CAL

[redacted]

EDUCATION & CITIZENSHIP

University of Rhode Island, Kingston, RI

Ph.D Mathematics, *May 2017*

- *Advisor*: [redacted]
- *Thesis Title*: Bifurcation of Some Planar Discrete Dynamical Systems with Applications

Rhode Island College, Providence, RI

M.A. Mathematics, *May 2013*

- *Advisor*: [redacted]

Mohammed V University Of Rabat -Faculty Of Science-, Rabat , Morocco

B.Sc Applied Mathematics, *June 2006*

Citizenship

- [redacted]

EXPERIENCE

Postdoctoral Teaching Scholar September 2019 - Present
Texas Tech university *Lubbock, TX*

Served as an instructor for the following courses:

- MTH 2450: Calculus III With Applications(2 sections) Fall 2021
- MTH 3370: Elementary Geometry Fall 2020
- MTH 2371: Elementary Analysis (2 sections) Fall 2020
- MTH 3342: Math Stats for Engineers/Scientists Summer 2020
- MTH 2300: Statistical Methods Summer 2020
- MTH 2450: Calculus III With Applications Spring 2020
- MTH 1452: Calculus II With Applications Fall 2019

Visting Assistant Professor September 2017 - June 2019
Trinity College *Hartford, CT*

Served as an instructor for the following courses:

- MTH 231: Calculus III Spring 2019
- MTH 234: Differential Equations Spring 2019
- MTH 207: Statistical Data Analysis Fall 2018
- MTH 299: Independent Study Fall 2018
- MTH 131: Calculus I Fall 2018
- MTH 127: Functions, Graphs and Modeling Fall 2018
- MTH 202: Intro to Difference Equations Summer 2018
- MTH 132: Calculus II Spring 2018
- MTH 207: Statistical Data Analysis Spring 2018
- MTH 131: Calculus I Fall 2017
- MTH 207: Statistical Data Analysis Fall 2017

Graduate Teaching assistant/Instructor September 2014 - May 2017
University of Rhode Island *Kingston, RI*

Served as an instructor for the following courses:

- MTH 142: Intermediate Calculus with Analytic Geometry Spring 2017
- MTH 141: Introductory Calculus with Analytic Geometry Fall 2016
- MTH 108: Topics in Mathematics Fall 2016
- MTH 215: Introduction to Linear Algebra Summer 2016
- MTH 141: Introductory Calculus with Analytic Geometry Spring 2016
- MTH 141: Introductory Calculus with Analytic Geometry Fall 2015
- MTH 131: Applied Caluclus I Summer 2015
- MTH 111: Precalculus Spring 2015
- MTH 111: Precalculus Fall 2014

Adjunct Mathematics Instructor Fall 2012 - Spring 2013
Rhode Island College *Providence, RI*

During my second year of Masters I served as an instructor for the Following course:

- MTH 010: Basic Mathematics Competency Fall 2012
- MTH 010: Basic Mathematics Competency Spring 2013

Mathematics Tutor

- *University of Rhode Island (Academic Enhancement Center)* Fall 2014-Spring 2017
- *Rhode Island College (Math Learning Center)* Spring 2013

Tutored Mathematics and Statistics courses of all undergraduate levels to individuals on one-to-one basis and groups of students as well. I also worked with students with special needs, and adults with limited mathematical background.

WebWork Problem Writer Summer 2016
University of Rhode Island *Kingston, RI*

Created and coded a collection of Precalculus problems used for online homework assigned to students taking MTH 111 at the university of Rhode Island.

Mathematica Problem Writer Summer 2016
University of Rhode Island *Kingston, RI*

Created a collection of Mathematica projects that will be assigned to students taking MTH 141 at the university of Rhode Island.
The projects consist of real world problems that the students will be guided to solve using Mathematica based on concepts of calculus that they acquired.

RESEARCH INTERESTS

Difference equations, Discrete dynamical systems and Bifurcation theory along with its application to biological models.

PUBLICATIONS AND WORK IN PROGRESS

- The Neimark-Sacker bifurcation and asymptotic approximation of the invariant curve of a certain difference equation.
  Published:
  ❑ [redacted], [redacted] *and* [redacted]
  ❑ Journal of computational analysis and applications, Vol 23, NO.8, 2017.

- The invariant curve caused by Neimark-Sacker bifurcation of a certain difference equation.
  Published:
  ❑ [redacted], [redacted] *and* [redacted]
  ❑ International Journal of Difference Equations, Vol 12, Number 2, pp. 267-280.

- Global Dynamics of Delayed Sigmoid Beverton-Holt Equation
  Published:
  ❑ [redacted] and [redacted]
  ❑ Journal of Discrete Dynamics in Nature and Society, Vol 2020, Article ID 1364282, 05-26-2020

- Book Review of :Difference equations for scientists and engineering: interdisciplinary difference equations.
  Published:
  ❑ [redacted]
  ❑ Journal of Difference Equations and Applications, 26(5), pp. 727–728, 06-28-2020

- On a discrete mathematical model of tumor–immune system interactions with blockade of immune checkpoints
  Published:
  ❑ [redacted] *and* [redacted]
  ❑ Journal of Difference Equations and Applications,Vol 28 issue 1, Pages: 73-108

- Analysis of a Continuous SI Epidemic Model
  In Progress:
  ❑ [redacted]*nd* [redacted]

CONFERENCES AND TALKS

- **On a discrete model of tumor-immune system interactions** — September 2021
  TTU Biomathematics Seminar — *Lubbock, TX*

- **TEXAS TECH MATH CIRCLE** — December 2019
  Complex numbers and applications — *Lubbock, TX*

- **Joint Mathematics Meetings Special Session Organizer** — January 2018
  Bifurcations of Difference Equations and Discrete Dynamical Systems — *San Diego, CA*

- **A Difference Equation with Neimark-Sacker Bifurcation.** — January 2018
  Joint Mathematics Meetings — *San Diego, CA*

- **Global Dynamics for Competitive Maps in the Plane.** — May 2017
  AMS 2017 Fall Spring Eastern Sectional Meeting — *New York, NY*

- **On the k-th Order Pielou equation and a Global Stability Result** Novemember 2016
  U.R.I Difference Equations Seminar *Kingston, RI*

- **The invariant curve caused by Neimark-Sacker Bifurcation.** September 2016
  AMS 2016 Fall Eastern Sectional Meeting *Brunswick, ME*

- **The Neimark-Sacker Bifurcation of a Certain Diff. Equation** November 2015
  AMS 2015 Fall Eastern Sectional Meeting *Brunswick, NJ*

- **The Neimark-Sacker Bifurcation of a Certain Diff. Equation** November 2014
  U.R.I Difference Equations Seminar *Kingston, RI*

- **IMS XXV Conference at Stony Brook University** May 2015
  Attended *Stony Brook, NY*

UNDERGRADUATE RESEARCH AND MENTORSHIP

Trinity College, Summer 2018

- [redacted]

GRADUATE COURSEWORK

- ❑ Real Analysis
- ❑ Topology
- ❑ Measure Theory
- ❑ Complex Analysis
- ❑ Linear Algebra
- ❑ Functional Analysis
- ❑ Probability Theory
- ❑ Statistics
- ❑ Numerical Analysis
- ❑ Ordinary Differential Equations
- ❑ Difference Equations
- ❑ Bifurcation Theory
- ❑ Dynamical Systems
- ❑ Ergodic Theory
- ❑ Abstract Algebra
- ❑ History of Mathematics

RELEVANT SKILLS

- **LaTeX**: Experience creating different types of documents and presentations.
- **Mathematica**: Experience for teaching and research.
- **Matlab**: Experience for teaching and research.
- **WebWork**: Experience coding problems.
- **Sakai, Blackboard, Moodle**: Experience Managing courses and supervising. online assignments and projects.
- **programming**: C++, Python.

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Faculty Search Committee
Department of Mathematics & Statistics
Northern Arizona University

May 2, 2022

To Whom It May Concern,

This letter is intended to express my strong interest in the position of Assistant Teaching Professor at Northern Arizona University's department of Mathematics & Statistics. I obtained my Doctoral Degree from the University of Rhode Island, where I served as a graduate teaching assistant and a per-course instructor. I am currently a Postdoctoral Teaching Scholar at Texas Tech University and my primary areas of research are Difference equations and Discrete Dynamical Systems. I believe that my aggregated personal and professional experiences in higher education, and dedication to excellence in Mathematics teaching and research make me a strong candidate for this position.

During my academic and professional career I have had the opportunity to teach various undergraduate courses designed for STEM and non-STEM majors, ranging from developmental courses to linear algebra, including Introductory College Algebra, Statistics and Calculus; courses that strived to incorporate a multitude of technological components such as: WileyPlus, MyStatLab, Webassign and Wolframe Alpha. My professional experience has helped me acquire the skills needed to effectively teach the mathematical content, model the mathematical thinking and incorporate the technological tools that students require to be successful in both their further coursework and future professions.
I have successfully incorporated the element of a tailored curriculum into a summer course that I instructed during my inaugural year at Trinity College, where I served as a Visiting Assistant Professor. This course enabled me to present materials that are directly related to my research to a small group of students through seminar style instructions.

In my graduate work, I focused on the impact of nonlinear perturbation on a class of Difference equations and biological models. In particular, ones that exhibit "Naimark-Sacker bifurcation". Moreover, I was able to make a contribution into the theory by generalizing and extending some global stability results which can be applied to solve many of the conjectures and open problems in the field.
Furthermore, while being a Postdoc at Texas Tech University, I had the opportunity to successfully analyze a multi-dimensional discrete time cancer model of Tumor immune system interactions. I am confident that my dedication and strong-will to strive for success will help me collaborate and direct both graduate and undergraduate research at Northern Arizona University.

The topics and subjects that my research covers, are not only interesting in their own right, but can be introduced to and explored by students with a background in the theory of linear algebra, differential equations and Real Analysis. While conducting a college-funded research at Trinity college in the Summer of 2018, I was enamored by the multidimensional exploration of mathematical modeling conducted by my research team comprising of undergraduate students. My prime goal is to make my area of research more accessible to both graduate and undergraduate students by developing new courses and involving these students with research projects.

With my enthusiasm to become a faculty member of your department, I am eager to apply my educational background, and my ability to interact with students from different backgrounds to make a considerable contribution to your institution. I am sure that given the opportunity, I will bring my experience together with my commitment to make a positive impact on the minds of tomorrow as well as contribute to the enrichment of the mathematics curriculum in your department.

Finally, I would like to mention that I enjoyed working in diverse environments, and that I am willing to relocate to further enrich my professional experience.
I have enclosed my curriculum (including a list of publications and work in progress), contact information for my references all-together with my teaching and research statements.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

[redacted]

Diversity statement

[redacted]

I was born in Morocco, a country that possesses a diverse and lively history that witnessed a long succession of different ruling bodies, such as Berbers, Jews, Romans, Arabs, French and Spanish. Diversity is reflected on all aspects of Moroccan life, namely the language, clothing, cuisine and culture. It is a country where traveling from region to region seems more like traveling from country to country. When I was 16 years old my family moved to Algeria a culturally and historically rich North African country. While there I completed my middle-school and high-school studies. I believe that speaking different languages, having lived in different countries and experiencing all which I have-when coupled with my inherent ability to adapt and thrive in a new environment-lays the foundation which ultimately shapes my personality and makes me a person that is open to multiculturalism and diversity.

In my native Morocco, I was fortunate enough to gain admission to the Rabat Mohamed V University in Morocco, a destination for students from all regions of Morocco as well as students from French speaking African countries. It was a great opportunity for me to interact and begin developing a deep understanding of the obstacles and struggles that foreign students can, and do, face. Following my graduation I moved to the United States, the land whom's foundational philosophy is predicated upon an all-encompassing codification of human rights, diversity acceptance and recognition of equal-opportunities. Nonetheless, my The move to the states did bring with it a host of difficulties; with my immediate family back in Morocco, I was charged with supporting myself entirely through my own devices for the first time in my life. I worked at several jobs earlier on, most of which did not require a college diploma. My degree from Morocco, I quickly learned was an credential that most employees were unsure how to properly assess.

Hoping to better my prospects of gainful employment, I learned about the M.A program in Mathematics at Rhode Island College (R.I.C) and decided to enroll. At R.I.C I was so fortunate to find a gifted faculty dedicated to excellence graduate teaching. Under their tutelage, I pursued further graduate level coursework and was honored to receive a position as an adjunct instructor. I earned my master's degree and successfully joined a Phd program at the University of Rhode Island (U.R.I) in Kingston.At U.R.I, I was given the opportunity to serve as a Graduate teaching assistant, a tutor and a per course instructor.

Upon obtaining my Doctoral Degree, I was privileged to become a Visiting Assistant Professor at Trinity College. A major draw of Trinity was its preceding reputation as an institution with culturally rich and diverse students and ideas. While performing my duties I have had an excellent opportunity to connect and interact with students and faculty members from different backgrounds. I was even fortunate enough to mentor a small group of international students through a college funded summer research.

My personal and professional experiences in higher education have made me aware of greater dimensions of diversity. In fact, I am impressed by the success that the department of mathematics at U.R.I achieved in balancing the gender-ratio among graduate students and faculty, as well as encouraging the contributions of individuals from different backgrounds and origins much like myself. I believe that it is our greatest purpose as educators to create a world where everyone has equal rights and equal opportunities to succeed. This means every single person is valued, heard, respected, empowered, and made to feel a true sense of belonging. It is my prime duty as an instructor and as a mathematician to strive for an environment that is friendly and attracting students from underrepresented groups such as:

- International students, most of whom do not speak English as their first language and who needed someone to understand their struggle and difficulties to adapt to a new environment and perhaps even a totally different educational systems.

- Students with different disabilities that required special care and patience to help achieve their goals and live a life to its fullest.

- Women and minorities, who may need needed to be encouraged to understand that despite, the stress of being in the minority and/or the socio-economic challenges they face, they can take advantage of their potentials and abilities to engage in learning and contributing to the world of Mathematics.

- Student veterans, a college population who required assistance in order to successfully transition from the rigors of military life to civilian and academic environments.

On the other hand, I consider that the core mission of any educational institution is to serve the interests of the state and the country, therefore establishing and fostering diversity among students and employees. I see this as not just a critical function, but a duty.

I believe that student-body diversity allows for the introduction of new ideas, perspectives, experiences and expertise, all of which lead to abundant creativity, innovative problem solving and improved decision making. Moreover, by understanding the variety of students and differences in learning styles, one can create an effective educational environment where the minds of tomorrow feel safe and comfortable to explore the beauty of mathematics and contribute to it through their own ideas.

For as long as I am an instructor I will continuously encourage my audience members and invite them to take part in the discoveries of the welcoming and supportive world of Mathematics; a world whose language is universal and a common ground to all of us.

Teaching statement

[redacted]

In my opinion, Mathematics is the field which studies abstract subjects that can often relate to nature. As a mathematician, I try to connect these abstracted insights to real-world situations, and explain phenomenons that are otherwise indiscernible. It is crucial that this point - that mathematics is in fact universal, and governing - be emphasized to and understood by the student. Therein, the most important of all aspects related to a mathematician is the ability to teach and transmit his or her knowledge to students. To teach a student is to allow him or her to comprehend various topics, and perceive them for what they truly are.

I believe that the main goal of a mathematics teacher is to ensure that students will leave his or her class with a complete understanding of the material. This is a process that expands gradually in the mind of a student. My job is to act as a guide, allowing the student to move through the course and take in the material. Within the student, this type of growth is facilitated in a relatively clear way: concise explanation of the concepts, followed by an illustration of the concepts and their applications, starting from the simplest and straightforward examples and gradually moving to ones at a higher level of difficulty. That being said, a necessary and perhaps essential part of this process is garnering an interactive classroom. I view lecturing then, as a two way form of communication. Discussion is much more important (and useful) than just having information flow in one direction. This is why I strongly encourage and, work to ensure, my students feel safe and comfortable expressing their opinions, ideas and concerns. For instance: when solving problems on the board I will always ask if someone has a suggestion or a starting point in mind. Often, I would then ask what the next step may be. My goal here is to have them explore deep into their minds, and to find out what inspires them to make such a choice. This process is constantly reiterated until we ultimately reach a conclusion to the problem. I have found this turns out to be a smooth and enjoyable task involving all of us.

Also while lecturing, I find it very useful to ask questions testing my audience's understanding of subjects. Any insight allows me to adjust my teaching if necessary and find out whether I should readjust my focus. In addition, allowing students to converse with one another - sharing ideas and approaches - is essential to create a positive dynamic in the classroom. I strongly believe in the effectiveness of group work. In class I have success when joining groups of students from different levels and backgrounds together to solve assigned problems. The groups work together in and out of the class to complete projects specifically tailored to the material currently being taught. Sometimes, in groups and in an environment other than the classroom, ideas are shared more freely and students are more comfortable in exploring the material.

Another essential part of my teaching philosophy addresses homework and testing. Outside of the class, I expect my students to supplement their learning by solving problems and practicing their skills. Practice problems range from basic applications up through difficult and thought pro-

voking - the goal is to begin to make them think critically. Weekly quizzes allow me to ensure that my students have not and will not fall behind, that they are studying and that they are ready for new topics. In addition, I get to explore the way my students think: I can more clearly identify their weaknesses and can more aptly emphasize crucial learning points in the next classes.
Before each exam I provide a worksheet or, 'practice exam,' that I have prepared beforehand. I also run a comprehensive review session outside of normal class hours. My exams are fair and well balanced; not too hard, nor too easy. Whether it is and exam, quiz or homework, I always make sure that students receive constructive feedback instead of simple grades and scores. After exams, I provide students with the class average as well as, a rough idea of the scoring distribution; the percentages above 70, 80 and 90. This is so they can get an idea of where they rank with respect to their peers.

I also have experience working as a tutor: first at the Math Learning Center of Rhode Island College, and later, at the Academic Skills Center at the University of Rhode Island. Through these experiences I gained invaluable skills and techniques. I believe I am more capable of working with students on a one-to-one basis and explain concepts at a more personalized level because of my time working as a tutor. This plays a major role when I begin to hold office hours. Office hours, I feel, are crucial for establishing a productive interaction with students outside of the classroom. It is a time when they get to know me as an individual and, a time when I get to know quieter students who are often reluctant to speak in class. Furthermore I gain a better understanding of their study habits, skills, motivation, and comprehension of the course material. Office hours then provide an opportunity for me to offer them suggestions, help prepare them for exams and improve their overall performance.

In retrospect, I am glad to say that I have truly found my life's passion. Mathematics is a beautiful field and to share it with others is the most rewarding of all pursuits. My research was marred with great difficulty, having gotten to where I am today required overcoming various obstacles and adapting continuously. My efforts were fueled by the desire to be a great ambassador of the field. This self awareness and ability to adapt, lends itself well to the demand put upon a teacher, who must always adjust to the ever changing environment of the classroom. In the future I will continue to supplement the field of academia, not only through the advancement of my research but also through teaching and fostering the great minds of tomorrow.

Future Career Path Statement

My teaching experience during and after my graduate studies opened my eyes and mind to the importance of my role as a professor, and taught me to make quality teaching a priority in my career. I have chosen a teaching path in higher education because I know that I have the skills and the potential to make a positive impact in the minds of tomorrow and therefore have my own contribution to the future of our country.

By applying for the position of Assistant Teaching Professor at Northern Arizona University, I am seeking a permanent position where I can enrich my professional experience. In addition to teaching and coordinating courses at different levels, I aspire to be involved in curriculum and assessment development, decision making and engaging in activities and services within your institution.
Furthermore I am confident that I can make my area of expertise more accessible to both graduate and undergraduate students by developing new courses and collaborating with them in research projects.

I know I can bring value to your institution and would love the chance to discuss how my experience and skills can contribute to the growth and success at Northern Arizona University. Thank you for taking the time to review my application.

Research statement

[redacted]

My research interests are on the global dynamics of non-linear difference equations and discrete dynamical systems. In particular the ones that exhibit "Naimark-Sacker" bifurcation as well as the basins of attractions of equilibrium points and periodic solutions of monotone dynamical systems. The field of difference equations is rich of open problems and conjectures with numerous applications to physics, economics, social sciences, engineering and Biology, see [1].

1 A Discrete cancer model

Cancer is a leading cause of death worldwide. It is a broad group of diseases involving unregulated cell growth [25, 34]. In particular, cancer cells have defects in regulatory circuits that govern normal cell proliferation and homeostasis. It is suspected that growth signaling pathways suffer deregulation in all human cancerous tumors [25, 34]. Traditional treatments of malignant tumors consist of surgery, chemotherapy, and radiation therapy. In recent years, immunotherapy has emerged as a promising approach to treat cancer. Cancer immunotherapy aims to augment the patient's own immune system to fight cancer and it includes different modalities such as vaccines, oncolytic virus, cytokine, adopted cell transfer and immune checkpoint inhibitors [25, 33].

The T cells consist of CD8 and CD4 T cells and are the major anti-tumor cells. The $CD8^+$ T cells are also called cytotoxic T lymphocytes (CTLs). They are the primary killers of tumor cells, and are also referred to as effector cells [25, 34]. An activation of $CD8^+$ T cells requires two signals. The first signal occurs when a naive $CD8^+$ T cell encounters and interacts with an antigen presenting cell such as a dendritic cell through the T cell receptor [21]. The second signal, the co-stimulation signal, is provided by the interaction between CD28 on the membrane of T cells and B7 on antigen presenting cells [21]. However, CTLA-4 (cytotoxic T lymphocyte antigen-4) molecules are expressed by activated T cells such as $CD4^+$ T cells and regular T cells and can out-compete CD28 for binding to B7 and thus dampen the co-stimulatory signals [21, 25].

Once T cells are activated by antigen stimulations, they express high levels of PD-1, a receptor for transmitting signals that restrain the T cells' function. When PD-1 positive T cells come to the tumor sites, their PD-1 will be engaged by PD-L1 expressed by most cancer cells to induce T cells death or reduce the T cell's ability to kill tumor cells [21, 25]. The PD-1, PD-L1, and CTLA-4 are collectively called immune checkpoint molecules since they function as barriers for restraining immune responses [25]. Therefore, the immune checkpoint blockade therapy is an immunotherapy to restore the function of anti-tumor immune cells by blocking the pathways used by cancer cells for controlling immune cells [25]. There are several drugs approved by the FDA specifically for blocking these immune checkpoint proteins and the therapy has revolutionized the treatment of malignant tumors [25].

Over the last few decades, a variety of mathematical models [22, 23, 24, 26, 27, 28, 33, 35] have been constructed to study the roles of immune cells upon tumor dynamics and treatment effectiveness. Majority of these models, however, are based on differential equations and there are only a few discrete–time models developed to study tumor growth. An earlier discrete model proposed by Moghtadaei et al. [30] in 2013 built on the well–known tumor–immune models of ordinary differential equations by applying the Mickens nonstandard finite difference scheme [37] to obtain a system of two difference equations of first-order. The authors illustrated numerically that the map can induce periodic and chaotic dynamics. A more recent model of difference equations studied by Songolo and Ramadhani [32] that appeared in 2017 was also obtained by applying nonstandard finite difference schemes to a tumor model of ordinary differential equations with anti-cancer therapies. The model is a system of four first–order nonlinear difference equations. The authors concluded that there exists a separation line between basins of attraction of the tumor–free equilibrium and the tumor–present equilibrium with largest number of cancer cells [32].

Recently, Serre et al. [31] developed a discrete–time model of tumor–immune interactions with combined treatments of radiation and immunotherapy of anti-PD-1 or anti-PD-L1 along with anti-CTLA-4. Their model was numerically simulated for a short period of time to show the conformations between model solutions and several experimental data. Subsequently, Li and Xiao [29] constructed a model of difference equation based on the model of Serre et al. with some major modifications. They studied asymptotic dynamics of the model by verifying that either a period-doubling or a Neimark–Sacker bifurcation can occur when the unique interior equilibrium loses its stability [29].

Motivated by the work of Serre et al. [31], I derived a discrete–time model of tumor–immune interactions and provided an analytical study of the resulting system. In particular, it is shown that the tumor will grow to unboundedly large if either its growth rate exceeds a critical value or if the tumor size is large upon being detected by the health personnel. The model exhibits a saddle-node bifurcation at the critical growth rate and the system has two coexisting equilibria when the tumor growth rate is smaller than the threshold. It is proven that the larger tumor is always unstable whereas the equilibrium with the smaller tumor may undergo a Neimark-Sacker bifurcation. In addition, sufficient conditions are provided for which the smaller tumor is asymptotically stable. Numerical simulations with parameter values taken from [31] are explored.

As noted above, Li and Xiao [29] also studied a variation of the model given by [31], where they assumed that the primary immune response is constantly proportional to the effector cells. Similar to my assumption, the secondary immune response at time n in [29] is also constantly proportional to the primary immune response at time n so that the resulting difference equation is first-order. Further, the tumor growth rate in [29] is modeled by a Ricker type function to avoid unbounded solutions. In this investigation, the tumor growth rate follows from the original model given by Serre et al. [31]. We will show that the tumor will grow unboundedly large if the tumor growth rate is large or if its initial mass is beyond a threshold.
My model derivation is based on [31]. Let T_n be the tumor mass on day n, measured in grams, and $\mu > 0$ denotes tumor's intrinsic growth rate. In the absence of the immune system and treatments, the tumor will grow exponentially given by $T_{n+1} = T_n \exp(\mu)$. The tumor releases

antigens which will be picked up by dendritic cells of the innate immune system and present them to the adaptive immune system to initiate tumor killing by effector cells [36]. Let A_n denote the amount of tumor antigens on day n, which are released by tumor cells at a constant rate ρ. The natural decay rate of the tumor antigens is denoted by λ. The compartment L_n models effector cells at the tumor site, which receive stimulation from the tumor antigens at a rate $1-\lambda$. The natural loss rate of immune cells is a constant and is given by ϕ. These parameters satisfy $0<\lambda,\ \phi<1$.

The tumor cells are killed by the immune cells. Serre et al. [31] separate the immune responses into the primary and the secondary immune responses. The primary immune response on day n is given by

$$Z_{\mathrm{prim},n}=\frac{aL_n}{1+\dfrac{bT_n^{2/3}L_n}{1+p_1}},$$

where $a>0$ is the proportionality of the primary response due to effector cells and $b>0$ is the intrinsic ability of the tumor to down–regulate the immune system. The anti-PD-1 or anti-PD-L1 drug is denoted by p_1. The power $2/3$ is adopted since it provides a better fit to experimental data according to the numerical study carried out in [31]. The product $bT_n^{2/3}L_n$ can be viewed as an amount of immuno–modulatory factors produced by the tumor cells to diminish primary immune responses whereas the treatment p_1 can help curtail this negative effect from cancer cells.

The secondary immune response in [31] depends on cumulative primary responses and is given by

$$Z_{\mathrm{sec},n}=\sum_{k=0}^{n}\frac{\sigma(1+c_4)}{r+c_4}Z_{\mathrm{prim},k}, \tag{1}$$

where $\sigma>0$ is the inclination of the primary immune response to induce a secondary immune response and c_4 is the anti-CTLA-4 drug. The term $r>1$ is a constant so that in the absence of anti-CTLA-4 treatment, $c_4=0$, the propensity to induce a secondary immune response per time step is σ/r, which is smaller than σ. If CTLA-4 inhibitor is taken into account, i.e., $c_4>0$, then $\dfrac{\sigma(1+c_4)}{r+c_4}>\sigma/r$. After incorporating the anti-tumor effects of the immune responses, the tumor mass at time $n+1$ is then reduced to

$$T_{n+1}=T_n\exp\Big(\mu-Z_{\mathrm{prim},n}-Z_{\mathrm{sec},n}\Big). \tag{2}$$

If $Z_{\mathrm{prim},n}+Z_{\mathrm{sec},n}<\mu$, the immune system slows down tumor growth while the immune system can shrink the tumor if $Z_{\mathrm{prim},n}+Z_{\mathrm{sec},n}>\mu$. The time unit is a day and the unit of tumor is in gram. There are no units given in [31] for other state variables A and L and parameters.

In this work, we assume that the past primary immune responses upon the secondary immune response are weak so that their contributions to the secondary immune response can be ignored. Consequently, the secondary immune response at time n is proportional to the primary immune response at time n and is given by

$$Z_{\mathrm{sec},n}=\frac{\sigma(1+c_4)}{r+c_4}Z_{\mathrm{prim},n},$$

where σ, r and c_4 have the same biological interpretations as in (1). The tumor equation under the anti-tumor effects of the immune responses with immunotherapies of anti-PD-1/anti-PD-L1 and anti-CTLA-4 then becomes

$$T_{n+1} = T_n \exp\Big(\mu - (1 + \frac{\sigma(1+c_4)}{r+c_4})\frac{aL_n}{1 + \frac{bT_n^{2/3}L_n}{1+p_1}}\Big).$$

Let

$$c = 1 + \frac{\sigma(1+c_4)}{r+c_4} \text{ and } p = \frac{b}{1+p_1}. \tag{3}$$

According to the above elaboration, the model then takes the following form

$$\begin{aligned} T_{n+1} &= T_n \ \exp\Big(\mu - \frac{acL_n}{1+pT_n^{2/3}L_n}\Big), \\ A_{n+1} &= (1-\lambda)A_n + \rho T_n, \\ L_{n+1} &= \lambda A_n + (1-\phi)L_n, \\ T_0 &> 0,\ A_0 \geq 0,\ L_0 \geq 0, \end{aligned} \tag{4}$$

where $0 < \lambda,\ \phi < 1,\ \rho,\ p,\ a,\ \mu > 0$, and $c > 1$.

By using the substitution

$$\alpha = ac\rho\lambda,\ \beta = p\rho\lambda \tag{5}$$

and the transformation

$$X_n = T_n,\ Y_n = \frac{A_n}{\rho},\ Z_n = \frac{L_n}{\rho\lambda}, \tag{6}$$

system (4) becomes

$$\begin{aligned} X_{n+1} &= X_n \ \exp\Big(\mu - \frac{\alpha Z_n}{1+\beta X_n^{2/3}Z_n}\Big), \\ Y_{n+1} &= X_n + (1-\lambda)Y_n, \\ Z_{n+1} &= Y_n + (1-\phi)Z_n, \\ X_0 &> 0,\ Y_0 \geq 0,\ Z_0 \geq 0, \end{aligned} \tag{7}$$

where $0 < \lambda,\ \phi < 1$ and $\mu,\ \alpha,\ \beta > 0$. The goal of this study is to investigate system (7).

2 Work on difference equations

I also investigated some contemporary problems in the field of difference equations and discrete dynamical systems which range from global attractivity results for difference equations to the different types of bifurcations for systems of difference equations in the plane. My goal was to explore the impact of different perturbations of the Beverton-Holt and the sigmoid Beverton-Holt models with delay that describe the growth or decay of single species in population dynamics [1, 2, 3].

The classical Beverton-Holt model is given by the equation

$$x_{n+1} = \frac{x_n}{f + cx_n}, \quad n = 0, 1, \ldots,\ c > 0,\ f > 0,\ x_0, x_1 \geq 0, \tag{8}$$

and the Beverton-Holt model with delay is given by:

$$x_{n+1} = \frac{x_{n-1}}{f + cx_{n-1}}, \quad n = 0, 1, \ldots,\ c > 0,\ f > 0,\ x_0, x_1 \geq 0. \tag{9}$$

The sigmoid Beverton-Holt with delay is given by

$$x_{n+1} = \frac{x_{n-1}^2}{f + cx_{n-1}^2}, \quad n = 0, 1, \ldots,\ c > 0,\ f > 0,\ x_1 \geq 0 \ and\ x_0 \geq 0, \tag{10}$$

The dynamics of Equation (10) is well known, see [4], and is given as:

1. If $f > \frac{1}{4c}$ then the unique equilibrium point $E_0 = (0, 0)$ is globally asymptotically stable.
2. If $f = \frac{1}{4c}$ then there are two equilibrium points $E_0 = (0, 0)$, $E_1 = (\frac{1}{2c}, \frac{1}{2c})$ in addition to one minimal period two solution $\{P_x, P_y\} = \{(\frac{1}{2c}, 0), (0, \frac{1}{2c})\}$, each with the basins of attraction, see [4].
3. If $f < \frac{1}{4c}$ then there are three equilibrium points $E_0 = (0, 0)$,$E_- = (\frac{1-\sqrt{1-4fc}}{2c}, \frac{1-\sqrt{1-4fc}}{2c})$ and $E_+ = (\frac{1+\sqrt{1-4fc}}{2c}, \frac{1+\sqrt{1-4fc}}{2c})$ in addition to three minimal period two solutions, see [4] for the basins of attractions

In order to investigate the impact of perturbation on the above biological models I considered the following equations:

$$x_{n+1} = a + \frac{x_n^2}{x_{n-1}^2}, \quad n = 0, 1, \ldots,\ a > 0, x_1 \neq 0, x_0 \neq 0, \tag{11}$$

$$x_{n+1} = \frac{x_n}{cx_{n-1}^2 + dx_n + f}, \quad n = 0, 1, \ldots,\ c, d, f > 0, x_1 \geq 0, x_0 \geq 0, \tag{12}$$

$$x_{n+1} = \frac{x_{n-1}^2}{cx_{n-1}^2 + dx_n + f}, \quad n = 0, 1, \ldots,\ c, d, f > 0, x_1 \geq 0, x_0 \geq 0. \tag{13}$$

Equations (11) and (12) belong to a category of difference equations with a unique positive equilibrium which exhibits the Neimark-Sacker bifurcation, and the key question here is whether local asymptotic stability of the equilibrium implies global asymptotic stability.
Equation (13) on the other hand exhibits a completely different dynamical behavior which is more or less similar to the sigmoid Beverton-Holt model (10), however the study of its dynamics requires bringing the equation into a two dimensional competitive system and using the theory of global stable and unstable manifolds for monotone systems [5, 6] to determine the basins of attractions of its equilibrium point(s) and minimal period two solutions whenever they exist.

2.1 The Global Dynamics and Bifurcations of Equation (11)

In the first research project I considered Equation (11) which has a unique equilibrium point whose characteristic equation has complex conjugate roots. The local stability of this equation is described as:

1. Locally asymptotically stable for $a > 1$;
2. Non-hyperbolic for $a = 1$;
3. Unstable (repeller) for $a < 1$.

By investigating the global dynamics, I showed that the equation exhibits Neimark-Sacker bifurcation at the critical value $a_0 = 1$ and therefore showed the existence of an attracting closed invariant curve encircling the equilibrium for $a<a_0$; a close enough to a_0. My major tool in proving this result is the "Neimark-Sacker bifurcation" theorem, [7, 8].

In addition, I provided an asymptotic formula for the invariant curve using Murakami's method [9]. As far as global asymptotic stability of the equilibrium is concerned, I used the embedding method of Janowski and Kulenović [10] to show that every solution of Equation (11) is a solution of the following equation:

$$x_{n+1} = a + \frac{a^2}{x_{n-1}^2} + \frac{a + x_n}{x_{n-2}^2}, \quad n = 0, 1, \ldots,$$

for which every solution must converge to the unique equilibrium $\bar{x} = a + 1$ for $a \geq \sqrt{2}$. The tool for this global asymptotic stability result is the following theorem of Kulenović and Ladas [11]:

Theorem 1 *Let I be a compact interval of the real numbers and assume that $f : I^3 \to I$ is a continuous function satisfying the following properties:*

1. *$f(x, y, z)$ is non-decreasing in x and non-increasing in y and z*
2. *The system* $\begin{cases} f(M, m, m) = M \\ f(m, M, M) = m \end{cases}$ *has a unique solution $M = m$ in I.*

Then the equation $x_{n+1} = f(x_n, x_{n-1}, x_{n-2})$ has a unique equilibrium $\bar{x}$ in I and every solution of it that enters I must converge to $\bar{x}$. In addition, $\bar{x}$ is globally asymptotically stable.

The following figures illustrate the global dynamics of Equation (11).

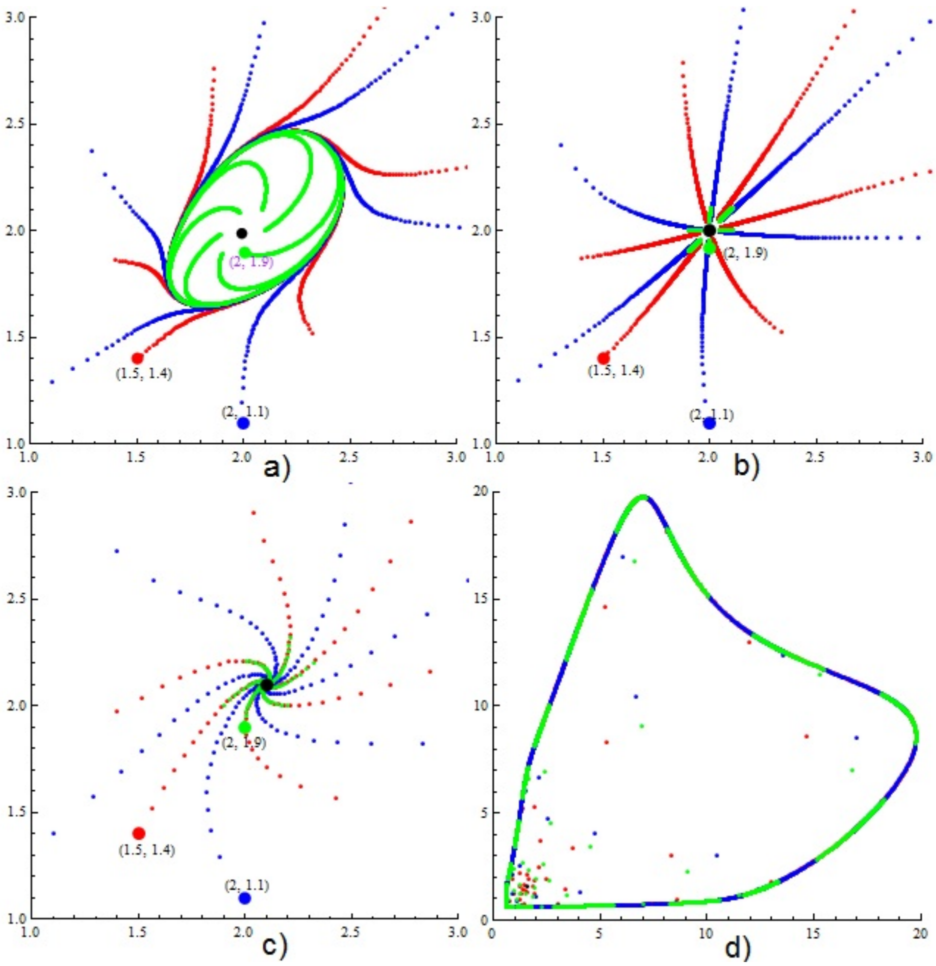


Figure 1: a) Phase diagrams when $n = 10,000$ and a) $a = 0.99$ b) $a = 1$ c) $a = 1.1$ d) $a = 0.589$.

2.2 The Global Dynamics and Bifurcations of Equation (12)

In this project I considered the global dynamics of Equation (12), which is one of the perturbation of Beverton-Holt equation (8). As is well known Equation (8) exhibits simple global dynamics where the zero equilibrium is globally asymptotically stable for $f \geq 1$ and the positive equilibrium is globally asymptotically stable for $f < 1$, see [1, 3]. This dynamics can be shortly described in the language of bifurcation theory by saying that there is a single change of stability or transcritical bifurcation at the critical value $f = 1$.

Clearly for $f \geq 1$ the zero equilibrium $\bar{x}_0$ is unique and globally asymptotically stable. On the other hand if $f < 1$ the zero equilibrium loses its stability, turns into a saddle point and allows coexistence with a positive equilibrium that is locally asymptotically stable for $\frac{1}{2} \leq f < 1$. Furthermore, I noticed that the positive equilibrium $\bar{x}$ is associated with complex conjugate charactaeristic values such that when $f < \frac{1}{2}$ its stability is subject to the following conditions:

1. If $c < \frac{2d^2}{(1-2f)^2}$ then $\bar{x}$ is locally asymptotically stable;

2. If $c = \frac{2d^2}{(1-2f)^2}$ then $\bar{x}$ is non-hyperbolic;

3. If $c > \frac{2d^2}{(1-2f)^2}$ then $\bar{x}$ is a repeller

Using Naimark-Sacker bifurcation theorem, I proved that Equation (12) exhibits Neimark-Sacker bifurcation for the critical value $c_0 = \frac{2d^2}{(1-2f)^2}$ and showed the existence of a local attracting invariant and closed curve encircling the equilibrium for $c < c_0$; c close enough to c_0. I also used Murakami's method [9] to algebraically approximate the invariant curve.

As of global stability I used a change of variable as well as the embedding method [10] to bring Equation (12) to the form:

$$z_{n+1} = 1 + (\frac{c}{d^2 z_{n-1}^2} + f) + (\frac{c}{d^2 z_{n-1}^2} + f)(\frac{c}{d^2 z_{n-2}^2} + f) z_{n-1}$$

Then I extended Theorem 1 to apply for functions that aren't necessarily monotone which allowed me to prove global asymptotic stability of the positive equilibrium $\bar{x}$ for $c < \frac{d^2}{1-f}$.

The following is my extension of Theorem 1:

Theorem 2
Let $\mathcal{S} \subseteq \mathbb{R}^k$, $f : \mathcal{S} \to \mathbb{R}$ and I a compact interval of the real line.

Suppose there exists a continuously differentiable function $G : I \times I \to I$ satisfying the following properties:

1. *$G(x, y)$ is non-decreasing in x and non-increasing in y*
2. *for all $m, M \in I$, $m \leq x_1, ..., x_k \leq M \Rightarrow G(m, M) \leq f(x_1, ..., x_k) \leq G(M, m)$*
3. *$G(x, y)$ has a unique fixed point $\bar{x}$ in I*
4. $\begin{cases} G(M, m) = M \\ G(m, M) = m \end{cases}$
   (a) *has "a unique solution $M = m = \bar{x}$ in I*

   " or " alternatively:

   (b) *has "two solutions $M_1 = m_1 = \bar{x}$, $M_2 \neq m_2$ and $G_x(\bar{x}, \bar{x}) - G_y(\bar{x}, \bar{x}) < 1$"*

Then:

1. *$\bar{x}$ is also a unique fixed point for $f(x_1, ..., x_k)$ in I*
2. *every solution of the difference equation $x_{n+1} = f(x_n, ..., x_{n-k+1})$ in I must converge to $\bar{x}$*

The results I obtained for Equation (12) show that this equation as a perturbation of Equation (9) undergoes major dynamic changes in such a way that in addition to exchange of stability bifurcation another more complicated bifurcation occurs indicating the possibility of chaotic dynamics or periodic solutions of unknown periods.

2.3 The Global Dynamics and Bifurcations of Equation (13)

In this project I considered the global dynamics of Equation (13), which is one of the perturbations of sigmoid Beverton-Holt equation (10). As is well known Equation (10) exhibits an interesting global dynamics with up to three equilibrium solutions and up to three period-two solutions, with different basins of attractions [4]. The dynamics of Equation (10) can be described as the sequence of exchange of stability bifurcations and period-doubling bifurcations [5]. I turned Equation (13) into a two dimensional dynamical system using the following substitution: $x_{n-1} = u_n,\ x_n = v_n$ with a corresponding map T of the form:

$$T\left(\begin{smallmatrix} u \\ v \end{smallmatrix}\right) = \left(\begin{smallmatrix} v \\ \frac{u^2}{cu^2+dv+f} \end{smallmatrix}\right).$$

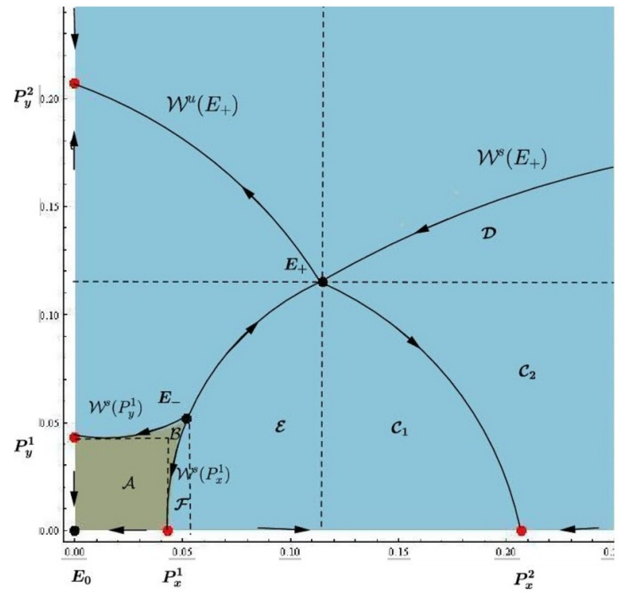
I have showed that this system has the following local dynamics:

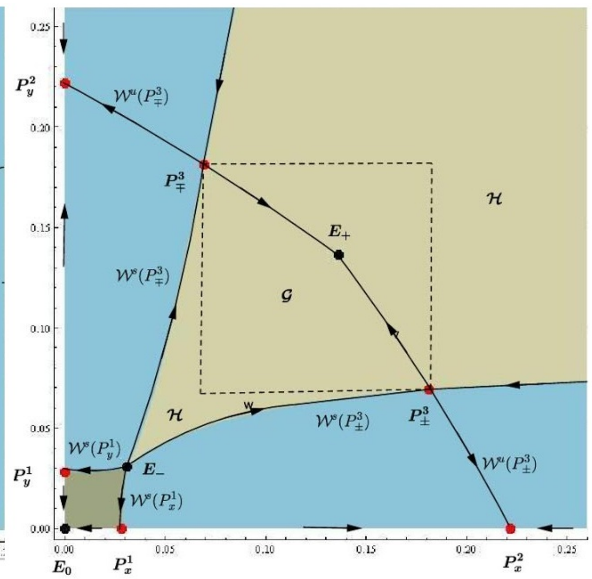
1. If $4fc>1$ then there are no period-two solutions and $E_0 = (0,0)$ is the unique equilibrium.
2. If $4fc = 1$ then there is one minimal period two solution and $E_0 = (0,0)$ is the unique equilibrium.
3. If $4fc<1$ and $(1-d)^2 - 4fc<0$ then there are two minimal period-two solutions and $E_0 = (0,0)$ is the unique equilibrium.
4. If $4fc<1$ and $(1-d)^2 - 4fc = 0$ then there are two minimal period-two solutions and two equilibrium points.
5. If $4fc<1$ and $0<(1-d)^2-4fc \leq 4d^2$ then there are 3 equilibrium points and two minimal period-two solutions.
6. If $4fc<1$ and $(1-d)^2 - 4fc>4d^2$ then there are 3 equilibrium points and 3 minimal period-two solutions.

It is a fact that the second iterate T^2 is **strongly competitive** and clearly all period-two points of T turn out to be the equilibrium points for T^2 [5, 6]. In addition I studied the stability at each of the equilibrium points and applied the theory of invariant manifolds for discrete competitive systems to find all the basins of attractions [5, 6].

There is an extensive literature on competitive and cooperative systems and many mathematicians participated in the development of this theory such as A. Brett, D. Clarke, J. Cushing, E. Dancer, J. Franke, P. Hess, M. Hirsch, S. Kalabušić, U. Krause, M. R. S. Kulenović, G. Ladas, O. Merino, E. Pilav, J. Selgrade, H. L. Smith, P. Takac, H. Thieme, A.-A. Yakubu, [2, 3, 5, 6, 12, 14, 15, 16, 17, 18, 19, 20]. Competitive and cooperative systems are used to model different interactions between two or more subjects in population dynamics, economics and biochemical networks. An extensive theory has been developed especially in the case of competitive and cooperative interactions between two species, where different scenarios such as competitive exclusion, competitive coexistence and the Allee's effect have been understood [2, 5, 6].

The following figures illustrate the global dynamics of the second iterate in the cases 5 and 6 stated above.





3 In Progress/ Future Work

I expect to extend the obtained global dynamics results for Equation (13) to a general second order difference equation

$$x_{n+1} = f(x_n, x_{n-1}), \quad n = 0, 1, \ldots, \tag{14}$$

where f is continuous function, decreasing in the first and increasing in the second variable and thus extend and generalize some results in [4].

I am also working on generalizing Theorem (3) to achieve stronger conditions subject to which local asymptotic stability implies global asymptotic stability.
Moreover I will be considering the study of a collection of difference equations that are perturbations of Beverton-Holt models.

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