TOWARDS THE DEVELOPMENT OF MARKETABLE PRODUCTS

James B. Johnston

Institute of Environmental Studies
University of Illinois
Urbana, IL 61801

The papers that make up this section deal primarily with fermentative pathways familiar to every microbiologist. Yet the individual papers present their subjects from very different points of view. The perspective of basic research, study for the sake of advancing understanding, is certainly well represented in all of the papers. But, to varying degrees, these papers touch on potential applications of the metabolisms being considered. Implicit in Young's description of alcohol dehydrogenase gene cloning for instance, is the opportunity to manipulate these genes to achieve new approaches to alcohol production. Similarly, Clark's study of E. coli mutants might serve as a model pointing to industrial applications through the profound analysis of the regulation of fermentative metabolism. The other two contributors, in contrast, explicitly discuss potential practical uses of their organisms and related mutants. Hillman describes the occurrence of lactate dehydrogenase deficient Streptococcus mutans and its potential to colonize the mammalian oral cavity with a consequent decrease in dental caries. Higgins reviews a broad range of cooxidative applications of methanotrophs and their enzymes, including some quite novel attempts to supply reducing power to isolated mixed function oxygenases through electrodes and oxidation-reduction dyes.

It is important in a volume discussing the opportunities for microbial production of chemicals through genetic intervention to consider at least cursorily the potential for application of the basic research advances described. A brief consideration of an historical example will illustrate the kinds of considerations that might favor or prevent the realization of an industrial application.

From before World War I until slightly after World War II, a
large percentage of the butanol produced in North America came from the clostridial fermentation of molasses or corn starch (1). This industry could produce net conversion of up to one third of these carbohydrate substrates into marketable solvents, although these were produced as dilute beers containing from 1.7 to 2.4% solvent that had to be concentrated and fractionated by distillation. The fermentation was subject to attack by bacteriophage or by contamination with lactic acid bacteria. The industry eventually fell victim to shifts in the prices of sugar feed stocks and the availability of far cheaper petroleum-based solvent substitutes.

The acetone-butanol industry was the first aseptic industrial fermentation; it also stands as one of the first industrial fermentations to attempt genetic intervention to improve the process, although these interventions were empirical in design. The factor limiting the final concentration of solvent in the beer produced was the tolerance of the organisms for the solvent. Attempts were made to screen for spontaneous and induced mutants that could tolerate higher than normal solvent concentrations. Similarly, it was found that the producer organisms could be "immunized against phage by serial transfer through media containing the virus" (1). This must surely be one of the first examples of the deliberate selection of a relevant mutation to improve an industrial process.

The history of the acetone-butanol fermentation industry teaches that the realization of improvements in industrial fermentation might actually come from genetic manipulation affecting metabolisms far removed from the actual production of the chemical product, for example manipulations affecting the organisms' ability to produce and withstand high concentrations of the desired product or to withstand phage or other competing organisms. Secondly, it teaches that any potential industrial fermentation will have to satisfy overall economic criteria including the relative market value of starting materials and final products, the costs of energy to support the overall process and the availability of competing substitute materials produced by other means. In general, chemical products of microbial origin often fail to meet these criteria because they are produced as dilute solutions and require costly, energy intensive processes to concentrate the product before marketing it. The obvious exceptions are those chemicals that have a high market value that can offset these energy costs, or chemicals that can be produced in no other way except fermentation.

The new era of genetic intervention to create opportunities for chemical production will presumably differ from the past by its theoretical rather than empirical basis. The lessons of past fermentation industries can now, in principle, be re-evaluated from the perspective of a detailed knowledge of the detailed biochemical and genetic basis of the industrially important microbial functions. For instance, genes may be arranged to create organismic tolerance