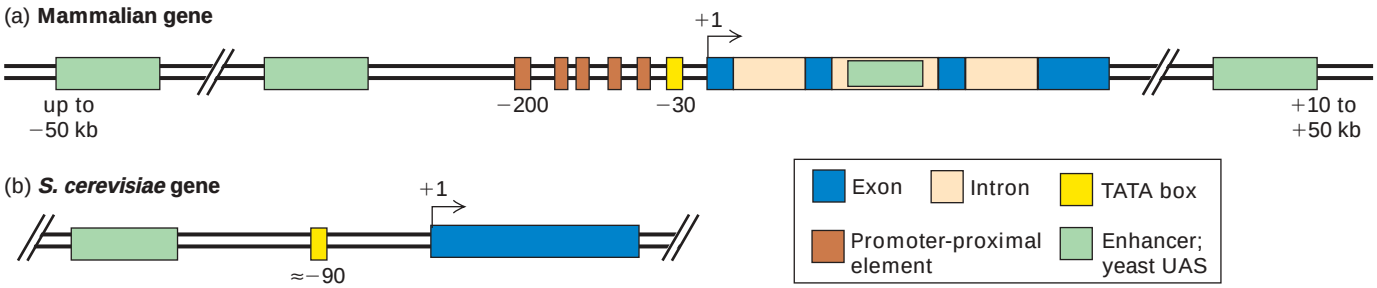

▲ FIGURE 11-12 **General pattern of control elements that regulate gene expression in multicellular eukaryotes and yeast.** (a) Genes of multicellular organisms contain both promoter-proximal elements and enhancers, as well as a TATA box or other promoter element. The promoter elements position RNA polymerase II to initiate transcription at the start site and influence the rate of transcription. Enhancers may be either upstream or downstream and as far away as 50 kb from the transcription start site. In some cases, enhancers lie within introns. For some genes, promoter-proximal elements occur downstream from the start site as well as upstream. (b) Most *S. cerevisiae* genes contain only one regulatory region, called an *upstream activating sequence (UAS),* and a TATA box, which is ≈90 base pairs upstream from the start site.

similarly to enhancers and promoter-proximal elements in higher eukaryotes. Most yeast genes contain only one UAS, which generally lies within a few hundred base pairs of the start site. In addition, *S. cerevisiae* genes contain a TATA box ≈90 base pairs upstream from the transcription start site (Figure 11-12b).

KEY CONCEPTS OF SECTION 11.2

Regulatory Sequences in Protein-Coding Genes

- Expression of eukaryotic protein-coding genes generally is regulated through multiple protein-binding control regions that are located close to or distant from the start site (Figure 11-12).
- Promoters direct binding of RNA polymerase II to DNA, determine the site of transcription initiation, and influence transcription rate.
- Three principal types of promoter sequences have been identified in eukaryotic DNA. The TATA box, the most common, is prevalent in rapidly transcribed genes. Initiator promoters are found in some genes, and CpG islands are characteristic of genes transcribed at a low rate.
- Promoter-proximal elements occur within ≈200 base pairs upstream of a start site. Several such elements, containing ≈10–20 base pairs, may help regulate a particular gene.
- Enhancers, which contain multiple short control elements, may be located from 200 base pairs to tens of kilobases upstream or downstream from a promoter, within an intron, or downstream from the final exon of a gene.
- Promoter-proximal elements and enhancers often are cell-type-specific, functioning only in specific differentiated cell types.

11.3 Activators and Repressors of Transcription

The various transcription-control elements found in eukaryotic DNA are binding sites for regulatory proteins. In this section, we discuss the identification, purification, and structures of these transcription factors, which function to activate or repress expression of eukaryotic protein-coding genes.

Footprinting and Gel-Shift Assays Detect Protein-DNA Interactions

In yeast, *Drosophila,* and other genetically tractable eukaryotes, numerous genes encoding transcriptional activators and repressors have been identified by classical genetic analyses like those described in Chapter 9. However, in mammals and other vertebrates, which are less amenable to such genetic analysis, most transcription factors have been detected initially and subsequently purified by biochemical techniques. In this approach, a DNA regulatory element that has been identified by the kinds of mutational analyses described in the previous section is used to identify *cognate* proteins that bind specifically to it. Two common techniques for detecting such cognate proteins are **DNase I footprinting** and the **electrophoretic mobility shift assay.**

DNase I footprinting takes advantage of the fact that when a protein is bound to a region of DNA, it protects that DNA sequence from digestion by nucleases. As illustrated in Figure 11-13, when samples of a DNA fragment that is labeled at one end are digested in the presence and absence of a DNA-binding protein and then denatured, electrophoresed, and the resulting gel subjected to autoradiography, the region protected by the bound protein appears as a gap, or "footprint," in the array of bands resulting from digestion in the absence of protein. When footprinting is performed