Towards Predicting Multi-Million Neuron Interconnectivity involving Dendrites-Axon-Soma Synapse: A Simulation Model

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Abstract

The Multi Million Neuron Interconnectivity involving-Dendrite Axon Soma Synapse (MMINi-DASS) prediction model [2] was proposed to overcome the severe shortcomings of population model. The shortcomings include inability to provide insight into synapse dynamics, fault simulation, learning process, balance, memory, and spatio temporal information processing of the brain in a realistic manner. The mathematical intractability of predicting millions of neuronal interconnectivity is circumvent in the MMINi-DASS by employing a simulation model. The focus of this paper is towards developing a simulation model whose computational complexity gets drastically reduced over that of MMINi-DASS model, while preserving all its merits. The expected computation reduction is such that silicon supercomputer itself can execute the simulation model without employing molecular supercomputers as in [2].

Keywords: simulated annealing, expected current, dendritic and telodendric structure prediction, cable theory, population model, spatio-temporal, BOLD (Blood Oxygen Level Dependent) response, fault simulation, fMRI (functional Magnetic Resonance Imaging)

1. Introduction

The understanding of the biophysics of computation of the brain and subsequently modeling it requires the complete realization of its different functions [7].This requires special emphasis on neurons, the basic building blocks of the Central Nervous System(CNS).The understanding of the various parts of the neuron is quintessential, especially that of the dendrites, telodendria and the set of associated synapses. This is crucial in realizing the vast expanse of interconnectivity that gives brain its structure and behavior.

However predominant models, have realized functionalities in various cortices by assuming the neurons collectively as a population [4].

Although such mathematical models confirm to the natural response of a region, they are biologically unrealistic; in the sense that they do not involve connectivity with respect to dendrite, soma, axon and synapses. A population considers its neurons as non - interacting [4] which does not provide insight in explaining: synapse dynamics, learning process, balance, memory, spatio temporal information processing in a realistic manner.

Such major drawbacks can be annulled if connectivity and information processing are realized at the single neuron level, across the neuronal population taking dendrites, axon, soma and synapse (DASS) models into account. An earlier novel attempt was made to establish the interconnectivity at the neuronal level. The simulation model that was proposed, Multi Million Neuron Interconnectivity involving Dendrites-Axon-Soma-Synapse (MMINi-DASS) [2] is tractable in predicting brain morphology. A major application of this is fault simulation, which helps to analyze brain diseases and disorders. Based on the realistic class of models included for the DASS, the MMINi-DASS model will aid in discovering new medicine through fault simulation.

The neuronal connectivity of a brain region is initially generated under a particular distribution. A Simulated Annealing (SA) based optimization algorithm [1] is used to reconfigure the connectivity by scheduling the parameters: neuron cell body geometry, axon length, number of dendritic branches, tree tapering coefficient etc., involved in describing the connectivity. In all 35 parameters were considered [2]. The SA algorithm is iteratively applied until the spatio-temporal neuronal activity matches with the BOLD response of the region obtained from its fMRI.

[Ψ] Names in alphabetical order

This MMINi-DASS Interconnectivity simulation model demands massive memory and complex computation [2].The complexity arises due to formation , partitioning and tracking intermediate connectivity matrices and deterministically solving the DASS models in each iteration.

We attempt to overcome the computational complexity of MMINi-DASS prediction model without actually solving the equations of the mathematical models [6] associated with the DASS structure. We resort to a prediction based simulation methodology employing the SA algorithm. For example, dendritic branch current is predicted without solving the cable model equations, using only the current injected through the dendrite.

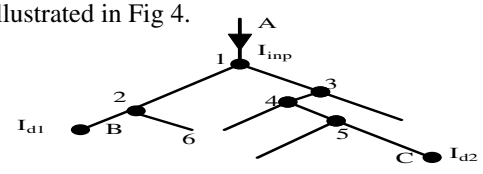
As a modest beginning we predict the dendritic structure and its associated electrical activity as a spin off, using a predictive simulation model, LNCNP is elaborated in section 2. Extensive simulation and results are given in section 3. Extension of this model to MMINi-DASS using a grid based approach will lead to drastic reduction in the computational complexities and is discussed in section 4.

2. Length and Number of Child Nodes Prediction (LNCNP)

We have formulated a novel prediction based simulation model, LNCNP for dendritic structures. We describe in the subsequent sections, the concept of LNCNP model, the algorithm adopted for the simulation, the simulation flow and the outcome of our experiment.

2.1 LNCNP model

In the LNCNP simulation model, using the electrical activity in the dendritic arbor we estimate the system parameters. The system parameters here refer to the number of expected child nodes (Tn) for any node and the expected length of a branch between any two levels (TL). A node, ie., branching point in the dendritic structure and the level of a node are illustrated in Fig 4.



I_{inp} : current from axon
path1: A-B ; 2 levels
path2: A-C ; 4 levels
I_{d1}: current at level 2 path1
I_{d2} : current at level 4 path2
Tn1: number of expected child nodes for B
Tn2 : number of expected child nodes for C
TL1 : expected branch lengths between 1,2
TL2 : expected branch lengths between 2,6

Fig 4: Arbitrary Dendritic Tree

After fixing the system parameters, the probabilities (p_n and p_l) of the individual parameters are found under a suitable distribution. The expected current in a branch at any level L within a partition, is given by:

$$I_{exp} = [\, p\_n * p\_l \,]^{L} * I_{inp}$$

$$L \leq \text{Total number of levels}$$

The LNCNP model differs from the previous models, vis-à-vis the fact that the information about the system parameters are abstracted by considering the dendrite as a logical entity rather than a physical entity from the beginning. Such an approach helps to alleviate the problem of handling and maintaining the connectivity matrices and drastically reduces the associated computations. This problem now reduces to that of optimizing the parameters of the system to arrive at the best configuration which corresponds to the desired electrical activity. Such a near optimal configuration of the system is achieved by employing Simulated Annealing algorithm that schedules the parameters dynamically [1].

2.2 An Unpartitioned Approach

The following algorithm explains the method of evaluating the most desired current, procured from a set of branch currents Id, for which LNCNP is initiated. The branch current set of interest is known from the electrical activity of the tree(by experimental means[5]). Iinp refers to the root node or axon current.

Step 1: Get the root node or axon current (I_{inp}), current array (say $I_d()$ set of N-values, denoted as $I_d(1), I_d(2), ..., I_d(N)$)

Step 2: for i: = 1 to N, repeat Step 3

Step 3: for j: = 1 to N

$$error[i]: = \sum (abs\,[I_d(j) - I_{inp} * \{I_d(i)/I_{inp}\}\text{^}\, j\,])$$

Step 4: Least Error: = min (error[i])

Step 5: Locate the I_d with the Least Error calculated in Step 4.

Step 6: This I_d, I_{inp} are the input for the LNCNP algorithm

The temperature parameters are the system parameters, that is, the arbor specification explained in section 2.1.Cost function refers to intermediate current values during optimization. The LNCNP simulated annealing algorithm that determines these system parameters is given in fig 1.

Step 1: Start
Step 2: Assume Random initial values for temperature parameters (TP)
Step 3: From values in Step 2, calculate the Cost Function C(S)
Step 4: Repeat Steps 5 to 12 until difference of the cost function and the desired current is lesser than tolerance (ξ)
Step 5: While Not near a local minimum repeat steps 6 to 10
Step 6: Modify TP randomly and calculate corresponding cost function C(S')
Step 7: DEL: = C(S) - C(S')
Step 8: prob: = min(1,$e^{-(\Delta/(k1 * TL))}$, $e^{-(\Delta/(k2 * TN))}$)
Step 9: if(random(0,1) < prob)
S: = S'
Step 10: End
Step 11: Update TP
Step 12: End
Step 13: Output Best/Optimal Solution

2.3 Need for Partitioned Approach

The unpartitioned simulation of the entire tree follows a single set of parameter values. Such characterization weakly correlates to the actual arbor. Hence we evolve a partitioning approach and initiate LNCNP on these partitions, each of which provide a set of parameters. The figure of merit of such an approach is more in accordance to the electrical activity of the arbor. Such partitioning also supports parallel evaluation of dendritic logical structures shown in Fig 4.

3. Simulation and Results

We performed extensive simulation in C platform and the following modules were implemented. The simulation flow is shown in Fig 2.

Modules:

Id_set: Accept the input current for any branch at the desired level and the root node/axon current of the tree.

N_way: Computes best partition sets.

Unpartition: Finds branch for which error, as defined in section 2.2, is minimum.

LNCNP: Runs simulated annealing to schedule system parameters.

The following results were obtained from simulation of a purkinje cell's dendritic structures.The data for mean number of branchlets for any node and branch length of a telodendria were obtained from [3],[4].

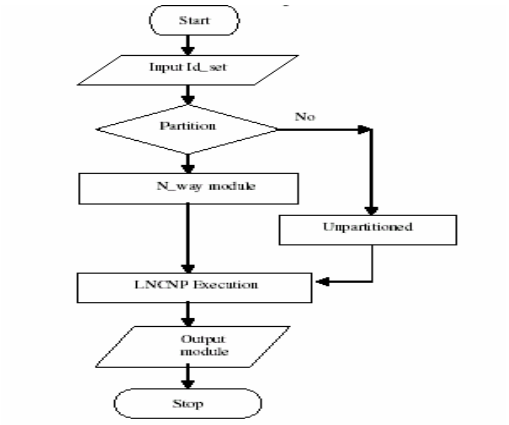


Fig 2: Simulation flow

4. Discussion

In the previous sections, we have presented our model, LNCNP for predicting the parameters required in establishing dendritic structure and computing its branch current. Here we discuss how LNCNP can be scaled up to achieve MMINi-DASS.

4.1. Extending LNCNP to MMINi-DASS- A Grid Based Approach

- Grid partition the arbor for determining the structure of the dendritic and telodendritic trees. Each cell in a grid A represents either a branch of the arbor or is void.

Maximum number of levels =10								
No. of Desired	Root node		Desired	Partition I		Partition II		
Currents	Current(mA)	Level	Current(mA)	length (m)	no. of nodes	length (m)	no of nodes	Optimum Partition Set
		2	10					
		3	7					
		4	2.4					
4	32	5	1	0.011547	15453	0.009292	14313	(1,2) (3,10)
		1	7.5					
2	15	2	3	0.010156	17185	0.007517	17041	(1),(2,10)
		3	9					
2	26	4	3	0.015073	20337	0.006884	14862	(1,3),(4,10)

TABLE 2: PARTITIONED

- In a hyper grid B, each cell represents either a grid A or a soma-axon pair or soma-axon-synapse triplet or a synapse alone.

No. of Desired Currents	Root node Current(mA)	Level	Desired Current(mA)	Optimized length (m)	Optimized node
		1	7.5		
2	15	2	3	0.01181	14399
		1	8		
		2	4		
3	10	5	1	0.015804	16403
		2	10		
		3	7		
		4	2.4		
4	32	5	2	0.016483	13419
		3	4		
2	26	4	3	0.012552	15286
		2	10		
		5	1.87		
		6	1.1		
4	37	8	0.32	0.011927	15478

TABLE 1 : UNPARTITIONED

- Abstract the elements of grid B into a cell of grid C. Each cell in grid C is thus a collection of a few interconnected neurons.
- Grids of type C form the cells of a hyper grid D. This hyper grid represents the MMINi-DASS interconnectivity. The diagrammatic representation of the grid approach is shown in Fig 3.

Each cell in the hypergrid D is computationally independent of its neighbors. From grid D the structure is established when the BOLD response obtained by the simulation model matches with that of the BOLD response from the fMRI. Until a near optimal solution is obtained, partitioned parallel computing is possible. During the execution of our predictive MMINi-DASS model, when we approach the neighborhood of near optimal solution, this model is replaced by deterministic models of DASS. The LNCNP and its extension to MMINi-DASS reduce computation drastically. However to achieve better accuracy, the deterministic approach is followed in the near neighborhood of the optimal solution.

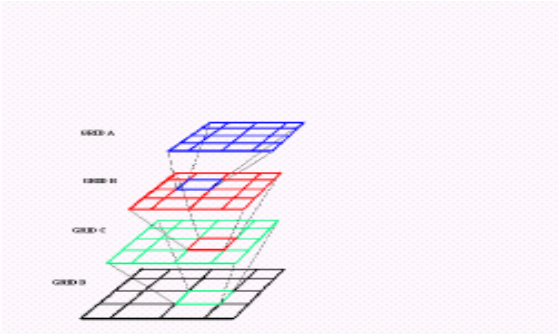


Fig 3:The grid of multi million neurons

5. Conclusion

Our primary focus is to build a tractable simulation model that reduces computational complexity drastically. Thus conventional silicon supercomputers [9-10], suffice for establishing MMINi-DASS, instead of awaiting for molecular computers which may be realized after a decade or more. This paper is a major initiative towards realizing MMINi-DASS prediction employing silicon supercomputers as a follow up of [2].

6. References

[1] S.Kirkpatrick, C.D.Gelatt, Jr., M.P.Vecchi- "Optimization By Simulated Annealing", Science, Volume 220, 1983, 671-680.

[2] N.Venkateswaran, Rajesh Ramaswamy- "Partitioned Parallel Processing Approach for Predicting Multi-Million Interconnectivity in the Brain: Involving Soma-Axon-Dendrites-Synapse", BICS, 2004.

[3] Brain Facts and Figures http://faculty.washington.edu/chudler/facts.html.

[4] Wulfram Gerstner and Wemer M.Kistler - "Spiking Neuron Models: Single Neurons, Populations, Plasticity", Cambridge University Press, August 2002.

[5] Eric de Schutter's homepage : http://www.bbf.uia.ac.be

[6] Henry C Tuckwell, "Introduction to Theoretical Neurobiology Vol I: Linear Cable Theory and dendritic Structure", Cambridge University Press 1988.

[7] Christof Koch & Idan Segev, "Methods in neuronal modeling: From Ions to Networks", 2nd Edition, MIT Press, 1998.

[8] N.Venkateswaran, Arrvindh Shriraman, Adithya Krishnan, Srinivas Sridharan, Niranjan Kumar Soundararajan-"The MIP project: Evolution of a novel Supercomputing Architecture", MEDEA Workshop-PACT Conference, September 2003.

[9] N.Venkateswaran, Arrvindh Shriraman, Adithya Krishnan, Srinivas Sridharan, Niranjan Kumar Soundararajan- "Memory In Processor: A novel design paradigm for Supercomputing architectures", ACM SigArch Computer Architecture News, June 2004.