2. Executive Summary

The area in this nomination is applied mathematics and statistics with applications in the biological sciences. UNC Charlotte clearly has existing strength in this area, and we believe that it forms an emerging area of excellence for the university. With additional resources, we would like to establish a Center for Mathematical Biosciences that would bring together researchers from across the university working in this area and catalyze collaboration. Here we discuss several ongoing research themes that could form the foundation for such a center.

Research Theme 1 (Lead: Y. Diao). Computational/statistical methods with applications related to drug development/disease treatment. The aim of this research direction is to use mathematical/statistical tools to tackle important problems in cell biology and microbiology. For example, a current project (Y. Diao & collaborators in applied math, biology and microbiology) concerns the 3D structure of the DNA of a class of parasites called Trypanosomatid parasites. These parasites cause deadly diseases (such as leishmaniasis and Chagas disease), but current treatments are toxic and difficult to administer. New anti-trypanosomatid drugs are difficult to develop due to the amazingly complicated 3D structure of the kDNA (hence the need for a good understanding of it). Another project (D. Chen, S. Li & collaborators at Mayo Clinic) concerns analyzing the overwhelmingly large and complicated genetic data from patients of Alzheimer's disease and control groups with an aim to develop an innovative data analysis pipeline for information "identification, implementation, and causal inference". Success of this research will reveal novel insights into the genes and pathways of AD, and hence is potentially helpful for drug targets therapeutics.

Research Theme 2 (Lead: X. Li). Multiscale modeling in bioprosthetic heart valves (BHVs) damage progression. BHVs are artificial replacements for diseased valves that mimic the structure of native valves. BHVs have advantages in immunogenicity and hemodynamics over other designs and therefore have become the preferred replacement valve over the last decades. However, the life span of BHVs remains limited to 10-15 years, and the mechanisms that underlie BHVs failure remain poorly understood. A central theme of this research direction is the development of a computational approach to improve the existing knowledge of the mechanism of BHVs failure, but also to help critically extend its lifespan. One example of this research direction is a current project (X. Li & collaborators) aiming at developing nonlocal-to-local coupling methods and numerical solvers to combine local mechanics with mesoscopic physical laws, which aims at modeling the interactions of blood fluids and aortic walls at the critical region of leaflets.

Research Theme 3 (Lead: K. McGoff). Dynamical models in genomics and epidemiology. Broadly speaking, this program seeks to understand the "rules" that govern the behavior of biological systems over time. Many biological systems exhibit complex behavior over time. For example, the gene expression profiles of mammals exhibit possess organ-specific circadian rhythms, and important dynamical patterns have been observed in systems ranging from the human microbiome to the spread of infectious diseases in a population. Understanding such "rules" requires research on both the theoretical and the applied aspects of dynamical systems, *i.e.*, complex systems that evolve over time. One ongoing project in this direction (K. McGoff & collaborators in biology) involves understanding the dynamic host-parasite interactions that cause malaria. A second ongoing project (K. McGoff & collaborators in epidemiology) involves understanding the dynamics of COVID-19 transmission using mathematical and statistical modeling.

Existing and emerging excellence. Collectively, the participants in this nomination have a strong record of collaborative research in the areas identified in the three themes, and some of them have already received recognition at the national level. This strong record of success justifies this nomination to be in the category of "Existing and Emerging Excellence". Drs. Xingjie Helen Li and Kevin McGoff both joined UNCC in 2015, and each of them has already received the prestigious NSF CAREER Award (which is a national recognition), as well as an additional NSF grant. Dr. Yanqing Sun is the recipient of 6 NSF grants (PI) and two NIH R37 MERIT Awards (co-PI) and her research is being processed for analyses of COVID-19 vaccine trials. Dr. Duan Chen was co-PI of an NSF grant, and Dr. Yuanan Diao was PI on 4 NSF grants (all of these were collaborative research projects). Dr. Gabor Hetyei was PI on 2 past grant awards (one from NSA and one from the Simons Foundation) and is PI on a current grant from Simons Foundation. Dr. Shaoyu Li was co-PI of an AHRQ R21 grant and has several grant proposals pending.

3. Evidence of Strength and Excellence

Participants in this nomination consist of fourteen faculty members from six departments. The participants from the Department of Mathematics and Statistics include: Duan Chen, Yuanan Diao, Gabor Hetyei, Shaoyu Li, Xingjie Li, Kevin McGoff and Yanqing Sun.

Evidence of Excellence: Individual Team Members.

Dr. Chen specializes in scientific computing and mathematical biology and has published more than 20 academic papers. Dr. Chen has established interdisciplinary collaborations with applied mathematicians and biologists across the nation (for example at NSF funded Mathematical Biosciences Institute and Mayo Clinics). His work has been well-recognized domestically and internationally, and it has been disseminated in US R1 universities and national/international institutions. Dr. Chen's research work was supported by NSF DMS-1619713 (2016–2019) and he is actively seeking external funding support. After joining UNCC, Dr. Chen has supervised multiple undergraduate and graduate theses.

Dr. Yuanan Diao specializes in knot theory with applications to biological sciences. He has more than 110 publications and has numerous collaborators including researchers in biology, microbiology and physics. These collaborations led to 4 funded NSF grants (he was PI for all of them): NSF DMS-0310562 (2003–2006), DMS-0712958 (2007–2010), DMS-0920880 (2009–2013) and DMS-1016460 (2010–2013). At UNCC, Dr. Diao has supervised a total of 5 doctoral students (3 graduated and 2 current), an undergraduate honor thesis and many undergraduate senior projects. His past and current students co-authored 22 papers with him (including an undergraduate student).

Dr. Gabor Hetyei specializes in combinatorics and graph theory, areas of mathematics with a wide variety of applications in the biological sciences. Dr. Hetyei has published 49 papers. He is PI on 3 external grant awards: #514648 (2017–2022) and #245153 (2012–2017) from Simons Foundation, and H98230-07-1-0073 (2007–2009) from National Security Agency. At UNCC he has supervised 3 doctoral students, one undergraduate honor's thesis and many undergraduate senior projects.

Dr. Shaoyu Li leverages her statistical theory to come up with compelling statistical methods and computational algorithms for cutting edge research and applications in biomedical research and public health through collaborations. She has published 25 papers (including more than 10 statistical methodological papers). These collaborations have led to an AHRQ R21 grant (AHRQ 1R21 HS 23875-01, 2015–2017, co-PI), two pending grants and two grant proposals to be submitted soon. Dr. Li supervised 8 master students and 5 undergraduate senior projects. Currently, she is supervising 1 Ph.D. student, 1 master student, and 2 undergraduate senior projects.

Dr. Xingjie Li has built interdisciplinary collaborations with mathematicians, physicists and engineers from domestic R1 universities and international institutions as well as senior scientists from Oak Ridge National Laboratory and Sandia National Laboratories. She has published more than 20 papers in leading peer reviewed journals, received several external grants, including (1) the Simons Foundation Collaboration Grant from Sep. 2016 to Aug. 2018; (2) the NSF DMS-1720245 from Sep. 2017 to Aug. 2020; and (3) the NSF CAREER award: DMS-1847770 from Jul. 2019 to Jun. 2024. Meanwhile, Dr. Li has been supervising undergraduate research and graduate thesis topics since 2016.

Dr. McGoff has a proven track record of success in interdisciplinary collaborations with mathematicians, statisticians, biologists, and epidemiologists. His collaborators almost all work at domestic R1 institutions or their international equivalents. Altogether, he has published 18 papers in top tier peer reviewed journals, and he received substantial external funding. In particular, he has served as PI for two grants: NSF grant DMS-1613261 ($225,000 from 2016 to 2019) and NSF CAREER grant DMS-1847144 ($419,367 from 2019 to 2024). Additionally, Dr. McGoff has supervised 10 undergraduate students in summer undergraduate research projects (REUs) and 12 undergraduate theses. He is currently advising one Master's student and one Ph.D. student at UNC Charlotte and co-advising a doctoral student at UNC Chapel Hill.

Dr. Yanqing Sun has made outstanding contributions in developing statistical methods to solve many complex problems arising from medical and public health studies. Her research has been funded both by NSF and NIH continually since 2003 (PI on 6 NSF grants, co-PI on 2 NIH R37 grants with more than 2

millions dollars to UNCC). She played a significant role in the national HIV vaccine efficacy trials and some methods developed by Dr. Sun are currently being processed for analyses of COVID-19 vaccine trials. Dr. Sun has published over 60 peer-reviewed statistical papers in statistical journals. She has supervised 17 Ph.D. students (13 graduated and 4 current) and published twenty five statistical papers with her students.

Emerging strength of the proposed area as a whole.

As described above, the individual math/stat researchers in this nomination have a demonstrated record of excellence. Within the math department, they have worked with each other in various ways, and these interactions have been quite successful. Furthermore, their collective research expertise covers a wide range of topics, including both domain specific topics like kDNA modeling, AZ data analysis, and vaccine efficacy trials, and also more broadly applicable theories/methods such as dynamical systems theory, mathematical modeling, mathematical computation, and statistical inference. This collective expertise has substantial overlap with the research interests of many faculty members across UNCC, and the potential for high impact inter-disciplinary collaboration is high. Indeed, we have received enthusiastic interest in this nomination from UNCC researchers from outside the Department of Mathematics and Statistics, which we describe in the following paragraph. Taken together, we strongly believe that this team is a source of emerging excellence for the university.

Dr. Kausik Chakrabarti (biology) studies the mechanisms of regulation of gene expression at the post-transcriptional and translational level and defining the modulatory pathways of genome integrity in blood-borne pathogens, Plasmodium falciparum (Malaria) and Trypanosoma *brucei* (Neurodegenerative disease), and in human cancers. Trypanosoma *brucei* is in fact a kDNA used by Dr. Diao and his collaborators to test their kDNA model. Dr. Jun-Tao Guo (bioinformatics) aims to have a better understanding of protein-DNA interactions in order to advance our knowledge of the mechanisms of specific protein-DNA recognition, since this knowledge bears implications in the design of novel therapeutic molecules. The goal of his lab is to develop computational tools and resources for studying protein-DNA interactions and this is an area that Dr. Duan Chen's expertise may fit. Dr. Donald Jacobs (physics) works in biophysics, where he applies rigidity theory to study mechanical stability of proteins and has been working on the open challenge of predicting protein thermodynamics, flexibility and dynamics at a pragmatic level useful for drug discovery workflows. Dr. Irina Nesmelova (physics) focuses on the molecular logic underlying biological function. Her research projects include structure-function-dynamics of proteins, protein-protein interactions and translational diffusion of proteins. Her research could use statistical inference and could yield fruitful collaboration with Drs. S. Li, McGoff and Sun. Dr. Robert Reid (bioinformatics) uses computational technology and statistics for biological data analysis in his research. He and his collaborators saved valuable time and money analyzing massive data sets. Drs. Chen and S. Li also work on massive data sets so they could collaborate in the future. The research of Dr. Alireza Tabarraei (mechanical engineering) is on multiscale modeling, computational materials science and nano materials failure mechanics and aligns well with Dr. X. Li's expertise. Dr. Shan Yan (biology) is interested in crucial issues in maintaining genomic stability, including checkpoint activation, DNA damage repair, and translesion synthesis (TLS) in response to DNA replication stress and oxidative stress as well as other stressful conditions. He uses statistics in his research and has already teamed up with some stat faculty members in the math department.

Potential use of additional resources.

With additional resources, we anticipate that we will be able to create a robust, cohesive, productive and successful research group that will help the university to advance toward the goal of becoming an R1 university. In particular, we would like to establish a Center for Mathematical Biosciences at UNC Charlotte. Establishing a center would confer many benefits to the university, *e.g.*, raising the profile of our research and collaborations, opening new opportunities for external funding, and attracting students and faculty. However, in order to establish such a center, we would need substantial additional resources to expand our current program (with our current teaching duties and limited man power, we simply cannot meet the demand). We envision an incremental process in which the university could provide resources in the form of increased funding for graduate students, postdoctoral positions, and/or seed funding to further develop our interdisciplinary collaborations. Leveraging these resources, we would hope to put ourselves in a position to be more competitive for significant external funding for the center.

4. Alignment with Regional and National Priorities

The proposed research programs in this nomination align very well with the mission of the university and the regional, national and international priorities. Its success has direct impact on medical, health and economical development for the Charlotte region, the nation and the globe.

National Priorities. One of the "NSF's 10 Big Ideas" (https://www.nsf.gov/news/special_reports/big_ideas/life.jsp) is *Understanding the Rules of Life*, and this Big Idea perfectly aligns with the research of this proposed area of excellence. Life on our planet is arranged in levels of organization ranging from the molecular scale through to the biosphere. There exists a remarkable amount of complexity in the interactions within and between these levels of organization and across scales of time and space. For example, within an ecosystem, biotic, abiotic and environmental components of the system can all interact within a single process, as in the nitrogen cycle. One of the NSF "Rules of Life" goals is to enable discoveries that will allow us to better understand such interactions and identify causal, predictive relationships across these scales – so-called "rules" for how life functions. The participants in this nomination are already conducting research towards this goal, and we believe that UNC Charlotte can emerge as a national leader in the use of mathematical and statistical methods for understanding the rules of life.

Furthermore, the research conducted in this area aligns with many national health priorities. For example in the kDNA project currently undertaken by Dr. Diao and his collaborators, the goal is to understand what is the 3D geometric as well as topological structures of the kDNA minicircle/maxicircle networks, and what roles such structures play in the cell development of the parasites. In the AD study headed by Drs. D. Chen and S. Li, a different approach using a combination of mathematical modeling and statistics is developed to tackle genes whose differential expression are causal to Alzheimer's disease. This is an important study since AD affects 5.7 million patients with annual cost of more than $230 billion in the US. Dr. McGoff's work on inference of dynamic host-parasite interactions could lead to novel treatments for malaria. Also, in the midst of a global pandemic, mathematical and statistical models of infectious diseases form an important source of information for our public health officials, and further development of such models will be crucial for our national preparedness for future epidemics.

In 2021, the U.S. government announced the launch of a Material Genome initiative (MGI) to accelerate material design, discovery and analysis and in 2021, the NSF updated the Future Manufacturing (FM) program solicitation (NSF 21-564) to support fundamental research and education in order to enable new manufacturing capabilities that do not exist today. Research Theme 2 in this nomination aims to develop robust mathematical models for biological materials and reliable numerical solvers which align perfectly with these goals. In a recent joint work with collaborations from Lehigh University, UC San Diego and Oak Ridge National Laboratory, Dr. X. Li presented a new high order numerical method as well as rigorous analysis to describe complex physics in a randomly heterogeneous materials, modeling the interactions between fluids and the peridynamic shells which can deal with multiple types of microstructural damages. This work provides a road map to add uncertainty quantification in biological materials modeling in a non-intrusive manner and achieves convincing results that are compared to the exponential data.

Regional and University Priorities. As an urban research university in North Carolina, it is UNCC's mission to leverages its location in the state's largest city to offer internationally competitive programs of research and creative activity, exemplary undergraduate, graduate, and professional programs, and a focused set of community engagement initiatives. The Department of Mathematics and Statistics has played an important role in supporting the university's mission. The department has a very strong graduate program in applied mathematics/statistics with national rankings of #108 and #97. For context, only ten other programs at UNCC have a higher rank, and the overall ranking of UNCC is #227. In the last 5 years (2016 to 2020), the program has graduated 43 Ph.D. students and 50 Master's students. The program also has an excellent track record of students' job placement. Our graduates are placed into high-paying jobs as well as academic jobs in the region and around the country. The program also has significant engagement with the Charlotte business industry and mathematical/statistical consulting is of growing demands. The successes of the programs in this nomination will have funded research opportunities for our graduate as well as undergraduate students, which will further strengthen our undergraduate and graduate programs. This aligns well with the mission of UNCC.

5. Supporting Documents

Part 1. List of participants and leads/co-leads (* indicates math/stat faculty), along with their titles, roles, and areas of expertise.

Yuanan Diao*	Professor Mathematics	Lead	Dynamical Systems, Functional Analysis, Mathematics Modeling, Mathematical Biology, Knot Theory
Xingjie Li*	Asso. Professor Mathematics	Co-Lead	Computational Mathematics, Mathematical Modeling, Mathematical Materials
Kevin McGoff*	Asso. Professor Mathematics	Co-Lead	Dynamical systems, systems biology, time series gene expression modeling, infectious disease modeling
Kausik Chakrabarti	Asst. Professor Biology	Participant	RNA in Genome Regulation, RNA-Protein Interactions, Cell Proliferation and Genome Integrity, Plasmodium Falciparum (Malaria) and Trypanosoma *brucei* (Neurodegenerative Disease)
Duan Chen*	Asso. Professor Mathematics	Participant	Computational Mathematics, Mathematical Modeling and Mathematical Biology
Jun-Tao Guo	Professor Bioinformatics	Participant	Structural Bioinformatics, Proteins Structure Prediction, Protein-DNA Interactions, Evolution of Regulatory Pathways
Gabor Hetyei*	Professor Mathematics	Participant	Enumerative & Algebraic Combinatorics, Commutative Algebra, Graph Theory
Donald Jacobs	Professor Physics	Participant	Computational/Statistical Physics, Condensed Matter, Molecular Biophysics, Structural Biology, Computational Biology, Data Analysis and Modeling
Shaoyu Li*	Asst. Professor Statistics	Participant	Statistical Genetics & Genomics, Statistical & Computational Methodologies, Cell-Type Specific Transcriptional Changes Associated with Human Diseases, Statistical Design & Analysis Methods for Mobile Health Studies
Irina Nesmelova	Asso. Professor Physics	Participant	Experimental Biophysics, Structure-Function-Dynamics Of Proteins, Protein-Protein Interactions, Translational Diffusion Of Proteins
Robert Reid	Asst. Professor Bioinformatics	Participant	Computational Technologies, Statistics For Biological Data Analysis, Sequence, Variant & Pathway Analysis, Genome Sequence Assembly
Yanqing Sun*	Professor Statistics	Participant	Survival Analysis, Parametric and Nonparametric Methods, Estimation and Hypothesis Testing, Vaccine Efficacy Trials
Alireza Tabarraei	Asso. Professor Mechanical Engineering	Participant	Multiscale modeling, Computational Materials Science, Nano Materials Failure Mechanics
Shan Yan	Professor Biology	Participant	Molecular Mechanisms of Genome Integrity, Cancer Biology, Cell Biology, Molecular Biology, Developmental Biology, Environmental Health

Part 2. 2-page CVs of the participants (attached).