Project Summary

Vision: Through NSF funding provided by this RII, Mississippi will become a national leader in modeling and simulation of complex systems. Focusing on our State plan for economic growth and building on strengths at our four research institutions, we will develop foundational infrastructure and human capital across a broad spectrum of application areas that will yield next-generation science and technology advances in computational simulation and modeling of biological and biologically-relevant systems. We will address three critical focus areas—biological systems simulation, computational biology, and computational chemistry—and then integrate technologies from these three multidisciplinary areas to address emerging scientific and workforce development challenges. Researchers from diverse fields will collaborate on complex multidisciplinary problems, train students who will become the next generation of research leaders, and build a computationally skilled workforce. Scientific goals include:

A. **Multi-Scale Simulation of Biological Systems (BioSim)** – Develop accurate models of physiologic behavior and apply these models to realistic problems having biological significance.

B. **Modeling Biological Networks (CompBio)** – Develop novel cyber-enabled data mining, data integration, data tracking, and model learning algorithms for building accurate, understandable models of biological networks.

C. **Modeling and Simulation of Nanoscale Chemistry (CompChem)** – Develop an understanding of fundamental nanoscale chemical phenomena through modeling and simulation to improve synthetic control, assess the environmental impact, and facilitate biomimetic design of nanosystems.

Strategies for growth include recruiting, educating and graduating students, particularly those from underrepresented groups; supporting and mentoring new faculty hires or faculty making career changes; and providing seed grants for faculty to enter our RII research areas. Our **potential impact** will be to develop a highly skilled, diverse workforce to foster the transition from an industrial to a knowledge-based economy in Mississippi.

Scope and organization. This proposed RII is essential to strengthen, grow, and propel the three research groups to national competitiveness. Our major goal is to capitalize on our previous investments by: 1) strengthening the quality of research in each area; 2) increasing statewide collaborations in each area; and 3) establishing meaningful research collaborations between the three groups in emerging research areas. Each research area, composed of collaborative research teams with representatives from our four research institutions, is directed by a lead investigator for the research area and a coordinator at each institution. Research areas will focus on specific investigations and, through a collaborative network that utilizes cyberinfrastructure, integrate research foci to address complex, multidisciplinary problems.

Our research, education, and workforce development activities are tightly integrated. BioSim, CompBio and CompChem share the *central thematic link* of modeling and simulating biological and biologically-relevant complex systems. BioSim research will focus on the development of a multi-scale simulation framework for investigation of human biological processes and will make this framework freely available via cyber-infrastructure for research, education, and training purposes. This framework will enable the prediction of biological function ranging from fluid and structural mechanics to cellular level physiology to molecular chemistry. CompBio will develop novel cyber-enabled algorithms to model and simulate complex biological networks supporting transformational research in data-sparse species of economic and environmental importance to the State. These algorithms will provide the computational framework to generate predictive models of emergent behaviors by integrating and mining diverse high-throughput data sets. CompChem will develop a systematic understanding of the relationships between the organization and properties of matter at the atomic, molecular, and supramolecular levels across size scales from approximately 1 to 100 nanometers. This understanding will dramatically improve our ability to design and synthesize controlled nanoscale objects with specific properties. In years 3-5, we will also identify and develop *application links* by incorporating scientific and technological breakthroughs by the focus groups to address challenging multi-disciplinary problems that cannot currently be addressed effectively via computational methods.

Education activities are consistent throughout the three focus areas and include providing professional development workshops in computational sciences for secondary teachers and community college faculty, recruiting students from secondary schools and community colleges, offering undergraduate assistantships for students during the academic year or summer, and supporting graduate students.

We will continue to **develop human capital** in the faculty ranks and student populations and increase the pipeline in STEM areas by supporting and mentoring faculty and by conducting education activities for secondary teachers and graduate and undergraduate students.

It is critical for the small and geographically disperse group of faculty within our State to develop a larger, virtual community building strong and competitive research teams to address large multidisciplinary research problems. Consistent with our State's vision for science and technology, we will directly impact three major areas of **cyberinfrastructure** development, all relying heavily on HPC computation and simulation methods that can only be effectively performed with the most powerful computers available. Each focus area is developing a virtual community through cyber-enabled consortia, linked via an umbrella website encompassing the activities of all personnel and institutions involved in our EPSCoR effort and through collaboration and teambuilding software. We will make extensive use of the Mississippi Center for Supercomputing Resources, which provides high performance computing research support at all eight publically funded institutions of higher learning, for performing the research tasks of this effort. We will further increase inter-institutional access to other in-state HPC resources through the development of our collaborative research projects.

Mississippi's diverse population provides an opportunity to improve the recruitment of underrepresented minorities in the computational sciences and increase the number of underrepresented graduate/undergraduate students. **Diversity, outreach and communications** are closely tied to our goal of growing a diverse, highly skilled workforce. Accomplishing this goal will make Mississippi competitive for funding in support of gaining national and international prominence in modeling and simulation, and for attracting new, high-technology industries to the State. We will use start-up funds to recruit and retain faculty from groups currently underrepresented in STEM fields. Through our secondary teacher workshops we will impact instruction and career knowledge in the computational sciences in secondary schools with large minority student populations. We will provide research experiences for undergraduates by reserving 25% of our assistantships for underrepresented students including those recruited from minority serving institutions. We will transition undergraduates into graduate programs at our four research institutions. We will fund travel by Mississippi undergraduate and graduate students and faculty to research institutions in other countries. Our international exchange program will foster international collaborations among scientists, grow our network, and give students the opportunity to gain the skills needed in our highly interconnected global scientific communities and economies.

We will use enhanced cyberinfrastructure to establish both student and faculty networks. The research leadership will meet once a month via video conferencing or groupware to enhance collaboration among the three focus areas. Two meetings each year for all participating faculty and student researchers will disseminate research results and facilitate inter-disciplinary collaborations,

Sustainability will result from our becoming nationally competitive in modeling and simulation of complex systems. We will impact the workforce by increasing the pipeline of students moving into computational sciences related careers and build a skilled, collaborative network of researchers who will successfully compete for extramural funding in project research and related areas.

Project **evaluation** will 1) formatively study, using a systematic structure, the quality of the implementation of this RII and project progress toward meeting milestones and intended outcomes, and 2) summatively assess, both annually and at the end of the grant, the effectiveness and overall impact of project components on improving discovery and learning, developing a nationally and internationally competitive, diverse Mississippi STEM workforce, facilitating science-based economic development in Mississippi, and expanding scientific literacy of Mississippi citizenry.

Management of the project will be led by project director Sandra Harpole, assisted by project administrator Teresa Gammill. Other members of the management team include science coordinator Susan Bridges and an education and outreach coordinator. The management team is guided by the Mississippi EPSCoR State Committee, which includes the chief research officers of our four research institutions as well as government and business leaders. The National Advisory Board (NAB), to meet twice yearly, will provide direct input to the research accomplishments and education and outreach to the PD and the individual researchers and recommend mid-course modifications. Rose Shaw, external evaluator, and Maxine Harper, internal evaluator, will collect and track data and provide both formative and summative reports to the PD and the NAB.

Intellectual merit. Our integrated research in modeling and simulation of complex systems will make seminal contributions in the areas of multi-scale simulation of biological systems (BioSim), modeling of biological networks (CompBio), and modeling and simulation of nanoscale chemistry (CompChem).

BioSim will develop a multi-scale simulation framework for investigation of human biological processes and make this framework freely available via cyber-infrastructure for research, education, and training purposes. The approach will tightly integrate: 1) a macro-scale Quantitative Human Physiology (QHP) model to determine the mechanisms responsible for alterations in human pulmonary and cardiovascular physiology; 2) meso-scale computational fluid dynamics (CFD) simulations of individual organs and organ systems; 3) meso-scale probabilistic simulations of organ and organ system subcomponents where deterministic simulations are not practical with current computing capabilities; and 4) micro-scale modeling and physiochemical characterization of inter-component interactions. As a compelling demonstration problem of practical significance, we will apply our multi-scale framework to the simulation of inhalation exposure to nanoparticles and the resulting deleterious effects on respiratory and cardiovascular function.

CompBio will develop new cyber-enabled algorithms to model complex biological networks supporting transformational research in data-sparse species of economic and environmental importance by addressing three key aspects of building biological networks: 1) data integration and mining, 2) data provenance, and 3) modeling, reconstruction, and simulation of complex biological networks. Our data integration algorithms will build on our pioneering use of Gene Ontology from relatively data-sparse species to apply graph based and binary data models for integration of heterogeneous genomics data at the functional level. We will build a flexible data provenance system for biological modeling that enables tracking of data from experiments through data mining and integration to model building and will extend to grid-scale. We propose new models for learning biological networks that combine Bayesian learning and numerical optimization, that can identify the most robust relationships with data sparse systems, and that use novel approaches for explaining model response.

CompChem will address three interrelated components for modeling and simulation of nanoscale chemistry. As a foundation, we explore new methods for theoretical characterization of nanoscale materials with particular emphases on using QM methods to predict changes in the structure and electronic properties of nanomaterials for sensors, using QSPR/QSAR models to predict nanotoxicity, and using integrated QM methods to study metal clusters. Computational and experimental chemists will collaborate to couple predictions about structure and properties with synthesis and characterization applied to three high impact applications: organometallic nanotubes containing nanopores, “magic”-sized gold nanoparticles, and the polyhedral oligomeric silsequioxanes. Finally, we will use simulation to study complex nanoscale processes in nature such as biopolymer hydration, large-scale enzyme motion, and molecular recognition and then use these results to develop bioinspired nanoscale materials.

Broader Impacts: We will impact the diversity of the computational sciences community of faculty and students in Mississippi and contribute to the development of a skilled workforce that will assist Mississippi in transitioning to a knowledge-based economy. We will contribute to the broader computational sciences community by investigating specific complex biological systems and processes with significant societal impact.