oligosaccharide (the *dolichol pyrophosphate-oligosaccharide*) with 14 sugars is transferred to the amino group of asparagine.

The 14-sugar residue is first "trimmed" by a set of specific glycosidases. In yeast, oligosaccharide processing often stops in the ER, leading to *simple glycoforms* (or high mannose or oligomannose forms). The initial trimming takes place in the ER, followed by transfer to the Golgi apparatus where final trimming occurs, followed by addition of various sugars or aminosugars. These units are added through the action of various glycosyltransferases using nucleotide-sugar cosubstrates as sugar donors. In insect cells high levels of N-acetylglucosaminidase activity results typically in dead-end structures with a mannose cap. *Complex glycoforms* have sugar residues (N-acetyl glucosamine, galactose, and/or sialic acid) added to all branches of the oligosaccharide structure. *Hybrid glycoforms* have at least one branch modified with one of these sugar residues and one or more with mannose as the terminal residue.

4.6. METABOLIC REGULATION

Metabolic regulation is the heart of any living cell. Regulation takes place principally at the genetic level and at the cellular level (principally, control of enzyme activity and through cell surface receptors). Let us first consider genetic-level changes, as these fit most closely with our discussion of transcription and translation.

4.6.1. Genetic-level Control: Which Proteins Are Synthesized?

As the reader will recall, the formation of a protein requires transcription of a gene. Transcriptional control of protein synthesis is the most common control strategy used in bacteria. Control of protein synthesis in eucaryotes can be more complex, but the same basic concepts hold. In the simplest terms, the cell senses that it has too much or too little of a particular protein and responds by increasing or decreasing the rate of transcription of that gene. One form of regulation is *feedback repression*; in this case, the end product of enzymatic activity accumulates and blocks transcription. Another form of regulation is *induction*; a metabolite (often a substrate for a pathway) accumulates and acts as an *inducer* of transcription. These concepts are summarized in Figs. 4.9 and 4.10. In both cases a repressor protein is required. The repressor can bind to the *operator* region and hinder RNA polymerase binding. For repression, a corepressor (typically the end product of the pathway) is required, and the repressor can block transcription only when bound to the corepressor. For induction, the inducer (typically a substrate for a reaction) will combine with the repressor, and the complex is inactive as a repressor.

Note in Figs. 4.9 and 4.10 that several genes are under the control of a single promoter. A set of contiguous genes, encoding proteins with related functions, under the control of a single promoter–operator is called an *operon*. The *operon* concept is central to understanding microbial regulation.

Control can be even more complex than indicated in Figs. 4.9 and 4.10. The lactose (or lac) operon controls the synthesis of three proteins involved in lactose utilization as a carbon and energy source in *E. coli*. These genes are *lac z*, *lac y*, and *lac a*. Lac z encodes