UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Balcony, Easel 89

11:00 AM to 1:00 PM

Energetics of Nickel Adsorption on Ceria Thin Films by Calorimetry

Ziareena (Reena) Almualem, Recent Graduate, Chemistry (ACS Certified)
Mentor: Charles Campbell, Chemistry
Mentor: Zhongtian Mao, Chemistry

Metal catalysts exhibit greater catalytic activity as nanoparticles rather than bulk-like particles. Metal oxide supports can promote the activity and stability of metal catalysts due to the strong metal-support interaction, which can change the electronic properties and structure of metal nanoparticles. Metal-on-oxide-support systems are important for fundamental research and applications in heterogeneous catalysis. Nickel-based catalysts are widely used in industrial purposes such as carbon monoxide oxidation for industrial exhaust cleaning. However, nickel can rapidly deactivate due to solid carbonaceous material (coke) formation and nanoparticle coalescence (sintering) on the surface during a catalytic reaction. Metal oxide supports, such as ceria (CeO_2), improve metal catalytic performance by preventing coke formation and sintering, and in particular, ceria has a high oxygen storage and release capacity during catalytic reactions. Here, the adsorption energies, growth morphology, and charge transfer of adsorbed nickel on stoichiometric ceria (CeO_2(111)) and reduced ceria (CeO_1.8(111)) thin films at 300 K and 100 K are studied using single-crystal adsorption calorimetry (SCAC) in ultra-high vacuum (UHV) and surface sensitive techniques such as low-energy He^+ ion scattering spectroscopy (LEIS), X-ray photoelectron spectroscopy (XPS), and low energy electron diffraction (LEED). The initial heat of adsorption of nickel atoms on stoichiometric ceria was ˜45 kJ/mol greater at 300 K than at 100 K and ˜65 kJ/mol greater than reduced ceria at 300 K. The calorimetry results indicate that nickel prefers step edges over terraces and binds stronger to stoichiometric ceria than reduced ceria due to nickel's oxophilicity. LEIS growth mode measurements indicate that nickel grows as 3D nanoparticles. XPS charge transfer experiments show that adsorbed nickel transfers electron charge to ceria below a coverage of 2 monolayers. These results encourage additional study of the adsorption energetics of other group 8 transition metals on ceria supports.

SESSION 1K

PHYSICS: FUNDAMENTAL AND APPLIED

Session Moderator: Alejandro Garcia, Physics

MGH 254

12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Investigating The Effect of Temperature Gradients on An Improved Test of The Equivalence-Principle by Constructing A Thermal Monitoring System

Yifei Bai, Senior, Physics: Comprehensive Physics, Mathematics
Mary Gates Scholar, UW Honors Program
Mentor: Jens Gundlach, Physics
Mentor: Charles Hagedorn, Physics, CENPA

Our research group performs one of the highest-precision tests of Einstein's equivalence principle, perhaps the most fundamental property of gravitation, using a sensitive rotating torsion balance. Among the leading experimental challenges are temporal and spatial temperature variation. Notably, horizontal temperature gradients across the apparatus, if not properly characterized, can emulate an equivalence-principle violating signal. We have implemented thermal shielding and run tests to measure the thermal effects on our measurement. Past tests have shown a need for both absolute and differential temperature sensors with higher sensitivity. Hence, my research project focuses on investigating the effect of temperature gradient on our experiments by constructing a thermal monitoring system. I have designed, laid out, constructed, and tested sensitive bridge thermistor circuits that can function as both absolute and differential temperature sensors. Current tests of our prototypes have shown that temperature sensitivities reaching 10 micro-Kelvin in one second (10^-5K/Hz^0.5). We are scaling-up these sensors and plan to deploy them in this academic year. Successful completion of this project will yield improved understanding of the temperature gradients within our experimental apparatus, allowing us to test the equivalence principle with yet higher precision.

POSTER SESSION 2

Commons West, Easel 23

1:00 PM to 2:30 PM

A Torsion Balance to Measure Gravitational Gradients

Nicholas Orndorff, Junior, Pre Engineering
Mentor: Charles Hagedorn, Physics, CENPA

The equivalence principle maintains that all mass is equally affected by gravity and is fundamental to our understanding of gravitational physics. Torsion balance experiments at the University of Washington have tested the equivalence principle at the 10^-13 level. Torsion balances are susceptible to systematic uncertainty caused by changing gravitational gradients formed in the environment, e.g. rainfall saturation in nearby hills. If changing gravitational gradients could be continuously monitored, then the full torsion balance sensitivity (differential accelerations below $10^-15 m/s^2$) could be reached. The goal of this project is to measure and correct for gravitational gradients. Simultaneously monitoring gravity gradients and testing the equivalence principle requires the construction of a concentric torsional gradiometer. Such an instrument has never been built before, requiring unique geometrical design constraints. Several functional prototypes have been constructed along with a complimentary data acquisition system. Improved equivalence principle limits will further constrain the unification of gravity with the standard model of particle physics.

POSTER SESSION 2

Balcony, Easel 106

1:00 PM to 2:30 PM

Human Stem Cell Derived Cardiomyocyte Maturation is Regulated by Glucose Levels and Metabolic Hormone Supplementation

Heather May Klug, Senior, Biochemistry
UW Honors Program, Washington Research Foundation Fellow
Mentor: Charles Murry, Pathology
Mentor: Elaheh Karbassi

Methods to differentiate stem cells into cardiomyocytes have been well established. However, a limitation for the successful application of these cells for research and medicine has been their fetal-like phenotype with respect to cell size, contractility, calcium handling, metabolism, and electrophysiology. We sought to increase the maturity of human pluripotent stem cell derived cardiomyocytes (hPSC-CMs) through metabolic pathway regulation. We hypothesized that switching the main metabolic substrates from glucose to fatty acids, mimicking the switch from placental to breast milk nutrient consumption that occurs during development, will increase hPSC-CM maturation. RUES2 embryonic stem cells were differentiated into cardiomyocytes and then treated with base media with varying glucose and calcium concentrations and fatty acid supplementation. Using quantitative PCR to measure gene expression, we measured an inverse relationship between glucose levels and markers of cardiomyocyte maturation: increased expression of cardiac troponin I relative to skeletal troponin I isoforms (TNNI3:TNNI1), increased expression of metabolic (CPT1B, PPARGC1A) and electrical maturity markers (KCNJ2, RYR2). These maturation markers were not influenced with fatty acid supplementation but were enhanced upon the addition of thyroid hormone and dexamethasone. We further quantified nucleation and sarcomere spacing to assess structural features of maturation using confocal microscopy. To understand the mechanisms by which media nutrients and signaling molecules cause phenotypic changes we investigated the relationship between maturation and global epigenetic state. Western blot revealed increases in global acetylation levels, measured by histone H3 acetylation, linked to maturation signaling. These findings depict a direct relationship between glucose metabolism and the development of a mature phenotype in hPSC-CMs, mediated by epigenetic mechanisms.

POSTER SESSION 2

MGH 241, Easel 150

1:00 PM to 2:30 PM

Effect of SS-31 on SOD1KO Model of Sarcopenia

Kevin Andrew Nguyen, Senior, Biology (Physiology)
UW Honors Program
Mentor: David Marcinek, Radiology
Mentor: Matthew Campbell, Radiology

Sarcopenia, or age-related of loss of muscle mass and function, is associated with a decline in quality of life for elderly populations and few effective treatment options. Sarcopenia is linked to mitochondrial dysfunction and elevated mitochondrial oxidant production. We are investigating the role of mitochondrial oxidative stress in sarcopenia using a mitochondrial targeted therapeutic and a mouse model of accelerated sarcopenia. SS-31 is a mitochondrial targeted peptide that associates with cardiolipin, decreases oxidant production, and increases ATP production. Superoxide dismutase 1 knockout (SOD1KO) mice lack superoxide dismutase 1 (an enzyme that converts the oxidant superoxide into hydrogen peroxide and molecular oxygen) resulting in an accelerated sarcopenia phenotype. We are testing whether treatment with SS-31 preserves muscle function in the SOD1KO mice. We hypothesize that improving mitochondrial function with SS-31 treatment will delay the decline in muscle function in the SOD1KO mice. To test this, we are administering SS-31 to SOD1KO mice through surgically-inserted osmotic pumps for 8 weeks between 3 and 5 months of age (the

published timeframe for the onset of skeletal muscle decline in SOD1KO mice) and performing in vivo muscle function measurements of the gastrocnemius before pump insertion and monthly after pump insertion for 3 months. We compare muscle functional measurements with histological and biochemical analyses of mouse tissue samples upon euthanasia and determine skeletal muscle fiber type, metabolite and protein concentrations, and muscle fiber respiration and oxidant production. We expect SOD1KO mice with SS-31 to have a lower rate of decline in muscle force production and increased fatigue resistance over time, higher max ATP production, and decreased oxidative stress. The effect of SS-31 on muscle function, mitochondrial quality, and redox homeostasis has exciting potential as a translational therapeutic treatment for human sarcopenia.

POSTER SESSION 2

Balcony, Easel 105

1:00 PM to 2:30 PM

Investigating the Role of Sarcomere Structure in the Proliferative Capacity of Cardiomyocytes to Improve Methods of Cardiac Regeneration

Anna Whitney Klug, Senior, Bioengineering
Levinson Emerging Scholar, Mary Gates Scholar
Mentor: Charles Murry, Pathology
Mentor: Christine Yoo

Myocardial infarction (MI) is the leading cause of death globally. Methods to regenerate cardiac tissue after MI has focused on inducing proliferation in adult cardiomyocytes near infarcted tissue or injecting stem cell-derived cardiomyocytes with proliferative capacity into the infarcted tissue. However, optimal regeneration has not been achieved with these methods, as the mechanism behind adult cardiomyocyte proliferation is not well understood and proliferative stem cell-derived cardiomyocytes are phenotypically and functionally immature. Exploration of the mechanism of cardiomyocyte proliferation is therefore necessary to enable optimal regeneration of cardiac tissue and function and MI. We hypothesize that the sarcomere structure, the basic muscle unit of the cardiomyocyte, is the limiting factor in proliferation of cardiomyocytes. To investigate this hypothesis, we have performed a thorough characterization and comparison of stem cell-derived wild type cardiomyocytes (WTC-CMs) and troponin I double knock out cardiomyocytes (TNNIDKO-CMs) which have an incomplete sarcomere structure due to the lack of troponin I. After confirming TNNIDKO-CMs and WT-CMs only vary in their sarcomere structure, we developed a coculture platform to demonstrate the mechanical weakness of TNNIDKO-CMs sarcomere structure. We then performed proliferation assays utilizing multiple proliferation markers to observe if proliferation was higher in the TNNIDKO-CMs with the incomplete sarcomere structures. Preliminary results have shown that TNNIDKO-CMs are more proliferative than WTC-CMs, thus implicating that sarcomere structure plays a role in controlling cardiomyocyte proliferation. Successful characterization of TNNDKIO-CMs and their increased proliferative capacity will elucidate the sarcomere structure's role in proliferation as well as develop a more comprehensive understanding of the underlying mechanism behind proliferation to help progress therapies for regeneration of cardiac tissue after MI.

POSTER SESSION 2

MGH 241, Easel 148

1:00 PM to 2:30 PM

Characterization of Dynorphin/KOR Circuitry in the Mouse Brain

Sanne Marie Casello, Senior, Neurobiology
Mentor: Charles Chavkin, Pharmacology
Mentor: Antony Abraham, Pharmacology

Chronic stress induces the release of neuropeptides including dynorphin, which activates kappa opioid receptors (KOR) to encode the dysphoric components of the stress response. Dynorphin/KOR actions on dopamine neurons have been shown to underlie aversive learning, and it is hypothesized that potentiation of cocaine reward following stress is likely to occur through similar neural mechanisms. In this study, we investigate the neural substrates underlying stress-mediated enhancement of cocaine reward. First, we verified the reliability of a KOR (KT2) antibody. Immunostaining specificity was verified using KOR-Cre mice which express Cre-recombinase in KOR-containing neurons. By combining cell-specific targeting using Cre-dependent viral expression of fluorophores and immunohistochemistry staining, we confirmed the specificity of anti-KT2 to KOR containing neurons. Using this antibody and an anti-tyrosine hydroxylase antibody, we examined the co-localization of KOR and dopamine in the ventral tegmental area (VTA). Immunohistochemical analyses showed that KORs were expressed in a majority of dopamine neurons in the medial and lateral VTA. Furthermore, we investigated dynorphin-KOR circuitry in the mouse brain. Dynorphin-containing neurons projecting from the prefrontal cortex (PFC) and dorsal raphe nucleus (DRN) to the VTA were identified by injection of a retrograde virus (CAV2-DIO-ZsGreen) into the VTA of prodynorphin-Cre mice. In a separate cohort, an excitatory opsin (Channelrhodopsin2) was injected into the DRN of pDyn-Cre mice with an optic fiber implant. The DRN region was then optically stimulated and resulting KOR phosphorylation was measured in the VTA thereby verifying dynorphin-releasing projections from the DRN to the VTA. This projection was further investigated by examining the effect of DRN dynorphin on stress-induced potentiation of cocaine conditioned place preference (CPP). We found that deletion of dynorphin

from the DRN, but not PFC, blocked stress induced enhancement of cocaine CPP. In conclusion, this experiment demonstrates a functional dynorphin/KOR circuit from the DRN to the VTA that mediates stress-induced increases in drug reward.

POSTER SESSION 3

Commons East, Easel 62

2:30 PM to 4:00 PM

The Impact of Small-Molecular Inhibitors on Error-Correction Mechanisms in Cricket Spermatocytes

Lyda Ebadani, Senior, Public Health-Global Health
Julia Tryon, Junior, Biology (General), Spanish
Mentor: Charles Asbury, Physiology and Biophysics

Chromosome segregation during mitosis and meiosis ensures accurate division of a cell's nucleus to produce daughter cells that each contain a proper set of chromosomes. An important hallmark of mitotic and meiotic cell division is the attachment of microtubules to protein structures called kinetochores. The phenomenon is susceptible to error, causing mis-segregation of chromosomes, which can result in aneuploidy, miscarriage or cancer. During the 1960s, Dr. Bruce Nicklas established the present model for how meiotic error correction transpires. By directly manipulating individual chromosomes in grasshopper spermatocytes, he misaligned individual chromosomes from the metaphase plate and then observed as the chromosomes spontaneously realigned. Dr. Nicklas' work demonstrated that mechanical tension is required for stabilizing proper kinetochore-microtubule attachments, and that the lack thereof results in detachments that allow the chromosome to reorient correctly. The Asbury Lab aims to further his experiments by using small molecular inhibitors in combination with micromanipulation to determine the role of enzymes such as Aurora B kinase in chromosomal error correction. Here, we tested the impact of Aurora B kinase, using a small molecular inhibitor that has been reported in human cancer models, AZD. Cricket spermatocytes were dissected and soaked in a solution of insect medium and AZD. After treatment, the spermatocytes were spread on a glass slide and filmed under a phase-contrast microscope for three hours. Metaphase cells were filmed because it is expected that Aurora B kinase releases erroneous attachments during this phase of cell division. Our results show that AZD treatment of cricket spermatocytes delays the transition from metaphase to anaphase, confirming that Aurora B kinase plays an important role in chromosome segregation in these cells. Our latest work focuses on fluorescent tagging of chromosomes to better distinguish misaligned chromosomes and to further understand the mechanisms of error correction.

POSTER SESSION 4

Balcony, Easel 93

4:00 PM to 6:00 PM

Heats of Adsorption of N2, CO, Ar and CH4 versus Coverage on the Zr-Based MOF NU-1000: Measurements and DFT Calculations

Graeme Oliver Vissers, Senior, Biochemistry
Mentor: Oscar Vilches, Physics
Mentor: Charles Campbell, Chemistry
Mentor: Wei Zhang, Chemistry

Metal-organic frameworks (MOFs) represent an important new class of adsorbent materials, catalysts, and catalytic supports. As such, it is important to fundamentally understand its adsorption capacity and selectivity of simple gases. NU-1000 is a prototypic zirconium-based MOF which has shown to be thermally stable up to 250 C and has a number of interesting catalytic and adsorbent properties. It is composed of zirconium oxide nodes connected by pyrene linkers with COO- end groups. We determined the isosteric heats of adsorption (Qst) versus coverage of four gases (N2, CO, Ar, and CH4) on NU-1000 by measuring volume-pressure equilibrium isotherms at very low coverages (under 0.1 monolayer) and above 90K. We then compared our experimental measurements to density functional theory (DFT) calculations of adsorption enthalpies at 77 K for the zero-coverage adsorption of the same gases at seven different types of sites of the MOF lattice. These comparisons showed remarkable agreement between the measured and theoretical isosteric heats in trend as well as reasonable agreement in magnitude, indicating that the sites predicted by DFT calculations are populated sequentially in order of decreasing absolute enthalpyt. This study further increased our understanding of adsorption on this prototype MOF at very low coverages and reaffirmed the accuracy of theoretical calculations.

POSTER SESSION 4

Balcony, Easel 107

4:00 PM to 6:00 PM

Development of an Immunohistochemistry (IHC) Platforms to Screen Conventional and Single Domain Antibodies

Luke C. Thurber, Senior, Bioengineering
Usman Moazzam, Freshman, Pre-Health Sciences
Jordan Pashupathi, Sophomore, Engineering Undeclared
Mentor: Jean Campbell, Pathology

The tumor microenvironment (TME) dictates the outcome of many immuno-oncology therapies for solid tumors. To better understand the dynamic milieu of the TME, new multiplexed, spatially-resolved histologic techniques are being developed.

A key limitation to evolving these techniques is identifying specific and selective antibodies that perform well in an immunohistochemistry (IHC) platform. The over-arching goal of this project is to develop a flexible, high-throughput platform to empirically test the IHC staining characteristics of antibodies in formalin-fixed paraffin-embedded (FFPE) tissues with improved throughput and lower test volumes. Essential elements in our platform design include: 1) flexibility to test a variety of biologic materials, which is dependent on the test antigen, 2) compatibility with manual and semi-automatic tissue microarray (TMA) builder, 3) easy use for pathologic assessment, and 4) future compatibility with fully-automated tissue staining instrumentation. Using computer-aided design software, and a stereolithography printer, we prototyped a guide template to build recipient TMA FFPE blocks. To screen for a variety of antigens in TMA "cores", we prepared cell lines, and acquired mouse tumor xenografts and human tissues. Standard IHC techniques were used to screen hybridoma supernatants generated from mouse immunizations. We have designed and tested six different multi-well slide-based IHC screening platforms. The current format consists of a six by four array of 2 mm cores. We have screened antibodies from two different mouse hybridoma campaigns. Thus far, we have identified candidate IHC antibodies for exogenous epitopes to identify chimeric antigen receptor T cells used to treat solid tumors, and a fusion protein hypothesized to be an oncogene in pediatric liver cancer. This project developed a single-slide antibody screening prototype for IHC. The device offers the flexibility to test multitude of tissues, and is built with design considerations for future automated tissue staining compatibility.

POSTER SESSION 4

Commons East, Easel 8

4:00 PM to 6:00 PM

Space: The Final Countdown

Daniel Loewito, Sophomore, Physics, Math, Shoreline Community College
Mentor: Charles Dodd, Geography, Shoreline Comunity College

What drives a space program? As more and more countries search for new areas of expansion, we must ask ourselves: who among them will be the leaders of space exploration in the 21st Century? This question has become extremely relevant due to the presence of a possible Modern Space Race. 2018 – 2020 will see more space missions from more countries than at any time since the Cold War Space Race. Although it is not a race to score firsts, there is a definite air of competition in the current space exploration scene. This literature review examines the driving factors behind the first space race and the current state of the emerging actors in space exploration. Studying the Cold War Space Race is important in helping us understand what sustains such a large-scale competition for space, along with the consequences that it might bring. For example, space and culture formed an interdependent relationship that seemed to feed into each other in a closed and self-sustaining cycle in that the space race generated a space-based culture in the United States, which in turn supported the US space program's continued existence. Comparing the two different races may lead to a better understanding of the state of the Modern Space Race.