Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Nikhil Cheerla and Anika Cheerla
High School: Monta Vista High School, Cupertino CA
Mentor: Dr. Andrew Beck and Dayong Wang
Project Title: Mitosis Detection And Tumor Grading Using Deep Convolutional Neural Networks

Analyzing mitosis proliferation is crucial to physician grading of tumor severity and prognosis. Despite the time and effort poured into automated mitosis detection, no systems have been able to perform at the level of skilled pathologists, who manually examine slide images for mitotic cells.

We build a 100-layer deep GoogLeNet-derived mitosis detector with aggressive data augmentation, and train it with our novel multi-stage bootstrapping algorithm to extract meaningful training examples from highly imbalanced data. Our deep convolutional neural network achieves an F1 score of 0.85 on the 717-image TUPAC dataset. This trained model also generalizes well, surpassing the best F1-scores obtained in previous mitosis competitions.

We then develop a pipeline to grade whole slide images using an intuitive ROI selection algorithm and the trained mitosis detector. The genes identified by our continuous mitosis scores outperform pathologist scores in their association to cancer and cell cycle functions/ pathways. Finally, we build a gene-level model to predict the mitosis scores from RNA-sequence data. From this model, we extract 10 gene predictions possibly linked to tumor mitotic activity.

We hope our research is a step towards a future where physicians use precise, deep-learning- enabled analyses of mitotic activity to diagnose and treat patients.

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Math : Science : Technology
Regional Finalist

Names: Vineet Edupuganti
High School: Oregon Episcopal School
Mentor: Dr. Raj Solanki
Project Title: Development of a High-Performance Biodegradable Battery for Transient Electronics

Traditionally, emphasis has been placed on durable, long-lasting electronics. However, electronics that are meant to intentionally degrade over time can actually have significant practical applications. Biodegradable, or transient, electronics would open up opportunities in the field of medical implants, where the need for surgical removal of devices could be eliminated. Environmental sensors and, eventually, consumer electronics would also greatly benefit from this technology. An essential component of transient electronics is the battery, which serves as a biodegradable power source. This work developed a biodegradable battery using a magnesium-based anode and an iron cathode. Discharge tests showed that magnesium alloy AZ31 extends battery lifetime by over six times, as compared to pure magnesium. With AZ31, the maximum power and capacity of the fabricated device were 67 μW and 5.2 mAh, respectively, though the anode area was just 0.8 cm^2. An equivalent circuit model was developed that accurately captured device behavior, taking into account its intentional degradation, allowing for application-based optimization without extensive experimental testing. The size of the device and the power it produces are in accordance with expected levels for low-power transient systems, indicating that the batteries developed in this research are sufficient for deployment in several application areas.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Kathy Liu
High School: West High School
Mentor: Dr. Jin Liu
Project Title: Nature-Based Solid Polymer Electrolytes for Improved Safety, Sustainability and Efficiency in High-Performance Rechargeable Batteries

Sustainable battery innovation is crucial for meeting accelerating energy demands. Replacing flammable battery liquid electrolytes with solid polymer electrolytes (SPEs) can drastically improve safety, decrease cost, and enable lightweight and flexible designs. SPEs also may be key to realizing much higher capacity lithium sulfur (Li-S) batteries (theoretical capacity 1675 mAh g^{-1} compared to 170 for current Li-ion) by resolving poor cycling caused by polysulfide dissolution in liquid electrolytes. However, SPE application is barred by lower electrochemical performance and poorly scalable processes. This project presents a novel high performance SPE based on sucrose. Electrolyte synthesis was developed and optimized, resulting in higher Li^+ ion mobility than most SPEs and liquid electrolytes, and remarkable 100-fold ionic conductivity improvement compared to polyethylene oxide, the most popularly researched SPE host. Notably, the SPE exhibits excellent electrochemical properties at room temperature and across a wide range, meeting diverse battery needs. Structural characterization confirmed successfully enhanced ion conduction sites from simple cross-linking. Application in all-solid-state Li-S batteries produced impressive performance over hundreds of cycles at both 25 and 45 °C, indicating the efficacy of the SPE as an efficient, low-cost, and high capability electrolyte and Li-S reaction stabilizer for more powerful, secure, and sustainable next-generation energy storage.

Siemens Competition
Math : Science : Technology
Regional Finalist

Name: Sagar Maheshwari
High School: Unionville High School
Mentor: Dr. Gil Alterovitz
Project Title: SiteKey: A Novel Binding Site Predictor for Ordered Proteins Interacting with Intrinsically Disordered Proteins

Intrinsically disordered proteins (IDPs) and intrinsically disordered regions (IDRs) are segments of proteins that lack a defined tertiary structure, giving them the ability to interconvert among a range of conformations and folds. This structural plasticity adds to the complexity of predicting protein behavior and treating numerous diseases. For example, a key tumor suppressor protein p53 has significant regions of disorder and has been associated with lung, breast, and brain cancer. While we now have effective algorithms for predicting ordered binding partners of IDRs, an algorithm for identifying and characterizing binding sites on such proteins has remained elusive, despite some effort. Here we present a novel machine learning algorithm *SiteKey* — a random forest classifier, trained on features derived from both protein sequence and structure, capable of identifying these binding sites with 88.4% accuracy and an area under the ROC curve of 0.9441. These results should provide a new approach to rational drug design in which binding regions can specifically be targeted to prevent major diseases, including cancer.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Rajiv Movva and Randy Zhao
High School: The Harker School
Mentor: Remzi Celebi
Project Title: Computational Prediction of Synergistic Chemotherapy Combinations Reveals Master Regulators of Efficacy

Chemotherapy is a routine treatment approach for early-stage cancers, but the effectiveness of such treatments is often limited by drug resistance, toxicity, and tumor heterogeneity. Combination chemotherapy, in which two or more drugs are applied simultaneously, offers one promising approach to address these concerns, since two single-target drugs may synergize with one another through interconnected biological processes. However, the identification of effective dual therapies has been particularly challenging; because the search space is large, combination success rates are low. Here, we present a computational framework to predict synergistic drug pairs using the largest available combinatorial cell line screening dataset, combining our knowledge of the drugs applied and cell line gene expression to establish gene-drug interactions. Our machine learning model reached an unprecedented Pearson correlation of 0.70 (prediction vs. experimental synergy data) and displayed high concordance with previous drug combination studies. Further, we analyzed our model's predictions to better understand the molecular processes underlying synergy and discovered that key regulators of tumorigenesis such as *TNFA* and *BRAF* are often targets in synergistic interactions, while *MYC* is often duplicated. We ultimately present novel hypotheses for synergistic drug pairs and their mechanisms that are supported by both computational predictions and biological understanding.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Andrew Shao and Arushi Sahai
High School: Lynbrook High School and Menlo School
Mentor: Dr. Elisa Toloba and Prof. Raja Guhathakurta
Project Title: Studying “Orphan” Globular Clusters in the Virgo Cluster of Galaxies

We present a sample of “orphan” globular clusters (GCs) with previously unknown parent galaxies, which we determine to be remote satellites of M87, a massive elliptical galaxy at the center of the Virgo Cluster of Galaxies. Because GCs were formed in the early universe along with their original parent galaxies, which were cannibalized by massive galaxies such as M87, they share similar age and chemical properties. In this study, we first confirm that M87 is the adoptive parent galaxy of our orphan GCs using photometric and spectroscopic data to analyze spatial and velocity distributions. Next, we increase the signal-to-noise ratio of our samples’ spectra through a process known as coaddition. We utilize spectroscopic absorption lines to determine the age and metallicity of our orphan GCs through comparison to stellar population synthesis models, which we then relate to the GCs’ original parent galaxies using a mass-metallicity relation. Our finding that remote GCs of M87 likely developed in galaxies with ~10^{10} solar masses implies that M87’s outer halo is formed of relatively massive galaxies, serving as important parameters for developing theories about the formation and evolution of massive galaxies.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: John Winnicki and Andrew Winnicki
High School: Punahou School
Mentor: Dr. Wen-Ming Chu
Project Title: Double Deficiency of Gαi1 and Gαi3 Leads to Chronic Inflammation-Associated Tumorigenesis

The role of the heterotrimeric Gi1 and Gi3 G proteins in tumorigenesis has not been studied; we now demonstrate that they link inflammation to cancer. Their α-subunits, Gαi1 and Gαi3, are downregulated in 30% of human colorectal cancers, including colitis-associated cancer (CAC). These deregulations are significantly associated with poor survival of human colorectal cancer. We assessed their impact in a CAC mouse model, and found that double Gαi1 and Gαi3 (Gαi1/3) deficiency promoted CAC initiation and progression through STAT3 activation, iNOS induction, myeloid-derived suppressor cell (MDSC) expansion, and CD8 + dendritic cell reduction. Gαi1/3 ablation diminished SHP2 in response to IL6, augmenting STAT3 activation, which stimulates MDSC expansion and inhibits dendritic cell development. Our study suggests that Gαi1 and Gαi3 act as tumor suppressors.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Brian Xia
High School: Canyon Crest Academy
Mentor: Steven de Belle
Project Title: Transgenerational programming of longevity with a low-protein diet: Animal model, E(z)/EZH2-mediated H3K27 trimethylation and early-life epigenetic “immunization” to prevent aging-related diseases

Longevity-extending interventions often prevent multiple aging-related diseases (ARDs) [1-3]. Long-lasting and transgenerational effects on health and disease of early-life nutrition have also gained increased attention [4, 5]. However, such studies have been compromised due to their time-consuming nature and lack of a model system. Here I address whether early-life nutrition programs longevity across generations, H3K27me3 serves as one underlying mechanism, H3K27me3 inhibition extends longevity by preventing ARDs, and similar mechanism functions in humans. Integrative methods were employed for longevity analysis, western blotting and disease characterization across F0–F2 generations after various early-life treatments in F0 flies; and bioinformatics analyses were performed with public metadata and literature information. The low-protein diet was found to 1) reduce longevity across generations, establishing the first animal model to study transgenerational inheritance of nutrition-programmed longevity [6]; 2) upregulate E(z)-mediated H3K27me3, leading to its further characterization as one underlying epigenetic mechanism and identification of EPZ-6438 to extend lifespan [7]; and 3) cause multiple ARDs which could be fully alleviated by post-eclosion administration of EPZ-6438, stimulating my proposal of early-life epigenetic “immunization” to prevent ARDs. Importantly, human EZH2-p53 pathway was found to regulate longevity and same ARDs, supporting H3K27me3 inhibition as a potential multi-disease therapy in humans.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Catherine Zeng
High School: Mission San Jose High School
Mentor: Souful Bhatia, Michigan State University
Project Title: Investigation of H/D Exchange in Aromatic Compounds with a Heterogeneous-Based Electro-Activated Palladium Catalyst

Deuterium-labeled compounds have applications across various industries, ranging from the mechanistic understanding of chemical and biological reactions to their use as internal standards and in the development of optical materials. Recently, they have also been proposed as medicinal agents. By transforming the metabolically labile carbon-hydrogen (C-H) bond to a relatively stable carbon-deuterium (C-D) bond, pharmaceutical companies have introduced deuterium-labeled compounds as an alternative to metabolically labile drugs. Traditionally, hydrogen-deuterium exchange (H/D exchange) has been achieved in high temperature and pressure environments or in a homogenous environment using a transition metal, both of which are unsuitable in an industrial setting. There is a need for a mild, inexpensive, site-selective and environmental-friendly heterogeneous-based approach to develop deuterated compounds. In this project, I develop a new method of H/D exchange for aromatic compounds that utilizes electric current to activate palladium catalyst in an aqueous environment (D_2O). The results showed successful deuterium incorporation into a number of different aromatic compounds, and provided additional insight for the interaction of palladium catalyst with its organic substrates.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Daniel Zhang & Edward Zhang
High Schools: Westview High School & Torrey Pines High School
Mentor: Dr. Jie Zhu, University of California, San Diego
Project Title: *Identification of Novel CpG Biomarkers by Genome-wide Methylation Profiling for Early Diagnosis and Prognosis of Leukemia*

Clinical cancer diagnosis faces many challenges, particularly in its low sensitivity and accuracy for early tumor detection. This project aims to develop a noninvasive early diagnostic platform using leukemia as a model system. Methylation pattern of CpG islands is an epigenetic regulator of gene expression, and extensive alterations of CpG methylation are well documented in cancer. Using genome-wide methylation profiling and computational analysis, we investigated the ability of CpG methylation status to differentiate acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) from normal blood. We discovered four and seven novel CpG biomarkers in AML and ALL blood samples, respectively. These methylation panels could distinguish AML or ALL from normal blood with more than 97% accuracy. Importantly, these CpG islands control genes like MNDA, RBP5, TCF25, GDF15, etc. Expression of these genes are downregulated or upregulated in leukemia, which is consistent with their CpG methylation profiles. We also developed a methylation-based survival classifier which successfully divided patients into high-risk and low-risk groups, with significant differences of clinical outcome in leukemia subtypes. Together, these findings demonstrated that our CpG panels can be highly sensitive and specific in the accurate diagnosis of AML and ALL with implications for prognosis and treatment selection.