Phage Lambda and Lysogeny

I. Lambda Life Cycle (Chapter 7 pages 180-188)
   Replication
   Enters as Linear DNA, 12bp overhangs at each end
   Circularizes upon entering
   Early theta phase replication, just like on the E.coli chromosome
   initiation: lambda O, P proteins analogous to the DnaA DnaC proteins
   the rest use the host's replication proteins
   Late phase rolling circle replication for amplification
   Gam protein inhibits RecBCD activity
   required for the transition from early to late phase replication
   Uses the cos sites to cut/package the concatamers of DNA into phage heads

II. Going Lysogenic
   Requires CI, CII, and CIII gene products (Clear plaques when mutated)
      1) pR and pL Promoters that are active at infection. Make CII and CIII respectively.
         CII acts as a transcriptional activator for CI repressor and (int)egrase
         CIII prevents CII degradation
      2) CII activates pRE (CI transcription) and pl (int transcription)
         CI represses expression of pR and pL turning off expression of lytic genes
         int (a site-specific recombinase) integrates lambda into the chromosome
         Integrates between gal&bio operons on the E.coli chromosome
         attB (BOB') attP(POP') are the integrase attachment sites
         Bacteria and Phage DNA
   Regulating lysogeny
      CI form a homodimer (two CI molecules)...
      ...and binds to the operators OL1
         OL1 and OR1 are bound first
         Shuts off pR and pL
         OL2 and OR2 are bound second (binding occurs quickly/cooperatively)
         Activates pRM
         At high concentration OL3 and OR3 also eventually bind
         Shuts off pRM
         CI also provides immunity from further infections of lambda

III. Induction (Waking the sleeping prophage)
   Following DNA damage, RecA induces CI protein cleavage
   Once Repressors are cleared off, pR and pL are active again,
   pL eventually makes int & xis
   pR makes cro...then O P... and eventually late phage gene products
   Preventing re-repression
      Cro binds to the operators in reverse order, OR3 OR2 OR1
      Binding to OR3 OR2 inhibits CI activation of pRM
      Eventual binding to OR1 prevents CI repression of pL
      Upon Integration, the RNaseIII site downstream of int & xis...disconnected
      these genes
      ... so both int and xis are expressed from pL and are **not** degraded

IV. Hair Triggers
   CI binds as a homodimer...
   ...leaving the operators open until a critical concentration of CI is reached.
Once the critical concentration is reached...
...cooperative binding of CI to OR2 OR1 shut down lysis (pR and pL) quickly

Also, once CI is degraded below the critical concentration...
...the operators are released (cleared of repressor) very rapidly.

V. Competition
  Cro vs CII immediately following infection
  If the cell is cranked up and growing fast...
  ...lots of transcription/translation occurs very rapidly...
  ...Cro made in sufficient quantities early on...
  ...some activated RecA may also be present to degrade the early CI made...
  ...O P replicate lambda, increasing the number of sites that need repressing...
  ...and the cell goes lytic.
  If the cell is growing slow or on limited resources...
  ...transcription/translation occur more slowly...
  ...some CI has a chance to be made before Cro can shut it down...
  ...no activated RecA is around to degrade the CI...
  ...the replication machinery is not present to create more lambda molecules...
  ...and the cell goes lysogenic.