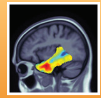
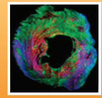
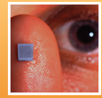
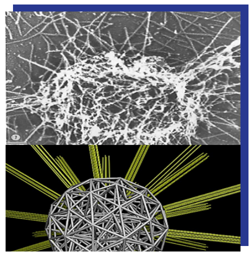
NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

Computational Modeling

National Institutes of Health

What is computational modeling?



Model of platelet structure helps to predict movement patterns of activated platelets.
Source: Danny Bluestein, Stony Brook University

Computational modeling is the use of computers to simulate and study the behavior of complex systems using mathematics, physics and computer science. A computational model contains numerous variables that characterize the system being studied. Simulation is done by adjusting each of these variables alone or in combination and observing how the changes affect the outcomes. The results of model simulations help researchers make predictions about what will happen in the real system that is being studied in response to changing conditions. Modeling can expedite research by allowing scientists to conduct thousands of simulated experiments by computer in order to identify the actual physical experiments that are most likely to help the researcher find the solution to the problem being studied.

A key feature of today's computational models is that they are able to study a biological system at multiple levels, including molecular processes, cell to cell interactions, and how those interactions result in changes at the tissue and organ level. The ability to study a system at these multiple levels is known as multiscale modeling.

How can computational modeling accelerate discovery?

To gain a better understanding of how computer modeling works, let's think about baking a cake that has 20 ingredients. If you want to know how each ingredient contributes to the outcome of the cake, one option would be to bake 20 cakes and leave out a different ingredient each time. Such an approach would be extremely time-consuming. Alternatively, you could enter all 20 ingredients into a computer model, including the known properties of each ingredient. You could then run a simulation in which a different ingredient is left out each time. In a matter of seconds, the computer could tell you how each of the 20 cakes would likely turn out if baked in real life.

Let's say you now want to know how changing the amount of each ingredient will affect the cake. In your computer model, you could adjust the amounts of each of the 20 ingredients any number of times until the outcome of your simulation is a cake that suits your needs (e.g. fluffy, sticky, soft, hard, etc.). In real life, you would need to bake 190 cakes to find out the results of changing any 2 ingredients; 1,140 cakes to find the results of changing any 3 ingredients; and 4,845 cakes to find the results of changing any 4 ingredients. The power of computational modeling is that it allows scientists and engineers to simulate variations more efficiently by computer, saving time, money and materials.

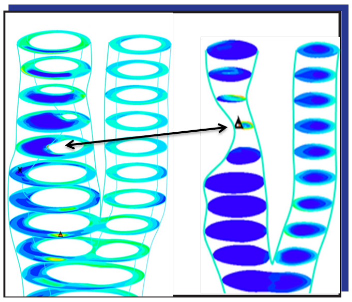
What are some examples of computational modeling and how it is used to study complex systems?

- **Forecasting the weather.** Weather forecasting uses computer models that analyze and make predictions based on numerous atmospheric factors. This is helpful for protecting life, property, and crops, and helping utility companies plan for increases in power demand, especially when extreme climate shifts are expected.
- **Building better airplanes.** Flight simulators re-create aircraft flight using the complex equations that govern how aircraft fly and the reaction of the aircraft to external environmental factors, such as turbulence, air density, and precipitation. In addition to being used to train pilots, flight simulators are used to design aircraft and test how aircraft might be affected by different conditions.
- **Studying earthquakes.** Computational modeling is used in the study of earthquakes, with the goal of saving lives, buildings, and other types of infrastructure. Computer simulations model how the construction, composition, and motion of structures, and the surfaces on which they are built, interact to affect what happens during an earthquake.

How can computational modeling improve medical care and/or biomedical research?

- Researchers are developing models of the structure and function of blood vessels, blood flow, and heart valves to optimize the design of implanted devices such as artificial heart valves and coronary artery stents. Computational models also aid in the creation of decision tools for doctors that can provide guidance for the treatment of cardiovascular disease, based on detailed analysis of specific characteristics of each patient.
- Computer models of the human cornea can help simulate laser eye surgery and refine the technique. They are also used for virtual training of physicians in how to perform the procedure.
- Researchers use computational modeling to help design drugs, early in the development process, that will be the safest for patients. Identifying which drugs are the least likely to have adverse side effects also has the potential to reduce the many years needed to bring a promising candidate drug from the experimental stage to winning approval as a safe and effective medication.

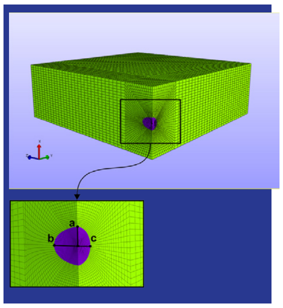
What are NIBIB-funded researchers developing in the area of computational modeling?



Model of clogged arteries identifies areas of wall damage (left) and points of high stress from blood flow (right), which predict atherosclerotic plaque rupture.
Source: Dalin Tang, Worcester Polytechnic Institute.

Improving healing of chronic wounds. Chronic skin wounds, especially in people suffering from conditions such as diabetes and obesity, are a significant health and economic problem in the U.S. and worldwide. Healing requires recruitment of new skin fibroblasts into the wound region, which is directed by a protein called platelet-derived growth factor (PDGF). Although much is known about the signals that activate PDGF, little is known about how different concentrations of PDGF are distributed throughout the wound site and how this orchestrates the movement of fibroblasts into the wound to promote healing. NIBIB-funded scientists are developing a computer model that incorporates a wealth of experimental data about the signals that activate PDGF. The model will be used to understand and predict the key triggers of the healing process at multiple levels, including self-assembly of contractile proteins, cell migration, and cell to cell interactions to form new tissue. The model will be used to identify, test and refine wound-healing approaches for patients with persistent chronic wounds.

Reducing osteoarthritis following knee surgery. Anterior cruciate ligament (ACL) tears are a common knee injury. ACL reconstructive surgeries are often successful at improving joint stability, but patients have a high risk for developing early onset osteoarthritis (OA). Researchers are working to understand why OA develops in these patients, and the best treatment strategy to lower the risk. They are creating a new multi-scale computational model to examine the mechanics of walking in terms of muscle, bone, and soft tissues. The model will be used to test key surgical variables affecting cartilage stresses after ACL reconstruction that are believed to increase osteoarthritic changes to the joint, which include ACL graft stiffness, and the angle of ACL attachment to the bones. The model will then examine the influence of surgical procedures on knee mechanics using MRI. The studies aim to identify clinical and surgical protocols that can best reduce the risk for early onset OA following ligament injury and surgical repair.



This model predicts changes in stress within a tissue in response to changes in physical and chemical properties.
Source: Jay Humphrey, Yale University.

Multiscale modeling of microbial biofilms for improved treatment of antibiotic resistant infections. The majority of naturally occurring bacteria grow as biofilms—large numbers of bacteria that self-organize into three-dimensional structures—which often renders them resistant to antibiotic treatments. Although they represent the vast majority of microbial life on the planet, the basic structural and biochemical characteristics of biofilms are still poorly understood. Scientists are combining computational and experimental tools to address the challenge of characterizing, predicting, and treating these complex systems. The goal is to develop an experimentally driven computer model that generates accurate predictions of biofilm behavior. The predictions will be used to develop novel ways for treating resistant biofilms found on the surfaces of implanted medical devices, such as urinary and venous catheters, breast implants, and pacemakers.

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The NIBIB supports the Interagency Modeling and Analysis Group (IMAG) which coordinates the Multiscale Modeling (MSM) Consortium of investigators who develop multiscale models to solve various biomedical, biological and behavioral research questions.