Chapter 16

LARGE-SCALE FINITE ELEMENT ANALYSIS OF THE BEATING HEART

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ABSTRACT

The regional mechanics of the beating heart are directly related to factors such as ventricular pumping performance, coronary blood flow, myocardial energetics and oxygen consumption, vulnerability to ischemia and injury, hypertrophy and remodeling, and arrhythmogenesis. Important characteristics include: the complex three-dimensional geometry and fibrous architecture; the nonlinear, nonhomogeneous, anisotropic material properties of the myocardium; the hierarchical collagen connective tissue matrix; the time- and history-dependent active tension development of the cardiac muscle cells; and the three-dimensional anisotropic patterns of cardiac impulse propagation. To model these features realistically requires large-scale computational analysis with sophisticated numerical methods. As described in the chapter by Dr. Hunter and colleagues, an accurate three-dimensional finite element model has been developed to describe the geometry, fiber architecture, and extracellular matrix structure of the heart. The model is based on extensive anatomical measurements in the left and right ventricles (LV and RV) of the canine heart. In this chapter, we illustrate some new approaches to the special problems of large-scale finite element modeling in biomechanics using examples from the analysis of stress and electrical activation in the heart. Prospects for further progress—particularly in coupled problems such as cardiac electromechanics—are examined in light of new developments in high-performance computing.

I. INTRODUCTION

The heart is a complex three-dimensional structure with mechanical and electrical properties that are nonlinear, nonhomogeneous, anisotropic, and time dependent. As described in the chapter by Hunter and co-workers, the thick ventricular walls have a helical fibrous architecture with a continuous transmural variation of pitch from that of a left-handed helix at the outside surface (epicardium) to a right-handed helix at the inside (endocardium). There is also a complex hierarchical connective tissue matrix, which affects both the mechanical and electrical conduction properties of the intact ventricular wall. The heart tissue (myocardium) undergoes large elastic deformations, exhibits some viscoelastic behavior, is biphasic in nature (being 80% water), is residually stressed, and develops history-dependent uniaxial force along the muscle fibers during active muscle contraction. The sequence of mechanical contraction is triggered by a depolarizing stimulus that propagates anisotropically through the excitable cellular medium. Wall deformation in turn affects the impulse propagation. In this chapter, we describe the computational analysis of stress and electrical activation in the heart, building on the structural framework established earlier (Chapter 15).

II. VENTRICULAR WALL MECHANICS

The distribution of wall stress in the normal and diseased heart is of fundamental importance because it affects major physiological factors such as (1) the pumping performance of the ventricles, (2) the oxygen demand of the tissue, (3) the distribution of coronary blood flow, (4) the vulnerability of regions to ischemia and infarction, (5) the stimuli to growth and remodeling during development and disease, and (6) the risk of arrhythmias. There have been no successful methods developed to measure stress in the intact heart wall—primarily because of its large deformations and the tissue injury caused by implanted transducers. However, regional distributions of
three-dimensional finite deformations in the intact heart wall of the resting and beating canine heart have been measured using biplane radiography of closely spaced metal implants.\textsuperscript{52, 60, 84, 85} These experiments also provide data to validate models of stress distributions in the intact heart during the cardiac cycle.

The distributions of stress in the ventricles of the heart are determined by the three-dimensional structure of the ventricular walls, the boundary conditions imposed by cavity and pericardial pressures and the fibrous valve ring at the base of the ventricles, and the mechanical properties of the myofibers and their collagen interconnections in the relaxed and actively contracting states. Many of these factors have been quantified in experimental studies. For example, Streeter and Hanna\textsuperscript{74, 75} and Nielsen and co-workers\textsuperscript{58} made detailed studies of the three-dimensional geometry and myocardial fiber architecture of the ventricles of the dog heart. Measurements of LV and RV pressures in patients and animal subjects are quite routine. Additionally, extensive data have been collected on the passive and active uniaxial material properties of isolated papillary muscles and trabeculae from various mammalian species.\textsuperscript{63, 77} Although fully triaxial material testing still presents significant technical difficulties, biaxial stress–strain testing has been performed in excised two-dimensional sheets of passive canine myocardium,\textsuperscript{13, 89} epicardium,\textsuperscript{35} and pericardium.\textsuperscript{47}

To keep the stress analysis mathematically tractable, many workers have developed models of LV mechanics using simplified geometric or material approximations.\textsuperscript{6, 15, 27, 36, 59, 79} Some useful insights into the basic mechanics of the ventricular wall have been obtained from these analyses. For example, the importance of including the thick-walled LV geometry, nonlinear stress–strain relations, and large elastic deformations has been demonstrated.\textsuperscript{14, 54} The helical fibrous arrangement has been shown to produce torsional deformations during systole (contraction) and diastole (filling). Torsion, in turn, acts to equalize the distributions of fiber stress and strain across the wall.\textsuperscript{2, 27} The significance of transverse shear strains also has been examined.\textsuperscript{36}

However, many important aspects of cardiac mechanics are too complex to be studied with simple analytical models. They are not suitable for analyzing the nonhomogeneous effects of three-dimensional variations in the geometry, fiber orientations, and mechanical properties of the heart, nor can factors such as ventricular interactions\textsuperscript{72} or the motion constraints imposed by the pericardium,\textsuperscript{23} valve rings, and papillary muscles\textsuperscript{31} be included. One important source of heterogeneity in ventricular mechanics is the pattern of activation of the myocardium. During normal "sinus" rhythm, activation is relatively synchronous, but there is nevertheless a difference of 50–100 ms between the earliest and latest activated points in the wall. The duration of the cardiac action potential also varies with position across the wall. In focal arrhythmias, asynchronous activation can significantly impair the mechanical function of the ventricles. Regional changes in the mechanics of the ventricular myocardium also occur in many other disease conditions. In myocardial infarction, for example, part of the ventricular wall becomes fibrous and scarred with no active function. In systemic hypertension, the wall changes shape in the LV, but not necessarily in the RV. Together, these factors contribute to the regional variations in local ventricular deformation that have been observed in a variety of experimental preparations and clinical studies. To interpret and understand these observations, more sophisticated models that require computational solution are needed. The most versatile numerical technique for these problems is the finite element method, in which the dependent variables are discretized by piecewise polynomial approximations over finite subdomains (elements) and expressed in terms of parameter values at interelement connection points (nodes).
III. FINITE ELEMENT STRESS ANALYSIS

As early as 1906, researchers first began suggesting the solution of continuum mechanics problems by modeling the body with a lattice of elastic bars and employing frame analysis methods. In 1941, Courant recognized piecewise polynomial interpolation over triangular subregions as a Rayleigh–Ritz solution of a variational problem. Since there were no computers at the time, neither approach was practical, and Courant's work was largely forgotten until engineers had independently developed it. By 1953, structural engineers were solving matrix stiffness equations with digital computers. The widespread use of finite element methods in engineering began with the classic papers by Turner et al. and Argyris and Kelsey. The name "finite element" was coined in 1960, and the method began to be recognized as mathematically rigorous by 1963.

Many finite element models of ventricular mechanics have been proposed, although most of them did not include the nonlinear kinematic terms associated with large deformations because iterative solution to the nonlinear governing equations at each load step is required. The importance of adopting nonlinear finite deformation theory for the analysis was demonstrated by Janz et al. However, their model, along with a few subsequent finite element models based on finite deformation theory and most of the linear models, treated the myocardium as an isotropic material. The effect of the ventricular muscle fiber distribution has been modeled with finite elements that possess material anisotropy with respect to a continuously varying fiber axis or, more commonly, by using a number of concentric elements each with a constant fiber direction. The incompressibility of the heart muscle, which is composed mostly of water, was usually accounted for by assuming that the myocardium has a Poisson's ratio close to 0.5. More correctly, in the context of finite deformations, the hydrostatic pressure—an extra dependent variable arising from the kinematic incompressibility constraint—is introduced as a Lagrange multiplier in the strain energy function.

Although some models consider muscle activation and contraction, others have been concerned with the prediction of end-diastolic stresses and sarcomere length distributions, a prerequisite for a realistic model of active ventricular contraction. However, suitable data are also required to validate finite element models. Since wall stress cannot yet be measured, regional distributions of ventricular wall strain are needed throughout the cardiac cycle. Whereas a large body of information is available on wall motions in the beating heart, regional measurements of three-dimensional strain suitable for rigorous validation of ventricular models have only appeared in recent years, and these data remain incomplete. Consequently, few finite element stress analyses have been directly verified with experimental strain data.

Important requirements, therefore, of a finite element model suitable for studying the regional mechanics of the normal and diseased heart are:

1. An accurate representation of the three-dimensional geometry and fibrous architecture of the left and right ventricles
2. Analysis of the kinematics of large deformations including the incompressibility constraint
3. A constitutive law for the nonlinear anisotropic elastic properties of the resting tissue
4. A model of the activation and tension development of the muscle fibers
5. Detailed regional measurements of three-dimensional wall strains for model validation
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Such a numerical model falls into the category of large-scale computational analysis, and a complete implementation requires the highest performance supercomputing power available. The following section outlines our methods and progress toward these aims, compares model-predicted strains with experiment, and points to further requirements and new challenges for the modeling of cardiac wall mechanics.

IV. THREE-DIMENSIONAL NONLINEAR FINITE ELEMENT MODELING OF THE HEART

Using the structural and anatomical framework described in Chapter 15, we have implemented the first three-dimensional finite deformation stress analyses of both ventricles of the beating dog heart and compared the predictions with transmural distributions of nonhomogeneous three-dimensional finite strains in our laboratory. The model still contains many simplifications to be computationally feasible, but establishes the basis for realistic simulation of ventricular wall mechanics.

Our finite element method was specifically developed for continuum analysis of the heart. Hence, the approach includes several special features uncommon to conventional finite element methods. The Galerkin finite element equations for three-dimensional finite elasticity (virtual work formulation) were derived in prolate spheroidal coordinates, which are well suited to describing the ventricular geometry. Using conforming isoparametric elements with tensor-product basis functions for each of the geometric coordinates, the ventricular geometry was accurately approximated with only 24 three-dimensional elements and 41 nodes. By formulating the governing equations in a coordinate system that simplifies the geometric description of the deforming body, the greater algebraic complexity was more than compensated by a significant reduction in the number of degrees of freedom required for the finite element discretization. This also considerably simplified prescription of the boundary conditions. The element equations were integrated by a Gaussian quadrature scheme and collected into the global system by the standard finite element assembly process. Force boundary conditions arising from the prescribed boundary pressures appear on the right-hand side of the system. Constrained displacement degrees of freedom were eliminated from the system during the assembly.

The resulting nonlinear system of global equilibrium equations was solved for the unknown nodal displacement and hydrostatic parameters using a Newton method, which minimizes the residual (error) for each equation to within a prescribed numerical tolerance. The nodal parameters of the undeformed geometric coordinates and muscle fiber angle were inputs to the model. The unknown dependent variables in the formulation were the nodal parameters of the deformed geometric coordinates and an additional element variable—the hydrostatic pressure—which arises from the incompressibility constraint equation. Therefore, this finite element problem was a “mixed” formulation. With such formulations, a compatibility condition that relates the pressure and displacement approximating spaces must be satisfied to ensure that a given displacement field corresponds to a unique solution for the hydrostatic pressure. In practice, this requires that for a linear nodal interpolation of the geometric parameters \( C^0 \) continuity), a single constant hydrostatic pressure parameter \( C^{-1} \) continuity) is all that can be permitted for each element to avoid numerical ill-conditioning. Since the incompressible deformation of thick-walled vessels results in a nonlinear transmural distribution of hydrostatic pressure, several finite elements, each with a constant pressure, are usually required through the wall thickness. Alternatively, fewer elements with a higher order of transmural interpolation for the
geometric and pressure variables may be used. To date, we have retained the linear transmural interpolation used for the undeformed geometric coordinates (Chapter 15), and hence the hydrostatic pressure variable was constant in each element.

For incompressible bodies, the kinematics of the deformation are constrained by the condition that the volume of any arbitrarily small part of the wall must remain constant. For most finite element schemes, this condition can only be satisfied in the average sense for the entire element. However, a significant improvement in the distributions of the stress and strain solutions within the element was obtained using an “isochoric” interpolation of the transmural coordinate that allows the kinematic incompressibility constraint to be satisfied more accurately within the element.50

The material anisotropy of the heart muscle was defined by referring the stress components at any point in the element to a system of local material coordinates, which is orthogonal in the undeformed state and has one axis aligned with the fiber direction interpolated from the nodal fiber angle parameters. The myocardium was modeled as a transversely isotropic material, although further extensions to orthotropy will be required to include the effects of the collagen connective tissue sheets described in Chapter 15. The constitutive law for the resting tissue was given by an exponential strain energy function

$$W = \frac{1}{2}C(e^Q - 1) - \frac{1}{2}p(I_3 - 1),$$

$Q = b_1E_{FF}^2 + b_2(E_{CC}^2 + E_{TT}^2 + E_{CT}^2 + E_{TC}^2) + b_3(E_{FC}^2 + E_{CF}^2 + E_{FT}^2 + E_{TF}^2).$

Here, $p$ is the hydrostatic pressure Lagrange multiplier and $I_3$ is the third principal invariant of the strain, which is constrained to equal 1 for incompressible materials. The material parameters had previously been optimized to predict strains measured in the isolated arrested dog heart during passive LV filling.27 This optimization and direct measurements by other workers89 indicate that the normal passive tissue is several-fold stiffer in the fiber direction than in the transverse plane.

Systolic contraction was modeled by adding to the stress tensor an active uniaxial fiber tension $T$, which was a function of time $t$, mean intracellular calcium concentration $[Ca]$, and sarcomere length $l$.25 A Hill-type equation for chemical equilibrium of dilute solutions represented the sigmoidal dose–response relation for developed tension as a function of $[Ca]$:

$$T_0 = T_{\text{max}} \frac{[Ca]^2}{[Ca]^2 + ECa_{50}^2} C_i,$$

where $T_{\text{max}}$ is the peak tension developed at maximum $[Ca]$. The leftward shift observed experimentally in this relation with increased sarcomere length was modeled by treating the calcium sensitivity $ECa_{50}$ as length-dependent:

$$ECa_{50} = \frac{[Ca]_{\text{max}}^2}{e^{B(i-l_0)} - 1},$$

where $l_0$ is the sarcomere length at which no active tension is developed. The time course of tension during an isometric twitch was contained in the term $C_i$, which was
### TABLE 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Passive</td>
<td></td>
</tr>
<tr>
<td>$C_0$</td>
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</tr>
<tr>
<td>$b_1$</td>
<td>18.5</td>
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<tr>
<td>$b_2$</td>
<td>3.58</td>
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<tr>
<td>$b_3$</td>
<td>1.63</td>
</tr>
<tr>
<td>Active</td>
<td></td>
</tr>
<tr>
<td>$T_{max}$</td>
<td>135.7 kPa</td>
</tr>
<tr>
<td>$[Ca]_{max}$</td>
<td>4.35 $\mu$M</td>
</tr>
<tr>
<td>$B$</td>
<td>4.75 $\mu$m$^{-1}$</td>
</tr>
<tr>
<td>$i_0$</td>
<td>1.58 $\mu$m</td>
</tr>
<tr>
<td>$t_0$</td>
<td>0.1 s</td>
</tr>
<tr>
<td>$m$</td>
<td>1.048 s$\mu$m$^{-1}$</td>
</tr>
<tr>
<td>$k$</td>
<td>$-1.429 s$</td>
</tr>
</tbody>
</table>

also a function of sarcomere length, as suggested by Tözeren:

$$C_t = \frac{1}{2}(1 - \cos \omega t),$$

where

$$\omega = \begin{cases} 
\frac{t}{t_0}, & \text{when } 0 \leq t < t_0, \\
\frac{t - t_0 + t_r}{t_r}, & \text{when } t_0 \leq t < t_0 + t_r, \\
0, & \text{when } t_0 + t_r \leq t.
\end{cases}$$

Here, $t_0$ is the time peak isometric tension, and the duration of relaxation $t_r$ is proportional to the sarcomere length:

$$t_r = ml + k.$$
end-diastolic volumes were 40.7 and 34.1 ml, respectively. All three deformed prolate spheroidal nodal coordinates were interpolated using trilinear basis functions. For adequate convergence of the stress solutions, the original 24-element mesh described earlier was subdivided into five elements transmurally to give a total of 60. Circumferential and azimuthal displacements were constrained during filling at all of the nodes at the base. Radial displacements were also prevented on the basal epicardial nodes to simulate the constraint to dilation of the valve annuli imposed by the stiff collagenous valve rings. The model deformed during passive loading with larger circumferential and radial strains on the endocardium than the epicardium but negligible transverse shearing, in agreement with experimental observation in the potassium-arrested dog heart.\(^{53,60}\) Also in agreement with our experiments, shear strain in the circumferential–longitudinal plane was negative, which is consistent with the small left-handed torsion exhibited by the model.

Figure 1b shows the end-systolic shape of the model at ventricular pressures of 2.1 kPa (RV) and 14 kPa (LV). The end-systolic ventricular volumes were 13.8 ml (RV) and 16.5 ml (LV). Under these loading conditions, the LV stroke volume was 17.7 ml (a 52% ejection fraction) and the RV value was 26.9 ml (66%). When the RV end-systolic pressure was increased from 2.1 to 4.7 kPa, the RV end-systolic volume rose to 18.6 ml, and the difference between the RV and LV stroke volumes fell from 9.3 to 5.4 ml. The displacement boundary conditions for systolic contraction were the same as those for filling, except that radial contraction was not prevented at the base. During ejection, the valve annuli did not change dimensions much, but enforcing the constraint led to large stress concentrations.
Comparing Figure 1b with Figure 1a shows that there was substantial wall thickening and transverse shearing during systole. The heart also twisted during ejection in the opposite sense to that seen in filling. Unlike diastole, however, there was a marked transmural variation of angular displacement in systole. It tended to be greatest at the subendocardium so that radial element boundaries at end-diastole became curved in the circumferential plane at end-systole. To see how well these deformations agreed with experimental results, we compared transmural distributions of end-systolic strains in the LV free wall (37% along the apex-base axis) with three-dimensional strain measurements at the same location in the open-chest, anesthetized dog. Normal and principal strain components agreed well with experimental data. Circumferential and longitudinal systolic shortening both increased in magnitude from epicardium to endocardium. Circumferential shortening was greater than longitudinal shortening and was very closely predicted, whereas longitudinal strain was slightly underestimated by the model. Radial systolic wall thickening also exhibited the increase from epicardium to endocardium seen in the laboratory. However, model thickening strains were greater than the mean experimental results, although within 1 standard deviation of the data. Part of this discrepancy may reflect the effect of altered coronary blood volume during the cardiac cycle due to the phase difference between coronary artery and venous flow. Whereas the model deformations were constrained to be strictly isochoric, the experimental measurements suggest a small loss of wall volume during systole.

Also in agreement with observation, the principal angle of greatest systolic shortening was close to the fiber angle near the epicardium, but not at the endocardium. The principal axis at the subepicardium was oriented approximately 30° clockwise of circumferential, whereas at the subendocardium, it was approximately circumferential. These results also fell within the experimental range.

Although normal strain and in-plane shearing behavior of the model were consistent with our experimental data, the transverse shear strains differed substantially. Azimuthal (longitudinal–radial) and axial (circumferential–radial) shear strains are usually positive and greatest at the endocardium. The model predicted large end-systolic transverse shear strains that were mostly negative and greatest at the midwall. One explanation for this significant discrepancy may be that contraction of the papillary muscles was not included in the model. It is likely that the force exerted by the papillary muscles at their endocardial insertions to the free wall affects the pattern of transverse shears. Another shortcoming of the model is the absence of the sheets of connective tissue coupling adjacent fiber layers. Their structure and orientation suggests that they play an important role in the shearing properties of the wall.

In contrast to the principal strains, the maximum principal stress coincided closely with the fiber stress, and shear stresses in the fiber coordinate system were negligible. End-systolic radial and cross-fiber stresses were similar and generally compressive. Hence, whereas the three-dimensional deformation of the ventricular wall has a complex transmural pattern, the stress distribution is quite simple: that is, a fiber stress embedded in a hydrostatic pressure field. The fiber stress depends on the fiber orientation and the sarcomere length; the pressure field varies from the LV pressure at the endocardium to the pericardial pressure at the epicardium. Therefore, since the important stress result at end-systole is the dominant fiber stress component, it is imperative that the model includes a realistic description of the fiber angle field and makes accurate predictions of sarcomere length.

In the midanterior region, where experimental strains were measured, the fiber stress was quite uniform, lowest at the endocardium, and with a slight peak at the
midwall. Fiber stress was less uniform in the posterior wall, where it was actually compressive near the endocardium. The peak fiber stress was higher in the midposterior wall and occurred at the subepicardium. High transmural gradients of sarcomere length and fiber stress were also found near the apex, which suggests that these regions may be most vulnerable to ischemia.

The foregoing discussion is intended to demonstrate the need for complex computational models of cardiac wall mechanics. However, such models are also computationally expensive. Our original implementation of this model required three days to solve on a VAXstation 3100 workstation. Hence, it was necessary to improve the performance of the computations substantially. An analysis of the computational algorithm reveals that the greatest amount of processing time in this problem is spent evaluating the integrands of the element equations that are summed and assembled into the global system. For the numerical solution of the highly nonlinear equations, an immediate reduction in the number of these computations can be achieved by not updating the Jacobian matrix at each Newton iteration. In the modified Newton method, the Jacobian is not recomputed at each iteration, but reused. By only updating the Jacobian when the summed error of the system in successive iterations does not fall by a sufficient amount, improvements of four- to six-fold were obtained. Further improvements were possible using quasi-Newton methods such as the BFGS update, independently suggested in 1970 by Broyden, Fletcher, Goldfarb, and Shanno. Here, the factorization of the previous coefficient matrix is used to update the Jacobian efficiently without recomputing the element equations. Another algorithmic improvement has been the use of a line search routine. From successive solution increments, quadratic interpolation is used to search for a scaling factor for the solution vector that minimizes the residual. Although the line search routine generally increases the processing time to reach equilibrium for a given load step, it can widen the convergence window and thus make larger load steps possible.

Further improvements in the computational performance were achieved by porting the code to a faster workstation. Our laboratory DECstation 5000/200 workstations are based on the MIPS RS3000 RISC (reduced instruction set computer) microprocessor. This allows a higher clock speed and more efficient architecture than conventional complex CISC computers. Together with faster memory and data throughput, this exercise speeds the model execution by a factor of 10. Finally, by porting compute-intensive parts of the code to the Cray Y-MP 8/64 vector supercomputer and optimizing the code for the vector architecture of the machine, another improvement of 5-12 times has been achieved. Details of optimization for vector supercomputing are described later. The combined result of these performance enhancements is an improvement of around 500-fold. Thus, a complete three-dimensional simulation of the mechanics of a single cardiac cycle for both ventricles requires about 10 min of execution time using the supercomputer.

The current model is still, however, quite simple. The main shortcoming of the time-varying elastance model is that although it predicts behavior at the end of ejection accurately, it does not accurately model the whole cardiac cycle of contraction and relaxation. Therefore, we have recently developed a modified convolution integral formulation for strain history-dependent muscle force generation. Although this constitutive law is readily implemented, it significantly increases the memory requirements and computation time. Moreover, to be useful, it relies on an accurate description of the sequence of activation that triggers contraction. This activation sequence is governed by the nonlinear dynamics of anisotropic impulse propagation in the excitable medium.
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V. CARDIAC ELECTRICAL DYNAMICS

Cardiac cells are electrically excitable and tightly coupled to each other. With a sufficiently strong electrical stimulus, the myocyte, which normally supports a negative transmembrane potential gradient at rest, may be transiently depolarized. The time course of excitation and recovery during this cardiac "action potential" is governed by ionic currents which flow across the membrane through specialized voltage-dependent ion channels specific to various ionic species, especially sodium, potassium, and calcium. Following the rapid onset of the action potential, a subsequent stimulus will fail to elicit another response until the cell has recovered sufficiently; this interval is called the absolute refractory period. During the "relative refractory period," subsequent action potentials can be evoked, but the threshold stimulus is raised.

The heart has a variety of cell types with different electrophysiological properties. Some cells, like the cardiac pacemaker cells of the sinoatrial node, are spontaneously excitable. Neurohumoral agents such as acetylcholine that alter the heart rate do so by changing the period of the spontaneous pacemaker oscillations. During normal "sinus" rhythm, the action potential propagates along the cell membrane and to neighboring cells, following an orderly pathway through the specialized conducting system of the atria and ventricles and finally reaching the ventricular myocardium. During the normal progress of this wave of excitation and recovery, each cell is excited only once during the heartbeat. However, some disorders of cardiac impulse propagation can lead to life-threatening "reentrant" arrhythmias in which the normal topology of the activation wave is modified.

A detailed understanding of global activation and recovery patterns has been elusive because of the geometric and structural complexity of the heart and the fine spatial scale, relative to the whole organ, of the activation patterns. Recent progress has come through large-scale computerized electrode mapping experiments which have clearly demonstrated the role of reentry in ventricular tachycardia (VT) and fibrillation (VF). However, the resolution of these experiments is fundamentally limited by the tissue damage caused by the recording electrodes. Computer models are essential to aid in the interpretation of sparse mapping data, suggest new experiments, and provide insights into the physics of cardiac action potential propagation.

VI. MODELS OF ACTIVATION PATTERNS

There have been many computational models of the electrical activity of the heart. The models can be grouped into three general categories: cellular automata, resistively coupled networks, and continuum models.

A. CELLULAR AUTOMATA MODELS

Most models have used the cellular automata approach in which the domain is subdivided into many discrete cells. The degree of excitation and recovery of the cells is described by a finite number of states. The transition of a cell from one state to the next is governed by a time delay and a set of rules based on the states of the neighboring cells. One of the earliest cellular automata models was the two-dimensional simulation of atrial tissue reported by Moe et al. Propagation between hexagonal cells followed an isotropic, nearest-neighbor rule. The transition from the absolute refractory state to three successive relative refractory states and back to the resting state followed fixed time courses. By randomly distributing the
absolute refractory period throughout the domain and applying rapid stimulations, the authors were able to induce a fractionated, disorganized activation pattern similar to atrial fibrillation. This study therefore supported the idea that nonuniform dispersion of refractoriness is a factor in the initiation and maintenance of atrial fibrillation.

Thakor and Eisenman\textsuperscript{78} extended Moe's analysis to a three-dimensional geometry. Using the same conduction and state transition rules but cube-shaped cells arranged to approximate the geometry of a dog heart, repeated extrastimuli could induce activation patterns similar to VT and VF. However, this model did not include the fibrous anisotropy of the myocardium, and conduction from a cell could only spread to the six neighbors with shared faces, not those at the corners. The nonuniform dispersion of the refractoriness hypothesis was also supported by the two-state cylindrical model of Smith and Cohen.\textsuperscript{73}

In other models, refractory inhomogeneities were restricted to a region of the myocardium. In a two-dimensional, five-state, nearest-neighbor model,\textsuperscript{66} refractory periods were uniform, except in a simulated ischemic zone near the center of the domain where contours of the refractory period were arranged into eccentric ellipses. Reentry was induced by a premature stimulus at a coupling interval less than the longest refractory period. This resulted in a long line of functional conduction block and a figure-eight reentry pattern (two counterrotating vortices). Bailie et al.\textsuperscript{3} used a simpler three-state model with prolonged refractory period in a simulated ischemic region. Because the ischemic zone was located at the edge of the domain instead of in the center, a single reentrant vortex was formed. In these two models, there was no fractionation of the wavefronts into the multiple wavelets that are thought to be characteristic of VF. Thus, in these simple cellular automata models, the initiation and stability of reentrant activation patterns is critically dependent on the distribution pattern of refractory periods.

A possible mechanism for the refractionation of a reentrant vortex that does not rely on material inhomogeneities was suggested by Gerhardt et al.,\textsuperscript{21} who used a two-dimensional cellular automata model that resembles the continuous FitzHugh–Nagumo equations.\textsuperscript{16} In this model, cell activation was not governed simply by the immediately neighboring cells, but rather by the number of activated cells in the adjacent region. The kinetics were described by a two-state excitation variable and an integer-valued recovery variable that increased linearly with time after excitation until it reached a maximum, at which point the excitation variable returned to the rest state. The return of the recovery variable to zero could also be affected by the state of the neighboring cells. These features allowed this model to represent the electronic interactions in excitation and recovery in a simplified way. Thus, it was able to approximate the dependence of propagation speed on wavefront curvature,\textsuperscript{82} which may be particularly important near the core of a reentrant vortex. For certain parameter choices, propagation wavefronts were observed to break (the waveback would catch up with the wavefront), and the broken ends of the wave would shed new vortices. Repetition of this process resulted in a chaotic activation pattern reminiscent of VF in an initially homogeneous medium without nonuniform refractoriness.

The cellular automata approach has the advantage of being simple, flexible, and computationally efficient. However, rule-based propagation and discrete membrane potential waveforms preclude an accurate representation of the electrotonic interactions between neighboring regions of myocardium. This limitation is most evident in recovery: cells that cannot adequately "feel" the potential of their neighbors must follow a preprogrammed time course of recovery. Therefore, an approach based more directly on the physics of the excitable medium is necessary to understand the complex factors that affect reentrant activation in the arrhythmias.
B. RESISTIVELY COUPLED NETWORK MODELS

Resistively coupled network models have been used to describe more realistically the extracellular coupling between cells. The electrotonic spread of excitation is modeled by connecting each cell to its neighbor through a network of resistors. The action potential within each cellular element is modeled by a continuous membrane kinetics law. In an early model by Gul’ko and Petrov,\(^\text{28}\) each element in a two-dimensional domain was connected through a resistance to its nearest neighbors. The speed of propagation was shown to be dependent on the curvature of the wavefront. Reentrant vortices could be initiated by a stimulus placed in the wake of a passing wavefront, showing that nonuniform dispersion of refractoriness is a sufficient condition for the initiation of reentry. In a similar study by Van Capelle and Durrer,\(^\text{82}\) the state of each element was described by two variables, which were evolved by two coupled nonlinear first-order differential equations.

The network approach was also used by Lesh et al.,\(^\text{49}\) who coupled a two-dimensional resistive network to the Beeler-Reuter membrane model.\(^\text{4}\) They showed that intrinsic differences in action potential duration between individual myocytes are masked by low-resistance cellular coupling. When the coupling resistance is increased—as might occur in ischemia—the nonhomogeneous behavior becomes evident. Recently, Leon and Roberge\(^\text{48}\) used a similar model to study the effects of anisotropic extracellular coupling on the membrane capacitance “charging factors,” “safety factors,” and propagation velocities. All were found to be greater for transverse than longitudinal propagation, and the results agreed quite well with experimental data from isolated cardiac muscle.

Therefore, resistively coupled network models have been valuable for identifying the microstructural basis of normal and reentrant activation patterns. Since they are based on a reasonably detailed knowledge of membrane ion channel kinetics and physical assumptions about cell-to-cell coupling, they are much less arbitrary than cellular automata models, but accordingly, more complex and computationally expensive. They may provide a basis for developing new macroscopic models, but it is clearly infeasible to extend them to the scale of the whole heart, and even three-dimensional analyses may not be practical with current computational power.

C. CONTINUUM MODELS

All continuum models can be described in the context of bidomain theory,\(^\text{64}\) which models the intracellular space and the interstitium as two anisotropic domains separated by a membrane. If the anisotropy of cellular and interstitial conductivity are the same, then the problem may be expressed as a two- or three-dimensional extension of the continuous cable theory reaction–diffusion equation:

\[
\frac{\partial u}{\partial t} = D_1 \frac{\partial^2 u}{\partial x^2} + D_2 \frac{\partial^2 u}{\partial y^2} + D_3 \frac{\partial^2 u}{\partial z^2} + I_{\text{ion}},
\]

where \(u\) is the transmembrane potential and \(D_i\) are the diffusion coefficients for ionic current in each of the three principal coordinate directions. The nonlinear ionic term \((I_{\text{ion}})\) models the membrane kinetics. Continuum models are potentially the most realistic, and they also have the potential to be solved using methods such as finite element analysis that can incorporate the complex geometry and heterogeneous structure of the heart.

The majority of model studies of reentrant activation patterns have used the FitzHugh–Nagumo system of equations on simple rectangular domains.\(^\text{11,86}\) Winfree
and colleagues have shown that in two dimensions, two counterrotating reentrant vortices (or "rotors") are formed at the two points where a critical contour of stimulus strength crosses a critical excitation phase contour. That is, figure-eight reentry can result from a properly timed stimulus in the relative-refractory wake of an activation wavefront. In three dimensions, the paired rotors become vortex filaments. Nonuniform anisotropy has not previously been studied in these continuous systems, and the computational approaches used have not been amenable to solution on realistic geometries with nonuniform fiber orientations.

The standard FitzHugh–Nagumo system can be written as

\[ \frac{\partial u}{\partial t} = \nabla \cdot (D \nabla u) + c_1 u(u-a)(1-u) - c_2 v, \quad \frac{\partial v}{\partial t} = b(u - dv), \]

where \( u \) is the excitation variable and \( v \) is the recovery variable. The second spatial derivative term in the first equation represents electrotonic diffusion, which may be different in each direction. The reaction terms representing the ionic currents are governed by two nonlinear first-order differential equations. The cubic term in the first equation has three fixed points: \( u = 0, u = a, \) and \( u = 1. \) The points \( u = 0 \) and \( u = 1 \) are stable and represent the resting and excited states, respectively. The point \( u = a \) is not stable and represents the activation threshold. In other words, a point in the domain will tend toward \( u = 0 \) as long as potential fluctuations do not exceed \( a. \) If they do, the point will become excited and tend toward \( u = 1. \) The appearance of \( u \) in the second equation makes recovery dependent on the potential of neighboring regions of the myocardium. The appearance of \( v \) gives recovery an exponential time dependence. Hence, this reaction–diffusion system is based on membrane physics of action potential propagation, and although the ionic currents are approximated by a phenomenological equation, this particular choice of nonlinearity has the basic properties of excitation, recovery, and refractoriness for appropriate choices of the constants.

Winfree has also reported preliminary propagation studies using the Beeler–Reuter membrane model for the ionic currents. These simulations showed the spontaneous fractionation of reentrant activation waves. This was attributed to the lack of synchrony between the Na and Ca activation mechanisms.

The main drawback of the continuum approach is its computational expense. These models must be run on high-performance computer systems in order to allow the investigator to adequately explore the model's parameter space—or in three dimensions to get any results at all. Continuum models also ignore the discreteness of cell-to-cell coupling. Discontinuities on the microscopic level have effects on propagation that are not predicted by continuum theories; however, the effects of discreteness can be simulated by appropriate modifications to the diffusion behavior to account for the intracellular coupling. There is, therefore, a need to develop efficient computational techniques for solving excitable systems like the FitzHugh–Nagumo equations on domains with the complex three-dimensional geometry and structure of the heart.

VII. HYBRID FINITE ELEMENT MODEL OF THREE-DIMENSIONAL IMPULSE PROPAGATION

To allow the behavior of the FitzHugh–Nagumo system and other continuum models for excitable media to be analyzed with a realistic representation of the cardiac geometry and fiber architecture, we have developed a hybrid collocation–
Galerkin finite element method. The field variables, the local fiber direction, and the geometric coordinates are all interpolated by Lagrange or Hermit tensor-product finite elements in two or three dimensions. The basis functions for the excitation and recovery variables are bicubic or tricubic Hermite polynomials that ensure the continuity of at least the first spatial derivatives (second in three dimensions) and cross-derivatives across element boundaries. To permit anisotropic propagation with respect to a fiber axis that varies spatially within a single finite element, the equations are transformed to a local orthonormal coordinate system with one axis that is always in the fiber direction.

To evolve the solution in time, the method of collocation is used to assemble the partial differential equations into a system of ordinary differential equations that are satisfied exactly at collocation points within each finite element. The main difficulty with conventional collocation methods is handling the boundary conditions for different mesh topologies. To overcome this problem and yield a numerically well-posed problem, we adopted a Galerkin finite element approach in which the no-flux boundary condition is weighted by the basis function subset that supports the solution on the boundary and is integrated over the surface. The resulting system of ordinary differential equations is solved through time using an adaptive Runge-Kutta or Adams scheme from a numerical algorithm library.

Accuracy and convergence of the method for the FitzHugh-Nagumo equations with normal and reentrant activation patterns are described in a recent paper. On a regular mesh with isotropic diffusion, a fully developed traveling wavefront was supported over three elements, and the waveforms of excitation and recovery matched the analytic solution with negligible error. Reentrant activation could be initiated on two-dimensional meshes as small as $6 \times 6$ elements. Solution times for a 196-element model (900 nodal parameters) were approximately 8 s per rotor (vortex) period with compute-intensive parts of the code distributed across the network to a Cray Y-MP 8/64 supercomputer.

The method has been implemented for two or three dimensions, but extensive testing has only been conducted for the former. Analyses have been performed to study the effects of geometry, fiber angle, and ionic current terms on activation patterns. The importance of including the diffusive electrotonic coupling has been demonstrated by studying propagation on irregular domains. The effect of nonuniform fibrous anisotropy was also studied by introducing a spatially varying fiber angle in a square domain. An initially elliptical wavefront propagating from a point stimulus could be made to bend into a banana shape and eventually break up on the convex side. Finally, to improve the shape of the model activation waveform, we have developed a modification to the FitzHugh-Nagumo equations to prevent the excitation variable from overshooting and becoming negative during recovery.

A. COMPUTATIONAL CONSIDERATIONS

Current models have up to 1000 parameters and can be feasibly executed on our high-speed RISC workstations. The Cray reduces computation times to only a few seconds. The largest three-dimensional models of the entire heart may involve up to 150,000 degrees of freedom or more. This will place the model in the category of large-scale supercomputer simulations, but still within current capacity. Substantial sophistication in three-dimensional graphics will also be required to visualize the results of these complex models, which will each use an hour or more of supercomputer time. However, when the model is coupled with nonlinear finite deformation stress analyses, the activation sequence governs the mechanical contraction. Mechanical contraction, in turn, alters the geometry of the excitable medium, requiring the
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colligation equations to be reassembled at each mechanical time step. Other coupled problems in cardiac mechanics will also be computationally demanding. One example is the solid–fluid mechanical coupling between the heart wall and ventricular blood. Another is the coupling between stress in the wall and the transport of coronary blood and oxygen to the tissues. The relationship between wall mechanics and tissue metabolism and energetics is also a major field of interest in cardiac physiology.

VIII. DISTRIBUTED ELECTROMECHANICS

We have developed efficient finite element analyses for modeling the mechanics and electrical dynamics of the intact heart. With optimized code, the solutions are feasible on modern vector supercomputers. However, the mechanics and electrical dynamics of the heart are closely coupled. Electrical excitation triggers muscle contraction and large deformations affect the geometry of the excitable medium. Because the time and space constants of the two problems are significantly different, it is presently infeasible to model the coupled problem in three dimensions using vector supercomputers. The complex geometry makes two-dimensional analysis of questionable value. We will need to take advantage of new advances in computational science and technology to attack these problems. As yet, this work is for the future; however, progress has recently been made toward obtaining the detailed experimental data that will be required to validate such models. Therefore, in this section, we describe new experiments in our laboratory to measure regional distributions of electrical activation and mechanical function in the beating dog heart.

The study of myocardial activation coupled to muscular contraction is essential to an understanding of cardiac performance in the normal heart and the functional changes that occur in disease states such as VT, ischemia, and myocardial infarction. Therefore, we developed a new method for simultaneously mapping the surface distributions of activation and finite deformations across the LV epicardium. In four anesthetized, open-chest canines studied recently, arrays of 25–53 radiopaque bipolar electrodes (RBEs) were saturated 5–10 mm apart to the anterior–lateral LV epicardium. Simultaneous records were made of the three-dimensional positions of the RBEs using high-speed biplane cineradiography (16 mm, 120 frames per second) and the local activation waveforms using a 56-channel mapping system (Bard Electrophysiology, Billerica, MA). The sinus node was crushed, and the heart was paced either from the right atrium (control) or from both the right atrium and the LV.

Least-squares finite element analysis was used to fit parametric polynomial surfaces to the RBE coordinates in the end-diastolic and subsequent systolic frames. Continuous distributions of epicardial strain obtained from these fitted functions showed that ventricular pacing from the center of the RBE array caused early epicardial shortening near the pacing site and circumferential lengthening by the end of ejection. Isochronal contour maps of the activation times showed that the relatively simultaneous epicardial activation in control pacing became asynchronous with ventricular pacing, with activation times varying up to 70 ms across the array. Thus, the synchrony and efficiency of mechanical contraction is closely determined by the activation sequence. Coupled three-dimensional models will be required to analyze these results in detail and extend them to other regions of the ventricular walls.

IX. HIGH-PERFORMANCE COMPUTING FOR LARGE-SCALE MODELS

The practical limitations of large-scale computational models are defined by the available resources for implementing vast numerical computations with reasonable
speed. Progress in modeling over the past 10 years has taken advantage of several developments in computer hardware, software, and numerical algorithms. Two important advances in computer hardware have been the availability of high-performance graphics workstations and vector supercomputers. Access to these resources by researchers has been made possible by the widespread appearance of fast local and wide-area networks that link remote sites.

Most modern graphics workstations achieve high computational performance by the use of RISC architectures. Examples are the SPARC processor used by Sun Microsystems (Mountain View, CA) and the R3000A chip manufactured by Mips (also from Mountain View, CA) and used by several vendors. By using reduced instruction sets, single microprocessor computers achieve enhanced performance by a variety of architectural innovations not readily achieved in conventional complex CISC designs. Recent processors, such as the IBM RS6000, have employed "superscalar" architectures. They have the advantage that, by using several functional units, more than one instruction can be executed per machine clock cycle. It is generally agreed that the rapid rate of advance in performance (~100-fold) in the last 5 years will continue for the foreseeable future. However, it is also important to recognize that the newest chips are beginning to approach the theoretical limits of clock speed. The newly announced Dec Alpha chips are reported to run at up to 200 MHz compared with about 1 GHz for the fastest scalar supercomputers. Therefore, increasingly, new computers will rely on the use of "multiprocessor" architectures. Indeed, multiprocessing is an already well-established feature of workstation design. Specialized chips are commonly used for many specialized tasks such as graphical display, input-output control, and memory management. The network also allows conventional workstations to work together in a "multicomputer" system. However, to take advantage of multiprocessor architectures and distributed systems requires significant innovations in algorithm design and programming, many of which are still in their infancy.

The high-speed network has also given researchers access to expensive vector supercomputers such as the Cray Y-MP vector computer. In these systems, advanced but expensive technology is applied to achieve the highest possible 64-bit single processor performance and to optimize all aspects of the design. The vector supercomputer is presently the only platform for many of the largest complex modeling problems in biomechanics and other fields. Even so, vector processors also impose constraints on the algorithm. Performing simultaneous computations on large sets of data requires that those computations do not contain dependencies—i.e., that the results of operations on one piece of data do not affect concurrent computations. Fortunately, it is not too difficult to vectorize finite element calculations with modern optimizing compilers, but the effectiveness of the optimization depends on the proportion of operations that can be vectorized and the vector lengths that can be achieved. However, incremental improvements in supercomputer performance generally require a complete redesign of the architecture or replacement with costly new processors. The processor on the new Cray C90, for example, is about four times faster than that of the Cray Y-MP. Therefore, to enhance performance further, up to 16 parallel 1-Gflop* processors will be available on one machine. Here again, therefore, we see hardware speed being improved by increasing reliance on multiple processor design.

A much less expensive alternative to a few monolithic processors with large memory (coarse-grained parallelism) is a massively parallel design employing

* Giga-floating-point operations per second.
Hundreds or thousands of microprocessors, each tightly coupled with much less memory per node (fine-grained parallelism). However, as the number of processors increases, computational performance depends on the ability of the programmer to distribute the tasks of the algorithm efficiently among the processors. For practical applications in biomechanics, it is fair to say that, as yet, the potential advantages of most multiprocessor architectures have not been exploited due to the substantial difficulties of parallel programming and the associated computational overhead. Although parallel computing is growing rapidly, it is still at the stage where the programmer must be aware of the design details of the computer architecture. This is complicated for applied researchers by the large variety of parallel architectures that have been developed and by the even more bewildering array of names that have been used to describe them. Therefore, we conclude this chapter with a brief survey of parallel computer systems and programming considerations. A more detailed overview is given by Nielsen.57

X. PARALLEL COMPUTING

There are two main forms of parallel processing systems. Multicomputer (or “distributed”) systems consist of heterogeneous processors, typically physical computer nodes with their own local memory, linked by a network. We will concentrate on “multiprocessor” systems, which are faster and more specialized because they consist of more tightly coupled and homogeneous processors whose memory may be local to the processor element, shared between elements, or a combination of each. Multiprocessor architectures may be classified according to their processor and memory organization or by the degree of parallelism of the instruction and data streams. From the latter approach, Flynn18 suggested the following four categories for computer architectures: single-instruction single-data (SISD), single-instruction multiple-data (SIMD), multiple-instruction single-data (MISD), and multiple-instruction multiple-data (MIMD).

In SISD computers, only one instruction is executed per instruction cycle, and the memory affected is only used by that instruction. This is the architecture of most conventional single-processor computers, and this classification also includes “pipelined” processors, where several instructions are processed simultaneously, but only one is completed per machine clock cycle. That is, one instruction may begin before its predecessor has been fully completed. SIMD machines have multiple identical processing elements, each with its own data memory. Every processor simultaneously executes the same instruction using its own data controlled by a master processor. The MISD architecture is largely a theoretical idea rather than a practical design model. The processors of MISD computers share the same data memory, but execute different instruction streams. MIMD is the most general design, each processor having independent instruction and data streams. MIMD machines are distinguished by whether their memory is shared or distributed between processors. We may therefore consider the Cray Y-MP with eight processors as a coarse-grained, tightly coupled, shared memory, MIMD machine.

Parallel computers are more commonly classified by the organization of their processors and memory and the coupling between them. Vector parallel processors are SIMD computers in which all of the processors perform the same instruction on different components of a vector of data. Since these operations are independent, the data elements do not interact. Vector operations are typically performed in parallel pipelined stages, and the vector processor may be controlled by a SISD host computer that also performs the scalar operations and those involving data interaction. In array
processors, multiple SISD processing elements with their local memory are arranged in a grid. Array processors are SIMD machines that usually occupy slots on the backplane bus of a SISD host computer that broadcasts the same instruction to every processor in the array. They are often used for specialized applications on simple data structures such as image processing. In addition to the local memory, there are one or more bit planes of array memory matched to the array configuration (e.g., image frame buffers). An extension to array processors are systolic arrays such as the Systolic Linear Algebra Processor. They are also SIMD architectures, but the processors are specialized for particular operations and to allow multidirectional data flows between processing stages. Thus, each piece of data is operated on more than once before being returned to memory. Although they are very useful for special applications, systolic arrays have not been used for cardiac modeling in spite of their name.

Cubes of dimension $n$ are parallel architectures with $2^n$ processors. In a dimension-3 cube, the eight processors are arranged at the corners of a cube. In higher dimension cubes, called hypercubes, inner cubes are embedded in outer ones. The processors exchange messages, and memory may be local or shared. Hypercubes have the advantages of a symmetrical architecture and short interprocessor communication paths. Examples of hypercubes are the Intel IPSC/2, which is a coarse-grained MIMD machine with 128 Intel i860 processors, and the Connection Machine (Thinking Machines, Cambridge, MA), which is a massively parallel fine-grained SIMD architecture consisting of four dimension-14 hypercubes, each with 16K 8-bit processors. The two-dimensional models of the FitzHugh–Nagumo equations implemented by Kogan et al. on a Connection Machine are the only cardiac models we know of that have been run on a massively parallel supercomputer.

Another name that is often heard in this context is the transputer. Transputers are not parallel architectures, but simple high-speed RISC chips with on-chip memory and serial links designed specifically for building parallel systems. A variety of MIMD parallel processors have been built as special-purpose accelerator boards for conventional microcomputers using Inmos transputer chips (Colorado Springs, CO), which can be programmed using the proprietary high-level language OCCAM.

New developments in parallel computer systems and programming will gradually make them more accessible tools to researchers implementing complex biomechanics models. The task is to implement the model algorithms so that as much as possible of the computation can be executed in parallel, while the overhead of interprocessor communications is minimized. Therefore, the approach is governed by the problem. For example, in the finite element stress analysis, the largest proportion of the computation time is occupied in the integration of the element stiffness matrices. If the computations for each element can be distributed to a separate processor on a shared memory SIMD or MIMD computer, then significant advantages should be achieved for sufficiently large problems. How many elements must be assembled in parallel to achieve a practical advantage is not clear for our present models.

On the other hand, in the activation models, the most computationally intensive part of the problem is solving the large linear system of equations. Algorithms and even specialized architectures for solving dense linear systems of equations on parallel machines have been developed and are reviewed by Gallivan et al. However, finite element models typically lead to sparse systems since the effects of a given nodal parameter are confined to the immediately adjacent element. The larger the finite element mesh, the more sparse becomes the global system of equations. A variety of approaches to sparse linear systems have been taken. For simple problems, suitable ordering of the global degrees of freedom leads to banded coefficient matrices. For an $n \times n$ matrix with a bandwidth of $m$, banded solvers can reduce the
factorization time from on the order of $n^3/3$ for a full system to $np(2p + 1)$; the back-substitution time is also reduced from on the order of $n^2$ to $n(3p + 1)$.$^{12}$ When memory was a limitation for large problems, frontal decomposition methods that were based on the element connectivity of the mesh were popular.$^{39}$ However, in most modern finite element codes, the numbering of nodes and elements is no longer critical. Instead, sparse matrix solvers for systems with arbitrary sparsity patterns are usually used. Heath et al.$^{32}$ recently surveyed parallel direct algorithms for sparse symmetric linear systems. However, because the sparsity pattern is not preserved in the factorization, the task of parallelizing direct algorithms is difficult, and most attempts have been confined to shared-memory MIMD multiprocessors. A simpler and more successful alternative to direct methods is the use of iterative algorithms. We anticipate that careful exploitation of multiprocessing systems for the parallel computation of multiple element matrices and the iterative solution of sparse systems will contribute significantly to the improvements in computational performance needed to model large coupled problems such as cardiac electromechanics and ventricular fluid–solid interactions. Together with suitable experimental data for validation, these models promise to enhance our understanding of the complex regional function of the normal and diseased heart.

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