BA3009 – Principles of Neurobiological Research

2006 – 2007 COURSE BOOKLET AND TIMETABLE

Objectives of the course

The aim of this course is to give students an understanding of the process of research, from formulation of hypotheses to choice of experimental systems and techniques, conduct of research, data analysis and statistics, conclusions and consideration of the wider context of the research field. In particular, we will teach students how to analyse scientific papers, to appreciate the limitations of research techniques and the advantages and disadvantages of various experimental and animal model systems. An understanding of the logistics of research strategy and practical considerations such as timescale and funding are also developed. Students will also participate in practical demonstrations of techniques used in contemporary neurobiological research. Developmental neurobiology provides the knowledge base for this course. The course is based around small group *tutorials* and laboratory *workshops.*

By the end of the course students are expected to have

1. gained an understanding of the key experimental systems and techniques used in neurobiological research and their applications
2. developed the ability to evaluate critically and to analyse scientific papers, focussing on the Figures and the quality of the data

Allocation of marks

60% - two hour examination

20% - 2000 word workshop report

20% - assessed presentation

Timetable

The course runs in Semester A on Wednesdays, from Wednesday 27th September until Wednesday 15th November. All tutorials take place in the small conference room (to left of the lift) on 4th Floor New Hunt's House, except the tutorial on Wednesday 8th November, which will be held in the CAL lab of New Hunt's House. All workshops take place in the research laboratories of the 4th Floor New Hunt's House.

Private study time

Private study time on this course can be beneficially used to look at relevant journals and practise data interpretation, in particular by focussing on the Figures within individual papers, and whether the authors' conclusions follow from their data. A large number of past exam questions and examples will also be provided at the second tutorial, and you can work through these in your own time.

Course organisers and tutors

Course organiser: Dr Uwe Drescher
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Course tutors: Dr David Chambers, Professor Jim Cohen, Dr Uwe Drescher, Dr Britta Eickholt, Dr Jon Gilthorpe, Professor Sarah Guthrie, Dr Corinne Houart, Dr Richard Wingate, all based on the 4th Floor New Hunt's House, and Dr Paul Francis from Wolfson CARD

Assessed presentation guidelines

During this course you will be assessed via one assessed presentation, one assessed workshop report and a two hour examination. For the tutorial, pairs of students will select a topic from a list of Experimental Systems which have been used extensively in the last decades to elucidate basic principles of developmental neurobiology and the molecules controlling these processes (see Appendix 1). Your presentation should last about 15 minutes, with 5 minutes for questions (20 minutes in all). You should give a PowerPoint

presentation with an Introduction to the experimental system you and your colleague have chosen. You should describe the system from a cell biological view, identify its main molecular players and their function within it, possibly describe in more detail for one selected gene/protein its particular function in this system, describe how this system relates to overall neural development, and suggest new directions of research, i.e. aspects of this system which you think should be better understood. A few references should be given that best describe basic features of this system. A handout of your presentation should be given to your colleagues and tutors.

Assessed workshop report

The workshop on “zebrafish as a model system” has been selected as the subject for an assessed write-up. You should produce a 2000 word report, giving an Introduction to the zebrafish as a model system, a detailed account of the experimental methods that were demonstrated during the workshop, the results you observed and their interpretation. You should include the experimental questions that such techniques may be used to address, their advantages and their limitations. It is not expected to be thoroughly researched in the same depth as an essay, but rather to provide an indication of your understanding of the day’s work. The write-up should be divided into subheadings as in a scientific paper – Introduction, Methods, Results and Discussion. Information about the zebrafish can be found on the Zebrafish information network (ZFIN), which can be accessed via the MRC Centre Webpage and further information can be obtained from the organiser of the session, Dr Corinne Houart.

Two hour examination

This exam will recapitulate the key features presented in the tutorials. The exam questions focus on data analysis and interpretation, experimental strategy and design.

Timetable with Learning Objectives

Wednesday 27th September

10 am – 12 noon **Tutorial:** Microscopy techniques (*Richard Wingate)*

2 pm – 5 pm **Workshop:** Microscopy techniques *(Richard Wingate, Jon Gilthorpe)*

The tutorial will outline the basic principles of light microscopy in practical terms. This will include the anatomy of the microscope, the optimisation of bright-field illumination, fluorescence and laser scanning confocal imaging, and digital photography. The workshop will provide hands-on experience of fluorescent material, bright field photomicroscopy and a demonstration of time-lapse imaging of cells labelled with green fluorescent protein (GFP).

Wednesday 4th October

10 am – 12 noon **Tutorial:** Experimental strategy and design *(Uwe Drescher)*

Wednesday 4th October

1 pm – 3 pm **Tutorial:** Data analysis I *(Uwe Drescher)*

These two tutorials will set out the major points in the planning and conduct of laboratory research, including the pitfalls and problems. It will be described how to formulate hypotheses and predictions and how to design critical experiments to test them. Sample questions for the examination will also be worked through, highlighting the major points to bear in mind in data analysis. Advice on the preparation of presentations on 'Experimental Systems' will also be given.

Wednesday 11th October

10 am – 12 noon **Tutorial:** Molecular approaches to neurobiology *(David Chambers)*

Some of the molecular techniques currently used to investigate developmental neurobiology will be listed together with information about how to find out more about these techniques and interpret them when encountered in scientific papers. These techniques will include: in situ hybridisation, RT-PCR on embryos, in vivo genes overexpression or knock-down, generation of transgenic mice.

2 pm – 4 pm **Tutorial:** Use of microarrays and bioinformatics *(David Chambers)*

An outline will be provided of contemporary techniques in screening gene arrays to search for genes involved in specific developmental processes and the development of specific cell types will be given. Technical and experimental design considerations and strategies in using databases to search for candidate genes and to investigate gene function will be explained.

Wednesday 18th October

10 am – 1 pm **Tutorial:** Assessed Presentations on the use of different animal model systems in neurobiological research *(Jim Cohen, Uwe Drescher, Sarah Guthrie, Britta Eickholt, and Richard Wingate)*

Pairs of students will select an experimental system from a list (Appendix 1). In15 minutes, they will give describe the system from a cell biological view, identify its main molecular players and their function within it, possibly describe in more detail for one selected gene/protein its particular function in this system, describe how it relates to overall neural development, and suggest new directions of research, i.e. aspects of this system which you think should be better understood.

2 pm – 3 pm Feedback and discussion on tutorial presentations *(Uwe Drescher)*

Feedback will be given on the morning's tutorial presentation in the use of different model organisms. Students who require further feedback will be able to talk to the tutor individually.

Wednesday 25th October

10 am – 12 noon **Tutorial:** *In vitro* models of neuronal development and axon guidance *(Jim Cohen)*

2 pm – 5 pm **Workshop:** *In vitro* models of neuronal development and axon guidance *(Jim Cohen, Sarah Guthrie)*

Tissue culture in vitro models are widely used in developmental neurobiology research. In this tutorial and workshop we will discuss the variety of in vitro approaches that can be employed, including their advantages and disadvantages, and their relevance to various areas of neurobiological study. In the workshop session, students will form small groups and go round the laboratory looking at various prepared examples of culture techniques. Means of quantification of these cultures will also be discussed. Among the likely examples to be

included will be organotypic cultures, collagen gel co-cultures, dissociated neuronal cultures and ‘stripe’ assays to assess the role of various guidance cues.

Wednesday 1st November

10 am – 1pm **Tutorial:** Zebrafish as a model system *(Corinne Houart)*

2pm – 5pm **Assessed workshop:** Zebrafish as a model system *(Corinne Houart)*

The choice of zebrafish as a model organism to study developmental biology has been made based on four main advantages: the zebrafish can be kept in aquaria with great ease, the females lay a large number of eggs at least once a week, the embryos are accessible from the moment they are fertilised and the embryos are optically clear at all stages of development. In the early ‘80s, these advantages had encouraged a group of American researchers to explore ways to begin genetic studies on this species.

Since then, the scientific community has collected more than a thousand mutations affecting a variety of developmental processes. The identification of the genes involved in these processes is the task of the near future. Such work is possible thanks to the elaboration of genetic maps of the zebrafish genome and will be greatly helped soon by the sequencing of the zebrafish genome. The practical will illustrate the two main strengths of the zebrafish: cell biology and genetics. A description of the main steps in zebrafish development (video) will be followed by an introduction to the mutations that brought about important findings with respect to the early development of the vertebrate brain. The students will be able to observe embryos carrying such mutations and describe their visible morphological defects. A couple of the most classical techniques in cell biology and molecular genetics will also be demonstrated.

Wednesday 8th November

10 am – 12 am **Tutorial:** Statistical analysis *(Paul Francis)*

This session introduces the concepts of how to describe data statistically depending on the nature of the data and then looks at ways of examining whether differences between groups can be attributed to chance or if there is a statistically significant difference. It is then up to

the researcher to decide if it makes biological sense. There will then be a short introduction to the statistical programme on the PAWS machines called SPSS using some supplied data.

Wednesday 15th November

10 am – 12 am **Tutorial:** Discussion of projects *(Sarah Guthrie)*

Handing out of course examination forms. Discussion of course for student feedback.

Assessed workshop report must be handed in by 5pm on Monday 20th November at U. Drescher's office (room 4.26C)

Appendix 1

Experimental systems

- patterning: hox genes in specifying antero-posterior patterning: specification of rhombomere identify
- patterning: interpretation of gradients: sonic hedgehog signalling in patterning along the dorso-ventral axis
- patterning: the mid/hindbrain boundary as an organising centre for brain development
- cell migration: neural crest cell migration into branchial arches
- axon guidance: the role of netrins and slits in the guidance of commissural axons to and from the midline
- axon guidance: role of the Eph family in development of the retinotectal projection (model for topographic maps)
- synapse formation: the role of agrin/MuSK in the development of the neuromuscular junction
- naturally occurring neuron death: the role of the neurotrophin family in the innervation of limb buds