1. INTRODUCTION

Mammalian cell technology deals with three interrelated cell culture aspects: cells and their characteristics, media composition and physical environment (see fig. 1).

- Cells are sensitive to shear forces, have a long generation time and are of the suspension or anchorage-dependent type.
- Culture medium is composed of a large number of chemically defined components, mostly supplemented with undefined protein-rich serum.
- Physical environment, like temperature, mass transfer and shear forces.

A hollow fibre bioreactor aims to improve the conditions for cell culture, both on the level of physical environment and medium composition. Cells immobilized in the extra-capillary compartment of a hollow fibre bioreactor are much less exposed to shear forces than cells cultured in stirred or airlift fermentors. As firstly shown by Knazak (1972) cells can be maintained for several months in such a system. Nutrients and oxygen are supplied via the capillaries. Waste products and carbon dioxide are removed via the same membranes (see fig. 2).

The large surface area, provided by the hollow fibre membranes, makes the bioreactor a versatile system: both sus-
pension and anchorage-dependent cells grow in these bioreactors. Membranes are available with various pore sizes. The mass transfer through the fibre wall of medium components and cell growth factors and cell products are influenced by the membrane characteristics, like wall thickness and cut-off values. This communication shows that a large variety of cell lines can be grown in a culture medium without serum or other proteins at very high densities, if dialysis membranes are used. High concentrations of product are obtained and harvested on a semi-continuous basis.

Fig. 2. Hollow fibre bioreactor. Cells are grown in the extra-capillary compartment of the bioreactor. Nutrients, wastes and gases are exchanged over the membranes. (Research within Akzo, 1987)