



**Figure 10.6.** Measured oxygen concentrations in a 20-m<sup>3</sup> production fermenter (figures in circle are model estimates). (With permission, from N. W. F. Kossen, in T. K. Ghose, ed., *Biotechnology and Bioprocess Engineering*, United India Press, New Delhi, 1985, pp. 365–380.)

great variability in oxygen concentration in the reactor with some values at zero. This heterogeneity means that cells pass periodically through anaerobic regions. Since many cells have regulatory circuits to respond to changes from aerobic to anaerobic conditions, these circuits may be constantly altering cellular metabolism.

Traditional scale-up is highly empirical and makes sense only if there is no change in the controlling regime during scale-up, particularly if the system is only reaction or only transport controlled. Common scale-up rules are the maintenance of constant power-to-volume ratios, constant  $k_{LA}$ , constant tip speed, a combination of mixing time and Reynolds number, and the maintenance of a constant substrate or product level (usually dissolved-oxygen concentration). Each of these rules has resulted in both successful and