Failure in Sight for
A Mathematical Model of the Heart

By Barry A. Cipra

In the desert
I saw a creature, naked, bestial,
Who, squatting upon the ground,
Held his heart in his hand
And ate of it.

I said, "Is it good, friend?"
"It is bitter—bitter," he answered;
"But I like it
Because it is bitter,
And because it is my heart."

—Stephen Crane, *The Heart*

Charles Peskin is looking forward to giving his computer a heart attack.

More precisely, Peskin, a mathematician at the Courant Institute of Mathematical Sciences, has plans to study heart attacks and other cardiac disasters with a detailed computer model of the human heart that he and colleague David McQueen, a mechanical engineer at New York University, have been perfecting since the late 1970s. As the John von Neumann lecturer at the 1999 SIAM Annual Meeting in Atlanta, Peskin described recent progress with the Courant heart model and the mathematics underlying it.

Although fine-tuning of the model continues, "we're ready to move to applications," Peskin says. He foresees simulating such things as leaky heart valves, scar tissue, and the effects of surgical procedures. The antiseptic environment of computation should give researchers insights into cardiac phenomena now known only through clinical studies of people who are seriously, often desperately, ill.

Charles Peskin of the Courant Institute of Mathematical Sciences gave the 1999 John von Neumann Lecture, "The Immersed Boundary Method for Biological Fluid Dynamics," at the 1999 SIAM Annual Meeting in Atlanta. "As we'll see in Charlie's lecture," said SIAM president Gilbert Strang during the Atlanta prize session, "there is a stronger movement in SIAM toward mathematics in biology and medicine, possibly toward a new activity group." Indeed, as of 2000, SIAM members have the option of joining ten activity groups, the newest being the SIAM Activity Group on the Life Sciences.

Fluids and Fibers

The heart (so to speak) of the computer cardiac model is the immersed boundary method, a mathematical technique invented by Peskin. Roughly speaking, the immersed boundary method combines the Navier–Stokes equations for fluid flow with Hooke's law for springs—in this case, the flexible fibers of the heart wall. (As Peskin semi-jokingly puts it, the correct answer to the question "What is life?" is "fiber-reinforced fluid.") Fluid and fibers (or rather, the sheets of fiber that constitute the immersed boundary) exert varying forces on one another. Most importantly, the boundary constantly changes shape—not only in continuous response to the fluid, but also in response to its own internal mechanisms, as when muscles "decide" to contract.

Although approximations invariably come into play when solutions are sought, the method itself has a perfectly rigorous derivation, Peskin explains. Lagrangian coordinates lend themselves to an initial description of the immersed boundary. The conversion to Eulerian coordinates changes the representation of the boundary into one that involves the Dirac delta function. (Roughly speaking, Lagrangian coordinates follow the trajectories of moving particles, while Eulerian coordinates keep track of changing conditions at points in a fixed frame of reference.) For numerical purposes, the delta function is replaced by a smoothed-out approximation—one of many tricks employed to get good answers out of the computer without waiting forever.

As it is, heartbeat computations are strenuous exercise, best done on a su-percomputer. Peskin and McQueen work primarily with the Pittsburgh and San Diego supercomputing centers. One of the recent advances has been to parallelize their code for the immersed boundary method. They've gotten "optimal" speed-up with eight processors, and "near optimal" with 16 (see Table 1 on the next page). The upshot is that the computation of a heartbeat, which formerly took a week to complete, can now be done in less than a day.

The hard part was parallelizing (and vectorizing) the computations of fluid–fiber interactions. Part of the difficulty is that the fiber points keep moving around, making it hard to structure the computation. In addition, computing the interactions involves the summation of force contributions from fiber points acting on fluid points, and vice versa. Simply parallelizing a serial do-loop for computing such a sum is guaranteed to produce wrong answers.

Peskin and McQueen's strategy for coping with these problems is to organize the fluid data into columns and use a linked-list structure to keep track of fiber points within each column. They parallelize the computations by distributing columns that don't

overlap to separate processors. (The linked list has to be updated each time the fiber points move, but that can also be done in parallel because the fiber points move only short distances at each timestep.)

The somewhat cumbersome linked list is actually unnecessary on the new Tera MTA. The acronym stands for "multi-threaded architecture"; as part of that architecture, the Tera includes a "full–empty" bit in each word of memory, which can be interpreted as indicating whether what's stored in that location is available or not. This allows for "lightweight" synchronization: Individual threads might be delayed, but the processor as a whole stays busy. Peskin and McQueen's code is now being used as a benchmark for the Tera.

Whatever machine it's running on, the model typically computes with the heart floating in a $128 \times 128 \times 128$ grid (with periodic boundary conditions, for simplicity), anchored (elastically) at the arteries—computer animations show the heart tugging down and away as it expels blood during systole, in accord with the motion of a real heart. (Were it not tied down, Peskin points out, the computer heart would shoot like a squid through the computational grid.) The model includes approximately 4000 fibers, wrapped in a complex, toroidal geometry, each with an assigned tension and a schedule for

Extending mutual congratulations at the award ceremony in Atlanta are Peskin and his Courant colleague Robert Kohn, who received the first Ralph E. Kleinman Prize (for his work in homogenization theory, optimal design, inverse problems, and the mathematics of materials science) at the meeting.

contraction. Since the entire circulation is not modeled, blood enters the computational domain from one (conceptual) reservoir and exits into another, with each reservoir exerting an appropriate amount of pressure.

Ideally, Peskin and McQueen would like to compute several successive heartbeats, to let the flow settle into a natural rhythm. So far, they've gone no further than a beat and a half (diastole–systole–diastole). Even so, when a full cycle is played repeatedly, it gives a realistic impression, one that captures flow features familiar to cardiologists from experimental and clinical studies.

The model is far from perfect, however. While watching it may convince the layperson, physiologists can easily spot things that are qualitatively wrong. Much of Peskin and McQueen's work in recent years has been to correct one "obviously wrong" thing after another. Most recently, they've realized that the model's outflow valves offer too much resistance. "The tissue that surrounds the rings on which the valves are mounted, we didn't give it the right properties on the first try," Peskin explains. But he's hopeful that the end is in sight. "There was a long series of things that were wrong. This [the outflow valve problem] is, I think, one of the last ones."

Computational Cardiology

Once the qualitative features are in hand, Peskin says, the model will require quantitative comparisons with experimental data, and additional, minor adjustments are bound to be necessary. "But I also think that once we get it qualitatively right, then it'll be ready for use," he adds.

One use will be in studies of specific heart problems. "For example, in a valve disease, the valve could be leaky, so we would make the valve leaky in the model and see what it does," Peskin explains. Similarly, after a heart attack, the fibers that die get soft initially but then harden as the tissue scars. "We could simulate the different stages of that and see what consequences it has for the heart motion as a whole," he says. Such computations could give insight into why heart attacks vary in severity.

The heart model should also help with the design of pacemakers and implanted defibrillators, for which an electrical lead is threaded into the heart and attached to the heart wall. When the heart beats, it exerts force on the lead, both through the flow of fluid and through the motion of the wall, and the lead has to be attached firmly enough to withstand the tugging. But if it's attached too

No. of CPUs	Elapsed Time (seconds)				GFLOPS	Speedup
	Fluid	Fiber	Push	Move		
1	2.71	0.107	2.64	2.75	0.258	1.0
2	1.37	0.0574	1.34	1.40	0.508	2.0
4	0.703	0.0325	0.677	0.704	1.00	3.9
8	0.383	0.0198	0.356	0.365	1.89	7.3
16	0.399	0.0149	0.234	0.199	2.50	9.7

Table 1. *Parallel Vector Performance. Optimal and near-optimal speedups for Peskin and McQueen's heart code. The roughly two billion floating-point operations for a single timestep require approximately 8 seconds on a single processor of a Cray C-90. Each timestep involves the fluid and fiber acting on themselves, the fiber "pushing" the fluid, and the fluid moving the fiber. (From "Shared-memory Parallel Vector Implementation of the Immersed Boundary Method for the Computation of Blood Flow in the Beating Mammalian Heart," by David M. McQueen and Charles S. Peskin; http://math.nyu.edu/~mcqueen/.)*

firmly, it might disrupt the natural motion of the wall. There's also the question of how much effect the lead has on the fluid flow. "All those things could be tested in the computer model," Peskin says.

Another potential application is in analyzing a new surgical procedure for treating congestive failure resulting from enlargement
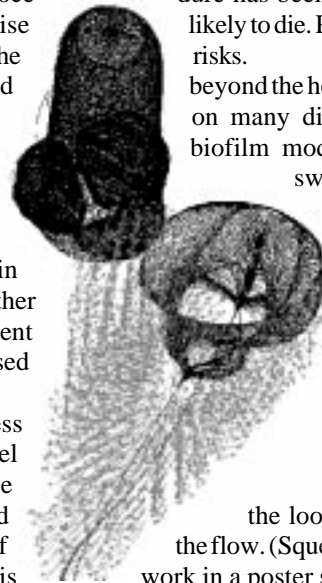
of the heart. Part of the force generated during contraction comes from the natural curvature of the heart wall. If the heart is enlarged, this component of the force decreases, which places an extra burden on the muscle. The new procedure, named for Randas Batista, the Brazilian surgeon who developed it, corrects for this problem in the most radical way imaginable: by cutting out a chunk of living heart tissue and sewing the rest back together. The Batista procedure has been successful in clinical studies, but it remains experimental and is reserved for people who are otherwise likely to die. Peskin and McQueen's computational heart could help researchers perfect the procedure and reduce the risks.

Peskin is also keen on uses of the immersed boundary method beyond the heart model. Lisa Fauci of Tulane University has been using the method to study swimming organisms on many different scales, from sperm to eels. In his von Neumann lecture, Peskin showed a video of a biofilm model Fauci has developed with Robert Dillon of Washington State University. In the model, swimming bacteria are attracted to pollutant chemicals, which they then eat, thus alleviating the pollution.

Aaron Fogelson of the University of Utah has been using the method to study platelet aggregation during blood clotting. (His computer animations, Peskin observes, can be interpreted either as a wound healing or as an incipient stroke, depending on whether you like your glass half empty or half full.) Dean Bottino, a PhD student of Fauci's, now at the University of Utah, has developed an immersed boundary model for cell locomotion.

Computational blood flows into the left ventricle during diastole. The aortic valve (upper left) is closed, and the mitral valve (lower right) is open. The "tails" on the fluid particles indicate the direction of their motion.

Eunok Jung, a current student of Peskin's, is studying valveless pumping—which occurs, for example, during CPR. Jung's model consists of a closed loop of tubing, part of which is flexible and can be squeezed. Her two-dimensional simulations show that net flow around the loop can be produced by periodic squeezing, even though there are no valves to control the direction of the flow. (Squeezing at the "wrong" frequency, however, can make the flow reverse direction.) Jung presented this work in a poster session sponsored by the Association for Women in Mathematics at the SIAM meeting.

Peskin thinks the immersed boundary method even has a future in molecular dynamics, where macromolecules like proteins are situated in a bath of water molecules. The goal is to follow the brownian motion of the macromolecule while treating the water molecules as a classical, continuum fluid. "The crucial thing there will be to include random forces," Peskin says. Many more applications are likely in the future. Indeed, if there's any boundary to the method itself, it's an awfully flexible one.

Barry A. Cipra is a mathematician and writer based in Northfield, Minnesota.