RESEARCH PROGRAMS IN

BIOLOGY

GRADUATE SCHOOL OF ARTS AND SCIENCE

BOSTON COLLEGE
FOCUS ON RESEARCH

Research lies at the heart of the biology experience at Boston College. The department offers a wide array of opportunities for scientific investigation within the areas of molecular cell biology and genetics, cell cycle, neurobiology, developmental biology, structural and cellular biochemistry, vector biology, infectious disease, and bioinformatics. Specific areas of research in the department include the following:

❖ The role of methylation in cellular aging and in maintaining protein stability
❖ Nuclear import and export of viral and cellular macromolecules
❖ Glucose detection and cAMP signaling in fission yeast
❖ The genes that cause epilepsy in mice, and the neurochemistry of seizure susceptibility
❖ Cell cycle control in B lymphocytes, by B cell antigen receptor (BCR)-mediated signal transduction and growth arrest by inhibitory BCR co-receptors
❖ The molecular genetic analysis of soluble-compound chemotaxis in *C. elegans*
❖ Developmental regulation of expression and molecular evolution in *Drosophila* eggshell genes
❖ The molecular organization of amyloids in Alzheimer’s and other neurodegenerative diseases
❖ DNA replication and nucleosome assembly in mammalian cells
❖ Synaptic ribbons and the use of mutant mice to study retinal structure and visual function
❖ Regulation by and detoxification of metal ions in yeast
❖ Control of cytoplasmic polyadenylation in developing systems
❖ Regulation of cytokinesis in animal cells
❖ Membrane adhesion proteins in demyelinating diseases
❖ Chromosome and microtubule dynamics in fission yeast, *Schizosaccharomyces pombe*
❖ Host-parasite interactions between malaria parasites and their mosquito hosts
❖ Genetic and cell biological analysis of Notch-mediated signal transduction in *Drosophila*
❖ Computational biology/bioinformatics

Research Facilities

Our department, in Higgins Hall, is well-equipped for modern molecular, genomic, and proteomic research, biochemistry, imaging, and bioinformatics.

Departmental genomics and proteomics infrastructure includes capacities for Beckman and LiCor DNA sequencing and DNA fragment polymorphism analysis, Affymetrix microarray spotting and scanning, Beckman robotics, and Alpha-Innotech two-dimensional gel proteomic analysis. We possess state-of-the-art cell culture and protein purification systems, including the BioCad SPRINT perfusion chromatography system, HPLC, FPLC, and preparative isoelectric focusing.

Our imaging facilities include a Leica confocal microscope, a Phillips transmission electron microscope, departmental and individual laboratory Zeiss and Nikon fluorescence and Nomarski compound microscopes, Molecular Dynamics phosphoimager and densitometer workstations, and x-ray diffraction capability. Our digital graphics and image processing facility includes numerous MacIntosh (G4) workstations with multiprocessor CPU configurations, coupled with high-resolution scanners. A large-format poster printer and dye sublimation printers support preparation of high-quality posters and print communications.

We have initiated development of a bioinformatics server platform, to which undergraduates, graduate students, and faculty have access, expanding departmental computing capabilities beyond our MacIntosh, IBM, Sun, and Silicon Graphics workstations. Our bioinformatics server, clavius.bc.edu, is currently comprised of a 20 CPU rack-mount computational cluster, with 1.2 terabytes of fiber-attached network storage. The server is heterogeneous, comprised of dual processor Intel Pentium III/Linux and dual processor Apple/Mac OS X nodes. Research computing time, available free of charge, affords substantial research and educational opportunities for students and faculty.
Assistant Professor Stephen Wicks and Ph.D. Student Brian D’ell Orfano review a genetic mapping experiment designed to identify a gene required for normal detection of water soluble compounds (chemotaxis). Dr Wicks’ laboratory is interested in the neurobiology of the chemosensory system. They are using molecular genetic, cell biological, and behavioral techniques to examine the chemosensory system of the small nematode roundworm, Caenorhabditis elegans. They are hoping to better understand the interactions of the various cell types that occur during the formation of an intact sensory organ, as well as the function of the intact organ in adult animals.
The Biology Department at Boston College offers programs of study leading to the M.S. and Ph.D. degrees in Biology with concentrations in several fields of study, including the following:

- Bioinformatics
- Cell Cycle
- Developmental Biology
- Immunology
- Molecular Cell Biology & Genetics
- Neurobiology
- Structural & Cellular Biochemistry
- Vector Biology

### Programs at a Glance

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<th>M.S.</th>
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<td>Total Enrollment</td>
<td>30</td>
<td>10</td>
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<tr>
<td>80% range of GRE</td>
<td>1200-1300</td>
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<td>Average GPA</td>
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<td>Average Age</td>
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M.S. Program

During the first year, students are required to complete the graduate core curriculum, BI 611, BI 612, BI 614, and BI 615 (Advanced Genetics, Graduate Biochemistry, Graduate Molecular Biology, and Advanced Cell Biology). M.S. students participate in two nine-week laboratory rotations during the first year and select their thesis research laboratory during the second semester. Typically, three additional graduate courses, at least one of which is a graduate seminar course, are required, as well as four courses directed toward completion of a thesis. M.S. candidates must submit and orally defend a written thesis based on their research.

Ph.D. Program

The basis of the Ph.D. program is the development of a body of original research that is publicly presented and defended in a publishable Ph.D. dissertation.

During the first year, students are required to complete the graduate core curriculum, BI 611, BI 612, BI 614, and BI 615 (Advanced Genetics, Graduate Biochemistry, Graduate Molecular Biology, and Advanced Cell Biology). Ph.D. students also take five additional graduate courses, at least three of which are graduate seminars.

The graduate seminars stress critical and creative thinking through the discussion of research literature in specialized fields. Students are also encouraged to explore the many different areas of research represented by the faculty and therefore are required to complete three nine-week laboratory rotations during the first year. Students then select their thesis research laboratory at the end of their third rotation.

To advance to candidacy for the Ph.D., students must successfully present and defend a research proposal before a faculty committee. The dissertation committee formed for each student meets annually to evaluate the student’s progress and to offer scientific advice. Ph.D. candidates are required to write a dissertation and defend it in a publicly presented seminar.
**THE COURSEWORK**

**BI 506 Recombinant DNA Technology**
This course will describe the theory and practice of recombinant DNA technology, and its application within molecular biology research. Topics will include the cloning of genes from various organisms, plasmid construction, transcriptional and translational gene fusions, nucleic acid probes, site-directed mutagenesis, polymerase chain reaction, and transgenic animals. The goal of the course is to make the research-oriented student aware of the wealth of experimental approaches available through this technology.

**BI 507 Computational Biology**
Introduction to computational molecular biology, with focus on the development and implementation of efficient algorithms for problems generally related to genomics. Sample topics include sequence homology and alignment, phylogenetic tree construction ("All about Eve"), hidden Markov models and their applications (e.g., multiple sequence alignment, recognition of genes), RNA secondary structure prediction, protein folding on lattice models, and determination of DNA strand separation sites in duplication and replication. Algorithmic content of course: genetic algorithms, simulated annealing, clustering, dynamic programming, recursion.

**BI 509 Vertebrate Cell Biology**
This is an advanced cell biology course focusing on the integration of gene activity, subcellular structure, extracellular signals, and specialized function in vertebrate cells. The course will involve an in-depth study of differentiated cell types, including erythrocytes, nerve and muscle cells, epithelia, and cells of the immune system. The molecular and genetic bases for diseases affecting these cell types will be discussed. The course will also include recent developments in the area of cell cycle control and the transformation of normal cells into cancerous cells.

**BI 510 General Endocrinology**
Many tissues (e.g., the brain, heart, kidney) as well as the classical endocrine organs (e.g., adrenal, thyroid) secrete hormones. This course is concerned with normal and clinical aspects of hormone action. The effects of hormones (and neurohormones) on intermediary metabolism, somatic and skeletal growth, neural development and behavior, development of the gonads and sexual identity, mineral regulation and water balance, and mechanisms of hormone action will be considered.

**BI 515 Biophysical Chemistry**
This course includes lectures on a number of the most important physical-chemical methods for determining the structures of macromolecules. Topics include electrophoresis, sedimentation, viscosity, light scattering, UV and visible spectroscopy, CD spectroscopy, x-ray crystallography, and NMR spectroscopy.

**BI 533 Cellular Transport and Disease**
The biology of intracellular traffic is in an exciting period of development. New techniques of molecular and cell biology are leading to discoveries of the transport signals and the major carriers. Topics covered in this course include: (1) transport of proteins and different classes of RNAs into and out of the nucleus, (2) transport of proteins into mitochondria and into ER, and (3) vesicular transport. Specific transport deficiencies causing diseases will be discussed. In addition, the course will describe how different viruses (HIV, papillomaviruses, adenoviruses, influenza virus) exploit the intracellular transport pathways of host cells during their life cycle.

**BI 535 Structural Biochemistry of Neurological Disease**
Structural biology relates molecular form to biological function, characterizing biological processes in terms of various molecular structures and the interactions of their constituents. This course introduces students to the principles and practices of structural biology, particularly in respect to its applications to understanding neurological diseases. Lectures that introduce and discuss various methodologies will be followed by demonstrations of the actual techniques, focusing primarily on membrane and x-ray fiber diffraction, and electron microscopy.

**BI 538 The Cell Cycle**
The cell cycle ensures successful cell division and multicellular development. Its importance is evident by the recent Nobel Prizes awarded in medicine. Mutations in cell cycle and checkpoint genes are found in many cancers, and basic research is expected to provide novel therapies. While the concept of "cell cycle genes" emerged from genetic approaches in yeast, it is applicable to all eukaryotes. Topics covered include: cell division cycle (cdc) genes, cyclin dependent kinases as universal regulators, phosphorylation and irreversible degradation as means to control cell cycle progression, checkpoint pathways, and the role of nuclear import and export in checkpoint control.

**BI 541 Immunobiology**
This course will focus on the regulation of the immune response at the molecular level. Topics will include the regulation of B and T cell development; function of B and T lymphocytes in the immune response; the molecular basis underlying the generation of antibody and T cell receptor diversity; and antigen processing via MHC I and MHC II pathways. The course will place a heavy emphasis on experimental approaches to studying immune regulation and will make extensive use of the research literature in order to cover recent advances in areas such as lymphocyte activation, tolerance, and clonal deletion.
BI 554 Physiology
This is a study of the fundamental principles and physicochemical mechanisms underlying cellular and organismal function. Mammalian organ-systems will be studied, with an emphasis on neurophysiology, cardiovascular function, respiratory function, renal function, and gastro-intestinal function.

BI 555 Laboratory in Physiology
This laboratory course investigates both the four major organ systems (respiratory, cardiovascular, renal, and gastro-intestinal) and neurophysiology. The majority of the course consists of computer simulations and tutorials. A few wet labs will be used to illustrate specific principles.

BI 556 Developmental Biology
Developmental biology is in the midst of a far-reaching revolution that profoundly effects many related disciplines, including evolutionary biology, morphology, and genetics. The new tools and strategies of molecular biology have begun to link genetics and embryology and to reveal an incredible picture of how cells, tissues, and organisms differentiate and develop. This course describes both organismal and molecular approaches which lead to a detailed understanding of (1) how it is that cells containing the same genetic complement can reproducibly develop into drastically different tissues and organs; and (2) the basis and role of pattern information in this process.

BI 557 Neurochemical Genetics
This course covers classical, biochemical, and molecular genetics related to inherited disorders of the nervous system. Attention is devoted to such current topics as trinucleotide repeats, genomic imprinting, genetic heterogeneity, and gene-environmental interactions. These topics are presented in relationship to a number of neurological diseases including Huntington’s disease, Tay-Sachs disease, phenylketonuria, Alzheimer’s disease, multiple sclerosis, autism, and complex multifactorial diseases such as mood disorders and epilepsy. Also presented are strategies for gene and dietary based therapies for neurological diseases. Reference materials include handouts of current research articles.

BI 570 Biology of the Nucleus
This course provides an in-depth treatment of the molecular biology of DNA and RNA, with particular emphasis on the control and organization of the genetic material of eukaryotic organisms. Topics covered include chromatin structure and function, DNA replication, nucleosome assembly, introns, RNA processing, and gene regulation.

BI 580 Molecular Biology Laboratory
An advanced project laboratory for hands-on training in the experimental techniques of molecular biology under close faculty supervision. In addition to formal lab training and discussion sections, students will have access to the lab outside class hours to work on projects intended to produce publication quality data. Methods taught will include macromolecular purification, electrophoretic analysis, recombinant DNA and cloning techniques, DNA sequencing, polymerase chain reaction, and the use of computers and national databases for the analysis of DNA and protein sequences. Ideal for students who desire a solid introduction to the methods of molecular biology through practical training.

BI 581 Neuroscience
This course presents selected topics in the broad field of neuroscience, focusing primarily on the mammalian nervous system. The course text (Neuroscience: Exploring the Brain by Bear, et al.) is designed for future neuroscience researchers and premedical students. Topics include historical foundations of neuroscience, synaptic and neurotransmitter systems, neuroanatomy, fundamentals of the nervous system organization, neural development, sensory and motor systems, motivation, and learning and memory. Readings from the text are supplemented with handouts related to current research articles.

BI 611 Advanced Genetics
This course is designed for graduate students who have successfully completed an undergraduate genetics course. Topics include the principles of DNA replication and repair, transmission genetics, microbial genetics, transposition, epistasis and complementation, and gene mapping.

BI 612 Graduate Biochemistry
This course is designed for graduate students who have successfully completed an undergraduate biochemistry course. The course concentrates on the biochemistry of biologically significant macromolecules and macromolecular assemblies. Topics include the elements of protein structure and folding, principles of protein purification and analysis, enzymology, nucleic acid biochemistry, and the structure and function of biological membranes.

BI 614 Graduate Molecular Biology
This course concentrates on the biochemistry of biologically significant macromolecules and macromolecular assemblies. Topics include the elements of protein structure and folding, principles of protein purification and analysis, enzymology, nucleic acid biochemistry, and the structure and function of biological membranes.

BI 615 Advanced Cell Biology
Topics include the principles of cellular organization and function, regulation of the cell cycle, and interactions between cells and cellular signaling pathways.

Examples of 800 level graduate seminars offered over the past few years:

BI 819 Advanced Topics in Biochemistry
BI 834 Seminar in Translational Regulation
BI 835 Seminar in Structural Neurochemistry
BI 848 Seminar in Cellular Biology: Nuclear Import and Export Pathways
BI 864 Seminar in Developmental Biology
BI 865 Seminar: Cell Motility
BI 867 Current Topics in Chromosome-Microtubule Dynamics
BI 880 Responsible Conduct of Research and Professional Development
The nuclear DNA of eukaryotes is organized by structural and regulatory proteins to form the nucleoprotein complex termed chromatin. The primary functional unit of chromatin is the nucleosome, a particle containing histone proteins and approximately 200 base pairs of DNA. Research in my laboratory is directed toward understanding the processes involved in nucleosome assembly during DNA replication. Just as the DNA in dividing cells must be replicated once each cell cycle, so too must sufficient histones (and other chromatin proteins) be synthesized to assemble nucleosomes on the newly replicated DNA. The proper assembly of chromatin during cell division is of vital importance, because the presence or absence of nucleosomes (and the precise positioning of nucleosomes with respect to DNA sequences) can determine which genes are transcribed, and when. To make our results as relevant as possible to human cell biology, our experiments are performed using HeLa cells, a transformed human cell line.

The faithful transmission and assembly of chromatin requires that many independent cellular processes be coordinated. As DNA is being replicated, histones are synthesized, then modified by enzymatic acetylation, transported to the nucleus, and assembled into nucleosomes. Moreover, supercoiled chromatin higher-order structures must first "unwind" to allow access to the DNA, and then condense again after replication is completed. In my laboratory the specific questions currently being investigated include: the modification status of parental histones that are segregated to progeny chromosomes, and the mechanisms of histone deposition onto newly replicated DNA; the involvement of histone acetylation in nucleosome assembly, and the properties of the enzymes (histone acetyltransferases) involved; the role of histone phosphorylation and methylation in regulating chromatin folding; and the isolation and characterization of somatic nucleosome "assembly factors," to define the in vivo assembly pathway.

In order to address these questions we use a number of approaches, including DNA replication systems (in vivo and in vitro), histone acetylation assays, in vitro assembly reactions using purified components, and yeast molecular genetics. We also take advantage of antibodies directed against specific histones, histone modifications, and non-histone chromatin proteins, to purify and analyze newly replicated nucleosomes and their assembly intermediates. Our aims are to identify major cellular components needed to generate nucleosomes in vivo, and to characterize the stages of chromatin biosynthesis. Ultimately, these studies should provide a better understanding of the regulation of chromatin organization during DNA replication, and of the processes involved in the faithful assembly of transcriptionally active and inactive chromatin structures.

Representative Publications

Research in the laboratory is in a sub-area of cell biology. Specifically, we are interested in how cells change shape or form and how that is precisely regulated using the cytoskeleton. Molecular motors using cytoskeletal tracks are required for such intracellular movements as cytokinesis, endocytosis, exocytosis, axonal transport and organellar movement in general. Although motors are required, many relatively basic questions are unanswered. Work in the laboratory focuses on one of these problems. A critically important cell shape change under investigation is cytokinesis, the division of the cytoplasm during mitosis that is mediated by an actin-myosin based contractile ring in the cleavage furrow. One of the outstanding questions in the study of cell division is how timing and placement of the contractile ring is coupled to mitotic controls. Using micromanipulation, reverse genetics, as well as biochemical approaches in dividing echinoderm eggs, we have sought to determine how the timing of cytokinesis is coupled to the mitotic cycle. These experiments suggest that the timing of cytokinesis is a function of the delivery of a positive cleavage stimulus to the cortical cytoskeleton. We have found that cytokinesis in embryonic cells requires inactivation of the mitotic spindle checkpoint but not mitotic exit. We also find that new membrane addition occurs in a final stage of cytokinesis and requires mitotic exit. Studies are underway to determine the nature of the cleavage stimulus and the response system orchestrating the assembly and dynamics of the contractile ring.ing to identify the protein that the antibody recognizes. This work involves the techniques of molecular biology, cell biology, and biochemistry. This protein will very likely serve as a unique marker for these neurons and perhaps allow us to extend our understanding of synaptic vesicle exocytosis/endocytosis in neurons.

Representative Publications


My laboratory at Boston College is interested in understanding the molecular signaling pathways that regulate antigen-dependent humoral immune responses. An effective humoral response requires a given B lymphocyte population to express a repertoire of receptors capable of recognizing a distinct array of antigens (Ags), while at the same time maintaining tolerance. Ag-specific B cells can undergo activation/proliferation, or programmed cell death. These “fate” decisions are dependent on the developmental stage of the lymphocyte, Th cell help, and signal input from co-receptors, which serve to modulate B-cell antigen receptor (BCR) signaling threshold. Our research contributions can be grouped into four areas: 1) regulation of CREB phosphorylation; 2) regulation of cyclin D2 gene transcription; 3) the role of cdc37/hsp90 molecular chaperones in negative signaling following BCR and FcγR co-cross-linking; and 4) identification of molecular components involved in CD5+/B-1 cells proliferation.

Our approach to identify protein kinases necessary for linking the BCR to CREB S133 phosphorylation has been comprehensive in nature, utilizing highly selective cell permeable activators/inhibitors of kinases and mice null for individual protein kinases linked to the B-cell signalosome. We are currently evaluating the requirement for novel PKC isoform(s) in BCR-induced CREB S133 phosphorylation.

Emphasis is to define signalosome components and downstream signaling pathways that contribute to de novo cyclin D2 gene expression in mature B cells. A requirement for functional hsp90 and MEK1/2 in BCR-induced cyclin D2 transcription has been uncovered. We are also currently using mice deficient in the p85α gene product of PI-3K to evaluate the role of PI-3K in cyclin D2 gene expression.

We are also investigating whether negative signals triggered by BCR-FcγR co-cross-linking promote growth arrest by targeting components of the cyclin D2-ckd4-pRb pathway. In B cells undergoing negative signaling, cyclin D2-ckd4 complexes are disrupted and unable to phosphorylate pRb. During this time, cdc37 is inducibly phosphorylated and along, with hsp90, does not stably bind cdk4. Thus, inhibition of cdc37 function by phosphorylation may likely contribute to the observed growth arrest.

Studies continue to investigate the unique hyperresponsiveness of peritoneal B-1/CD5+ cells with respect to proliferation. B-1 cells proliferate in response to activation of PKC alone, whereas B-2 cells require PKC activation and calcium mobilization. We have also found that cyclin D3 protein accumulates, coincident with S phase entry, suggesting that cyclin D3 holoenzymes contribute to endogenous pRb phosphorylation during G1/S transition.
Large scale DNA sequencing has ushered in a new era in biology. There are now hundreds of organisms in which nearly all the genomic sequence is known, making it possible to thoroughly analyze and compare species at their most atomistic genetic level. At the same time, massive phenotypic datasets, such as whole-genome expression arrays, have become increasingly available. My lab is interested in computational and mathematical approaches to analyzing such large data sources, to understand how genomes function and evolve.

1. Detecting Functional Sequences in DNA through Comparative Genomics

Comparative sequence data can be used to infer the functional sequences within genomes. Just as morphological features conserved among species (e.g. all vertebrates have a spine) are likely to be important to those species, conserved DNA sequences are likely to be functional. One of the lab’s goals is to identify DNA sequences that regulate the transcription or translation of nearby genes. For example, we have used comparative techniques to identify functional sites in the promoters of the Saccharomyces genus of yeasts. Such sequence comparisons can yield predictions of not only individual DNA/protein binding sites, but also broader features, such as the types of genes likely to be under the most complex regulation. The lab also collaborates with several experimental groups to validate functional sequence predictions, in species including malaria and zebrafish.

2. Identification of Neutral Mutation Rates

Evaluating the functional significance of conserved sequences is still a major challenge, partly because the mutation patterns of non-functional, or neutral, DNA are not well understood. Another direction of the lab is therefore to characterize neutral mutation rates. One puzzle is why neutral rates are uniform in some species, such as the sensu stricto yeasts, while rates vary by location in species such as mouse and human. Some current questions include what sequence features can affect mutation rates, and also whether mutational heterogeneity can have a selective benefit.

3. Evolution of Transcription Factors and Their Binding Sites

Currently, only a small fraction of the binding sites for transcription factors are known. As more transcription factor binding sites are discovered and mapped to their counterparts in other species, it will be possible to learn how transcription regulation has evolved. We are interested in computational methods to study transcription evolution, using both sequence and experimental data. Some questions in which we are interested are: How quickly do binding sites and transcription factors change between different species? How much of this change is neutral? And, how much is due to selection?

Representative Publications


My research focuses on computational biology/bioinformatics. Topics of interest include RNA and protein structure determination, application of machine learning methods to biological classification problems, time warping applications to functional genomics, and extensions of sequence alignment algorithms. As previous Genzten Chair of Theoretical Computer Science at the University of Munich, I played a key role in developing a Bioinformatics Program there, and published *Computational Molecular Biology: An Introduction*, John Wiley & Sons, Ltd. (2000). For the past three years, I have co-organized the MIT Bioinformatics Seminar.

Before pursuing computational biology in the Biology Department, my research focused on theoretical computer science (an area at the intersection of mathematics and computer science), and I worked on topics such as complexity of propositional proof systems, bounded arithmetic, complexity of higher type functionals, and Boolean functions and circuits.

**Representative Publications**


My laboratory research has focused on the symbiotic association of nitrogen-fixing Rhizobium meliloti with its host plant alfalfa. The specific interaction of the bacteria with alfalfa root hairs results in the development of root nodules, differentiated plant structures containing intracellular bacteria. These bacteria reduce atmospheric nitrogen to ammonia, thus providing a major source of available nitrogen for human consumption. The development of root nodules and the subsequent ability to fix nitrogen requires new gene expression from both symbiotic partners. My lab has investigated the induction of nodule-specific plant genes using a variety of bacterial mutants, each blocked at varying stages of intracellular development. Our results from numerous studies have shown that induction of certain nodule-specific genes requires entry of the bacterium into the plant cell but is independent of further bacteriod development. This may reflect a developmental program that is initiated by the infecting bacterium, but subsequently facilitated by plant processes. Following this reasoning, we hypothesized that plant developmental mechanisms may be conserved, and used PCR to identify several MADS box genes whose expression is found in the infected cells. Since plant MADS box genes have been implicated in flower development, it is intriguing to speculate that similar mechanisms may be involved during nodule development. Currently, we believe that three alfalfa MADS box genes are involved in a signal transduction pathway that is initiated by the infecting bacterium and results in differentiation of the infected cell. The infected differentiated cell has the appropriate environment to support the nitrogen-fixing bacteria. Further work is needed to identify the ultimate target genes and to determine the extent to which various programs for organ development overlap.

After a fellowship and sabbatical leave at the Radcliff Public Policy Center, I developed a new research interest revolving around science policy and career development. Currently, I am working with colleagues in the Carroll School of Management to examine success strategies for mid-career scientists working in academia. Our goal is to identify institutional, cultural and personal factors that influence research productivity through one’s mid-life, a period of documented transition. Special attention is being directed to the research success of women, and the unique problems that they face as an academic scientist.
The protozoan parasite *Toxoplasma gondii* is a member of the phylum Apicomplexa and can cause severe disease in humans. This parasite is easily grown and manipulated *in vitro* and has in recent years developed as a safe and versatile model for other apicomplexan parasites (e.g. malaria). We are using and developing forward, reverse and functional genetic tools using enzymatic as well as fluorescent protein reporter assays in combination with cell sorting and fluorescence microscopy to learn more about the parasite’s cell biology.

Parasite replication is conserved, yet are variations on a theme in different apicomplexan parasites. *Toxoplasma* divides by an internal budding process called endodyogeny where two daughters are being assembled inside the mother, which is significantly different from mammalian cell division. The parasite’s cytoskeleton, consisting of microtubules as well as a membrane skeleton in combination with intermediate protein filaments (the inner membrane complex or IMC) serves as a scaffold for daughter assembly. Recently we identified several components that act in the cytoskeleton assembly as well as daughter formation which are currently being characterized in detail.

Host cell invasion is an essential step in the life cycle of Apicomplexa and identifying essential steps and/or molecules in the process would provide attractive potential therapeutic targets. To identify key molecules in invasion, a set of conditional parasite invasion mutants has been generated through random as well as insertional (conditional) mutagenesis. Mutants are being analyzed through a set of cell biological assays while at the same time the mutated genes are being identified using DNA library complementations as well as plasmid rescues.

A third field of interest is the interaction of the parasite with its host cell. Although there is plenty evidence the parasite modifies its host cell to ensure its own survival, exactly how the parasite achieves this is unclear. It is also unclear if there are any essential host cell components the parasite requires from the host cell, which would be good interference targets as well. Several genetic screens using flow cytometric cell sorting as well fluorescent protein based growth screens are either planned or underway.
Gene expression can be regulated at several different levels. While the primary control of gene expression is at the level of transcription (synthesis of specific mRNAs from a DNA template) in recent years it has become apparent that regulation at the level of translation (the synthesis of proteins from messenger RNA) is also very important.

Translational regulation linked to changes in mRNA poly(A) tail length is necessary for progression through meiosis, early development and localized translation at the neuronal synapse. This mechanism is called "polyadenylation induced translation". Essentially, mRNAs containing a long poly A tail (50-300 nt) are translated, whereas those with a short poly A tail (<50 nt) are not. Molecular events that alter the length of the poly A tail therefore directly influence the translation of the mRNA.

Our research is currently focused on dissecting the molecular machinery of polyadenylation-induced translation and the signal transduction cascade that regulates this process during Xenopus oocyte meiosis.

We use Xenopus oocytes and eggs because we can obtain large amounts of material for examining the molecular machinery of polyadenylation-induced translation and we can induce the meiotic signal transduction cascade by adding progesterone to explanted oocytes. Microinjection allows us to explore the influence of various mRNAs and proteins on meiosis and the metabolism of components of meiosis and polyadenylation-induced translation.

Current projects include analysis of the regulation and metabolism of CPEB, identification and characterization of XGef and CPEB interacting proteins, and exploration of the role of XGef and small GTPases in progesterone stimulated meiosis.
How do eukaryotic cells sense their environment and regulate biological processes in response to environmental signals? To address this question, my lab studies how glucose triggers repression of transcription of the fbp1 gene in the fission yeast Schizosaccharomyces pombe. Depending upon the carbon source in the medium, S. pombe cells regulate fbp1 transcription over a 200-fold range.

Combining classical yeast genetics with molecular biology, we have identified a number of genes required for both repression and derepression of fbp1 transcription. Glucose repression requires the function of nine git genes leading to the activation of protein kinase A (PKA; cAMP-dependent protein kinase). These genes include seven genes required for activation of adenylate cyclase, one gene encoding adenylate cyclase (git2/cyr1), and one gene encoding the catalytic subunit of PKA (pka1/git6). Four of the genes required for adenylate cyclase activation encode alpha, beta, and gamma subunits of a heterotrimeric G protein, the same type of protein that regulates mammalian adenylate cyclase activity, and a seven transmembrane protein that may function as a glucose receptor. We are presently studying the interactions between these proteins and adenylate cyclase. We have also found that both adenylate cyclase and phosphodiesterase activities are regulated to control cAMP signaling. The remaining three git genes, appear to work independently from the G protein. The git1 protein is unique to S. pombe, while git7 and git10 have orthologs in other organisms that have been shown to physically interact and to work in a variety of processes. We are currently studying the roles of these proteins in cAMP signaling, as well as the mechanisms by which they carry out these roles.
Functional sequence variations cause phenotypic differences, and can lead to hereditary diseases. Functional or not, polymorphisms are landmarks allowing us to track how segments of DNA have been passed down through past generations. My laboratory is interested in various aspects of sequence variation research.

**Polymorphism discovery tools.** Building on PolyBayes, a SNP discovery tool we have developed at Washington University, we continue working on efficient, accurate, mathematically rigorous polymorphism discovery algorithms that can detect genetic variations in DNA sequences from varied sources and quality standards.

**Population Genetic modeling.** Large data mining efforts found millions of polymorphic sites in the human genome. These large data sets make it possible to study the molecular and demographic processes that have shaped the genome landscape of human variations. Our primary interest is in interpreting the effects of long-term demographic history on genome-wide human variation data using coalescent modeling approaches, and determining the model structures and model parameters that best account for the observed patterns. This will allow us to better understand human pre-history and to obtain quantitative computer models of human polymorphism structure.

**Human haplotype structure.** An ambitious initiative, the International HapMap project is underway to map out human haplotype structure at the kilobase scale in hundreds of reference samples from a handful of populations. Its utility for medical research will be determined by the degree to which allelic association patterns observed within the HapMap reference samples actually pertain to patients. An important research focus of my lab is to understand the demographic differences in the haplotype structure among human populations and to develop tools with which to extrapolate the strength of allelic association from reference samples to clinical samples.

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Representative Publications


The basic paradigm for nuclear import is that a protein containing a nuclear localization signal (NLS) interacts directly, or via an adapter, with an import receptor belonging to the karyopherin beta/importin beta (Kap beta/Imp beta) superfamily; is translocated through the nuclear pore complex and released in the nucleus. We had previously identified and characterized several nuclear import pathways for proteins containing a classical nuclear localization signal: hnRNP A1 and Influenza virus RNA.

My current research program focuses on the identification and characterization of the nuclear import pathways for the proteins and DNA of human papilloma viruses (HPVs). More than 100 HPV genotypes have been isolated and characterized, with roughly half infecting the skin and the other half the oral/anogenital mucosal epithelial tissues. Mucosal HPVs have demonstrated varying degrees of oncogenic potential. High risk HPVs, such as types 16, 18, and 45, are frequently detected in invasive cervical carcinomas. Low risk HPVs, such as types 6 and 11, are more often associated with benign exophytic condylomas. HPVs are small, nonenveloped, icosahedral DNA viruses that infect squamous epithelial cells. The virion particles (52-55 nm in diameter) consist of a single molecule of 8 kb double-stranded circular DNA contained within a spherical capsid composed of 72 homopentameric L1 capsomeres and L2 molecules of L2 minor capsid protein. During the late phase of viral infection, HPV L1 major capsid proteins enter the nuclei of terminally differentiated epithelial cells and, together with the L2 minor capsid proteins, assemble the viral DNA into virions.

Nuclear import and export of HPV proteins and nucleic acids are crucial for the viral life cycle and pathogenesis. Projects in my lab include: identification and characterization of the nuclear import pathways for L1 and L2 capsid proteins and for E6 and E7 oncoproteins of both high and low risk HPVs; the molecular mechanisms for nuclear import of HPV genomic DNA; and nuclear export pathways for E6 oncoproteins and viral transcripts. Our studies defining the transport pathways for HPV proteins and nucleic acids will make a significant contribution to the understanding of the HPV life cycle and pathogenesis.

Representative Publications

Research in my lab is being conducted in three areas: signal transduction during development in the fruit fly, *Drosophila melanogaster*; host-parasite interactions in the malarial mosquito, *Anopheles gambiae*; and endosymbiosis, pathogenesis, and bleaching in marine invertebrates.

Mechanisms that underlie the adoption of cell fates in *Drosophila* also operate in other multicellular organisms, including humans. We are focusing on understanding in flies the Notch signal transduction pathway, which also operates in humans and is central to the correct specification of cell fates and hence to pattern formation within embryonic, larval, and adult tissues. We are studying the Delta-Notch pathway—implicated in lymphoma and genetic syndromes in humans—using morphological, genetic, molecular, and cell biological approaches. These studies focus on understanding the regulation of signalling by Delta, a cell surface protein; the relationship between the structure of the Delta protein and its function as a signal during development; and the mechanisms by which Delta stimulates activation via proteolysis of the cell surface receptor Notch. This aspect of our research is of particular interest because Delta stimulates proteolysis of Notch by a *Drosophila* homologue of Presenilin, an intramembrane protease that has been implicated in Alzheimer’s disease in humans.

The continuing transmission of human malaria depends, in part, on reproduction of the malarial parasite, *Plasmodium spp.*, within mosquitoes. We are investigating the midgut, one of the mosquito tissues central to the reproduction of malarial parasites, using morphological, molecular, and cell biological techniques. We are also investigating cellular and molecular aspects of interactions between malarial parasites and the midgut during the course of parasite reproduction and growth in the malarial vector mosquito *Anopheles gambiae*, using molecular genetics and DNA microarray-based gene expression profiling. By better understanding this important host-parasite interaction, we hope to develop approaches to disrupt it, thereby reducing the transmission of malaria within human populations.

Coral and other marine invertebrates often harbor unicellular endosymbionts. Such endosymbionts provide photosynthetic resources to the host, and the host provides endosymbionts with nitrogenous resources and physical protection. We are studying one such endosymbiont, the dinoflagellate *Symbiodinium microadriaticum*, in an attempt to better understand the establishment and maintenance of these endosymbiotic relationships in corals (*Acropora spp.*) and anemones (*Aiptasia spp.*). These studies will extend our understanding of the mechanisms of endosymbiosis between dinoflagellates and invertebrates, an interaction vital to the health and diversity of tropical coastal marine ecosystems.

**Representative Publications**

The goal of our research is to understand the physiological significance of a protein carboxyl methyltransferase (PCMT) that esterifies unusual isoaspartyl residues in proteins. Isoaspartyl residues are not incorporated into proteins during translation, but arise spontaneously during aging. The introduction of an isoaspartyl residue into a protein produces a “kink” in the protein backbone, which can inactivate the protein. In purified systems, PCMT initiates the structural repair of the damaged substrate, and it has been proposed that PCMT helps to prevent the accumulation of damaged proteins in cells. Judging from the nearly ubiquitous distribution of PCMT activity in living organisms, PCMT function may be a fundamental component of cellular protein metabolism. We are currently using both biochemical and genetic experiments to study the significance of PCMT activity.

To define the biochemical pathway initiated by carboxyl methylation, we have been following the fate of isoaspartyl-containing proteins following their microinjection into Xenopus laevis oocytes. These experiments have shown that cells recognize isoaspartyl-containing substrates as abnormal and target them for degradation unless they are modified by PCMT, consistent with the role of PCMT in protein repair. We have further characterized the degradation pathway and found that proteins are degraded by the 26S proteasome in a novel pathway that does not involve ubiquitination.

We are also using the fruitfly Drosophila melanogaster to understand the effects of PCMT during aging. Drosophila makes a particularly suitable model for these studies because of the reproducible phenotypes associated with the aging process, which occurs over a period of about six weeks. In addition, many of the fundamental mechanisms underlying development and neural function are conserved from Drosophila to mammals. We have recently shown that overexpression of PCMT in adult flies causes a dramatic extension in the adult lifespan at 29 degrees centigrade, but not at 25 degrees centigrade. The results suggest that protein repair is important in the control of lifespan. PCMT function may be particularly important at slightly elevated temperatures, where proteins are more flexible and prone to isoaspartate formation. We are now constructing other Drosophila mutants to determine if there is a quantitative relationship between the level of PCMT expression and longevity.
The interests of my laboratory center around the molecular and developmental biology of the fruit fly *Drosophila melanogaster*. We utilize the follicular epithelial cells of the ovary to investigate the mechanisms which allow genes to be turned on and off in a sex-, tissue-, and developmental stage-specific manner. These cells produce proteins which form the protective eggshell surrounding the mature oocyte. Our laboratory and others have characterized many of the genes and proteins involved in making the two layers of the eggshell: the vitelline membrane (VM) and the chorion.

In the case of the genes encoding the proteins for the vitelline membrane, we have found that they are expressed only in the adult female, only in the follicular epithelium, and only during stages 8, 9, and 10 of egg chamber development. Our long-term goal is to elucidate the details of how such a specific pattern of control of gene expression is regulated. To this end we have cloned the genes for two vitelline membrane proteins, VM26A1 and VM34C, and fused their modified upstream regulatory regions to b-galactosidase and chloramphenicol acetyl transferase reporter genes. These constructs have then been reintroduced into flies via P-element-mediated germline transformation. Using this approach, we have been able to define roughly 100 base pair long regions adjacent to both genes which contain the key, independently acting sex-, tissue-, and stage-specific control functions. In addition, we have found a number of dependent control elements which require a functional independent element and which affect the spatial pattern of expression within the follicular epithelium and the quantitative levels of expression. We are now utilizing these defined cis-acting elements and gel retardation assays to search for the transacting molecules involved in switching on the VM genes. We have identified one factor which binds specifically to the key independent control region of the VM26A1 gene. Current work involves characterizing this factor and recovering a clone for its gene from an ovarian cDNA expression library.

A second area of research in the lab involves the field of molecular evolution. While sequencing the genes for VM proteins, we discovered that hidden within the coding sequence of each gene was a highly conserved 38-40 amino acid peptide we call the VM domain. We immediately wondered if the conservation of this VM domain extended beyond the melanogaster species, and hence might serve as a new model for the evolution of insect eggshells in general via the formation of a multi-gene family. We are currently using PCR and other techniques to search for VM domain-related sequence in other classes of insects.

**Representative Publications**


My research interests have included the biological roles of metal ions such as zinc and iron as well as the mechanisms for protection against the toxic effects of metals such as cadmium and copper, using the fission yeast *Schizosaccharomyces pombe* as a model system for eukaryotic cells. Recent studies have examined mechanisms for protection against copper and cadmium. The properties of metal-binding peptides known as Class III metallothioneins, as well as the conditions for their synthesis, have been the object of several studies.

Work on copper resistance has involved the isolation of a copper-resistant strain of *S. pombe*, which, unlike *S. cerevisiae*, does not contain a gene for a Class II metallothionein that accounts for copper resistance in the latter organism. Rather, the resistance trait in *S. pombe* results from a single recessive chromosomal mutation that appears to affect the properties of the cytoplasmic membrane with the consequence that entry of copper into the cell is inhibited.

Studies involving resistance to cadmium ions have focused on the synthesis of Class III metallothioneins (sometimes called phytochelatins) that have the overall structure \( [\gamma\text{Glu-Cys}]_n\text{Gly} \). These peptides, present in higher plants, occur in *S. pombe* as well, and their synthesis is stimulated in response to a variety of metal ions, cadmium being the most effective. Peptide synthesis is catalyzed by the constitutive enzyme \( \gamma\text{Glu-Cys} \) dipeptidyl transpeptidase (phytochelatin synthase), that uses glutathione \( (\gamma\text{Glu-Cys-Gly}) \) as an initial substrate. Complexes are formed with metal ions and several peptide molecules, often of heterogeneous lengths, frequently containing inorganic "labile" sulfide as well. Our work has focused on delineation of the stoichiometries and structures of the complexes formed with cadmium and zinc, as well as the conditions required for their formation and their possible biological functions in addition to a likely detoxifying role.

Representative Publications


Our research program focuses on dietary therapies for epilepsy, brain cancer, and neurodegenerative lipid storage diseases. These therapies include caloric modification, fasting, and the ketogenic diet. Our goal is to manage complex diseases through principles of metabolic control theory. This theory is based on the idea that compensatory metabolic pathways are capable of modifying the pathogenesis of complex neurological diseases despite the continued presence of the genetic or environmental defects responsible for the disease. By shifting the brain metabolic environment, diet therapies can potentially mask or neutralize molecular pathology. The neurochemical and genetic mechanisms of these phenomena are under investigation in genetic animal models and include the processes of inflammation, programmed cell death, angiogenesis, and bioenergetics.

Representative Publications


I advocate a multidisciplinary approach for addressing questions regarding the insect transmission of pathogens. Using tools from the diverse scientific disciplines of molecular biology, biochemistry, cell biology, immunocytochemistry, genomics, and proteomics, my laboratory investigates how the malaria parasite is transmitted from one human to another by using the mosquito as vector. The projects of my laboratory can be classified into four major areas: (1) the development of the mosquito stage of malaria parasites; (2) the biology of the mosquito as it relates to malaria transmission; (3) molecular interaction between the malaria parasite and mosquito; and (4) mosquito responses to malaria parasite invasion.

Our goal is to identify crucial parasite and mosquito molecules that can be targeted to develop malaria transmission-blocking strategies.

Soon after the ingestion by mosquitoes with blood, the parasites emerge from the gametocyte as male and female gametes, which fertilize to form zygotes. The zygote transforms into a motile ookinete and exits from the blood bolus. The ookinete crosses the midgut epithelium and lies between the midgut cells and the basement membrane, where it develops as an oocyst. Inside the oocyst, the parasite multiplies to form thousands of sporozoites. In about two weeks, sporozoites are released from the oocyst into the insect blood, invade the salivary gland and remain there until injected into a human during a subsequent blood meal.

My lab has shown that chitinase secreted by the malaria parasite is required for its escape from the blood bolus. Blocking chitinase activity in the mosquito midgut blocks *Plasmodium* development in the mosquito. This makes chitinase a candidate for development of a malaria transmission-blocking vaccine. In a series of subsequent studies, we described the cellular compositions of *Aedes aegypti* mosquito midgut. We have discovered that a carbohydrate-mediated ligand helps the avian malaria parasite, *Plasmodium gallinaceum*, which we use as a model, adhere to the midgut epithelium. We also find that the parasite appears to preferentially invade a specific cell type in the mosquito midgut. Recently, we discovered a novel differential partitioning of maternal lipids in the mosquito, where phospholipids are accumulated in the larval intestine.

Transmission of the malaria parasite by mosquitoes suggests that the parasite sporozoite stage is able to evade the potent insect antimicrobial immune response, which efficiently clears bacteria and fungi from the insect blood. To understand how the sporozoites survive in the mosquito, we have been using transgenic insect and gene microarray technologies. We have found that the malaria sporozoite modulates expression of a number of *Drosophila* genes involved in immunity, signal transduction, and metabolic pathways. Research to identify the *Anopheles* homologues of these *Drosophila* sporozoite-responsive genes and to determine the effects of malaria parasite infection on these genes is currently underway.

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### Representative Publications


My laboratory is interested in how cells keep their chromosomes intact. The ends of linear chromosomes pose a particular problem, because they must be differentiated from broken DNA ends that result from DNA damage. Most eukaryotes solve this problem by capping their chromosomes with specialized protein: DNA structures, or telomeres. Telomeres shield the chromosome ends from the checkpoint proteins that survey the genome looking for DNA damage, and from the enzymes that degrade and repair broken DNA ends.

Telomeres are not completely impenetrable—they must transiently open to allow telomerase to gain access to the chromosome end. Telomerase is the enzyme that adds new telomeric DNA onto the ends of chromosomes, and thus compensates for the inability of conventional DNA polymerases to fully replicate linear DNA molecules. In humans, telomerase is turned off in most terminally differentiated cells, but telomerase is reactivated in most types of tumors, and this reactivation correlates with the ability of tumor cells to proliferate indefinitely. Therefore, understanding how telomerase is regulated is of great interest to cancer biologists.

We are studying telomeres and telomerase in a model organism that proliferates continuously, the budding yeast Saccharomyces cerevisiae. We use genetics and biochemistry to investigate how the telomere is remodeled and how telomerase activity is regulated over the course of the cell cycle. Telomerase contains both protein and RNA components, and interactions between these components and specific telomere binding proteins are emerging. We are currently investigating how these interactions contribute to the recruitment, activation and release of telomerase at telomeres.

We have also uncovered a mechanism by which telomerase can be recruited to broken DNA ends, where it can instigate a crude form of DNA repair: telomerase can add telomeric DNA to the site of the break, which enables the broken chromosome to be capped with a telomere. This telomere healing mechanism is costly to genome integrity, since all DNA sequence distal to the break is lost, however it enables the checkpoint to be released and the cell to resume growth. We are working to understand the regulatory circuits that control telomerase activity at broken DNA ends. We are also investigating whether some types of chromosomal damage are dependent on this mechanism for DNA repair, and whether potential sites for telomere healing are nonrandomly distributed across the genome.

Representative Publications


My laboratory is interested in the neurobiology of the chemosensory system. We use molecular genetic, cell biological, and behavioral techniques to examine the chemosensory system of the small nematode roundworm, *Caenorhabditis elegans*. We are interested in two distinct aspects of this problem.

First, we wish to understand the development of the various cell types that must interact during the formation of an intact sensory organ. How is the regulation of this process organized? How is the developmental program executed? Many human sensory disorders arise as a consequence of errors in the development and maintenance of the sensory organ. Understanding the genetic control of this process in *C. elegans* may help us diagnose and treat these human diseases. To study this process in *C. elegans* we take advantage of an assay of structural integrity of the adult organ. When animals are soaked in a lipophilic dye, the dye is occluded from entering the animal at all points except the exposed tips of the chemosensory neurons. The sensory neuronal membrane thus fluoresces with the intercalated dye in a wild type animal. Mutations that perturb the development of the sensory organ (the “amphid” in the worm) or the sensory neurons themselves, lead to a dye-filling defective (Dyf) phenotype. We then clone these mutations using modern molecular genetic and genomic technologies.

Second, we also wish to understand the functioning of the intact chemosensory system. That is, once the chemosensory organ is in place, how does the animal come to select one taste over another? This is a complex question that we try to address in two ways. First we execute genetic screens—based on direct assays of behavior—for animals that can taste, but that have an altered preference for one taste relative to another. Second, we turn to nematodes in the natural world and try to understand the impact of strain variation on taste preference. Not all isolates of *C. elegans* share the same taste preferences, just as not all people share the same taste preferences. Since all strains are raised under identical conditions in the lab, much of this strain variation must be under a genetic locus of control. Each of these approaches presents a unique set of challenges to the geneticist, and consequently we have developed, and continue to refine, new methodologies and resources for forward genetics in *C. elegans*.
Boston College is a coeducational university with an enrollment of 8,900 undergraduate and 4,600 graduate students representing every state and more than 95 countries. Founded in 1863, it is one of the oldest Jesuit, Catholic universities in the United States. US News & World Report ranks Boston College 38th among national universities.

Boston College confers more than 3,800 degrees annually in more than 50 fields of study through 11 schools and colleges. Its 641 faculty members are committed to both teaching and research, and have set new marks for research grant awards in each of the last 10 years.

The University’s 116-acre main campus is located in an open suburban setting six miles from downtown Boston, with direct access to the city via public transportation. The past decade has seen the construction or substantial renovation of 10 campus buildings.

Graduate Housing

A wide variety of affordable rental housing is available in the local communities of Newton, Brighton, and Brookline. Many other nearby cities and towns are accessible via bus and trolley (two lines are within a few minutes’ walk from campus) as well as by several major roadways. The Boston College Housing Office is available to offer assistance in obtaining housing for incoming graduate students.
The City of Boston, founded in 1630, is the largest metropolis in New England, and is among America’s most vital cities as a center of trade and finance, education and research, art and culture.

Boston and Bostonians have been at the heart of movements and events that have shaped the United States, from the American Revolution to the computer revolution. This translates into a community that is at once rich in intellectual, cultural, political, and historical traditions, and alive with innovation and invention.

The city is known for its medical facilities and high tech companies, and for the educational institutions that support them. Boston College is one of more than 50 universities and colleges located within the Boston area. Among these are Harvard University, Massachusetts Institute of Technology, Boston University, Northeastern University, Brandeis University, Tufts University, Wellesley College, and many specialized professional, art, and music schools. This unmatched concentration of academic, cultural, and intellectual activities in the Boston area draws an extraordinary variety of young people from around the world. The rich academic environment, in combination with Boston’s thriving biotechnology industry, also provides graduate students a wealth of opportunities to discuss advances in pure and applied research with many of the top scholars in the field.

Boston is also a city that knows how to have fun. It offers residents and visitors alike a wide variety of ways to engage the mind, body, and spirit: national touring acts in concert at the Fleet Center, or quiet acoustic performances at Club Passim in Harvard Square; world-renowned exhibits at the Museum of Fine Arts, or funky one-artist shows at a Newbury Street gallery; a Red Sox game in famed Fenway Park, or an afternoon of skating at the Frog Pond on Boston Common.

For information about current news and events in the city, you can start by visiting www.boston.com.
Applicants for graduate training should have a bachelor's degree and undergraduate coursework in calculus, physics, biochemistry, biology, and chemistry, including organic chemistry. Strong consideration is given to letters of recommendation, particularly from faculty closely familiar with the applicant's research experience. The application deadline for fall admission is February 1st, but applications received after this date will be evaluated on a continual basis until April 15th. Applications submitted after February 1st may be at a disadvantage for financial aid consideration. All applicants, including those from foreign countries, must complete the Graduate Record Examination (GRE). Applicants whose native language is not English must achieve a score of 550 or better (written test) or 213 or better (computer-based test) on the Test of English as a Foreign Language (TOEFL).

International Students can consult Boston College's Graduate International Student Association web page at www.bc.edu/bc_org/svp/st_org/gisa/ for additional relevant information.

Financial Assistance

Financial support for students accepted into our graduate program generally includes stipends and remission of tuition and fees. Our base stipend covering the 12-month calendar year is awarded in the form of research assistantships, fellowships, or teaching assistantships, and summer support is provided from faculty research or university funds. Research assistantships are provided with funds from faculty research grants, while teaching assistantships are provided based on service in undergraduate lecture or laboratory courses.
Associate Professor Laura Hake and Postdoctoral Associate Susana Martinez review an autoradiogram of an in vivo phosphorylation assay. Dr. Hake’s laboratory is interested in the molecular mechanisms of RNA regulation during gametogenesis and early development. Their current focus is on the mechanisms of cytoplasmic polyadenylation during early development of *Xenopus laevis*. 