

include larger molecules, such as cyclodextrins or peptides, in which case they resemble GPs that bear sugars, lipids, and other groups added by posttranslational modification.

To what extent has similarity in surface properties led to analogs of biological functions? Some of these functions can indeed be found for NPs (see the figure, panel A). For instance, analogs of the bimolecular GroEL protein complex were found in cadmium selenide, gold, and nickel-palladium NPs (6). Bayraktar *et al.* observed formation of pair complexes of gold NPs with cytochrome c and cytochrome c peroxidase (3). Tuning the size and the charge should make it possible for the NP spheres to mimic either the cylindrical channel of GroEL or the semispherical binding patch of cytochrome c peroxidase.

Enzymatic activity has been observed in the NPs developed by Scrimin and co-workers, which have stabilizers including peptides forming a complex shell. For instance, successful hydrolysis of a phosphate bond of phosphodiester to create a functional replica of a ribonuclease can be achieved (7), and gold NPs modified with beta-cyclodextrin possessed esterase activity (8).

Recent studies also indicate that NPs can self-assemble into complex microscale superstructures such as chains, sheets, and twisted ribbons (9–11). Parallels can be made with GPs such as amelogenin (12) assembling in chains, S-layer proteins and chaperonin assembling in two-dimensional sheets (13), and GPs in the capsid of tobacco mosaic virus forming helical tubules (14). The accurate description of the self-assembly process was also achieved in computer simulations that incorporated force fields around the NPs similar to those used previously for proteins (9, 15). The similarity of the chemical behavior of NPs and GPs is not accidental but is based on analogous structure as well as thermodynamic and kinetic behavior of nanoscale structures in aqueous media.

Other emblematic functions of GPs have also been identified in recent publications but with lower degrees of experimental proof and functional resemblance (see the figure, panel B). For example, proteins can facilitate transport of DNA across cellular membranes. Bharali *et al.* found that NPs can efficiently do the same and cross cellular membranes themselves (16). They can support transfection of cells with genes replicating the function of bacterial SpoIIIE protein (17). The positive charge of the NPs and tight coiling of DNA around them resemble histone-DNA interactions and may account for the high efficiency of NPs as transfection vectors. Formation of extensive networks of NPs or gels

(18) can be compared with structural function of different proteins, but adequate replication of gel and network formation will require the demonstration of the reversibility of such reactions and different mechanical properties of the gels. Proteins perform a variety of functions when bound to DNA. Such binding occurs with NPs but without specificity (19).

It should be possible to replicate other functions of GPs that depend mainly on surface interactions by using NPs (see the figure, panel C). A logical extension of previous works is molecular engineering of the NP surface to reach specific and reversible binding of both small and large biomolecules, including DNA. These functions can find extensive use in biotechnology to control pathways of bacterial biosynthesis with NPs. Nanoscale systems with dynamic stimuli-responsive NP networks will lead to new sensing platforms and fluids with unusual flow responses reminiscent of many biological fluids. NP interactions with membrane receptors might have produced cell signaling events, but these effects remain to be investigated systematically (20, 21). Another potentially prolific direction is NP design to perform chiral catal-

ysis and inhibition of specific enzymes. If these functionalities are realized, they should enable medically relevant drug design, as well as clarifying the health effects of NPs present in the environment.

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10.1126/science.1190094

PLANT SCIENCE

Communal Benefits of Transgenic Corn

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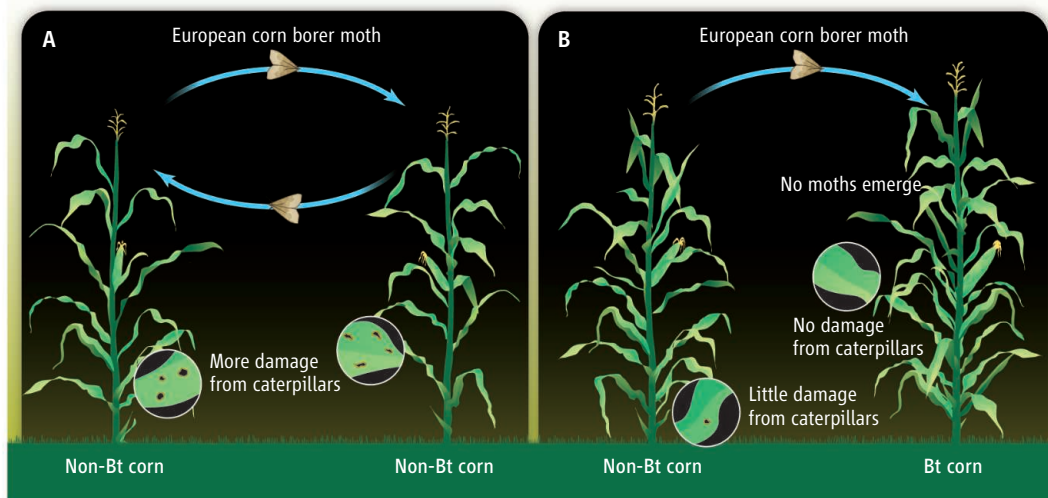
Genetically engineered corn plants can reduce pest damage on neighboring, unmodified plants.

Genetically engineered crops represent one of the most controversial and rapidly adopted technologies in the history of agriculture. First grown commercially in 1996, transgenic crops covered 135 million hectares (ha) in 25 countries during 2009 (1). To reduce reliance on insecticide sprays, corn and cotton have been genetically engineered to make insecticidal proteins derived from the common bacterium *Bacillus thuringiensis* (Bt). These Bt toxins kill some devastating insect pests, but unlike broad-spectrum insecticides, they do little or no harm to most other organisms, including people (2). Many pests have rapidly evolved resistance to insecticides, however, spurring concerns that adaptation by pests could quickly reduce the

efficacy of Bt crops and the associated environmental, health, and economic benefits (3–7). On page 222 of this issue, Hutchison *et al.* (8) rein in some of those concerns, documenting a landmark case in which Bt corn has remained effective against a major pest for more than a decade, yielding billions of dollars of estimated benefits to farmers in the midwestern United States.

Hutchison *et al.* describe Bt corn's suppression of the European corn borer (*Ostrinia nubilalis*), an invasive insect introduced into the United States in 1917. The caterpillars of this moth chew on leaves and tunnel in corn stalks. Before the advent of Bt corn, it caused losses of \$1 billion per year in the United States (8). However, susceptible caterpillars of this pest do not survive on Bt corn that produces toxins active against the larvae of Lepidoptera (moths and butterflies) (8).

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Halo effect. Bt corn planted near non-Bt corn can provide the unmodified plants with indirect protection from pests. European corn borer moths lay eggs indiscriminately on Bt corn and non-Bt corn, but their caterpillars survive and become moths only on non-Bt corn. (A) With only non-Bt corn, moths move between plants and lay eggs, and caterpillars damage plants. (B) Moths do not emerge from Bt corn plants, reducing the number of eggs and subsequent damage on non-Bt corn near Bt corn. Yield is highest for Bt corn (B), lowest for non-Bt corn (A), and intermediate for non-Bt corn near Bt corn (B).

Although it is not surprising that planting millions of hectares of Bt corn reduced the damage caused by the European corn borer, Hutchison *et al.* discovered that most of the economic benefits from 1996 to 2009 were associated with planting corn that does not make Bt toxins (i.e., non-Bt corn). This somewhat counterintuitive result arises from three facts: Farmers paid a premium of about \$10 to \$20 per ha for Bt corn seed; on average, non-Bt corn was more abundant than Bt corn; and pest populations decreased dramatically on non-Bt corn plants.

The suppression of pests on non-Bt plants near Bt plants—called the “halo effect”—was predicted on theoretical grounds by Alstad and Andow in 1996 (3). The halo effect occurs with European corn borer because females lay eggs indiscriminately on Bt and non-Bt corn, and the caterpillars hatching on Bt corn die (8) (see the figure). If Bt plants account for a substantial percentage of the available host plants, regional pest populations can be greatly reduced, resulting in less damage to non-Bt plants. Although the halo effect was seen before (6, 9, 10), Hutchison *et al.* are the first to report an economic analysis of this phenomenon based on large-scale, long-term data. They demonstrate that planting non-Bt corn pays off because farmers avoid the extra cost of Bt seed, yet still get some pest control benefits generated from neighboring Bt corn.

The immediate economic gains farmers reap from planting non-Bt corn could boost their compliance with the “refuge” strategy, which is designed to delay the evolution of pest resistance to Bt corn (3–5). In the United States, the Environmental Protection Agency

(EPA) requires farmers to plant refuges of non-Bt corn near Bt corn (2, 11). Refuges promote the survival of susceptible insects to mate with resistant insects that survive on Bt corn. If inheritance of resistance is recessive, the hybrid progeny from such matings will die on Bt crops, substantially slowing the evolution of resistance. This approach works best if the dose of toxin ingested by insects on Bt plants is high enough to kill all or nearly all of the hybrid progeny (12). Moreover, as the toxin dose increases, so too does the magnitude of resistance required for survival on Bt plants (13). Whereas mutations providing small decreases in susceptibility to Bt proteins are relatively common, those conferring sufficient resistance to enable survival on some types of Bt corn are exceedingly rare in the European corn borer (14, 15).

Although refuges have probably helped Bt crops remain effective longer than expected in most cases, some populations of at least four major pests have evolved resistance to Bt crops (12, 13, 16). Analyses of global resistance monitoring data suggest that the evolutionary principles underlying the refuge strategy can explain why some pest populations have evolved resistance faster than others (7, 12). In each case of field-evolved resistance to Bt crops, the high-dose standard was not met, refuges were scarce, or both (7, 12).

New tools to combat pest resistance to Bt crops include a wider array of toxins, including toxins genetically modified to counteract resistance (17). Also, to thwart resistance, plants that produce two or more distinct Bt toxins targeting the same pest are becoming increasingly important. For example, a

type of Bt corn registered in the United States in 2009 produces five distinct Bt toxins; three of these target caterpillar pests including European corn borer and two kill corn rootworm beetles (*Diabrotica* species) (11). Whereas the EPA had previously required non-Bt corn refuges planted in separate fields, rows, or strips, in April 2010 it approved sales of mixtures of corn seeds with and without Bt toxins that kill corn rootworms (11). This seed mixture approach ensures that farmers comply with the refuge strategy, and may be especially useful on small farms in developing countries where planting separate refuges is not practical. With the shift to seed mixtures and multitoxin

Bt corn, the EPA has dropped the minimum percentage of corn that farmers must plant in non-Bt corn refuges from 20% to as little as 10% (seed mixtures) or 5% (multitoxin plants) (11). No one knows how fast insects will adapt to Bt corn under these new conditions. As we scramble to stay one step ahead of the pests, let's keep in mind the groundbreaking report by Hutchison *et al.* affirming the adage that diversity breeds success.

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18. I thank the U.S. Department of Agriculture–National Institute of Food and Agriculture program for support.