and also briefly consider control of premature termination of transcription. RNA processing and various posttranscriptional mechanisms for controlling eukaryotic gene expression are covered in the next chapter. Subsequent chapters, particularly Chapters 13, 14, and 15, provide examples of how transcription is regulated by interactions between cells and how the resulting **gene control** contributes to the development and function of specific types of cells in multicellular organisms.

11.1 Overview of Eukaryotic Gene Control and RNA Polymerases

In bacteria, gene control serves mainly to allow a single cell to adjust to changes in its environment so that its growth and division can be optimized. In multicellular organisms, environmental changes also induce changes in gene expression. An example is the response to low oxygen (hypoxia) that is described in Chapter 15. However, the most characteristic and biologically far-reaching purpose of gene control in multicellular organisms is execution of the genetic program that underlies embryological development. Generation of the many different cell types that collectively form a multicellular organism depends on the right genes being activated in the right cells at the right time during the developmental period.

In most cases, once a developmental step has been taken by a cell, it is not reversed. Thus these decisions are fundamentally different from the reversible activation and repression of bacterial genes in response to environmental conditions. In executing their genetic programs, many differentiated cells (e.g., skin cells, red blood cells, and antibody-producing cells) march down a pathway to final cell death, leaving no progeny behind. The fixed patterns of gene con-

trol leading to differentiation serve the needs of the whole organism and not the survival of an individual cell. Despite the differences in the purposes of gene control in bacteria and eukaryotes, two key features of transcription control first discovered in bacteria and described in Chapter 4 also apply to eukaryotic cells. First, protein-binding regulatory DNA sequences, or control elements, are associated with genes. Second, specific proteins that bind to a gene's regulatory sequences determine where transcription will start, and either activate or repress its transcription. As represented in Figure 11-1, in multicellular eukaryotes, inactive genes are assembled into condensed chromatin, which inhibits the binding of RNA polymerases and general transcription factors required for transcription initiation. Activator proteins bind to control elements near the transcription start site of a gene as well as kilobases away and promote chromatin decondensation and binding of RNA polymerase to the promoter. Repressor proteins bind to alternative control elements, causing condensation of chromatin and inhibition of polymerase binding. In this chapter we consider how activators and repressors control chromatin structure and stimulate or inhibit transcription initiation by RNA polymerase.

Most Genes in Higher Eukaryotes Are Regulated by Controlling Their Transcription

Direct measurements of the transcription rates of multiple genes in different cell types have shown that regulation of transcription initiation is the most widespread form of gene control in eukaryotes, as it is in bacteria. *Nascent-chain analysis* is a common method for determining the relative rates of transcription of different genes in cultured cells. In this method, also called *run-on transcription analysis,* isolated nuclei are incubated with ^{32}P-labeled ribonucleoside triphosphates for a brief time (e.g., 5 minutes or less). During

▶ **FIGURE 11-1 Overview of transcription control in multicellular eukaryotes.** Activator proteins bind to specific DNA control elements in chromatin and interact with multiprotein co-activator machines, such as mediator, to decondense chromatin and assemble RNA polymerase and general transcription factors on promoters. Inactive genes are assembled into regions of condensed chromatin that inhibit RNA polymerases and their associated general transcription factors (GTFs) from interacting with promoters. Alternatively, repressor proteins bind to other control elements to inhibit initiation by RNA polymerase and interact with multiprotein co-repressor complexes to condense chromatin.