DNA looping occurs during bacterial gene regulation

- **Lac opeon**
  - Originally thought to contain a single operator, but secondary operators located nearly.
  - A *single tetrameric Lac repressor* can bind two operators simultaneously, looping out the intervening DNA.
  - *Strengthens* the overall interaction of the Lac repressor with DNA and thereby leads to greater levels of repression
DNA looping occurs during bacterial gene regulation

- Bacterial gene activator

- NtrC

- DNA looping readily allows the bacterial gene activator NtrC to contact RNA polymerase directly even though the two proteins are bound several hundred nucleotide pairs apart.
Figure 7-42  Molecular Biology of the Cell (© Garland Science 2008)

Figure 7-42a  Molecular Biology of the Cell (© Garland Science 2008)
Bacteria use interchangeable RNA polymerase subunits to help regulate gene expression

- A *sigma* subunits is required for the bacterial RNA polymerase to recognize a promoter.

- *Most bacterial* produce a whole range of sigma subunits.

- Permits *one large set of genes* to be turned off and a new set to be turned on simply by replacing one sigma subunit with another.

- *Very efficient*; it bypasses the need to deal with genes one by one.
Bacteria use interchangeable RNA polymerase subunits to help regulate gene expression

- Bacterial viruses, *SPOI*
  - Infects the bacterium *B. subtilis*.
  - *Uses the bacterial polymerase* to transcribe its genes.
  - *Early genes, called 28*, encodes a sigmalike factor, which binds to RNA polymerase and displaces the bacterial sigma factor.
  - *Middle genes, called 34*, displaces the 28 product and directs RNA polymerase to transcribe the “late gens”.
  - By this strategy, sets of virus genes are expressed *in the order in which they are needed*; this ensures a rapid and efficient viral replication.

### Table 7–2 Sigma Factors of *E. coli*

<table>
<thead>
<tr>
<th>SIGMA FACTOR</th>
<th>PROMOTERS RECOGNIZED</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma^{70}$</td>
<td>most genes</td>
</tr>
<tr>
<td>$\sigma^{32}$</td>
<td>genes induced by heat shock</td>
</tr>
<tr>
<td>$\sigma^{28}$</td>
<td>genes for stationary phase and stress response</td>
</tr>
<tr>
<td>$\sigma^{54}$</td>
<td>genes involved in motility and chemotaxis</td>
</tr>
<tr>
<td>$\sigma^{24}$</td>
<td>genes for nitrogen metabolism</td>
</tr>
<tr>
<td></td>
<td>genes dealing with misfolded proteins in the periplasm</td>
</tr>
</tbody>
</table>

The sigma factor designations refer to their approximate molecular weights, in kilodaltons.
A eucaryotic gene control region consists of a promoter plus regulatory DNA sequences

- **Gene looping**
- **Spacer DNA**
  - provides the flexibility needed for efficient DNA looping.
- **Gene regulatory sequence**
  - Allows the genes of an organism to be turned on or off *individually*.
  - Of the roughly 25,000 human genes, *an estimated* 8% (~2,000 genes) encode gene regulatory proteins.
Eucaryotic gene activator proteins promote the assembly of RNA polymerase and the general transcription factors at the startpoint of transcription

- **Enhancers**
  - The DNA sites to which eucaryotic gene activator proteins bind.
  - Their presence “enhanced” the rate of transcription initiation.

- The simplest gene activator proteins
  - *Two distinct domains* (DNA binding domain + activation domain).
  - A *chimeric protein*
Figure 7-45 Molecular Biology of the Cell (© Garland Science 2008)

(A) Gal4 protein
Gal4 DNA-binding domain
Gene for galactokinase
TATA GENE ON mRNA

(B) Gal4-LexA chimeric protein
Recognition sequence for Gal4
LacZ gene recognition sequence for LexA
TATA GENE OFF
mRNA

Figure 7-45a Molecular Biology of the Cell (© Garland Science 2008)
Eucaryotic gene activator proteins also modify local chromatin structure

- **General idea**
  - The GTFs, mediator, and RNA polymerase seem unable on their own to assemble on a promoter that is packed in standard nucleosomes.
  - Such packing may have evolved to prevent “leaky” transcription.
  - Four of the most important ways of locally altering chromatin
    - Nucleosome remodeling
    - Histone modification
    - Nucleosome removal
    - Nucleosome replacement
  - Writing and reading the histone code during transcription
Gene activator proteins work synergistically

- **Working synergistically**
  - Gene activator proteins often exhibit transcriptional synergy, where several activator proteins working together produce a transcription rate that is much higher than that of the sum of the activators working alone.

- **An order of events leading to transcription initiation** of a specific gene.
  - Does histone modification always precede chromatin remodeling?
  - Does mediator enter before or after RNA polymerase?
  - *Different for different genes.*
Eucaryotic gene repressor proteins can inhibit transcription in various ways

- Six ways in which eucaryotic gene repressor protein can operate
  - competitive DNA binding
  - masking the activation surface
  - direct interaction with the general transcription factors
  - recruitment of chromatin remodeling complexes
  - recruitment of histone deacetylase
  - recruitment of histone methyl transferase
Figure 7-50a  Molecular Biology of the Cell (© Garland Science 2008)

Figure 7-50b  Molecular Biology of the Cell (© Garland Science 2008)
Figure 7-50c Molecular Biology of the Cell (© Garland Science 2008)

**direct interaction with the general transcription factors**

Figure 7-50d Molecular Biology of the Cell (© Garland Science 2008)

**recruitment of chromatin remodeling complexes**