ROSE-HULMAN INSTITUTE OF TECHNOLOGY 5500 WABASH AVENUE TERRE HAUTE, IN 47803 PHONE: 812-872-6822 FAX: 812-877-8545 WWW.ROSE-HULMAN.EDU

APPLIED BIOLOGY AND BIOMEDICAL ENGINEERING DEPARTMENT

Research Opportunities in the Applied Biology Program at Rose-Hulman Institute of Technology

The faculty members of the Applied Biology program are dedicated to preparing broadly-trained biologists. We believe an important aspect of that education involves research experience. Therefore, every student majoring in applied biology at Rose-Hulman gains considerable research experience.

1. All students majoring in applied biology perform a year-long senior thesis research project in which they are mentored one-on-one with a faculty member.
2. Many students opt to perform independent research for a term or more under the guidance of a faculty mentor prior to the thesis.
3. The Interdisciplinary Research Collaborative, a summer research experience, is an opportunity for applied biology students to perform faculty-mentored research as a part of an interdisciplinary program including chemists, biochemists, physicists, mathematicians, and engineers.
4. Our applied biology students are competitive in obtaining research experiences for undergraduates at large research-oriented universities and internships.
5. Our students present their research at local, regional, and national professional conferences.
6. Current research projects are diverse in nature. Some are truly applied projects funded by industry while others examine more basic research problems.

On-going research projects among the faculty in the Applied Biology and Biomedical Engineering :

An examination of virus species and their zoonotic transmission among amphibians

In recent years, many viruses (such as Hantaviruses and SARS coronavirus) have emerged in the human population. The emergence of these new viruses has focused much attention on the monitoring of viruses and their diseases. Even with all this focus, the scientific community is unable to predict when and if a new virus will emerge. The focus of this research is to employ the techniques of molecular biology to probe for viruses in nature and to examine their patterns of emergence. Amphibians serve as a good model to study the emergence of viruses because the amphibian population has been declining globally and at least one family of viruses, the iridoviruses, has been implicated in mass die-offs worldwide. It is important to search for other potential viral disease threats prior to their emergence in the amphibian population. This study seeks to investigate the emergence of viral diseases in amphibians by tracking the prevalence and transmission of viruses in amphibian populations. Specifically, iridoviruses are monitored using PCR-based methods in local (Vigo County, IN) amphibian populations. In addition, viruses that have yet to be discovered in the same populations will be identified using a PCR-based method using degenerative primers.

Implications of evolutionary pressure via sexual selection on human mate choice behaviors

The strategies used by men and women to choose relationship partners have developed in our evolutionary history, and reflect the constraints and needs of attracting, acquiring, maintaining, and protecting mating relationships. Further, elements of the current environment present novel challenges to our suite of evolved behaviors. Research on these issues seeks to elucidate both historical influences on mate choice and which novel elements have the most significant influence on mate choice patterns. A variety of research strategies are applied to these questions – surveys and data-gathering from both males and females, alternate analysis of existing data, and mathematical modeling. Recent lessons learned include that RHIT men with girlfriends are

taller than men without girlfriends, but the two groups were similar in other biometrics and their likelihood of participating in varsity sports, and that students as participants in sexual selection research have different interpretations than do researchers of adjectives used to describe behavioral traits. Both of these lessons are appropriate for further investigation.

Biochemical characterization of plant disease defense mechanisms

Unlike animals, which have evolved an elaborate immune system for recognizing general pathogen invasion, plants have developed an extensive surveillance system that can recognize specific pathogen gene products. In this so-called "gene-for-gene" resistance, the products of specific plant-derived genes (known as resistance, or "R" proteins) recognize the products of specific pathogen genes (known as avirulence "avr", or effector molecules) and signal downstream defense responses in the plant. NDR1 (non-race specific disease resistance) is a gene in Arabidopsis thaliana that is required for disease resistance mediated by at least three different resistance genes. As a result, plants that lack a functional copy of NDR1 are susceptible to a range of pathogens. Despite the crucial role of NDR1 in disease resistance, little is known about the molecular function of NDR1. Recent evidence suggests NDR1 exists in a complex with other disease resistance proteins at the plasma membrane. The composition of this protein complex, as well as its dynamics during infection, is not yet known. The primary goal of this research is to understand the role of NDR1 in disease resistance, including its interaction with plant and pathogen proteins during infection. Current research activities include site-directed mutagenesis of putative functional domains, and mutant screens for dominant suppressors of NDR1. Furthermore, there are a number of Arabidopsis sequences that have high similarity (>60%) to NDR1. Until recently, it was thought that these sequences were non-functional pseudogenes. Recent RT-PCR data indicate that at least two of these genes, tentatively called "NDR2" and "NDR3" are expressed in planta. Through epitope-tagging and over-expression experiments, whether NDR2 and NDR3 encode functional proteins and participate in bacterial disease resistance is being investigated. The knowledge gained from this research, including the cloning and characterization of novel disease resistance genes, will help elucidate the molecular basis of disease resistance and contribute to the general understanding of the biochemical signaling events involved in resistance pathways.

Development and analysis of collagenous biomaterials for soft tissue engineering

The abundance and structural importance of collagen in the body make this biomaterial a logical choice for the development of a broad spectrum of tissue engineering applications. The relative biocompatibility of collagen has motivated many researchers to culture cells within collagen gels to create soft tissue equivalents in vitro. However, many of these efforts have met with limited success because the constituent cells dramatically contract the gels over time – resulting in a construct which is only a fraction of the original size, and containing a population of cells that has suffered a large degree of apoptosis. To address these problems, an approach from the field of composite materials is being utilized, wherein the inclusion of short fibers (aspect ratio greater than 10, but not continuous) within a matrix enables the modulation of overall composite properties with relatively minimal increases in material fabrication complexity. The composite materials consist of type I collagen fibers embedded in Type I collagen gels. Long continuous fibers placed within the composites (when desired) alter the tensile tangent modulus of the constructs; the gel phase of the composites is hospitable to cell culture. Recent work at Rose-Hulman developed new techniques to produce collagen fibers with specified cross-sectional areas and shapes, and provided the first experimental data on collagen gel-fiber mechanical

interactions. This past year, work focused on characterizing and selectively controlling mechanical properties of collagen fibers, gels, and fiber/gel composites. Recently a set of long term, in vitro, factorial-design experiments were concluded that quantitatively explored the effects of: included fiber size, total fiber mass, the inclusion of macropores within our composite biomaterials, and the application of a periodic compressive mechanical stimulus, on a number of biomaterial aspects (including: composite compressive modulus, constitutent cell viability, and cellular production of glycosaminoglycan, elastin, and matrix metalloprotease). The largest, mechanically-sound, biologically-viable cell/composite constructs to the knowledge in the field to date has been constructed. A recent discovery that pre-chondrocytes behave differently in our collagen composite biomaterials than do pre-adipocytes, osteoblasts, or fibroblasts was identified. This work implies that expensive continuous-stir bioreactors (the standard in the field) for cartilage tissue engineering may not be necessary. Currently the effects of strategically varying key parameters of our collagen fiber preparation protocol are being explored by seeking improved mechanical strength, greater fiber-gel interactions, and the characteristic nonlinear stress/strain behavior observed in natural collagenous tissues.

In vitro control of H2O2 and O2 concentrations in cell culture

Cells sense O2 concentrations that are below the concentrations required for their energy metabolism and respond with regulative processes. In addition to these stress responses, cells are normally in the body exposed to a wide range of O2 tensions from 21% atmospheric to less than 1% O2, dependent on their location in the body. Like oxygen, H2O2 has a dual role for cell health. Cells sense toxic cellular H2O2 concentrations, endogenously produced as part of metabolism or inflammation, and initiate a multitude of adaptive responses. On the other hand, low cellular H2O2 levels are necessary signal messengers for normal cell behavior, independent of any stress response. The increasing demand in studying cellular functions in cultured cells under various levels of oxygen and hydrogen peroxide (H2O2) is only partly fulfilled by conventional approaches such as hypoxia chambers, bolus additions of H2O2 or redox-cycling drugs. This project includes the validation of a mathematical model of the recently developed enzymatic GOX/CAT system that allows the independent control and maintenance of both H2O2 and hypoxia in cell culture. The Gox/Cat system can be used in studies that aim at better understanding a wide variety of inflammatory diseases such as rheumatoid arthritis, heart disease or diabetes.

A lumped-parameter model of mitral valve blood flow: left ventricular, diastolic e-wave filling

A computer model of early diastolic (E-wave) left ventricular filling through the mitral valve is being developed. This lumped-parameter model will be clinically useful, for example in the diagnosis of diastolic dysfunction. The computer model is based on the solution of the ordinary differential equations describing flow through the mitral valve, as well as equations that model the intrinsic and extrinsic behavior of a variable orifice area mitral valve (mimicking the opening and closing of the valve leaflets). The model was developed and calibrated using porcine data collected at the Laboratory for Experimental Heart Surgery at the University of Heidelberg, and/or using parametric values from the medical and scientific literature. The model has now been further validated in twelve canine trials, also collected at the Laboratory for Experimental Heart Surgery.

Development of a procedure for in vitro culture of amoebocytes from the American horseshoe crab

Bacterial contaminants known as endotoxins are fatal when they come in contact with our bloodstream. Thus, most injectable drugs, invasive medical devices, and vaccines must be tested for these contaminants prior to their use, and amoebocytes from horseshoe crabs form the basis of this test. (The Limulus amoebocyte

lysate (LAL), the test most widely used for screening for endotoxins, is a $60 million dollar industry.) Currently, amoebocytes are obtained by bleeding collected animals. However, the recent decline in horseshoe crab populations has brought into question the long term viability of this methodology. The goal of this research is to develop the methodology required to achieve in-vitro amoebocyte production via organ-cultured gill lamellaed. If successful, this technology might someday be commercialized with the potential to supplement or replace the current method of obtaining these cells.

Studying the effects of change to photoperiod on retinal sensitivity in the American horseshoe crab

Studies have shown that the breakdown and resynthesis of membrane containing light-sensitive pigment in the eyes of animals is a ubiquitous process; however, it is not yet understood why this membrane is recycled on a regular basis. The turnover of light-sensitive membrane is very energy intensive and disorders in this process can lead to Seasonal Affective Disorder (SAD) or retinal degeneration. The obvious explanation that membrane turnover occurs to replace damaged or worn out parts is not supported by experimental evidence. One hypothesis proposes that the regular turnover of light-sensitive membrane helps to modulate quantum catch such that eyes capture approximately the same number of photons each day, regardless of season. Experiments from this lab, using horseshoe crabs as a model system, do not support this hypothesis and have led to of an alternative idea known as the “dawn-dusk hypothesis.” According to this hypothesis, one function of membrane turnover is to regulate quantum catch at dawn and dusk in order to ensure that animals are able to properly entrain their biological clocks to sunlight independent of season. Current research in this lab is systematically studying how changes in photoperiod (either duration or intensity) affect retinal sensitivity.

Ribosomal proteins and the accuracy of translation

This research project focuses on the role of ribosomal proteins in maintaining the accuracy of translation and antibiotic resistance or sensitivity in eukaryotes. The work is facilitated by yeast strains harboring known nonsense suppressor or antisuppressor mutations in various ribosomal protein genes, such as RPS2, RPS9 and RPS23. Functional interactions between the proteins encoded by these genes have been established, and they are thought to be an integral part of the “accuracy center” in the ribosome. Certain changes in these proteins can lead to suppression of all three types of nonsense. Although, the specific types of nonsense and the degree to which each is suppressed is dependent on the particular change present in the associated ribosomal protein, as well as the presence or absence of other suppressor or antisuppressor mutations. In general, changes in these proteins, alone or in combination, can have diverse affects on the accuracy of translation and antibiotic interactions. One goal of this research is to better understand the action of such suppressor and antisuppressor mutations. To this end, diagnostic systems are being developed to allow for analysis of the amino acid substitutions that result from such suppression events in-vivo. Such analyses in strains harboring various changes in these accuracy center proteins should lead to better understanding the role these proteins play in tRNA selection. And similar analyses in the presence or absence of specific antibiotics will further elucidate the activity of those compounds. Another line of research is focused on uncovering the change(s) responsible for an antibiotic-dependent phenotype we induced in yeast. Preliminary studies suggest that the phenotype does not affect mitochondrial function. As such, this could be the first instance of non-mitochondria-associated antibiotic-dependence identified in a eukaryote. And because of yeast’s well characterized genetic system and amenability to manipulation the projects supporting these lines of inquiry provide exceptional opportunities for undergraduate research training.

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Microalgae biodiesel research

Environmental and economical concerns associated with global fossil fuel consumption have inspired a surge in alternative energy research. One area of research is biodiesel production from lipid-producing crop plants, including sunflowers and soybeans. Through the process of transesterification, lipids from plants are easily converted into fatty acid methyl esters (FAMEs), the primary component of diesel. Converting agricultural land from food production to energy production, however, is still a major political and economic obstacle to large-scale implementation. Consequently, research has recently focused on the use of lipid-producing microalgae as a source of biodiesel. Microalgae, such as Chlorella vulgaris and Neochloris oleoabundans, produce up to 40% lipids per dry weight. Preliminary studies have indicated that biodiesel production from algal lipids require substantially less acreage than crop plants, with less overall energy input (such as fertilizing, tilling, and harvesting). To this end, this research is focused on the optimization of microalgae growth and lipid production. Specifically, this project is currently testing the effects of elevated carbon dioxide and hormones on microalgae growth and lipid yield.

Study of biomechanical conditions surrounding total joint prostheses

A research collaboration with orthopedic surgeons from the Center for Hip and Knee Surgery in Mooresville, IN is ongoing to study the mechanical conditions in bones surrounding total joint prostheses, with the goal of discovering which conditions lead to premature failure of these components. Synthetic bones are coated with a photoelastic polymer, implanted with a prosthesis, then loaded to physiologic loads with a mechanical testing apparatus. A polariscope can be used to quantify the changes in the photoelastic coating and correlate them with surface shear strain in the underlying bone. To study total knee replacement, surgeon-controlled parameters such as polyethylene liner thickness, tibial tray conformity, and angle of implantation are varied in order to determine how each of these factors can be optimized by the surgeon in order to minimize mechanical conditions in the bone that might accelerate prosthesis loosening. The same factors can also be studied by measuring strains with a series of strain gauges or mathematically modeled using finite element analysis. By comparing the results from these three different measurement techniques, definitive recommendations will be made to surgeons regarding their technique and prosthesis selection that will help to prolong the life of total joint prostheses in patients.

Evaluation of hand motor function via force production of the thumb and/or index finger

Most activities of daily living required precision handling and power grasps. These motions require force production and control in multiple directions by the digits of the hand. Current clinical practices use key pinch and power grasp dynamometers to assess the motor functions of the hand. This project will investigate a way to provide a more comprehensive and descriptive method of assessing hand function.

Motion and/or gait analysis

This research evaluates human motion by investigating the impact of footwear on gait and balance. In particular, the determination of the biomechanical impact of activities like Zumba, Ballroom Dancing, and Tai Chi on balance and gait (particularly on ‘older’ subjects) is being investigated.