

# **New Directions in Applied Mathematics and Number Theory: A conference in honor of Dorothy Wallace's retirement**

## **Talk Titles and Abstracts**

### **Friday, June 23, 2023**

**Clyde Martin** (Texas Tech University)

**Title:** *Where would I be without Dorothy?*

**Abstract:** Some ruminations about my work with Dorothy and some of the work that we have done together and some work that I hope we do in the future.

**Yixuan He** (Harvard Medical School)

**Title:** *Prediction and stratification of disease risk through integrative multi-omics analysis of global biobanks*

**Abstract:** Human diseases and traits are influenced by a combination of genetic and environmental factors. Genetic risk scores, which reflect the aggregate genetic predisposition from many markers across the genome, are being developed and updated for disease prediction and risk stratification. However, environmental risk scores are still limited to a handful of exposures selected a priori, and it is unclear whether exposures cumulatively impact disease risk burden. In current-day biobank and high dimensional epidemiologic cohort 'omic data, there exist new opportunities to systematically consider the effects of multiple exposures and their interactions with the genome. In this talk, I will provide a roadmap for assessing cumulative genetic and environmental risk for several common disease in diverse populations using biobank level multi-omic data.

### **Saturday, June 24, 2023**

**Heiko Enderling** (Moffit Cancer Center)

**Title:** *Mathematical modeling of cancer radiotherapy*

**Abstract:** Radiation therapy is a mainstay of cancer treatment, with more than 50% of all cancer patients receiving radiation at some point of their clinical care. Mathematical modeling has a long history in radiation oncology, and recent modeling approaches saw translation into prospective clinical trials. Here, we will present the different mathematical modeling approaches to simulate radiation response, and their implication on personalizing radiation dose and dose fractionation, towards a novel concept of adaptive radiation therapy. Using patient data, we develop, calibrate, and validate the models before making predictions on novel therapies.

**Meifang Li** (Dartmouth, Geography)

**Title:** *From Student to Scholar: A Journey of Intellectual Growth with Professor Wallace*

**Abstract:** As a joint student fortunate enough to have been mentored by the distinguished Professor Wallace, I am honored to share the invaluable lessons and inspiration I have gained from our partnership. In this talk, I will trace the evolution of me from a student to a scholar that has taken place under Prof. Wallace's mentorship, exploring how her guidance has deepened my understanding of complex mathematic concepts and nurtured my growth and development.

**Bijoy Ghosh** (Texas Tech University)

**Title:** *Nonlinear and Optimal Gaze Pointing Control Problems in Human Binocular Eye Rotation*

**Abstract:** In this talk I shall revisit binocular eye movement control problem as a constrained dynamics on  $SO(3)$  from the point of view of a nonlinear multi input multi output system. In the mid-nineteenth century, Donders had proposed that for every human head and eyes rotating away from the primary pointing direction, the rotational vectors are restricted to lying on a surface, called the Donders' surface. Additionally, when eyes are gazing at a moving point target, their gaze directions always intersect. The binocular eye motion can be viewed as a nonlinear dynamical system on a Riemannian Manifold, and we explore how eyes can be optimally controlled to track point targets in visual space.

**Alisa DeStefano** (Holy Cross)

**Title:** *A dynamical system on the torus: observability and number theory*

**Abstract:** Dynamical systems on the torus consisting of winding lines of irrational slope have been studied extensively in the fields of dynamical systems and ergodic theory. Here, we will consider two problems from control theory and one problem from number theory involving this dynamical system. The first problem involves constructing a dynamical system that is observable by any nonconstant continuous observation function on the torus. Results from number theory involving rational approximation and continued fractions are used extensively in this construction. The second problem involves output digitization for three observable linear systems. This leads to studying winding lines with irrational slope on the torus and determining what information can be recovered about the system from the output. The third problem involves using the dynamical system to obtain probabilistic versions of classic results in the theory of Diophantine Approximation.

**Jason Rosenhouse** (James Madison University)

**Title:** *Connection Problems in Cayley Graphs of Matrix Groups*

**Abstract:** Network designers face competing concerns. A network needs to be resilient, in the sense that it should not be possible to fracture the network just by cutting a small

number of edges. But an excessive number of edges makes the network costly to implement in practice. In combinatorics, graphs striking the best possible balance between resilience and cost are referred to as "expanders." We will discuss the expansion properties of Cayley graphs arising from certain matrix groups. These graphs arise naturally in several contexts relevant to number theory and geometry.

**Maeve McCarthy** (Murray State University)

**Title:** *A mathematical model of phenotypic plasticity for Arizona Tiger Salamanders*

**Abstract:** Phenotypic plasticity is the ability of an organism to change its phenotype in response to changes in the environment. General mathematical descriptions of the phenomenon rely on an abstract measure of "viability". In the case of the Arizona Tiger Salamander, the organism has a point in its development when, upon maturing, it may take two very different forms. One is a terrestrial salamander (metamorph) that visits ponds to reproduce and eat, while the other is an aquatic form (paedomorph) that remains in the pond to breed and which consumes a variety of prey including its own offspring.

A seven dimensional nonlinear system of ordinary differential equations is developed, incorporating small (Z) and large (B) invertebrates, Ambystoma young of the year (Y), juveniles (J), terrestrial metamorphs (A) and aquatic paedomorphs (P). One parameter in the model controls the proportion of juveniles maturing into A versus P. Solutions are shown to remain non-negative. Every effort was made to justify parameters biologically through studies reported in the literature.

A sensitivity analysis and equilibrium analysis of model parameters demonstrate that morphological choice is critical to the overall composition of the Ambystoma population. Various population viability measures were used to select optimal percentages of juveniles maturing into metamorphs, with optimal choices differing considerably depending on the viability measure. The model suggests that the criteria for viability for this organism vary, both from location to location and also in time. Thus, optimal responses change with spatiotemporal variation, which is consistent with other phenotypically plastic systems.

**Frederika Retzeperis** (Icahn School of Medicine)

**Title:** Exploiting interactions between ploidy and host physiology in Glioblastoma

**Abstract:** Whole-genome doubling drives rapid tumor evolution and is a hallmark of many cancers, including Glioblastoma (GBM), with an incidence of ~14%. Despite aggressive treatment, GBM remains uniformly lethal, with a median survival of 14-16 months. The prognosis worsens in individuals aged 65 and older, with a median survival of under 7 months. While comorbidities contribute to the increased risk in older patients, age-related changes in the tumor microenvironment likely also contribute. Aging brains exhibit higher rates of polyploidy, hypoxia related gene expression, and glucose levels, as well as reduced stiffness. The average ploidy of 20 different cancer types correlates with the oxygen levels

recorded in their respective tissue of origin (Spearman  $r = 0.66$ ,  $P = 0.002$ ). We thus propose that metabolic substrates in the GBM microenvironment differentially influence cell fate decisions in cancer cells of different ploidy. We address this hypothesis with integrated in-vitro and in-silico experiments and multi-omic and imaging analysis of primary and recurrent GBM. We genetically engineered cell lines to represent diploid and tetraploid lineages and assessed their migratory patterns under variable glucose and serum gradients. Additionally, we performed RNA-seq and whole genome sequencing on multiple regions from one patient-matched primary and recurrent GBM. Pre- and post-surgery MRI data were registered to a standard space to approximate the spatial distribution of tumor cell densities. Leveraging this data, we developed and calibrated a novel Stochastic State-Space Model (S3MB) to simulate re-growth of recurrent GBM.