



Large scale modelling of two-dimensional cardiac tissue using parallel methods

N. Maglaveras^a, K. Margaritis^b, J. de Bakker^c,
F.J.L. van Capelle^c, M. Allesie^d, M. Strintzis^a
& C. Pappas^a

^a*Aristotelian University, Thessaloniki, Macedonia, Greece*

^b*University of Macedonia, Thessaloniki, Macedonia, Greece*

^c*University of Amsterdam, Amsterdam, Holland*

^d*University of Limburg, Maastricht, Holland*

ABSTRACT

Finite difference and iterative methods are used to simulate two-dimensional impulse propagation in cardiac tissue. The model used takes explicitly into account the effects of cytoplasmic and junctional resistances. An initial parallel approach for the implementation of the iterative methods (Gauss-Seidel in our case) based on the systolic array method is presented. The number of iterations needed for convergence of the iterative methods at each time step is examined in conjunction with changes in the spatial distribution of the electrophysiologic parameters such as coupling resistance. Electrograms and propagating action potentials (PAP) are calculated for cases simulating infarcted hearts by placing dead cell barriers in the model cardiac tissue sheet. The shapes of the electrograms and PAPs are critically depending on the position of the recording site relative to the dead cell barriers.

INTRODUCTION

The study of propagation of the cardiac impulse in myocardium is very important in determining the causes of dangerous arrhythmias. Although numerous studies have been done in multidimensional tissue preparations studying the nature of the propagating action potential (PAP) [1], relatively few simulation studies have appeared in the literature in the above mentioned areas [2]. The basic problem for simulating multi-dimensional propagation is computing power and uncertainties concerning the simulation of the membrane ionic currents and the structure of the spatial distribution of the electrophysiologic parameters in the myocardium, especially of the cytoplasmic and junctional resistances.

Recently due to the introduction of the massively parallel machines, and due to the more extensive use of supercomputers, it was possible to simulate certain arrhythmogenic phenomena in the heart such as reentry [3]. A number of questions though are still unanswered concerning the relationship between arrhythmias, the pathway direction, and the extracellular field recorded.

This work is aiming in the following goals. 1. To describe a model of cardiac tissue that takes into account the effects of the cytoplasmic and junctional resistances in impulse propagation. 2. To introduce some initial ideas for parallel implementation of such models in large scale simulations, and to study the numerical effects of spatial inhomogeneities in electrophysiological parameters in the computational accuracy and speed. 3. To explore the relationship between the impulse pathway, and the extracellular recordings in the presence of inexcitable barriers.

METHODS

The electrical equivalent of the network is shown in Figure 1. Each cell is broken up in 4 segments (3 cytoplasmic and 1 junctional). In the transverse direction there are two junctions per cell. The ratio between the cytoplasmic resistance R_c and the longitudinal junctional resistance R_j is 1:5 ($R_c=0.315$ MOhms and $R_j=1.575$ MOhms). The value of the transverse resistance R_{ij} is 0.8 MOhms. The space increments used were $\delta x=25 \mu m$ and $\delta y=10 \mu m$. The membrane capacitance C_m was $1 \mu F/cm^2$ and the ionic current followed the Beeler and Reuter (BR) formulation [4]. The conservation of current law was used at each node, which resulted in a finite difference formula at each node, which if we use the Crank-Nikolson implicit representation has the following form for each node.

$$ky_{i-1,j}V_{i-1,j,t+\delta t} - kx_{i,j-1}V_{i,j-1,t+\delta t} + (2 + kx_{i,j} + kx_{i,j-1} + ky_{i,j} + ky_{i-1,j})V_{i,j,t+\delta t} - kx_{i,j}V_{i,j+1,t+\delta t} - ky_{i,j}V_{i+1,j,t+\delta t} = ky_{i-1,j}V_{i-1,j,t} + kx_{i,j-1}V_{i,j-1,t} + (2 - kx_{i,j} - kx_{i,j-1} - ky_{i,j} - ky_{i-1,j})V_{i,j,t} + kx_{i,j}V_{i,j+1,t} + ky_{i,j}V_{i+1,j,t} - 2(\delta t/C_m)I_{ion,i,j,t} \quad (1)$$

where in (1) $kx_{i,j}=\delta t/Rx_{i,j}C_mS_vV$ and $ky_{i,j}=\delta t/Ry_{i,j}C_mS_vV$, V the volume of each segment, $Rx_{i,j}$ being either R_c or R_j , $Ry_{i,j}$ being R_{ij} or infinite, and S_v the surface-to-volume ratio for each segment taken $4000 cm^{-1}$. For dead cells all coupling resistances were considered infinite. Isochrones were constructed finding the dv/dt_{max} for all segments in our network.

For extracellular field calculations, volume conductor theory was used [5], assuming that we deal with a 2-D muscle where the extracellular field is assumed uniform, since no restricted extracellular space exists. Mirror image source contributions are also taken into account. All programs were written in FORTRAN and PASCAL and implemented on a DEC VAX 9000 supercomputer with 2 CPUs.

Boundary conditions were symmetry of propagation for the stimulus rows and columns and sealed ends for the far ends. The resulting linear system of equations that needs to be solved at each time step has the form $AV^{t+\delta t}=b$, with A a large sparse non-symmetric matrix [6]. It should be noted that A is highly non-symmetric even for the homogeneous sheet case, since there are asymmetries within each cell. Thus, iterative methods are used to solve this system. The desired accuracy for our purposes was 10^{-8} . Various iterative methods were used, but the Gauss-Seidel method was the most appealing one. It is important to note that the number of convergence steps depend largely on the eigenvalues of A and on the norm of $AV^{t+\delta t} - b$. Thus, we monitored the number of steps required for convergence to our desired accuracy for different spatial configurations of coupling resistances, and for different time steps. In particular Figure 2 shows the

isochrones and representative PAPs for the nominal case, where the anisotropy ratio is 1:4.1 ($\theta_x=50$ cm/sec, $\theta_y=12$ cm/sec). It is shown that the number of iterations is increased when δt is increased, when spatial nonuniformities in R_i are increased, and when a large amount of segments are in the fast upstroke phase where the changes in the nonlinearities of the ionic currents are substantial. Figure 3 shows the iterations needed for convergence for a case analogous with that of Figure 2, for a 100 by 100 array of segments and for $R_j/R_c=5$ and $R_j/R_c=13$. In these cases, the isochrone patterns were the same, and the PAPs had minor differences. However, the number of iterations for convergence at each time step is substantially increased (almost doubled) in the second case. In the second case there are more eigenvalues of matrix A that lie closer to the boundaries between stability and instability, which seems to effect the number of iterations. Also, we should note that the number of iterations is decreased as the spatial gradient of voltage is smoothed out.

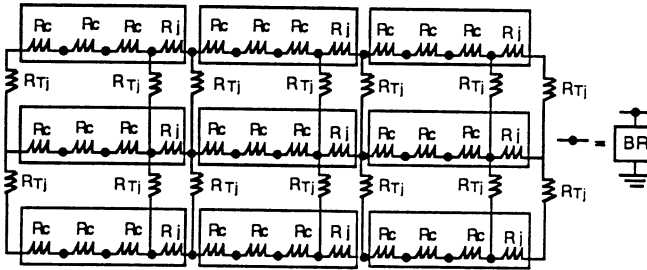


Figure 1. Electrical equivalent of the two-dimensional model of the cardiac muscle. Each cell is broken up in 4 segments, 3 cytoplasmic and one junctional.

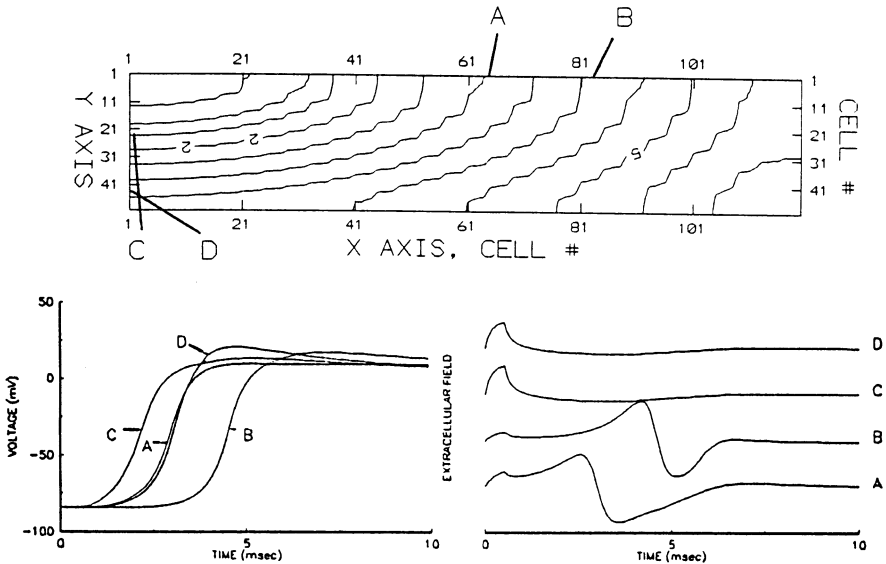


Figure 2. Isochrone profiles and representative PAPs from a 50 by 120 homogeneous anisotropic sheet of cardiac elements.

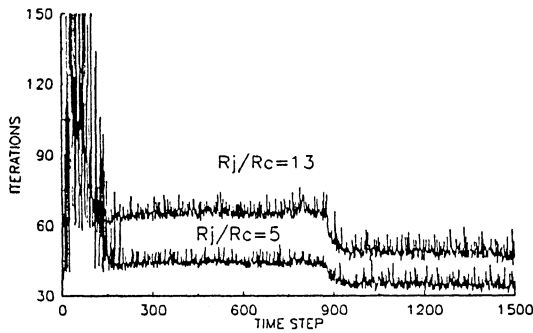


Figure 3. Number of iterations for a 100 by 100 array of elements with same anisotropy ratio, but different R_j/R_c .

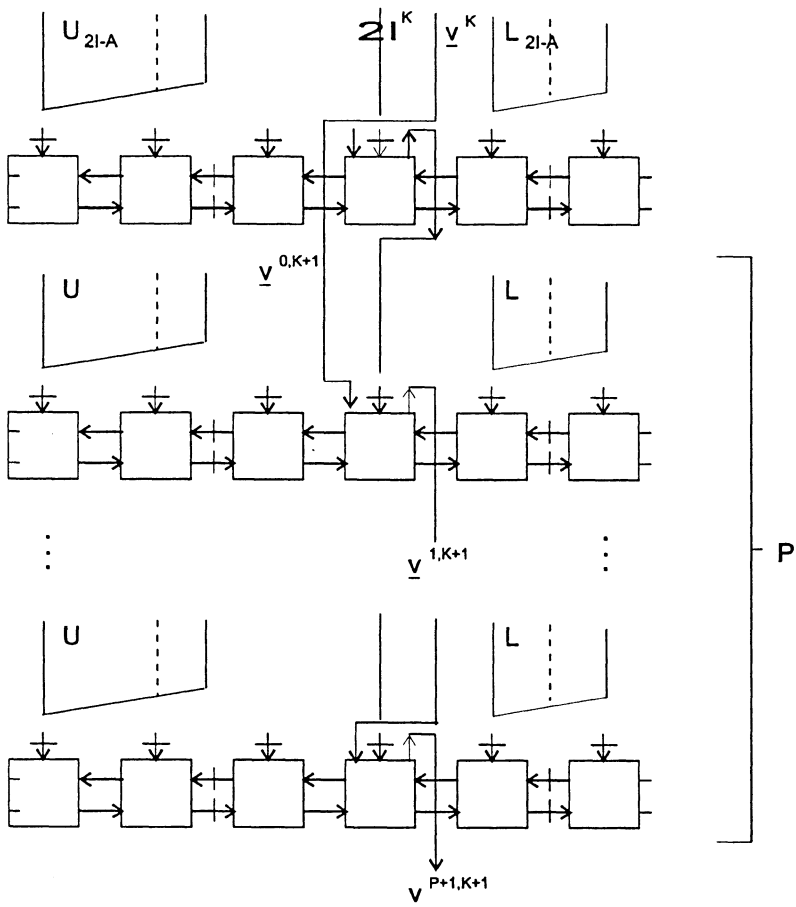


Figure 4. Parallel implementation of Gauss-Seidel method using systolic array architectures.

Such systems need to be solved using parallel processes, if we are to simulate complex arrhythmia phenomena. Thus, we present a first approach of implementation of the problem in a systolic environment. In particular, two things need to be considered. 1. The solution of the ODEs describing the ionic currents. 2. The solution of the system $AV^{t+\delta t} = b$ at each time step using iterative methods. Here, we will present a systolic theoretical design for the Gauss-Seidel solution (the second problem) of such a linear system.

The Gauss-Seidel and SOR iteration (GS) for our problem is defined by equation (2):

$$\underline{V}^{p+1} = \omega L \underline{V}^{p+1} + [(1 - \omega)I + \omega U] \underline{V}^p + \omega g \quad (2)$$

where $L(U)$ is strictly lower(upper) triangular matrix and $L+U=M$, where M is the Jacobi iteration matrix of A , defined as $M=D^{-1}E$ for $A=D-E$ where D a diagonal matrix. It should be noticed that in the Crank-Nicholson implicit scheme there are two iterative processes: one explicit, for advancing the calculations from one time step to another, and another implicit, for the correlation of the grid-point values at the same time step. By combining the finite difference approximation scheme (eq. (1)) and the Gauss-Seidel iterative method (eq. (2)), the following equation is derived:

$$\underline{V}^{p+1,k+1} = \omega L \underline{V}^{p+1,k+1} + [(1 - \omega)I + \omega U] \underline{V}^{p,k+1} + \omega g^k \quad (3)$$

Where $M=D^{-1}[D-(2I+A)]$, $g^k=D^{-1}[(2I-A)V^{k+2}]$ and $L+U=M$. Also $\underline{V}^{0,k+1}=\underline{V}^k$ and $\underline{V}^{p+1,k+1}=\underline{V}^{k+1}$ for p sufficiently large. Equation (3) indicates that there are several levels of modifications that take place during the iterative PDE solution. The innermost level consists of updating the grid point values, which are modified during the implicit application of the iterative method (superscript p). The next level involves the succession through different time steps, denoted by superscript k , i.e. during the explicit application of iterative methods. At the same level there is the modification of the ionic current vector, once for each time step according to the results of the previous time step and some initial approximations. Finally, the outermost level refers to the coefficient matrices which may be recalculated for selected time steps or remain unchanged throughout the computation depending on the cardiac muscle model that is simulated. The formulation of the coefficient matrix and ionic current vector are not discussed herein. The potential parallelism of the two innermost levels depends both on the iterative method used for the linear system solution and on the parallel algorithm / architecture implementing the iterative method.

Systolic algorithms and architectures for implementing the iterative methods discussed in the previous section have been presented in [7] - [8]. The main building block of these systolic designs is a systolic array performing matrix-vector multiplication and addition, i.e. $y=Ax+b$, herein termed 'matrix-vector inner product step' (mvips). In Figure 4 the systolic implementation of the Crank-Nicholson scheme is shown. Each explicit iteration step consists of a pipeline of implicit iteration steps. The first stage of the pipeline performs a mvips operation so that the right hand side vector of the implicit iteration is calculated. Then there are p mvips computations producing the grid values for the next time step. Notice the difference of the interconnections between the first and the remaining stages of the pipeline: the result of the first stage takes the place of the right hand side vector of the implicit iteration, while $\underline{V}^k$ is used as the initial approximation vector, i.e. $\underline{V}^{0,k+1}$, with the appropriate input delay. The output

vector $\underline{V}^{p+1,k+1}$, after p implicit iterations, for p sufficiently large, is the final result for time step k , i.e. $\underline{V}^{k+1}$. This vector is used as the input for the mvips stage of the next explicit iteration as well as initial input of the next implicit iteration.

RESULTS - DISCUSSION

Figure 5 shows the results from a case where the impulse propagates in a tortuous fashion through a 30 by 160 sheet of elements. In particular, a longitudinal plane wave was elicited by simultaneously stimulating cells 1 to 10 of column 1. Figure 5 also shows the iterations needed for convergence for the Gauss-Seidel method. We observe that the number of iterations depends strongly on the length of the wavefront. When we are at a time instant where the isochrone pattern is complex, the number of iterations increases. This shows that the computing time needed for the solution of these systems does not only depend on the eigenvalues of A , but also on the isochrone patterns.

Figure 6 shows an analogous case with the one in Figure 5, for longitudinal plane wave propagation. Only here, the sheet dimensions are increased and small nonconducting openings exist along the dead cell barriers. We can see from the extracellular field patterns that in the middle of the corridors between the dead cell barriers, the electrograms exhibit multiple peaks, resulting from local activation, and from the remote sites in the proximal corridors. The electrograms in the vicinity of the edge of the barriers exhibited either multiple peaks due to the functional block area, or an increased negative deflection. When sometimes it becomes difficult to distinguish the local from the remote components, we can record the extracellular field further away from the tissue. In this case, the local component would be dramatically reduced, while the remote one would be unchanged. Also, the PAP shapes are markedly different, and in the case of site D, we observe a prolonged foot in the initial phase, due to the electrotonic interactions taking place in the vicinity of the nonconducting opening.

Thus, we have presented a paper that deals with a two-dimensional cardiac tissue model. We developed an initial approach to parallel implementations using systolic array architectures, and we investigated the effects of spatial nonuniformities in electrophysiologic parameters and in time step, in the number of iterations required for the iterative method used (Gauss-Seidel in our case) to converge at each time step. We observed that increased time step increases considerably the number of iterations, while the isochrone shape is very important in determining the number of iterations at each time step. Concerning electrophysiological characteristics, we observed that dead cell barriers, create dramatic changes in PAP and extracellular field shapes, and can create prerequisites for dangerous arrhythmias.

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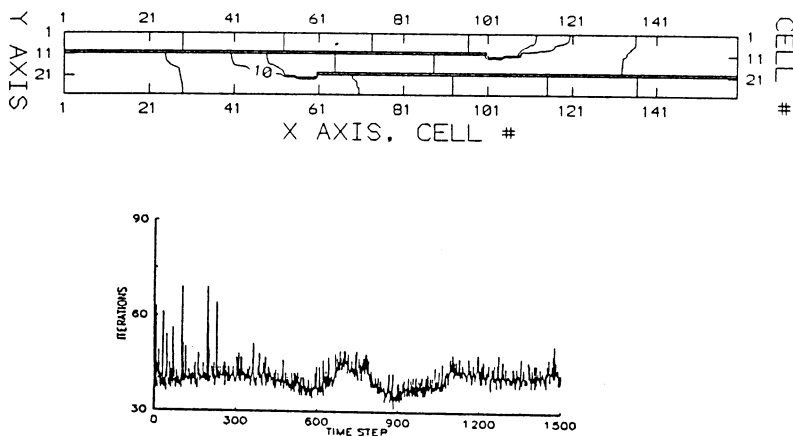


Figure 5. Isochronal map and number of iterations for a tortuous pathway. We observe that at the instant where the wavefront turns around the upper barrier (around time instant 8 msec corresponding to the 800 time step) there is a significant increase in number of iterations.

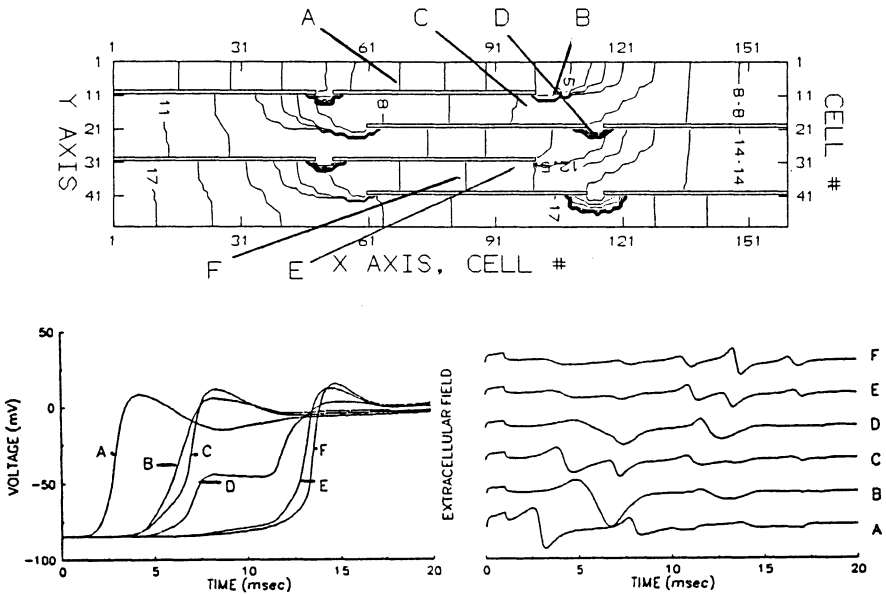


Figure 6. Isochrones, PAPs and extracellular field recordings from a case with small openings within the dead cell barriers. Observe the multiple peaks at electrograms C, E and F, and the difficulty of identifying the activation time in electrogram D. Observe the long foot in PAP D.