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ARTICLE

# Novel primary literature-based alternative to comprehensive final examination for undergraduate virology course

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**Abstract**

A novel approach is described using primary literature manuscripts for the final examination of an upper level undergraduate course in virology. This innovative technique was applied as an alternative to a core comprehensive final examination. A recent primary literature paper in virology was assigned several weeks before the end of the semester. Students were instructed to procure the electronic version of the manuscript, and to thoroughly read, highlight and outline the manuscript in advance. The examination was administered with an open book format and students were encouraged to bring laptops to access information as needed to answer questions. This primary literature-based examination format is presented here as an alternative to a comprehensive final exam. By comparing student examination scores for both final examination formats over a period of 11 years, it was determined that student performance was strong and not statistically different when compared to conventional comprehensive final examinations. Thus, the examination format described here was a useful assessment tool that provided students with valuable exposure to the discipline specific primary literature. While this article describes an application to an undergraduate virology course, the same examination techniques could be successfully applied to examinations in undergraduate or graduate classes in any areas of biochemistry and molecular biology.

**KEYWORDS**

assessment development, curriculum development, virology

## 1 | INTRODUCTION

From 1990 to 2018, the author has been offering Biology 364 (Virology) as an elective, single semester, 3.0 credit hour undergraduate course within the Department of Biology; Program in Biochemistry, Cell and Molecular Biology (BCMB) at the University of Scranton (Pennsylvania, USA). The course enrollees were primarily pre-health professional and pre-graduate school students who represented a highly competitive cohort. The course was purposely constructed to provide relevant content and challenging assessment approaches, to develop a broad knowledge base and the skills to perform well on the Medical College Admissions Test (MCAT) or the biology subject test of the Graduate Record Examination (GRE). Until 2010, there was an optional 2.0 credit laboratory component to the virology course. The present author described the use a non-infectious technique that

  

uses commercially available PCR primers and template as a model for HIV diagnosis for the concurrent laboratory component of the course.[1]

The lecture component of the course stressed molecular virology and clinical applications: molecular and serological diagnostic protocols, vaccination strategies, and antiviral chemotherapy of viral diseases affecting humans. The examinations were multiple choice format, five choices each, with some questions in the style of brief patient case presentation vignettes (see Figure 1 for sample questions). Examinations typically contained 40 multiple choice questions, and 5–7 short answer questions.

The course was purposely designed to prepare students to develop examination skills that would be useful

Which of these is not important for gene expression of retroviruses to ultimately produce viral proteins?

1. Self cleavage of protease from polyprotein
2. Ribosome frameshift
3. Splicing of RNA transcripts
4. Generation of – sense RNA
5. Action of cellular DNA dependent RNA polymerase

Mapping near the 3' terminus of the ALV packaged genome

1. Is a polypurine tract
2. Is a primer binding site
3. Is a cap
4. Is a Psi region
5. Is a long terminal repeat

Mr. John Diss, a 54 year-old mail carrier, presents with a temperature of 99.1F, and is complaining of chronic fatigue and yellowing of the skin and sclera. Serological testing shows the presence of HBsAg in his serum. He does not recall if he ever received a vaccine for hepatitis B virus. From this information, you may conclude that:

1. He must have been vaccinated at an early age
2. He is a chronic carrier of HBV
3. He has cleared an earlier infection
4. He has an active infection of HBV
5. Mr. Diss suffered a transfusion associated infection

Pick the false statement

1. Women with cervical cancer can be seronegative to HPV serotypes 16 and 18
2. Women with frank anogenital warts are likely infected with either HPV serotype 6 or 11
3. Some women with cervical cancer never had frank anogenital warts
4. Some women with cervical cancer were never infected with HPV serotypes 16 or 18
5. None of the above

Poliovirus encapsidates in its virions

1. The genomic RNA and RNA dependent RNA polymerase, surrounded by a capsid
2. One subgenomic mRNA surrounded by a capsid
3. One large, negative sense ssRNA, surrounded by a capsid
4. An RNA dependent RNA polymerase, in addition to the genomic RNA, surrounded by a capsid
5. None of the above

You are given that an RNA virus is phenol sensitive. From that information alone, you may conclude that:

1. It has a genome of multipartite positive sense molecules
2. Each of its nested RNAs is a messenger
3. It will either package a protein necessary for genome replication or expression, or have an envelope
4. It must produce one large polyprotein from its genome
5. You cannot conclude that any of those statements are true.

SHORT ANSWER FORMAT:

An asymptomatic person is accused of transmitting to their partner a genital herpes infection during a single episode of unprotected intercourse two weeks ago.

The person accused supplies a blood sample which is tested. The blood test detects serum HHV-2 IgG but not IgM; and is negative for both HHV-1 IgG and IgM. What can you reasonably conclude? (4 points for a complete answer)

**FIGURE 1** A sample of multiple choice and short answer questions from virology examinations, showing the depth of understanding required to answer correctly

for them in medical school. The author was concerned that examinations did not challenge the skills to read, understand, and critically analyze data in the primary literature. The topic of the present manuscript is the intentional re-design of the final examination to achieve that objective.

The course originally included four written examinations. The first three examinations were held at approximately weeks 3, 6 and 9. Those examinations were allotted the 75 min period for a normal class time and together, contributed 60% of the final semester average. (As an example of examination style and format, Figure 1 includes questions that appeared in examinations of the 2016 course.)

The fourth (final) examination, was worth 40% of the final semester average, was administered during the assigned day during finals week, and by institutional policy, had a time period set at 120 minutes. The virology final examination was a comprehensive exam, which, although it stressed the last quarter of the course material, was intended to assess student learning over the entirety of the semester. The comprehensive final examination would be typically 75 multiple choice questions and 10–20 short answer questions. The time each student spent on the examination varied considerably, with many students leaving early (~75 minutes), most students finishing before 120 minutes, and 4 or fewer students still writing after time was called at 2 hr. Student opinion was consistently against a comprehensive final exam; students posed a valid argument questioning the value of rememorizing vast volumes of material, the majority of which was already tested on previous examinations.

Aside from the general dislike of a comprehensive final, there was another consideration for the instructor. There was a personal concern that the comprehensive final took away from some of the most important course material covered in the final 3 weeks: content on the Family *Retroviridae*. The instructor sought an alternative testing tool that would: (a) give the Family *Retroviridae* its own dedicated portion of the final examination, and at the same time, (b) apply a creative way to incorporate primary literature reading into the course curriculum.

The new format adopted an approach that "the final examination" was effectively *two* different examinations. The first final examination was dedicated exclusively to the Family *Retroviridae* and it was composed of 50 multiple choice questions. The second final examination was dedicated exclusively to student understanding of a manuscript from the primary literature, with the intention that a carefully chosen virology manuscript could test a range of topics covered over the entire course. The second final examination was mostly short answer format, with the reasoning that students would do more careful deliberative thinking, rather than writing, or choosing from a menu of multiple choice responses.

Each of the two final examinations carried equal semester grade weight, and students were given the freedom to decide on how to spend their allotted 120 min. They had 2 hr to complete two examinations. To create a more interesting learning experience, the primary manuscript final was "open book" and further, students had the option to choose one classmate to collaborate with during the second examination. Importantly, the open book format and the option to pair up did not detract from the rigor of the exam. What those options did was to make the exam less intimidating, particularly since most students had little, if any, meaningful experience in reading the primary literature.

The complete "ground rules" for the primary literature final examination are presented in Figure 2, listing the instructions the students received, usually 4–5 weeks before the semester ended. To illustrate the format and content of this kind of examination, the complete final examination from the fall 2016 semester is included as Figure 3. The assigned manuscript for that year reported on the detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil.[2] The manuscripts for each year were different, carefully chosen to be very recently published or in press at the time,[3] and to cover techniques and concepts discussed over the entire semester. The manuscripts were carefully chosen to include a distinct emphasis on both molecular and clinical virology; sample manuscripts are referenced.[2–6]

## 2 | DATA COLLECTED

Examination score data were available for the years 2008–2018 (2018 was the last instance that the course was taught by the author). To investigate whether the revised format comprehensive final examination was an equivalent assessment tool, two comparisons were made. First, calculations were performed to determine if there were statistically significant differences between exam scores from the new (primary literature format, years 2011 through 2018) to the old format (years 2008–2010). Two-tailed Student's *t*-tests were applied to determine if the difference between the means was significant for the two formats; and ANOVA was applied to determine whether there were statistical differences within the year ranges of each format.

Secondly, comparisons were made between the (primary literature-based) final examination grades and

- **You are to use on campus electronic library resources to locate the assigned manuscript:**
- **Calvet, et al, (2016) Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. *Lancet Infectious Disease* 16:653-660**. It is recommended that you have the manuscript available to you when you are taking the examination.
- **You are likewise responsible for locating the GenBank sequence of the Zika virus genome sequence H/PF/2013 (KJ776791.1)**. It is recommended that you have the printout available to you when you are taking the examination. Between now and the day of the exam, you should read the paper for a thorough understanding. In class, I will review for you my hints for reading a scientific manuscript. Having said that, in the interest of fairness, I will not answer any individual questions about the manuscript before or during the examination.
- On the day of the examination: you will have the option to work alone or with one student currently enrolled in the class. If you work with a partner, you will submit one examination in for grading. Both partners will receive the same grade. In the unlikely event that you cannot agree on an answer to a particular question, you have the option to each submit a separate answer, and your grades will reflect that option.
- Each student will have two hours to complete two final examinations. The first exam will cover lecture material since the third examination, printed on white paper. That is a standard, closed book examination for which the Academic Honesty Policy is in effect, as stated in the course syllabus. When you have completed the first exam to your satisfaction, submit the exam to me and you will receive your second final examination, printed on different colored paper. (NOTE: For obvious reasons, once you have submitted the first exam, **you may not have it returned to you**, even if you have time remaining in the two hour examination period.)
- You may begin working on the second examination as soon as you receive it. If you chose to work with a partner, they can join you after they have submitted their first examination and received their second examination. I recommend that you move to a location in the classroom where you will have privacy to discuss your responses.

**FIGURE 2** "Ground rules" for the second final examination, provided to students when they received the citation for the assigned manuscript

the other four examinations for the same student cohort within a chosen specific year, 2016. Two-tailed Student's t-tests were applied to determine if the difference between the means of the four examinations was significantly different than the mean of the final examination.

## 3 | RESULTS

The goal was to establish a revised comprehensive final examination format that would: (a) provide a component dedicated to course material in the Family *Retroviridae*, but more importantly (b) challenge students to procure,

- The second examination is open book format. I define open book format to mean that you may use lecture notes and supplemental electronic assignments and figures posted on Desire2Learn. You may use your laptop computers, and you are free to use any resources available to you on the internet. You are free to use an electronic version of the manuscript and the published genome sequence, should you find that helpful. You may NOT use your computer or phone to contact any other person for assistance. Likewise, you may not contact any other student in the class, with the sole exception of your partner, if you have one.
- You will find that the second final examination will not require much writing on your part. Many of the questions are carefully crafted to be answered, YES, NO, or CANNOT TELL FROM THE INFORMATION PROVIDED IN THE MANUSCIPT. The third option will require you to have a full and complete understanding of the manuscript; what information is included, and what information is not included.
- Recall that this manuscript-based examination replaces a traditional comprehensive final examination. Having said that, appreciate that concepts from the entire semester will likely appear on your examination. Prepare accordingly.
- Your grades will be posted to you in the electronic gradebook of Desire2Learn when all exams have been graded. You can calculate your final letter grade from the average of five examinations, as outlined in the course syllabus.

**FIGURE 2** (Continued)

read, outline, and discuss with colleagues the experimental design and data analysis of a primary literature manuscript in the field of virology. Moreover, the goal was to create an assessment tool that demonstrated equivalent student performance patterns (i.e., not significantly more or less difficult) compared to the comprehensive final exam format used in the past. That goal was achieved.

Table 1 shows that by examining mean student grades from the new format final examination (years 2011–2018) to mean student grades from the old format final examination (years 2008–2010), there was no statistically significant difference (Student's *t*-test, $p = .6366$). Grade ranges were nearly identical. Moreover, applying ANOVA analysis, there was no statistically significant difference within the grades from years 2011–2018 ($p = .9920$), or within the grades from 2008–2010 ($p = .8692$).

Table 2 examines grade performance within the specific student cohort from the 2016 class. Using Student's *t*-test analysis, there was no statistically significant difference ($p = .9385$) between the mean of the primary literature final exam, compared with mean from the previous four examinations, for the same students within the 2016 cohort.

These data demonstrate that the novel primary literature final examination was an effective, fair and consistent assessment tool for student performance within a particular class cohort, and also over an 8 year period.

## 4 | DISCUSSION

This examination format challenged students to read manuscripts in the primary literature. Specifically, students were evaluated on their understanding of the following types of content: molecular organization of the viral genome; strategies for viral gene expression (in the context of what they learned from lecture content); known functions of viral proteins, and possible functions of putative translation products predicted from an analysis of a viral genome; antigenic determinants; and molecular properties of the virus that may influence disease pathogenicity or virulence.

- Does Zika virus produce a viral protease?
  - Circle YES or NO
- Does Zika virus package an RNA dependent RNA polymerase?
  - Circle YES or NO
- Is Zika virus sensitive or resistant to phenol extraction?
  - Circle YES or NO
- Does Zika virus produce sub-genomic messengers *de novo*?
  - Circle YES or NO
- In these documents, is there evidence that Zika virus has a 5' cap on its genome?
  - Circle YES or NO
- In these documents, is there evidence that Zika virus has a 3' non-coding region in its genome?
  - Circle YES or NO
- The NS5 gene of Zika is
  - Protease
  - Capsid
  - Cannot tell from the information provided
- Does the Zika virus genome have a non-translated leader sequence?
  - YES or NO or CANNOT TELL FROM THE INFORMATION PROVIDED
- What is the first amino acid incorporated into viral protein?
  - If impossible to know from the information provide, say so, for full credit.
- Did the strain isolated from patient 1 have exactly the same sequence of the strain that was included for the reading assignment?
  - YES or NO or CANNOT TELL FROM THE INFORMATION PROVIDED
- The sequence provided includes the short sequence TGGGTCT at the end.
  - What is remarkable about that short sequence, for a virus like Zika virus?
  - Explain how this remarkable sequence appears here, based on your understanding of the **Methods** section of the assigned manuscript.
- How many messenger RNAs does Zika have to express its genome?
- Is the genomic RNA polyadenylated?
  - YES or NO or CANNOT TELL FROM THE INFORMATION PROVIDED
- What is the nonsense triplet that ends the first Zika virus open reading frame?
  - Circle UAA UAG UGA or CANNOT TELL FROM THE INFORMATION PROVIDED
- Does the genomic RNA produce a complement during its eclipse period?
  - YES or NO or CANNOT TELL FROM THE INFORMATION PROVIDED
- The sequence provided is:
  - The genome
  - The complement to the genome
  - CANNOT DETERMINE FROM THE INFORMATION PROVIDED

**FIGURE 3** The actual 2016 final examination questions from assigned manuscript of Calvet et al.[2]

Additionally, this examination format employed different techniques of evaluation, as questions were posed in various configurations. For example, multiple choice answers did not always present an obvious correct answer from a menu of choices (posing a choice: "that answer cannot be answered from the information

- At which nucleotide does the first open reading frame end?
  - o ___ or indicate if CANNOT DETERMINE FROM THE INFORMATION PROVIDED

- The information provided shows only one strand of nucleic acid. Is it possible from this information to know the complete opposite strand?
  - o YES or NO

- What can you say about the size of Zika virus based on experimental techniques described in the MATERIALS section? (5 points for answer with explanation)

- In your own words (not the words of the authors), describe how the strain of Zika virus genome ended up as DNA during this study. (You are not allowed to use any text from the paper, which does not actually directly answer the question posed) No more than one sentence.

- What is the evidence that Patient 2 fetus with microcephaly was actually the result of CMV infection and not Zika? No more than one sentence.

  - Is there a discussion of a specific Zika virus protein involved in mosquito infections? YES or NO

  - How many serotypes are there of Zika virus? ___

MULTIPLE CHOICE QUESTIONS

This paper is the first report of:

1. Anti-Zika IgM in serum
2. Anti-Zika IgG in serum
3. Zika virus genome detected in amniotic fluid
4. Microcephaly associated with Zika virus infection
5. Zika virus in the Brazilian province of Paraiba

The first 5' AUG

1. Is actually found on a negative strand of RNA
2. Is found at nucleotide 1
3. Was not actually found on the genome
4. Is found at nucleotide 108
5. This information in not available from the assigned documents

The number of amino acids coded for with the first open reading frame is about

1. 1800
2. 3400
3. 10800
4. 5200
5. Cannot tell from the information provided

**FIGURE 3** (Continued)

presented in the manuscript"). To answer in that context requires a full understanding of the manuscript, rather than a simple search to find an obvious answer hidden in the body of the paper. As another example, open ended short answer questions demanded that students be able to critically analyze what was included (and not included) in figures and tables.

It is noteworthy that with this new format, students tend to stay working for entire 120 min final examination period, compared to the original format, where students were leaving after only 75 min, as noted above. That observation suggests that while the grade averages are comparable with both formats, students were more deliberate in devoting more time when challenged with interpreting the primary literature, even working with a partner.

It would have been useful to get data from University sponsored course evaluation assessment tools regarding how the new format was perceived by students (such as open ended questions: "Do you believe that the second final examination was a fair assessment of your semester performance in this class?," "Did you find the use of primary professional literature to be a useful exercise in your learning progress?" etc.). Unfortunately, that assessment tool was not possible since the University of Scranton course evaluation system was intentionally set up to close to student responses before the final examination week began. On the other

**TABLE 1** ANOVA analysis (top) and Student's *t*-test (bottom) of student performance comparing the new (primary literature) final examination with the conventional comprehensive final examination format

| | Range (%) | Median (%) | Mean (%) | *SD* | *n* | ANOVA *p* value |
|---|---|---|---|---|---|---|
| New format | | | | | | |
| 2018 | 60–94 | 81 | 82.0 | 10.11 | 26 | |
| 2017 | 60–99 | 87 | 82.4 | 11.46 | 22 | |
| 2016 | 68–98 | 81 | 81.7 | 7.31 | 19 | |
| 2015 | 72–95 | 81 | 81.4 | 6.42 | 22 | |
| 2014 | 64–95 | 83 | 81.0 | 8.75 | 25 | .9920 |
| 2013 | 66–95 | 80 | 80.5 | 9.64 | 20 | |
| 2012 | 67–94 | 82 | 82.9 | 7.26 | 21 | |
| 2011 | 64–95 | 83 | 82.3 | 7.76 | 27 | |
| All 8 years | 60–99 | 83 | 81.9 | 8.81 | 182 | |
| Old format | | | | | | |
| 2010 | 62–99 | 83 | 84.0 | 9.96 | 24 | |
| 2009 | 72–97 | 81 | 81.7 | 6.46 | 21 | .8692 |
| 2008 | 59–100 | 82 | 82.1 | 10.63 | 22 | |
| All 3 years | 59–100 | 82 | 82.6 | 9.66 | 67 | |

| | Aggregate mean (%) | Student *T*-test *p* value |
|---|---|---|
| New format (8 year period 2011–2018) | 81.9 | .6366 |
| Old format (3 year period 2008–2010) | 82.6 | |

*Note:* Statistical analyses were performed using Excel software. Student's *T*-test with two-tailed distribution, two-sample equal variance. ANOVA formatted for single factor, alpha at .05.

**TABLE 2** Student's *t*-test statistical analysis of student performance comparing primary literature final examination with the previous four examinations in the same student cohort in 2016

| | Range (%) | Median (%) | Mean (%) | *SD* | *n* | Student's *t*-test *p* value |
|---|---|---|---|---|---|---|
| Primary literature final exam | 68–98 | 81.0 | 81.7 | 7.31 | 19 | .9385 |
| All four other exams for same class | 48–100 | 84.5 | 82.3 | 10.33 | 76 | |

*Note:* Statistical analyses were performed using Excel software as described in Table 1.

hand, in meeting students after the semester ended, a consensus could be summarized as: "*It was not nearly as bad as I had anticipated it would be. It actually wasn't that bad*."

## 5 | FUTURE DIRECTIONS

With the incorporation of primary literature into the final examination, this can be viewed as a significant first step. A logical next step might be to include more exposure to the primary literature into an undergraduate or graduate virology course through the novel "flipped classroom" instructional strategy. In this potential application, students would be assigned to read (one or two) additional primary literature readings throughout the semester, with the assignment to independently prepare for individual and group assessment in the classroom. For many students, this would be a valuable learning tool that will prepare them for further education, as many medical schools (including the institution at which this author currently teaches) are incorporating the flipped classroom model into their curricula.[7]

The present manuscript describes a specific application to a virology course. Nonetheless, this same format could be applied to any biochemistry or molecular biology class, undergraduate or graduate, for the meaningful incorporation of primary literature into course content and student assessment.

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