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A Study of Neuronal Properties, Synaptic Plasticity and Network Interactions Using a Computer Reconstituted Neuronal Network Derived from Fundamental Biophysical Principles

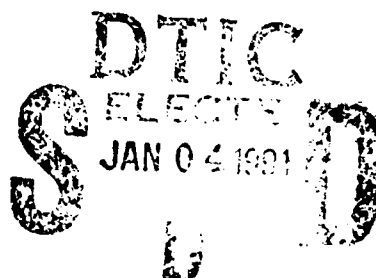
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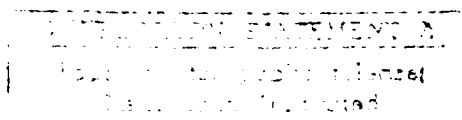
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31

Progress Summary

The neural simulator program *MacNeuron* is currently implemented on the Macintosh IIci computer with executable versions using either the Motorola 68020 or 68000 processor and with or without the Motorola 68881 math co-processor. A preliminary version of the program showing some features of the user-interface compiled with the 68020/68881 options is included with the progress report. A preliminary user manual is also included which describes the execution environment of the program. Currently, the program consists of more than 15,000 lines of Pascal code, and the program is still in its development and testing stages where more codes will be generated and modified. The program is written in Object Pascal using the THINK Pascal compiler incorporating the class-structure of the THINK Class Library for building the neuron-class structure. Since substantial efforts have been put into designing a generalizable generic neuronal stimulator for realistic neuron simulation, it becomes more apparent that the same simulation program can encapsulate the similar structure of an integrate-and-fire reduced model of the *MacNerveNet* program. The incorporation of the *MacNeuron* and *MacNerveNet* into one single hybrid model program as envisioned in the original grant proposal is taken into account in the design of the *MacNeuron* program. Independent efforts to develop the *MacNerveNet* program has been re-directed to incorporate the program into *MacNeuron* to maximize the program development results.

The current implementation of the user-interface of *MacNeuron* encapsulates the building process of a neuron and network by forming instances of the basic elements in a compartmental model. The menu-driven window user-interface environment is used in describing the morphological structures of a neuron by its compartmental elements of membrane and ionic channels. A text-based script description of the above user-specification equivalent is currently under development where the menu-driven iconic specification of the simulation parameters can be interchanged with the text-based script-file specification. Thus, the simulation can be run with full user-control (using iconic interface) or execute under totally hands-off background mode (using text-based batch interface) in the next version. Currently, the program is under testing phase where the numerical integration routines and other simulation routines are undergoing thorough testing and validation.

An integrate-and-fire model of a network of neurons for decoding interspike-intervals of spike trains which forms a topographical mapping of the input spike train, converting serial signal into bands of parallel signal for processing was developed. The network uses time-delayed elements for extracting the interspike-intervals of the input spike train. The successive layers of the network extract and eliminate higher-order interspike-intervals. The network can also be considered as a band-pass filtering device where the interspike-intervals of the input spike train be represented by the firing of the specific neuron on the output layer. The variability (or jittering) in the firing times of spikes can be represented by one axis of rows of neurons in the two-dimensional representations in the output layer while the

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interspike-intervals are represented by the firing of the neurons on the other axis of the two-dimensional array of output neurons. The unique design architecture for signal processing using pulse-coded signal implemented by a neural network is filed for patent protection. The patent application is currently being made through Baylor College of Medicine.

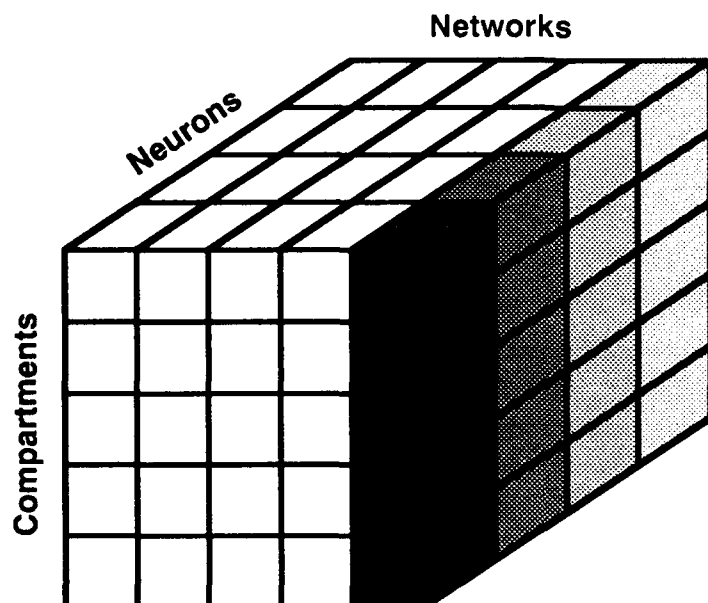
Specific Program Progress

MacNeuron:

The *MacNeuron* program is the detailed biophysical/biochemical simulation model of compartmental neurons. The design goal of the program is to develop an easy-to-use generalizable simulation program for performing neurobiological experiments using a computer model that can be used by both experimentalists and theorists. Different numerical algorithms are incorporated into the program that are selectable by the users. Since different algorithms have their inherent characteristics of computational speed and error control, the model is designed to use a variety of algorithms to provide flexibility that other similar neural simulator models do not offer. The numerical integration algorithms incorporated into the program includes Euler, Gear, Runge Kutta Fourth Order and Runge Kutta Mearson methods currently, and the implicit integration algorithm will be added later. The program is modularized such that more advanced numerical algorithms can be added to the system with little difficulty, thus making the program very generalizable. Similarly with the same design goal, the algorithm for computing the input/output relationships of a neuron can be generalizable such that the simulation can include as much biophysical/biochemical processes in a spatial-temporally realistic neuron as specified by the user or the simulation can include simplified reduced integrate-and-fire "point neuron" formulation. This approach is essentially the hybridization method for including the *MacNeuron* and *MacNerveNet* projects into one single simulator that was proposed in the original grant proposal.

The construction of a system of neural networks (or the brain) can be modeled conceptually in the following way in our model. The basic elements for building neurons and network in the model can be considered in terms of "compartments". The compartments are divided into two classes: the membrane compartments and chemical compartments. The membrane compartments are electrical equivalent patches of membrane that can be connected to form the morphology of a neuron, and chemical compartments are volume spaces that separate different species of ions or ligand/neurotransmitters or other chemicals such as secondary messengers where chemical reactions occurs. These *compartments* can then be connected together to form a *neuron*. The *neurons* are then connected to form a *network*. The *networks* are connected to form a *brain*. Thus, a neuron is composed of interconnecting compartments; a network is composed of interconnecting neurons, which, in turn, forms interconnections with the compartments. Conceptually, this hierarchical structure can be represented graphically by a cube, with one dimension representing the compartments, another dimension representing neurons (which are composed of compartments in the compartment-dimension), and another dimension

representing networks (which are composed of neurons in the neuron-dimension) as in the following figure.



A neuron can be considered as composed of a collection (or vertical column in this figure) of interconnecting compartments. A network can be considered as composed of a collection (or a vertical slab in this figure) of interconnecting neurons. A brain can be considered as composed of a collection (or a cube in this figure) of interconnecting networks. Thus, hybridization or generalization between a detailed biological-realistic network and a reduced integrate-and-fire neural network can be accomplished conceptually by this figure, where an integrate-and-fire networks are essentially composed of single-compartment "point neurons" represented by a two-dimensional horizontal slab in the above figure whereas a detailed compartmental networks are composed of multi-compartment neurons represented by a three-dimensional cube in the above figure.

Different parts of the program are implemented, and after the pieces are thoroughly tested, they will be put together to form a functional program for simulation. The development of the graphical output of the program is deferred until the new version 7.0 release of the Macintosh operating system by Apple Computer to incorporate the new inter-application communication feature where the graphical output can be performed by a high-quality graphics/charting program.

Publications by the Principal Investigator during 1989 and 1990

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- Alkon, D. L., Vogl, T. P., Blackwell, K. T., Tam, D. C. (1990) *Neural network models of conditioning and action*. In: *Memory Function in Neural and Artificial Networks*. (M. L. Commons, S. Grossberg, J. E. R. Staddon, eds.) Lawrence Erlbaum Associates: Hillsdale, New Jersey. (in press)
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- Alkon, D. L., Vogl, T. P., Blackwell, K. T. and Tam, D. C. (1989) Pattern recognition and storage by an artificial network derived from biological systems. *Neural Network Models of Conditioning and Action: the Twelfth Symposium on Models of Behavior at Harvard University.*

Submitted publications

- Tam, D. C., Knox, C. K., Friehs, G. M. and Ebner, T. J. Characteristics of visually guided two-dimensional arm movements in the primate with visual feedback alteration. *(submitted to the Journal of Neurophysiology)*