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Integrating developmental biology into the undergraduate curriculum at the University of Bath, United Kingdom

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ABSTRACT The undergraduate curriculum for bioscience degrees at the University of Bath is outlined, and the place is described of the developmental biology components within it. In the first year, all students receive four lectures on animal development and four on plant development. In the second year, many choose substantial lecture and practical courses on animal development , which outline the early development of *Xenopus*, mouse and *Drosophila*. The third year is usually spent on placement, with a company or research institute, a few of which are developmental biology-based, and may also involve some distance learning. The fourth year is spent back in Bath. Students interested in developmental biology can opt for advanced courses covering vertebrate organogenesis, developmental neurobiology and plant development. There are also one-semester, final-year projects spent in the labs of faculty members, several of whom specialise in developmental biology and offer projects accordingly.

KEY WORDS: *developmental biology lecture, practical class, tutorial, placement, project*

Background Information

Scholarly Interests of Author

I have been active in developmental biology research for 28 years, mostly using *Xenopus* as the experimental organism. I have worked on limb development and regeneration, on the inductive interactions leading to early body patterning, and on the development of the gut. Current interests are the molecular basis of metaplasias in the gut and the molecular mechanisms involved in regeneration of limb and tail. I have also written three books: *From Egg to Embryo* was intended to introduce molecular biologists to the world of classical experimental embryology; *Egg and Ego* to introduce biology students to the world of academic science; and most recently *Essential Developmental Biology* is an undergraduate textbook.

Books Published

SLACK, J.M.W. (1991). *From Egg to Embryo: Regional Specification in Early Development* (second edition). Cambridge University Press, Cambridge.

SLACK, J.M.W (1999). *Egg and Ego. An Almost True Story of Life in the Biology Lab*. Springer, New York.

SLACK, J.M.W. (2001). *Essential Developmental Biology*. Blackwell Science, Oxford, UK.

Representative Publications

DALE, L. and SLACK, J.M.W. (1987). Fate map for the 32 cell stage of *Xenopus laevis*. *Development* 99: 527-551.

SLACK, J.M.W., DARLINGTON, B.G., HEATH, J.K. and GODSAVE, S.F. (1987) Mesoderm induction in early *Xenopus* embryos by heparin binding growth factors. *Nature* 326: 197-200.

SLACK, J.M.W., HOLLAND, P.W.H. and GRAHAM, C.F. (1993). The zootype and the phylotypic stage. *Nature* 361: 490-492.

General Teaching Philosophy

I favour traditional "top down" teaching methods, at least in the early years. Although this is out of fashion in teaching circles, I feel that students have to have some knowledge to think about and discuss, and the most painless way for them to acquire it is to have someone explain it to them. At the same time, I do not encourage respect for "ex cathedra" authority. I try to explain what is the evidence for major results, and emphasise that things continually change in research. I also encourage discussion in tutorials with groups of 4-5 students, although only after they have read up on a subject.

I like to get across the idea that developmental biology is a synthetic discipline that unites anatomy, genetics and molecular biology. Students can find this difficult as they are used to simple, linear subject matter. To reduce the "epistemological obstacles" I believe that each model organism should be introduced separately and that no prior knowledge should be taken for granted. I also firmly believe that plants and animals should be kept separate. Although there are some principles in common, the actual molecular biology of plant and animal development is substantially different, and I feel

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nothing is achieved by trying to force them into a common mould. I also believe in the minimisation of detail. The subject is now exceedingly complex with so many genes and pathways, often known by different names in different model organisms, that a ruthless selection of topics is necessary if students are not to be overwhelmed.

Finally I think the key to maintaining interest is to persuade the audience that the subject is really important: both intellectually important as a "centre piece" of modern biology, and practically important as the source of new technologies from IVF to transplantable stem cells. Only a minority of students will themselves become research workers, so the outcomes of the teaching are just as important for those who will work in industry, or become High School teachers, or work outside science altogether. They need to know that the subject is exciting, that it has a central position in modern biology, and that it is going to be ever more important to the outside world. (note: although this is my personal philosophy, it is not necessarily shared by the other faculty mentioned in the article!)

The University of Bath is a small university in the West of England, specialising in science and technology. It is highly ranked in the various national league tables and is usually listed among the top ten UK universities. Bath itself is a historic city, well known to tourists in the UK, but the university was only founded in 1966. Although there are also two medically oriented departments, activity in developmental biology is confined to the Department of Biology and Biochemistry. In this department, we run 9 undergraduate degree programmes consisting of all combinations of three subjects and three programme types:

The subjects are:

1. Biology
2. Molecular/Cellular Biology (MCB)
3. Biochemistry.

The programme types are:

1. MBiol 4 years, year 3 being a research-based professional placement with distance learning. The general orientation of the degree is toward research.
   (MBiochem is similar but with 2 professional placements of 6 months in years 2 and 3)
2. BSc with placement: 4 years, year 3 is professional placement, but may not be research-based.
3. BSc: 3 years full time in Bath.

Hence the 9 degrees are:

Biology BSc, BSc with placement, MBiol
MCB BSc, BSc with placement, MBiol
Biochemistry BSc, BSc with placement, MBiochem

The structure is modular, but all students take Biol0006 Cell and Molecular Biology in year 1, which contains 4 lectures on animal development by J.M.W. Slack and 4 lectures on plant development by R.J. Scott. After this, all the developmental biology units are optional (Fig. 1). All three degrees have access to Biol0035 Genes and Development 1 in year 2. All can do Biol0036 Genes and Development Practicals in year 2, (MBiochem, just half of it). Biology and MCB students can do Biol0067 Genes and Development 2, Biol0101 Neurobiology-development, and Biol0069 Plant Development in the final year. A few students, particularly those on MBiol and MBiochem programmes, do their professional placements in developmental biology labs, several of which are in the USA. All programmes except BSc Biochemistry include a one-semester project in the final year based in a research lab in Bath, and this may also consist of developmental biology. Students who have taken advantage of all these possibilities will be very well informed by the time they graduate, although the majority will have done just one or two components.

General Considerations

Faculty members always think that their own research area is very interesting and needs to be presented to students. The students, on the other hand, may need some persuading that a subject is really important. This is particularly the case for developmental biology as they tend to find it rather difficult. This is partly because of the intense level of detail that the subject now contains, and partly because of its integrative character, requiring as it does a simultaneous grasp of anatomy, molecular biology and genetics.

I myself feel that the integrative character makes it a very valuable subject to study at undergraduate level. I also believe that developmental biology will be of increasing practical importance in the coming period. This is not in the obvious area of human developmental defects, but rather in the area of pharmaceuticals, where assays based on *Xenopus*, *C. elegans* or *Drosophila* can be adapted for high throughput screening of compounds affecting a variety of signalling pathways or transcription factors. In time there will also be a large industry involved with the technology of tissue regeneration and organ replacement, for which persons knowledgeable about developmental biology will be in demand.

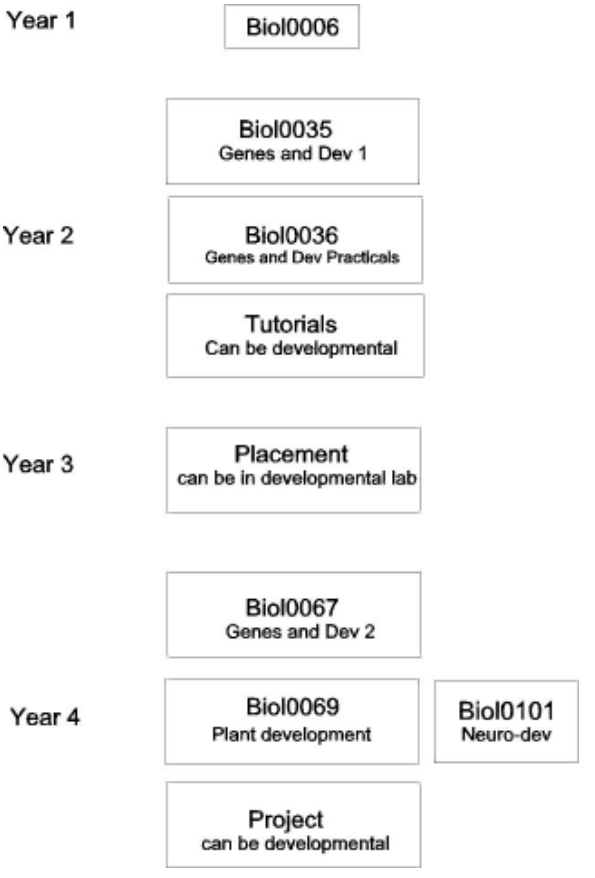

Fig. 1. Schematic of developmental biology options in the Bath 4-year Biology and MCB programmes.

To make the subject palatable at undergraduate level, I feel it is important to keep the detail to a bare minimum and to treat just one model organism at a time. Although bright graduate students may be expected to jump from sea urchin gastrulation to *Xenopus* gastrulation to dorsal closure in *Drosophila* in quick succession, this does not come naturally to undergraduates who have never seen the embryos of the organisms concerned.

"Developmental biology" tends to mean animal development. Although some of the logic of plant development is similar, the actual molecules involved are very different, and my own view is that it makes sense to deal with plant development in a plant science context. So, although we introduce both animal and plant development in year 1, the subsequent courses have separate prerequisites reflecting the scientific gap between them.

The following is a summary of the content of the course units that we offer:

Biol0006: Cell and Molecular Biology, Year 1

The course consists of 36 lectures. Enrolment is about 200. Assessment is by examination. Only 8 lectures are devoted to developmental biology, as follows:

J.M.W. Slack

1. Introduction
2. Developmental genetics
3. Inducing factors
4. Mammalian development

R.J. Scott

1. Plant development - an overview.
2. Body plan specification - seaweed and superweed.

3 and 4. Genetic regulation of flower development - an ABC.

Biol0035: Genes and Development I, Year 2

The course consists of 36 lectures, the first 18 given by J.M.W. Slack and the second 18 by V. Subramanian. It is intended as a self-contained basic grounding in animal development. Assessment is by examination. Enrolment is about 60-80.

Aims & Learning Objectives

To introduce the study of animal development, making use of the three most important animal models viz. *Xenopus*, *Drosophila* and the mouse, to demonstrate basic embryological concepts and the functions of developmentally important genes. After taking this course the student should be able to:

* demonstrate a knowledge of the descriptive embryology of the three model species.
* demonstrate a knowledge of selected methods for the study of gene expression, overexpression and ablation.
* discuss how information from anatomy, molecular biology and genetics can be integrated in the explanation of a particular developmental process.

Content

Xenopus development covering normal development, fate mapping, specification map, induction, morphogen gradients, DV patterning in egg, mesoderm induction, dorsalisation, neural induction, AP patterning. *Drosophila*: development covering normal developmental genetics, dorsoventral and anteroposterior patterning. Mouse: development covering gametogenesis and fertilisation, normal pre- and post-implantation development, ES cells, transgenesis and targeted mutagenesis. Cell adhesion. Extracellular matrix. Cell movement and morphogenesis.

week	lecture	topic
1	1	Introduction to developmental biology
	2	*Xenopus*-normal development
	3	*Xenopus*-gastrulation
2	4	*Xenopus*-fate and commitment
	5	*Xenopus*-dorsoventral polarity
	6	*Xenopus*-inductive interactions
3	7	*Xenopus*-criteria for assessing molecular candidates
	8	*Xenopus*-activins and FGFs
	9	*Xenopus*-Wnts and BMPs
4	10	*Drosophila*-normal development
	11	*Drosophila*-techniques
	12	*Drosophila*-dorsoventral pattern, maternal
5	13	*Drosophila*-dorsoventral pattern, zygotic
	14	*Drosophila*-anteroposterior pattern, maternal
	15	*Drosophila*-gap and pair-rule genes
6	16	*Drosophila*-segmentation
	17	*Drosophila*-Hox genes
	18	Revision session
7	19	The mouse as a model
	20	Classical approaches and methods
	21	Molecular approaches and methods
8	22	Gametogenesis
	23	Fertilisation
	24	Preimplantation development
9	25	Embryonic stem cells
	26	Embryonal carcinoma cells
	27	Genetic analysis 1- homologous recombination and conditional recombination
10	28	Genetic analysis 2- ectopic expression and conditional expression
	29	Genetic analysis 3- gene regulation
	30	Revision session
11	31	Cell movement and cell adhesion
	32	Implantation and gastrulation
	33	Genetic regulation of gastrulation
12	34	Extraembryonic membranes
	35	Mammalian fate maps
	36	Revision session

At this stage the students are given extra reading, especially review articles, but they tend to do rather little. Recommended textbooks are *Essential Developmental Biology* by Slack and *Principles of Development* by Wolpert.

Biol0036: Genes & Development Practicals, Year 2

The course consists of 11 class practicals each lasting 3 hours. 5 are given by V. Subramanian and 6 by D. Tosh. It is intended as an introduction to the practical side of the subject and has Biol 0035 as a prerequisite. Assessment is by practical write-up. Enrolment is about 40.

Aims & Learning Objectives

To introduce students to the appearance of *Xenopus*, insect and mouse embryos; to the use of dissecting and compound microscopes; to simple microsurgical procedures and to immunohistochemistry and *in situ* hybridisation. After taking this course the student should be able to:

Fig. 2. Practical class, during which *Xenopus* embryos are handled. *Part of Biol0036 Genes and Development Practicals.*

* recognise the stages of *Xenopus* and mouse embryos.
* carry out simple experiments on *Xenopus* embryos.
* relate the appearance of two-dimensional microscope sections to three-dimensional embryos.
* identify selected *Drosophila* mutants
* carry out immunohistochemical or *in situ* hybridisation procedures

Content

11 laboratory practical sessions: sorting and staging *Xenopus* embryos (Figs. 2,3); embryo culture; maternal inheritance; simple micromanipulations; interpretation of sections; morphology of insect embryos; isolation of preimplantation mouse embryos; analysis of a gene trap ES cell line; *in situ* hybridisation and immunohistochemistry.

Each session lasts 3 hours and they are on Monday and Friday, allowing either a 3-day or 2-day period between practicals for culture or for washes, etc.

Biol0067: Genes & Development 2

This course has Biol0035 (Genes and development 1) as a prerequisite and is taken by final year students with a serious interest in developmental biology. Enrolment is about 25. It consists of 24 lectures, 12 given by V. Subramanian and 12 by J. Slack. Assessment is by examination (80%) and a coursework essay (20%).

Aims & Learning Objectives

To provide an advanced course in developmental biology that will communicate the excitement of recent research advances. After taking this course the student should be able to:

* understand the basic principles underlying invertebrate development and organogenesis in higher organisms
* relate the mechanisms of development to cellular and molecular events
* understand the applications and implications of research in developmental biology to human developmental defects.

Content

This course builds on Biol0035 to give a comprehensive grounding in developmental biology. The vertebrate development lectures cover Hox genes, somitogenesis, myogenesis, neural development, epithelial-mesenchymal interaction, limb development and regeneration, and developmental defects. Invertebrate model organisms are increasingly being used for molecular genetic analysis of genetic systems important in human medicine. The course will introduce the important model organism *Caenorhabditis elegans* and extend the analysis of *Drosophila* development to include the mechanism of segmentation and the patterning of the imaginal discs.

This is for final year students. The final year may be year 3 or 4 depending on whether the students have done a professional placement in year 3. By this stage, the students are expected to be able to be able to read primary papers in journals such as *Development* and *Developmental Biology*.

Biol0101: Neurobiology - Development

This is a half course (12 lectures) for final year students taught by R.N. Kelsh, and has a prerequisite of Biol0028 Cellular Neurobiology. Enrolment is about 30. Assessment is by examination.

Aims and Learning Objectives

To provide a detailed understanding of selected examples of the origins of neural tissues and the mechanisms that control their development. After taking this course the student should be able to:

* outline the processes involved in generating a nervous system
* explain current models of the mechanisms of neural plate specification and patterning.

Content

Neural development, including neuronal specification, survival and proliferation, and axon guidance to target tissues.

Biol0069: Plant Development

This course is taken by final students with a serious interest in plant development. It consists of 24 lectures by R.J. Scott. Enrolment is about 20. Assessment is by examination (80%) and a coursework essay (20%).

Prerequisites are: Biol0038 (Environmental physiology) or Biol0031 (Plant biotechnology).

Aims and Learning Objectives

To provide a molecular genetic description of the main developmental pathways operating within the higher plant life cycle and to illustrate the principal experimental techniques used in plant developmental biology. After taking this course the student should be able to:

* understand the principal mechanisms that 1) regulate body plan specification in plants 2) pattern the flower and the root and 3) regulate leaf development
* describe the processes of cell and tissue differentiation at the molecular genetic level
* design experimental approaches to investigate developmental pathways in *Arabidopsis*

Content

The course starts by contrasting life cycles and styles of higher plants with that of animals; next we consider the establishment of the basic body plan of plants and again contrast the mechanisms adopted in plants with that of various animal models. The various molecular genetic techniques used in plant development research are then described and illustrated with a focus on plant embryogenesis. Cell fate specification is described in some depth with frequent examples from various organisms. Post-embryonic development is illustrated by using flower development. Cell and tissue differentiation is described using anther and carpel development as examples.

Other Teaching that may involve Developmental Biology

Projects

All faculty members accommodate final year undergraduates in their lab for a one-semester research project. These are often supervised by postdocs or senior postgraduate students in the lab. Examples of recent projects in the developmental biology area are

Adams

1. Application of GFP-fusion proteins to studies of cell movements in the early zebrafish embryo.
2. Cell rearrangement in the early development of the zebrafish (*Danio rerio*).
3. Green fluorescent protein: An application in the quantitative analysis of morphogenesis in the zebrafish.
4. Cell behaviour during zebrafish morphogenesis

Kelsh

1. Comparison of neural crest markers in wild-type and colourless zebrafish
2. An attempt to rescue the enteric phenotype in zebrafish colourless mutants
3. *sox10* expression in the melanophore lineage
4. Investigation of the role of *sox10* in zebrafish epiphysis development

Slack

1. Creation of an expression vector for transgenic applications
2. Notch overexpression and inhibition gives an insight into developmental pathways in *Xenopus* laevis
3. Subcloning genes with a suspected involvement in *Xenopus* limb regeneration
4. Expression analysis of patterning genes within the embryonic gut of *Xenopus* laevis.

Subramanian

1. Analysis of the skeletal defects of *Mll/p53* double mutants
2. Molecular basis of intestinal defects in *mel 18 -/-* and *Cdx1 -/-* mice
3. *In vitro* studies on the effect of a *Mll* exon 5 truncation on cell proliferation and transformation.

Tosh

1. The effects of oncostatin M on the hepatic metaplasia of the pancreas
2. Role of FGFs in the transdifferentiation of pancreas to liver

Ward

1. Determining the effect of insulin-like growth factor-2 on the cell composition of the mature mouse placenta.
2. Expression of the mDab protein in mice with cerebellar ataxia.
3. Characterisation of a transgene-induced mutation associated with defective spermatogenesis in mice.

Projects are assessed by the supervisor and another faculty member (the assessor). the supervisor marks on the basis of lab performance and the quality of the written report. The assessor marks on the basis of a *viva* (an oral examination) and the written report.

Tutorials

Each faculty member has a tutorial group of about 4 students. He/she will set them work each fortnight during year 1 which consists of essays, calculations or literature searches. In year 2 the tutorial work consists of longer essays and critiques of primary scientific papers. These are often conducted by postdocs, although the faculty member retains overall responsibility for the teaching. As tutorials are intended to develop presentational skills, there is no specific syllabus, but developmental biology topics may be covered, particularly in year 2.

Placements

The majority of Bath students do programmes involving professional placement in year 3 (or 6 months of year 2 and 3 for MBiochem). A small number of MBiol placements are based in academic developmental biology labs, for example in 2002/3 Bath students are with the following:

Fig. 3. Student working with embryos under the microscope.

1. Gregor Eichele, Max Planck Institut für Experimentelle Endokrinologie, Hannover, Germany.
2. Sander van den Heuvel, Harvard University, Cambridge, Mass, USA
3. Alejandro Sanchez Alvarado, University of Utah, Salt Lake City, Utah, USA.
4. Robert Schwartz, Baylor College of Medicine, Houston, Texas, USA

Postgraduate Education

Graduate training in the UK is usually much shorter in duration than in the USA or continental Europe. The majority of graduate students do Ph.D.s, which are research only and for which funding lasts only 3 years. The thesis must be submitted before 4 years are up; otherwise the host department may face sanctions from the funding bodies. All the faculty members active in developmental biology offer Ph.D. projects.

The majority of Bath students will have done 4-year degrees including a professional placement, so are reasonably well prepared to start laboratory research. But most UK bioscience graduates will just have done 3-year BSc degrees, with quite limited practical experience, and it is increasingly felt that it is very hard to complete a Ph.D. within 3 years when starting from this background.

To bridge the gap many universities run a 1-year MRes (Master of Research), which consists of some high level courses and some laboratory rotations. We are planning to introduce this in Bath in the near future to cater for 3-year BSc graduates.

From this year we also offer the “newroute” or “integrated” Ph.D., which is a national initiative of 21 universities, including Bath. This is a Ph.D. more similar to the US model, which lasts 4 years with some taught material in years 1 and 2 and laboratory rotations in year 1. It is mainly designed for overseas students.