaves would absorb sunlight more efficiently than leaves of any other color. Obviously plant evolution was driven by other needs, and in particular by the need for protection against overheating. For a plant growing in a hot climate, it is advantageous to reflect as much as possible of the sunlight that is not used for growth. There is plenty of sunlight, and it is not important to use it with maximum efficiency. The plants have evolved with chlorophyll in their leaves to absorb the useful red and blue components of sunlight and to reflect the green. That is why it is reasonable for plants in tropical climates to be green. But this logic does not explain why plants in cold climates where sunlight is scarce are also green. We could imagine that in a place like Iceland, overheating would not be a problem, and plants with black leaves using sunlight more efficiently would have an evolutionary advantage. For some reason which we do not understand, natural plants with black leaves never appeared. Why not? Perhaps we shall not understand why nature did not travel this route until we have traveled it ourselves.

After we have explored this route to the end, when we have created new forests of black-leaved plants that can use sunlight ten times more efficiently than natural plants, we shall be confronted by a new set of environmental problems. Who shall be allowed to grow the black-leaved plants? Will black-leaved plants remain an artificially maintained cultivar, or will they invade and permanently change the natural ecology? What shall we do with the silicon trash that these plants leave behind them? Shall we be able to design a whole ecology of silicon-eating microbes and fungi and earthworms to keep the black-leaved plants in balance with the rest of nature and to recycle their silicon? The twenty-first century will bring us powerful new tools of genetic engineering with which to manipulate our farms and forests. With the new tools will come new questions and new responsibilities.

Rural poverty is one of the great evils of the modern world. The lack of jobs and economic opportunities in villages drives millions of people to migrate from villages into overcrowded cities. The continuing migration causes immense social and environmental problems in the major cities of poor countries. The effects of poverty are most visible in the cities, but the causes of poverty lie mostly in the villages. What the world needs is a technology that directly attacks the problem of rural poverty by creating wealth and jobs in the villages. A technology that creates industries and careers in villages would give the villagers a practical alternative to migration. It would give them a chance to survive and prosper without uprooting themselves.

The shifting balance of wealth and population between villages and cities is one of the main themes of human history over the last ten thousand years. The shift from villages to cities is strongly coupled with a shift from one kind of technology to another. I find it convenient to call the two kinds of technology green and gray. The adjective "green" has been appropriated and abused by various political movements, especially in Europe, so I need to explain clearly what I have in mind when I speak of green and gray. Green technology is based on biology, gray technology on physics and chemistry.

Roughly speaking, green technology is the technology that gave birth to village communities ten thousand years ago, starting from the domestication of plants and animals, the invention of agriculture, the breeding of goats and sheep and horses and cows and pigs, the manufacture of textiles and cheese and wine. Gray technology is the technology that gave birth to cities and empires five thousand years later, starting from the forging of bronze and iron, the invention of wheeled vehicles and paved roads, the building of ships and war chariots, the manufacture of swords and guns and bombs. Gray technology also produced the steel plows, tractors, reapers, and processing plants that made agriculture more productive and transferred much of the resulting wealth from village-based farmers to city-based corporations.

For the first five of the ten thousand years of human civilization, wealth and power belonged to villages with green technology, and for the second five thousand years wealth and power belonged to cities with gray technology. Beginning about five hundred years ago, gray technology became increasingly dominant, as we learned to build machines that used power from wind and water and steam and electricity. In the last hundred years, wealth and power were even more heavily concentrated in cities as gray technology raced ahead. As cities became richer, rural poverty deepened.

This sketch of the last ten thousand years of human history puts the problem of rural poverty into a new perspective. If rural poverty is a consequence of the unbalanced growth of gray technology, it is possible that a shift in the balance back from gray to green might cause rural poverty to disappear. That is my dream. During the last fifty years we have seen explosive progress in the scientific understanding of the basic processes of life, and in the last twenty years this new understanding has given rise to explosive growth of green technology. The new green technology allows us to breed new varieties of animals and plants as our ancestors did ten thousand years ago, but now a hundred times faster. It now takes us a decade instead of a millennium to create new crop plants, such as the herbicide-resistant varieties of maize and soybean that allow weeds to be controlled without plowing and greatly reduce the erosion of topsoil by wind and rain. Guided by a precise understanding of genes and genomes instead of by trial and error, we can within a few years modify plants so as to give them improved yield, improved nutritive value, and improved resistance to pests and diseases.

Within a few more decades, as the continued exploring of genomes gives us better knowledge of the architecture of living creatures, we shall be able to design new species of microbes and plants according to our needs. The way will then be open for green technology to do more cheaply and more cleanly many of the things that gray technology can do, and also to do many things that gray technology has failed to do. Green technology could replace most of our existing chemical industries and a large part of our mining and manufacturing industries. Genetically engineered earthworms could extract common metals such as aluminum and titanium from clay, and genetically engineered seaweed could extract magnesium or gold from seawater. Green technology could also achieve more extensive recycling of waste products and worn-out machines, with great benefit to the environment. An economic system based on green technology could come much closer to the goal of sustainability, using sunlight instead of fossil fuels as the primary source of energy. New species of termite could be engineered to chew up derelict automobiles instead of houses, and new species of tree could be engineered to convert carbon dioxide and sunlight into liquid fuels instead of cellulose.

Before genetically modified termites and trees can be allowed to help solve our economic and environmental problems, great arguments will rage over the possible damage they may do. Many of the people who call themselves green are passionately opposed to green technology. But in the end, if the technology is developed carefully and deployed with sensitivity to human feelings, it is likely to be accepted by most of the people who will be affected by it, just as the equally unnatural and unfamiliar green technologies of milking cows and plowing soils and fermenting grapes were accepted by our ancestors long ago. I am not saying that the political acceptance of green technology will be quick or easy. I say only that green technology has enormous promise for preserving the balance of nature on this planet as well as for relieving human misery. Future generations of people raised from childhood with biotech toys and games will probably accept it more easily than we do. Nobody can predict how long it may take to try out the new technology in a thousand different ways and measure its costs and benefits.

What has this dream of a resurgent green technology to do with the problem of rural poverty? In the past, green technology has always been rural, based in farms and villages rather than in cities. In the future it will pervade cities as well as countryside, factories as well as forests. It will not be entirely rural. But it will still have a large rural component. After all, the cloning of Dolly occurred in a rural animal-breeding station in Scotland, not in an urban laboratory in Silicon Valley. Green technology will use land and sunlight as its primary sources of raw materials and energy. Land and sunlight cannot be concentrated in cities but are spread more or less evenly over the planet. When industries and technologies are based on land and sunlight, they will bring employment and wealth to rural populations.

In a country like India with a large rural population, bringing wealth to the villages means bringing jobs other than farming. Most of the villagers must cease to be subsistance farmers and become shopkeepers or schoolteachers or bankers or engineers or poets. In the end the villages must become gentrified, as they are today in England, with the old farm workers' cottages converted into garages, and the few remaining farmers converted into highly skilled professionals. It is fortunate that sunlight is most abundant in tropical countries, where a large fraction of the world's people live and where rural poverty is most acute. Since sunlight is distributed more equitably than coal and oil, green technology can be a great equalizer, helping to narrow the gap between rich and poor countries.

My book *The Sun, the Genome, and the Internet* (1999) describes a vision of green technology enriching villages all over the world and halting the migration from villages to megacities. The three components of the vision are all essential: the sun to provide energy where it is needed, the genome to provide plants that can convert sunlight into chemical fuels cheaply and efficiently, the Internet to end the intellectual and economic isolation of rural populations. With all three components in place, every village in Africa could enjoy its fair share of the blessings of civilization. People who prefer to live in cities would still be free to move from villages to cities, but they would not be compelled to move by economic necessity.

LETTERS

'Our Biotech Future' October 11, 2007

'Our Biotech Future': An Exchange September 27, 2007

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1. *
See Carl Woese, "A New Biology for a New Century," in *Microbiology and Molecular Biology Reviews*, June 2004 (http://dx.doi.org/10.1128/MMBR.68.2.173-186.2004); and Nigel Goldenfeld and Carl Woese, "Biology's Next Revolution," *Nature*, January 25, 2007. A slightly expanded version of the *Nature* article is available at http://arxiv.org/abs/q-bio/0702015v1. ↩