EXAMPLE – High Quality Research Proposal for PURA Salary Award application

Proposal by BME student, Brian Nguyen

Overview of Proposed Work

Approximately 800,000 ligament, tendon, and joint capsule injuries occur every year [1] and often natural healing [2] or surgery [3] does not provide a full recovery of such injuries. Tissue engineering of ligaments, tendons, and joint capsules may be an important way of resolving many of the problems encountered with the repair of related injuries. Specifically, using a scaffold in conjunction with transplanted cells may provide an effective means of repair or replacement of injured connective tissue [4]. A possibility is that a temporary scaffold encapsulated with adult stem cells would be injected into the injured area and then cured to hold the cells in place. It would provide temporary structural support allowing the stem cells to differentiate into relevant connective tissue. The biomaterial would then degrade over time and only native (healed) tissue would remain.

In the Temenoff laboratory, hydrogels are being used as a biomaterial that would provide a carrier for stem cells to differentiate into tendons or ligaments. Different types of hydrogels can be created through combining molecules of different molecular weights. In this case, poly(ethylene glycol) diacrylate (PEG-DA) with a molecular weight of 3,400 Da can be mixed with a novel polymer, oligo(poly(ethylene glycol) fumarate (OPF), with molecular weights of either 3,000 Da or 10,000 Da. This will result in crosslinked hydrogel networks of different mesh sizes. OPF contains ester bonds in the fumarate groups that are susceptible to hydrolytic cleavage and is therefore expected to degrade in an aqueous environment. The hydrogels can also be laminated. The process works by adding a second layer to the hydrogel before it has completely crosslinked [5].

It has been found that stem cells encapsulated in a hydrogel would differentiate into tendon/ligament cells in response to tensile loading [6]. To mimic this, a tensile culture system would be used to create cyclic tension on the hydrogel/cell constructs over a period of time (1 week, 2 weeks, 4 weeks or 6 weeks). However, little is known about degradation properties of these hydrogels under dynamic loading. Therefore, a study will be performed to determine differences in the degradation profile of various types of hydrogel carriers under cyclic tension. This will prove useful for further studies in the Temenoff lab, as the degradation rate of the hydrogel will have effects on the function of cells embedded in these hydrogels in future experiments.

Objectives for Semester's Research

The project given to the student involves four main assignments: fabrication, testing, data recording, and data analysis of hydrogels. Two groups of hydrogels are to be fabricated. One group will include homogenous hydrogels of a single OPF type , while the second group will include laminated hydrogels with two different layers of material each using OPF of a different molecular weight. To create the samples, various types of OPF will be combined with PEG-DA and equal amounts of N, N, N', N' -tetramethylethylenediamine (TEMED) and ammonium persulfate (APS). After raising the temperature of the mixture to 37 °C, crosslinking will occur in approximately 10 minutes. The hydrogels will then be placed in saline in a tensile culture system and continuously stretched to 10% past their original length.

The data to be recorded includes the hydrogels' mechanical properties (tensile strength, failure strength, elasticity, failure strain, etc.) and its change in mass (wet/dry weight) over different time intervals (approximately weekly over 6 weeks). The data to be analyzed includes the creation of a degradation curve of the hydrogel over time and determination of any significant differences of hydrogels with different mesh sizes and number of laminated layers. Through this analysis, this study will provide a better understanding of how OPF hydrogels degrade under cyclic tensile loading.

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EXAMPLE – High Quality Research Proposal for PURA Salary Award application

Proposal by Jignesh Shah, CHBE

Model for Solubility of Pharmaceutical Compounds

Pharmaceutical compounds often exhibit polymorphism i.e. they can exist in more than one crystal habit or form. These polymorphs have quite different physical properties (such as melting points and enthalpies of fusion) and, in turn, exhibit different solubility behavior, stability and bioavailability in solvents. As a result, product recovery during crystallization of the pharmaceutical compounds depends on the polymorph that is more stable at the given conditions. In formulating an effective drug, therefore, it is essential to determine the solubility of all polymorphs of the drug, and the conditions at which each polymorph is stable.

In the proposed work, I will evaluate the applicability of different thermodynamic models for the prediction of the solubility of organic compounds. One such model was proposed by Mirmehrabi, Rohani, and Perry (a), (b). Their model correlates the activity coefficient of an organic compound in a liquid solution and this can then be used to obtain the concentration (solubility) of the organic compound.

I propose to first test the model on solubility data for compounds with only one crystal structure and relate the parameters of the model to physical properties of the solid. The model will then be extended to polymorphic systems. The first step (testing the model on compounds that exhibit a single crystal structure) is expected to be completed this semester (Fall 2006). Based on this work, the goals for the next semester (Spring 2007) are as follows: (i) identify various crystal structures of compounds like cimetidine, mexiltine HCl, and diflunisal; (ii) test the model for the solubilities of these structures; (iii) relate model parameters to the physical properties of the polymorphs.

The polymorphs will be identified experimentally by melting, quenching, and/or precipitation from weak solvents. As the name suggests, melting involves the heating of the drug to its liquid state and then cooling at different rates. In the quenching method, the crystals will be obtained by extremely rapid cooling of the pure compound. The weak solvent method is executed by adding an anti-solvent to the solution and forcing the solid to precipitate out. Crystal structures thus obtained will be characterized using DSC (Differential Scanning Calorimetry), SEM (Scanning Electron Microscopy), and powder X-ray diffraction. Of these, DSC will help identify solid phases and heat of transition between different phases. The physical properties of these structures will be analyzed using SEM, while the actual crystalline structure will be determined using powder X-ray diffraction method. Also, MATLAB and MS Office applications like Word, Excel, and PowerPoint will be used to analyze the collected data, document the results, and present them.

The project will be carried out under the mentorship of Dr. Amyn Teja and co-mentorship of his graduate student, Angel J. Olivera-Toro in School of Chemical and

Biomolecular Engineering building (Ford Environmental, Science, and Technology building).

(a) Mirmehrabi, Mahmoud, Sohrab Rohani, and Luisa Perry. "Thermodynamic Modeling of Activity Coefficient and Prediction of Solubility: Part 1. Predictive Models." Journal of Pharmaceutical Sciences 95.4 (2006): 790-797.
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EXAMPLE – High Quality Research Proposal for PURA Salary Award application

Proposal by Deborah Peak, ISYE

Monitoring of Fluid Loss in Prepubescent Girls versus Young Women

Although much research exists about hydration and the needed amounts of fluid needed to maintain a healthy level of hydration, it still remains difficult to determine the proper amount of fluid necessary to stay hydrated. Researches continue to debate how to determine the proper amount of fluid necessary to maintain proper hydration levels. Some research provides a specific amount of liquid to be consumed per day, while others cite the body's thirst reflex as an indicator of necessary fluid intake.

The increase in occurrence of hyponatremia further stresses the need to determine the adequate intake of fluids, as it proves that too much fluid can result in the same dangerous side effects as dehydration, in extreme cases. Hyponatremia also proves that there is a maximum level of fluid intake the body can healthfully maintain.

Therefore, knowing the adequate level of fluid intake and its dependency on age is important. Most research on fluid loss focuses on men's fluid loss in comparison to boys, yielding results that show men lose significantly more fluids than boys. But significant research has not been conducted to determine the fluid loss rates of young girls.

Through participation in research conducted by Dr. Millard-Stafford and the Exercise Physiology Laboratory in the School of Applied Physiology I will help determine the fluid loss in young girls compared to the loss in mature women. As female who regularly participate in exercise, hydration plays an important factor in my preparation and participation in exercise. Also having personally experienced hyponatremia, I understand the importance of knowing the body's adequate level of fluid intake. By comparing the average levels of fluid loss during exercise it would be possible to know the average adequate amount of fluid needed for females at different ages. The accuracy of the body's thirst reflex will also be assessed.

Prior testing subjects, I will participate in a pilot test of this experiment to indicate the outcomes that will result from testing. This trial will also serve to indicate which areas of the experiment require improvement in order to gain more accurate results. With another undergraduate student, I will also assist to recruit subjects for participation in this experiment. During testing, I will assist in all aspects of data collection and data analysis.

To research this difference in fluid loss, ten prepubertal girls will be matched with ten adult women based on fitness level, determined by VO_{2max}. These subjects will participate in a series of fitness tests and provide information on their fluid and food intake through out the period of research that will be used to monitor their fluid intake and loss.

A preliminary fitness test will determine the VO_{2max} of each participant using a continuous, maximal grated treadmill test. The subjects stride lengths will be measured; other general descriptive data including height, weight, and percent body fat composition will also be determined in this test. Subjects will give a urine sample to determine their urine specific gravity before exercise. The measured stride length will be use in conjunction with the FitSense shoe pedometer, to determine the step count of the subject during treadmill test and the remaining research period. The pedometer will also be used to determine the accuracy of step counts for the prediction of fluid loss during this test and throughout the remaining research period.

The exercise test will occur on the following day and consist of intervals of walking and running at different levels of exertion on the treadmill while in a climate controlled room of 55% relative humidity and 30 degrees Celsius. Periods of rest will occur during these intervals. Preliminary measurements including resting heart rate, oxygen consumption through expired gases (VO_2), urine specific gravity, core temperature, body fatness, total body water, and body weight and height. The subject’s heart rate, core temperature, perceived thirst and exertion, VO_2, and respiratory exchange ratio will be measured on intervals throughout the exercise. The difference between post-exercise and pre-exercise weight and urine specific gravity will be used to determine the fluid loss during the exercise. The body’s perception of thirst will also be compared to the results of exercise tests.

The Sensor Medic 2900 Metabolic Cart will measure the VO_2, caloric expenditure, and respiratory exchange ratio. Core temperature will be measured using the CorTemp Wireless Ingestible Temperature Sensor, an internal ingestible thermometer. A Xitron 4200 Hydra Bioelectrical Impedance device will determine total body water. The Jackson Pollock equation for females will be used to determine body fatness. Heart rate will be measured using the Polar Heart Rate Monitor.

EXAMPLE – High Quality Research Proposal for PURA Salary Award application

Proposal by LCC student, Lindsay Chatel

The History of Pain: Modern Understanding of Medical Development and Social Influence on Pain Perception

Overview of Proposed Work

Modern studies of chronic pain have caused physicians to question their prior understanding of pain's fundamentals. When diagnostics fail to catalogue pain as a physical symptom, it must originate through a mental stimulus. In order to access pain's psychological components, chronic pain may be recognized as the possible result of societal responses to medical innovation. To define pain as it is understood today one must provide a new assessment of pain, its history, its cultural factors, and its pervasive influence. This research project focuses on the history of pain as it is expressed and treated in early modern surgery. Drawing on Atul Gawande's The Pain Perplex, this project explores the historical progression of pain perception as it has been influenced by medical developments in addition to cultural and social reactions to such innovations. As Gawande and others have recently argued, pain has a history; linked to cultural and political influences, pain becomes a window into our deepest held beliefs, preoccupations, and anxieties. In People in Pain, Mark Zborowski, a twentieth-century anthropologist, found that patients understood their pain in culturally specific ways. The importance of such patients' linguistic expression will generate a range of insights into early modern patients and the cultural specificity which influences their particular pain. It is my goal to research the historical development of human understanding of pain with emphasis on the influences of situational medicine and society. Through my research I seek to better understand the role which historical development plays on the subject of pain. This includes understanding its sources, developing treatments, and extending those treatments for misunderstood cases. Such is the process of learning which has shaped our modern understanding of pain as both a mental and physical experience which may be expressed in various ways and initiated by various stimulants. One such stimulant is surgery.

This project considers the relationship between surgery and pain in order to explore the historical development of our ideas and assumptions about pain. A range of sources, including surgery manuals where surgeons developed instruments and treatments will examine these factors. In doing so, said research provides a catalogue of Renaissance conceptions and practices related to surgical pain and the instruments that cause it. To supplement these surgery manuals, case studies of surgeons' practice also representatively characterize the patient. Doctors began to recognize the relevance of pain in treatment only during the 1800's. The development of anesthetics was the first major medical step towards dealing with human suffering that was caused by disease. Since this innovation, doctors have further developed understanding as far as how we feel pain and how this pain can be dealt with. Today we have pain clinics which focus on alleviating chronic pain. However, despite such institutions, our understanding of pain remains elementary. Is pain physical or mental? How do we experience it and how should it be relieved? What does the history of pain tell us about the cultural factors determining an individual's experience? Working with Professor Klestinec, I wish to pursue further the cultural and historical significance of pain in order to understand its lasting influence. Together with Professor Klestinec, I will focus on theories of pain (those espoused in Hippocratic medical treatises, in Descartes' writings, and in Renaissance surgery manuals). I will also query the rise and impact of anesthesia, the emergence of a science of pain, neurophysiology, the mapping of pain pathways, and the Gate Control Model. This research will draw from philosophical and medical texts as well as case studies of chronic pain including: nausea, migraines, back pain, and phantom limb pain. This research will show that pain is not simply a symptom of some other hopefully treatable condition. Rather pain has the ability to stand alone as a chronic condition. This research seeks to show not only how medical perspectives have changed but also how these perspectives continue to shape the way we feel pain. From this research and weekly meetings with Professor Klestinec, I will complete a final paper, and in-depth study of the cultural and historical significance of pain for surgeons, medical authority, and patients. Understanding the history of pain, one can better understand where our collective knowledge stands today. This historical progression will be understood through pain recognition, the development of theories, case studies, a shift in ideas and practices within the medical world, and analysis of pain as both mental and physical. Through this study, I hope to further my own awareness while adding to a more exact understanding of the nature of pain as we experience it.