

The tools that more than doubled world grain harvests since 1960 have lost their edge. Bold efforts to bioengineer crops seem the only hope for a new surge in harvests

Crop Scientists Seek a New Revolution

Every year, the U.S. National Corn Growers Association sponsors a competition among farmers for the highest maize yield. The contestants have always vied furiously for the title in this agricultural Superbowl, but now some scientists are taking an interest, too. During the 3 decades of the competition,

FUTURE FOOD

Much of the world is awash in grain, but future abundance will depend on whether researchers can repeat the stunning advances of the Green Revolution. This special report examines the prospects for doing so.

A NEW REVOLUTION BIOENGINEERING

U.S. maize harvests have risen continuously from an average of 5 metric tons per hectare in 1967 to 8 t/ha in 1997, according to the U.S. Department of Agriculture (USDA). Yet the highest, prize-winning yields have stayed roughly constant (except in years of flood or drought), at about 20 t/ha for irrigated fields. "It's a striking pattern," says Kenneth S. Cassman, an agronomist at the University of Nebraska, Lincoln: "Steady progress upward on the average, but at the top—the best of the best—it doesn't appear that the maize yields have changed in 25 years."

The apparent ceiling on maize yields—and hints of similar ceilings for rice and wheat—has led Cassman and other researchers to argue that cereals harvests have physical limits, and farmers may be nearing them. Agricultural economist Vernon Ruttan of the University of Minnesota, St. Paul, says that while he was working at the International Rice Research Institute (IRRI) in Los Baños, the Philippines, in the early 1960s, "it was fairly easy for me to tell myself a story about where future yield increases were going to come from." Today, he says, "I can't tell myself a convincing story about where the growth is going to come from in the next half-century."

If the question is whether farmers can raise average yields closer to the maximum, says Thomas R. Sinclair of the USDA Agricultural Research Service at the University of

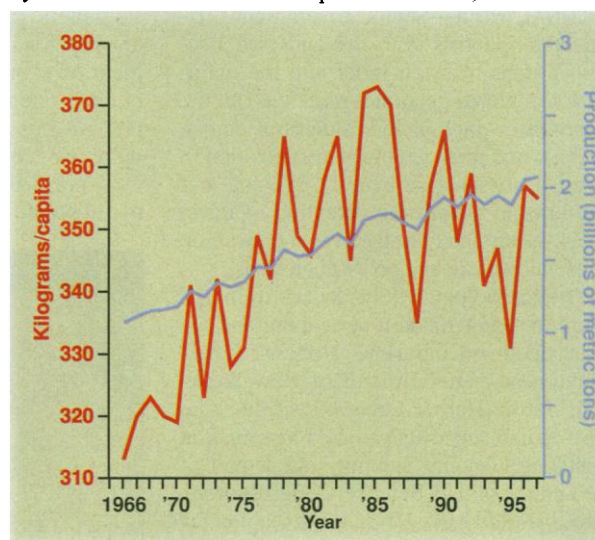
Florida, Gainesville, "I would guess that there is" some room for advancement. But if the question is whether breeders can raise the "physiological potential" of cereal crops, Sinclair says, "I don't think the evidence there is very encouraging. ... It's hard to see where improvements in that would come from."

The stakes are enormous. In the 1950s and '60s, agricultural scientists at IRRI and the International Maize and Wheat Improvement Center, a Mexico City-based laboratory better known by its Spanish acronym, CIMMYT, developed the package of improved crop varieties and agricultural management techniques collectively known as the Green Revolution. The critical advances of the Green Revolution—and other work by the 16 international agricultural research centers that make up the Consultative Group on International Agricultural Research (CGIAR)—helped world grain harvests more than double since 1960. Despite a huge population increase since then, per capita food production has grown by almost a quarter; the number of people eating less than 2100 calories per day, a standard index of malnutrition, has fallen by three-quarters. Driven by soaring harvests of rice, wheat, and maize, the world's most important crops, the global boom in agricultural production is one of the century's greatest technological achievements.

Now, though, researchers will have to do it all over again. By 2020, global demand for rice, wheat, and maize will increase 40%—an average annual increase of almost 1.3%—according to a projection released in August by Mark W. Rosegrant, Claudia Ringler, and Roberta V. Gerpacio of the International Food Policy Research Institute (IFPRI), a CGIAR think tank in Washington, D.C. "What everyone wants to know," Rosegrant says, "is whether that additional

demand can be met, and whether it can be met without undue environmental or economic cost."

Since the early 1980s, says the United Nations Food and Agricultural Organization (FAO), global cereals harvests have been rising at a rate of about 1.3% per year—just enough to meet the projected increase in demand. But this rate of increase is half what it was in the 1970s, suggesting the possibility of a long-term falloff. Most of the relative decline is due to economic upheavals in formerly communist nations and planned reductions in incentives like farm subsidies in other developed countries, which have



Just keeping up. World grain harvests continue to rise, but because of population growth, per capita production has flattened.

caused farmers to take land out of cereals production. But productivity increases—rises in cereal yields per hectare—have been slipping, too, from 2.2% per year in 1967–82 to 1.5% per year in 1982–94.

To many agronomists, the slackening is a sign that the now-familiar tools of the Green Revolution are facing diminishing returns. The burgeoning harvests the world will need tomorrow will have to come, they say, from radically new, completely untried innovations in genetic engineering. But even if those innovations pan out—which is far from certain—researchers fear

SOURCE: FAOSTAT (<http://faostat.fao.org>)

that farmers may not have enough water to grow the new crops or may be forced to use so much fertilizer on marginal land that they will poison ecosystems and permanently damage soils. "When you add up everything that has to be done, and the narrowing range of options for how to do it, the challenge is dauntingly large," says Tony Fischer, crop-sciences program manager at the Australian Centre for International Agricultural Research in Canberra.

Not everyone shares this alarm, as vigorous debate at recent meetings in Baltimore* and Irvine, California, showed.† "People have been predicting yield ceilings for millennia, and they've never been right," says Matthew Reynolds, a plant physiologist at CIMMYT. Indeed, some skeptics argue that the slowdown in productivity growth might actually be a sign of progress, because it shows that many nations are enjoying food surpluses. As for meeting future demand, they say, it is a good bet that some of the many efforts to re-engineer crops will pan out. "If I were an agricultural policy developer in a developing country today, I'd be more worried about too much food in the world than too little, because it would drag the prices down," says D. Gale Johnson, an agricultural economist at the University of Chicago. With varying degrees of caution, official projections from the World Bank, FAO, and IFPRI agree with Johnson: Agricultural researchers can repeat the Green Revolution.

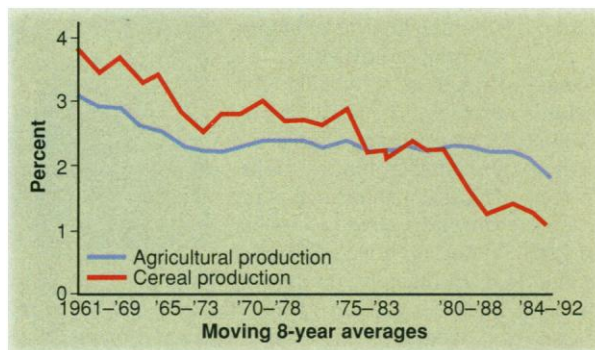
But the plant breeders themselves are not sanguine. "Those maximum rice yields have been the same for 30 years," says Robert S. Loomis, an agronomist at the University of California (UC), Davis. "We're plateauing out in biomass, and there's no easy answer for it."

* "Post-Green Revolution Trends in Crop Yield Potential: Increasing, Stagnant, or Greater Resistance to Stress?" 90th annual meeting, American Society of Agronomy/Crop Science Society of America/Soil Science Society of America, 19 October 1998. The papers have been submitted for a forthcoming special issue of *Crop Science*.

† "Colloquium on Plants and Population: Is There Time?" 5–6 December 1998, Beckman Center of the National Academies of Sciences and Engineering, Irvine, California. Papers at www.lsc.psu.edu/NAS/The%20Program.html

Exploited opportunities

When scientists speak of yields, they can be referring either to a crop's "actual yield"—the harvests produced in real-world conditions—or its "potential yield"—the theoretical maximum weight of grain a unit of land can produce, given perfect weather, optimal



Slower growth. Annual increases in cereal production have slowed since the Green Revolution of the 1960s and 1970s.

use of fertilizers, and no pests or pathogens. Yields can thus be raised either by lifting actual yields closer to the ceiling, usually by improving crop management or developing strains that are resistant to pests, disease, and stresses, or, more ambitiously, by raising the ceiling itself.

The Green Revolution did both. Plant breeders at CIMMYT and IRRI dramatically increased the potential yield of wheat and rice by creating shortened, "dwarf" varieties with strong stalks that could hold more grain. This boosted the "harvest index"—the percentage of the plant's mass that is grain—to about 50%, almost double the previous figure (*Science*, 22 August 1997, p. 1038). Dwarfing didn't work on maize, the third major cereal, because the shorter plants shaded themselves too much. So maize

breeders took a different approach, says Don Duvick, an agronomist at Iowa State University in Ames: producing strains that could be planted more densely. "We were able to breed to withstand the stresses of that [crowding] and get the yields up in that way."

In addition to these triumphs of plant breeding, the Green Revolution had two other, equally important reasons for its success: chemical fertilizer and irrigation. Be-

tween 1961 and 1996, according to FAO statistics, global fertilizer use more than quadrupled, rising from 31 million metric tons to 135 Mt. Meanwhile, the world total of irrigated land almost doubled, from 139 million ha to 263 Mha.

Those trends are now stalling. In developed countries, for example, heavy fertilization boosted yields but also contaminated water supplies, leading environmentalists to argue that farmers should cut back, not increase, fertilizer use. Moreover, poor nations in places like Africa cannot afford agricultural chemicals, limiting their use where they are most needed. Rosegrant projects that fertilization will continue to rise but that the rate of increase will fall sharply. Future harvest boosts, he believes, will come less from using more fertilizer than from using existing levels more efficiently. "By working hard," he says, "you can squeeze out increases inch by inch."

One hope for squeezing higher yields out of the same input, according to John Sheehy, an agricultural systems modeler at IRRI, is to track fertilization more closely to plants' nitrogen requirements. "Rice accumulates half its nitrogen by the time it acquires a quarter of its above ground biomass," he says. To maximize yields, farmers thus need "a huge basal application" of fertilizer in the first 40 days after sowing, followed by gradually diminishing levels thereafter. In preliminary tests at IRRI, a tracking regimen lifted yields by as much as 20%. But, as Sheehy concedes, such intensive management is easier in laboratories than in farmers' fields. "Translating this work into the

real world will be a challenge," he says.

Prospects for expanding irrigation are only somewhat better. Irrigation, too, has caused environmental damage, depositing toxic salts on poorly drained agricultural land. And because irrigation is already used in most of the areas where it is practical, future water projects will be increasingly expensive. Worst of

all, the International Water Management Institute, a CGIAR laboratory in Sri Lanka, projects that by 2025 as many as 39 countries—including northern China, eastern In-

"People have been predicting yield ceilings for millennia, and they've never been right."

—Matthew Reynolds

"When every step forward is harder to take, that's a sign of diminishing returns."

—Kenneth Cassman

dia, and much of Africa—will be so short of water that they will be forced to reduce irrigation rather than expand it.

Researchers like Sandra Postel of the Global Water Policy Project in Amherst, Massachusetts, believe that technological innovation can advance water-use efficiency, even in poor countries. Rather than watering crops by flooding whole fields, for example, farmers in parts of northern India are employing cheap, movable plastic pipes dotted with pinholes to “drip-irrigate” their fields. New, low-cost, high-efficiency sprinklers are also under development. But Postel expects the gains to be modest: “To satisfy the nutritional needs of 8 billion people and protect the environment, we’ll have to get twice as much agricultural productivity out of each unit of water we’re using.” She regards the task as “doable, I guess, but an awful lot of things are going to have to come out just right.”

Immovable ceilings?

Given the difficulties of raising yields by improving the use of agricultural inputs, many agronomists believe that a second Green Revolution will have to rest even more heavily than the first on creating crop varieties with higher potential yields. Again, traditional strategies may be losing their

opportunity has been pretty well exploited.”

In recent years, Sinclair says, plant breeders have succeeded mainly in creating varieties that are less susceptible to pests and disease, or that can tolerate hostile environmental conditions, like drought or salty soil. “The problem,” he says, “is that pest resistance isn’t increasing potential yield. It’s just protecting what you have already.” In his view, “we’re getting better at approaching the ceiling. What has been elusive is actually raising the ceiling.”

Worse, breeders are finding it increasingly hard to keep even the current small harvest increases coming. “Average annual maize yields keep right on going up by 90 kg/ha” in the major maize-producing U.S. states, says Cassman, “but the investment in maize-breeding research has gone up four-fold. The efficiency of translating this investment into yield is therefore down by 75%.” He adds, “When every step forward is harder to take, that’s a sign of diminishing returns.” Still more troubling to Cassman, this ever-increasing effort is required to produce a constant linear rise in yields, when the projections by FAO, IFPRI, and the World Bank are for an exponential increase in demand.

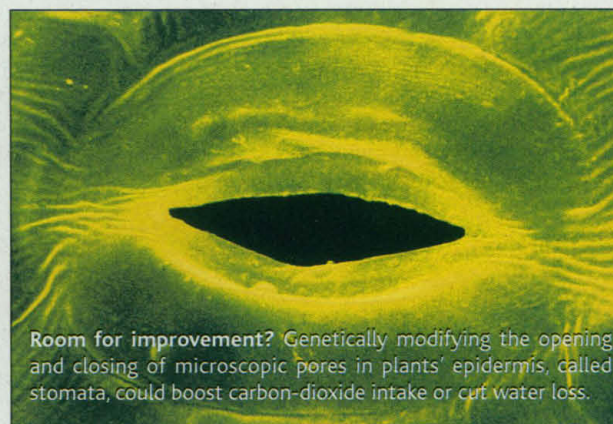
Some agronomists believe traditional plant breeding still has plenty of life left. Chinese rice researchers, for example, are exploiting the surge of productivity



Good breeding. Green Revolution strains of maize and wheat (*below right*), planted next to taller traditional varieties.

edge. “Most plant breeders and those who work in association with them would go along with the idea that there’s very little scope in wheat and rice for increasing the harvest index beyond the present value of about 50%,” says Roger Austin, an agricultural consultant in Cambridge, England. Breeding still shorter plants ultimately produces such a low, uneven canopy of leaves, he says, that it is “difficult to get uniform interception of light,” which interferes with photosynthesis; breeding for thinner, lighter stalks makes plants more likely to collapse under the weight of their own grain. As for further crowding of maize, in Sinclair’s view, “that

and vigor often seen in first-generation crosses to develop a “superhybrid” rice (see sidebar, p. 313). But other post-Green Revolution efforts to breed more productive varieties have run into difficulties. After 10 years, an ambitious IRRI program to design



Room for improvement? Genetically modifying the opening and closing of microscopic pores in plants’ epidermis, called stomata, could boost carbon-dioxide intake or cut water loss.

a “new plant type” of rice that would combine multiple innovations is a study in frustration.

Rice grows as a clump of as many as 30 stemlike “tillers” that bear the flowers and grain on “panicles.” Because a third or more of the tillers may not end up producing grain, the designers of the new plant type proposed creating rice cultivars that would have fewer tillers with bigger, more productive panicles. The smaller number of tillers would also reduce the diameter of the plant, allowing farmers to plant more of them in the fields. Moreover, IRRI breeders wanted the new plant type varieties to have thicker, more upward-angling leaves, which would catch more sunlight than current varieties, boosting the rate of photosynthesis. By combining all these changes, IRRI hoped to lift potential yields in the tropics to 12 t/ha, compared to today’s potential yield, which has stagnated at about 10 t/ha.

Because indica, the most common subspecies of cultivated rice, did not seem to have genes for reduced tiller number, IRRI began the new plant type in 1990 with germ plasm from another subspecies, tropical japonica. This indeed increased the size of the grain-bearing panicles, but the bigger panicles did not fill up with rice, because the plants could not shunt enough energy into them. Making the plants more compact compounded the problem, because the crowded “spikelets” atop the panicles couldn’t develop properly. “When you say you can make a watch run better by fixing up these six pieces, it affects the other pieces, too,” Iowa State’s Duvick says. “You fix A, you hurt B.”

At the Baltimore meeting, IRRI crop physiologist Shaobing Peng, who helps direct the new plant type project, revealed that last summer some new plant type rice finally produced better yields than conventional varieties—a sign that IRRI may be on the right track. But the new plant type was still extremely vulnerable to stem borers, a com-



CREDITS: (CLOCKWISE FROM TOP) D. M. PHILLIPS/VISUALS UNLIMITED; CIMMYT; CIMMYT

Crossing Rice Strains to Keep Asia's Rice Bowls Brimming

BEIJING, CHINA—While plant breeders in most of the world fear that grain yields are plateauing (see main text), Yuan Longping thinks a big jump in rice productivity is just around the corner. Yuan, the director of the National Hybrid Rice Research and Development Center in Changsha, Hunan Province, says he is on the verge of creating a superhigh-yield hybrid that promises jumps of 15% to 20% in potential rice yields over existing hybrids.

Yuan cautions that the results are based on tiny test plots and must be confirmed in larger trials over the next 2 years. Even if the new strain does live up to expectations, say other plant breeders, consumers may turn up their noses at the quality of the rice. But scientists who have heard his preliminary results think Yuan is on to something big. "When I hear Yuan Longping's enthusiasm about this and when I think about his track record, I take note of what he's saying," says Neil Rutger, director of the Dale Bumpers National Rice Research Center in Stuttgart, Arkansas. "If [the yields are] what he claims, it is a significant achievement," adds Sant Virmani, deputy head of plant breeding at the International Rice Research Institute in Los Baños, the Philippines.

Yuan's efforts make use of the fact that the first generation of hybrid plants is typically more vigorous and productive than either parent—a poorly understood phenomenon called heterosis. To take advantage of heterosis, virtually all the maize in developed countries is grown from first-generation (F1) hybrid seed. But corn is much easier to hybridize than rice. Because rice is self-pollinating, getting hybrid seed requires developing lines of plants in which the male organs are sterile and can only be pollinated by the other parental line. A third line of plants is required to provide pollen to reproduce the male-sterile line for the next growing season. The technique is not only laborious but also produces small quantities of seed. As a result, hybrid rice in most countries has taken a back seat to inbred rice, in which part of one year's crop can be kept as seed for the next.

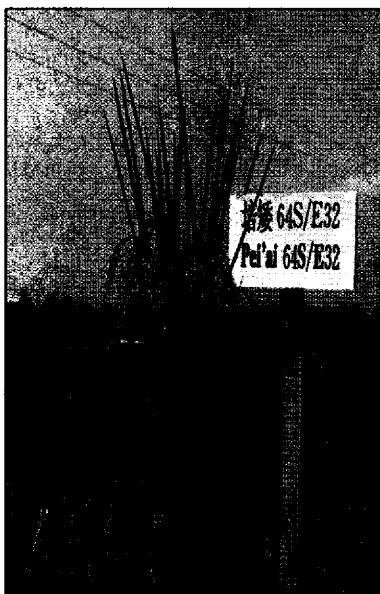
Not in China, however. In the 1970s, Yuan made production of F1 hybrid rice seed viable with techniques that tapped his country's cheap labor. He sprayed the male-sterile plants with a growth hormone so that the panicles, or grain clusters, would emerge from the rice leaf sheath to catch pollen that was shaken loose by ropes dragged over the male-line plants. Hybrid rice now accounts for half of China's rice acreage and yields an average of 6.8 tons per hectare compared with 5.2 tons for conventional rice. By Rutger's calculation, the increased output feeds an additional 100 million Chinese every year.

China's success has inspired hybrid rice production in India, Vietnam, and the Philippines. Several more countries are developing hybrid rice varieties suited to their own growing conditions. But even

higher yields will be needed to meet Asia's projected food demand.

To Yuan, the answer was to cross more diverse parent strains in order to achieve even greater heterosis and higher yields. Unfortunately, the more diverse the parents, the greater the chance that the offspring will be sterile, growing vigorously but producing little rice. But in the mid-1980s, Hiroshi Ikehashi, a plant breeder at Kyoto University in Japan, identified a gene in certain species of japonica rice native to Indonesia that promotes fertility in hybrids. This wide compatibility gene, which has proven relatively easy to transfer through crossbreeding, was the breakthrough Yuan needed.

Rather than count on heterosis alone to raise yields, however, Yuan also decided to incorporate morphological improvements. Since 1996, his group has selectively bred potential parents for long, narrow, and very erect top leaves. This configuration, Yuan believes, captures sunlight more effectively. He's also bred plants to grow large panicles that hang close to the ground, reducing the risk of lodging, or falling over. "Both hybridization and morphological improvements are important," Yuan says. "I don't think you can rely on just one or the other."



Hybrid vigor. Chinese rice breeders hope this cross between strains having narrow, erect leaves will push up yields.

In 1997, one of the crosses yielded an average of over 13 tons per hectare—well above the 10.5 tons for existing hybrids grown under ideal conditions. Although that test took place on just a fraction of a hectare, the group achieved similar results last summer in trials at four separate locations totaling more than 2 hectares. If he can get 12 tons per hectare for two consecutive years, Yuan says, "I will declare that the goal of the super-hybrid rice-breeding program is achieved." He is so confident of success that he invited participants at an international conference in Cairo last

fall to visit China and witness this year's harvest.

But yields aren't everything. "The value of superhybrids will very much depend on the grain quality," warns Miroslaw Maluszynski, a plant geneticist at the International Atomic Energy Agency in Vienna, Austria. Yuan agrees that hybrid rice became popular in China because people "needed calories more than quality." And quality is still critical in more affluent nations such as Japan and South Korea. "Where quality is important, hybrid rice won't sell," says Shigemi Akita, a crop physiologist at the University of Tokyo.

Still, Yuan and others are confident that hybrids will play an increasingly important role in filling Asia's rice bowls. Studies of heterosis "are still at a juvenile stage," he says. "The very high-yield potential of hybrid rice has not yet been fully tapped." —DENNIS NORMILE

mon pest. "The tillers are strong but not tough," IRRI's Sheehy says. "Borers chew right through them, which poses a genuine research problem." Although he believes the new plant type will eventually be "vindicated," its progress is a sobering reminder of the difficulties of raising yield.

"We've been working on rice yields for so many years without making the kind of progress we'd like to make," Peng says. "We

may be able to create the new plant type without biotech, but that is where new opportunities will have to come from in the future."

Big biotech

Peng and the other agronomists who regard genetic engineering as the key to surpassing the yield barrier have more in mind than the products of today's biotech industry, which now cover almost 20 million ha in North

America alone. The vast majority of these crops are the result of single-gene transfers, in which one or more genes coding for desired characteristics—such as herbicide resistance or an antibacterial compound—are smuggled into the organism from an outside source. Such efforts, although important to raising actual yields, are unlikely to raise potential yields. To break yield barriers, the plants will have to be thoroughly re-engineered.

Among the more widely discussed biotech possibilities is altering the stomata, the porelike openings that stipple a plant's epidermis and control the in- and outtake of oxygen, carbon dioxide, and water. In most plants, the stomata are edged by two cells that resemble a pair of parentheses. When the plant takes in water, the stomatal cells swell open, allowing water to escape and permitting gas exchange; when the surroundings become drier or hotter, the stomata close. Because the stomata stay open longer than needed, most of the water that wheat and rice take in ends up in the atmosphere rather than being used in photosynthesis. "If you're irrigating, you might put up with the water loss in the name of getting the greatest biomass possible," says UC Davis's Loomis. "But if you're dry-land farming in Kansas, it might not be a good deal—you're using up water too fast."

To allow dry-land crops to use water more efficiently, stomata might be bioengineered to close more readily; in water-rich areas, they might be modified to stay open even longer. "That would give you better ventilation in the leaf, decreasing the canopy temperature and giving you better transport of CO₂, both of which could boost the rate of photosynthesis," says Fischer of the Australian Centre for International Agricultural Research.

Researchers have their eyes on two molecular targets that play a role in regulating the stomata: the plant hormone abscisic acid, which triggers closing, and an enzymatic process called farnesylation, which seems to impede ABA (*Science*, 9 October 1998, pp. 252, 287). By altering farnesylation, researchers may, in theory, be able to adjust plants' sensitivity to ABA and thus the tendency of the stomata to close. That task is daunting enough, but other researchers would like to go even further and tinker with the mechanisms of photosynthesis itself (see next story).

Many economists are confident that such efforts will eventually pay off and drive up crop yields again. But agronomists tend to view biotech as a long shot. Controlling such basic multigene traits, Fischer warns, is a "complex, unpredictable" task. Photosynthesis, notes Sinclair, is a process that evolution hasn't changed fundamentally "in a couple billion years." And even if the work is a technical success, the payoff may be minor, as traditional plant breeding has already pushed up crops' harvest index and ability to capture sunlight about as high as they can go. As Sinclair put it at the Irvine meeting, "Some of the hope for biotechnology seems analogous to the dreams of mechanical perpetual motion devices over a century ago: No matter how finely tuned the machine, reality does not allow output to exceed input."

Still, altering photosynthesis is "the great white hope" of the future of agricul-

ture, as agricultural consultant Austin puts it. "All the relatively obvious steps have been taken. Photosynthesis is what's left."

Money woes

Re-engineering photosynthesis—or fundamentally improving crops in some other way—will require years of costly basic research, in Cassman's view. But a crucial source of support for agricultural science is eroding. For more than a century, according to Phil Pardey, an economist at IFPRI, government funding has supported long-term agricultural research. Although the biotech boom has spearheaded a recent massive increase in private-sector spending on agricultural R&D, notes Duvick, a former research director of agribusiness giant Pioneer Seeds, "even the big companies don't do a lot of long-term research."

But despite opposition from both the academic and corporate community,

IRRI's budget in constant 1994 dollars has dropped from a high of \$46.5 million in 1990 to \$32.7 million in 1997, according to CGIAR figures. Similarly, CIMMYT's funding fell from \$40.2 million in 1988 to \$28.4 million in 1997. "We're taking away funding with the assumption that we've made it," says Dennis A. Ahlburg, a demographer at the London School of Hygiene and Tropical Medicine's Centre for Population Studies. "But if we don't continue to support [agricultural research], we'll slide backward."

"The scientific challenge [of feeding the world] has been grossly understated," Cassman says. "But even if I'm wrong, and we somehow can do it without special effort, I think you'd like to have a margin of security. ... We are talking about the prospects for producing enough food to feed people in the next century, and a margin of security seems justified."

—CHARLES C. MANN

FUTURE FOOD ►BIOENGINEERING

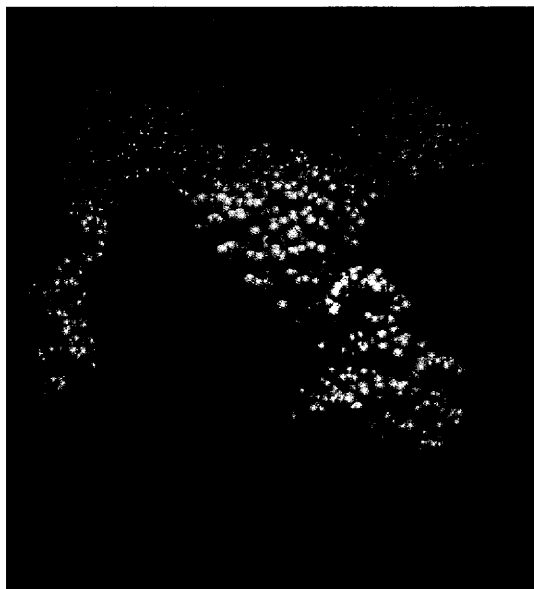
Genetic Engineers Aim to Soup Up Crop Photosynthesis

To improve crops' ability to turn atmospheric carbon into food, researchers hope to alter the principal enzyme or supercharge it with CO₂

Few nonbiologists may have heard of ribulose-1,5-bisphosphate carboxylase-oxygenase, the enzyme known as RuBisCO, but its importance is hard to overstate. The principal catalyst for photosynthesis, it is the basic means by which living creatures acquire

the carbon necessary for life. By interacting with atmospheric carbon dioxide, RuBisCO—the world's most abundant protein—initiates the chain of biochemical reactions that creates the carbohydrates, proteins, and fats that sustain plants and other living things, ourselves included. But the enzyme also has another distinction, according to T. John Andrews, a plant physiologist at The Australian National University in Canberra: "RuBisCO is nearly the world's worst, most incompetent enzyme—it's almost certainly the most inefficient enzyme in primary metabolism that there is."

RuBisCO's ineffectiveness has been a spur to scientists since it became fully apparent in the 1970s. Indeed, the quest for a better RuBisCO is "a Holy Grail in plant biology," says George Lorimer, a biochemist at the University of Maryland, College Park, who worked with the Swedish team that mapped the enzyme's structure in 1984. "Everyone always goes in with the hope of changing the face of agriculture." Despite more than 20 years of effort, the hopes have not yet paid



The enzyme that feeds the world. RuBisCO, which captures carbon dioxide and helps turn it into starches, sugars, and other compounds, is a target for genetic engineers.

CREDIT: JOURNAL OF MOLECULAR BIOLOGY 259, 160 (1996)