GLOBAL CHALLENGES AND BIOTECHNOLOGY

Jennifer Kuzma

A bus runs on diesel fuel made from soybeans.

AP/WWP/NREL

Biotechnology, if used appropriately, has the potential to provide more and healthier foods, reduce dependence on fossil fuels, and offer more effective cures for diseases. Enzymes that can break down plant material into biofuels such as ethanol will eventually lead to the more cost-effective production of sustainable bioenergy products. A new bioengineered form of rice bolstered with vitamin A may help reduce blindness stemming from vitamin deficiency in developing countries.

But these and other applications carry risks that need to be addressed through regulatory and safety regimes. Governments and other organizations also need to step in and invest in biotech research and development tailored toward products that can help developing countries and assist these nations in building the capacity to benefit from bio-innovation.

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> *Science can only ascertain what is, but not what should be, and outside of its domain, value judgments of all kinds remain necessary.*
> — Albert Einstein

For centuries, humans have harnessed the power of biological systems to improve their lives and the world. Some argue that biotechnology began thousands of years ago, when crops were first bred for specific traits and microorganisms were used to brew beer. Others define the beginning of biotechnology as the emergence of techniques allowing researchers to precisely manipulate and transfer genes from one organism to another. The discovery of the structure of deoxyribonucleic acid (DNA) in the 1950s marks the start of this era. Genes are made up of DNA and are expressed into proteins, which do chemical work and form structures to give us specific traits. In the 1970s, scientists discovered and used the power of natural "scissors"—proteins called restriction enzymes—to specifically remove a gene from one kind of organism and put it into related or unrelated organisms. Thus, recombinant DNA technology, or what most experts now label as modern biotechnology, was born.

The pioneers of biotechnology could not have envisioned our current abilities to engineer plants to resist disease, animals to produce drugs in their milk, and small particles to target and destroy cancer cells. However, biotechnology is more than engineering—it is also a set of tools for understanding biological systems. Genomics is based on these tools and is the study of genes and their functions. We have determined the composition of, or "sequenced," the entire set of genes for humans and several other organisms using biotechnology. Genomic information is helping us better to evaluate the commonalities and diversity among organisms and human beings and to understand and cure disease, even tailoring treatments to individuals.

Biotechnology, or really any technology, does not exist in a vacuum. It is derived from human efforts and affected by social, cultural, and political climates. Society drives and regulates technology, attempting to minimize the downsides and maximize the benefits. Many natural and physical scientists would prefer that the separation between social and ethical concerns and science and technology be well defined. Recent controversies over the use of genetically engineered organisms in food and agriculture have illustrated that this boundary is not so clear. Not only are there safety concerns about genetically engineered organisms, but there are also cultural differences in acceptance of the products.

International contexts for technologies are important and should be considered. Biotechnology is not a panacea for global problems, but it is a tool that holds a great deal of promise if used appropriately. On the other hand, there are social systems that are affected by new technologies and fears of creating greater divides between rich and poor if technology is not accessible to all sectors of society. With this context in mind, this article outlines several global challenges and considers how biotechnology can be harnessed to meet them in sustainable and equitable ways.

Nati Harnik/AP/WWP

Pellets of plastic made of maize are poured into a dish.

THE ENERGY CHALLENGE, CLIMATE CHANGE, AND THE ENVIRONMENT

Fossil fuels are a finite energy resource, and we are expending them more quickly than nature can replenish them. Biotechnology has a role to play in the use of more renewable sources of energy. Biomass energy, for example, is a carbon-neutral energy source, as plants eventually take as much carbon from the atmosphere as they release. Researchers are engineering better cellulases—enzymes that can break down plant material into biofuels such as ethanol. Better cellulases will eventually lead to the more cost-effective production of sustainable bioenergy products.

Some believe that climate change will have the greatest impacts on the poor, who do not have the resources to move or adapt when natural disasters strike or their surroundings change. Not only would a transition to biomass energy have positive environmental effects; it could also lead to economic development in rural communities all over the world. Farmers could grow crops for their food, feed, and energy needs. However, they must have access to the technology that makes biomass conversion possible. Getting technologies to rural areas and building capacity to operate such systems will be challenging.

Other examples of the energy and environmental applications of biotechnology include microorganisms engineered to produce hydrogen gas from organic waste, plants engineered to make biodegradable polymers, molecular machines based on plant photosynthetic proteins to harness energy from the sun, bacteria engineered to break down environmental pollutants, and biosensors developed to rapidly detect harmful environmental contaminants. The environmental applications of biotechnology are often overlooked and underfunded, yet the sustainability of our planet in the face of an increasing population is an issue of utmost importance.

AGRICULTURE, FOOD QUALITY, AND SECURITY

Biotechnology has taken off in areas of food and agriculture. For example, cotton, soybeans, maize, and other crops have been engineered to contain proteins from the bacterium *Bacillus thuringiensis* (Bt) that protect them from insect pests. Bt crops are grown widely in many countries. The cultivation of Bt cotton in China has significantly reduced the use of chemical pesticides that are dangerous to human health, benefiting rural farmers.

On the other hand, there have been concerns associated with Bt crops. Starlink was a Bt maize variety approved only for animal feed in the United States, given questions about its potential to be a human allergen. However, it eventually contaminated some maize-based products in the human food supply. Also, the genes for Bt proteins have been discovered in Mexican maize varieties, although Mexico has a moratorium on planting Bt maize. This contamination has caused concern because Mexico is the geographic center of diversity for maize, and many want to preserve native varieties for cultural and agronomic reasons. Therefore, in order to reap the benefits of genetically engineered crops, it is important that good international biosafety regimes be developed to avoid future mishaps and enhance confidence in the use of these crops.

Healthier and more nutritious foods are also being developed via biotechnology. For example, more than 100 million people are affected by vitamin A deficiency, which is responsible for hundreds of thousands of cases of blindness annually. Researchers have engineered a variety of rice to supply the metabolic precursor to vitamin A. This "golden rice" is being bred with local varieties to enhance its properties for growth in developing countries. Intellectual property hurdles have been overcome to distribute the rice for free to subsistence farmers—this is especially important because the cost of seed could otherwise be prohibitive. Researchers are developing other crops that have increased quantities of iron, vitamin E, essential amino acids, and healthier oils.

For the future, additional applications of biotechnology to food and agriculture could prove useful. The United Nations Environment Program ranks freshwater shortages as the second greatest environmental problem, behind climate change, for the 21st century. Drought- and salinity-tolerant crops tailored to developing countries could greatly enhance food security in areas where a combination of natural disasters and marginal land are sure to lead to famine in a given year. Through genomics and modern biotechnology, we are getting closer to understanding, identifying, and engineering the many traits that control water use and salt utilization in plants.

HEALTH AND MEDICINE

Medical applications of biotechnology are better known in the public's eye. Stem cells and cloning have gained unusual prominence in national and international politics. Stem cells are the early-stage cells in an organism that have been shown to give rise to different kinds of tissues. They have successfully replaced or repaired damaged tissue in animal models, and they hold great promise for treating human diseases such as Alzheimer's and diabetes. Although the vast majority of people agree that cloning to produce humans (reproductive cloning) is unacceptable, therapeutic cloning, in which the cloning process is used only to harvest stem cells, is hotly debated. Therapeutic cloning could supply stem cells that exactly match a patient, minimizing the serious risks associated with tissue rejection. These methods hold great promise. However, the ethical, cultural, and policy issues associated with them will continue to occupy scientists and politicians in the foreseeable future.

A fundamental application of biotechnology to medicine is in drug discovery. Humans have discovered drugs from natural sources by trial and error since the beginning of history. Now genomics and its companion field for proteins—proteomics—have allowed us to discover drugs more systematically. The automation of biochemical binding assays in small chips called microarrays enables scientists to screen thousands of chemical compounds for their effectiveness against disease-causing proteins in a very short time. This high-throughput screening, as it is called, would not have been possible without years of serious investment in basic biotechnology research.

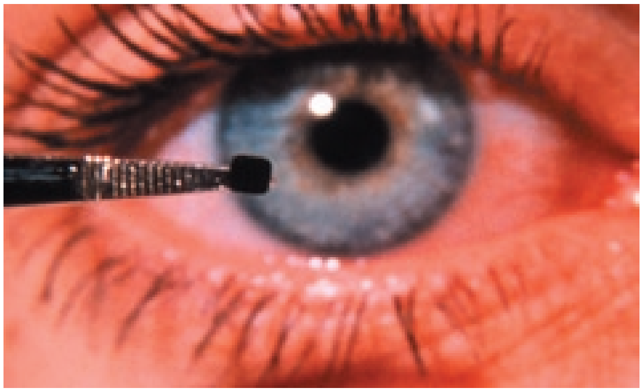
With microarray analysis, the activity of thousands of genes can be quickly measured. Many researchers are harnessing this tool to determine early gene activity when humans are infected with pathogens. Rapid, noninvasive screens are envisioned for the future, and they will be especially important for infections that require immediate treatment in order to reduce spread and save lives, such as infections resulting from a bioterrorist attack. Nanosensors are being developed from particles that are about 50,000 times smaller than the diameter of human hair to detect protein and gene expression in individual cells

Jay Laprete/AP/WWP

A patient undergoes gene therapy.

in the body, thus allowing the assessment of the health of cells at early stages of disease. The U.S. government is spending millions of dollars on nanosensors that can be placed in the blood of astronauts to monitor continuously for space radiation exposure.

Gene therapy, in which genes are delivered to specific diseased organs or tissues in the body to overcome metabolic deficiencies or other disease, is another area of great promise. The use of viruses to deliver genes has shown risks to human health, making trials with these viruses controversial. The convergence of nanotechnology with biotechnology will allow for safer gene delivery methods that are not based on viruses. Chemically synthesized nanoparticles that carry genes or therapeutics specifically to diseased cells are currently being tested in animals.


Markus/Matzel/Peter Arnold, Inc.

A micro device for a retina implant.

Biotechnology also plays an important role in preventing disease. Vaccines produced by recombinant DNA methods are generally safer than traditional vaccines because they contain isolated viral or bacterial proteins, as opposed to killed or weakened disease-causing agents. However, many citizens in developing nations do not have access to any vaccines, let alone ones derived from biotechnology. Currently, most vaccines require cold storage and professional administration through injection. Therefore, researchers are working on genetically engineered plants to deliver vaccines through food. The cost of plant-derived, orally administered hepatitis B vaccine is estimated to be one-sixth that of current hepatitis B vaccines. Enough antigen to immunize all babies in the world each year could be grown on approximately 80 hectares of land. However, as with Bt crops, there are general concerns about pharmaceutical crops because they may cross-pollinate with food crops in the field. It will be especially important to develop biosafety regimes that either use crops that do not cross-pollinate (for example, male sterile) or isolate the pharmaceutical crops (for example, in greenhouses).

THE CHALLENGES

It is striking that a number of the above examples relate to the Millennium Declaration, an agreement reached in 2000 by more than 170 countries to address poverty, economic development, and environmental preservation. Yet science and technology are seldom integrated with international programs focused on social and economic development. There has been significant progress in meeting some of the goals of the Millennium Declaration, such as reducing poverty, increasing primary education and gender equality, and lowering child mortality. However, less progress has been made in fighting global disease and improving environmental sustainability. These are challenges in which biotechnology can play a role.

Investments in science and technology by any nation will eventually bear economic fruit. However, investments to address the social, political, cultural, and ethical issues surrounding applications of biotechnology are equally important. There are good ways to foster open dialogue on such issues. We may never agree on some applications of biotechnology, such as therapeutic cloning, but dialogue leads to better understanding of each other's views and respect for our differences.

We should not minimize the potential health and environmental risks of biotechnology. We need to fund studies of these effects by independent organizations. Regulatory systems should be streamlined to be effective, efficient, and transparent. Currently, there are few incentives for the independent study of regulatory systems and policy.

Finally, we need to invest in technologies that are tailored toward helping developing countries and building capacity in their communities, for example, through education, training, and assistance with intellectual property issues. Biotechnology investments have primarily been made in developed countries and on products that will offer financial returns. This focus is natural for the private sector, but a broader agenda is needed. Governments and other organizations should step in and invest in research and development in developing countries and in products that can benefit those countries. Through increased awareness of the social context of biotechnology and commitments to resolve existing issues, one can envision a future in which biotechnology is harnessed responsibly to help all nations and all people. ■

The opinions expressed in this article do not necessarily reflect the views or policies of the U.S. government.

A CHEMICAL REACTION FOR BIOTECHNOLOGY:
The 2005 Nobel Prize

Cheryl Pellerin

A chemical reaction with great commercial potential in the pharmaceutical, biotechnology, and food industries caught the eyes of the Royal Swedish Academy of Sciences this year. The academy awarded the 2005 Nobel Prize in Chemistry to three scientists—Americans Robert Grubbs and Richard Schrock, and Frenchman Yves Chauvin—for developing a reaction that streamlines the development and industrial production of bioengineered drugs, plastics, and other materials in a way that makes such production less expensive and more environmentally friendly.

"Metathesis is ... an important weapon in the hunt for new pharmaceuticals for treating many of the world's major diseases," the Royal Swedish Academy of Sciences said in announcing the prize. The work by the Nobel Prize winners, it said, will aid researchers in their efforts to develop biotech medicines to address such illnesses as bacterial infections, hepatitis C, cancer, Alzheimer's disease, Down's syndrome, osteoporosis, arthritis, inflammation, fibrosis, and HIV/AIDS.

The reaction that Grubbs, Schrock, and Chauvin developed is called "olefin" metathesis. Olefin metathesis starts with a carbon chain that has a carbon-carbon double bond, which is ordinarily hard to break. A special catalyst—a substance that increases the reaction rate without being consumed in the process—that has a carbon-metal double bond is added. During the reaction, all the elements of the carbon chain and the catalyst combine to form a single ring. The ring then breaks apart, and a carbon atom from the carbon-metal double bond has changed places with a carbon atom from the carbon-carbon double bond. The resulting two substances are a new chemical compound and a modified catalyst. Synthesizing this new compound in any other way would have been very complicated and required many more reaction steps.

"The discovery of metathesis involved finding ways to break [the carbon-carbon] bonds and reform them very easily under very mild conditions," according to Charles Casey, professor of chemistry at the University of Wisconsin and past president of the American Chemical Society.

Many industrial biotechnology companies use olefin metathesis to produce candidates for drugs and other compounds. Metathesis can also be used to synthesize a naturally occurring substance, such as an insect hormone, and produce it in large quantity for use as a natural insecticide.

"There are all kinds of complex organic molecules that we'd love to synthesize," Casey said, "and these [metathesis reactions] are some of the most efficient ways to do it." ■

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