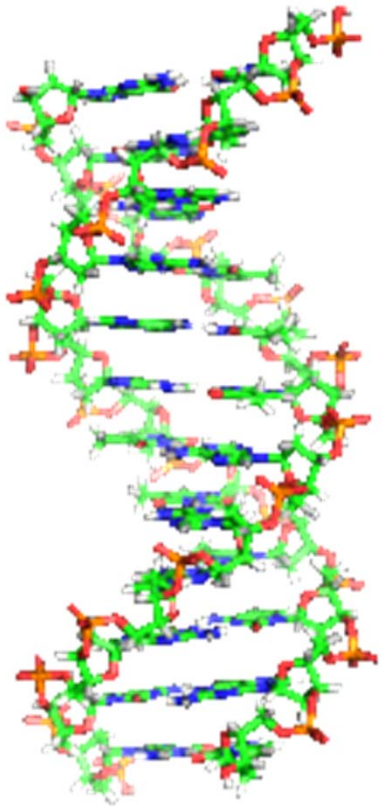
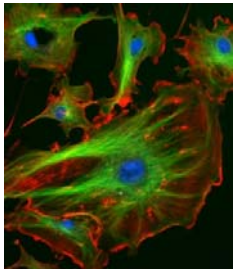


Lecture 5: From Transcription to Translation



Section A: From Nature to Concepts

Genes & Society
LSM3201 / GEK 1527

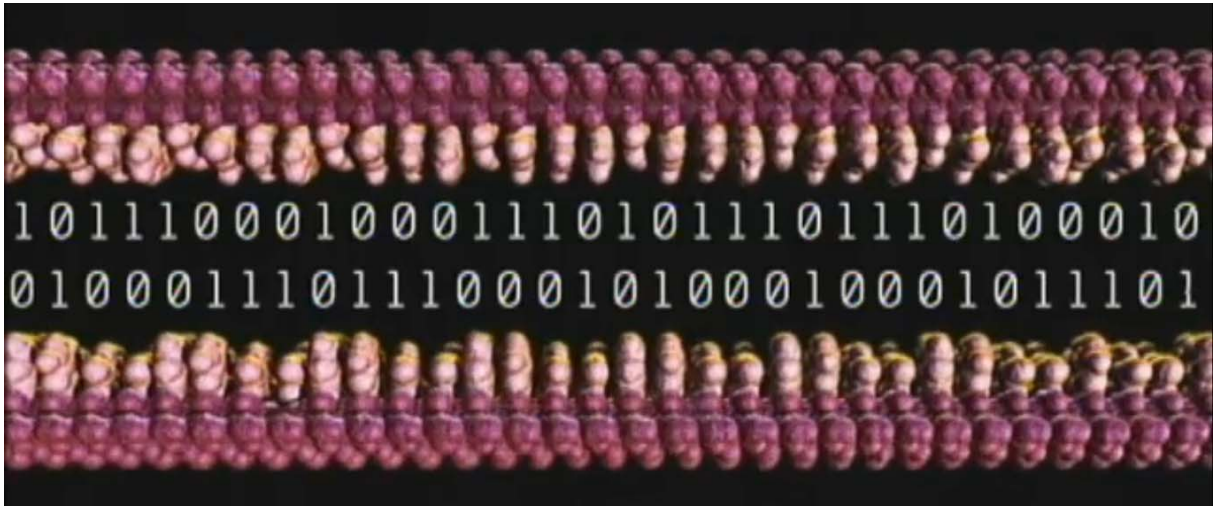
The understanding of life is a great subject. Biological information is the most important information we can discover, because over the next several decades it will revolutionize medicine. ***Human DNA is like a computer program but far, far more advanced than any software ever created***.

- Bill Gates (Founder of Microsoft)

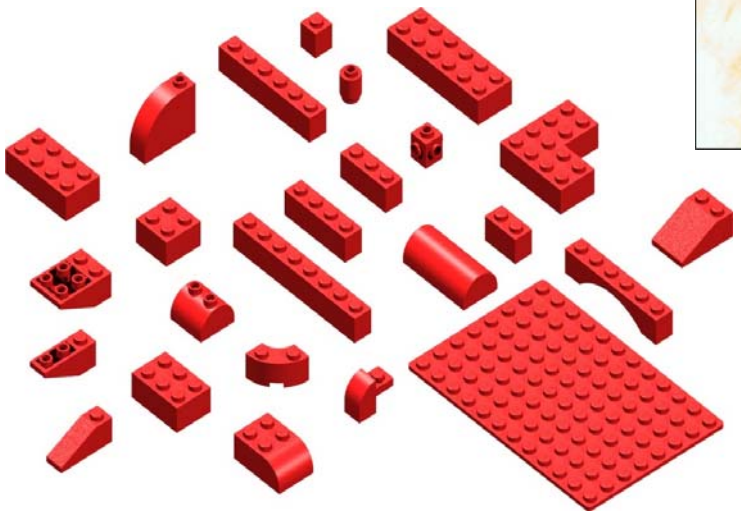
The DNA Software

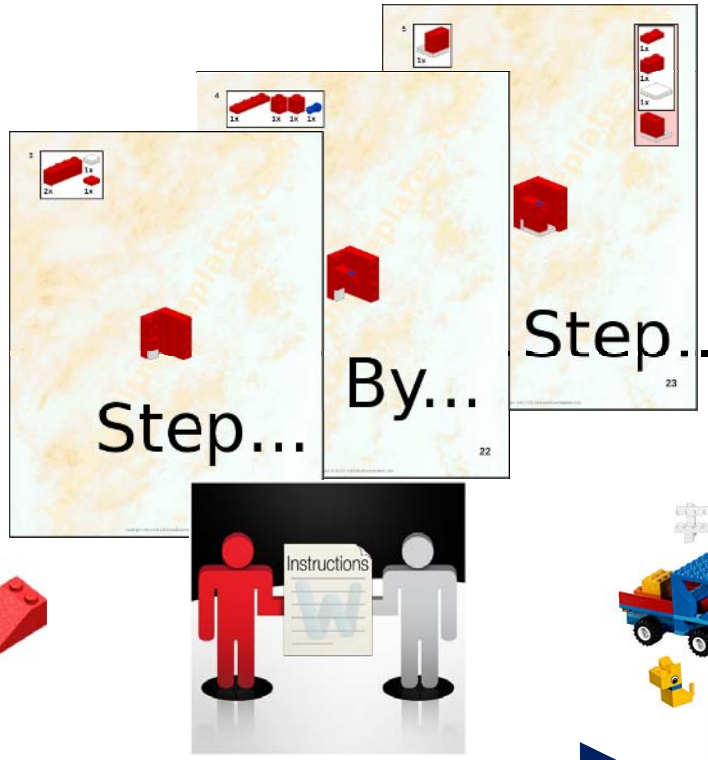
Check out how DNA can be encoded with information following a similar manner as how computer fundamentally encodes information using binary system.

http://www.hhmi.org/biointeractive/paired-dna-strands



Instruction (Gene) to assemble Lego Bricks (amino acids) into virtually any 3-D objects (proteins) that bring together an imaginary world (biological world).



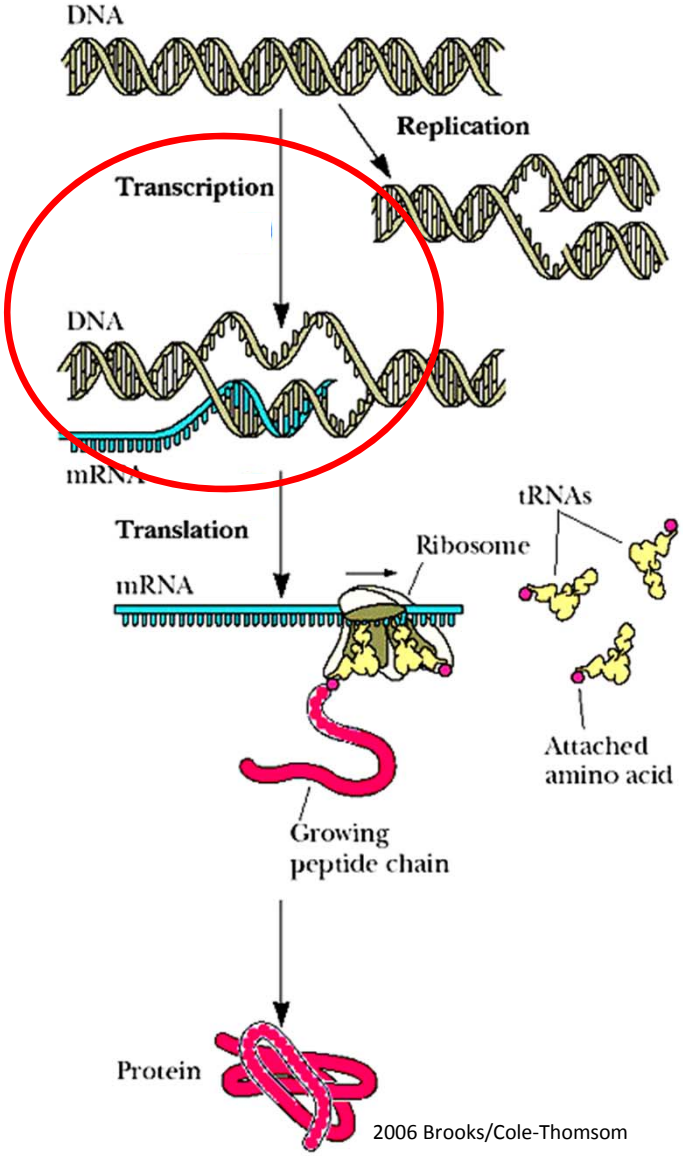


https://brickbuiltnameplates.com/

http://www.getacoder.com/blog/?tag=free-work

http://www.photoshoproadmap.com/Photoshop-blog/building-a-lego-bricks-photoshop-brushes-set/

http://bunkerlawgroup.com/2010/12/28/the-employee-handbook/



Central dogma of Molecular Biology: Flow of Genetic Information From DNA to Protein

Replication: DNA replication yields two DNA molecules identical to the original one, ensuring transmission of genetic information with high fidelity.

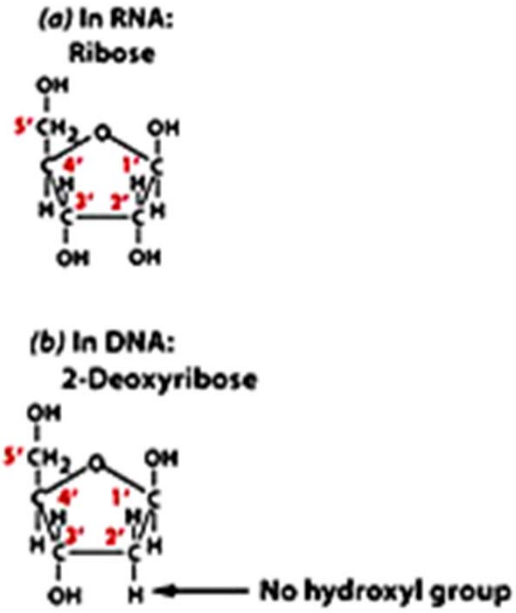
Transcription:
making of mRNA from DNA

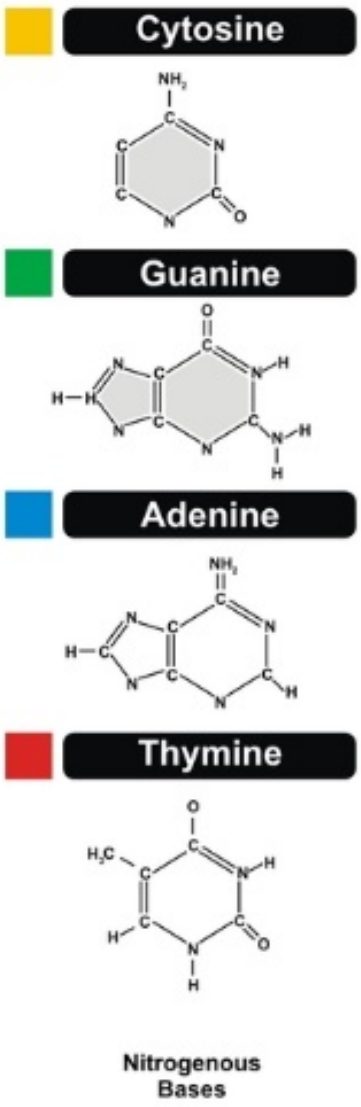
Transcription: Information encoded in the nucleotide sequence of DNA is transcribed through synthesis of mRNA whose sequence is dictated by the DNA sequence.

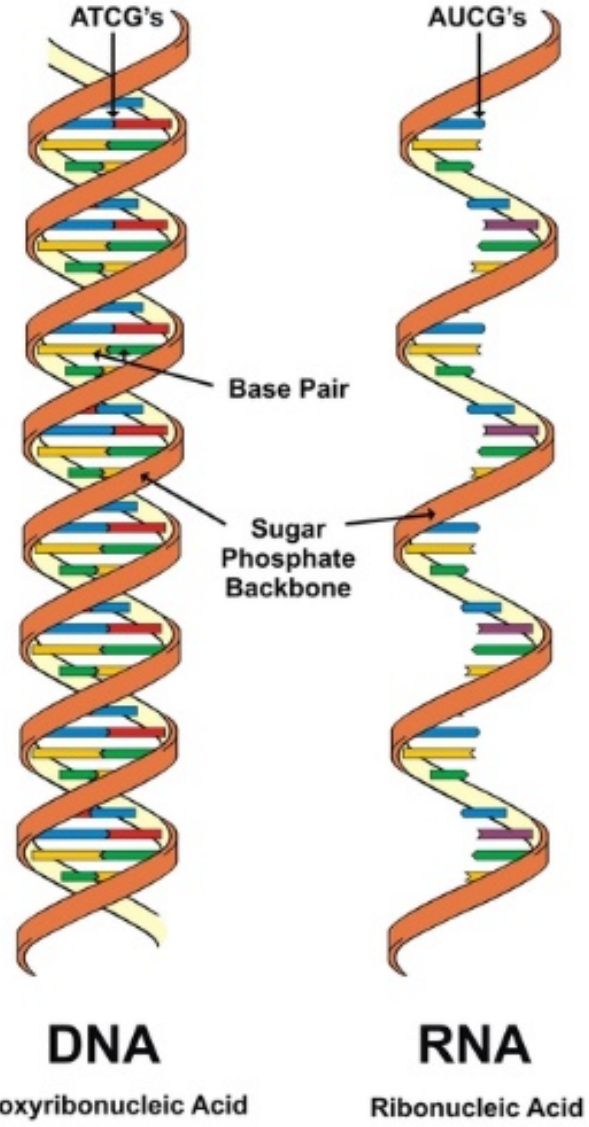
Translation:
the making of *proteins from mRNA*

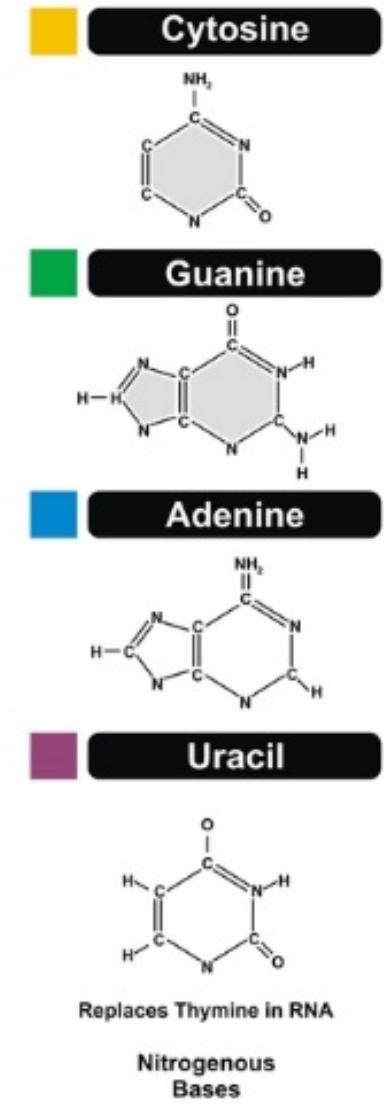
Translation: As the sequence of mRNA is read (as groups of three consecutive nucleotides) by the protein synthesis machinery (tRNA, rRNA, other proteins) it is translated into the sequence of amino acids in a protein. This information transfer system is encapsulated in the dogma: DNA → RNA → protein.

DNA vs. RNA









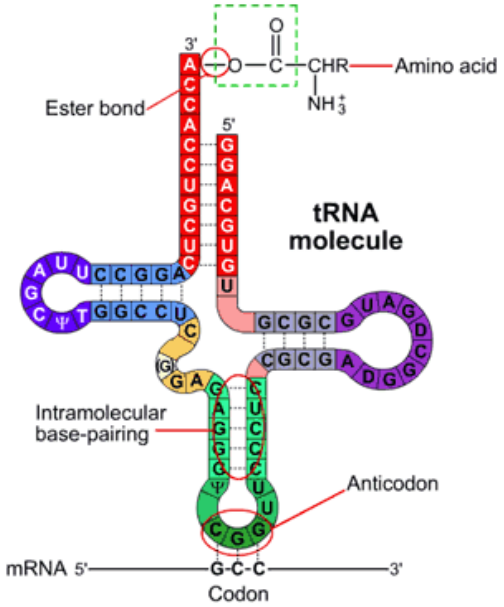
http://www.livescience.com/37247-dna.html

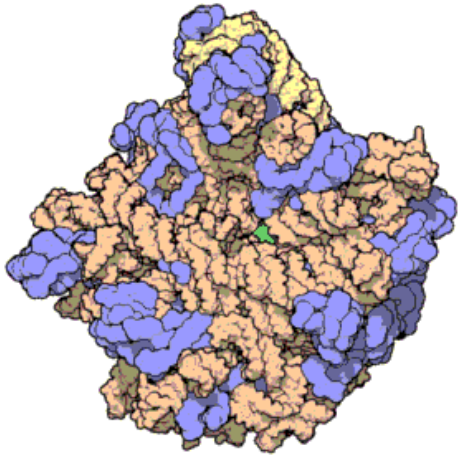
Classes of RNAs

1. **Messenger RNA or *mRNA* : "carries" the genetic information out of the nucleus for protein synthesis.**

2. **Transfer RNAs or *tRNAs* : "decodes" the information from mRNA by bringing the correct amino acid into place.**

3. **Ribosomal RNAs or *rRNAs (pink & beige)*: associate with ribosomal protein (blue) to form ribosome which is a "factory" for protein synthesis**

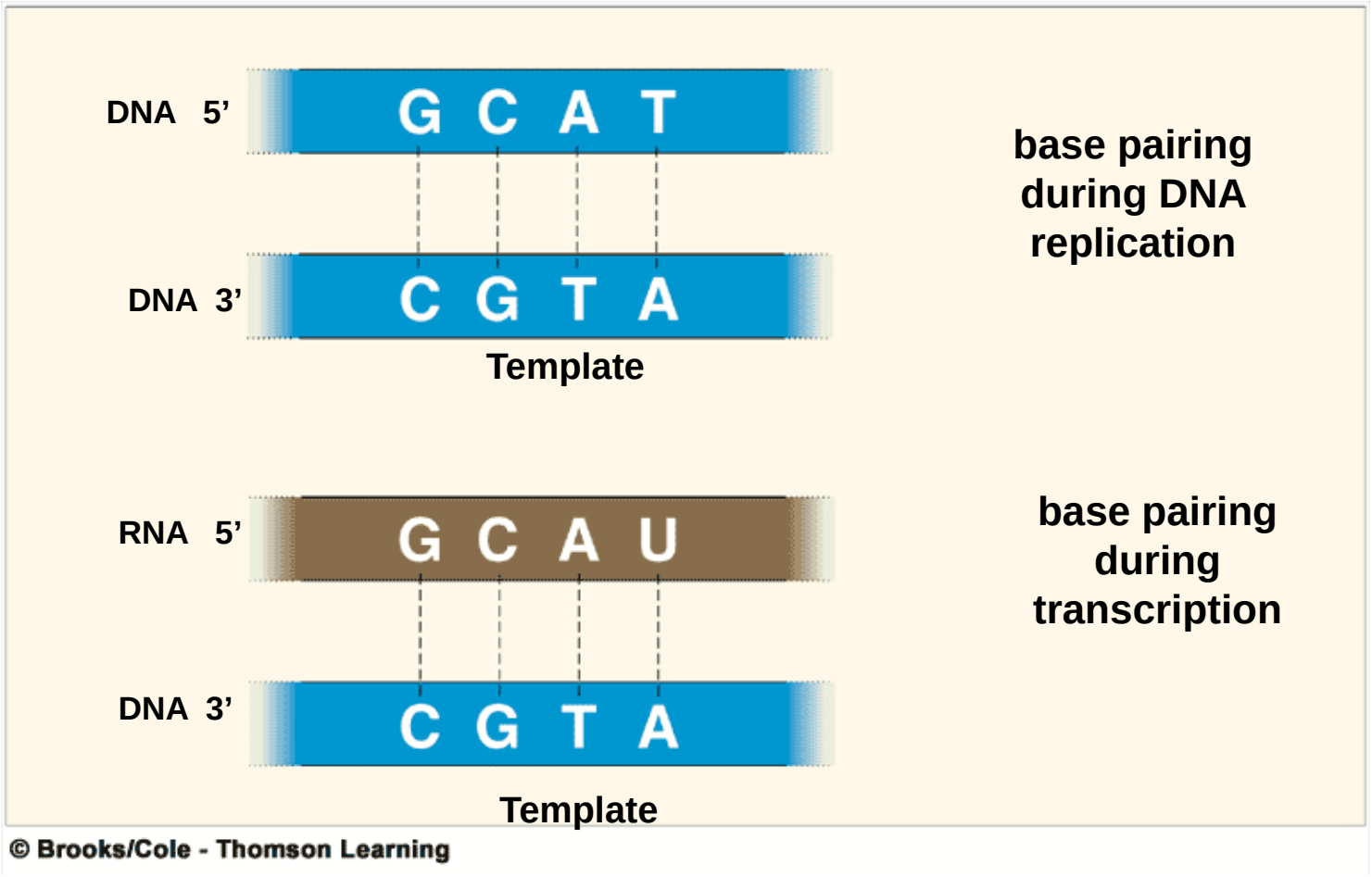




http://www.wiley.com/college/boyer/0470003790/structure/tRNA/trna_intro.htm

http://mcmanuslab.ucsf.edu/sites/mcmanuslab.ucsf.edu/files/put_your_BMS265_images_here/ph_large_subunit.gif

Transcription: making of messenger RNA (mRNA) by "*copying*" information from DNA



- Antiparallel and Synthesis Directionality (5' to 3') apply.
- All bondings (phosphodiester and hydrogen bonds) apply.
- Nucleotide base-pairing rules apply (except that T is replaced by U).

Non-template/ coding / sense / inactive strand:

5'….GGG CCC ATA TAT TTC TAA CTT……3'
3'….CCC GGG TAT ATA AAG ATT GAA……5'

DNA

Nucleic acid language

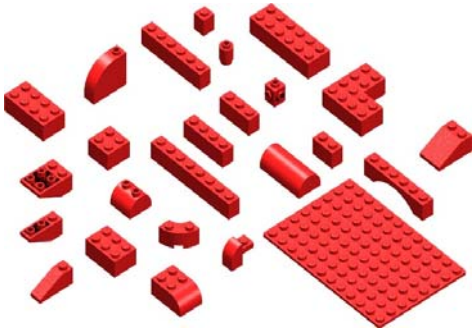
Transcription

Nucleic acid language

template / non-coding / antisense / active strand

5'….GGG CCC AUA UAU UUC UAA CUU……3' mRNA

….this mRNA will then serve as template for protein synthesis



Translation

Amino acid language

Refer to genetic codon dictionary

….Gly Pro Ile Tyr Phe "STOP" protein

What is needed for Transcription?

1. A Template is needed (no need primer)
2. Manpower (enzyme RNA polymerase)
3. Building Blocks are needed (free available NTPs)

Check out IVLE Animations

Try transcribing this out at DNA Interactive in copying the code! http://www.dnai.org/a/index.html

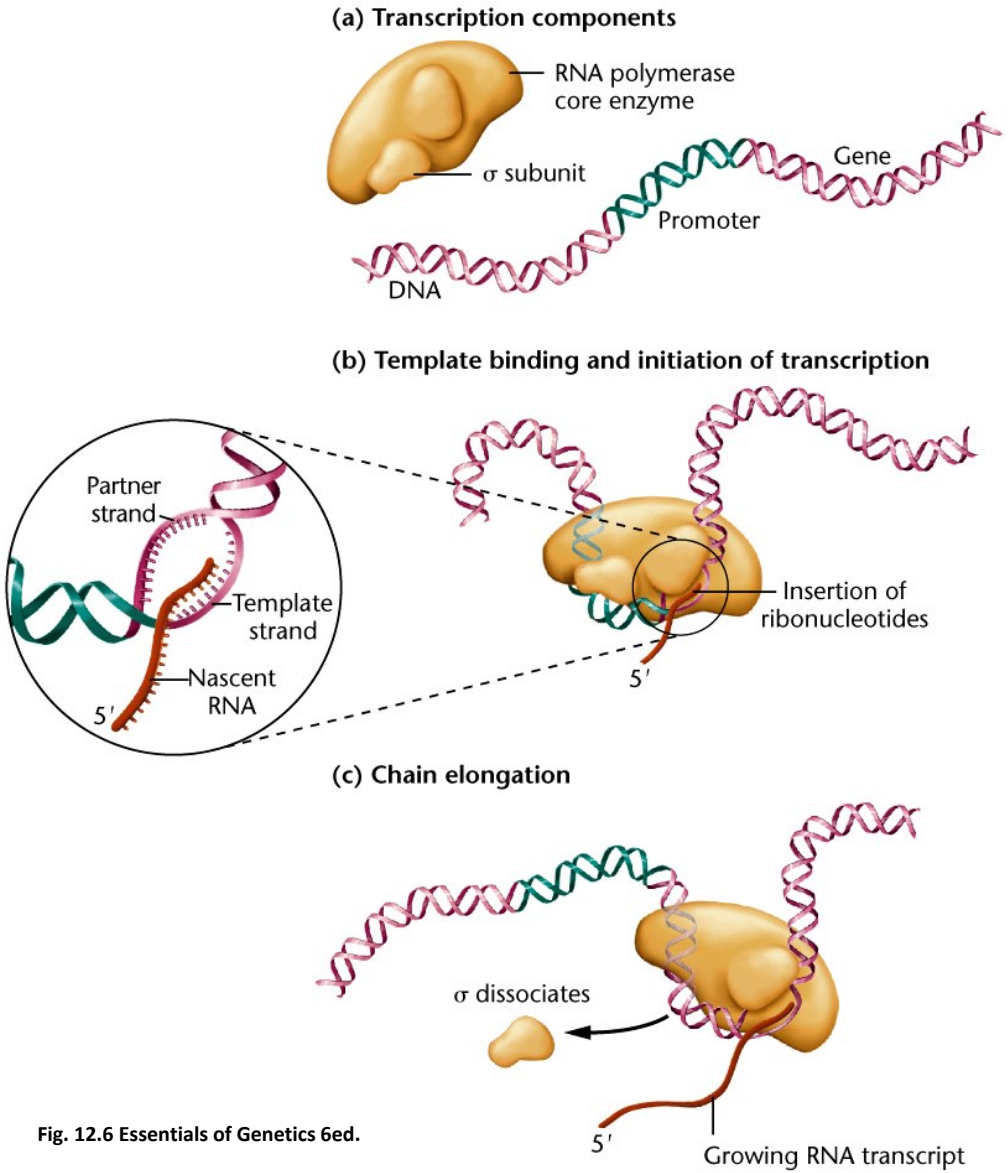


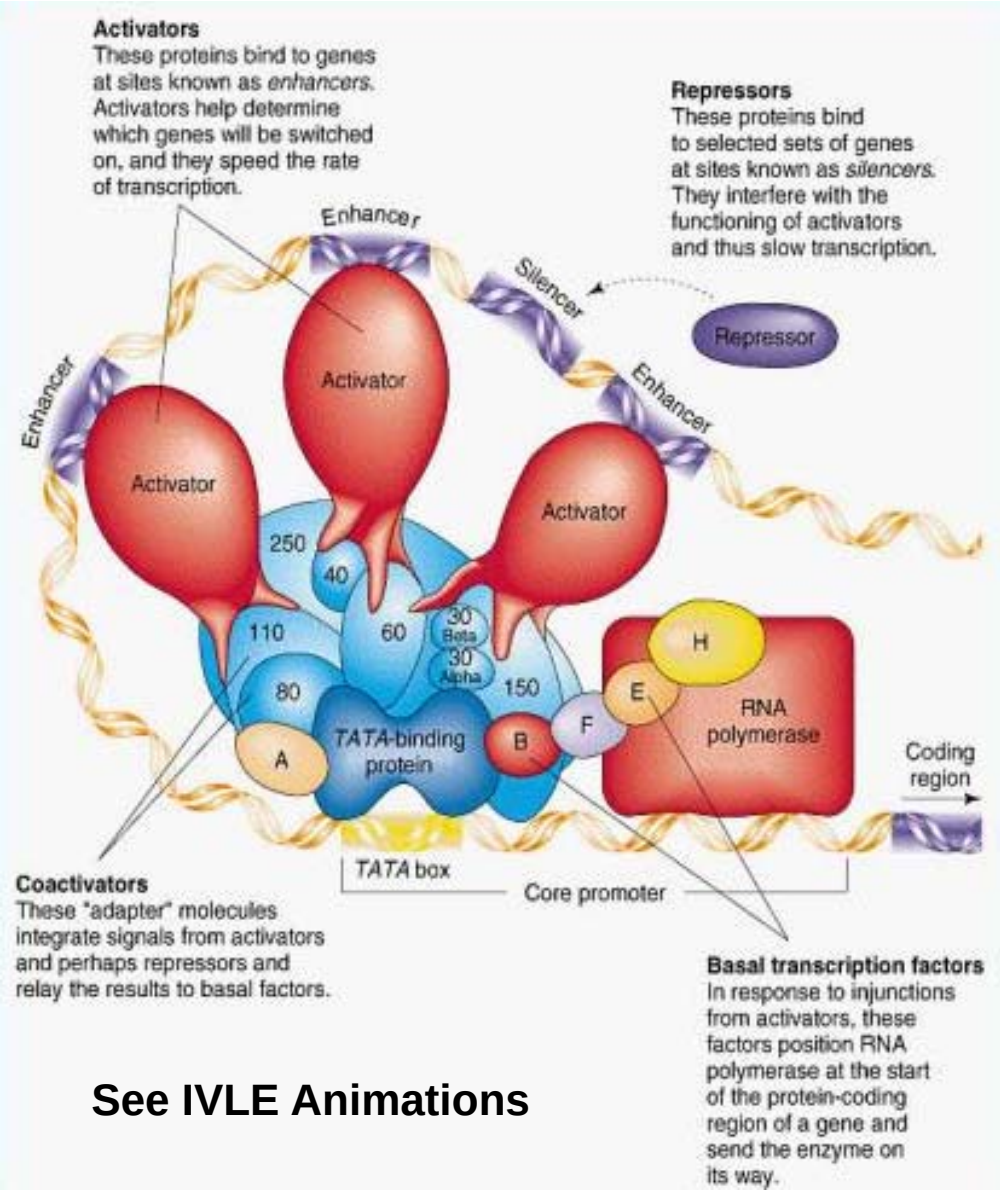
Fig. 12.6 Essentials of Genetics 6ed.

Transcription process:

(a) The components of the process involved a multi-subunit RNA polymerase including σ subunit that binds to the DNA at the promoter region of a gene.

(b) Template binding at the promoter site involves the σ subunit of RNA polymerase that recognizes specific sequences on the promoter and subsequent initiation of RNA synthesis.

(c) Chain elongation occurs after the σ subunit has dissociated from the transcription complex, and the enzyme moves along the DNA template high .



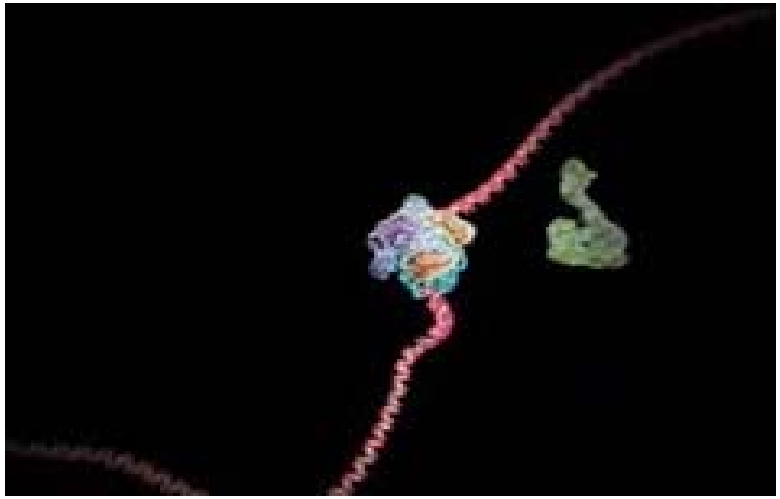
See IVLE Animations

Transcription regulation in eukaryotic cells are more complex involving multiple factors.

Depending on external chemical signals, specific cellular factors interact with:

1. **Each other (activators and coactivators)**
2. **General/Basal transcription factors (including RNA Polymerase)**
3. **Specific promoter sequences and upstream element (including enhancer)…**

…to direct the transcription of particular gene(s).

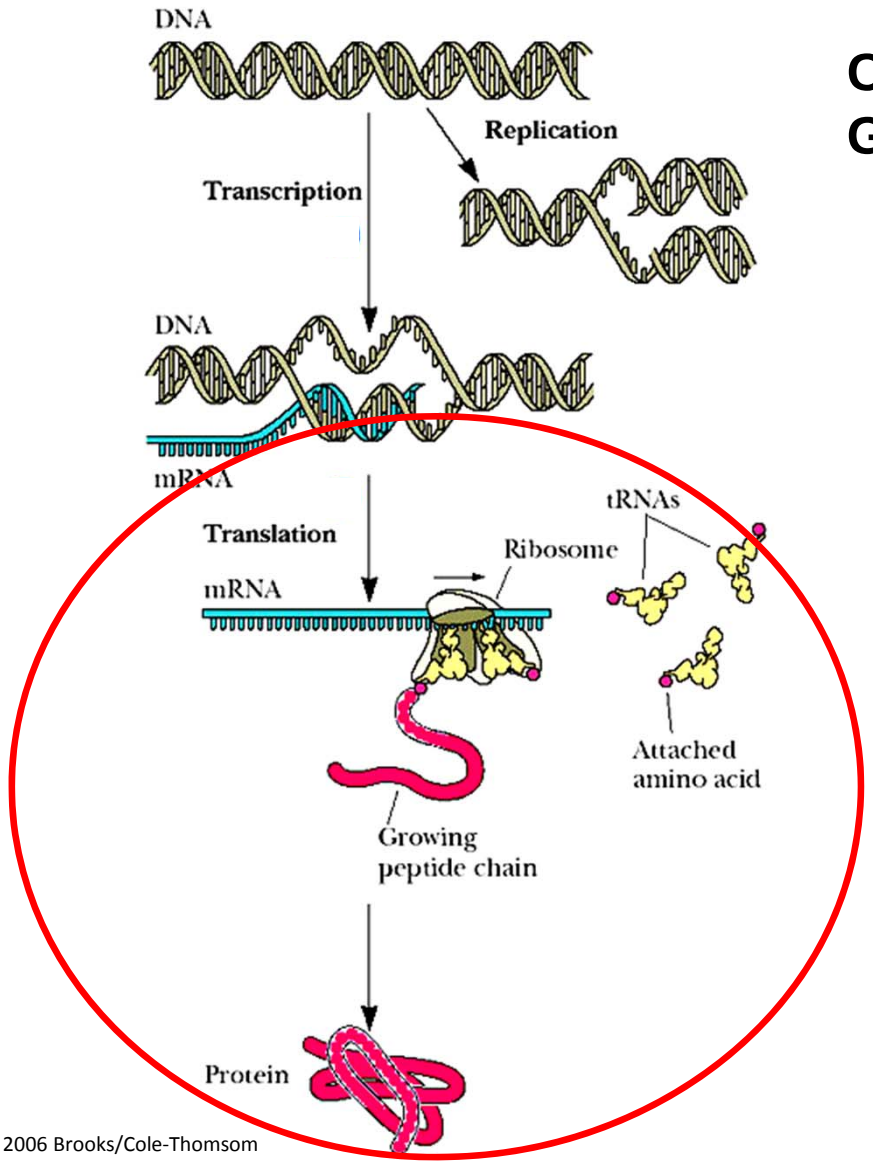


Check it out on the IVLE

http://www.dnai.org/a/index.html

1. Transcription is the process of copying RNA from DNA for gene expression. It begins with a bundle of factors assembling at the start of a gene. A gene is simply a length of DNA instructions stretching away to the left. The assembled factors trigger the first phase of the process, reading off the information that will be needed to make the protein.

2. The blue molecule racing along the DNA is reading the gene. It's unzipping the double helix, and copying one of the two strands. The yellow chain snaking out of the top is a copy of the genetic message RNA. The building blocks to make the RNA enter through an intake hole. They are matched to the DNA - letter by letter - to copy the As, Cs, Ts and Gs of the gene. The only difference is that in the RNA copy, the letter T is replaced with a closely related building block known as "U". You are watching this process - called transcription - in real time. It's happening right now in almost every cell in your body.



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Central dogma of Molecular Biology: Flow of Genetic Information From DNA to Protein

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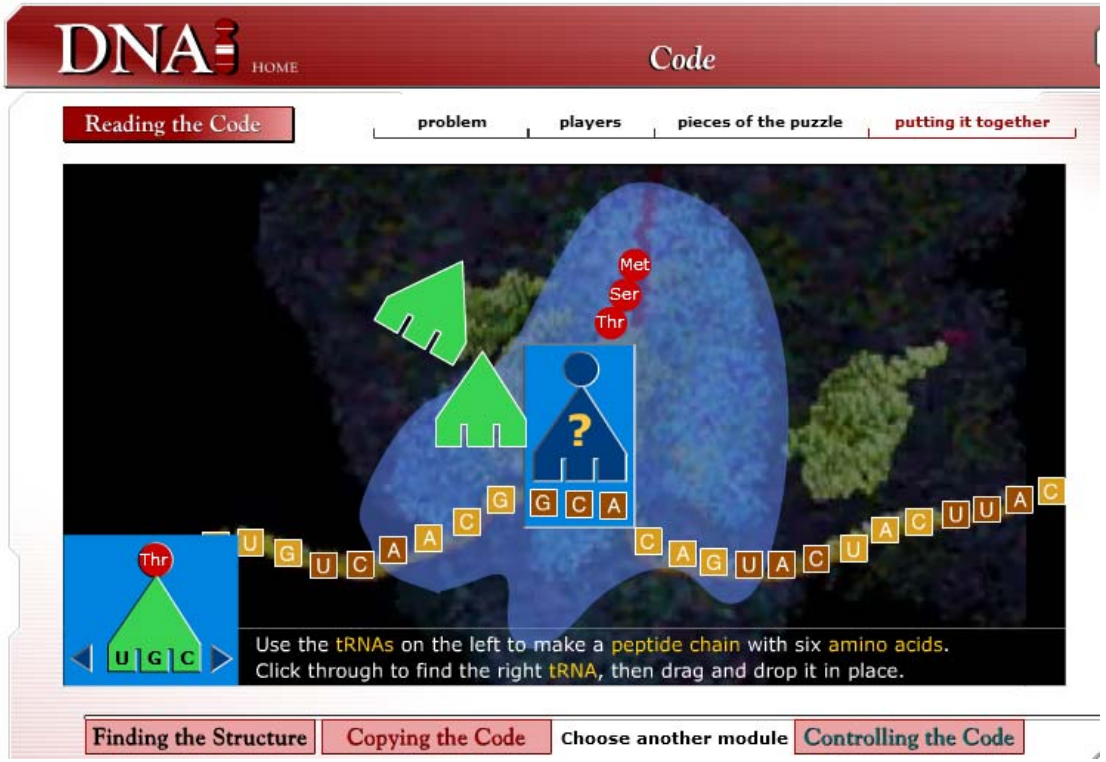
What do you need in order to make a molecule of protein?

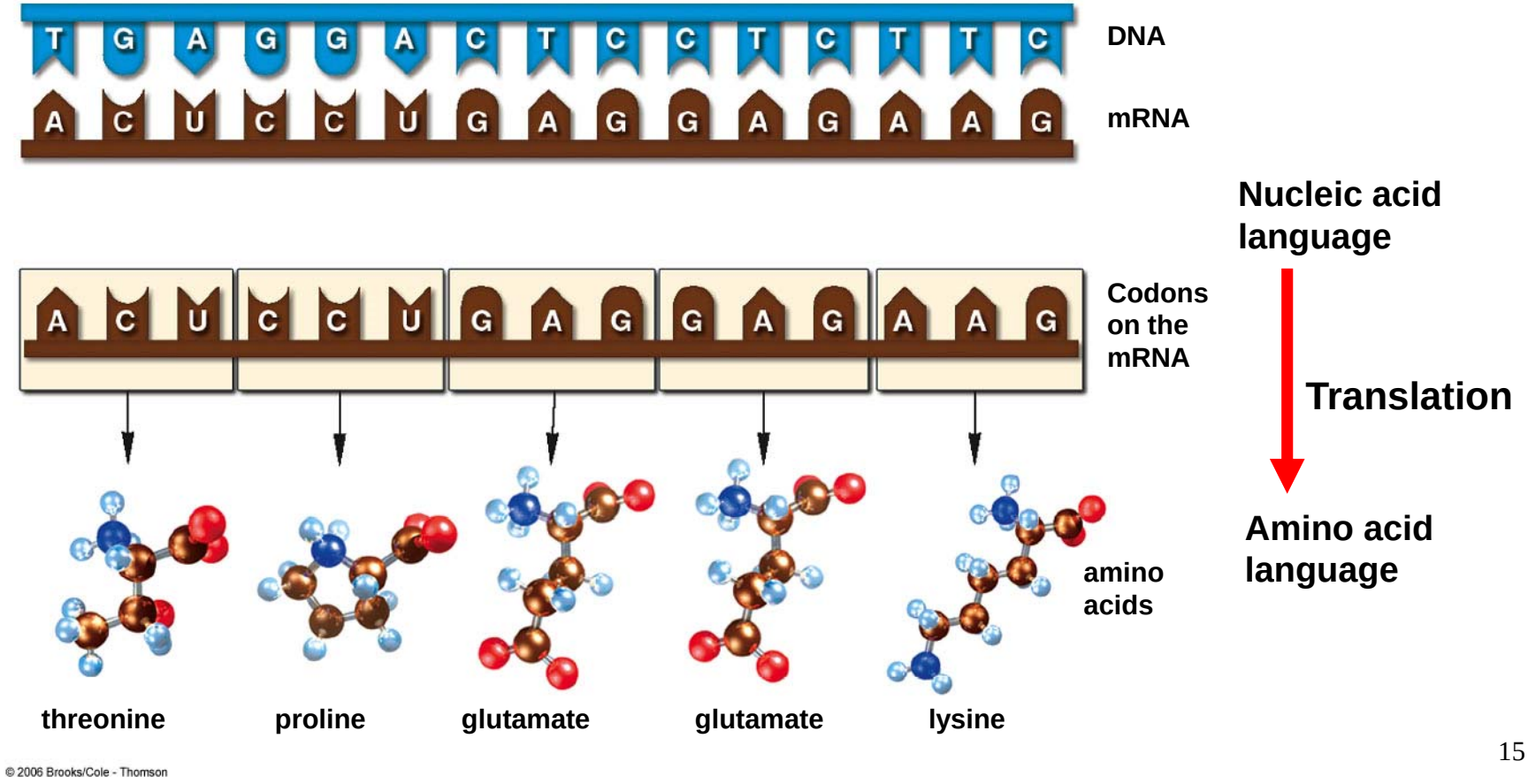
1. A transcript of the instruction (the mRNA)
2. Manpower (the ribosome + tRNAs)
3. The building blocks (amino acids)



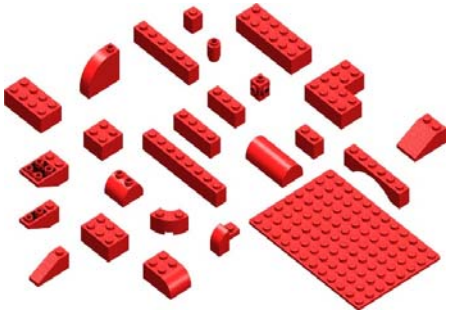
Check on the IVLE animations

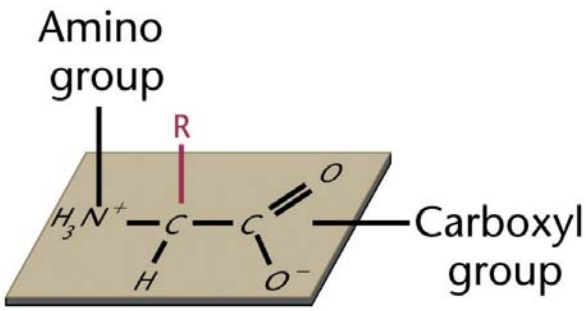
Try translating this at Reading the Code at DNA Interactive! http://www.dnai.org/a/index.html

An mRNA transcript is produced from a gene region of DNA. The nucleotide sequences will be translated to amino acid sequences by a translation machinery reading three nucleotide sequences as one codon which specify one amino acid following a genetic code (genetic dictionary).



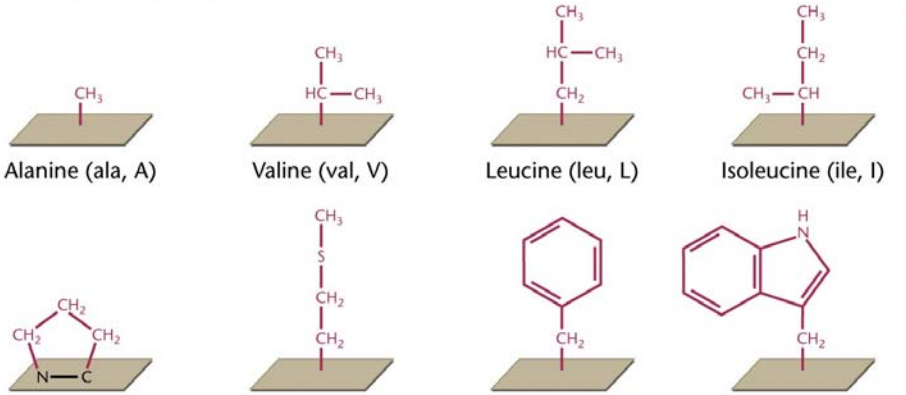
20 Amino Acids



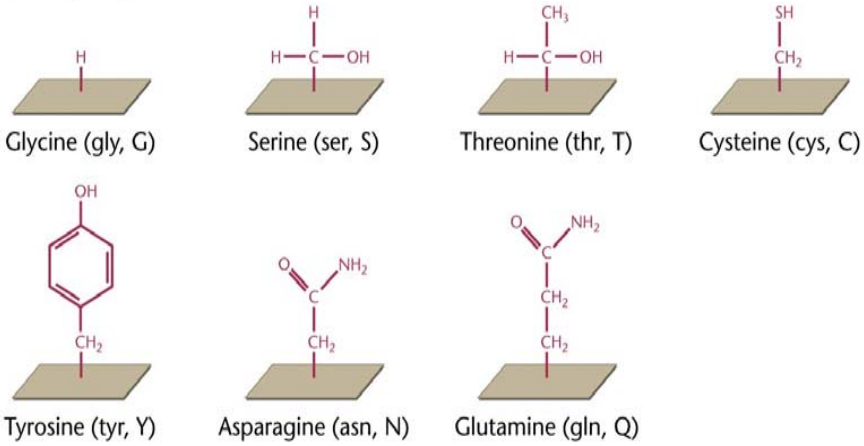


Amino acid structure

1. Nonpolar: Hydrophobic



2. Polar: Hydrophilic



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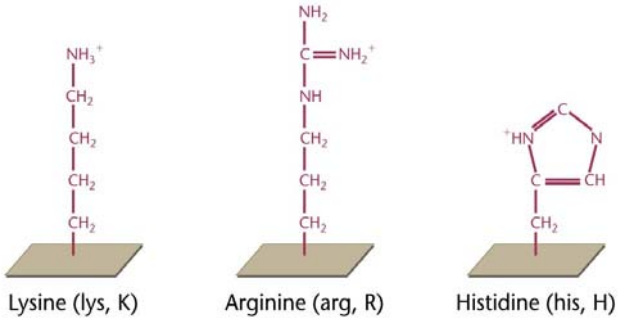
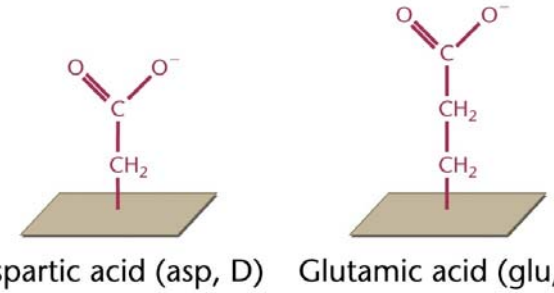
3. Polar: positively charged (basic)



4. Polar: negatively charged (acidic)



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DNA words are three letters long.

22

DNA FROM THE BEGINNING

The genetic code had to be a "language" – using the DNA alphabet of A, T, C, and G – that produced enough DNA "words" to specify each of the 20 known amino acids. Simple math showed that only 16 words are possible from a two-letter combination, but a three-letter code produces 64 words. Operating on the principle that the simplest solution is often correct, researchers assumed a three-letter code called a codon.

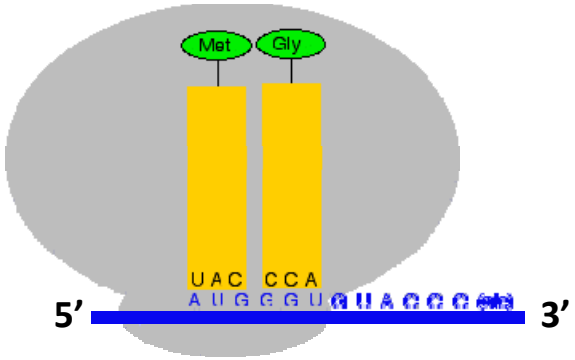
Research teams at University of British Columbia and the National Institutes of Health laboriously synthesized different RNA molecules, each a long strand composed of a single repeated codon. Then, each type of synthetic RNA was added to a cell-free translation system containing ribosomes, transfer RNAs, and amino acids. As predicted, each type of synthetic RNA produced a polypeptide chain composed of repeated units of a single amino acid. Several codons are "stop" signals and many amino acids are specified by several different codons, accounting for all 64 three-letter combinations.

http://www.dnaftb.org/22/

Check out the Triplet code:
http://www.hhmi.org/biointeractive/triplet-code

What Is the Genetic Code?

- **Specific consecutive three nucleotides found within the coding region of the mature mRNA that code for an amino acid are know as codons.**
- **There are a total of 64 codons (4^3) which make the genetic code. All the codons have meaning. Of the 64 codons, 61 specify particular amino acids. Remaining three - UAA,UAG, UGA- specify no amino acids as they are the stop/termination codons.**
- **The genetic code is degenerate. With the exception of Met and Trp, every amino acid is coded by more than one codon. Example: Arg, Leu, Ser, are represented by six different codons.**
- **The genetic code is 'universal'; similar in prokaryotes and eukaryotes (with few exceptions).**



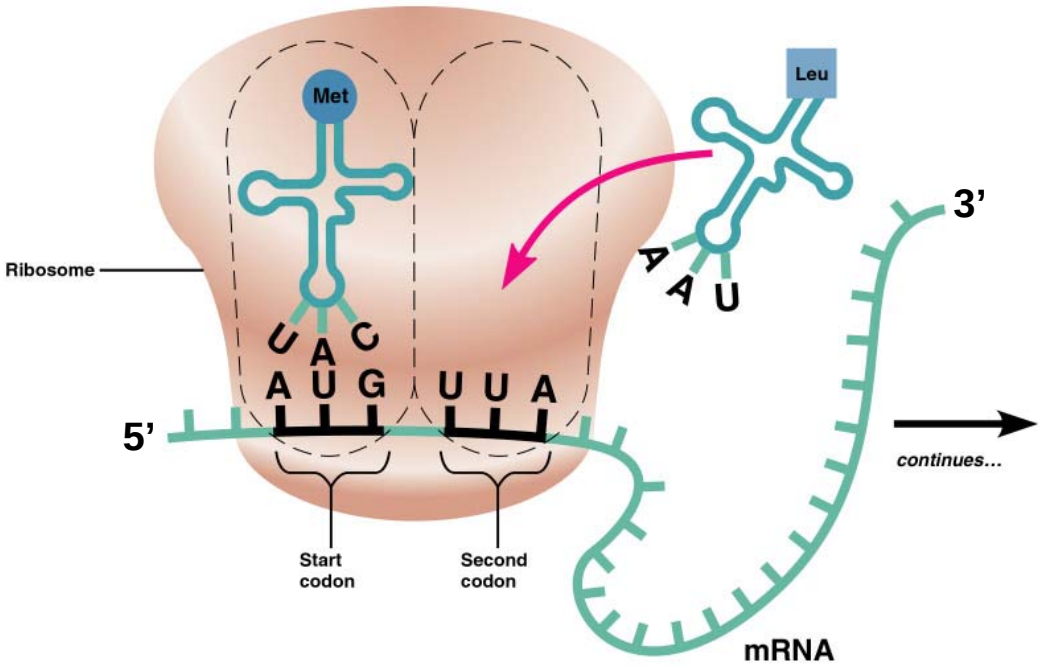
2nd base in codon

1st base in codon	U	C	A	G	3rd base in codon
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Start Codon Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

http://cronodon.com/BioTech/Ribosomes.html

The Genetic Code in Translation

tRNA brings corresponding amino acid into place according to the codon being read on the mRNA.



2 On the assembled ribosome, a tRNA carrying the first amino acid is paired with the start codon on the mRNA. A tRNA carrying the second amino acid approaches.

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2nd base in codon

1st base in codon	U	C	A	G	3rd base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
Start Codon	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Translation: Protein Synthesis

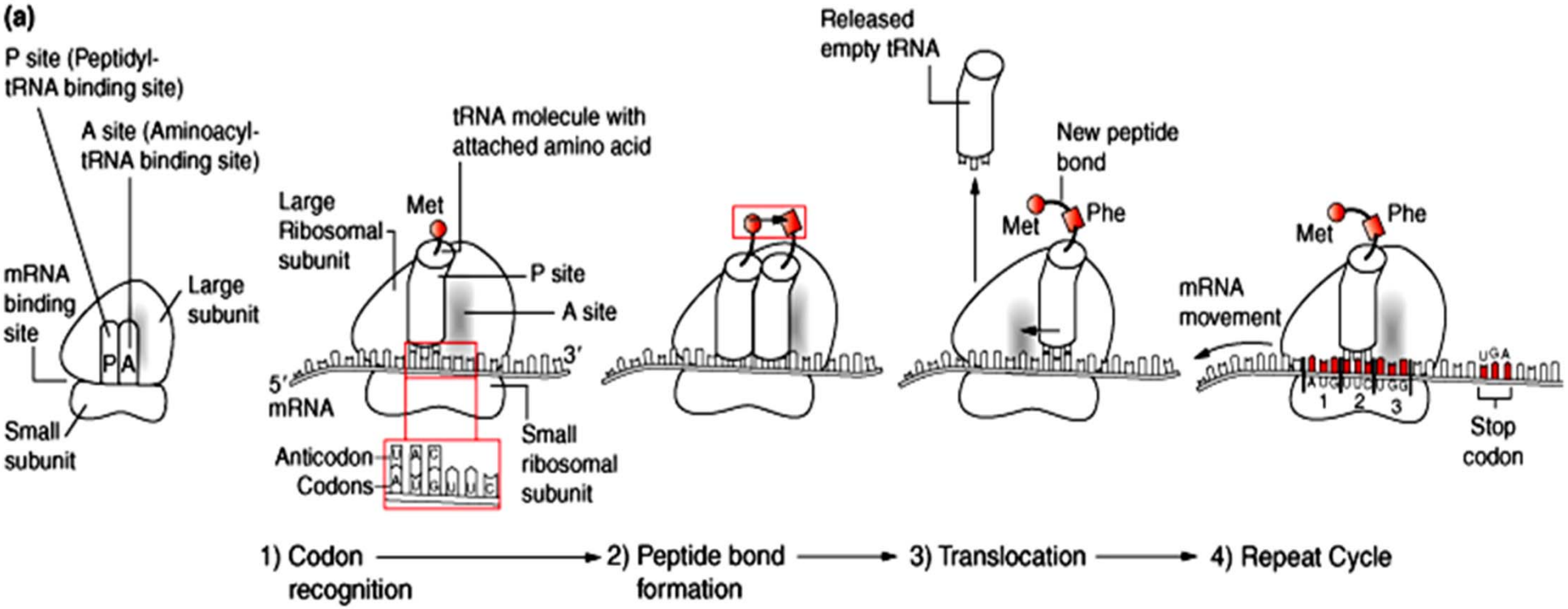
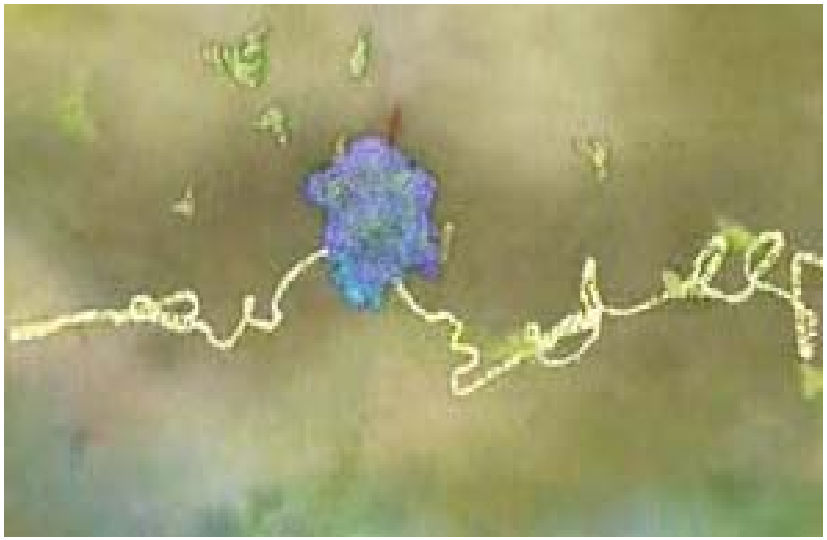
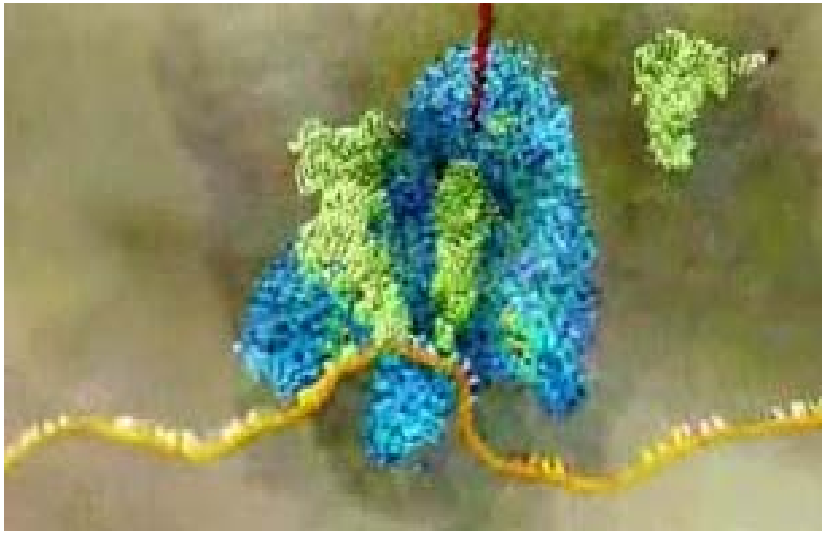


Fig. 2.13 Pearson Introduction to Biotechnology





Check this out on IVLE or

http://www.dnai.org/a/index.html

1. When the RNA copy is complete, it snakes out into the outer part of the cell. Then in a dazzling display of choreography, all the components of a molecular machine lock together around the RNA to form a miniature factory called a ribosome. It translates the genetic information in the RNA into a string of amino acids that will become a protein. Special transfer molecules — the green triangles — bring each amino acid to the ribosome. The amino acids are the small red tips attached to the transfer molecules.

2. Now we come to the heart of the process. Inside the ribosome, the RNA is pulled through like a tape. The code for each amino acid is read off, three letters at a time, and matched to three corresponding letters on the transfer molecules. When the right transfer molecule plugs in, the amino acid it carries is added to the growing protein chain. Again, you are watching this in real time. And after a few seconds the assembled protein starts to emerge from the ribosome.

Protein folding and post-translational modification to produce functional proteins in eukaryotes

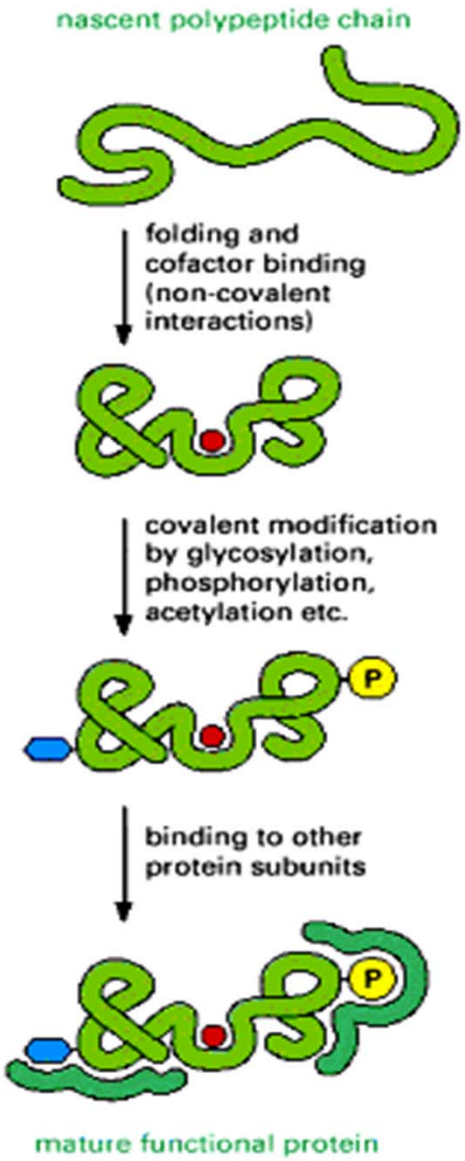
To be useful to the cell, the completed polypeptide chain must:

- fold correctly into its three-dimensional conformation,

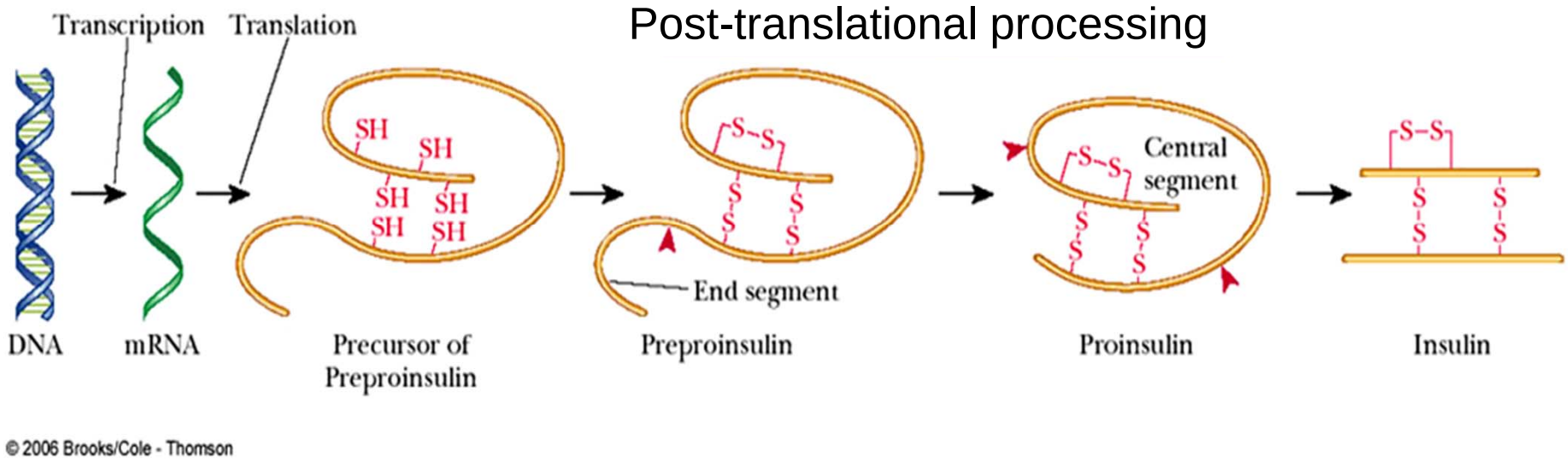
- bind any cofactors required, and

- assemble with its partner protein chains (if any). These changes are driven by non-covalent bond formation.

In addition, many proteins also have covalent modifications made to selected amino acids known as post-translational modification. Although the most frequent of these are protein glycosylation and protein phosphorylation, more than 100 different types of covalent modifications are known (involved covalent modifications) .



Post-translational modification of Preproinsulin to Insulin



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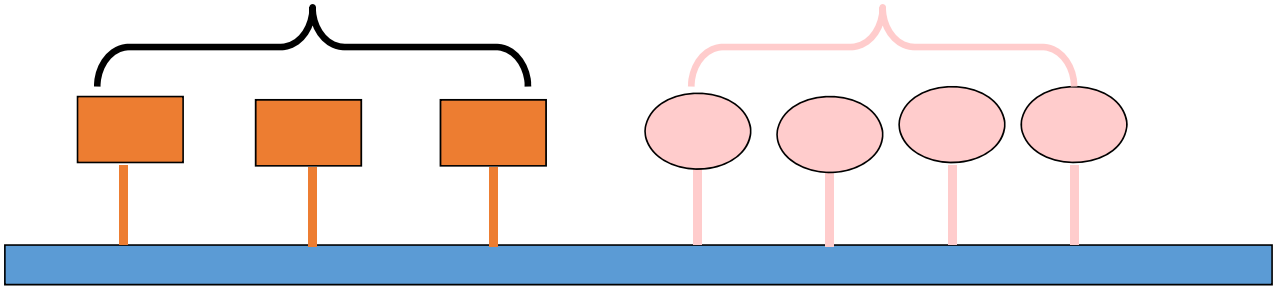
After a precursor of preproinsulin is formed by the transcription–translation process, it is transformed into preproinsulin by formation of three disulfide bonds. Specific cleavage that removes an end segment converts preproinsulin to proinsulin. Finally, two further specific cleavages remove a central segment, with insulin as the end result.

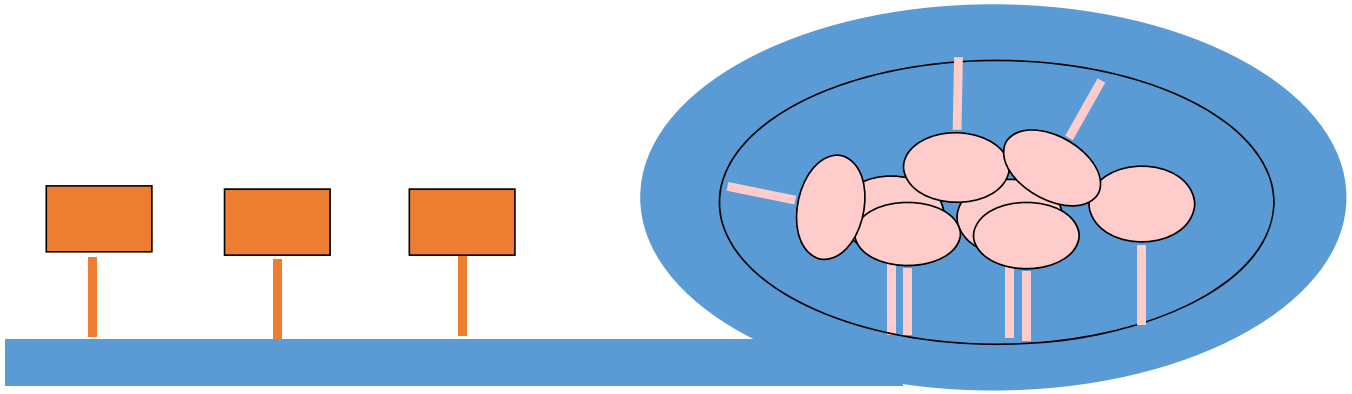
Protein sequence

side chains that like water (hydrophilic)

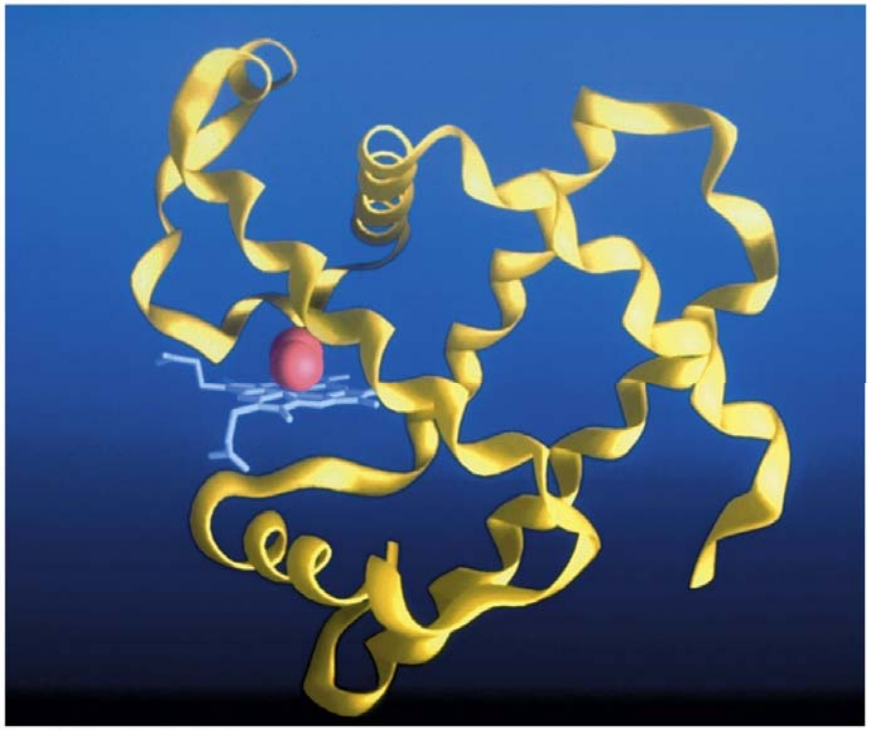
side chains that do not like water (hydrophobic)



Protein structure in water



What does a protein look like?



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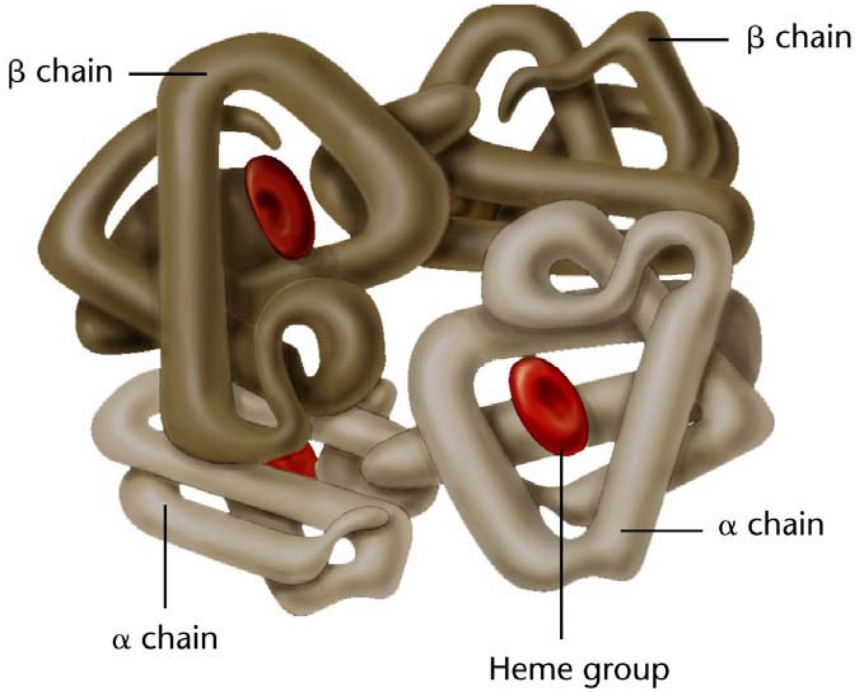
Tertiary Structure
(myoglobin in muscle cells)



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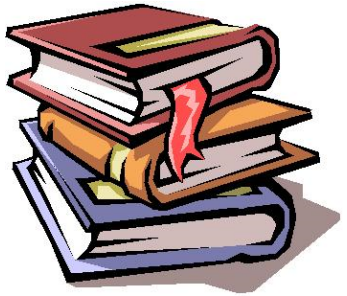
Quarternary Structure
(hemoglobin in red blood cells)

Summary of Transcription & Translation

- RNA is made up of polymers of ribonucleotide [ribose sugar, base (A,C,G & U), phosphate] and usually single-stranded.
- RNA is transcribed by RNA polymerase using DNA as a template in a process called transcription and all 4 ribonucleoside triphosphates (NTPs, i.e. ATP,CTP,GTP &UTP). A primer is not required.
- RNA polymerase binds to promoter sequence on DNA and 'reads' the template strand from 3' to 5' direction. The newly-synthesized RNA extends from 5' to 3' direction.
- *Translation is a process of synthesizing a chain of amino acids (polypeptide) based on the mRNA sequence.*
- Translation takes place within *ribosomes* in the *cytoplasm* with the help of *tRNAs* that carry specific amino acids corresponding to the mRNA codon sequence.
- Genetic code/dictionary describes the nucleotide triplets (codons) that code for the 20 amino acids including chain initiation and termination for translation.
- The amino acid sequence will determine the structure (following folding & modifications), the properties and function of the polypeptide or protein.

Additional Enrichment Materials



- **IVLE Animations: Transcription_with narration; RNA polymerase II; Transcription Video; Translation_with narration; Translation polyribosome; Translation Video.**
- **Useful Weblinks:**
- **Check out Paired DNA strands encoding information similar to binary system:**
- http://www.hhmi.org/biointeractive/paired-dna-strands
- **Check out the triplet code:**
- http://www.hhmi.org/biointeractive/triplet-code
- **Check out "Copying and Reading the Code" within "Code" in DNA interactive:** http://www.dnai.org/a/index.html
- **Check out Learn Genetics: Learn about RNA the versatile molecule & transcribe & translate a gene**
- http://learn.genetics.utah.edu/content/molecules/
- http://learn.genetics.utah.edu/content/molecules/transcribe/