

## **CELL SIGNALING SEMINAR** Biology 4550/5550 spring 2007

### **BRING THIS PACKET TO INITIAL LECTURES- IT INCLUDES LECTURE NOTES**

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**TEXTBOOK:** Molecular Biology of the Cell by Alberts et al.. THIS IS A NEW EDITION (4<sup>TH</sup>). . Your textbook from General Cell Biology 3611 is very helpful and I also highly recommend Molecular Cell Biology.

CD for the course is also required; it has lecture notes, video/animations, and PowerPoint slides from our textbook (which you will use in your PowerPoint lectures). It also other course info. Note that if you want to print off lecture PowerPoint slides, you can print more than one slide per page in the science computer lab on the third floor (located between the bio and chem. Office). After purchasing the CD, click on the file that begins with "START HERE..."

### **REQUIRED OF STUDENTS:**

Since this is a senior and graduate level course, I expect every student to be familiar with General Biology and General Cell Biology topics. For a more specific review of this beginning material, read the signal transduction chapters of "The World of the Cell" by Becker et al. (sixth ed is current-this is the text used by our Cell Biology 3611 class). There will be homework, written summaries of research papers, essay exams and 2 PowerPoint presentations (see below). In addition, FOR GRADUATE STUDENTS, A 15 PAGE TYPED SINGLE SPACED PAPER IS DUE ONE WEEK BEFORE FINALS. The paper will describe in layman's terms the paper that the graduate student has orally presented before the class. The format: introduction (typical values are given: 3-4 pages), methods (5 pages), results (5 pages), discussion (2 pages). Include illustrations (perhaps those from your talk) in the 15 pages (using a typical reference/bibliography format for papers that you cite). Thus, your written paper will be similar to scientific papers, but remember, your oral presentations will be dramatically different from this format!!

### **COURSE STRUCTURE:**

I will lecture for a period of time then students will give two oral presentations. My lectures will discuss the scientific method and then go on to explain principles of cell signaling. Subtopics under scientific method include hypothesis testing, scientific writing, basic statistics, graphical analysis and scientific fraud. We will develop a general understanding of how various cell functions are controlled; for example, how do hormones which are located in the blood stream tell a cell to begin the process of cell division (and how this goes awry in cancer)?

### **GRADE:**

Your grade is dependent upon homework, tests, your one page summaries and your two oral presentations. The graduate students have a paper in addition. The test is given after the end of Dr. Stith's lectures and during final's week. For sample essay questions, see

later section of this packet.

**COURSE SUMMARY:** Many of these **cell signaling or signal transduction** processes involve two basic principles. First, the hormone must act across the plasma membrane; this is referred to as '**transduction**' (to transduce is to convert a message-as in a hormonal message-into another form- a signal inside the cell; do not confuse this definition with that used in molecular biology). The consequence of this first finding is that water-soluble hormones must transfer their message across the impermeable lipid membrane; a **hormone receptor** is required (note that this does not hold for most steroid hormones) and often intracellular second messengers (the first messenger would be the hormone) are produced directly from membrane phospholipids. Hormone receptors are transmembrane (integral) proteins (from cell biology 3611: what secondary structure does the receptor have as it passes through the membrane?).

The second basic finding is that most hormonal signals induce their biochemical changes in the cell through changes in the amount of phosphate bound to proteins. Putting a highly charged phosphate functional group (from cell biology 3611: what atoms are present in this functional group? which are charged?) on a protein will cause new ionic bonds to form and this will dramatically change the 3-D structure of the protein (turning the protein off or on). **Protein kinases** put the phosphate on a protein, whereas **phosphatases** remove the phosphate; these two types of enzymes are controlled by hormones. Increasing amounts of phosphate on some proteins will increase the protein's activity, and with other proteins, the opposite is true.

Using these two guiding principles of cell signaling, we will explore the myriad of unique cell signaling systems. Along the way, we may also delve into the control of protein synthesis, membrane channels, fertilization, cell division, intracellular calcium release, intracellular pH, and specific enzymes. **SO IN CONJUNCTION WITH MY LECTURE DISCUSSIONS, READ THE PERTINENT PART OF THE TEXT** (we cannot cover all topics in the text in lecture but your talk may be on any appropriate topic from the text).

### **STUDENT PRESENTATIONS:**

After my introductory lectures, the participants will be required to find, research and present two 20-25 minute lectures on the topic of their choice (the length of time can vary from semester to semester depending upon class enrollment and class periods available). The area of the lectures will be connected with cell signaling. I will assist in the definition of the topic, **approve the topic to be discussed** and **assist in the understanding of the original research papers** that will be used to develop the presentation. As is common for upper level courses, it is important to talk to me outside of class about the methods and background info (these are actual research papers that are difficult to understand). **However, do not show up just before your talk and expect to redo the slides in the minutes before the presentation time.** Attendance for all classes is mandatory- especially important for the student talks. I need a title for your talk **ONE MONTH AHEAD OF TIME!! TWO WEEKS BEFORE YOUR TALK I NEED A**

ONE PAGE SUMMARY OF YOUR TOPIC AND A COPY OF ONE ARTICLE THAT REPRESENTS THE BULK OF YOUR TALK. (put your name on the paper with the date of your talk; see example provided in this packet). I EXPECT TO SEE USE OF FIGURES FROM OUR TEXTBOOK IN YOUR TALK (electronic versions of the text figures are available on class CD-ROM).

**University policies to remember:**

Biology department Policy: “If you have a grievance with this course or with the instructor, it is necessary to proceed as follows with respect to resolving it. First, you must meet with the instructor or teaching assistant to discuss your grievance. If it is not resolved to your satisfaction, you may then contact the chair of the department to discuss the grievance further. However, you must follow this procedure. Keep in mind that it is in your best interests to approach the issue in a professional and diplomatic manner.”

**Spring 2007 CLAS Academic Policies**

The following policies pertain to all students and are strictly adhered to by the College of Liberal Arts and Sciences (CLAS).

- Every student **MUST** check and verify their schedule prior to the published drop/add deadlines. Failure to verify a schedule is not sufficient reason to justify a late add or drop later in the semester. It is the student’s responsibility to make sure that their schedule is correct prior to the appropriate deadlines.
- CLAS students must always have an accurate mailing and email address. Email is the official method of communication for all University of Colorado at Denver and Health Sciences Center business. Go to <http://www.cudenver.edu/registrar> to update and/or change your email address.
- Students are **NOT** automatically added to a course off a wait list after wait lists are dropped. If a student is told by a faculty member that they will be added off the wait list, ***it is the responsibility of the student to complete the proper paperwork to add a course.*** Students are **NOT** automatically added to a course from the wait list after the 5<sup>th</sup> day of the semester when wait lists are dropped.
- Students must complete and submit a drop/add form to make any schedule changes. ***Students are not automatically dropped from a class if they never attended, stopped attending or do not make tuition payments.***
- Late add’s will be approved ***only*** when circumstances surrounding the late add are beyond the student’s control and can be documented independently. This will require a petition and documentation from the student. Late add’s will only be approved if the student has not taken any exams, quizzes, or has not completed any other graded assignments. Independent verification of this from the professor of record will be required. Please note that the signature of a faculty member on an add form does not guarantee that a late add petition will be approved.
- Late drops will be approved ***only*** when circumstances surrounding the late drop are beyond the student’s control and can be documented independently. This will require a petition and documentation from the student. Please note that the signature of a faculty member does not guarantee that a late drop petition will be approved.
- Students wishing to **graduate in spring of 2007 must meet with their academic advisor by the end of the drop/add period** to obtain a graduation application. This application must be completed and submitted by 5 PM on January 31, 2007. You can obtain an application **ONLY** after meeting with your academic advisor. **There are no exceptions to this policy or date.**
- Students are responsible for completing financial arrangements with financial aid, family, scholarships, etc. to pay their tuition. Students will be responsible for all tuition and fees for courses they do not officially drop using proper drop/add procedures and forms.
- Students who drop after the published drop/add period will not be eligible for a refund of the COF hours or tuition.

### Spring 2007 Important Dates

- **January 16, 2007;** First day of Class
- **January 18, 2007;** Last day to be added to a wait list
- **January 18 – January 31, 2007;** Students are responsible for verifying an accurate spring 2007 course schedule via the SMART registration system. Students are NOT notified of their wait-list status by the university. All students must check their scheduled prior to January 31, 2007 for accuracy.
- **January 19, 2007 at 5PM;** Wait lists are dropped. Any student who was not added to a course automatically from the wait list by this date and time MUST complete a drop/add form to be added to the class. Students are NOT automatically added to the class from the wait list after this date and time.
- **January 22, 2007;** First day an instructor may approve a request to add a student to a course using the Schedule Adjustment Form (drop/add form).
- **January 25, 2007;** Last day to add a course using the SMART Web Registration system. **Students MUST check their registration to verify what classes they are enrolled in.**
- **January 31, 2007 at 5 PM;** Last day to add structured courses without a written petition for a late add. **This is an absolute deadline and is treated as such.** This deadline does not apply to independent study, internships, and late-starting modular courses.
- **January 31, 2007 at 5 PM;** Last day to drop a spring 2007 course with a full tuition refund and no transcript notation. Drops after this date will appear on your transcript. **This is an absolute deadline and is treated as such.**
- **January 31, 2007 at 5 PM;** Last day to completely withdraw from all spring 2007 courses with a full tuition refund and no transcript notation. Drops after this date will appear on your transcript. **This is an absolute deadline and is treated as such.**
- **January 31, 2007 at 5 PM;** Last day for students to apply for Spring 2007 Graduation. Students MUST see their CLAS advisor to obtain a Graduation Application.
- **January 31, 2007 at 5 PM;** Last day to request pass/fail option for a course.
- **January 31, 2007 at 5 PM;** Last day to request a no credit option for a course.
- **January 31, 2007 at 5 PM;** Last day to register for a Candidate for Degree.
- **January 31, 2007 at 5 PM;** Last day to petition for a reduction in thesis or dissertation hours.
- **April 2, 2007 at 5 PM;** Last day for Non-CLAS students to drop individual classes or withdraw from all classes without a petition and special approval from the student's academic Dean. **This is treated as an absolute deadline.**
- **April 13, 2007 at 5 PM;** Last day for CLAS students to drop individual classes or withdraw from all classes without a petition and special approval from the student's academic Dean. **This is treated as an absolute deadline.**
- **No schedule changes will be granted once finals week has started. There are NO exceptions to this policy.**

Snowy day policy: some class days might coincide with large snow fall. If classes are not officially canceled (check radio or TV news or 556-8376 or 556-2401), class will be held.

Keep track of the drop deadline (tenth week of the semester).

The departmental policy is that incompletes will be granted only when a majority of the course requirements have been completed and only one or two items remain to be completed. Incompletes are not to be given in which the student is to retake the entire course or even most of the course. No incompletes will be granted after the start of quiet week without a doctor's note. **If repeating this course, it must be completed in its entirety. There will be no exceptions to this departmental policy.**

Make sure that you have read the Student Code of Honor booklet to understand your responsibilities.

### **REQUIREMENTS FOR THE COURSE:**

Grades dependent upon:

- a. homework; statistics, writing 20 pts each= 40 pts total
  - b. paper: graduate students only; 50 pts
  - c. exam: 100 points, midway in semester
  - d. talks: first talk: 60 pts, second talk: 60 pts= total of 120 points
  - e. final 100 points.
- a) You have read pertinent sections of the book, handouts or information on Dr. Stith's web sites before the lectures; this will form a foundation for the upcoming discussions. Remember that this is an advanced seminar that requires input from the students. Your grade is dependent upon homework, tests, your one page summaries and your two oral presentations. The graduate students have a paper in addition.
- b) Give me a copy of the research paper that is covered by your talk. Try to pick a paper that has methods you are familiar with and pick a paper that is not too difficult (I can help). Papers published in Science have been difficult for students to present (due to their short nature). If you find that the paper involves quantum physics, and you know nothing of the methodology, choose a paper that involves simpler methods. Please see me when you have chosen a paper to confirm that it is appropriate (see later discussion on papers).  
Please choose a scientific paper as soon as possible (optimally, three weeks before your talk) so that you can confirm the paper with me and you can write up the page or two describing the paper.  
On the cover page, include your name and date of presentation. Make sure that the copy is legible and that the first page has the journal reference (journal title, volume, page and year) as it will be photocopied again for the other students. Part of your grade depends upon this cover page and paper summary.
- c) Note that attendance, completion of homework, exam, involvement in discussions, effort spent trying to improve your understanding of course material and readings, oral presentations, and following procedures outlined in this handout will determine your grade.
- d) **MANY STUDENTS DO VERY POORLY ON THEIR FIRST TALK; YOUR GRADE WILL REFLECT HOW WELL YOU CORRECT THE ERRORS OF YOUR FIRST TALK. IN OTHER WORDS, YOUR GRADE WILL REFLECT HOW MUCH EFFORT YOU PUT INTO IMPROVING YOUR SECOND TALK.**
- e) I may be able to offer important suggestions and help outside of class.
- f) let me know ahead of time if you need special AV equipment.
- g) remember: each talk is to be about 25 minutes, and that some of our meetings may have three speakers. Part of your grade will be whether your talk is about 25 min.
- h) Do not let things slide to the last minute and remember that attendance is a large part of the grade.
- i) A major point of this course is to develop communication skills; that is, to present information in a clear manner. Your development of these skills will provide the basis for your grade. Communication skills:

- 1) do not talk to the screen or blackboard (make eye contact) or block the overhead projector with your shoulder
- 2) it is best to write down all important statements before your talk-if you are to use the overhead, it may be best to have the talk's outline written out on the clear acetate sheets before giving the talk. Do not write down too much on each overhead.
- 3) have a written outline of your talk (we don't need to see a detailed outline)
- 4) use the board or overhead
- 5) **assume that the other students do not know anything or remember anything from your first talk**

j) You should be able to take criticism of the talk (it is important to note that we are attempting to improve or refine our presentation skills). When I gave a poor grade to one student, he said that he understood the material. Whether the student actually understood the material or not was not the issue (he did not understand the material as well as he thought; this is a major reason for poor presentations); his presentation or communication skills were poor (he did not follow the suggestions presented here) and he did not show any improvement from the first to the second talk.

k) **MOST IMPORTANT--EVEN WITH A GENERAL SCIENTIFIC PAPER AS THE BASIS OF YOUR TALK, TRY TO BE NARROW IN YOUR FOCUS WHEN YOU GIVE YOUR TALK.** Don't try to cover the whole field and speak only in generalities. That is, don't try to summarize a topic and **do not use a review paper for the basis of all of your talk.** Limit your overview to the first 5-8 min of the 25 min talk. In the past, one student simply got up and resummarized a review paper. Almost everything that he went over was incorrect. He did not pick one aspect/topic from the review and center in on it; he did not go to any of the original literature. He picked an old out-of-date review with out-of-date and even incorrect statements. Since the student did not understand the basis of the generalities of the review, he made many incorrect assumptions. As a result, the student understood very little and presented material that was wrong. Another student gave a poor talk due to the following: he spent over 20 min summarizing the field and very little information was actually related to the data (that were hurriedly mentioned at the end). Evaluation and presentation of original data is what I emphasize in this course.

Instead of regurgitating or rereading a review, I would rather see you struggle (and hopefully succeed to some extent) to understand a single topic based on the original literature (the key word is "focus"-don't repeat a review of a general topic).

l) **IN THE TALK, TRY TO USE ONLY A FEW FIGURES FROM THE PAPER(S) AND MAKE SURE THAT YOU UNDERSTAND THE FIGURES--THEIR METHODOLOGY AND CONCLUSION.** Typically, you do not have time to present all figures; choose the important ones. For the background information in the introduction, use our textbook illustrations; even if I did not talk about it in lecture, there is probably a slide related to your presentation.

First: ask yourself why the experiment was done. You might have a slide stating a question; does aspirin work through map kinase?

**Second, VERY IMPORTANT:** even though the paper does not usually show a flow chart of the steps that produced the data in the figure (or in the text), **YOU SHOULD**

**MAKE A FLOW CHART** (using pictures more than words) OF THE EXPERIMENTAL STEPS. This helps you understand the results and is a tremendous help to your audience. Illustrate procedures used (e.g., for immunofluorescence, show the stack of molecules used to identify the location of the antigen).

You will have to refer to earlier papers to understand the methods used; look in cell or biochemistry textbooks, Methods in Enzymology or other literature for explanations of technique. You may spend 10-15 min explaining the basis of just one figure; then showing and explaining the conclusions of the one figure may take another 5-10 min!!

In other words, center in on the figures of a paper. Illustrate and write out every procedure used; know why they performed each step (if the paper does not state why and you cannot find out why by looking at other references listed in the bibliography, ask me). Consider **redrawing complex figures to simplify**. Leave out part of the figure if you do not fully understand the result and if it is non-essential; you can present what you want as long as there is no large gap in logic. If the photocopy is illegible (do your best here), redraw the figure clearly by hand. For complex figures, break them down into parts and make a drawing illustrating what each lane or part represents. Summarize each figure with a statement and a drawing before going on to the next figure. **MAKE SURE THAT YOU COPY THE FIGURES LARGE ENOUGH TO BE SEEN; USE THE ENLARGE FUNCTION OF THE COPY MACHINE!!**

Rewrite the axes from the figure; for example, instead of putting down the rather meaningless "3240/380 ratio" as a label for the y axis, use a definition of what the label means (in this case, it means the "intracellular calcium concentration"). Ask yourself what the axes represent.

When actually presenting a figure, the first thing to do is to go over the X and Y axes and say what they represent.

When writing on the overhead, write in large print so that everyone (even 20 feet away) can read your statements.

For every figure, make a flow chart of the method and present this before you actually show the figure.

For every figure, present a concise conclusion of the data.

As you may note from the above, a clear description of the methods used is important. You must understand the method to be able to criticize a conclusion made from the data. If you understand the method, you will present the data in a clear manner. With this in mind, check the library for biochemical methods books (there are many in our library, more in UCHSC's Denison library). There are various book series that describe methodology; e.g., Methods in Enzymology, Methods in Cell Biology. You may spend 15 min per figure in the paper.

m) Use a **conclusion or summary page** (use acetate for overhead as I can give you some); present this at the end of the talk.

n) **ASK YOURSELF IF THE CONCLUSIONS PRESENTED IN THE PAPER ARE JUSTIFIED BY THE DATA PRESENTED!!!** What holes do you see in their logic? Do you see any other experiments that should have been performed? Are the authors

assuming too much? If you do not ask yourself these questions in preparing the talk, I will ask you to answer these questions during the talk.

You can outline your talk by using a few figures from a paper; then build up supporting information (e.g., information on methods used to produce figure). Try to stay clear of sweeping statements that you cannot back up.

Ask yourself if the conclusions in the paper are justified by the data (I will ask you this during your presentation).

o) **IMPORTANT: DO NOT DISCUSS METHODS DURING THE FIRST TALK AND THE RESULTS DURING THE SECOND; KEEP DISCUSSION OF THE METHODS AND THE RELATED RESULTS TOGETHER!!** You will have to "rewrite" the paper—that is, the paper has methods listed separately from the results. In an oral presentation, you will have to present a method, then the results, then present a second method and the second figure of results.

p) **SINCE YOU HAVE ONLY TWO 25 MIN talks, I RECOMMEND THAT YOU DISCUSS ONLY ONE PAPER IN BOTH TALKS.** You would have to split one paper into two sections for the two talks (say, figures 1-4 for talk one, fig. 5-8 for the second talk)—this will take some careful planning.

q) Talk slower than you believe necessary. In this way, you can think before you make a statement or answer a question. Thinking is important. Also, it is easier for the audience to follow.

Don't refer to "things" or "stuff;" use the proper name for a chemical or procedure.

r) If your two talks discuss related topics, begin the second talk by briefly reviewing the first talk.

s) Practice the talk beforehand, you might want to have some padding in case there are questions.

t) One student said that he could not summarize all the information for a certain topic in one 25 min talk. I reminded him that Nobel Prize winners often summarize all of their life's work in a relatively short talk. An important skill that is a goal of this course is **how to summarize and present** the more important information and **leave out details that are not needed**. Make sure that the talk is organized; that is, the ideas flow from one to another in a logical manner (don't leave out an important piece of information that allows one to jump from point A to point B). The importance of focusing in on one certain aspect of a paper is another lesson of this course.

Another student said that he had given many scientific talks and didn't like the fact that I offered constructive criticism. Poor presentations are often not criticized (the data are something else). Believe me, poor speaking skills or presentations will hurt your career. One goal of this course is to improve presentation skills (clarity of speech and presentation of ideas, whether logical progression of facts is used, etc.) is very important.

u) Don't mislead the audience by emphasizing matters of marginal importance.

v) Tips for a good oral presentation (see *The Scientist*, Oct. 13, 1997, page 14): Show enthusiasm, use some short, punchy sentences, raise and lower your voice and keep to your time limit. Don't read from overheads or speak in a monotone, state too many facts (information overload), speak too quickly, use jargon (explain the terms used), or use visuals with too much detail in them. **The importance of a good oral presentation to your career is emphasized in the article.** The article emphasizes that, in shorter talks such as those in this course, it is very important to know what to cut and what to include. This requires practicing the talk.

**IN SUMMARY, the structure of the talks should have:**

1. a 5 min introduction. For example, if you are talking about the acetylcholine receptor, start your talk about the importance of acetylcholine in the body. Or if you are discussing one aspect of the mechanism of insulin, first talk about insulin effects and then show all the steps of the insulin pathway (see lecture). Point out the one step you will be discussing.
2. 5 min on techniques used for the first figure or result. Assume that the audience does not know anything about the technique involved. Draw a flow chart. See Methods in Enzymology., biochemistry books. The audience should understand the methods and their limitations.
3. 5 min; show the table or figure. First, define what the axes are.
4. 1-2 min summary of the conclusions from the figure or table. Make a drawing representing the conclusion. Defend author's conclusions or say that the conclusions are not appropriate.
5. Repeat steps 2-5 for the next figure.

**Books on Oral Presentations:**

Technical Presentation Workbook: Winning Strategies for Effective Public Speaking by Jerry Wircenski (New York, American Society of Mechanical Engineers Press, 1996).

Communicating Science: A Handbook, by Michael Shortland and Jane Gregory (New York, John Wiley and Sons, 1991)

Dazzle'em with Style; the art of oral scientific presentation.

by Robert RH Anholt (WH Freeman and Co, NY).

This book presents a checklist:

1. create an informative title.
2. place your presentation in context of a major scientific principle. (if talking about cell division, mention cancer).
3. focus on a single issue and adjust it to the interests of your audience.
4. identify the underlying question you will address, divide it into subquestions and answer each question.
5. follow a logical line of thought.
6. minimize the use of jargon.
7. avoid backtracking, and always return to the point.
8. end with a concise, clearly formulated conclusion.

9. design visual displays to be simple, error-free and clearly visible.
10. practice your presentation to build confidence in delivery skills.

Anholt emphasizes that, to keep the interest of the audience, you should make your talk a series of questions. Answer the questions with results from experiments.

### POSSIBLE TOPICS

These topics are the "hot" topics of Cell Signaling; one of the topics may be chosen for your talk. I encourage forming teams so that others in the group do not cover the same material but each speaker can build upon what others have said. First, chose a topic area (say "the mos protein; how does it cause cell division or cancer?") with the help of the list below, lectures and the reading of the text. The review articles found in Current Opinions in Cell Biology are excellent. They are short and provide background; **pick one of their highlighted references for your actual talk.** You can search for papers on various topics for free if you go to the web site of Pub Med at the National Library of Medicine- <http://www.ncbi.nlm.nih.gov/PubMed/>

Second, for background info, look the key word ("mos") up in an advanced cell biology or medical textbook; I recommend Molecular Biology of the Cell or Molecular Cell Biology.

Third, pick an actual research paper (not a review) and prepare an oral presentation.

Your grade is dependent upon your understanding of this material and the effort shown to follow the talks of other students and contribute to discussions (of course, the grade is also dependent upon your talk).

#### TOPICS:

1) ras oncogene: cover Harvey vs. Kirsten; See Sci 248:67 (1990); Nat 343:377, 1990. GAP (see Frank McCormick refs),  $k_{rev}$ =Rap and NF1 regulation (see Kitayama et al., 1989; Lapetina et al., 1989). An important discovery over the past year; ras may act through raf-1 (another oncogene). Also an important new control factor described: SOS. (NOTE oncogenes cause cancer; induce abnormal cell division).

Rho and Rac are members of the ras family but they are involved in microfilament regulation (thus, stress fibers, focal contacts, lamellopodia); see Curr. Opinion in Cell Biology 9:86, 1997.

2) A major cancer causing protein is called SRC- it is an oncogene: see Oncogene 5:161, 1990; incl. mechanism involving ras (see Tony Pawson ref; Mol Cell Biol 8:324, 1988; Sci 248:79; 241:42) and src (see PNAS 86:7017, 1989). MY LAB IS VERY INTERESTED IN THE ROLE OF SRC IN XENOPUS (A RECOGNIZED EXPERIMENTAL ANIMAL) BIOLOGY- SEE ME ABOUT THIS IMPORTANT TOPIC.

3) mos oncogene: especially as applies to Xenopus biology; George Van der Woude. Mos may act directly upon MEK.

4) p34 or cdc2 gene product; the enzyme that induces cell division. As applies to Xenopus biology. See Nat 343:233, 1990; EMBO J 8:3985 (1989). Regulation by cyclin. More recent references: Bioessays 17:471, 1995; Current Opinion in Cell Biology 6:877, 1994

5) Lysophosphatidic acid is a soluble lipid found in blood that binds to a receptor, activates a G protein, and turns on the map kinase path to induce cell division. See: Curr. Opinions in Cell Biology 9:168, 1997

6) Protein Kinase C; an enzyme that may cause cancer. Does it also work through ras or raf-1? NEW:: TPA goes through raf marginally but mostly through an action on MEK kinase see Ken Bloomer in yeast where PKC hits MEK K (pck1). See recent review by A. Newton: Curr Opinion in Cell Biology 9:161, 1997

7) Insulin; its receptor, ras and protein kinase C pathway (see Mol Cell Biol. 9:4312, 1989). An important discovery: insulin acts through IRS-1 and IRS-2 (do a literature search).

8) Role of phospholipase D in insulin action and cell signaling. See Proc. Natl. Acad. Sci USA 92:12151, 1995.

9) Integrins are membrane proteins that bind to the extracellular matrix and microfilaments inside the cell. They are involved in many cell processes (including cell movement and division). A family member is what sperm binds to on the surface of the egg. See: Curr Opinion in Cell Biol. 9:725, 1997.

10) The map kinase path. A hormone binds to a receptor, activating a tyrosine kinase to activate Grb/sos, ras, raf, MEK1,2, ERK1,2. ERK is also called map kinase, and the kinase is believed to regulate numerous paths. Cur Opinion in Cell Biology 9:180, 1997.

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### **General Description of Science:**

The Scientific Attitude, by Frederick Grinnell

A Handbook of Biological Investigation, by J. W. Ambrose, III and K. P. Ambrose (very good overview of almost all aspects of hypothesis development, science writing, statistics and graphics).

Statistical Concepts; a basic program, F.L. Brown, J.R. Amos, O.G. Mink (very good review because it is so short)

Asking Questions in Biology, C. Barnard, F. Gilbert, P. McGregor (offers very good practice in development of clear hypotheses).

Scientific Integrity, Francis Macrina (1995, ISBN 1-55581-069-1C). This book may become a required text for the scientist of the future; it has sections on mentoring, scientific record keeping, authorship and peer review, use of animals in research, conflict of interest, ownership of data and intellectual property.

The **nature of science** is that facts can be put together to link seemingly totally unrelated fields (facts are important but how we put together is intelligence):

From Connections by James Burke, on the **nature of scientific research**: A... "Scottish mechanic once made a minor adjustment to a steam pump and triggered the whole Industrial Revolution. A nineteenth -century weatherman developed a cloud-making device that just happened to reveal to Ernest Rutherford, a physicist he knew, that the atom could be split. Thanks to a guy working on hydraulic pressure in Italian Renaissance water gardens we have the combustion engine. A silk loom and the 1890 U.S. census gave birth to the computer. Gaslight and the American War of Independence were responsible for raincoats. Glassmaking and English clay made possible transatlantic navigation...The process does not fall neatly into categories such as those we are taught in school. For example, most of the elements contributing to the historical development of transportation had nothing to do with vehicles. So there are no rules ...Things almost never turn out as expected. When the telephone was invented, people thought it would only be used for broadcasting. Radio was intended for use exclusively onboard ships. A few decades ago, the head of IBM said America would never need more than four or five computers." Some in Congress want to drastically cut back on research funding (especially those that they believe are worthless; they say that we should only fund certain specific categories, such as cancer research): what do you think this would do to progress?

The nature of Biological research and the value of hard work:

"The molecular biologist Sydney Brenner once thought of founding a journal called the Journal of Zombie Biology.... "because that's all you have to do. You just wind yourself up in the morning, and go to the lab and just do things...many of the answers come from just doing things. Biology isn't a subject in which you can have great thoughts in the bath." Leo Szilard said: "When he was a physicist he could lie in the bath and think for hours, but in biology he was always have to get up to look up another fact." From Paula E. Stephan and Sharon G. Levin in Striking the Mother Lode in Science: The Importance of Age, Place and Time (Oxford Univ. Press).

### **General References on careers in science:**

A Ph.D. is not enough; a guide to survival in science; Peter J. Feibelman.

Conquering Grad School; what you need to know; James Barner, Wishbone Publishing, \$19.95, ISBN 0-9641365-3-8; PO Box 274-B25, Plainfield, IL 60544-0274

The Ultimate Grad School Survival Guide, Lesli Mitchell, Peterson's Guides, \$15; tele: 1800-338-3282. This book offers suggestions on choosing an advisor, writing, networking, and how to get a job.

To be a Scientist; Donald Braben, \$15, Oxford Univ. Press, 1800-451-7556.

Summary of suggestions for a successful scientific career (from a booklet entitled: Careers in Biological Sciences: Advancement for Women and Minorities):

1. find a well-placed supportive mentor who can give you advice on scientific and political issues.
2. have your papers and grants read by colleagues before you send them out and attach a very enthusiastic cover letter. The cover letter should say why the paper/grant is interesting and important (use phrases such as: "we show for the first time...will be of interest to many fields...).
3. respond to criticism of the paper or grant in a positive manner (long critiques do not mean rejection). In resubmitting, make sure that you clearly state how you addressed the

comments.

4. publish, publish and publish.
5. ask NSF or NIH program administrators for assistance in the preparation of your grant.
6. specific grant writing tips: study successful ones, give realistic budgets, state your aims and number them (only a couple is best), critically evaluate existing knowledge, and write your abstract last. Emphasize proven techniques, have reference letters from experts in the use of the technique (as advisors) but use the techniques on a unique and important problem.
7. before achieving tenure, give service only if it benefits yourself (i.e., devote yourself to research and teaching and say no to committees).
8. make no enemies, don't isolate yourself, develop friends among faculty and students, avoid stridency, be a team member.
9. learn to write well.
10. go to small meetings (larger meetings may not be as valuable).
11. keep on top of these issues: how much do my colleagues earn? What were their stating salaries? When will I get promoted? "Market yourself" by making clear what you do is significant. NIH's Adolphus Toliver has three "P's": prance-rush into your colleague's office to tell about your publications; preen-in order to impress people; and pout-know exactly when and how to pout without offending anybody.
12. be prepared for rejection, bounce back quickly.
13. save time for thinking; ask what new directions your research program could go into; which way science is going, and reflect on the "why" of past success.

#### **When reading a manuscript:**

1. read for overview; get main idea, scan text. Conclude if work is trivial. Read the abstract and discussion.
2. Line by line, careful reading.  
Are methods adequate? Do the data support the assertions or conclusions?
3. Examine the style of presentation; are the data better presented in a table or a figure?

#### **On the nature of intelligence**

##### I) Critical Thinking

Reference: Critical Thinking by Vincent Ryan Ruggiero (College Survival Inc, PO Box 8306; Rapid City, SD 57709). See list in book for other references.

(See quotes on pg. 4)

##### **Critical thinking skills:**

Recognizing fact versus opinion.

If you state a fact that is not common knowledge, or that can't be easily verified, briefly state where you got the information.

If you state an opinion include the opposite opinion in your summary.

If you are not sure whether a statement is a fact or an opinion, treat it as an opinion.

Characteristics of critical thinkers:

Critical thinkers are honest with themselves (I can drink a six pack and drive perfectly).

Critical thinkers resist manipulation (advertising)  
Critical thinkers realize that they are confused and then try to remedy the situation by trying to find an answer.  
Critical thinkers try to find an answer by asking lots of questions.  
Critical thinkers base their judgments on evidence (not on what they feel).  
Critical thinkers do not exaggerate or over-simplify or over-generalize. (All televangelists are crooks).  
Critical thinkers look for connections between subjects (we can use the chemical concept of pH to explain many biological processes).  
Critical thinkers are intellectually independent (they use other people's conclusions or ideas but do not always "go with the crowd" - fads or beliefs change with time and society).  
Critical thinkers are not stubborn.  
Critical thinkers will listen.  
Critical thinkers will change their opinion in light of new evidence.

2) From: Emotional Intelligence by Daniel Goleman and article in Time (Oct. 2, 1995): the central trait for "being smart:" IQ and brain power may not be as important as being able to regulate "emotion in a way that enhances living." In short, being able to put off instant reward for long term reward, being able to handle anger, frustration, loneliness and to use worry/stress to focus the mind not cloud it (i.e., hard for depressed or angry students to study), and being an optimist to overcome obstacles that will cause others to give up. Another characteristic of those with high EQ (emotional quotient): being able to work with others (form study groups).

### **Scientific Writing:**

Visit my library to look at the following books:

Writing to Learn Biology, by Randy Moore

A Short Guide to Writing About Biology (2nd Ed), by Jan A. Pechenik

The Elements of Style (3rd Ed), by W. Strunk, Jr., and E. B. White

Writing a Successful Grant Application, by Liane Reif-Lehrer

Writing Papers in the Biological Sciences, by Victoria E. McMillan.

Research: how to plan, speak and write about it. Clifford Hawkins, Marco Sorgi.

Writing to learn biology. Randy Moore.

Scientific Style and Format; the CBE manual for authors, editors and publishers

(published by Cambridge University Press).

**GRADUATE STUDENTS: USE THIS INFORMATION FOR YOUR PAPER!!**

#### **Good scientific writing is**

1. simple and concise (see later exercises); write the way that you speak to simplify.

Original: Dantzer (1977) suggested the use of tranquilizers to minimize the stress associated with fighting among pigs. Randai (1977) also suggested that sedatives could be used to control fighting when mixing unfamiliar sows. Straw bedding has been recommended to reduce fight in pigs (Ewbank and Meese, 1971). Fraser (1975) found straw bedding reduced abnormal behavior in tethered sows.

Trimmed version:

Tranquilizers or other sedatives (Dantzer, 1977; Randai, 1977) or straw bedding (Ewbank and Meese, 1971; Fraser, 1975) may be useful in minimizing stress, fighting and abnormal behavior in pigs.

2. Make sure of the meaning of every word.

A. connotation: how a word relates to others in the sentence.

Keep related words together (see Strunk);

He explained to me what it meant.

He explained what it meant to me. (better)

It is noteworthy that after the egg is pipped, the chick begins to vocalize.  
this says that it is noteworthy that the egg is pipped. Change to:  
After the egg is pipped, it is noteworthy that the chick begins to vocalize.

B. Intrinsic- actual meaning of the word. For example:

varying concentration means varying through time

various concentrations means the concentrations are stable through time and that there are different values.

infer; derive by reason, to infer conclusions

imply; to express indirectly.

refer; vs. allude-refer indirectly, can't allude directly or specifically.

aliquot- to divide into equal parts. I do not aliquot 5 mls from the solution; I would sample the solution.

Title: don't say "Studies on..." or "Effects of calmodulin..." but the title should reflect the conclusion: "Calmodulin decreases sodium ion flux..."

### **FIFTEEN ESSENTIAL RULES OF GRAMMAR**

1. Don't use no double negative.
2. Make each pronoun agree with their antecedent.
3. Join clauses good, like a conjunction should.
4. About them sentence fragments.
5. When dangling, watch your participles.
6. Verbs has to agree with their subjects.
7. Just between you and I, case is important too.
8. Don't use run-on sentences they are hard to read.
9. Don't use commas, which aren't necessary.
10. Try not to ever split infinitives.
11. Its important to use apostrophe's correctly.
12. Proofread your writing to see if any words out.

(from The Wildlife Society News, No. 113, Dec. 1967)

### **OTHER TIPS ON WRITING:**

1. What is the difference between "affect" and "effect?" In most cases, affect is a verb (to influence) and effect is a noun (result). Poor grammar can affect your grade; the effect is a low grade. Rarely, effect can be a verb (to accomplish).
2. It is not PC to say "The physician gave his patient a pill." One way around sexism is to say "The physicians gave their patients pills." Note that "A physician gave their patients a pill" is not correct.
3. Do not put one comma between the subject and the verb. Two commas are ok. This is incorrect: "The dog who was an aggressive pit bull, chased the cat." Another comma before "who" makes the sentence correct.
4. SEPARATE NOT SEPERATE; OCCURRED NOT OCCURED (in general, if a verb ends with a single consonant, double the final consonant if the accent is on the last syllable of the verb, e.g., oc-cur').
5. In a paper, results are often in the past perfect. Generalizations from published work is usually in the present tense.
6. Infer is to derive by reason. As in: infer the conclusions.  
ImPLY is to express indirectly. It is impossible to allude directly to something; use refer if there is a specific reference.
7. Aliquot is to divide into equal parts. You cannot aliquot out 50  $\mu$ L from 2 mls. Use the word "sample."
8. Put related words together: "It is noteworthy that after the egg is pipped the chick begins to vocalize." This sentence suggests that it is noteworthy that the egg is pipped.
9. Note that data is plural ("The data are...") and datum is singular.
10. When combining two sets of data with their own standard deviations: the total standard deviation is the square root of the sum of the variances.
11. Definitions should be given at the first use of the unabbreviated word:  
"The insulin receptor kinase activity (IRK)....."

### **WRITING SKILLS; HOMEWORK**

I suggest that you review basic grammar and style; a good reference is The Elements of Style by W. Strunk and E.B. White (3rd. ed). It is short (85 pages) and inexpensive. Each of the following contains one or more mistakes of punctuation, grammar or diction. Excerpts from this book are on our class web site (read and use the readings). Indicate the

necessary corrections or re-write the examples. **For questions 17-30**, record the page number or rule number from Elements of Style that explains your answer. A key will be given out later.

1. Revise the following phrases and sentences in order to make them shorter and simpler.
2. During the period that...
3. ...in the environs of....
4. ...at a high speed level...
5. X produced an inhibitory effect on the formation of Y
6. It was possible to obtain semi-preparative quantities of the substance.
7. Solvents were pre-cooled to 0 deg. C prior to use...
8. One lot contained particles greater than 75 microns, and this material was shaken on a sieve prior to use to remove particles in excess of this size.
9. In designing delivery systems for offensive use, in the committee's opinion, the basic prerequisite of these is the delivery accuracy of these systems.
10. Glycerol ether of varying degrees of unsaturation....
11. A method is described for use on unfractionated human plasma that is superior to that now in use.
12. Following the incubation,
13. Early treatment may greatly improve mortality.
14. Conversely, the opposite is true in special circumstances.
15. By this we do not mean to infer that his conclusions were wrong...
16. Experiments have been made on the effect of low and high temperatures on thyroxine production of mammals and of low temperature on avian thyroxine production.  
-----for below, reference page or rule number from Elements of Style.
17. Snakes, lizards, and turtles make up the Class Reptillia.
18. Hormones, that are produced in the pancreas, reach the liver via the portal blood.
19. Neither heat or acidification to pH 4 reduce the activity of the extract.

20. This enzyme enolase was completely denatured at 45 deg. C.
21. The major pests are the flies, mosquitoes, and the leeches.
22. Previously, the anthrone method was used, but now we employ the glucose oxidase procedure.
23. Locomotion in this species depends upon pseudopodia and flagellae are lacking.
24. The wings and tail are black, and the crest yellow.
25. This sophisticated technique is basically different than older methods.
26. The pheromones, vis-a-vis most vertebrate hormones, are unusual in several ways.
27. The fresh skin is first defatted with gasoline. Then it is washed with hot detergent solution. Finally, it is stretched and allowed to dry.
28. We have alluded specifically to the fact of the system's departure from steady state conditions.
29. Varying levels of acidity were applied, but without significant affect on the efficiency of extraction.
30. To support this hypothesis is tantamount to acceptance of the postulate that none of the vital species-specific system parameters in this animal are being expressed inside of a realistic range of values.

### **STATISTICS:**

(the equations do not print well for the web; see hardcopy)

Parametric tests are typically used by cell biol./biochemists. For both of the two major tests that we use- the t Test and regression analysis- the data must fall into a "normal distribution" or bell-shaped curve (see other restrictions below for t Test). Nonparametric data are analyzed by psychologists (does the patient feel better? often not numbers but involves ranking of happiest to saddest patient, etc.).

We use statistics to disprove or support the Null hypothesis (that nothing is changed). What is the probability of saying that there is a significant change and then be incorrect (that is, the Null hypothesis is correct yet we say that it is wrong)? We usually set this probability at 5% (0.05) of the time. That is, only 5% of the time will we be incorrect if we say that there is a significant difference between control and experimental groups. 95% of the time we will be correct when we say there is a difference. Sometimes 10% (will be incorrect 10% of the time) or 1% (esp. in medical research) is used.

1) **Difference: t test**; a parametric test for differences between the means of two samples. There are two types; one assumes that the variances between the two samples is the same, the other doesn't. We compare a calculated t value ( $t_{\text{calc}}$ ; calculated from the data) with a critical t value ( $t_{\text{crit}}$ ).

Assumes: 1. individual observations are independent of each other (if you continue to poke a patient for blood, they will become more and more apprehensive, this may alter the hormones in the blood; and the observations on hormone level would not be independent.

2. the distribution of observations are continuous; that is, you can have 41.14 and 41.15, any values possible.

3. The observations are normally distributed (not skewed, but a bell-shaped curve)

4. make sure that you use the correct form (do you assume that the variances are the same?).

draw a bell shaped curve:

### Commonly used equations describing a population:

The width of the bell-shaped curve can be represented by the variance "v" (or its square root, called the standard deviation or "S"):

$$S = \sqrt{v} = \sqrt{\frac{\sum X^2 - \frac{(\sum X)^2}{N}}{N-1}} = \sqrt{\frac{\sum (Xi - \bar{X})^2}{N-1}}$$

This number is used to calculate the t value ( $t_{\text{calc}}$ ) and:

N= number of data points and  $\bar{X}$  is the symbol for the average.  $Xi - \bar{X}$  is the difference between a datum and the average (it can be a negative number). Note the difference between  $\sum X^2$  and  $(\sum X)^2$ . (of course,  $\Sigma$  is the summation symbol).

Note that the standard error of the mean can also be calculated:

$$\text{Std. Err Mean:} = S / \sqrt{N}$$

### Pooled vs. paired t test; when to use?

If you use the paired t test, you must use the same person for both control and experimental groups. That is, you take the blood pressure of the person, inject the drug and then take the blood pressure again on the same person. If you have a group of twenty people, you would do this for all of them. If a few people happen to be athletes, their abnormally low blood pressure would increase your variance. However, with the paired t test, this problem would be minimized. If you use the pooled t Test (one group of people for the control group, a totally different group of people for the experimental group), and if you have a few people with abnormal blood pressure, the variance in your control data

would be greater. This would compromise your ability to determine if there was a change in the blood pressure with the drug.

Equation for the Pooled t test:

$$t_{calc} = \frac{|\bar{X}_1 - \bar{X}_2|}{\sqrt{\frac{N_1 S_1^2 + N_2 S_2^2}{N_1 + N_2 - 2}} \sqrt{\frac{N_1 + N_2}{N_1 N_2}}}$$

Instead of  $N_1 S_1^2 + N_2 S_2^2$ , many books suggest replacing it with:

$$(N_1 - 1)S_1^2 + (N_2 - 1)S_2^2$$

Note the use of the absolute value in the numerator. The "S" (stand. Dev.) or N (number of data points) terms refer to either group one or two (see subscript).

Degrees of freedom =  $N_1 + N_2 - 2$

Equation for the Paired t Test:

$$S_d = \sqrt{\frac{\sum d_i^2 - \frac{(\sum d_i)^2}{N}}{N - 1}}$$

$$t_{calc} = (\text{averagedifference}) / (S_d / \sqrt{N})$$

The degrees of freedom = (no. of pairs of data = N) - 1

Where  $d_i$  is the difference between the before and after data points (obtained from the same person or sample). This could be a negative number (e.g., 100-105 = -5). N is the number of data pairs (in the homework, this would be 10). To obtain the "averagedifference," add up all the differences (there would be 10 for the homework) and obtain an average (e.g., -5, 5, 0, 10 for four pairs of data points would total 10 and average would be 10/4).

After calculating the  $t_{calc}$  value, use the degrees of freedom to find a  $t_{crit}$  from a table (see our course web site for this table). Make sure that you always use a two-tailed test (unless there is a situation where you know that there is only an increase possible). If the calculated t value is less than the critical t value, then we do not reject the Null hypothesis. That is, if the calculated t value is less than the critical t value (found in the table), then there is no difference between the two groups (the drug has no effect).

## II) Trend: regression analysis (p. 66 and 136 from Barnard et al.)

With this analysis, you can quantify trends and thus predict new values of Y if given X values. You can also state whether a change in X actually alters Y values. That

is, does higher doses of a drug produce any effects at all?

Assume this equation for a line:  $Y = bX + a$

Null hypothesis is  $b=0$  (slope is zero; show graph)

Assumptions: 1) The values of X are fixed by the experimenter and the values of Y are free to vary.

2. Y is continuous whereas X can be discrete.
3. The values of Y are from a normal distribution
4. Variance around the regression line is the same for all XY pairs.

PROCEDURES: Calculate slope and intercept (see below). If you want to, you can also use the F test to see if slope = 0 or not( see p.74 of Ambrose).

### Equations for regression analysis:

$$\text{slope} = \frac{\sum XY - \frac{(\sum X \sum Y)}{N}}{\sum X^2 - \frac{(\sum X)^2}{N}}$$

$$\text{y intercept} = \frac{(\sum Y * \sum X^2) - (\sum X * \sum XY)}{(N \sum X^2) - (\sum X)^2}$$

$$\text{REGRESSION COEFF.} = \frac{\sum XY - N\bar{X}\bar{Y}}{(N-1)S_x S_y}$$

(regression coefficient r is a measure of how well the data fit the regression line)

Where  $\bar{X}$  is the average of the x's and  $\bar{Y}$  represents the average of the y's.  $S_x$  is the standard deviation of the X data points.

### Possible Concerns with statistics:

1. Note the effect of sample number: Fig. 3.2 (p. 43) on right is significant because of the large number and left figure is insignificant.

2. Confounding errors: is there more enzymatic activity as the embryo grows? so graph enzyme activity versus age. But as the embryo ages, the number of cells increase. Thus, enzyme activity increases with age, but one a per cell basis, the enzyme activity does not increase and this is what the researcher actually wanted. In child development, you find that larger children are less susceptible to viruses; is this an error? larger children are older children and they may have developed immunity over younger children

and size has nothing to do with it. So, take children of one age, and separate by size.

3. Pseudoreplication: take one patient, do the test 15 times on this patient vs. take 15 patients, do test on each patient one time. Which is better?

Remember to include sample size, average and std. dev. (or std. error) when reporting data. In a paper, identify the type of statistical test used.

### **STATISTICS HOMEWORK:**

Calculate whether a drug had any effect on the blood pressure:

PATIENT	BEFORE	AFTER DRUG
1	100	100
2	100	105
3	105	100
4	110	100
5	100	110
6	105	100
7	105	110
8	100	105
9	95	100
10	90	100

For your homework, do the calculations by hand (not using a computer program) just this once to get an understanding of the equations. You can use a computer program to check your calculations but I want to see all the intermediate steps in your calculations.

Use the **pooled** t test to calculate a t value; is there a significant difference after the drug? Do you support the null hypothesis (which is what?).

Use the **paired** t test to calculate a t value; is there a significant difference after the drug?

Compare the two tests; what is the relative tcalc with the two methods using the same set of data? Which test would you prefer to use?

Given the following data, what is the **regression line and the regression coefficient?** (data are in x-y pairs). Show all calculations.

-2, 1          -1,2          0, 6          1, 8          2, 8



$t_{CRIT}$

df	.1	.05	.01	.001
1	6.314	12.706	63.657	636.619
2	2.920	4.303	9.925	31.598
3	2.353	3.182	5.841	12.941
4	2.132	2.776	4.604	8.610
5	2.015	2.571	4.032	6.859
6	1.943	2.447	3.707	5.959
7	1.895	2.365	3.499	5.405
→ 8	1.860	2.306	3.355	5.041
9	1.833	2.262	3.250	4.781
10	1.812	2.228	3.169	4.587
11	1.796	2.201	3.106	4.437
12	1.782	2.179	3.055	4.318
13	1.771	2.160	3.012	4.221
14	1.761	2.145	2.977	4.140
15	1.753	2.131	2.947	4.073
16	1.746	2.120	2.921	4.015
17	1.740	2.110	2.898	3.965
18	1.734	2.101	2.878	3.922
19	1.729	2.093	2.861	3.883
20	1.725	2.086	2.845	3.850
21	1.721	2.080	2.831	3.819
22	1.717	2.074	2.819	3.792
23	1.714	2.069	2.807	3.767
24	1.711	2.064	2.797	3.745
25	1.708	2.060	2.787	3.725
26	1.706	2.056	2.779	3.707
27	1.703	2.052	2.771	3.690
28	1.701	2.048	2.763	3.674
29	1.699	2.045	2.756	3.659
30	1.697	2.042	2.750	3.646
40	1.684	2.021	2.704	3.551
60	1.671	2.000	2.660	3.460
120	1.658	1.980	2.617	3.373
∞	1.645	1.960	2.576	3.291

for a deg of freedom of 8,  
assume 0.05,  
 $t_{crit} = 2.306$ .  
For a signif. difference,  
 $t_{calc} > 2.306$

Abridged from Table III of R. A. Fisher and F. Yates: "Statistical Tables for Biological, Agricultural, and Medical Research," published by Oliver and Boyd Ltd., Edinburgh.  
Abridged with permission of the authors and publisher.

## **SAMPLE QUESTIONS CONCERNING CELL SIGNALING**

(see below examples of the type of questions that will be on our essay exam). Remember to read the textbook sections that pertain to the lectures. Remember, in essay exams, make sure that you do not spend too much time on one question and then end up with unanswered questions at the end of the time period. Remember to use diagrams to illustrate an answer.

Taken from:

[http://www.foothill.fhda.edu/fac/klenkeit/generaldoc/answering\\_essay\\_exams.htm](http://www.foothill.fhda.edu/fac/klenkeit/generaldoc/answering_essay_exams.htm)

Emphasis will be placed on writing and essay exams in all of my courses. The following are some hints/techniques for effective writing and taking essay exams. Please feel free to stop by my office or email me and discuss this material if you have questions.

Much of the advice that follows may seem elementary to those who already have extensive experience with in-class essay exams. Reviewing the basics is, however, a good idea. You might compare my list with your own experiences.

### **Taking exams**

1. Prepare for the exam by going over the study guide. Look over the [Guide to writing social science essays & exams](#) for tips on organizing and outlining your essays.
2. Get a normal night's sleep before an exam. Pulling an all nighter often results in muddled responses in essays.
3. Read the entire exam paper through before you begin to write. Note all of the instructions given about the number and choice of questions. **Underline** or **circle** directions such as "choose" or "cite a specific example from XXX article."
4. The next step is to make a rough time budget. Note the point value (or percentage value) of each question. Then decide how long to spend on each question and stick to your time plan.
5. Select those questions that you feel quite sure that you can answer. This seems obvious advice, but students sometimes tackle questions because they seem more difficult. They think that the instructor will be impressed by their efforts to deal with the harder question. This is nearly always a mistake. Pick the question that you are most confident about answering.
6. Make sure that you interpret the question correctly. A question that asks you to compare and contrast means that you are to do both. Too often with such questions, students only offer contrasts and do not give any comparisons.
7. Some of the terms that are used frequently in essay questions are listed below. Make sure that you are clear about the meaning of these terms.

Make a brief outline of the main points you want to make and jot terms you will incorporate and examples you might use. Once you have a brief outline, begin writing and check off each point in your outline as you complete it. Since you have done your thinking/organizing at the beginning (your outline) you do not have to constantly stop and decide where you are in your answer. This saves time.

8. Avoid lengthy introductory paragraphs on most in-class essay exams. Jump right in to answer the question. Make a thesis statement that addresses the question and then back it up with a specific example or examples.

9. Never do less than the required number of answers. If you see that you are running short on time leave that answer unfinished or as briefly as possible summarize the last part of the answer. Go on to the next question. Write something -- even a brief summary will usually earn some points, while a blank answer will earn zero.

10. Write legibly. If the reader cannot decipher your handwriting your grade may be penalized.

11. Leave time, if you can, to re-read your paper before you hand it in. Mistakes can be made when writing quickly and a re-read will allow you to make corrections. A negative may be omitted, for example, making nonsense of a sentence. You may have written the word "to" when you meant to use "too". You may have written there when you meant their. You may have failed to explain or define a term that you used.

### **Forming a thesis statement**

The thesis statement is possibly the most important element of your written work. In one simple statement it tells the reader what you will be writing about. In other words, the thesis should be a summary of what the essay is going to talk about. The thesis statement should be straightforward and declarative. The rest of the essay should support or expand upon the thesis.

An example of a thesis statement for web assignment 2 might be: "The dual labor market theory best describes the impetus for migration between Pakistan and Saudi Arabia." This tells the reader that the author is going to first summarize the dual labor market theory, then relate it to evidence about migration between Pakistan and Saudi Arabia.

While English papers and term papers often have a thesis statement at the end of an introductory paragraph, for short essays and exams, start out with the thesis. This way you don't waste any valuable time or space warming up to the topic, but you get right to the point. The shorter the written work is supposed to be, the more quickly you should give the reader your thesis. For more about the fundamentals of writing essays see the [Guide to writing social science essays & exams](#).

## Key terms in exam writing

Some terms that are frequently used in essay-type questions are listed below. Make sure that you are clear about the meaning of these.

<b>Compare</b>	Look for similarities and differences between
<b>Contrast</b>	Set in opposition in order to bring out differences
<b>Criticize</b>	Give your judgment about the merit of theories, or opinions, or about the truth of facts. You should back your judgment up by a discussion of specific evidence.
<b>Define</b>	Set down the precise meaning of a word or phrase.
<b>Describe</b>	Give a detailed or graphic account of.
<b>Discuss</b>	Investigate or examine by argument, sift and debate, giving reasons pro and con.
<b>Evaluate</b>	Make an appraisal of the worth of something from the perspective of its truth or utility; include to a lesser degree your personal opinion.
<b>Explain</b>	To make plain, to interpret, and to account for.
<b>Illustrate</b>	Use a figure or diagram to explain or clarify. <u>Or make clear by use of concrete, specific examples.</u>
<b>Interpret</b>	Expound the meaning of; make clear and explicit; usually also giving your own judgment.
<b>Justify</b>	Show adequate grounds for decisions or conclusions.
<b>Outline</b>	Give the main features or general principles of a subject
<b>Relate</b>	To show how things are connected to each other, and to what extent they are alike, or affect each other.
<b>Review</b>	To make a survey of, examining the subject critically.
<b>State</b>	Present in brief, clear form.
<b>Summarize</b>	Give a concise account of the chief points or substance of a matter, omitting details and examples.
<b>Trace</b>	Follow the development or history of a topic from some point of origin.

[this list adapted from Bird, C. and Bird, D. M., *Learning More Effective Study*, New York. Appleton-Century-Crofts 1945 pp 195-8]

**MODIFIED FROM:** Professor Kevin Hopkins, Widener-Harrisburg; for more detail, see:<http://academic.udayton.edu/legaled/barpass/Essay/Advice05.htm>

The overall purpose behind the essay examination is to: (1) test your knowledge and understanding of the case materials covered during the semester (i.e. can you identify from the exam fact pattern the relevant issues/areas of law to be discussed); and (2) test your ability to apply the ideas to new and/or factually similar situations.

To do this successfully, it is critical that you know the applicable idea. You must also, however, be able to convey this information as quickly as possible and in some type of structured written format. I offer the following approach to **reading the essay exam question** and organizing your thoughts. Remember: you should spend at least 1/4 to 1/3 of the allotted time for each question outlining and organizing your thoughts.

1. Browse through the **entire** exam packet first to assess the applicable time allotments for the questions, and to make sure your examination packet is complete (i.e. no missing pages, etc.).
2. For each specific fact pattern/exam question, I suggest that you go immediately to the end of the fact pattern and read the specific question to be addressed. This will usually be the last sentence of the fact pattern, or the last paragraph and may contain words such as "evaluate all possible ...," "name the steps," etc..
3. Once you have determined what the question is asking, quickly read the entire fact pattern first for a basic understanding of the facts, high-lighting and noting the obvious issues and facts that will be important in assessing the issues. You can do this by using hi-liters/colored pens, and making minor notations in the margins of the examination page.
4. Reread the question again, but this time, take it more slowly. During this review of the question, continue to look for and to note issues (i.e. causes of action or legal problems/situations covered during your review of the substantive law materials) but begin to really focus on those facts that will be critical for THE ANSWER.
5. You are ready to outline the ANSWER. You could begin by restating the question, then listing parts of the answer and illustrating with a diagram.

Ask yourself: Have you identified the issues involved in the problem? Have you alerted the reader "up front" to the issues to be decided? Have you properly "wrapped up" your argument for a specific issue before moving on to the next issue? Have you provided a conclusion for the reader? Have you answered the question posed? Is your answer responsive to the question? This is critical. Finally, does your answer reflect all of your knowledge of the cause of action, the applicable counter arguments and defenses?

1. diagram the regulation of ras p21. Include regulatory proteins.
2. " PI turnover
3. " cAMP system
4. discuss receptors; affinity measurements (between receptor and hormone), structure and action
5. diagram cell cycle regulation

## HOMEWORK AND NOTES FOR VIDEO ON MOLECULAR BIOLOGY TECHNIQUES.

This section may not be used this year- this will be decided later in the semester. Much of your reading will involve knowledge of methods; a video that will review basic DNA terminology and techniques of molecular biology will be shown. Please complete questions after viewing the video (this may require reviewing basic Biology 2051; see ch. 19 in Campbell's textbook; see me or look in reserves in library for a copy). I will check to see that you have attempted to answer the questions listed below (note some are already answered). One week after the video, I will collect all answers for grading. Write out the questions on other paper (not below). I encourage you to work in groups (but hand in your own written answers). As with our lecture on statistics and writing, you will not become a molecular biologist with this brief review/introduction. From the *video or other sources (e.g., advanced cell text noted earlier)*, Define:

1. DNA cloning
2. DNA structure; backbone is made up of \_\_\_\_ and \_\_\_\_\_. Rungs of the ladder are the four nucleotides: \_\_\_\_\_ and they pair up as following:
3. RNA differs from DNA: it is single stranded not ds; uses nucleotide \_\_\_\_ not \_\_\_\_; uses ribose not deoxyribose.
4. T F (circle one) A chromosome is one DNA molecule, with many genes.
5. Replication of DNA:
6. Transcription:
7. Codon:
8. Translation:
9. Plasmids: small, circular DNA found in cytoplasm of bacteria.
10. Vector: a carrier, typically a virus or plasmid, of foreign DNA into a cell (usually a bacterium).
11. Transformation: to put DNA into a cell
12. bacteriophage:
13. mutation:
14. restriction enzymes: cut DNA at recognition sites
15. DNA ligase: anneals DNA fragments
16. DNA polymerase (e.g., Klenow, T4): enzymes that made DNA

II) Making Genomic libraries and Gene Cloning: Briefly, take all DNA from human cells, make fragments with restriction enzymes, put all fragments (including human insulin gene) into plasmid (a vector), then put plasmid into bacteria (transformation). As bacteria grow, they replicate all DNA including human insulin gene. Then isolate DNA from bacteria; now have millions of copies of human insulin gene; now you can sequence the DNA.

17. What's easier to use to isolate DNA? Cesium chloride gradient or DNA resin?
18. What is ethidium bromide used for? Is it dangerous? Limits?
19. DNA subcloning:
20. when a tet gene is in a bacterium (in a plasmid), it will prevent or allow (circle one) bacterial growth in presence of tetracycline.

III) Draw a series of pictures describing DNA hybridization: which bacterium picked up the fragment of DNA that contains the human insulin gene? Procedure: make a replica, release DNA from cells, denature (two DNA strands separate at high temperature), add

DNA to a filter where it binds, add radioactive DNA probe from insulin gene to locate insulin gene. This identifies which bacteria picked up the insulin gene (vs. other genes).

VOL. 2. Note I skip less important and more complicated procedures. In very general terms,

21. Describe steps of a Southern blot:

22. Describe Dot blot:

23. Describe DNA sequencing:

24. define a Point mutation:

25. Describe PCR: (purpose: to make large quantities of DNA)

26. Describe Polyacrylamide gel electrophoresis

27. Western blot: (purpose: to quantify amount of a certain protein)