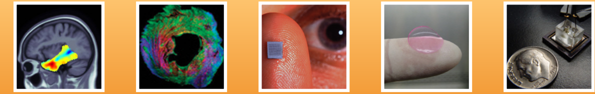
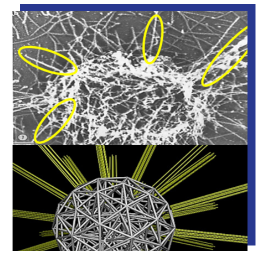
NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING



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 mathematics, physics and computer science to study the behavior of complex systems by computer simulation. A computational model contains numerous variables that characterize the system being studied. Simulation is done by adjusting these variables and observing how the changes affect the outcomes predicted by the model. 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.

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, explaining to the computer what each ingredient does and how it interacts with other ingredients. 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 both time, money and materials.

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

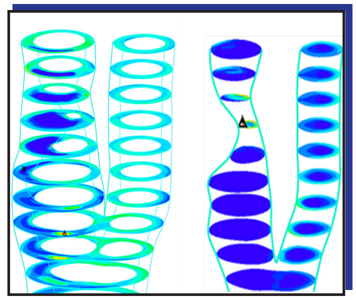
Computational modeling is used to study a wide range of complex systems. Some examples include:

- ***Forecasting the weather.*** Weather forecasting uses computer models that analyze and make predictions based on numerous atmospheric factors. This is important for many reasons including 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 for the design of aircraft and research into 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.
- ***Household items.*** Computational models are used to develop many, if not most, of the items we use in our home. For example, packaging of household chemicals (e.g. for hygiene, laundry, cleaning) and food (e.g. coffee, potato chips, cookies), production of textiles (e.g. fabric, clothes) and even designing diapers utilize many complicated mathematical methods and modeling tools.

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

- ***Treatment of heart disease.*** Researchers are developing models of the mechanics of blood vessels, blood flow, and heart valves. These models can then be used in a number of ways, including optimizing the design of implanted devices such as artificial heart valves and coronary artery stents. Researchers are also using computational models to develop decision tools for doctors that can provide guidance for the treatment of cardiovascular disease based on detailed analysis of specific characteristics of each patient.

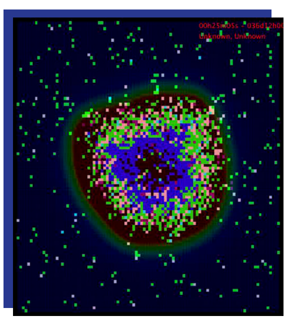
- ***Vision surgery.*** With the increase in laser vision surgery, scientists are using computational modeling to improve the procedure and reduce the chance of poor results. Specifically, biomechanical models of the human cornea are being developed to simulate laser surgery and refine the technique. Another important use of these models is for virtual training of physicians in how to perform the procedure.
- ***Predicting drug side effects.*** Researchers are using computational modeling to predict potential side effects of drugs. This approach offers the possibility of choosing the design of a drug, early in the development process, that will be the safest for patients. This approach may also allow researchers to identify possible new uses for medications that are already on the market. 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 an approved, safe medication for diseases and conditions that lack effective treatments.



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.

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

Designing precise drug delivery systems. An exciting area of research is targeted drug delivery, which uses extremely small and versatile vehicles known as nanoparticles. Scientists are able to synthesize nanoparticles composed of discrete molecules, chemicals and other physical characteristics that enable the particle to deliver a therapeutic agent to a specific disease site, while avoiding interactions with healthy tissues. NIBIB-supported researchers are using computational models of the complex interactions of nanoparticle systems within the biological environment of the human body. Such modeling simulates the fate of nanoparticles that have different designs; the goal is to develop improved, more precise nanoparticle drug delivery systems.



Computational model showing molecules moving in and out of the site of tuberculosis granuloma formation.
Source: Denise Kirschner, University of Michigan

Modeling pathogen and immune responses to treat tuberculosis. Tuberculosis remains a worldwide problem, infecting one third of the population. Current therapy is difficult for patients to adhere to, as it requires 6 months of treatment with multiple antibiotics. Researchers are using a combined experimental/computational approach to develop a realistic model that describes the immune response to infection with the bacteria that causes tuberculosis. The goal is to predict the outcome of treatment strategies that boost immunity during antibiotic treatment. Results from the model will be used to develop improved therapies that optimize the combined effects of antibiotic treatment and the immune response. This approach will also provide data and tools to the broader community of researchers investigating various areas related to tuberculosis, immunity, and computational modeling.

Combining imaging for the complete picture. In recent years, there has been rapid progress in the development of imaging technologies to study brain structure and function. Researchers are now working to acquire more detailed information by using combinations of imaging techniques, including functional magnetic resonance imaging (fMRI), diffuse optical tomography (DOT), electroencephalography (EEG) and magnetoencephalography (MEG) measurements. This requires integrating imaging experiments using two or more techniques simultaneously to optimize details of brain structure and function. Researchers will use computational models that combine multiple imaging modalities for research studies and clinical management of patients. This approach will have important implications for understanding the dynamics of normal brain function, and how these dynamics change in illnesses such as epilepsy, Alzheimer's disease, stroke and Parkinson's disease. The technique can also be used to monitor brain function during sleep, under anesthesia, and in patients treated in the intensive care unit.

Optimizing conditions for tissue repair. Tissue failure, due to trauma, age and disease, has created a demand for successful tissue replacement and regeneration strategies. At present, such approaches are hampered due to the inability to design biomaterials that meet the specific needs of each repair site. Researchers are developing a modeling toolkit that would predict the best biomaterial composition for different biological environments -- such as in different parts of the body. The current focus is on load-bearing biomaterials for repair of bone and related tissues. Importantly, the components of the modeling toolkit will have broad utility for a range of biomaterial and regenerative applications, including repair of tendon, cornea, and blood vessels.

NIBIB Contacts

National Institute of Biomedical Imaging and Bioengineering
6707 Democracy Blvd.
Suite 200
Bethesda, MD 20892
Phone: 301-496-8859
info@nibib.nih.gov
www.nibib.nih.gov

Office of Science Policy and Communications
Press Office:
Phone: 301-496-3500
Fax: 301-480-1613
nibibpress@mail.nih.gov

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.

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

National Institute of Biomedical Imaging and Bioengineering