So far we have considered only inlet gas streams. With fermentations involving pathogens (disease-causing organisms) or recombinant DNA, *all organisms* must be removed from the exhaust gas. The concentration of microbes in the exit gas is far higher than in the inlet gas. Catalytically aided combustion (incineration) of the exit gas is an effective, but expensive, solution. Consequently, filtration of the exit air is of increasing importance.

10.5. SUMMARY

Scale-up of reactors is a task primarily for the biochemical engineer. Three basic reactor types for the aerobic cultivation of suspended cells are (1) *systems with internal mechanical agitation*, (2) *bubble columns*, and (3) *loop reactors*. Although the bubble and loop reactors offer advantages in terms of energy efficiency and reduced shear damage to cells, the traditional stirred-tank system is more flexible and can better handle broths that become highly viscous.

The primary limitations on the size of stirred-tank bioreactors are gas supply (e.g., O_2) and heat removal. The value of k_La, the *volumetric transfer coefficient*, is of prime concern. Its value depends not only on the equipment used, gas flow rates, and agitator speed, but also on the nature of the fluid (salt content, presence of surface active agents, and viscosity). The properties of the fluid can change during the fermentation. By directly monitoring oxygen concentration in the gas phase and the dissolved-oxygen level, it is possible to make on-line estimates of k_La. If the rate of oxygen uptake is known, the rate of heat generation can be readily estimated in aerobic fermentations.

Scale-up is difficult, because conditions in a large vessel are much more heterogeneous than in a small vessel. If geometrically similar tanks are used, it is impossible to maintain shear, mixing times, and k_La simultaneously identical in both the large and small tank. Scale-up would be simplified if good reaction models could be coupled to good transport models; since this is not yet possible, *scale-down techniques* are a good alternative.

Bioreactor instrumentation and control are less advanced than in the petrochemical industry. Improvements in sensor technology and the dynamical models of bioreactors are critical to improvements in control technology.

The large-scale bioreactor places heavy demands on processes to *sterilize* (kill or remove all organisms from) fluids entering the bioreactor. Liquid streams are thermally sterilized or filter sterilized. Steam terilization is preferred, but the sterilization process must not damage the ability of the medium to support growth. Since longer periods of exposure to high temperatures are necessary to assure sterility in larger volumes of liquid, the sterilization process can alter the medium composition more for large-scale than for small-scale systems. This is an additional factor that can lead to differences in productivity upon scale-up. *Continuous sterilization* protects the medium components from degradation better than batch sterilization, because the heat-up and cool-down periods are greatly minimized. *Filter sterilization* of liquids is used when the medium contains particularly heat-sensitive components. Air streams are typically filter sterilized. Surface filters (membrane cartridges) are commonly used in gas sterilization.