

In addition to these challenges in reactor design, there were similar hurdles in product recovery and purification. The very fragile nature of penicillin required the development of special techniques. A combination of pH shifts and rapid liquid-liquid extraction proved useful.

Soon processes using tanks of about 10,000 gal were built. Pfizer completed in less than six months the first plant for commercial production of penicillin by submerged fermentation (Hobby, 1985). The plant had 14 tanks each of 7000-gal capacity. By a combination of good luck and hard work, the United States had the capacity by the end of World War II to produce enough penicillin for almost 100,000 patients per year (see Figs. 1.2 and 1.3).

This accomplishment required a high level of multidisciplinary work. For example, Merck realized that men who understood both engineering and biology were not available. Merck assigned a chemical engineer and microbiologist together to each aspect of the problem. They planned, executed, and analyzed the experimental program jointly, "almost as if they were one man" (see the chapter by Silcox in Elder, 1970).

Progress with penicillin fermentation has continued, as has the need for the interaction of biologists and engineers. From 1939 to now, the yield of penicillin has gone from 0.001 g/l to over 50 g/l of fermentation broth. Progress has involved better understanding of mold physiology, metabolic pathways, penicillin structure, methods of mutation and selection of mold genetics, process control, and reactor design.

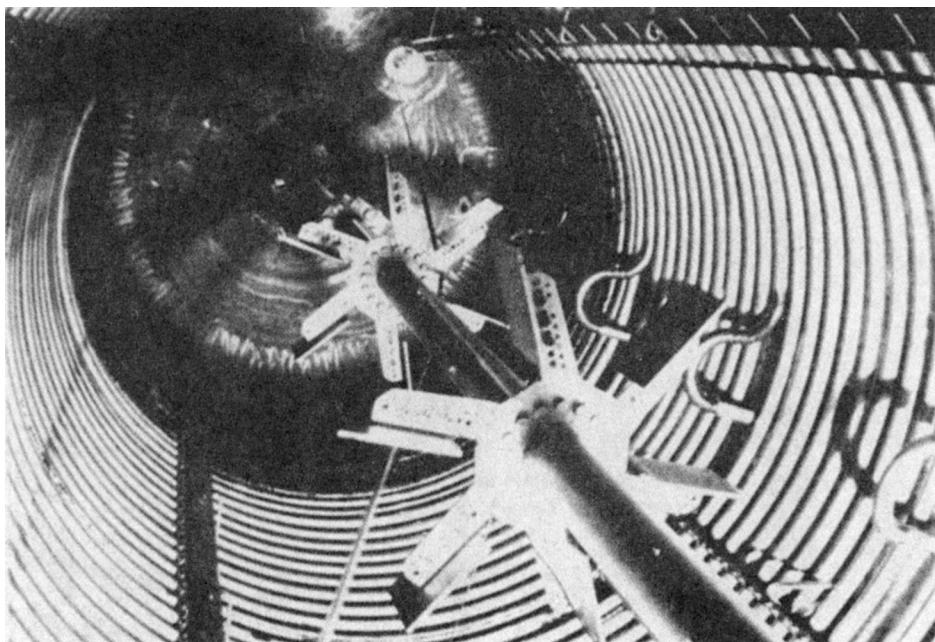


Figure 1.2(b). Inside view of a large antibiotic fermenter. (From *Trends in Biotechnology* 3 (6), 1985. Used with permission of Elsevier Science Publishers.)