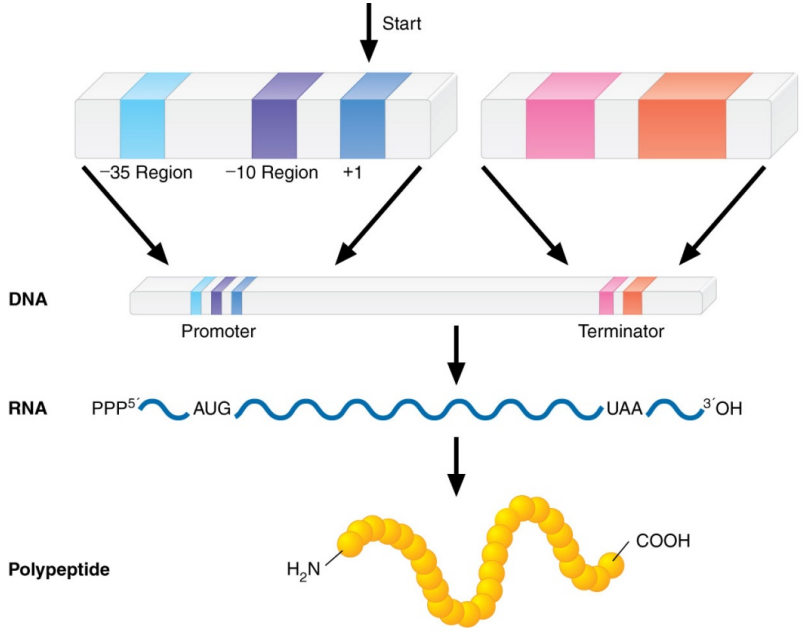
Chapter 18

Overview

Converting Genetic information in molecules of life

- **Replication** – producing new DNA molecule
  - ✓ Necessary when cell divides during mitosis
- **Transcription** – production of RNAs
  - ✓ rRNA-protein synthesis; mRNA-recipe; tRNA-gets amino acid
- **Translation** – conversion of genetic information into proteins
- **Central Dogma**
  - ✓ **DNA→RNA→proteins**



Chapter 18: Overview

- Successful information-based system involves conservation and transfer
  - DNA - stable structure that maximizes storage and duplication
  - RNA - more reactive with numerous roles in protein synthesis and gene expression regulation
- Decoding DNA requires DNA-protein interactions
  - Major and minor grooves facilitate sequence-specific binding
    - Contact between amino acid residues and edges of bases
- DNA-binding proteins - most possess twofold axis of symmetry

1. Helix-turn-helix
2. Helix-loop-helix
3. Leucine zipper
4. Zinc finger

- Accurate DNA synthesis; effective DNA repair mechanisms
  - Variation may also be important for adaptability to environments
    - Caused by genetic recombination and mutation

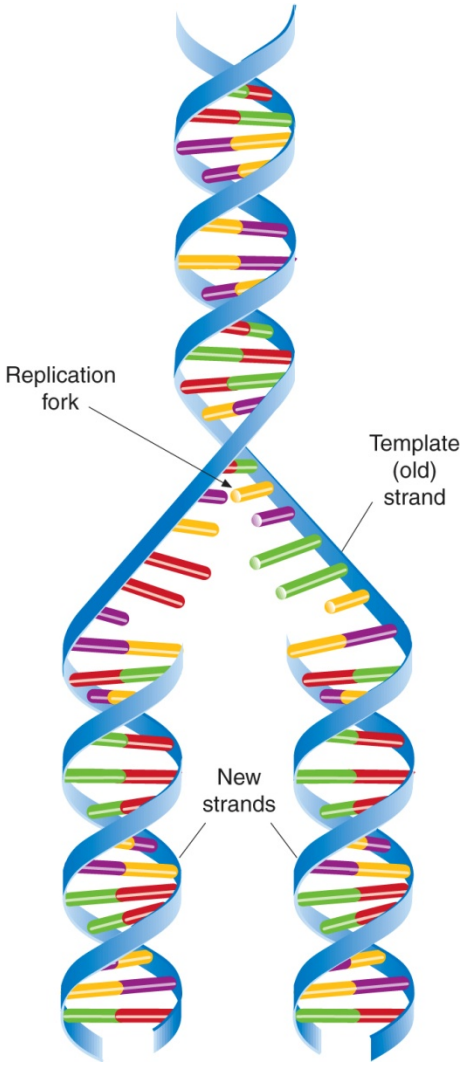


Figure 18.2 Semiconservative DNA Replication

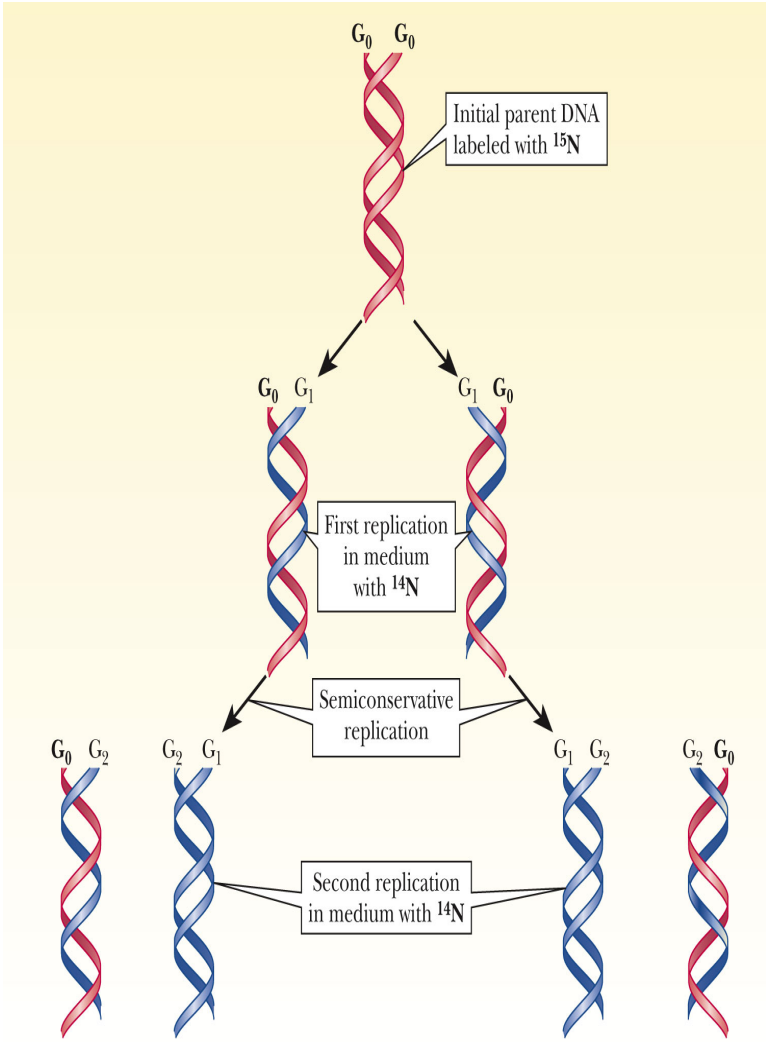
Semiconservative replication

- Separation of 2 original strands
- Each serves as a template for synthesis of a complementary strand (daughter)
  - 1 original strand/1 new strand
- **Meselson and Stahl** established using radio-labeled $^{15}NH_4Cl$
- **Replication factories** – specific nuclear or nucleoid compartments where replication takes place

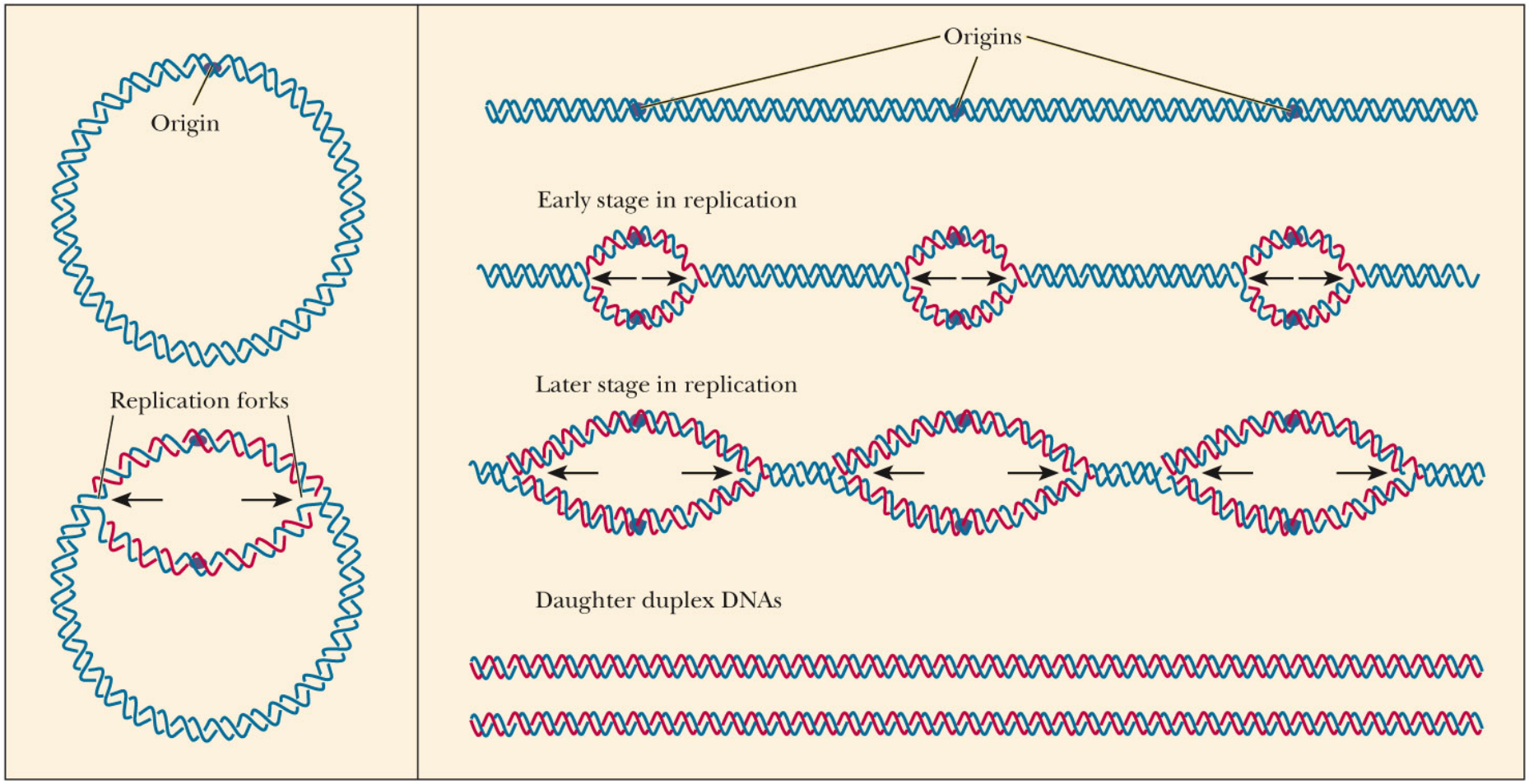
DNA Synthesis in Prokaryotes

- **Helicases** - unwind DNA
- **Primer synthesis** – required for initiation
- **DNA polynucleotide synthesis** – synthesis of complementary strand

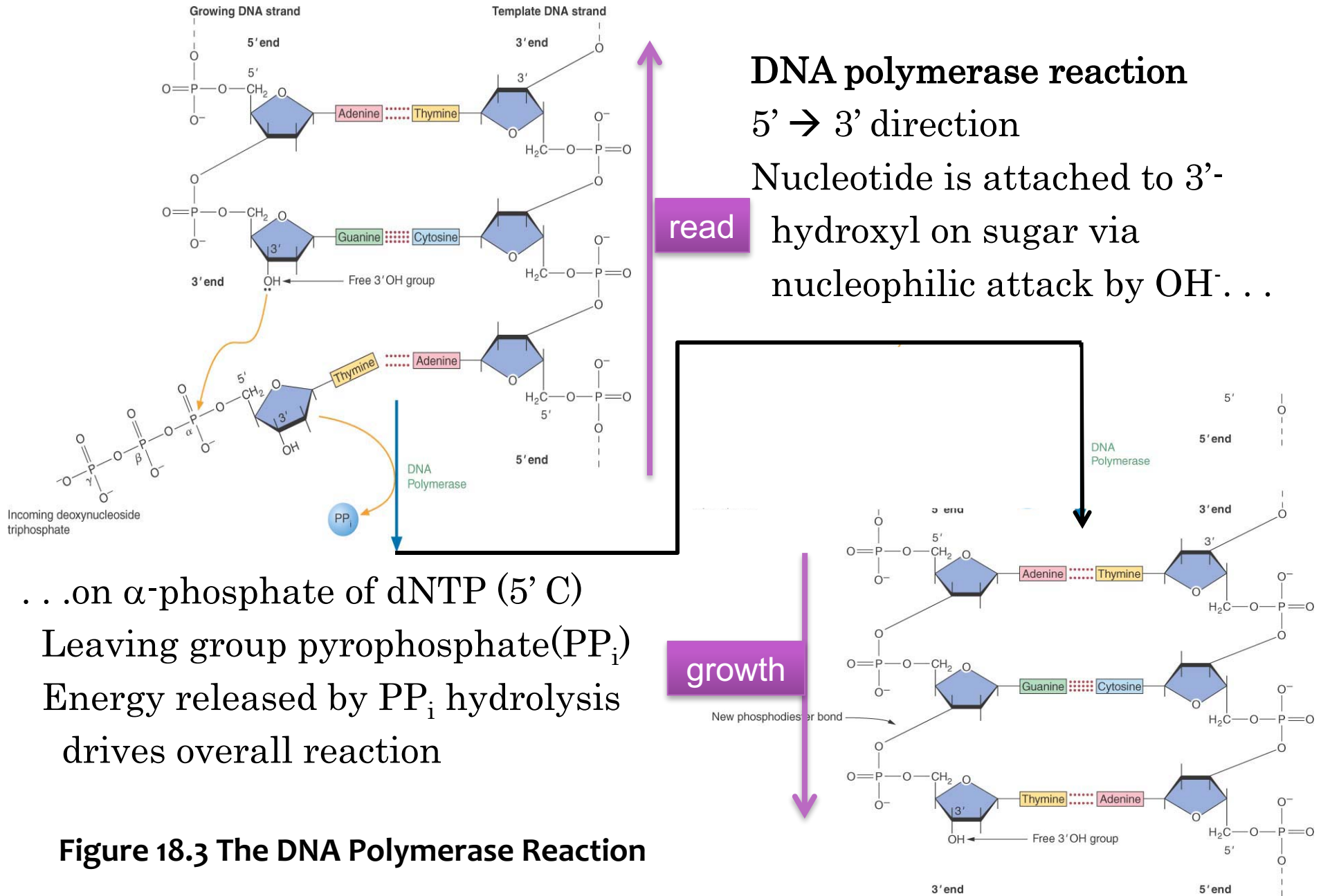
- **Replication**
  - Separation of the two original strands
  - Synthesis of two new daughter strands using the original strands as templates
- **Semiconservative replication:** each daughter strand contains one template strand and one newly synthesized strand
  - Incorporation of isotopic label as sole nitrogen source ($^{15}NH_4Cl$)
  - Observed that ^{15}N-DNA has a higher density than ^{14}N-DNA, and the two can be separated by density-gradient ultracentrifugation



Origin of replication – point where replication will begin



Replication forks– Y shaped region of an unwinding DNA double helix undergoing replication



DNA polymerase reaction

5’ → 3’ direction

Nucleotide is attached to 3’-hydroxyl on sugar via nucleophilic attack by OH^-. . .

. . .on α-phosphate of dNTP (5’ C)

Leaving group pyrophosphate(PP_i)

Energy released by PP_i hydrolysis drives overall reaction

Figure 18.3 The DNA Polymerase Reaction

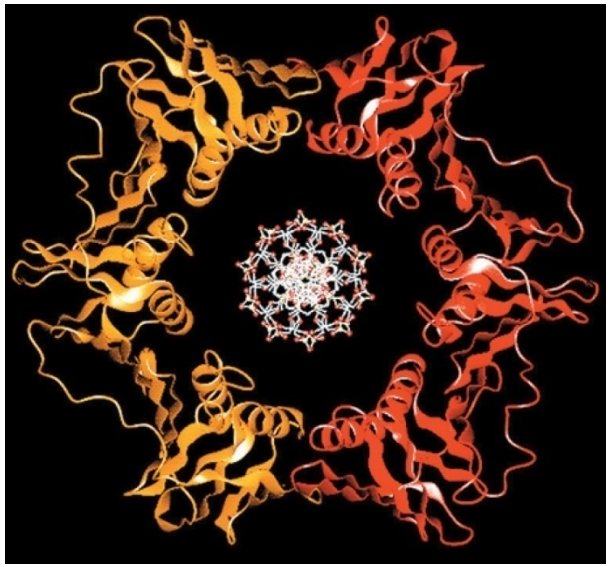


Figure 18.5 Cross Section of the β_2-Clamp of DNA Polymerase III

- DNA polymerase III (pol III)
  - Catalyzes the nucleophilic attack of the 3′-hydroxyl group onto the α-phosphate
  - Pol III holoenzyme - at least 10 subunits
  - Core polymerase is formed of three subunits: α, ε, and t
  - β-protein (sliding clamp) is two subunits and forms a donut-shaped ring around the template DNA
  - γ-complex (clamp loader) transfers sliding clamp

- **Replisome** - two pol III holoenzymes, **primosome** and DNA unwinding proteins
  - DNA polymerase I - 3 catalytic activities
    - **5' → 3' exonuclease** activity
    - 5' → 3' template directed polymerase activity
    - 3' → 5' **exonulease** activity
  - DNA polymerase II, IV, V - DNA repair enzymes known as *translesion* repair enzymes
    - Part of the SOS response - prevent cell death
- **DNA ligase** catalyzes the formation of the phosphodiester bond between adjoining nucleotides
- **DNA topoisomerases** – control supercoiling, relieve torque

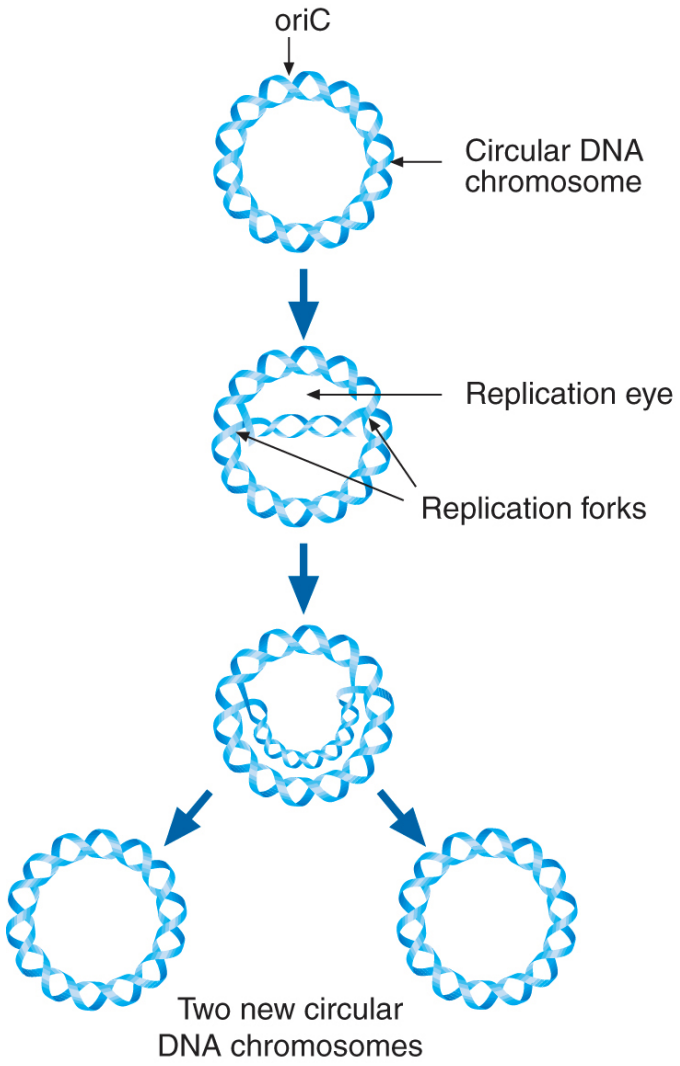
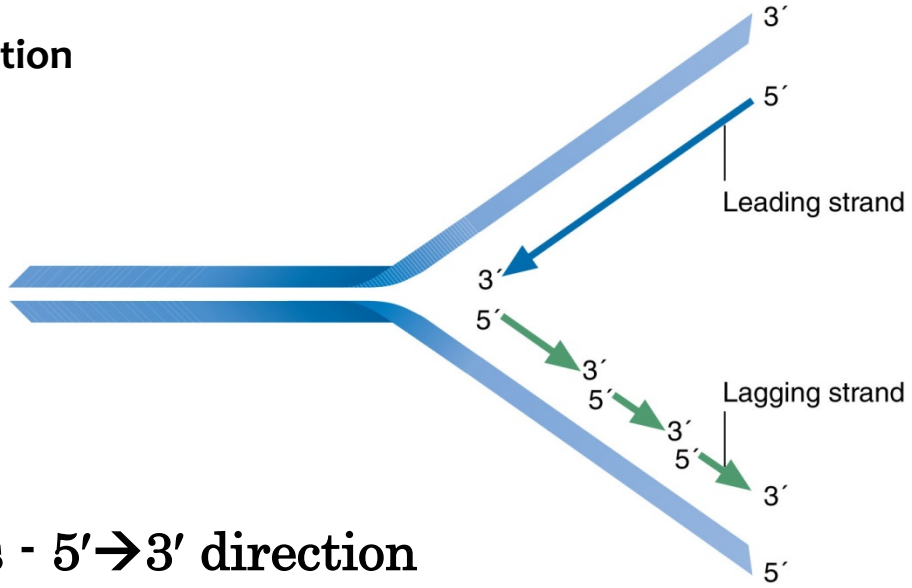


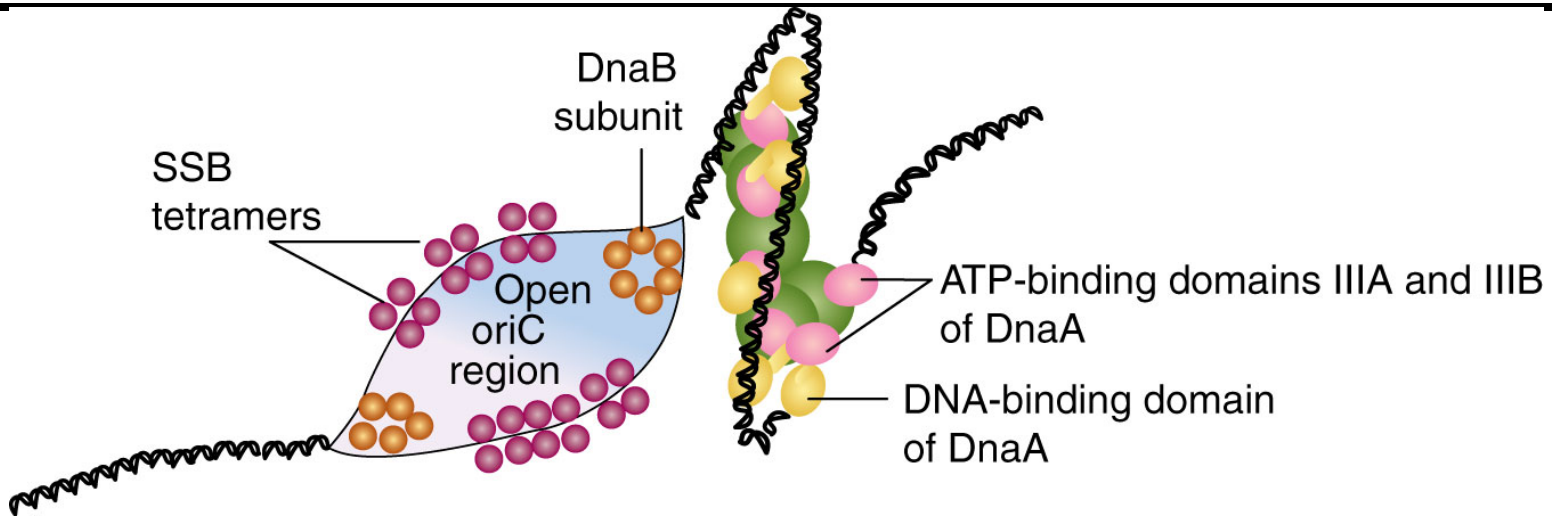
Figure 18.6 Replication of Prokaryotic DNA

- Type I topoisomerases produce transient single-strand breaks
- Type II topoisomerases produce transient double-strand breaks
  - **DNA gyrase**—in prokaryotes helps separate replication products & create negative (-) supercoils
- *E. coli* – high ATP/ADP ratio; DnaA, begins at origin of replication, **oriC**
  - Bidirectional from oriC: **5' -> 3' & 3' -> 5'**
  - Each **replication fork**:
    - **helicases** – unwind double helix
    - **Replisome** – molecular machine that carries out DNA replication
  - **Replicon** - One origin of replication unit and regulatory sequences

Figure 18.8 DNA Replication at a Replication Fork

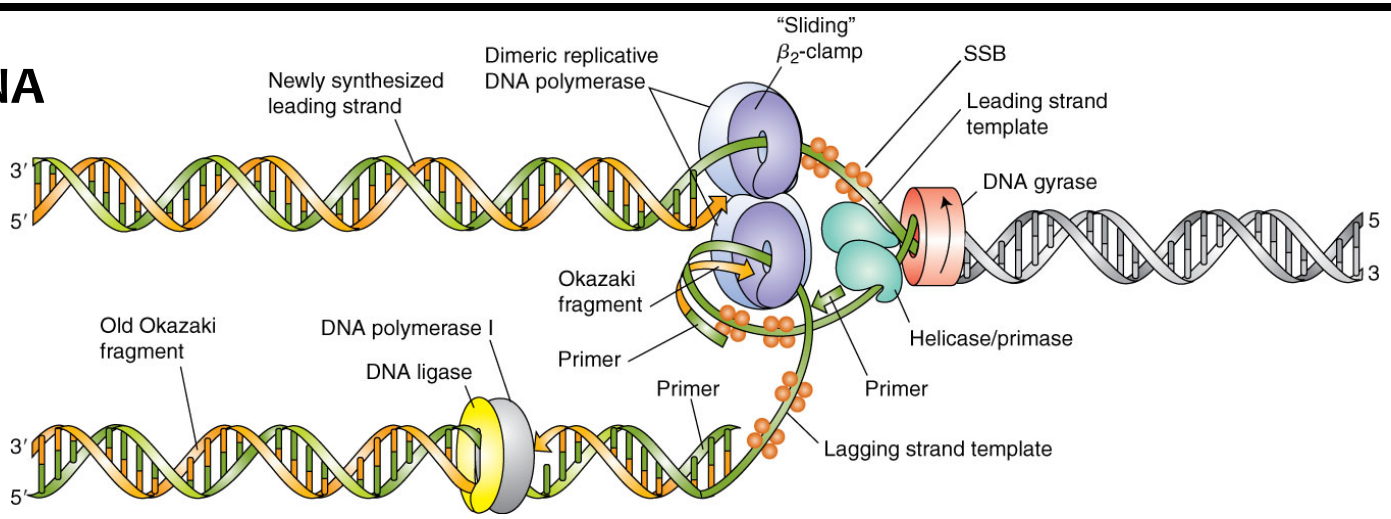


- **DNA synthesis - 5′→3′ direction**
- **DNA polmerase reaction** – nucleotide attaches to 5’ end
  - Incoming nucleotide (5’-triP nucleophile) adds to 3’-hydroxyl on sugar on end of chain
  - 3’-hydroxyl grp attacks P adjacent to sugar being added
  - Elimination of pyrophosphate, formation of phosphodiester bond
- **leading strand** – continuously synthesized
- **lagging strand** –semi-continuous
  - **Okazaki fragments** – short 5’->3’ segments; joined by **DNA ligase**



- **DNA-binding domain**
  - DnaA proteins bind within oriC (DnaA boxes) – yellow beads
  - DnaA-DNA complex forms; requires ATP (pink beads) & histone-like protein (HU); complex opens
  - DnaB helicase (orange beads) binds to DNA; helix is unwound & replication fork moves forward
  - Topoisomerases relieve torque ahead of the replisome
  - Single Stranded Binding proteins (SSB)– binds to single strand DNA to keep strands apart (purple)

Figure 18.10 *E. coli* DNA Replication Model

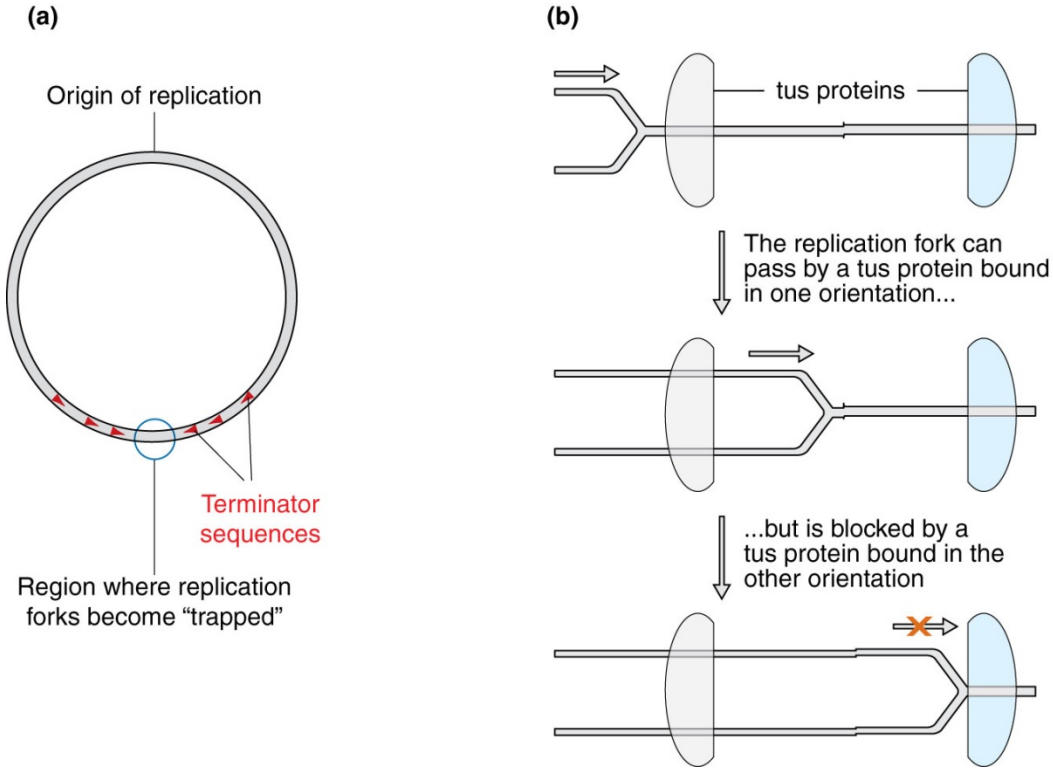


DNA synthesis requires:

- All **4** deoxyribonuleotide triphosphates & Mg^{2+} (ATP, CTP, TTP, GTP)
- **RNA primer** required for pol III to initiate DNA synthesis
  - All **4** ribonucleoside triphosphates (ATP, CTP, UTP<, GTP)
  - Leading strand, only a single primer is required
  - Lagging strand, a primer is required for each Okazaki fragment
- Pol III synthesizes at the 3′ end of the primer
  - RNA primers are removed by pol I
  - DNA ligase then joins Okazaki fragments
- Tandem operation of pol III complexes requires lagging strand to be looped around replisome

- DNA replication takes place only once each generation in each cell
- Errors in replication (**mutations**) occur spontaneously only once in every 10^9 to 10^{10} base pairs
  - Can be lethal to organisms
- **Proofreading** - DNA pol I and III, and postreplication repair mechanisms
  - 15 eukaryotic DNA polymerases; 3 (α, β, ε) in nuclear replication
    - ε corrects α errors
    - β is a nuclear repair polymerase

Figure 18.11 Role of Tus in DNA Replication Termination in *E. coli*



- Replication ends - replication forks meet at the other side of the circular chromosome at the termination site (ter region)
  - ✓ 6 termination sequences (orange arrows)
  - ✓ Replication forks become 'trapped' in ter region
- DNA-binding protein **tus** - binds to the ter causing replication arrest

DNA Synthesis in Eukaryotes

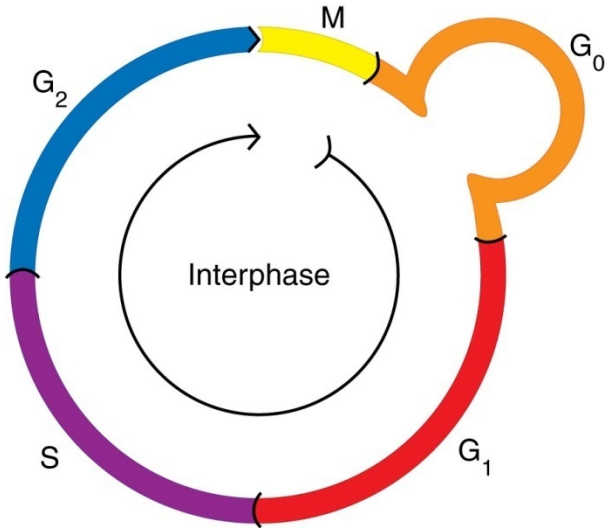


Figure 18.12 The Eukaryotic Cell Cycle

- **15 DNA Polymerases**
  - Three (α, δ, and ε) are involved in nuclear DNA replication
  - Pol γ replicates and repairs mitochondrial DNA
  - Polymerases β, ζ and η function in nuclear DNA repair
- **Timing of replication**—limited to S phase in cell cycle
- **Replication rate** – slower 50 bp per second per replication fork due to complex chromatin structure
- **Replicons**—compresses replication of large genomes into short periods
- **Okazaki fragments** are from 100 to 200 nucleotides long

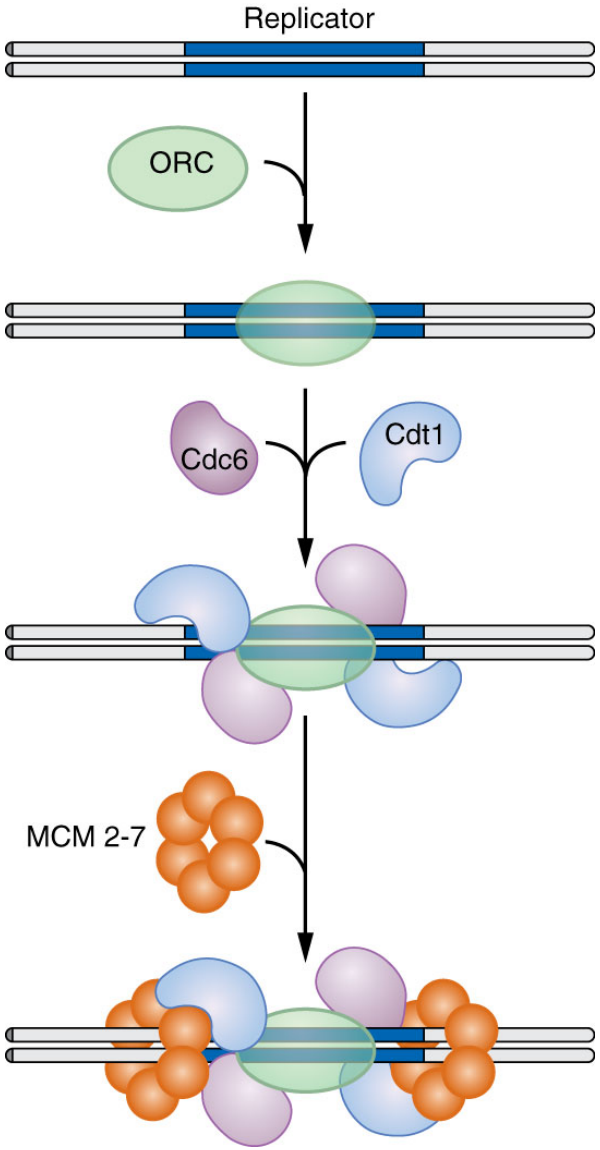


Figure 18.14 Formation of a Preinitiation Replication Complex

Eukaryotic Replication Process – begins with assembly of pre-initiation replication complex (preRC)

- **Preinitiation replication complex** (preRC) – initiates replication
  - **origin replication complex** (ORC) binds to DNA initiation region (origin)
    - Recruits Cdc6 & CdrI
  - **MCM complex** (helicase) is recruited
    - Allows replication proteins to load onto replication fork
- **Licensed preRC** -active initiation complex
  - Requires pol α/primase, pol ε, and accessory proteins
  - Cell cycle regulating kinases then phosphorylate and activate
- **Replication licensing factors (RLFs)** - proteins bind to ORC, complete preRC structure

- **Replication protein A** (RPA)- stablizes newly separated strands
  - **Primase** – synthesizes RNA primers
    - Pol α/Primase extends primers by short DNA strand (~20nt)
- **Replication factor C (RFC)** - clamp loader
  - Controls attachment of polymerase δ and ε to continue process
- Replication continues until replicons meet and fuse
- 3' end of lagging strand – no space for new RNA primer
  - End of chromosome susceptible to nuclease digestion

- **Telemeres**– mini-satellite sequences at end of linear chromosome
- **Telomerase** – overcomes susceptibility to nuclease digestion
  - Ribonucleoprotein with reverse transcriptase activity
  - RNA base sequence complementary to the TG-rich sequence of telomeres
  - Uses sequence to synthesize a single-stranded DNA to extend the 3′ strand
  - **Telomere end-binding proteins (TEBPs)** –binds to GT rich telomere sequences
  - **Telomere repeat-binding factors (TRFs)**– secure 3' end
- During normal human aging - telomeres shorten
  - Once reduced to a critical length - chromosome replication cannot occur;causes cell death
  - 90% of all cancers have hyperactive telomerase

Average natural mutation – 1/100,000 genes/generation

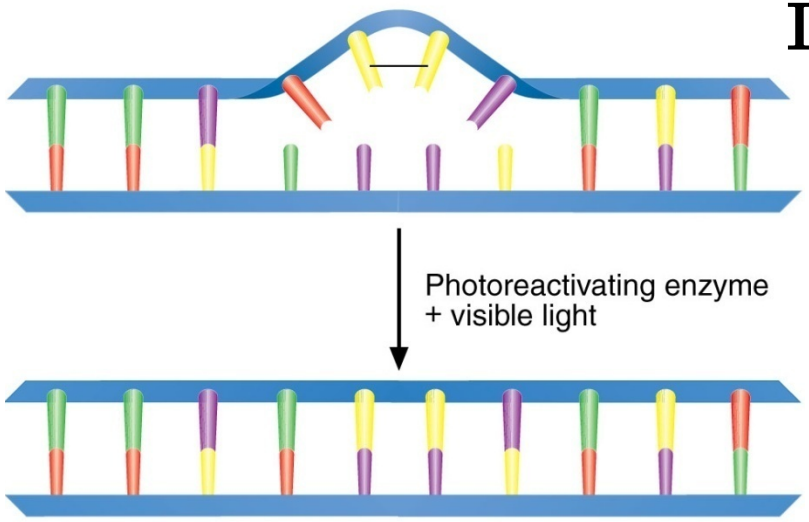


Figure 18.18 Photoreactivation Repair of Thymine Dimers

Direct Repairs – photoreactivation repair of thymine dimers

- Occurs in bacteria, archaea, protozoa fungi, plants, & animals (not humans
- DNA damage repaired without removal of nucleotides
- **DNA ligase** – repairs breaks in phosphodiester linkages
- Pyrimidine dimers - restored to original monomeric structure
- Hydrogen bond - UUsing photoreactivating enzyme and visible light

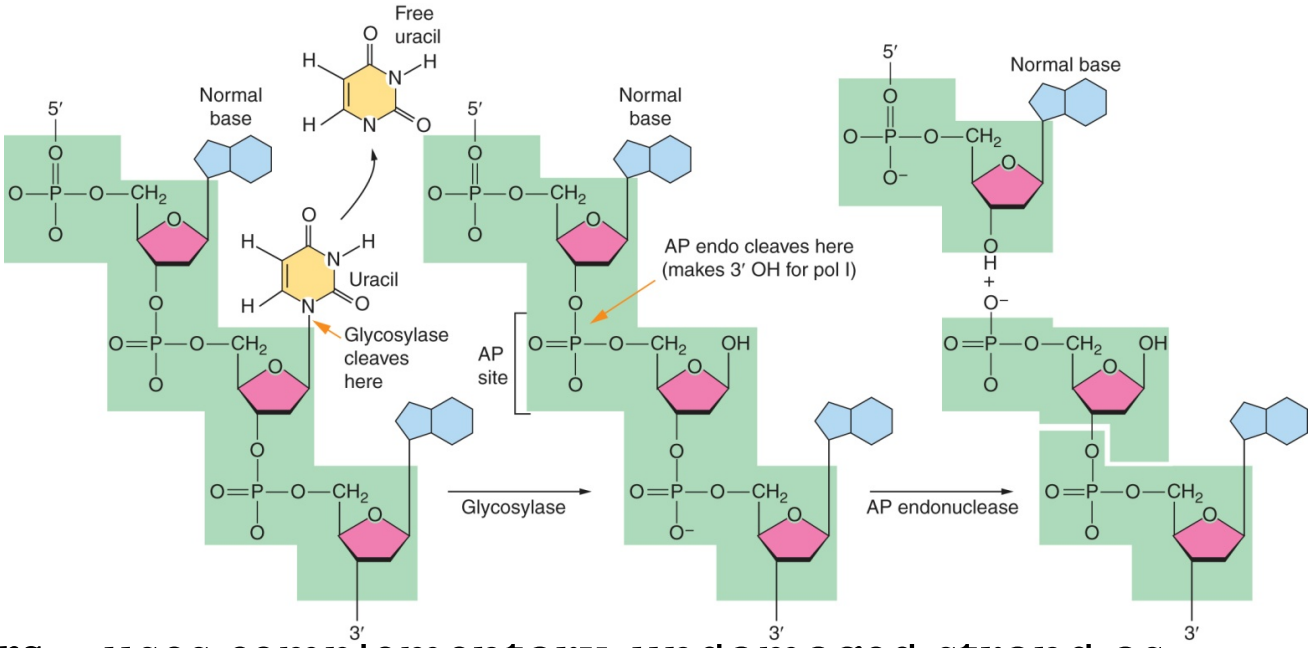
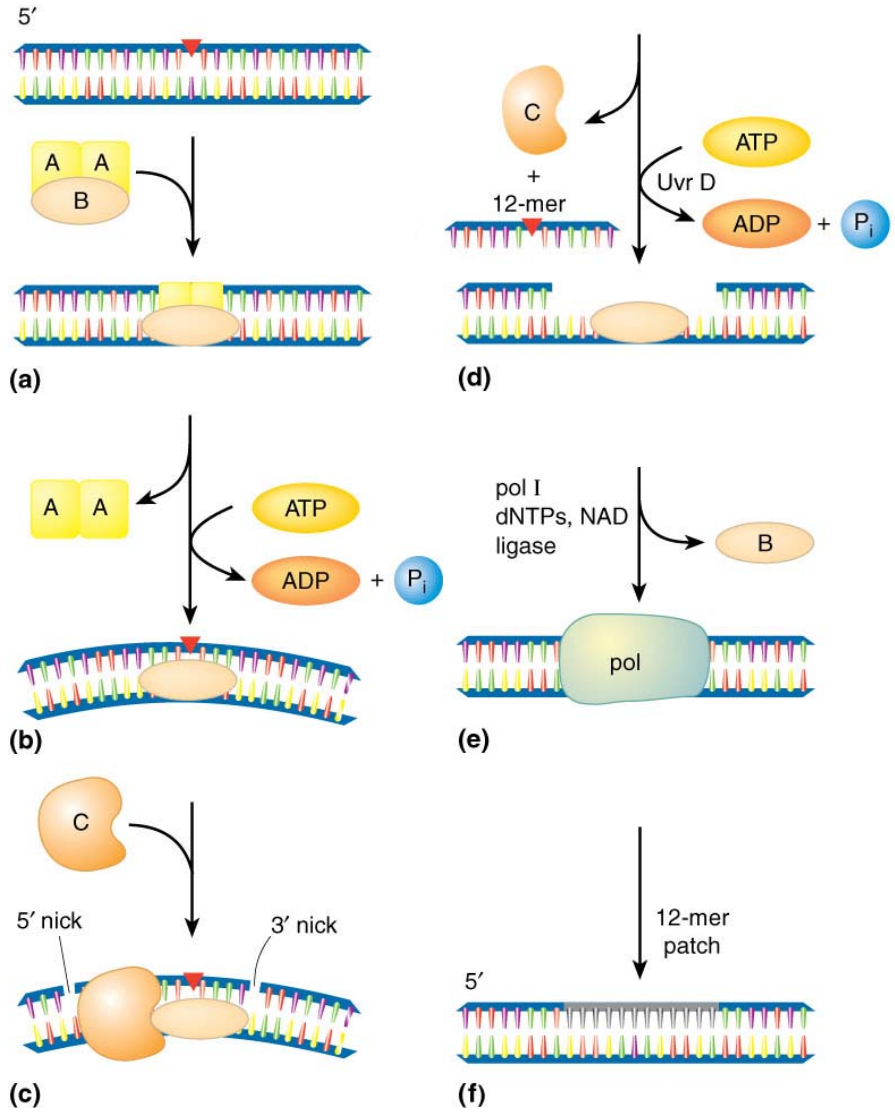


Figure 18.19 Base Excision Repair

Single Strand Repairs – uses complementary, undamaged strand as template

- **Base excision repair** removes then replaces individual nucleotides whose bases have undergone damage
  - **DNA glycosylase** cleaves N-glycosidic linkage between damaged base and deoxyribose of nucleotide
  - Nucleases – remove purines or pyrimidines (apurinic or apyrimidinic sites)
  - DNA polymerase & DNA ligase – repair gap
    - pol I in bacteria; DNA polymerase β in mammals



Nucleotide excision repair - removal of bulky (2-30 nt) lesions; gap is filled

- **Global genomic repair**
  - excision enzymes recognize distortion rather than base sequence
  - *E. coli* - excision nuclease cuts DNA
    - removes 12 to 13 nt ssDNA sequence containing the lesion
    - pol I and DNA ligase – repair gap

Figure 18.20 Excision Repair of a Thymine Dimer in *E. coli*

- **Transcription coupled repair** - strand being actively transcribed
  - Damage is recognized when RNA polymerase is stalled
  - **Mfd** (transcription-repair coupling factor) displaces polymerase and recruits $UvrA_2B$ to initiate damage removal
- **Mismatch repair (MMR)** - corrects helix distorting base mispairings resulting from proofreading errors or replication slippage
  - Key feature is the capacity to distinguish between old and newly synthesized strands
  - Methylation of parent strand results in hemimethylated daughter strands

Double-strand breaks (DSBs) - can result in a lethal breakdown of chromosomes

- Caused by radiation, ROS, DNA damaging agents, or as result of replication errors
- Repaired by two mechanisms: non-homologous end joining (NHEJ) and homologous recombination
  - NHEJ is error prone because there is no requirement for sequence homology
  - Recombination will be explained next

DNA Recombination – principle source of genetic variations that make evolution possible

- Rearrangement of DNA sequences by exchanging segments from different molecules
  - Two types of recombination:
    - **General recombination** occurs between homologous DNA molecules (most common during meiosis)
    - **Site-specific recombination**—the exchange of sequences only requires short regions of DNA homology (e.g., **transposition**)

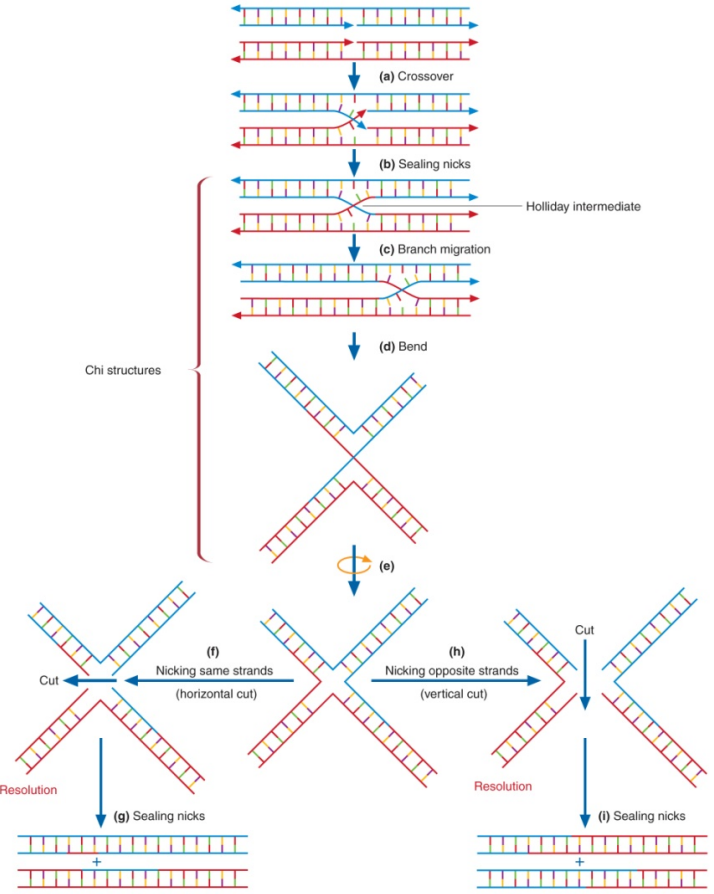
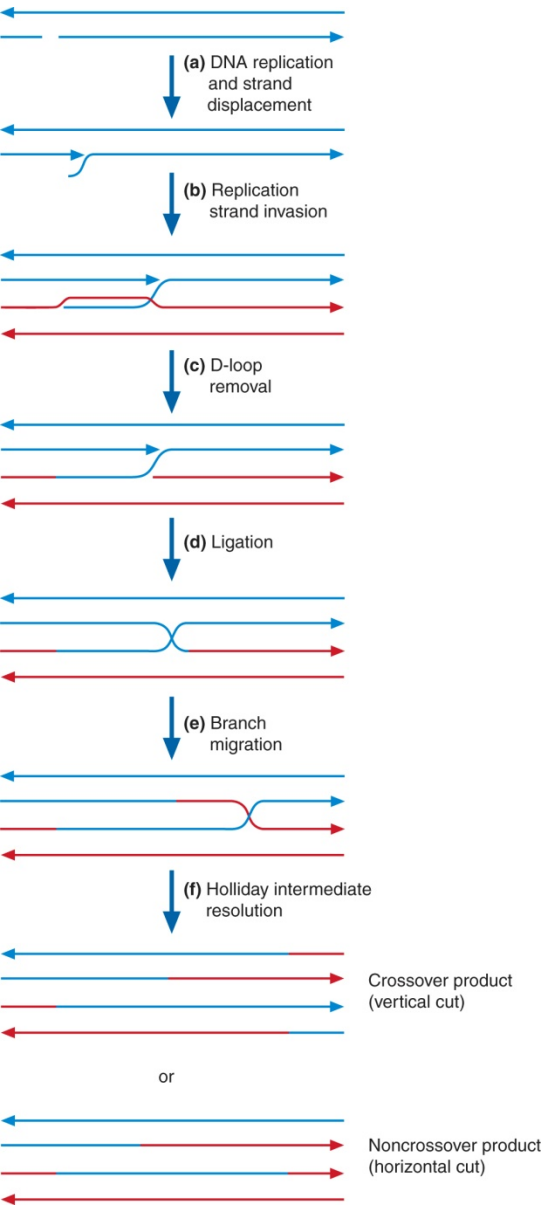


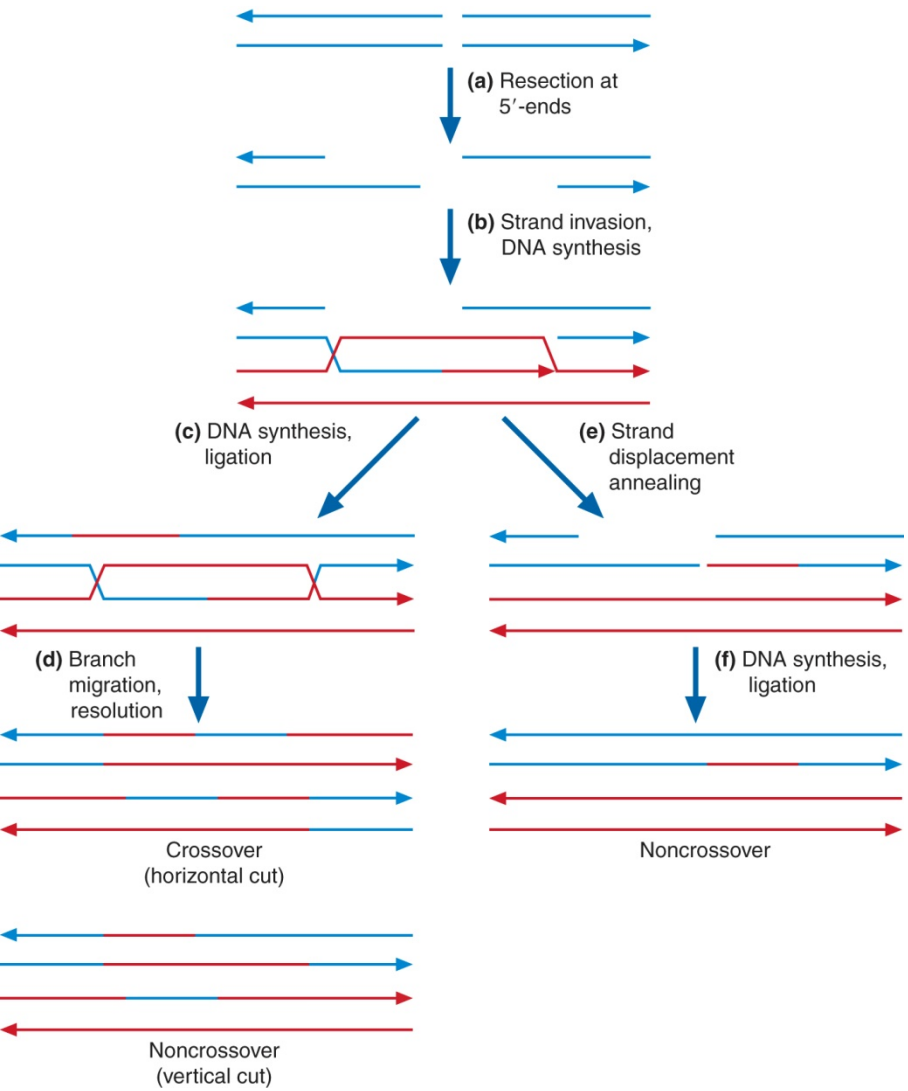
Figure 18.21: The Holliday Model

General Recombination

- Holliday model (1964)
  1. Two homologous DNA molecules become paired
  2. Two of the DNA strands, one in each molecule, are cleaved
  3. Two nicked strand segments cross over, Holliday intermediate
  4. DNA ligase seals the cut ends
  5. Branch migration leads totransfer of a segment of DNA from one homologue to the other
  6. Second series of strand cuts occurs
  7. DNA polymerase fills gaps, DNA ligase seals cut strands



- **Messelson-Radding model**
  1. One strand of two homologous DNA molecules is nicked
  2. Extension causes displacement of strand on other side of nick
  3. D-loop is cleaved, invading strand is ligated to newly created 3′-end of the homologous strand
  4. 3′-end of newly synthesized strand & the 5′-end of a homologous strand are ligated forming a Holliday junction
  5. Branch migration may occur
  6. Strand nicks and Holliday junction resolution result in a crossover or non-crossover product



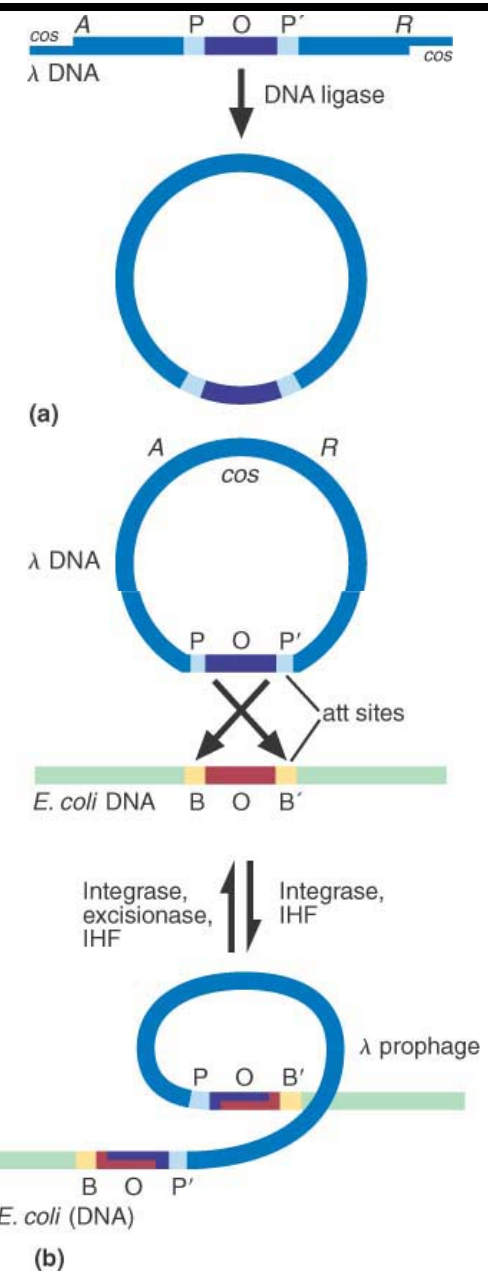
Double-strand break repair model

1. Endonuclease induces a DSB in one pair of homologous chromosomes
2. Exonucleases degrade the 5′-ends leaving 3′-end tails
3. One 3′-end tail invades the homologous DNA molecule and forms a D-loop
4. DNA polymerase extends the invading and noninvading 3′-tail
5. Branch migration and end ligation result in Holliday junction formation
6. Resolution of 2 Holliday structures can give noncrossover or crossover products

- DSBR occurs in mitosis, without crossover products
  - **Synthesis-dependent strand annealing model** explains this phenomena

- **Bacterial Recombination** is involved in several forms of intermicrobial DNA transfer:
  1. **Transformation** - naked DNA molecules enters the cell through small holes in the cell wall
  2. **Transduction** - bacteriophage inadvertently carries bacterial DNA to a recipient cell
  3. **Conjugation** - unconventional sexual mating involving passing DNA from a donor cell through a sex pilus to a recipient cell

- **Eukaryotic Recombination** occurs during first phase of meiosis to ensure accurate homologous chromosome pairing and **crossing over**
  - Similar to prokaryotic recombination but has a larger number of proteins because of the more complex genomes
  - Rad52 is believed to be the initial sensor of DSBs
    - MRN complex – creates scaffold stabilizing DNA ends at DSBs
      - Recruits & activates ATM – regulates damage response
    - Rad51, BRCA1, and BRCA2 are involved in DSB repair



Site Specific Recombination and Transposition - short segments of homologous DNA called **attachment** (att) **sites** or **insertional** (IS) **elements**

- Recombination can lead to insertions, deletions, inversions, and translocations
- Integration of bacteriophage λ DNA into *E. coli* chromosome requires homologous att sites in phage and bacterial genomes
  - A viral recombinase (λ integrase) and a bacterial gene product (integration host factor) are also required for λ prophage formation
  - Results in insertion of λ genome into bacterial chromosome

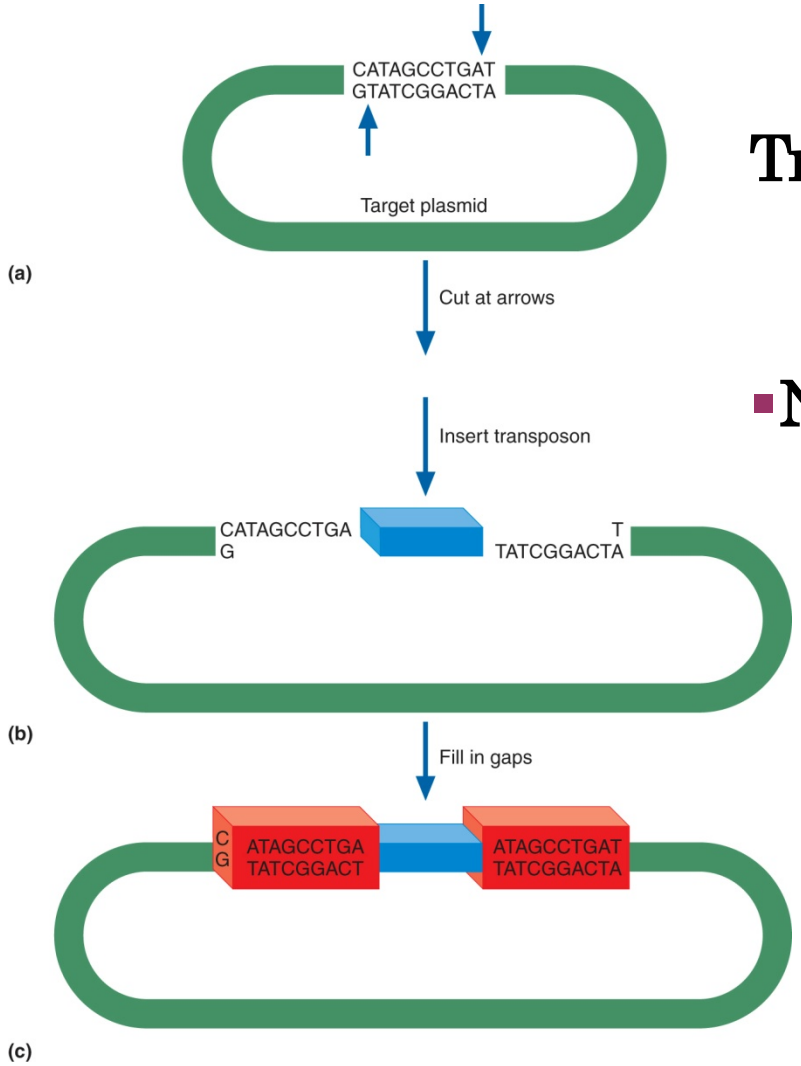


Figure 18.27 Nonreplicative Transposition

Transposition – move DNA sequence from one site to another in genome

- **Nonreplicative transposition** -double-stranded cut in the donor DNA
  - Spliced into the staggered ssDNA cut ends of the target site
  - DNA repair system fills the gaps in target DNA
  - Transposons – "jumping genes"

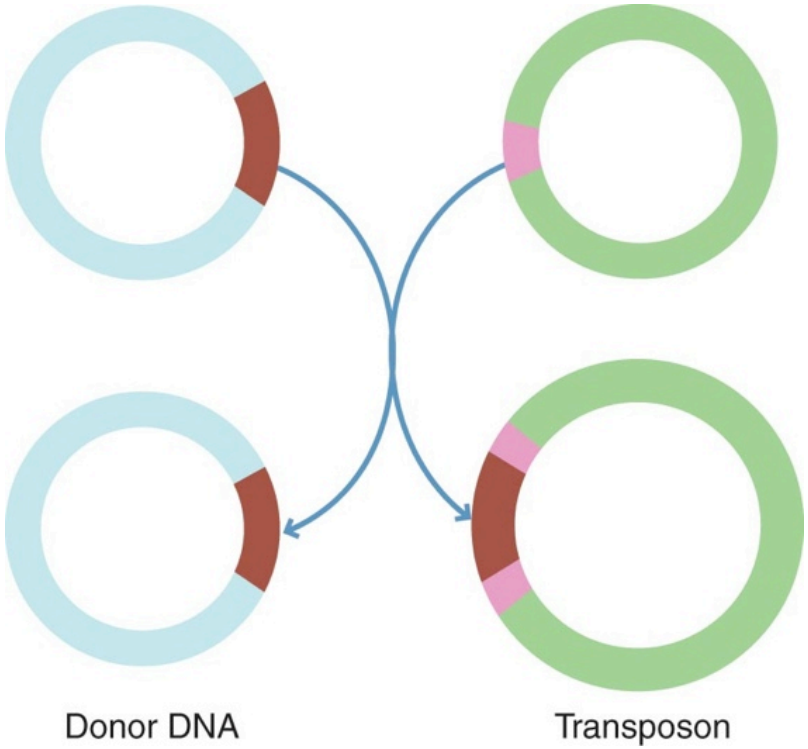


Figure 18.28 Replicative Transposition

Replicative transposition - transfer of one strand of donor DNA to target position

- Duplication of the transposon rather than insertion at the new site
- Involves an intermediate, co-integrate, resolvase (catalyzes the site-specific recombination)

Transcription – creation of RNA from DNA sequences

- RNA polymerase – enzyme catalyzing the addition of ribonucleotides in a 5′→3′ direction
- All 4 ribonucleoside triphosphates required, Mg^{2+}
- Primer is not needed, DNA template is required
  - Only 1 strand of helix is used
- **Nontemplate strand** (+) - same base sequence as the RNA, except transcript has uracil for thymine
- **Template strand** (-) - antiparallel to the new RNA strand
  - Contains initiation & termination signals
  - Enzyme moves in 3'-to-5' direction
  - RNA created in 5' → 3'

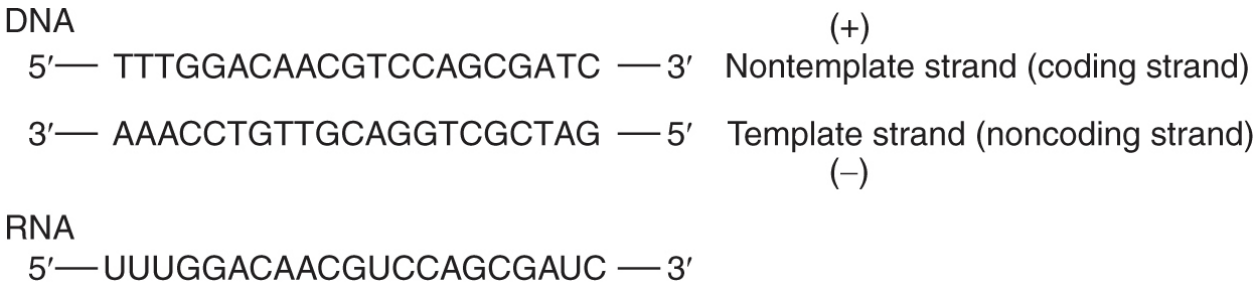
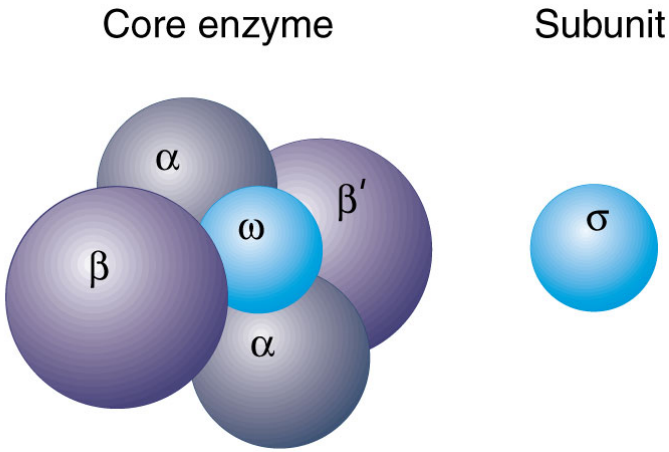


Figure 18.31 DNA Coding Strand

Figure 18.30 *E. coli* RNA Polymerase



Transcription in Prokaryotes

- RNA polymerase in *E. coli* catalyzes the synthesis of all RNA classes
- **Core enzyme** (α_2,β and β′) catalyzes RNA synthesis
- **Holoenzyme** – complete enzyme ($\alpha_2\omega\beta\beta'\sigma$)
  - σ subunit promotes core assembly and σ–factor functions in transcription initiation
- **Promoters** – RNA polymerase binds to DNA at start of transcription

Section 18.2: Transcription

RNA Polymerase slides down DNA 3' -> 5' to promoter sequence

- **Upstream** of start of transcription
- **3 components** – 2 consensus sequences, 3rd TSS
  - **Transcription start site (TSS)** -position +1
  - **Consensus sequences** at -10 region (Pribnow box) and -35 region
  - **Core promoter** - -35 element to TSS
- **Chain initiation** – RNA pol recognizes -35 region
  - **Closed complex** – forms when promoter binds
- **Open complex** - break hydrogen bonds; unwind a short segment of DNA at Pribnow box
- RNAP catalyzes the addition of first nucleoside triphosphate
  - 10 nucleotides synthesized – RNAP clears promoter region
  - σ factor is released, ready for elongation

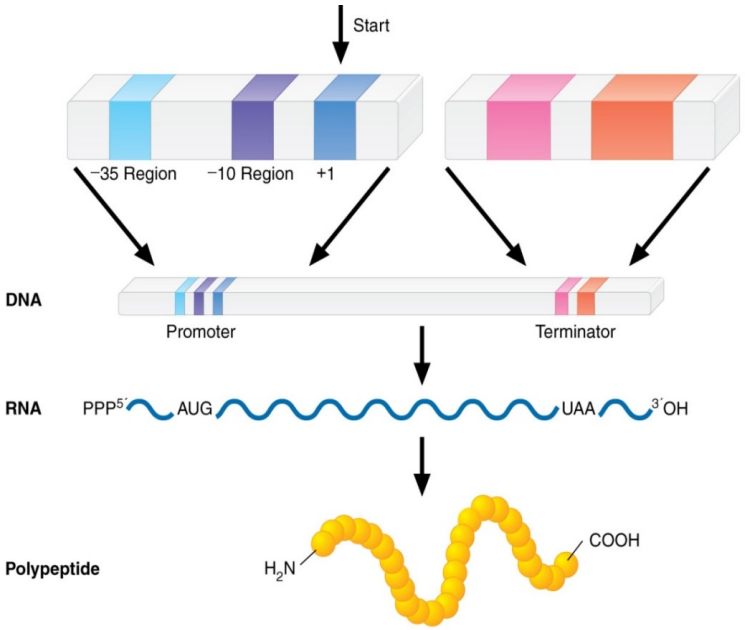


Figure 18.32 Typical *E. coli* Transcription Unit

Section 18.2: Transcription

- **Transcription bubble** - unwound DNA of 12–14 bp
  - Contains RNA-DNA hybrid
- Template strand enters active site through channel
  - Active site lies between β/β' subunits
- Nontemplate strand loops away from active site into its own channel
- Both strands emerge, re-forming a double helix

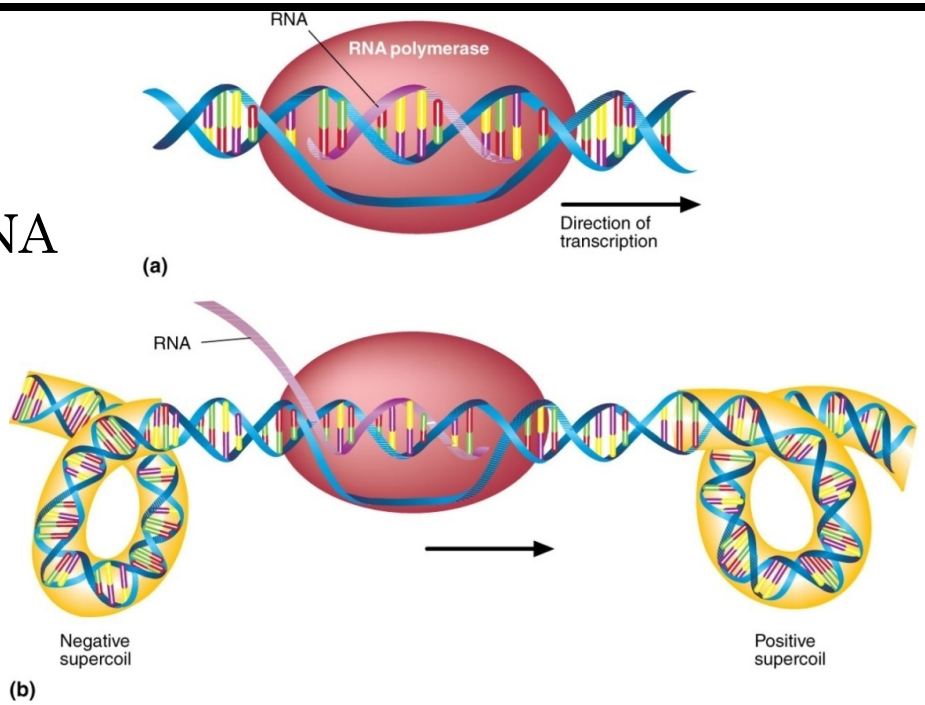
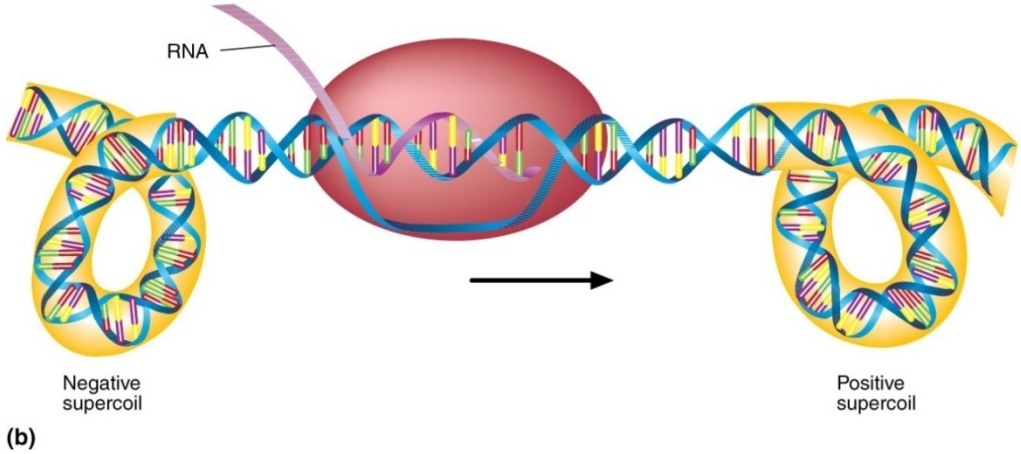


Figure 18.31 Transcription in *E. coli*

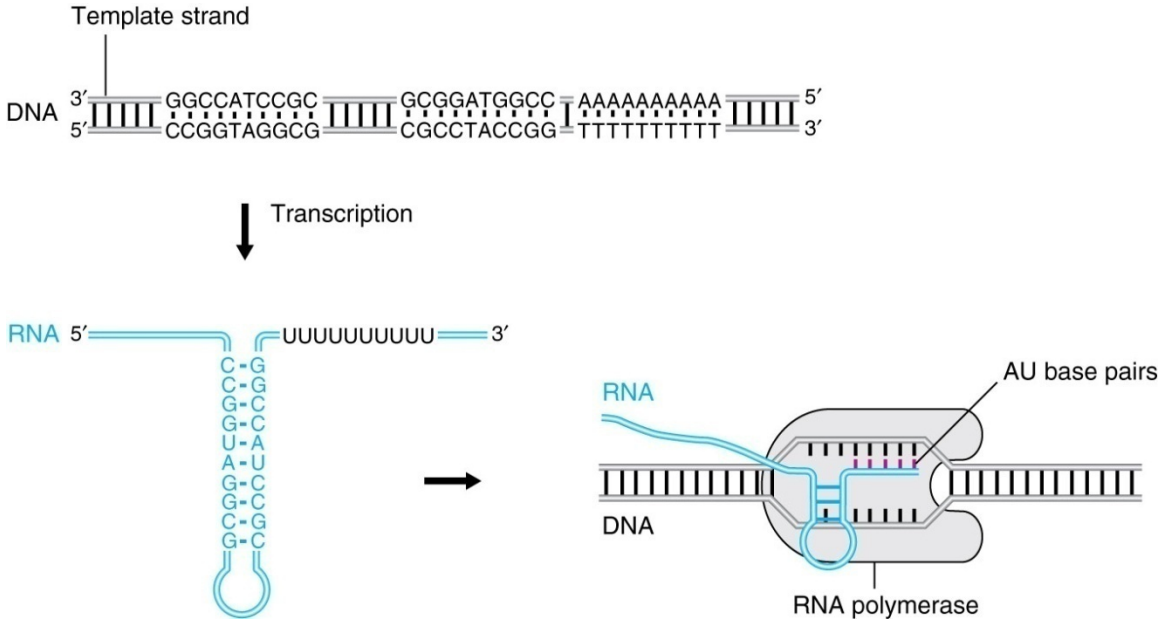


Growing RNA chain exits through a channel

- ✓ Positive supercoils ahead of transcription; negative supercoils behind
- ✓ **Topoisomerases** relieve the supercoils, advance bubble
  - ✓ No relax – RNA chain wraps around helix every 10bp

- Termination signal - ends transcription

Figure 18.34 Intrinsic Termination



- **Intrinsic termination** – controlled by **termination sites**
  - 2 inverted repeats spaced by few other bases
  - Sequences of complementary bases, loop back on themselves
    - DNA encodes a series of uracils
  - Forms a stable hairpin causing RNA polymerase to slow or stop
    - Series of A-U base pairs between template strand & RNA
  - RNA transcript is released due to weak base-pair interactions

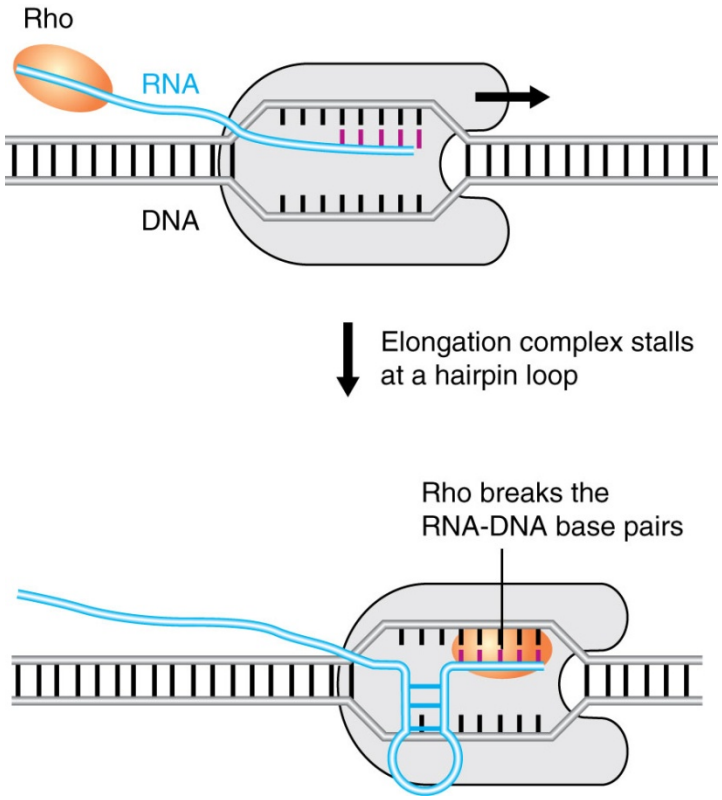


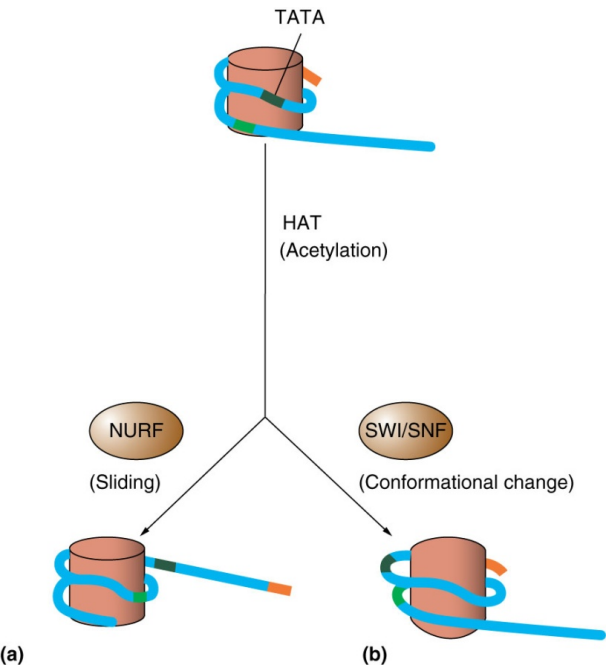
Figure 18.35 Rho-Dependent Termination

rho-dependent termination – aid of ATP-dependent helicase **rho factor**

- Rho binds to a specific recognition sequence on the nascent RNA chain, upstream from termination site
  - Chases polymerase; when hairpin loop forms, stalls allowing rho to catch up
- Unwinds the RNA-DNA helix to release the transcript

Transcription in Eukaryotes

- Polymerases are similar in structure and function – 1 vs 3
- Initiation factors are distantly related, but perform similar functions
- Regulatory mechanisms differ significantly in both organisms



- One major difference is the limited access to DNA of the transcription machinery
  - Chromatin least partially condensed
  - **Transcription premissive** - histone tails modified by histone acetyl transferases (HATs)
  - **Chromatin remodeling complexes** – weakens histone-DNA contacts
    - SWI,SNF, and NURF

- **RNA Polymerase Activity**
  - **RNA polymerase I (RNAPI)** transcribes larger rRNA (28S, 18S, and 5.8S) in the nucleolus
  - **RNA polymerase II (RNAPII)** produces the precursors of mRNA, miRNAs and most snRNA
  - **RNA polymerase III (RNAPIII)** is responsible for transcribing the precursors for tRNA, 55 rRNA, U6 snRNA, and the snoRNAs
- Requires various transcription factors bound to the promoter to initiate transcription

Eukaryotic promoters- Pol II core promoter can be focused or dispersed

- Focused - transcription start site (TSS) and core promoter elements (CPE)
  - TATA box - consensus sequence, TATAA
  - **TFIID** - TATA-binding protein (TBP) binds to TATA box.
    - Other core elements include the Inr (initiator), BRE (B recognition element), and DPE (downstream promoter element)
- Dispersed genes -multiple TSSs, distributed over a broad region of 50-100 basepairs
  - Typically occur within CG islands
    - Facilitate nucleosome destabilization

RNA polymerase II (RNAP II)

- 12 subunits in humans
  - RBP1, largest subunit, forms part of the enzyme's active site; binds DNA
  - Contains C-terminal domain (CTD)
    - Unphosphorylated allows RNAPII to bind promoters
- RNAP II machinery - set of five transcription factors and a 20-protein mediator complex
  - General transcription factors (GTFs): TFIIB, TFIID, TFIIE, TFIIF, and TFIIH are the minimum required for accurate transcription
    - Facilitate promoter recognition, preinitiation complex formation, and ATP-dependent DNA unwinding

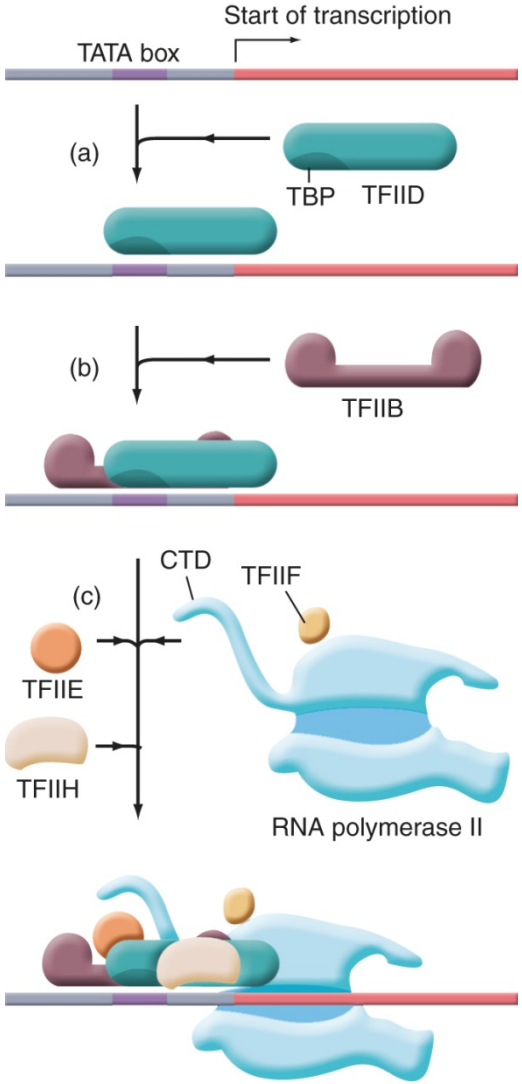
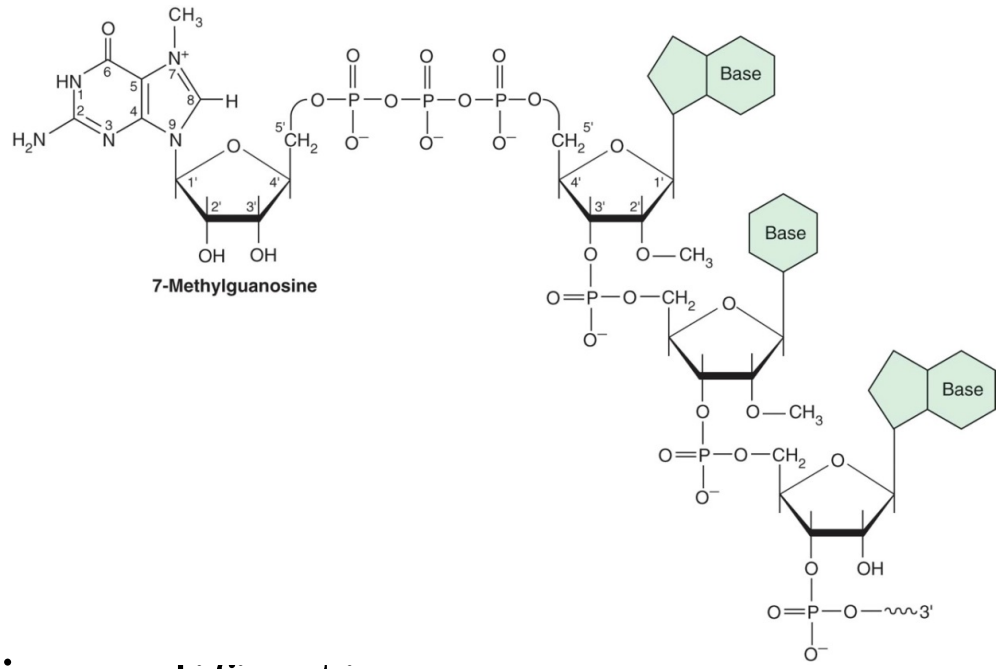


Figure 18.44 Preinitiation Complex Formation at a TATA Box

- **PIC assembly** - binding of TBP subunit of TFIID to the TATA box.
  - Other GTFs: TFIIA, TFIIB, TFIIF, mediator
  - TFIIH acts as an ATP-dependent helicase
  - Promoter clearance occurs after 23 nt
- **Elongation** - promoter clearance; mediator dissociation
  - Termination Sequence - poly(A) sequence, (5′-AAUAAA-3′)
  - Poly(A) tail- (100–200 adenylate residues) to end of the transcript

Figure 18.45 The Methylated Cap of Eukaryotic mRNA



- **RNA Processing-** enzymatic modification
  - **Trimming** -removal of leader (5') and trailer (3') sequences
  - **capping** – protects 5' end from nucleases
    - Synthesized when the transcript is about 30 nt long

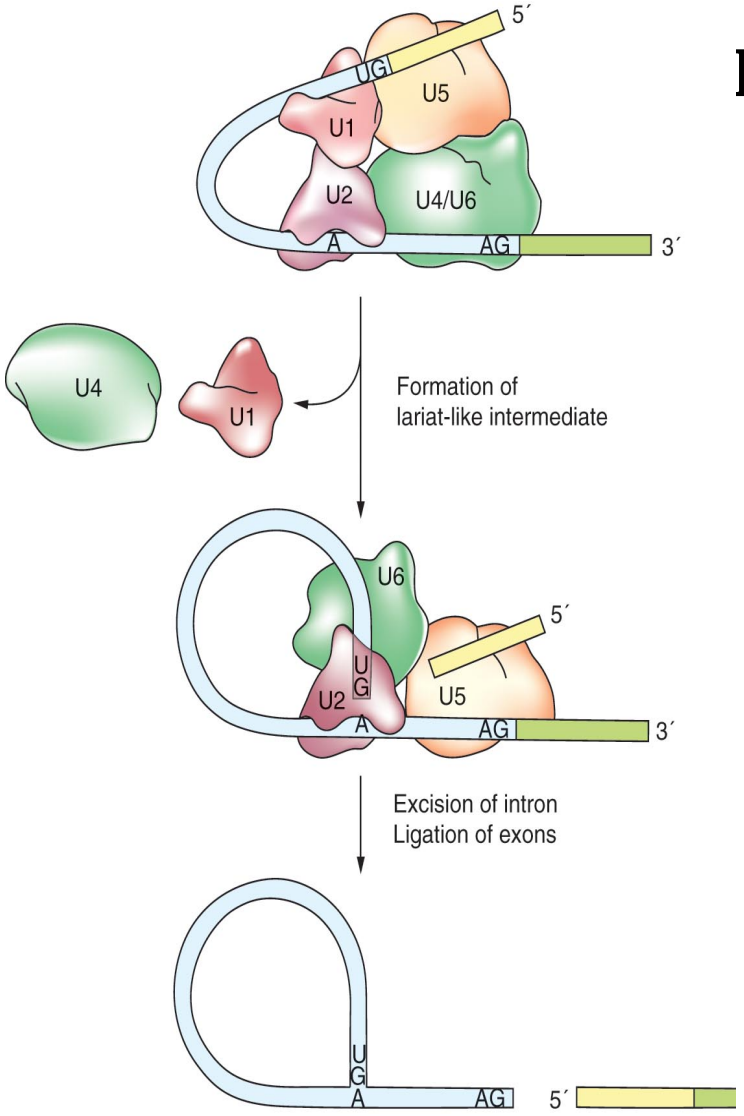


Figure 18.47 RNA Splicing

RNA splicing - removal of introns from an RNA transcript

- **Spliceosome** – removes introns; links exons together forming a functional product
- **Splicing reaction**

1. A 2′-OH of an adenosine nucleotide within intron attacks a phosphate in 5′ splice site, forming a lariat
2. Lariat is cleaved; two exons joined when 3′-OH of the upstream exon attacks a phosphate adjacent to the lariat
   - 5′ splice site is the **donor site** and the 3′ splice site is the **acceptor site**
- Four active spliceosomes form with each pre-mRNA to form a **supraspliceosome**

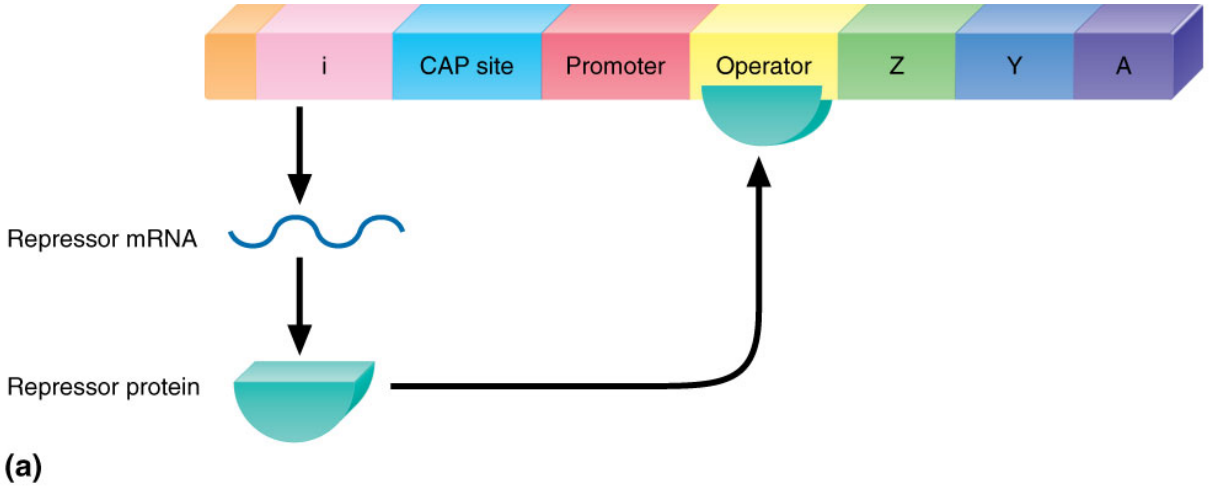
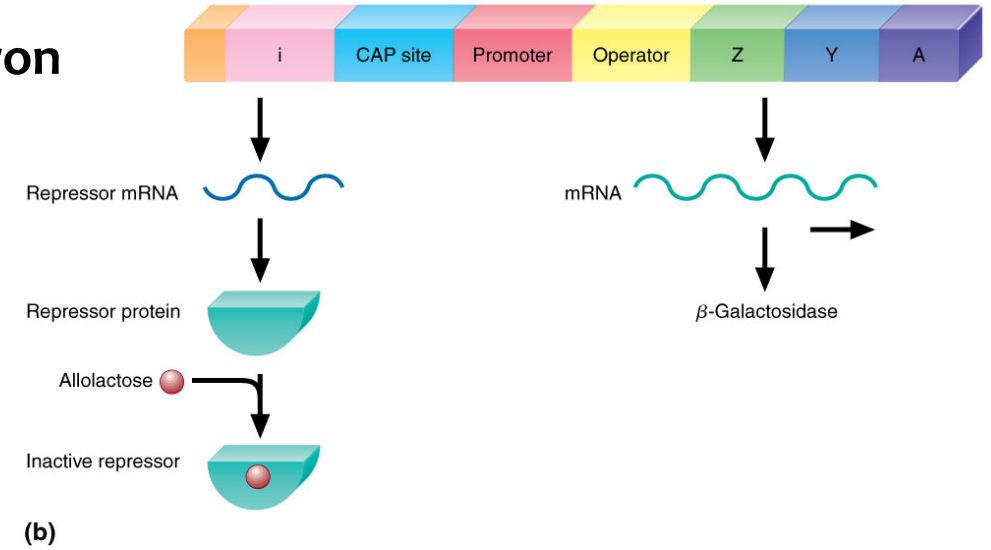


Figure 18.50 Function of the *lac* Operon

- ***lac* Operon** -control element / structural genes that code for enzymes responsible for lactose metabolism
  - Structural genes Z, Y, and A encode for β-galactosidase, lactose permease, and thiogalactoside transacetylase, respectively
  - *lacI* gene encodes for a repressor that binds to the operator of operon as a tetramer
    - *lac* operon is repressed when its inducer allolactose is not present due to *lac* repressor binding

Figure 18.50 Function of the *lac* Operon



- When lactose is present, some of the lactose is converted to allolactose by β-galactosidase
  - Allolactose binds the repressor, changing its conformation and promoting its dissociation from operator
  - *lac* operon becomes active and stays active until lactose is consumed

Genomic Control

- Chromatin structure
  - Structural organization of genome – chromatin remodeling
- Transcription factor-regulated RNA polymerase complex formation
  - Particular set of proteins that assembles on a regulatory DNA sequence
- Less common examples include gene rearrangements and gene amplification

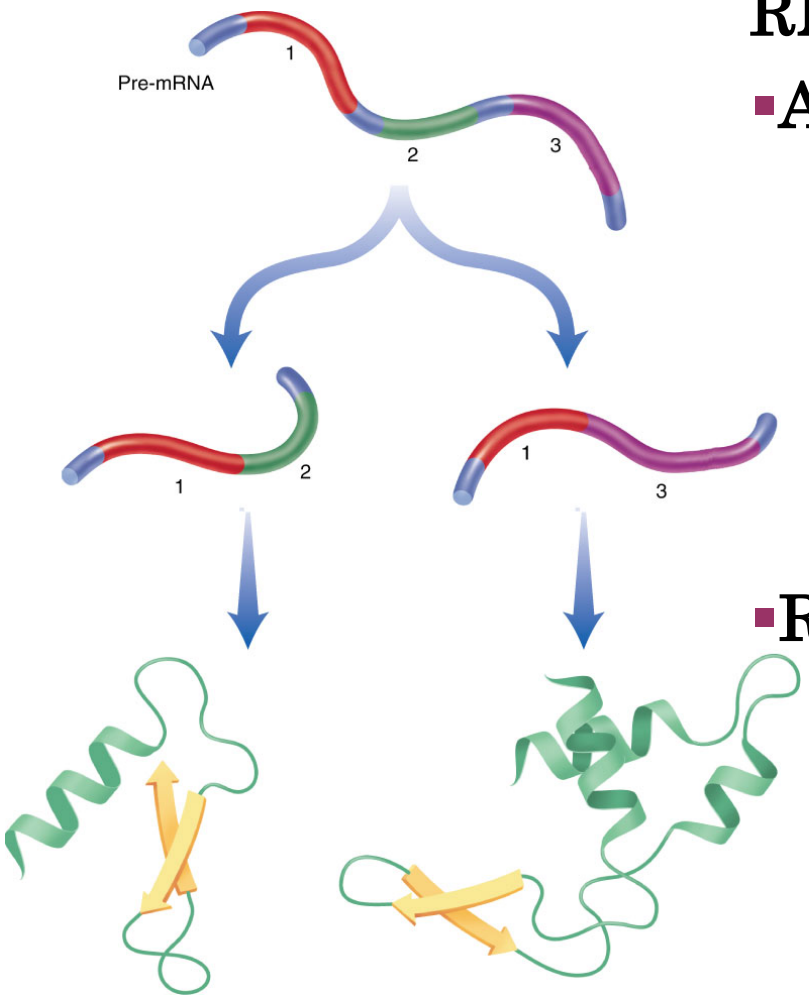


Figure 18.52 RNA Processing

RNA processing

- **Alternative splicing** - Joining of different combinations of exons to form cell-specific proteins
  - Vertebrate tropomyosin gene - 13 to 15 exons; five common in all isoforms
    - Remaining exons are alternatively used in different mRNAs
- **RNA editing** - After transcription, base changes
  - RNA stability, translation initiation, alteration of splice sites, and amino acid sequence changes

Posttranscriptional Gene Silencing

- miRNAs inhibit translation by binding to complementary sequences in the 3′-UTR of target mRNAs
- Humans are estimated to have as many as a thousand miRNAs believed to regulate about one-third of human genes
- miRNA-mediated gene silencing utilizes components of RNA interference
  - Limited to protection against viruses & transposons
- Cells use small-interfering RNAs (si-RNAs) to recognize and degrade target mRNAs

- **mRNA Transport** - out of the nucleus requires three phases: processing, docking and passage through nuclear pore complexes (NPC), and release into the cytoplasm

- **Translational Control**—Covalent modification of several translation factors has been shown to alter translation rate in response to various stimuli

Signal Transduction

- Cells alter gene expression patterns in response to environmental signals
  - Initiated by binding of a ligand to a receptor; then initiates a signal transduction cascade
  - Induce two classes of genes at the end of their signal transduction cascades
    - **Early response genes** are rapidly activated (within 15 minutes); often transcription factors
    - **Delayed response genes** - induced by activities of transcription factors and proteins produced during the early response phase