

that the necessary bottles would fill a row stretching from New York City to San Francisco. Engineers generally favored a submerged tank process. The submerged process presented challenges in terms of both mold physiology and in tank design and operation. Large volumes of absolutely clean, oil- and dirt-free sterile air were required. What were then very large agitators were required, and the mechanical seal for the agitator shaft had to be designed to prevent the entry of organisms. Even today, problems of oxygen supply and heat removal are important constraints on antibiotic fermenter design. Contamination by foreign organisms could degrade the product as fast as it was formed, consume nutrients before they were converted to penicillin, or produce toxins.



Figure 1.2(a). Series of large-scale antibiotic fermenters. (With permission, from T.D. Brock, K.M. Brock, and D.M. Ward. *Basic Microbiology with Applications*, 3d ed., Pearson Education, Upper Saddle River, NJ, 1986, p. 507.)