Instrument Society of America

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Biochemical Measurement and Control

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Foreword

I have watched a company struggle to become a biochemical force of the future through the commercialization of recombinant DNA technology. I have sat through countless seminars designed to teach me how to evolve into a biochemical process control engineer. Unfortunately, nothing was ever said about biochemical measurement and control. Furthermore, I could not find any books on the subject. What was taught in the seminars was what was available in the open literature, which was the principles of biochemistry and fermentor design. Since these facts had little to do with the actual job at hand, they were easily forgotten and relegated to a stack of reference books on my shelf. Everything I learned of importance to me as I functioned in this emerging industry was the result of actual applications and discussions with suppliers and contractors to the biochemical industry. What I learned is summarized in this book, with the hope that it will lighten the load of those instrument and control engineers who wish to make the same transition. There is no information included on cell chemistry. The information on biochemical processes is cursory only. Some of the statistics will

be outdated by the time the book is published. Its only intent is to impress the reader with the potential impact of recombinant DNA technology to provide motivation and a framework for learning how the job of the instrument and control engineer will change as the technologies continue to expand and develop.

Gregory K. McMillan
St. Louis, Missouri, 1987

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CHAPTER 1

An Industrial Perspective

What are biochemical measurement and control? They are the industrial measurement techniques and process control strategies used to get living cells or parts of living cells to produce commercial quantities of useful substances. Each living cell is a sophisticated catalytic reactor that can convert nutrients and sugar into products, as shown in Figure 1.1. The enzymes act as specific catalysts, and the nucleus serves as a control center with the blueprints for chemically complex products.

Why all the fuss about biochemical production? How did it happen that GenenTech® (a genetic engineering firm) set a record

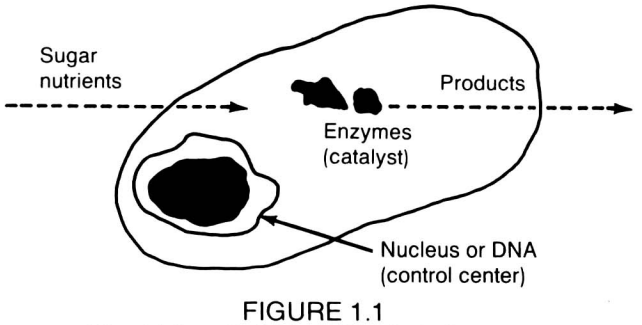

FIGURE 1.1
The Living Cell as a Catalytic Reactor

for the fastest price rise per share by increasing from $35 to $89 in 20 minutes? We are on the verge of harnessing the ultimate technology, the life process, to provide products to help solve the world's problems. Besides the global benefits of longer life and improved quality of life, there are some local benefits of significant importance to industry in view of its current problems.

Industry has suddenly found itself overwhelmed with competition in the commodity product market. There is a glut of cheap commodity chemicals produced by mature processes. The commodity intermediates (e.g., ethylene) tend to be produced close to the source of cheap feedstocks (e.g., Middle East), while commodity finished goods (e.g., textiles) tend to be produced close to the source of cheap labor (e.g., Far East). It is almost impossible for the West to compete with underdeveloped countries where the wages are a few dollars per hour or with oil-rich countries where natural gas is essentially free (it used to be flared). The United States has moved from a role as supplier of products to the Third World to the role of buyer of products from the Third World. While the economy has been temporarily buoyed by the increase in services (marketing, distributing, advertising, and accounting) for the increase in foreign products, the long-term effect of the continual outflow of money for foreign goods cannot be anything but disastrous. An economy based on local services and foreign industrial production is doomed to failure.

American industry would like to capitalize on its leadership position in basic research and technology development to devise processes for new products. These would generally be high value-added products priced at dollars per gram instead of cents per kilogram like commodity products. The competition would be limited by patent protection and the profit margins would be large. Biochemical specialty products fit this mold. The goal is to learn how to monitor and control the most technically advanced reactor system known — the living cell — to produce incredibly pure quantities of incredibly complex chemical compounds. Some of these compounds as pharmaceuticals will bear the price of several hundred dollars per gram.

1.1
Products

The recent progress in the understanding of the body's defense mechanisms and how cells become vulnerable to attack or