are capable of self-replication but have a more restricted range of cells into which they may differentiate. In the hematopoietic system one type of progenitor cell can give rise to the myeloid cells (e.g., red blood cells or erythrocytes, platelets, macrophages, etc.) and the other to lymphoid cells (e.g., T-cells and B-cells). The progression of differentiation depends on a large number of hematopoietic growth factors. Hematopoiesis, the process of generating these blood cells, takes place in the bone marrow. *Ex vivo* hematopoiesis is an alternative or supplement to bone marrow transplants. Hematopoietic stem and progenitor cells can be recovered from human blood, particularly umbilical cord blood.

There are many challenges to generating commercial-scale systems for hematopoiesis. Coculture with stroma cells from the bone marrow is necessary to generate necessary growth factors, so bioreactors must accommodate adherent cell growth. Three basic reactor types are under development. Fluidized bed reactors with macroporous supports mimic structures much like that in bone. However, there are challenges in controlling surface chemistry and maintaining the appropriate mix of cell types. Cell sampling and control of reactor conditions can be problematic.

Flatbed reactors (e.g., modified T-flasks with continuous flow possible) can carry stroma and facilitate analysis and design, since the geometry is well defined. Direct microscopic observation of cells is possible. Automated flatbed systems have been used to generate cells for human clinical trials.

Membrane-based units, such as hollow-fiber reactors, are potential solutions. This is an efficient design that is fairly easy to characterize. However, cell observation and harvesting are considered problematic. Another alternative is the possible use of spheroid cultures (a natural aggregation of a mixed population of cells), which can be done in suspension-type bioreactors.

Bioreactors for production of other tissue types from other stem cells are a real possibility. There is far less experience with bioreactors for other stem cells/tissues, but the principles the reader has learned in this book should be applicable to these challenges.

15.4.2. Extracorporeal Artificial Liver

Liver failure is a major medical problem. The liver performs many metabolic functions (carbohydrate, fat, and vitamin metabolism, production of plasma proteins, conjugation of bile acids, and detoxification), of which detoxification is the most critical. In some cases, a failing liver may recover if the metabolic and detoxification demands on it can be reduced; an artificial liver may provide the respite necessary for self-repair of a liver. In other cases an artificial liver may serve as a bridge to a transplant.

Due to the spatial and metabolic complexity of the liver, an implantable artificial liver is a distant objective. However, an extracorporeal device to serve as temporary assist device is realistic (such a system is in clinical trials). A promising design is a hollow-fiber system using porcine (pig) hepatocytes. Such cells are relatively easy to obtain in large quantities and maintain a satisfactory level of differentiated cellular activity in regard to detoxification. A disadvantage is due to limited lifespan (and proliferative ability). The membrane that separates these cells from the blood provides protection against adverse immune reactions. The issues in the design of such hollow-fiber reactors are similar, whether the reactor is to be used in a bioprocess operation or in a biomedical application.