GRADUATE TEACHING FELLOWS' PROGRESS IN THEIR RESEARCH
(as of January 2006, with some updates as of August 2007)

TABLE OF CONTENTS

Patrick Gorman, Lehigh University, STEM Graduate Teaching Fellow, Harrison Morton Middle School, Mathematics

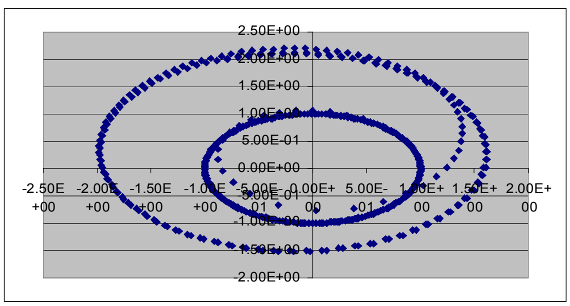
I am currently attending Lehigh University as a mathematics graduate student, participating in the STEM project as the graduate fellow on the mathematics team at Harrison Morton Middle School. For the years prior to the STEM project, I was a Teaching Assistant in the mathematics department at Lehigh University. I have earned a Master's Degree in Mathematics from Lehigh University, and am currently pursuing a Ph.D. degree in applied mathematics. The focus of my applied mathematics research is in the field of astrophysics working with my advisor Dr. George McCluskey.

The problem I am currently researching is that of extra solar planets. In the past few years, the fields of astronomy and astrophysics have been greatly boosted by the discovery of well over one hundred extra solar systems of planets, which are basically other stars which have at least one planet which orbits. Current methods of detecting these planets are in the early stages and are done from only earth-based telescopes. The lack of precision from these telescopes has resulted in the ability to almost exclusively discover planets whose sizes are of the same order of magnitude of Jupiter. With the success of the detection of these planets, there are many projects in the works to launch space telescopes designed exclusively to detect planets around other stars. These more accurate telescopes will be able to not only detect the large planets, but also Earth size planets orbiting other stars. This is of course motivated by the ever-burning question of whether it is possible there is other life in the universe. The discovery of these planets could be a clue in determining the likelihood of extraterrestrial life.

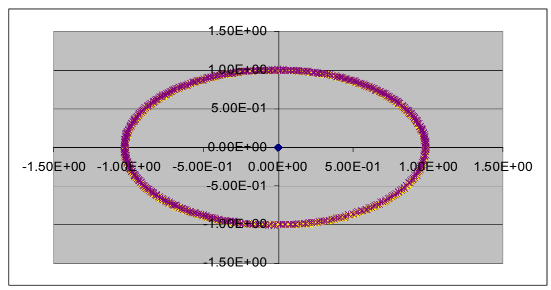
My research is based on this idea of the search for Earth like planets in extrasolar systems. The goal of my research is to determine the regions of stability for Earth size planets in an extrasolar system. In particular, I am interested in stable orbits of an Earth size planet in a binary star system rather than in a system with a single star. An added factor of another planet of the size of Jupiter in the system will also be explored. Two major problems to explore arise from this research subject. The first is to be able to simulate a system of two stars with an Earth size planet and a Jupiter size planet. The second is to determine what exactly is stable in a mathematical sense.

The simulation of these systems is accomplished using a modified version of a program written in the c language called NBI. This is an N-Body Integrator in which the initial conditions of the system are inputted into the program and it calculates the positions and velocities of all the objects in the simulations over a certain period of time. An initial set of simulations was done with three objects. The first object was a central star exactly the size of the sun. The second object was a planet exactly the size of the Earth, placed at one astronomical unit away from the central star and put into an initially central orbit. The third object was the variable in the simulations. It was the second star in the binary system, which was placed at positions varying from three astronomical units from the central star to twenty astronomical units from the central star. The other parameters of the second star that were varied are its mass, which was varied from one-tenth of the mass of the sun to twice the mass of the sun, and its eccentricity, which was varied from zero which is a perfectly circular orbit to nine-tenths. Using these conditions, hundreds of simulations were conducted. These simulations were done with no particular stability criterion other than to see whether the Earth size planet was kicked out of the binary system or not. This data will be used to see what conditions for the binary system to use when expanding the simulations to include a second planet of the size of Jupiter. The current simulations being run include the Jupiter size planet. Of particular interest is if when the two planets are put in some kind of resonance, is the system more stable than when they are not? This is being researched because of the many resonances that exist in our own solar system. Another object that may be added to the simulation at a later point is a moon orbiting the Earth size planet. This is because of recent studies that show that life may not have been possible even on our Earth without the stabilizing force of the Moon.

The problem of what is stable is the area of the project I am currently focusing on. During the initial sweep of simulations, the only stability criterion used was to determine the percentage the Earth varied off of its initial circular orbit. This is a rudimentary determination of how stable the orbit is, but is by no means mathematically sound. I am currently researching the possibility of using what is called a Frequency Map Analysis, which uses a fourier analysis of orbital elements to observe possible instabilities in the orbit. Once the fourier analysis is working, a more thorough search for stable orbits will be done. Upon completion of my research I hope to teach at the university level and continue doing outreach in a similar manner as the STEM program at Lehigh.



Example of unstable Earth orbit



Example of Stable Earth/Moon Orbit

Donna DeMarco, Lehigh University, STEM Graduate Teaching Fellow, Broughal Middle School, Technology

I joined the Lehigh University STEM project in June of 2004 as part of the supplement. This year, even though the supplement was not renewed, Lehigh University generously continues to fund me so I can remain a part of the STEM project. I appreciate the STEM leadership team's, and Lehigh University's, support and faith in me so I can continue to contribute to the STEM project.

I currently attend Kutztown University full-time. I am pursuing my Masters of Science, Computer & Information Science. Courses I've completed include Object-Oriented Analysis, Database Management, Web-based programming, Compiler, Operating Systems, Networking, and Information Security. Kutztown's masters program does not require a thesis. Instead, a comprehensive exam is given at the completion of the course requirements. This exam is an extensive in-depth written essay and programming test based on four of the graduate level courses taken. I successfully passed this exam and will be graduating May 2006.

I am also taking courses at Lehigh University in the College of Education, and P.C. Rossin College of Engineering and Applied Science, and I participated in summer workshops.

Once I complete my Masters of Science, Computer & Information Science, I plan to apply to Lehigh University's College of Education Ph.D program in Learning Sciences & Technology. The Learning Sciences and Technology (LST) Ph.D. program focuses on the systematic study of the psychological, social, and technological processes that support learning.

I plan to participate in the Instructional Design and Development concentration, which focuses on the design, development, and evaluation of innovative learning products in educational settings. This may include corporate settings, online teaching settings (particularly in higher education), or non-traditional settings (like museums, historical sites, and the like). I am already interacting with other Lehigh Ph.D candidates to become more familiar with the program and current research in the field of computer science.

I enjoy working with all the members of the STEM project. I really enjoy teaching the students in grades 6, 7 and 8 at Broughal Middle School. It's very rewarding to see the students involved and participating in class and using the tools we developed for them. Our goal is to seamlessly integrate the technology into the class so the students are using the technology as another tool in their toolkit of learning.

Chris Janneck, Lehigh University, STEM Graduate Teaching Fellow, Harrison-Morton Middle School, Technology

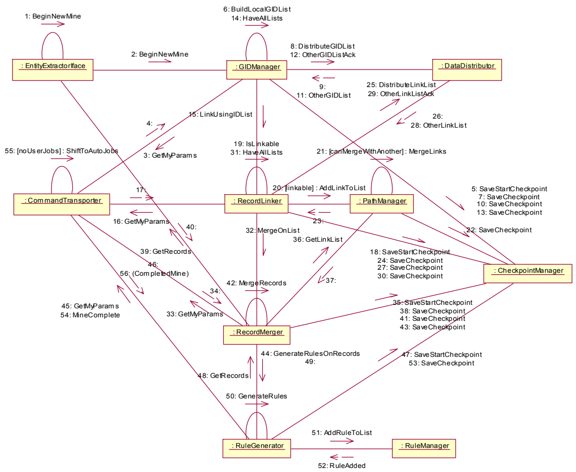
Chris Janneck is a new graduate fellow on the Harrison-Morton Middle School Technology Team this year. Coming onboard during the summertime, his research work under the grant has fallen under two major categories. The first assignment has been as a lead designer, manager and developer of the D-HOTM system, implementing an algorithm that is breaking new ground in the area of distributed data mining. His second charge has been the establishment of his own Ph.D. research program, under his new academic advisor, Prof. Pottenger.

The D-HOTM System, Version 1

The Distributed Higher-Order Text Mining (D-HOTM) system strives to be among the first applications developed using the distributed abilities of the Text Mining Infrastructure (TMI), developed by the Parallel and Distributed Text Mining Lab at Lehigh University. D-HOTM will be used for the study of several aspects of distributed mining, including wide-area MPI cluster performance, interactive mining and steering, and the performance of several distributed association rule mining (D-ARM) algorithms. D-HOTM is a hybrid approach including information extraction and distributed data mining capabilities. Most notably, it is the realization of the Distributed Higher-Order Association Rule Mining (DiHO ARM) algorithm, also developed in the lab. This algorithm surpasses traditional ARM algorithms in several key ways, including allowing distributed mining natively, in the absence of an *a priori* known global schema, across hybrid forms (neither horizontally nor vertically, only) of data fragmentation.

The D-HOTM system is comprised of three top-level components. The first, used by the Investigator, is the Controls component. This serves as the front-end of the system, accepting input directly from the user to establish all the parameters of the D-HOTM mining job. These parameters are then passed to the core of the system, the D-HOTM component itself. This component performs the distributed mine, contacting any necessary databases and sites, utilizing the TMI and the Global Justice XML (GJXML) data model for transmission of data. Once the mine is completed and results are collected, they are passed to the Analysis component. This component will provide various abilities to sort, organize, filter, and visualize the mining results, to the Investigator.

At the time of this report, the first functional version of the D-HOTM system has been completed. This initial version acts as a proof-of-concept for the D-HOTM design, including a functional core component (housing the DiHO ARM algorithm), inter-process communication using the Message Passing Interface (MPI), data input through a simple XML format and output in the form of association rules, i.e. “if-then” statements. This system has been tested on the National Center for Supercomputing Applications’ (NCSA) Tungsten Supercluster (of Xeon Linux machines). As this system has great potential application in the law enforcement domain, the test data is a simulated set based on methamphetamine trafficking. Future versions of this system will focus on more fully developing the Controls and Analysis components of the system, and improving the stability and efficiency of the computational processes.



Collaboration Diagram of DiHO ARM

Ph.D. Dissertation Proposal

The focus of his dissertation will center on the appropriate intertwining of the areas of computational steering, distributed computing and textual link analysis, to develop a theoretical framework and implementation that demonstrates the effectiveness and usefulness of combining these primarily disparate fields. His research will aim to bring these disciplines together for the purposes of performing textual link analysis, across distributed systems, in an interactive and engaging manner – an approach not fully realized in today's work. If successful, his work will elucidate the effectiveness of interactive analysis and exploration in link analysis, as compared to the traditional batch and off-line systems. In lieu of the benefits of visualizing intermediate results and interactive classification systems, his approach may provide substantial benefits in terms of computational speed and accuracy of results, especially with very large and distributed datasets.

His dissertation proposes to study, develop, and integrate the field of interactive computational steering with distributed text-based link analysis. Completion of his work will involve several key phases – first, to complete a more thorough literature search on the application of visualization and steering technologies to link analysis techniques and algorithms. Second, to develop a theoretical framework for the understanding of human-in-the-loop steering as applied in text-based mining and analysis domains. This phase will also include the adaptation and enhancement of theoretical frameworks for distributed higher-order linkage (currently under development in the lab), as well as defining appropriate metrics for measurement of performance. Third, to design and develop systems for computational steering, analysis, and exploration of intermediate and final results that, when used in conjunction with a distributed link analysis framework, will demonstrate the feasibility, usability, and correctness of the underlying theory.

The overarching goal of his work is to provide the theory, techniques, and an implementation that promote a greater understanding of the data being analyzed, through a powerful interface that mitigates information overload, all in a real-time distributed working environment.

If successful, his work will provide a strong foundation, both theoretical and implemented, in the area of distributed data analysis – an area that, given the direction of present-day information infrastructures, will only continue to grow in years to come. There are several specific fronts to which his work may be applied. In terms of link analysis, most work is currently done using relational databases and other well-defined data structures. His work will utilize and expand the D-HOTM framework, which is based on free-text extraction and analysis, where significant amounts and types of data are presently stored. Second, currently all known link analysis algorithms operate under the requirements of a known global schema, and (if using distributed data) under horizontal or vertical fragmentation. The DiHO ARM algorithm operates without any of these restrictions, and his work will continue to explore the possibilities and success of using such a process. Third, all known link-analysis work is done in a batch-style format, with analysis always done as post-processing on the end results. His work will allow users to monitor the processing, make changes, and perform analysis throughout the computational process. This ability will greatly enhance productivity especially in highly computation-intensive applications where an incorrect parameter may invalidate many days of computation. Plus, this will allow users to see the intermediate steps of computation, further providing credence to the generated results. Fourth, the vast majority of computational steering and visualization efforts are focused in the biomedical field, or other fields where visualization techniques have been time-tested and applied. Currently, there are no well-defined or generally accepted visualization techniques for textual link analysis, and so his work hopes to find one or more appropriate techniques for this area. Fifth, his work will aim to demonstrate the feasibility of human-in-the-loop processing, and provide experimental results comparing this with more automated analysis techniques in terms of computation time, accuracy, and the like. Sixth, while work has been done applying computational steering for the purposes of reducing computational time, no known work has applied these techniques to enhance the accuracy of generated results. His work will also study the computation time versus accuracy tradeoff, aiming to provide an ability to control this tradeoff, as well as studying the effects of having such a control. Seventh, and finally, the implemented system will itself be a research platform, designed to allow the incorporation of different data sources, of different analytical and visualization components, and the insertion of different algorithms and computational processes.

Sally Moritz, Lehigh University, STEM Graduate Teaching Fellow, Dieruff High School, Computer Science

Learning object-oriented design and programming is a challenging task for many beginning students. Yet object orientation is a critical paradigm of modern software development. In recent years, this has motivated the development of new curricula and tools to support their pedagogies. However, student achievement in first-semester courses, as well as enrollment and retention rates (especially for women and minorities), remains a concern. New tools and techniques are needed to engage students and enable more of them to be successful in a CS1 course. This need inspired two avenues of research: a new "design first" curriculum that uses elements of Unified Modeling Language (UML) to teach students problem-solving and design skills before procedural code, and an intelligent tutoring system (ITS) that observes students as they create UML class diagrams and offers customized assistance when they need it.

The design-first curriculum is similar to the "objects first" approach in that it teaches object concepts early. Anecdotal and experimental evidence supports the hypothesis that objects first is more effective than teaching procedural concepts first. However, this approach still emphasizes coding and syntax rather than problem solving. When presented with a problem, many students don't know where to begin. They need guidance on how to analyze a problem and develop a plan for solving it. The design-first curriculum begins by teaching students a procedure for creating a UML class diagram, given a problem description in English. It then continues with use cases and a project-driven rather than syntax-driven approach to learning Java.

The design-first curriculum has been used successfully over three semesters at Dieruff High School. The curriculum and results from the first year at Dieruff have been disseminated through several publications and conference presentations, and shared via the web with high school and college teachers.

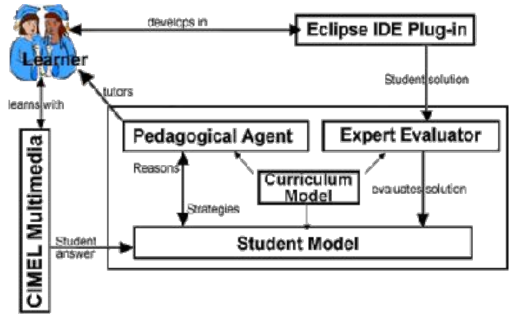
We constructed an integrated development environment (IDE) using freely available software (the Eclipse IDE combined with DrJava, an interactive Java processor for students, and an interface to enter UML class diagrams developed at Lehigh). This environment generated code stubs from class diagrams, thus supporting students as they moved through the development process from design to coding. But novices need more than syntax error messages; they need give problem-specific advice and help when they get stuck. Students at Dieruff had human tutors: their teacher and a graduate teaching fellow. But good human tutors are often not available. Intelligent tutoring systems (ITS) can provide customized help to students when they need it.

A team of three graduate students has designed and implemented DesignFirst-ITS, which observes student work in the LehighUML tool. It monitors a student's work on a class diagram to solve a given problem, and offers hints and advice if the student makes an error. The ITS has been tested, producing significant results in version has been tested at Lehigh University and Whitehall High School; all of students successfully produced UML class diagrams and showed significant pretest/posttest improvement in their understanding of OO concepts.

An ITS must be able to solve the problems that are presented to the student, or at least evaluate the student's work. Several models exist for accomplishing this task, but all are limited in the number of different solutions they accept as correct. This is not a problem in many domains, but it is in object-oriented design. For any given problem, there are often many different solutions that are acceptable. While scaffolding is desirable to guide novices through a new procedure, students who follow a different but fruitful path should not be deterred. I have built an expert module for the ITS that can not only generate its own solutions, but also recognize and accept valid solutions that are different from prior known solutions. Called the Expert Evaluator (EE), it analyzes each action the student enters in the LehighUML editor and determines the correctness of the step and concept applied. If incorrect, the EE also determines the type of error committed, and recommends an alternative to the incorrect action. This information is made available to the two other components of the ITS: the student model, which estimates the student's knowledge of the concepts applied in the problem, and the pedagogical agent, which chooses appropriate feedback and presents it to the student.

The Expert Evaluator must employ software engineering principles to analyze a problem description and identify solution components within it. Software engineering research has developed a body of processes and guidelines for human developers to follow, and metrics for measuring the quality of a design. Research has also produced tools which extract design elements from system requirements. However, these tools are used to provide a starting point for human designers, or as a brainstorming aid, but not as a means of automating the generation of software systems. The difficulty lies in two aspects of the problem: requirements are described in natural language, so any design tool must overcome the problem of natural language translation, and system requirements don't include all details explicitly (some are assumed as common knowledge, others are inadvertently omitted until they are remembered later in the development cycle).

Prior research has had some success in generating designs for simple problems on the same scale as those typically assigned to beginning students. Also, problem descriptions provided to students should be complete and explicit; a much lesser amount of prior knowledge can be assumed of beginners than of experienced developers. Thus, the goals of this research are to demonstrate that the automation of software engineering processes and principles can effectively develop solutions for small-scale, well defined problems; can assist teachers in producing more complete and accurate problem descriptions; can accurately evaluate student designs, including recognizing acceptable novel solutions; and can provide pedagogically useful information about the student's work to the student model and pedagogical agent components of an ITS.



In May, 2006, Ms. Moritz completed her General Exam. Since then she has implemented Solution Generator. When evaluation of the Solution Generator is complete, Ms. Moritz will complete her dissertation.

Steven Sweeney, Lehigh University, STEM Graduate Teaching Fellow, Spring Garden and Fountain Hill Elementary School, Physics

I have been continuing my work towards obtaining my Ph.D. in physics here at Lehigh University. A great deal of progress has been made towards finishing up our current research project for publications. I do experimental work in the area of Atomic, Molecular, and Optical (AMO) physics. My current area of focus is atomic energy pooling collisions in excited cesium atoms.

Atoms can be described as being in a number of energy states depending on whether they have been excited, usually by use of a tuned laser. These energy states are discreet levels predictable through the use of quantum mechanics. We know the precise energy these atoms sit at, the wavelength of light needed to transfer the atoms to another energy level following established transition rules, and the normal lifetime of these states (i.e., the amount of time an excited atom can exist before emitting a photon and dropping to a lower energy state).

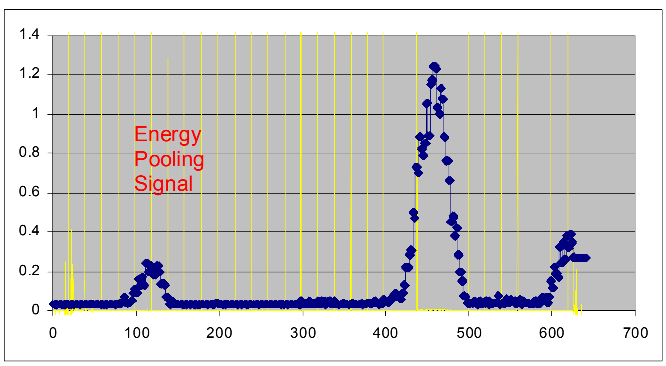
A common method of interaction between atoms in a vapor is a collision. In a macroscopic model using identical hard spheres, such as ball bearing, the product of a collision would be a transfer of kinetic energy between the two colliding bodies. In atomic physics, however, there is a much more interesting possibility. Two excited atoms, each with a certain amount of energy above the atomic ground state, can collide. When they do this, there is a chance that they will take their excited energies and "pool" them together to create a highly excited atom and a ground state atom. This occurs when the energy of the initial atoms combined is roughly equal to the energy of the highly excited atom. For our experiment, we use a titanium-sapphire laser to produce a constant population of atoms in the $6P_{3/2}$ excited state. At the same time, a pulsed dye laser is used to excite cesium molecules to a repulsive state, producing ground state atoms along with atoms in the $5D_{3/2}$ and $5D_{5/2}$ excited states in a process called photodissociation. The energy of the $6P_{3/2}$ and $5D_{3/2}$ atoms is roughly 26231.75cm^{-1}. For cesium, the energy of the $7D$ levels is roughly 26050cm^{-1}, just below the combination of our initial excited atoms. Our goal is to measure the effect on the likelihood of this energy pooling collision happening as a function of the velocity of the initial atoms.

Previous experimental and theoretical work done on these measurements have always been done using an average velocity distribution for the atoms. We think that there should be a dependence on velocity. Collisional cross-sections tend to always show some kind of velocity dependence, and it would seem odd for energy pooling collisions to break this trend. We hope to use the knowledge gained from this experiment to look at other more interesting states in the future.

As mentioned above, we are using the energy pooling collision $5D_j(fast) + 6P_{3/2}(slow) \rightarrow 7D + 6S$. We can adjust our photodissociation to pump our cesium molecule to different heights the repulsive state, causing the resulting atoms to come out of the molecule with a specified kinetic energy and velocity. This is done by adjusting the wavelength of laser light from our pulse dye laser. The shorter the wavelength produced the more energy in the photons, leading to more energy in the atoms released from the molecule. To be sure that we are looking at the effects of only these fast atoms, we must only look for collisions that occur a very short time after the initial laser pulse, which in our case has been a window of 150ns. For Cs vapor at 180°C used in this experiment, other collisions will cause the atoms to lose their specific velocity and will rather take on an averaged velocity distribution like the one used in previous work.

Preliminary results show that there is a definitely dependence of the energy pooling cross-section on the initial velocity of the $5D_{3/2}$ and $5D_{5/2}$ atoms. There is a possibility of seeing even more of an effect in other collisions. As said, our initial atoms already posses enough combined energy to produce our highly excited atom. Our hope is to be able to perfect our technique enough to be able to look at collisions where the energy of the initial excited atoms is just less that the energy of the highly excited atom we are looking for. Because of this, there must be some kinetic energy in the initial atoms to help overcome this difference. We expect that there might be some kind of velocity threshold where just below the likelihood of energy pooling in nearly zero and above is much more likely to happen.

Once our initial work on the $5D_j(fast) + 6P_{3/2}(slow) \rightarrow 7D + 6S$ collision is finished, we plan on publishing this work and proceeding one towards other collisions in cesium, granted that we are able to process the extremely small signals that are obtained from these types of collisions. Following that, I plan on proposing my doctoral research this spring on this continued work and possibly molecular research involving rovibrational spectroscopy of diatomic alkali gases.



Velocity Dependence of Energy Pooling Collisions

Kelley C. Caflin, Lehigh University, STEM Graduate Teaching Fellow, Freedom High School, Chemistry

To implement quantitative solid state NMR two techniques are being implemented. The first is the use of an electronic reference signal in the place of the internal standard. This reference signal is used to standardize signals allowing for comparison of samples. The second technique is the use of chemometrics, a method for prediction of unknown samples with the use of mathematical modeling. Using both techniques together, it is believed that quantitative ssNMR is possible with a great deal of accuracy and precision. The reference signal that used in this work is the electronic reference to access in vivo concentrations (ERETIC) method reported by Akoka et al.. This method uses an electronic device to create a reference signal, a pseudo- FID (free induction decay) that is recorded during the acquisition of the true signal. An electronically produced signal is therefore present in the spectra. The calibration of the ERETIC signal is done using a known sample and the use of the areas underneath both the reference and ERETIC peak. Once the calibration is complete the ERETIC signal can be used to quantify any compound by a relationship of the now “known” concentration of the ERETIC signal and the areas of the two peaks. For our purposes, this signal can be used to normalize the differing intensities of the ssNMR signals caused by retuning of the probe. This signal will make it possible to compare one sample to another more easily.

The chemometrics approach used in this application is a multivariate calibration technique. Another benefit of chemometrics is the multichannel advantage. All of the data from the spectrometer contains valuable information about the system of study. When all the information is used, unlike earlier methods where a single resonance is used, the model accounted for all of the information, rather than a limited data model, and should have less variance in the prediction.

The first study done was to determine the variance caused by retuning the probe after the introduction of each sample into the spectrometer. The variance was tested by putting the sample into the spectrometer and retuning the probe five times. The sample used was L-valine. The pulse program 5CP213 was used and 512 acquisitions were recorded for each trial. Data was transferred from the 300 MHz NMR to a computer to be processed.The software used to process the spectra was NUTS®.

The binary system, L-valine and N-acetyl-L-valine, training set consisted of six samples with each component ranging from 0 to 100% of the sample in 20% increments, i.e. 20/80 or 40/60. The multivariate calibration used in all cases was classical least squares (CLS) because of its simplicity. In this case linear additivity is assumed. The CLS model is

$$[\ Y\ ] = [\ C\ ] \bullet [\ b\ ] + [\ E\ ] \qquad \text{Eq. 2}$$

where Y is the response or output of the instrument, C is the concentration, b is the model, and E is the error.

The first thing noticed was that the first unknown was predicted more accurately than the third unknown. The third unknown was analyzed several days after the completion of the training set, possibly creating some sort of bias. The second conclusion is that the best results were obtained using a line broadening term of 30 Hz and the greatest signal to noise ratio.

In order to determine the best way to construct a training set for a multiple component system, a theoretical study was performed. Spectra for this study were created using programming in MatLab®. The Gaussian function was used because it is the basic line shape of the true peaks in a solid-state NMR spectrum. The first step was to create a two component system. The next step was to create a training set and use it to predict "unknown" samples. . Predictions from the models showed promise for "unknowns" comfortably within the range of the calibration set, most giving a value less than a 2 %RSD with the largest being about 3.5%. The training set was then reconfigured to contain more samples. Each component ranged from 0 to 100% at 10% increments, thus creating 11 samples. Unknowns with percentages again at the ends of the model were tested. Results still showed rather large %RSD, but not as great as the previous predictions with the largest at 12%. It can be seen in Figure 1 that as the resolution between the peaks decreases, the ratio of the %RSD to resolution increases.

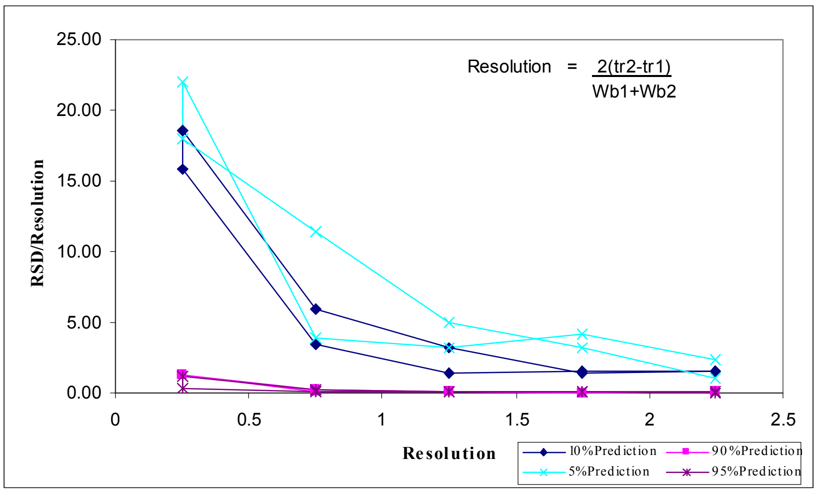


Figure 1- 100-0% in 10% Intervals- 11 Sample Calibration Set. Shows as the distance between two peaks decreases the predicted value become less accurate.

As a result of this study, information on the construction of training sets was obtained. Like the first study, the predictions of the concentrations of the components became less accurate as the resolution between peaks decreased. A new and surprising finding was that the limited training set with only single and binary samples did as well if not better at predicting the concentration of three component samples than the full training set. This is a promising development in the use of chemometrics in prediction of multiple component systems.

Melodie Kent, Lehigh University, STEM Graduate Teaching Fellow, Harrison-Morton Middle School, 6th Grade Science

Patients with diseases such as Acute Lung Injury (ALI) or Adult Respiratory Distress Syndrome (ARDS), require mechanical ventilators to help them breathe. These diseases lead to liquid buildup in the lungs and the collapse of small pulmonary (lung) airways. During mechanical ventilation, liquid-filled and collapsed airways experience repeated opening and closing events. This cycle damages the layer of epithelial cells in the lung that normally provides a barrier, which prevents fluids from entering the lung. As a result, mechanical ventilation often leads to more liquid in the lungs, more lung injury, and deteriorating pulmonary health. This progression is called ventilator-induced lung injury (VILI) and leads to a 30 % mortality rate. Although we understand that mechanical ventilators can exacerbate lung injury, we are not certain whether biomechanical or biological mechanisms are responsible for this injury. We hypothesize that the flow of air bubbles in fluid filled lungs during mechanical ventilation may have a large affect on patient morbidity[i].

For the last six months, I have been testing the effects of passing bubbles over lung epithelial cells in a narrow channel. My results indicate that passing the bubble over the lung epithelial cells causes cell necrosis (immediate cell death). Other researchers in this field have shown that bubble-induced shear and pressure stresses and flow patterns kill the cells[ii]. Under the most stressful conditions, about 30% of the cells die within 5 minutes. However, additional cell death occurs over longer periods of time. These long-term consequences may be mediated by chemical signals similar to those found in programmed cell death, or apoptosis. Interestingly, recent research indicates that blocking the chemicals that lead to programmed cell death can prevent cellular injury.[iii]

The goal of my proposed research is to identify the factors that lead to cell death following the passing of an air bubble over the cells and to determine if mechanical and/or chemical mediators can be used to prevent cellular injury. I will perform a physical *in-vitro* experiment of the mechanical ventilation process and observe the cellular response using cell culture and florescent microscopy techniques. I will approach this project in three phases:

1) *Set up an in-vitro test system.* Preliminary tests performed in our lab used a POC (perfusion open-close) chamber system and a syringe pump to expose epithelial cells to the flow of air bubbles at different velocities. When an injury occurs as a result of this bubble, certain internal parts of the cell are exposed. These parts can be observed using fluorescence reagents that bind to specific exposed proteins and as a result fluoresces a specific color that determines if the cell is alive or dead. For my project, I plan to modify this system so that the cells grow on a collagen substrate which mimics their *in-vivo* environment. I am also interested in growing cells on flexible membranes so that I can quantify the effects of cell stretching as bubbles deform the membrane. Finally, I will add temperature controls to the system so that cells in long-term tests experience typical *in-vivo* conditions.
2) *Measure cellular responses under different mechanical conditions*. In my experiments, I will oscillate a bubble across a bank of cells to mimic the

conditions during inspiration and expiration. I will vary the bubble speed, channel height, and frequency of oscillation. These variables directly modify the mechanical stresses felt by the cells. The mechanical stresses generated during bubble oscillation will be quantified with computational fluid dynamics (CFD) techniques. These stresses may result in either immediate cellular death or programmed cellular death. In addition, biological mechanisms may allow the cell to repair damages that would otherwise lead to cell death. As a result, I will develop fluorescence staining protocols to quantify five possible cell states: 1) Alive and uninjured, 2) Dead due to injury, 3) Repaired and healthy 4) Repaired but self-destructing, or 5) Uninjured and self-destructing. I will compare the stress magnitudes to cell injury and death rates.

3) *Measure cellular responses under different biological conditions.* Changes in the biology of the cell may have a significant impact on how the cell responds to mechanical stresses. I will apply chemical treatments like cytoskeleton disrupters and polymerizers to break down or stiffen the cells[iv]. The results from altering structural properties will be compared to the responses of normal epithelial cells using fluorescence techniques. This comparison could help us determine how the mechanical and structural properties of the cell influence their viability.

The research plan proposed above outlines an *in-vitro* simulation to understand mechanical ventilation's affect on lung injury. Specifically, mechanical ventilation may be conducted under various conditions, such as high/low pressures or high/low frequency [v]. Therefore, the ventilation of fluid filled lungs may result in a variety of bubble speeds/frequencies and pressures. Our *in-vitro* models were designed to accommodate these varying mechanical conditions. The value of this study is directly linked to the advantage of having a carefully-controlled *in-vitro* system rather than an animal because our current system provides more efficient means of evaluating how epithelial cells respond to a given mechanical stimulus. Knowledge of the cell injury and death patterns, which occur under these conditions, may lead to treatment strategies that mitigate cell death and patient mortality.

My interest in the project arose initially from constant involvement on bio-engineering projects and finally by becoming involved with this specific project for my senior thesis. My senior thesis included construction of a flow chamber from raw materials. This chamber is currently under revision and will serve as our primary chamber.

My proposed research is part of a larger project on the effects of mechanical ventilation overseen by Dr. Samir Ghadiali, my advisor in the Mechanical Engineering at Lehigh University. However, the inter-disciplinary nature of my project requires input from two of Lehigh's Biological Sciences professors, Dr. Jennifer Swann and Dr. Linda Lowe-Krentz. I am currently broadening my biology basics by taking cell biology based grad courses and continuing my preliminary lab work in a bio-mechanics lab. My previous experience with building this chamber, biology course work, and preliminary lab testing all contribute to my extensive knowledge and skill set necessary to conduct this experiment immediately.

Lehigh University not only has the necessary equipment and facilities, but they also have the financial resources to support my research activities. Lehigh has received a $1.38 million grant from National Science Foundation to help establish the bio-engineering program. My advisor, Dr. Ghadiali, has also received numerous fellowships and grants from organizations such as the Parker B. Francis Foundation and the American Heart Foundation.

The knowledge gained during my dissertation research will help identify the source of ventilation lung injury and may therefore help develop less injurious treatment therapies. My excitement for this project comes from knowing that these findings may be the difference between life and death.

---

[i]Ciubotaru, MD ,Ronald L., Scott K. Epstein, MD, FCCP, John B. Wong, MD. 2005. Effect of failed extubation on the outcome of mechanical ventilation. *Chest Journal*. 112:186-192
[ii] Bilek, A.M., K.C. Dee, and D.P Garver. 2003. Mechanisms of surface-tension-induced epithelial cell damage in a model of pulmonary airway reopening. *J Appl Physiol.* 94:770-783
[iii] Hagimoto, Naoki. Thomas Martin, Gustavo Matute-Bello, Morio Nakamura. 2005. Apoptosis and Epithelial Injury in the Lungs. *Proc Am Thorac Soc*. 2:214-220
[iv] Hubmayr, Rolf D., Nicholas E. Vlahakis, Richard E. Pagano, Mark A. Schroeder. 2002. Role of Deformation-Induced Lipid Trafficking in the Prevention of PM Stress Failure. Am *J Respir Crit Care Med*. 166:1282-1289
[v] Francois Lemaire. 2001. Influence of Tidal Volume on Alveolar Recruitment. *Am J Respir Crit Care Med.* 163:1609-1613

Preliminary Design of Flow Chamber
(Bird's Eye View)