Predicting the Morphology of Arbitrary Dendritic Trees through Simulated Annealing

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Abstract- The inter-neural connectivity plays a major role in the various regions of the brain affecting their functionality. In this regard, the knowledge of the dendritic interconnect structure is imperative. There are quite a few experimental approaches currently available to explore the dendritic connectivity which have their own shortcomings. On the other hand, a theoretical approach would be helpful in developing simulation and fault models for the dendritic tree structure which has wide applications in research and diagnostic purposes. In this paper, we propose a powerful approach based on a randomized algorithm, to predict the dendritic tree structure connectivity. This approach involves two finite steps, one dealing with the topological aspects and the other dealing with the fixing up of the physical length of each of the dendritic branches. The randomized algorithm employed is the simulated annealing[kigv83] and it is powerful in the sense that it can overcome local minima to achieve global minima to obtain near optimal solution. We also propose in this paper an integrated approach in which simulated annealing[kigv83] algorithm is simultaneously employed on both the dendritic structure prediction and the length prediction with dynamic scheduling[vanaa87]. This ensures faster convergence towards optimal solution. Extensive simulation have been carried out and results are presented demonstrating the efficacy of the method.

***Index terms* - algorithm, biological neural networks, cable theory, dendrites, dendritic prediction, morphology, simulated annealing, unrestricted partition.**

1 Introduction

Understanding the brain's function, requires the knowledge of inter-neural connectivity. These connections are established through Dendrites and the Telodendria. The dendrites receive the vast bulk of cell's synaptic input and perform sub-linear summation. The telodendria is complementary to dendrites, having divergent structure. For some neuron types, spatially extended dendritic trees exist to provide space for a large number of quasi-independent dendritic compartments where the synaptic input to each compartment is boosted by an expansive non-linearity. The connectivity is complex. This can be appreciated by the fact that a microliter of a cortex contains approximately 10^5 neurons, 10^9 synapses and 4kms of axons, with the axons and the dendrites together occupying $(3/5)^{th}$ of the neuropil volume[chk2002]. To understand the overall information processing in any region of the brain it is imperative that we to know the exact connectivity across neurons. However it is very difficult to access most neurons and determine their dendritic structures precisely. Experimental approaches to determine dendritic structures include imaging techniques, neuron staining techniques, radioactive tracers and voltage sensitive dyes. Each of these techniques have their own advantages and disadvantages. Imaging techniques have a comparatively low resolution while staining techniques like silver staining are hazardous and less compatible with mass spectroscopy. Colloidal Coomassie Staining has a detection limit 10 to 50 times lesser than silver staining whereas Nissl stains detect only those portion of the cell which contained large amounts of RNA. Radioactive tracing is an invasive technique that leads to degeneration of cell bodies. However, these techniques are employed by experimental neuroscientists.

This paper embraces a theoretical approach towards

the investigation of dendritic structural connectivity. Theoretical prediction of dendritic structure is a Non-Polynomial(NP) complete[hor78] problem eluding convergence to a near optimal solution. This necessitates evolution of algorithmic techniques to determine the dendritic structures. Here application of a randomized algorithm, the simulated annealing[kigv83] is proposed to determine the complex dendritic structures. A two step approach, SPLP(Structure Prediction and Length Prediction)is adopted with the first step involving the determination of the connectivity details and the second, for fixing the individual branch lengths to match the observed input-output voltage transients which is dealt in section 3. Section 5 deals with a more powerful approach InSPLP(Integrated Structure Prediction and Length Prediction)integrating both the processes is evolved to achieve faster convergence towards a near optimal solution.

2 Mathematical Modeling of Arbitrary Dendritic Trees

The voltage transients at any point in the dendritic tree is modeled as a system of Partial Differential Equations (PDEs) derived from cable theory[tuckwell88]. By Laplace Transformation, these PDEs are transformed to s-domain. The boundary conditions give rise to a system of simultaneous equations which is solved by matrix methods. The following is a general set of equations for an arbitrary dendritic tree:

$$\frac{\partial V_{j,k}(x,t)}{\partial t} = \frac{\partial^2 V_{j,k}(x,t)}{\partial x^2} - V_{j,k}(x,t) + I_{j,k}(x,t) \quad (1)$$

$j = 1 \ldots n \quad , k = 1 \ldots k_j$ for each j, where j is the node number and k_j is the total number of converging branches at the node j,(refer fig.1)
and the boundary conditions are

$$\frac{\partial V_{j,k}(0,t)}{\partial x} = 0 \quad (2)$$

where j is the node upon which the k^{th} input converges(refer fig.1).

$$\begin{aligned} V_{j,1}(L_{j,1},t) &= V_{j,2}(L_{j,2},t) \\ &= .. \\ &= V_{j,k_j}(L_{j,k_j},t) \\ &= V_{jj,p}(0,t) \end{aligned} \quad (3)$$

where j is any node from which a branch converges to jj, p is the p^{th} converging branch to the node jj(refer fig.1).

$$\begin{aligned} &\frac{1}{r_{j,1}}\frac{\partial V_{j,1}(x,t)}{\partial x} + \frac{1}{r_{j,2}}\frac{\partial V_{j,2}(x,t)}{\partial x} \\ &+ \ \ldots \\ &+ \frac{1}{r_{j,k_j}}\frac{\partial V_{j,k_j}(x,t)}{\partial x} \\ &= \frac{1}{r_{jj,p}} V_{jj,p}(x,t) \end{aligned} \quad (4)$$

where j is any node from which a branch converges to jj, p is the p^{th} converging branch to the node jj, $r_{m,n}$ is the axial resistance of the n^{th} branch converging on the m^{th} node(refer fig.1).

$$\frac{\partial V_{j,1}(L_{j1},t)}{\partial x} = 0 \quad (5)$$

where j is the output terminal node. The structure of a

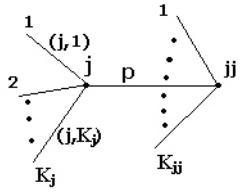

Figure 1: Model Representation for the generic dendritic equations:j, jj are nodes.

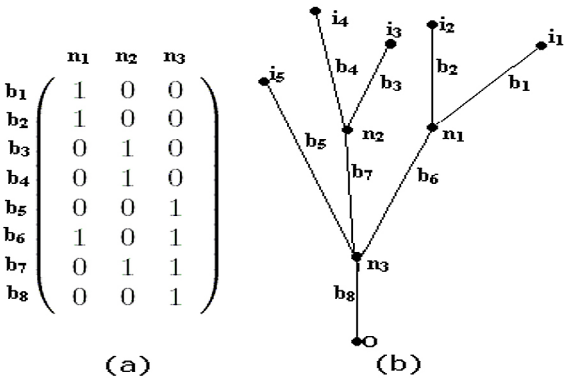

Figure 2: Incidence matrix representation and its interpretation as structure.

dendritic tree is represented by incidence matrix as in graph theory[nar74]. The dendritic branches form the edges while the dendritic nodes form the vertices. Incidence matrix representation for an arbitrary tree with 5 inputs is given in fig.2. The rows correspond to the branches while the columns correspond to the nodes of the tree. The given tree thus has 8 dendritic branches and 3 nodes. The incidence matrix represents only the arborescence of the dendritic tree and does not convey details about the physical length of individual branches.

Step 1 : Obtain the number of inputs as N.
Step 2 : Determine the unrestricted partitions of all numbers from N to 2. Let them be represented as levels from N to 2 respectively.
Step 3 : Take the first partition of N and find the number of summands.
Step 4 : Go to that level that equals the number of summands.
Step 5 : Take the partition at that level and find the number of summands.
Step 6 : Repeat the steps 4 and 5 until the number of summands is two. This determines one tree structure.
Step 7 : Now perform the entire procedure exhaustively to find all combinations for every partition of N.
Step 8 : Stop.

Table 1: Structure prediction algorithm for the SPLP approach

3 Structural and Length Prediction Algorithm for Dendritic Tree-the SPLP approach

In this paper two approaches towards dendritic tree prediction are put forth. The first, SPLP involves a two step process while the second, InSPLP marries the two process into an integrated approach. The following sub-sections are devoted towards discussing the first approach while the subsequent section presents an algorithm for the second approach.

3.1 Structural Prediction

The prediction of the dendritic tree structure does not lead to a unique solution due to its Non-Polynomial (NP)[hor78] characteristics. Given the number of inputs to be N, an algorithmic approach is devised to predict arbitrary dendritic tree structures. The number of ways of forming the first level of nodes is in fact a problem in unrestricted partitioning[apos98] of N into positive integers i, such that for all i, $1 \leq$ i $\leq$ N-1. This step is carried out recursively till the final node is reached. Thus partition matrices (refer fig.3) are obtained. The algorithm is given in Table 1.

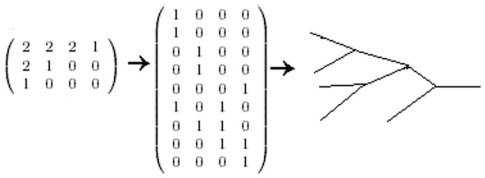

Figure 3: Structural prediction flow:from partition matrix to incidence matrix to structure interpretation.

3.2 Length Prediction

The determination of the structural geometry involves the prediction of length as well. In the previous subsection we had obtained the dendritic structural solution space. The branch lengths of the obtained dendritic structures are predicted employing simulated annealing[kigv83] to match the observed transient input and output signals. The dendritic branch is modeled as a Linear Time Invariant (LTI) system and the phase response corresponding to each input are determined. Path length for each input is determined from the pseudo-propagation velocity(eqn.(6)) and their respective phase response to achieve faster convergence and better accuracy. The algorithm is presented in Table.2.

$$v = \sqrt{\frac{d}{R_m R_i C_m^2}} \tag{6}$$

where
d - diameter of the cable
R_i - axial resistance
R_m - membrane resistance.

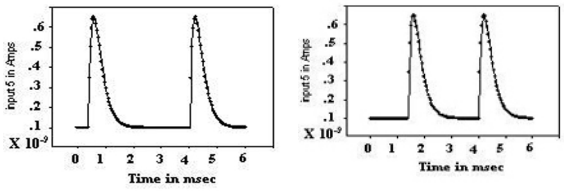

Figure 4: input currents at input terminals 1,2 for the reference structure in fig.7

4 An Integrated Approach for Predicting Dendritic Tree Structure along with their Branch Lengths(InSPLP)

The SPLP procedure for dendritic tree prediction is suitable for small number of inputs due to the NP completeness[hor78] of the structure prediction process.

```
obtain individual path lengths from
each input to the output;
  initial state length = L;
V0 = output required;
while(not all structures are
        completed)
begin
  initial state_structure = S;
  initial state_length = L;
     //corresponds to temperature
     //in the simulated
     //annealing algorithm.
  while(d > optimum value)
  begin
      while(d < d_pre)
      begin
          L' = neighbour of L such
               that total path
               length condition is
                satisfied;
          V = output voltage for
                 the state(L,S);
          d_pre = d;
          d = function of
                   correlation(V,V0);
          //d corresponds to energy
          //in the simulated
          //annealing algorithm.
          //problem is to minimize d.
          prob = min(1,exp{-d/L})
          if (random(0,1) >= prob)
              L = L';
          end
      end
      update L;
  end
  output best solution;
end
```

Table 2: Simulated annealing[kigv83] algorithm for Length prediction through the SPLP approach. Path length were obtained using fig 7, output voltage (fig.6) was obtained by using a reference structure with individual branch lengths with input currents (fig.4,5,6)

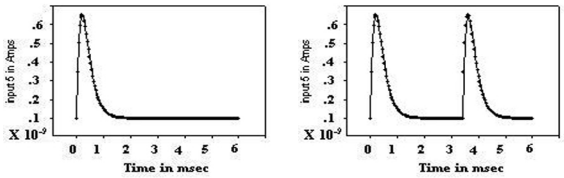

Figure 5: input currents at input terminals 3,4 for the reference structure in fig.7

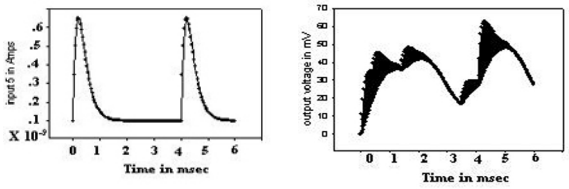

Figure 6: input currents at input terminals 5, voltage at the output terminal for the reference structure in fig.7

Thus an integrated approach (InSPLP) for combining both the structure prediction and branch length prediction is proposed towards obtaining a near-optimal solution with a faster convergence. The path length constraint is determined as in the case of the SPLP algorithm using eqn.6. The InSPLP algorithm(table 3) employs dynamic scheduling[vanaa87] to incorporate simultaneous structure as well as length prediction as opposed to the sequential prediction of structure followed by length in the SPLP approach . Superior performance of the InSPLP approach is attributed to the direct convergence to a single optimal solution without predicting all the structures separately as opposed to the SPLP. It may be recalled that in the SPLP approach we obtain optimal branch lengths for all the possible structures permissible for a given number of inputs. The algorithm for InSPLP is given in Table.3.

The structure prediction part of the SPLP approach is NP complete[hor78] with respect to the number of inputs to

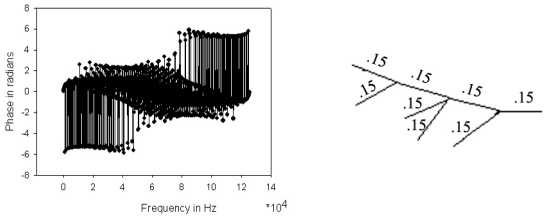

Figure 7: Phase plot for the reference structure (figure in the right). The length of individual branches is in terms of λ, the electrotonic length chosen to be 0.01cm.

```
obtain path length from each input to
         the output;
Input to the tree defined;
 Initial state :
   Initial length = L;
   Initial structure = S; T_L = L;
 //corresponds to temperature 1 in the
 //multi-temperature simulated annealing
 //algorithm.
 T_S = S;
 //corresponds to temperature 2 in the
 //multi-temperature simulated annealing
 //algorithm.
 V0 = Required output voltage waveform;
 count = 1;
 V= Output voltage for the state(L,S);
 d = function of correlation(V,V0);
//d corresponds to energy in the
//simulated annealing algorithm.
//problem is to minimize d
 while (d > optimum value )
 begin
   while(d < d_pre)
   begin
    if(count == 1)
       L' = neighbouring solution of L
            such that the path length
            condition is satisfied;
       S' = S;
    end
    if (count == 0)
       S' = neighbouring solution of S;
       L' = L;
    end
    d_pre = d;
    V = output voltage for state(L',S');
    d = f(correlation(V,V0));
    prob =
      min(1,exp(-d/T_L),exp(-d/T_S))
    if ( random(0,1) >= prob)
      y =
      min(exp(-d/T_L),exp(-d/T_S))
      if ( y == exp(-d/T_L))
         count = 0;
      end
      if ( y == exp(-d/T_S))
          count = 1;
      end
    end
   end
 end\\
```

Table 3: Simulated annealing algorithm for Integrated Structure Prediction and Length Prediction(InSPLP). Path length were obtained using fig 7, output voltage (fig.6) was obtained by using a reference structure with individual branch lengths with input currents (fig.4,5,6)

the tree structure. This problem of NP completeness[hor78] is overcome in the InSPLP approach. The InSPLP approach thus offers faster convergence towards the solution making it suitable for predicting connectivity in large neural networks including synaptic contacts. Predicting the structure of an entire neural assembly may need a different partitioning approaches involving multiple scheduling parameters which may be difficult to model. The computation intensiveness of the problem necessitates a hardware based solution. To meet this end the DDNAM Array Architecture[ψnam2] proposed by the authors are under investigation for parallel simulation of these methodologies.

5 Simulation Results

This section presents the simulation results for SPLP and InSPLP approach.

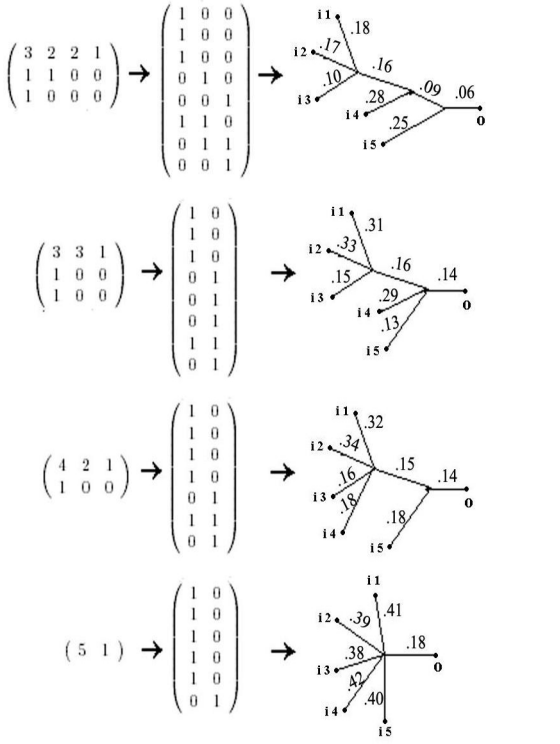

Figure 8: Intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths for 4 out of 12 (of the remaining 8, 4 are in fig.9 and 4 are in fig.10)distinct structures using SPLP approach.

5.1 Simulation Results for the SPLP approach

The simulation results presented were performed for a five input tree. For five inputs twelve distinct structures are possible and permutation of the terminal input locations further yields 246 possibilities. Here simulation results for the 12 distinct structures are presented in figures (8), (9) and (10). The results of the NEURON Simulation Environment[hica97] is taken as the experimental standard. The dendritic tree used as reference for the simulation is shown in fig(7). The output signals obtained from the SPLP algorithm are correlated with the output simulated on NEURON[hica97], when this correlation is best the corresponding matrix yields the predicted structure. The figures (8), (9) and (10) depict the optimized length values for each branch of the predicted structures obtained using the SPLP procedure. Each figure gives the intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths. All the dimensions are in terms of electrotonic length, λ, which is chosen to be 0.01cm.

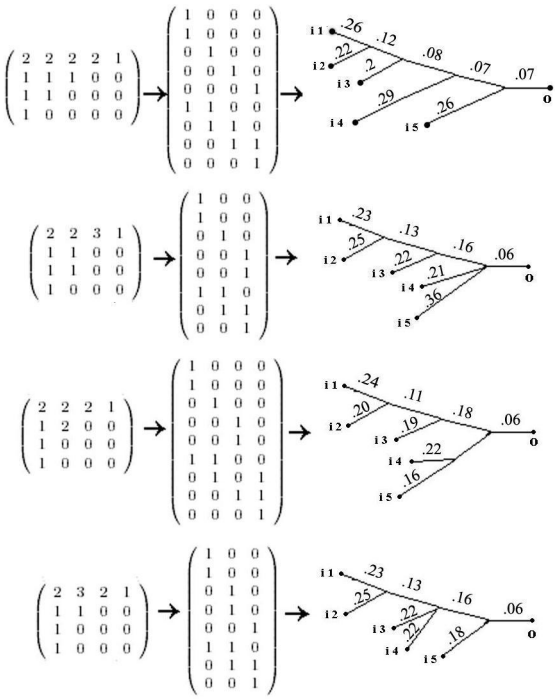

Figure 9: Intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths for 4 out of 12 (of the remaining 8, 4 are in fig.8 and 4 are in fig.10)distinct structures using SPLP approach.

5.2 Simulation Results for the InSPLP approach

The simulation results presented for the InSPLP were performed for a five input tree as in the SPLP approach. Except for the algorithm of the InSPLP (table 3) the simulation procedure is same as described for the SPLP approach. Here only a single best solution is obtained due to the nature of the InSPLP algorithm. Figure (11) depicts the optimized length values for each branch of the predicted structure obtained using the InSPLP procedure. The figure gives the intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths.

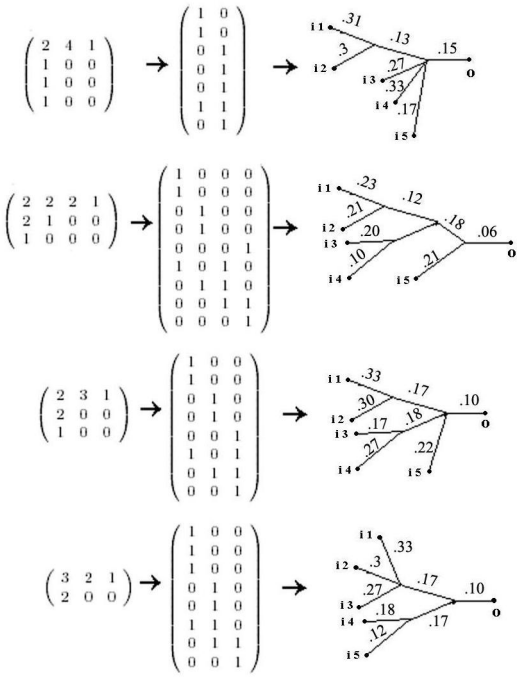

Figure 10: Intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths for 4 out of 12 (of the remaining 8, 4 are in fig.8 and 4 are in fig.9)distinct structures using SPLP approach.

6 Conclusion

This paper presents a simulated annealing[kigv83] based methodology for predicting the complex morphology of dendritic structures. We have presented two simulated annealing[kigv83] based algorithms, SPLP and the InSPLP. It has been shown that InSPLP is more efficient with respect to solution convergence and also easily amenable for extending the same technique for predicting complex neural

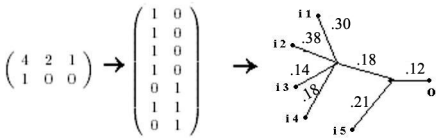

Figure 11: Intermediate results of the simulation flow from the partition matrix to the incidence matrix to the final predicted structure having optimized branch lengths using In-SPLP approach.

assembly including the synaptic contacts. Extensive simulation results are presented to demonstrate the capability of the presented methodologies for predicting the dendritic morphology. The experimental structure used as reference was simulated using the NEURON[hica97] software package. The accuracy of both the presented approaches are very well brought out by correlating the simulation results namely the output signal variation with that of the output simulated by the NEURON[hica97]. It is our earnest opinion that these prediction algorithms will be useful and also can supplement to a large extent, the structural prediction carried out using imaging techniques which have certain drawbacks. Further the most important application of the prediction methodologies is in fault simulation. The predicted structure can be altered according to the requirements of fault simulation and the behaviour of the neural assembly can be investigated.

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