

# Tulane

## **BIOMEDICAL ENGINEERING Senior Projects Class of 2001**

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BMEN 490-491: Research & Professional Practice

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**Table of Contents**  
**2000-2001 Biomedical Engineering Senior Projects**

*Ali, Rehan Z. Three Dimensional Reconstruction of Bovine Lamina Under Elevated Intraocular Pressure (01-01).....5*

*Bhattacharya, Jinia Interstitial Fluid Flow of Ligamentous Tissue Under Mechanical Stress (01-02).....5*

*Binchi III, Fermo A. Biomaterials Laboratory Demonstration (01-03).....5*

*Blidner, Richard Andrew Peripapillary Scleral Thickness in the Perfusion Fixed Monkey Eye (01-04).....5*

*Bridges, Kimberly The Development of a Non-Contact Method of Measuring Cross-Sectional Area of Engineered Tissues (01-05).....6*

*Cheema, Naveed Rosen Ali Elastic Properties of Acellular Agarose Gel Disks as a Funtion of Gel Concentration (01-06).....6*

*Eisenstatt, Thomas An Analysis of Traffic Congestion at the I-10/I-610 Highway Interchange (01-07).....6*

*Filanowski, Amanda Jane Factors Affecting Dental Material Alloying Composition and Toxicity (01-08).....7*

*Jiang, Jing Immunohistochemisty and Western Blot Analysis of GAP-43 and p75 NGF-Receptor in Human Peripheral Nerve Neuroma (01-09).....7*

*Johnston, Lisa Danielle The Effect of Chitosan Solutions on the Tear Break Up Time In Rabbits (01-10).....7*

*Kinsey, Nicole M. A Motorized Tricycle (01-11).....8*

*Lay, Andrea N. Mechanical Properties of Tissue-Engineered Ligament Analogues (01-12).....8*

<i>Levy, Sara M. Development and Validation of a Viscoelastic Creep Test Method That Maintains a Biological Environment (01-13)</i> .....	<b>8</b>
<i>Mejia, Amilcar Ramon Chavarria Business Plan for G &amp; A Biopolymerica (01-14)</i> .....	<b>8</b>
<i>Reynolds, Kathryn R. DNA Chip Technology: The Social, Ethical, and Legal Issues Related (01-15)</i> .....	<b>8</b>
<i>Ruckdeschel, Rachel A. Reentry in a Geometrically Accurate Model of the Atria (01-16)</i> .....	<b>9</b>
<i>Silver, Andrew M. Morphometric Study of the Human Knee Joint (01-17)</i> .....	<b>9</b>
<i>Skok, Jennifer Protocol for Dispersing and Extruding Collagen Fibers (01-18)</i> .....	<b>9</b>
<i>Smith, Jeremiah D. Remote Subcutaneous Measurement for the Prevention of Congestive Heart Failure (01-21)</i> .....	<b>10</b>
<i>Tackett, Stacie Assistive Technology: Increasing Medication Adherence in the Elderly Using Personal Digital Assistants (01-22)</i> .....	<b>10</b>
<i>Taylor, Brian Characterization of a Posterior Ciliary Artery Insertion and Exit Positions within Perfusion Fixed Normal and Early Glaucoma Monkey Eyes (01-23)</i> .....	<b>10</b>
<i>Tsai, Tzuchi Car Adaption for a Hemiplegic (01-24)</i> .....	<b>11</b>
<i>Vanderpool, Vanessa Angiotensin II as a Transcriptional Regulator of the Bradykinin B<sub>2</sub> Gene Receptor (01-25)</i> .....	<b>11</b>
<i>Vest, Sydney Swimming Performance in Fish: Part I, The Construction of a Flow Tank (01-26)</i> .....	<b>11</b>
<i>Yuan, Winson Hand Tremor Measurement of Ophthalmic Surgeons (01-19)</i> .....	<b>11</b>
<i>Ziauddin, Rafi Mohamed A Glaucoma Drainage Device Based on the Starling Resistor Principle (01-20)</i> .....	<b>12</b>

*NOTE: (01-) = accession number*

**THREE DIMENSIONAL RECONSTRUCTION OF  
BOVINE LAMINA UNDER ELEVATED INTRAOCULAR PRESSURE**

Student: Rehan Z Ali

Advisor: Dr. Roger W. Beuerman

Glaucoma is a widespread optical disease characterized by an elevated intraocular pressure. It has been suggested that said pressure may constrict the lamina cribosa, squeezing these passageways through which the optic nerve travels. Through the use of a confocal microscope, this study will acquire several series of images at varying depths and pressures in a bovine eye. These images, after manipulation to ensure an accurate final depiction, are fed into a computer program that constructs a three dimensional portrayal of this structure. Through analysis of this data a better understanding of glaucoma and its effect upon eyesight is gained.

By analyzing the images at various depths under increasing pressures, changes within the laminar structure can be observed. While there is only a slight change in structure when images are compared from 12mmHg to 24mmHg, there is a drastic shift in the laminar beams when the 60mmHg image is observed. The beams within the structure appear to move out and away from the center of the structure. Beams bend and appear to stretch, this forces some of the holes to become larger, while others decrease in area. This phenomenon is observed at all depths of the lamina, from top to bottom. Such movement undoubtedly creates strains on the nerves passing through these passageways, and could be cause of some Glaucoma.

**INTERSTITIAL FLUID FLOW OF LIGAMENTOUS  
TISSUE UNDER MECHANICAL STRESS**

Student: Jinia Bhattacharya

Advisor: Dr. J-K Francis Suh

Several studies have been conducted in the past that have dealt with the movement of interstitial fluid into and out of soft tissue, especially in diarthrodial joints such as the knee. Two methods are used to analyze this phenomenon, laboratory experimentation and computer modeling. In previous experiments, it has been shown that fluid is exuded out of the tissue under tensile stress. On the other hand, computer models produced by finite element methods predict the opposite results. The purpose of this study is to use a unique experimental method to determine the fluid flow direction, and thereby eliminate the discrepancy between the two methods.

This study involved the use of rabbit flexor tendons. Tendons can be characterized as a biphasic material, consisting of both an incompressible solid matrix and fluid. When these tissues are stretched longitudinally, deformation occurs in both the longitudinal and lateral dimensions. This allows for the determination of the tissue's Poisson's ratio. Computer models have suggested a Poisson's ratio of approximately 0.3, which implies an increase in tissue volume and therefore the imbibing of fluid into the tissue matrix. However, experimentation has shown that there is a decrease in tissue volume due to fluid exudation, resulting in a Poisson's ratio of greater than 0.5.

In this study, the Young's modulus and Poisson's ratio of the flexor tendon were determined. It was hypothesized that the Poisson's ratio would be greater than 0.5 to suggest a decrease in tissue volume due to the exudation of interstitial fluid from the tissue under tensile stress. The Young's modulus was found to

be approximately 390 Mpa, which is comparable to values presented from past research. The determination of the Young's modulus served as a validation for the research methodology in this study. The Poisson's ratio of the flexor tendon was then found to be 2.3. This value supported the hypothesis that the Poisson's ratio would be greater than 0.5, thereby suggesting that interstitial fluid is actually exuded from, not imbibed into, the tissue under tensile loading. It is expected that the results of this study will help to modify the existing computer models and lead to a more accurate characterization of the mechanical properties of soft tissues.

### **BIOMATERIALS LABORATORY DEMONSTRATION EXPERIMENTS**

Student: Fermo A. Bianchi, III

Advisor:

Four biomaterials laboratory experiments were designed to provide concrete demonstrations to students in Biomaterials and Materials Science classes. The phenomena examined were creep, corrosion, phase changes/thermal expansion, and fracture mechanics. We have developed working models for creep, corrosion, and fracture mechanics. The thermal expansion/phase change experiment can hopefully be developed further in future projects.

The three experiments examined thus far have turned out to be valuable representations of phenomenon that are constantly occurring in the worlds of biomaterials and materials science. We feel that the concept developed for the Phase Change/Thermal Expansion laboratory will, in the future, lead to a fourth working experiment.

### **PERIPAPILLARY SCLERAL THICKNESS IN THE PERFUSION-FIXED MONKEY EYE**

Student: Richard A. Blindner

Advisor: Dr. Claude F. Burgoyne

**Purpose:** To measure the thickness of the peripapillary sclera in 9 normal monkey eyes perfusion-fixed at an intraocular pressure (IOP) of 10 mm Hg. To additionally assess the affects of acute and chronic IOP elevation on the thickness of the peripapillary sclera by comparing data from the perfusion-fixed eyes at IOP 10mm Hg to IOP 30/45 mm Hg normal and IOP 30/45 glaucomatous monkey eyes. Characterization of peripapillary scleral thickness is necessary to build computational finite element models of the load-bearing tissues of the monkey optic nerve head and posterior scleral shell.

**Methods:** Both eyes of 9 mature male Rhesus monkeys were cannulated and the IOP within one normal eye was set to 10 mm Hg and the contralateral eye that was either normal (acute elevated IOP) or given early experimental glaucoma (chronic elevated IOP) was set to 30/45 mm Hg. After 15 minutes, all monkeys were perfusion-fixed with gluteraldehyde and both eyes were enucleated. The ONH of each study eye was trephined (6mm), sagittally sectioned (4  $\mu\text{m}$ -along either the superior-inferior or nasal-temporal axis), and stained with Van Gieson's. Within the OHN region (defined as those sections with an open Bruch's membrane), high-resolution (approx. 2  $\mu\text{m}/\text{pixel}$ ) digital images of every 24th histologic section were obtained, yielding images at 96  $\mu\text{m}$  intervals. Scleral thickness was measured in these images at 100  $\mu\text{m}$  intervals, beginning at the posterior scleral canal opening (PSCO) and proceeding out 1500  $\mu\text{m}$  from the PSCO. Measurements for each eye were grouped into either the superior (S), inferior (I), nasal (N), or temporal (T) quadrant. Measurements within each quadrant were subdivided into central (center 50%) and peripheral (outlying 25%) regions. Within the central region, an ANOVA was employed to assess the effects of quadrant and distance from the PSCO on peripapillary scleral thickness and to determine statistical difference between treatment groups.

**Results:** Scleral thickness within the central region was thinnest in the N quadrant (291  $\mu\text{m}$ ,  $p < 0.0001$ ) and thicker in the S (369  $\mu\text{m}$ ), I (372  $\mu\text{m}$ ), and T (369  $\mu\text{m}$ ) quadrants. In all quadrants, the sclera was thinnest at the PSCO (248, 240, 201, and 201  $\mu\text{m}$  in the S, I, N, and T quadrants, respectively,  $p < 0.0001$ ), and thickest 800 to 1000  $\mu\text{m}$  respectively). When comparing differences between treatment groups the data indicates a thinning of the peripapillary sclera for both acute and chronic elevated IOP.

**Conclusions:** Peripapillary scleral thickness varies depending on the quadrant and the distance from the PSCO. Because it is thinner, the sclera immediately adjacent to the PSCO, especially in the nasal quadrant, is likely to experience higher stresses than the more peripheral sclera for a given level of IOP. While our

ANOVA shows significant differences between the treatment groups, the small sample size limits the confidence with which we view our results. Thinning of the sclera due to acute or chronic elevated IOP may amplify the stress concentrations already present in the peripapillary sclera.

### **THE DEVELOPMENT OF A NON-CONTACT METHOD OF MEASURING CROSS-SECTIONAL AREA OF ENGINEERED TISSUES**

Student: Kimberly A. Bridges

Advisor: Dr. Glen Livesay

**Introduction:** One of the most important areas of research concerning soft tissues is the accurate determination of material properties. Knowledge of the material properties of human ligaments allows design parameters to be identified to create engineered tissue replacements. With improved design criteria for engineered tissues, more successful and accurate reconstruction of damaged tissues will be realized. Additionally, an accurate system of determining materials properties will allow investigations into the remodeling of fibroblast-seeded collagen scaffolds as a function of controlled loading in culture.

**Motivation:** Since the soft tissues of the human body are highly deformable, accurate determination of cross-sectional area remains an experimental challenge. Direct contact with the tissue may alter the specimen's cross-sectional area and therefore the apparent material properties. Further, care must be taken that the tissue is not permanently damaged in a way that would affect subsequent testing. Current studies indicate that optical, non-contact methods may be the best solution to this problem, but drawbacks still exist. Repeatability, speed of measurement, minimizing the influence of outside variables, and accurate measurement of concavities are just a few of the new problems introduced by optical measurement methods.

**Objectives:** The overall goal of this project is to review past research conducted on cross-sectional area measurement and to design a system that can be applied to both normal and tissue-engineered ligaments. A non-contact method will be developed and tested for accuracy and repeatability on non-biologic materials of known shape and cross-sectional area. Future studies will examine soft tissue specimens such as the anterior cruciate ligament and engineered tissues.

### **ELASTIC PROPERTIES OF ACELLULAR AGAROSE GEL DISKS AS A FUNCTION OF GEL CONCENTRATION**

Student: Naveed Roshan Ali Cheema

Advisor: Dr. J-K Francis Suh

This study used unconfined compression tests to investigate the material properties of agarose gel as a function of gel concentration. After obtaining lateral displacement and reaction force data, equilibrium stress, longitudinal strain, and lateral strain were computed to obtain values for the final results: Young's Modulus and Poisson's Ratio. The reaction force data was also used to generate stress-relaxation plots. The fact that agarose exhibited proper stress relaxation demonstrated that agarose has fluid phase support and that it may conform to the linear BPE model. The Young's Modulus and Poisson's Ratio data also illustrated that 4% agarose had values comparable to those of articular cartilage, suggesting that it is structurally similar enough to be used for tissue engineering purposes.

In summary, this project studied the material properties of agarose as a function of concentration through the use of unconfined compression testing of gel plugs. It has been demonstrated that agarose is indeed structurally and behaviorally very similar to articular cartilage through the presentation of stress-relaxation curves and Young's Modulus and Poisson's Ratio data. Agarose has been found to have significant fluid phase support. Additionally, it has been suggested that 4% agarose is the best suited for tissue engineering purposes.

### **AN ANALYSIS OF TRAFFIC CONGESTION AT THE I-10/I-610 HIGHWAY INTERCHANGE**

Student: Thomas Eisenstatt

Advisor: Dr. John H. Grubbs

**Abstract:** Traffic congestion affects the country in many ways. Everything from grapes to grandparents relies on our highways to get from one place to another and congested highways hamper the free flow of goods and people across our country. In order to prevent congestion from happening in the first place, its causes must be determined. By studying the relationship between traffic velocity and traffic density, it was determined that as the density of traffic reached a certain point, the ability of traffic to flow in a normal manner ceased.

**Conclusion:** In order to maintain optimal traffic flow, traffic densities should be maintained at lower levels than those present during rush hour and other high volume periods. There are different options that could be considered. One option would be to increase the number of lanes available. This endeavor was carried out and completed on the I-10/I-610 interchange during the summer of 2000. However congestions still occurs as demonstrated by the data collected after this date. A second option would be to develop alternate routes that parallel the single expressway that connects the city of its suburban areas. These routes exist in the form of highways with side street access, a lower speed limit, and traffic lights. These factors discourage commuters from taking advantage of these routes. Expansion of these routes would be beneficial, but may incur public resistance to change these highways from neighborhood arteries to metro arteries. As an alternative, a light rail system, if installed, would alleviate this problem.

### **FACTORS AFFECTING DENTAL MATERIAL ALLOYING COMPOSITION AND TOXICITY**

Student: Amanda Jane Filanowski

Advisor: Dr. Kirk J. Bundy

**Abstract:** The composition of dental alloys must be constructed carefully in order to ensure that they will have acceptable physical and biocompatibility characteristics. Mechanical, electrochemical, and aesthetic considerations must all be taken into account when designing a dental material. I have explored the alloy composition of representative dental alloys to determine how toxicity is affected by changing alloying composition, while maintaining structural integrity. I used results from the Microtox bacterial bioluminescence assay and a predictive mathematical model to predict the toxicity of several different alloy compositions within five classes of dental alloys: cobalt-chromium, nickel-chromium, titanium, stainless steel, and amalgam. Unexpected results from the Microtox testing imply that the bacteria should be exposed to some toxicants for longer periods of time than are now the standard in order for the metal to express its true toxic effect. An error within the mathematical model that predicted inaccurately high toxicities was also discovered.

E-pH diagrams were utilized to see if hexavalent chromium, a carcinogenic substance, would possibly be produced by the corrosion of a Co-Cr-Ni-Mo alloy under oral conditions. The presence of hexavalent chromium in the form of chromate and dichromate was predicted by the diagrams and chemical analysis work should be done to see if it is an actual corrosion product under those conditions.

**Conclusion:** Within established guidelines for the composition of these alloys there appears to be similar toxicities within each class. However, within each class the use of elements that seem to increase toxicity should be limited. Further work should be done to explore the toxicity of dental materials. The predictions made in this study should be tested through Microtox analysis of the dental alloys and as more species are tested, the toxicity of different alloys as well as ceramics and polymers should be explored. The use of silver, mercury, and other bactericidal agents within dental alloys and their resulting toxicity to both the patient and the bacteria must also be explored further.

The predictive mathematical model should be reviewed and errors relating to the prediction of high toxicity in compounds comprised of low toxicity constituents should be eliminated. In the future, it may be appropriate to take Microtox light attenuation measurements at exposure times longer than 15 minutes in order to present a more accurate picture of toxicity. The possible presence of hexavalent chromium due to corrosion of dental alloys should also be investigated due to the possible carcinogenic effects of the ion.

# **IMMUNOHISTOCHEMISTRY AND WESTERN BLOT ANALYSIS OF GAP-43 AND P75 NGF-RECEPTOR IN HUMAN PERIPHERAL NERVE NEUROMA**

Student: Jing Jiang

Advisor: Dr. Roger Beuerman

**Abstract:** The growth-associated protein (GAP)-43 is a major component of the axonal growth cone. The low affinity nerve growth factor receptor, p75, was also investigated, as it has been found to be upregulated in the dorsal root ganglion cell, at the same time as GAP-43. The objectives of this study were to determine whether GAP-43 and the low-affinity nerve growth factor receptor p75 are elevated in traumatic neuromas. Follow up study is done to determine whether there is a correlation between the relative amounts of GAP-43 or p75 and characteristics such as times elapsed between injury and repair. We studied traumatic neuromas from twenty-one randomly selected patients. Monoclonal antibodies for GAP-43 were used to localize this protein in frozen tissue sections from these human peripheral nerve neuroma as well as normal nerves. Immunohistochemistry and double-labeling Immunofluorescence techniques were used to detect GAP-43 and p75 NGF-R. Quantitative Western Blot analysis identified GAP-43 protein. Strong positive staining for GAP-43 was detected in axons of human peripheral nerve neuromas. Axons were specifically identified by using anti-NGF receptor antibody that can specifically bind to axons in a double-label Immunofluorescence examination. In contrast, normal human peripheral nerve as well as monkey and rat sciatic nerve showed weak stains. Furthermore, the nerve trunks in the neuroma were observed to be markedly enlarged and thickened as compared to axons in normal human peripheral nerve. Also, significant increase in GAP-43 levels in all neuroma specimen harvested within 13 months of injury as compared to normal nerve were shown. Specimen harvested at and after 14 months of injury showed a precipitous drop in GAP-43 levels to that of normal nerve or lower. High GAP-43 levels were also correlated with transection injury, high postoperative sensory grade, and pain. P75 remained elevated without consistent decrease in our population. Our study shows that AP-43 in neuroma may relate to regulation or modulation of the growth cone mobility during axonal regeneration, suggesting that GAP-43 may play an important role in the formation of human peripheral nerve neuroma. Expression of intra-axonal GAP-43 varies over time after injury, remaining elevated for approximately the first year, then decreasing abruptly to normal or subnormal levels. These results prove that peripheral nerves should be repaired early, if repair is necessary. In addition, the experiments showed that genetic up-regulation of GAP-43 continues for months or years if regeneration is not complete.

## **THE EFFECT OF CHITOSAN SOLUTIONS ON THE TEAR BREAK UP TIME IN RABBITS**

Student: Lisa Danielle Johnston

Advisor: Dr. Jean T. Jacob

The goal of this thesis was to test the hypothesis that a solution made from chitosan, a polymer derived from the exoskeleton of certain arthropods would increase the longevity of the tear film.

To test the chitosan polymer on the stability of the tear film, dry eyes were first induced in laboratory rabbits by removing the lacrimal glands in three successive surgeries. One eye had the glands removed while the other served as a control. Using a range of concentrations, pH, and osmolality, the chitosan solution was drop applied to the rabbits eyes. The tear break-up time of each rabbit's tear film was observed through a tearscope to determine which solution led to the longest tear break-up time. Chitosan is a demonstrated mucoadhesive so it should increase tear break up time significantly once the most effective concentration, pH, and osmolality of the solutions are found.

In the formulations of solutions it was discovered that a higher deacetylation of chitosan might be needed to achieve neutral solutions that did not hinder tear film stability. Other polymers were used in combination with chitosan to obtain solutions with a neutral pH and low osmolality.

More research is needed to fully understand any benefits chitosan may have on the tear film. Use of a chitosan with higher deacetylation and experimentation with different solvents could show that chitosan does have beneficial qualities to stabilize the tear film and relieve dry eyes.

### **A MOTORIZED TRICYCLE**

Student: Nicole M. Kinsey

Advisor: Dr. David A. Rice

Cerebral palsy is a condition caused by a brain lesion resulting in loss of movement. Many children with cerebral palsy have trouble doing everyday normal activities. My client is a three-year-old child with cerebral palsy. He has limited movement in his limbs and poor trunk support. These limitations keep him from sitting and standing on his own. The purpose of this research is to build a motorized tricycle that the client could use. Through the use of this tricycle the client will be integrated into a playroom environment by playing independently and interacting with his peers. The goal is to increase the client's social abilities as well as increase physical abilities. I modified a Mongoose Moto Goose tricycle by adding a specialized seat and motorizing it. The seat is a child carrier seat that is designed to be attached to the back of a bicycle. Motorization was accomplished through building a skateboard unit that the tricycle rests in and is then pulled. The client activates the motorization with a switch on the handlebars. The client is very enthusiastic about the tricycle. Through use of the tricycle my client should increase his independence by interacting with peers and increase his physical skills.

### **MECHANICAL PROPERTIES OF TISSUE-ENGINEERED LIGAMENT ANALOGUES**

Student: Andrea N. Lay

Advisor: Dr. Glen A. Livesay

Creating a tissue-engineered ligament that performs acceptably on the cellular scale, as well as on the scale of whole tissues, requires detailed knowledge of the relationships between macroscopic and microscopic structures and biomechanical function within ligamentous tissues. The goal of this work was to construct simple fibrous tissue scaffolds and determine the fundamental mechanical properties of these scaffolds before and after culture with rat fibroblasts.

### **DEVELOPMENT AND VALIDATION OF A VISCOELASTIC CREEP TEST METHOD THAT MAINTAINS A BIOLOGICAL ENVIRONMENT**

Student: Sara M. Levy

Advisor: Dr. Glen A. Livesay

In the past twenty years, injury to soft tissues, such as tendons and ligaments, has become a common injury among younger individuals because they are participating more in sports and other recreational activities. The current study will experimentally determine the viscoelastic responses for soft tissues in order to de-

velop a method to test the creep behavior of soft tissue in a biological environment and identify a pattern common to the viscoelastic behavior inherent to soft tissue. Sixteen rat tail collagen specimens were creep tested in order to characterize their viscoelastic responses at low loads in an environmental chamber that controlled was controlled for moisture and temperature. A pulley system and a parallel attached LVDT were used for testing and data acquisition. There were no significant patterns of viscoelastic behaviors identified from investigating the amount of creep and rate of creep at equilibrium. Control of biological parameters were met with some limitations based on a lack of species knowledge. This obstacle has raised an important concern to develop more accurate biological protocols for testing materials to quantify inherent soft tissue viscoelastic behaviors that should be incorporated into the design of ACL reconstruction grafts.

### **BUSINESS PLAN FOR G&A BIOPOLYMERICA**

Student: Amilcar Ramon Chavarria Mejia

Advisor: Dr. Donald P. Gaver

The information presented in this senior thesis provides the foundation for the establishment of a biomedical engineering company, G & A Biopolymerica (GAB). This company will manufacture new types of

polymer brushes suitable for biomedical applications such as orthopedic implants, medical equipment, and pulmonary investigations (biopolymer brushes). The extensive study of polymer brushes has concluded that when two surfaces are coated with these brushes, the force required to slide them against each other reduces dramatically. This is the most significant attribute of polymer brushes, which allows them to act as a lubricating film between two sliding surfaces.

FAB theoretically predicts that the desired coefficient of friction for orthopedic implants could be attained with the application of biopolymer brushes. As a result, the amount of wear experienced by the parts of an implant will be considerably lower. This would lead to an increased life span in orthopedic implants and better quality of life to those who benefit from these implants. Other applications in medical equipment and pulmonary investigations have the potential to generate large profits for GAB.

The format of this document follows the standard outline for a business plan and not that of a scientific paper in order so that it may suitably present both the business and engineering aspects of GAB to any pertaining investing parties who may wish to invest in its creation.

### **DNA CHIP TECHNOLOGY: THE SOCIAL, ETHICAL, AND LEGAL ISSUES RELATED**

Student: Kathryn R. Reynolds

Advisor: Dr. Mary K. Pelias

DNA chips, also known as microarrays, are paving a smoother road in the field of genetics. Until recent technological advances, traditional methods in molecular biology generally dealt with one gene in one experiment. Obtaining a complete picture of how genes interact with one another to express a certain characteristic or trait was a tremendous task to take on. In order to gain a great understanding of how genes work in concert, a new method was needed to allow scientists to view gene expression at a genome-wide level.

Creation of DNA chips, 2-centimeter-square arrays of known DNA fragments—short oligonucleotides or longer strands of complementary DNA (cDNA) - on a solid substrate such as glass, silicon, or a nylon membrane, allow the simultaneous analysis of large numbers of nucleic acid hybridization experiments in a highly reduced amount of time. Depending on the organism and the size of its genome, the microarray can consist anywhere from a particular subset of genes to an entire set of genes from a genome. Two major applications for the DNA microarray technology exist: 1) Identification (gene/gene mutation sequences) and 2) Determination of expression levels. Of genes. At Affymetrix, one of the pioneer companies for DNA chips, current manufacturing methods allow ~300,000 unique oligonucleotides (each 500-5000 base pairs long) to be synthesized on a 1.28 by 1.28-cm array. These DNA chips range in price anywhere from \$45 to \$850. The scanners and fluidics stations needed to analyze the chips and conduct the experiments can cost more than \$100,000. In order for DNA chips to become diagnostic devices, they would need to come dramatically down in price. Besides the outrageous price range, which could be chalked up to gene chips being a new product and experiencing all the initial setbacks during the first stages of production, the real hurdle to overcome is the amount of data obtained needing to be analyzed and interpreted. The ultimate task is weeding out the “junk mail” to find the “letter” you have been waiting for.

### **REENTRY IN A GEOMETRICALLY ACCURATE MODEL OF THE ATRIA**

Student: Rachel A. Ruckdeschel

Advisor: Dr. Natalia A. Trayanova

This research aims to identify the effects that the three-dimensional structure of the atria has on the spread of normal atrial excitation and the formation and propagation of reentrant waves that underlie atrial flutter and fibrillation. A three-dimensional computational model of the atria that incorporates many features of atrial anatomy has been constructed using custom C code. Normal activation of the model atria proceeds from the right atrium to the left by way of Bachmann’s bundle without the rim of the fossa ovalis as a preferential conduction pathway. Several experimentally observed atrial reentries were simulated using the model created. Upon examination of the reentrant pathways utilized in the model, it was found that reentry in the left atrium makes use of an intercaval region of slow propagation and the pulmonary veins a anatomical obstacles to generate a figure-of-eight reentrant wave, and reentry in the right atrium anchors to the tricuspid ring or the inferior vena cava to form a single loop reentrant circuit. Left atrial reentry is sustained

by hidden propagation along the subepicardial layers of the left atrium. Reentry in the right atrium initiated near the inferior vena cava utilizes the muscular sheath surrounding the coronary sinus for back propagation to help sustain the reentrant wave. Individual removal of the crista terminalis, the pectinate muscles, the crista terminalis along with the pectinate muscles, and the coronary sinus sheath from the model atria revealed that these structures can provide a pathway for more rapid activation of the region surrounding the inferior vena cava but are not necessary components of any of the observed reentrant pathways. The model's three-dimensional structure is clearly critical in initiating and maintaining atrial reentry along the observed pathways.

### **DNA CHIP TECHNOLOGY: THE SOCIAL, ETHICAL, AND LEGAL ISSUES RELATED**

Student: Kathryn R. Reynolds

Advisor: Dr. Mary K. Pelias

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Creation of DNA chips, 2-centimeter-square arrays of known DNA fragments—short oligonucleotides or longer strands of complementary DNA (cDNA) - on a solid substrate such as glass, silicon, or a nylon membrane, allow the simultaneous analysis of large numbers of nucleic acid hybridization experiments in a highly reduced amount of time. Depending on the organism and the size of its genome, the microarray can consist anywhere from a particular subset of genes to an entire set of genes from a genome. Two major applications for the DNA microarray technology exist: 1) Identification (gene/gene mutation sequences) and 2) Determination of expression levels. Of genes.

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### **ANALYSIS OF 3D MODELING OF CT IMAGES FOR KIDNEY TRANSPLANT**

Student: Amaya Dwan Lambert

Advisors: Dr. Douglas Slakey, Dr. David Rice

Laparoscopic surgery, a minimally invasive technique, is becoming the preferred method for living related kidney donation. Since each donor's anatomy is unique, it is vital that the surgeon understands the details of the kidney and surrounding anatomy. Helical CT scan images reconstructed into three dimensions create a comprehensive road map to aid in surgical planning and avoid complications. Unfortunately, with current mechanisms, the 3D reconstruction process is exceedingly cumbersome and time consuming. A user-friendly environment for the CT scanner and reconstruction mechanism promotes effective anatomic communication by the radiologist to the transplant physician.

This study explores the GE Medical Systems Advantage Windows Workstation version 1.2 (AW 1.2) currently in use at the Tulane University Medical Center (TUMC). Through observation and questionnaire it evaluates the mechanisms for which the AW 1.2's user-friendliness could be maximized. Using the results of the study, a user's guide was created and refined to aid the TUMC radiology staff with the reconstruction process. The ultimate result is a reduction in time spent and

increased user satisfaction.

### **MORPHOMETRIC STUDY OF THE HUMAN KNEE JOINT**

Student: Andrew M. Silver

Advisor: Dr. Glen A. Livesay

Morphometrics, the study of shape and shape change, is widely used in many scientific disciplines, however, little or no work has been performed in the biomechanics field to study the effect of shape on the function of joints. This study investigates the shape differences between pairs of left and right knees of human subjects. Before human knee testing could begin, both 2-D and 3-D ideal objects were tested using various methods to establish that Morphometrics could be used for this study of the human knee joint. These objects were rotated, enlarged, and deformed to ensure that Morphometrics would only detect a shape change when one was present. Following this validation, a 3-D model of the human knee joint was digitized and studied, to show that Morphometrics can work with complex 3-D objects. The final stage of the project focused on the human knee joint. Human subjects were digitized, and comparisons were made between their pair of left and right knees. It was found that there is an average shape difference between left knees and right knees as a whole across subjects, as well as a difference within each person's pair of knees. Future studies will look at how shape is related to mechanical function in the joints of the human body. With the validation of the Morphometrics program, a method for quantifying shape differences has been established. The next step is to perform mechanical tests on the measured joints and compare their responses with one another to determine if geometric availability will have a substantial effect on overall joint function, and now that hypothesis can be tested.

### **PROTOCOL FOR DISPERSING AND EXTRUDING COLLAGEN FIBERS**

Student: Jennifer Skok

Advisor: Dr. Kay C Dee

The anterior cruciate ligament (ACL) is an intraarticular ligament of the knee that functions as a joint stabilizer. The ACL is often injured in sports and motor vehicle accidents and, due to the poor inherent healing capacity of the ligament, the injury often requires operative intervention. Over 60,000 ACL reconstructions are performed each year in the United States alone. Although a variety of biological and polymer grafts have been studied to replace ACL, an ideal graft has not yet been developed or has a graft received unconditional approval by the Food and Drug Administration.

One alternative approach to ACL reconstruction is to replace the ruptured ACL with a resorbable scaffold that induces neoligament formation in the knee joint while mechanically supporting the joint during healing. The ligament analogue composition would consist of a resorbable collagen fiber scaffold seeded with fibroblast cells, which attach to and proliferate on the collagen fibers and deposit new collagen within the analogue. The goal of this research project was to develop a reliable and repeatable procedure for creating collagen fibers, which would be used to construct the ligament scaffolds.

Collagen fibers have been created using the following two step process, dispersion and extrusion, which was developed and tested in this research project.

### **THE RESPONSE OF DISTAL AIRWAY EPITHELIAL CELLS TO FLUID SHEAR**

Student: Adam M. Sorokin

Advisor: Kay C Dee

Infants born prematurely often require mechanical ventilation and are at risk for Respiratory Distress Syndrome (RDS). To simulate the environment the alveolar epithelium experiences *in vivo*, an epithelial-like transformed cell line, L2, was subjected to 30 minutes of 5 and 15 dynes/cm<sup>2</sup> of shear stress in a parallel flow chamber. Cells were then tested for changes in NO\* production, proliferation, and physical damage. No significant changes in NO\* production were found, but some general trends were observed. Compared to control conditions, L2 proliferation increased significantly after 5 dynes/cm<sup>2</sup>, but significantly decreased after 15 dynes/cm<sup>2</sup>. Membrane damage evaluation was inconclusive, but viability evaluation indicates that

the employed levels of shear stress were not lethal to adhered cells.

### **THE DEVELOPMENT OF A MODEL OF LEUKOCYTE ADHESION**

Student: Joel Beaird Springer

Advisor: Dr. Donald Gaver

Our goal is to model the process of leukocyte adhesion to endothelial cells in the vasculature. The adhesion sequence occurs in three phases: initial contact, cell rolling, and subsequent firm adhesion. This adhesion sequence depends on the interaction between the surrounding fluid and the cell's membrane structure. The simulation begins immediately proceeding the initial contact phase and continues until firm cell adhesion. A two-dimensional, extensible elastic ring represents the cell's membrane. This membrane deforms as a function of the external fluid stress field. The cell binds to the substrate wall using ligand bonds. Whether the leukocyte adheres depends upon the reaction kinetics of these ligand bonds. The ligand bonds in the contact region between the cell and the substrate behave as elastic springs. An imposed fluid stress acts on the cell via a homogenous, incompressible Newtonian fluid in shear flow and produces a total drag force. The boundary element method of integration determines the imposed shear and normal stresses along the cell's membrane. The interplay between the drag force and the adhesion force produced by the ligand bonds causes membrane shape deformation and either cell rolling or firm adhesion.

To disperse the collagen, a 1% solution of bovine collagen and 0.005N HCl, pH2, was blended, centrifuged and stored in a refrigerator for no longer than one week. The collagen solution was extruded, in small volumes of 5mL or less, from a plastic syringe using a syringe pump. The solution was pumped through an 18 gage needle and polyethylene tubing, weighted at the exit end with a 30 gram standard weight, into 100 mL of pre-warmed polymerizing buffer in a 100 mL graduated cylinder. The solution soaked in the buffer for 45 minutes and was transferred by funnel and filter paper to 200 mL of 95% ethanol, in which it soaked for four hours. Fibers were then removed by fine forceps and dipped in 100mL of dH<sub>2</sub>O. The fibers were then strung over parafilm covered glass slides, which were stood up on their sides and left to dry overnight. The fibers were removed, measured and found to have an average width of 1 millimeter and an average length of 30 millimeters. The fibers were flat and consistent in width and length. New drying methods could produce differently shaped fibers. Now that these uniform fibers have been created, they can be used in future studies to create cell-seeded ligament scaffolds for clinical testing as ligament replacements in animals and humans.

### **REMOTE SUBCUTANEOUS MEASUREMENT FOR THE PREVENTION OF CONGESTIVE HEART FAILURE**

Student: Jeremiah D. Smith

Advisor: Dr. Cedric F. Walker

Congestive heart failure (CHF) is the most common reason for hospitalization of the elderly. In a study in 1999, administrators suggested congestive heart failure most frequently for videoconferencing/telemonitoring system. This disease has vital signs able for remote monitoring and significant to the treatment. Since fluid retention is an indication of congestive heart failure worsening, the most important sign a VCTM system can transmit is the edemic conditions. Currently, the VCTM systems for CHF only relay information about the weight of a patient and do not consider the edemic conditions. This project uses infrared LEDs and photodetectors to make tangent lines to a patient's ankle. The tangent lines give estimates of the radii at various positions on the ankle. The numerical values for the radii are compared to base level radii to determine if the patient is experiencing any fluid retention. This information. Along with the patient's weight is relayed through the phone lines to a nurse's station. With the addition of the edemic conditions, the physician is provided with a clearer view of the patient's situation.

### **ASSISTIVE TECHNOLOGY; INCREASING**

## **MEDICATION ADHERENCE IN THE ELDERLY USING PERSONAL DIGITAL ASSISTANTS**

Student: Stacie Tackett  
Advisor: Dr. David A. Rice

The failure of the memory required to carry out planned actions at appropriate times constitutes prospective memory. Normal functioning in every day life requires this type of memory. Prospective memory failure commonly appears in elderly adults and can lead to medication nonadherence. Nonadherence can cause declining health, unnecessary hospital visits, and early admission into nursing homes and assisted living facilities.

Increasingly complex medication regimens of the elderly increase the demands on prospective memory and in doing so, increase the rate of medication nonadherence. The small proportion of nursing home residents due to problems associated with memory failure can benefit from a developed reminding system tested in this project.

Four subjects tested the system during a control period consisting of a written list constructed individually by each subject and an experimental period consisting of a Palm-based reminding system developed by the researchers. The developed reminding system included a Palm V personal digital assistant, an attachable Palm V modem, an interactive webpage, an Internet browser, and a medication reminding program entitled *On-Time-Rx*. This program contained an essential log that recorded the response and times of the subjects being tested.

This research evaluated existing technology in coordination with existing software to produce a reminding system to eventually test the improvement of medication adherence in elderly adults. This research determined that a Palm-based reminding system provided a more efficient reminder than a paper-based system. The preliminary testing data showed that using the Palm increased the success of the subjects. The data also showed that the Palm greatly reduced the number of tasks completed both early and late. The accuracy of the Palm-based system was tested, but results showed extreme similarity to those of the paper-based system. The accuracy results did, however, confirm the validity and consistency of the recorded data. Researchers also assessed the interactive webpage set up for use in the project to determine if a web-based reminding system would be useful in the future and how easily users could access it.

Advancing technologies provided numerous opportunities for the healthcare industry. Medication adherence is one field that has had great success with past technologies. This success prompts the continued research and development of new ideas and systems to further increase the medication adherence of those in need. This project focuses on a target population whose medication nonadherence is contributed to memory failure associated with aging. The preliminary testing of the reminding system presented in the project proved the usefulness and benefits that this system can provide. Further testing on the target populations could provide additional evidence of the need for this type of reminding system.

## **CHARACTERIZATION OF POSTERIOR CILIARY ARTERY INSERTION AND EXIT POSITIONS WITHIN PERFUSION FIXED NORMAL AND EARLY GLAUCOMA MONKEY EYES**

Student: Brian Taylor  
Advisor: Dr. Claude F. Burgoyne

**Purpose:** To study the positioning of the Short Posterior Ciliary Arteries (SPCs) as it relates to the sclera around the optic nerve head (ONH).

**Methods:** Using digital imaging technology, images are acquired of the sclera around the optic nerve head from sagittal sections of 2 rhesus monkey eyes. These images are taken from slides on which the sagittal sections approximately 4-6 microns in thickness have been mounted. The eyes have been fixed at varying intra-ocular pressures (IOP) and some have had glaucoma induced. Using these images and a custom computer program, measurements are made in order to better characterize the positioning of the short posterior ciliary arteries (SPCAs).

**Results:** The positioning of the SPCAs with relation to the ONH show that most are between 1001-2000 microns away from the Scleral canal.

**Conclusion:** The SPCAs are positioned relatively close to the ONH. Due to the position, the SPCAs are

positioned in an area of high stress-concentration. Further computer modeling can be done to reconstruct to vessel in 3 dimensions in order to incorporate the arteries into the lab's Finite Element Models.

### **CAR ADAPTION FOR A HEMIPLEGIC**

Student: Tzuchi Tsai

Advisor: Dr. David A. Rice

My client suffered a stroke in childhood leaving her without efficient control over her right leg and arm. In general, reaching over to her right side and performing tasks with her left hand presents a problem for her. Consequently, operating a left hand drive car poses some trouble for her. When starting the ignition, she has difficulty turning the key because the ignition is behind the steering wheel on the right. The major problem is selecting gears. On an automatic transmission, both the gear selector and its inter-lock button must be operated simultaneously. The goal is to have the client be able to operate the gear selector on the left side and turn the ignition with less strain. The design presented here moves the gear selector with a handle on the left side. A bicycle brake wire system provides the inter-lock control. A lever attached to the key offers necessary leverage for the left hand. These designs improve the accessibility of a standard car without requiring irreversible modifications unimpaired drivers can operate the vehicle normally with the adaptation in place.

### **ANGIOTENSIN II AS A TRANSCRIPTIONAL REGULATOR OF THE BRADYKININ B<sub>2</sub> RECEPTOR GENE**

Student: Vanessa Vanderpool

Advisor: Dr. David A. Rice

Angiotensin II (Ang II) and bradykinin are two hormones present in the kidneys. By means of the angiotensin type-I receptor (AT<sub>1</sub>), angiotensin II has many effects including vasoconstriction, directly increasing sodium reabsorption, and stimulating the release of angiotensin. The bradykinin B<sub>2</sub> receptor (B<sub>2</sub>R) is the primary receptor for the peptide bradykinin; affecting vasodilation, cell growth, inflammation, and electrolyte excretion. Previous studies have shown that bradykinin and Ang II play important roles in the regulation of arterial blood pressure and fetal kidney development; however, little is known about their transcriptional regulation.

The present study proposed that angiotensin II (Ang II) transcriptionally regulates B<sub>2</sub>R expression in animals and cells treated with Ang II to determine if expression levels were upregulated. Analysis of B<sub>2</sub>R protein levels in adult rats treated with Ang II showed no significant difference when compared with protein extracted from rats infused with saline ( $14.7 \pm 1.3$  vs.  $15.1 \pm 0.2$ , n=9,  $P=0.771$ ). On the other hand, analysis of IMCD3 cells showed increased B<sub>2</sub>R and AT<sub>1</sub> protein levels when treated with Ang II. Unfortunately, only one trial was completed, establishing a need for further investigation. Transfected IMCD3 cells treated with various doses of Ang II showed no significant difference between cells treated with Ang II and untreated cells when analyzed by CAT assays. However, we believe that this is due to erroneous harvesting times, requiring an alteration in the protocol. In summary, the results of this study were inconclusive yet did not discard Ang II as a possible regulator, necessitating further investigation.

### **SWIMMING PERFORMANCE IN FISH: PART 1. THE CONSTRUCTION OF A FLOW TANK**

Student: Sydney Vest

Advisor: Dr. Craig Hood

After an extensive research of the flow characteristics through and around pipes, a flow tank was constructed that will enable the future study of the effects of flow rate on swimming performance in the Blacktail Shiner, *Cyprinella venusta*. The flow tank was built based on a previously published design (Blazka et al., 1960; Beamish, 1978; Adams et al., 1997; Hove et al., 2000) and a flow tank used by researchers at the Waterworks Experimental Station (U.S. Army Corp of Engineers, Vicksburg, MS). Designs for the external and internal flow tank sections were developed and the sections manufactured by a commercial company (Cadillac Plastics, Inc.) using Plexiglas® to construct the inner flow tube and the outer rectangular

tank. A motor was purchased that provided 18.9lb –in of torque, a 0-100 speed dial from a distributing company, as well as a propeller with a blade diameter (blade tip to blade tip) of seven inches. The motor was used to create a variable flow through the flow tube. Microturbulent flow filters were built using half-inch diameter PVC pipe. These flow filters were positioned inside of the flow tube and served the purpose of regulating turbulent flow. The top of the rectangular tank was made to be removable with a six-inch diameter whole cut in it at the opposite end of the propeller as an entrance for the flow meter.

Upon completion of the flow tank, a flow meter (Marsh-McBirney Model 2000) was used with special adapters to obtain flow (velocity) readings at eight distinct points in the tank. A straight extension was used to measure five points on the outside edge of the flow tube and an angled apparatus was used to obtain three more readings from points six and a half inches inside of the tube. Three trials were run in which readings from the flow meter were obtained from each of the eight sites for positions 40, 50, 60, and 70 on the motor speed dial. It was determined that velocity in the flow tank was minimal near the center of the cross-sectional area of the tube and far away from the motor, resulting in a reverse parabolic velocity profile. This reverse profile was due to the propeller creating a force on the walls of the tube rather than a uniform force along the cross-sectional area as in normal laminar flow.

The finalization of this project signifies the completion of one part of a two-part project. This tank will be used to test swimming performance in the Blacktail Shiner, *Cyprinella venusta*.

### **HAND TREMOR MEASUREMENT OF OPHTHALMIC SURGEONS**

Student: Winston Yuan

Advisor: Dr. David A. Rice

Physiological tremor is an involuntary, roughly sinusoidal component inherent in normal human hand motion. It has been found to consist of a “mechanical reflex” component, which depends on mechanical properties, and a second component that is thought to originate from the central nervous system and has a frequency range of 8-12 Hz. Due to the limited surface of the eye and its delicate tissue properties, such small-scale tremors could pose a serious problem for ophthalmic surgeons during surgery. We have built a simple laboratory tremor measurement device that is based upon the principles of a magnetic coil induction system using a moving magnet phonocardiode. The model device will be used to test ophthalmic surgeons’ hand tremor under simulated anterior segment surgery conditions. The ultimate goal is to quantitatively measure the effects of stimulants like caffeine, sedatives, beta-blocking agents, drugs such as propranolol and other activities on the surgeons’ hand tremor during surgery.

### **A GLAUCOMA DRAINAGE DEVICE BASED ON THE STARLING RESISTOR PRINCIPLE**

Student: Rafi Mohamed Ziauddin

Advisor: Dr. David A. Rice

Glaucoma is a group of disorders of the eye in which the intraocular pressure (IOP) is elevated. This increased pressure can damage the optic nerve, and, if left untreated, cause blindness. In complicated or severe cases, the implantation of a glaucoma drainage device (GDD) may be necessary. Such devices use a thin tube to drain excess aqueous humor from the anterior chamber of the eye to a bleb. The fluid is dispersed from the bleb via diffusion through the surrounding tissues. Several such devices are currently used. Restrictive GDDs contain a valve to regulate flow while nonrestrictive GDDs offer little resistance to the flow of aqueous humor. Soon after implantation of nonrestrictive GDDs, the patient’s IOP may drop below normal, which may lead to suprachoroidal hemorrhage and other complications. Restrictive GDDs help prevent this; however, an elevated IOP is often observed following implantation. We propose controlling pressure using the Starling resistor principle. The device consists of a collapsible channel enclosed by a fluid-filled pressure chamber. The pressure of the chamber regulate the flow through the channel. Such a device may limit both postoperative hypertensive and hypotensive phases. *In vitro* testing showed that flow was tightly controlled by chamber pressure. The model showed that control can occur in a planar structure in which the pressure chamber does not completely surround the collapsible channel. Future studies require sizing the GDD for implantation as well as evaluation the device *in vivo*.

