What can Multiscale Models do for Precision Medicine?

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Profile:

Grace C.Y. Peng received the B.S. degree in electrical engineering from the University of Illinois at Urbana, the M.S. and Ph.D. degrees in biomedical engineering from Northwestern University. She performed postdoctoral and faculty research in the department of Neurology at the Johns Hopkins University. In 2000 she became the Clare Boothe Luce professor of biomedical engineering at the Catholic University of America. Since 2002, Dr. Peng has been a Program Director in the National Institute of Biomedical Imaging and Bioengineering (NIBIB), at the National Institutes of Health. Her program areas at the NIBIB include mathematical modeling, simulation and analysis methods, and next generation engineering systems for rehabilitation engineering, neuroengineering and surgical systems. In 2003, Dr. Peng lead the creation of the Interagency Modeling and Analysis Group (IMAG), which now consists of program officers from ten federal agencies of the U.S. government and Canada (www.imagwiki.org/mediawiki). IMAG has continuously supported funding specifically for multiscale modeling (of biological systems) since 2004. IMAG facilitates the activities of the Multiscale Modeling (MSM) Consortium of investigators (started in 2006). Dr. Peng is interested in promoting the development of intelligent tools and reusable models, and integrating these approaches in engineering systems and multiscale physiological problems.

Abstract

1. Introduction – What is Precision Medicine?

In 2011, the National Academy of Sciences (NAS) published a report entitled, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease."[1]This report has spurred many talks and discussions in the scientific arena in the United States to examine how we can manage the explosion of disease-relevant data, and better integrate the knowledge gained from basic biomedical research with medical histories and health outcomes of individual patients. The NAS Committee concluded it is time now to modernize the human disease taxonomy that informs healthcare decisions, by more precisely defining and classifying diseases. A *New Taxonomy* would precisely define diseases based on their intrinsic biology, in addition to traditional "signs and symptoms"; and incorporate a deeper understanding of disease mechanisms, pathogenesis, and treatments in a dynamic, iterative fashion – continuously incorporating newly emerging disease information. The New Taxonomy would require an *Information Commons* in which data on large populations of patients become broadly available for research use, and a *Disease Knowledge Network* that adds value to these data by highlighting their inter-connectedness and integrating them with evolving knowledge of fundamental biological processes. The result would be "Precision Medicine".

1.2. *IMAG and the MSM Consortium*

Since 2003, the Interagency Modeling and Analysis Group (IMAG), a coalition of program officers from 10 government agencies in the United States and Canada, has been promoting funding activities in the area of modeling and analysis of biomedical, biological and behavioral systems[2], with a particular emphasis on multiscale modeling. Since 2006, IMAG has facilitated the activities of the Multiscale Modeling (MSM) consortium, which is made up of investigators in the field. Each year, the IMAG MSM Consortium meets to discuss timely issues that concern the field of multiscale modeling. This year, on October 22-23, 2012, the MSM Consortium decided to focus its discussions on "Multiscale Modeling for Precision Healthcare"[3]. Four sets of MSM Consortium panelists were asked to read the NAS report on Precision Medicine[1], collect other sources of relevant information, and comment on the following questions: 1) Data-driven models, physiological models and structural models – can they be tailored to individuals for precision healthcare? 2) Can computational biology facilitate precision healthcare? 3) How can we utilize clinical data to inspire MSM research for precision healthcare? 4) How do we incorporate verification, validation and uncertainty quantification in MSM for precision healthcare? The panelists led the MSM Consortium in an interactive discussion on each of these questions, and that the views expressed below are those of the MSM Consortium, not the NIH or other government agency members of IMAG.

2. MSM and Precision Medicine

Though the NAS report on Precision Medicine[1] does not refer to computational models, the MSM Consortium concluded that multiscale models will be necessary platforms to derive knowledge from clinical and scientific data and to integrate knowledge for the purpose of informing diagnoses, supporting therapeutic decisions and predicting clinical outcomes. At the same time the improved data resources, through the New Taxonomy, Information Commons, Disease Knowledge Networks recommended in the NAS report, will all be critical in enabling the application of multiscale models to precision medicine. A recently published review article by Winslow et al.[4] defines *computational medicine* as the means to use quantitative multiscale models to understand altered structure and function in disease, and develop new methods for disease diagnosis and treatment.

The MSM Consortium also discussed the use of computational (systems) biology models, and its unique ability to link molecular scales with

macro-scale information. Though computational biology models have already shown success in correlating high-dimensional, high-throughput data with disease diagnosis, there is a need to increase the influence of mechanistic hypotheses in the modeling cycle[5]. The MSM Consortium also discussed the need for good clinical data appropriate for models, as well as a need to better engage the clinical community in the modeling discussion. Finally, the MSM Consortium conducted an extensive discussion on model validation, verification and uncertainty quantification (VV&UQ). The Consortium identified the need to develop model evaluation criteria at the beginning of the model development process, and that VV&UQ should be addressed in the context of a model's use case and level of criticality of the clinical decision being made.

In conclusion, multiscale modeling has the potential to play a critical role in implementing the goals of precision medicine. While most diseases present clinically at tissue, organ and whole body scales; they are frequently treated with molecular interventions. Multiscale models are among the most rigorous tools available to integrate a hierarchy of information at different scales and predict the dynamic state of a patient and the progression of disease.

References

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