and amplification that will be far superior to the standard method in supplying stable strains of microorganisms useful in large-scale applications. In the new method, foreign genes or genes of interest carried on a plasmid are introduced directly into the main chromosome of the microorganism. A specific gene of interest has been inserted in the bacteriophage *E. coli* and has subsequently been observed to be amplified. This leads to improved stability and productivity of recombinant DNA microorganisms. These microorganisms can be produced in quantities required by large-scale industrial biocatalyzed processes. In addition to the potential for aiding in large-scale chemical production by biocatalysis, this research should also be applicable to the production of pharmaceuticals and biological materials.

Designing Biocatalysts for Energy-Efficient Chemicals Production

There are several technical barriers to the development and application of biocatalysts for the production of fuels and chemical feedstocks. The development of a molecular-level reaction model for enzyme systems is an initial scientific step in solving these problems. Over the past three years the California Institute of Technology, with DOE funding, has worked to develop software for computer-based graphic displays of three-dimensional structural models of molecules. The models permit the user to display and rotate a three-dimensional representation of the structure of any biological molecule of interest such as an enzyme or pharmaceutical. The interaction of the atoms in the molecule and any structural changes imposed by the user-specified conditions (e.g., increases in temperature, pressure, or the removal/substitution of any given atom) can be displayed. The models simulate real molecules by using a set of analytic force fields to describe the interactions among the atoms. When use of the models for predicting the molecular structure of the enzyme thermolysin as a function of temperature and inhibitors was undertaken, excellent agreement with crystallographically determined structures of thermolysin resulted. This tool is now being used to design new molecular structures for use in drugs, catalysis and for a wide variety of other applications. The simulation models may enable the design of supports for immobilizing enzymes without degradation of performance and enable the design of enzymes for selectivity and resistance to poisons.

Efficient Aerobic Fermentation

Biocatalysts have the ability to facilitate desired chemical reactions in one step by lowering the activiation energy barrier. Unfortunately, the availability of oxygen necessary for microorganisms is a major constraint in the growth and production of microorganisms within the bioreactor used in aerobic fermentation. Biochemical engineers have devised a variety of bioreactor geometry and stirrer configurations to minimize this problem. Under DOE sponsorship, a breakthrough technology with broad applications has been developed for aerobic fermentation using genetically engineered microorganisms. Professor James E. Bailey of the California Institute of Technology has shown that the oxygen limitation problem can be minimized by genetically inserting a hemoglobin gene into *E. coli* bacteria. It was clearly demonstrated that *E. coli* possessing plasmids containing hemoglobin, an oxygen carrier, grew more efficiently at a lower oxygen concentration (by a factor of two) than those without the hemoglobin gene. This method can dramatically improve the growth and productivity of genetically engineered aerobic microorganisms. The production of aerobically fermented products in the United States in 1987 was about 300 million pounds. Use of these genetically engineered microorganisms can help resolve critical barriers which currently impede the production technology of energy-efficient aerobic fermentation processes. Two broad-based patents covering the above technology have been filed by Professor Bailey.