Agriculture: The Foundation of the Bioeconomy

Ganesh M. Kishore
Burrill & Company
San Francisco, CA

These are some of the most exciting times in agriculture. Agriculture is in the news practically every day, and not just in the United States. It is also in the news in Asia, Africa, South America, and Europe because of developments not only in food production but also in terms of leveraging agricultural products for biomaterials and renewable fuels. It is my thesis that if we get agriculture right, it is possible to meet—sustainably—many of humanity's needs, independent of whether a person is living in the United States or in Timbuktu.

Key Issues

Number one, of course, is the energy issue. The economic growth that is occurring in many parts of the world, especially in the BRICK[1] nations, is causing a huge surge in demand for fuel. Resultant uncertainty over access to fuel is creating its own set of issues including the need to create enough storage of liquid transportation fuels.

The number-two issue is food. This economic growth is not only driving energy consumption but also demands for improved quality of food. In fact, within the next 20 years, we have to produce 50% more food from the same amount of land with similar inputs, which will require significant inputs of technology. Debates about food versus fuel, (non) acceptance of genetically modified (GM) crops and a number of other issues will continue via the Internet with massive dissemination of misinformation. It is possible

[1]Brazil, Russia, India, China and Korea

that many technologies that should see the light of day will not be accepted readily. We have the job of improving public acceptance via education, if these technologies are to serve society on a global basis.

A key point is that genetics has come of age. Native traits present in crop species coupled with molecular breeding technologies will deliver significant increases in agricultural productivity. Lignocellulosic technologies will be critical. Significant innovations are needed to help agriculture meet societal demands for biofuels, bio-chemicals and biomaterials not only in terms of sustainability but also to meet required quantities.

Revolution

The biotechnology revolution is occurring before our very eyes, driven, in part, by developments in DNA sequencing and DNA synthesis. Ten years ago, it took billions of dollars to finance the sequencing of the human genome. Within the next 5 years, it is likely that an individual can have her/his genome sequenced for less than $10,000.

This remarkable progress in the arena of sequencing has implications for our ability to discover traits, whether for crops or for microorganisms. New disciplines in biology are possible, allowing us to look at systems as opposed to isolated biochemical reactions. In fact, 30 years ago when I was doing my graduate research, if you isolated a protein, purified it to homogeneity and studied its properties, you would get a PhD. Sometime later if you isolated and sequenced a gene, that was sufficient for a Ph.D. Today, we can sequence a gene in a matter of minutes. And today, we are asking questions about how systems are put together with a host of biochemical reactions in the context of the cell they are a part of. Systems biology is going to have profound implications not only for crop genetic engineering but for microbial genetic engineering as well.

Usable Solar Energy

Sunlight is abundant. In one hour, the sun emits more energy than human society consumes in one year; there is enormous potential for solar energy to be converted into usable forms. Microbial and plant systems have the ability to transform light into chemical energy, the most portable known form of energy.

Renewable fuel standards have been established on a global basis. I am not sure which of the regions of the world meet these standards and which will revise the mandates that they have set for themselves. Whatever, the number projected in terms of biofuels use is huge. Whether it is 50 billion gallons or 100 billion gallons, it is a significant number that we should work towards if we are to address climate change and the need for sustainable renewable energy, for which everyone is clamoring. This is also important for the economies of nations in Africa and Asia if they are to grow, because they have the potential to contribute to the energy needs of the planet.

Fundamental Considerations

As we look at biofuels or biomaterials—or even vitamins and other types of organic molecules—three fundamental considerations emerge. Number one is the feedstock, the source, whether it is sugar or lignocellulose or starch. The feedstock is going to be regiondependent. In the Midwest, corn is as good a feedstock as any. On the other hand, in India or Brazil, sugar cane is the ideal crop. In arid environments, jatropha, sweet sorghum or some other crop tolerant of moisture stress could be the feedstock of choice.

Second is the technology. The technology that we have today is mostly focused on biochemical methods, but thermochemical and chemical approaches are also being refined. In fact, nanotechnology and nanocatalysis are coming into play; I expect that these will make significant inroads and effectively compete with biotechnology in this space.

And third is the fuel itself. Many of my friends say that ethanol is good for human consumption, but not so good for automobiles. Better fuels are to be made. Butanols are the first step in this direction, but there is no reason why we cannot make the very same fossil fuels that we already put in our gas tanks. My message is: stay tuned. We are in the first inning of a nine-inning game.

For agriculture to reliably meet the demands being placed on it—whether related to food, feed or fuel—it has to take care of itself first. Farmers in many nations already cannot afford fertilizers or pesticides. We will not be able to afford to continue to use fertilizers synthesized by today's highly energy-intensive processes. Likewise, we cannot continue to discharge nitrous oxide gases, methane and a number of other effluents from agriculture. If agriculture is to be a major contributor to renewable energy, it needs to take care of inputs. It also needs to make sure that productivity is consistent, sustainable and reliable.

The International Panel on Climate Change predicts rapid further accumulations of carbon dioxide, methane and NO_X gases in the atmosphere in the near future. Agriculture's role needs to be addressed urgently. Fertilizer use is a major contributor to atmospheric NO_X. Methane comes mainly from paddy fields and cows. We need to address these molecules if agriculture is to play increasing roles in our society in terms of materials and energy.

I alluded to the fact that breeding and biotechnology will make major contributions to enhancement of agricultural productivity. Indeed, we now have the base sequence of the corn genome. We have sequenced several plant species and with molecular techniques it is possible to move genes and traits from one type of corn to another. Corn of tropical origin was rarely used in the breeding of temperate genotypes until about 10 years ago because it took breeders about 15 years to get rid of imported deleterious traits. With molecular tools, we now can do in 2 years what used to take 10. Over the past 50 years, corn yields have grown at 2% per year. Utilizing biotechnological methods, yield increases as high as 5% per year are projected.

Biotechnology's Potential

Biotechnology has had a major impact on agriculture over the past 12 years. It had zero value in 1995 whereas in 2007 it was a $7.5 billion industry. It has the possibility of being a $60 billion to $120 billion industry by the year 2020. Of course, it is important to make the discoveries, but technology alone will be insufficient if regulations and policies do not keep pace. Now is the time for modification of agricultural policies that hinder international movement of agricultural goods and stand in the way of people feeding each other and meeting each others' fuel needs. In fact, if 800 million people on this planet are hungry today, it has nothing to do with agricultural productivity or technology. It has everything to do with the local politics and the local systems that prevent food movement across boundaries.

Agricultural biotechnology has the potential to create even more value if GM crops are accepted, provided, of course, that they meet scientific and other types of regulatory standards. About twenty-two nations are cultivating genetically engineered crops. The latest entrants to the scene are in Asia; China and India, in particular, are adopting biotechnology in a major way. Expect India to accept biotechnology in an even more significant fashion in the foreseeable future as *Bt* vegetables and *Bt* rice, and other crops of that ilk, come into the market place. South America, which resisted the adoption of biotechnology, is now witnessing the benefits to its farmers and to agribusiness in general, from Roundup Ready corn and Roundup Ready soybean. Europe, especially France, remains problematical for those promoting biotechnology. I hope that science and wisdom will prevail upon the regulatory authorities so that GM crops will soon be cultivated by French farmers.

Bt and Roundup Ready

The first major biotech product was insect-resistant corn (*Bt*), aimed at controlling the European corn borer, which damages the stalk and ear, and can lower productivity by up to 20 bushels per acre. When the product was being developed at Monsanto, we thought that it would have application on 2 million to 3 million acres. Today it is grown on nearly 50 million acres across the United States because the damage from European corn borer was vastly underestimated. Furthermore, we have come a long way since 1999. Today, we don't talk about controlling one insect like European corn borer, we talk about controlling black cutworm, corn earworm, western bean cutworm—a series of caterpillar insects that lower productivity depending upon region—as well as rootworm, a major pest that damages the roots of corn. Products now on the market—"triple stacks"—have two *Bt* genes, one for above-ground insects and another for below-ground insects and a gene that imparts resistance to the herbicide Roundup, which helps in weed control.

The Roundup Ready trait (resistance to the herbicide glyphosate) is available in soybean, corn, cotton and canola. When I was with Monsanto, people asked why we were wasting our time and resources working on this product, since weed control had been adequately accomplished. They did not appreciate the importance of no-till farming, which has seen wide adoption by soybean growers. No-till practices are now used on 90% of the soybean that is cultivated in the United States, and it is making inroads with corn as well. If we are to reduce farmer-dependence on fuel, especially for their tractors, no-till farming is a great way to go. It is also helps prevent topsoil loss, which is essential to sustainability.

New Technologies

As we stack insect- and weed-control traits, we are beginning to recognize that they work in synergy in terms of yield protection. When we have a triple stack, the value to the crop isn't 3×, but more like 3.6×. In fact, we are beginning to recognize that these are outstanding abiotic-stress protectors, shielding crops against the effects of drought, heat and other environmental insults. For example, resistance to corn rootworm, concomitant with the *Bt* trait, results in greater absorption of soil moisture than from a root treated with chemical insecticide. Three years ago, for example, a major drought in Illinois led to predictions of 60 to 65 bushels of corn per acre, whereas many farmers who planted *Bt* corn harvested 140 to 150 bushels per acre.

Drought tolerance remains a major objective for a number of companies. Both of my former employers, DuPont and Monsanto, are working on technologies to improve it. In fact, water use is a major issue that all biotechnological processes need to address. Whether it is the cultivation of a crop or the conversion of the sugar from that crop into end-products like ethanol or butanol, water management is fundamentally important. Of course, in agriculture if we have deprivation of water even for short periods of time, it can have major implications for productivity. One of the reasons for the current food-versus-fuel debate is because Australia, Africa and parts of Europe suffered droughts simultaneously, causing global shortages of wheat and rice grains.

Moisture deficiency lowers yields of corn also. Although hybrids have been bred to improve productivity, especially in terms of the water responsiveness, we need better traits than what we have been able to find within the corn germplasm. At Pioneer, they evaluate their corn genotypes in terms of water responsiveness in "managed crop plots" in California where there is no rain. The amount of moisture in the soil is directly proportional to what has been provided through the sprinkler system. Monsanto and Syngenta have their own managed trials in which genes are being tested for drought-tolerance attributes. I predict that, by the year 2012, drought-tolerant genotypes of corn, canola and rice will be commercially available.

There is much excitement among researchers also with respect to nitrogen-use efficiency. Corn and rice genotypes are being developed that, with 75% of current fertilizer-application levels, show no yield penalty. Similarly, genes are being discovered that, when introduced singly into canola or soybean, have the potential to increase yields by 10% to 15%. I expect these products to reach the marketplace in the 2014–2015 timeframe.

On a global basis, agricultural productivity is less than what it could be. For example, the productivity of corn in China is about half of what it is in the United States. If new technologies are not deployed in other countries and if fertilizer and water-management capabilities are not available, there is no way we can use available arable land with optimum efficiency. Genetic engineering and a number of other technologies have not found full acceptance, and, of course, in many developing countries fertilizers are unavailable and/or soil fertility is low. We must find ways to reverse these trends.

This leads me to the thesis that it should be possible to improve US corn productivity more than the 3% per year seen over the past decade. I believe that it will be more like 5% to 6% very quickly, because we now have access to genomic tools unavailable just 5 years ago. We now have access to a large number of plant DNA sequences, and comparative genomics, bioinformatics as well as improved understanding of the synthetic relationships between plant species will allow much more rapid crop improvement than was possible by traditional breeding alone.

Extended Gene Pool

Traditional breeding has harnessed less than 10% of what is possible. Furthermore, wild relatives of crop plants contain genes that can protect their domesticated counterparts against disease and insect predation. These "interesting" genes can also increase growth rate, yield, photosynthetic efficiency and other attributes. The time has come to dip into this reservoir of genes and traits.

My colleagues at Pioneer have used tropical corn as a source of disease-resistance genes for temperate germplasm, to facilitate no-till farming. (No-till temperate corn is usually subject to disease and insect pressures.) With molecular breeding tools, this was achieved in just 2 years. We can expect further rapid progress of this kind in the future, including exploitation of genes in teosinte, one of the precursors of modern corn.

Implications of Increased Crop Yields

If we can increase yields of corn significantly, what is the potential in terms of biofuels production? At current yields of 150 bushels per acre, ethanol productivity (from endosperm, pericarp and stover) is approximately 510 gallons per acre. If we can push corn yields to 250 bushels per acre, with improved lignocellulosic technology to convert some of the stover and the cob to ethanol, there is no reason why we can't achieve 1,000 gallons per acre of corn over the course of the next 12 years.

For those who ask where 15 billion gallons of ethanol will come from, we actually have the potential to produce anywhere from 30 to 50 billion gallons of ethanol by the year 2020. We have some things to attend to, including the major byproduct of ethanol (and butanol) fermentation: distillers dry grains (DDGs). Today, DDGs are used to feed ruminant animals and with dilution with corn it can be fed to non-ruminants. However, if we produce 15 billion gallons of ethanol we do not know what we will do with the resultant DDGs other than drying and sending them to China, an expensive proposition. Application of lignocellulosic technologies to DDGs for additional biofuels production is an exciting proposition; the protein by-product can then be used as feed for a number of species, monogastric and ruminant.

If you are in Brazil and you are looking at corn, you are looking at the wrong crop. Sugar cane is the right crop for Brazil, which has the potential to be the Saudi Arabia of biofuels. Few of the technologies that we are applying to corn have been applied to sugar cane. By applying technologies developed for corn to sugar cane, there is no reason why we can't double or even triple sugar-cane productivity. Improving traits, like drought tolerance, has the potential to further improve the productivity of sugar cane. Also, applying lignocellulosic technology to sugar cane bagasse, might double biofuel productivity beyond what is obtained today. If I were in the business of starting companies I would concentrate on improving sugar-cane germplasm. Brazil already has mountains of bagasse next to the sugar-cane factories that is burned to generate electricity that is fed to the grid. But, there is huge potential to make liquid transportation fuels using bagasse.

Another crop that has potential in relatively dry regions, including southern Texas and across the tropics, is sweet sorghum. Sweet sorghum is capable of producing sugar and grain as well as producing biomass, all of which can be fed into the biofuels/biomaterials industry. In fact, this crop is now being promoted by ICRISAT[2] and other research institutions.

Unacceptable Loss of Carbon

John Pierce[3] and his colleagues at DuPont are working on lignocellulosic technologies. I hope they succeed because if these technologies can be made to work economically—producing sugar at the same price as that from sugar cane—it augurs well for the development of a new bioproducts industry. We need this technology very badly.

However, whether the sugar is of lignocellulosic origin or whether it's from sugar cane or is cornstarch glucose, when fermented by yeast or bacteria, 35% of the carbon is lost as carbon dioxide. The plant has already done the hard job of fixing the carbon dioxide and giving up a third of that carbon is simply unacceptable. Those interested in winning the next Nobel Prize should work on this challenging aspect.

Butanol

Currently there is an ethanol glut. Although available in many locations, it cannot be moved economically to where it is needed, like Delaware and California. For this reason, ethanol may not be the ideal fuel, which is where butanol comes in.

Butanol has many advantages over ethanol. It has higher energy density, is noncorrosive, and is readily miscible with gasoline so that it can be premixed and shipped. Also, it does not require a flexible-fuel engine. It has all the attributes that one would look for in an ideal biofuel. Two isomers, n-butanol and isobutanol, are being investigated, which have the added possibility of conversion to kerosene jet fuel as well as biodiesel. We do not have to wait for the production of biodiesel from algae or jatropha. We can actually use the lignocellulosic substrate, produce the butanol and polymerize it to diesel, kerosene or jet fuel. The most important breakthrough needed is the cost-effective production of these isomers. Scientists at a company DuPont has invested in, Gevo, are close to demonstrating cost-effective production of isobutanol. And I'm sure that DuPont researchers will soon report developments in this area as well. Stay tuned.

Biodiesel

Fatty-acid esters are being investigated from the perspective of B2 and B10 supplements to the diesel engine. The reason why the ethanol industry grew so rapidly in the United States was because it became the oxygenate replacing MTBE. We had to go to anhydrous ethanol as opposed to the hydrous ethanol, which the Brazilians use with their flex-fuel systems. Now there is opportunity to have the low-sulfur standard or the no-sulfur standard in diesel and to provide lubricity with fatty-acid esters. However, the problem is an insufficient supply of vegetable oil, even globally. The most efficient vegetable oil crop available is palm, which produces between 4½ and 6 tons of oil per hectare. It is the most efficient photosynthetic conversion available. In fact, being in the humid tropics,

[2]International Crops Research Institute for the Semi-Arid Tropics, Hyderabad, India

[3]See pages 25–38.

they "work" 365 days a year and there is no shortage of water. Having its DNA sequence will have tremendous impact on breeding; palm has seen no genetic improvement for 30 years. Bringing molecular tools, including trait technologies, to bear with this crop could double its oil yield.

Similarly, opportunities exist to significantly increase yields of rapeseed, which might be cropped three times annually in some regions.

Several colleagues, especially in India, are focused on jatropha. However, although it grows in arid environments, to be economically productive, jatropha needs to be fertilized and drip-irrigated. With these inputs, why not develop a biofuel crop that has potential as a food crop in times of need? Jatropha also has safety issues: it produces phorbol esters and a ricin-like toxin. None of these issues have been addressed.

Interest has increased recently in algae as a feedstock for biodiesel production. There is potential to produce vast amounts of oil on only a few acres. However, economic analyses indicate costs in the range of $15 per kilogram of oil, which compare poorly with palm and soybean oils at around $1 per kilogram. Algae offer prospects of rapid genetic manipulation. Increasing photosynthetic yields is more likely in algae than in plants. And we can create fluxes through the lipid pathway with synthetic biology, and increase lipid productivity. We can also make molecules that are expressed in algae with application directly as fuels. My thesis is that algae have great potential, but it will take some time to realize it.

Renewable Materials

We have the opportunity to produce renewable materials as well as biofuels. In fact a number of monomers are already being produced. As a venture capitalist, I get to review a lot of business plans. We see every type of possibility, including diacids, diols and diamines. It is almost as though we are looking at nylon and polyester development in the chemical industry 30 to 40 years ago.

Take-Home Messages

Regarding food versus fuel, 90% of what we read in the newspapers is erroneous. To get the facts, go to the sources, read the original articles and make up your own mind. Corn is being blamed as responsible for global food shortages. Although the United States has consumed significant amounts of corn for biofuel, this usage is unconnected to shortages of rice, wheat and fruits and vegetables. At most, corn may account for 20% of the current food shortage. Corn is less efficient than sugar cane or sweet sorghum in terms of its biofuel-energy content, but it's a good starting point on which we can build.

Applications of biotechnology have created value. Ethanol use by US transportation systems along with carbon dioxide savings from tractors (resulting from no-till practices) means that carbon dioxide reduction in the United States has been significantly greater than in Europe over the past 10 years through deployment of superior technologies.

Grain shortage is an important issue. Grain stocks are at all-time lows in the United States, India and parts of Latin America. A crop failure will constitute a major problem. We cannot address this without deploying modern technologies.

A hundred years ago, we were asking whether we should use ethanol and biodiesel in our engines or fossil fuels. Ford, Diesel and the Rockefellers had that dialog when the discovery of tetra-ethyl lead changed the direction of that particular history. With the development of biotechnology tools we have the potential to get back on track with renewable systems similar to those that prevailed for 10,000 years of human development. During two ice ages, 10,000 years ago and 5,000 years ago, human beings resorted to agriculture to survive. Mesopotamian agriculture, initiated 10,000 years ago, and further expansion of agriculture by the Romans 5,000 years ago were related to climate change. We must look at biotechnology as an opportunity to address climate change again.

We can silence the tsunami of food versus fuel. The prospects for agriculture are bright provided we learn how to apply innovation, provided we learn how to imagine and provided we create policies that allow that innovation to manifest itself.

GANESH KISHORE is managing director at Burrill & Company and CEO of the Malaysia Life Sciences Capital Fund. After receiving a PhD in biochemistry from the Indian Institute of Science, he obtained postdoctoral training in chemistry and biology and served as a Robert A Welch Fellow at the University of Texas at Austin. He then joined Monsanto as a senior research biochemist responsible for developing processes for the synthesis of aspartame, the active ingredient of NutraSweet and Equal. He subsequently led the development of the technology behind Roundup Ready.

He was named a distinguished science fellow, the highest honor bestowed upon scientists at Monsanto and was appointed assistant chief scientist. He also won the Queeny Award. As the leader of Plant Sciences Research at Monsanto, he directed the development and commercialization of most of the agbiotech products on the market today.

Dr. Kishore joined DuPont in 2002 as chief technology officer for its Agriculture and Nutrition Platform and took over the role of chief biotechnology officer in 2005. He guided the acquisition of several key technology companies and bolstered the biotech competence within DuPont, which he left in 2007 to join Burrill.