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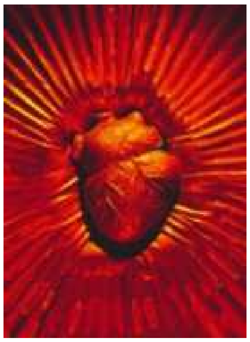
Working a Beat

By Jacob Berkowitz

In the fall of 2001 an article was published in Cardiac Electrophysiology Review that summarized the current work on computer modeling of atrial fibrillation, the debilitating quivering of the heart's upper chambers. All things being equal, there was probably about as much chance that Wonho Oh would ever see the article as he would get hit by lightning. Except for one thing—the article's concluding statement that "the final limitation of simulations is the inadequacy of available computer resources to handle all the details."



Not long after the article appeared, the Brookhaven National Laboratory mathematician and supercomputing scientist received a call from Flavio Fenton, the Director of Electrophysiology Research of the Heart Institute at the Beth Israel Medical Center in New York City.

That call began Oh's ongoing journey to help develop better simulations of the heart's electrical activity, especially arrhythmia, or irregular beating, using the power of parallel supercomputing. It's a pursuit that puts Oh (who has no training in biology) at the forefront of research into an ailment that accounts for one-third of all cardiac deaths in the United States.

Oh was introduced to heart electrophysiology because Flavio Fenton's rabbit heart ventricle simulations were slow enough to give an eager researcher a heart attack. Working on a single processor workstation, it took about three hours to model a single second of electrical activity in a rabbit's ventricles—the heart's two lower chambers and pumping workhorses. At this rate it would be impossible to achieve Fenton's goal: modeling fibrillation and arrhythmia in the human atria and ventricles. Human hearts are at least four times larger in diameter than a rabbit's, but the increase in computing power required is even greater, reflecting the cubic rise in volume of the larger heart.

Model Complexity

In order to study fibrillation, Fenton needed to significantly increase the complexity of his models—another factor that would require more computing power. He needed to create bi-domain models that accurately reflect the fact that the heart's ion-mediated electrical current travels into and out of cells. Earlier heart electrophysiology models treated this bioelectrical system as a mono-domain one, with electrical activity limited to cells' interiors.

"When you go from mono-domain to bi-domain you need to solve not only a partial differential equation but also a Poisson equation, and this involves more computing power. The bottleneck is the Poisson equation. It couples the partial differential equations for the intra- and extra-cellular environments. Unless you have a fast algorithm, the same method for the mono-domain can be at least ten times slower with the Poisson," says Fenton, who is also a visiting research scientist in the physics department at Hofstra University in Hempstead, NY.

Interestingly, it was Oh's experience working with geologists studying flow through porous media that prepared him to help cardiologists.

"I was solving oil reservoir equations," says Oh, who's also a professor State University of New York in Stony Brook. "These involved an elliptic partial differential equation that looks similar to the bi-domain equation. The major difference is that the heart problem includes a time derivative, it changes with time."

Electrical Pump

While most of us know the heart as a pump, fewer of us think of the large, essential muscle in our chests as an electrical pump. Yet, it is electrical activity that regulates the heart's normal, steady rhythm of between 60 and 90 contractions a minute. In a healthy heart the cardiac rhythm originates in a small area located in the upper part of the right atrium called the sinoatrial node. The impulses from the heart's natural pacemaker travel as an electrical wave through the atria, and then—after a hundredth-of-a-second delay allowing for blood to enter the ventricles—through the cells of the ventricles. This electrical stimulation causes the cells to contract forcefully , pumping blood through the body.

Arrhythmia occurs when, as a result of structural or dynamical problems, one of these electrical waves is locally blocked and breaks, turning the wave into a potentially deadly spiral of electrical activity.

"When these spiral waves are produced in the heart, they have a much faster frequency than your normal pacemaker," says Fenton. "Since they rotate much faster, they take control and your heart starts pumping much faster—called tachycardia. Then the spirals tend to break into multiples. And when you have a few of these spirals all over your heart, each one at a very high frequency and out of phase from the others, then the whole heart is just quivering and not pumping anymore."

About ten percent of all Americans over the age of 65 have some level of chronic atrial fibrillation, a condition that results in weakness and numerous long-term circulation problems. Ventricular fibrillation always results in death if not treated within minutes.

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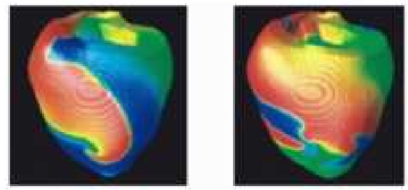
Heart Modeling

In the early 1980s, Beth Israel Medical Center cardiologist Dr. Steven Evans began collaborating with a mathematician to numerically model the heart's electrophysiology. In 1998, he recruited Fenton, who was then working in high energy physics, to further pursue the computational modeling of this electrical activity.

The pursuit of heart electrophysiology modeling is driven by the fact that cardiologists are already well aware of the potential to treat arrhythmia. Patients with abnormal heart rhythms can undergo what has become a standard diagnostic procedure known as an electrophysiology study. A catheter is inserted into a patient's femoral vein in the groin, and then guided up into the heart. The doctor then stimulates the heart with electrical signals to make it beat at various rates, and to observe any irregularities. Based on this test, the cardiologist can use a variety of drugs, surgical techniques, or a small, automatic defibrillator worn by a patient, to prevent arrhythmia or to convert irregular rhythms back to normal.



The problem is that even given these medical techniques, cardiac arrythmias are still a major killer, and their cause and dynamics—the breaking of the electrical wave and spiral wave behavior—still remain largely a mystery.

The Code

Working with experimental data, Brookhaven's Oh is methodically developing the parallel supercomputing code and algorithms that will enable Fenton, Evans and other researchers to minutely model atrial and ventriclar activity with greater precision and speed than ever previously achieved.

Initially he's developing a three-dimensional slab model, one that will act as a validation and testing ground for building the parallel code.

"When you stimulate a part of the slab tissue, you expect a certain behavior of the electrical potentials, as seen experimentally. At this point, I have a basic set of code and I have been testing it in a serial fashion in a single processor with a small tissue sample to see whether the resulting potentials look reasonable. Qualitatively its working, the wave is propagating, but I still need to confirm it quantitatively," Oh says.

After this initial phase is completed, the electrophysiologists will get what they are waiting for—movement of the model to Brookhaven's Galaxy cluster parallel supercomputer. The Galaxy cluster consists of 77 Pentium III dual processor nodes, each with one gigabyte of memory. The nodes currently communicate through a Message Passing Interface (MPI) library, though Oh says he plans to use OpenMP format as well as MPI in the near future. (The OpenMP format allows multiple threads on a single node and eliminates unnecessary message passing between the processors on a single node.)

"The final goal is to make my code work for parallel machines so that I can get the result very quickly," says Oh. "The real challenge is that you want to have a scalable algorithm, so that once you have numerous processors available the computing speed grows at the same rate as the number of processors."

Lifesaving Knowledge

It is this speed at the bi-domain, human ventricles or atria level that will significantly advance the theoretical understanding and, it is hoped, treatment of arrhythmia, says Fenton.

"The speed of parallel supercomputing allows for a parameter search, one that explores the whole range of possible conditions, such as ischemia (reduced blood flow) to the levels of sodium ions. You need to be able to do a lot of different simulations with many different parameters, and you can't do it if it takes a day to do one simulation—then you don't get anywhere."

Getting somewhere in science is always important, but never more so than when the prospect of lifesaving knowledge is on the horizon. Sophisticated new simulations of fibrillation and arrhythmia in human hearts hold the promise of providing the in-silico pre-screening of new anti-arrhythmia drugs, more effective defibrillators, and improved surgical techniques to treat arrhythmia.

All of this is being aided by a computer scientist who at the start of the project had to reach for a dictionary to understand cardiac terminology.

Concludes Oh: "Simulations are not going to replace experimental data. But numerical simulations are highly reproducible—they're not dependent on the conditions present in an experiment which make it difficult to reproduce them. Once you know that what you're simulating is identical to the experiments, then you can do more replicates and do them faster without harming anything."

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Brookhaven

Wonho Oh
Wonho Oh received his B.S. in mathematics from Yonsei University and his Ph.D. in applied mathematics from the State University of New York at Stony Brook. He is currently an Assistant Professor in the Department of Applied Mathematics and Statistics at the State University of New York at Stonybrook, as well as an Assistant Scientist in the Center for Data Intensive Computing at Brookhaven National Laboratory.

Flavio H. Fenton received a B.S. degree in physics from Universidad Nacional Autonoma de Mexico (UNAM) in 1990 and the M.S. and Ph.D. degrees in physics from Northeastern University in 1992 and 1999, respectively. Since 1999 he has worked as a visiting research scientist at Hofstra University and, since 2001, as Director of Electrophysiology Research at the Heart Institute, Beth Israel Medical Center, New York. His current research interests focus on models of cardiac cellular electrical activity and computer simulations of arrhythmias.

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Contact:
Wonho Oh
who@bnl.gov

Flavio Fenton
Flavio.H.Fenton@hofstra.edu

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