tiguous genes under the control of a single promoter–operator is called an *operon*. More global control through *regulons* is also evident. Some gene products are not regulated, and their synthesis is constitutive.

Once a protein is formed, its activity may be continuously modulated through *feedback inhibition*. A number of alternative strategies are employed by the cell to control the flux of material through a pathway. Another form of regulation occurs through the interaction of extracellular compounds with cell surface protein receptors.

4.9. APPENDIX: EXAMPLES OF REGULATION OF COMPLEX PATHWAYS[†]

In *E. coli* the conversion of aspartic acid to aspartyl phosphate is mediated by three isofunctional enzymes, of which two (designated as **a** and **c** in Fig. 4A.1) also mediate the conversion of aspartic acid semialdehyde to homoserine. Enzyme **a**, possessing both these functions, is feedback inhibited, and its synthesis is repressed by threonine. Enzyme **c**, which similarly possesses both functions, is inhibited, and repressed by lysine. The third, aspartokinase (enzyme **b**), is not subject to end-product inhibition, but its synthesis is repressed by methionine (Table 4A.1).

The enzymes of the L-lysine branch (**m–q**) and the L-methionine branch (**r–v**) catalyze reactions leading in each case to a single end product and are subject to specific repression by that end product (L-lysine and L-methionine, respectively).

The third branch of the aspartate pathway is subject to much more complex regulation, for two reasons. First, L-threonine, formed through this branch, is both a component of proteins and an intermediate in the synthesis of another amino acid, L-isoleucine. Second, four of the five enzymes (**e–h**) that catalyze L-isoleucine synthesis from L-threonine, also catalyze analogous steps in the completely separate biosynthetic pathway by which L-valine is synthesized from pyruvic acid. The intermediate of this latter pathway, α-ketoisovaleric acid, is also a precursor of the amino acid L-leucine. These interrelationships are shown in Fig. 4A.1(b).

L-isoleucine is an end-product inhibitor of the enzyme **d**, catalyzing the first step in its synthesis from L-threonine; this enzyme has no other biosynthetic role. L-valine is an end-product inhibitor of an enzyme (**e**) that has a dual metabolic role, since it catalyzes steps in both isoleucine and valine biosynthesis. In certain strains of *E. coli*, this enzyme is extremely sensitive to valine inhibition, with the result that exogenous valine prevents growth, an effect that can be reversed by the simultaneous provision of exogenous isoleucine. The L-leucine branch of the valine pathway is regulated by L-leucine, which is an end-product inhibitor of the first enzyme, **i**, specific to this branch. These interrelationships are shown in Fig. 4A.1(b).

As shown in Table 4A.2, many of the enzymes that catalyze steps in the synthesis of L-isoleucine, L-valine, and L-leucine are subject to repression only by a mixture of the three end products, a phenomenon known as *multivalent repression*. However, the five enzymes specific to L-leucine synthesis are specifically repressed by this amino acid alone.

[†]With permission, from R. Y. Stanier and others, *The Microbial World*, 5th ed., Pearson Education, Upper Saddle River, NJ, 1986.