Patient-specific Heart Modeling for Personalized Cardiac Therapy

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Response to NIH RFI on Science Drivers Requiring Capable Exascale HPC

The Specific Scientific Challenge

Heart disease persists as a leading human health issue worldwide reflecting our inability to predict adverse cardiac events for individual patients, as well as longstanding challenges in evaluating efficacy and risks of novel therapies on a clinically relevant population. We propose a new generation of patient-specific, multi-scale computational models that simulate cardiac performance and response to therapeutic intervention. These models would feed patient-specific data into a whole heart model that simulates the interaction of the chemical, cellular, whole organ and vascular system. These models could be correlated with large medical image data sets to obtain the necessary geometric and structural data to construct patient specific heart models and help select treatments based on the outcomes of other similar patients. With this capability, we could predict, through patient-specific simulation, how much time would pass before a specific person might have a "heart attack," which would represent a disruptive breakthrough in the fight to conquer cardiovascular disease.

Such models would require the following capabilities:

1) Patient-specific cardiac anatomy and muscle fiber direction,
2) Functionally accurate finite element models of whole-heart contractile performance incorporating electro-mechanical coupling and solid-fluid interaction,
3) Multi-scale modeling from sub-cellular signaling to whole organ function in health and disease
4) Systems-level coupling of cardiovascular physiology and metabolic function, and
5) Functional outputs to simulate clinically measureable indices of cardiovascular performance and correlate with other high dimensional data sets such as medical records and genomics data.

Early versions of (1)-(5) already exist, including: magnetic resonance imaging and diffusion tensor imaging (from Mount Sinai) that provide patient specific cardiac anatomy and fiber architecture; validated finite element models of the mechanical function of a healthy whole heart (developed at IBM and dubbed Cardioid). Disease models are currently under development in collaboration between Mount Sinai and IBM. Electromechanical coupling and solid-fluid interaction models are under active development by colleagues at other leading research institutions including The Johns Hopkins University and Stanford University. Our approach is synergistic with the multi-scale modeling and systems biology coupling at other partner institutions like UC San Diego. The Mount Sinai Health System is the largest medical network in New York and provides unparalleled access to cardiologists and cardiac patients. IBM's Cardioid model has been used to simulate the introduction of an anti-arrhythmic drug into the bloodstream and watch its absorption.

The Potential Impact

The ability to predict the timing and severity of a heart attack brings the possibly of prevention through the application of specific therapies prior to the expected attack. This information may also help individuals to choose healthier lifestyles. For those patients unable to avoid the impact of heart disease, the ability to optimize patient-specific therapies in silico would maximize therapeutic outcomes and reduce the disease burden for a substantial segment of society. It could impact the national economy by reducing health care costs associated with the greatest health problem in the developed world. It would also streamline the discovery and development of novel drug-, gene-, and cell-based treatments that could generate revenue as the next generation of cardiac therapies. These models will advance the field tremendously by both increased predictive ability and being highly customized based on individual patient data.

The Specific Limitations of Existing HPC

Exascale-sized data repositories with secure encryption capabilities will also be required for machine learning to help correlate data from simulations with patient medical records and genomic data to help develop a specific precision therapy for a specific patient. Expert systems such as Watson could help correlate disparate data sets to suggest effective treatment plans.

Related Research Areas

Related research areas that may benefit include modeling of other debilitating diseases that require patient-specific detail and could be minimized by advanced warning, such as aortic aneurysm or intervertebral disc herniation. Solving multi-scale cell-to-organ biology problems would impact research areas in diseases such as diabetes, neurodegeneration, and various age-related illnesses. Similar approaches could help inform other organs models such as the brain. Successful multi-physics integration of solid mechanics, fluid dynamics, and electrical conduction systems could impact the study of human physiology in extreme conditions such as high altitude, deep sea, or outer space exploration, and could directly translate to a wide range of industrial applications including future energy, transportation, and manufacturing systems.

Computational Parameters Expected in 2025

The simulation for the finite element models for the contractile performance in Cardioid ((2) above) already require petascale computing capabilities. This model has already been run on 1.6 million compute cores on Sequoia BlueGene/Q at Livermore National Laboratory, simulating an hour of heart activity in seven hours of wall clock time at 0.1mm resolution. The combination of higher resolution, additional multi-physics and other multi-scale models correlated with image, genomic and medical records will clearly constitute an exascale simulation. In addition, ideally the simulations would run in hours or less for practical utility in a healthcare setting.

Other Capabilities Needed

In addition to increased computational horsepower to run these multi-scale, multi-physics, patient-specific cardiac models, other capabilities needed by the end-to-end system will include enhanced 3D visualization tools for interacting with the medical image data and for finite element modeling assembly and inspection for multi-physics compatibility; analytical tools for machine-learning interpretation, and accessible presentation (including to physicians and patients) of the complex multi-dimensional data sets generated by the model simulations; data encryption capabilities to ensure confidentiality of patient medical records; and data storage and sharing capabilities to transfer and integrate image data, medical records, and modeling software across multiple sites and platforms. Tools for automated image registration and segmentation and feature extraction will need to be developed and validated as current tools are only semi-automated. Simulation software that accurately mimics the chemicals and their coordinated efforts with cells, organs and the entire vascular system also need to be developed and validated. The resolution of Cardioid needs to be improved to 0.05 mm for greater accuracy.