Welcome to Genome 371!

If you are **not registered**…

- please don't take a seat!

  (class is full)

- see Anne Paul (outside) to get on the wait list

If you are registered and would like to **switch quiz sections**…

- hang on until the mid-lecture break and see Anne Paul

You **must attend** a quiz section this week to remain registered for the course

Genome 371—Introduction to Genetics

Lectures: Foege 060
Quiz Sections:
Hitchcock 443

Instructors:
Stan Fields
Josh Akey

Associate:
Anne Paul

Teaching Assistants:
Ray Malfavon-Borja
Alex Nord
Cait Rippey

Gen371— Handouts

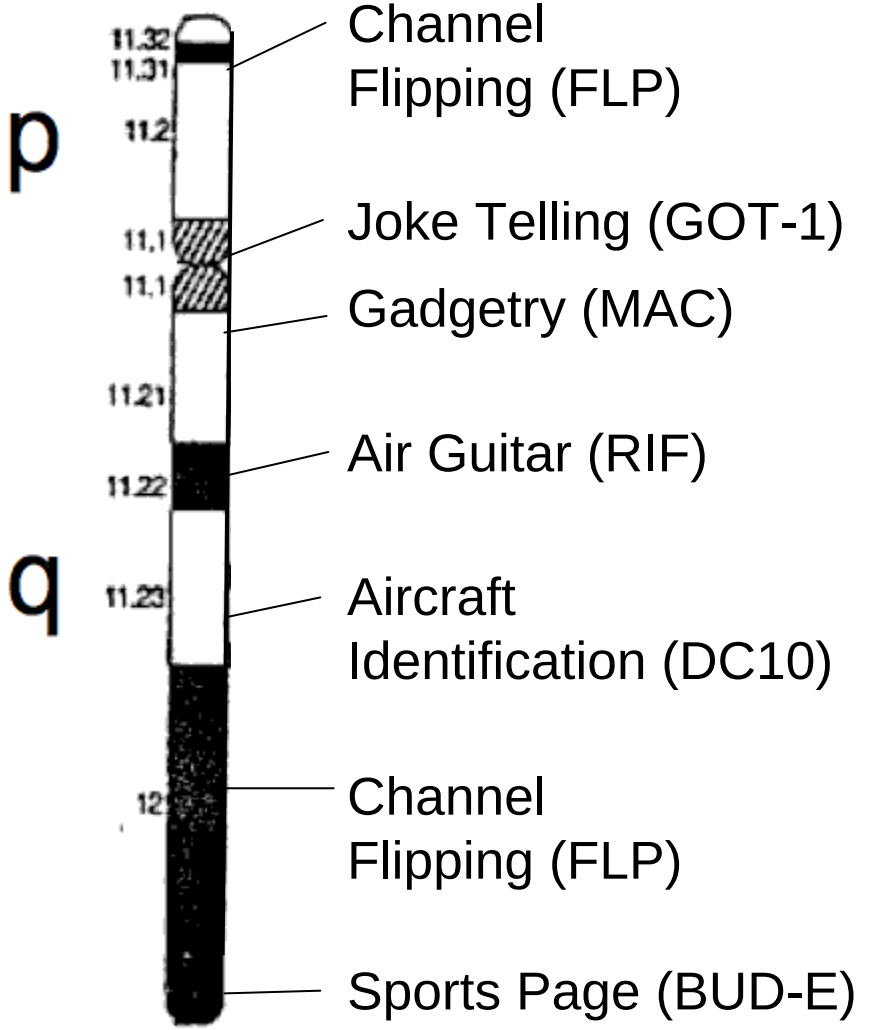
- Syllabus/Lecture notes
- Office hour poll

At mid-lecture break:

- Office hour poll returned
- Exam conflict form

  (ask during break if you need one)

The Y Chromosome



What do we mean by **genetics**?

How biological information is…

- encoded within cells
- read and used
- transmitted to progeny

Studying genetics…

- Use defects in the code (mutations) to understand how a process normally works…
- Use sequence information to get new insights

Throughout the quarter… logic, not memorizatio

What this course is about

Patterns of inheritance

- how are traits inherited?
- how are traits determined by genes?

Mutant analysis

- how biological processes are studied by analyzing mutants

Genomics and human health

- what we can learn by studying whole genomes

Throughout the quarter . . .

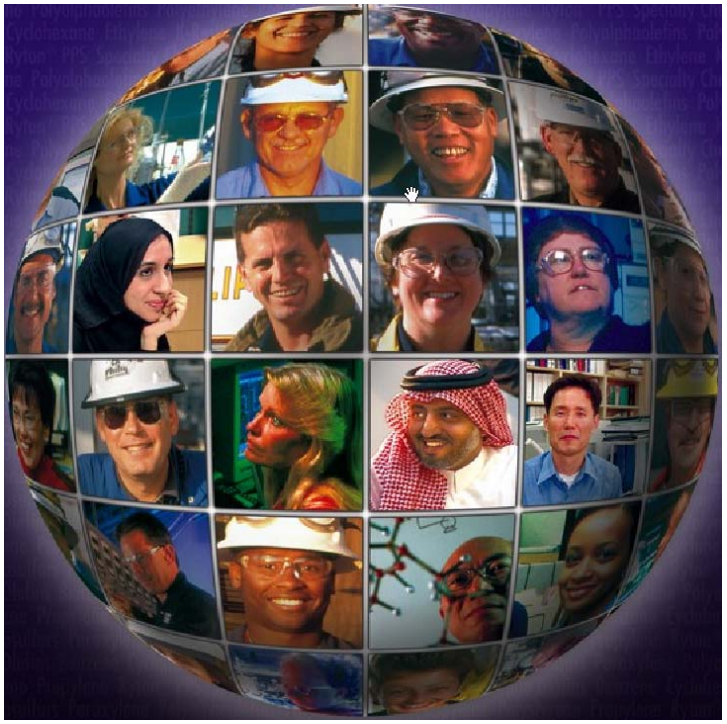
- how and why model organisms are used
- how that information applies to humans

Why might we want to learn this material?

Insight into diversity?

Variation in **phenotype** (observed physical traits)…

and variation in **genotype** (underlying genetic encoding)

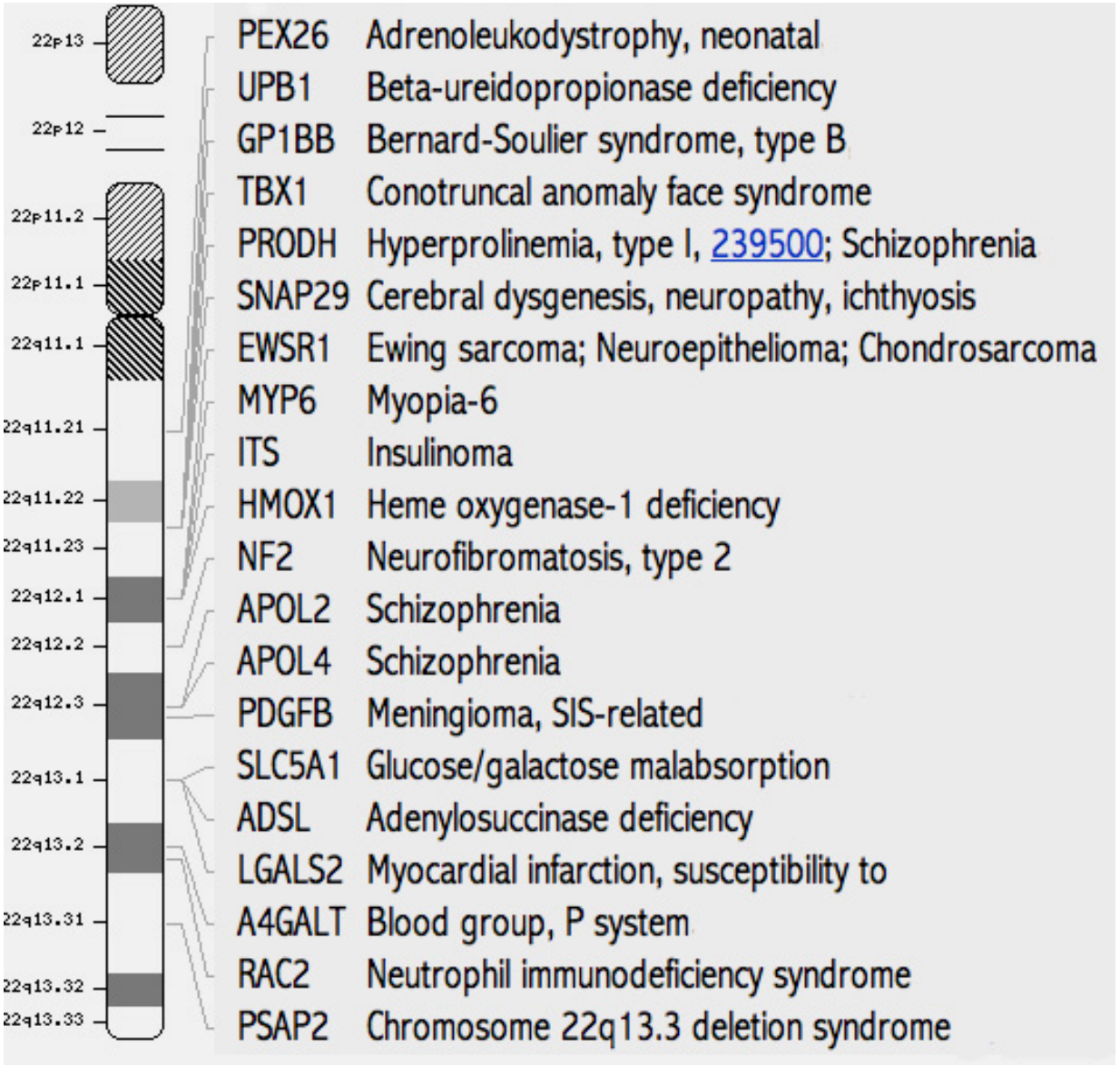


from Chevron Phillips

from catoftheday.com

Insight into our origins?

Insight into health?



Aside: what is a genome?

The genetic material in one complete set of chromosomes inherited from a parent

Diploid organisms (like us)… two genomes per cell (one from mom, one from dad)

What do we mean by **genetics**?

How biological information is…

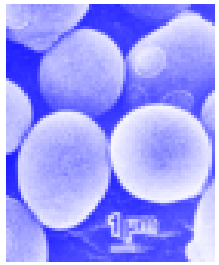
- encoded within cells
- read and used
- transmitted to progeny

Studying genetics…

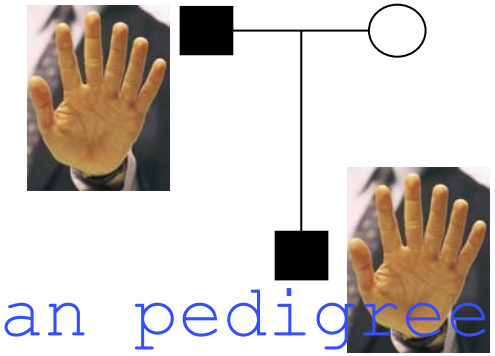
- Use defects in the code (mutations) to understand how a process normally works…
- Use sequence information to get new insights

Throughout the quarter… logic, not memorizatio

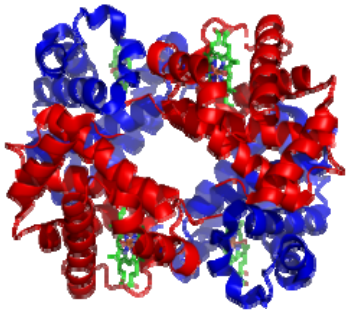
Common theme: linking genotype & phenotype



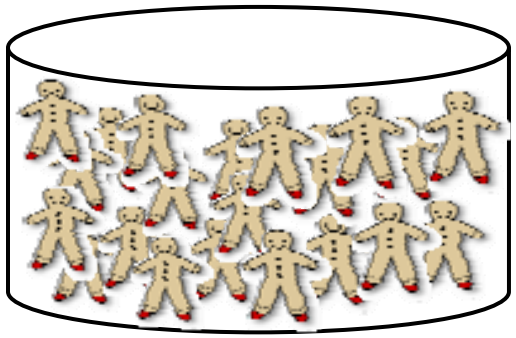
Mutant identified
in a model organism



Human pedigree
segregating a trai



Protein acting in
a biological process



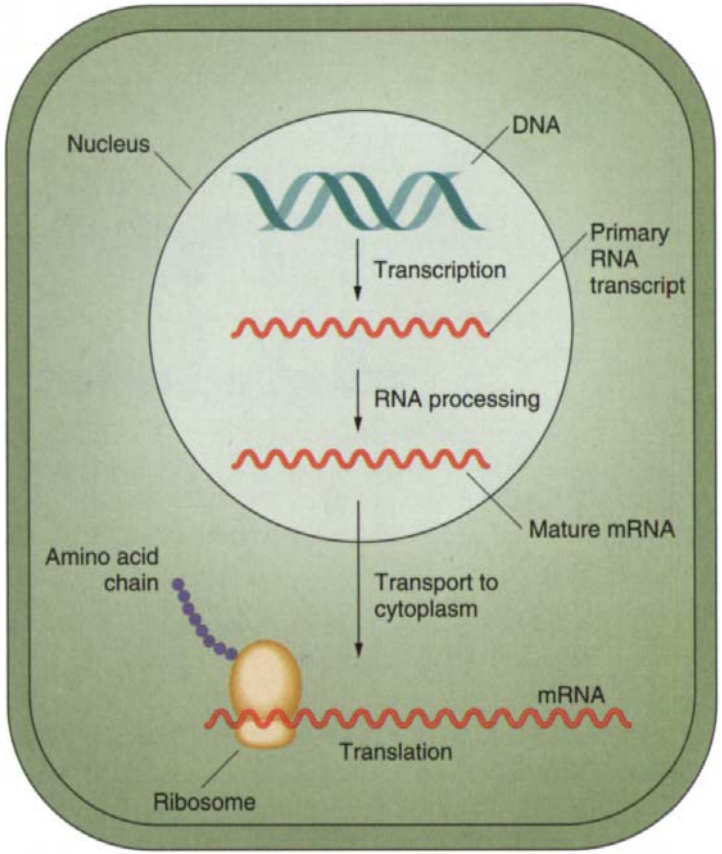
Association s

```
 946 ATT GTC TGT AGC CGA TTG GAG GAG TAC AAC AGC CAT
1009 GGA CCT TTA CGG CGT AAT CCT GGA AAC CAT GAC AAA
1072 GCT GAT GTA GAA TTT TGC CTG AGT TTG ACC CAA TAT
1135 AAT TTC AGC TTT AGA AAT ACA CTG GAA GGA TTT GCT
1198 TCT CAA AGC AGC ATG CAC AAT GCC TTG CAC ATC TAT
1261 GGA TCT GCC AAC GAT CCT ATC TTC CTT CTT CAC CAT
1324 TGG CTC CGA AGG CAC CGT CCT CTT CAA GAA GTT TAT
```

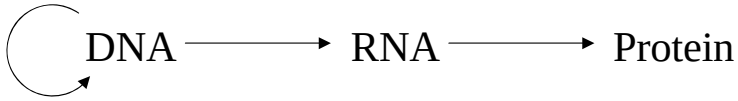
Sequence analysi

Today

How are traits determined by genes?



Review of the "Central Dogma" of genetics



Genes encode proteins.

The activities of proteins produce visible traits.

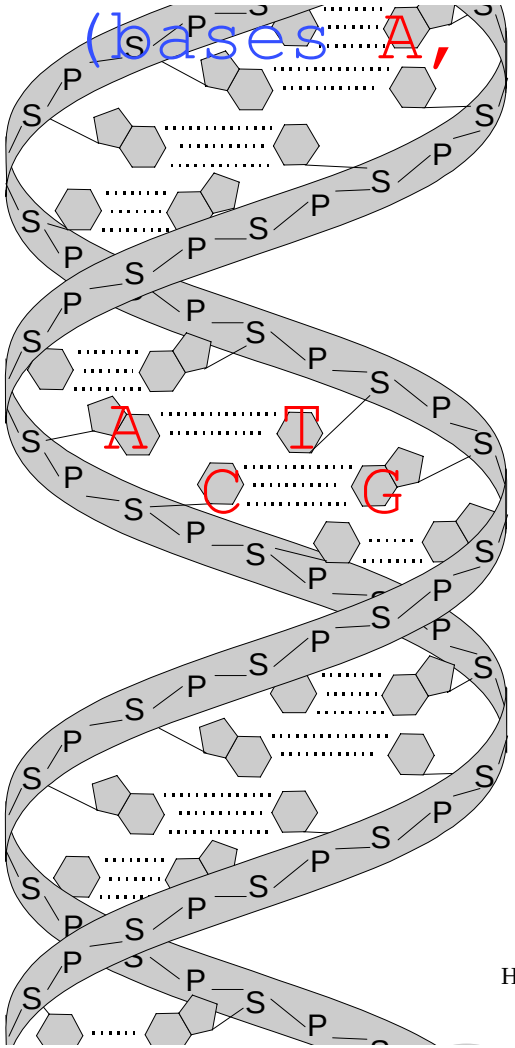
Genes that don't encode proteins

Looking for open reading frames (ORFs)

DNA and the flow of information

The genetic material: DNA

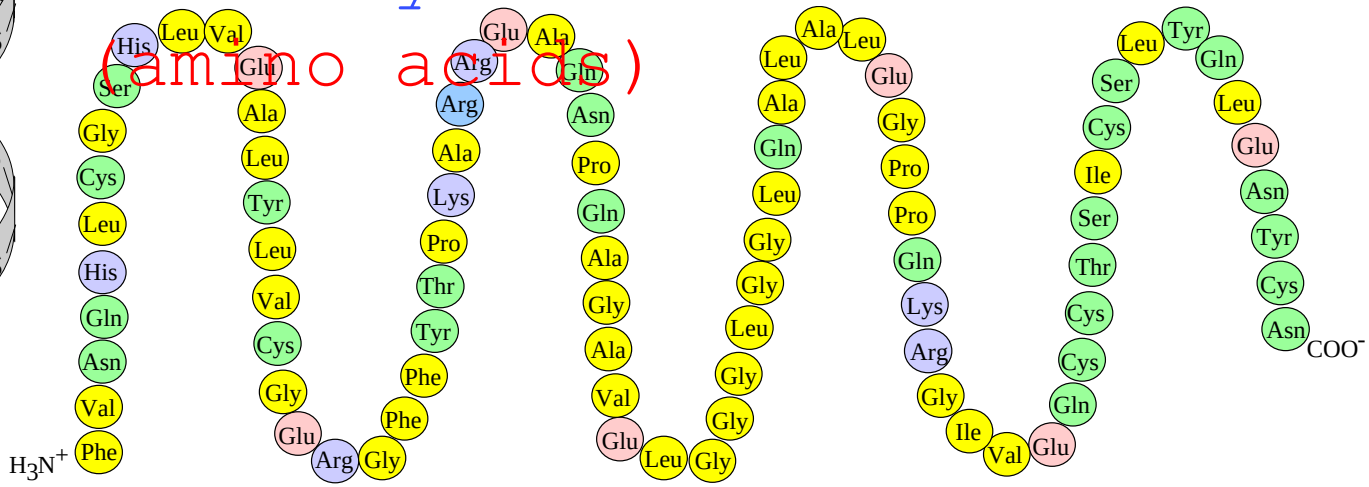
- Four kinds of subunits (bases A, C, G, T)



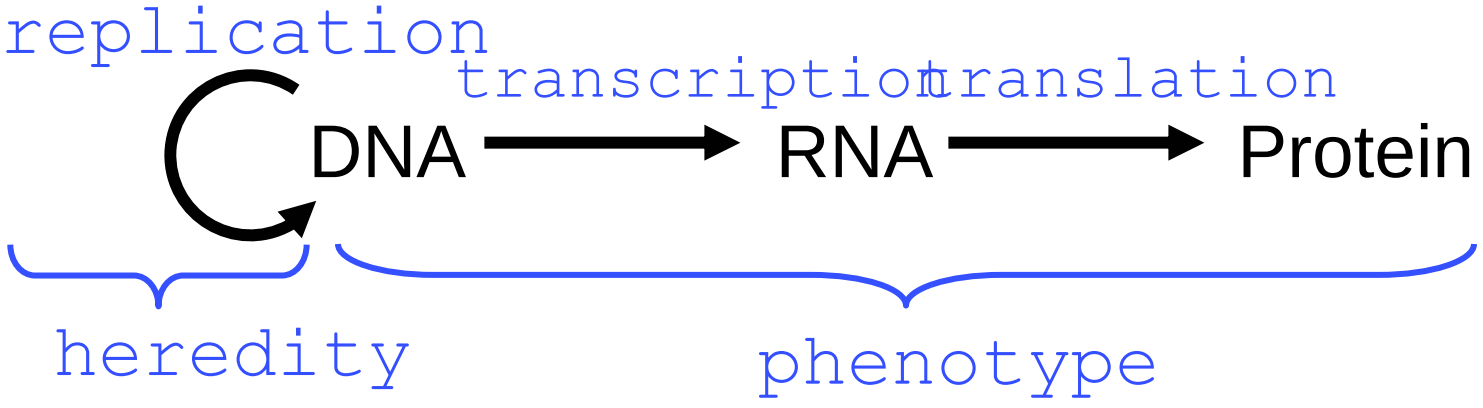
A coding problem

Activities within the cell performed by proteins

- Twenty kinds of subunits (amino acids)



The “Central Dogma” of molecular biology



Information into protein only flows one way

A universal code: 3 nucleotides = 1 amino acid

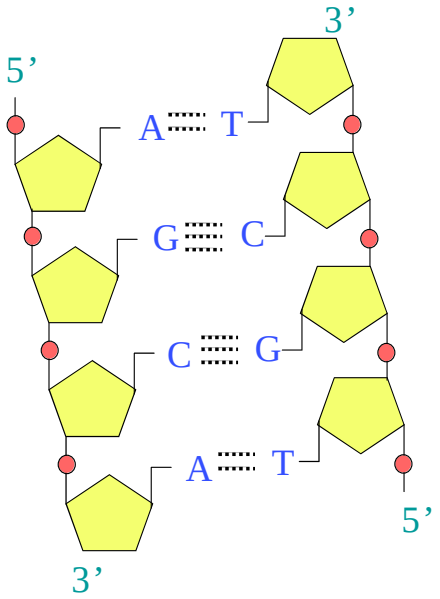
About these lecture notes…

http://courses.washington.edu/gensc371
Username: gensci371
Password: 2010

-Don't worry about copying down every word, worry more about understanding what's being said!

-Handouts, problem sets, practice

The structure of DNA cont'd



- Information content is in the sequence of bases along a DNA molecule

  rules of base pairing → each strand of the double helix has all the info needed to recreate the other strand

- Redundancy in the code

  multiple ways that DNA can specify a single amino acid

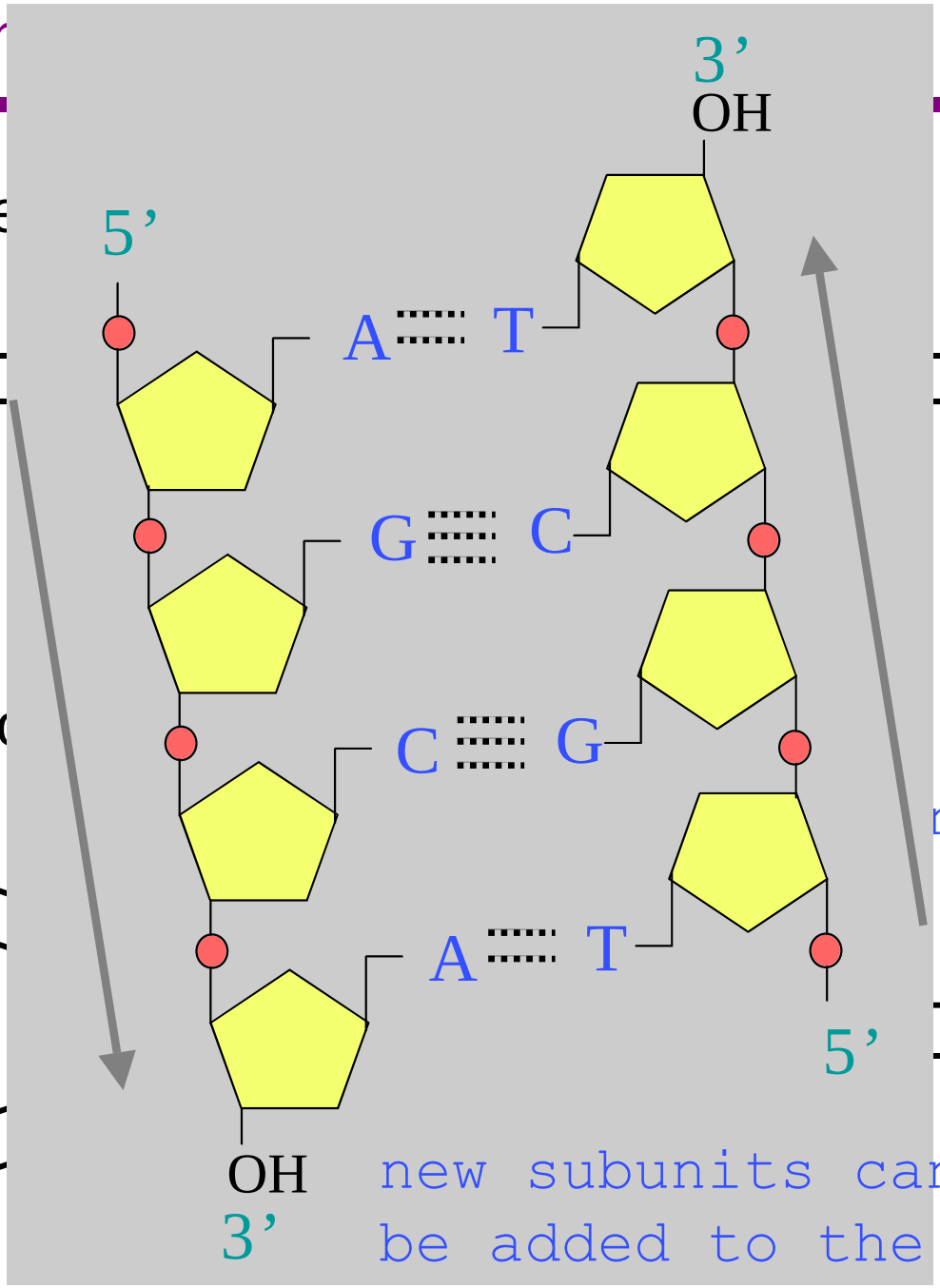
- Genetic variation — differences in the base sequence between different individuals

  why individuals vary in their phenotypes

Review of th

DNA structure

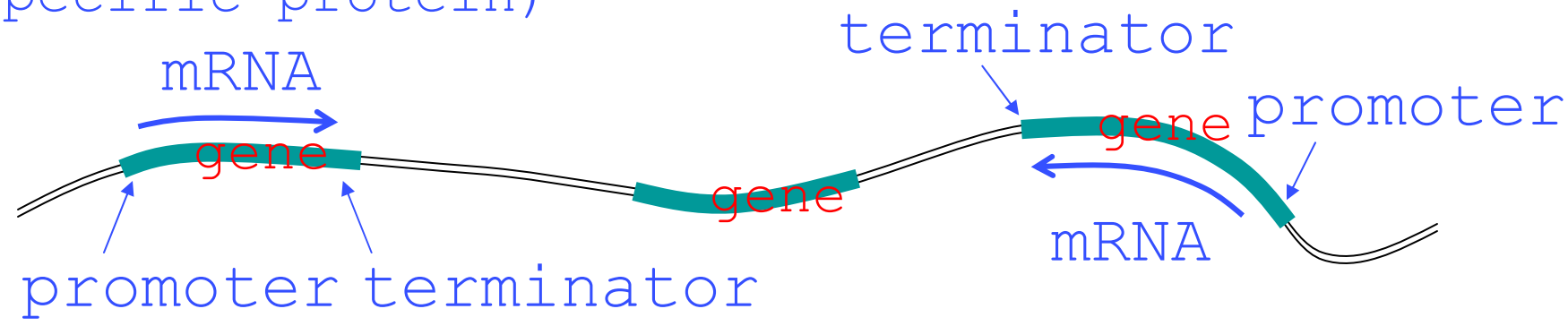
DNA replicatio



Review of the Central Dogma (cont)

Genes — specific segments along the chromosomal DNA that code for some function

Transcription: "copy" gene into RNA (to make a specific protein)

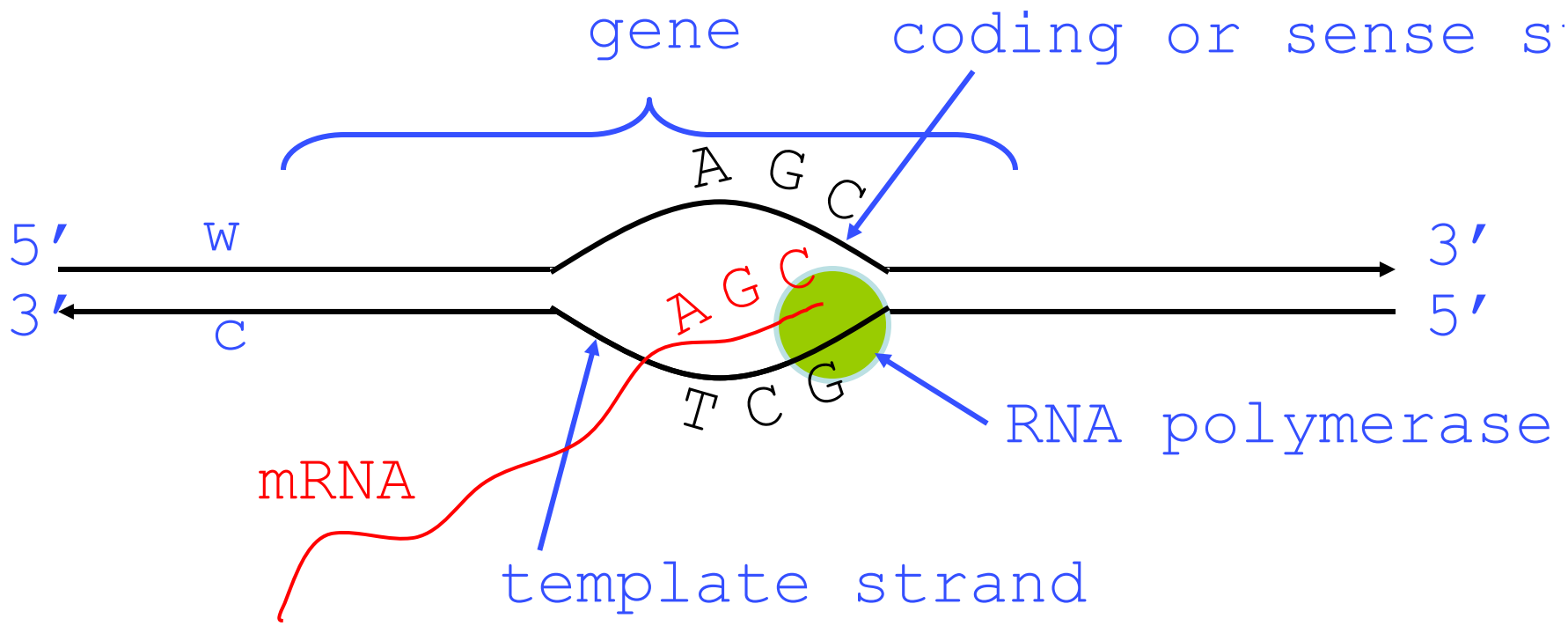


QuickTime™ and a
Animation decompressor
are needed to see this picture.

Review of the Central Dogma (cont.)

Transcription: "copy" gene into RNA to make a specific protein

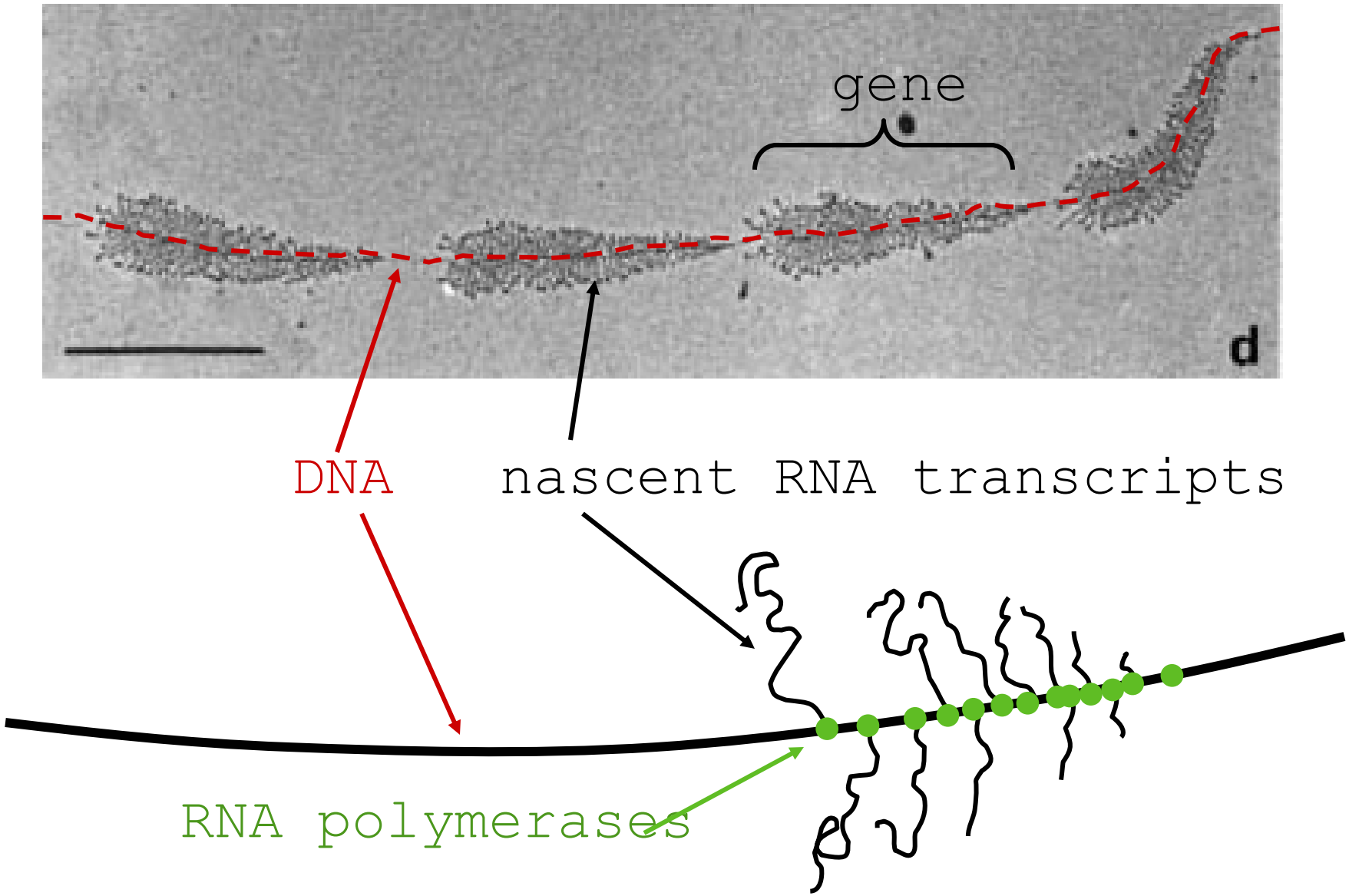
ribonucleic acid… uses uracil (U) in p



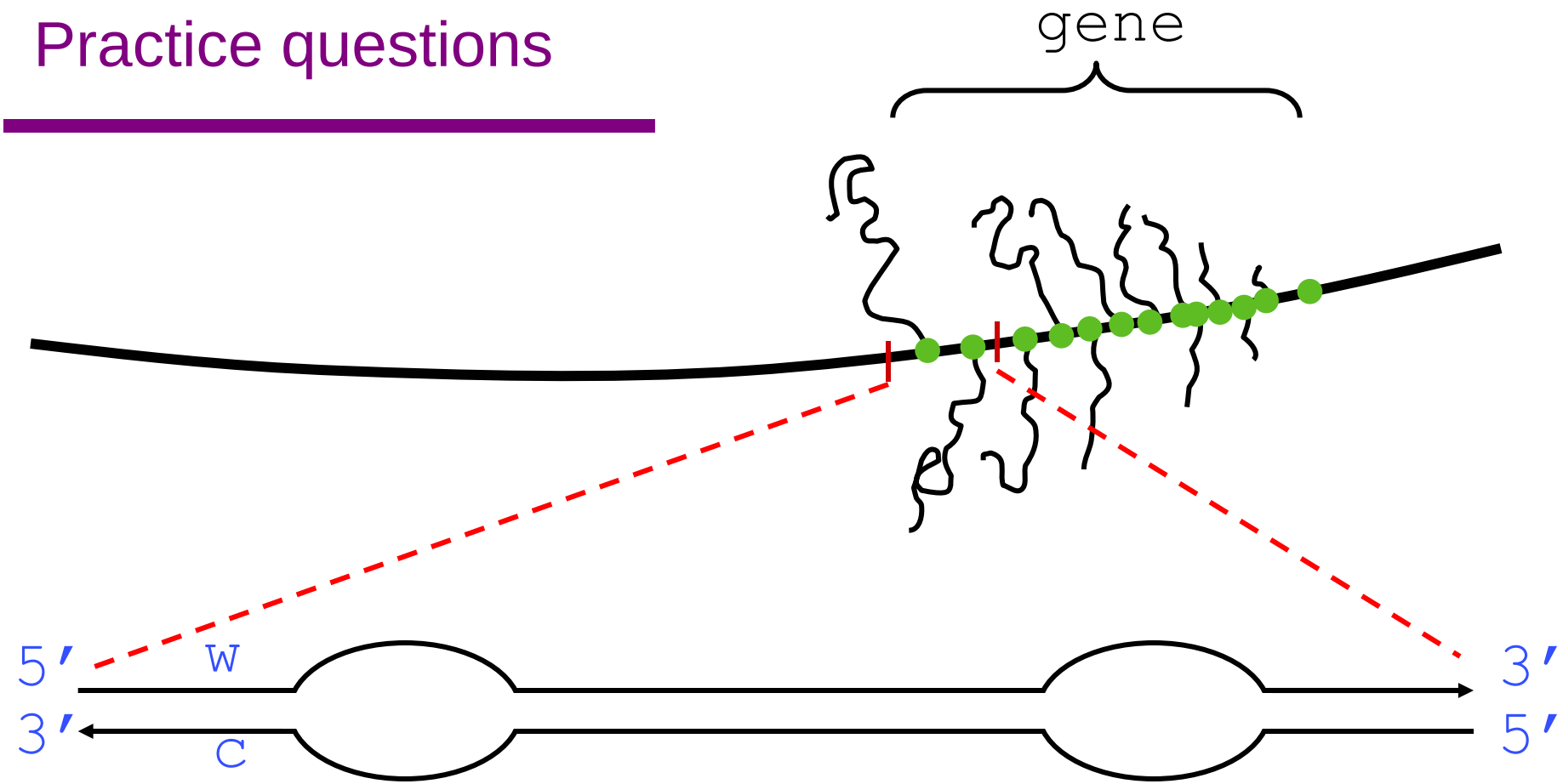
Where's the 5′ end of the gene? of the mRNA?

Which way is RNA polymerase moving?

Transcription in vivo

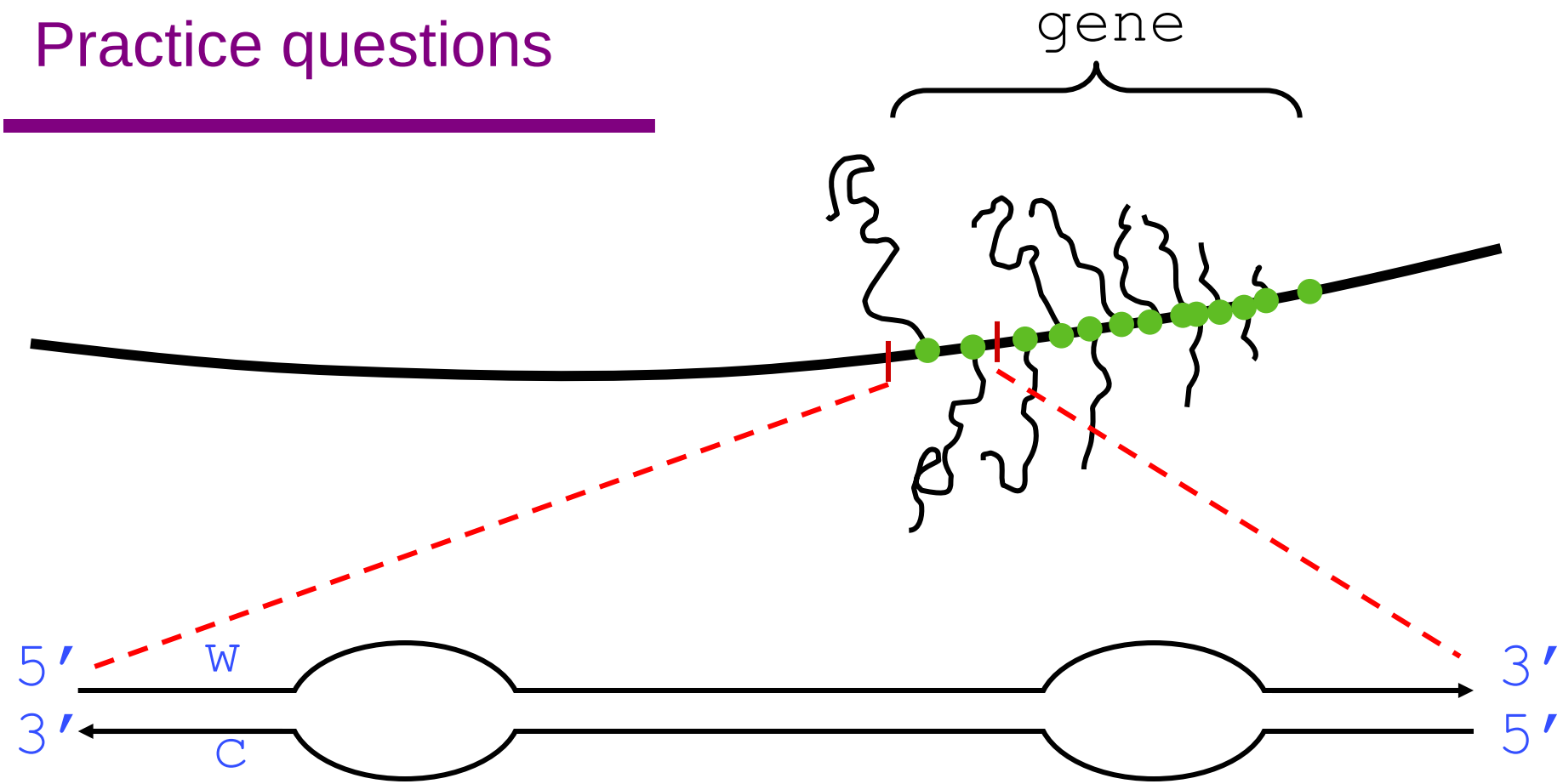


Practice questions



1. Which way (to the right or left) are RNA polymerases moving?

Practice questions



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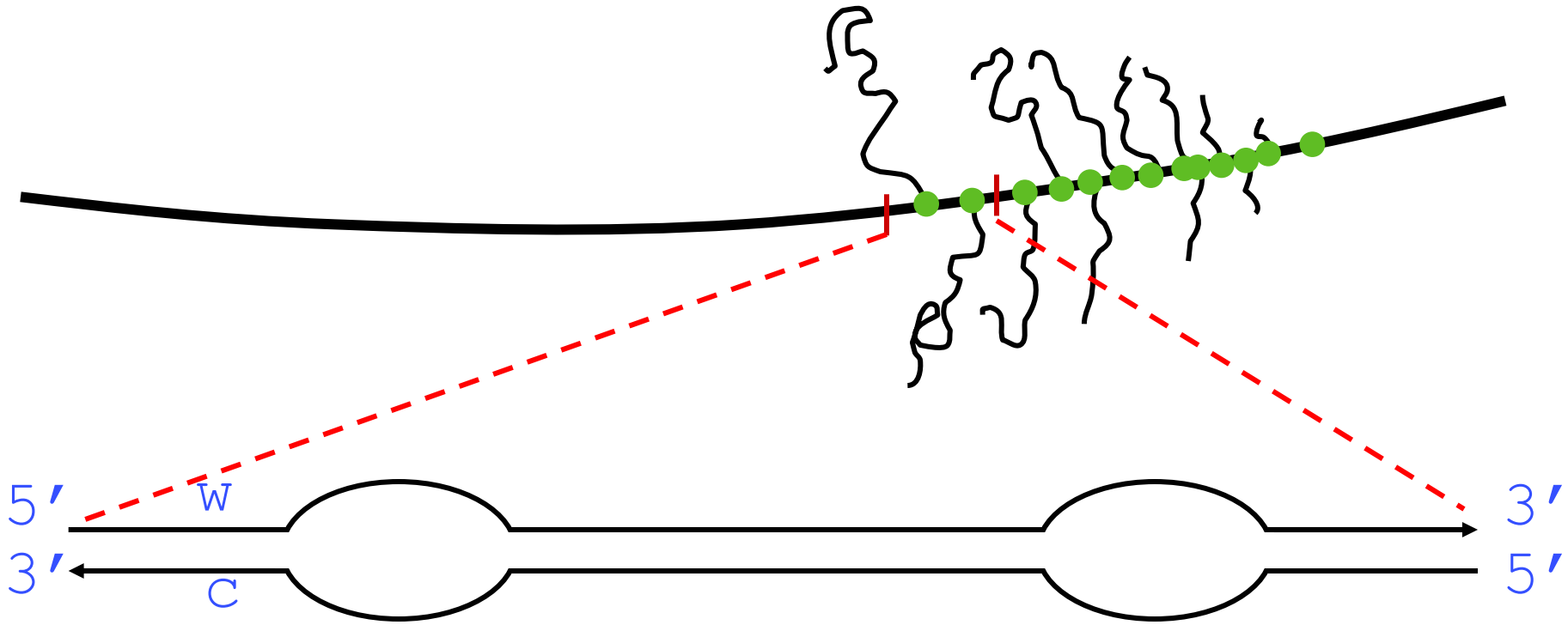
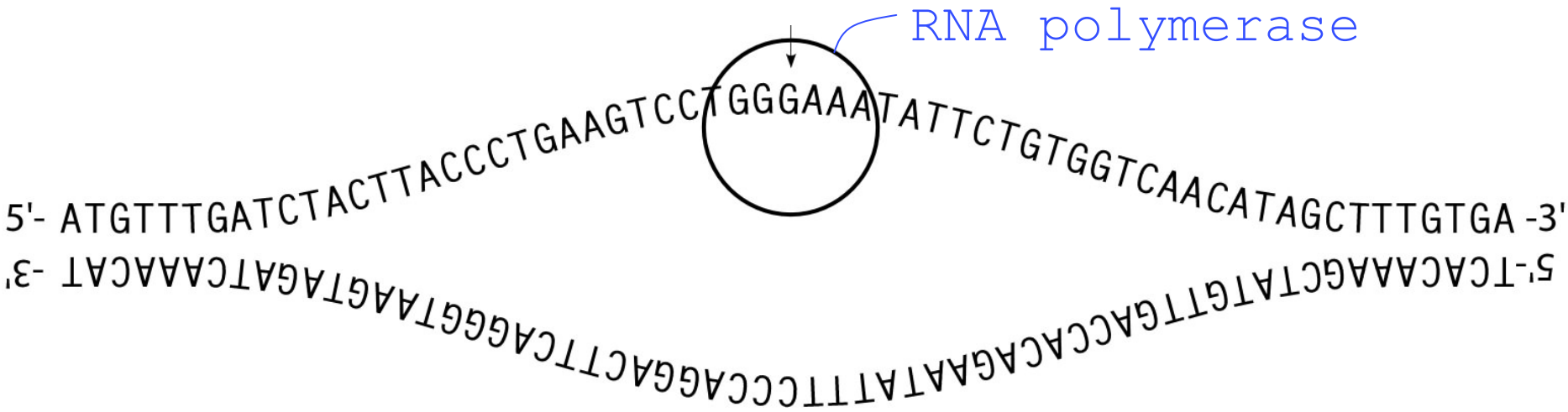


2. Where is the promoter? To the right or the left of the gene?

3. Which strand (W or C) is the template strand?

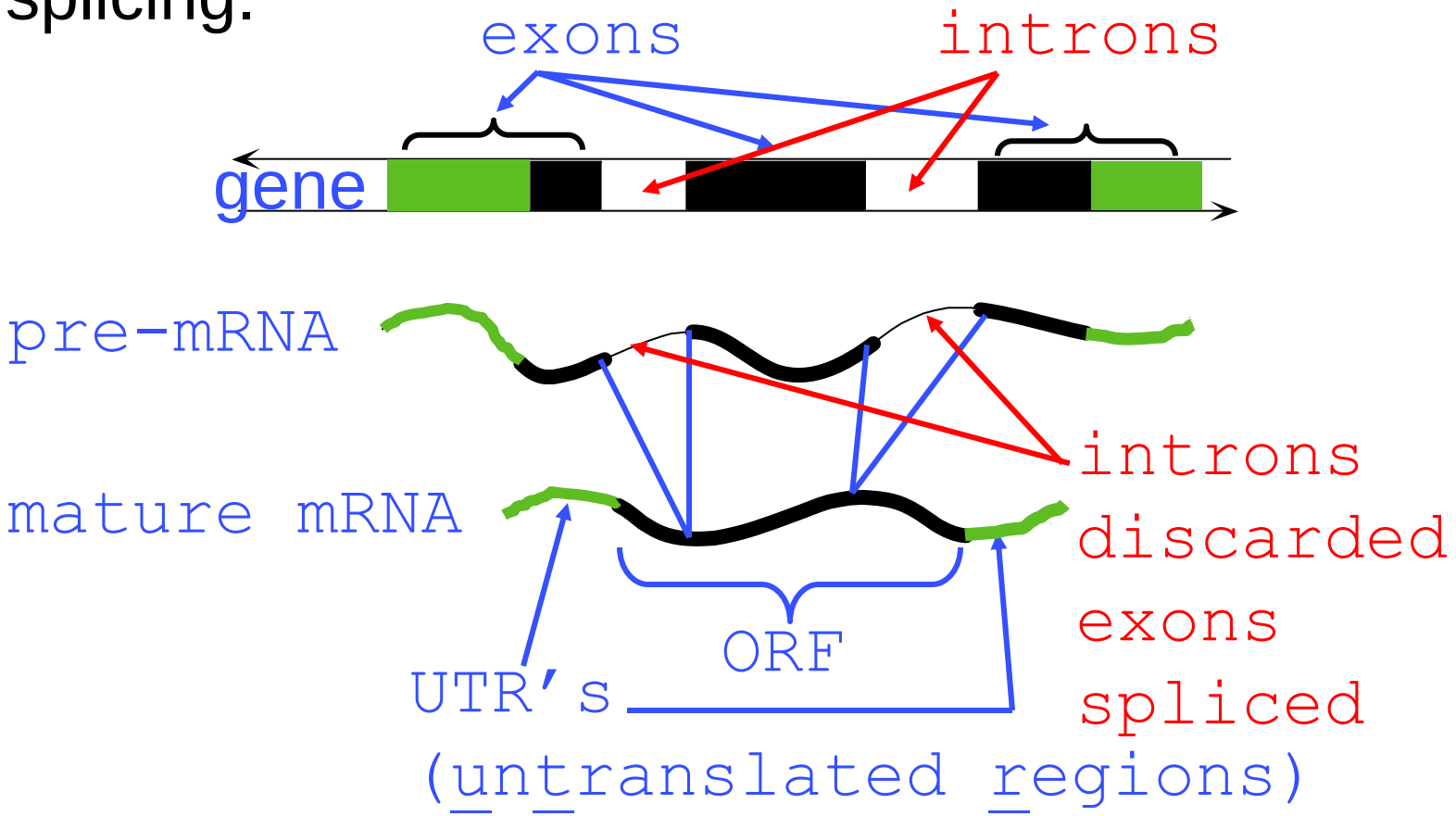


4. Zooming in on a transcription bubble… draw the first base of the RNA (the arrow marks the transcription start site). Mark the 5’ and 3’ ends of the base you just added.

5. Draw the next 10 bases of RNA that will be made. To which side of the first base will you add these next 10? Which strand on the DNA is the coding strand? Which is the template strand?

Review of the Central Dogma (cont.)

Eukaryotic genes are interrupted by introns (non-coding information). They must be removed from the RNA before translation in a process called "splicing."



Beyond the Basics

Gene or No Gene?

A gene is often a segment of DNA that encodes a protein.
How about DNA that encodes:

a micro RNA that binds to an mRNA to inhibit

an RNA spliced out of an intron and used for an antisense transcript?

a long non-coding RNA of no known function?

a pseudogene?

Course mechanics

Resources

» **Web site:**

http://courses.washington.edu/gensci371

Restricted areas…

Name = **gensci371**

Password = **2010**

» Notes, Problem sets, Practice exams

» Videos of lecture available

» Go-Post discussion board:

Science only! TA assistance

» **Office hours!**

Course mechanics

Lecture format — solve problems as we go along
(don't just wait for the answers)
— **ask questions**

Quiz sections — Wed/Thu Hitchcock 443
starting this week
material in the quiz sections will help you
understand the course

Textbook not required (based on feedback)
but standard genetics texts on reserve
(in Odegaard); relevant pages in syllabus

Pubmed (search "Books" by topic)
http://www.ncbi.nlm.nih.gov/pubmed/

Course mechanics

Office/help hour scheduling—

based on forms provided at the break

Make use of one-on-one help!

Help hour times / location will be posted

Course mechanics

Grades

1 mini-test (35 points) (Next Monday)

2 in-class exams (200 points total)

1 final (100 points)

Exams

Exam conflict policy

Group study is encouraged!

Missing an exam

- Illness
- University sponsored conflict (submit an exam conflict form by Friday, April 3)

No make-up minitest

What will exam questions look like?

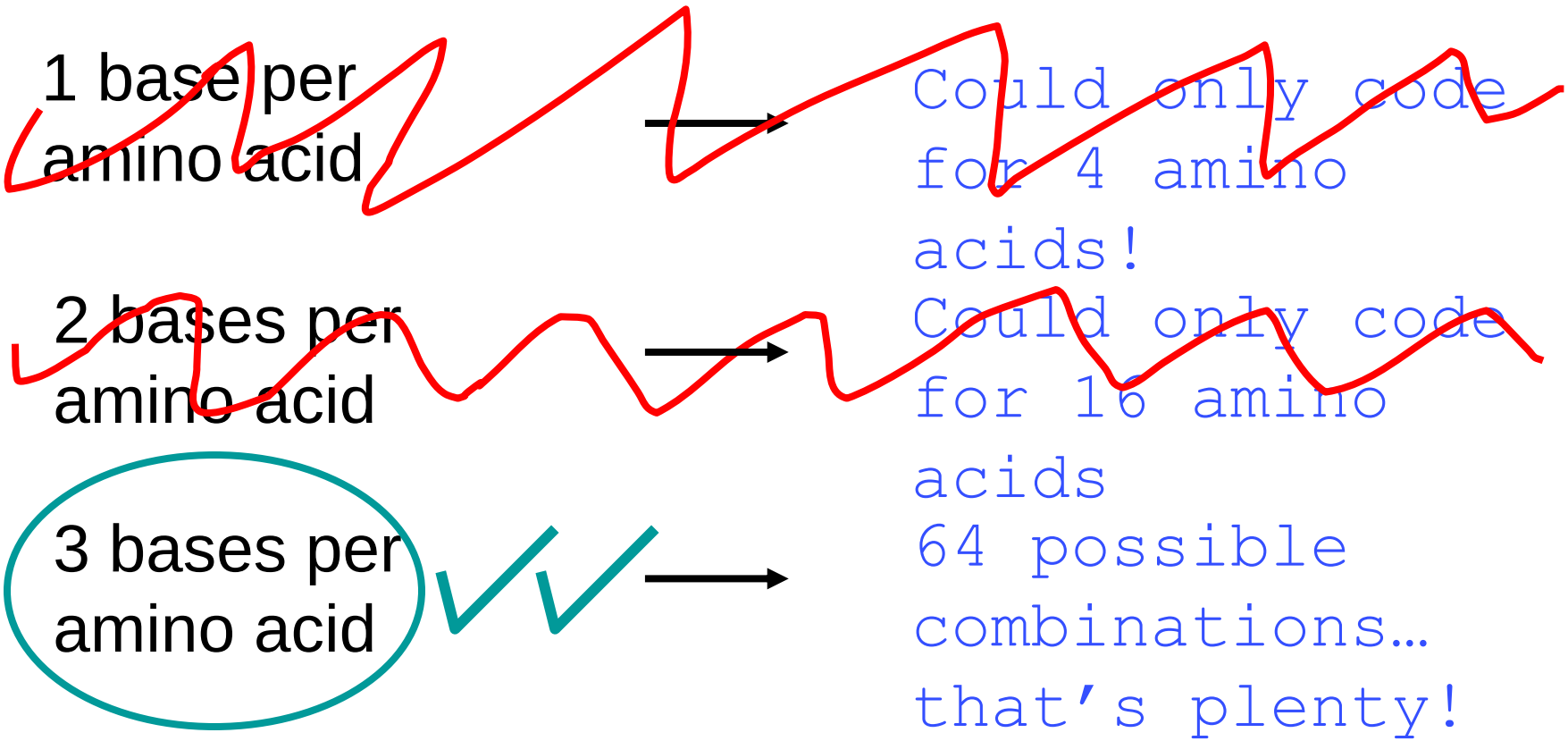
You will not be asked to repeat back what you heard in class…

You will be asked to analyze data or to design tests of hypotheses

Review of the Central Dogma (cont.)

Translating the nucleic acid code to a peptide code…

Possible coding systems:



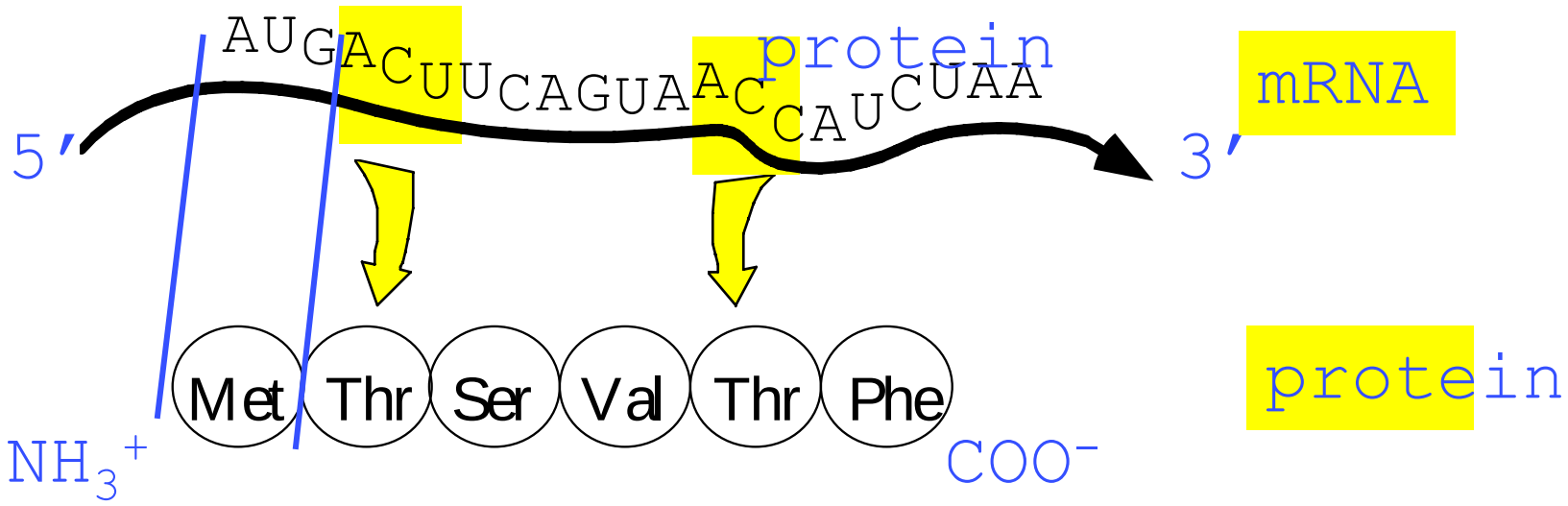
The triplet code

3 bases = 1 amino acid

More than 1 triplet can code for the same amino acid

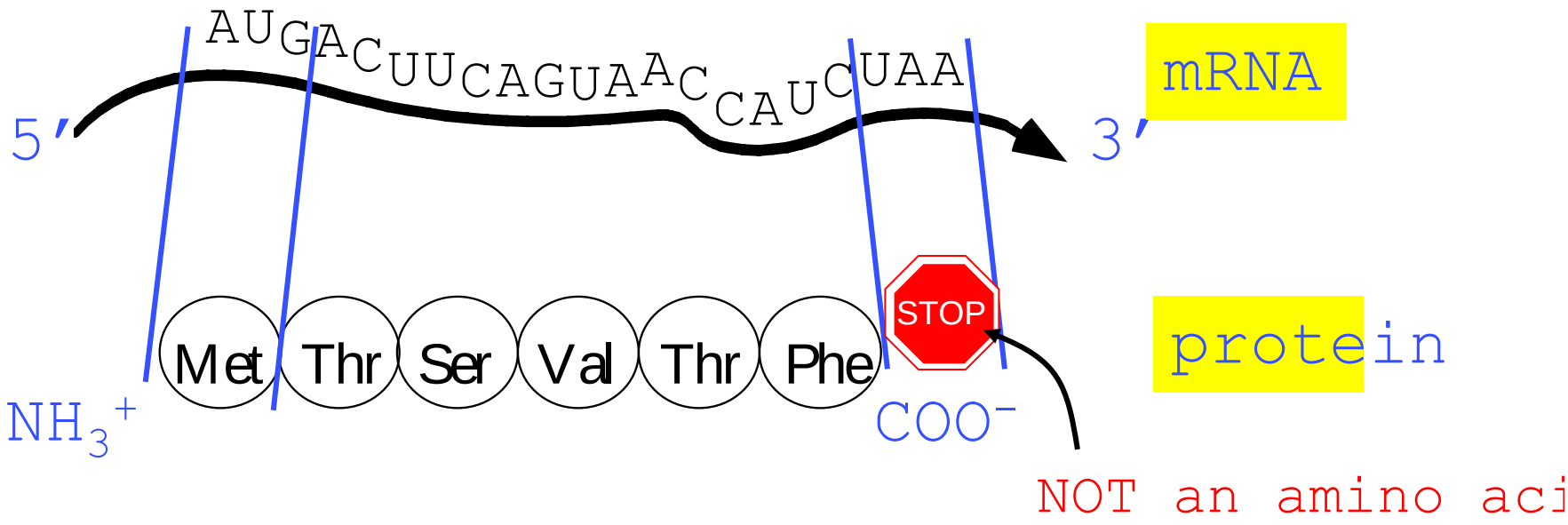
codon

Translation: read the information in RNA to order the amino acids in a protein



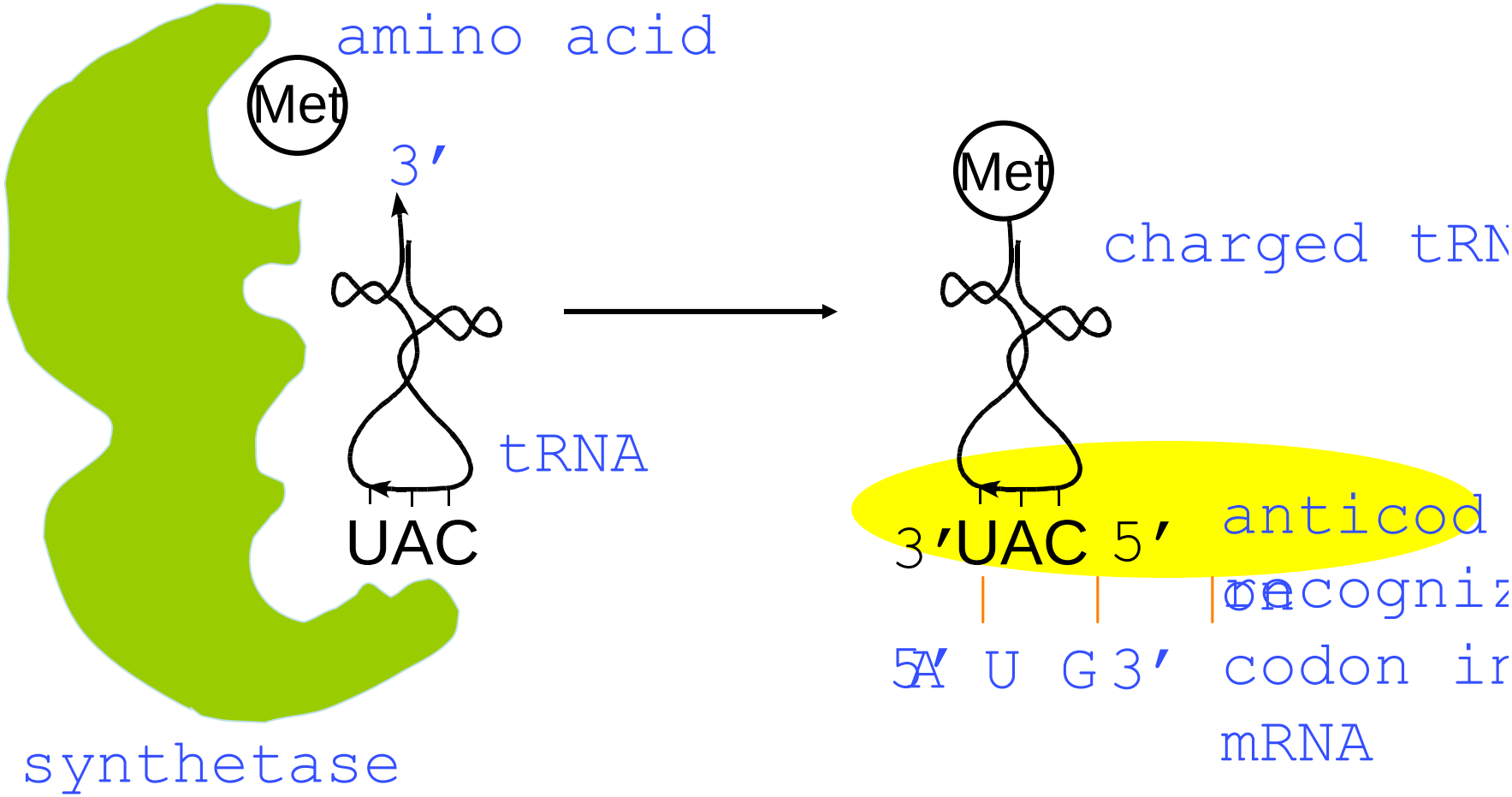
Punctuation:

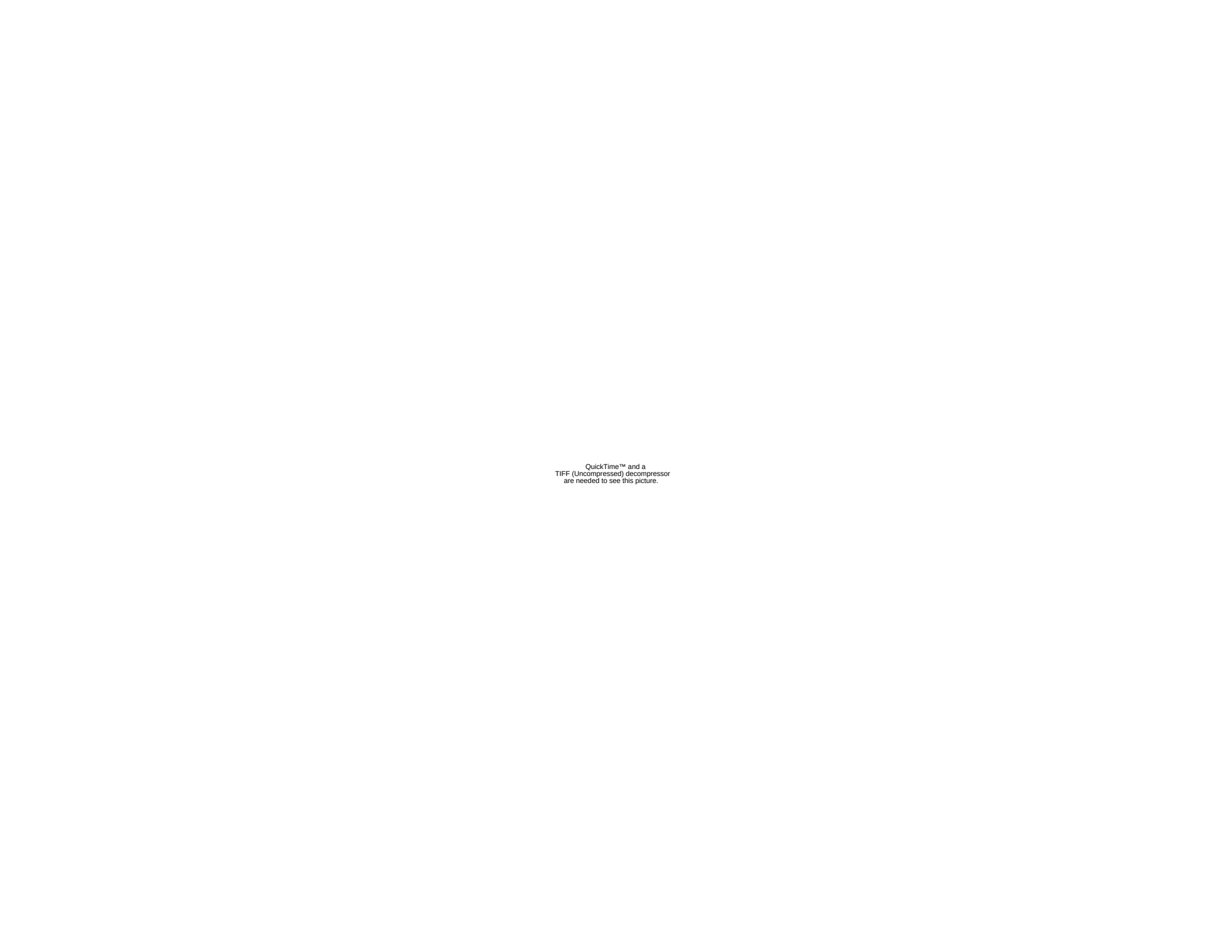
sta AUG = methionine, the
rt: first amino acid in
(almost) all proteins
sto UAA, UAG, and UGA.
p:



The Genetic Code: Who is the interpreter? Where's the dictionary? What are the rules of grammar?

tRNA = transfer RNA

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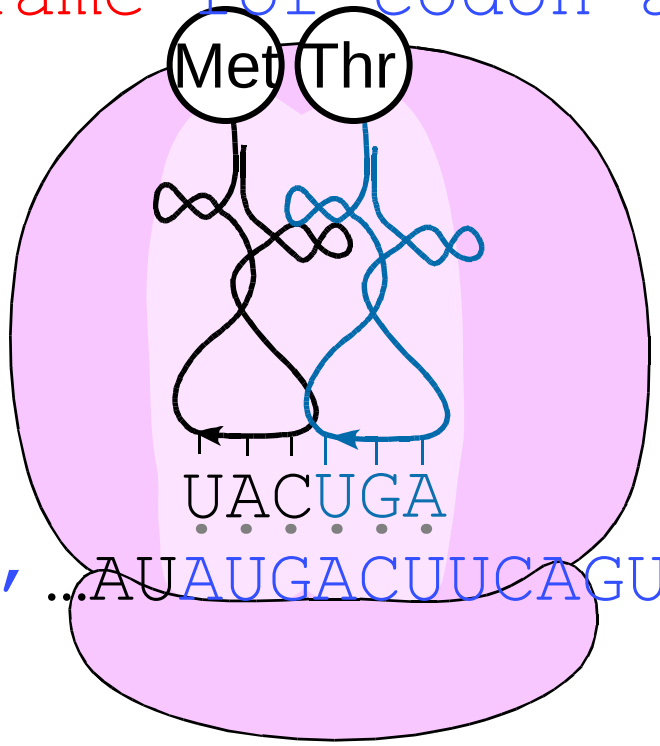
are needed to see this picture.

The **ribosome**: mediates translation

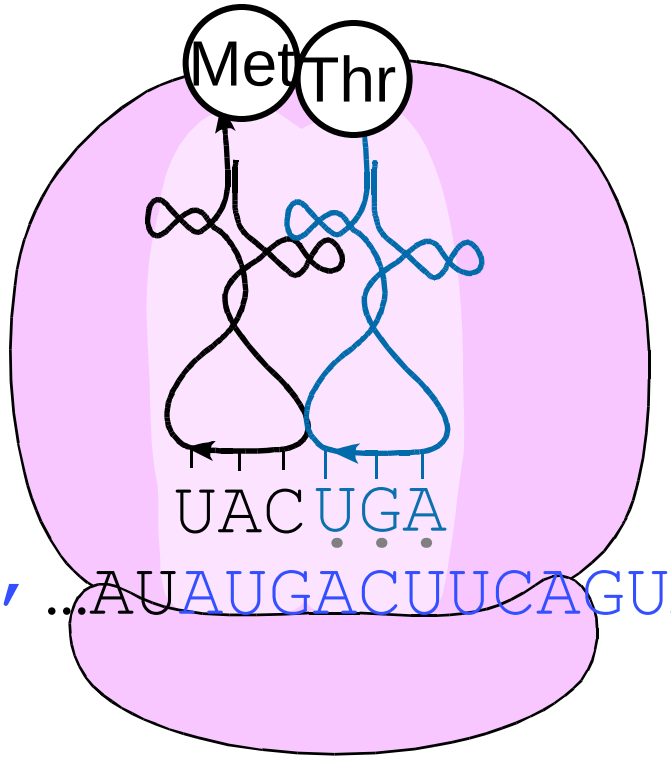
Locates the 1st AUG, sets the reading frame for codon-anticodon base-pairing



ribosome

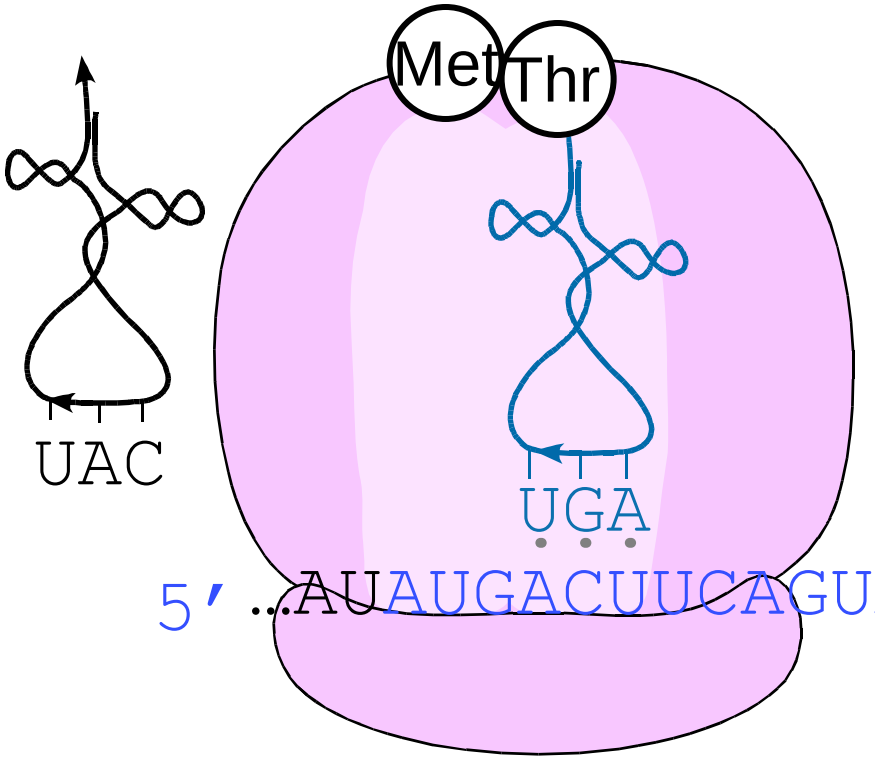
After the 1st two tRNAs have bound…

the ribosome breaks the Met-tRNA bond; Met is instead joined to the second amino acid



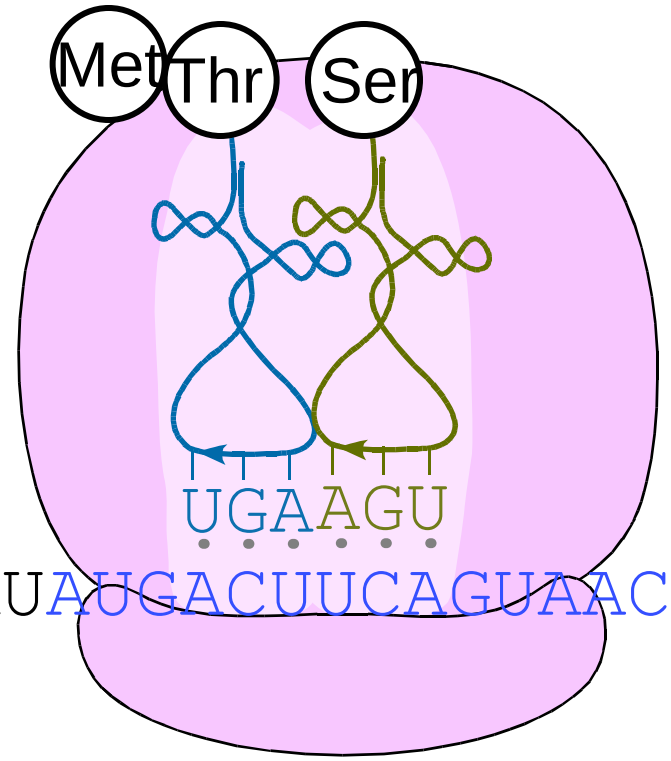
ribosome

the ribosome breaks the Met-tRNA bond; Met is instead joined to the Thr-tRNA



…then ribosome moves over by 1 codon in the 3′ direction

and the next tRNA can bind, and the process repeats



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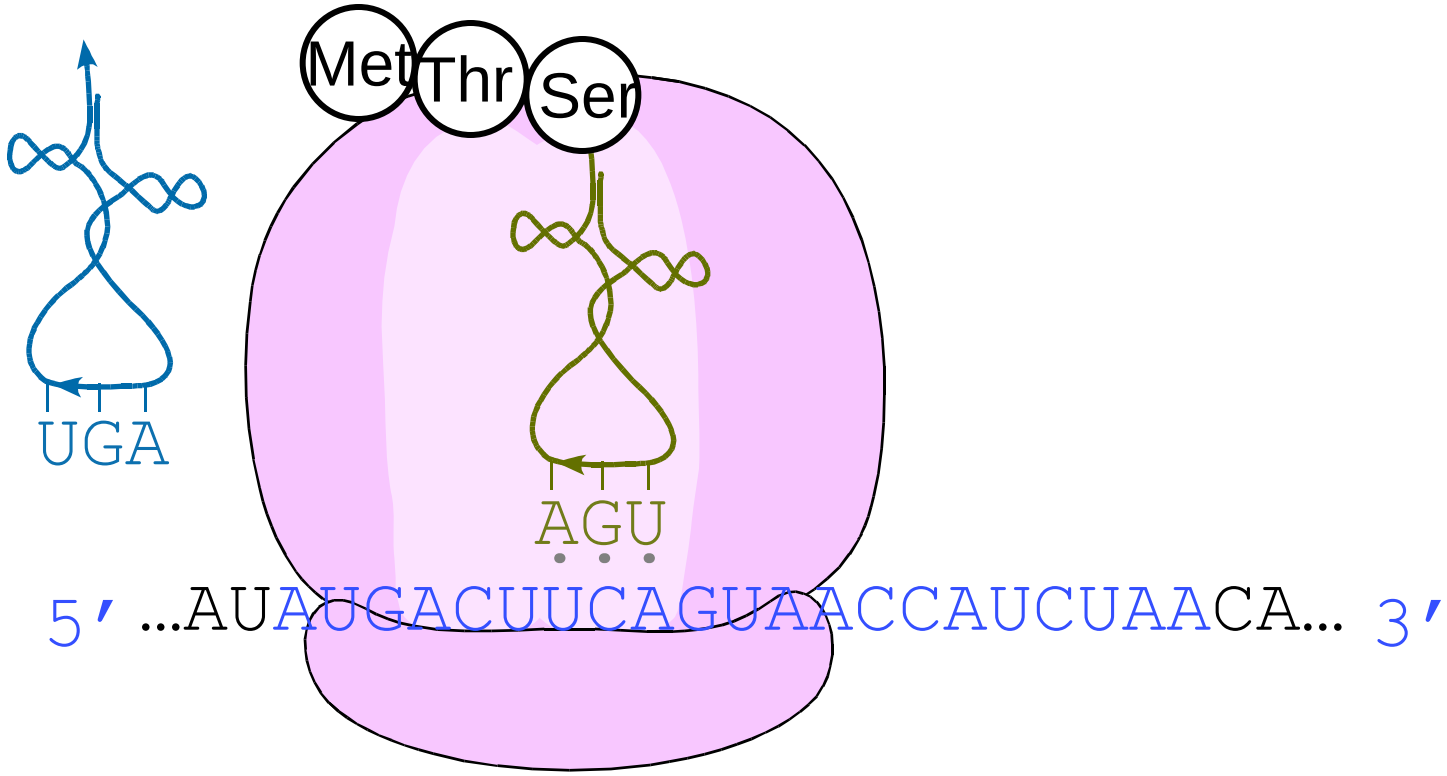
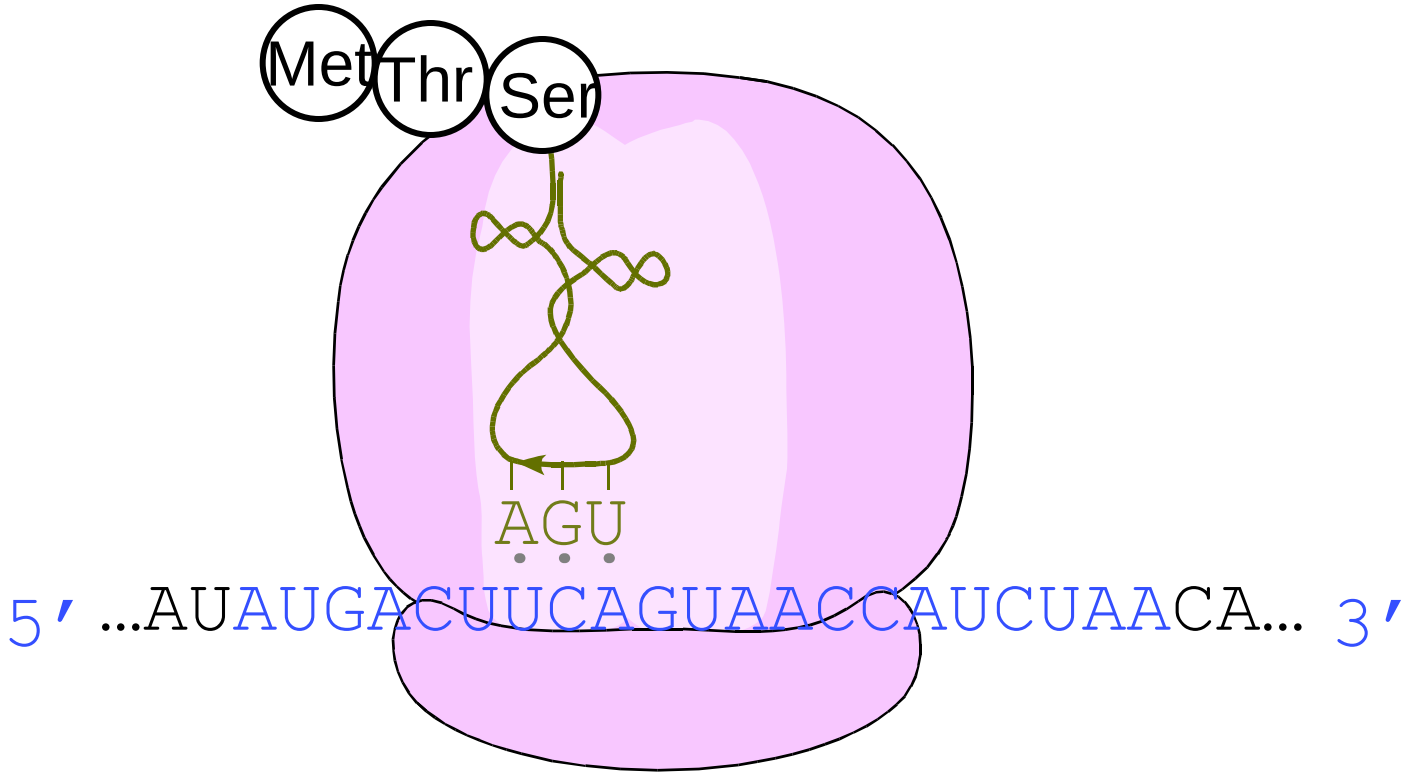
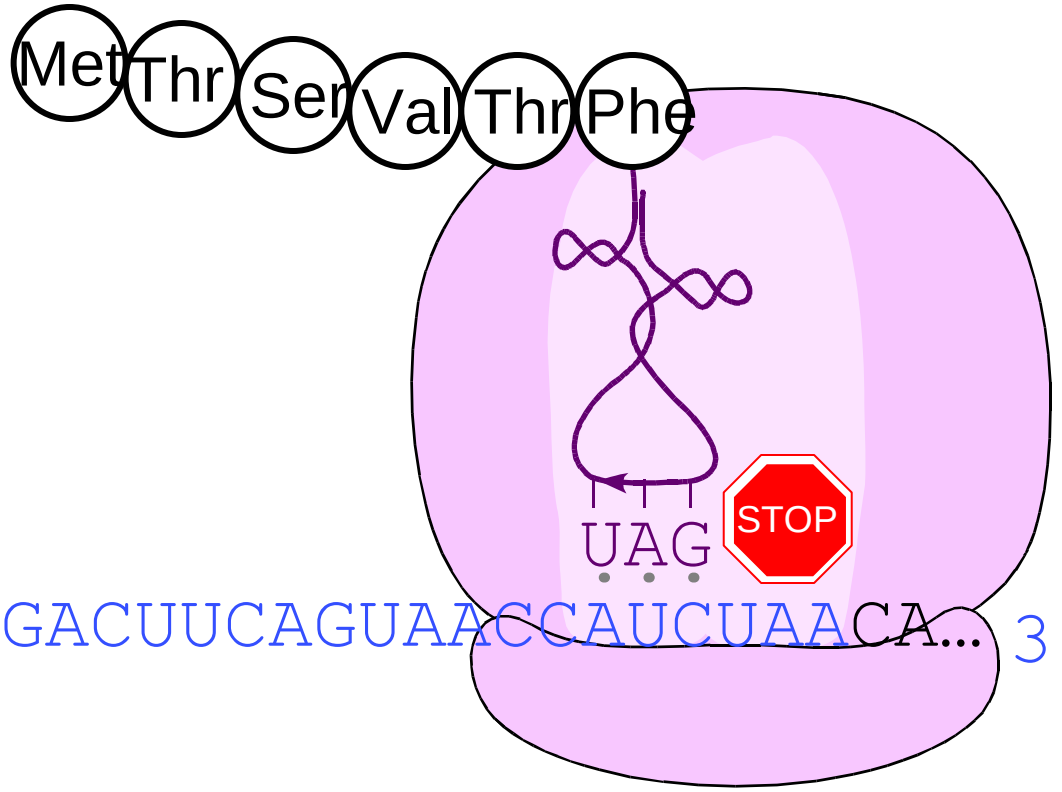
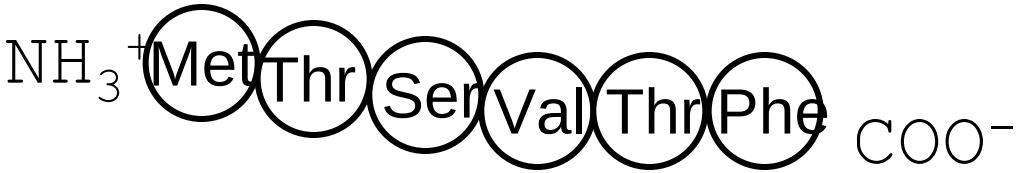

Met
Thr
Ser
UGA
AGU
5′ …AUAUGACUUCAGUAACCAUCUAACA… 3′


Met
Thr
Ser
AGU
5′ …AUAUGACUUCAGUAACCAUCUAACA… 3′

When the ribosome reaches the Stop codon… termination



The finished peptide!

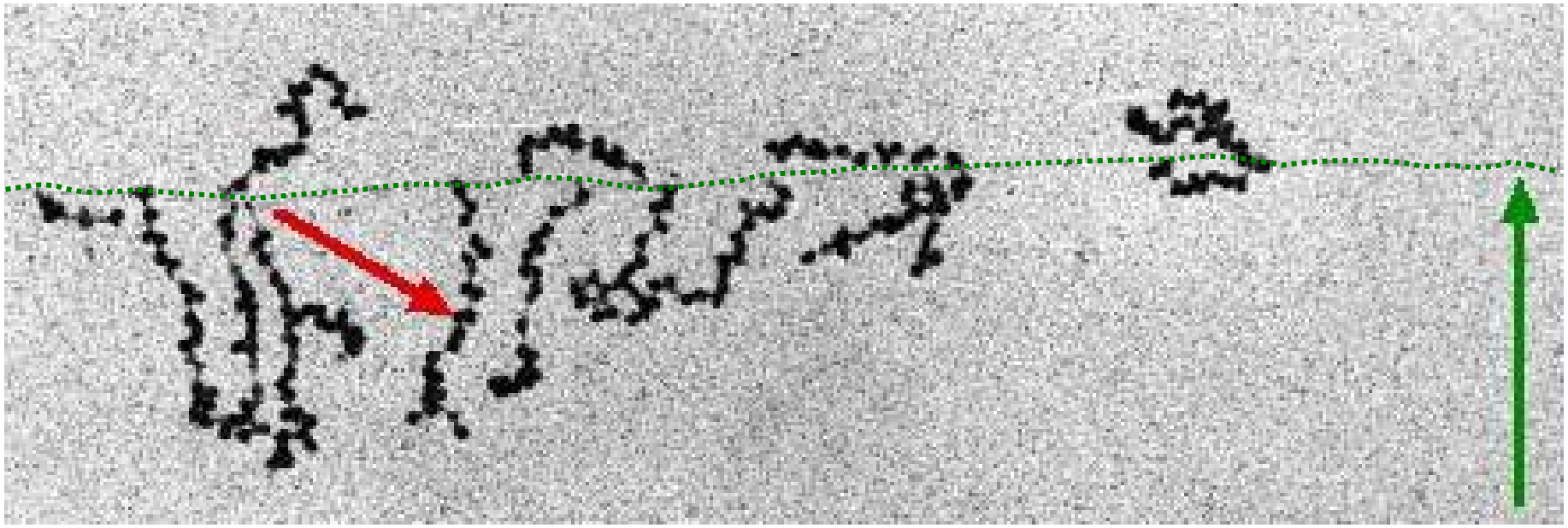


5′ …AUAUGACUUCAGUAACCAUCUAACA… 3′

Practice questions… homework

Coupling of transcription and translation

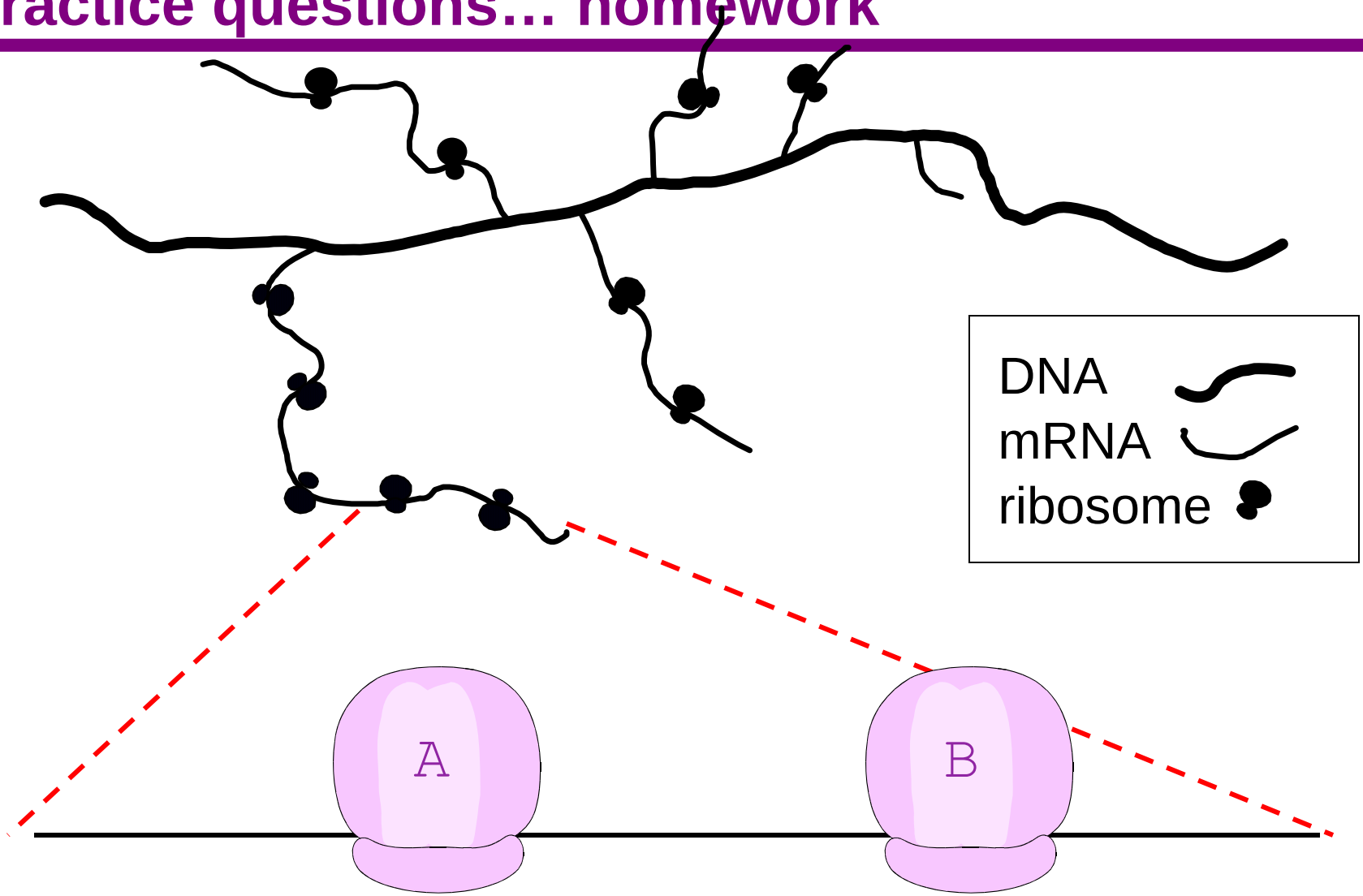
. . . in prokaryotes, like E. coli.



DNA

mRNAs covered
with ribosomes

Practice questions… homework



1. Label the 5’ and 3’ ends of the mRNA, then answer the following questions:

2. Which way (to the right or to the left) are ribosomes A and B moving?
3. Toward which end (left or right) is the AUG start codon?
4. Which ribosome (A or B) has the shorter nascent polypeptide?
5. Which end of the polypeptide (amino or carboxy) has not yet been synthesized?

Reading Frame: the ribosome establishes the grouping of nucleotides that correspond to codons by Start counting triplets from this base AUG ed.

Open Reading Frame: ORF: from the first AUG to the first in-frame stop. The ORF is the information for the protein.

More generally: a reading frame with a stretch of codons not interrupted by stop

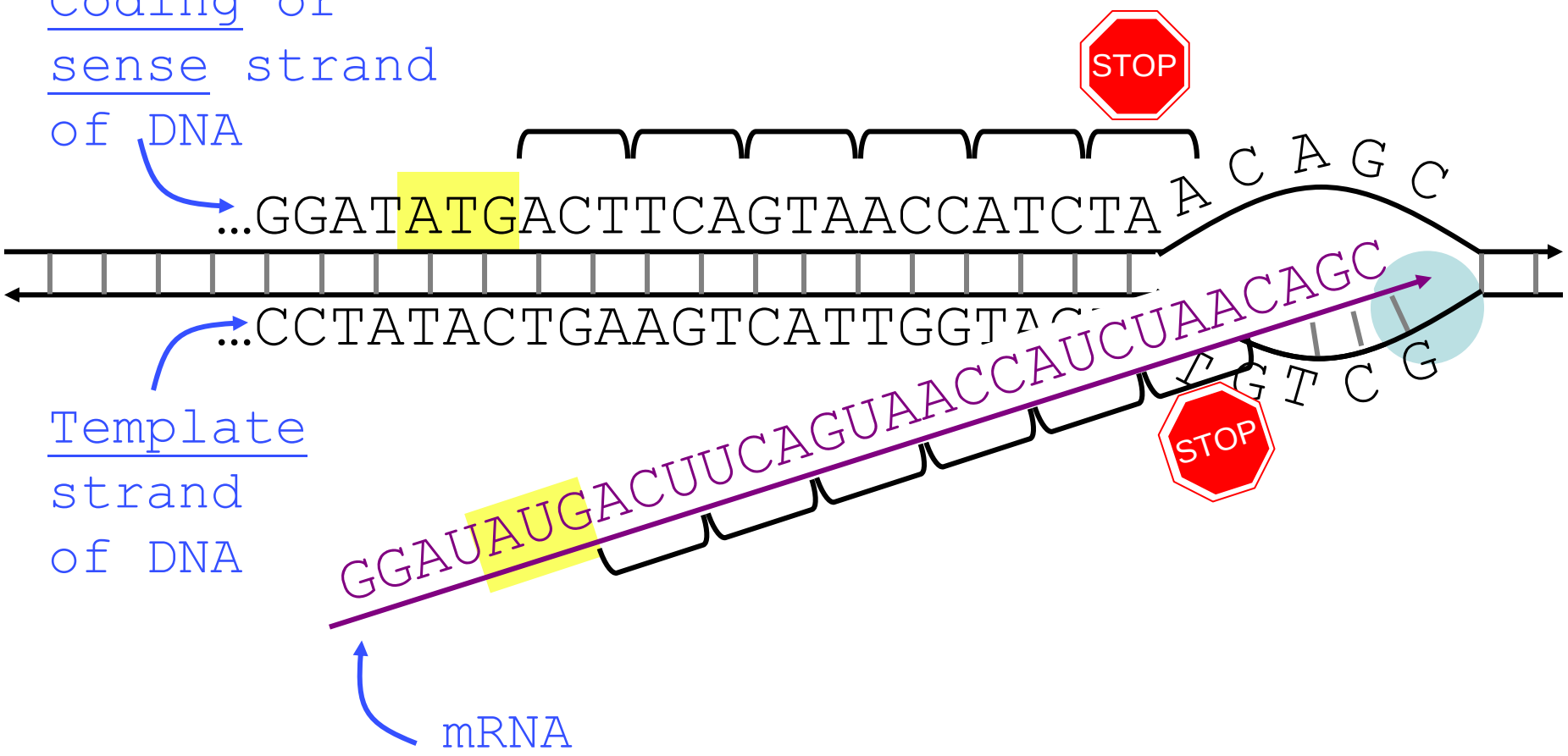
Looking for ORFs

- read the sequence 5′ → 3′, looking for stop
- try each reading frame
- since we know the genetic code—can do a virtual translation if necessary

Something to think about…

- what might the presence of introns do to our virtual translation?

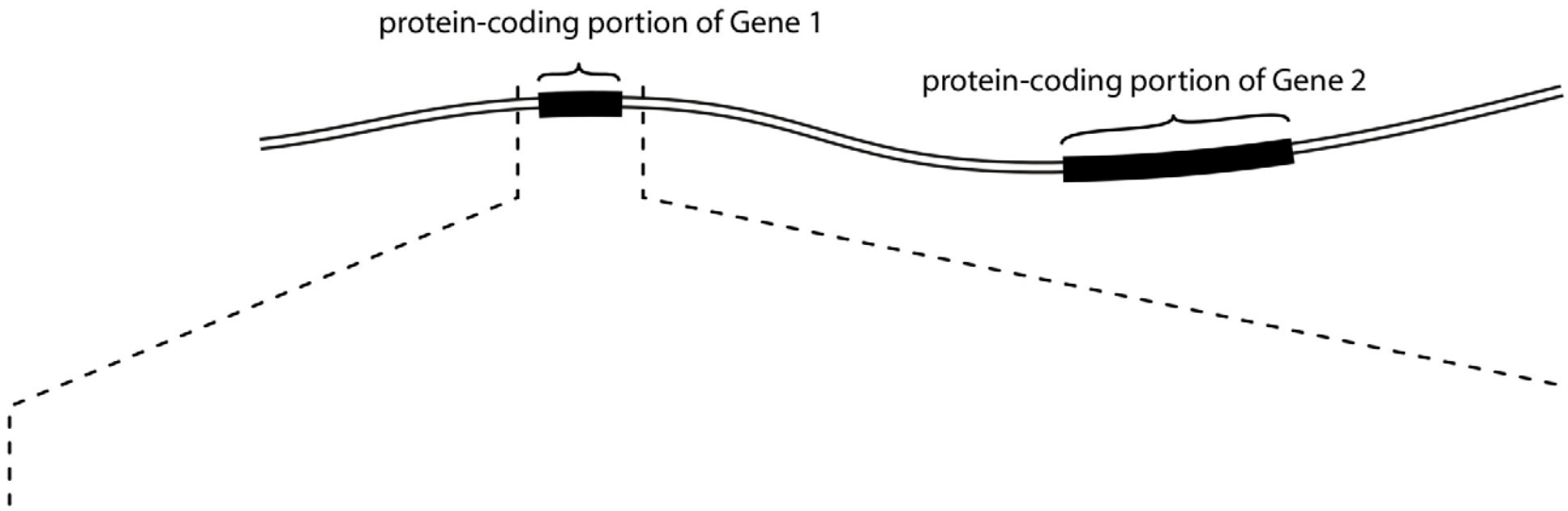
Identifying ORFs in DNA sequence



Looking for ORFs

Practice question

Practice questions



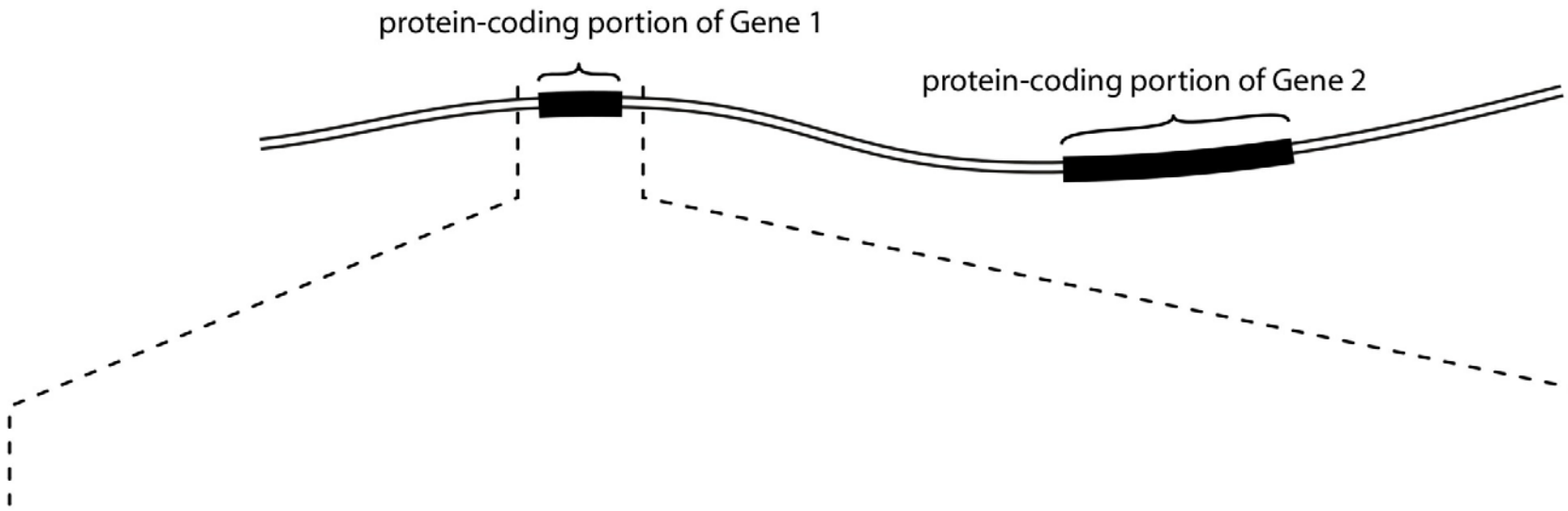
5'-GATTAAAAGAATGAGATTTCCTTCAATTTTTACTGCAGTTTTATTCGCATAAGCCCGACT-3'
3'-CTAATTTTCTTACTCTAAAGGAAGTTAAAAACTGCAGTAAAATAGCGAAGCTTACGGGA-5'

transcription

5'-AAAAGAAUGAGAUUUCCUUCAAUUUUUACUGCAGUUUUAUUCGCAUAAGCCCGACU-3'

1. Which strand on the DNA sequence is the coding (sense) strand? How can you tell?

Practice questions



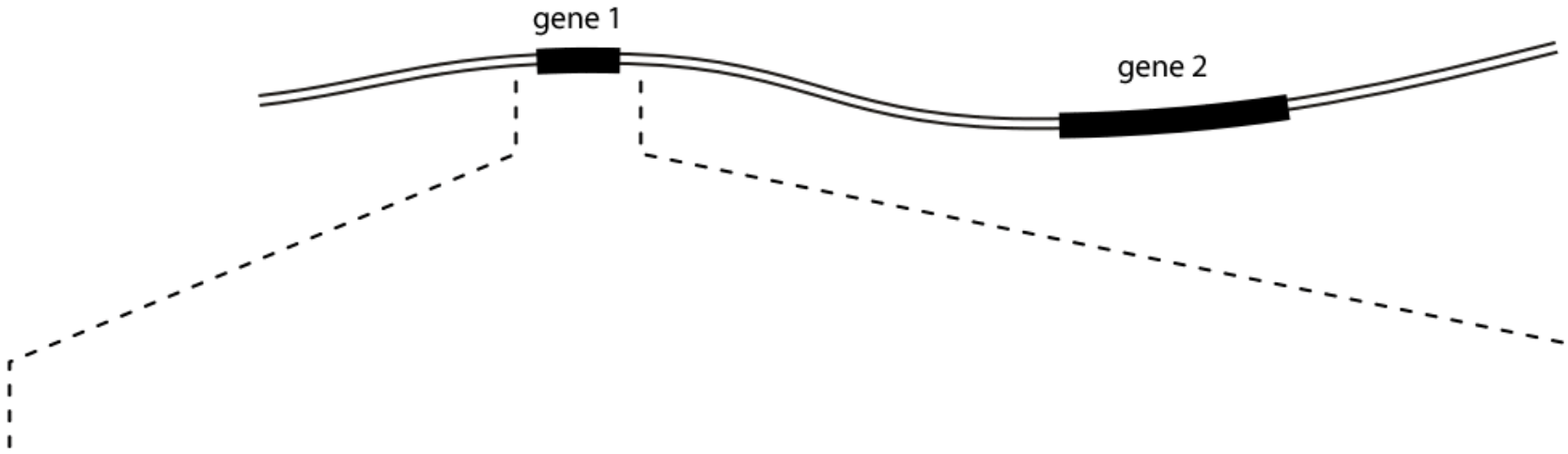
5'-GATTAAAAGAATGAGATTTCCTTCAATTTTTACTGCAGTTTTATTCGCATAAGCCCGACT-3'
3'-CTAATTTTCTTACTCTAAAGGAAGTTAAAAACTGCAGTAAAATAAGCGTATTCGGGCTA-5'

transcription

5'-AAAAGAAUGAGAUUUCCUUCAAUUUUUACUGCAGUUUUAUUCGCAUAAGCCCGACU-3'

2. On the DNA sequence, circle the nucleotides that correspond to the start codon.

Practice questions



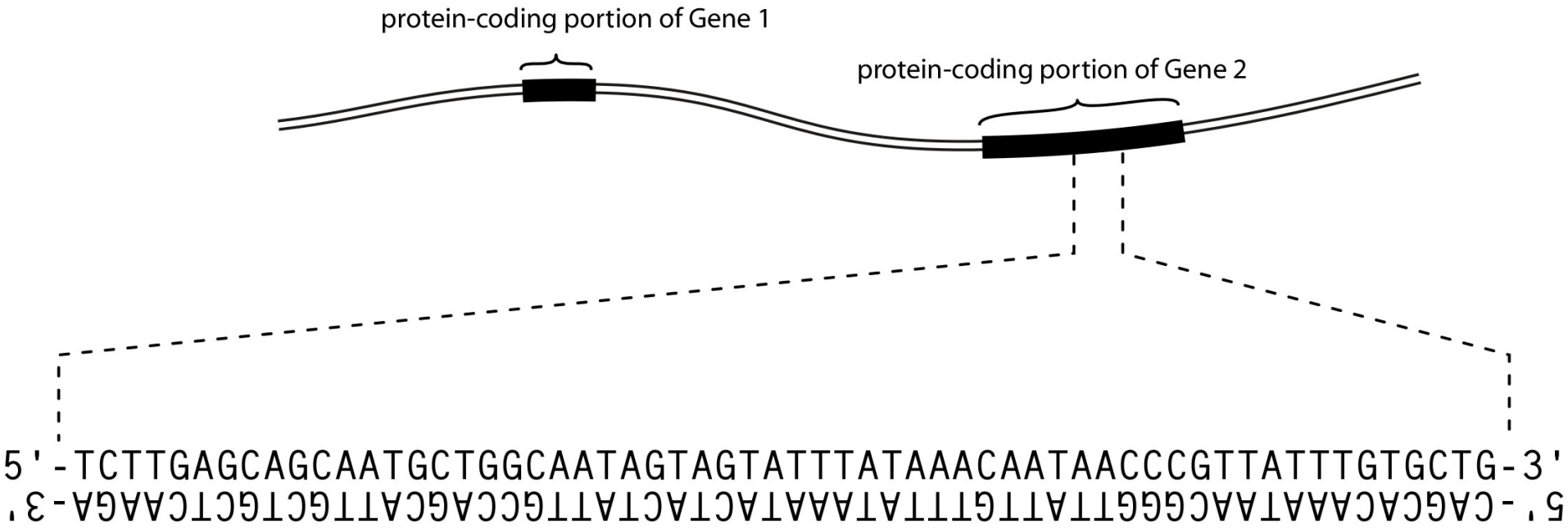
5'-GATTAAAAGAATGAGATTTCCTTCAATTTTTACTGCAGTTTTATTCGCATAAGCCCGACT-3'
3'-CTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAAATAAGCGGGCTTATC-5'

transcription

5'-AAAAGAAUGAGAUUUCCUUCAAUUUUUACUGCAGUUUUAUUCGCAUAAGCCCGACU-3'

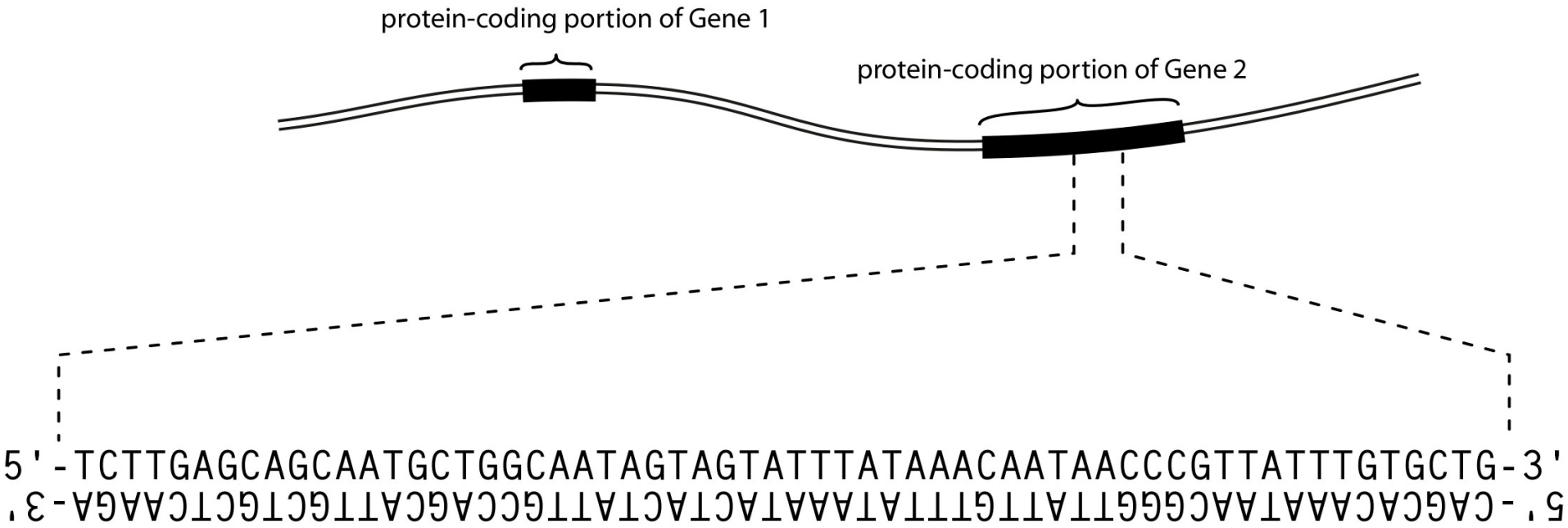
3. How many amino acids are encoded by this gene?

Practice questions



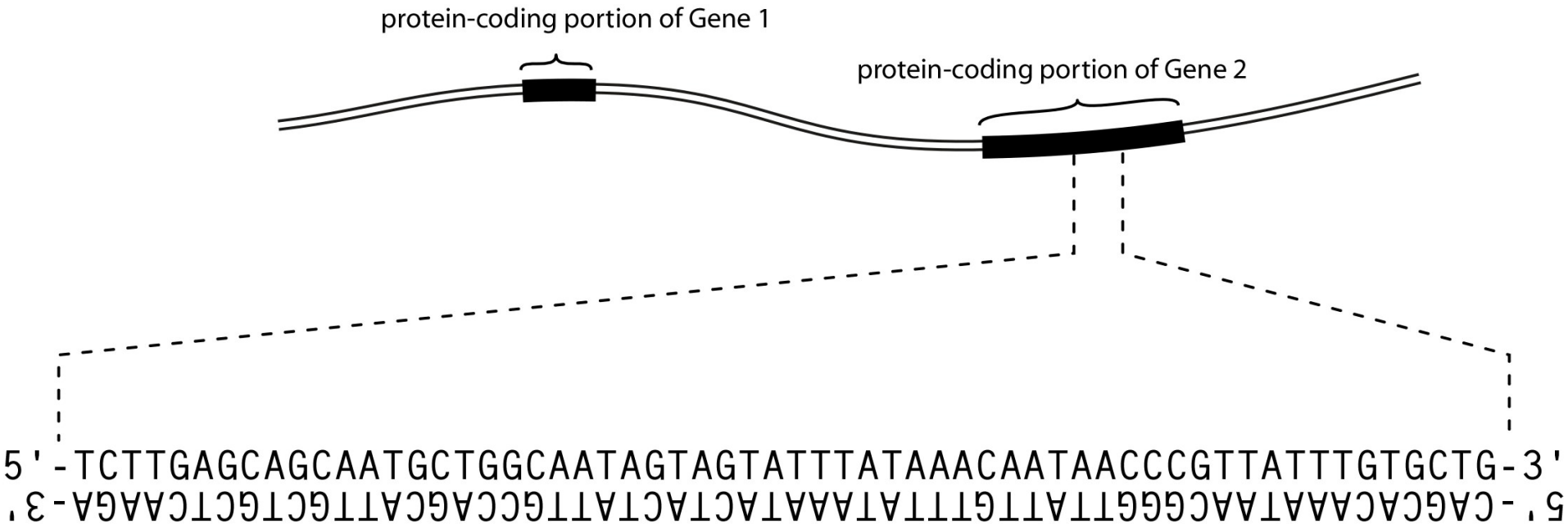
1. Do you expect the start and stop codons of gene 2 to be represented in the DNA sequence that is shown?

Practice questions



2. How many potential reading frames do you think this chunk of DNA sequence contains? How did you arrive at your answer? Would the answer be the same if you didn't know that this sequence came from the middle of a gene?

Practice questions



3. …

   On the appropriate strand, mark the codons for the portion of gene 2 that is shown.

Finding genes in DNA sequence

Warm-up to QS1

Given a chunk of DNA sequence…

GGGTATAGAAAATGAATATAAACTCATAGACAAGATCGGTGAGGGAACATTTTCGTCAGTGTATAAAGCCAAA
GATATCACTGGGAAAATAACAAAAAAATTTGCATCACATTTTTGGAATTATGGTTCGAACTATGTTGCTTTGAA
GAAAATATACGTTACCTCGTCACCGCAAAGAATTTATAATGAGCTCAACCTGCTGTACATAATGACGGGATCTT
CGAGAGTAGCCCCTCTATGTGATGCAAAAAGGGTGCGAGATCAAGTCATTGCTGTTTTACCGTACTATCCCCA
CGAGGAGTTCCGAACTTTCTACAGGGATCTACCAATCAAGGGAATCAAGAAGTACATTTGGGAGCTACTAAGA
GCATTGAAGTTTGTTCATTCGAAGGGAATTATTCATAGAGACATCAAACCGACAAATTTTTTATTTAATTTGGAA
TTGGGGCGTGGAGTGCTTGTTGATTTTGGTCTAGCCGAGGCTCAAATGGATTATAAAAGCATGATATCTAGTC
AAAACGATTACGACAATTATGCAAATACAAACCATGATGGTGGATATTCAATGAGGAATCACGAACAATTTTGT
CCATGCATTATGCGTAATCAATATTCTCCTAACTCACATAACCAAACACCTCCTATGGTCACCATACAAAATGG
CAAGGTCGTCCACTTAAACAATGTAAATGGGGTGGATCTGACAAAGGGTTATCCTAAAAATGAAACGCGTAGA
ATTAAAAGGGCTAATAGAGCAGGGACTCGTGGATTTCGGGCACCAGAAGTGTTAATGAAGTGTGGGGCTCAA
AGCACAAAGATTGATATATGGTCCGTAGGTGTTATTCTTTTAAGTCTTTTGGGCAGAAGATTTCCAATGTTCCA
AAGTTTAGATGATGCGGATTCTTTGCTAGAGTTATGTACTATTTTTGGTTGGAAAGAATTAAGAAAATGCGCAG
CGTTGCATGGATTGGGTTTCGAAGCTAGTGGGCTCATTTGGGATAAACCAAACGGATATTCTAATGGATTGAA
GGAATTTGTTTATGATTTGCTTAATAAAGAATGTACCATAGGTACGTTCCCTGAGTACAGTGTTGCTTTTGAAA
CATTCGGATTTCTACAACAAGAATTACATGACAGGATGTCCATTGAACCTCAATTACCTGACCCCAAGACAAAT
ATGGATGCTGTTGATGCCTATGAGTTGAAAAAGTATCAAGAAGAAATTTGGTCCGATCATTATTGGTGCTTCCA
GGTTTTGGAACAATGCTTCGAAATGGATCCTCAAAAGCGTAGTTCAGCAGAAGATTTACTGAAAACCCCGTTT
TTCAATGAATTGAATGAAAACACATATTTACTGGATGGCGAGAGTACTGACGAAGATGACGTTGTCAGCTCAA
GCGAGGCAGATTTGCTCGATAAGGATGTTCT

How do you find out if it contains a gene? How do you identify the gene?

Finding sense in nonsense

cbdryloiaucahjdhtheflybitthedogbutnotthecatjhnhajctipheq

Finding genes in DNA sequence

Warm-up to QS1

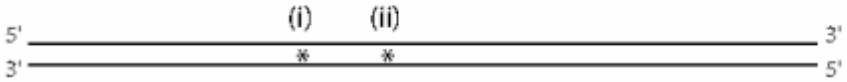
Given a chunk of DNA sequence…

GGGTATAGAAAATGAATATAAACTCATAGACAAGATCGGTGAGGGAACATTTTCGTCAGTGTATAAAGCCAAA
GATATCACTGGGAAAATAACAAAAAAATTTGCATCACATTTTTGGAATTATGGTTCGAACTATGTTGCTTTGAA
GAAAATATACGTTACCTCGTCACCGCAAAGAATTTATAATGAGCTCAACCTGCTGTACATAATGACGGGATCTT
CGAGAGTAGCCCCTCTATGTGATGCAAAAAGGGTGCGAGATCAAGTCATTGCTGTTTTACCGTACTATCCCCA
CGAGGAGTTCCGAACTTTCTACAGGGATCTACCAATCAAGGGAATCAAGAAGTACATTTGGGAGCTACTAAGA
GCATTGAAGTTTGTTCATTCGAAGGGAATTATTCATAGAGACATCAAACCGACAAATTTTTTATTTAATTTGGAA
TTGGGGCGTGGAGTGCTTGTTGATTTTGGTCTAGCCGAGGCTCAAATGGATTATAAAAGCATGATATCTAGTC
AAAACGATTACGACAATTATGCAAATACAAACCATGATGGTGGATATTCAATGAGGAATCACGAACAATTTTGT
CCATGCATTATGCGTAATCAATATTCTCCTAACTCACATAACCAAACACCTCCTATGGTCACCATACAAAATGG
CAAGGTCGTCCACTTAAACAATGTAAATGGGGTGGATCTGACAAAGGGTTATCCTAAAAATGAAACGCGTAGA
ATTAAAAGGGCTAATAGAGCAGGGACTCGTGGATTTCGGGCACCAGAAGTGTTAATGAAGTGTGGGGCTCAA
AGCACAAAGATTGATATATGGTCCGTAGGTGTTATTCTTTTAAGTCTTTTGGGCAGAAGATTTCCAATGTTCCA
AAGTTTAGATGATGCGGATTCTTTGCTAGAGTTATGTACTATTTTTGGTTGGAAAGAATTAAGAAAATGCGCAG
CGTTGCATGGATTGGGTTTCGAAGCTAGTGGGCTCATTTGGGATAAACCAAACGGATATTCTAATGGATTGAA
GGAATTTGTTTATGATTTGCTTAATAAAGAATGTACCATAGGTACGTTCCCTGAGTACAGTGTTGCTTTTGAAA
CATTCGGATTTCTACAACAAGAATTACATGACAGGATGTCCATTGAACCTCAATTACCTGACCCCAAGACAAAT
ATGGATGCTGTTGATGCCTATGAGTTGAAAAAGTATCAAGAAGAAATTTGGTCCGATCATTATTGGTGCTTCCA
GGTTTTGGAACAATGCTTCGAAATGGATCCTCAAAAGCGTAGTTCAGCAGAAGATTTACTGAAAACCCCGTTT
TTCAATGAATTGAATGAAAACACATATTTACTGGATGGCGAGAGTACTGACGAAGATGACGTTGTCAGCTCAA
GCGAGGCAGATTTGCTCGATAAGGATGTTCT

How do you find out if it contains a gene? How do you identify the gene?

Practice question (homework)

The diagram below represents the region of cat genomic DNA that contains the *tyrosinase* gene (needed for fur pigment production). The asterisks marked (i) and (ii) show the locations of two mutations that have been found in this gene (in separate cats). Mutation (i) causes fur pigmentation to be much more intense than normal, but no amino acid changes were found in the tyrosinase protein in this mutant. Mutation (ii) is a TCA→TGA change that results in a truncated, non-functional protein.



(a) Based on what you have been told about mutation (i), suggest a hypothesis to explain the altered fur phenotype.

(b) Mark the start codon of the tyrosinase gene in the diagram above by drawing a small circle at its approximate location on the **coding strand**. Your answer here should not contradict your answer in (a).

(c) In the close-up representation of a transcription bubble in the tyrosinase gene (below), mark the coding (sense) and template strands... again, consistent with your answer in (a). Draw a circle to mark the location of the RNA polymerase and draw a short RNA transcript with its 5' and 3' ends marked. Is the promoter to the left or to the right? Circle one: Left Right

(d) The picture below represents electron micrographs of tyrosinase mRNAs from the two mutants (i and ii) as they are being translated by ribosomes. [The proteins being made are not shown.] Both mRNAs are in the same orientation (i.e., both have their 5' ends on the same side). Identify which mRNA is from which mutant. Then mark the 5' and 3' ends on one of the mRNAs and put a box around the approximate location of the start codon.