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## **Fermentation: An Art from the Past, a Skill for the Future**

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The origins of fermentation are lost in ancient history, perhaps even in prehistory. We know that the ancient Egyptians and Sumerians both had knowledge of the techniques used to convert starchy grains into alcohol. For most of history these processes, or similar ones based on fruit juice conversion, have represented the most commonly accepted interpretation of the word 'fermentation'.

However, 'fermentation' has many different and distinct meanings for differing groups of individuals. In the present context we intend it to mean the use of submerged liquid culture of selected strains of microorganisms, plant or animal cells, for the manufacture of some useful product or products, or to gain insights into the physiology of these cell types. This is a relatively narrow definition, but would include the 'traditional' fermentations described above. By contrast, the modern fermentation industry, which is largely a product of the Twentieth century, is dominated by aerobic cultivations intended to make a range of higher value products than simple ethanol.

In recent years there has been a tremendous expansion in the use of fermentation technology by individuals with less training in the subject than previous exponents of these techniques. This book is aimed at scientists and engineers relatively new to the subject of fermentation technology, and is intended to be the text equivalent of the briefings and chats that mentors in this area would have with newcomers. It is meant to be a means of passing on the experiences we have had in many years of fermentation to relative newcomers to the subject, so that perhaps, you will be able to avoid some of the more obvious pitfalls we fell into. It is specifically not intended as a reference text to the principles underlying fermentation science and engineering, as such volumes already exist. Each

chapter in this book is accompanied by a short ‘further reading section’ or supporting reference section, which generally contain a list of a few book chapters, or relevant reviews supporting the material in the chapter.

The fermentation industry today is very much in a state of flux, with rapid changes in location, product spectrum, and scale of processes occurring. To a large extent this has been brought about by macroeconomic forces compelling the relocation of large scale bioprocesses outside high labour cost regions, but also by the successful deciphering of the human genome with its myriad of new therapeutic targets, and the significant advances in the construction of advanced fermentation expression systems for making novel proteins and antibodies.

Thus, fermentation skills and knowledge are now essential to driving forward systematic research into drug/receptor interactions, function of membrane proteins in health and disease, and are powering an unparalleled expansion in our capability to combat serious diseases in the human population, including cancers, degenerative illnesses such as Alzheimer’s, and increasingly common complaints of developed societies such as asthma. The new fermentation-derived medicines, including biopharmaceuticals, hold out the prospect of improved specificity of treatment, and decreased side effects. It is truly a revolutionary period in clinical medicine as these new agents manufactured by fermentation routes enter the market. The ‘new’ fermentation products, therapeutic proteins, antibodies (simple and conjugated) are more complex and costly than previous products, but, in essence, the need to focus upon the fermentation step is now clearer than ever. Basically, the ‘quality’ of these products (the potency, efficacy, stability and immunogenicity) is determined by the upstream or fermentation stage, so the need for a clear understanding of what happens in that stage, how it can best be monitored, controlled, and carried out in a reproducible fashion, is greater than ever. It is in exactly these areas that the many often highly capable individuals entering fermentation are unwittingly deficient in background.

The long heralded era of personalized medicine may well be imminent due to recent advances in cultivation and replication of stem cells. This will make the need for scientists and engineers who understand culture techniques even greater in coming years. Thus, the demand for fermentation skills is likely to increase in the immediate future. Fermentation has contributed much to the well-being and wealth of human populations over millennia; it will continue to do so to an even greater extent in the future. We hope this book will help those coming recently to this field to contribute more effectively to that process.