Rabi Scholars Program
Annual Research Symposium

Friday, 8 October 2010
12:00 Noon-2:00 pm
603 Schermerhorn

Elizabeth Allocco
Mentor: Professor Jennifer Manly, Columbia University, The Taub Institute

Cultural Factors in Neuropsychological Testing

It has been estimated that the number of people over the age of 65 who suffer from Alzheimer's disease (AD) will more than double by 2050, to reach a number between 11 million and 16 million people. The disease will be burdensome both on the population level, where it will place a strain on the healthcare system, and on the individual level, where it will affect both patients and caregivers. This burden will be especially high among African Americans, who experience prevalence between double and triple that among whites. Preemptive efforts are being made to understand why AD is more prevalent in African Americans, and to develop methods to diagnose AD and other dementias more accurately. The California Verbal Learning Test II (CVLT II) is an assessment of learning and memory that may be used in the diagnosis of AD. The current standards of normal and pathological performance on the test may not lead to accurate diagnosis in non-white cultural groups. Preliminary findings of its use in a population of older African Americans, both with and without memory problems, indicates that the word recall strategy used by African Americans on the CVLT II is not accounted for in the normative data used to score the test. It may therefore produce an inaccurate picture of their cognitive state and complicate the effort to understand the diagnosis of AD in African Americans.

Rohan Bhandari
Mentor: Professor Richard Osgood, Jr., Columbia University

An Empirical Determination of Image States in Graphene Through Two-Photon Photoemission

This project sought to experimentally validate the theoretical values that have been calculated for image states on Graphene and so gain insight into its electronic properties. An image state refers to an electron that has been excited outside of the surface of the metal, and its resulting electric field. Graphene is of particular interest, because it exhibits very curious electronic properties: its electrons are able to travel relatively long distances before colliding with other electrons. Also, these electrons behave as Dirac particles, essentially acting as particles in an accelerator, while actually traveling relatively slowly and residing in a metal. Using a high frequency (on the order of a femtosecond) laser to bombard the Graphene surface with photons, image states were probed with the use of two-photon photoemission (2PPE). By measuring the surface electrons' energies, we can infer the energy of the excited electron as it moved through Graphene. Through analysis of these data, we are able to determine properties of these electrons and their resulting image states.

Samuel Beck
Mentor: Professor Anthony Mezzacappaa, Oak Ridge National Laboratory

Spectral Analysis of Kinetic and Magnetic Energies in Core-Collapse Supernova Simulations

Core-collapse supernovae are an important part of the life of our universe because they produce many of the heavier elements that are critical to life. However, the specifics of how core-collapse supernovae occur remain a mystery. One such question is how supernovae could create the enormous magnetic fields that we observe around neutron stars. Several simulations to date have indicated somewhat informally that most growth in magnetic field strength occurs through two processes, turbulence of the highly conductive plasma and stretching of the magnetic field lines. If this is the case, then a spectral analysis should reveal growth in magnetic energy primarily at shorter wavelengths, where these two processes dominate. By creating a highly parallelized algorithm to perform this spectral analysis, some evidence has been found to support this conclusion.

Nate Booth
Mentor: Professor Deb Roy, MIT

Event Segmentation for Video Retrieval

Segmentation of observed behavior into discrete events is a normal part of human perception. Similar segmentation performed by a computer can facilitate various computer operations, such as video retrieval. This paper examines the way humans segment events and presents an algorithm for a computer to replicate the human event segmentation process, with a focus on applying that algorithm to video retrieval. Segmentation was done on naturalistic video of human behavior from the Human Speechome Project. We designed various methods to score agreement between human subjects on where one event ends and another begins. We used these scoring methods to test the performance of an algorithm that automatically separated video into segments. Finally, we attempted to use this algorithm to improve the performance of an engine that finds video clips matching natural language descriptions.

Alice Chang
Mentor: Professor Ronald Breslow, Columbia University

Synthesis of Water-soluble Polyimidazoles and their Effects on the Kinetics of RNA Cleavage

The goal of the project is the synthesis of small, water-soluble molecules bearing imidazole units. Imidazole in the histidine side chain is central to the activity of the enzyme RNAse A, whose imidazole rings catalyze the RNA cleavage by a bifunctional acid-base mechanism. Because RNA cleavage takes place in solvent water, any water-soluble polyimidazoles we design could be effective enzyme mimics and potential drugs. A novel imidazole compound was designed and used toward amide bond formation with the triamine. The product was easily purified in high yield. Future plans include trying metal ligands and different amine substrates, reducing agents, and protecting groups. Once a promising water-soluble polyimidazole is made, RNA cleavage experiments can be conducted.

Vadim Chanyshev
Mentor: Professor Daniel Rabinowitz, Columbia University

The St. Petersburg Paradox

The St. Petersburg Paradox is a relatively well known problem in game theory, which is famous for having no numerical solution. The problem describes a lottery game that is played by flipping a coin as many times as needed until it results in tails. Every time the coin is flipped, however, the payoff is doubled. The paradox of the problem is that the expected payoff is impossible to calculate. However, that does not mean that the game is not playable in practice. Working on this problem in the past I have found a way to estimate the expected payoff at a certain confidence level, which is useful for finding the average loss the lottery can expect to have with each game it allows its customers to play. This summer I developed a process to calculate exactly what the chance is of the lottery going bankrupt after any number of games played by its customers. This process makes it possible to quickly generate thousands of possible sequences of outcomes which can then be distributed in a systematic fashion. After that is done, I am able to find the probabilities of any of these sequences occurring. This will, in the end, allow me to take the sum of these probabilities and find the risk of the lottery going bankrupt with an undefined loss or making a profit.

Woo Chang Chung, Joon Ho Kang & Hyoun Ju Sohn
Mentor: Professor Abhay Narayan Pasupathy, Columbia University

Atomic Force Sensors with Sub-Angstrom Resolution

Traditional cantilever atomic force microscope (AFM) sensors use amplitudes of several angstroms to scan surfaces, thus limiting their resolution and vibrational performance. We describe the use of a high-stiffness length extensional quartz resonator (LER) oscillating at 1 MHz with sub-angstrom amplitudes as a force sensor for AFM. We use sharpened carbon fibers as force-sensing tips that are mechanically attached to the LER without degradation of the quality factor of the resonance. We describe the sharpening procedure used to generate carbon fiber tips with 100-200 nm curvature radius, as well as the assembly of the sensing device. Resonance frequency varies according to the distance between the sample and the tip, and by measuring the change in resonance frequency of LER we are able to plot the force curve. The distance was controlled at the nanometer scale using the piezo-distance coordinator, and the resonance frequency at each displacement was measured with a lock-in amplifier. Force curve graphs show the attractive and repulsive force regions of the tip-surface interaction. We demonstrate that these sensors can be used to perform high-quality simultaneous electron tunneling and force measurements.

Jay Dhuldhoya
Mentor: Professor Lily Wu, David Geffen School of Medicine, UCLA

Employing Lymphangiogenesis and Chemokine Induced Migration Assays to Study the Role of CCR7 in Prostate Cancer Metastasis

Prostate cancer mortality is commonly the result of metastatic dissemination of the primary tumor to distant sites. Recent evidence suggests that the lymphatic system may be in important conduit for the spread of tumor cells to regional and distant lymph nodes. Furthermore, we have shown that overexpression of the lymphangiogenic factor VEGF-C increases the incidence of prostate cancer metastasis to drainage lymph nodes. Analysis of these lymph node metastases showed upregulation of the chemokine receptor CXCR4, implicating its role in the metastatic process. CXCR4 and its ligand SDF-1 (CXCL12) normally function to traffic immune cells through the lymphatic system. Aberrant expression of these chemokine receptors on tumor cells may allow them to utilize this chemotactic system to traffic to distant sites. First, we investigated the pathway of lymphangiogenesis in the presence of different cell types that comprise a tumor. Lymphatic endothelial cells (LECs) were transfected with red fluorescent protein (RFP) and plated on top of a layer of matrigel and tube formation was observed. The experiment was also performed after mixing LECs with one or more of the following cell types: Hi-Myc prostate cancer cells, Hi-Myc overexpressing VEGF-C, 3T3 fibroblasts, and J774 macrophages. Data was collected by a live cell scope which took bright field and fluorescent images of the sample every 15 minutes over a 12 hour time period. Image and video results show a significant increase in branching and vessel length when the LECs are plated in combination with tumor cells or fibroblasts. Another principle objective was to see the effects of CXCR4 overexpression on the migration of tumor cells to lymphatic vessels. A layer of LECs was plated below an 8 μm thick transwell insert. Wild type Hi-Mycs expressing GFP and CXCR4 Hi-Mycs expressing RFP were plated on top of the transwell insert and both cell types migrated through the insert toward the LECs. After 8 hours, on average 20% more CXCR4 Hi-Mycs migrated through than did WT demonstrating the chemokine axis likely plays a direct role in trafficking tumor cells to the lymphatic system. More quantitative analysis needs to be done, but it seems that CXCR4 and VEGF-C reinforce each other with tumor cells producing VEGF-C to increase lymphatic growth, which in turn releases more chemokine signaling to traffic the tumor cells.

Alexandru Georgescu
Mentor: Professor Robert Mawhinney, Columbia University

Lattice Quantum Chromodynamics

There are four fundamental forces in nature: gravitational, electromagnetic, weak and strong. The quantum theory of the strong interaction, called quantum chromodynamics, is mediated by gluons "pulling together" quarks. For example, a proton is the result of three quarks kept together by the strong force. At the moment, we are unable to calculate the integrals required by this theory analytically and our only method of getting any theoretical result is Lattice Quantum Chromodynamics. This consists of discretizing space-time and treating it numerically on a grid, and it leads to many theoretical difficulties as space-time is inherently

continuous and not a grid. However, it is currently our best approach. My work consists of writing simulations for Lattice QCD and fitting data with the purpose of determining whether the particle called the sigma meson, whose existence is governed by the strong force, becomes a stable particle at high enough energies.

Zachary Gray
Mentor: Professor Amber Miller, Columbia University

Constructing Frequency Selective Surfaces for Observation of the CMB

The Cosmic Microwave Background (CMB) is a bath of electromagnetic radiation spread isotropically throughout the sky. Its uniform temperature (2.7 K) suggests that the constitutive photons were once in thermal contact, providing sufficient motivation for the Big Bang theory. In order to study the CMB, Frequency Selective Surfaces (FSS) are needed to filter well-defined CMB frequencies from foreground noise. Specificity for a given frequency can be achieved by etching a conducting material such as copper onto a substrate in an appropriate periodic pattern. The relationship between frequency transmittance and surface pattern is the subject of this study.

Stephen Hancock,
Mentor: Dr. Richard Norton, University of Oxford

Slow-Motion Manifolds in Equation for Phase Separation

We study the nonlinear diffusion equation u_t = e^2u_xx - f(u) with boundary conditions u_x(0,t) = u_x(1,t) = 0 and x in (-1, 1), as the diffusion coefficient e approaches 0. Here f is a smooth odd function with exactly three distinct zeros at 0 and +/-1. We further assume f'(+/-1) > 0, from which it follows that F(u) for which F'(u) = f(u) has two equal minima at u = +/-1. We can also write our equation as a gradient flow of an energy functional as u_t = -dI(u)/du, where I(u) is the integral over x from 0 to 1 of e^2u_x^2/2 + F(u). Thus the solution seeks to decrease energy at the fastest rate.

This equation is the simplest mathematical model for the coexistence of two phases of a substance at its transition temperature. In this context, u is an order parameter related to the microscopic structure of the matter in such a way that u near -1 corresponds to one of the two phases (e.g. liquid) and u near 1 corresponds to the other phase (e.g. solid). F(u) is the free energy of the matter, and its two equal minima correspond to the fact that the two phases have the same free energy at the transient temperature. The e^2u_x^2/2 term in the expression for I(u) is added to penalize high gradients of the order parameter and hence to model the tendency of the substance to minimize the number of interfaces separating the two phases.

For e small, the solution should behave like u_t = -f(u) for fixed time, which rapidly approaches a step function with values at u = +/-1. This steepening will be balanced by diffusion, and we end up with a metastable pattern of small-width transition layers between these two limits. It can be shown that u = +/-1 are the only stable stationary solutions, so in

general the layers must move, although they do so over an extremely long time scale of order exp(-A/e).

One can obtain a system of ODEs for the slow motion of these layers, and one of my major results is recovering a derivation of these equations, previously done in the unpublished notes of J. Neu. Another theoretical result is two proofs giving a quantitative upper bound on the smallness of epsilon required for the development of transition layers, one drawn from the approximations made in my derivation of the equations of motion and the other using an energy-type method.

Max Horlbeck
Mentor: Professor Jonathan Weissman, UCSF

Working Toward a Human EMAP

Epistatic Mini-Array Profiles (EMAPs) are a method for discovering novel genetic interactions, and quantifying existing ones, in order to elucidate molecular pathways. Originally developed in yeast, they use a two-dimensional matrix of double gene disruptions to discover novel genetic interactions and assign functions to uncharacterized genes. We are currently implementing the EMAP method in human cell lines by knocking down genes using RNAi. We infect cells with short hairpin RNA (shRNA) libraries to knock down gene expression, and treat cells with toxins that exploit specific cellular pathways. The cell population enriches for shRNAs that confer resistance to the toxin, identifying genes involved in those pathways. Because shRNAs have highly variable effectiveness and have not been characterized as well as short interfering RNAs (siRNAs), we test the enrichment of 30 shRNAs per gene. I first demonstrated that enrichment corresponds with target mRNA knockdown, although the proportionality depends on the gene being targeted. Using this information, I analyzed properties of the shRNAs and targets that correlated with enrichment. Properties shown to be important for siRNA effectiveness, as well as other factors like target secondary structure, did not appear to have a significant effect. In addition, I investigated potential off-target effects in the experiment using a genetic algorithm approach, and identified the subcellular localization of uncharacterized hits by fluorescence microscopy.

Jonathan Huggins
Mentor: Professor Liam Paninski, Columbia University

Optimal Experimental Design for Sampling Voltage on Dendritic Trees

This research used statistical and optimization techniques to better understand measurements taken from individual neurons in the brain and to determine how to make the most useful measurements possible. Within a neuron, signals are sent electronically as a voltage. Measuring the voltages gives insight into the properties of the neuron and how the neuron is processing information. There are various techniques for measuring the voltage across a neuron's membrane, but these measurements can be taken at only a few locations at a time and are quite inaccurate (noisy). Therefore, the voltages at all other points along the neuron must be inferred and the noisy data must be "smoothed out." Utilizing a common statistical

tool called a Kalman filter, this research sought to smooth the data and perform the inference by choosing observation locations that were as meaningful as possible (they reduced the expected error of the predictions the filter would make). These optimized observation schemes were compared to some very simple ones like taking random observations or taking observations evenly spaced over the whole neuron. Our observation schemes were 30-100% better than the naïve ones, depending on how many observations were being made simultaneously.

Michael Kennelly and James Nugent
Mentor: Dr. David Kagan, Columbia University

Methods for Modeling Compactification of Calabi-Yau Manifolds

Superstring theory predicts six additional spatial dimensions in addition to the three dimensions of space and one of time with which we are familiar. Assuming that string theory is correct, the extra dimensions provide a means of unifying the four known fundamental interactions of physics, the Strong Nuclear, Weak Nuclear, Electromagnetism, and Gravitation. However, since we do not interact with these dimensions in our macroscopic life, a theoretical approach is necessary to explain why we do not see them. The most standard approach is to compactify them, that is, to make them very small. While there are many shapes that these compactified dimensions could take, the primary candidate is a class of manifolds called a Calabi Yau manifold.

We sought to develop computational techniques to analyze fourteen such Calabi Yau Manifolds that were identified. These fourteen manifolds were chosen because they allow a direct, hands-on set of examples for studying the physics of giving such parameters a large mass. Using Mathematica and C++, algorithms for modelling the geometry of these Calabi Yaus were developed using Meijer G functions and Hypergeometric functions. They were then revised to maximize both accuracy and processing time. These general algorithms could then be used to explore some of the physics involved in introducing large masses for the parameter field controlling certain geometrical aspects of the Calabi Yau.

Alexis Kurmis
Mentor: Professor David Schiminovich, Columbia University

Decoding Galaxy Properties Using Infrared Observations from the Spitzer Space Telescope

The study of galaxies and their evolution requires conversion of the measurements of flux, color, angular size and other spectral and morphological signatures into physical measurements such as stellar (and dark matter) mass, temperature, luminosity, physical size, age, chemical content and structure. Measuring these physical properties is important because it permits a direct test of models of galaxy formation that predict how galaxies will be distributed among these properties.

The data for this project are images and spectra of galaxies that have been studied as part of the Sloan Digital Sky Survey (SDSS), a large optical survey that has been carried out over

the past decade. Our data include ultraviolet images from the Galaxy Evolution Explorer mission (GALEX) as well as mid-infrared images and spectra from the Spitzer Space Telescope.

As part of this project, we studied correlations among the observed quantities (wavelength, flux, and ratios of emission lines), and used a new software package called Processing to improve the display and interpretation of results. The data for each galaxy were fitted to multiple physical and empirical models to determine both what type of galaxy it is, and whether we could constrain physical conditions within the galaxy (dust mass, hardness of UV radiation field) that depend on various factors, including the rate of star formation and the presence of a supermassive blackhole. We demonstrate that the addition of mid-infrared measurements, and in particular a measurement of the Mid-IR spectral slope, provides new insight into the diagnostic diagram, and valuable information regarding the physical conditions within the galaxies in our sample.

Andre Lazar
Mentor: Professor Michael Sheetz, Columbia University and University of Singapore

Stretching Filamin at the Cell Edge in the Context of Cell Motility

Understanding the actin cytoskeleton is central to figuring out how both mechanical and chemical signal transduction occurs in the cell. Actin-based cell motility is a complex mechanical system involving many structural and signaling proteins. The current model for cell motility is based on focal adhesions, which are large complexes of many actin-binding (and other) proteins. Filamin is an integral protein in the actin cytoskeleton, binding both to actin (and helping to form the actual network), other filamin proteins (dimers) and to different proteins associated with focal adhesions. We investigated Filamin A's mechanical conformations in relation to its various functions by tracking the hypothesized stretching in the cell. Filamin is stretched in the cell in order to expose previously hidden domains, which allow it to strengthen focal adhesions. We show through fluorescence microscopy and statistical analysis that Filamin is indeed stretched in the cell in excess of 500nm.

Christopher Lopez
Mentor: Dr. David Shea Vela-Vick, Columbia University

Legendrian Knots and the Characteristic Algebra

We studied an invariant of Legendrian knots called the characteristic algebra. A Legendrian knot is a closed curve in 3-dimensional space R^3 that is tangent to a contact structure on R^3. Contact structures originated in Sophus Lie's seminal work on differential equations and have applications in areas of physics – such as optics and thermodynamics – and applied mathematics – such as control theory. We used analogues of standard results from algebraic topology to determine if the abelianized characteristic algebra, a simplified version of our Legendrian knot invariant, distinguishes topological knot types. The desired equivalence had already been shown for the special case of Legendrian twist knots; we used algebraic

topology results to investigate the conjecture in the case of the subclass of rational Legendrian knots.

Man-Yu Moy
Mentors: Dr. Yongbo Lu, Dr. Rena D'Souza, Texas A&M Health Science Center

Twist2 & E12 Regulation of Fgfr2 Expression in MDPC During Tooth Development

Tooth agenesis is a tooth developmental anomaly in which certain teeth fail to develop at all and in familial tooth agenesis, the basis for this disorder is genetic. Incidence of tooth agenesis varies from 1.6-20% of the population depending on the tooth. Tooth agenesis, whether due to genetics or not, can compromise oral health, orofacial balance, speech development, and self-esteem. Hence, understanding the genetic basis behind familal tooth agenesis is an important first step toward treatment or prevention of the condition.

Twist1 and Twist2 are two transcription factors that have been found to regulate mesenchymal dental pulp cell (MDPC) differentiation in tooth development. There is evidence that Twist1 upregulates production of growth factor Fgfr2 in MDPCs. Meanwhile, another MDPC regulatory protein E12 has been found not to upregulate Fgfr2 by itself. However, coexpression of Twist1 and E12 creates a synergistic effect that greatly enhances Fgfr2 expression. In this study it was hypothesized that due to the similar nature between Twist1 and Twist2, Twist2 should upregulate Fgfr2 in MDPCs as well and Twist2 and E12 should produce the same synergistic effect. The effect of Twist2 on Fgfr2 expression was determined as were the synergistic effects with E12. Results showed that Twist2 does in fact upregulate Fgfr2 in MDPCs and like Twist1 has a synergistic effect with E12 on Fgfr2 production.

Dan Margulies
Mentor: Professor Nicholas J. Turro, Columbia University

Click Functionalized Small Molecules for Construction of Complex Architectures

Dendrimers are large molecules constructed out of smaller units through sequential branching; they are a subcategory of polymers. Click chemistry is a chemical methodology based on the use of reactions that are high yielding, easily purified, and modular. Of particular note are the Cu(I) catalyzed Azide-Alkyne Cycloadditon (CuAAC) and the Diels-Alder cycloaddition (DA). Dendrimers have been shown to have application in studying the interaction between large molecules in aqueous solution. Additionally, dendrimers are being considered for use as transport capsules for drug delivery and molecular encapsulation. Surface functionalization using click chemistry permits the customization of dendrimeric materials. Dendrimers can be constructed to have free alkyne termini on their surfaces and internally, allowing for click chemistry with azide functional small molecules. Small molecules incorporating azide functionalities were synthesized by DCC coupling of 6-azidohexanol and carboxylic acids, for functionalization of alkyne terminal click polymers and polymeric architectures. Structures were confirmed using ^{1}H NMR and ATR-IR spectroscopy. Future research includes construction of click dendrimers, and the use of the

above molecules in studying their internal structure. Photoactive aromatic ketones (benzophenone, xanthone) can be used to study photo-radical crosslinking in the polymeric structure. Fluorescent groups (pyrene) can be used to determine surface coverage and reaction yield, as well as for fluorescence imaging.

Julia Oktawiec
Mentor: Professor Jeannette Chloe Bulinski, Columbia University

Investigation of the Effect of Novel Profiling Compounds on Microtubule Destabilization

Microtubules are important components of the cell's organizational and mechanical structure, with diverse functions that range from organizing the chromosomes during mitosis to helping transport proteins and organelles around the cell. As a result of microtubules' integral role during cell division, drugs that act on them often have significant effects that can be exploited to treat certain diseases, such as cancer, which rely on rapid proliferation of affected cells. A recent study looked at a set of potent novel profiling compounds (NPCs), NPC4, NPC7 and NPC25, that appear to act as microtubule destabilizing drugs (Wolpaw et al., unpublished). Microtubule sedimentation assays were performed to examine the NPCs' effect on microtubule polymerization. However, their action did not appear to be as potent as existing microtubule destabilizing drugs, especially in vitro, in the presence of the microtubule-stabilizing drug Taxol. Images from immunofluoresence confirmed earlier data that the NPCs acted similarly to microtubule destabilizing drugs, by acting on the ends of the microtubules. Future experiments to test the in vitro effects of these compounds on tubulin isolated from bovine brain tissue and from cancer cells are needed to elucidate their mechanisms of action.

Jungsik Park
Mentor: Professor Michael Strano, MIT

Carbon Nanotube-Guided Thermopower Wave Velocity Oscillations

The Strano group at MIT recently caused powerful thermopower waves of energy to shoot through the nanotubes – wire-like molecules billionths of a meter across. The minuscule tubes coated with a chemical fuel can act as a power source with 100 times more electrical power by weight than conventional batteries. Just a tiny amount of energy is needed to generate the energy wave. Not only that, these devices can maintain their power indefinitely until used, unlike the conventional batteries. Therefore, it is expected that these thermopower waves can replace conventional fuel cells, an electrochemical cell that converts a source fuel into an electrical current. Studying aspects of the thermopower waves during this summer, we found that wave velocity of the waves oscillates for certain values of the chemical reaction kinetics and thermal parameters. Using Comsol Multiphysics, we theoretically simulated this phenomenon. As a result, we could obtain two phases of distinct oscillations as the value of beta (inverse adiabatic temperature) increased. As the oscillation of thermopower waves is linked to oscillations in the voltage generated by the reaction, we can design new types of nanoscale systems capable of generating alternating current.

Milesh Patel
Mentor: Professor Brent Stockwell, Columbia University

A Kinome shRNA Screen Identifies the Role of Phosphorylase Kinase in Mediating Erastin-induced Cell Death

The purpose of this study was to define a novel cell death mechanism induced by Erastin, a compound found to selectively kill tumor cells harboring oncogenic RAS mutations. Our approach was first to identify genes mediating Erastin induced cell death (EICD). We used shRNA technology to knockdown the expression of specific kinase genes in two cancer cell lines, HT1080 and U2-OS, and then measured resistance to Erastin treatment. Genes important to the Erastin cell death mechanism showed significant rescue when those genes were suppressed using shRNAs. From our initial screen, primary hits (genes that showed significant rescue) were retested in a number of different biological replicates to ensure their validity. We identified four genes – PHKG2, PIK3R3, NRAS and KRAS – that should play crucial roles in EICD. shRNA is prone to off-target gene knockdown. Therefore, only genes for which at least two different shRNAs targeting the same gene showed decreased expression using RT-qPCR were considered hits. We performed three follow-up experiments on PHKG2, the catalytic subunit of phosophorylase kinase (PHK), to confirm its role in EICD. Calcipotriol indirectly activates PHK; treatment with Erastin and calcipotriol showed greater cell death than Erastin treatment alone. K252a inhibits PHK; treatment with Erastin and K252a showed less cell death than Erastin treatment alone. PHK activity is also dependent on the presence of calcium; removing intracellular calcium with BAPTA-AM showed suppression of EICD. Since PHK activates glycogen phosphorylase, an enzyme that metabolizes glycogen into glucose-1-phosphate, these preliminary results suggest glucose metabolism may play a significant role in EICD.

Alexander Perry
Mentors: Dr.Aaron Lauda and Dr. Sabin Cautis, Columbia University

Categorification of Quantum Groups.

We studied the categorified representation theory of U_q(sl_2), the quantized enveloping algebra of the Lie algebra sl_2. Lie algebras arise in mathematics as a way to study Lie groups (groups with a compatible differential structure) – given a Lie group, the tangent space at the identity is naturally a Lie algebra. The Lie algbera sl_2 is the simplest and most basic Lie algebra. Given a Lie algebra g, the enveloping algebra U(g) is an associative algebra with the same representation theory as g. Quantum groups are deformations U_q(g) of the enveloping algebra U(g) of a Lie algebra depending on a parameter q. The structure of their representation category can be used to give invariants of knots. This is an instance of general philosophy that we can study algebra by diagrammatics/geometry and low dimensional topology by "quantum" algebra. Part of this program involves "lifting" the algebra to categories – and even so-called "higher" categories – to get more refined geometric invariants. Aaron Lauda realized U_q(sl_2) as the Grothendieck ring of a 2-category, and showed with Mikhail Khovanov how to categorify its representations. The goal now is to study the 2-representations of this 2-categorification. As a first step we found

this summer an explicit basis for the algebras whose category of modules categorify the U_q(sl_2) representations. We are currently extending the 1-categorical action of U_q(sl_2) on these module categories to 2-morphisms.

Pawel Przytycki
Mentor: Professor Chris Wiggins, Columbia University

Using Protein-Protein Interaction Data to Increase Statistical Significance in Genome Wide Association Studies

A variation in a single nucleotide between members of a species is called a single-nucleotide polymorphism (SNP). The goal of genome-wide association study (GWAS) is to uncover correlations between genotypic variations, such as SNPs, and observable traits (phenotypes) such as race or a disease. It is hoped that such genetic associations can help identify the genes or genomic regions that impact a given trait. However, because the entire genome, with thousands or millions of SNPs, is being examined for possible association, many statistical tests are being performed at the same time and the problem of multiple hypothesis testing arises. The goal of this project is combine known protein-protein interaction (PPI) information with genotypic variation data in order gain more statistically significant associations. PPI networks have been shown to be modular in nature, meaning that proteins can be grouped into functionally coherent clusters. We hypothesized that such clusters co-evolved and thus rather than testing for association of individual SNPs with a given trait one can test for association of genotypic variation of whole clusters with that trait. Three tag SNPs were chosen to represent each cluster and we tested the independence of these triplets of SNPs versus bipolar disorder. Finding five SNP sets that were significantly correlated with the disease, we validated the method through literature searches and found that three of the genes associated with these SNPs have some known association with the disease. This method seems to have found disease correlated SNPs that would not have been found without clustering, suggesting the utility of this new approach.

Cecilia Schudel
Mentor: Professor Julia Hirschberg, Columbia University

Realizing Emotional Faces in a Text-to-Scene Conversion System

For those without special training in computer graphics, it has traditionally been a challenge to render complex 3D images, especially those that convey realistic human emotion. WordsEye (Coyne & Sproat, 2001) is a text-to-scene program that represents a user's text input with a 3D image using computer graphics. In this project, we succeeded in improving WordsEye's emotion-modeling capabilities and developed an extensive library of facial expressions. The face library was built using the FaceGen 3D graphics package, which allows for high-level control of facial features based on statistical modeling. We incorporated FaceGen capabilities into WordsEye, allowing users to choose faces of well-known people and specify particular emotions for these faces in their input.

We tested the success of our augmented version of WordsEye in a Harlem-based summer enrichment program for 6th grade students, who used the system in an English literature class. Before the class began, students provided a writing sample. Over the course of five weeks, students were asked to re-create scenes from Aesop's *Fables* and George Orwell's *Animal Farm* in WordsEye. They then provided a new writing sample at the end of the class. Our findings showed that students who used WordsEye as a part of the class scored significantly higher on written essays than students who took the same course without WordsEye. One student explained how WordsEye increased his understanding of course assignments: "When you read a book, you don't get any pictures. WordsEye helps you create your own pictures, so you can picture in your mind what happens in the story." Future work includes fully integrating all of FaceGen's face-manipulation capabilities into WordsEye and developing an analysis component for WordsEye to infer emotions from input text and select the appropriate emotional face.

Jenny Shao
Mentors: Dr. Malcolm Moore and Dr. Server Ertem, Sloan-Kettering Cancer Center

Identification of Cancer-Stem Cell Specific Agents via High-throughput Screening

The resistance of ovarian cancer to current therapies such as chemotherapy and radiation pose a significant impediment to designing treatments for later-stage cancer patients. Previous studies conducted in the lab have given rise to a promising hypothesis, namely that this resistance may be traced back to a specific tumor population now known as cancer stem cells (CSCs). As the name implies, this group of cells exhibit stem cell-like properties, especially that of self-generation, and are capable of generating tumors *in vivo*. By identifying the chemical and biological agents that are effective against CSCs, this research sought to determine the mechanisms of CSCs responsible for their resistance. Experimental results obtained shed light on clinical observations. An analysis of high-throughput data showed that primary clinical compounds such as Taxol yield very low efficacy on the CSCs. Indeed, the CSC cell population was confluent at high dosages of the clinical compounds and only effective at concentrations that would be lethal to the patient. Further, the time course demonstrated that resistance increased significantly as the CSC cell population (and corresponding tumor) matured. Since CSCs have thus been shown to be resistant to current clinical drugs and chemotherapy, the results obtained suggest that CSCs may be a primary cause of resistance in ovarian cancer.

Katharina Shaw
Mentors: Dr. Weimin Liu, Dr. Yingying Li, & Dr. Beatrice H. Hahn, University of Alabama

Detection of Plasmodium vivax*-like Parasites in Wild-living African Apes*

The human malaria parasite *Plasmodium vivax* is responsible for 25-40% of the ~515 million annual cases of malaria worldwide. While *P. vivax* accounts for over 50% of malaria cases outside of Africa, it is not thought to be transmitted in western and central Africa because of the very high prevalence of the red blood cell Duffy-negative phenotype in local populations (a condition thought to confer resistance against blood infection with *P. vivax*). Nonetheless,

there are persistent reports of travelers returning from these geographic regions with *P. vivax* infections, which raises the question: Is there currently a non-human reservoir of *P. vivax* in western and central Africa? I used conventional PCR and single genome amplification (SGA) strategies to show that wild-living African apes are naturally infected with *Plasmodium* parasites that are nearly identical to human *P. vivax*. These findings suggest that there might be an ape reservoir of human *P. vivax* infection in central Africa, which could explain the presence of this parasite in travelers from this geographic region.

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The Categorification of Quantum Groups

Quantum groups are algebraic structures whose representation theory can be used to construct invariants of knots. A knot invariant is a function from the set of all knots to any other set defined in such a way that the function does not change for equivalent knots. Equivalent knots are defined to be knots which can be transformed into one another through a series of moves such as (un)twisting and (un)looping (but not cutting). In other words, knot invariants help us to determine which knots are different.

A categorified quantum group is a more sophisticated algebraic structure that can be used to give more interesting invariants of knots and conjecturally 3-manifolds, or even 4-manifolds, which are higher dimensional analogues of knots.

One interesting aspect of categorified quantum groups is that they can be defined using a diagrammatic calculus. In this calculus, complicated algebraic computations can be reduced to manipulations involving planar diagrams. One of the central themes is turning algebraic problems into diagrammatics where topological intuition can be applied.