Today’s class

• Extra-credit essay
• Activity on mitosis, meiosis, and inheritance
• Lecture and activities on the lecture
Extra-credit

• One (minimum) to two pages, single-spaced, 12 point font, 1 inch margins, 4 or more references
• 4% (max) extra-credit
• Write the essay on one of the following topics:
  – What are prions? What makes the unique? What is the connection between prions and mad cow disease? Are you concerned about prions?
  – What is de-extinction? How is it done? What are some of the candidate species being considered? Do you agree with this practice? Why?
  – What is the Enviropig? Who created it? How did they create it? Why was it created? Do you think the Enviropig is valuable? Why?
  – Who is Oxitec? How is Oxitec modifying mosquitoes to reduce the spread of mosquito-borne diseases? What diseases are they targeting? Have they tested their mosquitoes? Do you think these mosquitoes are valuable? Why?
  – What is biofortification? What are the three ways it can be done? What are the differences between the three methods? Has it been implemented? Where and how? Do you agree with this practice? Why?
How was DNA discovered?

- Frederick Griffith's experiment
- Scientists Oswald Avery, Colin MacLeod, and Maclyn McCarty isolated DNA, RNA, and proteins from the S strain bacteria in the dead mice
- They used enzymes that specifically degraded each component
- Then used each mixture separately to transform the R strain
- Martha Chase and Alfred Hershey's experiment
- Around this same time, Austrian biochemist Erwin Chargaff found that the amounts of A, T, G, and C varied from species to species
  - But he noticed that the amount of A = the amount of T and the amount of G = the amount of C
Cell Physiology

- Virtually all cell function is a result of proteins and their interactions
- Information for every protein is stored in DNA
DNA and Genes

Gene: **DNA code for a specific final protein**

- 20 amino acids (protein monomers)
- DNA codons (triplet of DNA bases) code for a specific amino acid
  - (codons usually written in RNA form)

General gene structure:

```
ATG  CAA  TGC  TGG  AAT  CCA  TGC  TCG  TAG
```

Start codon  Stop codon
Quick Check, remembering all the way back to week 1 . . . .

• What type of macromolecule is DNA?
  1. Protein
  2. Nucleic acid
  3. Carbohydrate
  4. Lipid
DNA is made of nucleotide monomers composed of a sugar (deoxyribose), a phosphate, and a base.
DNA Nucleotides Differ in their base
Structure of Deoxyribonucleic Acid (DNA)

- Two long chains of nucleotides
  - A, T, G, C
- Backbone of P and deoxyribose
  - Covalent bonds (phosphodiester bonds)
- Chains held together by hydrogen bonds
  - A=T, G=C
- Twists around in a double helix
- Strands are antiparallel
The Watson-Crick Model of DNA Structure

(a) Hydrogen bonds hold complementary basepairs together in DNA
Green = purines
Purple = pyrimidines

(b) Two DNA strands form a double helix

(c) Four turns of a DNA double helix
How does DNA replication happen?

- Matthew Meselson and Franklin Stahl's experiment
DNA Replication

- DNA serves as its own template

https://www.youtube.com/watch?v=5qSrmeiWsuc
DNA Replication - semiconservative

Original DNA strands:
Complementary sequences
(H bonds holds strands together)

Strands unwind (helicase enzyme)
H bonds separated

DNA Polymerase (enzyme)
installs new nucleotides

New backbone bonded together (enzyme)
(covalent bonds)
Summary of replication

DNA ligase

DNA polymerase I

DNA polymerase III

Primase

RNA primer

Helicase

Topoisomerase

Lagging strand

Leading strand

Okazaki fragments

Sliding clamp

Single-strand binding protein

DNA polymerase III

5'

3'

5'

3'
Telomere replication

- In humans, a six base pair sequence, TTAGGG, is repeated 100 to 1000X
- Telomerase
  - Catalytic part
  - RNA template
- Happens only in germ cells and adult stem cells
DNA Replication: You as the Polymerase

- Imagine you are DNA polymerase
- Write the sequence of the complementary DNA strand for the following DNA sequence

ATGCGTTATCTTTTCGGGATAG
Uncorrected Mistakes in DNA Replication Leads to Mutation

– DNA replication:
  • Normally accurate
  • Proofread and corrected

– Changes in DNA sequence: mutations
  • Point mutations
  • Frameshifts mutations
Main two categories - mutations

**Point Mutations**
- Silent: has no effect on the protein sequence
  - ![Diagram](chart.png)
- Missense: results in an amino acid substitution
  - ![Diagram](chart.png)
- Nonsense: substitutes a stop codon for an amino acid
  - ![Diagram](chart.png)

**Frameshift Mutations**
- Insertions or deletions of nucleotides may result in a shift in the reading frame or insertion of a stop codon.
  - ![Diagram](chart.png)
Uncorrected Mistakes in DNA Replication Leads to Mutation

– DNA replication:
  • Normally accurate
  • Proofread and corrected

– Changes in DNA sequence: mutations
  • Substitutions (one base or more changed for another)
  • Insertions (new base or bases added)
  • Deletions (base or bases lost)
  • Inversions (piece of DNA flips direction)
  • Translocations (pieces of DNA swapped)
Substitution Mutation

(a) Nucleotide substitution

original DNA sequence

```
ACTCTCTGAGGAG
TGAGGACTCTCT
```

substitution

```
ACTCTCTGTGAGGAG
TGAGGACCTCTC
```

nucleotid pair changed from A–T to T–A

Fig. 11-8a
Insertion Mutation

(b) Insertion mutation

original DNA sequence

A C T C C T G A G G G A G
T G A G G A C T C C T C

1 to many bases inserted

T–A nucleotide pair inserted

Fig. 11-8b
Deletion Mutation

(c) Deletion mutation

original DNA sequence

1 to many bases deleted

C–G nucleotide pair deleted

Fig. 11-8c
Inversion Mutation

Fig. 11-8d

Piece of DNA is now backwards
Translocation Mutations

(e) Translocation

original DNA sequences

break

DNA segments switched

break

Fig. 11-8e
How Else Do Mutations Occur?

• Spontaneous mutations
  – Mistake during replication (0.2 to 1 in each replication)

• Induced mutations
  – DNA damage from chemicals (mutagens)
    • Reactive Oxidative Species ($O^{-}_{2}$)
  – DNA damage from UV radiation (sunlight, tanning, UV light boxes)
  – DNA damage from X-rays
Mutations of hemoglobin are well-characterized

<table>
<thead>
<tr>
<th>Table 12-4</th>
<th>Effects of Mutations in the Hemoglobin Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DNA (Template Strand)</strong></td>
<td><strong>mRNA</strong></td>
</tr>
<tr>
<td>Original codon 6</td>
<td>CTC</td>
</tr>
<tr>
<td>Mutation 1</td>
<td>CTT</td>
</tr>
<tr>
<td>Mutation 2</td>
<td>GTC</td>
</tr>
<tr>
<td>Mutation 3</td>
<td>CAC</td>
</tr>
<tr>
<td>Original codon 17</td>
<td>TTC</td>
</tr>
<tr>
<td>Mutation 4</td>
<td>ATC</td>
</tr>
</tbody>
</table>
Genetic Information Flows from DNA to RNA to Protein

(a) Transcription

Translation of the mRNA produces a protein molecule with an amino acid sequence determined by the nucleotide sequence in the mRNA.

(b) Translation

Translation of the mRNA produces a protein molecule with an amino acid sequence determined by the nucleotide sequence in the mRNA.

Transcription of the gene produces an mRNA with a nucleotide sequence complementary to one of the DNA strands.
Transcription, Going from DNA to RNA

DNA: set of instructions for how to make an organism

• DNA provides instructions for protein synthesis
  – DNA in eukaryotes is kept in the nucleus
  – Protein synthesis occurs at ribosomes in the cytoplasm

• RNA serves as an intermediate
  – Made from DNA template (transcription)
  – The messenger RNA

https://www.youtube.com/watch?v=h5mJbP23Buo
Quick Check

• Is this DNA or RNA?
  – AUCCGCUUCCAAAU
# Differences between DNA and RNA

<table>
<thead>
<tr>
<th></th>
<th>DNA</th>
<th>RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strands</strong></td>
<td>Two</td>
<td>One</td>
</tr>
<tr>
<td><strong>Sugar</strong></td>
<td>Deoxyribose</td>
<td>Ribose</td>
</tr>
<tr>
<td><strong>Types of bases</strong></td>
<td>Adenine (A), thymine (T)</td>
<td>Adenine (A), uracil (U)</td>
</tr>
<tr>
<td></td>
<td>cytosine (C), guanine (G)</td>
<td>cytosine (C), guanine (G)</td>
</tr>
<tr>
<td><strong>Base pairs</strong></td>
<td>DNA–DNA</td>
<td>RNA–DNA</td>
</tr>
<tr>
<td></td>
<td>A–T</td>
<td>A–U</td>
</tr>
<tr>
<td></td>
<td>T–A</td>
<td>U–A</td>
</tr>
<tr>
<td></td>
<td>C–G</td>
<td>C–G</td>
</tr>
<tr>
<td></td>
<td>G–C</td>
<td>G–C</td>
</tr>
<tr>
<td><strong>Function</strong></td>
<td>Contains genes; the sequence of bases in most genes determines the amino acid sequence of a protein</td>
<td>Messenger RNA (mRNA): carries the code for a protein-coding gene from DNA to ribosomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ribosomal RNA (rRNA): combines with proteins to form ribosomes, the structures that link amino acids to form a protein</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transfer RNA (tRNA): carries amino acids to the ribosomes</td>
</tr>
</tbody>
</table>
Why does transcription happen?

- DNA is too large, too valuable to leave the nucleus
- Can’t get to the ribosomes to give instructions for making proteins
- Sends a temporary copy made of RNA
- Process of making this copy is called transcription
- Specific type of RNA produced in transcription is messenger RNA (mRNA)
Steps in transcription

One strand is the coding strand (or sense strand or non-template strand), and the other is the noncoding strand (also called the antisense strand, anticoding strand, template strand, or transcribed strand).
Step 1: Initiation

- Transcription factors form the **preinitiation complex** in the promoter region and recruit the RNA polymerase.
Step 2 - Elongation

- RNA polymerase adds ribonucleotides
Step 3 - termination

• RNA polymerase finds a termination signal 1,000 to 2,000 bases after the end of the gene
Step 4 – On to another gene
Eukaryotes: mRNA is **Processed** to Get Ready for Translation

(a) Eukaryotic gene structure

- **Exons (the code)**
- **Introns (spacers)**

(b) RNA synthesis and processing in eukaryotes

![Diagram of mRNA processing in eukaryotes]

- **Transcription**
  - Pre-mRNA
  - An RNA cap and tail are added
  - RNA splicing
  - Finished mRNA
  - Finished mRNA is moved to the cytoplasm for translation

**Alternate splicing:** multiple proteins from 1 gene

Introns are removed
Prokaryotic transcription

- No nucleus – transcription and translation simultaneously
- Don’t have introns
From RNA to protein

- Sequence of nucleotide bases in DNA is a code for making proteins
- To uniquely code for each of the 20 amino acids, how many bases must code for a single amino acid?

<table>
<thead>
<tr>
<th>Number of bases</th>
<th>Code pattern</th>
<th>Total number of unique codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 base forms code</td>
<td>4 unique codes - A, T, C, G</td>
</tr>
<tr>
<td></td>
<td>pattern</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 bases form code</td>
<td>= 16 unique codes (too few)</td>
</tr>
<tr>
<td></td>
<td>pattern</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3 bases form code</td>
<td>= 64 unique codes (just right)</td>
</tr>
<tr>
<td></td>
<td>pattern</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4 bases form code</td>
<td>= 256 unique codes (too many)</td>
</tr>
<tr>
<td></td>
<td>pattern</td>
<td></td>
</tr>
</tbody>
</table>
How Is the Information in DNA Used in a Cell?

- The genetic code uses three bases to specify an amino acid (codon or triplet)
  - Each codon specifies a unique amino acid in the genetic code
  - **start codon** (AUG), three **stop codons** (UAG, UAA, and UGA)
  - More than one codon for some amino acids
    - Degenerate code
      - Silent mutations
# Codon Table

<table>
<thead>
<tr>
<th>First base of codon</th>
<th>Second base of codon</th>
<th>Third base of codon</th>
</tr>
</thead>
<tbody>
<tr>
<td>U</td>
<td>UUU</td>
<td>UGU</td>
</tr>
<tr>
<td></td>
<td>UUC</td>
<td>UGC</td>
</tr>
<tr>
<td></td>
<td>UUA</td>
<td>UGA</td>
</tr>
<tr>
<td></td>
<td>UUG</td>
<td>UGG</td>
</tr>
<tr>
<td>C</td>
<td>CUU</td>
<td>CGU</td>
</tr>
<tr>
<td></td>
<td>CUC</td>
<td>CGC</td>
</tr>
<tr>
<td></td>
<td>CUA</td>
<td>CCA</td>
</tr>
<tr>
<td></td>
<td>CUG</td>
<td>CCG</td>
</tr>
<tr>
<td>A</td>
<td>AUU</td>
<td>AGU</td>
</tr>
<tr>
<td></td>
<td>AUC</td>
<td>AGC</td>
</tr>
<tr>
<td></td>
<td>AUA</td>
<td>AGG</td>
</tr>
<tr>
<td></td>
<td>AUG (met, start codon)</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>GUU</td>
<td>GGU</td>
</tr>
<tr>
<td></td>
<td>GUC</td>
<td>GGC</td>
</tr>
<tr>
<td></td>
<td>GUA</td>
<td>GGA</td>
</tr>
<tr>
<td></td>
<td>GUG</td>
<td>GGG</td>
</tr>
</tbody>
</table>

- **UUU**: Phenylalanine (phe)
- **UUC**: Leucine (leu)
- **UUA**: Valine (val)
- **UUG**: Valine (val)
- **CUU**: Leucine (leu)
- **CUC**: Leucine (leu)
- **CUA**: Leucine (leu)
- **CUG**: Leucine (leu)
- **AUU**: Isoleucine (ile)
- **AUC**: Isoleucine (ile)
- **AUA**: Isoleucine (ile)
- **AUG**: Methionine (met, start codon)
- **GUU**: Valine (val)
- **GUC**: Valine (val)
- **GUA**: Valine (val)
- **GUG**: Valine (val)

- **UU**: Serine (ser)
- **UAC**: Serine (ser)
- **UAA**: STOP codon
- **UAG**: STOP codon
- **CAU**: Proline (pro)
- **CAC**: Proline (pro)
- **CAA**: Proline (pro)
- **CAG**: Proline (pro)
- **ACU**: Threonine (thr)
- **ACC**: Threonine (thr)
- **ACA**: Threonine (thr)
- **ACG**: Threonine (thr)
- **AAA**: Lysine (lys)
- **AAG**: Lysine (lys)
- **AGU**: Asparagine (asn)
- **AGC**: Asparagine (asn)
- **AGG**: Asparagine (asn)
- **GAU**: Aspartic acid (asp)
- **GAC**: Aspartic acid (asp)
- **GAG**: Aspartic acid (asp)
- **GAA**: Glutamic acid (glu)
- **GAG**: Glutamic acid (glu)
- **GGU**: Glycine (gly)
- **GGC**: Glycine (gly)
- **GGA**: Glycine (gly)
- **GGG**: Glycine (gly)

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Base pairing – complementary

- Aminoacyl tRNA Synthetases add AA to tRNAs; “charging” tRNAs
- tRNAs translate RNA into protein
Translation: Going from mRNA to Protein

• mRNA, tRNA, and ribosomes cooperate to synthesize proteins
  – Three steps
    1. Initiation
    2. Elongation
    3. Termination
Initiation of Translation

A tRNA with an attached methionine amino acid binds to a small ribosomal subunit, forming a preinitiation complex.

1. The preinitiation complex binds to an mRNA molecule. The methionine (met) tRNA anticodon (UAC) base pairs with the start codon (AUG) of the mRNA.

2. The large ribosomal subunit binds to the small subunit. The methionine tRNA binds to the first tRNA site on the large subunit.
Elongation of the Protein

Elongation:

4. The second codon of mRNA (GUU) base-pairs with the anticodon (CAA) of a second tRNA carrying the amino acid valine (val). This tRNA binds to the second tRNA site on the large subunit.

5. The catalytic site on the large subunit catalyzes the formation of a peptide bond linking the amino acids methionine and valine. The two amino acids are now attached to the tRNA in the second binding site.

6. The "empty" tRNA is released and the ribosome moves down the mRNA, one codon to the right. The tRNA that is attached to the two amino acids is now in the first tRNA binding site and the second tRNA binding site is empty.
Termination: Stopping Protein Synthesis

7 The third codon of mRNA (CAU) base-pairs with the anticodon (GUA) of a tRNA carrying the amino acid histidine (his). This tRNA enters the second tRNA binding site on the large subunit.

8 The catalytic site forms a peptide bond between valine and histidine, leaving the peptide attached to the tRNA in the second binding site. The tRNA in the first site leaves, and the ribosome moves one codon over on the mRNA.

9 This process repeats until a stop codon is reached; the mRNA and the completed peptide are released from the ribosome, and the subunits separate.
Visualizing Translation: Movie Time!

• https://www.youtube.com/watch?v=gG7uCskUOrA
Complementary Base-Pairing Is Critical to the Process of Decoding Genetic Information

Fig. 12-8

(a) DNA
complementary DNA strand

(b) mRNA
codons

(c) tRNA
anticodons

(d) protein
amino acids
methionine glycine valine etc.
Gene regulation – cells can control protein synthesis 5 ways

- Transcription
- mRNA processing – alternative splicing
- Translation
- Modification
- Degradation
Transcriptional repressors bind to promoter regions and block transcription.
Spliceosomes can splice pre-mRNAs in different ways.
Gene regulation – post-transcriptional gene regulation

RNA stability can be varied by adding or not RNA-binding proteins and microRNAs.
Phosphorylating a protein can activate it. Dephosphorylating it can deactivate it.
Gene regulation – post-translational regulation

Ubiquitinizing a protein gives it a death sentence.
Genetic Linguistics

• Does the DNA code mean the same to all species?
• Will every species read DNA the same way?
• If we put the gene for a human protein into another species, will it make the same protein?
Experiment

- Jellyfish are cool
- Some of them make a protein known as GFP that glows green when exposed to UV light
Experiment

• What if we take the gene for this protein and put it into bacteria?
• Will the bacteria make GFP? Or will they translate the genetic code differently?
Experiment

• What if we take the gene for this protein and put it into bacteria?
• Will the bacteria make GFP? Or will they translate the genetic code differently?
Experiment
Experiment

• What does this tell you about the genetic code?
The code is universal!

• They make the same protein!
• What does this tell you about the genetic code?
• It’s universal! An mRNA codon will be translated into the same protein, no matter the species
• We exploit this in so many, very cool ways
  – Recombinant DNA technology
GloFish – color from anemones, coral, and jellyfish
GFP as a marker - Tracking proteins