PERSPECTIVES: THE RICE GENOME

World Poverty and Hunger—the Challenge for Science

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We are living in the age of science. There are more scientists alive and practicing today than in all the previous periods of history combined. Science permeates the cultural outlook of our societies and the worldview of more people than ever before. Science has contributed to enormous achievements in human welfare. Thanks to numerous scientific advances, we are now moving to the third global revolution, a new world that has never been more promising, or more perilous.

The first of the great global revolutions was the agrarian revolution that settled people in small communities and launched civilizations. By the banks of the Nile and along other great rivers of the world, our ancestors established the foundations of organized society and fashioned the wise constraints that make people free. They created the wonders of the ancient world. Even today, it is the surpluses produced by farmers that make city life possible.

The second great global revolution, the industrial revolution, was the harbinger of enormous change in production methods, and in the relationship of people to the final product on which they labored. The artisan became a worker; processes of production and specialization led to an enormous burst of output, bringing big improvements for much of humanity during the next two centuries.

The Third Global Revolution

Our world is undergoing a third transformation, one so profound that its contours can only be dimly perceived, its driving forces barely understood, and its momentous consequences hardly imagined. Indeed, it provokes fear as much as it seduces the imagination.

Driven by ever more powerful computers and ever-faster communications, the digital language of bits and bytes allows us to merge the realms of words, music, image, and data as never before. It creates new industries; the old disappear. With the click of a mouse and the flight of an electron, billions of dollars move across the globe. The Internet has revolutionized the very meaning of time and space. Currently, there are about 2 billion pages on the Internet, which will increase to 8 billion pages by 2005. Will these be the forces of homogenization or of diversity? Will they be used to crush the weak or to afford them new opportunities?

From informatics to biology, the revolution continues. We have decoded the DNA blueprint of life, are learning to manage the deployment and expression of genes, are mobilizing bacteria to do our work, and are manipulating the very building blocks of life. Our new capacities pose new and profound ethical and safety issues. Unlike the past, the new issues of proprietary science will also complicate our future.

"…a world divided cannot stand; humanity cannot survive partly rich and mostly poor."

The Paradox of Our Times

Consider the paradox of our times. We live in a world of plenty, of dazzling scientific advances and technological breakthroughs. Yet our times are marred by conflict, violence, economic uncertainty, and tragic poverty. A sense of insecurity pervades even the most affluent societies. Nations are looking inward, and the rich turn their backs on the poor. Even though we may have pushed back the specter of a nuclear holocaust, other challenges that are just as serious and as daunting loom ahead: globalization, environmental pollution, poverty, and hunger.

Much has been done to make the world a better place. The 20th century was one of struggle for emancipation. The colonies were liberated; many women got the franchise; and racial, ethnic, and religious minorities and nonconformists were acknowledged to have political and civil rights arising from their common humanity. There have been many socioeconomic improvements over the last 40 years: developing countries have doubled school enrollments, halved infant mortality and adult illiteracy, and extended life expectancy at birth by 20 years. Despite these advances, much remains to be done. A global developmental agenda demands our efforts and our solidarity.

Today:

- 1.2 billion people live on less than a dollar per day.
- 1 billion people do not have access to clean water.
- More than 2 billion people have no access to adequate sanitation.
- 1.3 billion people, mostly in cities in the developing world, are breathing air below the standards considered acceptable by the World Health Organization.
- 700 million people, mostly women and children, suffer from indoor air pollution due to biomass-burning stoves, equivalent to smoking three packs of cigarettes per day.
- Hundreds of millions of poor farmers have difficulty maintaining the fertility of soils from which they eke out a meager living.

To this stock of problems, we can now add a slew of new challenges. The human population is increasing by 80 million persons a year, mostly in the poorest countries. Dramatic overconsumption and waste in wealthy nations and population pressure in poor countries are putting enormous pressures on the ecosystems on which we all depend.

The world's marine fisheries are grossly overexploited. Soils are eroding. Water is becoming scarcer. Deforestation is continuing. We must redouble our efforts to address the global challenges of desertification, climate change, and biodiversity. Agriculture must be transformed to promote sustainable food security for the billions of hungry people in the world. The challenges of urban poverty and environmental destruction are unprecedented, and will only increase with the urban populations of developing nations expected to treble over the next two generations. In the 47 "least developed" countries of the world, 10% of the world's population subsists on less than 0.5% of the world's income. Some 40,000 people die from hunger-related causes every day. One sixth or more of the human family lives a marginalized existence. Therein lies the challenge before us. Will we accept such human degradation as inevitable? Or will we strive to help the less fortunate? Will we regard ourselves as no longer responsible for future generations, or will we try to act as true stewards of Earth? It is not resources that are lacking; it is the will to harness them. Indeed, the world has never been richer, and the future promises even more.

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A Growing Gap Between Rich and Poor

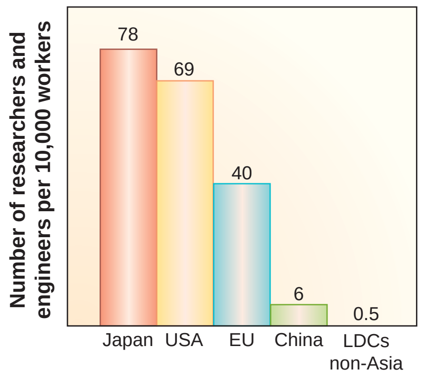
It is inconceivable that there should be some 800 million persons going hungry in a world that has the resources to provide for that most basic of all human needs. In the 19th century, some people looked at the condition of slavery and said that it was monstrous and unconscionable—that it must be abolished. They were known as the abolitionists. They did not argue from economic self-interest but from moral outrage. Today the condition of hunger in a world of plenty is equally monstrous and unconscionable and must be abolished. We must become the "new abolitionists." We must, with the same zeal and moral outrage, attack the complacency that would turn a blind eye to this silent holocaust, which claims tens of thousands of hunger-related deaths every day.

Addressing the American people, Abraham Lincoln said that a house divided cannot stand; a nation cannot live half slave and half free. Today, I say that a world divided cannot stand; humanity cannot survive partly rich and mostly poor.

Despite our enormous productivity, the undeniable benefits of globalization and trade, and the amazing achievements recorded on the social indicators for most of Earth's people, there has been an alarming rise in inequality both between and within countries.

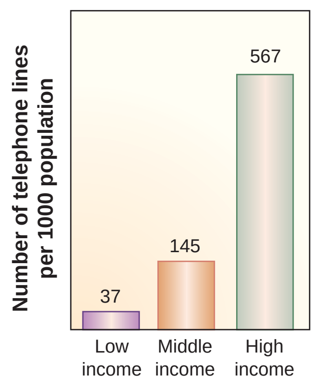
The top 20% of the world's population consumes 85% of the world's income, the remaining 80% live on 15%, with the bottom 20% living on 1.3% of the world's income. And these disparities are growing. A generation ago, people in the top 20% were 30 times as rich as those in the bottom 20%. Now, they are more than 70 times as rich, yet will not give 0.3% of their income for the poorer 80% of humanity. The richest three persons on the planet have more wealth than the combined GDP of the 47 poorest countries. The richest 15 persons have more wealth than the combined GDP of all of sub-Saharan Africa with its 550 million people!

If indeed we are moving toward a knowledge-based society, then connectivity and the preparation of human capital and its deployment will be the key to enabling poor developing countries to improve their situation. Yet, here too, the figures are troubling. There is a vast and growing gap in the production and availability of scientists and engineers between the wealthy Northern Hemisphere and the poorer Southern Hemisphere. Whereas the United States and Japan have about 70 researchers and engineers per 10,000 population, and China can claim six, the poorest developing countries in Africa have fewer than one (see the figure this page, top). In 2000, telephone lines per thousand persons numbered 567 in high-income countries, and 145 and 37 in middle- and low-income countries, respectively (see the figure this page, bottom). At the turn of the millennium, personal computers per 10,000 persons stood at 1800 for the rich, 230 for middle-income countries, and only one for the poor. The rich account for 88% of all Internet connections, yet constitute only 15% of the world's population.



The power of human capital. The United States and Japan have about 70 scientists and engineers per 10,000 population, China can claim six, and the least developed countries (LDCs) of Africa have fewer than one.

The future does not look any more promising. Tertiary school enrollments in 1980 in the low-, middle-, and high-income countries stood at 4, 11, and 34%, respectively (see the figure next page, top). By 1996, these figures stood at 5, 15, and 58%, respectively. There are a few exceptions, such as the Republic of Korea and Singapore, which have joined the high-income enrollment statistics (see the figure next page, bottom). Such quantitative indicators do not take into account the enormous differentials in quality of education, especially at the primary and secondary levels.



Who is connected? Two years ago, there were 567 telephone lines per 1000 persons in high-income countries, 145 per 1000 in middle-income countries, and 37 per 1000 in low-income countries.

SOURCE: (BOTTOM) WORLD DEVELOPMENT INDICATORS, 2000

What Science Can Do

It is against this backdrop that we must address how science can meet head-on the challenge of world poverty and hunger.

On the positive side, science can help to feed the hungry, heal the sick, protect the environment, provide dignity in work, and create space for the joy of self-expression. Yet, on the negative side, lack of opportunity to master science and the new technologies will accentuate the divide between rich and poor. On an average per capita basis, the rich countries have about 40 times the income levels of the poor, but they invest 220 times as much in research.

To these troubling trends we must add the special challenge of dealing with the emergence of private sector–driven science, which increasingly poses the problem of how to protect intellectual property rights without impeding free access to research tools and the equitable sharing of benefits with the poor who cannot afford to pay. The power of patents and intellectual property regimes to mobilize private sector funding in research is clear. In 1999, one corporation, IBM, had more patents (2756) than 134 countries combined (2643). In the new biological sciences this is even more true. Patents are taken out not just on finished products, but also on processes and intermediate inputs. And even though there is a research exemption, it does not hold for products of research that have wide applicability and could be marketed. This issue will lead us to a world of scientific apartheid unless it is addressed in an imaginative way that does not stifle innovation or prevent the flow of private capital into research.

However, it is much more than a matter of money. Never before has the need for the scientific enterprise in developing countries or its potential for success been greater. And yet as that enterprise reveals the marvels of genes and the secrets of atoms, many in the developing world are looking with suspicion on the new, and are trying to erect barriers to limit where minds may range.

The Values of Science

There is a central core of universal values that any truly modern society must possess, and that science promotes. These are rationality, creativity, the search for truth, adherence to codes of behavior, and a certain constructive subversiveness.

The physicist, biologist, and writer Jacob Bronowski (*1*) defined science as "the organization of our knowledge in such a way that it commands more of the hidden potential in nature." Science goes far beyond the utilitarian application of knowledge; it impacts an entire world outlook, from cosmology to what makes us human. Values are not rules. They are, in Bronowski's words, "those deeper illuminations in whose light justice and injustice, good and evil, means and ends are seen in fearful sharpness of outline."

Science values originality as a mark of great achievement. But originality is a corollary of independence, of dissent against the received wisdom. It requires the challenge of the established order, the right to be heard however outlandish the assertion, subject only to the test of rigorous method. Independence, originality, and therefore dissent—these are the hallmarks of the progress of contemporary civilization. It is well established that effective pursuit of science requires the protection of independence. Without independence of inquiry, there can be no true scientific research. The safeguards that independence requires are obvious: free inquiry, free thought, free speech, tolerance, and the willingness to arbitrate disputes on the basis of evidence. These are societal values worth defending, not just to promote the pursuit of science, but to yield a more tolerant society that adapts to change and embraces the new.

Can such ideas resonate in a society wracked by poverty and hunger, riven by civil strife and worried about fiscal crisis? I can already hear the naysayers, and their emphasis on pragmatism, realism, and the urgent. But they are wrong. Science does have the capacity to capture the imagination and to move the emotions. We must see science as an integral part of our culture, which informs our worldview and affects our behavior. Even more, science is itself a culture of global dimensions, or at least a cultural current that affects strongly the society where it flourishes. It brings imagination and vision to bear on concrete problems and theoretical speculation. The poet William Blake said, "What is now proved was once only imagin'd." Imagination and vision are at the very heart of the scientific enterprise.

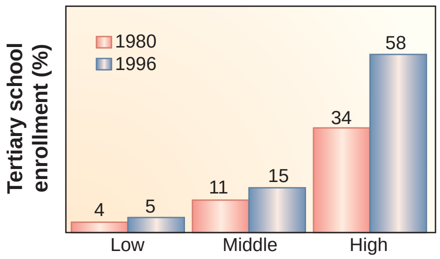
Setting the Agenda

For science to realize its full promise and become the primary force for change in the world, it requires that scientists work to

- engage scientific research in the pressing issues of our time
- abolish hunger and reduce poverty
- promote a scientific outlook and the values of science
- build real partnerships with the scientists in the South.

It is inconceivable that of the 1233 drugs that have been approved in the last decade, only 11 were for treating tropical diseases, and of these, half were intended for livestock, not humans. It is inconceivable that many of the persistent issues of child nutrition that could be tackled by changing the nutritional content of crops are receiving so little attention. We need more examples like Quality Protein Maize (QPM) and vitamin-A rice (Golden Rice).

We need to engage in real collaboration between centers in the North and South, and to engage scientists in the South in common research endeavors. Only by joint efforts will the values of science be strengthened and the scientific outlook promoted in societies where strong currents of obscurantism and xenophobia vie with rationality and tolerance for the hearts and minds of people.



Tertiary school enrollments. In 1980, tertiary school enrollments stood at 4, 11, and 34% for low-, middle-, and high-income countries, respectively. In 1996, this had risen to 5, 15, and 58%, respectively.

These efforts also need to involve the public, for only by such involvement do institutions flourish. Robert Putnam's pioneering work in Italy in the 1990s showed how institutional performance dramatically improves with greater civic involvement and support (*2*).

Such joint efforts require addressing the many issues that govern the practice of science in developing countries, from policy to institutions to human resources to finance. In order to promote true partnerships between the North and South, we will have to think beyond occasional intergovernmental protocols. We need to bring together the public and private sectors, government and civil society, national and international community groups and foundations, all forged into true and caring coalitions.

Implementing this agenda will mean

- not just new science and technology, but also relevant science and technology
- not just communications, but also content
- not just technology transfer, but also real collaborations that promote the values of science and the scientific outlook.

This last point emphasizes process as much as outcome, for the process itself promotes fundamental ethical values that are at the heart of what good science is all about. In the words of Bronowski, "Those who think that science is ethically neutral confuse the findings of science, which are, with the activity of science which is not."

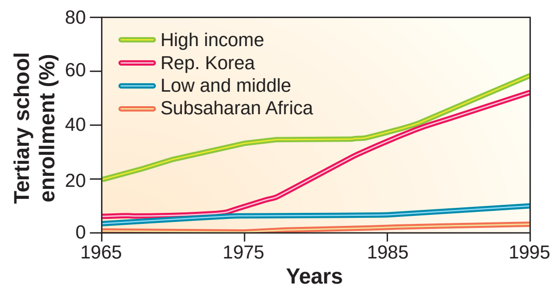
The Way Forward

Clearly it is essential to fully integrate the international scientific community, without which there can be no effective practice of science. But scientists' voices must be heard loudly and clearly in the national discourse of their own societies. This absence not only severs science from its salutary effect on the modernization of societies, but also undermines the public support necessary for its pursuit.

To the members of the scientific community in the industrialized world I say: You cannot let the talents of 80% of humanity flourish only if they leave their native lands or remove themselves from their societies. You must extend additional efforts to reach them and assist in the strengthening of the scientific enterprise in the South.

To the members of the scientific community in the developing world I say: We are at a crossroads. Either we are going to reassert the importance of science and the scientific outlook, or we are going to witness our societies increasingly marginalized in the world of the information age.

The scientific communities of the developing world either will become more and more detached from their own societies, or will reassert the links of the scientific outlook and its values in the mainstream of the modernization efforts of their changing societies. They must by their engagement help to create the "space of freedom" that is necessary for civilized constructive social discourse, and essential for the practice of science. This commitment is the only way to create centers of excellence in the developing world and to ensure that the benefits of progress accrue to all the poor and the marginalized. It is these "values of science" that can unleash the full measure of



Tertiary school enrollments over time. Whereas tertiary enrollment continues to increase in high-income countries, it has changed little in middle- and low-income nations. The exceptions are the Republic of Korea and Singapore, which show increases in tertiary school enrollments comparable to those in high-income countries.

SOURCES: LEFT, WORLD DEVELOPMENT INDICATORS, 1999; RIGHT, TASK FORCE, 2000 their talent and their genius. All of that, however, requires liberating the mind from the tyranny of intolerance, bigotry, and fear, and opening the doors to free inquiry, tolerance, and imagination.

With centers of excellence in the developing world, there can be real partnerships between North and South. The promise of science can be fulfilled to make the new century one free of hunger and of absolute poverty, accurately described as a condition beneath any definition of human decency. All of that, however, requires our joint commitment as scientists to work for the benefit of the entire human family, not just the privileged minority who are lucky enough to live in the most advanced industrial societies. These tasks are enormous. But the longest journey starts with a single step. So let us start. If not us, who? If not now, when?

References

1. J. Bronowski, *Science and Human Values* (Harper and Row, New York, 1956).
2. R. D. Putnam, *Making Democracy Work: Civic Traditions in Modern Italy* (Princeton Univ. Press, Princeton, NJ, 1993).

PERSPECTIVES: THE RICE GENOME

The Most Precious Things Are Not Jade and Pearls...

Pamela Ronald and Hei Leung

"The most precious things are not jade and pearls but the five grains." The five grains referred to in this Chinese saying are most likely to be rice, wheat, millet, sorghum, and maize (*1*). These cereal grains account for up to 60% of the calories consumed by people in the developing world (*2*). We could also apply this saying to the valuable genetic information that cereals contain—especially rice. With a genome significantly smaller than those of other cereals, rice is an excellent model for genetic and molecular studies (*3*). The publication of draft genome sequences of two major subspecies of rice (*indica* and *japonica*) on pages 79 and 92 of this issue (*4*, *5*), provides a rich resource for understanding the biological processes of plants and promises to positively impact cereal crop production.

If the world's population continues to grow as predicted for the next 20 years, global cereal yield must increase 80% over the 1990 average to feed these additional people (*6*). Compounding the problem is that areas of productive farmland continue to be lost through urbanization and degradation of existing agricultural soils (*7*). Although achieving food security will require a multitude of social and economic solutions, the new knowledge derived from genomics research will make an important contribution. The challenge ahead for the plant research community is to design efficient ways to tap into the wealth of rice genome sequence information to address production constraints in an environmentally sustainable manner.

Taxonomically, all cereals belong to one of the two major groups of flowering plants: the monocotyledonous plants (monocots). Completed in 2000, the genome sequence of the weed *Arabidopsis thaliana* provided our first complete view of the genome of a dicotyledonous plant (*8*). With the availability of the rice genome sequence, we can now directly compare the genome of a monocot to that of a dicot and to genomes of other sequenced organisms. A significant observation is that over 80% of *Arabidopsis* genes have close counterparts (homologs) in rice whereas only 50% of rice genes have homologs in *Arabidopsis*, suggesting that all rice genes are essentially a superset of *Arabidopsis* genes (*4*). Furthermore, at a significant level of similarity, 85% of proteins examined in cereals have a related protein in rice (*3*). This observation poses some interesting questions regarding what the additional rice genes do. Assuming functional conservation, the extensive DNA sequence similarity between rice and other cereals will provide a short cut to the isolation of genes of agronomic importance in cereals as well as in other crop species. Thus, genomewide analyses affirm that rice is indeed a model species for cereal research with practical applications in both monocots and dicots (see the Perspective by Bennetzen on page 60).

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Comparative genomic analysis enables biologists to assign a tentative function to a gene according to what that gene does in another species. For instance, the rice genome sequence reveals a network of genes encoding phosphate transporters, first identified in yeast, that are likely to be important for uptake of this macronutrient from soils (*5*). Genes controlling disease resistance, tolerance to abiotic stresses, or synthesis of essential vitamins can also be predicted by comparative genome analysis (*8*–*10*). This information facilitates the formulation of clearly defined hypotheses regarding which genes govern specific biochemical and metabolic pathways. Experiments can then be designed to determine whether the gene of interest has the predicted contribution to that pathway. For example, the presence of candidate sequences for phosphate transporters can be tested for correlation with phosphate-uptake efficiency in rice populations exhibiting variability for this trait (*11*).

The task of the protein encoded by the candidate gene can be further validated by whole plant approaches, typically by overexpressing the gene of interest (by hooking it up to a strong regulatory domain) or by knocking out its function, a field of study called reverse genetics (see the figure). For example, if a gene is hypothesized to govern disease resistance, overexpression of the gene or disruption of its activity should lead to a detectable alteration in resistance to disease, thus confirming the original prediction. Large collections of

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