plied sciences (especially bioprocess engineering and industrial microbiology) and sustained availability of finances for new biotechnology firms throughout their early stages.

- It identifies and proposes options for policy issues that have arisen or may arise in connection with the commercialization of biotechnology. Some issues, such as the economic healthiness of the plurality and flexibility of firms commercializing biotechnology, are especially provocative in that they relate to high technology more generally.
- It emphasizes, sometimes through its very limitations, the pace and variability of the evolutionary changes through which biotechnology is passing. It also cautions the reader that any valid consideration of that elusive animal, "competitiveness in biotechnology," requires an appreciation of the way in which diverse elements are inextricably interwoven.

The OTA report, *Commercial Biotechnology, An International Anaylsis*, is an important and comprehensive document that will be used by the U.S. Congress to evaluate policy options and legislative choices over the next few years. However, its effect and stature may be as great internationally as domestically, thanks to its excellent, comprehensive review of each of the major nation's positions and potential for development. The report will become a standard reference work and may prove to be the basis for much decision-making for governmental organizations, large commercial groups, and new biotechnology firms.

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**RESEARCH PAPER ANALYSIS**

# BACTERIAL FITNESS AND GENETIC ENGINEERING

Genetic engineering companies may soon find it necessary to hire molecular geneticists with expertise in the area of microbial evolution. The reason for this lies in the growing interest in the fitness and adaptation of genetically engineered microorganisms, both in the laboratory and following release into the environment. The reproductive fitness of plasmid-carrying bacteria depends on the stability and partitioning of plasmids into daughter cells as well as the "metabolic load" of the plasmids on cellular growth. The stability of several cloning vectors has been shown to be due to a partition locus (*par*) that acts to ensure uniform distribution of plasmids into daughter cells[1–3]. Recently, the *par* locus in plasmid pSC101 has been isolated and shown to consist of a 395 base pair DNA fragment that, although it encodes no proteins, controls the partitioning of plasmids from one cell generation to the next[4].

The usefulness of cells carrying plasmids containing foreign DNA depends not only on their stable transmisssion during growth, but also on the fitness of the plasmid-carrying cells relative to plasmid-free cells that might arise. If plasmid-free cells are more fit under a given set of growth conditions, the plasmid-carrying cells will be displaced from the population rapidly. Indeed, this is what one generally finds when plasmid-carrying and plasmid-free strains are grown together in chemostats under a variety of limiting conditions.

However, some reported results raise questions as to the generality of this rule. Several groups have demonstrated that λ lysogens of *Escherichia coli* reproduce more rapidly than non-lysogens when strains are grown together in glucose-limited chemostats[5,6]. Recently, Hartl and coworkers have shown that a small accessory DNA element, IS50R, markedly increases the growth rate of *E. coli* in glucose-limited chemostats[7]. This finding raises the intriguing possibility that insertion sequences (IS), which are ubiquitous in the genomes of microorganisms, may, under certain environmental conditions, confer a selective growth advantage that more than compensates for their metabolic burden. In the parlance of evolutionists, accessory genetic elements such as the *par* locus and insertion sequences may enhance bacterial fitness, and this may be an important force in the selection of these elements during the course of evolution.

In this issue of BIO/TECHNOLOGY Edlin and co-workers provide additional evidence for this view. They have shown that in glucose-limited chemostats the presence of a 1.8 kb λ *cos* DNA fragment in a plasmid increases the fitness of bacteria harboring such a plasmid to the level of their plasmid-free counterparts. The growth rate of bacteria carrying the *cos* fragment on a plasmid is 20% higher than the growth rate of bacteria lacking this fragment. It remains to be shown whether the 1.8 kb fragment contains an expressed protein (which seems to be the case for IS50) or whether some non-expressed sequence (the *cos* region itself is the most likely candidate) is responsible for this increased fitness.

In a practical vein, the fitness of genetically engineered bacteria may ultimately determine their value as biotechnological tools. A topical case-in-point are the "ice-minus" bacteria[8], whose usefulness depends on their reproductive fitness vis-à-vis wild type bacteria after being released into the environment. With a number of laboratories now pursuing questions of bacterial fitness, some of the molecular mechanisms by which accessory genetic elements affect bacterial growth, survival, and reproduction should soon be known.

**Harvey Bialy, Ph.D., is research editor of BIO/TECHNOLOGY.**

**References**

1. Meacock, P. A. and Cohen, S. N. 1980. Partitioning of bacterial plasmids during cell division: a cis-acting locus that accomplishes stable plasmid inheritance. Cell **20:**529–542.
2. Skogman, G., Nilsson, J., and Gustafsson, P. 1983. The use of a partition locus to increase stability of tryptophan operon-bearing plasmids in *E. coli*. Gene **23:**105–115.
3. Nordstrom, K., Molin, S., and Aagaard-Hansen, H. 1980. Partitioning of plasmid R1 in *E. coli*. Plasmid **4:**215–227.
4. Miller, C. A., Tucker, W. T., Meacock, P. A., Gustafsson, P., and Cohen, S. N. 1983. Nucleotide sequence of the partition locus of *E. coli* plasmid pSC101. Gene **24:**309–315.
5. Edlin, G., Lin, L., and Kudrna, R. 1975. λ-lysogens of *E. coli* reproduce more rapidly than non-lysogens. Nature **225:**735–737.
6. Dykhuizen, D., Campbell, J. H., and Rolfe, B. G. 1978. The influence of λ-prophage on the growth rate of *E. coli*. Microbios **23:**99–113.
7. Hartl, D. L., Dykhuizen, D., Miller, R. D., Green, L., and de Framond, J. 1983. Transposable element IS50 improves growth rate of *E. coli* cells without transposition. Cell **35:**503–510.
8. Powledge, T.M. 1984. Public education urged to counter biotec critics. BIO/TECHNOLOGY **2:**10–12.