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Intellectual Merit: A major goal of mathematical models and analysis in biology is to provide insight into the complexities arising from the non-linearity and hierarchical nature of biological systems. Primary goals of the proposed Center will be to **foster the maturation of cross-disciplinary approaches in mathematical biology** and **foster the development of a cadre of researchers who are capable of conceiving and engaging in creative and collaborative connections across disciplines to address fundamental and applied biological questions.** Our vision for the proposed Center is to efficiently utilize NSF funding: 1) to address key biological questions by facilitating the assembly and productive collaboration of interdisciplinary teams; and 2) to foster development of the critical and essential human capacity to deal with the complexities of the multi-scale systems that characterize modern biology.

We propose a variety of routes to achieve the above goals, based upon our prior successes in developing new interdisciplinary collaborations nationally and internationally, and on the successful efforts at other Centers. Initially, we will develop a series of **small working groups** on emphasis areas at several levels of biological organization that will benefit from interdisciplinary efforts (human origins, infectious disease management in systems involving wildlife hosts, multi-scale analysis of cellular processes, intragenomic conflict). Some groups will be formed in response to requests from a government agency partner. These initial emphasis areas will then be **expanded, based upon proposals from the research community and collaborative efforts with industry and government agency partners**. Workshops assembling larger groups of researchers will assess somewhat broader problems, with dual goals of fostering language-building across disciplines and defining specific issues to be addressed by future working groups.

Human capacity building will be fostered through: direct mentoring of new researchers (including undergraduate and graduate students and post-doctoral fellows); outreach efforts in collaboration with professional societies to educate biologists about mathematical and computational approaches found to be broadly useful in biological application; connections to institutions serving under-represented groups; a 'research experience for undergraduates' program that will incorporate high school teachers; and varying levels of tutorial workshops designed to enlighten biologists about key quantitative methods – for example, the application of high performance computing methods to analyze biological problems which involve large data sets, spatial information, and dynamics. At the same time, we will assist mathematicians to identify new mathematical challenges arising from current biological research.

Broader Impacts: The nature of the questions addressed by the Center will span all of biology, thus impacting both basic and applied science. These **impacts will necessarily be broad**, ranging from specific models and applications (physiological integration, disease projection, reserve design) to fundamental questions about human origins, biosphere functioning, and the emergence of biological patterns at diverse scales. The Center will become a primary location for the rapid analysis of numerous questions of direct public policy concern, from the impacts of biofuel development, to the ongoing challenges of invasions of non-native species, to global change issues related to human activity. As a specific initial venture to address national needs, we will collaborate with Great Smoky Mountains National Park to develop methods of particular interest for natural area management that will be transferable to numerous U.S. locations.

Mathematical biology has to date benefited from the large impact of relatively few individuals and programs that have trained the vast majority of active researchers at this interface. The proposed Center will foster the next step: **continuing the development of individuals trained at this interface**, but also **fostering the development of entire programs that are equipped to educate the array of mathematically competent, biologically knowledgeable and computationally adept researchers** needed to address the vast array of challenging questions in this century of biology. Fostering high quality interdisciplinary programs, focused particularly on underrepresented groups, will be a major emphasis of the Center.

Rationale for the Center:

The field of mathematical biology has undergone significant transition over the last decade, with research becoming much more closely linked to observation and experiment. Rather than starting from mathematical abstractions, it is now common for researchers to 1) begin with observations; 2) use those to suggest promising methods, tools and models; and 3) proceed to analysis, simulation, evaluation and application. Across the spectrum of the life sciences in which mathematics has been contributing new insights, data are increasingly used to focus conceptual models as the first step in problem formulation. There is a close connection to biological reality, abstracted as necessary, to phrase compelling and worthwhile biological questions, derive the import of assumptions, and reach new biologically-relevant conclusions based upon the math.

A parallel trend is seen in practice: no longer is mathematical biology solely the domain of theoreticians with objectives of abstraction and generality. Models and analysis are serving to directly improve public policy, health practice, and natural resource management. The vision expressed in the early 1990s as to the potential contribution to basic science has been realized and exceeded. Today, we see innovative and successful application for the purpose of informed decision-making in industry (development of pharmaceuticals, food safety actions) and government (disease and threat surveillance), as well as forays into areas such as economics and human social systems. Concurrently, the explosion in data gathering capacity arising from technological advances has provided new challenges to the cohesive structuring of biological knowledge at every level - from within the cell to across the planet.

In conjunction with the above is the continual strengthening of interactions between biology and other fields and a growing appreciation that advances in biology necessitate ongoing efforts to enhance interdisciplinary collaboration. Integration with other sciences has been particularly evident in suggestions on the education of future research biologists[87] and underpins an array of open theoretical biological questions.[88] The proposed activities of this Center will serve as a fulcrum to leverage quantitative approaches to advance biology over the near- term (next decade) and long-term (next several decades) by: 1) **fostering new collaborative efforts to investigate fundamental and applied questions arising in biology using appropriate mathematical and computational methods** and 2) **enhancing the critical and essential human capacity to analyze complex biological questions**, producing a diverse cadre of individuals who can not only conduct the research themselves, but can also lead the development of new educational programs.

The proposed activities for the Center complement each other in meeting the above goals. Interdisciplinary research succeeds in a number of different formats and the Center activities that foster these include the development of working groups on specific problems, collections of working groups that involve collaborative activities between groups each with somewhat different issues to address around a larger central problem, workshops that focus larger groups of researchers on major areas that require prioritization and structuring before smaller working groups can address them efficiently, and activities built around longer-term commitments of effort by visiting researchers, staff, post-docs and students. Open-ended discussions in collaboration with industry and government partners will assess the feasibility and efficacy of developing working groups for these more application-driven areas, and will suggest projects for longer-term research collaborations involving Center staff. A key area for interaction with industry partners IBM and ESRI concerns the potential high-performance computing approaches, linked with appropriate visualization, to provide new models and insights in challenging multi-scale problems. This integrated approach to the interdisciplinary research efforts of the Center will expand upon the structures built at other NSF-funded Centers – particularly those addressing the multiple-scale research questions to be addressed and the mixture of basic and applied problems at the math/biology interface.

Consistent with this mixed-format approach to research is an associated mixture of approaches for educational and outreach activities. Short-term introductions to particular research methods (developed as tutorials), more intense exposure to new research themes for visiting undergraduates and graduate students, and extensive long-term collaborations involving post-doctoral fellows will all contribute to the objective of building a cadre of researchers who are "fearless" in their ability to mix biological, mathematical and computational approaches in addressing biological questions. A major objective of the Center to is to *foster the development of entire programs to educate the array of mathematically competent, biologically knowledgeable and computationally adept researchers* needed to address the vast array of open questions in this century of biology. Given this objective, we propose to expend a major fraction of the resources of the Center on post-doctoral fellows who will likely be the largest contributors to the development of programs elsewhere upon completing their tenure at the Center. Assessing the impact of this investment in fostering other interdisciplinary programs require a several decade overview. To help shorten this time period, we propose that part of the Center's outreach efforts will be to identify institutions - particularly those that serve under-represented groups - that offer opportunities for rapid development of such programs and encourage connections with Center post-docs and students. In collaboration with agency partners, notably initially the National Park Service, we propose outreach initiatives to a larger public that will illustrate the interconnections between the scientific fields that contribute to natural system management. Through this outreach, we will collaborate in the establishment of displays and interactive computer models arising from Center activities in highly-visible public locations such as National Park visitor centers.

Research activities:

There are several outstanding institutional models from which to choose best practices to accomplish our vision, including other Centers supported by NSF. In addition to collaboration with the wide-ranging activities of these other Centers and institutions, we propose to meet our objectives by building upon our thirty years of leadership, experimentation and experience with the unique interdisciplinary program in mathematical ecology and evolution at the University of Tennessee.[12,29,58] In the course of our innovative and iterative attempts to engage multiple disciplines in fruitful discovery, we have found that we must painstakingly cultivate the conditions for producing 1) the requisite **intuition** of life scientists for mathematics and of mathematicians for biology; 2) a common **language** that can be rapidly acquired by the participants in working groups for a specific biological question; and 3) agreement **on appropriate mathematical tools** for addressing the problem of concern. We have most effectively nurtured that sense of intuition and that common language and tool set by engaging interdisciplinary teams focused upon questions that are sufficiently biological in nature but that also require the quantification and abstraction of mathematics, a thread common to many suggestions.[9,16,49,55,72,73,78,94,103]

The proposed Center activities are designed to produce an expanding cohort of young researchers skilled in translating and adapting perspectives and solutions across mathematics and biology, within their respective sub-fields, and in both basic and applied science. To the task of making connections and fostering productive collaborations, we bring an established reputation for leadership and commitment to path-breaking interdisciplinary work;[1,7,8,24,25,37,45,60,62,63] a particular affinity for guiding gifted students from many fields and diverse backgrounds;[1,4,5,7,8,34,44,45,61,100] and a conviction that information and understanding should be widely disseminated and shared.[37,99,108]

Our enterprise will be led by distinguished faculty across several units of UT, in collaboration with colleagues at Oak Ridge National Laboratory, industry partners including IBM and ESRI, and government agency partners including the National Park Service. Our colleagues link as well to a vast array of significant national and international research efforts and institutions operating at the interface between math and biology. We view as critically important to the continuing enhancement of modeling methods in application to biology a high level of competence and thoroughgoing experience with

computational science. To that end, locating the Center at Tennessee would ensure that it has at hand the extensive computational resources of UT/ORNL, including both some of the world's most advanced hardware and the human expertise to effectively use this hardware across the sciences.

Major research-focused initiatives we propose for the Center to meet our objectives are:

1. To increase the cadre of scientists in the US with experience at the interface of mathematics and biology required to address the range of open scientific and practical problems in biology, we envision several routes to success based upon our experiences at Tennessee[12,29,50,58] as well as in our leadership roles at other major Centers (including the NSF Mathematical Biosciences Institute). Our goal is to make it possible for individuals from diverse backgrounds at different levels of experience to be able both to express their biological questions mathematically and to evaluate the alternative biological and mathematical assumptions inherent in these types of analyses. This objective will be met by offering residences for both post-doctoral fellows and graduate students for short-term (several weeks to months) as well as longer-term (1-2 year) periods, in addition to providing space for both junior and senior researchers who wish either to participate in collaborative projects for short periods or to spend a sabbatical at the Center. Ongoing programs at the Center will include short, research-level overviews in numerous areas of biology and mathematics, led by leading researchers at the math/biology interface. These programs will be made broadly available electronically (with interactive feedback) to individuals not in residence at the Center, and will be timed so as to supplement the activities of working groups.

Table 1
Major Initiatives

- Human Capacity Building among diverse groups at the interface of math and biology
- Collaborative Working Groups and workshops focused on basic and applied issues and national needs
- HPC and spatio-temporal issues within biology (in collaboration with Industry Partners)
- Education – REU, UBM, Mentoring Network, Tutorials
- Outreach and Professional Societies

2. Provide an opportunity for collaborative working groups across disciplines to analyze a variety of problems in biology that require mathematical formulation and analyses to investigate them effectively. We have been building such teams across disciplines here at the University of Tennessee for many years, involving collaborators from many units.[1,24,62,67,70,71,75,82,99,107] (Our recent NSF funding has supported students and collaborators based in Geography, Computer Science, Electrical Engineering, Mathematics, Ecology and Evolutionary Biology, the College of Veterinary Medicine and Forestry, Wildlife and Fisheries.) We have developed and organized workshops for diverse groups with widely-varying levels of quantitative experience, including Short Courses on the Mathematics of Biological Complexity (www.tiem.utk.edu/courses/) designed for biologists with little formal math training and several workshops on Computational Science for Natural Resource Managers designed for field practitioners.[37,109] Through our many leadership roles in international and national organizations, the senior personnel of this proposal have also organized a vast array of workshops and courses at other institutions around the world and have an exceptional network of contacts for prospective participants in working groups at the Center. The Center will support on average 20 working groups and 4 workshops per year.

3. Provide opportunities for implementation and education in high performance computing (HPC) in application to biological problem solving.[37,75,82,106,108,109] This includes hands-on short-term workshops as well as longer-term collaborative projects. Both will employ the expertise of staff based in the Center who are knowledgeable about both biology and the variety of high performance computational facilities and approaches available, including particularly that of the NSF-supported TeraGrid. Sessions on the application of high performance computing to biology will be both formal and informal, through the participation within the Center of UT/ORNL faculty and staff with extensive HPC and biology experience. However, it is not our intent to replicate the role of computational biology centers already established with concentration in bioinformatics and cellular-scale analyses. Rather, the Center would provide avenues for biologists to collaborate with computational scientists to develop <u>new</u> directions.[37,49]

4. Provide a central location for activities at all levels for math biology education, including educational research initiatives to assess the impact of these activities, and serve as an archive for materials and previous efforts across different levels. The emphasis will be first at the undergraduate level, building upon our previous experience developing the undergraduate set of quantitative courses for biologists highlighted in the BIO2010[87] report, running a long-term REU site and one of the first UBM programs[58] and our contacts with the ongoing NSF-funded UBM sites and those supported by the NIH Division for Minority Oriented Research Experiences programs emphasizing quantitative training in biology. A summer REU program will bring both undergraduates and appropriate educators (both high-school and 2-year school) to participate in activities of the Center, with mentoring provided by Center faculty and post-docs. We propose to develop an education assessment protocol, broadly applicable at institutions involved in math and biology educational activities, to evaluate impacts of these programs relative to more traditional, single discipline undergraduate training. Concurrently, we will build upon the pre-college and general public education activities of several Center collaborators to expand these to incorporate math/biology linkages. In addition to sponsoring formal workshops on implementation and assessment of the variety of educational activities in this area supported by NSF and other agencies, we propose to work closely with the variety of UBM programs supported by NSF to involve their participants in activities at the Center, either in person or remotely, and in particular we will organize a summer conference at the Center for UBM participants.

5. As a research outreach activity to the broader scientific community, we will cooperate with professional societies to present sessions on the mathematical connections to biology at meetings and venues both nationally and internationally. While there exist ongoing sessions related to biological applications at the major mathematical society meetings, relatively few professional biological societies offer such sessions at the math/biology interface. We argue that a very cost-effective method to advance the development of a mathematical view in many sub-disciplines within biology is to regularly illustrate the benefits of such approaches at society meetings. The Society for Mathematical Biology (SMB) has established a small grants program for this purpose but it has been little used to date. We plan to improve this situation in collaboration with the SMB and the American Institute of Biological Sciences (AIBS), a consortium of almost 200 professional societies in biology, in addition to other societies with an international span. The Center leadership team includes current and former Board members and officers of AIBS and SMB.

In all of the above, we will use the expertise of a Committee to Promote Diversity, to consist of five members external to UT, as a set of advisors to enhance the ethnic and gender diversity of participants in all Center activities. The explicit goal is to build upon the long-term success at UT in the gender diversity of our graduate and undergraduate efforts in mathematical biology (e.g. of our current math biology group of Ph.D. students, five are male and six are female, and of the 30 math biology students who have completed Ph.D.s at UT, 14 were female and 16 were male) to ensure access and participation at all levels of Center activities by individuals from under-represented groups. This Committee will be led by the Associate Director for Outreach, Education and Diversity, Dr. Suzanne Lenhart. We already have agreement from a math biologist from a historically-black college to serve on this Committee. Additional members will be recruited from contacts with the array of organizations the senior personnel have been involved with that promote diversity such as the National Association of Mathematicians, and individuals from diverse backgrounds with whom the Center personnel have collaborated in numerous biological and mathematical settings. One of the senior personnel of the Center, Agricola Odoi, will also serve on this Committee ensuring that his experiences as a scientist from a minority ethnic group will be used in planning broad participation in Center activities. The committee will suggest possible workshop and working group participants as well as assist in recruiting a diverse pool of post-docs. Diversity in participants will be one consideration in the guidelines for working group proposals as part of the vetting

process carried on through the Board of Advisers. Two members of the Committee to Promote Diversity, including its Chair (selected by its membership), will serve on the Board of Advisers

While questions and issues addressed by working groups and workshops at the Center will be chosen in large part through a proposal process open to the scientific community and vetted by our Board of Advisors, we propose to use two general scientific themes as starting points for intellectual inquiry. Several reports proffer current and future challenges in mathematical biology[16,49,55,72,73,78,94] and in related educational issues.[9,48,50,58,103] We will particularly request proposals from the open scientific community that deal with two general themes:

(a) How do the properties of integrated biological systems arise from the properties of the components? This is a central question in all of science but arises particularly in the hierarchical structured systems that characterize biology at all levels. General issues of emergence of biological pattern have long interested theoreticians, with recent mathematical methods in networks and agent-based modeling methods[1,25,28,75,82] offering new opportunities to investigate whether general properties lead to pattern and how this is driven by particular processes operating at each level in the hierarchy.

(b) How can we effectively integrate mathematical formulations operating at different hierarchical levels in biological organization into a system-level view? The field of multi-scale modeling now incorporates many approaches and is promulgated in the scientific journals of various disciplines. Systems biology presents opportunities far beyond a focus on gene regulatory networks. We have had considerable experience developing a multi-modeling framework to address landscape-scale problems arising from plans for Everglades restoration.[25,51,75,82] These are hybrid methods, which link together different mathematical approaches for interacting components of systems operating at different scales and hierarchical levels. The hybrid approaches typically applied in physical sciences are far too restricted to carry over simply to the varying temporal and spatial scales of many interacting biological processes. Examples we expect the Center to focus upon include: integrated whole-organism physiology, offering opportunities for great advancement through multi-scale modeling, with potential treatments for treatment of illness; models for disease spread that account for human-management and individual behavioral syndromes across populations;[31] and integrated models at cell-scale that incorporate differing levels of resolution of within cell processes.[88]

Developing a set of working groups arising from proposal submissions focused on either the above two themes or on new themes proposed by our Board of Advisors will require some time. In order to establish research activities at the Center quickly, we propose to focus initial Center research activities around the following **emphasis areas** that we believe offer new opportunities for major advances. During the **initial two years of the Center we intend to focus approximately 30% of the activities on these emphasis areas and 30% on the issues developed below in the section on National Needs**. The remaining 40% will be focused on proposals from the community and those arising from agency partners. For years 3-5 of the Center, we expect that these initial emphasis areas will make up approximately 20% of the Center's research-focused activities, with 80% being associated with externally-generated proposed activities, vetted by the Board of Advisors.

We have chosen the initial emphasis areas listed below in combination with those in the section on National Needs to include a range of problems across biology in order to entice a diverse collection of biologists and mathematicians to become acquainted with the activities of the Center and to provide a diversity of potential fields for post-docs and visitors. They have also been chosen owing to the strong interest and expertise available among Center collaborators to rapidly initiate working groups on them and the likelihood that results from these working groups would generate considerable public interest. Thus, we propose a mixture of activities covering different biological areas ongoing over the course of any year rather than a large focus on any single area each year, as has been the practice at the

Mathematical Biosciences Institute. Depending upon evaluations of the activities of these emphasis areas and those described below under National Needs, we expect that working groups associated with these activities could continue well beyond the initial two years of the Center.

(A) Intragenomic Conflict Emphasis Area

Inefficiency, redundancy, and sub-optimality are common observations when one analyzes the interaction of genes within an organism. These observations appear to contradict the idea of adaptation as formulated by Darwin in The Origin of the Species. However, in recent years what seemed to be dead ends of the evolutionary process are being explained as the evolutionary outcome of genes selected to maximize their own fitness at the expense of other genes and their host organisms. This explanation opens up the general issue of what circumstances will lead to genetic cooperation versus competition. This new paradigm provides a framework to study conflict and cooperation between different genes of different types according to their probability and mode of transmission. The complexity and the dynamical nature of gene interactions imply that a solid mathematical theory of these processes will be very useful. How genetic conflict shapes genetic mechanisms and systems is research that could greatly benefit from formal mathematical models, in particular optimization models, models of frequency-dependent selection, linear and non-linear replicator dynamics, game theory, and network/graph theory.

Table 2

Research Themes:

- Biological patterns emerging from properties of systems components
- Multiscale approaches to hierarchical biological systems

Initial Research Emphases:

- A. Intragenomic conflict
- B. Multi-scale simulation of cellular processes
- C. Human origins
- D. Natural systems dynamics
- E. Infectious diseases in systems with wildlife hosts

This focus entails a number of possible approaches and links, including: Gene Networks,[2,11,22,95] the Mathematical Theory of Epigenetics,[23,53,105] Sexual Conflict and Intrafamilial Conflict (Kin Selection, Parent-Offspring Conflict),[13,40,46,104] Evolutionary Theory of Selfish Cell Lineages (Cancer, Apoptosis, Restriction Modification Systems)[35,84,91] and Genomic Architecture.[76,102] No one working group would cover all of these in conjunction with this emphasis area, but we anticipate that much could be accomplished through establishing 2-3 groups over the first 2 years of the Center.

(B) Multi-scale Simulation of Cellular Processes Emphasis Area

A major challenge in mathematical and computational biology is to provide self-consistent descriptions of biological phenomena across ranges of time- and length-scales. We propose to pursue this by integrating molecular-level and coarse-grained, mesoscopic descriptions of cell-scale systems biological behavior.

This effort will require discussions and collaborations to develop parallelizable multi-scale methods and tools. Such multi-scale techniques will require care to ensure self-consistency, involving seamless transfer of molecular-level simulation results to input for modeling at higher levels within-cell. The mathematical approaches will include multigrid methods, continuum mechanics, graph theory and covariance analysis.[3,81,85] Applications of successful results will range from the atomistic description of drug/receptor interactions via modeling the chemical structures of many drug candidates with varying levels of detail, the molecular structure of possible cellular (protein) targets for a new drug, interactions between drug candidates and protein receptors, and systems-biology level modeling of complexes and organelle subsystems. The program will integrate work at the UT/ORNL Center for Molecular Biophysics with UT biological and mathematical groups and a variety of US and international researchers. The availability at the proposed Center of access to and expertise in the UT NSF Track II supercomputer and the Jaguar Petaflop Cray XT4 machine at ORNL will greatly enhance the ability of results from working groups to be evaluated quickly through differing implementations. Multi-scale descriptions of dynamics and

structure arising from this emphasis area will also be extremely useful in interpreting neutron scattering experiments on various biological systems at different length and time scales performed at the ORNL Spallation Neutron Source.[81]

(C) Human Origins Emphasis Area

Decades of intensive work by generations of evolutionary biologists have led to a dramatic increase in our understanding of how new species arise[17,41,42,43,44] – the central theme of Darwin's revolutionary book.[19] We believe that the time is ripe for attacking the ultimate speciation event - the origin of our own species.[20] Arguably, no area of evolutionary biology is as compelling to general audiences as those related to human origins; the topic underpins discussions of our place in the universe, of morality and cognition, and of our fate as a species. It is now widely recognized that many features of modern human behavior, psychology, and culture may be explained to a certain extent in terms of selective factors that operated during the Pleistocene. Any general theory of the origin of humans will include a significant quantitative/mathematical component that will have to deal with a combination of ecological, genetic, cultural, and social factors, processes, and changes. We propose to stimulate the development of interdisciplinary, multi-scale mathematical models focusing on different aspects of human origin and evolution.

No single working group can could possibly address the myriad issues associated with this emphasis area, but initial sets of Center activities would be devoted to: models of selection, migration, and drift in spatially structured populations and reconstruction of human history and migration patterns from molecular data;[18,30,97] models of the evolution of languages and reconstruction of human history and migration patterns from linguistic data;[69,74,89] models of gene-culture coevolution;[15,98] emergence of social networks (in mammals, apes, and humans) as a result of competition and cooperation;[54,56] reinforcement learning and games on graphs with dynamic linking as an alternative to classical game-theoretical approaches;[64,68,77,101] coalitions in apes, contrasting theories and data;[26,47,66] models of the evolution of individuality, different levels of selection and the emergence of higher-level units of biological organization from lower-level units.[83,90,111]

National Needs:

A main objective of the Center is to provide a base to carry out the interdisciplinary research that characterizes much of modern biology, from fundamental questions to those with direct applications. We plan to use our extensive experience from research collaborations with a variety of government agencies, including the US Geological Survey, the US Fish and Wildlife Service, the National Park Service, the Environmental Protection Agency and the Nuclear Regulatory Commission to maintain an ongoing "research resource" in quantitative modeling linked to biology. Our **goal is to become the first-choice location for development of models, quantitative analysis of alternative management, and application of modern computational science to practical issues raised by the sponsoring agencies of CIMBS, and additional agencies that might benefit from the expertise we gather at the Center**. We expect that many of the initial applications will arise from the sponsoring agencies, on issues we are specifically requested to address. Below we present first a general procedure for how the Center would respond to partner agency requests, followed by descriptions of additional emphases areas for activities during the initial years of the Center operations with 30% of the initial two years of the Center activities focused on the below endeavors. As an illustration of our response methodology, we discuss applications arising from discussions with a partner agency, Great Smoky Mountains National Park (GSMNP). Second, we point out several disease issues that we propose as emphases, noting that disease arises in many contexts providing the possibility to leverage mathematical efforts in application to one area to benefit others, as has been true for many efforts in mathematical epidemiology.

D) Natural Systems Dynamics Emphasis Area (GSMNP Partnership): As an example of the manner in which we propose to meet our general goal, we propose a direct collaboration with GSMNP having several objectives: (1) to develop a set of quantitative approaches to general issues of importance to the National Park Service (NPS) in that these arise in many contexts at different locations; (2) to focus these efforts initially on particular case studies developed in conjunction with the research and management staff of GSMNP, developing models and methods that have high likelihood of being transferable to other components of the NPS; (3) to extend these methods through application to case studies at other NPS locations; and (4) to use the extensive outreach opportunities to the general public provided by NPS interpreters to visitors at NPS units as a means to broaden public appreciation of the utility of quantitative approaches in addressing issues of national concern related to natural system management.

The general procedures for the response of the Center to concerns brought to us from other agencies will be our proposed procedures in the GSMNP partnership. The steps are to (i) identify a set of appropriate, tractable (e.g. not requiring large expenditures for additional data collection) projects through a small working group including representatives from the agencies involved, members of the Center staff including post-docs and students, and external mathematicians and biologists with appropriate expertise; (ii) prioritize these projects and develop suggested teams as working groups to address those assigned highest priority; (iii) provide resources for the working group to conduct its effort with an explicit set of deliverables and deadlines (with an evaluation process to ensure each project is proceeding in a timely manner); (iv) publish the results in several formats including scientific journal publications, technical reports appropriate for agency use (e.g. with appropriate software and documentation of its use); and (v) develop several forms in which the results may be used in outreach to inform and educate the public.

We have already initiated step (i) with GSMNP and here briefly outline several initial projects that illustrate our planned activities related to this portion of the Center's activities. We have chosen these issues based upon not only their intrinsic interest to GSMNP, but their potential for transferability and connections to issues related directly to other areas of concern such as animal disease. These projects are:

a. Wildfire analysis and control: With support from NSF, the PI and collaborators have been developing a unique set of procedures linking the use of HPC to wildfire scenarios modeled in a GIS, with focus on optimal placement of fire control such as fire-breaks. This effort uses HPC to evaluate potential responses to fire outbreaks at numerous locations, providing a "look-up table" of initial best responses that are then employed in a real-time manner within a GIS as decision support associated with any particular fire. GSMNP is faced with similar issues of wildfire management, but with different criteria for decisions because of the benefit of some fires in providing successional habitat, while still containing the spatial extent of the fire. There is a trade-off between long-term management objectives including biodiversity impacts, and short-term responses by fire control teams to suppress fires. The mathematical issues posed by the need for spatial control given multiple criteria are quite challenging. In addition, the requirement of availability of the decision support tools in the GIS context familiar to NPS staff and the ready need for such methods in many public land management systems indicate that this project would have broad impact.

b. Emerging diseases: GSMNP expends about $300K per year to harvest and limit damage caused by feral hogs that root and particularly impact wetlands and high-elevation fragile habitats. Pseudorabies is a disease of swine, spread by direct contact between individuals and existing in other hosts including possibly deer. It is of great concern in North Carolina owing to the large economic impact that would arise if swine exports from the State were quarantined. Concern has arisen that the GSMNP population could potentially act as a source for pseudorabies in part because of illegal releases of hogs from quarantined States in the Park and surrounding National Forest land. The State of North Carolina has requested an increased monitoring and harvest effort in GSMNP to limit the likelihood of pseudorabies spread to domestic/commercial populations, but it is not clear where and how to focus additional effort.

This matter leads to general issues of population management tied to spatial disease spread and optimal spatial harvesting methods that would be broadly applicable, given the presence of hogs in many National Parks and other protected areas, such as Nature Conservancy reserves and Forest Service natural areas.

An additional disease-related issue concerns chronic wasting disease and the efforts to enhance the population of elk that has recently been re-established in GSMNP. This disease has limited the ability of the Park to import elk from elsewhere because of the possibility of enhanced transmission of this disease to other species. While the PI has been investigating models for optimal augmentation of small populations from reserve populations,[10] this effort has not included disease impacts. Trade-offs in management associated with a desire to sustain a new population while reducing potential disease spread is a general issue in wildlife disease management that has application in many contexts.

c. Invasive species control: GSMNP is affected by a flood of invasives that have greatly impacted the system already (e.g. the balsam wooly adelgid has devastated the high-elevation Fraser fir population), and the Park expends considerable effort attempting to limit the impact of particularly harmful invasives. New potentially harmful invasives arise regularly, including Didymo or "rock snot" (*Didymosphenia geminata*), an invasive diatom that is being seen in more and more locations with cold, nutrient-poor waters, and fire ants, which have been found to impact local ant diversity and interact with fire-disturbed areas in ways that may exacerbate their impact. The recent arrival of both hemlock woolly adelgid and gypsy moth in GSMNP also raises concern about potential landscape-level consequences. Guidance is needed on prioritizing not just which invasives to focus limited control efforts upon but where as well. With prior NSF support, the PI and collaborators have developed a tool for analyzing alternative spatial management of old-world climbing fern (*Lygodium microphyllum*) in south Florida. Extending these methods to account for trade-offs in monitoring versus control and providing GIS decision support, including situations in which it is necessary to account for spread from neighboring locations (e.g. requiring the Park to be viewed in a landscape context), would provide a generally applicable tool of use in many different land-management situations.

d. Biodiversity: The All-Taxa Biodiversity Inventory (ATBI) is an ongoing project to characterize, as completely as possible, the diversity of taxa within GSMNP. The ATBI project has resulted in the discovery of hundreds of new species (874 species new to science and 5207 new Park records). The ATBI represents one of the most comprehensive inventories in the country on federal lands and uses citizen-scientists in the project both to enhance community and visitor understanding and to promote biodiversity concepts to the public. NSF has funded several project elements, yet the concept of developing probabilities of occurrence within the Park still needs exploration. Given that significant knowledge has been gained of effort expended and "return" in terms of new species found, the data might be usefully applied to important general issues of how many species there are on the planet.[79] A very practical issue of direct import to the Park is where and on which taxa to focus continuing effort, and how to use the experiences of the ATBI to guide similar attempts elsewhere. This issue may be thought of as an optimal stopping time problem in stochastic processes, but it has not been analyzed in that context.

E) Infectious disease dynamics and management in systems that include wildlife hosts: Recent analysis of 335 new diseases that emerged between 1940 and 2004 concludes the rate of new infectious diseases in humans is increasing, more than half of the diseases jumped from animals to humans, and most of these originated in wildlife.[57] This and many other studies reflect the growing intersection between people, domesticated animals and wild species.[21] A major emphasis of the proposed Center will be on animal disease, and we propose to initiate activities within this emphasis on several particular diseases for which expertise exists at Tennessee and that are expected to generate results with general applicability to disease problems elsewhere..

Center collaborators have developed models for rabies in raccoons (Asano et al, Ding et al), bats (Dimitrov et al.), and tick-borne disease.[38] Novel approaches in these have been the use of optimal control to consider potential "best" control strategies, and methods to link detailed physiological responses and characteristics of individual behavior to population-level responses. Optimal spatial control methods for raccoons and the placement of oral rabies vaccines in space may be applied to other disease situations, an example being tick-borne disease.[38] Bat rabies modeling efforts span cross-scale influences on disease dynamics from genes, to individuals, to epizootic structures in bat populations and metapopulations. A novelty of the multi-disciplinary experimental and modeling approach carried out at Tennessee in bat modeling is that it integrates physiological and immunological differences among individuals in response to pathogen exposure, dose, and virulence, to project population-level, ecological, and evolutionary outcomes for hosts and diseases. This development of viral disease models across scales allows extrapolation from data collected at observable scales to estimate parameters of processes operating at unobserved scales. Similar multi-disciplinary, multi-scale studies of tick/pathogen disease dynamics are also in progress at Tennessee. These efforts on rabies and ticks are mentioned here to illustrate expertise available through both the UT Institute for Environmental Modeling and the UT Center for Wildlife Health that may be drawn upon to assist in modeling efforts. Modeling is a critical tool due to challenging aspects of wildlife-associated disease that must be addressed for management to succeed:

- The systems that are of significant public concern are inevitably multi-host, with one or more wild species interacting with livestock, companion animals and/or humans;
- Species can act as reservoirs, vectors, spillover hosts, or dead-end hosts, which adds great complexity (particularly when invertebrate vectors with complex life-cycles are involved);
- Treatment/management of such problems typically requires population-level intervention (rather than individual treatment) – for example, vaccination campaigns, habitat management, culling;
- Given the expense of population-level management, and the complexity/uncertainty of outcomes, deterministic or stochastic simulation modeling is often used but rarely has incorporated an explicit spatial control context;
- Quantification of wildlife/domestic animal/human interactions almost inevitably requires that landscape features and behavioral patterns of movement, interaction and habitat preference be considered – requiring GIS and spatial statistical tools.

An overarching goal of working groups and modeling activities in this emphasis area will be to *predict and manage* outcomes better, which necessitates accounting for disease dynamics and making assumptions about future trends in environmental factors affecting disease transmission. Real-world options for management require an economic analysis, typically in some cost-benefit (or cost-efficiency) method. One general issue that has been little addressed from an optimization perspective is the appropriate balance of surveillance *versus* intervention; associated with this issue is the question of which species should be targeted. Significant research expenditures on these topics are being made by a variety of agencies (e.g., the NIH MIDAS program), and our proposed effort for the Center will complement these efforts. We will ensure that this is so through careful discussion, early in the process, with CIMBS agency partners and the variety of researchers involved in disease modeling at other institutions.

UT researchers, including many at the College of Veterinary Medicine and various departments in the College of Agricultural Science and Natural Resources, have expertise in numerous animal disease systems. The proposed Center provides an opportunity to link mathematical approaches with this local biological expertise, to address issues that would be prioritized by the management of the Center with input from agency representatives and the Board of Advisers, while remaining cognizant of research activities elsewhere. We argue that, rather than doing generalized disease modeling, the efforts of the Center will be most effective if models are motivated by explicit disease systems. Several examples are cited below to suggest the breadth of possible case studies for which expertise is available among our collaborators and through the Center for Wildlife Health. These would be used as initial emphases,

guided by advice from outside UT. We acknowledge that not all of these particular cases might be addressed during the first two years of Center activity.

(a) Bovine tuberculosis: Because of its ability to infect humans, and its negative effect on the commercial trade of livestock, bTB has been a priority disease for eradication from livestock in the United States for a century. Indeed, bTB has largely been eliminated from the country's livestock, with New Mexico and Michigan being among the last remaining persistent pockets present in the U.S. because of maintenance of the disease in free-ranging wildlife. Internationally, no single strategy has proven successful for wildlife bTB control; in New Zealand intensive culling of the wildlife reservoir has succeeded,[14] whereas in the UK it has not.[27] Biologists thus need species- and area-specific scientific guidance about what densities maintain bTB as self-sustaining in wildlife populations, and analytical tools for projecting the ongoing course of the outbreak under different management scenarios. Such tools can provide critical information for use in setting area-specific harvest quotas, communicating with the public, and projecting personnel and budget requirements over time. Although many modeling studies exist internationally, the application of optimal control methods in conjunction with spatial modeling requires new models. One of our senior personnel (G. Hickling) has extensive international expertise in this disease system, and is presently collaborating with Michigan and Australian researchers on a spatial models of wild deer bTB.[14,92]

(b) Syndromic surveillance: Threats from a number of emerging, re-emerging and exotic diseases of both domestic and wild species make it increasingly important to detect disease outbreaks as early as possible. Disease outbreaks typically offer a very short window of opportunity for effective response. Therefore, early detection and quick action are critical to protect animal populations and minimize health and economic impact of outbreaks. Sound statistical/mathematical algorithms must be developed to efficiently identify significant outbreaks. Traditional methods of outbreak detection are not time-sensitive, as it takes time to get laboratory results leading to delays in outbreak detection. Therefore, better real-time syndromic surveillance systems are needed.

One of our senior personnel (A. Odoi) and collaborators from University of Kentucky are developing an early outbreak detection and alarm/alert system – the Automated Surveillance Data Analysis System (ASDAS). ASDAS is designed to automatically prepare and analyze syndromic surveillance data and send e-mail alerts when significant disease clusters/outbreaks are detected. The system has been tested on outbreaks of horse diseases in Kentucky, has utility for all domestic and wild species, and could adapted to be a nation-wide syndromic early warning system. The current system is focused on database and GIS issues associated with surveillance data. There are many mathematical and computational opportunities to improve this system, including addition of a risk assessment component.

The Spatial Analysis and Decision Assistance (SADA) project of the UT Institute for Environmental Modeling for which L. Gross is a co-investigator, applies a variety of spatial statistical methods and Bayesian approaches to ecological and human risk assessment associated with toxicants. The methods incorporated in SADA have potential application to disease outbreaks, with further development to account for disease dynamics and organism demography, and would leverage previous risk assessment efforts to expand the methods being incorporated in ASDAS.

(iii) Spatial aspects of resistance in Staphylococcus: Staphylococcus is a pathogen for many species of animals as well as humans. Methicillin-resistant *Staphylococcus* (MRSA) infections are becoming increasingly important causes of both nosocomial and community-acquired infections in both domestic animals and humans and cross-transmission between domestic pets and humans is thought to occur. The seriousness of the resistance problem is exacerbated by the fact that the organisms are frequently resistant to most of the commonly used antibiotics making treatment and control of the infection difficult. One of the senior personnel for the Center (A. Odoi) is collaborating with several UT faculty to determine the

geographical and temporal patterns in distribution of cases of *Staphylococcus* infections in canines and assess if there is any community predilection for the disease. One of the P.I.'s current graduate students (E. Bodine) has collaborated on models for the spread of MSRA in a human population.[65] These models are in a non-spatial context, but the structure may be fruitfully extended to a metapopulation framework linked to the canine population data and could provide a method to assess risks of resistance outbreaks in a spatial context.

The above components of Center activities illustrate in part how there is a role for the Center in explaining and offering support to apply methods that have not yet been extensively implemented across biology or to address national needs related to biology. One example we have noted is the application of optimal control theory,[71] which has been employed in relatively few contexts in biology mainly by our collaborators[33,39,59,61,62,63,67,78] yet offers great potential in application to difficult spatio-temporal management issues.[36,38,39,110] This method goes beyond the standard approach to management problems in which a variety of potential scenarios are assessed. Spatially-explicit scenario analysis involves considerable difficulty in determining ranking of alternatives. In response to this, the P.I. and collaborators have developed HPC methods to evaluate the robustness of scenario rankings to uncertainty in inputs and assumptions.[36] We expect that many of the problems noted above would benefit from the use of HPC when spatial issues are included. While HPC methods have become common in certain limited areas of biology, the opportunities afforded by parallel processing to rethink our models (to account directly for the concurrency and synchrony occurring at many scales in biological systems) have been pointed out for individual-based models[1,75,82] but rarely implemented.

Education and Outreach:

A diverse array of activities are planned for these aspects of the proposed Center, with varying target audiences and associated methods. As illustrated in Figure 1, these may be grouped into those oriented towards a pre-college and general public audience, a college audience, and a professional audience, with elements overlapping all of these. Educational activities beyond those associated with the outreach components will include formal and informal training components (tutorials, graduate student and post-doctoral mentoring) and opportunities for self-advancement (teaching opportunities for post-doctoral fellows). These activities will be under the direction of Suzanne Lenhart, as Associate Director for Outreach, Education and Diversity, with the assistance of an Outreach Coordinator who will report to Lenhart. The Outreach Coordinator will collaborate in developing activities described below, with particular emphasis on pre-college activities. This Coordinator will also supervise the development of an archive for materials and program information for math biology education across different levels, including evaluative methods for this material.

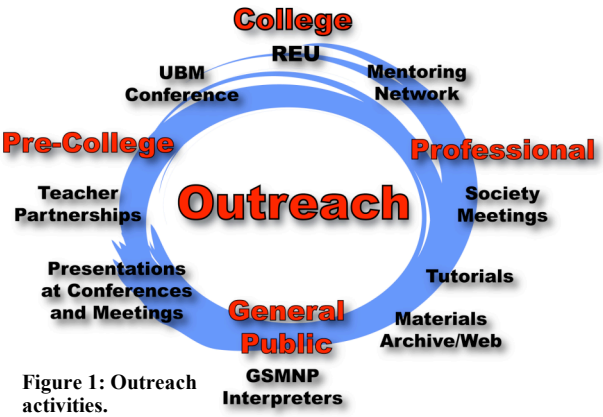

Figure 1: Outreach activities.

Lenhart brings to this effort great experience in outreach, having devoted many years as mentor to the math club at a local high school with weekly meetings to prepare students for math contests. She was Director of one of the largest and longest-running Research Experience for Undergraduates (REU) programs in the US, is a past-President of the Association for Women in Mathematics (AWM), and is a member of the Scientific Board of the American Institute of Mathematics. She will work closely on these activities with two other senior personnel: Susan Riechert, who has for over a decade led a large *Biology in a Box* outreach project, that has

provided hundreds of exercises for elementary through high school students at schools in over a dozen Tennessee counties; and Cynthia Peterson, who has led many educational activities associated with the Genome Science and Technology Graduate Program at UT, led the creation of a new Ph.D. program at UT in Scalable Computing for Biology and has developed extensive contacts with institutions serving under-represented groups. Several proposals for funding of graduate students at the intersection of biology and quantitative science are presently under review, led by Dr. Peterson and including the P.I. of this proposal as part of the leadership team. Any funding arising from these other proposals will supplement the opportunities available to Center participants.

At the pre-college level, the Center will use the results from its activities to support speakers and demonstrations, at teacher and student gatherings. For example, the National Convention of Mu Alpha Theta (the national high school math honor society) will be held in Knoxville in July 2009, with an expected attendance of over 700 students and 100 high school teachers. Lenhart is an organizer of this convention and will ensure that Center activities are highlighted. Other outreach efforts will expand on current activities including workshops for middle school students and teachers held several Saturdays each year, called SHADES (Sharing Adventures in Engineering and Science), organized by the local chapter of AAUW. The workshops focus on 'hands on' activities and both Riechert and Lenhart have been active in these efforts. Many of the senior personnel of the Center have been active in the annual Darwin Day events which have expanded from the initial activities at UT to many events world-wide and we will assist these activities in emphasizing the importance of quantitative methods in evolution.

In collaboration with GSMNP, we will develop compact modules to be used by National Park interpretive staff, who have extensive contact with Park visitors. The objective will be to motivate what a model is, how models can be used to assist Park management of the biota, and how math is used to analyze these models. We will use examples from Center activities, and develop more complex examples that could be used in Visitor Center displays and on web sites to illustrate the application of modeling to address issues in the Park. Although details of these modules may be specific to GSMNP, the general approaches will be readily applied in many other locations including State natural areas and preserves.

Lenhart is one of the co-organizers of the newly formed AWM Teacher Partnership program, to match teachers at various levels with mathematicians working in colleges, government or industry. The partners communicate via email and with all the participants via a listserve, and allows for classroom visits and joint projects. Interested teachers request a partner through information on a website, and a committee makes the pairings. This program started in August 2006 and has matched 56 pairs so far. We will establish a similar partnership through the Center, as one aspect of our “distributed mentoring” activities, with emphasis on high school teachers in either biology or math interested in making connections between the fields. We will collaborate with AWM in establishing this program and will publicize it through the several biology and math societies that have high representation of high school teachers.

At the college-level, each summer we will host a conference for undergraduates and will encourage participation by high school biology and math teachers from the surrounding region. The conference will focus on student research presentations, especially students from ongoing or past UBM and REU programs. Directors of the current UBM programs will be asked to serve on the organizing committee of this conference and give recommendations of students to participate. The conference will also include talks and career informational panels, involving research biologists and mathematicians. We will limit the size of this conference to a total of 50 participants (30 students, 10 faculty of UBM and REU programs and 10 high school teachers) to ensure interaction between participants. This activity will be at a scientific level that would be understandable to the high school teachers in attendance.

The Center will host an REU program for seven weeks each summer. Ten undergraduate students including math and biology majors will participate in this program. The students will work in groups on

research projects arising from current projects at the Center and directed by a faculty member in conjunction with a post-doc or a graduate student. Two teachers from local high schools will also be invited to participate in this summer activity. Lenhart was the director of the math REU program at UT for 15 years and involved local teachers in several of these. Gross and Lenhart directed a UBM program with math and biology majors in which students developed their own projects, performed experiments, developed models and analyzed the results.[58] While not allowing time for a fully new project to be developed by each REU team, evidence from many years of directing REU programs at UT indicates that these have provided motivation for many students to go on to graduate training in math and biology.

We will develop a Mentoring Network in Math Biology as an extension of the very successful mentoring program sponsored by the SMB at its annual meetings. As active researchers in math biology, the senior personnel get regular information requests from undergraduates at institutions that lack local expertise in the field, asking for advice on topics including careers and courses. The "distributed mentoring" we have carried out in response to these requests often entails regular email and occasional phone conversations with the student, and many times has resulted in the student going on to pursue a graduate degree either at UT or elsewhere. In collaboration with SMB and other professional societies, we will implement a 'matching service' for such requests, taking responsibility for ensuring that the matches are appropriate and monitoring them for quality of response. The initial group of mentors will be the faculty and post-docs in the Center; we will expand this pool as necessary by recruiting from the math biology community.

As outreach for professional development, we propose to collaborate with professional societies in biological fields to support and enhance the offerings related to mathematical and computational science at their annual meetings. Although large sessions devoted to quantitative ideas are common in some biological societies, there are many with no such emphasis. The Center will encourage development of symposia and other sessions (including tutorial ones) on relevant mathematical themes as appropriate in professional biological societies with little prior emphasis on this. We will begin this project with societies with strong emphasis on biological education, in conjunction with SMB and programs such as BioQuest, and then branch out to other societies in various sub-disciplines of biology that have historically been somewhat less oriented towards mathematical methods.

The Center will hold 3-4 tutorial sessions each year. Some will encourage the development of HPC understanding and skills among biologists with computational skills but a lack of experience with HPC approaches. We will ensure that all post-docs and graduate students associated with the Center develop their knowledge of HPC potential. All post-docs will be assigned a primary and secondary mentor (one from each of a more quantitative or biological area) and the application process will request potential post-docs to suggest potential mentors. Post-docs will be given the opportunity to teach some undergraduate courses if desired, and be assigned a mentor for teaching. Weekly seminars will be held, organized by the post-docs with recommendations from Center researchers. Long-term visitors to the Center will be expected to develop collaborations with post-docs and faculty of the Center, with their applications evaluated based upon the nature of their proposed interactions.

Communication, Knowledge Transfer and Informatics:

An objective of the Center is to enhance the development of programs at the math and biology interface at a variety of locations, and especially to establish these at institutions with the potential to enhance the diversity of future researchers. A very small set of programs (including ours at UT) have educated the vast majority of researchers actively involved in math biology. Though the field has expanded over the past several decades, there are still relatively few biology programs with expertise among their faculty sufficient for educating biology students in the quantitative methods now becoming prevalent in research. Similarly, few math programs have been able to attract the relatively limited number of highly qualified Ph.D.s in math biology being produced, in part because of resource constraints associated with limited

faculty positions. Faculty demographic trends offer great potential for a major set of math faculty opportunities at the biology interface and the ongoing technologically-driven advances in mathematical and computational biology, in conjunction with the advice of reports such as BIO2010, have caused biology programs to emphasize recruitment of quantitatively-skilled biologists.

The Center will develop connections to a few of institutions with large numbers of under-represented groups in STEM fields with the aim of fostering a few excellent programs at the math biology interface. The PI has been an adviser to mathematics and biology programs at several institutions appropriate for this activity, and Peterson has been active in developing connections to such institutions in conjunction with proposals to bring students from these institutions to UT. These proposals do not provide a mechanism for the reciprocal relationships needed to build expertise at these institutions. We propose to encourage the post-docs, and some faculty, of the Center to participate in longer-term visits to these institutions. This would not be in the formal manner of the NIH-funded Institutional Research and Academic Career Development Award program, which requires post-docs to teach courses at institutions that primarily serve under-represented communities. Rather, we will develop a long-term relationship between the Center participants and 3-4 institutions that will assist them (including short-courses for faculty, research mentoring for students) in developing their potential to enhance the quantitative components of their biology curriculum and the biological components of their math curriculum. Metrics of success would be: the numbers of students from these institutions who go on to pursue either REU programs in quantitative biology or math biology, or go on to do graduate work in these; the number and type of collaborations between the Center participants and the faculty and students at these institutions; and curricular modifications made at these institutions to integrate math and biology.

We propose several additional methods to enhance knowledge transfer arising from Center activities. This includes the development and maintenance of an archive of publications carried out with Center support. A component of the archive will be software and products developed through the Center, for which we will develop an appropriate database and metadata structure, as well as redundant back-up servers in two locations to reduce the likelihood of data loss. The Center will encourage and sponsor activities at professional society meetings to enhance the connections between math and biology and to encourage attendees to become cognizant of the resources available through the Center. The archive of educational material related to math biology will be one component of the web resources provided by the Center to enhance knowledge transfer as well as the proposed Mentor Network.

We have two industry and one government agency partners already established. We will develop procedures to actively seek and add new partners based upon the recommendations of the Board of Advisers and the needs associated with the research activities of the Center. By the 3rd year of the Center, we will have approached various agencies and organizations as potential financial sponsors for projects that will enhance Center activities. In this endeavor we will use the expertise of other NSF-supported Centers, while following UT regulations regarding IP arising from financial connections with industrial partners. Regarding other Centers, we will request that the CIMBS Director participate in the all-Director meetings of appropriate Centers supported by NSF.

The Center informatics staff will be extensively trained in computational science, and knowledgeable about the application of HPC to biology. The PI has supervised many such staff members through The Institute for Environmental Modeling, most of whom have MS-level training in either math or computing and who have become experts in biological fields and co-authored papers at the math biology interface. Access to mathematical and standard programming language software, workstations capable of significant computation, and appropriate servers for email and web-services (including support for Win, Mac and Linux OS) will be provided and the Center will maintain a mid-range cluster. Audio-visual equipment will ensure both high quality visualization capacity locally and the capability for interactive collaborations between groups of various sizes from external locations.

References: Those listed in **bold** were supported by NSF awards to the PI or Senior Personnel.

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Computing resources at the University of Tennessee and Oak Ridge National Laboratory

Teraflop-scale supercomputers are available through The National Center for Computational Sciences (NCCS) at Oak Ridge National Laboratory (ORNL) and UT's managed computational resources. UT-Battelle management of ORNL has resulted in a partnership that provides a unique synergy of resources and experience on a wide array HPC platforms. The relationship has resulted in bringing leading HPC scientists to UT and ORNL through joint appointments and the creation of the Joint Institutes such as the Joint Institute for Computational Science (JICS) and Joint Institute for Biological Science (JIBS). Three of the major computational resources available to CIMBS participants, located within NCCS and the associated UT Centers, are UT's "Track2" HPC, the Cray XT4 "Jaguar" and the Blue Gene /P.

The UTK Joint Institute for Computational Science (JICS) has received funding under the NSF 05-625, Towards a Petascale Computing Environment for Science and Engineering, for a Mid-Range HPC deployed and supported by The National Institute for Computational Sciences (NICS). NICS is delivering a 1-petaflops (PF) peak performance Cray XT5 (code-named Baker) system, with 100 terabytes (TB) of memory and 2.3 petabytes (PB) of disk. The XT5 is designed specifically for sustained application performance, scalability, and reliability, and will incorporate key elements of the Cray Cascade system to prepare the user community for sustained, high productivity, petascale science and engineering. The proposed system holds Cray Baker compute blades each with eight "Montreal" AMD Opteron processors with eight cores at 3.0 GHz. The system has 100 TB of memory across the machine. NICS and Cray, in partnership with AMD, will provide and support this system. To deliver this new capability to the science and engineering communities, the team will establish a major new petascale computing environment—fully integrated with the TeraGrid. As part of TeraGrid it will be nationally available to researchers. UT management will allow for priority access to a portion of process time to UT researchers, including participants in CIMBS, and have the benefit of locally available support and workshops.

The Cray XT4 "Jaguar" is one of DOE's Leadership Computing Facilities hosted at NCCS. It was ranked number 2 on the top500 supercomputer list in 2007 and is the most powerful supercomputer available for open scientific use. Jaguar currently exceeds the 100 teraflops calculation level with ongoing upgrades to 250TF in the first quarter of 2008. Future plans aim to reach a petaflop, or 1 quadrillion mathematical calculations per second, by 2009. Jaguar is composed a combination of XT3 and XT4 systems connected through a Cray SeaStar router through HyperTransport. The resulting interconnect has very high bandwidth, low latency, and extreme scalability.

A second generation Blue Gene/P providing 8000 processors capable of 27 teraflops has been installed in the NCCS at ORNL. While small on the typical Blue Gene scale, it provides a unique platform for HPC implementation with the combination of OpenMP across cores and MPI between nodes. The existence of larger Blue Gene Installations at IBM that could be made available through the Industry Partnership relationship with IBM included in this CIMBS proposal also allows for the ability to upscale with the same design if the computational needs merit.

These large-scale HPC systems supplement a variety of smaller clusters available for research at UT as well as the proposed small-scale development cluster to be installed for the CIMBS. Extensive experience is available at UT to allow CIMBS participants to readily obtain support for HPC implementation on all of the above machines, with an additional advantage that a number of the Senior Personnel and Collaborators on this proposal have utilized these HPC facilities for biological applications and can provide advice for CIMBS participants, including how to effectively transition models between single processor desktops, multi-core machines, clusters, and HPC.

Appendix A1: Senior Personnel

Principal Investigator:
Louis Gross, Prof, UT Ecology & Evolutionary Biology and Mathematics and Director, Institute for Environmental Modeling

The PI has considerable leadership experience at similar Centers (Chair of the Board of Governors of the Mathematical Biosciences Institute from 2004-2006; co-Director of 7 courses and workshops on mathematical ecology at The International Centre for Theoretical Physics in Trieste, Italy, from 1986-2000) and in professional societies (President of the Society for Mathematical Biology from 2003-2005; Ecological Society of America, Program Chair 2007-2008, Theoretical Ecology Section Chair, 2001-2002; American Institute of Biological Sciences, Board of Directors, current). He has directed The Institute for Environmental Modeling at UT for 10 years, with a full-time staff of 8 to 14 scientific and computational researchers, not counting post-docs and students. He has been lead PI on over $8M of externally funded projects since 1990, including NSF support for two ITR, one DUE and one QEIB over the past decade, involving faculty and students from many different departments, and has mentored 13 post-doctoral fellows. Starting with workshops he organized in the early 1990's, he has devoted significant effort to educational initiatives in mathematical biology and has led over 20 workshops and short-courses related to quantitative training for life scientists since 1990. From his long service to the UTK Faculty Senate, including as President from 2006-2007 and Chair of the Budget Committee from 2002-2004, the PI has extensive understanding of procedures, including fiscal and personnel, at the University.

Senior Personnel (* indicates Directors):

*The below individuals have agreed to serve in both an advisory role to the Center (a * indicates those listed who will serve as Associate Directors) and as a pool of possible post-doctoral mentors for the Center. They provide local expertise in fields related to many Center activities including possible working groups. All have agreed to assist the Center as appropriate, and all will receive release-time funding provided by UT over the initial years of Center activity in order to assist in the growth of the Center.*

Michael Berry, Prof, UT Electrical Engineering & Computer Science
He is an expert on text mining, parallel computation and application of high performance computing in genomics and environmental biology and has served as Head of the UT Computer Science Department. Applications he has led the development of include the Land-Use Change Analysis System and the Regional Simulation Model for spatial environmental impact analysis, and he has been a long-term collaborator of the PI on three separate NSF-funded projects applying parallel and grid-computing to natural resource problems.

Virginia Dale, Group Leader, ORNL Landscape Ecology & Regional Analysis Group
She is an ORNL Distinguished Scientist with extensive experience applying computational methods to land-use and global change utilizing simulations linked to GIS. She is the editor-in-chief of the journal Environmental Management and has served on numerous boards including the EPA Scientific Advisory Board.

Sergey Gavrilets, Distinguished Prof, UT Ecology & Evolutionary Biology and Mathematics *
He is a leading researcher in theoretical and computational evolutionary biology with extensive international collaborations. He has authored a major monograph applying mathematical methods to the issue of speciation, and directs a large and active group of post-doctoral fellows and students from several disciplines. He regularly teaches and leads courses at several international locations.

Michael Gilchrist, Asst Prof, UT Ecology & Evolutionary Biology
His research efforts in bioinformatics include developing statistical models to answer questions on protein function and expression through the use of genome scale datasets, and addressing questions in parasite replication, the evolution of virulence and host immune system activation.

Graham Hickling, Assoc Prof, UT Forestry, Wildlife & Fisheries; Director, Center for Wildlife Health *
He is Director of the Center for Wildlife Health and constitutes a direct linkage from the proposed management team for the Center to the expertise and capabilities in the agricultural units of the University as appropriate to develop Center activities in response to disease and outbreak/threat issues. He has research experience in disease-related problems across several taxa, is a member of the Wildlife Disease Working Group of The Wildlife Society and was vice-President of the New Zealand Ecological Society.

Suzanne Lenhart, Prof, UT Mathematics *
She is a leading applied mathematician with research publications spanning many areas of biology including HIV, TB, bioreactors, bioeconomics, cardiac function and population dynamics. She has authored a major text on optimal control for biologists, has been a leader in several major professional societies (SMB, SIAM, and President of AWM), and has extensive experience in outreach. She has been a long-term collaborator of the PI on three separate NSF-funded projects applying optimal control methods to natural resource problems.

Agricola Odoi, Asst Prof, UT Comparative Medicine, Veterinary College
He is an epidemiologist with expertise in spatial disease and the use of GIS models. He brings an international perspective from his educational background in Uganda and Kenya and extensive ongoing collaborations in Africa.

Cynthia Peterson, Prof, UT Biochemistry & Cellular and Molecular Biology
She is Director of the UT Genome Science and Technology Graduate Program with extensive knowledge of applications of computational methods in structural biology. She has been very active in building collaborations between UT and minority serving institutions.

Dan Simberloff, Gore Hunger Prof of Environmental Science, UT Ecology & Evolutionary Biology
He is one of the world's leading ecologists with numerous awards including the Ecological Society of America's highest award, the Eminent Ecologist Award. He maintains an extensive world-wide field research program focused on issues of biological invasions and global change and has been a leading innovator in the application of statistical methods to large ecological data sets. Among his many service activities, he was a member of the National Science Board and he has directed over 30 graduate students.

Jeremy Smith, Governor's Chair and Prof, UT-ORNL Joint Institute for Biological Sciences and Director, Center for Molecular Biophysics
He is a leading computational scientist in the area of molecular biophysics, with broad ranging research interests in areas such as hydrogen production and bioethanol, single-molecule spectroscopy for cancer detection, and atomic-detail physics of photosynthesis. He maintains extensive international collaborations and has mentored numerous post-doctoral fellows and junior scientists.

Francisco Ubeda de Torres, Asst Prof, UT Ecology & Evolutionary Biology
He is a researcher in theoretical and mathematical genetics, with particular interest in the role of conflict in transmission and expression including genomic conflict and imprinting, the evolution of mutualism, and the use of genomic databases to evaluate theory.

UT and ORNL Senior Collaborators:

The below individuals serve as a pool of possible post-doctoral mentors for the Center as well as providing a variety of local expertise in fields related to possible working groups. All have agreed to assist the Center as appropriate, with possible release-time funding provided by UT when needed to support Center activities.

Vasili Alexiades, Prof, UT Mathematics
Jerome Baudry, Asst Prof, UT Biochemistry & Cellular and Molecular Biology
Elissa Chesler, Scientific Program Director, ORNL Mammalian Genetics & Genomics
Jack Dongarra, Distinguished Prof, UT Electrical Engineering & Computer Science
Jim Drake, Assoc Prof, UT Ecology & Evolutionary Biology
Hong Guo, Asst Prof, UT Biochemistry, Cellular & Molecular Biology
Thomas Hallam, Emeritus Prof, UT Ecology & Evolutionary Biology and Mathematics
Henriëtte (Yetta) Jager, Research Staff, ORNL Environmental Sciences
Igor Jouline, Assoc Prof, UT Microbiology and ORNL Computer Science & Mathematics
Mike Langston, Prof, UT Electrical Engineering & Computer Science
John New, Prof & Head, UT Comparative Medicine, Veterinary College
Wilfred M. Post, Senior Research Scientist, ORNL Environmental Sciences
Vladimir Protopopescu, Senior Research Staff, ORNL Computer Science & Mathematics
Susan Riechert, Distinguished Service Prof, UT Ecology & Evolutionary Biology
Shih-Lung Shaw, Prof, UT Geography
Ken Stephenson, Prof, UT Mathematics
Michael Vose, Assoc Prof, UT Electrical Engineering & Computer Science
Steven Wise, Asst Prof, UT Mathematics
Russell Zaretzki, Asst Prof, UT Statistics, Operations & Management Sciences

Industry Partners:

IBM – Dr. Kirk Jordan, Emerging Solutions Executive, IBM Strategic Growth Business/Deep Computing

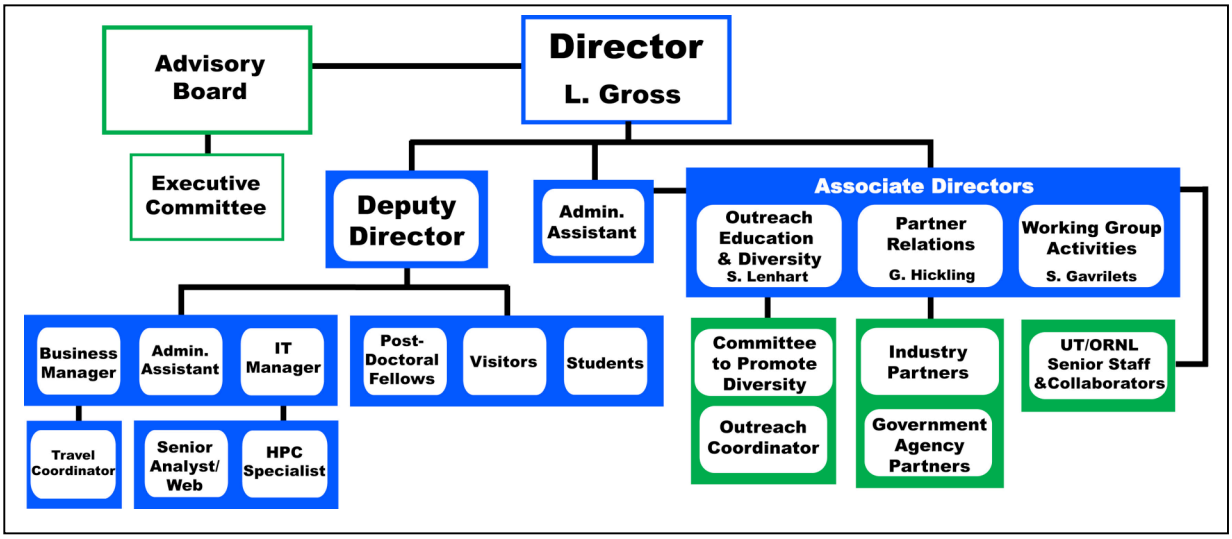
ESRI Inc. – Dr. David Maguire, Chief Scientist and Director

Government Partners:

Great Smoky Mountains National Park – Chief Nancy Finley, Resource Management and Science

Appendix A2: Management Plan

The University of Tennessee has extensive formal management experience for major research and educational facilities, including its cooperative role as manager of Oak Ridge National Laboratory with Battelle. Thus, there is a wide array of expertise available internal to the University to assist the Directors and initial leaders of the Center to effectively develop its facilities, staff, and activities. The Plan outlined here focuses on (i) Organizational reporting and structure; (ii) Operating management; and (iii) Assessment. The underlying tenets of this Management Plan are that flexibility in response to needs for the Center require that the organizational structure be capable of considered, deliberate, and yet rapid decision-making, and that this need for flexibility must be concurrent with accountability to the University and Foundation. As the award procedure for the Center is through a cooperative agreement, it is expected that representatives from the various funding agencies will participate in a variety of capacities in the activities and planning of the Center, but that the day-to-day operations of the Center would be managed by the Center Directors and staff, who are UT employees.



Organizational reporting and structure:

The Center will report through the Vice Chancellor for Research at the University. Given the interdisciplinary nature of the Center activities and the expectation that the Center will incorporate activities involving joint UT/ORNL faculty and staff, faculty and staff of the Institute of Agriculture, as well as collaborating faculty from several Colleges (including Agricultural Sciences and Natural Resources, Arts and Sciences, Business, Veterinary Medicine and Engineering) it is necessary to have reporting be at an appropriate administrative level.

The PI will be the founding ***Director*** with an initial tenure of three years. Following this period, a formal assessment will determine whether the Director will be retained, the assessment to be carried out by the UT Office of Research in conjunction with input from the Board of Advisors (BOA). The Director will be the primary contact with the BOA and its Executive Committee and will have overall responsibility for all activities of the Center. The Lead PI has extensive experience managing interdisciplinary research projects involving a dozen staff members. A ***Deputy Director*** will be responsible for the day-to-day operational activities of the Center, and thus will be someone with appropriate scientific credentials (e.g. a Ph.D. in a field related to the Center) and personnel management experience. The Deputy Director will

have responsibility for the searches for postdoctoral fellows, and will be the point of contact for all short- and long-term visitors. The Deputy Director, in collaboration with the Director, will establish mentors for post-docs and regularly evaluate the success of these. Note that all of the senior personnel and the collaborators have experience attracting and directing post-docs, with most having had extensive experience (e.g. have directed five or more such post-docs). A search for this position will begin as soon as the Center is funded, with the Director and Associate Directors serving as the search committee.

There will be three Associate Directors who will make up the management team of the Center along with the Director and Deputy Director, and will be initially three of the Senior Personnel on this proposal. The ***Associate Director for Outreach, Education and Diversity*** (S. Lenhart) will have oversight of all outreach and education activities for the broad community, be responsible for supervising the Outreach Coordinator, and will work closely with the Committee to Promote Diversity (CPD) to ensure that opportunities for participation in all Center activities are made available to diverse students and researchers. She will also have responsibility to plan tutorials, based upon recommendations from partners and in collaboration with the other Directors. The ***Associate Director for Partner Relations*** (G Hickling) will be the lead contact for all initial industry (ESRI, IBM) and government agency (GSMNP) partners, as well as for the CIMBS supporting agencies. He will develop, with CIMBS partners, plans for Center activities to meet their particular needs and collaborate with the other Directors and staff to initiate them. The ***Associate Director for Working Groups*** (S. Gavrilets) will be responsible for leading the assessment of working group and workshop proposals (in conjunction with the BOA and CPD), and collaborating with Center staff to organize all working groups and workshops once selected. The final selection of these activities will be made by the team of Directors based upon input from the BOA and CPD. All Associate Directors will utilize the expertise of UT/ORNL Senior Personnel and Collaborators in planning and carrying out Center activities.

An ***Information Technology Manager*** will have responsibility for all IT support, for basic hardware and connectivity, software and applications for collaborative services, and for high performance computing (HPC). All IT staff (an ***HPC specialist*** and a ***Senior Analyst*** with web and database experience) will report to the IT Manager. We have already identified current UT staff who have long experience collaborating with the PI on computational problems in biology who would be available and excellent choices to fill these IT positions.

A ***Business Manager*** will oversee all aspects of finances, accounting and budgeting for the Center. This person will be expected to have knowledge of financial accounting systems in place at UT, human resource policies and procedures for staff, and be capable of providing concise summaries of all financial activities of the Center. Reporting to the Business Manager will be a ***Travel Coordinator*** who will manage all travel and visa arrangements for all visitors and Center staff and researchers. One ***Administrative Assistant*** will report to the Deputy Director and assist in the meeting the needs of the post-docs and visitors, and another ***Administrative Assistant*** will report to the Director and assist in the activities of all Associate Directors. An ***Outreach Coordinator*** will report to the Associate Director for Outreach, Education and Diversity and will be responsible for developing and managing outreach and education initiatives, as well as assist in planning tutorials.

A ***Board of Advisors*** (BOA) will be established consisting of a group of researchers and educators external to UT who will be expected to fulfill two main obligations: (i) review the activities of the Center annually and provide a report outlining their assessment of the strengths and weaknesses of the Center to both NSF and other cooperating agencies, and to UT; and (ii) provide a means to externally review proposal submissions to the Center for activities to be held at the Center. We anticipate the need to have a fairly large group (20 members) on the BOA based on the proposed diversity of activities and fields encompassed by the Center. All BOA members would be involved in proposal evaluations, however a much smaller Executive Committee (4 members plus a Chair, elected by the members of the BOA),

would be charged to carry out the assessment of the Center activities and the effectiveness of the Director. In selecting BOA members, the need for expertise in the array of scientific areas will be taken into account, as well as the need for expertise in evaluation and assessment procedures and diversity of background. A ***Committee to Promote Diversity*** (CPD) will be established consisting of 5 members external to UT plus one UT researcher, with a task of providing advise and assistance to the Center on enhancing the ethnic and gender diversity of participants in all Center activities, including selection of BOA members. The CPD will select its Chair from among its external-to-UT members to serve a 2-year term, and this chair along with one additional non-UT member of the CPD will serve on the BOA. Selection of the membership of the BOA and the CPD will be made by the leadership team of the Center, with input from the various Agency cooperators, and open requests for participation made to the research and education communities.

Operating management:

The major Center activities will be managed by the above described leadership team consisting of the Directors. This team will hold regular monthly meetings with all Center staff with supervisory responsibilities (e.g. the IT and Business Managers) as well as the Outreach Coordinator. The major activities of working groups and workshops involves three components: proposal solicitation, evaluation and selection; working group and workshop planning and hosting; and assessment. Proposals will be solicited through an array of electronic and in-person requests at diverse venues. Proposal evaluation will be carried out by the BOA as advisory to the Director who along with the other Directors will make the final determination of which proposals to support. Guidelines for proposal submission and evaluation will be broadly disseminated and developed with input from the CPD and the BOA, and advice from other NSF Centers who have similar activities. The Associate Director for Working Groups will coordinate all planning for working groups and workshops. All educational and outreach activity coordination will be led by the Associate Director for Outreach, education and Diversity, who shall also be charged with investigating additional funding mechanisms to support educational and outreach activities.

Assessment:

Standard University operating procedures requires any Center to be reviewed by the Research Council of the Faculty Senate every five years, but the Center will have an annual review by the Vice Chancellor for Research, as well as an annual review conducted by the BOA Executive Committee. These reviews will be coordinated so as not to be overly burdensome. The format of the evaluation by the BOA Executive Committee would be two-fold: (a) assessment of the quality of activities carried out at the Center and (b) evaluation of the leadership of the Center. Both components would be provided as reports to the funding agencies and the Vice Chancellor for Research. UT has a very formalized set of procedures for personnel evaluation and in order to reduce duplication of effort, the personnel evaluations carried out by the BOA of the Director would be coordinated with that of the Vice Chancellor. Consistent with UT personnel evaluation procedures, the Director would carry out a yearly evaluation of all Center staff. Assessment methods for the working group, workshop and tutorial activities will be developed by the Associate Director of Outreach, Education and Diversity, utilizing several mechanisms and with input from evaluation and assessment expertise available at UT. These assessments will be tabulated by the administrative assistant to the Directors with regular reports provided to funding agency representatives and the BOA.

In the third year of Center activities, an evaluation of the Center leadership will be carried out by a committee chosen by the Vice Chancellor for Research with input from the BOA. The evaluation committee will include representation from internal and external to UT, and will make a formal recommendation regarding any suggested changes in the leadership team to the Vice Chancellor who will consult with funding agency partners of the Center regarding any modifications of Center leadership.

Appendix A3: Intellectual Property Rights:

The general guideline for rights and access to all intellectual property, inventions, creative works, and models produced through activities of the Center is that these shall be provided in an open access manner to all interested parties, including public distribution through the web sites of the Center, but subject to the rules and regulations of the employers of the individuals involved in the creation of these works. The University of Tennessee has a formal IP policy specified by the Board of Trustees that notes:

"**Article II A: General**: Domestic and foreign rights to certain inventions and creations developed by University personnel in performing the duties of their employment by the University or through their substantial use of facilities or funds provided by the University shall be assigned to the University pursuant to a revenue sharing plan for inventor(s) and creator(s)."

where

"Funds and facilities provided by government, commercial, industrial, or other public or private organizations and administered and controlled by the University shall be considered to be funds and facilities provided by the University."

The University specifically defines **Inventions** as: "All inventions, discoveries, computer programs, software and/or codes, methods, uses, products or combinations, whether or not patented or patentable at any time under the Federal Patent Act as now existing or hereafter amended or supplemented." This would therefore encompass most of the products to be produced through the Center, except for copyrightable written material that do not fall under this definition (e.g. technical reports and scientific journal articles would be the main ones) but are considered Creations.

With regard to both **Inventions** and **Copyrightable** material, the University IP policy states:

"Rights to inventions which are subject to the terms of a sponsored research or other agreement between the University and a third party are **subject to the terms of the applicable agreement**, or, in the absence of such terms, the rights to the inventions shall be assigned to the University pursuant to a revenue sharing plan for inventor(s)."

This statement provides the mechanism under which we propose to manage IP rights arising from activities at the Center carried out by University of Tennessee employees who receive financial support either directly from Center funding, or indirectly through cost-sharing provided by the University in support of the activities of the Center. ***For these employees, the University waives its rights asserted under Article II A above, and instead authorizes the distribution of all inventions and creations produced by these employees through open access methods, including distribution through web sites maintained by the Center.***

All employees of the University involved in activities at the Center whose efforts are funded in part through either direct Center funds, or indirectly through cost-sharing provided by the University in support of the activities of the Center, will be required to sign a statement agreeing with this principle of open access. This does not constrain the rights of such employees to submit for publication results from their activities at the Center in whatever venue they wish, as operationally we will maintain for open access the original form of the publication at the time it is submitted for publication. Access to the final published version will be maintained either through direct inclusion on the Center web sites when this is legally allowed, or through links to web pages of the author where applicable.

Similarly, it does not constrain the rights of these employees to develop monographs and texts for which they may receive financial gain, as these are covered by a separate section of the University IP Policy that encourages the production of scholarly and educational materials in this form (e.g. textbooks) without

requiring that it be assigned to the University. The Center will conform to this in that it will benefit the development of the scientific fields supported by the Center to encourage production of major scholarly and educational works such as textbooks by leading researchers and educators in these fields. Thus, unless the Center specifically contracts for production of such a major work, the rights to such will be owned by the authors and not required to be freely available through open access.

The above statements apply to University employees. The general policy of the Center will be ***to request that similar guidelines be followed for Center participants who are not University employees***, however such individuals may be constrained by policies of their own employers. We do not believe it would be in the best interest of the Center to constrain the range of individuals involved in Center activities to those whose employers agree to the open access principles described here. Therefore we will request, but not insist, that all participants involved in Center activities who are not University employees sign a statement similar to that developed for University employees regarding providing open access to their works produced in conjunction with Center activities. We will for example request authorization for open publication on the Center web sites all presentations made at the Center, including when appropriate video of such presentations.

The University also has under review policies for Research Data including maintenance and archiving that we propose to follow with regard to all data (this includes computer codes, publications, model descriptions, etc.) produced through the activities of the Center. This policy requires archiving data for a period of at least three years after the conclusion of a sponsored project, and the University commits itself to carrying this out with regard to all data produced through Center activities. In particular, data archives will be maintained in two separate locations with daily backups, in order to provide redundancy in the event of loss of data at one location.

The PI has had considerable experience managing large data sets and associated metadata from his research efforts in constructing large spatially-explicit computer-based models for assessing the biotic impacts of Everglades restoration. Federal geospatial metadata standards (e.g. FGDC) are not designed to deal with complex output from models, however new metadata approaches were developed by the UT Institute for Environmental Modeling to deal with complex spatio-temporal data arising from models. The Center will incorporate metadata standards in its databases, consistent with federal ones but appropriate for the diversity of data and products to be built at the Center, using prior expertise developed at Tennessee as well as that arising from projects such as the USGS National Biological Information Infrastructure and the NSF-supported SEEK (Science Environment for Ecological Knowledge) project.

Appendix A4: Institutional Capabilities
UT maintains one of the leading research and education groups in mathematical biology in the US and, as the below commitment indicates, offers its strong endorsement of the goals of the proposed Center.

Commitment of UT to the Success of the Center

The University of Tennessee strongly supports this proposal and through its submission indicates its willingness to share the costs associated with the establishment and maintenance of the proposed Center. To further the activities of the Center, UT commitments will include the following:

1. Space: UT will provide adequate temporary facilities to initiate workshop activities of CIMBS by January 1, 2009. These facilities will include: offices for 10 staff members, 12 post-docs, 4 long-term visiting researchers, 4 short-term visiting researchers and shared office space for an additional 15 workshop visitors. UT will provide all furnishings for these offices including desks and workstations. The approximately 8,000 sq ft facilities will include two small (12 person) conference rooms plus one larger (40 person) conference/presentation room, each with video projection and flat screen capabilities built in, plus a lounge area. The location will be on-campus within a 5-minute walk of the main locations of biological science and mathematics on campus, and a 5-minute shuttle-bus ride from the facilities in veterinary medicine and animal disease located on the western portion of the campus. The Center will have control to limit access to the facilities to only Center-affiliated individuals. The current status of this location is that approximately one-half of the facility has already been renovated, and this renovated space includes offices so that the initial staff of the Center can be located there by September 1, 2008. Within two years (by January 2011), UT will provide a permanent location for the Center, covering one complete floor (approximately 12,000 sq ft) in a building in the center of campus. This facility will be modified as per designs by the Center staff and external advisers, including all the above mentioned capabilities, with a larger conference facility with then-current technology remote connection capacity (e.g. Access Grid or better). This permanent location will be within the same facility as one of the leading computational science centers in the world (UT Innovative Computing Laboratory), enhancing opportunities for collaboration. This permanent location is a 3-minute walk from the mathematics and biology units on campus, and a 5-minute shuttle bus ride from the facilities in veterinary medicine and animal disease located on the western portion of the campus.

2. Computational facilities: UT will provide workstations (with a 3-year replacement cycle); accessories adequate for each of the Center offices (gigabit connectivity to central servers plus wireless access for portables); and access to a diversity of hardware, including the proposed in-house cluster (136 processors) and ORNL- and UT-based High Performance Computers (HPC). UT will identify the Center as a priority user of the NSF Track 2 HPC facility, with the Center guaranteed a portion of Track 2 discretionary allocation (as needed) for use in research conducted through the Center. UT will provide access to current computational software packages at no cost to the Center.

3. Additional Faculty: The University of Tennessee has strongly supported for three decades one of the major research and educational groups in mathematical biology in the world. The primary biological research areas of the main group of faculty involved has been ecology, evolution and epidemiology, with additional expertise in bioinformatics and genomics provided by younger faculty. The University recognizes that it would be beneficial to the proposed Center to have a broader array of biological fields represented among its faculty in mathematical and theoretical biology. This would provide a more diverse array of opportunities for mentoring in particular sub-fields for the post-doctoral fellows who will be resident at the Center, as well as provide a more diverse collection of faculty available to assist in the variety of workshops sponsored at the Center.

Therefore, to further indicate the strong University support for this Center, UT will commit to maintaining and expanding the current very strong mathematical biology group by planning to add five new faculty members with expertise in mathematics and biological areas that expand on those which are the focus of the current faculty. While no one institution can cover the entire breadth of biological areas in which mathematical approaches have made significant advances, this University commitment will broaden the local expertise and therefore enhance the attractiveness of the Center programs to possible Center participants. The exact areas in which the new faculty hires will be made will be determined by the Center management in consultation with the faculty in life sciences and mathematics across Departments and Colleges at UTK. At least one of these positions will be in animal infectious disease modeling, with a home appointment in one of the biology departments or the College of Veterinary Medicine. Examples of additional fields in which we expect new hires would be made include biological networks, cell biology, host-pathogen-environment systems, and immunology. These hires will be made over the first three years of the Center's operation, and the new faculty are expected to have home appointments in a variety of departments, with some possibly holding joint appointments between two departments as is true for several of the current faculty.

4. Staff: UT will cover the 9-month salary of the Director of the Center, who shall not have any formal classroom teaching responsibility. UT will provide internal funding for release time for 3 FTE's each year for participation in Center activities by both UT faculty and ORNL staff, some of which will be used for scientific software professionals as part of a dedicated, multidisciplinary staff with experience in high performance computing applied to biological modeling and analysis. These funds will also be used to provide release time for the individuals included as Senior Personnel and Collaborators who will not be supported directly on the management team for the Center. One FTE will be used to support these Senior Personnel during the initial two-year period of the Center operation, providing support for the initial emphasis areas and working groups proposed as part of the initial period of operation.

5. Post-doc and Graduate Student Opportunities: UT will provide internal funding for teaching opportunities for those Center post-docs who desire it, providing funding for partial salary support for one semester of teaching experience for all post-docs desiring this. UT will provide internal funding for 4 graduate students to be affiliated research assistants at the Center, carrying out dissertation work in collaboration with Center staff and visitors. Additionally, currently there are several proposals pending at various agencies for graduate student training that would directly connect to the Center, and UT will leverage the Center activities to foster connections between these graduate students and the post-docs by offering the gradate students opportunities to collaborate with the post-docs and Center staff on the ongoing research activities at the Center.

Access: The Knoxville airport is a 20-minute drive from the Center location, served by over 70 outgoing direct flights daily with 8 to DC, 9 to Chicago, 8 to Atlanta, 8 to Charlotte, 4 to NYC/Newark and 6 to Cincinnati. A Four Points by Sheraton hotel is 3 blocks from the initial Center location, with excellent negotiated rates for UT, and we have obtained assurance from this hotel that there will be adequate space available for participants attending working groups as well as facilities for hosting receptions for each working group. Two other large hotels (Holiday Inn Select and Hilton) are 3 blocks from the Four Points.

Knoxville Attractions: Knoxville has a relatively low cost-of-living, one of the highest per capita collections of restaurants in the US, offers a diverse array of cultural activities close to the initial Center location (a traditional music and dance center 2 blocks away; within a 15-minute walk are two major venues for classical, pop and jazz, the Knoxville Art Museum, downtown with 12 weekly major touring artists free concerts each year, daily free noon-time concerts and many arts festivals which attract thousands of visitors, numerous restaurants and clubs, a major theatre for plays and the plethora of activities on-campus), and is less than an hour from the mountain streams of Great Smoky Mountains National Park. Field trips will complement Center activities.