Diversity and Strategies of Viral Genomes

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Abstract

In the first two activities, students working in small groups receive a series of model viruses. These include each of several types of nucleic acid genomes (DNA/RNA, ds/ss, +/- strands). In one set of activities, students sequentially examine the variety of modes by which the genomes are replicated and the dependence of mechanism upon the form of nucleic acid. In a second series of activities, small groups examine the steps in the normal flow of information from cellular genes to mRNA. Students then examine viral genomes of different compositions and identify how the message is made once the genome has entered the host cell. In the third activity, students are given a hypothetical protein, then they are directed to back-translate from the amino acid sequence to the original viral nucleic acid sequence found in that specific virus.

Activity

Invitation for User Feedback. If you have used the activity and would like to provide feedback, please send an e-mail to MicrobeLibrary@asmusa.org. Feedback can include ideas which complement the activity and new approaches for implementing the activity. Your comments will be added to the activity under a separate section labeled "Feedback." Comments may be edited.

Editor's Note (2008): This Curriculum Resource was published prior to establishment of current criteria of submission, and as such, does not contain all criteria required of current publications. However, the Editorial Committee felt that the activity itself remained worthwhile and relevant, and encourages potential users to contact the authors for clarification as needed. If you do update this activity for use with your students, and are interested in updating the resource for distribution in the library, please contact ASM at MicrobeLibrary@asmusa.org.

INTRODUCTION

Time Required.
Activity 1. 30 to 45 minutes
Activity 2. 20 to 35 minutes
Activity 3. 20 to 35 minutes

Pedagogical Function.
This activity was designed to help students understand the diversity of viral genomes and to identify strategies required for successful replication. Exploration of these viral lifestyles in a laboratory setting would be inaccessible for reasons of safety, time, and money. In lieu of direct experimentation, these exercises engage students by assigning them the jobs required for production of a new generation of viral particles. It thus gives students a venue for exploring the non-"central dogmatic" means by which viruses express and replicate themselves.

Learning Objectives.
At the completion of these activities, students should be able to:

- identify and differentiate pathways required for replication and expression of viruses which are RNA or DNA containing, single stranded, or double stranded, or of retroviruses.
- understand concepts of genome diversity (such as nucleic acid type, sense/antisense strandedness) and directionality (5'—> 3') of individual strands.

Background.
Before beginning any of these activities, students should be familiar with basic steps in the process of viral infection. They should also be aware that viral nucleic acids exist in an array of forms (Appendix 2) and that viruses can be classified by their genome structure (Appendix 3). The instructor may wish to introduce the students to the specific concepts pursued in these activities; namely, the steps in viral replication are dependent on genome structures (Appendix 4), and viral

transcription and translation strategies are dependent on genome structures (Appendices 5 and 6). Any of these appendices may be used as a student handout to supplement the instructions, or they can be used as visuals during pre- or postactivity discussion. Alternatively, these latter concepts may be more fully developed following the activities.
Appendix 2. Viral nucleic acids exist in an array of forms
Appendix 3. Viruses can be classified by genome structure
Appendix 4. The steps in viral replication are dependent on genome structures
Appendix 5. Viral transcription strategies are dependent upon genome structures (version 1) - expanded version with brief descriptions
Appendix 6. Viral transcription strategies are dependent upon genome structures (version 2) - condensed version

Activity 1. Before assigning the project, students should know the basics of nucleic acid structure (bases, base-pairing) and the canonical mechanism of DNA replication.

Activities 2 and 3. Before receiving the assignment, students should have covered the basics of nucleic acid structure (bases, complementary base-pairing for DNA and RNA), directionality (5'—> 3'), and sense vs. antisense (+ and -) strands. They should also be familiar with transcription and translation and with use of a codon table (Figures 7, 8, and 9).
Figure 7
Figure 8
Figure 9

PROCEDURE

Materials.
Activities 1 and 2. Instructions and worksheets for students to record results (Figures 1-5); tape; twelve 12- to 16-oz. drinking cups per team (one pair for each of six viral types); strips of paper in each of two colors (one color is RNA, the other is DNA), on which the written sequence of a small region of genetic material is typed for each of the six viral genome types to be demonstrated (see below).
Figure 1. Replication of Viral Genomes - Instructions
Figure 2. Viral Replication Worksheet (version 1). Identify an example virus, its associated disease, and the steps in its replication
Figure 3. Viral Replication Worksheet (version 2). Identify the steps in replication of a group of viruses
Figure 4. Preparation for Viral Transcription - Instructions
Figure 5. Preparation for Viral Transcription Worksheet

Genome types: see Appendix 1
Appendix 1. Steps in Activity 1

a. (-) strand DNA
b. (+) strand DNA
c. (+) strand RNA
d. (-) strand RNA
e. (+) strand of RNA of a retrovirus
f. double-stranded DNA

Sample sequence: 5'....AUGCAUGGAUCCAAAGGUAACUAA....3'

Activity 3. Instructions to students, worksheets for students to record results, and a codon table (Figures 6-10).
Figure 6. Back-Translation - Instructions
Figure 7. Back-Translation - Worksheet
Figure 8. Genetic Code Table RNA Codons and Corresponding Amino Acids
Figure 9. Codon Table for Back-Translation, version 1. An expanded and alphabetical listing of the single letter amino acid symbols and their associated codons
Figure 10. Codon Table for Back-Translation, version 2. A compact listing of the single letter amino acid symbols and their associated codons

Instructor Version.
Activity 1. Replication of viral genomes.
Students of mixed abilities will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to examine the variety of modes by which genomes of different nucleic acid structure are replicated.
Figure 1
Figure 2
Figure 3

Activity 2. Preparation for viral transcription.
Students of mixed ability will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to examine the normal flow of information from genes in cellular DNA to mRNA. They will then examine the steps completed by viruses.
Figure 4
Figure 5

Activity 3. Back-translation.
Students of mixed ability will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to convert a hypothetical protein to the nucleic acid form found in a specific virus.
Figure 6
Figure 7
Figure 8
Figure 9
Figure 10

Safety Issues. Not applicable.

ASSESSMENT and OUTCOMES

Suggestions for Assessment.

- Peer oral assessment is incorporated into the activities through group discussion and whole-class discussion and feedback.
- Immediate instructor feedback is incorporated in the "check-in" at the completion of each example; students must successfully complete each "genome" before receiving the next one.
- Concepts can be included on a subsequent quiz or exam.

Problems and Caveats.
Activity 1. Replication of viral genomes.
Students of mixed abilities will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to examine the variety of modes by which genomes of different nucleic acid structure are replicated.

1. Student teams receive a virus from the instructor's station composed of a paper strip (genome)encapsulated by a "capsid" made of two drinking cups taped together; the tape acts as "structural links." The team then "infects" a host cell, opening the "virion" and releasing the "genome" paper strip. The "genome" is labeled by its type (+ or - strand, RNA or DNA, single strand [ss] or double strand [ds], and it has a short nucleotide sequence "encoded."

2. Students will identify the next steps that occur, resulting in production of a replica genome. They accomplish this by writing the appropriate complementary sequence on the appropriate colored blank "genome" strip. They should also individually record these data on a worksheet (Figure 2 or 3) that they will submit for review. The worksheet should include spaces for them to describe the attributes of the genome of the original virion and space in which they sequentially list all steps in production of the new genome by writing the current sequence.
Figure 2
Figure 3

3. When the team believes they have correctly generated *all* the sequential intermediates *and* the replica genome, they take all the strips to the instructor. The instructor compares the submission to a key, checking for correct types, order of steps, directionality (5' to 3'), and sequence (T in DNA, U in RNA) of all sequences.

4. If correct, the instructor initials the assignment list, and the group receives the next virus. Each group should do at least a few viruses, depending on time available and how long it takes to get correct results. The same process is continued through the series.

Activity 2. Preparation for viral transcription.
Students of mixed ability will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to examine the normal flow of information from genes in cellular DNA to mRNA. They will then examine the steps completed by viruses.

1. Students begin by receiving a pair of narrow strips of paper labeled "+DNA" and "-DNA". These will feature complementary sequences to include a start codon, coding sequence, and a stop codon. They must then generate a message by writing the sequence of the (+) strand of RNA on the worksheet (such as Figure 7). They must also describe the fate of the mRNA–it will leave the nucleus and participate in translation on a ribosome (free in cytoplasm or bound to endoplasmic reticulum). Finally, they must translate the mRNA into a protein, using a codon table (Figure 8, 9, or 10). Students must submit the top portion of the worksheet for verification by the instructor before they receive the second portion of this assignment. The correctly completed first section will include original DNA strips taped on; written mRNA sequence, answers to requested items about stages (initial location, next steps in series; names of enzymes; changes in location; amino acid composition of protein). They thus need to demonstrate competence with the relationship of the cellular genome to mRNA, movement of mRNA from nucleus to cytoplasm, and colinearity of nucleic acids and amino acids in protein product.
Figure 7
Figure 8
Figure 9
Figure 10

2. Students will next identify the pathways for mRNA synthesis that occur when a viral genome enters a host cell. Student teams, upon successful completion of step 1, will receive a "virion" from the instructor: paper strip "genome" encapsulated by a two-drinking-cup "capsid" taped shut. Students "infect" a cell and must identify the subsequent steps necessary for transcription of this material to occur and the sequences generated for the final protein product and for any nucleic acid intermediates. Once complete, students again submit their results (the correct nucleic acid sequences, correct order of events, correct types and order of nucleic acid intermediates, correct protein sequence) to the instructor. Once successful, they receive the next virus. They sequentially work through the following viral types: (+) ss DNA virus, ds DNA virus, (-) ss RNA virus, and a (+) ss RNA virus.

Activity 3. Back-translation.
Students of mixed ability will work in small groups (size to vary; cap at 10 teams per class) in a guided design activity to convert a hypothetical protein to the nucleic acid form found in a specific virus.

1. Students begin by receiving the name of a virus and the amino acid sequence of a hypothetical protein from that virus. First they need to identify the virus and thus identify the form of viral nucleic acid found inside mature virions.

2. Using the amino acid sequence, students next will write out the mRNA sequence used to make the polypeptide. Several different versions of codon tables are included.

3. They need to evaluate this and decide if this is the form of nucleic acid to be packaged, based on the virus assigned to their team. If not, they must convert to the final nucleic acid form, i.e., DNA or RNA, ss or ds, and (+) or (-) strand before

submitting it for verification.

SUPPLEMENTARY MATERIALS

Possible Modifications.
Each activity may be divided among several groups, with each group working with a different virus. After all groups have completed the various stages of nucleic acid conversion required, there can be a class-wide debriefing, in which each group describes their assigned virus and the various strategies required to produce the next generation.

Alternatively, have students critique other students' work to determine if they have figured out the appropriate replication scheme or the appropriate protein. The instructor can verify, but additional learning can go on by having students critique one another.

The amount of detail required can be varied, based on time available and also on background of students. The two different versions of the worksheet for Activity 1 vary by the amount of information the students must supply and also by the amount of prompting given to them in soliciting answers. Examples are given of additional supporting material that can be used by faculty in preactivity lectures or that can be distributed to students.

Activity 2 can be modified by altering the sequence presented to the students in each part of the assignment. Specifically, the nucleic acid sequences can be manipulated to generate protein sequences with hidden phrases when transcribed and then translated using the single-letter alphabet symbol designations for the amino acids. This can be accomplished by back-translation – starting with the known (or desired) protein sequence and then identifying the corresponding RNA and DNA sequences. Traditionally, this has been done with a codon table (Figure 8); included here are two alternate presentations (Figures 9 and 10) in which the one-letter amino acid designations are listed alphabetically. Limits on the phrases possible are imposed by the lack of four letters (no J, O, U, or X) and the ambiguity associated with two letters (B and Z). However, wide arrays of messages are possible, and a small collection is included in Appendix 7, with all stages for these messages written in Appendix 8.
Figure 8
Figure 9
Figure 10
Appendix 7. Example Messages for Activities 2 & 3 (Hidden Messages) - no answers
Appendix 8. Example Messages for Activities 2 & 3 (Hidden Messages) - includes nucleic acid sequences

The identity of the virus or the protein sequence given to the students can be altered to modify Activity 3. Further, students can be instructed to construct their own polypeptide (their own secret message).

References
References

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Figure 1. Replication of Viral Genomes - Instructions

In this activity, you and the members of your team will examine the variety of mechanisms used by viruses for replication of their genomes. To begin, your team should receive a worksheet for recording your work. Please write the names of your team's members on the worksheet. You will also receive a "virus" from the instructor. Within the virus "capsid," you will find the viral "genome."

1. First, you need to observe and identify your virus and its pertinent characteristics.

- Tape the "genome" to the worksheet.
- Identify the "virus."
- Summarize the characteristics of the "genome" – DNA or RNA; ds or ss; (+) or (-) strand.

2. Next, you need to describe the steps in replication of the genome.

- Name the enzyme responsible for the next step – [DNA/RNA] – dependent [DNA/RNA] polymerase.
- Identify the source of the enzyme – host-encoded or viral-encoded.
- Write out the sequence of the nucleic acid synthesized by this enzyme.

3. Examine this product.

- Is this the final form of nucleic acid that will be packaged in new virions?
- If it is, submit your worksheet to the instructor for verification.
- If it is not the final sequence, repeat the preceding set of steps until you produce the final form.

After your instructor has verified your "replication" of the viral genome; you will receive another virus. Repeat these three sections for each virus your team is assigned to analyze.

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Figure 2.Viral Replication Worksheet (version 1)

Identify an example virus, its associated disease, and the steps in its replication.

Team members:

Virus ID:
Name an EXAMPLE virus:
Name the resulting DISEASE:
Tape the genome here. ß

Summary of genome characteristics (circle *one* of each):

DNA *or* RNA
(ds) *or* (ss)
(+) *or* (-)

Next step:
a) Identify the enzyme: [DNA/RNA] dependent [DNA/RNA] polymerase.

b) Identify the source of the enzyme: [host/virus]-encoded.

Write out the next sequence here. ß

Is this the finished replicated form of this genome?
If yes, submit this to your instructor.
If not, continue.

Next step:
a) Identify the enzyme: [DNA/RNA] dependent [DNA/RNA] polymerase.

b) Identify the source of the enzyme: [host/virus]-encoded.

Write out the next sequence here. ß

Is this the finished replicated form of this genome?
If yes, submit this to your instructor.
If not, continue on the back of this page.

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Figure 3. Viral Replication Worksheet (version 2)

Identify the steps in replication of a group of viruses.

Team members:

Virus ID:

Tape the genome here. ß

Summary of genome characteristics (circle *one* of each):

DNA *or* RNA
(ds) *or* (ss)
(+) *or* (-)

Write out the next sequence here. ß

Is this the finished replicated form of this genome?
If yes, submit this to your instructor.
If not, continue.

Write out the next sequence here. ß

Is this the finished replicated form of this genome?
If yes, submit this to your instructor.
If not, continue.

Write out the next sequence here. ß

Is this the finished replicated form of this genome?
If yes, submit this to your instructor.

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Figure 4. Preparation for Viral Transcription - Instructions

In this activity, you and the members of your team will examine the variety of mechanisms used by viruses to transcribe their genomes once they are inside a host cell. To begin, your team should receive a worksheet for recording your work. Please record the names of your team members. You will also receive a codon table to aid you in translating nucleic acid sequences into amino acid sequences. Begin by examining transcription of a "normal" gene from a host cell.

1. First, examine the host DNA.

- Tape the "gene" to the worksheet.
- Write the sequence of the mRNA transcribed from this gene.
- Describe the next steps:

  Where is this mRNA located within the cell?
  What happens to it next?
  What polymerase was used for transcription?
  Does the mRNA change locations within the cell?

- Write the sequence of the protein translated from this gene, using the codon table.
- Submit your worksheet to the instructor for verification.

2. You will receive a "virus" from the instructor. Within the virus "capsid", you will find the viral "genome." You need to observe and identify your virus and its pertinent characteristics.

- Tape the "genome" to the worksheet.
- Identify the "virus."
- Summarize the characteristics of the "genome" – DNA or RNA; ds or ss; (+) or (-) strand.

3. Next, you need to describe the steps in transcription of the genome.

- Write out any changes in the nucleic acid between the genome and the mRNA.
- Identify the steps.
- Name the enzyme responsible for producing the viral mRNA.
- Identify the location of these steps within the cell.
- Identify the source of the enzyme – host-encoded or viral-encoded.
- Write the sequence of the protein translated from this gene, using the codon table.
- Submit your worksheet to the instructor for verification.

After your instructor has verified your "replication" of the viral genome; you will receive another virus. Repeat sections 2 and 3 for each virus your team is assigned to analyze.

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Figure 5. Preparation for Viral Transcription Worksheet

Team members:

Part 1. Cellular transcription

Tape host (cellular) DNA "strands" here. ß

Write sequence of mRNA here. ß (5'Þ 3')

Next steps:

a. Name the current location of the mRNA in the cell.
b. Name the next steps in sequence.
c. Name the polymerases used in transcription.
d. Identify any changes in location of the mRNA in the cell.
e. Translate the mRNA into protein.

Write the protein sequence here. ß

Instructor initials ___

Part 2. Viral transcription

Virus ID:

Tape the viral genome here. ß

Write out any changes in nucleic acid form (from genome to mRNA) here. ß (5'Þ 3')

Next steps:

a. Identify the steps in series from viral nucleic acid to mRNA.
b. Name the enzyme(s) involved in producing the viral mRNA.
c. Identify the location of all events in the cell.
d. Name the source(s) of the enzyme(s).
e. Translate the mRNA into protein.

Write the protein sequence here. ß

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Figure 6. Back-Translation - Instructions

In this activity, you and the members of your team will convert the amino acid sequence of a polypeptide into the nucleic acid sequence of a designated virus. To begin, your team should receive a worksheet for recording your work. Please record the names of your team members. You will also receive a codon table to aid you in back-translating from amino acid sequence to nucleic acid sequence.

Note: In the spelling of some "proteins", a little latitude was exercised to obtain some phrases. This is due to the absence of four English alphabet letters (J, O, U, and X) from the single letter codes for amino acids. In addition, two letters (B and Z) are used to represent pairs of amino acids (B = asparagine and/or aspartic acid; Z= glutamine and/or glutamic acid).

1. First, examine the virus and the polypeptide sequence.

- Tape the "protein" to the worksheet.
- Summarize the characteristics of the "genome" – DNA or RNA; ds or ss; (+) or (-) strand.

2. Next, convert the amino acid sequence into an mRNA sequence.

- Write the mRNA sequence that would have been used to generate the "protein" using the codon table.
- Is this the final form of nucleic acid that will be packaged in new virions?
- If it is, submit your worksheet to the instructor for verification.

3. If this is not the final form of nucleic acid to be packaged in new virions, repeat the preceding set of steps until you produce the final form. When complete, submit your worksheet to the instructor for verification.

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Figure 7. Back-Translation Worksheet

Team members:

Tape the viral "protein" here. ß

Identify the virus.

Write sequence of mRNA here. ß (5' 3')

Next steps:

a. Name the current location of the mRNA in the cell.
b. Name the next steps in sequence.
c. Name the polymerases used in transcription.
d. Identify any changes in location of the mRNA in the cell.
e. Translate the mRNA into protein.

Write the protein sequence here. ß

Instructor initials ___

Part 2. Viral transcription

Virus ID:

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Figure 8. Genetic Code Table RNA Codons and Corresponding Amino Acids

First Base (5' end) ß	Second Base				Third Base (3' end) ß
	U	C	A	G	
U	Phe / F	Ser / S	Tyr /Y	Cys / C	U
	Phe / F	Ser / S	Tyr /Y	Cys / C	C
	Leu / L	Ser / S	{term}	{term}	A
	Leu / L	Ser / S	{term}	Trp / W	G
C	Leu / L	Pro / P	His / H	Arg / R	U
	Leu / L	Pro / P	His / H	Arg / R	C
	Leu / L	Pro / P	Gln / Q	Arg / R	A
	Leu / L	Pro / P	Gln / Q	Arg / R	G
A	Ile / I	Thr /T	Asn / N	Ser / S	U
	Ile / I	Thr /T	Asn / N	Ser / S	C
	Ile / I	Thr /T	Lys / K	Arg / R	A
	Met / M	Thr /T	Lys / K	Arg / R	G
G	Val / V	Ala /A	Asp / D	Gly / G	U
	Val / V	Ala /A	Asp / D	Gly / G	C
	Val / V	Ala /A	Glu / E	Gly / G	A
	Val / V	Ala /A	Glu / E	Gly / G	G

{term} = termination codon

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Figure 9. Reverse Translation Table – (Version 1) An expanded and alphabetical listing of the single letter amino acid symbols and their associated codons (a.k.a. - Code Your Own Protein Messages)

Alphabet Symbols	J,O,U,X	A			B*		
Amino Acids	*Not used.*	Alanine			Asparagine &/or Aspartic acid		
RNA Sequences		G	C	U C A G	G A	A	U C
DNA Sequences		G	C	T C A G	G A	A	T C

Alphabet Symbols	C			D			E			F		
Amino Acids	Cysteine			Aspartic acid			Glutamic acid			Phenylalanine		
RNA Sequences	U	G	U C	G	A	U C	G	A	A G	U	U	U C
DNA Sequences	T	G	T C	G	A	T C	G	A	A G	T	T	T C

Alphabet Symbols	G	H	I	K

Amino Acids	Glycine			Histidine			Isoleucine			Lysine		
RNA Sequences	G	G	U C A G	C	A	U C	A	U	U C A	A	A	A G
DNA Sequences	G	G	T C A G	C	A	T C	A	T	T C A	A	A	A G

Alphabet Symbols	L			M			N			P		
Amino Acids	Leucine			Methionine			Asparagine			Proline		
RNA Sequences	U	U	A G	A	U	G	A	A	U C	C	C	U C A G
	C	U	U C A G									
DNA Sequences	T	T	A G	A	T	G	A	A	T C	C	C	T C A G
	C	U	T C A G									

Alphabet Symbols	Q	R	S	T

Amino Acids	Glutamine			Arginine			Serine			Threonine		
RNA Sequences	C	A	A G	C	G	U C A G	U	C	U C A G	A	C	U C A G
				A	G	A G	A	G	U C			
DNA Sequences	C	A	A G	C	G	T C A G	T	C	T C A G	A	C	T C A G
				A	G	A G	A	G	T C			

Alphabet Symbols	V			W			Y			Z*		
Amino Acids	Valine			Tryptophan			Tyrosine			Glutamine &/or Glutamic acid		
RNA Sequences	G	U	U C A G	U	G	G	U	A	U C	G C	A	A G
DNA Sequences	G	T	T C A G	T	G	G	T	A	T C	G C	A	A G

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Figure 10. Reverse Translation Table (Version 2) A compact listing of the single letter amino acid symbols and their associated codons (a.k.a. - Code Your Own Protein Messages)

Alphabet Symbol	Amino Acid	RNA Sequences	DNA Sequences
J, O, U, X	*not used*	*none*	*none*
A	Alanine	GCU, GCC, GCA, GCG	GCT, GCC, GCA, GCG
B	Asparagine &/or Aspartic acid	GAU, GAC, AAU, AAC	GAT, GAC, AAT, AAC
C	Cysteine	UGU, UGC	TGT, TGC
D	Aspartic acid	GAU, GAC	GAT, GAC
E	Glutamic acid	GAA, GAG	GAA, GAG
F	Phenylalanine	UUU, UUC	TTT, TTC
G	Glycine	GGU, GGC, GGA, GGG	GGT, GGC, GGA, GGG
H	Histidine	CAU, CAC	CAT, CAC
I	Isoleucine	AUU, AUC, AUA	ATT, ATC, ATA
K	Lysine	AAA, AAG	AAA, AAG
L	Leucine	UUA, UUG, CUU, CUC, CUA, CUG	TTA, TTG, CTT, CTC, CTA, CTG
M	Methionine	AUG	ATG
N	Asparagine	AAU, AUC	AAT, ATC
P	Proline	CCU, CCC, CCA, CCG	CCT, CCC, CCA, CCG
Q	Glutamine	CAA, CAG	CAA, CAG
R	Arginine	CGU, CGC, CGA, CGG, AGA, AGG	CGT, CGC, CGA, CGG, AGA, AGG
S	Serine	UCU, UCC, UCA, UCG, AGU, AGC	TCT, TCC, TCA, TCG, AGT, AGC
T	Threonine	ACU, ACC, ACA, ACG	ACT, ACC, ACA, ACG
V	Valine	GUU, GUC, GUA, GUG	GTT, GTC, GTA, GTG
W	Tryptophan	UGG	TGG
Y	Tyrosine	UAU, UAC	TAT, TAC
Z	Glutamine &/or Glutamic acid	GAA, GAG, CAA, CAG	GAA, GAG, CAA, CAG

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Appendix 1. Steps in Activity 1

The list below shows various viral genome compositions on the left.
The steps the students must complete, in order, are shown on the right.

Group starts with:	Group completes:
ss (-) DNA	Þ (+) DNA Þ (-) DNA
ss (+) DNA	Þ (-) DNA Þ (+) DNA
ss (+) RNA	Þ (-) RNA Þ (+) RNA
ss (-) RNA	Þ (+) RNA Þ (-) RNA
ss (+) RNA (retroviral)	Þ (-) DNA Þ (+/-) DNA Þ (+) RNA
ds (+/-) DNA	Þ (+/-) DNA

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Appendix 2. Viral nucleic acids exist in an array of forms

Nucleic acid[a]	Strands present [b]	Type of strands [c]	Classification [d]
DNA	Double-stranded (ds)	(+/-)	I
	Single-stranded (ss)	(+)	IIa
	Single-stranded (ss)	(-)	IIb
RNA	Double-stranded (ds)	(+/-)	III
	Single-stranded (ss)	(+)	IV
	Single-stranded (ss)	(-)	V
	Single-stranded (ss)	("+")	VI

Adapted from: Pelczar et al., 1993.

a. Viruses have *either* RNA *or* DNA as the genomic material in a mature virion.
b. Strands present:
   Double-stranded = two complementary strands of the same nucleic acid
   Single-stranded = a single strand of one type of nucleic acid
c. Types of strands: By convention, the mRNA strand is identified as the (+) or "sense" strand. It is transcribed from and is complementary to the (-) or "nonsense" strand.

(+/-) =	Both sense and nonsense strands are present.
(+) =	Sense strand is present.
(-) =	Nonsense strand is present.
("+") =	Strand present has coding sequences, but it is NOT used as a message. Instead, a DNA intermediate must be synthesized, which in turn serves as a template for transcription.

d. Classification (following the Baltimore system), in which viruses are grouped by the form of nucleic acid in the virion. This grouping system focuses on the steps from the viral nucleic acid to reach viral mRNA since all viral mRNAs will be translated by the host ribosomes.

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Appendix 3. Viruses can be classified by genome structure

Genome	Classification	Example Viruses (& diseases)
(ds) DNA (+/-)	I	Poxviruses (smallpox) Herpesviruses (oral and genital herpes) Papovaviruses (warts)
(ss) DNA (+) (ss) DNA (-)	IIa IIb	Parvoviruses (gastroenteritis, Fifth disease)
(ds) RNA (+/-)	III	Reoviruses (Colorado tick fever, rotaviral diarrhea)
(ss) RNA (+)	IV	Picornaviruses (polio, colds) Togaviruses (rubella, encephalitis)
(ss) RNA (-)	V	Filoviruses (Ebola) Hantaviruses (hemorrhagic fever, respiratory distress) Orthomyxoviruses (influenza) Paramyxoviruses (colds, measles, mumps) Rhabdoviruses (rabies)
(ss) RNA ("+")	VI	Retroviruses (AIDS)

Collected from: Black, 1999; Dimmock and Primrose, 1994; Ingraham and Ingraham, 1995; Madigan et al., 1997; Perry and Staley, 1997; Prescott et al., 1999.

Curriculum Resources

Appendix 4. The steps in viral replication are dependent upon genome structures

Nucleic acid in virion	Steps required for production of new viral nucleic acids
(ds) DNA	ds (+/-) DNA Þ (+/-) DNA
(ss) DNA	ss (+) DNA Þ (-) DNA Þ (+) DNA ss (-) DNA Þ (+) DNA Þ (-) DNA
(ds) RNA	ds (+/-) RNA Þ ss (+) RNA Þ ds (+/-) RNA
(ss) RNA (+)	ss (+) RNA Þ (-) RNA Þ (+) RNA
(ss) RNA (-)	ss (-) RNA Þ (+) RNA Þ (-) RNA
(ss) RNA ("+")	ss ("+") RNA Þ (-) DNA Þ (+/-) DNA Þ (+) RNA

Adapted from: Ingraham and Ingraham, 1995; Madigan et al., 1997; Perry and Staley, 1997; Prescott et al., 1999; Tortora et al., 1992.

Curriculum Resources

Appendix 5. Viral transcription strategies are dependent upon genome structures (Version 1) – Expanded version with brief descriptions

Nucleic acid	Steps required for production of viral mRNA (and polymerases)	Source of RNA polymerase
(ds) DNA	Direct synthesis of mRNA from entering viral nucleic acid by host RNA polymerase; may occur from either strand. (DNA-dependent RNA polymerase)	Host-encoded
(ss) DNA	Entering ssDNA must be converted to dsDNA before transcription can occur. (DNA-dependent DNA polymerase)	Host-encoded
(ds) RNA	Viral polymerase produces mRNA from one (-) strand of viral RNA. (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA (+)	Viral RNA acts as mRNA. *or* Complementary strand of RNA is synthesized; this acts as template for production of viral mRNA. (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA (-)	Viral polymerase synthesizes mRNA using viral genome as template. (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA ("+")	DNA intermediate must be synthesized; it then serves as template for mRNA production. (RNA-dependent DNA polymerase *and* DNA-dependent DNA polymerase)	Host-encoded

Adapted from: Ingraham and Ingraham, 1995; Madigan et al., 1997; Perry and Staley, 1997; Prescott et al., 1999; Tortora et al., 1992.

Curriculum Resources

Appendix 6. Viral transcription strategies are dependent upon genome structures (Version 2) – Condensed version

Nucleic acid	Steps required for production of viral mRNA (and polymerases)	Source of RNA polymerase
(ds) DNA	(ds) DNA Þ mRNA (DNA-dependent RNA polymerase)	Host-encoded
(ss) DNA	1 2 (ss) DNA Þ (ds) DNA Þ mRNA (1 = DNA-dependent DNA polymerase, 2 = DNA-dependent RNA polymerase)	**1)Host-encoded** **2) Host-encoded**
(ds) RNA	(ds) RNA Þ mRNA (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA (+)	(ss) RNA acts as mRNA (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA (-)	(ss) RNA Þ mRNA (RNA-dependent RNA polymerase)	Virus-encoded
(ss) RNA ("+")	1 2 3 (ss) RNA Þ ssDNA (-) Þ dsDNA Þ mRNA (1 = RNA-dependent DNA polymerase, 2 = DNA-dependent DNA polymerase, 3 = dependent RNA polymerase)	1,2)Viral-encoded 3) Host-encoded

Adapted from: Ingraham and Ingraham, 1995; Madigan et al., 1997; Perry and Staley, 1997; Prescott et al., 1999; Tortora et al., 1992.

Curriculum Resources

Appendix 7. Example Messages for Activities 2 & 3 (Hidden Messages)

(short list of messages – examples for Activity 3)

A. Sample messages for use with "uninfected" cells:

HAPPYHEALTHYCELLSEQWENCE

B. Sample messages for use with "infected" cells:

VIRALSEQWENCE

ILIVEBYLYSIS

ILIKELYSIS

EKSPERIENCELYSIS

DIEVIALYSIS

DEATHVIALYSIS

RESISTANCEISFEWTILE

C. Sample messages for use with "infected" cells
that will overcome lysis:

ASSIMILATETHIS

Curriculum Resources

Appendix 8. Example Messages for Activities 2 & 3 (Hidden Messages)

(full entries)

NOTE: Listed below is a small selection of messages for use with Activity 2 (translation exercise). In the spelling of some "proteins," a little latitude was exercised to obtain some phrases. This is due to the absence of four English alphabet letters (J, O, U, and X) from the single letter codes for amino acids. In addition, two letters (B and Z) are used to represent pairs of amino acids (B=asparagine and/or aspartic acid; Z=glutamine and/or glutamic acid). Finally, periods were used to separate codons in the mRNA, as well as the corresponding sequences in the DNA; these serve as place markers and may be left in or removed as appropriate for the audience and the time alloted for the exercise.

A. Sample messages for use with "uninfected" cells:

HAPPYHEALTHYCELLSEQWENCE

Amino acid sequence: (NH_2) - HAPPYHEALTHYCELLSEQWENCE - (COOH)

mRNA sequence: (5') - CAU.GCU.CCU.CCC.UAC.CAU.GAA.GCU.UUA.ACU.
CAU.UAU.UGU.GAA.UUA.UUA.UCU.GAA.CAA.UGG.GAA.AAU.UGU.GAG. (3')

DNA sequence:
(5') - CAT.GCT.CCT.CCC.TAC.CAT.GAA.GCT.TTA.ACT.CAT.TAT.
(3') - GTA.CGA.GGA.GGG.ATG.GTA.CTT.CGA.AAT.TGA.GTA.ATA.

TGT.GAA.TTA.TTA.TCT.GAA.CAA.TGG.GAA.AAT.TGT.GAG. (3')
ACA.CTT.AAT.AAT.AGA.CTT.GTT.ACC.CTT.TTA.ACA.CTC. (5')

B. Sample messages for use with "infected" cells:

VIRALSEQWENCE

Amino acid sequence: (NH_2) - VIRALSEQWENCE - (COOH)

mRNA sequence: (5') - GUU.AUU.CGU.GCU.UUA.UCU.GAA.CAA.UGG.GAA.
AAU.UGU.GAA. (3')

DNA sequence:
(5') - GTT.ATT.CGT.GCT.TTA.TCT.GAA.CAA.TGG.GAA.AAT.TGT.GAA. (3')
(3') - CAA.TAA.GCA.CGA.AAT.AGA.CTT.GTT.ACC.CTT.TTA.ACA.CTT. (5')

ILIVEBYLYSIS

Amino acid sequence: (NH_2) - ILIVEBYLYSIS - (COOH)

mRNA sequence:

(5') - AUU.UUA.AUU.GUU.GAA.GAU.UAU.UUA.UAU.UCU.AUU.UCU. (3')

DNA sequence:
(5') - ATT.TTA.TAA.GTT.GAA.GAT.TAT.TTA.TAT.TCT.ATT.TCT. (3')
(3') - TAA.AAT.ATT.CAA.CTT.CTA.ATA.AAT.ATA.AGA.TAA.AGA. (5')

ILIKELYSIS

Amino acid sequence: (NH_2) - ILIKELYSIS - (COOH)

mRNA sequence: (5') - AUU.UUA.AUU.AAA.GAA.UUA.UAU.UCU.AUU.UCU.

DNA sequence:
(5') - ATT.TTA.ATT.AAA.GAA.TTA.TAT.TCT.ATT.TCT (3')
(3') - TAA.AAT.TAA.TTT.CTT.AAT.ATA.AGA.TAA.AGA (5')

EKSPERIENCELYSIS

Amino acid sequence: (NH_2) - EKSPERIENCELYSIS - (COOH)

mRNA sequence:
(5') - GAA.AAA.UCU.CCU.GAA.CGU.AUU.GAA.AAU.UGU.GAA.UUA.UAU.
UCU.AUU.UCU. (3')

DNA sequence:
(5') - GAA.AAA.TCT.CCT.GAA.GCT.ATT.GAA.AAT.TGT.GAA.TTA.TAT.
(3') - CTT.TTT.AGA.GGA.CTT.CGA.TAA.CTT.TTA.ACA.CTT.AAT.ATA.

TCT.ATT.TCT. (3')
AGA.TAA.AGA. (5')

DIEVIALYSIS

Amino acid sequence: (NH_2) - DIEVIALYSIS - (COOH)

mRNA sequence:
(5') - GAU.AUU.GAA.GUU.AUU.GCU.UUA.UAU.UCU.AUU.UCU. (3')

DNA sequence:
(5') - GAT.ATT.GAA.GTT.ATT.GCT.TTA.TAT.TCT.ATT.TCT. (3')
(3') - CTA.TAA.CTT.CAA.TAA.CGA.AAT.ATA.AGA.TAA.AGA. (5')

DEATHVIALYSIS

Amino acid sequence: (NH_2) - DEATHVIALYSIS - (COOH)

mRNA sequence:
(5') - GAU.GAA.GCU.ACU.CAU.UUA.UAU.UCU.AUU.UCU. (3')

DNA sequence:

(5’) - GAT.GAA.GCT.ACT.CAT.TTA.TAT.TCT.ATT.TCT. (3’)
(3’) - CTA.CTT.CGA.TGA.GTA.AAT.ATA.AGA.TAA.AGA. (5’)

RESISTANCEISFEWTILE

Amino acid sequence: (NH_2) - RESISTANCEISFEWTILE - (COOH)

mRNA sequence: (5’) - CGU.GAA.UCU.AUU.UCU.ACU.GCU.AAU.UGU.GAA.AUU.
UCU.UUU.GAA.UGG.ACU.AUU.UUA.GAA. (3’)

DNA sequence:
(5’)CGT.GAA.TCT.ATT.TCT.ACT.GCT.AAT.TGT.GAA.ATT.TCT.TTT.GAA.
(3’)GCA.CTT.AGA.TAA.AGA.TGA.CGA.TTA.ACA.CTT.TAA.AGA.AAA.CTT.

TGG.ACT.ATT.TTA.GAA.(3’)
ACC.TGA.TAA.AAT.CTT.(5’)

C. Sample messages for use with "infected" cells that will overcome lysis:

ASSIMILATETHIS

Amino acid sequence: (NH_2) - ASSIMILATETHIS - (COOH)

mRNA sequence:
(5’) - GCU.UCU.UCU.AUU.AUG.AUU.UUA.GCU.ACU.GAA.ACU.CAU.AUU.
UCU. (3’)

DNA sequence:
(5’)-GCT.TCT.TCT.ATT.ATG.ATT.TTA.GCT.ACT.GAA.ACT.CAT.ATT.TCT.(3’)
(3’)-CGA.AGA.AGA.TAA.TAC.TAA.AAT.CGA.TGA.CTT.TGA.GTA.TAA.AGA. (5’)

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