Poster
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Subthreshold Synaptic Computation in the Cell Body and Dendritic Trees of Neurons and its Role in Understanding Psychopharmacological effects*

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I-Advances in Psychopharmacology and the Problem of Interpreting the Dynamics of Therapeutic Effects

Although the action of psychopharmaca on neurotransmission is relatively well know any definition of psychopathological entities in terms of enhancement or else reduction of neurotransmission it is highly questionable. Namely if it is true that there occurs, in general, a depletion of catecholamines in Major depression as well as an higher level of activity of dopaminergic activity in Nucleous Acumbens in those cases of schizophrenia with perceptive and cognitive positive disturbances as well as a reduction of dopaminergic activity in the frontal lobe in the case of spectrum disorders with disturbance in social adjustment, and retirement there is no proof that therapeutic effects would result, in the strict sense, from the correction of these deviations.

It is very probable that nowadays we are not treating diseases but rather ameliorating symptoms that we have chosen as targets for our intervention. Furthermore it is probably convenient to invoke effects on some psychological functions to explain some remarkable therapeutic results that we are currently obtaining. This is the case concerning the reduction of drive as well as emotional expression in learning autokinesis and schizokinesis and reduction of anticipation processes concerning positive symptoms of

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acute schizophrenia as well as the reduction of the initiation of compulsive actions in the case of addicts to playing money games as well as compulsive behaviour in Obsessive-Compulsive disorder.

The same applies to Mooud disorders in which the affective level can be reduced in the case of Manic Disorders and enhanced in the case of Depression.

Other examples might be found as for instance disturbances of thought and of symbolic motion due to a disorganisation of the hierarchy of impulses to action.

Useful as it may be the contribution of this psychological structural approach we must admit that we have no explanation whatsoever for the amelioration we obtain concerning speech and thought contents in the case of obsessive-compulsive disorder, schizophrenia and phobic disorders.

To attain an understanding of the effects of drugs on thinking processes and cognition, in general, we would needs reliable information about characteristics of knowledge architectures in the Brain as well as event representation and finally about the encoding processes in terms of the first system of neurotransmission as well as second and third messengers systems.

It should be noted that as a matter of fact psychopharmaca act directly on neurotransmission and their effects on sequences of action potentials are indirect. We need a cogent understanding of sub-threshold synaptic computation in the cell body surface as well as dendro-dendritic in dendro-somatic networks.

We are still far away from having the knowledge we need concerning the representation of cognitive-affective events in the Brain. We do nevertheless know about powerful putative hypotheses concerning the representation not only of elementary data but also of relationships defined over those data and the representation of cognitive symbolic processes in general, in terms of sub-threshold synaptic computation in the cell body and dendro-dendritic networks.

Explanation of the therapeutic effects of drugs on thinking and cognition in general can be obtained in models constructed according with principles we present in the next section.

II-Synaptic and Symbolic Representation Structures and Processes Representation of Data and Functions and their Decoding

In artificial neural networks of the McCulloch and Pitts type events and computational procedures are separated. Events are represented by neuronal states 1 or 0 as well as by synaptic states of excitation or inhibition and computational operators are specified by neuronal thresholds, algebraic summation of synaptic excitation and inhibition as well as by the interpretation rules which specify the logical functions of such neurons (McCulloch and Pitts,1943). In a second proposal WS McCulloch introduced the concepts of pre-synaptic inhibition which allowed the representation of functions such as "exclusive or" or "equivalence" without the need of using calculations involving layers of formal neurons.

In 1995 we used the neurophysiological and biophysical results of (Graubard and Calvin, 1979), to develop a computational approach to dendro-dendritic processes of excitation and inhibition as well as dendro-dendritic interactions and propagation of dendritic signals. We tried to obtain a complete agreement with neurophysiological data concerning the graduate character of dendritic potentials along the dendritic tree and we studied architectures of dendro-dendritic formal networks considering in some detail the computational possibilities raised by dendro-dendritic interactions and propagation of dendritic signals always from more proximal to more distal sites in dendritic ramifications relatively to the respective cell bodies. It was possible to implement besides the trivial operations of summation and subtraction also the operations of multiplication and division. Convolution and correlation of two functions represented as arrays of finite differences were calculated using iterative operations which implied pre-synaptic facilitation and inhibition. The implementation of operations of multiplication and division required pre-synaptic facilitation or inhibition of synaptic terminals located in dendritic ramifications (J. Barahona da Fonseca et al,1995, I. Barahona da Fonseca et al, 1995). Non linear characteristics of these interactions were required for the formal representation of these operations and functions of convolution and correlation (see figure 1).

$$f_2(\tau) = \int_{-\infty}^{+\infty} f_1(t)\, h(\tau - t)\, dt$$

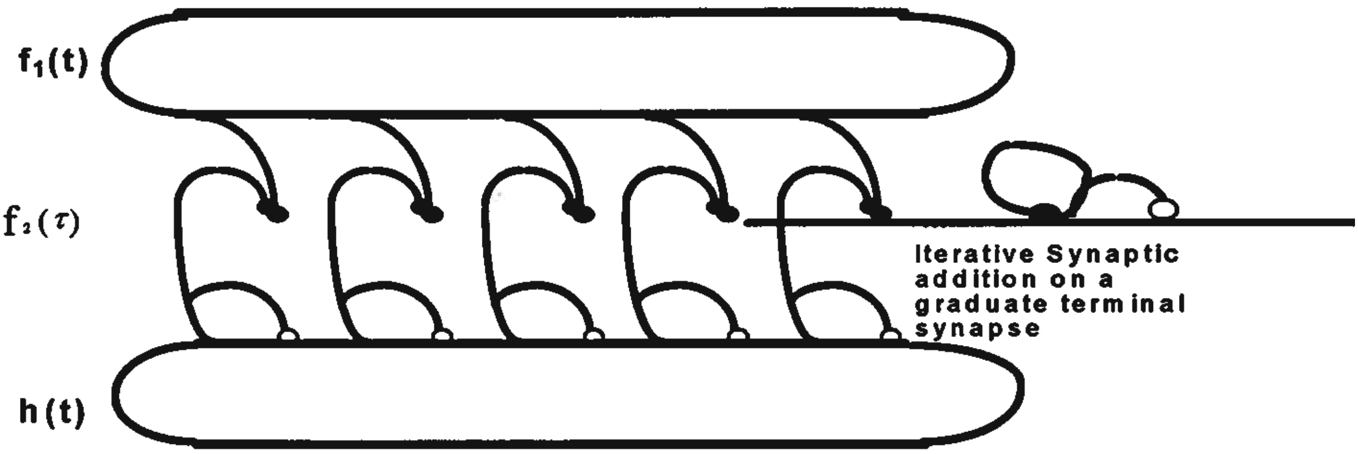

Figure 1- Convolution is represented using an iterative addition a number of times specified by a counter which determines the occurrence of pre-synaptic facilitation.

Logical functions were also represented in dendritic formal networks using synaptic interaction and a spatio-temporal distribution along dendro-dendritic networks. In both finite difference representation of signals and in computations as well as in the implementation of logical functions the approach required cohincidence interaction between synapses involving successive graduate signals which were undergoing spatial displacements. This spatio-temporal distributed computation was significantly different from the integrative model of (Hodgkin and Huxley, 1952).

Cell body synaptic interactions which would not attain the cell body threshold for action potentials was also examined leading to the concept of threshold synaptic computation and information processing in local and sub-neural circuits. Namely together with this approach concerning synaptic computation below the threshold for action potentials the computational possibilities of the second and third messenger systems and their interaction with the first system of neuro-transmission were also examined.

Using a combination of the three approaches it was then developed an hypothesis concerning the atribution of an hybrid character to neural messages. Besides carrying information about the operands on which synaptic dendritic and cell body operators would perform their computations it was hipothetized that afferent messages might also carry information which using the second and third system messengers would program in the strict sense the synaptic receptors allowing the implementation of sequences of operations according with a program involving the "routing" of messages to cell body and dendritic sites on which arithmetic as well as control operations would be implemented allowing a proper sequencing and hierarchyzation of operations. This view corresponds in fact to conceive a single neuron as if it was a network involving the second and third messenger routes together with relevant synaptic computation. All those processes would occur below the cell body threshold for action potentials. Furthermore messages would suffer a progressive control of their propagation to dendritic sites where subroutine operations would be performed. These control operations, facilitation or else inhibition might allow the substitution of a given building block of a program by other building blocks. These changes would imply a modification of program in its sequences and subroutines.

In this view programming messages would produce the representation of relationships defined over data and functions as well as their transformations. High level symbolic processes would be identified through their dimensional and referential aspects as well as through the characterisation of knowledge about relational structures included in the knowledge architecture of the system. Symbolic rules would be identified by their denotation and its meaning would be interpreted as some form of program. A further relevant remark is that the time structure and relationships which are required imply the hypothesis of time operations with a granular time and peculiar dimensional characteristics as well as a not linear or paralell or interewoven character which give to the time concept a role different from the linear parametric characteristics of physical time. Furthermore time operators require annihilation and creation of operational characteristics making signals become available or on the contrary making signals to fade out.

Decoding Operations

The encoding procedure for functions has been examined through the consideration of the role of synaptic interaction between the first system of neurotransmission and, on the other hand the second and third systems of messengers. These systems might encode the components of logical functions within the context of sub-threshold synaptic computation in the cell body and dendrites of neurons. That is, programming messages might implement arithmetic operations, control instructions, the organization of computational components and their ordering in adequate sequential, parallel or inter oven form.

On the other hand in a different computational compartment of sub-threshold synaptic operatium messages conveying logical or other functions would be decoded, identified and utilized. That would be a fundamental feature in pattern identification and processing in perceptive as well as in cognitive and decision making operations essential for adaptive behaviour structures. The most relevant consequence of this approach is to produce a self reflexive representation of the processes which are occurring within a neural network.

Our dendro-dendritic approach together with the concept subthreshold synaptic computation and changes of computational architecture introduced through heterosynaptic structures of programming interactions leads to higher order analog computation in the context of unbounded exponential computation. Polynomial type computation will introduce limits to the possibility of higher order programs and use of symbolic rules which will be dealt with in another place.