

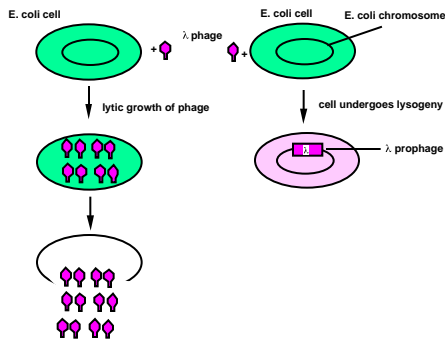
Bacteriophage lambda ()

Transcriptional switches can regulate cellular decisions

Lysis or Lysogeny

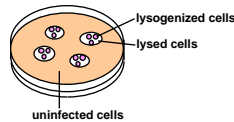
- **Lysis:** Infection by phage produces many progeny and breaks open (lyses) the host bacterium
- **Lysogeny:** After infection, the phage DNA integrates into the host genome and resides there passively
 - No progeny
 - No lysis of the host
- Bacteriophage lambda can do **either**.

Infection by temperate phage leads to lysis or lysogeny

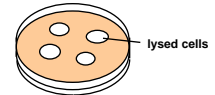


Temperate and lytic phage have a different plaque morphology

Temperate phage generate turbid plaques



Mutants of phage that have lost the capacity to lysogenize form clear plaques

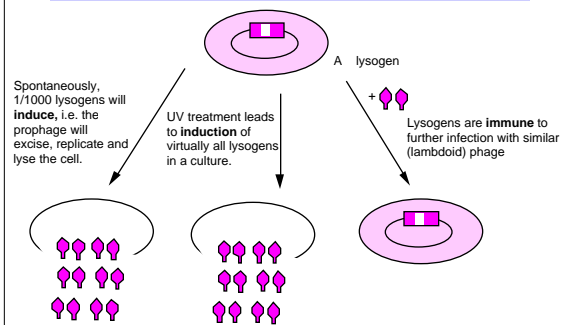


Lytic phage: clear plaques

Elements of lysogeny

- The phage genome integrated into the host bacterial genome is a **prophage**.
- Bacterium carrying the prophage is a **lysogen**.
- Lysogens are **immune** to further infection by similar phage because the phage functions are **repressed in trans**.
- **Induction** of the lysogen leads to **excision** of the prophage, **replication** of the phage DNA, and **lysis** of the host bacterium.

Induction and immunity of lysogens



Regulatory mutants of lambda

Clear plaque mutants

Need wild type for lysogeny:

Establishment Maintenance

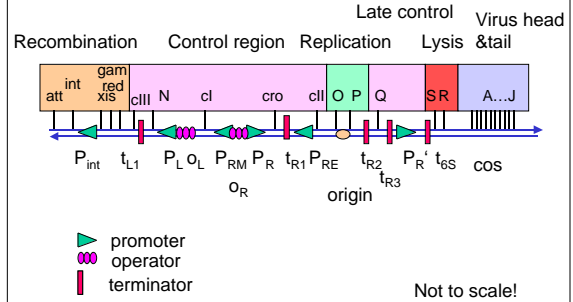
<i>cl</i>	Yes	Yes
<i>cII</i>	Yes	No
<i>cIII</i>	Yes	No

Act in *trans*

Virulent mutants (*vir*)

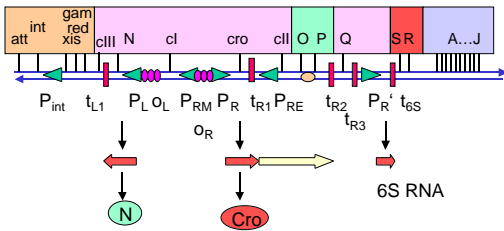
Act in *cis* : are double mutants in o_R &/or o_L

Genes are clustered by function in the lambda genome

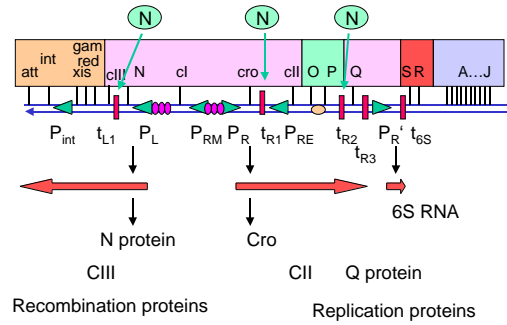


Immediate early transcription

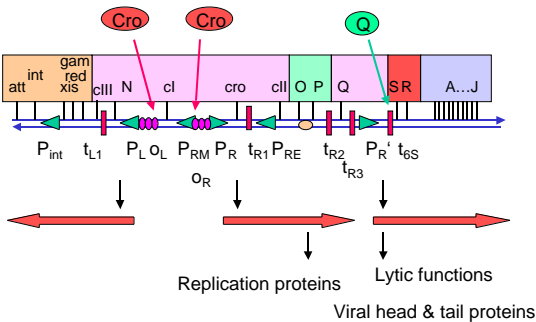
Transcription by *E. coli* RNA polymerase initiates at strong promoters P_R , P_R' , and P_L , and terminates at t 's.



Antitermination by N protein leads to early gene expression

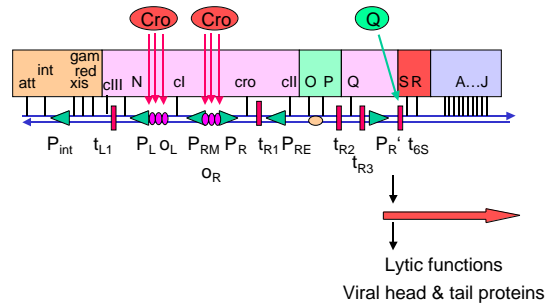


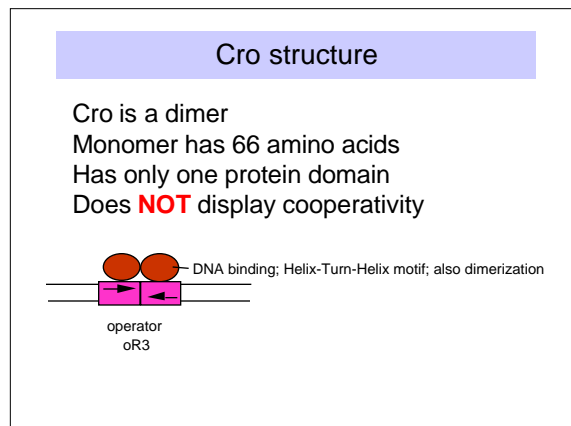
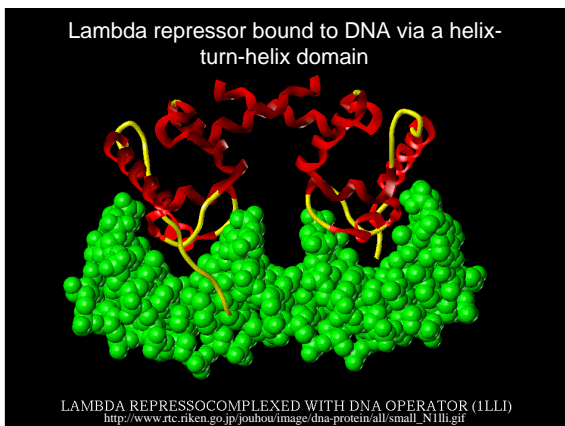
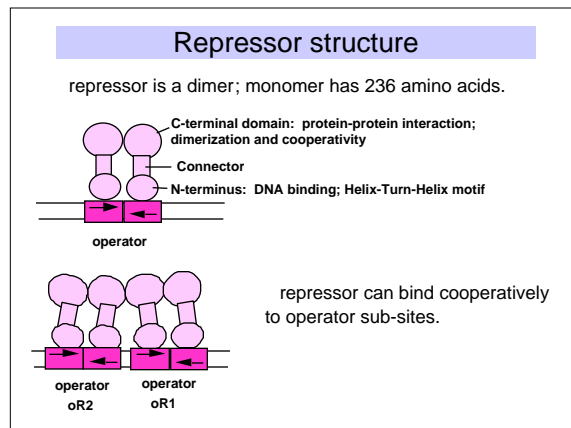
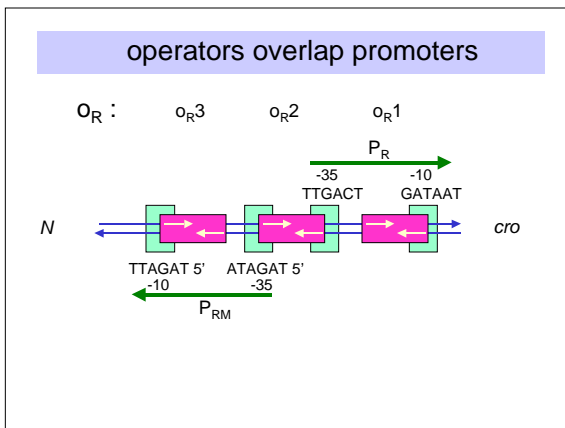
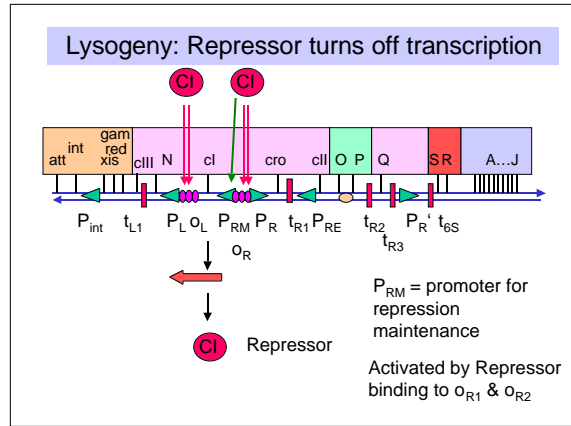
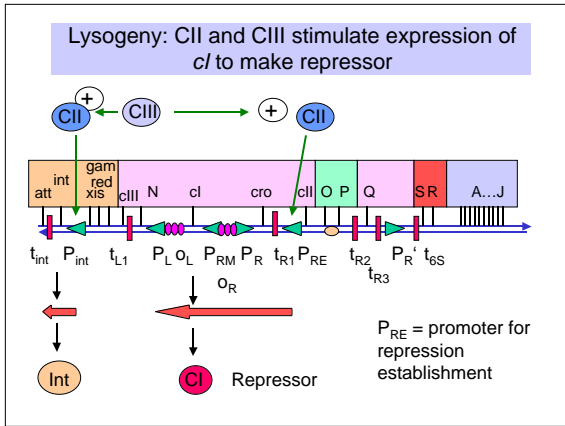
Lytic cascade: Cro turns off *cl*, Q protein action leads to late gene expression



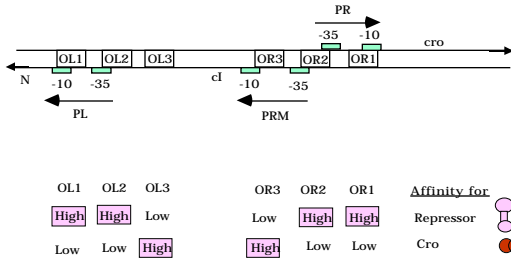
Late stage of lytic cascade

High concentrations of Cro turn off P_R and P_L . Abundant expression from P_R' .





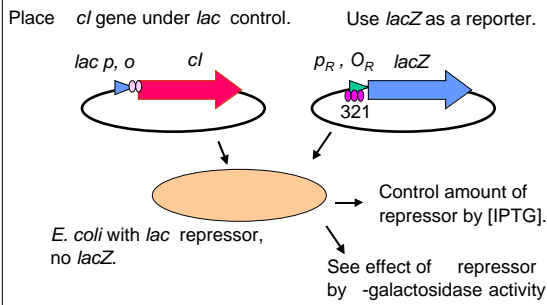
Competition between repressor and Cro for operator sites



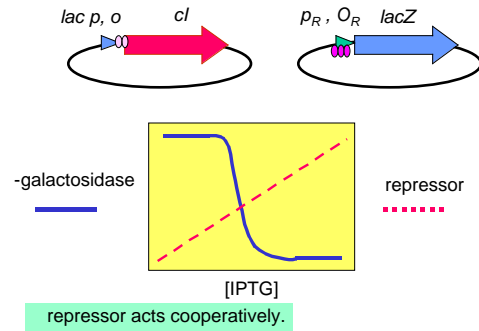
Use hybrid genes to dissect regulatory schemes

- Place a convenient reporter gene under control of the regulatory elements being studied
- Use a known regulatory region to control the *trans*-acting regulatory element

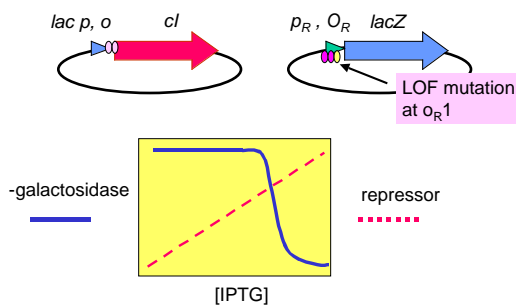
lac hybrid genes



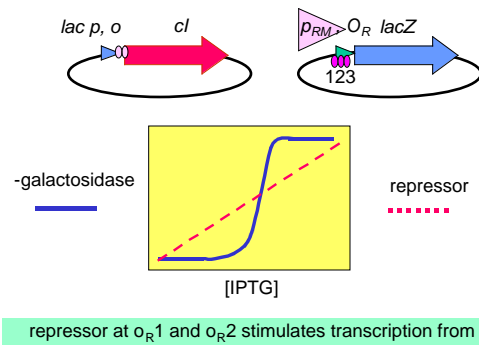
repressor will turn off expression from P_R & P_L

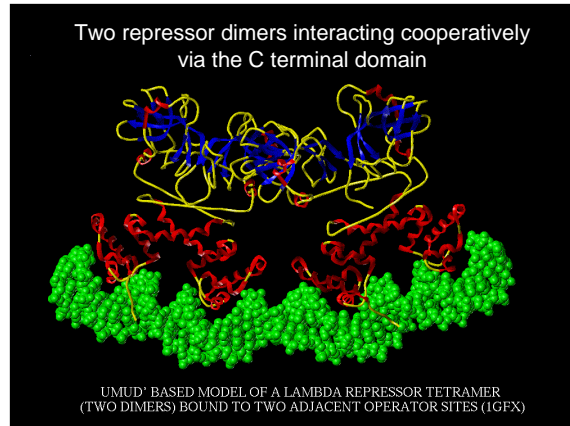
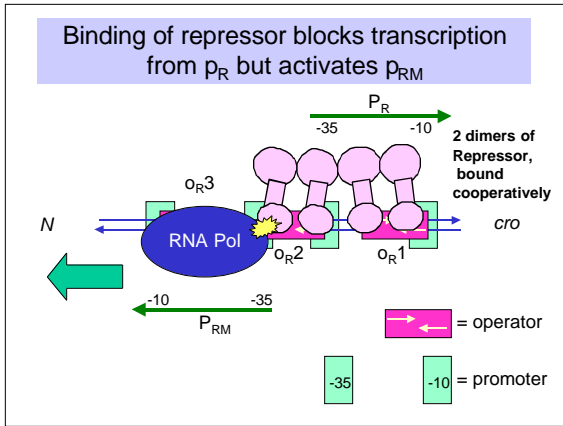


Mutation of o_R1 decreases affinity for repressor



Repressor will stimulate transcription from P_{RM}





- Bacteriophage : Events leading to lysis**
- lysis or lysogeny (cl or Cro?) ?
 - Both lysis and lysogeny:
 - P_R , P_L , $P_{R'}$ active : synthesize N, Cro
 - antitermination by N : synthesize cIII, cII, Q
 - Lysis:
 - Low [Cro] : binds O_{R3} , shuts off P_{RM} (cl)
 - High [Cro] : shuts off P_R and P_L
 - antitermination by Q + activation of $P_{R'}$ by Cro

- Bacteriophage : Events leading to lysogeny**
- lysis or lysogeny (cl or Cro?) ?
 - Lysis and lysogeny :
 - P_R , P_L , $P_{R'}$ active : synthesize N, Cro
 - antitermination by N : synthesize cIII, cII, Q
 - Lysogeny:
 - cII stimulate expression from P_{RE} (cl repressor) and P_{INT} (integrase)
 - cIII stabilizes cII
 - cl repressor shuts off P_R , P_L , $P_{R'}$ (no lytic functions), stimulates P_{RM}

- Factors favoring lysogeny cause increased concentrations of repressor vs. Cro**
- High multiplicity of infection
 - More templates produce more of the CII protein, which stimulates PRE.
 - Phage sense that it is too crowded.
 - Poor nutrient conditions for host
 - Low [glucose] leads to increase in [cAMP].
 - Increased [cAMP] will **repress** the host gene *hflA*.
 - Less HflA (a protease) leads to less degradation of the CII protein.

Homework problems provide a quantitative approach to the competition between Cro and repressor for the operators.