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List of CSI CRSP students and their abstracts presented at the 2017 CRSP Symposium

Exploring GBM-targeting drug synergism using 3D cell culture model system

Abisola Shittu and Briana Sampson
Mentor: Professor Nancy Liu-Sullivan

Glioblastoma multiforme (GBM) is the most aggressive form of primary CNS malignancy with an average survival rate of slightly over one year. There is no available efficacious chemotherapy for GBM. The only available drug called Tomozolomide (TMZ) is used to treat cancers metastasized to the brain from other organs. GBM does not response well to TMZ. This dire situation calls for the high need to discover novel treatment strategies for GBM. Transforming growth factor beta (TGFb) is a master cytokine that regulates key cellular processes including cell proliferation, differentiation, apoptosis, and migration. TGFb is found to be significantly elevated in GBM tissue, making it an attractive molecule as a therapeutic target. A TGFb inhibitor called LY2157299 is currently undergoing phase II clinical trial but only effective at GBM elimination for less than 50%, not an acceptable statistics for GBM patients. Under the mentorship of Dr. Nancy Liu-Sullivan of the College of Staten Island, we have explored combination possibilities of LY with other compounds that also influence cytokines signaling in GBM tumor sphere formation and migration. In my oral presentation, I shall describe our exciting findings and discuss the significance in addition to future perspectives.

Towards Real Time Crime Forecasting Using Machine Learning Methods

Tatiana Anderson
Mentor: Professor Feng Gu

Crime forecasting can be used to identify and analyze crime patterns and trends so that police officers can prevent and stop crimes before their occurrences. It is a challenging task to predict crimes because many factors decide the occurrence of a crime, such as individual characteristics, interactions with peers and families, time, available police resources, and situational factors including weather, events, lightning, audiences, etc. Traditionally, regression models, statistical approaches, and other simulation models are developed to qualitatively and quantitatively study the relationship between the occurrences of crimes and different factors for detection and prevention. But in many scenarios, it is hard to accurately predict real time crimes using those

methods due to many reasons including complexity of the system, interactions among different factors, and limited data availability. In this work, we plan to apply machine learning methods to forecast real time crimes by automatically detecting situational factors including liquor stores, bus or subway stations, demographics, etc of the occurred criminals. The criminal data from the Portland Police Bureau from 2012-2017 will be used to verify the effectiveness of the used methods.

Design and Feedback Control of a Robotic Arm

Mobin Uddin Chowdhury and Melvin Summerville
Mentor: Professor Aleksandar Haber

This project aims at developing a robotic arm with three degrees of freedom capable of performing precise positioning and trajectory tracking. The prototype will be developed from the scratch using affordable components such as Nema 23 stepper motors, Makerbeam aluminum extrusions, rotary encoders, Arduino microcontrollers, etc. Most of the moving parts including bevel gears, spur gears, and the rotary base will be 3D printed.
As a result of the first phase of the project, we present a robotic joint composed of a stepper motor, spur gear reducer, relative rotary encoder, electro-mechanical end stops, as well as an Arduino microcontroller. We have implemented a PID control algorithm whose purpose is to rotate the joint to a desired angle. The rotary encoder measures and sends the angle information to the microcontroller which then calculates the control actions for the stepper motor. The challenge is that the rotary controller is of a relative type, meaning that its zero position is determined by the system's initial position. Consequently, the desired angle cannot be achieved. This is solved by including an electromechanical end stop. When the system is started, the joint rotates until it reaches the end stop. The end-stop determines the zero position of the system, and starting from this position any desired angle of rotation can be achieved. The second problem we addressed is related to the fact that initially the stepper motor could not produce enough torque to lift the load attached to the joint. This challenge is resolved by designing a spur-gear reducer that amplifies the torque and reduces the rotation speed. We have 3D printed the reducer, and surprisingly, it is able to amplify the torque such that the load can be lifted. The next stage is to use the 3D printing technology to design and manufacture a moving base.

Neuronal Basis for the Late Onset Ataxia in Fragile X

Mathura Sothylingam and Luis Alvarez
Mentor: Professor Abdeslem El Idrissi

Fragile X syndrome is a genetic condition that is due to a trinucleotide CGG expansion in the premutation alleles along the promotor region of the FMR1 gene. Fragile X associated Tremor/ ataxia syndrome which is caused by these triplet expansion, is considered a neurodegenerative disorder affecting males with late onset (ages > 50 yrs). FMRP is an mRNA binding protein and has been shown to play a role as a transporter of mRNA. Therefore, the absence of FMRP causes improper shuttling of mRNA which leads to abnormal brain development. Since ataxia is a neurodegenerative disorder characterized by abnormal locomotor activity, we hypothesize that the lack of cerebral structure integrity in FMRP (-) brains may lead to underdeveloped Purkinje cells. The importance of Purkinje

cells in the cerebellum is due to their ability to act as a resistance modulators during a high volume of incoming signals from proprioceptors, basal ganglia and other areas of the brain. Thus, we can speculate that histopathologies of cerebellar structures may cause ataxia-like tremors later in life. Through IHC and confocal microscopy, we will be able to explore and compare the structures of the cerebellum in FVB/NJ wild type and KO mice. In order to confirm that ataxia does occur, the DigiGait ataxia machine will be used to measure the footsteps of both groups and evaluate forefront and hind leg coordination. We found a significant alteration in the dendritic tree of Purkinje cells using calbindin and tubulin as markers and a very pronounced aberration in locomotor activity that we think typifies ataxia in these mice.

Insulin receptor expression in the brain and its role in hyper-excitability

MD Zahirul Islam
Mentor: Professor Abdeslem El Idrissi

Brain homeostasis relies on a number of factors that regulate neuronal excitability. Surprisingly one of these factors coincide with the insulin neuroendocrine system. There is ample evidence that insulin play an important role in neuronal excitability. Previous studies have shown that taurine-fed mice have increased insulin sensitivity in the pancreas, when compared to controls during glucose tolerance test. These results also showed an increase in insulin and insulin receptors expression in the pancreas. Our hypothesis is, since insulin is secreted into the bloodstream and does indeed pass through the blood brain barrier, taurine supplementation may increase the expression of insulin and insulin receptors in the brain which determines the levels of excitability in each brain region. Thus we also believe that the increase in taurine supplementation can modulate neuronal excitability. It is important to note that neurons highly express insulin receptors. Furthermore, insulin crosses the blood-brain barrier through a high affinity uptake system. Once insulin passes to the brain, it binds to the insulin receptors and affect neuronal excitability via signal transduction pathway, with differential effects on brain structures. In the cortex and hippocampus, insulin receptor activation has been shown to increase excitability, whereas in the hypothalamus the effects of insulin are inhibitory.
We determined the expression of insulin/insulin receptors in the brain/pancreas through immunohistochemistry and confocal microscopy in 4 different group of mice; the wild type controls, fmr1 KO, taurine-fed (for two months prior to examination) wild type, and taurine fed KO. Our results show that insulin and insulin receptors expression and activation are highly regulated in these treatment groups and indicate that insulin, through activation of its cognate receptor, may regulate neuronal excitability.