Global tectonics
Part 1

Medicinal bananas and bionic eyes

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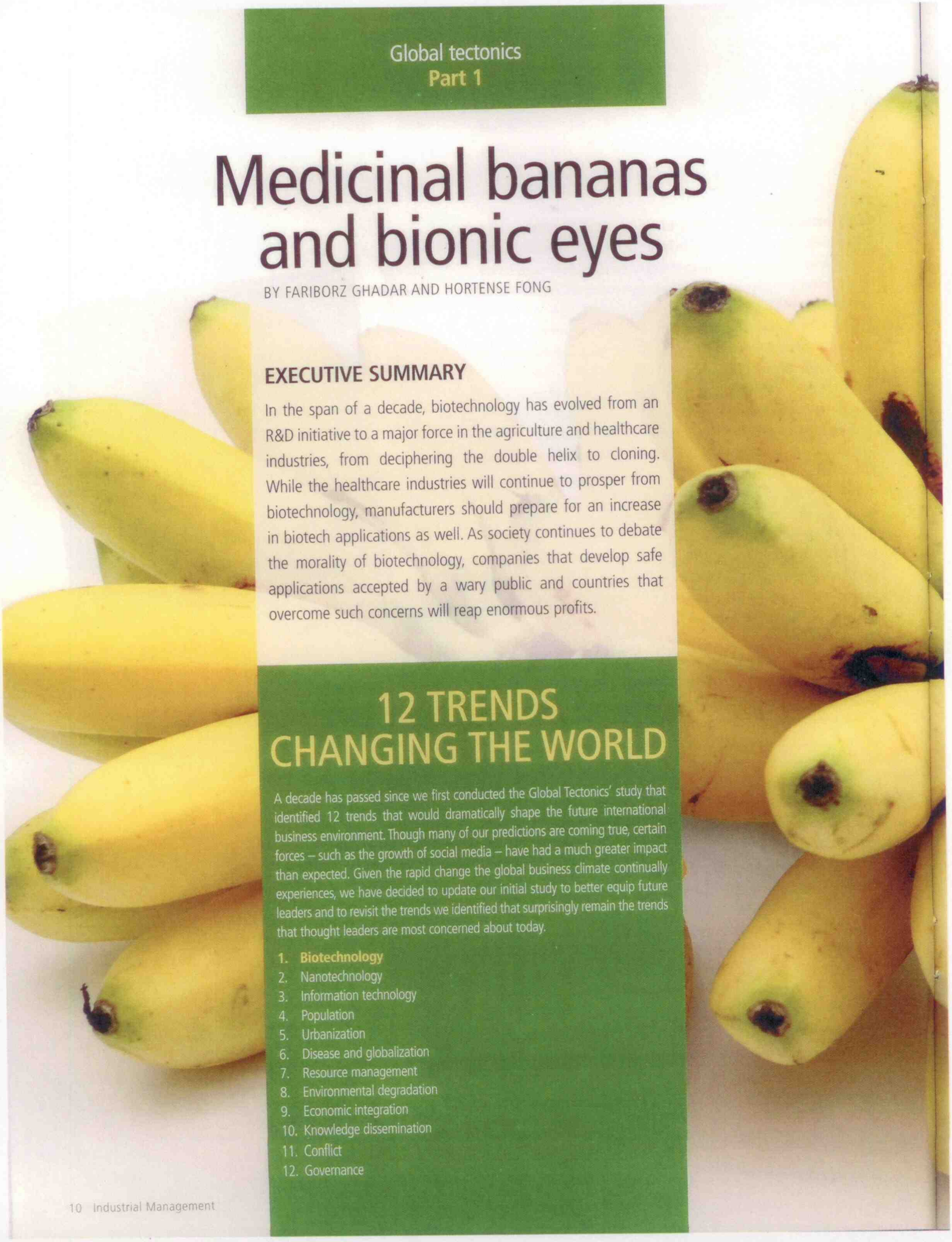


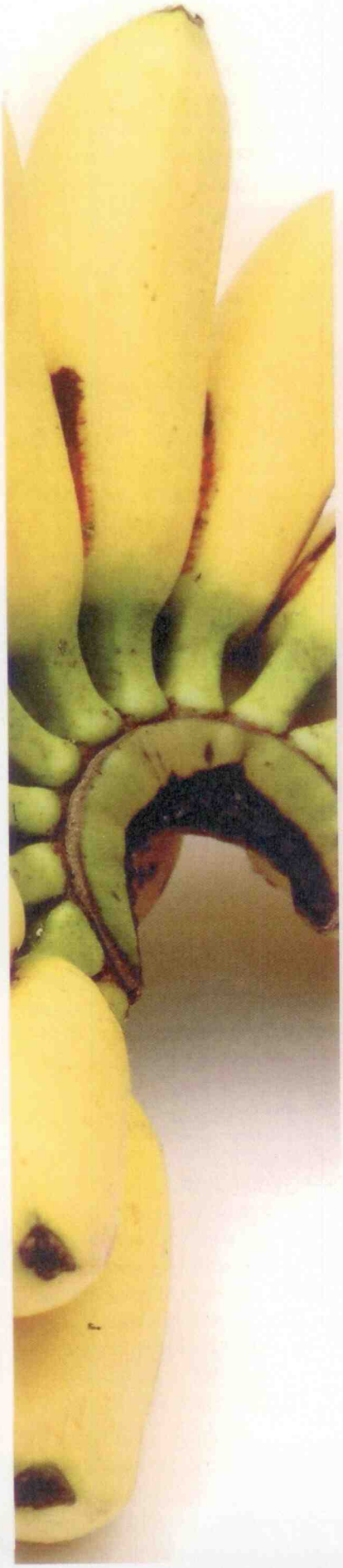
EXECUTIVE SUMMARY

In the span of a decade, biotechnology has evolved from an R&D initiative to a major force in the agriculture and healthcare industries, from deciphering the double helix to cloning. While the healthcare industries will continue to prosper from biotechnology, manufacturers should prepare for an increase in biotech applications as well. As society continues to debate the morality of biotechnology, companies that develop safe applications accepted by a wary public and countries that overcome such concerns will reap enormous profits.

12 TRENDS CHANGING THE WORLD

A decade has passed since we first conducted the Global Tectonics' study that identified 12 trends that would dramatically shape the future international business environment. Though many of our predictions are coming true, certain forces – such as the growth of social media – have had a much greater impact than expected. Given the rapid change the global business climate continually experiences, we have decided to update our initial study to better equip future leaders and to revisit the trends we identified that surprisingly remain the trends that thought leaders are most concerned about today.

1. **Biotechnology**
2. Nanotechnology
3. Information technology
4. Population
5. Urbanization
6. Disease and globalization
7. Resource management
8. Environmental degradation
9. Economic integration
10. Knowledge dissemination
11. Conflict
12. Governance



In February 2013, the U.S. Food and Drug Administration approved, for the first time, a bionic eye. The eye allows individuals with a blindness called retinitis pigmentosa to detect light and dark.

Then, in August 2013, two scientists, Rajesh Rao and Andrea Stocco, achieved noninvasive human brain-to-brain interfacing. Rao successfully controlled the hand movements of Stocco, who was all the way across the University of Washington's campus, with a brain signal transmitted via the Internet. In September 2013, Oregon Health & Science University reported the discovery of an AIDS vaccine candidate that appears to completely clear an AIDS-causing virus from the body.

Every day, mind-boggling breakthroughs are made in the realm of biotechnology. Biotechnology leverages a cell's manufacturing capabilities to put biological molecules, such as DNA and proteins, to use. The primary areas of biotech application are healthcare, food and agriculture, industry and the environment. Ernst & Young estimated the worldwide biotech industry revenue for publicly held companies to be $89.8 billion in 2012. Of that, the U.S. accounted for $63.7 billion. While most biotech developments still occur in the United States, more and more countries are investing in biotech, and the field soon will become global. Last year, *Scientific American* analyzed the biotech industry of 54 countries, 18 more countries than it took into consideration in 2009.

Because we now live in an era of biotechnology, companies will be made and destroyed with groundbreaking inventions. The trillion dollar question is: Where is biotechnology headed?

The current state

To answer this question, we should begin by analyzing where the technology is now.

Companies will be made and destroyed with groundbreaking inventions.

Currently, the pharmaceutical industry is perhaps the biggest beneficiary of biotech. When we look at the stock performances of enterprises that use biotech, the strongest performers are pharmaceutical companies, such as Gilead, Aegerion Pharmaceuticals Inc. and MannKind Corp.

Due to aging populations in developed countries and increased wealth and access to drugs in developing countries, global drug sales hit the $1 trillion mark last year for the first time in history. Genetically engineered drugs – drugs generated with living cells rather than with chemicals – account for an estimated 10 percent of the total global prescription drugs market.

Thus far, genetically engineered drugs target diseases such as various cancers, Alzheimer's, diabetes, multiple sclerosis, heart disease, AIDS and arthritis. Additionally, 650 new biotech drugs and vaccines targeting more than 100 diseases are under development. Large pharmaceutical companies, such as Pfizer and Merck, are investing in biosimilars, generic impersonations of biotech drugs, because of their profitability and the high sales growth of such drugs. Consumers benefit from this trend because they receive access to more drug choices and prices.

Agribio, or agricultural biotechnology, companies have benefitted from biotechnology the longest. Commercialization of biotech crops began in 1996, and as of 2012, genetically modified (GM) seeds are planted in 28 countries – 20 developing countries and eight industrial countries. In 2012, the U.S., Brazil, Argentina, Canada and India grew the most biotech crops. In contrast, the European Union continues to fight the use of GM crops through stringent regulations. Critics are concerned about the health and environmental effects of the crops as well as the concentration of supplying power by just a few corporations. In July 2013, Monsanto gave up trying to grow new

GM crops in Europe altogether. China also has faced major public opposition to GM crops.

The opposition to GM crops in Europe and China, however, is more than offset by their growth in many developing countries. According to the International Service for the Acquisition of Agri-Biotech Applications, "for the first time in 2012, developing countries planted more hectares than industrial countries." This trend is likely to continue because the benefits of biotech crops strongly appeal to developing countries. Biotech crops require less land to grow, are often resistant to disease and drought, and frequently reduce pesticide use and carbon dioxide emissions. Consequently, more than 90 percent of the 17.3 million farmers who grew biotech crops in 2012 were small, resource-poor farmers in developing countries. The global market value of biotech crops in 2012 was just short of $15 billion. Plans to introduce biotech crops to various Asian and African countries are already in the pipeline.

Besides crops, scientists also are altering the genetic sequences of animals. A genetically engineered salmon that grows twice as fast as regular salmon is in the FDA approval process. Scientists also have genetically engineered pigs, goats and cattle for various purposes. For example, the Enviropig digests and processes phosphorous better, making it more environmentally friendly.

Industrial and environmental biotech are the newest applications of biotechnology. Industrial biotech aims to create more sustainable manufacturing processes. For example, "green plastics" do not use petroleum in their production and instead use renewable crops. Compared to traditional manufacturing methods, industrial biotech methods produce a lower carbon footprint, create less waste and increase yields, resulting in lower costs. Since the turn of the century, the U.S. and the EU have invested billions in bio-based industrial research. In 2011, DuPont acquired global enzyme leader Danisco for $6.3 billion, making DuPont a leader in industrial biotechnology.

For decades, petrochemical companies, such as BP, Shell, DuPont and ExxonMobil, have invested heavily in synthetic biology research to try to develop a renewable fuel source. ExxonMobil plans to invest more than $300 million in Synthetic Genomics Inc. in hopes of developing an algae-based biofuel.

Like all progress in human history, there will be setbacks. Until disaster struck in 2012, Amyris was touted as the company that would hoist up the biofuels industry and transform the energy industry. Using genetically engineered yeast, Amyris turns sugar into the liquid fuel farnesene, which can act as a replacement for petroleum-based diesel. Not only does farnesene cut the amount of pollutants from vehicle exhaust pipes, but it is also a renewable resource, unlike petroleum.

The mistake Amyris made was in promising to produce a certain amount of farnesene in a given amount of time. Due to technical problems in trying to scale up production, the company failed to meet its 2012 deadline and its stock price, which was once as high as $33 a share, plummeted to $1.45 a share.

Going hand in hand with industrial biotech, environmental biotech aims to clean up existing waste. An example of such technology is the use of fungus in cleaning up toxic metals from water polluted by coal mines.

25 years down the road

Biotechnology, a global tectonic, is shifting the foundations of healthcare, agriculture, business and government. The discoveries made in the field could solve many global food, health and environmental problems, thus corporations and governments would be wise to keep their eyes and ears open to the developments in the field. Who will be the main biotechnology players 15, 20, 25 years from now?

The discoveries made in the field could solve many global food, health and environmental problems.

First, healthcare companies, particularly pharmaceutical companies, will continue to prosper as the global population ages and developing nations grow wealthier. According to the United Nations Population Fund, the older population "is growing at a faster rate than the total population in almost all regions of the world." An aging population means more drug purchases. Furthermore, market research firm Evaluate Pharma projects that, in 2014, 50 of the top 100 drugs will have been genetically engineered. As regulation and regulatory agencies catch up to the technological advancements, an unprecedented number of drugs and medical devices will be approved.

The real boom in biotech pharmaceuticals in the coming decades will occur in developing countries. The drug markets in developing countries are growing tremendously because of increased wealth and access to medicine, along with shifting disease patterns. China's pharmaceutical market, worth $108 billion in 2005, is estimated to grow to $900 billion by 2020. Additionally, the lower costs needed to produce a drug in developing countries make them an attractive investment.

In 25 years, we likely will be living in an era of personalized medicine. With the completion of the Human Genome Project in 2003, the decreased cost of personal genetic studies and an ever-growing genetic database, we are closer to an era of healthcare tailored to one's genetic makeup. Already, biotech has developed drugs for rare diseases previously thought incurable. Through personalized medicine, patients will receive the benefits of pharmacogenomics – the personalization of drugs through the matching of specific gene variations with responses to specific medications – and of gene therapy – the replacement of disease-causing genetic mutations with healthy genes.

If we focus less on the bio and more on the tech, we enter into a more

futuristic realm. Though we still do not know why we age, we have ironically discovered technologies that may allow man to live forever.

Consider the following facts: On May 8, 2013, George Laskowsky, chief technical officer of Thinker Thing, a Chilean tech startup, created the first ever real object with his mind. With an electroencephalography (EEG) headset on, Laskowsky was given shapes to choose from and, based on his levels of boredom or excitement picked up by the headset, the arm of a mythical creature was designed and then built by a 3-D printer. Now, recall the human brain-to-brain interface between Rao and Stocco, during which a brain wave was sent across the Internet. Who's to say that we will not be able one day to record all of the decisions a person would make in varying situations, download them onto a hard drive, and then upload the data to a robot?

Consequently, human-machine interfaces will be the next big area of biotech research and application. Already, we have the technology to control wheelchairs and cars with our minds. In 2009, Toyota and research lab RIKEN developed a wheelchair that can be controlled with brainwaves through an EEG cap. This idea was brought one step further with thought-controlled cars. Finally, bionic limbs are growing more and more advanced. By splicing a prosthetic to the wearer's residual nerves in the partial limb, scientists have been able to create a sense of "touch."

3-D printing also will contribute greatly to the area of prosthetics. Researchers at Princeton already have built a bionic ear by feeding a 3-D printer with biological and nanoelectronic inks. What is even more incredible is that the bionic ear can detect frequencies a million times higher than a normal ear can. In 25 years, 3-D printing will have solved the geometric complexities tissue engineers face today. Researchers will be able to create organs with blood vessels, such as livers, kidneys and hearts.

Despite Europe and China's current opposition, GM crops will continue to be grown, consumed as food and used in industry. China's citizens likely will come around as they learn more about GM crops and realize the large presence of GM foods in U.S. diets.

In 2010, the U.N.'s Food and Agriculture Organization predicted that global agricultural output must increase 70 percent by 2050 to feed the world's anticipated population of 9 billion. GM crops are one solution to the impending food problem. The fact that more than 90 percent of GM crop farmers are small resource-poor farmers in developing countries indicates a growing dependence on GM seeds. Many farmers rely on the drought-resistant, pest-resistant attributes of GM crops to feed their families and their country. Because of this growing dependence, governments likely will create regulations to prevent crop misuse and the corporate exploitation of farmers.

To increase the use of GM crops, companies must prove to consumers that their products are safe to eat and are not environmentally hazardous. The GM crop industry may turn to golden rice, which helps the body produce vitamin A, to prove the benefits of biotech. While most genetically engineered crops are designed to benefit farmers, golden rice was designed to benefit consumers, preventing blindness and death. (For more details, see the sidebar on Page 13.) The scientists who created golden rice, Ingo Potrykus and Peter Beyer, licensed their patent rights to Syngenta under the condition that the technology would be given to poor farmers in the developing world for free.

In 25 years, biofortified foods – foods nutritionally enhanced through genetic modification – will exist in diets throughout the world, decreasing nutrition-related diseases. We also will have foods that act as vaccines for diseases like hepatitis B and cholera; in fact, such a banana already exists. One of the main concerns about GM crops is their impact on biodiversity, and while some plants will go extinct as a result, new species also will develop.

With the tasting of the first piece of lab-grown meat in August 2013, the market of scientifically produced meats has opened up to consideration. We will see genetically engineered animal products in supermarkets in the decades to come. Thus far, no substantial scientific or legal arguments have been made against the genetically modified salmon seeking FDA approval.

Human-machine interfaces will be the next big area of biotech research and application.

Finally, industrial and environmental biotech companies will continue to snowball and grow. In 25 years, our manufacturing processes will be cleaner and cheaper than they are today. With 3-D printers and nanocapabilities that let us build things from individual atoms and molecules, we will be able to build essentially anything we can imagine. Consultants at Smithers Rapra, a global leader in rubber, plastics, polymer and composites testing and consulting services, predict that the global industrial biotechnology market will grow at around 20 percent a year between now and 2020.

Since the use of synthetic biology in industrial processes will result in a smaller carbon footprint, less industrial waste and higher yields, urban areas in developing countries likely will invest heavily in this technology. Rapid industrialization has led to water and air pollution, and rapidly growing urban populations place a strain on infrastructure. The countries that succeed in developing robotics and clean manufacturing will be the world's future manufacturers.

Perfect cluster conditions

Genomic medicine is projected to generate $350 billion worth of economic activity and millions of jobs. The advancements made in bioIT, 3-D printing, nanotechnology and robotics can be applied to biotechnology,

Golden rice: Fact vs. fiction

In August 2013, a torrent of news was released about the destruction of an experimental field of genetically modified golden rice in the Philippines. News networks reported that hundreds of angry farmers stormed the fields and ripped the golden rice plants out of the ground. The attackers claimed that multinational corporations are trying to take control of the country's rice seed industry and thereby take advantage of the Philippines. They further justified their actions by stating that golden rice puts the environment and the health of the public at risk. Greenpeace corroborated the attackers' health concern claim.

Upon hearing the news, Mark Lynas, a journalist and environmental activist, rushed to the scene to find out the facts of the attack. First, he discovered that the trial was completely funded by public sector groups, including the Philippine Rice Research Institute and the International Rice Research Institute. There was no private corporate involvement. Contingent upon successful field trials, golden rice seeds would then be given to farmers for free – without technology costs or royalties. He further learned from the project's senior manager, Raul Boncodin, that the attackers were activists and not farmers. Although farmers were present, they only stood on the side and watched. Local farm leaders were shocked and saddened by the destruction of the rice, reported the news site Slate.

Scientists all over the world also were saddened by the news because they knew that golden rice can prevent millions of deaths each year. Golden rice produces beta-carotene, the precursor of vitamin A, a deficiency of which can lead to blindness and death. Every year, a quarter-million to a half-million children become blind and 2 million people die due to a lack of vitamin A. Thousands of scientists signed a petition in support of golden rice and some expressed their frustration with the bundling of genetically modified crops and politics.

According to *Food Safety News*, Dr. Andrew Bartholomaeus, a toxicology expert at the University of Canberra, wrote, "As a toxicologist with 30 years of experience in food, cosmetics, pesticides and pharmaceuticals, I know the claims about risks of GM food are disingenuous and reflect a political rather than moral position. The lives of millions are at risk from the mindless actions of ill-informed anti-biotech activists."

creating the perfect recipe for a world-changing biotech cluster. Not only will the cluster create many lifesaving drugs and medical products, but it also will bring capital and jobs to the country that hosts it. The window of opportunity for hosting will be open only for so long, and the nation that controls the cluster will gain a significant head start in the field of biotechnology.

It is uncertain why clusters form where they do, but there are two steps a country can take to increase the likelihood of building a biotech cluster. The first is to build a genomic database because genomic medicine is highly data driven. The database should include information in areas such as disease outbreaks, family history and environmental exposures. Plunkett Research predicts that advances in systems biology – the use of molecular diagnostics, advanced computers and genetic databases – may lead to faster and cheaper drug development. Researchers now use genetic databases of virus sequences to try to predict which virus will cause the next epidemic.

The second step a country can take to kick-start a cluster's development is to offer a cluster-conducive environment through legislation and capital. For example, government can offer tax incentives and can build labs with equipment that normally would cost too much for a small enterprise to buy. Brazil, Singapore, China and India have invested heavily in biotechnology. China, for example, has built about 10 large science parks and many smaller ones, as well as provided tax benefits and grants. The government also has invested in young biotech companies and subsidized the costs of facilities. Brazil plans to reduce bureaucratic restrictions on research and development and incentivize academic and industrial collaboration.

As recommended during *Industrial Management's* first Global Tectonics article on biotechnology in 2005, "With so many possibilities and the expensive nature of R&D, countries would do well to concentrate their research dollars on developing areas of niche expertise and build critical alliances with other countries to share knowledge, resources and risk." In particular, "developed countries would do well to establish partnerships with research centers in poorer places as part of their foreign assistance packages." The developed country benefits with lower costs and the developing country benefits from the capital investment and knowledge-exchange.

Besides government, companies can support cluster growth by working with other companies. Pfizer has shared software for biotech drug research with some of its competitors, such as GlaxoSmithKline and Roche, in an effort to overcome technical obstacles. Pharmaceutical companies recognize the scientific benefits of information sharing.

Catching up to the speed of innovation

Every so often, we read headlines such as "Researchers grow human brains in a lab" and "Hello mothers, hello father," that leave us curious and terrified. The first article is about the use of stem cells to grow brains for research purposes. The second is about the combination of DNA from two women and one man to create a baby free of mitochondrial diseases. Biotech is a field filled with controversial subjects, and our typical response is to fight against ideas we find unnatural.

Biotech, however, has been used for centuries in making wine, beer and cheese, and in crossbreeding plants. The invention of the microscope gave us increased understanding of the cell and sped up innovation. But neither regulation nor society has caught up with the speed of invention in terms of health, legal, moral and religious ramifications. We do not yet know the long-term effects biotech will have on our health and the environment. Issues related to privacy and insurance practices are bound to arise.

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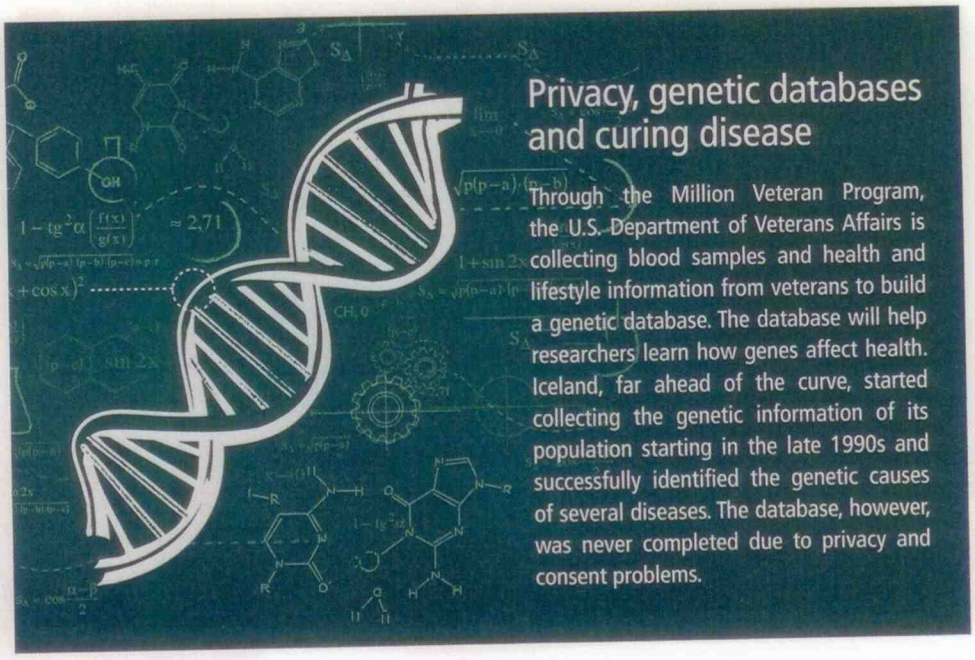
However, biotechnology holds great promise in mitigating a number of global problems, including disease, pollution and hunger, if implemented properly and with appropriate risk management. To develop public trust in GM crops, governments likely will implement regulations to control misuse, and corporations must develop transparency protocols. Biotechnology will transform our lives during the next 25 years. To guide its development, biotech companies will work together and governments will support biotechnology's growth. ❖



Privacy, genetic databases and curing disease

Through the Million Veteran Program, the U.S. Department of Veterans Affairs is collecting blood samples and health and lifestyle information from veterans to build a genetic database. The database will help researchers learn how genes affect health. Iceland, far ahead of the curve, started collecting the genetic information of its population starting in the late 1990s and successfully identified the genetic causes of several diseases. The database, however, was never completed due to privacy and consent problems.