

1. Total cell mass concentration may stay constant, but the number of viable cells may decrease.
2. Cell lysis may occur and viable cell mass may drop. A second growth phase may occur and cells may grow on lysis products of lysed cells (cryptic growth).
3. Cells may not be growing but may have active metabolism to produce secondary metabolites. Cellular regulation changes when concentrations of certain metabolites (carbon, nitrogen, phosphate) are low. Secondary metabolites are produced as a result of metabolite deregulation.

During the stationary phase, the cell catabolizes cellular reserves for new building blocks and for energy-producing monomers. This is called *endogenous metabolism*. The cell must always expend energy to maintain an energized membrane (i.e., proton-motive force) and transport of nutrients and for essential metabolic functions such as motility and repair of damage to cellular structures. This energy expenditure is called *maintenance energy*. The appropriate equation to describe the conversion of cell mass into maintenance energy or the loss of cell mass due to cell lysis during the stationary phase is

$$\frac{dX}{dt} = -k_d X \quad \text{or} \quad X = X_{so} e^{-k_d t} \quad (6.9)$$

where k_d is a first-order rate constant for endogenous metabolism, and X_{so} is the cell mass concentration at the beginning of the stationary phase. Because S is zero, μ_g is zero in the stationary phase.

The reason for termination of growth may be either exhaustion of an essential nutrient or accumulation of toxic products. If an inhibitory product is produced and accumulates in the medium, the growth rate will slow down, depending on inhibitor production, and at a certain level of inhibitor concentration, growth will stop. Ethanol production by yeast is an example of a fermentation in which the product is inhibitory to growth. Dilution of toxified medium, addition of an unmetabolizable chemical compound complexing with the toxin, or simultaneous removal of the toxin would alleviate the adverse effects of the toxin and yield further growth.

The *death phase* (or decline phase) follows the stationary phase. However, some cell death may start during the stationary phase, and a clear demarcation between these two phases is not always possible. Often, dead cells lyse, and intracellular nutrients released into the medium are used by the living organisms during stationary phase. At the end of the stationary phase, because of either nutrient depletion or toxic product accumulation, the death phase begins.

The rate of death usually follows first-order kinetics:

$$\frac{dN}{dt} = -k'_d N \quad \text{or} \quad N = N_s e^{-k'_d t} \quad (6.10)$$

where N_s is the concentration of cells at the end of the stationary phase and k'_d is the first-order death-rate constant. A plot of $\ln N$ versus t yields a line of slope $-k'_d$. During the death phase, cells may or may not lyse, and the reestablishment of the culture may be possible in the early death phase if cells are transferred into a nutrient-rich medium. In both the death and stationary phases, it is important to recognize that there is a distribution of