



FACULTY OF MEDICINE

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF PHARMACOLOGY

**PHAR 3102**

**Molecular Pharmacology**

COURSE OUTLINE

SEMESTER 1, 2011



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## PHAR3102 Course Information

Molecular Pharmacology (PHAR3102) is a 3<sup>rd</sup> year Science Course worth Six Units of Credit (6 UOC). The course is usually undertaken as part of a major in Pharmacology in a Bachelor of Science or Bachelor of Medical Sciences. This course builds on the information you have already gained in Introductory Pharmacology and Toxicology (PHAR2011)

### OBJECTIVES OF THE COURSE

This course will examine the molecular basis of drug action and explore how cutting edge biotechnology and biomedical research can advance pharmacological knowledge, increasing our understanding of how drugs work. The following areas will be studied in detail; genetic variability in drug action, protein structure-activity relationships, receptor-ligand interactions, signal transduction, biochemical and molecular aspects of G-protein coupled receptors and their signalling mechanisms. Research and analytical skills will be developed in practical classes.

### COURSE CO-ORDINATOR and LECTURERS:

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Course Coordinator:

Dr Angela Finch

Rm 408 Lowy Building ph: 9385 1325

Consultation times: Tuesday 12-1 pm

Co-coordinator

Dr Lu Liu

Rm 209 Wallace Wurth Building ph: 9385 8762

Consultation times: Wednesday 3-4 pm

Students wishing to see course coordinators outside consultation times should make an appointment *via* email.

Lecturers in this course:

Dr Angela Finch

a.finch@unsw.edu.au

A/Prof. Renate Griffith

r.griffith@unsw.edu.au

Dr Nicole Jones

n.jones@unsw.edu.au

Dr Trevor Lewis

t.lewis@unsw.edu.au

Dr Lu Liu

lu.liu@unsw.edu.au

A/Prof. Laurence Wakelin

l.wakelin@unsw.edu.au

### COURSE STRUCTURE and TEACHING STRATEGIES

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Learning activities occur on the following days and times:

- Lectures: Tuesday 10 am -12 pm
- Tutorials: Wednesday 12-1pm or Friday 1-2pm\*
- Practicals: Monday 10 am -1 pm or Monday 2-5pm\*

\* Once enrolled in one of the two sessions, students cannot change.

Students are expected to attend all scheduled activities for their full duration (2 hours of lectures per week and up to 4 hours of practical and tutorial sessions per week). Students are reminded that UNSW recommends that a 6 units-of-credit course should involve about 150 hours of study and learning activities. The formal learning activities are approximately 65 hours throughout the semester and students are expected (and strongly recommended) to do at least the same number of hours of additional study.

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Lectures will provide you with the concepts and theory essential for an understanding of molecular pharmacology. To assist in the development of research and analytical skills practical classes and tutorials will be held. These classes and tutorials allow students to engage in a more interactive form of learning than is possible in the lectures. The skills you will learn in practical classes are relevant to your development as professional scientists.

### **APPROACH TO LEARNING AND TEACHING**

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The learning and teaching philosophy underpinning this course is centred on student learning and aims to create an environment which interests and challenges students. The teaching is designed to be engaging and relevant in order to prepare students for future careers.

Although the primary source of information for this course is the lecture material, effective learning can be enhanced through self-directed use of other resources such as textbooks and Web based sources. Your practical classes will be directly related to the lectures and it is essential to prepare for practical classes before attendance. It is up to you to ensure you perform well in each part of the course; preparing for classes; completing assignments; studying for exams and seeking assistance to clarify your understanding.

### **STUDENT LEARNING OUTCOMES**

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PHAR3102 will develop those attributes that the Faculty of Science has identified as important for a Science Graduate to attain. These include; skills, qualities, understanding and attitudes that promote lifelong learning that students should acquire during their university experience.

#### Graduate Attributes

- A. Research, inquiry and analytical thinking abilities
- B. The capability and motivation for intellectual development
- C. Ethical, social and professional understanding
- D. Effective communication
- E. Teamwork, collaborative and management skills
- F. Information Literacy – the skills to locate, evaluate and use relevant information.

On completion of this course students should:

1. be able to describe the genomic regulation of drug action
2. be able to discuss the molecular pharmacology of receptors, channels and enzymes
3. have gained a knowledge of molecular biology techniques used in pharmacology
4. be able to accurately record experimental data and draw conclusions from experimental data
5. be able to demonstrate their ability to work in teams and communicate scientific information effectively

### **ASSESSMENT PROCEDURES**

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| • Progress exam (40 min duration)                 | <b>15%</b> |
| • Laboratory notebook                             | <b>10%</b> |
| • Molecular techniques wiki and learning activity | <b>10%</b> |
| • End of session examination (2 hours duration)   | <b>60%</b> |
| • Tutorial participation                          | <b>5%</b>  |
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The *practicals* are provided to support lecture material and practise analytical skills. The practical classes and tutorials help you to develop graduate attributes A, C, D & E. At the completion of the practical course you will be required to submit your laboratory notebook covering all of the practical sessions.

In the tutorial sessions students will work in teams to research a technique used in molecular pharmacology. They will submit an *information wiki* and facilitate a *learning activity* in the tutorial session. This assessment task will allow you to develop your research, information literacy, communication and time management skills, as well as allowing you to demonstrate your ability to work in a team and collaborate successfully (Graduate Attributes A, D, E & F).

Written assessment tasks must be submitted electronically *via* Blackboard, through Turnitin. A penalty will apply for late submissions (10% per day).

The *progress examination* will be held during the session on the 12<sup>th</sup> of April. This exam will give you feedback on how you are succeeding in the course. The *progress examination* and *end of session examination* will test not only your knowledge of the molecular pharmacology of receptors, channels and enzymes but also your ability to apply the knowledge you have acquired from multiple lectures to molecular pharmacology scenarios. The examinations may be in the format of MCQ, short or long answer questions. The questions will be based on the material covered in the lectures, practical classes and tutorials. Material covered prior to the progress exam may be again examined in the final exam. The examinations will address graduate attributes A and B. The end of session examination will be held during the official examination period.

## **TEXTBOOKS AND OTHER RESOURCES**

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A single primary text which adequately covers the content of this course has not been identified. Therefore each lecturer will provide you with additional resources to supplement their lecture material. These resources will take the form of text books, journal articles or web-based resources. If available, links to the electronic form of these resources will be put on the course Blackboard page.

“A pharmacology primer: theory, applications, and methods” by T. Kenakin will be used as a reference text for lectures given in weeks 9-12. The 2<sup>nd</sup> Edition of this text is available electronically via the UNSW library.

## **COURSE EVALUATION AND DEVELOPMENT**

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Each year feedback is sought from students about the courses offered in the Department of Pharmacology and continual improvements are made based on this feedback. The Course and Teaching Evaluation and Improvement (CATEI) Process of UNSW is the way in which student feedback is evaluated and significant changes to the course will be communicated to subsequent cohorts of students. Also a staff-student liaison group will be set up and students will be invited to become class representatives to seek feedback from their colleagues and meet with academic staff to discuss any issues that arise. Based on feedback given in these meetings changes will be implemented during the course and for future years.

*Based on the feedback received in 2009 and 2010 the following changes have been made: questions provided to help focus the reading of journal articles for tutorials, reduction in the proportion of total marks for the final examination, marks to encourage participation in tutorials, smaller practical classes and reduction in the length of each experiment to ensure it can be completed within a three hour practical class.*

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## GENERAL INFORMATION

The Department of Pharmacology is part of the School of Medical Sciences and is within the Faculty of Medicine. It is located in the Wallace Wurth building. General inquiries can be made at the BABS.SOMS.BEES (B.S.B.) Student Office, located on the Ground Floor Room G27, of the Biosciences Building. Office hours are 9.00 am - 5:00pm.

**Professor Margaret Morris** is Head of Department and appointments to meet with her may be made through the Administrative Assistants in Room G3 Wallace Wurth.

**Departmental Vacation Scholarships:** The Department of Pharmacology supports several summer vacation scholarships each year to enable good students to undertake short research projects within the department. For further details contact the Administrative Officer.

**There is an honours program conducted by the School.** The Honours program is coordinated by Dr Patsie Polly (patsie.polly@unsw.edu.au), Ph: 93852924. Any students considering an Honours year should discuss the requirements with the coordinator. Outstanding students may be considered for scholarships offered by the University and these are offered annually.

### **Postgraduate degrees**

The Department of Pharmacology offers students the opportunity to enter into the following graduate programs:

**Course Work Masters:** Masters in Drug Development. For more information contact Dr John Langlands (j.langlands@unsw.edu.au)

**Research Masters:** In Pharmacology. For more information contact the post-graduate coordinator Dr Pascal Carrive (p.carrive@unsw.edu.au)

**Doctorate (Ph.D):** In Pharmacology. For more information contact the post-graduate coordinator Dr Pascal Carrive (p.carrive@unsw.edu.au)

### **The School Teaching Administrator**

Ms Carmen Robinson is able to provide additional information on any courses offered by the School.

BABS.SOMS.BEES (B.S.B.) Student Office, G27 Biosciences Building.

ph:9385 2464,

Email: Carmen.Robinson@unsw.edu.au

## OFFICIAL COMMUNICATION BY EMAIL

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All students in the course PHAR3102 are advised that e-mail is the official means by which the School of Medical Sciences at UNSW will communicate with you. All e-mail messages will be sent to your official UNSW e-mail address (e.g. z1234567@student.unsw.edu.au) and, if you do not wish to use the University e-mail system, you **MUST** arrange for your official mail to be forwarded to your chosen address. The University recommends that you check your mail at least every other day. Facilities for checking e-mail are available in the School of Medical Sciences and in the University library. Further information and assistance is available from IT at UNSW (<http://www.it.unsw.edu.au/students/index.html>.)

**When contacting a lecturer with a query, it is essential that the following information is provided as a minimum: student name, student number, course number, course name.**

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## ATTENDANCE REQUIREMENTS

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Attendance at scheduled teaching activities is governed by the University's requirement that students attend at least 80% of all classes.

**Attendance at practical classes is compulsory, and must be recorded in the class roll at the start of each class. Arrival more than 15 minutes after the start of the class will be recorded as non-attendance. It is your responsibility to ensure that the demonstrator records your attendance and no discussions will be entered into after the completion of the class.** Satisfactory completion of the work set for each class is essential. It should be noted that non-attendance for other than documented medical or other serious reasons, or unsatisfactory performance, for more than 1 practical class during the session may result in an additional practical assessment exam or ineligibility to pass the course.

The University acknowledges that students are involved in many extra-curricular activities throughout their studies. The School of Medical Sciences is generally supportive of students' activities but must be confident that these do not significantly impact on attendance at scheduled teaching activities or completion of assessment requirements.

Guidelines on extra-curricular activities affecting attendance can be found on the School of Medical sciences Website.

[http://medicalsciences.med.unsw.edu.au/SOMSWeb.nsf/resources/Course+Outline+NEUR+2/\\$file/Extra-curricularActivitiesSOMS.pdf](http://medicalsciences.med.unsw.edu.au/SOMSWeb.nsf/resources/Course+Outline+NEUR+2/$file/Extra-curricularActivitiesSOMS.pdf)

## BEHAVIOUR IN PRACTICAL CLASSES

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The practical class is an opportunity for students to develop graduate attribute C by behaving in an ethical, socially responsible and professional manner within the practical class.

- Punctual arrival is expected.
- Turn off mobile phones before entering the class.
- A lab coat must be worn when required practical classes
- Enclosed shoes are compulsory.

Students must take due care with biological and hazardous material and make sure all equipment is left clean and functional. Those who don't adhere to these basic laboratory rules will be marked absent.

## PRACTICAL CLASSES

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In the interests of safety, special attention should be paid to any precautionary measures recommended in the notes. If any accidents or incidents occur they should be reported immediately to the demonstrator in charge of the class who will record the incident and recommend what further action is required.

### Animal Experimentation

The procedures used in the laboratory classes involving *the use of animals* have been approved by Animal Care and Ethics Committee (registration number ACE04/54B). All experiments undertaken in the Department of Pharmacology adhere to the NHMRC code of conduct for animal experimentation.

## NOTICEBOARDS

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Noticeboards for this course can be found on the 2nd floor of the Wallace Wurth building.

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Current timetables and information relevant to you will be displayed here and on the course page on Blackboard. It is your responsibility to check these regularly.

### **TECHNOLOGY ENABLED LEARNING AND TEACHING RESOURCES**

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The Department of Pharmacology has chosen to use the University's central Blackboard service to provide teaching material for all of its courses.

- To access these materials, go to the TELT, or Technology Enabled Learning and Teaching web site <http://telt.unsw.edu.au/>.
- Click on "Login to UNSW Blackboard" and log on using the "Web Single Sign On" service
- After logging on to Blackboard, look for the course PHAR3102. You should have access to it if you are properly enrolled.
- You can make use of Lectopia recordings taken of the lectures that are available on Blackboard. Lecture slides will also be made available on Blackboard.

### **HANDWRITING**

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Students whose writing is difficult to understand will disadvantage themselves in their written assessment. Make every effort to write clearly and legibly. Do not use your own abbreviations.

### **SPECIAL CONSIDERATION**

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**Please note the following Statement regarding Special Consideration.**

If you believe that your performance in a course, either during session or in an examination, has been adversely affected by sickness or for any other reason, you should notify the Registrar and ask for special consideration in the determination of your results. Such requests should be made as soon as practicable after the problem occurs. **Applications made more than three days after an examination in a course will only be considered in truly exceptional circumstances.**

When submitting a request for special consideration you should provide all possible supporting evidence (eg medical certificates) together with your registration number and enrolment details. Consideration request forms are available from the Student Centre in the Chancellery and from Course Offices. In exceptional circumstances further assessment may be given. **If you believe you might be eligible for further assessment on these grounds, you should contact the Course Authority or the relevant Course Office as soon as possible.** Please refer to <https://my.unsw.edu.au/student/resources/Policies> for further details regarding special consideration.

### **MISSED EXAMS**

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If in any circumstances you unavoidably miss an examination, you must inform the Registrar and also contact the relevant Course Office immediately. Normally, if you miss an exam (without medical reasons) you will be given an absent fail. If you arrive late for an exam no time extension will be granted. It is your responsibility to check timetables and ensure that you arrive with sufficient time. **PLEASE NOTE** that if you miss any examinations for medical reasons you must lodge a medical certificate with UNSW Student Central within **3 DAYS** (refer to <https://my.unsw.edu.au/student/atoz/SpecialConsideration.html> for further details). Your request for consideration will be assessed and a deferred exam may be granted. You cannot assume you will be granted supplementary assessment. The deferred exam may include a significant oral element.

**The supplementary exam will be held in the week starting the 11<sup>th</sup> of July, 2011.**

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## MISSED PROGRESS EXAM

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If you unavoidably miss the progress exam in PHAR3102, you must inform the course coordinator within **3 DAYS**. You must supply adequate documentation (e.g. medical certificate) to be considered for any supplementary progress exam.

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## MEDICAL CERTIFICATES

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Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other acceptable documentation to the course coordinator. **Certificates should be lodged no more than 3 days after an absence. Certificates lodged after 7 days will not be accepted.** The following details must be attached: Name, Subject number, Group number, Date of the class, Name of class/es missed.

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## STUDENT SUPPORT SERVICES

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Those students who have a disability that requires some adjustment in their teaching or learning environment are encouraged to discuss their study needs with the course coordinator prior to, or at the commencement of, their course, or with the Equity Officer (Disability) in the Student Equity and Disabilities Unit. Issues to be discussed may include access to materials, signers or note-takers, the provision of services and additional exam and assessment arrangements. Early notification is essential to enable any necessary adjustments to be made.

Student Equity and Disabilities Unit, Ground Floor of the Goodsell Building

**Tel:** +61 2 9385 4734/5434

**Email:** [seadu@unsw.edu.au](mailto:seadu@unsw.edu.au)

**Website:** [www.studentequity.unsw.edu.au](http://www.studentequity.unsw.edu.au)

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## STUDENT RIGHTS AND RESPONSIBILITIES

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<https://my.unsw.edu.au/student/resources/Policies.html#StudentResponsibilities&Conduct>

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## APPEAL PROCEDURES

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Details can be found at MyUNSW via the Student Central link.

<https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html>

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## GRIEVANCE RESOLUTION OFFICER

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In case you have any problems or grievance about the course, you should try to resolve it with the Course Coordinator (Dr Angela Finch ph:9385 1325) or the Head of Department (Prof Margaret Morris ph: 9385 1560). If the grievance cannot be resolved in this way, you should contact the School of Medical Sciences Grievance Officer, Dr P.Pandey (9385 2483, [P.Pandey@unsw.edu.au](mailto:P.Pandey@unsw.edu.au)).

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## PLAGIARISM

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The School of Medical Sciences will not tolerate plagiarism in submitted written work. The University regards this as academic misconduct. Evidence of plagiarism in submitted assignments, etc. will be thoroughly investigated and may be penalised by the award of a score of zero for the assessable work. Evidence of plagiarism may result in a record being made in the Central Plagiarism Register and the Faculty Students Ethics Officer being notified.

### What is Plagiarism?

Plagiarism is the presentation of the thoughts or work of another as one's own.\* Examples include:

- direct duplication of the thoughts or work of another, including by copying material, ideas or concepts from a book, article, report or other written document (whether published or unpublished), composition, artwork, design, drawing, circuitry, computer program or software, web site, Internet, other electronic resource, or another person's assignment without appropriate acknowledgement;
- paraphrasing another person's work with very minor changes keeping the meaning, form and/or progression of ideas of the original;
- piecing together sections of the work of others into a new whole;
- presenting an assessment item as independent work when it has been produced in whole or part in collusion with other people, for example, another student or a tutor; and
- claiming credit for a proportion a work contributed to a group assessment item that is greater than that actually contributed.†
- For the purposes of this policy, submitting an assessment item that has already been submitted for academic credit elsewhere may be considered plagiarism.
- Knowingly permitting your work to be copied by another student may also be considered to be plagiarism.
- Note that an assessment item produced in oral, not written, form, or involving live presentation, may similarly contain plagiarised material.
- The inclusion of the thoughts or work of another with attribution appropriate to the academic discipline does *not* amount to plagiarism.
- The Learning Centre website is the main repository for resources for staff and students on plagiarism and academic honesty. These resources can be located via:[www.lc.unsw.edu.au/plagiarism](http://www.lc.unsw.edu.au/plagiarism)

The Learning Centre also provides substantial educational written materials, workshops, and tutorials to aid students, for example, in:

- correct referencing practices;
- paraphrasing, summarising, essay writing, and time management;
- appropriate use of, and attribution for, a range of materials including text, images, formulae and concepts.

Individual assistance is available on request from The Learning Centre.

Students are also reminded that careful time management is an important part of study and one of the identified causes of plagiarism is poor time management. Students should allow sufficient time for research, drafting, and the proper referencing of sources in preparing all assessment items.

\* Based on that proposed to the University of Newcastle by the St James Ethics Centre. Used with kind permission from the University of Newcastle

† Adapted with kind permission from the University of Melbourne.

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## **Molecular Pharmacology LECTURE and PRACTICAL OUTLINES**

The course timetable is appended at the end of these notes and can also be found on Blackboard.

The course is divided into 5 main themes covering the molecular basis of drug action.

- **Genomic Regulation of Drug Actions**
- **Protein Structure**
- **Molecular Pharmacology of Receptors, Channels and Enzymes**
- **Signal Transduction and Modulation**
- **Receptor Theory**

### **Introduction to Molecular Pharmacology**

This lecture will give an overview of what is encompassed in the term “molecular pharmacology”. The impact molecular biology techniques have had on the study of pharmacology will be discussed. The role of molecular pharmacology in 21<sup>st</sup> century pharmacology will be explored.

### **Genomic Regulation of Drug Actions**

#### Pharmacogenetics and Pharmacogenomics

The concept of pharmacogenetics and pharmacogenomics will be covered in these lectures. The types of genetic mutations: single nucleotide polymorphisms; tandem repeat polymorphisms; gene insertion and deletion; gene duplications; alternative splicing and their effects on drug targets will be explored. The influence of genetic background on drug efficacy and the use of pharmacogenomics to individualise therapy will also be covered.

#### *In silico* Pharmacology: Practical

In this practical we will be searching for new isoforms of cytochrome P450 thought to be involved in inter-individual differences in drug metabolism and which contribute to either a lack of efficacy or adverse side effects of drugs. To identify a putative new CYP isoform, we will be using publically accessible databases, other computer based techniques and data obtained from RT-PCR.

#### The Regulation of Gene Transcription

This lecture will briefly discuss the process of gene transcription and go on to examine transcription factors in more detail – including their different structures and roles in biological functions such as development, responses to environmental stimuli (e.g. heat or low oxygen), and gene transcription. A number of examples of therapeutic agents that can act by modulating gene transcription – including hormones acting at nuclear receptors, will be discussed.

#### Pharmacological Regulation of Gene Expression: Practical

Drug induced changes of gene expression of transcription factors will be examined. Techniques learnt include tissue/cell culture, RNA isolation, RNA quantification, RT-PCR and gel electrophoresis. Primer design will also be introduced.

### **Protein Structure**

#### Protein Structure

Proteins are the largest class of drug targets and an understanding of their three-dimensional structure is essential for molecular pharmacology. This lecture will review the

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basics of protein structure. Students will learn about the structure and properties of amino acids and about the four levels of protein architecture, primary through to quaternary structure.

### Receptor-Ligand Interactions

In this lecture we will review the fundamental thermodynamic equations describing drug binding to a receptor focusing on the relationships between affinity, enthalpy and entropy, as they relate to the forces underlying molecular recognition. Of special importance will be a range of electrostatic forces, the hydrogen bond, hydrophobic bonding, and a variety of, little appreciated, entropic effects that have a profound influence on affinity and specificity.

## **Molecular Pharmacology of Receptors, Channels and Enzymes**

### GPCRs

This lecture will provide an introduction to the six GPCR families. It will explore the structural similarities and diversity between these families. Representative members from each family will be examined in more detail. The role of receptor dimerisation and receptor activity modifying proteins (RAMPs) in producing different receptor phenotypes will also be covered.

### GPCRs: Role of Structural Motifs

This lecture will take a more detail look at the key structural regions of GPCRs and their role in receptor activation and regulation. The structural regions examined will include the N-terminus, extracellular loops, specific transmembrane helices, the DRY motif, intracellular loops and tails.

### How Enzymes Work

This lecture will cover general principles of how enzymes work including; catalytic transition state, binding energy and reaction specificity, equilibrium constant and enzyme kinetics (the Michaelis-Menten equation).

### Drug Modulation of Enzyme Function

This lecture will cover the basic principles of how drugs modulate enzyme activity including competitive, non-competitive and uncompetitive inhibition. A brief overview of analytical techniques used in enzyme activity characterisation will also be given.

### Channels

This lecture will review ligand-gated ion channels, voltage-gated ion channels, osmolyte or mechanosensitive channels, transient receptor potential channels and gap junction channels. The diversity of the functions these ion channels perform and the diversity of the subunits that compose these ion channels will be introduced. Our understanding of how these channels function has been made possible through the application of a number of molecular techniques and from a growing number of crystal structures.

### Receptor Enzymes

Receptor enzymes transduce signals through a unique mechanism. They have ligand binding domains on the extracellular surface of the plasma membrane, and an enzyme active site on the cytosolic side. These two domains are connected by a single transmembrane domain. This important class of receptors will be introduced in this lecture with a particular focus on receptor tyrosine kinases.

## **Signal Transduction and Modulation**

### Second Messengers

This lecture will review the types of second messenger molecules. Several examples of second messenger systems, including: the phosphoinositol,  $\text{Ca}^{2+}$ , cAMP, cGMP and

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arachidonic acid systems will be covered. The main signal transduction pathways used by GPCR will be introduced in this lecture and the role of second messengers as drug targets will be explored.

### Guanine Nucleotide-Binding Proteins (G-proteins)

This lecture will review the members of the G-protein superfamily. It will explore the structural characteristics of this family and the mechanisms of G-protein activation and regulation, including the GTPase and GTP switch. G-protein dependent signalling pathways will be covered. The role of G-proteins in disease will be discussed.

### Regulation of GPCR Signalling

Mechanisms by which receptor desensitisation occurs, including internalisation, phosphorylation, binding of  $\beta$ -arrestins, and degradation will be covered. The role of homologous and heterologous in receptor regulation will be explored. Some of the key enzymes involved in modulation of GPCR signalling include; second messenger dependant kinases, G-protein receptor kinases and RGS proteins. The function and regulation of these enzymes will be covered.

### Receptor Internalisation & Alternative Signalling Pathways

Ligand mediated endocytosis and the regulation of this process will be discussed. The classification of desensitisation of GPCRs into Class A and Class B and the role of internalisation in non-G-protein mediated receptor signalling will also be discussed.

### Receptor Signalling: Practical

This practical will examine the ability of the  $\beta_2$  adrenergic receptor to activate extracellular signal-regulated kinase (ERK) via G-protein dependent and independent pathways.

## **Receptor Theory**

### Advanced Pharmacodynamics

The pharmacological concept of potency, efficacy,  $pD_2$ ,  $pA_2$  will be reviewed. The calculation of  $pD_2$  and  $pA_2$  values from dose-response curves of agonists and antagonists will be covered. Factors affecting pharmacodynamic variability and the role of this variability in drug efficacy and toxicity will be discussed.

### Determining Antagonist Potency: Practical

In this computer-aided practical the antagonist potency of mepyramine against histamine-induced contractile responses of guinea-pig ileum will be determined.  $EC_{50}$  values will be obtained from concentration-response curves generated by semi-log paper and Prism. The antagonist  $pA_2$  value will be calculated using the Arunklakshana & Schild method.

### Constitutively Active Receptors and Inverse Agonists:

The concept of constitutively active receptors will be discussed in this lecture. Examples of wide-type receptors, naturally occurring receptor mutants, receptor variants created by site-directed mutagenesis, showing constitutive activity will be covered. The concept of inverse agonism and its discovery through molecular pharmacology techniques will be discussed. Examples of inverse agonists will be given and their potential as therapeutics will be discussed.

### Allosteric Modulators:

This lecture will cover the principles of receptor allosteric modulation. The concepts of allosteric versus orthosteric binding sites will be explored. The allosteric mechanisms in activation of ligand-gated channels and GPCRs will be covered. The role of allosteric sites as novel drug targets will be explored.

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### Signalling-Bias,

Signalling-bias (also called; ligand-directed signalling, functional selectivity, agonist-directed trafficking, biased agonism, or protean agonism) describes the observation that different ligands acting on the same receptor cause different patterns of response. These observations have led to a change in the concept of the receptor as either off or on but rather existing in a spectrum of conformational states each of which gives rise to a different signalling outcome. This lecture will explore these concepts and the influence they have on drug development.

### Receptor Theory

Since the 1920's models have been developed to assist in the understanding of the complex events that occur upon ligand binding to receptor. The first simple model was the two-state model, however with advances in pharmacology (such as molecular pharmacology) this model could no longer explain the results obtained, this led to the development of more complex models; including the Occupational and Operational models of agonist action followed by the Ternary complex model and the Cubic ternary complex model. These lectures will discuss the development of these models and examine specific examples of experimental results which support the receptor states described by these models. The Induction versus Conformational Selection hypotheses of ligand action will also be covered.

### New concepts in Pharmacology

In this lecture we will discuss the emerging concepts in receptor pharmacology that are currently being published and debated at scientific meetings, including heteromers, bitopic ligands and signalling texture.

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## TIME TABLE

<b>Wk</b>		<b>Lecture</b> Tuesday 10-11am BioMedF	<b>Lecture</b> Tuesday 11-12pm BioMedF	<b>Practical</b> Monday 10-1 or 2-5pm ‡305 BioSci *202 or 204 WW	<b>Tutorial</b> Wednesday 12-1pm Mat 130 or Friday 1-2pmThursday Webster 250
1	28/2	Introduction to Molecular Pharmacology (A Finch)	Pharmacogenetics/genomics I (L Liu)		Introduction to Assessment Tasks (AF)
2	7/3	Pharmacogenetics/genomics II (L Liu)	Nuclear Receptors/Transcription Factors (N Jones)	<i>In Silico</i> Pharmacology *	Molecular Techniques Tutorial (AF)
3	14/3	Protein Structure (R Griffith)	Receptor-Ligand Interactions (L Wakelin)	Pharmacological Regulation of Gene Expression (Part A)‡	Journal Club (AF)
4	21/3	GPCRs: Introduction to Families A, B & C (A Finch).	GPCRs: Role of Structural Motifs (A Finch)	Pharmacological Regulation of Gene Expression (Part B)‡	Molecular Techniques Tutorial (LL)
5	28/3	Channels (T Lewis)	Receptor Enzymes (R Griffith)	Pharmacological Regulation of Gene Expression (Part C)‡	Journal Club (LL)
6	4/4	Enzymes ( R Griffith)	Enzyme Modulation (R Griffith)	Pharmacological Regulation of Gene Expression Data Analysis*	Molecular Techniques Tutorial (LL)
7	11/4	<b>Progress Exam</b>	Second Messengers (L Liu)	Receptor Signalling (Part A)‡	Journal Club (LL)
8	18/4	G-proteins (L Liu)	Regulation of GPCR Signalling (A Finch)	Receptor Signalling (Part B)‡	No tutorial due to public holiday
Mid-Semester Break					
9	2/5	Receptor Internalisation & Alternative Signalling Pathways (A Finch)	Constitutive Active Receptors (L Liu)	Receptor Signalling (Part C)‡	Molecular Techniques Tutorial (AF)
10	9/5	Allosteric Modulators (L Liu)	Advanced Pharmacodynamics ( L Liu)	Receptor Signalling Data Analysis*	Journal Club (AF)
11	16/5	Signalling Bias ( A Finch)	Receptor Theory I (A Finch)	Determining Antagonist Potency*	Molecular Techniques Tutorial (AF)
12	23/5	Receptor Theory II (A Finch)	New concepts in Pharmacology (A Finch)	Advanced Pharmacodynamics <u>Tutorial</u> *	Journal Club (AF)
13	30/5			Exam Revision /Mini-research symposium <u>12-1-2-3pm</u> *	



## Assessment Tasks

Task	Due Date
Molecular Techniques Wiki (draft)	Monday 9am one week before scheduled presentation
Molecular Techniques Wiki	Monday 9am the week of scheduled presentation
Learning Activity	During assigned tutorial
Progress Exam	Tuesday, 12 <sup>th</sup> April, 10am
Laboratory Notebook	Monday 23 <sup>rd</sup> May, 5pm
Final Examination	Official exam period

### Laboratory Notebook

You will be required to keep a laboratory notebook for all practical classes in this course. Keeping a laboratory notebook is an important skill for every scientist to develop. Laboratory notebooks are a complete record of all the procedures carried out and data collected for each experiment. Enough detail needs to be recorded so as someone could reproduce your experiment at a later date. A laboratory notebook is a legal document and as such certain conventions and procedures must be followed.

The requirements for laboratory notebooks are given below:

- The lab notebook must be a bound book and not a spiral notebook or loose sheets in a folder
- The first 2 pages should be reserved for a table of contents
- Each page is numbered
- All entries are to be made in blue or black ink.
- Never remove any pages from your laboratory notebook.
- All information should be recorded directly into your notebook. Write down in detail what you do for each step of the experiment and record your results as you obtain them. Graph, films, printouts etc should be stuck directly into your notebook. Do not record data or calculations on scraps of paper and later copy them into your book. Whilst your laboratory notebook should be legible and as neat as possible it is more important that you record all the information.
- If you make a mistake strike it through with a single line and initial and date the correction. Do not use correction fluid or scribble out the mistake. The mistake should still be readable as sometimes you will realize that the entry was not a mistake after all and will want to be able to read it.
- Do not skip pages in your laboratory notebook (for example to allow space for data that will be collected later) instead make reference such as "continued from page 2" or "continued on page 5". You can start a new a new experiment on a new page however any blank space on the preceding page must have an X put through it.
- Each entry in the laboratory notebook should begin with the date, the title and a brief description of the aims of the experiment.
- At the end of each day your laboratory notebook should be signed and dated by a witness ( *i.e.* a demonstrator)

**The following information should be recorded in your laboratory notebook for each experiment:**

1. A brief and informative title.
2. The aims of the experiment and any background information. This section should include two or three sentences in your own words explaining what the question is that you are asking (your hypothesis) and the methods you are using to answer your question. This section should be completed before you come to class.
3. Questions for each practical should be answered before you come to class.
4. A concise step by step description of what you actually do when performing the experiment (this can be in point form). Record any calculations you have done and the equipment, chemicals and solutions you have used.
5. Any observations (e.g. gel has a bubble, not all the sample loaded, current not stable). All data collected with correct units, titles and labelled axes on graphs, and titles and labels for all drawings, films and printouts.
6. A summary of the findings and conclusions. How do your findings relate to your original aims/hypothesis? If the results were not as expected, suggest possible reasons for this. How do your findings relate to other studies in the scientific literature?

Laboratory Notebooks are due before **5pm, Monday 23<sup>rd</sup> May**. Laboratory notebooks are to be submitted at the BABS.SOMS.BEES (B.S.B.) Student Office, G27 Biosciences Building. You will need to staple or use sticky-tape to attach the Assessment Cover Sheet to the front cover of your book.

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### Marking Criteria – Laboratory Notebook

Criteria	<i>Excellent</i> <b>&gt;8.5</b>	<i>Very Good</i> <b>8.4-7.5</b>	<i>Good</i> <b>7.4-6.5</b>	<i>Needs Improvement</i> <b>6.4-5.0</b>	<i>Unacceptable</i> <b>&lt;5.0</b>
<b>Organisation</b>  _____/10 x 0.5	Each experiment has a title and date and appears in the table of contents. Errors are neatly struck through, no correction fluid used. All entries in pen. Each page numbered. Each day is initialled.	Each experiment has a title and date and appears in the table of contents. Most errors are neatly struck through. All entries in pen. Each page numbered. Each day is initialled.	All but one experiment has a title and date and appears in the table of contents. Some errors are not neatly struck through. Some entries not in pen. Each page numbered. Each day is initialled.	Not all experiments have a title and date and appear in the table of contents. Not all errors are neatly struck through. Not all entries are in pen or each page numbered. One day not initialled.	Experiments lack a title and date and don't appear in the table of contents. Errors are not neatly struck through. Entries not in pen. Page numbers lacking. More than one day is not initialled.
<b>Safety</b>  _____/10 x 0.5	In attendance for every safety briefing. All safety summaries attached and signed.	In attendance for >90% of safety briefings. All safety summaries attached and signed.	In attendance for >75% of safety briefings. All safety summaries attached and signed.	In attendance for >50% of safety briefings. Most safety summaries attached and signed.	In attendance for <50% of safety briefings. >50% of safety summaries not attached and/or signed.
<b>Questions</b>  _____/10 x 1	All questions answered correctly.	All questions answered with minor errors	Questions answered, with some errors.	Not all questions answered, some answered with errors.	Majority of questions not answered or incorrect.
<b>Aims</b>  _____/10 x 2	The aims of each experiment or the question to be answered is clearly identified and stated.	The aims of each experiment or the question to be answered are stated. .	The aims of each experiment or the question to be answered are identified but more detail needed.	The aims of each experiment or the question to be answered are partially identified, however more details are needed.	The aims of each experiment or the question to be answered are not given.
<b>Experimental protocol</b>  _____/10 x 2	The protocol for each experiment is succinctly described with enough detail to allow another researcher to follow. All calculations are correct.	The protocol for each experiment is described with enough detail to allow another researcher to follow. Only minor errors in calculations..	The protocol for each experiment is described however, key information missing in some experiments. A few errors in calculations.	Describes how the experiments were done, but is difficult to understand. Errors in calculations. .	Does not accurately describe how the experiments were done. Calculations are incorrect or missing.
<b>Data</b>  _____/10 x 2	All data collected are presented. The data are clearly labelled. Correct units are given.	All data collected are presented. The data are clearly labelled with minor omissions. Minor errors in units given.	Data collected are presented and clearly labelled but with minor omissions. Errors in units given.	Some data not presented or not labelled. Errors in units.	Most of the data collected not presented. The data are not labelled. Correct units not used.
<b>Conclusions</b>  _____/10 x 2	A summary of the findings and clear and concise conclusions are given. Conclusions are correct and supported by references where appropriate.	A summary of the findings and conclusions are given. Conclusions are correct and supported by references where appropriate.	Summaries of the findings and conclusions are given. Minor errors in conclusions. More references needed.	Summary of the findings and conclusions are given, however more detail needed. Some conclusions are incorrect and or not supported by references.	Summary and conclusions do not accurately describe the results of the experiments or are not presented.

## Molecular Techniques Tutorial

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### Overview

Publishing a scientific paper is the primary way that a scientist contributes new knowledge or methods to the scientific community. Collectively, these journal articles chronicle advances in science and technology. Without this foundation of work—whether a seminal contribution or a simple finding—future experiments would have no context and scientific research could not progress. Thus, understanding the literature is vital to understanding scientific research.

To understand scientific literature, however, it is important to know what tools and techniques scientists use to ask and answer questions. Over the course of the semester, you will explore several molecular biology techniques that are essential to understanding the scientific papers publish in the area of molecular pharmacology. Each student group will design and lead an exploration of a laboratory technique that is found in the papers to be discussed in each tutorial.

### Instructions for the in-class activity

#### *Part 1: Make a wiki about the technique*

To help your classmates prepare for the activity you will design, your group will write a wiki about the technique that contains the following information:

- **How the technique works.** For example, describe the materials needed or provide an annotated diagram of the important steps involved, or the molecular process that occur during each step of the technique.
- **How the technique is used.** Include a description of what type of information this technique provides and what types of questions can be answered using the technique.
- Two **Hypotheses** that could be tested using this technique and two hypotheses that could not be tested using this technique. Include an explanation of why they can or cannot be tested using this technique.
- **Benefits and limitations of the technique.**
- **References.** List any resources that your group used to develop the fact sheet or in-class activity, and highlight other important resources where your classmates can find more information.

The Wiki should not be longer than 1000 words

The course coordinators are available at any point in the planning process to answer questions about the technique or this project.

### Researching your assigned technique

Places to look for general information:

- Textbooks
- Internet: Beware that not all sites will be accurate! Good information can usually be found at university websites, textbook publishers and scientific company websites.

Places to look for specific information:

- The library has many books covering molecular biology techniques
- The Current Protocols series of books are available in the library and electronically via the library catalogue. This series includes: Current Protocols in Molecular Biology, Current Protocols in Pharmacology, Current Protocols in Nucleic Acid Chemistry, Current Protocols in Human Genetics, Current Protocols in Bioinformatics, Current Protocols in Protein Science.
- Scientific literature (hint: limit your search to reviews or methods journals)
- Journal Websites

Cell - <http://www.cell.com/>

Science - <http://www.sciencemag.org/>

Nature - <http://www.nature.com/nature/index.html>

Molecular Pharmacology - <http://molpharm.aspetjournals.org/>

Trends in Pharmaceutical Sciences -

<http://www.sciencedirect.com/science/journal/01656147>

### **Part 2: Design and lead an in-class activity**

Each group will work together to design and lead an in-class activity that will:

1. Actively engage your classmates involved in learning and thinking about the technique
2. Help your classmates determine how well they understand the technique

The entire activity should take **no more than 15 minutes**. After the activity, plan to spend 5 minutes to tie everything together and answer any questions your classmates might have.

**All together, you will have 20 minutes of tutorial time, so use it wisely.**

**Some ideas for activities**

- **Take a quiz.** Give your classmates time to think about and answer the questions with a partner, then discuss the answers as a class.
- **Sequence the important steps in the technique.** Diagram each step on a separate sheet of paper. Have groups of students describe what is happening at each step, arrange the diagrams into the correct order, and explain why they ordered the steps in that way.
- **Act out the important steps of the technique.** Provide materials for your classmates to serve as critical molecules, reactions, or other “players” in technique, then have each person describe what their role is, and have the entire class act out the technique. Discuss key points afterwards.
- **Solve a scenario where the technique is done or used incorrectly** (e.g. steps missing or out of order, or incorrect conclusions drawn from an experiment). Have your classmates work together to determine the correct order of the steps, propose more appropriate conclusions (and justify their answers), or answer questions about the scenario.
- **Interpret data from an experiment** that employs the technique. Develop a series of key questions that will encourage discussion about what conclusions can be drawn from those data.
- **Compare and contrast.** Have classmates compare and contrast your technique with another related technique. Give your classmates a set of scientific questions and have them decide which technique to use for each and explain their decisions.

**Timeline (what is due when):****The Monday one week before you present**

The academic taking your tutorial (either Dr Finch or Dr Liu), will review your draft of the wiki and a description of your activity (and any accompanying visual aids, quizzes, etc.) and a meeting will be arranged where suggestions for improvement will be given.

**On the Monday before you present**

The coordinator will open your wiki for viewing by the whole course at 9am so that your classmates can study it before the tutorial.

**During tutorial on the day you present**

- Introduce the activity, give instructions
- Guide classmates in completing the activity
- Wrap-up; tie everything together and answer questions
- *Do not give a "lecture" on the topic the rest of the class will have covered that prior to the class by reading your wiki*

**What to do on the weeks another group will be presenting:**

Study the wiki to familiarise yourself with the technique so that you can participate meaningfully in the planned activity. You should come to class prepared to discuss any of the information found in the wiki and how the technique is used in the paper for discussion in the tutorial.

## Marking Criteria – Molecular Techniques Wiki

<b>Criteria</b>	<b>Excellent (&gt;8.5)</b>	<b>Very Good (8.4-7.5)</b>	<b>Good (7.4-6.5)</b>	<b>Needs Improvement (6.4-5.0)</b>	<b>Unacceptable (&lt;5.0)</b>
<b>Completeness</b>  _____/10 x2	The wiki contains all assigned elements and all details necessary to fully explain the technique. Your wiki can stand alone for the readers to use as a comprehensive source of information on the technique.	The wiki contains all assigned elements, but lacks a few minor details. Your wiki provides readers with most of what they should know about the technique but could be more comprehensive.	The wiki contains all assigned elements, but lacks some details. Your wiki provides readers with most of what they should know about the technique but lacks a key detail.	The wiki contains all assigned elements but lacks important details. Your wiki provides a general overview, but readers would need to look elsewhere to fill in the gaps.	One or more assigned elements are missing or incomplete. Your wiki lacks key information needed to give the reader a basic understanding of the technique.
<b>Accuracy</b>  _____/10 x2	All information included in the wiki is accurate. The reader can confidently rely on the wiki as a source of information about the technique.	The information is accurate except for a few minor errors. The wiki is useful as a resource but may mislead the readers on a few small details.	The information is accurate except for a few minor errors. The wiki is useful as a resource but may mislead the readers with some details.	The information contains several errors. While no significant errors are made, the wiki contains enough errors to detract from its usefulness as a source of information about the technique.	A significant error is made that causes confusion. The reader cannot depend on your work as a reliable source of information about the technique.
<b>Clarity</b>  _____/10 x 2	The wiki is well written and easy to read. All terms are clearly defined and topics are fully explained. Your writing allows readers to easily understand the meaning of all points presented.	The majority of the wiki is well written and easy to read, but a few minor terms or details are unclear. Your writing allows readers to understand the meaning of all points presented.	The majority of the wiki is well written and easy to read, but some terms or details are unclear. Your writing requires readers to infer your meaning regarding a few details.	Some parts are unclear or poorly written. The lack of clarity in your writing is distracting to readers and causes them to question your meaning, but they can still draw appropriate conclusions with some effort.	Major portions or key details of the wiki are unclear or poorly written. Your writing is unclear enough to cause the reader to misinterpret your meaning, leading to confusion about the technique.
<b>Creativity</b>  _____/10 x 2	The wiki makes optimal use of visual aids or other creative elements (pictures, drawings, flow charts, figures, etc.) to illustrate key points of the technique. Your creativity greatly enhances your wiki as a learning tool and provides additional means for the reader to gain understanding about the technique beyond what is stated in the text.	The wiki makes use of visual aids or other creative elements to illustrate key points of the technique. Your creativity enhances your wiki as a learning tool and allows the reader to gain greater understanding about the technique.	The wiki includes visual aids or other creative elements to illustrate the technique, but they are not original or inclusive of details specific to the technique. The readers gain something from the aids but may have trouble visualizing or fully understanding parts of the technique.	The wiki includes pictures or diagrams, but they do not contribute to the readers' understanding of the technique.	Visual aids or creative elements are not used. The reader does not gain a full sense of the technique from your information sheet.
<b>Individual contribution to the wiki</b>  _____/10 x 2	Contributes extensively to the researching, writing, and editing. Shows appropriate wiki etiquette when editing and respects the work of others	Contributes equally with other group members in researching, writing, and editing. Shows appropriate wiki etiquette when editing and respects the work of others.	Contributes to the researching, writing or editing. Displays appropriate wiki etiquette most of the time and generally respects the work of others	Provides minimal contribution to the researching, writing and editing. Displays appropriate wiki etiquette some of the time but often fails to respect the work of others	Does not contribute to the researching, writing and editing. Does not follow wiki etiquette and fails to respect the work of others

**Total \_\_\_\_\_/100**

### Marking Criteria – Molecular Techniques Learning Activity

<b>Criteria</b>	<b><i>Excellent</i> (&gt;8.5)</b>	<b><i>Very Good</i> (8.4-7.5)</b>	<b><i>Good</i> (7.4-6.5)</b>	<b><i>Needs Improvement</i> (6.4-5.0)</b>	<b><i>Unacceptable</i> (&lt;5.0)</b>
<b>Choice of content</b>  _____/10 x3	The activity addresses key or difficult aspects of the technique. Your classmates will leave with a deeper understanding or reinforced knowledge of the technique.	The activity addresses an important aspect of the technique. Your classmates will learn about the technique but would benefit more from a more in depth choice of content.	The activity addresses an important aspect of the technique, but not the most important or difficult aspects. Your classmates will learn something about the technique but would benefit more from a different choice of content.	The activity addresses a minor or easily understood aspect of the technique. This will not help further their understanding of the technique beyond what they could easily grasp on their own.	The activity does not address any important details of the technique or its uses. Your classmates will not learn from it.
<b>Knowledge of the technique</b>  _____/10 x3	The presenters serve as experts on the technique. The content of the activity is clear and accurate, and the group is able to provide thorough and accurate answers to all reasonable questions raised by the class. Your classmates can depend on you teach them all they need to know about the technique.	The presenters are knowledgeable about the technique. The content of the activity is clear and accurate. The group is able to accurately answer most reasonable questions raised by the class without assistance. You are able to give your classmates a sound knowledge of the technique.	The presenters have some knowledge of the technique. The content of the activity is clear and mostly accurate. The group is able to answer most reasonable questions raised by the class but requires assistance from the instructor in some cases. You are able to teach your classmates most of what they need to know about the technique.	The presenters know a little more about the technique than their classmates. Some content of the activity is unclear or inaccurate, or the group is only able to answer basic questions raised by their classmates about the technique. Your classmates cannot depend on you to teach them much about the technique.	The presenters do not understand the technique themselves. Much of the content of the activity is inaccurate or vague, or the group cannot answer basic questions about the technique. Your lack of preparation causes confusion for your classmates.
<b>Activity design</b>  _____/10 x3	The chosen activity engages all members of the class in learning about the technique. The activity is well-designed, creative, and generates useful discussion. Your classmates will gain something from the activity beyond what they would gain from simply reading the information sheet.	The chosen activity engages all members of the class in learning about the technique and generates good discussion. Your classmates will learn from the activity, but would benefit from a more creative format.	The chosen activity engages most members of the class in learning about the technique and generates some discussion but lacks originality. Your classmates will learn from the activity, but would benefit from a more engaging format or better planned activity	The chosen activity engages the class in learning about the technique but is not well-designed or does not generate useful discussion. Poor planning reduces the effectiveness of the activity in helping your classmates learn about the technique.	The chosen activity does not engage the class in learning about the technique. Your classmates could learn the information just as well by reading the information sheet.
<b>Group participation (group graded as a whole)</b>  _____/10 x1	All members of the presenting group work together to lead the activity and make sure it runs smoothly and all members of the group are willing and able to answer questions about the technique. Everyone contributes equally and works as a team.	All members of the presenting group participate in leading the activity and are willing and able to answer questions about the technique, but all do not contribute equally.	All members of the presenting group participate in leading the activity and are able to answer questions about the technique, however, the members of the group work independently rather than as a team.	Some members of the presenting group show little effort to participate in leading the activity or are not prepared to answer questions about the technique.	The presenting group does not work together to lead the activity and answer questions. Some members do not participate, or a lack of preparation and communication leads to confusion.



