

METHODS

Data Acquisition

UEGs from four pigs were utilized for this study. Data was originally acquired from seven pigs [21]. However, complete data from two pigs were not available. Since CSD and TCM methods require a center electrode and four orthogonal electrodes, complete data sets were necessary for these methods to be used to determine the locations of electrical activation sites. The data from the other pig had a very low signal-to-noise ratio and could not be used. Filtering with a 60-Hz filter did not improve the signals.

Anesthesia was induced in the pigs using 5% Pentothal. A continuous drip of pentobarbital was used to maintain adequate anesthesia. Skeletal muscle paralysis was induced and maintained with IV, succinylcholine. A femoral arterial line was set up for continuous monitoring of hemodynamics and blood gases. The levels of electrolytes and blood gases were maintained within normal limits. Body temperature was regulated and maintained at 37.0 degrees Celsius [21].

A median sternotomy was performed to open the chest of each pig. The exposed heart was suspended in a pericardial cradle. A plaque containing 121 unipolar, Ag-AgCl electrodes was placed on the hearts of each of the four pigs. The electrode plaque was sutured to the epicardium on the apex of the left ventricle. The electrodes were spaced 280 μm apart in an

array of 11 rows and 11 columns. The electrode diameter was approximately 120 μm . A diagram of the electrode plaque is shown in Figure 1. A 60 Hz AC current, which was delivered by two wire electrodes sutured 1 cm away from the unipolar electrode plaque, was used to induce VF in the pigs [21].

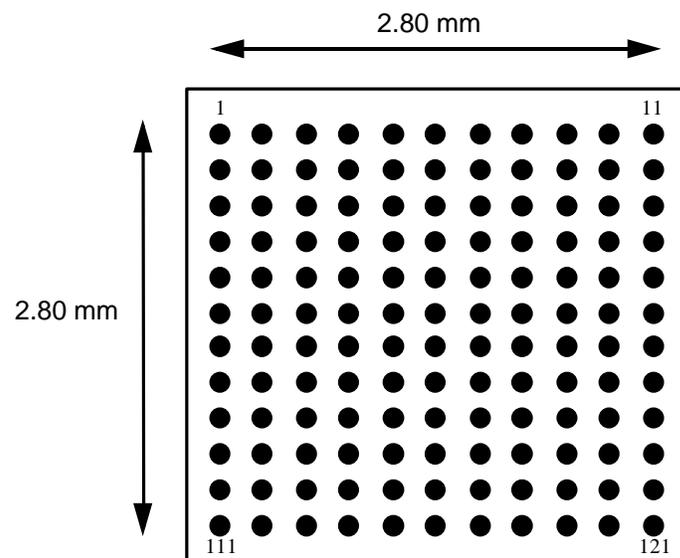


Figure 1. Electrode plaque used for recording UEGs. The 11 by 11 array of electrodes was sutured to the epicardium on the left ventricular apex. The small black circles represent the electrodes. The spacing between the electrodes was 280 μm .

UEGs were acquired during the first two seconds of VF from the heart of each pig. A sampling rate of 1 kHz with a high-pass filter at 0.1 Hz and a low-pass filter at 500 Hz was used. For each electrode on the plaque, a UEG consisting of 2000 data values was recorded [21]. Therefore, 121 UEGs consisting of 2000 data points in time were recorded for each of the four

pigs. Figure 2. shows a UEG recorded during VF and a UEG of a normal heart rhythm for comparison.

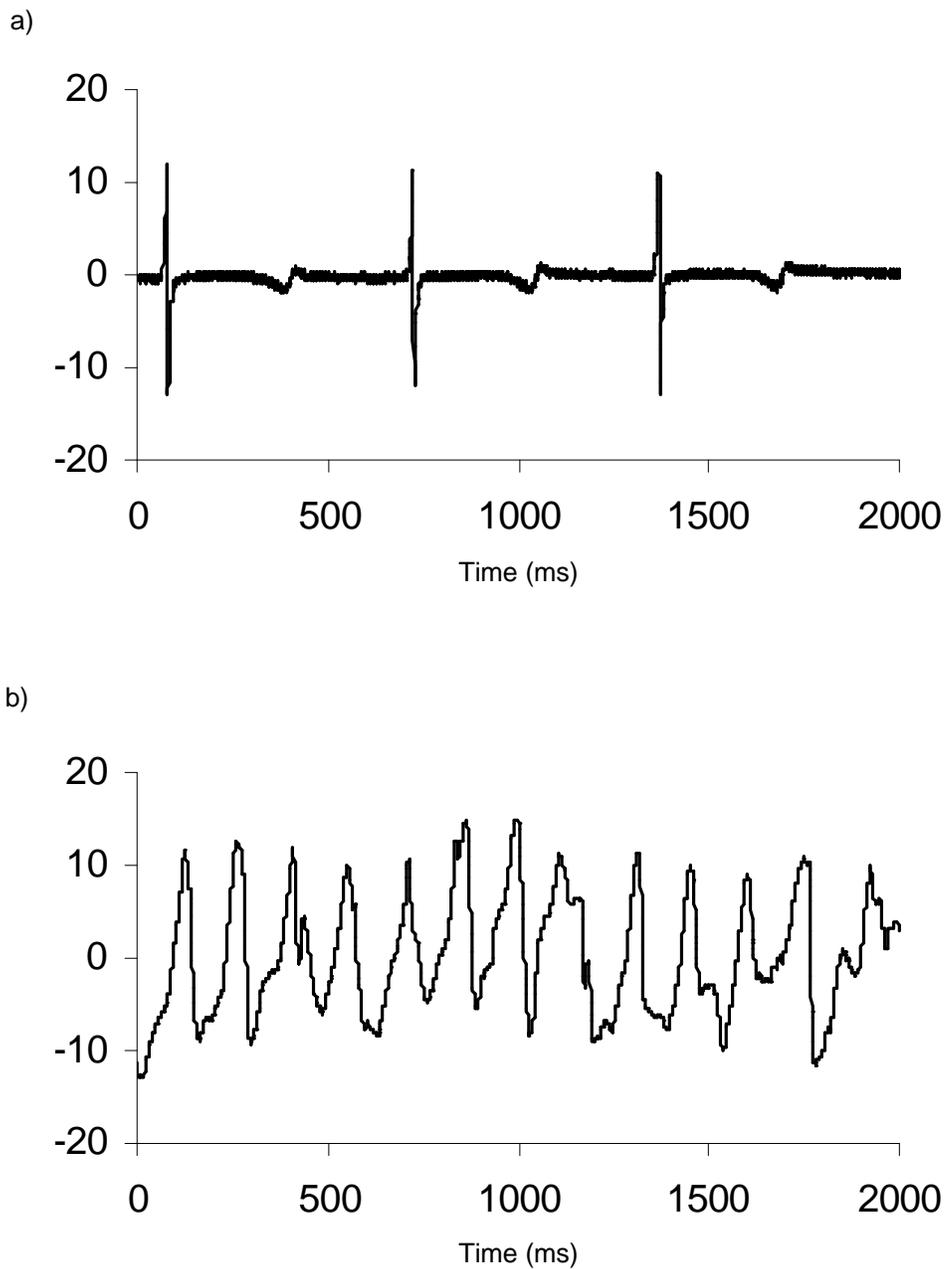


Figure 2. Comparison of UEG of normal sinus rhythm and UEG of VF. a) UEG recorded during normal sinus rhythm b) UEG recorded during VF.

Methods for Identifying Activations during VF

Three different methods were used to identify electrical activations during VF -- Rule Based Method (RBM), Current Source Density (CSD), and Transmembrane Current Method (TCM). RBM used negative derivatives to identify activations. The 3-point Lagrange method was used to calculate the derivatives for each UEG [22]. Derivatives less than or equal to -1.4 mV/ms and a minimum of 56 ms apart were considered to be true activations. Blanchard and her coworkers had found that -1.4 mV/ms was a threshold for the separation of local and distant activity. A derivative with a maximum magnitude more negative than -1.4 mV/ms represented local activation. Whereas, derivative magnitudes more positive than the threshold indicated distant activity [23]. The interval between activations of 56 ms represented a minimum beat-to-beat time and was based on a study that found the time between successive activations during VF in dogs to be 86 ± 15 ms. The 56 ms interval was two standard deviations from the mean [24]. An activation identified using RBM is shown in Figure 3.

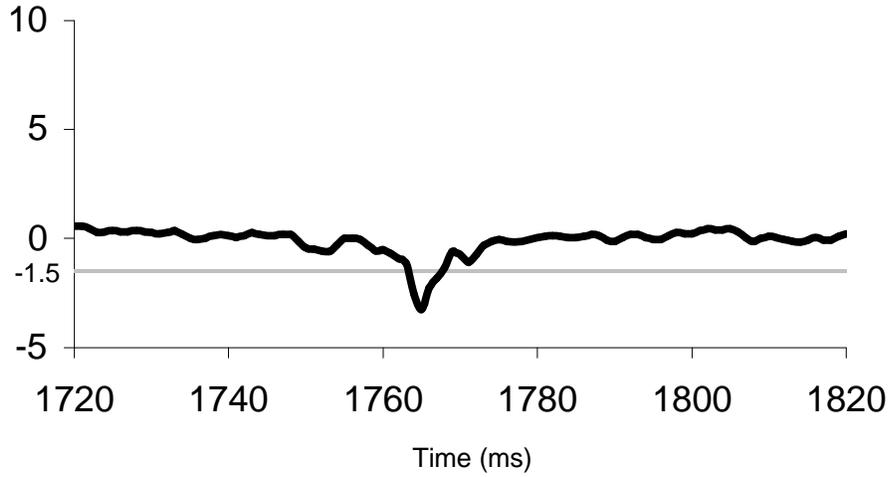


Figure 3. An electrical activation identified using RBM. The bold line represents the voltage derivatives as calculated with RBM. The activation is considered to have occurred at the time of the maximum negative derivative (1765 ms). The maximum negative derivative is significantly less than -1.5 mV/ms and can be considered to represent a true activation.

The CSD method relied on spatial derivatives to distinguish activations during VF. The following equation was used to calculate the CSD:

$$v_{\text{CSD}} = G[(v_1 - v_0) + (v_2 - v_0) + (v_3 - v_0) + (v_4 - v_0)] \quad (1)$$

where G is a scalar constant and v_0 is the center electrode [8]. v_1 , v_2 , v_3 , and v_4 are electrodes orthogonal to the center electrode, v_0 , and located diagonally two electrodes away from the center electrode as shown in Figure 4. This electrode spacing for the orthogonal electrodes was the configuration that worked the best. If the v_1 , v_2 , v_3 , and v_4 electrodes were moved closer to the center electrode, the CSD signal contained high levels of noise, and the sites

of electrical activation, which are generally represented by relatively large amplitude deflections, were not distinguishable. An electrical activation identified using CSD is shown in Figure 5. The time of the greatest absolute slope was considered to be the time of local activation [8].

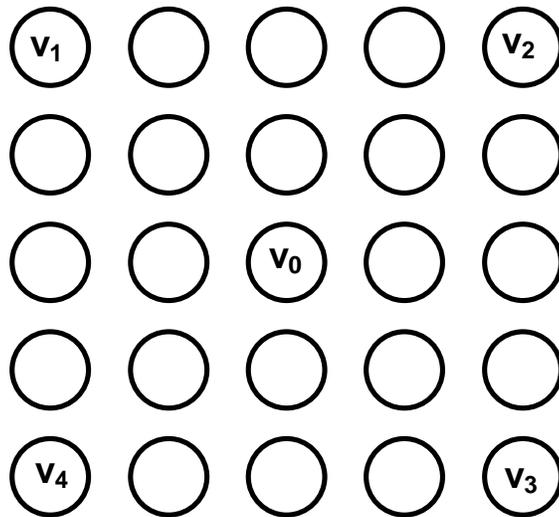


Figure 4. Electrode configuration used for CSD and TCM. v_0 is the center electrode and v_1 , v_2 , v_3 , and v_4 are the four orthogonal electrodes.

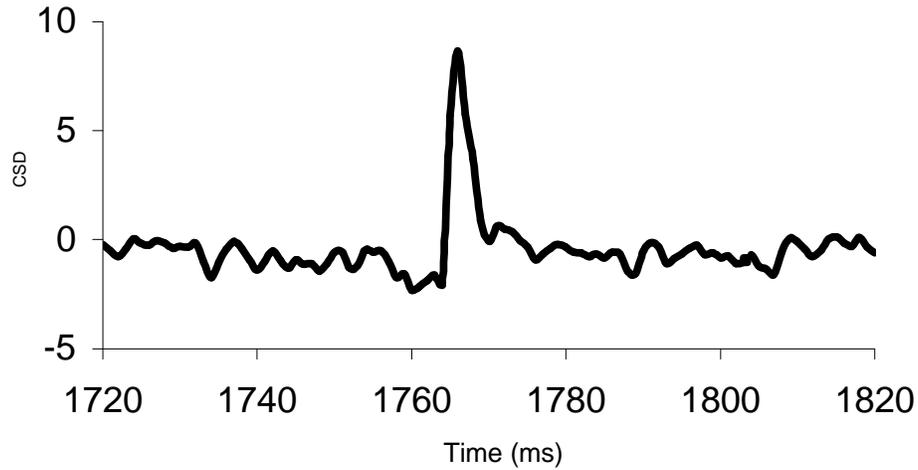


Figure 5. An electrical activation identified using CSD. The bold line is v_{CSD} . The local activation is considered to have occurred at 1765 ms, the time of the steepest absolute slope.

TCM, which was developed by Witkowski *et al.*, can also be used to differentiate between local activations and distant activity under certain conditions. As with CSD, TCM requires four orthogonal electrodes. The same orthogonal electrodes, v_1 , v_2 , v_3 , and v_4 were used for both TCM and CSD. (See Figure 4.) TCM is used to estimate a value that is proportional to the transmembrane current, I_m [25, 26]. The following equations were used to estimate I_m :

$$E_{surf} = (\text{sqrt} ((v_4 - v_2)^2 + (v_3 - v_1)^2)) / 0.792 \quad (2)$$

$$I_m = E_{surf}(t) - E_{surf}(t-1) \quad (3)$$

where E_{surf} is the surface potential, t is time and 0.792 mm is the distance between v_0 and each orthogonal electrode. Biphasic deflections of I_m , as shown in Figure 6., were used to identify local activations with the instant of local activation determined as the minimal dV/dt [6, 25].

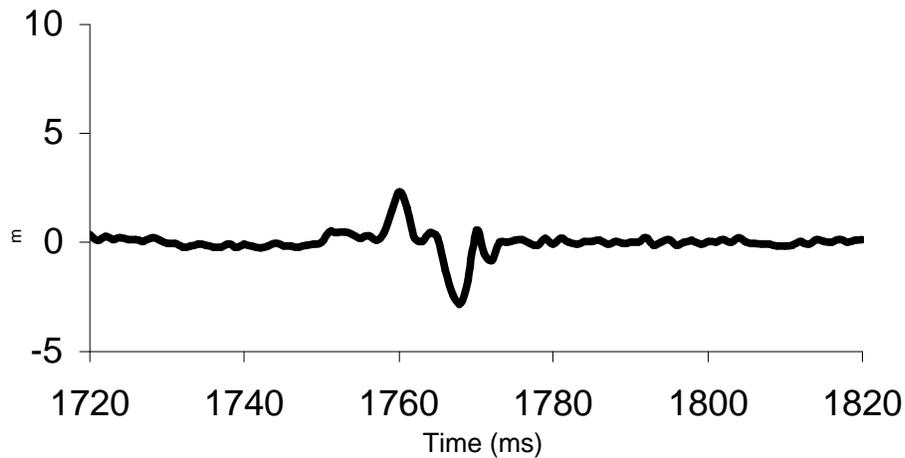


Figure 6. An electrical activation identified using TCM. The bold line is the TCM estimation of the transmembrane current, I_m . The electrical activation is represented by the biphasic deflection with the instant of local activation occurring at 1765 ms.

Artificial Neural Network Examples

Preprocessing was done on the UEGs with RBM, CSD, and TCM in order to create the training and test examples for the ANNs. A MATLAB program was used to calculate RBM, CSD, and TCM for all possible data points on a UEG. After the RBM, CSD, and TCM calculations were completed, the MATLAB program separated the processed data into two groups or classes of examples. The first class of examples represented

electrical activations. The other class of examples were examples at which activation had not occurred.

Furthermore, the ANN examples were also divided according to the types of data that the examples included. ANN examples were created that had only RBM and CSD data. Other examples included RBM, CSD, and TCM data. The examples with RBM and CSD data had 24 data points, and the examples that also included TCM information consisted of 47 data points.

The examples all had one data point that was the minimum value of the three-point derivative calculated using RBM. Only examples with derivatives more negative than -1.5 mV/ms were included as examples of activations. Since the previously determined threshold for a local activation was -1.4 mV/ms, this would ensure that the training examples were true activations [23].

The examples that were not activations all had maximum negative derivatives more positive than -0.2 mV/ms. Blanchard and her colleagues had determined that it was not possible to classify with certainty activations with derivatives between -1.4 mV/ms and -0.3 mV/ms as local activations or distant activity [7]. Therefore, none of the training examples had maximum negative derivatives in this range. The training examples that were not activations were known to not represent local activations.

The training and test examples also included a twenty-three data point time history of v_{CSD} , as calculated using the CSD method. For examples that

represented activations, the time of the local activation, which was determined by the steepest absolute slope, was the center point of the v_{CSD} time history. The 11 values of v_{CSD} prior to and the 11 values of v_{CSD} following the point of local activation were also included. Examples, that were not activations, had the 23 point v_{CSD} time history centered on the minimum voltage derivative. Figure 7a. shows an example of an activation with RBM and CSD data. In Figure 7b., an example that is not an activation is displayed.

The examples with RBM, CSD, and TCM data also included a time history of I_m . The time history of I_m , as determined using TCM, consisted of 23 data points. The data points were the value of I_m at the time of the maximum negative voltage derivative and the 11 prior and the 11 following values of I_m . An example of an activation determined with RBM, CSD, and TCM data is shown in Figure 8a., and an example that does not represent an activation is shown in Figure 8b.

Finally, each training and test example was marked with a target. A target is the desired output of the ANN for a given example. If an example was an activation, it was marked with a target of 0.9. An example that was not an activation was given a target of 0.1.

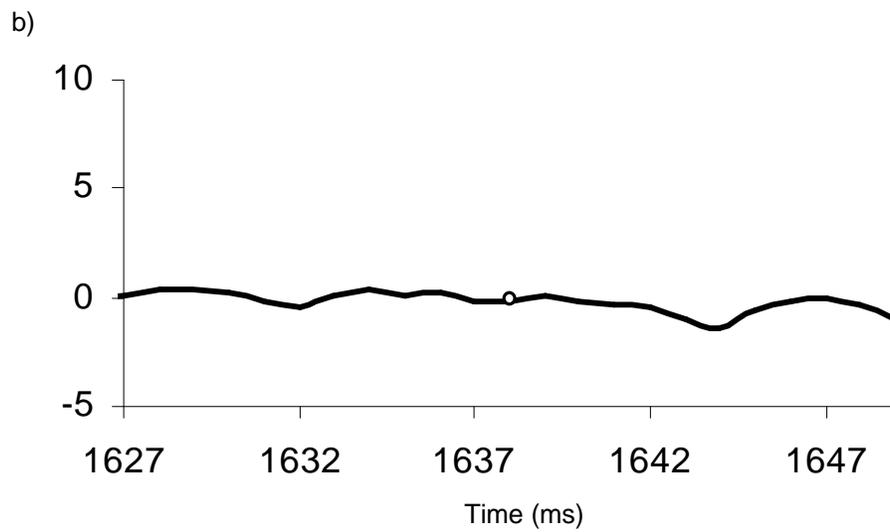
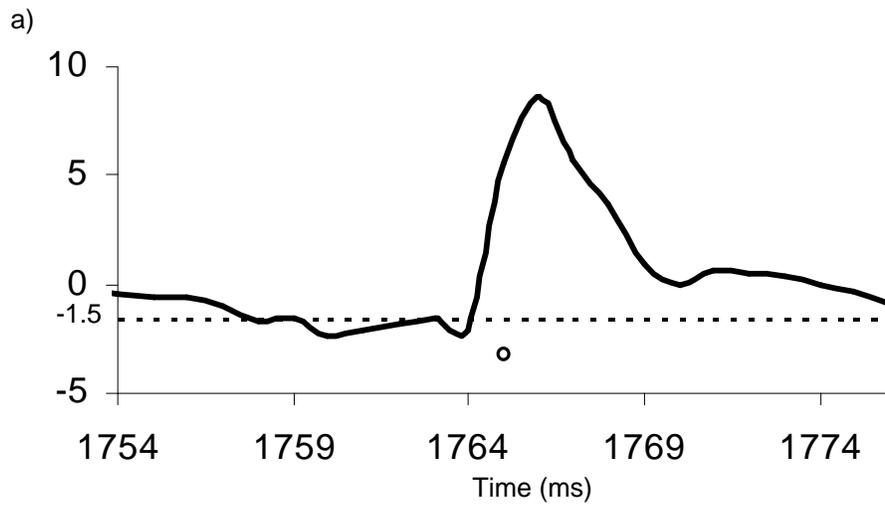


Figure 7. Artificial neural network examples with RBM and CSD data. The solid black line represents v_{CSD} and the small circle represents the data point that is the most negative value of the voltage derivative, as calculated with RBM. a) Example of an activation. b) Example that is not an activation.



Figure 8. Artificial neural network examples with RBM, CSD, and TCM data. The solid black line represents v_{CSD} , the gray line is the time history of I_m , and the small circle represents the data point that is the most negative value of the voltage derivative, as calculated with RBM. a) Example of an activation. b) Example that is not an activation.

Artificial Neural Network Architectures

Artificial Neural Network Using RBM and CSD Data

A simple feedforward ANN with three layers of neurons was constructed using a computer program written in the C language. The three layers were an input layer, a hidden layer, and an output layer. The ANN had 24 input nodes corresponding to the data points of the examples with RBM and CSD information. One input was for the minimum voltage derivative and the other 23 inputs were for the time history of v_{CSD} .

The ANN also had 30 hidden nodes. Experiments were done with several ANN architectures with different numbers of hidden nodes, and the ANN with 30 hidden nodes produced the lowest error rates. One output node, which indicated the results of network processing, was used. The target output for an activation was 0.9 and 0.1 if not an activation. A schematic diagram of the ANN using RBM and CSD data is shown in Figure 9.

The weights of the ANN were randomly initialized to values between -1.0 and 1.0. A weight is a parameter that represents the strength of a connection between two nodes in an ANN. The arrows between the input nodes and the hidden nodes and between the hidden nodes and output nodes in Figure 9 represent the connections between the nodes. As the ANN is trained and learning occurs, the weights change so that the ANN produces a better mapping of the inputs to the target function.

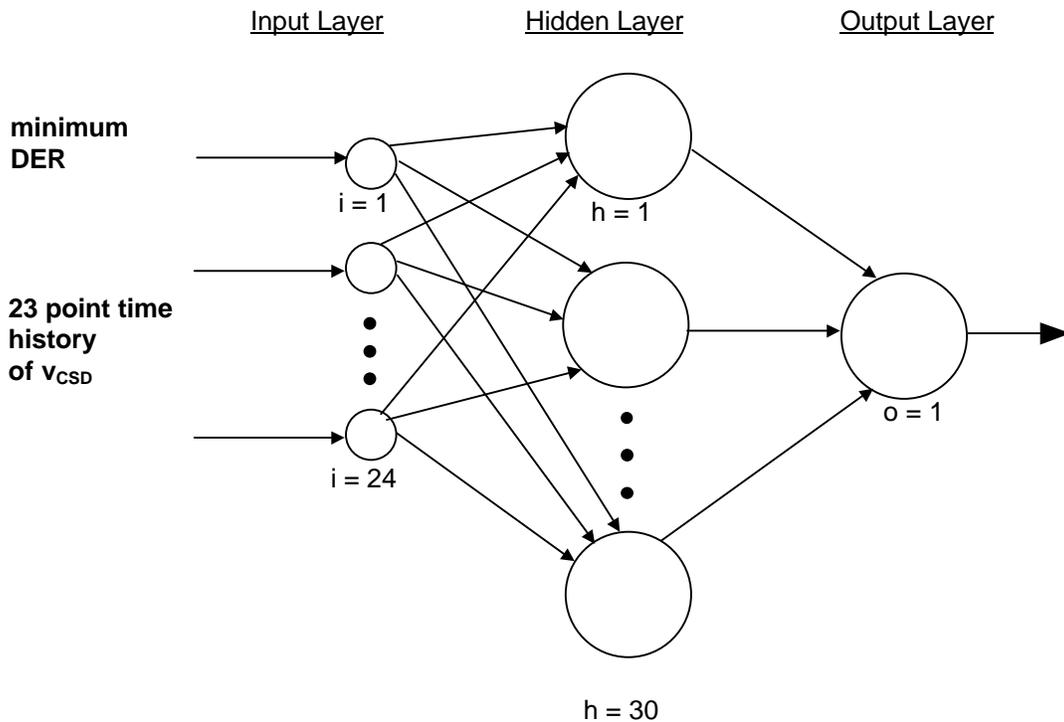


Figure 9. Schematic diagram of the architecture of the artificial neural network using RBM and CSD data.

Artificial Neural Network Using RBM, CSD, and TCM Data

The second ANN was also a feedforward ANN implemented as a C program. The ANN had an input layer, one hidden layer, and an output layer. Forty-seven inputs were needed for this ANN since it also utilized TCM data. The inputs for the ANN were the minimum value of the three-point derivative, 23 points for the v_{CSD} time history, and 23 points for the time history of I_m , as calculated using TCM. The first ANN did not include the inputs for the I_m time history.

This ANN also had 30 hidden nodes, which was the number that produced the smallest errors, and one output node. The target outputs of the network were again 0.9 for an activation and 0.1 for examples that were not activations. The weights were randomly initialized to values between -1.0 and 1.0. Figure 10. shows the schematic diagram for the ANN using RBM, CSD, and TCM data. Also, the similarities and differences between the inputs, numbers of nodes in each layer, and the outputs of both the ANN architectures are displayed in Table 1.

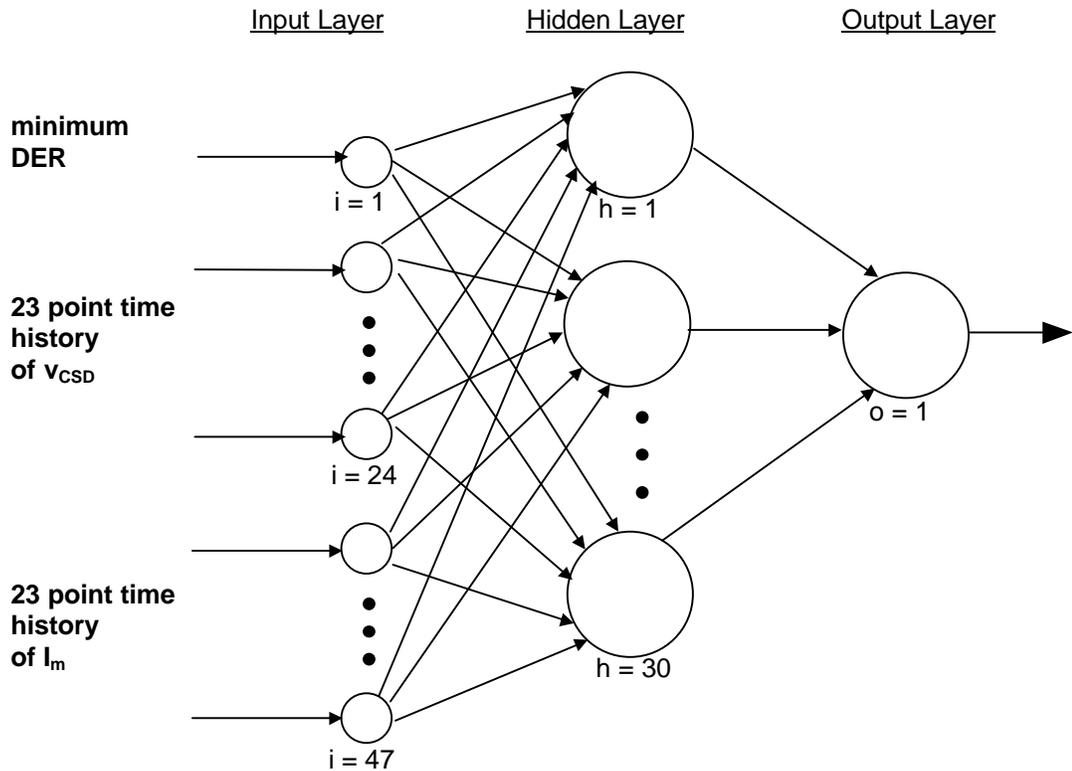


Figure 10. Schematic diagram of the architecture of the artificial neural network using RBM, CSD, and TCM data.

Table 1. Comparison of artificial neural network architectures. The inputs, outputs, and number of nodes used in each layer of the two ANNs are shown.

Neural Network	# Input Nodes	Inputs	# Hidden Nodes	# Output Nodes	Outputs
Neural network using RBM and CSD data	24	minimum value of derivative from RBM and 23 point time history of V_{CSD}	30	1	0.9 (activation) 0.1 (not activation)
Neural network using RBM, CSD, and TCM data	47	minimum value of RBM derivative, 23 point time history of V_{CSD} , and 23 point time history of I_m	30	1	0.9 (activation) 0.1 (not activation)

Artificial Neural Network Training Methods

The ANNs used for this research were feedforward networks with floating point precision and sigmoidal transfer functions. Supervised learning was used to train both the ANN using only data preprocessed with RBM and CSD and the ANN, which used RBM, CSD, and TCM data. The ANNs were trained using the Backpropagation of errors method [19, 20] with simple gradient descent [27]. For the training of both ANNs, two different methods of ordering the examples, staged training and non-staged training, were examined.

Staged Training

In staged training, the training examples were divided into four different training sets. There were 80 examples in each training set for a total of 320 training examples. The training examples were selected randomly from the four pigs. The examples were categorized into the different training sets based on the magnitude of the derivative value in the example, as calculated using RBM. The training sets were referred to as very high magnitude, high magnitude, medium magnitude, and low magnitude. Table 2. shows the magnitudes of the derivatives (DERs) that were included in each training set. Of the 80 examples in each training set, 40 were activations and were marked with targets of 0.9. The other 40 were not activations and had targets of 0.1.

Table 2. Training sets for staged training. The training sets are categorized by the magnitude of the derivative as calculated using RBM.

Training Set	Derivative Magnitudes (mV/ms)	
	Activations	Not Activations
very high magnitude	DER < -3.0	DER > -.05
high magnitude	-3.0 < DER < -2.5	-0.10 < DER < -0.05
medium magnitude	-2.5 < DER < -2.0	-0.15 < DER < -0.10
low magnitude	-2.0 < DER < -1.5	-0.20 < DER < -0.15

The ANN was trained in stages with the four training sets used in a specific order. A stage consisted of training the ANN with one of the four training sets to a $MSE < 0.001$. During the first training stage, the ANN was trained using the examples in the very high magnitude training set to a $MSE < 0.001$. Next, the ANN was trained to the same MSE with the high magnitude training set. Then the medium magnitude training set was used to train the ANN. Finally, the ANN was trained to a $MSE < 0.001$ using the low magnitude training set of examples.

Non-staged Training

For non-staged training, there was one large training set, which included all magnitudes of derivatives more negative than -1.5 mV/ms for examples of activations and more positive than -0.20 mV/ms for examples that did not represent activations. The same examples that had been divided into four training sets for staged training were placed in random order in one training set consisting of 320 examples. In the training set, 160 of the examples were activations with targets equal to 0.9 and 160 examples were not activations with targets of 0.1. The ANN was trained using the single training set to a $MSE < 0.001$.

Artificial Neural Network Testing

After training to a $MSE < 0.001$, the ANNs were tested using the same method for both staged training and non-staged training. Two sets of randomly selected, unseen test examples with 200 examples in each set were used. The term unseen is used to indicate that the test examples were not used during the training of the ANNs. Therefore, the first time the test examples were introduced to the ANNs was during the testing phase. In the first set of test examples, the examples included data obtained from preprocessing with RBM and CSD. The second set of 200 test examples had data from RBM, CSD, and TCM. Each set of test examples was applied to the appropriate ANN.

Both sets of test examples had 100 examples that were activations with targets of 0.9 and 100 examples that were not activations with targets of 0.1. The test examples all had low magnitude derivatives. For the class of examples that were activations, the derivatives were in the range of -2.0 mV/ms to -1.5 mV/ms. The examples that belonged to the class of examples that were not activations had derivatives between -0.20 mV/ms and -0.15 mV/ms.

An error was determined for each unseen test example that was input into the trained ANN. A squared error function was used to calculate the error. The squared error (SE) for each test example was calculated using equation 4.

$$SE = (O - T)^2 \quad (4)$$

In equation 4, O is the output of the ANN for the test example and T is the target, or desired output (0.1 or 0.9), for the same example.

The squared error was used to determine whether or not the ANN classified the test examples correctly as activations or not activations. If the squared error for a test example was greater than 0.25, then the error of the network output was higher than 0.5. Bishop showed that the error provides an estimate of the probability that a test example is classified incorrectly [28]. An error of 0.5 indicates the probability that the example is misclassified is approximately 0.5. Test examples for which the ANN generated a SE larger than 0.25 had an error greater than 0.5 and an estimated probability of more than 0.5 of being classified incorrectly. Therefore, test examples with SE higher than 0.25 were considered to have been misclassified.

In addition, two validation parameters based on definitions from the Association for the Advancement of Medical Instrumentation (AAMI) were used to evaluate the ANNs performance. First, the Sensitivity of the ANN was measured. Sensitivity is the quotient of the total number of test examples correctly assigned to a class by the ANN and the total number of test examples that belong to the class. Second, the Positive Predictiveness (+P) of the ANN was determined. +P is calculated as the number of test examples correctly assigned to a class divided by the total number of test examples

assigned to the class [15, 29]. Sensitivity and +P are both expressed as percentages. The Sensitivity and +P for the two classes of examples, activations and not activations, were determine.