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HARVESTING THE FRUITS OF GENETICS

We have entered the age of the gene. Watson and Crick's discovery of the structure of DNA in the last century and mapping the human and other genomes in this one have provided the keys to applied genetics. We have spent much of the last 30 years deciphering raw genetic data and converting it into information and knowledge. Today, that conversion accounts for almost one fifth of the U.S. gross domestic product (GDP).

Applications are everywhere, including health, behavior, forensics, livestock, fisheries, pest management, crops, food, forestry, microorganisms, chemical engineering, environmental engineering, materials, manufacturing, energy production, and information technology. Genetics improves on nature, enhancing human health, economic performance, and the environment. It alleviates arthritis, creates new foods such as the beetato, and made history of many crop pests such as the fungal rice blast. It creates new techniques, approaches, and even organisms, such as the toxagen, for breaking down many hazardous wastes. The table below highlights some of the important capabilities and consequences that genetics has brought to business and society over the last 35 years.

Application Area	Capability from Genetics	Examples of Consequences
Health	Identify, treat, and prevent genetic diseases and disorders	Elimination of almost 2,000 single gene diseases, such Huntington's Chorea; 50% reduction in diseases with genetic predispositions, including dozens of cancers
Behavior	Understand chemical, physiological, and genetic bases of human behavior	85% reduction of schizophrenia; overhaul of education curricula to tailor learning based on individual genetic/cognitive profiles

2025

Identification/ forensics	Unprecedented accuracy contributes to a decline in many crimes, including kidnaping and fraud	27% reduction in auto theft attributed to deoxyribonucleic acid (DNA) security locks
Livestock	Produce transgenic custom-designed livestock by calling up and obtaining genes from databases along the lines of cookbook recipes	Revival of the once-flagging pork industry with the advent of 37 popular varieties such as the ultra-lean "Pig-No-More"
Fisheries	Create and combine transgenic fish with different tastes and textures, doubling production from last century	Overwhelmed natural fisheries supplemented with aquafarms raising hearty new strains such as the "octosquid"
Pest management	Target specific pest species and behavior patterns and genetically engineer resistance to pests in crops	Crop loss due to pests reduced 63% in United States; elimination of Lyme disease and elephantiasis by genetic alteration of the vectors
Crops	Increase yields, growth rates, resistance to disease, longevity, and reduce the need for water and fertilizer	Irish potatoes, Kansas wheat, and Japanese rice continue to set yield records due to elimination of intermittent blights
Food	Add more foods to the human diet and customize foods to particular needs and requirements, such as tastes, preparation, and preservation	The number of foods making up the bulk (90%) of the human diet increases from 6 to 37; all 11 principal grains are dietarily balanced for protein.
Forestry	Develop superior and faster-growing strains through disease resistance, herbicide resistance, and artificial seeds	Worldwide tree/forest coverage doubles
Microorganisms	Widespread use in medicine, food and agriculture, chemicals, mining, waste management, and environmental cleanup	Use in bioreactors to produce commodity and specialty chemicals, medicines, and foods
Chemical engineering	Use databases of molecules and chemical reactions in more biologized industrial processes	Random hit-or-miss approach gives way to rational chemical design, contributing to the industry's 54% reduction in design time
Environmental engineering	Monitor, remediate, and enhance the environment, such as breaking down solid and toxic wastes to restore degraded ecosystems	Bioremediation now used as the primary cleanup mechanism in 40% of hazardous waste sites in the United States

Materials	Manipulate materials at the molecular or atomic level so manufacturers can customize materials for highly specific functions	35% of people in affluent nations use some form of biosensor to monitor their health
Manufacturing	Use more biological processes at smaller scales, approaching the nanoscale	Bioreactors in widespread use in the nondurable goods sector or affluent nation manufacturing
Energy	Expand the use of biomass and aid enhanced oil recovery	Conversion efficiency of biomass could triple with recent feedstock break-through
Information technology	Apply genetic algorithms in software programming	Neural network computers mimic the intelligence level of chimpanzees

For convenience, the term genetics, as used in this book, incorporates applied genetics, aspects of molecular biology, and biotechnology. Genetics is the key enabling technology of the 21st century, rivaling information technology, materials technology, and energy technology in importance. The effects of all of the enabling technologies are far-reaching across business and society, but advances in genetics in particular are fundamental to many science and technology areas and societal functions, including health and medicine, food and agriculture, nanotechnology, and manufacturing. Unlocking the secrets of genetics has required understanding the underlying physics, biophysics, and chemistry of DNA, such as how and why it conducts electricity.

Through genetics, we understand and manipulate:

- the structure and functions of complex biological molecules, particularly proteins, and employ rational design for synthesizing complex molecular assemblies and cells;
- the functions of many tissues, organs, and systems;
- gene expression to influence an organism's development, growth, and aging; and
- novel traits and novel organisms.

Rising public interest in genetics is tied to the growing realization that humanity is capable of directly shaping our and other species' evolution. We no longer have to wait for nature's relatively slow natural selection. Genetics brings the capability of speeding and redirecting evolution along paths of our choice. Adaptations that once took generations can now be made in months or years through genetic manipulation. For example, it was inevitable that rare genetic conditions such as autosomal dominant polycystic kidney disease, in which fluid-filled cysts form in the kidneys and in half the cases ultimately required dialysis or transplant, would be eliminated through natural selection in hundreds of years. With genetic therapy, however, that process was accelerated and accomplished in just 15 years from the first therapies to the ultimately successful one.

We not only use more biological and natural processes today, but we improve on them. Many biosynthetics are more suitable for human purposes than their natural analogs. For example, peptide nucleic acids (PNAs) that are used to block the message of colon cancer genes from being carried out can actually improve natural antibodies. Indeed with a-life (artificial life), we are rethinking the definition of life itself (see box below).

Artificial life enhances our understanding of natural life

Artificial life is devoted to the creation and study of lifelike organisms and systems built by humans. Computer-generated simulations synthesize evolutionary processes. The strong a-life school argues that these simulations are living things whose essence is information embodied in machines or robots. They point to computer viruses, which evolve strategies to prolong their existence, and suggest long-term issues of our responsibilities to new life forms.

The so-called weak a-life school avoids the living/nonliving question and focuses on their lessons for our and other species' evolution. Practical applications include the growing capability to evolve, rather than design, new products ranging from pharmaceuticals to robots. For example, thousands of tiny robots without advanced programming are simply set on a task. Those who perform best naturally are selected. After many iterations, a best candidate emerges, and the reasons why are probed and applied for future generations.

Harvard's first doctorate in a-life was granted in 2015.

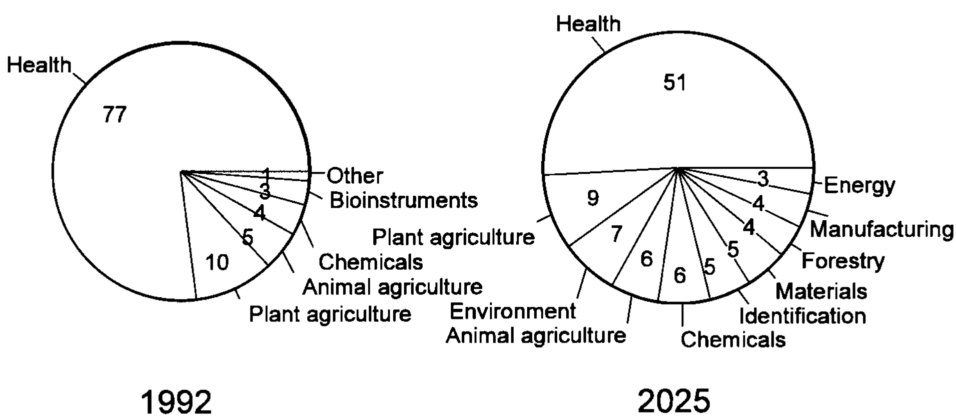
This power has inspired a profound global debate about how genetics should and should not be used. Net forums, electronic town meetings, newspapers, and journals are filled with discussions of what behavior society should encourage, given our growing capability to influence it.

We are still evolving a philosophy of how to incorporate genetics into our world view. Over the years, the nature/nurture debate often split along ideological lines, with conservatives tending to favor the gene-determinism notion, and the liberals favoring environmental determinism. Today, the ideological slant is largely relegated to the fringes, as consensus is growing that the ratio between gene determinism (nature) and environmental determinism (nurture) slightly favors the former—roughly 60% to 40%. A side effect of the debate is a great increase in the research demand for twins, as subjects for experiments aimed at proving the case of one side or the other.

On the economic front, genetics is rewarding those who invest in it for the long haul. It has been an industry for patient capital. Its spread over so many industries has made it an increasingly important factor of the national and global economy. There are several boom regions: San Francisco with its large number of genetics companies and its proximity to Silicon Valley; Boston with its universities; and Houston, which has diversified away from oil and energy to health-related genetics. There has also been a niche industry based in Salt Lake City that has grown up around the reliable genealogies kept by Mormons.

Genetics is not a typical industry, in that it is not measured as a separate entity. It is a part of, or embedded in, so many industries that government statisticians do not attempt such a measure. Economists' best guesses are that genetics accounts for about 20% of gross domestic product, or roughly $2 trillion in 2024. The only segment of the economy contributing more is information technology, which is estimated at 40% to 53% of GDP.

R&D Spending on Genetics: 1992, 2025



Genetic history: a new national pastime?

Newsgroups, videos, books, videoconferences, and courses have sprung around genetic history. Many people are interested in tracing their family's roots genetically. Thousands have gone so far as to obtain genetic samples of ancestors—even when it entails exhuming bodies.

A second thread is interest in the genetic history of other species. The restoration of the Mastodon in 2014 sparked interest in species restoration. The classic film *Jurassic Park* enjoyed a huge revival that year, especially when the interactive element was added to it. Plans to revive other species are under consideration. Politicians and the scientists involved are proceeding cautiously, but surely species restoration is an industry poised to explode in the 2030s.

Last century's emphases on using genetics for improving human health and battling human disease are being supplemented with more exotic applications, e.g., manufacturing and materials, human enhancement, energy, environmental engineering, and species restoration and management. The food and agriculture industries, for example, have been steadily expanding their use of genetics for decades. Advances have often come from applying what seemed like isolated breakthroughs into a systems framework. In 2020, for example, researchers in Egypt working on eradicating a species of locust engineered a microorganism that later proved useful in converting crop wastes into biomass energy.

Some false paths in genetics

Genetics involves a complex system of predispositions, biochemistry, and environmental factors. As a result, there were many wrong turns on the road to prosperity. There were many Interferons—a 1980s drug once hailed as a cure-all that ended up with limited use in cancer therapy. It turns out that finding the gene for a disease or disorder is one thing, and devising a safe, affordable test for it is quite another.

Lots of the failures came from petty schemes. The Burma government, for example, spent lots of money trying to develop and breed in a gene for submissiveness to authority, without success.

Some companies took a limited view of genetics as a manufacturing tool using recombinant DNA for making proteins. Their products often failed, as the synthetic proteins were difficult to administer as therapeutics, because they were big and fragile.

And, of course, there is the now infamous attempt to mimic human brain cells by trying to induce them to grow on a silicon chip.

Researchers in these early days often did not understand the underlying principles behind a purported breakthrough. Many discoveries or processes had to be worked out by trial and error. Gene therapy, for example, began with *ex vivo* injections into cells and their subsequent replacements—a process that had to be repeated as the original cells died off. It took another decade to work out the retroviral approach widely used today that is far less invasive, and much less expensive.

The pace of genetics developments

The speed at which developments have occurred has depended largely on four factors:

- the pace of technical progress (development of new technologies, such as for automating genome mapping and sequencing)
- the extent of unexpected complexities (for instance, changing a gene or two can alter more than just one function)
- economic considerations (costs, for example, including gene therapy treatments in standard insurance packages)
- social and ethical issues (for example, social resistance to genetic testing as a condition of employment)

Many times, progress in a particular area stalled and then a new finding reinvigorated the R&D community. Often, old ideas were rejuvenated as the supporting knowledge base that developed in the interim led to new insights.

Engineered biomass, for example, lay largely dormant for about two decades until the Cropagen treatment came along in 2020.

Genetics knowledge and capabilities are largely in the hands of World 1 nations, which have the knowledge base and infrastructure required to support the R&D fundamental to success in genetics. World 1 nations have so far realized their greatest share of profits from their home markets. Over the last 10 years, that gap has begun to narrow as burgeoning middle and destitute nation markets are tapped through alliance, acquisition, and licensing arrangements. Strategies for affluent markets differ considerably from those in Worlds 2 and 3. Customized genetic therapies, which are increasingly common in World 1, have barely found a market in the middle nations. Similarly, in food and agriculture, genetics has greatly increased the diversity of affluent nation markets, while its primary effect in middle-income and especially in destitute nations has been to increase the supply of staples.

THE WORLD 1 NATIONS—GENETICS: A LEADING KNOWLEDGE INDUSTRY

Genetics has been dominated by the affluent nations. It is knowledge work in every sense of the term. The technological and intellectual infrastructure required to be a major player has kept the affluent nations ahead of World 2 societies who are eager to catch up. The footsteps of nations like Thailand and India are getting louder, especially in plant genetics.

Health and food have been the big drivers of genetics in World 1. The United States sells more genetics-related products and services than anyone else, with Japan close behind. Europe continues to lag. The United States has been particularly strong in health and food, whereas Japan has been strong in environmental applications. Europe has been hampered by social objections to genetics. Last century, Germany passed one of the world's most comprehensive laws designed to regulate the use of recombinant organisms in laboratories and industry. This handcuffed genetics developments throughout Europe due to Germany's central role in the EC. Despite the removal of these restraints by 2009, it has proven difficult to catch up.

Cooperation among affluent nations regarding genetics has been strong. The cooperation has its origins in the various international genome projects. It arose largely from practical necessity, given the rapid dissemination of new findings since the establishment of the GlobeNet last century. The difficulty in keeping secrets and the growing web of global alliances made it more sensible to accommodate rather than fight. Of course, cooperation worked because the commercial interests were carefully negotiated. It continues with the move toward global management and regulation. The International

Organization for Standardization (ISO) 46000 standards for genetics were a capstone achievement in 2024.

A U.S. CASE STUDY: Still the leader in genetics

The U.S. R&D and science and technology base, supplemented with talent drawn from a global labor pool, remains first class. The large internal market for health spending was the early driver for genetics, but the emerging markets of the middle nations have become increasingly important. At the same time, these World 2 nations are becoming stronger competitors in the genetics marketplace.

Human health continues to drive genetics

Genetics is enabling health professionals to identify, treat, and prevent genetic diseases and disorders. The centrality of genetics in diagnosis and treatment is clear, particularly in early diagnosis, in testing for predispositions, and in therapies. There are thousands of diagnostic procedures and treatments for genetic conditions.

Diagnostics detect specific diseases such as Down's syndrome and behavioral predispositions such as depression. Treatments included gene-based pharmaceuticals, such as those using antisense DNA to block the body's process of transmitting genetic instructions for a disease process. In preventive therapies, harmful genes are removed, turned off, or blocked. In some cases, healthy replacement genes are directly inserted into fetuses, via injection, inhalation, retroviruses, and sometimes pills, to alter traits and prevent diseases. For those already sick or impaired, genetic therapies using similar techniques have an outstanding record of reversing or correcting conditions.

The evolution of health-related genetics

- Identifying single-gene diseases and disorders
- Identifying multiple-gene predispositions
- Developing tests for genetics flaws
- Mapping biochemical pathways and developing therapies and treatments
- Developing preventive methods
- Enhancement

Our understanding of genetic diseases is along a continuum. Three areas are under particularly good control. The best understood are the single-locus genes that are strictly heritable from parents. Next are the genes associated with the transition of normal cells to cancerous ones. This is particularly important because most cancer patients do not die of their initial tumors, but from metastasizing cells that manage to escape the tumor and grow into secondary tumors in other organs. The breakthrough was finding and developing a monoclonal antibody (MAB) treatment for the genes that code for cellular adhesion proteins central to a metastasis. A third area of solid understanding is in autoimmune disease genes. Defects in these genes cause the immune system to destroy healthy cells to which they accidentally bind. Understanding of these mechanisms continues to grow, and here again, MAB treatments are proving effective.

Although genetics will be the greatest driver of advances in human health this century, it is not a panacea for all human health problems. Health is a complex of interacting systems. The benefits of genetics are also weighted more heavily to future generations, because prevention is such an important component. Genetic therapies are ameliorating conditions in middle-aged and older Americans today that will not even exist in future generations. For example, psoriasis has been brought under control for many via gene therapy. The recent development of an effective prenatal diagnosis, however, means that no future child need be born with the condition.

Genetics and reproduction

Some of the uses of genetics in reproduction are:

- in utero testing for traits and predispositions
- in utero alteration of traits through genetic manipulation, including baldness, schizophrenia, diabetes, sexual predisposition, and some mental abilities
- gene replacement therapy
- intrauterine karyotyping by examining fetal cells in maternal blood
- replacement of defective fetal proteins in utero
- DNA-mediated gene transfer using retroviral vectors, including during in vitro fertilization
- enhancement therapy, such as for height; elucidation of the mechanisms for nearly all genetic diseases and the onset of most cancers and all autoimmune diseases
- automated genetic diagnosis; genetic testing of embryos for traits; DNA probes for diagnosis; identification of the genetic locus for every disease-related gene

First step: single-gene diseases and disorders

Almost half of the approximately 4,400 known genetically-based diseases and disorders (up from 4,000 last century)—caused by one or more genes—are now under effective control, that is, there is a preventive measure or therapy available. All human diseases and disorders have had their linkages, where they exist, to the human genome identified. The mapping of the genome has driven a move to more customized health care by enabling advances in diagnosis, prevention, treatment, and enhancement. Some diseases and disorders have been wiped out, in cases where access to care was widespread and affordable. Many rare diseases have been eliminated, as they were easier targets for researchers. More mainstream diseases such as cystic fibrosis and eczema, and conditions such as near-sightedness, have practically disappeared as well.

In some cases, a large percentage, but not all, of a disease's occurrences have been eliminated. Many Alzheimer's disease cases are linked to a single errant gene and can be repaired with gene therapy. Fifteen percent of arthritis cases have been eliminated over the last 15 years with genetic diagnostics and therapy. Researchers project that another 15% to 25% of arthritis cases can also be eliminated if the testing is more widely disseminated and the cost of the treatment is reduced, or insurance coverage of it expanded. Some cases, however, still elude researchers. Similarly, a small percentage of breast cancer cases have long been eliminated while others persist.

The mysterious role of "junk DNA"

As the human genome project found, most DNA does not code for genes. Of the three billion chemical bases that make up human DNA, only 3% code for proteins. The role of the rest of the 97% has long mystified researchers, but the pieces of the puzzle are slowly falling into place.

Experiments in which some of the junk DNA is removed, have shown that it plays a role in normal genome function, because complications develop in its absence. For instance, it appears to mediate and control gene expression, such as when and where they are turned on and off.

Some junk sequences, such as the Alu sequence, have remained the same for millions of years. Natural selection would preserve such a sequence this long only if it served some important function. Still, the details of its role and how it works remain to be discovered.

Sometimes, even if a single gene is found to be responsible for a disease or disorder, there can be many ways it can mutate. For instance, one study found 23 types of mutations that could occur on a gene linked to Type II diabetes. Similarly, although cancers arise from genetic regulation of cell growth going awry, they can be initiated many ways—from viruses, radiation, environmental poisons, defective genes, or combinations of these factors. Another common set of mutations are the repeats, which are like stammers in the genetic message. Triplet repeats, for example, have turned up in many places, ranging from cerebrospinal ataxia and speech impediments. And some disease genes have been identified without an effective treatment coming with it, as is the case with Lou Gehrig's disease.

The economic impacts of these findings have been significant. In the case of osteoporosis, for example, fixing a single gene that significantly increased the risk of getting the disease later in life saved almost $1 billion a year in the 1990s and 2000s—when $10 billion a year in medical bills were attributed to it. Of course, the procedure for fixing the gene cost money too, but far less than the care required when an elderly woman fell and broke her hip. A positive social impact was the addition of an average of three months to women's life expectancy. It has also improved the quality of life of older women, enabling them to stay active in political, social, community, and business life longer.

Identifying genetic predispositions

The chemical, physiological, and genetic bases of human behavior are generally understood. Direct, targeted interventions for disease control and individual human enhancement are commonplace. Brain-mind manipulation technologies to control or influence emotions, learning, sensory acuity, memory, and other psychological states are available and in widespread use. The incidence and severity of conditions, such as hyperactivity in children, have been substantially reduced. Each sensory activity can now be enhanced by genetic treatments where necessary. Near-sightedness, poor senses of taste and smell, and some forms of deafness can now be prevented or treated genetically, assuming that the appropriate prenatal diagnostics are performed.

Genetic predispositions have been identified for thousands of diseases, disorders, and behaviors. Some genes have been found to be responsible for a variety of disorders, such as the P16 and P53 genes for many cancers. P16s are housekeeping genes, which when functioning normally spot nucleotide mismatches and orchestrate repair enzymes. P53s are tumor suppressor agents that serve as brakes on abnormal cell growth. Both are susceptible to mutation leading to multiple types of cancers. Some forms of rarely fatal conditions, such as hay fever, have been discovered to have important genetic components.

Genetics has been used as ammunition in the nature versus nurture debate. Many on the nature side see genetics explaining everything, whereas the nurture side downplays the explanatory power of genetics. Most people fall between these two poles and see genetics as a powerful, but not an all-inclusive, explanatory tool. Current research is emphasizing the linkages, rather than an either-or approach. A team at the Institute for Psychiatric Genetics, for example, found that two organisms can have the identical genotype (the physical genes), but different phenotypes (how the genes are expressed) based on the environment in which they are in. If one version of a gene provides a better protein than another in a given environment, then that version will prosper. The implication is that with our growing genetics capabilities, we cannot only influence the phenotype but the genotype as well. For example, a person allergic to cats only finds out about his or her condition in the animal's presence. In addition to the obvious step of simply staying away from cats, he or she now has the ability to act on this information and use genetic therapy to alleviate the condition—and even enjoy the company of cats.

Questions of whether conditions have genetic predispositions have drawn the social and biological sciences closer together and stimulated joint R&D. A practical experiment underway in Australia—where it is very sunny, without many trees, and with a relatively thin ozone layer—is attempting to genetically predispose people to sun-avoidance.

There have been genetic links found for many behavioral conditions, such as drug and other addictions, alcoholism, sexual orientation, aggression, neuroses and manic depression. Great strides have been made in understanding many genetic origins. Unfortunately, the reality has often turned out less than the promise. For example, great expectations about genetic links to hyperactivity have fallen well below expectations—it turns out to be a complex condition with less than 10% of cases tied to a gene defect. Similarly, the magic genes for alcoholism, obesity, and other conditions have not eliminated these problems, but they have greatly increased the effectiveness of treatments.

There has been a 20% reduction in the crime rate this century. Although the degree to which this is related to genetics is arguable, most criminal justice experts attribute an important role to genetic testing. For example, genetic testing is often used for early intervention to influence the behavior of those predisposed to commit crime. In a finding with important implications for criminal justice, knockout mouse experiments, in which the gene for the serotonin receptor is "knocked out" or replaced by an inactive copy that holds its place, leads to more aggressive behavior in the mice. This research was important evidence for the concept that aggressive behavior in people could be linked to some dysfunctional serotonin systems. Treatments to balance serotonin levels continue to improve. Longitudinal studies with prison inmates are ongoing efforts to fine-tune these therapies. At the same time, studies linking genetics and criminal behavior have often had to tread carefully. It has just been since about 2013 that it has been politically safe to publish results that could be interpreted as having adverse implications for a social group. Even now such results are carefully couched, stating that genetic and behavioral links are primarily tendencies rather than immutable facts.

Researchers are investigating, for example, whether there is a genetic predisposition to accident-proneness. Similar research has been investigating the more general questions about predispositions to certain emotions, cognitive styles, and behaviors. Research indicates that most people change their behavior or alter their environment—such as avoiding smoking or milk or dairy products—after a genetic test reveals a predisposition.

Genetics has contributed to the understanding of personality, intelligence, behavior, psychoses, and neuroses. This understanding has driven as well as been driven by society's greater emphasis on mental and spiritual health and well-being vis-a-vis the physical aspects. There have been many defendants claiming in courts that "the genes made me do it," but the courts have not yet accepted this as a defense—although genetic information is factored into sentencing.

The most positive outcomes have been in education. Some progress comes from the correction of genetic disorders, such as locating and testing for a gene associated with dyslexia and devising the appropriate therapy. More recently, some teachers are designing classes for individual children based on their genetic makeup. A pioneering program at Penn State University found genetic markers that correlate with an individual's intelligence quotient (IQ). Subsequent research has been looking for and finding more and more genetic links to dozens of components of intelligence. The combined applications of this research are enabling custom-made education for some—mostly those who can afford to pay for it.

The links between genetics and brain science continue to solidify. The popularity of psychiatric genetics, first as a field of inquiry, and now one of the hottest majors on campuses across the country, portends strengthening of this link.

Genetics' contribution to brain science

Molecular biology, genetics, and immunology are providing a rich tool kit of new molecular tools for investigating the brain:

- *Antibodies* permit the visualization and localization of specific neurochemicals and cells.
- *Tissue cultures* allow brain cells to be cultured and studied in the lab.
- *Mapping* the human genome has generated new knowledge about the genetic basis of brain structure, development, and function.
- *Genetic engineering* creates tools for research, and treatments for mental and neurological disorders, such as growing neurons in culture and biochemically altering their development potential or function.

Brain science is evolving into a new enabling technology, on a par with genetics. Its rapid advances in the 21st century have carved a central role for it as a shaper of other sciences and technologies, as well as business and society. Geneticists are playing primary roles in brain science, helping to unravel brain structure and function at the level of genetic regulation, brain development, and neurotransmitter-receptor communications. Researchers have developed a genetic map for nearly all recognized brain disorders, along with a rough guide to the type and extent of environmental and psychosocial influences that interact with the genetic template. One of the painstaking successes is progress against the rare brain-related psychiatric disorder known as Wilson's disease, which had schizophrenic-like symptoms and sometimes killed people. The gene responsible for the toxic buildup of copper in this disease was identified last century, but it mutated in many ways and only persistence in identifying the biochemical pathways from gene to brain have enabled the present 55% success rate in reversing its effects.

Bioelectronics researchers have learned how to place embryonic brain cells on silicon chips and induce them to grow along desired paths. The next step, which has been researched without a breakthrough for decades, is to get the brain cells to grow connections to one another—in order to crudely mimic the circuitry of the brain. Enthusiasts believe it may be soon be possible to make biochips that drug makers could use to test new compounds or that may enhance human functions like memory or learning.

Developing tests for genetic flaws

There are thousands of diagnostics commercially available, ranging from those that identify specific diseases or disorders to cognitive and intelligence tests. Some are generic across the population, whereas others aim at specific racial, ethnic, or other groups. Tests have long been available for some diseases such as Charcot-Marie-Tooth disease, myotonic dystrophy, hereditary breast and ovarian cancer, and Alzheimer's Types 1 and 3.

Testing for flawed genes is now a $15 billion industry in the United States, including carrier screening, prenatal diagnostic testing, predisposition testing, and confirmatory diagnostic testing. A basic diagnostic test for the most common and harmful conditions is required for all pregnancies and is covered by all insurance plans. Mandatory diagnostics account for 70% of the industry today, due to their numbers. But the fastest growth is in more sophisticated tests for would-be parents, especially for those couples interested in enhancing their children's traits.

The mandatory diagnostic tests required for children to attend public schools screen for 253 diseases and disorders. Some of the tests are public health measures, such as susceptibility to the resistant forms of tuberculosis. Others are educationally oriented, such as tests for dyslexia, incidences of which, with the help of genetic therapy, have been reduced by 85%. Of course, other diagnostics are available in the schools, but they are administered on the basis of family history, or as a consequence of a student's symptoms and behavior.

Genetic diagnostics are also mandatory for admission to the military and many public service fields, such as police, fire, and education. Many insurance companies cover diagnostics, since detecting a potential condition or predisposition before it becomes a problem can save them money. Additionally, if a person applying for insurance is discovered to have a serious condition, such as a 90% likelihood of lung cancer, the insurance company can apply to the federal government to have the person placed in the national high-risk pool.

The insurance industry has been slow to get into genetic testing. Until 2005, they were using only the results of tests done by others. But as the costs came down, accuracy improved, and social objections lessened, the industry began doing some testing of its own. A key justification by the industry and its supporters for getting into testing was that insurers were willing to develop and pay for some sophisticated tests that would not have been developed at all or for a long time. The industry scored some important successes in collaboration with the big genetics companies, such as Genentech. For example, in 2017, a test for an elusive form of autism was developed that enabled parents to decide whether to risk having children with the condition. Isolating its genetic location also catalyzed research that has just recently led to the first promising therapy. The use of testing by insurance companies would not have passed muster, however, if the arrangement to cover high-risk applicants in a government-sponsored pool was not created by federal legislation in 2011.

A consequence of the boom in genetic testing has been a corollary boom in genetic counseling. The shortage of counselors in the late 1990s and 2000s has been addressed—some say a bit excessively if you take a look at the Network ads. At any rate, there has been tremendous development in the field of counseling over the last 20 years. The fundamental principle is that the person doing the science is not the person doing the counseling. It was learned that the skills required for the former were much different from the latter—and vice versa—and it was best to keep them separate.

Some decisions, such as what to do if one possesses a gene identified as directly responsible for a disease or disorder, have been fairly straightforward for most people. Few people choose to have a child that is genetically doomed. The exceptions are typically for one of two reasons. People are afraid of the results and avoid the tests, or they have religious or moral objections to tinkering with what is seen as God's plan. Even more difficult are cases where tests reveal a condition, but no treatment is available.

Public policy has often lagged the science and technology. Before the High Risk Insurance Act of 2011, people who refused a genetic test were often denied employment. There are still policy vacuums regarding some important genetics' issues. For instance, there is no formal public policy on parents who do plan to have children that diagnostics reveal will have serious genetic defects.

Many analysts regret the lost opportunity to design a proactive public policy covering such questions at the turn of the century, before developments took place that limited policymakers' flexibility. Now, people can assess whether or not they as individuals would be hurt by policy changes regarding genetics. Twenty-five years ago, when genetics was still fairly new and its eventual consequences unclear, there was a chance to make policy based on all people being treated as equally at risk, and subsequently being more willing to share that risk. Now, the federal high-risk insurance pool budget is strained, given its commitment to cover those people who insurance companies are not legally required to insure.

Mapping biochemical pathways and developing therapies and treatments

For many diseases and disorders, the intermediate biochemical processes that lead to the expression of the condition have been clarified—a recent estimate from Roberta Lee, head of the President's Advisory Board on Genetics, was that about 30% of the pathways are well understood. This information is particularly useful when combined with an individual's environmental, medical, and genetic histories. These histories are on record and under full control of the individual. They are protected on the network by cryptography or biometric identification of the user. Of course, some people still swear by their health smart cards, not trusting information only available through the network—despite the overwhelming evidence that you are more likely to misplace a card than lose information on the network.

The focus on biochemistry has created a boom for pharmaceutical companies. Today's pharmaceuticals have evolved generationally.

- The first generation consisted of recombinant DNA (rDNA) and MAB drugs based on making proteins.
- The next generation was antisense technology (the synthetic molecules that were easier to deliver than bulkier proteins) using compounds to block genetic instructions.
- The third generation involved the direct transfer of genes through hazardous and expensive bone marrow transplant or other implantation or injection.

A new generation of techniques is evolving from improvements in these three areas. For example, therapeutic gene pills are being tested now in the labs.

Biochemistry, and designing delivery systems appropriate to individual biochemistries, are the pharmaceutical industry's core competencies. Access to personal information has been essential to their success, as it enables the customization of treatments and dosages to the individual, rather than to a hypothetical average person.

Custom-designed drugs such as hormones and neurotransmitters are as safe and effective as those produced naturally within humans or other animals. Drugs are designed to act on individual cells rather than on organ systems as in the past. Drug manufacturing via genetic engineering offers greater precision, purity, and reproducibility of products, complete process control, the ability to improve or modify products, and the ability to create products that affect only the target site. Drugs made of genetic material, nucleic acids, carbohydrates, and nonexclusively protein-based synthetic molecules, such as PNA analogues of DNA or ribonucleic acid (RNA), are in widespread use.

Although the move to genetics-based treatments forced pharmaceutical companies to reevaluate their inventories to serve World 1 markets, it also opened opportunities in middle-income and destitute nation markets. The customized treatments in the affluent nations have remained beyond the means of most people in the middle-income and destitute nations. Mass-market-designed drugs, however, are affordable. Although some in these nations complain that they have financed the pharmacogenetic revolution in the affluent nations by buying these older generation products, there is little doubt that people's status in the World 2 and 3 societies has been significantly improved. In fact, an unanticipated consequence of the pharmaceutical boom in some less well-off nations has been a resurgence in population growth, as people live longer with the benefit of more sophisticated treatments. In Peru, for example, average life expectancy has increased four years so far this century.

The evolution of antisense

Antisense, or left-handed DNA, targets messenger RNA, binds to it, and keeps an unwanted message, such as triggering cancerous growth, from being transcribed. Antisense was invaluable to alleviating extreme obesity and many other metabolic conditions. Antisense is also used in many products, such as foods that people cannot metabolize, and therefore, do not gain weight from eating.

The path to success for antisense has taken decades. In retrospect, it was found that the following criteria had to be met for success in the marketplace. The criteria included:

(1) synthesized easily and in bulk
(2) stable in vivo
(3) able to enter the target cell
(4) retained by the target cell
(5) be able to interact with their cellular targets
(6) not interact in a non-sequence-specific manner with other macromolecules

An important area of progress coming from mapping the biochemical pathways is in alleviating common conditions. Arthritis, for example, has been reduced in severity by genetics-based therapies intervening in biochemical processes involved in the swelling of the joints. The greatest single success in treating cancers to date has been with suicide cells, which are targeted to the cancer via MABs and kill all cells that they sit in—including some healthy ones as well. Delivery mechanisms have also been a heavily researched area, with the key advance being the use of smart materials able to sense and respond to conditions in the body.

Genetic therapies are now routinely preventing and reversing conditions. One of the early diseases that effective genetic therapies were developed for was cystic fibrosis, which once afflicted one in 2,500 newborns. Most victims died before age 30. A therapeutic gene is spliced into a virus and inhaled into the lungs, where it prevents the growth of the deadly cysts.

By 2035 or so, nanomachines (one-billionth of a meter) in the bloodstream will monitor and in some cases compensate for chemical deficiencies. These self-assembled nanovessels are expected to float in the bloodstream and search for and destroy harmful bacteria, fat, or cancer cells.

Developing preventive methods

Prevention today is centered in reproduction. We have complete control of human reproduction, including when and how conception occurs, and what gender traits we want in the child. Based on techniques pioneered with cows, it is possible to detect the genetic defects in fertilized cells just days old via in vitro fertilization. A sample cell is screened for diseases and disorders, and if a harmful gene is found, the cells are discarded. These embryonic treatments and improved birth-control technologies, including the descendants of the RU486 morning-after pill have gradually lessened the once potent political issue of abortion—by avoiding it. Harris polls find that 73% of Americans now favor using gene therapy to improve babies' physical characteristics or intelligence, up from just 43% in 1992.

There was a great outcry in the late 1990s over reports of human embryos being secretly cloned in laboratories. Legislation banning human cloning was passed in 2003, although organs may be cloned. Developing other preventive methods required that legislation prohibiting tampering with genes be repealed, making it possible to alter genes linked to undesirable conditions—so that they need not be passed on to children. Most such laws were repealed by 2010, when legislation establishing a fixed list of genes that could be manipulated was passed. A panel meeting every three years reviews and adjusts the list. It considers the unanticipated effects of manipulating one function of multipurpose genes when making decisions on whether to add a gene to the list.

Genetic prevention has meant great progress over some cruder preventive measures of the past, such as removing breasts or thyroids to prevent future cancers. These procedures are still sometimes necessary, mostly for older people, who were born after prenatal preventive techniques were developed. The selecting out of harmful genes will eventually reduce them drastically, but mutation will always replace them to some low incidence.

Challenge for the next decade: enhancement

The human species is the first species to influence its own evolution. One of the first enhancements was the use of human growth hormone. There was a great deal of debate over whether this treatment was really necessary, because in many instances its use is more cosmetic than vital to health. Today, most insurance plans cover hormone treatment for dwarfism, but not to make short people taller—this coverage is only included in more expensive plans. An interesting social consequence is that height has become a measure of social status for some. Research has historically shown a correlation between income and height. With genetic enhancement, the correlation has been strengthened, as the enhancement therapy runs into thousands of dollars. People in households with incomes above $100,000 are on average roughly seven centimeters taller than people in households with incomes below $100,000.

Basic forms of physical enhancement come through transplanting organs including the heart, kidney, lung, eyes, ears, skin, endocrine glands, nerves, bowels, and pancreas. The organs come from other humans as transplants or from synthetics cloned in the lab. Organs grown in other animals for use in humans have been in R&D for decades without being able to get beyond the trial stage, except for skin and hair.

The trend is drawing attention to mental enhancement—primarily intellectual. Parents lacking math skills, for example, can now shop for genes predisposed to mathematical excellence, and have them inserted prenatally in their children. Other parents are selecting traits such as artistic ability, musical talent, or athletic prowess for their children. Of course, some challenging social questions are bound to arise as genetics leads to increasingly talented and intelligent children growing up in a society in which they are in many ways superior to their parents, teachers, and government authorities. Optimists anticipate a more informed and enlightened society. Pessimists worry about older people being warehoused in communities or homes for the genetically impaired.

In several parts of the world, particularly Asia, the understanding of human genetics has lead to explicit programs to enhance people's overall physical and mental abilities. Some countries, for example China, have adopted eugenics under the cover of enhancement. China long ago banned marriages that might produce children with mental or physical defects. It now forbids couples from having children whose genetic tests indicate having any of several hundred diseases or disorders. Despite the policy of strict control—including jail time for violators—in practice the controls are often evaded. A lesson many Western nations have learned is that public policy fails when it tries to reach 100% compliance. A combination of information and incentives generally proves more effective than mandates.

Slow but steady progress: aging and life extension

More people in World 1 societies are living to their mid-80s while enjoying a healthier, fuller life thanks in part to genetics' role in changing people's behavior regarding their health. Biologists now manipulate the genes involved in normal and abnormal development, growth, and aging, although no fountain of youth has been discovered. It is evident that aging is a complex set of processes and is not likely to be significantly influenced by any one discovery.

Genetics' greatest role in life extension has yet to arrive. Today, the average life expectancy is 85. Genetics promises to extend that average life expectancy to 100 by end of the century, when the first generation of children benefiting from genetics' advances will be reaching the end of their life. Advances include the use of prenatal gene tests that can indicate embryos likely to result in a fatal disease or serious disorder.

Two developments boosting life expectancy are genetics-based advances in reducing free radicals in the body, which have been found to hasten aging, and by increasing the body's production of free radical scavengers. Another promising area for life extension is continuing advances in programmed cell death, in which cells activate intrinsic death programs. Links to genetic activation have been found for a limited number of cells. Research is ongoing in developing genetic programs that cause cancer cells to die and immune cells to live longer.

Identification: the DNA does not lie

DNA identification has been the single most important advance for criminology in the last 50 years. It has contributed to declines in violent crime, the identification of deadbeat parents, and the prevention of fraud. For example, paternity suits in which the accused denied being the parent practically disappeared by 2006, because the threat of the test guaranteed that the guilty party would be identified.

Back in the 1990s, forensic application of DNA became popular in cases of rape, murder, and mayhem where there were blood samples. By the year 2000, the sharp decline in the cost of doing an identity match had led to massive DNA sampling. By 2002, legislation established a program to set up a DNA databank of children. An early application enabled parents to identify their children in cases of kidnapping or accidents.

Fortunately, the legislation involving access to genetic information was taken out of the hands of state governments, where the variations from one to another were quite extraordinary. One consequence was a small population boom in the Midwest that was attributed to people attracted by the generally strict privacy laws in these states. The Genetic Recording Act of 2004 built in substantial safeguards at the national level. One goal was to provide important biological data for individuals. For instance, the act addressed an anachronism of 20th century medicine, in which medical records were owned by doctors or hospitals rather than individuals, and placed medical histories under the full control of individuals.

There were also the epidemiological elements of genetic information that were quite important. Under the act, no use or application of genetic information was permitted that allowed a personal identifier, except at the request or with the permission of the individual. Epidemiology still obtained vital public health information without tying it to individuals, where it could possibly be used against them. Guaranteeing the anonymity of people's records boosted the supply and quality of public health data. In cases where data has been spotty, small royalties have been offered as an incentive.

A number of striking applications developed out of DNA databasing. One is tracking population flows and migrations. By 2012, it was established that the gene pool of self-reported black Americans consisted of about 37%

white genes, and the gene pool of self-reported white, non-Hispanics consisted of about 1.7% black genes. In the so-called "old confederacy" that rose to 13%.

DNA: the ultimate personal identifier

DNA is useful for identification because it is relatively inert, but it can be copied. This inertness is what makes it useful for identification purposes and why it can be recovered intact from ancient times. Controversies over the admissibility of DNA evidence in trials in the 1990s have long since blown over. Every state has developed DNA databases to varying degrees of sophistication. They started with taking blood samples of prisoners. Key data now are routinely noted on birth certificates.

The DNA identifiers code in an interesting way regarding older people. It became voguish around the turn of the century, when the great expectations for DNA identification were becoming real, for older Americans to leave a bequest of their tissue for analysis on behalf of their descendants. To some extent, a still popular process is exhumation sampling. Currently, about 19,000 graves are opened in the United States each year to exhume genetic samples. Both the cost and the legal constraints to prevent frivolous exhumation have kept the number relatively low. Of course, cell banks, in which people can leave a portion of their cells for descendants, should eventually eliminate the need for exhumation.

Unanticipated consequences sometimes arose from the forensic applications of DNA identification in violent crimes. For example, it led to a decline in instances of rape, but a simultaneous rise in murder associated with rape. This presumably was a response to reduce the likelihood of being identified as a suspect. The forensic applications also extended effectively to military injuries, deaths, and accidents, such as plane crashes.

Genetics helps manage the animal, insect, and microorganism kingdoms

The genomes of prototypical animals, fish, insects, and microorganisms, including goats, pigs, fruit flies, and locusts have been worked out. Knowledge of the genome has led to more refined management, control, and manipulation of their health, propagation, or elimination. Other species serve the needs of people while at the same time, the sustainability principle has led people toward a stewardship role for the planet, in which a balance is sought among the needs of people, other species, and the planet itself.

The biological functions and behavior of many animals and insects are manipulated through biochemical or genetic means. In agriculture and plant genetics, as with human health, working out the biochemical pathways dominated genetics at the turn of the century.

There are routine genetic programs for enhancing animals used for food production, recreation, and even pets. There has been a global boom in the goat population, as it turns out to be especially well suited to genetic manipulation. In the affluent nations, goats often produce pharmaceutical compounds, whereas goats in the middle and destitute nations produce high-protein milk. Enhancements in affluent nations are generally aimed at improving people's quality of life, whereas in the less-developed countries, more basic necessities are targeted. For example, work animals are the targets of massive investments in genetics applications and R&D.

Customized livestock

Genetic engineering of animals has enabled total control over livestock reproduction, leading to increased growth, shortened gestation, and higher nutritional value. Farmers can draw on a network cookbook of recipes for custom-designed livestock. They simply call up and obtain the genes they want from databases, transmit them to the local biofactories, and the animals with the desired characteristics are produced and shipped.

All transgenics must pass muster with the International Commission on Animal Care in Agriculture established in 2017. They are subject to an extensive physical examination, typically by virtual reality. Field visits occur only when something is suspected to be amiss. Transgenics must not threaten other species, and must not be in a condition of undue suffering as a result of the engineering—even where it might suit human purposes. The latter condition arose after horror stories of the treatment of transgenics. Network videos of hogs too musclebound to even stand led to public pressure to provide a reasonable standard of comfort for transgenics. The global network of animal rights groups has been effective in identifying and reporting scofflaws.

Transgenic animals, usually cows, sheep, or pigs, are used as living factories to produce needed proteins and other compounds internally or in their milk. These sites were once dubbed "gene pharms." The animals are bioreactors, producing, for example in the case of goats, a vital protein called AAT for fighting emphysema. Farmers also benefit from transgenics and other livestock by using engineered drugs and hormones to increase feed efficiency. Sometimes, the animal's digestion is modified to accommodate available feedstocks. Veterinary pharmaceuticals have boomed alongside human pharmaceuticals.

More varied menus from livestock genetics

Relatively few animals are grown on farms that grow human foods. They are generally handled as separate activities. The somewhat mislabeled fat-free swine came into substantial commerce in 2001. Swine have been among the most popular animals for genetic manipulation in agriculture because their size can be easily controlled from 15 to 100 kilos. Their genetic manipulation has been so fine-tuned that since 2006, at least 85 genetic varieties of swine have been introduced. A brief fad for duck-tasting pork settled down into a fairly steady but small seller. The introduction of chicken swine could not compete with the low cost of poultry itself. The growing popularity in venison in the early decades of the century has been even surpassed by the transgenic beefison, which has all the richness and flavor of venison, but the desirable physical and bulk characteristics of beef.

The economic ramifications have been impressive. Instead of, or in addition to, building a multimillion-dollar factory, pharmaceutical companies can either buy or lease farmland and raise a herd of livestock to breed the needed compounds, saving millions of dollars. The field has come a long way since the controversy over bovine somatotropin, the growth hormone supplementing the cow's natural hormones. In the 1990s, this case crystallized the fears of many people about genetics. A movement started to use milk only from "natural" cows. The agriculture industry was much more careful about subsequent introductions of genetically manipulated products, and over time the introductions engendered less and less opposition, to the point where they are routine and unnoticed today.

Strange bedfellows: animal rights and genetics

Animal rights activists have long protested against the use of animals for experimentation. They were successful decades ago in eliminating testing for nonessential experiments, such as for human cosmetics, by tapping the public's conscience. They were not successful in eliminating animal experimentation where human disease was the subject.

Ironically, given the perception that the activists were antiscience, genetics along with information technology have significantly reduced the need for animal testing. Animal testing has been increasingly replaced with toxicological models using genetics, experts systems, and computer simulations. Some genetic therapies prevent the onset of diseases and disorders, which took away the need for a drug treatment that may have used animal testing. Also, the use of technologies such as polymerase chain reaction (PCR) and cloning enabled the creation of synthetic substitutes for animal testing in some cases.

Transgenics are also adapted to withstand rough environments. Genes from the hearty llama in South America, for example, were introduced into their Middle Eastern relatives, the camel, and vice-versa, to greatly expand the range of each. Some species have been introduced into entirely new areas. The modification of parrots to withstand cold North American temperatures, for example, has been a boon to bird-watchers across the United States. Transgenic pets continue to be popular. Genes from mild-mannered Labrador retrievers, for example, have been bred into the fierce Pit Bull Terrier, and led to a resurgence of this breed once outlawed in many communities. Astromals^{tm}, four-legged 4-kilo fuzzy creatures with wings that can fly for short bursts, have been a big favorite of kids since 2019.

Experiments to use animals as breeding grounds for human organs continue on a small scale. It turns out that pig organs are the best candidates, but this research has been superseded by advances in synthetic organs. Animal experiments have been more useful in providing insight into their human counterparts. For example, experiments with growth and fatness in pigs in the 2000s vastly improved our understanding of human obesity. Cases of extreme obesity—where people weigh more than 200 kilos—are now successfully treated with a combination of gene and behavioral therapy. Unfortunately, those who could be helped do not necessarily come forward or cannot afford the treatment. Tests on other animals have led to sunless tans (certainly important, given the fragile ozone layer), 20-20 vision and better for the visually impaired, and most welcome for many, a full head of hair for those previously marked by their genes to be bald.

Fisheries and the coming aquaculture revolution

Genetic engineering of seafood has resulted in fish with different tastes and textures. In some cases, single species are directly modified, and in others, desirable qualities from different species are combined. For example, the tunasword, in which abundant tuna fish have been modified to taste like the less abundant swordfish, has brought the once-expensive taste of swordfish into the mainstream diets. A strain of oysters was modified to give it a less squishy texture, which was found to be a turnoff to many people squeamish about seafood. At the same time, another modified strain of nonedible oysters serve as natural filters for pollutants in many bays along the U.S. coastline.

Genetics advances have been helped along with a complementary growth in aquaculture. As fisheries across the globe had to be shut down in order to prevent their complete depletion from overfishing, aquaculture and genetics teamed to fill the gap, boosting output twofold over last century's average production. An unfortunate byproduct was a massive decline in employment for fisherman, and the resultant social problems of trying to retrain fisherman for other work—many were third, fourth, and fifth generation practitioners and strongly resisted the demise of their occupation. Although many natural fisheries have been restored, their careful management and advanced technologies have kept the demand for fishermen low.

Selective breeding techniques used in agriculture are now routinely applied to fish. Hearty species such as the tuna and catfish have become favored due to their suitability for fish farming and their receptivity to engineering. Fish farms prosper at sea as well as on land. Ocean ranches manage fish populations in their natural habitat. On land, tanks extending thousands of square meters house fish in environments designed to maximize their growth for human consumption—as with transgenic livestock, the fish farmers must provide a reasonable standard of comfort for their fish. Another genetics-led boom for fisheries came in krill and kelp, when they were modified to suit people's tastes. Krill dip became a national fad 10 years ago.

Pest management: outsmarting nature's evolutionary wonders

Genetics plays a central role in pest management, which has been evolving toward targeting specific pest species, in some cases targeting particular behavior patterns. Insects have proven remarkably adaptable to human efforts to eliminate them. An arms race between insects and pesticides has been marked by humans winning battles, but insects winning the war. Genetics is turning the tide.

Breeding pheromones into surrounding plants to lure pests away from their intended prey has been gaining favor over the last decade. There have been several course corrections, such as redirecting resources away from breeding in pesticide and herbicide resistance, as sustainability phased out the use of these chemical agents. Almost 75% of the year 2000 market for herbicides and pesticides has been replaced by biological or genetic alternatives. Sustainabilty advocates are pushing for total replacement in a decade.

Pests are now routinely sterilized through genetic engineering to disrupt their populations. Genetically engineered resistance to pests in crops is now common, through techniques such as inducing the plants to produce their own protective compounds. Genetics has enabled advances such as:

- crop plants altered one gene at a time to build in pest resistance
- insecticidal crops (inbred pest killing mechanism)
- crops that better tolerate negative environmental factors such as salinity and wind
- crops that store better
- products highly selective for pest species
- products that can be patented

Insect disease vectors are being targeted through genetic engineering to control their populations and thus the diseases they carry. The virtual elimination of malaria in World 3 took advantage of mixing in mosquitos bred without the capacity to carry malaria with their disease-carrying counterparts. Several generations later, fewer and fewer carried the disease. In combination with other public health measures, malaria cases are down 93% from last century. Other biological control methods used today include the synthesis of effective cost-competitive, pest-specific, safe substances that regulate growth, cause molting failures, accelerate aging, or otherwise breed in disinterest in destroying crops.

Boosting nature's bounty with plant genetics

Scientists have worked out the genome of prototypical plants, such as corn and wheat. This has led to more refined management, control, and manipulation of their health and propagation. The overarching goals are to reduce the time of the breeding cycle, speed up plant evolution, and develop patentable varieties.

Expanding diets through plant genetics

Genetics has expanded the number of foods in the human diet. Back in the 1980s and 1990s, there were about 3,000 edible plants. Three hundred of these were actually consumed around the world, 30 were significant in commerce, and 6 provided 90% of human nutrition. By 2010, the number of foods drawn into commerce had risen to 111, and today it is estimated that there are 212 in commerce in the United States, that number being made up of both modified and transgenic species.

The primary factors holding back many of these foods from entering into commerce was the presence of an unpleasant odor, a poor shelf life, or great difficultly in preparation time and energy. Those factors have been designed out. Other foods are from transgenic plants, not merely natural species that have been improved be genetic manipulation, but species that represent crossovers from distinctly different plant and animal genetic lines.

A second Green Revolution in agriculture

Farmers have near total control over plant genetics. Today's plants are more productive, more disease-, frost-, drought-, and stress-resistant, balanced and higher in protein content, lower in oils, and with more efficient photosynthesis rates or feed conversion rates than their 20th century predecessors. Natural processes such as ripening are enhanced through stimulatory microorganisms.

Genetics customizes and fine-tunes crops, building in flavor, sweeteners, and preservatives, while increasing nutritional value. Most crops are precisely suited to the resources at hand, to climate and other conditions, and to market needs. Many crops have gained 25% to 50% productivity over the last 25 years.

Some crops have been engineered for three decades now, including squashes, cotton, tomatoes, potatoes, sugarcane, soybeans, corn, peppers, peas, wheat, and rice. The money saved through these innovations has been quite formidable. For instance, last century, fungal rice-blast disease was costing rice farmers in Southeast Asia about $5 billion a year—with engineering, it is no longer a problem.

Linking farm and food

The close systems linkage between farm production and food preparation continues to grow. The integration of those two, while far along by 1997, really reached an unprecedented level by 2014. The optimization of food size, color taste, strength, cooking characteristics, and flavor to go through the food preservations processes (freeze-drying, frozen food preparation, open-stand sales, irradiating) have basically transformed the food delivery agency.

Five field tests conducted in all of the 1980s rose to hundreds in the 1990s and to thousands by 2020. The first step in agrogenetics centered around the cloning of known disease-resistance genes. Next was the identification of novel resistance genes and breeding them into populations. A more recent approach has been to genetically engineer plants to produce specific antibodies against their likely disease invaders. An example of this evolution was that crops were once, and in some cases still are, inoculated with nitrogen-fixing bacteria, but now they possess the characteristic through genetic engineering.

Genetics also plays a role in developing or enhancing soils for agriculture as well as environmental restoration. About 15% of the world's farms employ some form of restorative agriculture. A prime beneficiary has been Papua New Guinea, where thousands of square kilometers of deforested areas are now a healthy ecosphere once again and are producing valuable export crops such as mangos and kiwis. Farmers design crops and employ more sophisticated techniques to optimize climate, soil treatments, and plants. Crops are sometimes engineered to fit soils, or soil is engineered to fit crops.

Transgenics are not just in agriculture

Although agriculture has been the prime beneficiary of genetics, horticulture has also received a boost. Transgenic flowers, for example, combine heartiness, fragile beauty, colors, and textures in thousands of new varieties. A 2023 Net survey of the Flower Forum and its subgroups found that 76% of participants had at least one transgenic nonfood plant in their home.

Genetics also accounts for a large share of the millions of dollars spent on seeds, not only for crops, but also grass and flowers. The global seed market is in the tens of billions of dollars and continues to be a rich source of export income for the nation.

Expanding food choices

Foods for human consumption are more diverse as a result of agricultural genetics. Grocery shoppers sitting in front of their screen and ordering today have choices that would have bewildered people last century. Older people in the United States can barely conceal their amazement at how young people not only freely try new foods, but also seem to be in a continual search for the latest novel food. So many plants that once were not candidates for consumption have become standard fare, due to the removal of a noxious trait. For example, seaweed, always a part of some diets, became a widespread choice as its texture was made more palatable to a wider range of people and tastes.

Old fashioned foods linger on...barely

It has been recently estimated that 7% of the population prefer old-fashioned, that is pre-year 2000 plant and animal foods for a variety of reasons, and 3.5% exclusively consume them. The rest prefer them but consume them to varying degrees.

There is far less animal protein in diets in advanced nations today compared with the 1990s. Twenty-three percent of the U.S. population are vegetarians. Protein substitutes or enhancements, such as super-rich fish, are in widespread circulation. Even cultural staples, such as rice and beans in Mexico, are routinely altered nutritionally to have balanced proteins. There are more vegetables carrying proteins, for example, eggplant, potatoes, turnips, and radishes. Health, environmental, and ethical factors in tandem with better-tasting and more-convenient nonmeat foods through genetics have powered this change.

Synthetic and genetically manipulated foods can be matched to an individual consumer's taste, nutritional needs, and medical status. Many older people decry—most with good humor—the guilt- and consequence-free consumption of previously unhealthy foods, such as cake, cookies, and potato chips. A recent Net advertisement extolled the virtues of "extra-salty (artificial), low-cholesterol, cancer-busting french fries."

Food scientists have characterized molecular and structural properties of foods, and have identified structural-functional relationships and defined how these properties affect processing, storage, and acceptance of foods. They have determined the molecular and cellular bases of biological activities in food. Preservation methods have undergone a radical overhaul since the 1990s. Toxicity testing is much more sophisticated.

Genetic probes monitor safety and quality in food processing, such as the ability to detect single organisms, and more accurately set acceptable levels of microbes. This has been especially helpful to risk-benefit analysis routinely used in government risk-management programs.

Fine-tuning forestry

Forestry has drawn on genetic engineering and tissue culture to improve tree species, in the process becoming steadily more like agriculture. Genetic manipulation has resulted in superior tree strains through improved disease resistance, herbicide resistance, and artificial seeds. There have been substantial gains in productivity based on faster-growing species, better-quality lumber, and fine-tuned wood characteristics. The relatively long turnover time for gene testing in the field (5 to 15 years) was sped up by somatic embryogenesis, which enables the rapid multiplication of desirable genotypes.

Species are adapted to specific conditions and environments, including ones previously thought of as poor, or not even considered. Trees are routinely engineered for use in paper, with the important environmental characteristic of allowing nonchemical pulping. The introduction of the nitrogen-fixing-from-air capability into tree crops has been a boon to productivity and cost savings.

Forestry management has been driven by a doubling in global demand for forest products since 2005 and by environmental considerations, such as reforestation, biodiversity, and global warming. Genetics has also been instrumental in the global restoration of many denuded areas. The U.S. expertise has been critical in helping World 2 and 3 societies to get their environments into shape. Many of these nations, influenced by sustainabilty as well as economic opportunity, have come to view their forests and associated biodiversity as national assets.

Microorganisms are everywhere

Engineered microorganisms are used in the production of commodity and specialty chemicals as well as medicines, vaccines, and drugs. Groups of microorganisms, often working in sequence as living factories, produce useful compounds. They are also widely used in agriculture, mining, resource upgrading, waste management, and environmental cleanup. Oil- and chemical-spill cleanups have been a high-profile application that remains important today, even with double-hulled ships and other improved safety measures.

A boost to the application of engineered microorganisms came from the development of so-called suicidal microorganisms. They were developed in response to fears of runaways, particularly in bioremediation of solid and hazardous waste sites and agricultural applications such as fertilizers. Engineered microorganisms can self-destruct by expressing a suicide gene after their task is accomplished. An additional control element came with a detonator mechanism that can be activated in the event of a malfunction. Although they are not 100% effective, with redundant approaches there has never been a problem with large-scale releases.

Newer applications of genetics

Genetics has long been a force in human health, food, and agriculture. Over the last few decades, however, genetics has been having a greater impact across diverse industries, such as chemical engineering, environmental engineering, materials, manufacturing, energy, and information technology. It also contributes to the burgeoning field of artificial life.

The biologizing of chemical engineering

The various genome projects have created databases of molecules and chemical reactions. Chemical engineers have gained greater capabilities over processes at the industrial scale. Chemicals are now routinely devised to mimic and in some cases improve on those in nature.

Chemical engineering has been biologizing over the last 25 years. The challenge for chemical engineers today is to improve their understanding of more complex, weaker biological interactions and apply them to the chemical knowledge base. The hot research areas are in larger molecules, molecular recognition, attraction, and evolution and self-assembly in substances, and self-replicating systems. An expanding branch of chemistry known as combinatorics creates many variations of an existing molecule and then uses the ones that are interesting. Large libraries of molecules based on this approach are screened for effectiveness as drugs or other useful compounds.

Modified genes and biologically-active membranes are routinely synthesized in the lab. Chemical labs also synthesize gene-derived enzyme catalysts and other microorganisms not found in nature. Chemical processes are based more frequently on biocatalysts and their mimics and antibodies, as well as immobilized enzymes and their analogues. Synthetic bioactive agents inhibit or activate enzymatic or receptor functions.

Genetics has been critical to the chemical industry's shift away from bulk chemicals to higher value-added products. Genetics is especially useful for fermentation that produces amino acids, which are in turn used as food additives or as animal feed supplements. Dozens of industrial enzymes are used as biocatalysts in applications, such as producing simple sugars from more complex ones and breaking down cellulose in cotton to soften new blue jeans. Engineered enzymes offer the advantages of working at mild temperatures, producing chiral compounds, being biodegradable, not requiring organic solvents, and producing very specific reactions. Artificial DNA, synthetics not mimicking natural compounds, have brought new capabilities such as DNA chlorination and bromination that eliminate the troublesome byproducts characteristic of previous approaches.

Helping to clean the environment

Genetic engineering is used for a vast range of environmental services—from breaking down toxic wastes to restoring degraded ecosystems. Environmental applications of genetics have been gaining momentum since 2010. Of course, 13% of GDP growth in the United States over the last 35 years has been devoted to environmental cleanup or preservation.

Ecologists and environmentalists use genetics as a source of greater understanding of organisms' interactions in ecosystems and as a key to reclamation or bioremediation. Current research is looking into applications of genetics for totally artificial environments, as in space and seabed stations. More and more proposals for terraforming Mars are presented each year. The Senate held hearings on the subject in October 2023.

Bioremediation now accounts for almost 40% of the hazardous waste cleanup market. Engineered organisms speed cleanup, which would occur naturally but at nature's much slower pace. An important breakthrough for engineered organisms was developing the ability in 2003 to cost-effectively break down polychlorinated biphenyls (PCBs), which were once thought to be virtually indestructible. Microorganisms biologically convert or consume pollutants. Oil spill and hazardous waste cleanup were the first major commercial activities for biotechnology in environmental applications. Typically, the toxins and wastes are broken down to subatomic particles, reassembled, and converted into harmless or sometimes useful byproducts. An interesting application of DNA identification in forensics is determining who and what contaminated a soil. The ability to genetically manipulate organisms has introduced more transgenic species into the open environment, increasing the numbers of fish in the ocean and the survivability of vertebrates on land. There continues to be great interest in transgenic organisms as either threatening invaders or as with the goal of enhancing species or creating new balances among species. There have also been successful, small-scale projects of adapting animals to better suit their environment than the other way around. In cases where a food source was disappearing, genetic modifications have enabled species to adapt to a new food source. Genetic manipulation has presented fewer threats to the environment than many environmental groups had forecast.

Genetics is also contributing to making environmentally intrusive activities, such as mining and petroleum engineering, less damaging. In mining, engineered microorganisms assist in mineral leaching and metal concentration. In petroleum engineering, they ferment and emulsify the oil to help bring it to the surface.

Customizing materials at ever-smaller scales

The growing ability to manipulate materials at the molecular or atomic level is allowing manufacturers to customize materials for highly specific functions, such as environmental sensing and information processing. Genetics has made it possible to make more molecular structures and more complex materials using biological processes. For example, left-handed polymer molecules produced by genetics have properties that are different from their mirror opposites in nature, right-handed molecules. Their ability to attach to their opposites and prevent them from carrying out a harmful process—often referred to as jamming the lock—has made them a key tool in many pharmaceutical treatments.

Smart implants bridge the gap between the biological and electronic worlds. Implants with biomembranes control some of the body's biochemical functions, help target drug delivery, and are integral to synthetic organs and organoids (synthetic organs that induce the body to surround them or infiltrate them with tissues that produce hormones or perform other biological functions). Smart, inorganic materials are sometimes smarter than living biological ones today. Genetics produces polymers capable of bonding directly to living tissue for specialized applications, such as sensor implants to regulate blood pressure.

Japan has been particularly active in biosensors, which are devices that use immobilized biomolecules to interact with specific environmental chemicals. The activity can be detected and quantified through measuring changes in color, fluorescence, temperature, current, or voltage. Biosensors are routinely used in chemical processing and manufacturing for process monitoring and control, as well as further downstream in controlling industrial effluents.

Plants are bioengineered to produce raw materials for plastics, detergents, and food additives. For example, an engineered relative of rapeseed developed in 2017 produces a biodegradable plastic commonly used in food and beverage packaging.

Biologizing manufacturing

Manufacturing is becoming more like breeding. The expanding range of manufacturing applications includes molecular engineering for pharmaceuticals and other compounds, nanotechnology based on biological principles including self-assembly, rudimentary DNA chips, and biosensors. Biomanufacturing officially became a new subcategory within manufacturing in 2015—earning its own standard industrial classification (SIC). It now accounts for 1% of manufacturing under the revised classification scheme. Its share is expected to quadruple within a decade, especially as genetic engineering techniques are applied as part of custom production.

Enzymes, which were once too fragile for manufacturing applications, are now in widespread use. A Japanese approach pioneered in the 2000s is to subject enzymes to harsh conditions and cause them to mutate, so that they evolve an ability to withstand harsher conditions. A more recent innovation in 2021 was adapting microorganisms in the deep ocean that live on sulfur-based rather than oxygen-based systems for use in manufacturing processes involving sulfur.

A key consideration in biologizing is society's commitment to sustainability, which has driven a search for environmentally benign manufacturing strategies. Biological approaches, while typically slower than mechanistic ones, are more sustainable. The nondurable goods sector has been biologizing over the last two decades. All industrial enzymes are produced by genetic engineering today. Recombinant DNA has long been used in cheesemaking, wine-making, textiles, and paper production. Bioreactors, in which engineered living cells are used as biocatalysts, are now being used for new kinds of manufacturing, such as making new tree species, in addition to traditional applications in food processing, beverages, and chemicals. An especially attractive feature is that they can produce compounds that cannot easily be produced synthetically, due to high cost or environmental effects.

Nanotechnology is finally coming closer to delivery on some of its exotic promises last century. It is expected to be an increasingly useful tool for manufacturing in the next decade. Research has been focusing on methods for building materials and devices by manipulating atoms or molecules directly or through chemical or biological means. Self-assembly offers tremendous advantages in control and economy over conventional manufacturing. Self-assembled structures put themselves together based on attractive and repulsive forces between molecules, and could use a beaker on a table top rather than billion-dollar plants with clean rooms and vacuum chambers. Biological systems such as ribosomes remain the inspiration and models for assembler designs. Self-assembling nanomachines have been successfully programmed in the lab to build other nanomachines, but still too slowly to be commercially viable. The revolutionary potential is to change manufacturing from the top-down approach—using big materials and miniaturizing them by cutting, pounding, and winnowing—to a bottom-up approach—starting with atoms and biologically building them by self-assembly into molecules, and increasingly complex units.

Disappointing results in fueling alternative energy

Biomass energy has not lived up to the potential that many had forecast for it last century. In the United States and other World 1 nations, crop biomass has a small niche market. It has generally been unable to win out over competing uses for land—food and other commodity crops still typically earn more money than energy crops. In middle and destitute nations, the use of biomass has dropped almost by half, although this is explained by the fact that the unsustainable practice of using firewood and charcoal for fuel has been greatly reduced. The genetics revolution in biomass has bypassed many World 2 nations that lack the financial or technical resources to use it. Some middle nations, such as Thailand, however, are moving fast in these areas (see the middle and a destitute nation story later in this chapter.)

Energy from forests can be converted to natural gas with the aid of genetically engineered microorganisms. This gas can then be used in highly efficient gas-fired turbines. Genetics assists in energy conversion, including fermentation and other liquefaction techniques, as well as gasification tailored to feedstock species. An early technique was short-rotation wood-crop technology using genetic screening, physiological studies, and databases to improve yields. Genetics also plays a role in municipal solid waste conversion and processing, as well as producing energy from waste materials.

In the late 1990s, the discovery of microorganisms that thrive in petroleum provided a boost to enhanced oil recovery. The study of their structure and function led to the design of closely related engineered microorganisms that are pumped down into a well and sealed in. That leads to fermentation and, with the addition of water, promotes an emulsion that enhances production. Billions of barrels of oil in the United States have been recovered through enhanced recovery that otherwise would have remained in the ground.

Genetics, as pure information, links to information technology

Linkages between genetics and information technology are growing as researchers take advantage of the fact that genes are pure information. Information technology has long been a key enabling tool for genetics, handling the massive health-related genetics information in health smart cards, for example. A whole new discipline dubbed bioinformatics, or the science of biological computing, has sprung up to meet the enormous information needs of genome projects. The National Center for Biotechnology Information at the National Institutes of Health (NIH) and the European Bioinformatics Institute have worked together to integrate bioinformatic databases across the globe. Genome maps of any species are readily available to download from the Net practically anywhere. Other important applications over the last 35 years include:

- Artificial intelligence to determine changes in gene patterns
- Robots for doing genome sequencing and mapping and DNA replications
- Computer modeling and virtual reality for predicting molecular structures, which has been especially useful in pharmaceutical and in food processing for choosing enzymes, additives, and micronutrients

Evolutionary software engineering

Genetic algorithms are now commonly employed in computing. The principles of evolution are applied to computer coding. Pieces of computer code are viewed as analogous to chromosomes.

This approach has been used to program miniature robots by randomly generating the so-called chromosome codes and then selecting out the appropriate sequence when the robot behaved as desired. The chromosome pools of programs most closely matching the behavior are in turn combined in a process similar to reproduction.

Although the approach works, many trials are necessary to get the desired behavior. It is very slow and works only under limited conditions.

Genetics and information technology are now physically working together in advanced experimental computers. Biophotonic computers using biomolecules and photonic processors have set speed records for the fastest switching available. They are still in the laboratory, however, due to their high cost. Biomolecules appear capable of meeting the central hardware challenge of miniaturization, which has busied R&D labs since 2015 when Moore's Law (that computer capacity doubles every 18 months) finally collapsed as conventional semiconductor technology reached its physical limits. Bacteriorhodopsin's engineered descendants have the attractive features of serving as switches in logic gates, working in tandem with traditional silicon or gallium arsenide semiconductors. They are also being used in liquid crystal displays. Research continues into possible applications neural networks, although many scientists feel this particular path is an ill-fated detour. Analog biochips, which have been investigated since the early 1980s, have finally been yielding practical applications for tactile pattern recognition in computing environments using virtual reality over the last decade. They are synthetic organic organizations of molecules that in some cases can perform a chip function faster with greater storage density and smaller size.

Regulation supports genetics worldwide

Genetics continues to receive a great deal of regulatory attention. Fortunately the attention has been focused more on promoting better genetic science, technologies, businesses, and products, rather than churning old fears of runaway plagues or other genetic disasters.

Plant genetics and the associated risks are nothing new

Risk analyses of concerns about the release of genetically altered species concluded that humanity has long been altering plant genetics through traditional breeding practices. They added that no unique threat was posed with genetic manipulation. What is different today is the dramatic leap in capabilities to speed and enhance the process. Instead of waiting for generations for alterations to take effect, genes can be altered on the spot.

There have been localized problems with new breeds or new pest management strategies. Who can forget the Idaho potato blight of 2013, when an engineered microorganism targeting a potato pest turned out to rot the potatoes themselves. Fortunately the damage was contained to a couple of counties, and within three years the microorganism was wiped out.

The regulation of genetics has been a driver of the global management of global issues. This is a case where business has been out in front in calling for regulation. The regulatory situation 10 to 15 years ago was a mix of conflicting and confusing stipulations across hundreds of jurisdictions. What businesses were doing in one part of the world was illegal or prohibited in another. An early leader in international regulation was the United Nation's Codex Alimentarius Commission (CAC) that in 2015 adapted its charter of setting international standards for food products to include genetics or biotechnology products. Their voluntary standards were often adopted on a large enough scale to make de facto international standards. A promising development just 10 years ago was the renaming of HUGO, the Human Genome Organization, the international genome mapping agency, to GRO (Genetics Regulation Organization) —and the adoption of a new mandate, to harmonize conflicting genetics regulations. It is teaming with the sister regulatory bodies and is scheduled to promulgate the International Standardization Organization's latest work, ISO 46000 for genetics, along the revised previous lines of standards for manufacturing quality (ISO 9000), the environment (ISO 14000), telecommunications (ISO 22000), and energy (ISO 35000). It is a step forward, but the journey will be a long one.

DOTE leads the way in risk management

The Department of the Environment (DOTE) is the furthest ahead of any government agency in risk management. Over the last three decades, regulators have often responded to public fears of genetics inflamed by sensational media reports, rather than the available scientific evidence. Public fears generated political pressure that was in turn directed at regulatory agencies, sometimes forcing them to act counter to their best thinking.

Rather than wait for a crisis to develop, however, DOTE took advantage of research that clearly indicated that effective risk management should incorporate people's perceptions of a risk, even if they appear irrational or alarmist. They have been pioneering a shift in risk management from New Deal style paternalism of a 100 years ago, in which government knows best and takes care of everything, to an enabling model, in which regulators work closely with affected people and provide the most reliable information. People are involved in making the decisions that affect them. DOTE risk managers have been leading the way with this approach. Rather than dismissing people's fears, they are acknowledged. Often the fears are based on mistrust of the agency. It has taken years of providing credible information to build that trust, and maintaining it is an ongoing challenge.

Even the FDA, once one of the stodgiest paternalistic agencies, became so open and experimental to deal with the AIDS crisis last century, that it sometimes surged ahead of the activists demanding its reform. The same principle has applied to businesses that deal with DOTE and a local community together. Addressing constituent concerns and building a relationship based on trust also applies to businesses beyond risk management situations to being a key part of dealing with any customers or potential customers.

Because its effects are so far-reaching, jurisdiction for regulating genetics in the United States, unfortunately, remains dispersed across 10 agencies and institutions, although this was an improvement over the dozens of agencies a decade ago. Interagency cooperation is routine, leading to the gradual integration of state and local regulation at the federal level. In many states, it became politically popular to ban anything related to genetics. The first indicator of international resistance to gene-based change was banning dairy or beef products derived from cows given growth hormones. Later, legal restrictions on gene research, such as not being able to intervene in inheritance, were overturned. The antigenetics movement at the state and local levels gradually lost steam as genetics became demystified. People paid greater attention to it in schools, the workplace, and in public education campaigns.

The Departments of the Environment and Agriculture have overseen tens of thousands of field tests of engineered organisms since they began in the 1990s. A precedent-setting step in interagency cooperation also came in the 1990s when NIH's Recombinant DNA Advisory Committee voted its gene therapy subcommittee out of existence and forwarded new protocols to the Federal Drug Administration's (FDA's) Recombinant Advisory Committee (RAC).

Proposals to create a Department of Genetics or Biotechnology continue to spring up. So far, proponents have been unable to provide a compelling reason for consolidation. The strongest driver for consolidation at the national level turns out to be international pressure.

Cooperation spurs national and international genome programs

The human genome project was the big driver of today's advances in genetics. It was an international effort, although the bulk of the research was carried out in the United States. The genomes of most important species have been mapped, but work continues on mapping more of the planet's commercial species. The corn and cotton genomes were completed in 2000, rice (by Japan) in 2002, wheat (by Russia and the United States) in 2004, chicken and cattle in 2012, and the pig in 2014. One can think of the genome map's contribution to the understanding of species biology as comparable to that of the periodic table of elements for chemistry.

Gene hackers: the new breed

Despite tight controls over genes and the technologies for manipulating them, a new breed of hackers—gene hackers—has been raiding databanks and laboratories to create novel organisms. Incidents have been rare. The media attention they get makes them seem more frequent than they actually are.

There have been some gruesome results, some right out of science fiction—three headed frogs, stinky plants giving off incredibly foul odors, and of course, microorganisms such as the bacteria that poisoned Winchester, Massachusetts' water supply in 2019, killing a dozen people and making thousands ill. There are also heroic accounts. A gene hacker in 2007 secretly worked on a therapy for her fatally ill spouse, only to die herself when the effort went awry. This incident inspired the international blockbuster movie, *Altering Destiny*.

Automation greatly speeded the task of identifying and marking the three billion units of DNA that make up the almost 100,000 genes arranged over 23 pairs of chromosomes. If human genome were compiled in paper books, it would take 1,000 volumes the size of an old King James Bible to hold it all. Each human genome differs slightly from every other—roughly 0.1 of 1% or about three million nucleotides. Today's catalog of the human genome is a mosaic of a hypothetical average person. The human genome project was undertaken in the 1990s and was completed right on schedule in 2005. Whenever it looked like the goal would be missed, new advances, notably genomic mismatch scanning (GMS) and representational difference analysis (RDA) came along to speed the process.

Patent law evolves to keep up with genetics

U.S. law once gave the broadest protection to inventors, but the gradual harmonization of international patent law has lessened the differences among nations. Patent enforcement remains an issue as some countries, notably China and Korea, still resist. International agreement was necessary. For instance, the three basic tests are still (1) novelty, (2) not obvious, and (3) utility. The difference today is a stricter criterion for demonstrating utility. A precedent-setting case in 2001 was the invalidation of many cotton patents claimed by W.R. Grace, once a large multinational, because they were deemed to be too broad in seeking rights to any cotton created or modified by genetic engineering.

Patent law once prohibited the patenting of anything natural. The argument that eventually prevailed is that genes are not natural, even though the organism from which they are taken may be. NIH had sought to patent the human genome to prevent private entrepreneurs, and especially foreign capital, from controlling what was being created with U.S. public money. But when the U.S. Patent and Trademark Office rejected NIH's patent applications for 315 segments of gene codes in 1994, NIH decided not to appeal and to drop its other patent claims, believing that successful patents would impede research instead of stimulating it.

The graying royalty system

From the middle to the end of the last century, the most successful genetically manipulated food was hybrid corn, hybridized and grown by traditional, old-fashioned methods. The success of the product depended on two characteristics. The first was that the product itself was superior in all regards, and the second was that the farmer had to go back to the hybridizer each year for seed, thus tying it to an economic reward structure (the price of the seed). Virtually no genetic improvements were made in self-propagating crops, with the exception of several, notably rice, directed at poor nations' economic well-being. With the development of rapid, high-speed, low-cost DNA analyses, it became practical to identify the makeup of a carload or shipload of grain very easily, and the current national as well as international law provides a 25-year royalty fee for the developers of successful-in-commerce, self-propagated hybrid grains.

It is now estimated that 60% of all U.S.-grown and marketed grains and 34% of worldwide grains in international commerce are part of that royalty system. Royalties are in an unusual pattern; they start off low in the first five years of the introduction of the grain to propagate its use and they peak in the 12th to 17th year of use, and then gradually decline and fall to zero in the 26th year. In rank order of importance using the international royalty system are wheat, oats, rice, and rye.

The next part of the story involved a key researcher in patenting at NIH leaving to head a private, nonprofit venture, The Institute for Genomic Research (TIGR), and its profit-making ally, Human Genome Sciences (HGS), with ties to SmithKline as well. TIGR/HGS amassed a gargantuan amount of human expressed sequence tags (ESTs), which are gene fragments that can be used to rapidly track down genes of potential pharmaceutical value. The competition heated up as other big pharmaceutical firms, such as Merck, threatened to band together and bankroll a public database of ESTs. HGS eventually agreed to share the information with researchers if they gave HGS the right to be involved in any subsequent commercialization. A researcher looking for a defective gene similar to a certain known bacterial gene, for example, simply called HGS to see whether any of the genes in its files were similar, and, for a fee they would receive an answer and the necessary data. If the researcher subsequently used that information to develop a treatment for cancer or diabetes, HGS would seek a share in any subsequent marketing.

The impressive genetics tool kit

The basic tools of genetics have enabled advances in observing, locating, mapping, identifying, labeling, isolating, separating, describing, sequencing, altering, mutating, changing, moving, transferring, replicating, synthesizing, and designing. At the same time, homage should be paid to the many bacteria, the fruit fly Drosophila, and the mouse for being the testbeds to developing these capabilities.

THE WORLD 2 AND WORLD 3 NATIONS—A MIXED STORY FOR GENETICS

There have been some tremendous success stories as well as disappointments in the middle-income and destitute societies. Technology transfer remains a critical issue, especially for food production and distribution in the destitute nations. The hoped-for development of a “miracle” nutritional food has failed to materialize, but there have been sporadic success stories. Successful applications of genetics in the middle and destitute nations include:

- Transgenic livestock adapted to new, often harsh, environments
- Embryonic biomass industries based on engineered feedstock crops
- Near eradication of some infectious diseases, notably malaria
- A genetics-fueled second Green Revolution

- Unarable lands brought back into production
- A tourism boom spurred in part by genetic tools for enhancing biodiversity
- Reforestation and ecological restoration preserve valuable sources of pharmaceuticals for export
- A growing presence in international seed and plant markets, including a breakthrough for the papermaking industry

Despite genetics advances, destitute nations such as Haiti and Egypt still experience occasional episodes of widespread starvation. Many World 2 and 3 nations' leaders maintain that agricultural genetics has actually hurt their economies by developing new crops that lessen the need for their indigenous ones. Farmers there have been hurt by substitutes for their unique export crops, brewed up in affluent nation bioreactors.

At the same time, transgenics have been exploited throughout Worlds 1 and 2. Engineered goats, for example, have prospered in several climates and terrains. In addition to being readily adaptable to new environments, they are leaner, their milk is less fatty, and they use less space than cows. Breeding out their predisposition to rapacity has made them an ideal livestock.

Many middle nations have developed niche industries in genetics, but they generally have not posed a threat to affluent nation dominance. Thailand's amazing recent breakthrough in biomass energy, however, may change this situation within the next decade. All in all, genetics has been neither a panacea nor a poison for the middle and destitute nations. It is likely that its effects will be felt more strongly over the next decade, as products and services from the affluent nations continue to spill over into Worlds 2 and 3.

Genetics has not played as large a role in health in these nations as in the affluent ones. Middle nations have made a transition to the mass medicine once practiced in the affluent nations. The transition to custom medicine is likely to be made over the next few decades as people become increasingly well-to-do and able to afford the latest technologies.

Genetics has been most useful at the public health level in combination with education and other measures. Most nations have instituted at least a rudimentary form of diagnostic genetics testing and counseling. The benefits include not only healthier populations, but smaller ones as well. More families are accepting the idea that they need not have as many children as their parents. Large families were often a hedge against the fact that many children would not survive. As the survival rates for each child increases, the need for a large family declines. Another public health-based driver of genetics medicine has been the problems of megacities. The close living and working quarters promotes the rapid spread of infectious diseases. Engineered immune system boosters have been effective in sporadic cases, but have not yet been distributed widely enough to achieve their potential.

An ironic side effect of genetics-led advances in medicine and public health in some World 2 and 3 nations is that genetic disorders have been accounting for an increased proportion of disease. These regions have a far greater percentage of consanguineous marriages (between blood relatives), roughly 20% to 50% of marriages in some parts of Asia and Africa, which lead to greater genetic complications. This greater share of genetic disease has increased the importance of developing cost-effective genetic therapies for these regions.

India's second Green Revolution

Genetics has been a tool for igniting a second Green Revolution in agriculture. India's prospects at the turn of the century were marred by a burgeoning population drawing on increasingly tired and overworked cropland. Disaster would most certainly have struck if not for the introduction of synthetic soil supplements, crop strains that could accommodate the land's existing conditions, and widespread application of integrated pest management techniques. Another important tool was bringing underutilized varieties of plants with high yields and high nutritional value into people's diets. Genetic engineering for protection against pests attacking food in storage—historically a critical shortcoming in World 3 food systems—improved food availability by 20%.

Genetics plays an important role in developing synthetic soils that combat erosion and in some cases have made the unarable arable. In combination with new strains of plants with high yield and fast growth, the yield from marginal lands shoots up.

India has also been making a foray into commercial genetic engineering of flowers. It is now the world's leading producer of petunias. These and other flowers have inbred pest and heat resistance critical to success in the Indian biosphere, thanks to genetic engineering.

Kenya capitalizes on its biodiversity riches

Kenya today is the biggest tourist attraction outside World 1. It has been turning around its desperate status as a destitute nation from the last century. It is moving into the middle cut of nations—based mostly on political and economic reform following the death of President Daniel Arap Moi—but in part due to its use of genetics as a tool for the conservation of its rich biodiversity. It has worked with environmental organizations in World 1 to pioneer the applications of genetics to help indigenous species adapt to their human-modified environments, as well as modifying the environments to better suit the animals. They have also pioneered the storage of gene samples of species. The tourism associated with wildlife has long been the nation's number one industry.

Lions and elephants were on the road to extinction in the wild at the turn of the century. Dealing with poaching was certainly a critical factor, but genetics had a saving role as well. In 2003, the hundreds of lions remaining in the wild were attacked with a virus that threatened to wipe them out. DNA typing identified the responsible microorganism, and as many lions as could be approached were given a genetically developed vaccine that enabled them to fight the virus off. With elephants, the breakthrough was using genetics to boost their food supply that had been dwindling for years.

The nation discovered that adopting a systemic approach to maintaining and enhancing the biosphere worked much better than piecemeal or bandaid solutions that tended to favor one species at the expense of another.

Brazil's pharmaceutical and chemical cornucopia

Like Kenya, Brazil has found economic opportunity in protecting and enhancing its biodiversity. Brazil's niche has been in pharmaceuticals and other chemicals. It is tapping its lush tropical forests, which are storehouses of over half the worlds' plant and animal species, where in the past they were recklessly cutting them down. Brazil has also diversified into genetic engineering of crops as sources of new pharmaceuticals to supplement its natural stores.

Genetics-based forest reclamation strategies have been central to the nation's success in exploiting its biodiversity. Genes for rapid growth have been engineered into native rainforest tree species. In tandem with environmental engineering and ecological restoration projects, 53% of the rainforests once thought to be lost forever, have been restored.

Thailand's strong commitment to becoming the genetics tiger

While other Asian tigers such as Singapore and Taiwan have pursued their fortunes as global leaders in information technology and financial services, Thailand has been pursing the genetics path. There has long been relatively strong support for biotechnology among the population. Thailand first built a presence in the international trade in seeds and plants, which was once largely in the hands of the United States, Netherlands, and Italy. A key development for this industry was the development of genetic treatments adapting seeds and plants to Thailand's relatively hot climate. Thailand, and to a smaller extent India, is rebalancing this trade from affluent nation dominance to a more equitable distribution.

Thailand has risen to be among the world's leading producers of biomass energy based on genetically engineering feedstock crops from agricultural wastes. This ideas has long been investigated, but only became a commercial winner in the last decade with the development of an engineered microorganism that converted ordinary waste into feedstock for fuel cells—an increasingly important energy source in remote areas throughout the world. In addition, just last year a group of Thai researchers working in tandem with a U.S. team, pioneered the biomass-fed "silkworm" microbes for producing uniform, high-quality fiber for papermaking.

Critical Developments, 2000-2025

Year	Development	Effect
2000	Widespread use of antisense technology using compounds to block genetic instructions.	Genetics-based medicine breaks into the main-. stream
2001	The hectare of farmland dedicated to raising transgenic animals goes into production.	Huge costs savings in raising farm animals as biofactories compared with building multi-million-dollar plants.
2004	Genetic Recording Act of 2004 passed.	Substantial safeguards for people's genetic information reduces social resistance to genetic testing.
2005	The human genome completely mapped.	The knowledge base for medical intervention is established.
2005	Routine genetic testing and	Entrepreneurs respond to, and saturate, market counseling available. demand.
2006	Corn and cotton genomes mapped.	Genomes of other important species continue to be completed.
2010	U.N.'s CAC standard for several bioprocessed legumes adopted as de facto international standard.	Demonstrates that international cooperation is possible and can benefit all.
2011	High Risk Insurance Act passed.	Government-backed insurance pool to cover people diagnosed with genetic disease or disorder.
2012	Deadly fungal rice blast eliminated.	A billion-dollar problem disappears.
2014	Restoration of the mastodon.	Entertainment value of genetics established.
2014	Malaria virtually wiped out in the destitute world.	One of the toughest killers is finally stopped.
2015	U.N.'s CAC adapts its charter to include standards-setting for genetically altered foods.	Begins the institutionalization of international regulation of genetics.

2015	Identifying biochemical transmission pathways of genetic information.	Building on the genome map to further progress toward treatments and remedies.
2017	GRO formed on the skeleton of HUGO to oversee international regulation of genetics.	Institutionalizing cooperation on genetics matters.
2019	Map for all genetically-based brain disorders completed.	Integration with brain science forms the basis for a new enabling technology.
2020	Widespread therapies for single-gene disorders.	Genetics knowledge is increasingly translated into effective actions.
2020	Identification of genetic predispositions nearly complete.	Substantial progress in the thorny task of separating nature from nurture.
2023	Chemical composition for all human genes fully identified.	The basis for therapies and treatments is fully in place.
2024	ISO 46000 standards for genetics promulgated.	ISO international standards have long tradition of aiding global commerce.
2024	First successful mass-market gene pill.	Overcomes the delivery problem that has hampered gene therapies.
2025	Genetics the second largest industry in the United States behind information technology.	Indicator of U.S. evolution into knowledge industries.

Unrealized Hopes and Fears

Event	**Potential Effects**
Runaway genetically engineered microorganism causing death and destruction.	Wipeout of large segments of people, plants, or other species.
Many human diseases wiped out through genetics.	Savings in health spending, but potential for a population explosion at the same time.
Pollution-eating microbes eliminate hazardous and nuclear waste dumps.	Resolution of key environmental issues affect the vitality of the planet.
Biomass energy crop breakthrough. environment.	Provide energy without harming the
Discovery and manipulation of an aging gene that dramatically boosts life expectancy.	Profound reshaping of societies accustomed to 85-year lifespans.