$D = 0.3\ h^{-1}$			$D = 0.67\ h^{-1}$		
Time, h	Generation	f_-	Time, h	Generation	f_-
0	0	0.003	0	0	0.003
4.6	2	0.010	5.2	5	0.010
11.5	5	0.04	10.3	10	0.015
16.0	7	0.08	15.5	15	0.05
23.1	10	0.30	20.6	20	0.13
27.7	12	0.43	31.0	30	0.34
34.7	15	0.55	41.4	40	0.68
46.2	20	0.96	51.7	50	0.95

14.7. It has been claimed that gel immobilization stabilizes a plasmid-containing population. A factor suggested to be responsible for the stabilization is compartmentalization of the population into very small pockets. For example, the pocket may start with an individual cell and grow to a level of 200 cells per cavity. Develop a mathematical formula to compare the number of plasmid-free cells in a gel to that in a large, well-mixed tank.

14.8. You must design an operating strategy to allow an *E. coli* fermentation to achieve a high cell density (> 50 g/l) in a fed-batch system. You have access to an off-gas analyzer that will measure the pCO_2 in the exit gas. The glucose concentration must be less than 100 mg/l to avoid the formation of acetate and other inhibitory products. Develop an approach to control the glucose feed rate so as to maintain the glucose level at 100 ± 20 mg/l. What equations would you use and what assumptions would you make?

14.9. Develop a simple model for a population in which plasmids are present at division with copy numbers 2, 4, 6, 8, or 10. The model should be developed in analogy to eqs. 14.7 through 14.9. You can assume that dividing cells either segregate plasmids perfectly or generate a plasmid-free cell.

14.10. Assume you have an inoculum with 95% plasmid-containing cells and 5% plasmid-free cells in a 2 l reactor with a total cell population of 2×10^{10} cells/ml. You use this inoculum for a 1000 l reactor and achieve a final population of 4×10^{10} cells/ml. Assuming $\mu_+ = 0.69\ h^{-1}$, $\mu_- = 1.0\ h^{-1}$, and $P = 0.0002$, predict the fraction of plasmid-containing cells.

14.11. Assume you scale up from 1 l of 1×10^{10} cells/ml of 100% plasmid-containing cells to 20,000 l of 5×10^9 cells/ml, at which point overproduction of the target protein is induced. You harvest six hours after induction. The value of P is 0.0005. Before induction $\mu_+ = 0.95\ h^{-1}$ and $\mu_- = 1.0\ h^{-1}$. After induction μ_+ is $0.15\ h^{-1}$. What is the fraction of plasmid-containing cells at induction? What is the fraction of plasmid-containing cells at harvest?