

Commentaries

Biotechnology for Food, Energy, and Industrial Products New Opportunities for Bio-based Products

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Introduction

In 1936, McCarroll of the Ford Motor Company [1], stated:

"Everything pertaining to an automobile has its origin in the earth. There is no need to exhaust the mines and forests if the material required can be grown on the farm; and in addition the growing of the material on the farm will give to the farmer, when markets are developed, another source of cash. When the industrial market for farm products has been developed, it will not be long before there appears the farm-factory. In this farm-factory much of the processing by which the product is advanced into better condition for the raw material will be done in or near the fields where the raw material is harvested".

At the time of Mr. McCarroll's comments, all Ford cars were finished in an enamel in which soybean oil was used extensively (it was estimated that about a half-bushel of soybeans were used in the manufacture of every Ford car). By 1941, Henry Ford had produced his first automobile with an 'all plastic' body. The car climaxed a dozen years of research based on Ford's long-standing belief that someday he would "grow automobiles from the soil" [2]. The car made its appearance when a steel shortage threatened to cripple the automobile industry's non-defense production. Unfortunately, World War II forced industries to focus on meeting the needs of the Defense Department and plastic vehicle bodies had no place in the war effort.

This story of Henry Ford and plastic from soybeans is a lesson on how difficult it is to promote and sustain innovation. Almost 50 years would pass before both the industry and the public would again embrace bio-based products. In June 2002, the United Soybean Board in the United States released "The Soy Products Catalog: A Listing of Soy Industrial Products" [3]. The catalog listed more than 40 classes of consumer and industrial products, e.g., personal care products, cleaning products, industrial lubricants, and printing supplies.

This re-emergence of interest in bio-based products was a result of the timely coalescence of economic considerations, environmental concerns, and scientific advancements. There were concerns for finding sustainable resources (developing a bio-based economy to replace a petroleum-based economy), developing new energy sources (developing biomass resources to curb climate change), and taking advantage of the advances in the science of molecular biology (biotechnology and the elucidation of the genomes of plants and animals).

1 The Bio-based Economy

1.1 Developing bio-based products

In the past two decades much has been written about the changes required to feed a future world population of 10 billion or more. Having food is only part of the demand; there has been much less focus on the material needs of such a population. Accompanying any population growth are the legitimate desires for adequate energy, transportation, housing, schools, health facilities, communication networks, etc. Since World War II, a petroleum-based economy has provided for these needs, but there is a limit to the reservoirs of petroleum-based hydrocarbons. Switching to the use of renewable resources whenever the appropriate technology is available, is a more sustainable and environmentally responsible approach. Indeed, the conversion to a bio-based economy will take time, but there is now a major effort underway where plant/crop-based renewables are serving as complementary resources to conventional feedstocks to meet the ever-growing needs for chemicals, materials, and other products [4]. Biotechnology is key to the continued progress in this area.

Plant/crop-based (i.e., bio-based) resources are defined as source material derived from a range of plant systems, primarily agricultural crops, forestry products, and processing streams (including microbial) in the food, feed, and fiber industries. Plant-based inputs may take several forms including wood, cellulose, lignin, starch, amino acids, proteins, etc., and may be sourced from many different places, e.g., from biomass, crop residue, dedicated crops, and crop processing by-products. The current goal is economic and renewable suites of products from new biorefineries, which will include production of primary products and co-products together [4]. The primary bio-based products can include oils, commodity or specialty chemicals, and materials.

The key to building a bio-based industry is to identify 'platform chemicals'. These are chemicals that are easily obtained from plant/microbial sources and have excellent properties that lead to new products. The United States Department of Energy's current Biomass Initiative is providing matching funds to companies that have identified and are developing platform chemicals [5]. For example, DuPont has developed a fermentation-based process for 1,3-propanediol. The process starts with corn as a renewable carbohydrate feedstock and using a biocatalyst converts the carbohydrates to the 1,3-propanediol. The 1,3-propanediol is the key ingredient in Sorona™, Dupont's newest advanced polymer platform. In addition to benefits of softness, stretch recovery, vibrant color, and stain resistance, textiles made with Sorona™ have the dimension of being a natu-

rally sourced material [6]. Cargill Inc. has developed a process for the microbial conversion of glucose from corn to 3-hydroxypropionic acid, a platform intermediate that can be produced at a theoretical yield of 100% from glucose. By integrating fermentation with chemical processing, this novel intermediate can then be cost-effectively used to make other commercially valuable chemicals [7]. Not all 'platform chemicals' come from the fermentation of a feedstock.

The soybean is recognized as a source of food and feed, but two of its major components – oil and protein – offer significant utility as industrial chemical feedstocks [8]. In 1991, the Congress of the United States established the United Soybean Board to create greater demand for and increase the value of soybeans. The Board recognized the potential for industrial product development and launched a program involving industry, universities, private research organizations, and government agencies. The funding for the programs comes from a 'checkoff' program generated by the sale of soybeans. The focus of the industrial product development has been on five primary market segments: 1) coatings and printing inks; 2) adhesives; 3) lubricants; 4) plastics and composites; and, 5) specialty chemicals including solvents, surfactants, and pesticides [8].

Since the enactment of the Clean Air Act of 1990, many conventional chlorinated, fluorocarbon, and petroleum-based industrial solvents have been regulated out of traditional market applications. Methyl soyate, a soybean-oil-based methyl ester has gained market acceptance as an excellent solvent in applications such as parts cleaning and degreasing, paint and ink removal, and oil spill remediation [8]. It is also marketed in numerous formulated consumer products including hand cleaners, car waxes, and graffiti removal. The demands for products made from soybeans continue to increase, as does worldwide production. The 2001–2002 harvest for soybeans in the United States was 79 million metric tons produced on 29.5 million hectares. Brazil was second with 43.5 million metric tons produced on 16.4 million hectares; while Argentina was third with 29.5 million metric tons produced on 11.3 million hectares [9].

To be economically viable, the industrial production of bioproducts must be driven by high-volume, low cost raw materials. The sources of plants for bioprocessing are large and diverse. The real issue is one of cost of conversion to 'force fit' plant-derived materials into a manufacturing system that requires a different chemical strategy. Plant/crop-based renewables are not alternative sources, but rather they are additional sources of materials for use as industrial feedstock. With further development of new thermal, chemical, and biological processes, there are opportunities to expand the use of plant-based renewables in economically viable systems.

1.2 Developing renewable energy sources

There is now widespread acknowledgement that renewable bioresources have considerable potential to increase national energy security and to minimize anthropogenic effects on the environment. However, the transition to renewable resources from fossil fuels must meet certain replacements in the economic arena. It will require significant advances in science and technology development to both meet such criteria and to ensure sustainable enterprises.

From an energy perspective, there are many options on how to most effectively use biomass to generate energy. A major consideration is the source of biomass. In the United States alone, forestry sources and crop residues are a 260 billion-kilogram source of biomass that is not utilized today [4]. The Minnesota Agri-Power Project uses crop parts in an integrated manner. Some 620,000 metric tons of alfalfa are converted into feed with an additional net energy output. Specifically, the leaves are processed into a high-protein animal feed, while the stems are gasified and combusted to produce 75 megawatts of electricity per day [4]. Although many biomass materials can be used directly, most require conversion to either ethanol or to biodiesel. Biodiesel is produced from any fat or vegetable oil, such as soybean oil, through the chemical process of transesterification. Both the alcohol and biodiesel can be used as a diluent in commercial fuels.

In the United States the market potential for the production of ethanol from corn stover (the stock, cob, leaf and husk) is as high as 38 billion liters if cost of production can be reduced [10]. As noted, the stated issue is economics, but it is really an 'available technology' issue. A tremendous amount of research is being conducted on finding more efficient ways to convert biomass to fuels. New second generation biocatalysts are being evaluated for the simultaneous saccharification and fermentation of biomass-derived sugars for generating fuel ethanol [11]. If the plant-derived material is structural biomass then certain constituents, such as lignin and cellulose predominate and new techniques such as integrated combustion or organometallic chemistry may provide opportunities to better utilize this type of source [4].

As noted, biodiesel is the name of a clean burning mono-alkyl ester-based oxygenated fuel made from soybean oil or other vegetable oils or animal fats. Biodiesel is registered as a fuel and fuel additive with the U.S. Environmental Protection Agency [12]. It contains no sulfur or aromatics and meets the 2007 sulfur standards [12]. As the nations of Europe know, there are many reasons to support the production and utilization of biodiesel. Biodiesel can help cut emissions of carbon dioxide (the primary greenhouse gas contributing to global warming) by 80% compared to petroleum diesel. Biodiesel has the best energy balance of any liquid fuel. Every unit of energy needed to produce biodiesel results in 3.24 units of fuel energy [12]. Biodiesel is also the safest of all fuels to use, handle and store. It has a flash point much higher than that of petroleum diesel [12]. Of equal importance is that biodiesel is one of the few alternative fuels available that works within the existing diesel technology infrastructure. Thus, biodiesel is a way to clean up the air and improve domestic energy security without making drastic changes in the system.

1.3 Biotechnology and the elucidation of the genomes of plants and animals

Advances in agricultural biotechnology are producing a revolution in the knowledge about how plants and animals grow and produce useful products. These advances have tremendous importance to the countries of South America [13]. Trigo et al. [13] have noted that biotechnology holds potential for improving the competitiveness of regional agricultural production in world markets, as well as reducing the incidence of urban and rural poverty, given that the nutritional and income status of

the poor are highly dependent on the efficiency of staple food crop production. In addition, they noted that biotechnology is expected to:

- improve yield potential and stability (increasing tolerance to adverse effects) in both temperate and tropical crops,
- improve agricultural sustainability by increasing disease and pest resistance and supporting integrated pest management efforts, thereby lessening the use of toxic pesticides,
- improve the nutritional value of food crops, including the enhancement of vitamin and micronutrient content of cereal grains, and
- expand the potential uses of agricultural processes and products by using non-edible substances of food crops to produce medicinal products, fuel alcohol, and industrial oil, thereby increasing employment and income [13].

In an era of great regulatory uncertainty and government oversight, farmers are in a very risky business [14]. There is a vocal segment of the public that demands food grown without fertilizers or the use of pesticides. They want their animal products free of hormones, from 'free' ranging animals, raised under non-stress environments, and nurtured with the purity of bottled water. Yet, they demand all of this at a price that allows them to commit less than 15% of their income for food. Farmers know that to stay in business, feed their families, and plan for their future, they must maximize profits. That means keeping the cost of inputs such as fertilizers, pesticides, and tillage low to produce the largest yields that meet the highest standards of food quality for marketing. Farmers also know that to compete successfully, they need every opportunity and advantage that science and technology can offer. Increasingly farmers are being forced to raise crops on marginal lands (the impact of urban sprawl). They must compete for water rights with large cities, and find more efficient ways to harvest, process, and transport produce and livestock to global markets. This is the setting in which we now find the first 'fruits' of agricultural biotechnology. These are some of the reasons why farmers in North and South America have been so attracted to insect resistance, virus resistance, and herbicide resistant crops. Crops that produce higher yields, require less pesticide, and reduce tillage.

1.3.1 Plant biotechnology and field testing

Agricultural biotechnology is a collection of scientific techniques, including genetic engineering, that are used to modify or improve plants, animals, and microorganisms. These modern techniques have enabled scientists to move genes (and therefore desirable traits) in ways they could not before, and with greater ease and precision. Today, over 57 million hectares of genetically modified crops are planted annually. The bulk of these hectares are in the United States, Canada, Argentina, and China [15]. The science and technology required to manipulate the genes of plants and to understand the functions of those genes is progressing at an incredible rate [16] Thus, scientists are designing transgenic plants with phenotypes developed to provide direct benefit to the consumer. Crops are being genetically modified for enhanced nutritional or other health benefits. Exciting current examples include golden rice, cavity-fighting apples, antioxidant tomatoes, and edible vaccines in bananas [16].

In the United States, the Animal Plant Health Inspection Service (APHIS) has the regulatory responsibility for transgenic plants [17]. As of 28 May 2003, APHIS had approved 8,982 field tests under permits and notification from 223 different companies, universities, Federal laboratories, and institutes over the years from 1987 to date. The total number of approved releases under permits and notifications by phenotype included:

• Herbicide tolerance	2,970
• Insect Resistance	2,782
• Product Quality	1,850
• Virus Resistance	1,204
• Agronomic Properties	744
• Fungal Resistance	584
• Other	477
• Marker Gene	416
• Bacterial Resistance	100
• Nematode Resistance	11

The total number of approved releases under permits and notifications for the major regulated organisms included:

• Corn	4,170	• Alfalfa	175
• Potato	726	• Rice	156
• Soybean	675	• Beet	151
• Cotton	620	• Bentgrass	144
• Tomato	526	• Melon	132
• Wheat	296	• Lettuce	76
• Tobacco	215	• Poplar	67
• Rapeseed	177	• Squash	60

A total of 93 organisms have been genetically modified and field-tested in the United States. Transgenic corn accounted for 21% of the total worldwide acreage of transgenic crops planted [15]. Within the 'other' category of phenotypes (477 approved permits or notification) are the field tests of food crops to produce pharmaceuticals – so called pharm crops. Corn is particularly well suited to the production of drugs, especially for monoclonal antibodies [18]. Nature designed the corn kernel to store and accumulate large complex proteins. The monoclonal antibodies are large complex molecules created by instructions from the transgenes in the plant and subsequently stored in the kernel. Traditionally the monoclonal antibodies are produced in mammalian cell cultures and typically it costs about \$450 million to produce 500 kg per year, while the same amount could be produced in 200 hectares of corn and processed in a facility costing only \$80 million. The monoclonal antibodies are used to treat a host of life-threatening and chronic diseases, including cancer, arthritis, and heart disease [18]. The field testing of pharm crops, however, has not been without controversy [18]. APHIS has recently strengthened the permit conditions to field-test plants genetically engineered to produce pharmaceutical and industrial compounds [19].

1.3.2 Genomes and genetic engineering

Biotechnology is and will continue to be key to the sustainable development of agriculture and the associated bio-based industries. The first wave of transgenic crops (i.e., crops having resistance for herbicides, insects, and viruses) was dependent upon the solitary effects of single proteins that were virtually independent of plant metabolism [20]. The gene responsible for the trait was transferred from phylogenetically divergent organisms, and hence could not be readily obtained from traditional breeding. Today, genomic sequencing projects are rapidly revealing the content and organization of crop genomes [20]. Genomic information is doubling every 14 months. The scientific community has completed the sequencing of more than 100 genomes of plants, animals, microbes, and viruses. Today, we are able to isolate a gene from its genome background and deliberately modify its expression. Such genes will often modify metabolism in a manner similar to that of natural or induced mutations, making it possible to create desired phenotypes with greater precision and efficiency. Indeed, these types of genes are being used to engineer a variety of phenotypic changes,

including altered growth and development (e.g., altered flowering, fruit ripening, growth rates, yield), modified metabolism, increased tolerance to environmental stresses (e.g., frost, drought, salt), or novel disease resistance (e.g., viral, bacterial, or fungal resistance) [21]. These are exciting breakthroughs in research in biotechnology and genetically modified organisms, but at the same time public debate about genetically modified crops has intensified.

1.3.3 Animal biotechnology

In the 30 May 2003 issue of *Science Magazine* an article was titled 'First Cloned Mule Races to Finish Line' [21]. Scientists have now successfully cloned bovines, ovines, felines, rabbits, rodents, and pigs [21]. The importance of this announcement is not cloned animal, but rather the technology and science that are being developed from the research. The real goal of animal biotechnology is in animal improvement programs. Research is needed to discover, test, and implement improved genetic evaluation techniques for economically important traits of our domestic food animals [22]. Current research is directed at the genetic improvement of efficiency of yield traits (milk, fat, and protein) and non-yield traits that affect health, vigor, and profitability (longevity, conformation, reproductive efficiency, and mastitis resistance) [23].

Much progress has also been made to use transgenic animals as new sources of pharmaceuticals, such as human growth hormones, alpha antitrypsin (used for treating emphysema), and lactoferrin (used to treat gut infections in babies). Most of these human medications are obtained from the milk of transgenic animals, but recently efforts have been made to obtain 'pharmed' medicine from animal urine [24]. As with genetically modified plants, animal biotechnology has its environmental and public health and safety issues [25]. These must be carefully and seriously addressed if commercialization of this technology is to occur.

2 Public Acceptance of New Technologies

A revolution in agriculture and the development of bio-based products is under way. We can take charge and influence in a positive way the potential impacts that biotechnology and the bio-based economy will have on our society and the environment, or we can oppose the application of new technologies and maintain the status quo. Indeed, in Europe and a few countries outside of Europe, the need for biotechnology is being challenged. There are individuals and groups who are leading a campaign to spread fear of the products, disfavor of science and scientists, and hatred of the commercial sector [14,18]. Some of the fear of this new technology is based on legitimate concerns for the environment and human health [26], but much is tied to environmental extremisms, positions that are hard to understand for those peoples who depend upon agriculture for a living and who seek a better quality of life. Biotechnology and the bio-based economy are here to stay. The global community demands sustainable development, alternative energy sources, and environmentally compatible products. The future is now!

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