Example 14.3.

Derive equations to describe the dynamics of a plasmid-containing population when the plasmid-free host is auxotrophic for metabolite *M*. The metabolite is made and released from a plasmid-containing cell into the medium in a chemostat.

Solution This situation is similar to that in eqs. 14.7, 14.8, and 14.9, except for the production and release of *M*. The only modification is to add a mass balance for *M* and to alter the equations for μ_-. Let *M* be the concentration of *M*. Then

$$dn_+/dt = \mu_+ n_+ - Dn_+ - Rn_+ \tag{14.7}$$

$$dn_-/dt = Rn_+ + \mu_- n_- - Dn_- \tag{14.8}$$

$$dS/dt = D(S_0 - S) - \frac{\mu_+ n_+}{Ys_+} - \frac{\mu_- n_-}{Ys_-} \tag{14.9}$$

$$\frac{dM}{dt} = \delta\mu_+ n_+ - \frac{\mu_- n_-}{Y_{M_-}} - D\mathrm{M} \tag{14.42}$$

$$\mu_+ = \mu_{+\max} \frac{S}{K_{S_+} + S} \tag{14.11a}$$

$$\mu_- = \mu_{-\max} \frac{S}{K_{S_-} + S} \frac{M}{K_{M_-} + M} \tag{14.43}$$

where δ is the stoichiometric coefficient relating the production of *M* to the growth of n_+.

This set of equations would have to be solved numerically. However, the type of analysis used in Example 14.2 could be applied if *M* were supplied in the medium such that the residual level of $M >> K_{M_-}$.

Our discussion and examples so far have been for continuous reactors. For most industrial applications batch or fed-batch operations will be used. While continuous reactors are particularly sensitive to genetic instability, genetic instability can be a significant limitation for batch systems.

For a batch reactor, the cell-number balances are:

$$dn_+/dt = \mu_+ n_+ - P\mu_+ n_+ \tag{14.44}$$

$$dn_-/dt = P\mu_+ n_+ + \mu_- n_- \tag{14.45}$$

with the initial conditions of

$$@\ t = 0, \qquad n_{+0} = N_{+0}, \qquad n_{-0} = 0$$

Solving eq. 14.44 with these initial conditions yields

$$n_+ = N_{+0} e^{(1-P)\mu_+ t} \tag{14.46}$$

and eq. 14.45 using eq. 14.46 yields

$$n_- = \frac{P\mu_+ N_{+0}}{(1-P)\mu_+ - \mu_-}\left[e^{(1-P)\mu_+ t} - e^{\mu_- t}\right] \tag{14.47}$$