

A SHORT AND PERSONAL STORY OF SUZANNE TYC-DUMONT IN THE SCIENTIFIC CONTEXT OF THE TIME

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INTRODUCTION

The Symposium “The Functional Architecture of the Brain: from Dendrites to Networks” held in Marseille on may 4 and 5, 2006 wants to honour half century of scientific work in neurosciences of Suzanne Tyč Dumont, PhD of University of Geneva and Docteurès Science of University of Paris. Very young, during her University studies in Geneva she was assistant of Professor Guyenot in comparative zoology and genetics and of Professor K. Ponse in endocrinology. Then in London she worked with Professor G.W. Harris in neuroendocrinology, there she gained a life interest for Neurophysiology. In fact, following this last research experience she entered and still is in the field of Neurosciences. Starting as “Institut National d’Hygiène” fellow in Paris on 1956, she then entered permanently the “Centre National de la Recherche Scientifique” (CNRS) of which she is now Emeritus Director of Research. In Paris she has been Professor Paul Dell’s (98) pupil and collaborator for several years. From him she learned the early neurophysiology, the rigorous and imaginative reasoning, yet the scientific enthusiasm. In his laboratory she also benefited of the great experience of Doctor Marthe Bonvallet and Professor André Hugelin. In 1978 she succeeded Professor Dell at the direction of the laboratory of Neurobiology of the “Institut National de la Santé et de la Recherche Medicale” (INSERM U6) in Marseille, where she later created the Laboratory of “Neurocybernetique Cellulaire” of the CNRS. Among the scientific personalities that she met we must remember Hsiang-Tung Chang. We will see how he might have influenced the progression of her work.

During her scientific life she introduced to the experimental method and to thinking science students, young researchers as well as all ages collaborators, French and foreigners. All of them have expressed remarkable good opinions on her scientific work and leadership. They also emphasized her non conformistic attitude toward research and her pleasure in doing science. One of her collaborators has qualified her work as “the leftist physiology”, i.e. “the readiness to consider seriously data which did not exactly fit with the expected results”; others has declared learning from her “la satisfaction que peut apporter la contestation des dogmes scientifiques” or “elle a fait en sorte que la recherche soit un vrai plaisir. On a parfois galéré, mais on s’est

régalé grâce à elle”; and “elle a su former et animer une équipe au sein de laquelle l’amitié comptait autant que la performance et qui a su se serrer les coudes”. Finally a sentence of an unknown author circulated in her laboratory during the coffee break: “Madame Suzanne fait la révolution dans la sérénité”.

This symposium collects a series of conferences given by the former students, collaborators and friends of Suzanne Tyč-Dumont and is dedicated to her as witness of how she has enlightened their scientific work in several aspects of the functional architecture of the brain, from dendrites to networks. However, in order to chronologically summarize her own researches in neuroscience, it would be more appropriate to say “From networks to dendrites” since she started her career trying to understand how the reticular formation influences and regulates simple networks and landed in trying to understand how the dendrites of a single neuron process the incoming information. We will briefly comment on the scientific approach and accomplishments of the more outstanding researches performed by Suzanne Tyč-Dumont. We will place her work on the scientific and historical context of the time.

*I PERIOD: THE FUNCTION OF THE ACTIVATING RETICULAR
FORMATION: THE “MISE EN CONDITION” OF THE SENSORY
MOTOR SYSTEMS*

This group of researches was performed by Suzanne Tyč Dumont on the late 50th and the early 60th, it has been the subject of several publications (25-28, 67-69) in addition to the thesis presented to obtain the degree of “Docteur ès sciences” in 1964 (96). Dell’s laboratory was located in the “Centre Psychiatrique Sainte Anne” and the 50th were the years of the psychiatric revolution during which neurosurgery, electroshock and strait jacket were replaced by the psychopharmacology. They were also the years of the Algerian war and of the Algerian independence. In St Anne the researchers, particularly the youngest like S. Tyč-Dumont, were actively participating to the scientific and political events.

The scientific context of those years was very much oriented toward the study of the reticular formation, a study in which many scientists were involved. To illustrate this reticular era we have to remind briefly how developed the researches. Early anatomopathological observations, largely mentioned by Tyč Dumont (96), suggested that the mesencephalic brainstem structures which we can now identify as reticular, could be responsible for the sleep function. However, it was not before the electroencephalographic (EEG) machine was available to clinicians and neurophysiologists that the sleep and wakefulness states could be easily monitored in man as in animals (Berger 4; Rheinberger and Jasper, 1927). In the 30th, Bremer and his associates (10-13) recycled the Sherringtonian decerebration by transecting the brainstem at different antero-posterior levels with no loss of substance so that EEG activity could be recorded in the intact anterior part of the brain. Needless to remind the permanent sleeping “cerveau isolé” and the alternating sleep and wakefulness “encephale isolé” preparations largely used during the following several decades of

brain research. In the late 40th, the new golden era of the reticular formation opened with the work of Magoun and Rhines (83, 93) showing that it could be distinguished geographically as ascending (towards the cortex) and descending (towards the spinal cord) and functionally as facilitatory and inhibitory structures. The discovery of the function of the ascending reticular system, then called activating reticular formation, was published in 1949 by Moruzzi and Magoun (88, 80): a mesencephalic reticular stimulation evokes low voltage fast EEG activity and wake up the animal.

In the following years, an incredible amount of researches and symposia (see 81, 82, 32, 86, 87) were done in trying to integrate ascending and descending reticular functions. It was shown that the activating reticular system was tonically active to maintain wakefulness, and that it was collecting all kind of sensory inputs converging on single reticular units with neither clear functional nor clear geographic selectivity (14, 85, see 87) to maintain this tonic activity (see 87). Thus sleep was supposed to result from a reticular deactivation (21). But the activating reticular system was also shown to have an autonomous arousing activity at least partially independent of its sensory input while sleep would be precipitated by an active process of other part of the reticular system (3, 5, 79). A new collection of reticular input was also started by the Dell's group showing additional convergence from the vegetative system (22, 6), thereby participating to the "homeostasie réticulaire" (see 20). Other important aspects concern the reticular influence on motor reflex, on specific sensory systems, perception, habituation (42, 53, see 54, 66), consciousness (see 86). Finally, the description by Dement (23) of the periodical phase of sleep characterized by activated EEG activity, rapid eye movement and dreaming oriented another approach of the reticular research (see 91).

Perhaps the widespread reticular researches are better described humoristically as the "yelling reaction" (YR) by G. Percec (90), a famous French writer: "Since that time, numerous observations have been made that have tried to decipher the tangling puzzle as well as the puzzling tangle of the afferent and/or the efferent sides of the YR and led to the rather chaotic involvement of numberless structures and paths: trigeminal, bitrigeminal, quadrigeminal, supra-, infra-, and inter-trigeminal afferents have been likely pointed out as well as macular, saccular, utricular, ventricular, monocular, binocular, triocular, auditive and digestive inputs. Spinothalamic, rubrospinal, nigro-striatal, reticular ¹, hypothalamic, mesolimbic and cerebellar pathways have been vainly searched out for a tentative explanation of the YR organization and almost every part of the somesthetic, motor, commissural and associative cortices have been found responsible for the progressive building-up of the response although, up-to-now, no decisive demonstration of both the input and output of the YR programming has been convincingly advanced".

Therefore, at the time Suzanne Tyč-Dumont joined the reticular teams, the question was: what else can be done? She explained: "à mon sens il devait être plus facile de comprendre la fonction réticulaire en analysant les effet de la mise en jeu des sys-

¹ For brevity we report here only reference by Pompeiano, O., (91a) who report details about the reticular formation.

tèmes diffus sur les systèmes sensori-moteurs spécifiques. Ce sont leurs interactions qui doivent engendrer ce que Pieron, dès 1912 avait nommé la réactivité critique, c'est à dire la capacité d'élaborer des réactions appropriées à un complexe donné de circonstances". To do that she has tested the sensory (visual and acoustic) messages which independently reaches both the primary cortices and the activating reticular formation and the network of two cranial motor reflexes, the mouth opening and the vestibulo-ocular reflexes. The conditioning stimulus was the arousal reaction elicited by electrical or sensory activation of the mesencephalic reticular formation. The deal was to understand where and how the activating reticular formation was impinging upon the test networks and whether the ascending arousing signals had any meaning to the sensory and the motor functions.

On the motor side, the reticular arousal directly increases the excitability of the motoneurons. The reflexes however were not necessarily facilitated, while the vestibulo-ocular reflex was facilitated, the opening mouth was definitely reduced, both responses being evoked by the reticular or sensory stimulation as function of the degree of the reticular activation (Fig. 1). On the sensory side of the reflex, the reticular control also act peripherally, so that the reticular formation would be like a gate which regulate, admit or not admit the entry of the sensory message into the central nervous system, an idea which later will be largely exploited to explain the control of pain (84). However, this peripheral control affects the first interneurons of the polysynaptic reflexes, not the receptors nor the ganglionic cells. Interestingly, the very small muscles of the middle ear, stapedius and tensor tympani, are also facilitated, the result being a reduction of the very peripheral input of the acoustic signals with no influence on the acoustic receptors. This last result anticipate, in a way what we now know, that not only the somatosensory (42), but also the other receptor types are regulated by their own specific centrifugal system as first described by Galifret (31) in the visual system of the pigeon. Finally, the reticular arousal is independently facilitatory of the sensory signals at higher level, the thalamo-cortical (Fig. 2).

Some of the results were apparently contradictory: the facilitation of the motoneurons does not respect the principle of the reciprocal innervation and acts on both flexor and extensor motoneurons; a given network, as that of the mouth opening reflex receive from the reticular formation inhibitory signal on the sensory side and facilitatory on the motor side; on the sensory side, the arousal evoking stimulus may evoke opposite effects, either facilitatory or inhibitory; finally a tricking problem could be the respective latencies of the responses, since the conditioning reticular influence comes later, after the test response that has to be regulated is over.

Nevertheless, for the author there is no such contradiction insofar as one consider that the activation of the reticular system produce variable non unidirectional effect. In fact other observations rule out those contradictions. The principle of the reciprocal innervation is re-established (Fig. 3) and is presumably the net-result, at the central level, of the different influences imposed at different sites of regulation. The reticular inhibition of the sensory input of a reflex, might overwhelm the facilitation of the motoneurons of the same reflex. The facilitatory response of the sensory message at higher levels, is gradual (Fig. 2) and last only the first 300 msec of

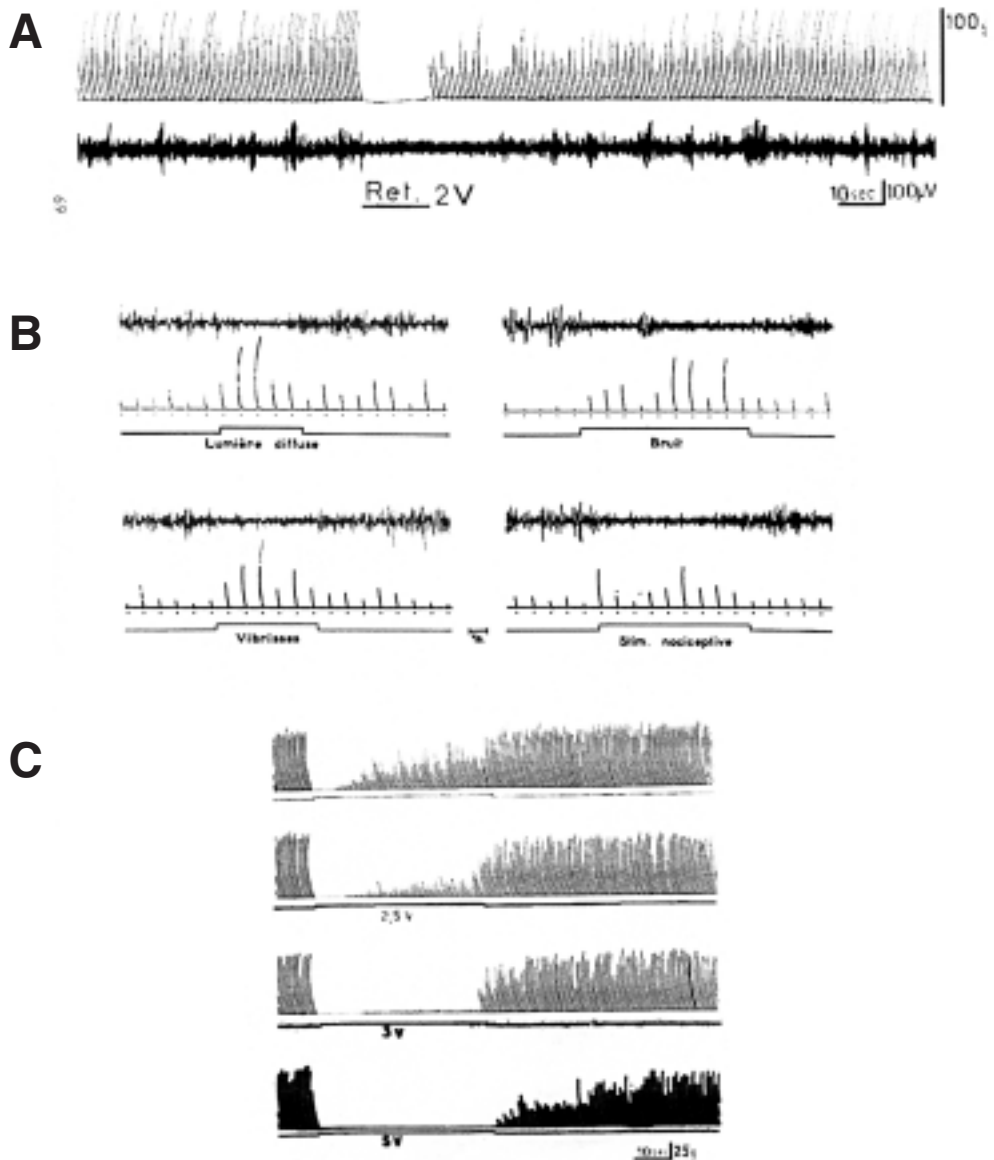


Fig. 1 - *The reticular arousal modify the amplitude of the motor reflexes.*

(A) Simultaneous modification (suppression) of the opening mouth reflex and of the cortical activity (desynchronization) during arousal evoked by mesencephalic reticular stimulation (Ret) at 300 c/s, 2V during 15 seconds. Encéphale isolé cat; isometric contraction of the digastric muscle by excitation of the ipsilateral side of the tongue (first line); EEG records (second line).

(B) Facilitation of the arousal reaction on the vestibulo-ocular reflex. Encéphale isolé cat, flaxedil; EEG records (first line); vestibulo-ocular reflex (second line); various arousing stimuli (third line).

(C) Modifications of the degree of inhibition of the opening mouth reflex as function of the reticular excitation. Contraction of the digastric muscle as in A (first line); reticular stimulation as in A but with increasing intensities (second line).

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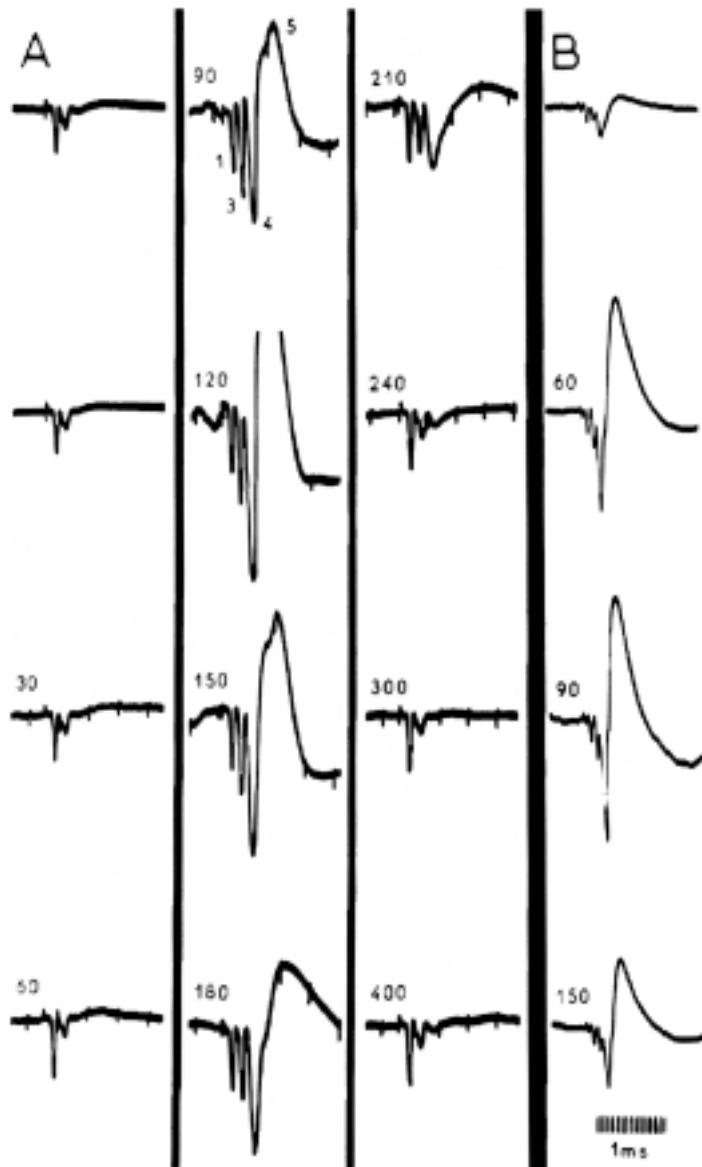


Fig. 2 - *The reticular arousal facilitates the cortical sensory responses.*

A. Facilitation of the visual evoked responses in the cortex during the first 300 msec of an arousal reaction. Encéphale isolé cat, flaxédil; monopolar record (on the visual cortex surface) of the potentials evoked by electric stimulation of the optic chiasma every 3 seconds (0.1 ms, 1.5 V). The arousal reaction started after the first two control responses. The following responses were recorded during 10 identical reticular stimulations delivered every 10 minutes. The visual potential was evoked at increasing times after the beginning of the arousal stimulation as indicated in the figure in ms.

B. An arousal reaction was produced by a clic acoustic stimulation. From top to bottom: a visual (as in A) control response, then three facilitated visual responses obtained 50, 90 and 150 ms after the acoustic stimulation.

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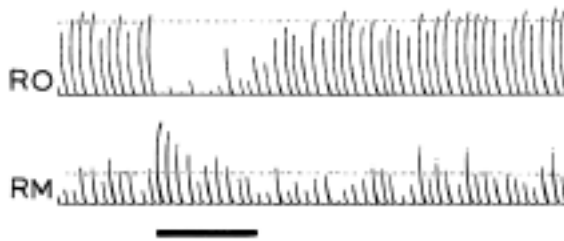


Fig. 3 - *Reciprocal effect of the reticular arousal on antagonistic reflexes.*

Opposite effect evoked by an arousal réaction on the polysynaptic opening mouth reflex and on the monosynaptic masseter reflex. Encéphale isolé cat, flaxedil; recording the isometric contraction of the digastric muscle (RO) and of the masseter muscle (RM) during the mesencephalic reticular stimulation (300/s, 3.4V) indicated by a thick horizontal line. The interrupted line show the amplitude of 10 control averaged responses. Note the simultaneous inhibition of RO and the facilitation of RM. From 96.

the arousal reaction; the inhibition of a polysynaptic reflex is also gradual and follow the changes of intensity of the arousal (Fig. 1C).

It is clear however that the mechanisms underlying the variabilities of the results obtained in such complex systems could not be at the time completely explained, they could only be interpreted. In fact very wisely the author interprete the interaction occurring between the “système diffus”, the activating reticular formation having multiple entry, multiple relays and long latency of activation, and the “system discret”, any specific sensory motor network, having a single entry, few relays and being activated with much shorter latency: “Pour comprendre cette interaction, il faudra considerer non pas la latence du signal parcourant le systèm discret par rapport à celle de la mise en jeu du système diffus, mais plutôt considerer leurs temps de latence respectives par rapport à celui de la réaction psychomotrice qui en résulte. Il devient alors évident que si la réaction réticulaire est lente vis à vis des transmissions intérieur des systèmes discrets, elle a cependant le temps d’intervenir avant la réaction psychomotrice. Nous concluons en proposant d’attribuer au système réticulaire activateur “une fonction dynamique de mise en condition” (96). S. Tyč-Dumont presented her reticular researches at the IBRO meeting in Pisa in 1961 (see 20) and at the meeting of La Havana in 1965 (97).

II PERIOD: TOWARD ELEMENTARY MECHANISMS

Of particular interest was the meeting in Cuba (97) where she met H.T. Chang for the first time. Chang was born in 1907, graduated from the University of Beijing and during the world war II went to USA where he worked in research for more than 10 years. Studying the cortical dendritic potentials, he was the first to hypothesize an active function of the dendrites. His idea was that the axo-somatic synapses provide a rigorous and fast transmission for reflex movements whereas the axo-dendritic synapse would mediate higher nervous activities like perception, consciousness, intelligence (16, 17). During that meeting he extensively explained to her his ideas and projects.

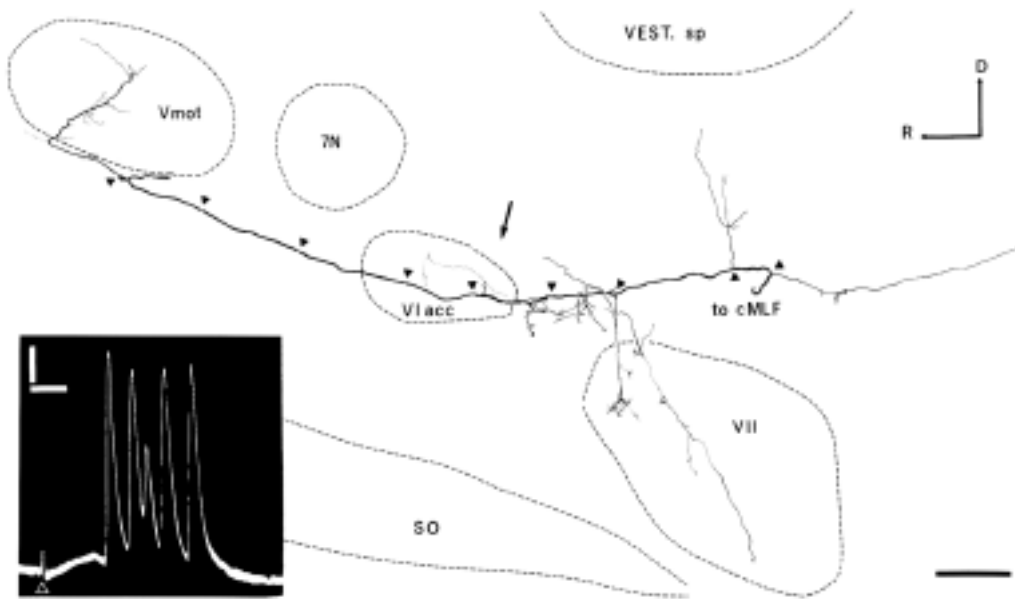


Fig. 4 - *Histological reconstruction of an entire trigeminal axon in the sagittal plane.*

The axon was identified by its intracellular response to stimulation of the vibrissae (lower left inset), then intracellularly injected with horseradish peroxidase. Note the wide distribution of the axonal branches to the brainstem motoneuron pools. V mot: motor trigeminal nucleus; 7n: facial nerve; VI acc: accessory abducens nucleus; VII: facial nucleus; cMLF contralateral medial longitudinal fasciculus; SO: superior oliva; VEST. sp: spinal vestibular nucleus; black triangles: Ranvier nodes; calibration 100 μ ; D: dorsal, R: rostral. Modified from 30.

S. Tyč-Dumont started a new laboratory with A. Hugelin in the new “Centre Hospitalo Universitaire” in the Saint Antoine hospital in Paris. After the researches on the reticular formation and because of the hypothesis formulated about its complex functions, she oriented the investigations toward the mechanisms of neuronal interaction inside complex systems, namely the synaptic transmission as revealed by intracellular recordings. Her choice of investigations has been the oculomotor system, focalizing on a simple trineuronal network, the vestibulo-ocular reflex of which she analyzed the intrinsic synaptic mechanisms including the nystagmic neurogenesis and its input and output relationships with other brain structures. For more informations about this work which lasted several Years, we send the reader to her publications (8, 33-37, 43-49, 52, 56-60, 63-65) and to the monograph of Horcholle Bossavit and Tyč Dumont (61)

At that time, for obvious technical reasons, intracellular neural recording and staining were only applied to the invertebrate neurons never to mammals. The first intracellular stainings in mammals were performed by Jankowska and Lindstrom (70) in the spinal cord and by Tyč-Dumont and her collaborators in the brain-stem neurons (35, 30). The method consisted of electrophysiologically characterize and injecting with a dye a neuron *in vivo*, than histologically reconstructing the same

whole stained neuron isolated among the neighbouring cells. One of this is illustrated in Fig. 4. She also coupled the electrophysiological method to the available sophisticated neuroanatomical (24, 7) and neurochemical (50, 51, 29) techniques. Parallel to the increasing complexity of the work, she build up her own group of collaborator and other external collaborative relations (1, 2, 15, 38, 62). Very special was the methodological collaboration with Jankowska in the laboratory of Lundberg in Göteborg where the mechanic shop developed a highly performant precision stereotaxic apparatus, the “transvertex”, for intracellular recording in brain-stem and medulla.

It is during these years of intense scientific activity that she applied to get the direction of the laboratory of neuroscience with the precious help of Georges Percé. Percé (1936-1982) is a very well known author whose contribution to the French literature is now largely recognized. For many years he was in charge of the library and of the editorial activities of the laboratory where she was working. His strong and pleasant personality has left permanent marks. The INSERM assigned to her the direction of a “Unité de recherche” in Marseille.

III PERIOD: THE DENDRITIC SPACE

As said before, one of the pioneer work done by Suzanne Tyč-Dumont was to adapt to the mammalian central nervous system the method of electrophysiologically characterize and injecting with a dye a neuron *in vivo*. The investigations had disclosed not only the variety of morphological features in a functionally homogeneous set of neurons, but also the variety of their neuritic extension which have been observed to overgrow the expected location. This is particularly impressing for the dendritic arborization which has the important function to receive and presumably to choose most of the input of the neuron. However, at that time, as the author pointed out (78), a strong interest had developed for the results that could be preferentially obtained from a bold neuron with a single point recording from the soma or from a piece of membrane. On the contrary, the idea of looking at the activity of such a widespread tentacular distribution displayed by a dendritic arborization was neglected in both the electrophysiological and the theoretical approaches. While the electrophysiological studies are very much dependent on the technical constraints, the simulation studies do not have such constraints. Nevertheless, Tyč-Dumont reoriented her investigations toward the studies of the dendritic space. For dendritic space is ment the activity displayed in all the branches of the entire arborization simultaneously. The challenge was to realize a general map of the whole neuron in which to view and study the space dependent activity as much as the time dependent activity of the dendrites. For that she developed completely new tools and, in the same time, used simulation methodes.

The first step was to reconstruct tridimensionally the dendritic arborization of the injected brain-stem motoneurons with a computer assisted microscope implemented by P. Gogan (8, 95). It must be noticed that the reconstruction was done at very high

resolution (1 micrometer), higher than that performed by others. With this material the dendritic geometry could be related to the electrotonic structure using the simulation method (8, 9, 55, 72). Curiously, at the same time, a physicist from the former Soviet Union was independently studying mathematical methods of branching axons and dendrites (74) and developed a software program for studies of synaptic interactions in anatomically and biophysically complex neurons. A young physicist student of Korogod, Ira Kopisova, managed to travel to Cambridge to present their prototype software KRONA at the physiological society meeting to which Tyč-Dumont was also attending. The two teams, from Dniepropetrovsk and Marseille met there and it was the beginning of a long fruitful collaboration which still lasts. The first simulation was performed by combining the 3D geometry of stained motoneurons acquired in Marseille with the biophysical membrane parameters computed in KRONA (75, 76). It was found that under steady state the dendritic arborization of the motoneurons has a stochastic electrotonic organization which depends on its local geometry, namely on the change of diameter of the dendritic tree and on the pattern of its branching points (9).

In a further step of the simulation, the motoneuron model included a soma emitting bursts of action potentials. It was observed that the back invasion of the dendrites from the somatic activity elicited variable changes, transient and geometry dependent, of the dendritic polarization (76). It was suggested that the back invasion acts as a retro-control, the function of which would be to regulate the access of the incoming input to the neuron. In fact, further simulation studies have shown that the charge transfert effectiveness along the dendritic tree is much higher in a resting neuron than in a neuron highly excited by intense synaptic activity (77, 78). In other words, at rest the whole dendritic tree will be equally efficient in transferring current to the soma therefore lacking spatial discrimination. On the contrary, an already excited neuron will develop a variable spatial distribution of the efficiency, such as to functionally switch off, say disconnect, the distal branches, and therefore their input connections, from the soma. Thus it appears that the pattern of effectiveness of the dendritic space is not steadily dependent on the geometry, it is also dynamically bounded to its activity (77) (Fig. 5).

As soon as solid results were obtained about the dendritic space, S. Tyč-Dumont went to present the data to the Shanghai workshop in neurobiology organized by IBRO, knowing that H.T. Chang would be at the meeting. Chang dream to build in Shanghai the first laboratory of tissue culture in order to have an easier approach to the dendritic hypothesis vanished with the cultural revolution, he was thus very interested on her work.

Parallel to and guided by the results obtained with the simulation work, on the assumption that theoretical results must be verified by an adapted experiment, Tyč-Dumont and Gogan developed new experimental tools to study the spatial dimension of dendritic neural activities. The goal was "to explore the space domain of the neuronal excitation on two scale of observations simultaneously by imaging the soma and the neurites of single neurons at high spatial resolution" (40, 39). This experiment could be done thanks to a very sophisticated optical setup capable of

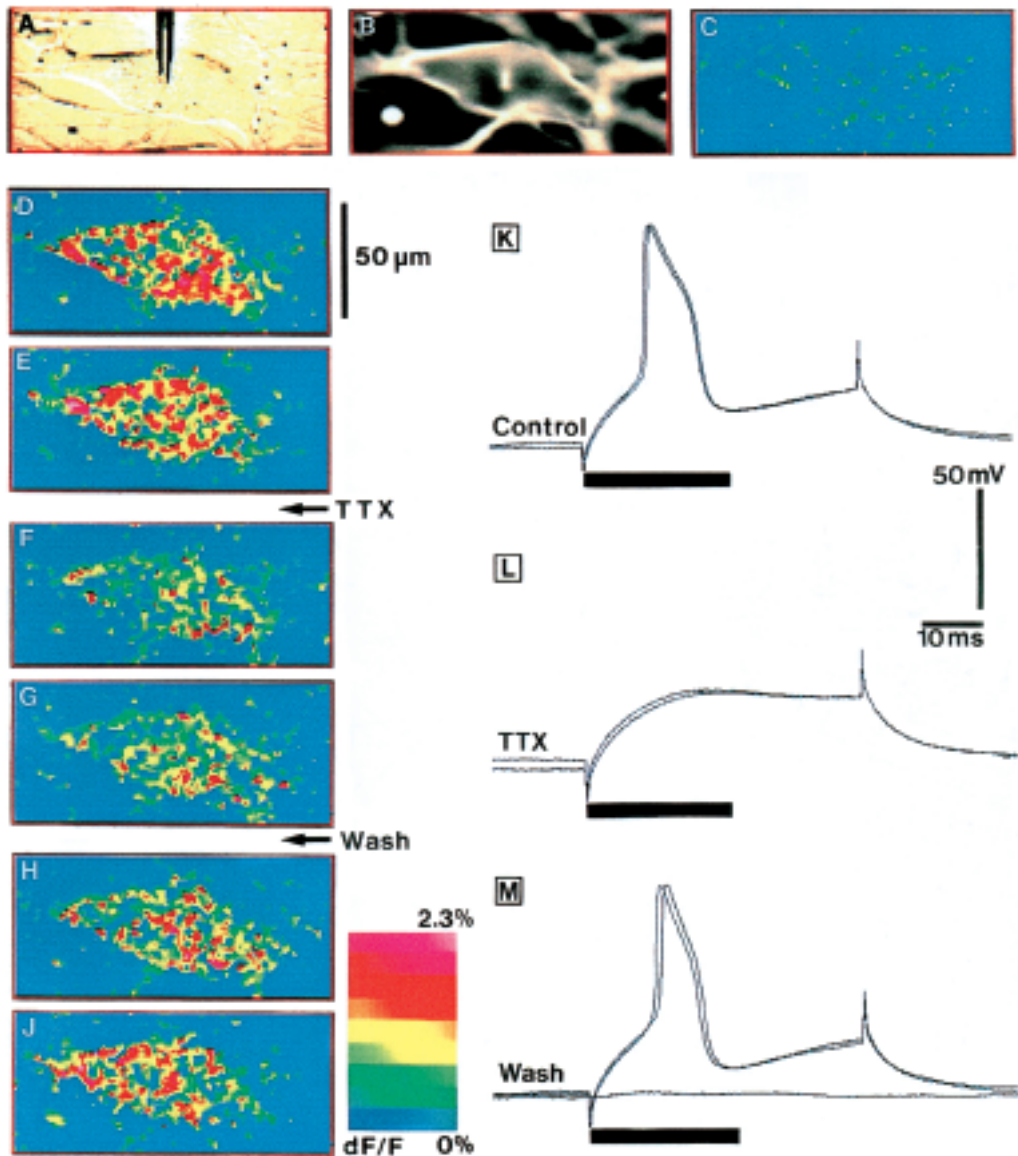


Fig. 5 - Effect of TTX blockage of fast sodium conductances on spatial patterns of depolarized sites. (A) CCD image of an impaled neuron with DIC optics. (B) fluorescence image of the same field after 10 min staining with a voltage sensitive dye (RH237); (C) processed image of the same field with the neuron at rest; (D-E) two processed images when the neuron is excited by an intracellular current pulse (0.5 nA) delivered at 20 sec interval, recorded in synchrony of the superimposed potentials shown in K; (F-G) Two successive processed images synchronized to the superimposed intracellular recordings shown in L after application of TTX in the bath. The fast sodium conductances are blocked and the number of depolarized sites greatly decreased; (H-J) two successive processed images synchronized to the intracellular recordings shown in M after washing the TTX from the bath. Black bars under the recordings in K, L, M indicate the open time of the CCD shutter. Modified from 39.

very high spatial resolution of image acquisition and processing. The material was an astronomical camera and dissociated neurons raised in culture and providing a monolayer of cells directly accessible to the image acquisition and to the electrophysiological manipulation. The activity of the cultured neurons was monitored by a fluorescent voltage sensitive dye. Conventional patch microelectrodes were used to record the neuronal activity, to control the membrane potential and to consistently evoke spike discharges. The experimental design was intended to visualize the map of the whole neuron, soma and neurites to detect the spatial distribution of the membrane polarization during excitation.

The work started with culture of simple neurons, the nodose ganglionic cells (39, 94). The first observation was that during an action potential generated in the soma, the map of the neuronal membrane (soma and dendrites) displays increased fluorescence. The increase is not uniform, is made of numerous patches of various sizes and intensities indicating different degrees of depolarization. While these patches are unevenly distributed, the distribution definitely changes when a new action potential is generated at the soma. The observed depolarizations were the result of the activation of the voltage-dependent sodium channels since the fluorescence was greatly decreased by tetrodotoxin application to the cultured cells (Fig. 6). Thus, the striking result is that identical action potentials activate different set of voltage dependent Na channels.

From this experimental evidence the authors raised several questions which can be summarized as follows: how the channels responsible for the generation of action potentials are distributed in the membrane, uniformly or clustered? How and where are they activated during successive action potentials? These questions were solved combining the results obtained from the imaging experiments on the nodose ganglionic cells with a mathematical model of the membrane (94). Superimposed images of sequential action potentials revealed that the voltage-dependent sodium channels had a preferential membrane distribution in clusters. Then the simulation model confirmed that the channels have indeed a definite spatial distribution in cluster and showed in addition that the variability of the images generated by successive action potentials results from the opening of the channels stochastically in the cluster. This work was the first attempt to investigate the spatial organization of ion channels in the membrane during excitation.

With these new results, once again S. Tyč-Dumont rushed toward Shanghai in 1995 to the meeting of asian physiology to meet Chang. Already aged of 88, he discussed her work with great satisfaction as if it would have been his own work.

A more advanced study using the same methodological approach was done on cultures of dissociated hippocampal cells, presumably the pyramidal neurons, therefore changing from simple ganglionic cells to complex neurons with well developed dendritic arborization. The results obtained in the hippocampal dendrites were homologous to those observed in the soma of the ganglionic cells: "a mosaic of depolarized sites changing site and intensity from one trial to another" (95). Moreover, a one way connection between two cultured neurons could be detected, the stimulation of one neuron evoking an action potential in the second one. The site

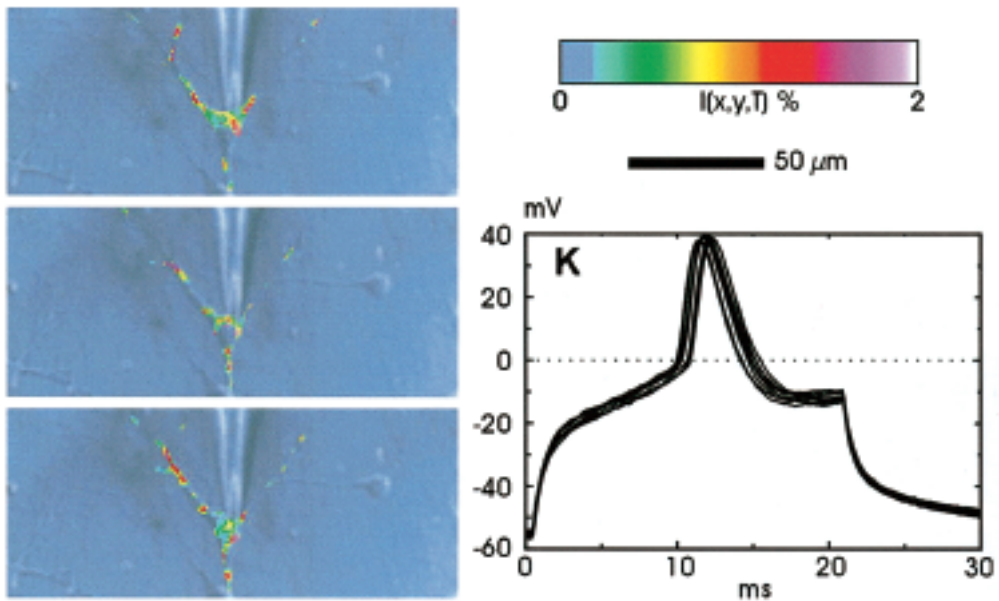


Fig. 6 - Trial-to-trial variability in spatial pattern of a live neuron.

Three processed images showing the relative changes in fluorescence $I(x,y,T)$ produced in one hippocampal neuron by three successive similar action potentials shown superimposed in K. The neuron was stimulated and recorded through a microelectrode inserted in the soma. Color scale: $I(x,y,T)$ in %. The exposure time was 30 ms as indicated by the abscissae in K and start at $t=0$ ms. Modified from 95.

of the presumed synaptic contact was identified on a dendrite by the local lightening in patches of membrane with the fluorescent dye on stimulation of the presynaptic neuron (Fig. 7).

Here again the authors complement the imaging experiments with the construction of a model simulating what was observed in the cultured neurons including amplitude and duration of the action potentials and the changes in the spatial map (95). The new approaches, at this phase of the image investigations, was to introduce the synaptically induced action potentials in both, the deterministic and the stochastic model. It was shown that the probability for a synaptic activity to evoke a spike depends on the stochastic activity of the channels, the geometry of the dendrites, the position of the channel clusters in the dendritic membrane and, of course, on the synaptic strength.

The conclusions of the authors (95) are that the neuronal membrane is a mosaic of dynamic domains randomly active in space and time. They introduced the notion of a “spatio-temporal flicker” and speculated that the dynamic of input-output function are not only conditioned by the synaptic input but also by the intrinsic stochastic spatial variability of the membrane which thus increases the repertoire of the neuronal processing. This new idea seems to complement recently theoretical work explaining the neuron as a mosaic of proteins (71, 41)

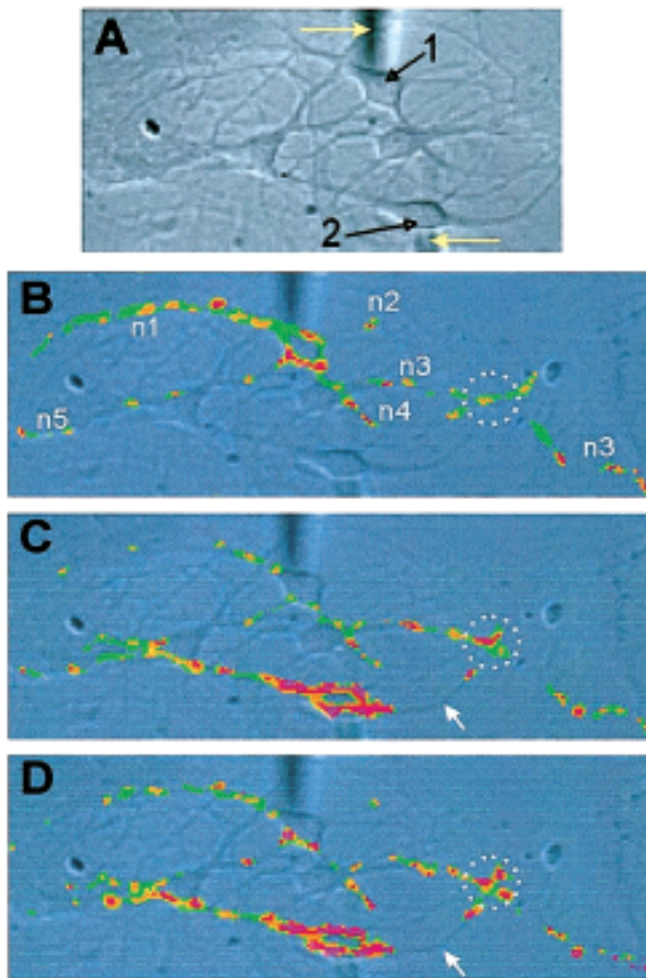


Fig. 7 - *Spatial pattern obtained in two live neurons by direct and synaptic stimulation.*

(A) image of the microscopic field containing four hippocampal neurons in culture using differential interference contrast optics. One microelectrode impaled neuron 1 and another neuron 2 (yellow arrows).

(B) Processed image $I(x,y,T)$ obtained after averaging ten successive trials when only neuron one was directly stimulated, producing action potentials. The neurites of neuron 1 were labeled n1-n5. Highly depolarized sites in the soma and neurites n1-n5 reveal the position of Na^+ channel clusters activated during the action potentials. Non significant signals were detected in the other neurons, indicating that neuron 1 send no functional connections to them.

(C) Processed image $I(x,y,T)$ obtained after averaging 10 trials when only neuron 2 was directly stimulated producing action potentials which triggered EPSPs and no action potentials in neuron 1 indicating a synaptic connection between neuron 2 and 1. Depolarized sites were obtained in neuron 2 and also in n3 and n4 of neuron 1 which displayed an almost silent soma.

(D) Processed image $I(x,y,T)$ obtained after averaging four trials when direct stimulation of neuron 2 produced action potentials which triggered action potentials in neuron 1. n3 and n4 of neuron 1 are ignited as in C, but now are also ignited soma sites and other neurites sites as in B.

Color scale: $I(x,y,T)$ in %. Dotted circles in B, C, D: zone of presumed synaptic contact from neuron 2 to neuron 1. Exposure time was 30 ms.

Modified from 95.

Unfortunately this outstanding work full of promises could not be taken further since, at the compelling retirement of Susanne Tyč-Dumont, the CNRS chose to change the scientific orientation of the laboratory. Nevertheless we believe that these ideas will have interesting future developments. And in fact, the new promises have started already with the work of Palmer and Stuart (89).

CONCLUSIONS

The conclusions coming out of this article concern the progression of the work of Tyč-Dumont from networks to dendrites. The very novel results acquired through the researches done on the dendritic space have revealed that the autoctonous activity of a neuron, say the electrotonic properties and the back invasion by the somatic action potentials, prepare to and modify the way in which a neuron reacts to new incoming activity. We are tempted to say that this cellular model is analogous to that formulated about the interaction between the activity of the “diffus” activating reticular system and the “discret” receiving network described back in the early years of her work (96). Both could explain why the same controlling system might have either positive (facilitatory) or negative (inhibitory) influence and why it will be more adapted if it comes later after the controlled system. In both cases the interaction will be a “mise en condition” based on the concept of plasticity which is an intrinsic property of the nervous system.

We like also to say a few words on behalf of the history of science. In 1995, when S. Tyč-Dumont went to Shanghai, H.T. Chang gave her a book concerning his own scientific life (18). The book was translated to French by C. Gipoulon (Université Paris VII) and adapted by G. Horcholle-Bossavit and S. Tyč-Dumont for the history of neuroscience in autobiography (19). How the repeated discussion with him could have influenced the progression of her work we do not know (does she know?). We do believe however that Chang must be considered one of her mentors.

This short review on the scientific career of Suzanne Tyč-Dumont wanted to trace the continuous dialectic progression of a scientific thinking, approach and planification together with her personality in the historical frame of the time, rather than a simple synthesis of her work. We had the pleasure to accomplish this manuscript with her vivid collaboration. She provided documents, interviews, discussions. We also had the help of her collaborators particularly for understanding her leadership.

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