

$$D = \mu_+ f_+ + \mu_- (1 - f_+) \quad (14.15)$$

Substituting eq. 14.15 into eq. 14.7 after eq. 14.7 is divided by N^t yields

$$df_+/dt = \mu_+ f_+ - f_+ [(\mu_+ f_+) + \mu_- (1 - f_+)] - Rf_+ \quad (14.16)$$

and, after rearrangement,

$$df_+/dt = f_+^2 \Delta\mu - f_+ (\Delta\mu + R) \quad (14.17)$$

where

$$\Delta\mu = \mu_- - \mu_+ \quad (14.18)$$

Equation 14.17 is a Bernoulli's equation. It can be solved in terms of a dummy variable $v = 1/f^+$, assuming a constant $\Delta\mu$ and R . A constant $\Delta\mu$ and R would be achieved only if the copy number distribution of plasmid-containing cells remained constant during the experiment. Also, strictly speaking, the assumption of constant $\Delta\mu$ is inconsistent with constant N^t . This analysis is best applied to situations where $\Delta\mu$ is not extremely large. The solution is

$$\frac{1}{f_+} = \frac{1}{1 - f_-} = \frac{\Delta\mu}{\Delta\mu + R} + ce^{(\Delta\mu+R)t} \quad (14.19)$$

where c is the constant of integration. The initial condition is $f_- = f_{-0}$ at $t = 0$. Then c must be

$$c = \left(\left[\frac{1}{1 - f_{-0}} \right] - \frac{\Delta\mu}{\Delta\mu + R} \right) \quad (14.20)$$

Once c is evaluated, eq. 14.19 can be rearranged to yield

$$f_- = \frac{(f_{-0}\Delta\mu + R)e^{(\Delta\mu+R)t} - R(1 - f_{-0})}{(f_{-0}\Delta\mu + R)e^{(\Delta\mu+R)t} + \Delta\mu(1 - f_{-0})} \quad (14.21)$$

Since f_{-0} is usually $\ll 1$, eq. 14.21 becomes

$$f_- = \frac{(f_{-0}\Delta\mu + R)e^{(\Delta\mu+R)t} - R}{(f_{-0}\Delta\mu + R)e^{(\Delta\mu+R)t} + \Delta\mu} \quad (14.22)$$

Further simplification is possible by considering three limiting cases:

- 1. $\Delta\mu \gg R$ (growth-rate-dependent instability dominant)
- 2. $\Delta\mu \leq R$ (segregational instability dominant)
- 3. $\Delta\mu < 0$ and $|\Delta\mu| \gg R$ (effective selective pressure)

These limiting cases yield:

Case 1: Where t is sufficiently small so that $\Delta\mu \gg (f_{-0}\Delta\mu + R)e^{(\Delta\mu)t}$, then

$$f_- \approx (f_{-0} + R/\Delta\mu)e^{\Delta\mu t} \quad (14.23)$$