Preface

There has been a rapid increase in the number and demand for approved biopharmaceuticals produced from animal cell culture processes over the last few years. In part, this has been due to the efficacy of several humanized monoclonal antibodies that are required at large doses for therapeutic use. There have also been several identifiable advances in animal cell technology that has enabled efficient biomanufacture of these products. Gene vector systems allow high specific protein expression and some minimize the undesirable process of gene silencing that may occur in prolonged culture. Characterization of cellular metabolism and physiology has enabled the design of fed-batch and perfusion bioreactor processes that has allowed a significant improvement in product yield, some of which are now approaching 5 g/L. Many of these processes are now being designed in serum-free and animal-component-free media to ensure that products are not contaminated with the adventitious agents found in bovine serum. There are several areas that can be identified that could lead to further improvement in cell culture systems. This includes the down-regulation of apoptosis to enable prolonged cell survival under potentially adverse conditions. The characterization of the critical parameters of glycosylation should enable process control to reduce the heterogeneity of glycoforms so that production processes are consistent. Further improvement may also be made by the identification of glycoforms with enhanced biological activity to enhance clinical efficacy. The ability to produce the ever-increasing number of biopharmaceuticals by animal cell culture is dependent on sufficient bioreactor capacity in the industry. A recent shortfall in available worldwide culture capacity has encouraged commercial activity in contract manufacturing operations.

However, some analysts indicate that this still may not be enough and that future manufacturing demand may exceed production capacity as the number of approved biotherapeutics increases. Animal cell culture has been used extensively for a variety of applications. Mammalian cells, especially Chinese hamster ovary (CHO) cells, have

become a dominant platform for the production of recombinant proteins that require proper holding and posttranslational processing and modifications. Dozens of recombinant protein biopharmaceuticals produced in animal cell culture, including therapeutic monoclonal antibodies, have been approved for marketing. Cultured animal cells, such as Vero and MDCK cells, have also been employed as the substrate for the virus propagation in the production of viral vaccines. Moreover, animal cell culture offers an important basis for gene and cell therapy, regenerative medicine, drug development and screening, and other biomedical applications. In the last few decades, there have been significant advances in animal cell culture technologies, which allow a remarkable increase in antibody concentrations to several g/l in industrial fed-batch processes of recombinant CHO cells. However, there is still a need for a chemical engineering approach to applications of genomics, proteomics, and metabolomics technologies, efficient and economical downstream processing, and innovation in vaccine manufacture processes. Cells, which are normally colourless, are fixed and stained for viewing under a microscope. Fixing is a process that stabilizes the chemical and structural characteristics of the cells. Cells are then stained with a dye or combination of dyes to highlight structural details. Different fixation and staining procedures highlight different structural features. The fixative methanol is good for monolayers. Hematoxylin, a powerful stain commonly used by cytologists, stains nuclear material bright blue to dark blue. Hematoxylin does not stain cytoplasmic material, however, so another stain must be employed, such as eosin, which stains cytoplasmic material light pink to red. Cell and organ cultures are used to maintain living animal cells and groups of cells outside the body (in vitro). With separate, living cell cultures, it is possible to see and study the behaviour of animal cells in greater detail than when they are in the animal. Cell culture also frees the cells from some of the controls that normally regulate their activities. Cells, or tissues, are kept alive for varying periods of time, at times undergoing repeated divisions over many generations. Cells grown and cultured for study have been taken from a wide variety of species, such as humans, monkeys, mice, dogs, cats, frogs, insects, fish and many others.

In the preparation of this book, it has been the author's aim to keep in mind not only the requirements of students in this subject but as well the needs of student.

—*Editor*