Electron Transfers and Holographic Molecules: Why Neuroscientists Should Take Quantum Phenomena into Consideration

Philippe Anglade*, Yamina Larabi-Godinot[†] and Shigeru Tsuji[‡]

ABSTRACT

Discoveries concerning the neurotransmission mode of the nerve impulse contributed a lot to the development of modern neurosciences. Neurons release chemical agents, such as neurotransmitters and neuromodulators, which bind to receptors of their target cells, enabling, thus, propagation of nerve impulse from cell to cell. In the nervous system, intercellular exchanges of information take place as bindings of ions or molecules to receptor proteins. These bindings induce changes in the conformation of the proteins which can, in this way, integrate and memorize physical and chemical alterations affecting the surrounding neurons. The researches on learning and memory are based on these concepts. However, the revolutionary advances in quantum physics allowed new hypotheses to be addressed in the functioning of the nervous system, particularly in the brain. Indeed, new technologies based on the application of quantum mechanics were recently devised, such as scanning tunneling microscopy and transient absorption spectroscopy. The use of these methods revealed that quantum particles, like electrons, might play so far unknown roles in the biological processes. Thus, electron transfers by tunneling effect have been evidenced between molecules of the photosynthetic and respiratory chains, retina and DNA. Moreover, such biophysical investigations established that proteins could function as holographic media, integrating and recording multiple particles emissions. These data suggest that, in the nervous system, a single molecule might integrate and memorize, in the shape of wave interference figures, a gigantic amount of physical and chemical signals arising from its surrounding medium.

Key Words: nervous system, receptor protein, electron transfers, holographic molecules, quantum memory

DOI Number: 10.14704/nq.2014.12.2.730 **NeuroQuantology 2014; 2: 237-246**

Introduction

In 2008, Shigeru Tsuji, the author of an important achievement in the histochemistry of the cholinergic synapse (Anglade and Larabi-Godinot, 2010), expressed his intent to investigate the active zone of the synapse with the aid of "quantum biology" (electron transfers). Beyond the fact that this denomination is rarely used, "quantum biology" is still not a well-established domain. This probably emphasizes the understandable difficulty for the neurobiologists to take into account the laws of quantum mechanics. In this context, the present paper aims at drawing attention to the urgency for introducing quantum physics in the researches concerning the nerve system, in particular on the neuronal synapses (Tarlaci, 2011).

Today, it is well established that nerve impulse propagates through highly specialized cellular entities, the neurons, considered as the

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 16 January 2014; **Revised:** 19 February 2014;
Accepted: 21 March 2014
***e*ISSN** 1303-5150

functional units of the nervous system. Likewise, it is known that the transmission of nerve signals from the neurons to their target cells is mediated by neurotransmitters which, after being released from the neuronal endings, bind to receptors located on the effector cells. The advances made in neurophysiology and pharmacology during the 20th century are furthermore, based on these fundamental concepts. However, the development of quantum physics gave rise to a revolution in many scientific areas. The laws of quantum mechanics that govern the atomic particles lead to conjecture that transmission and integration of information inside the brain do not only rest on these well-known neuronal concepts. Thus, ideas, which were rejected owing to their erroneous side, may come back into consideration with new significations.

At the end of the 19th century, many neurobiologists did not view the neurons as functional units of the nerve system. The most famous among them was the Italian medical doctor Camillo Golgi, who devised a histological staining of the nervous tissues that marked his epoch (Golgi, 1885). Golgi considered the brain as a diffuse nerve network, according to the "reticular" theory, shared at that time by a lot of scientists. Others, such as the Spanish histologist Santiago Ramon y Cajal, supported – and the future showed them to be right – the "neuronist" theory following which the neurons were entities anatomically separated from each other (Ramon y Cajal, 1906). Golgi assumed that the nerve impulse was propagating inside a network made of the anastomosed fibrilles of the neurons. The Italian histologist considered this network of amalgamated fibers and neurons as a true functional unit. While Cajal was first concerned about the details of his microscopic observations, Golgi was more careful of holding the idea of nervous network rather than defining its histologic basis. And contrary to a current opinion, Golgi hesitated for a long time to express his idea on the anatomical relationship between nerve fibrilles of adjacent neurons (Raviola and Mazarello, 2011). Only late, when he vehemently defended his reticularist theory, he strongly asserted that the fibrilles were amalgamated at their junction sites. Finally, the first observations of the nervous tissue by electron microscope clearly demonstrated that the neurons were separated each other at their junction zone, the synapse, by a gap called "synaptic cleft" (Palade and Palay, 1954 ; De Robertis and Bennett, 1955 ; Robertson, 1956). These data, in agreement with the demonstration of the chemical nature of the nerve transmission (Loewi, 1921) and with the description of the neuromuscular junction (Couteaux, 1947), definitely showed that the "neuronists" were right. The reticularist theory was then definitely forsaken.

However, the recent introduction of the concepts of quantum physics in the neurosciences resulted in new hypotheses about the presence, in the brain, of putative functional entities that were not based on the traditional concept of the neuronal unit (Atmanspacher, 2006). Moreover, recent experimental data on intermolecular transfers of quantum particles, such as electrons, have opened insights on unsuspected intermolecular communications (Gray and Winkler, 2005). Though these assumptions remained to be proved, they suggest that, without questioning the neuron as functional unit in the brain, there might also be unknown communication and integration modes of information, which do not correspond to the well described interactions between the neurons. Thus, the theses of some precursors, such as Pierre Flourens (1863; see below) or Camillo Golgi (1891), came back in a perspective that these authors were, nevertheless, far from conjecturing.

Molecular interactions are based on chemical bonds: a general concept in biology

The discovery of the elementary particles of the matter and the description of their properties has overthrown the understanding of the physical world. Indeed, it was shown that electromagnetic phenomena (light, electric current…) could be divided in finite numbers of elementary quantities of energy, called quanta. These quanta do correspond to matter particles, like photons or electrons. Thus, the electromagnetic phenomena are both waves and corpuscles (Segrè, 2007). These data enabled investigators to precise the structure of atoms and molecules. They showed that electrons were ordered in layers around the atomic nuclei, following discontinuous energy levels. Hence, they could establish that the chemical properties of atoms and molecules were mainly due to the electrons of the peripheral layers, owing to the essential role of these particles in the chemical bonds between atoms. New technological devices followed this revolution,

which induced a renewal of the concepts in biology.

In living organisms, chemical bonds are mainly due to electron exchanges between atoms that constitute ions or molecules. These interactions are composed of elementary reactions: oxidation, when an atom or a molecule donates one or several electrons, and reduction, when an atom or a molecule receives one or several electrons. Organic molecules, like amino acids, proteins or nucleic acids, interact by such oxidation-reductions to form more or less complex assemblies in the cells. Similar intermolecular bindings are the holders of information transfers from one molecule to another. Such information transmission often results in a "conformational" change of these molecular assemblies (Changeux, 1990). The structural modifications of the molecules can lead in turn to their functional alterations. Thus, complex interactions can take place between molecules to regulate the development and survival of the living organisms.

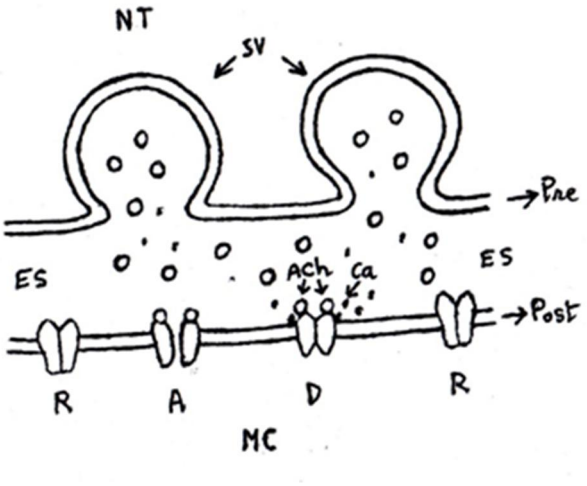

Figure 1. Schematic drawing of the conformational changes of the acetylcholine (ACh) nicotinic receptor of the neuromuscular junction. Synaptic vesicles (sv) of the nerve terminals (NT) of the neuromuscular junction merge with presynaptic membrane (Pre) and release ACh in the extracellular synaptic space (ES). ACh molecules (white circles) bind receptors located on the postsynaptic membrane (Post). This binding induces an alteration in the conformation of the receptor which changes from a resting (R) to an active (A) state. A steady release of ACh leads to a strong discharge of calcium ions (Ca – black dots) in the extracellular synaptic space. Then, Ca ions bind nicotinic receptors to a site different from ACh. The binding of Ca ions evokes a change in the conformation of the receptors which get a desensitized state (D) for which the affinity for ACh is altered. In that case, the desensitized state is the physiological outcome of the concomitant binding of ACh and Ca ions. This state of the receptor molecules corresponds to a local and temporary memory of a strong activity of the surrounding nerve endings. MC: muscle cell.

In the nervous system, specific molecules can receive and integrate information from surrounding cells by their binding sites

The nervous system is characterized by a high specialization of exchange and integration of intermolecular information. This feature has been well described by extensive studies on the nerve transmission at the level of the synapses of the neuromuscular junction (Changeux, 1990). Acetylcholine, the neurotransmitter released from the nerve endings, binds with nicotinic receptors of the muscle cell membrane. The binding takes place between the cationic quaternary ammonium radical of acetylcholine and *pi* electrons of amino-acid residues of the receptor protein (Beene *et al.*, 2002). This association evokes a conformational change of the protein by which a Na+ permeable ion channel opens in the middle of the molecule. The entering of Na+ ions in the muscle cell through the channels induces electrical depolarization of the muscular membrane, responsible for muscle contraction (Changeux, 1990).

The nicotinic receptor of acetylcholine became an important model to study the molecular mechanisms associated with learning (Changeux and Dehaene, 2008). In addition to the binding sites of acetylcholine, this protein is endowed with other sites that can bind, for example, inhibitors of nerve transmission or calcium ions. The binding of such ligands to the receptors can induce a change in the conformation of this protein (for that reason called "allosteric" protein) and, consequently, in its physiological functioning. Thus, after its conformational change due to the binding of acetylcholine, the receptor passes from a resting to an active state. This leads to the opening in the middle of the receptor of a channel by which Na^+ ions enter the muscle cell. On the other hand, a steady stimulation of the receptor by acetylcholine evokes desensitization of the protein that develops a new conformation by which it becomes less sensitive to the neurotransmitter than at resting state. This desensitized state is regulated by electric activity occurring after steady stimulation of the neurotransmitter or by binding of calcium released from active neighboring synapses (Changeux and Edelstein, 2005) (Figure 1). Thus, one receptor can integrate different signals originating from several synapses. In response, this receptor can develop a conformation reflecting, at one given time and

place, both the memory of its proper physiological state and of the activity of the surrounding cells (Changeux and Edelstein, 2005). Computerized models of such multiple integrations taking place on receptors may allow the investigation of the phenomena of signal integration at the level of neuronal networks (Changeux and Edelstein, 2005).

The sensorimotor synapse responsible for the reflex of the gill withdrawal of *Aplysia californica* (sea slug) is another cellular and molecular model of signal memorization and of learning (Bear *et al*., 1996; Kandel *et al*., 2000). A weak stimulation of the siphon of *Aplysia* leads to moderate withdrawal of the gill. A strong stimulation of the tail induces an important withdrawal of the gill. The alternative applying of these two stimulations provokes an increase in the response to a weak stimulation of the siphon (Bear *et al*., 1996; Kandel *et al*., 2000). This sensitization of the gill withdrawal would be due to a molecular complex compounded with a serotonin receptor (associated to a G protein) and with a molecule of adenylyl cyclase. This complex, located on sensory neurons of the siphon, can integrate two signals: the binding of serotonin, released from an interneuron following a strong stimulation of the tail of the animal, and the binding of calcium, entered after the action potential evoked by a weak stimulation of the siphon (Bear *et al*., 1996; Kandel *et al*., 2000) (Figure. 2). The consequence of the synergic action of these two signals is that intracellular cyclic AMP levels, measured during siphon stimulation, are greater in the case of conjugated tail stimulation. This increase in cyclic AMP levels successively leads to an activation of a Kinase A protein, an increase of the neurotransmitter release from the sensory neuron, and, thus, a greater response of the motor neuron of the gill (Bear *et al*., 1996; Kandel *et al*., 2000).

These two examples of extensive researches on the molecular and cellular bases for learning and memory indicate that, in the last decades, molecular biology has much progressed in elucidating intermolecular reactions and their multiple levels of integration. Physiological signals are collected by molecular receptors as bindings with ions or molecules coming from surrounding medium. These receiving molecular assemblies can integrate several signals at different binding sites. Owing to their bonds with the ligands, they develop new conformations that represent the memory of new physiological states of their surroundings at one given time. Thus, regulation of the development, survival, and reproduction of a living organism begins to be understood from molecular elementary chemical associations and dissociations of molecules. In other words, exchange of information and recognition between molecules passes through chemical bonds carried out by electrons.

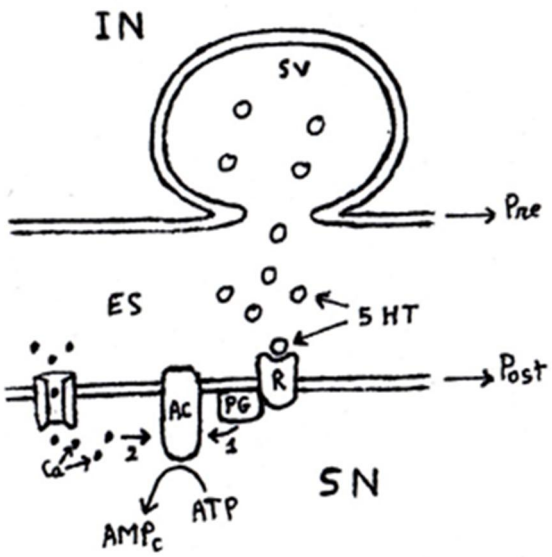

Figure 2. Schema of the molecular substrate of an associative learning in *Aplysia* (After Bear *et al.*, 1996). A strong stimulation of the tail of *Aplysia* induces a release of serotonin (5HT – white circles) from the endings of an interneuron (IN) which makes synapse with a sensory neuron (SN) of the siphon. The stimulation of the siphon results in calcium ions (Ca – black dots) entry in the sensory neuron (SN). The alternate application of the two stimuli induces an increase in the gill withdrawal caused by siphon stimulation. The increase of the reflex of gill withdrawal would be due to a molecular complex composed of a 5HT receptor (R) associated to a G protein (PG) and of an adenylyl cyclase molecule (AC). This complex, located on the sensory neurons of the siphon, can integrate two signals (cf. arrows 1 and 2): the binding of 5HT, released from the IN following a strong stimulation of the tail of the animal, and the binding of Ca ions on adenylyl cyclase, owing to weak siphon stimulation. The synergic action of these two binding results in an increase of the intracellular cyclic AMP (AMPc) levels measured during siphon stimulation. The raising of the intracellular cyclic AMP successively leads to an increase of the neurotransmitter release from the sensory neuron of the siphon and to a greater activity of the motor neuron of the gill. In one word, the conjugated bindings of two ligands on a neuronal molecular complex represent the biochemical substrate for the conditioning of the reflex of the gill withdrawal. Post: postsynaptic membrane; sv: synaptic vesicle filled with 5HT; ES: extracellular synaptic space. ATP: adenosine triphosphate, from which adenylyl cyclase catalyzes cyclic AMP synthesis.

Quantum particles are involved in the intermolecular information

Electron transfers between molecules

The revolution of quantum physics has opened new insights on the understanding of information exchanges between the molecules of the living organisms. Photosynthesis in plants and oxidative phosphorylation associated with respiration are, indeed, based on intermolecular transfers of atomic particles, like photons, electrons or protons. Biochemical reactions taking place during photosynthesis or respiration allow living beings to synthesize molecules that keep the energy necessary for development, survival and reproduction. These processes use energy stored in the light, in the shape of photons, or in the chemical bonds, formed by electrons. Electrons can be transferred along chains of molecules specifically set for their transport (Figure 3). These electron transfers are essential for the storage of energy in phosphorylated molecules (Winkler, 2006).

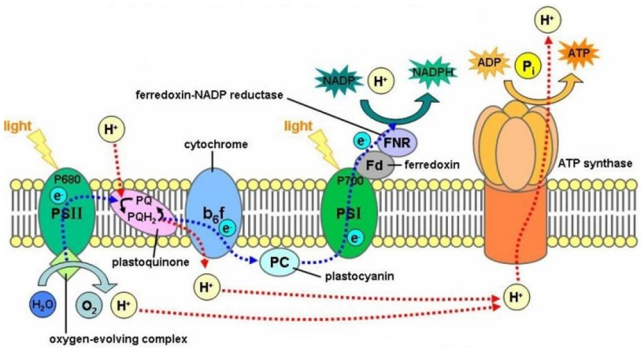

Figure 3. The steps in photosynthesis. Photosynthesis starts with the ionisation by light of a chlorophyll molecule. The ionising energy gains amount ΔE of energy according to the basic quantum mechanical equation ΔE=hc/λ. In ionisation, two electrons are released and are carried by what is known as the electron transport chain. These electrons are used in phosphorylation, and ATP (adenosine triphosphate), used as the source of energy in cells, is formed. In photosystem I (PS I), the electrons return to the chlorophyll. Photosystem II (PS II) is more complicated. NADP: nicotinamide adenine dinucleotide phosphate; H_+: hydrogen atom; e_-: electron (*from NeuroQuantology 2011; 4*: 692-701*)*.

According to the laws of classical physics (and to the common logic of the world visible to the naked eye), one object cannot pass through an energetic wall overtaking its own energy. However, following the rules of quantum mechanics, there is, under favorable conditions, some probability that one particle may "tunnel" through such an energetic barrier (Gray and Winkler, 2005). Biophysicists applied the discoveries of quantum physics to the study of the electron transfers taking place in photosynthesis and respiration. They showed that electrons could be transferred inside a protein or between two proteins following pathways predicted by tunneling phenomenon (Gray and Winkler, 2005). Like photons collected by pigments of photosynthetic chains or of retina, electrons act sometimes as waves, sometimes as corpuscles. These dual features explain their surprising properties (Gray and Winkler, 2005).

Recent investigations have focused on the factors that regulate the rate of the electron transfers occurring in photosynthetic and respiratory chains and in DNA molecules (Gray and Winkler, 2005). Electrons can tunnel from one protein to another within a distance of about 2 nm. Moreover, interval between some oxidation-reduction centers suggest that transfers of electron could occur on a distance far exceeding 2nm, by "hopping" several intermediate states of oxidation-reduction (Gray and Winkler, 2005; Warren et al., 2012). Electron transfers inside the folding of one protein or between two proteins are favored by water molecules "structured" by their hydrogen bonds (Mentré, 1995; Miyashita *et al.*, 2005; Lin *et al.*, 2005 ; Ball, 2007). Appropriate folding of the proteins is a key condition that allows long range electron flows between oxidation-reduction centers of two proteins. In one word, electrons can be transferred from a donor to an acceptor protein by tunneling, when the two proteins form a complex suitable for electronic coupling. The best electronic coupling is reached when electrons tunnel at optimal speed and minimal energy consumption (Winkler, 2006). It is worth noting that electron transfers kinetics can be regulated by the dynamics of the conformational changes occurring in the oxidation-reduction donor-acceptor complex (Gray and Winkler, 2005). Thus, pathways followed by electrons in an aqueous medium inside a molecule or between two molecules cannot be properly understood without the rules of quantum physics.

Holographic molecules

The early applications of quantum physics gave rise to the revolutionary finding of the hologram (Kock, 1981; Hariharan, 2002). A hologram is generated by recording, on an appropriate photographic medium, the

interference of two laser beams coming from a unique source of coherent light (Figure 4). The waves of the laser radiations are monochromatic, of a single frequency, and in the same phase. One part of the laser beam, used as reference, comes on the recording medium directly from the source. The other part comes from its reflection on the object taken in holographic recording. Thus, a hologram records a wave interference pattern. The image of the object is reconstructed by illuminating the hologram plate. When the light source is a laser beam identical to that which was used for the holographic recording, an accurate three-dimensional image of the object is obtained. A characteristic of this method is that each point of a hologram can restitute an image of the whole object. When splitting a hologram, the image of the complete object can be reconstructed from each of the splits. Moreover, the holographic image can reproduce very small details of the original object, even those which could not be detected by a naked eye. Thus, each point of a hologram can record the whole information of a physical object (Kock, 1981; Hariharan, 2002).

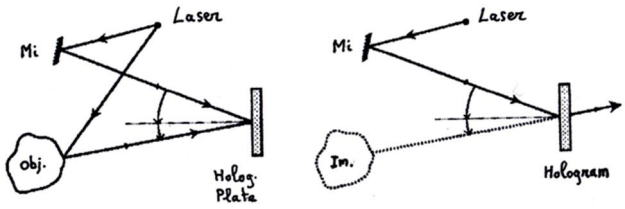

Figure 4. Principle of the recording (4a) and the image reconstruction (4b) of a hologram. Left. Hologram recording is obtained by the interference on a photographic (holographic) plate of two laser beams coming from a unique source of coherent (monochromatic and monophasic) light. One part of the laser light comes from the reflection on the object (Obj.) taken in holography. The other, used as reference, comes on the recording medium directly from the source. The wave interference pattern is thus recorded in the holographic plate. Mi: Mirror. Right: In order to get the best result, the holographic image (Im.) of the object is reconstructed by illuminating the hologram by a laser light identical to the source used for the recording process. In this case, each point of the hologram can restitute a three-dimensional image of the whole object in all its details.

The recent development of computer-generated holography has made possible to digitally generate a hologram. A holographic interference pattern can be digitally recorded or even computed without the need of any physical object being outside the computer. The corresponding holographic image is then obtained by interference with a display analogous to coherent light (Slinger *et al.*, 2005). Thus, holography is a general method of generating and observing interference patterns, not only of light but also of electron waves. Hence, an interference pattern generated by electrons may be also considered as a hologram. In this case, the image of the electron interference could be restituted by an electronic radiation identical to the incident electrons. It may be, then, hypothesized that such phenomena take place in living organisms. This is even more plausible, as photosensitizer pigments, such as rhodopsins of bacteria, are used for recording holographic data (Oesterhelt *et al.*, 1991; Barnhart *et al.*, 2004). Any protein involved in the process of electron transfers might also function as a "holographic molecule".

Holography can, thus, bring new insights on the recording and the processing of intermolecular information, which are essential for the nervous system functioning and, more generally, for any cellular interaction. The electrons involved in chemical reactions or transferred from a molecule to another could play a so far unexplored role in intra- or inter-molecular transmission and storage of information in living organisms, in particular through water structured in a specific manner around molecules (Mentré, 1995; Lin *et al.*, 2005; Ball, 2007). Such transmission and storage of information might take place in the nervous system, in particular at the level of the neuronal synapses. In this case, their study would renew the knowledge of the cellular and molecular phenomena associated with learning and memory.

Toward therapeutic applications

Diverse pathologies, in particular neurodegenerative diseases, are associated with deficits in mitochondrial electron transport chains (Trimmer *et al.*, 2009). Recently, researchers made cultures of modified neuronal cells transfected by mitochondrial DNA of patients with Parkinson's disease (Trimmer *et al.*, 2009). They showed that exposition to near-infrared laser light could restore axonal mitochondrial transport to normal levels (Trimmer *et al.*, 2009). This effect could be due to the absorption of laser light by photosensitizers, like the oxidized copper centers in complex IV of the electron transport

chain (Trimmer *et al.*, 2009). The absorbed light would thus increase levels of energy produced in mitochondria by activating oxidation-reduction reactions in the electron carriers of the respiratory chain. Such experiments suggest that treatments based on photoelectric phenomenon could be proposed in order to increase the activity of the surviving neurons in patients with Parkinson's disease or with other pathologies linked to deficits in oxidative phosphorylation.

The rules of quantum physics: a further step in the knowledge of the nervous system functioning?

The problem of the hypotheses linking quantum physics to brain

The discoveries of quantum physics led to new theories on the intellectual faculties associated with the brain activity. Like philosophers, neuroscientists have been struck by the fact that uncertainty was constitutive of an electromagnetic phenomenon and that the observation of such indetermination could be reduced to determined quanta of energy. Some of them found an analogy between this quantum theory and the mental process in which intent can rise from indecision and lead to a resolution, reducing all the possibilities to a single determined reality (Atmanspacher, 2006). Diverse hypotheses have been elaborated in order to cast some light on the problem of the relation between "mind" and "material" phenomena observed by neurobiologists in the brain (Atmanspacher, 2006; Clarke, 2010). The examination of these different approaches overcomes the aim of the present article. Nevertheless, it should be mentioned, here, that several structures have been proposed as being responsible for quantum processes associated with memory, consciousness and free-will. Among these structures are: assemblies of neurons linked to particular mental representations (Stapp, 1999), neuronal endings where the release of neurotransmitters would rest on "indeterministic" exocytosis of synaptic vesicles (Beck and Eccles, 1992), and neuronal cytoskeletal proteins suggested as the putative basis of coherent superimposition of several physical states for large assemblies of neurons (Hameroff and Penrose, 1996; Hagan *et al.*, 2002).

According to other theories, brain functioning might be analogous to the hologram principle (Pribram, 1991). Thus, the process linked to memory would not take place in defined areas of the brain, but would be present in the whole nervous system as interference patterns of electron waves encoded by mathematic formulas (Pribram, 1991). This hypothesis curiously reminds of the idea proposed in the 19th century by Flourens: each part of the brain would carry out the same functions as the whole organ (Flourens, 1863). The spreading of the interference patterns in the entire brain is also a remote echo of the theory of the diffuse nervous network (Golgi, 1891). These speculations on the links between quantum physics and consciousness or free-will are ingenious and stimulating. However, they suffer from the difficulty to clearly connect a mental state to physiological and biochemical phenomena. The interface between mind and matter remains, for the essential, an enigma for science.

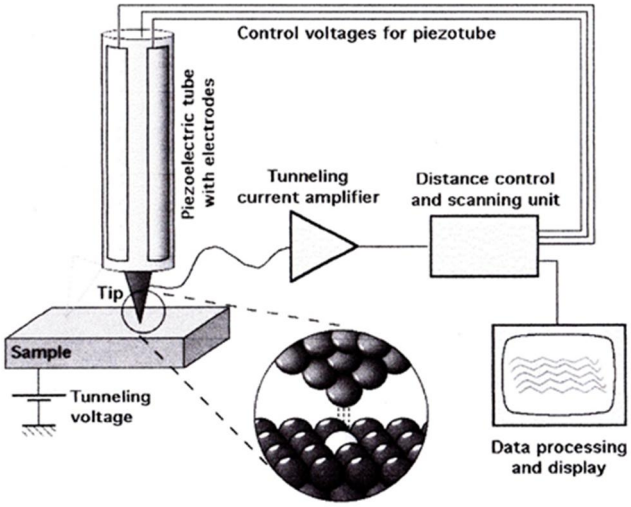

Figure 5. Schematic representation of a scanning tunneling microscope. The conducting tip of the scanning tunneling microscope (STM) scans the surface of the sample. When a voltage difference is applied between the tip and the sample, electrons can tunnel between the two. The variations of tunneling current are measured at a sample-tip distance (less than 1nm) kept constant by a piezoelectric mechanism controlled by computer. Conversely, it is possible to calculate the variations of the sample-tip distance when the tunneling current is maintained constant. The STM can display images of atomic surfaces or analyze local densities of energy states for restricted sites of the sample. Reproduced with the permission of M. Schmid (Creative Commons Attribution Share-alike 2.0 Austria License).

Looking for experimental data

Although a lot of hypotheses have been raised on the role of quantum phenomena in brain functioning, and more generally in the nervous system, experimental data are still lacking in

this domain. Recent works indicated that it was already possible to study electrons tunneling between two proteins (Lin *et al.*, 2005). *In vitro* researches use specific displays for probing surfaces at nanometer scale and characterizing electronic properties of macromolecules at atomic level. Thus, the scanning tunneling microscope can detect electron transfers with the aid of an electrode scanning the surface of the investigated structure (Binnig *et al.*, 1982) (Figure 5).

According to the prediction of quantum mechanics, this technique allows calculation of the alterations in the energy density of the atomic structures and observation of the probability of presence for the electrons of oxidation-reduction centers arrayed by conformational plasticity of the molecules. *In vitro* electron tunneling between two proteins can be studied by grafting the proteins on the surface of semi-conductor materials (Botelho do Rego *et al.*, 2013). Moreover, the transient absorption spectroscopy enables to investigate protons or electrons transfers after excitation by a laser light pulse of few nanoseconds or even few femtoseconds in the case of ultra-fast laser spectroscopy (Berera *et al.*, 2009; Irebo, 2010). In these techniques, the molecules can be included in suitable media, like crystals, for evaluating the electron transfer kinetics (Gray and Winkler, 2005). Schematically summarizing, the absorption changes and the emission lifetimes of the molecular species can be recorded by a photomultiplier, digitalized by an oscilloscope and transferred to a computer. Then, the data can be processed by statistics and read on equations graphs (Figure 6).

Neuronal synapses and quantum phenomena

It should be kept in mind that, in addition to the neurons, the nervous system comprises several types of glial cells, such as astrocytes, oligodendrocytes and macrophages. For several decades, it has been soundly established that glial cells were responsible for a large range of molecular interactions which were essential for the functioning of the nerve system (Kettenmann and Ransom, 2012). Nevertheless, the putative involvement of quantum molecular interactions in glial cells will not be discussed here, since the present report focuses on the implication of quantum phenomena in neurons and, particularly, in neuronal synapses.

Chemical and electrical synapses are the preferential areas for the transmission of the nerve impulse between neurons or between neurons and their effector cells. The chemical synapse is the site of neurotransmitter release from the membrane of presynaptic neurons. After their release, neurotransmitters bind receptors located on the membrane of the neighboring neurons, thus provoking nerve impulse propagation in these postsynaptic neurons. Electrical synapse (much less frequent than chemical synapse) is a structure where pores cross over the joined cytoplasmic membranes of two adjacent neurons (Furshpan and Potter, 1959). Thus, ions can directly pass from the cytoplasm of one neuron to another to perform an electronic coupling between the two neurons. This phenomenon results in a time reduction in the transmission of the depolarization wave (the nerve impulse) from one cell to another.

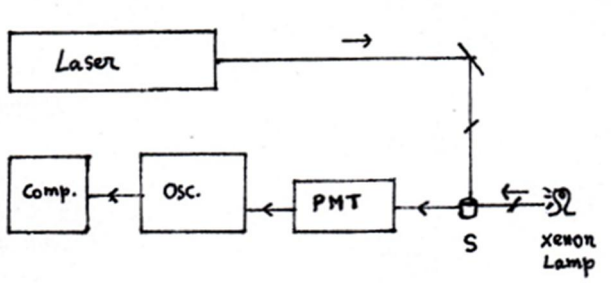

Figure 6. Schematic drawing of a device for transient absorption spectroscopy. A laser beam is pulsed onto the sample (S) in order to measure the absorption changes and emission lifetimes of the molecular species. An analyzing light (for example generated by a xenon arc lamp) passes through the sample before being directed to a photomultiplier (PMT). The resulting current is then digitalized by an oscilloscope (Osc.) and sent to a computer (Comp.) for the data processing. (Modified from T. Irebo, 2010).

Information transmission at the neuronal synapse through electron transfers following their properties of quantum particles has not been really considered until now. Nevertheless, new technologies, like scanning tunneling microscopy or transient absorption spectroscopy, must enable to study electron transfers between the numerous synaptic proteins associated to diverse activities: docking and fusion of synaptic vesicles with the presynaptic membrane, metabolic regulation at the level of the basal lamina of the synaptic cleft, neurotransmitter receptors or ion channels in the postsynaptic membrane. Methodological investigations could be undertaken in order to approach electron or proton transfers between proteins, not only *in*

vitro, but also on cultures of neuronal cells or on brain slices. In this context, it is worth noting that, in the neuromuscular junction, an increase of the nerve transmission was induced by methylene blue reduction at the level of the presynaptic membrane. This observation might be due to electron transfers from molecules of the presynaptic membrane to methylene blue located in the presynaptic cleft (Tsuji, personal communication).

Photosensitizer proteins, like rhodopsins of bacteria, can directly transduce light in electrical current (Oesterhelt *et al.*, 1991). These molecules are used as recording medium of holographic data with a resolution higher than the best photographic films (Barnhart *et al.*, 2004). The example of bacteriorhodopsins has opened new horizons since electrons are quantum particles endowed with characteristics similar to photons (Li et al., 2008). Indeed, synaptic proteins might be able to integrate electronic information as interference patterns of electron waves coming from multiples sources, in a way similar to holograms. According to this hypothesis, one molecule or, even, a center of oxidation-reduction inside one molecule would be the site of storing and integrating electronic information coming from cellular surroundings. Thus, experimental researches in this domain might induce a revolution in the concepts of transmission, integration and memorization of cellular and molecular information in the nervous system.

Acknowledgements

The authors wish to express their acknowledgements to Pr. J.-F. Lambert for his helpful reading of this manuscript. They also address their thanks to Mrs. T. Tsuji and Dr. M. Godinot who much encouraged this work.

References

Anglade P, Larabi-Godinot Y. Historical landmarks in the histochemistry of the cholinergic synapse: perspectives for future researches. Biomed Res 2010; 31: 1-12.

Atmanspacher H. Quantum approaches to consciousness. Stanford Encyclopedia of Philosophy, 2006; 15 Dec.

Ball P. Water as an active constituent in cell biology. Chem Rev 2007; 28 December: A-AI.

Barnhart DH, Koek WD, Juchem T, Hampp N, Coupland JM, Halliwell NA. Bacteriorhodopsin as a high-resolution, high-capacity buffer for digital holographic measurements. Meas Sci Technol 2004; 15: 639-646.

Bear MF, Connors BW, Paradiso MA. Neurosciences: exploring the brain. Williams and Wilkins (Pub.), USA, 1996.

Beck F, Eccles J. Quantum aspects of brain activity and the role of consciousness. Proc Nat Acad Sci 1992; 89: 11357-11361.

Beene DL., Brandt GS, Zhong W, Zacharias NM, Lester HA, Dougherty DA. "Cation-π interactions in ligand recognition by serotonergic (5-HT_{3A}) and nicotinic acetylcholine receptors: the anomalous binding properties of nicotine". Biochemistry 2002; 41: 10262-10269.

Berera R, Van Grondelle R, Kennis JTM. Ultrafast transient absorption spectroscopy: principles and application to photosynthetic systems. Photosynth Res 2009; 101: 105-118.

Binnig G, Rohrer H, Gerber C, Weibel E. Surface studies by scanning tunneling microscopy. Phys Rev Lett 1982; 49: 57-61.

Botelho do Rego AM, Ferraria AM, Rei Vilar M. Grafting cobaltic protoporphyrin IX on semiconductors toward sensing devices: vibrational and electronic high-resolution electron energy loss spectroscopy and X-ray photoelectron spectroscopy study. The Journal of Physical Chemistry C 2013; 117(43): 22298-22306.

Changeux J-P, Dehaene S. The neuronal workspace model: Conscious processing and Learning. In Byrne J (Pub), Learning and Memory: A Comprehensive Reference, 2008 Oxford, Vol. 1, pp. 729-758.

Changeux J-P, Edelstein SJ. Nicotinic acetylcholine receptors, Jacob O (Pub), Paris, 2005.

Changeux J-P. The TiPs lecture. The nicotinic acetylcholine receptor: an allosteric protein prototype of ligand-gated ion channels. Trends Pharmacol Sci 1990; 11: 485-492.

Clarke P. Determinism, brain function and free will. Science and Christian Belief 2010; 22: 1-16.

Couteaux R. Contribution à l'étude de la synapse myoneurale. Rev Canad Biol 1947; 6: 563-711.

De Robertis E, Bennett HS. Some features of the submicroscopic morphology of synapses in frog and earthworm. J Biophys Biochem Cytol 1955; 1: 47-58.

Flourens P. De la phrénologie et des études vraies sur le cerveau, 1863, Garnier frères (Pub), Paris, 304p.

Furshpan EJ, Potter DD. Transmission at the giant motor synapses of the crayfish. J Physiol 1959; 145: 289-325.
Golgi C. Le réseau nerveux diffus des centres du système nerveux. Ses attributs physiologiques. Méthodes suivies dans les recherches histologiques. Arch Ital Biol 1891; 15: 434-463.
Golgi C. Sulla fina anatomia degli organi centrali del sistema nervoso, "Revista sperimentale di Freniatria", 1885, reprint in Opera Omnia, 1903, Hoepli (Pub), Milano.
Gray HB, Winkler JR. Long-range electron transfer. Proc Nat Acad Sci 2005; 102: 3534-3539.
Hagan S, Hameroff SR, Tuszinski JA. Quantum computation in brain microtubules: decoherence and biological feasibility. Phys Rev 2002; E 65: 061901-1 to -11.
Hameroff SR, Penrose R. Conscious events as orchestrated spacetime selections. J Consci Stud 1996; 3: 36-53.
Hariharan P. Basics of Holography. Cambridge University Press, 2002.
Irebo T. Proton-coupled electron transfer from hydrogen-bonded phenols. Acta Universitatis Upsaliensis, 2010, Uppsala, Sweden.
Kandel ER, Schwartz JH, Jessel TM. Principles of neural science. Mc Graw-Hill (Pub), 2000, New-York.
Kettenmann H, Ransom BR. Neuroglia. Oxford University Press, 2012, 3rd ed., 912p.
Kock WE. Lasers and holography: an introduction to coherent optics. Dover Publications, 1981, Mineola, New-York.
Li Lu, Checkelsky JG, Hor YS, Uher C, Hebard AF, Cava RJ, Ong NP. Phase transitions of Dirac electrons in bismuth. Science 2008; 321: 547.
Lin L, Balabin IA, Beratan DN. The nature of aqueous tunneling pathways between electron-transfer proteins. Science 2005; 310: 1311-1313.
Loewi O. Ueber humorale Uebertrakbarkeit der Herznervenwirkung (II. Mitteillung). Pflüg Arch Ges Physiol 1921; 193: 201-213.
Mentré P. L'eau dans la cellule. Une interface hétérogène et dynamique des macromolécules. Masson (Pub.), 1995, Paris.
Miyashita O, Okamura MY, Onuchic JN. Interprotein electron transfer from cytochrome C_2 to photosynthetic reaction center: Tunneling across an aqueous interface. Proc Nat Acad Sci 2005; 102: 3558-3563.
Oesterhelt D, Bräuchle C, Hampp N. Bacteriorhodopsin: a biological material for information processing. Q Rev Biophys 1991; 24: 425-478.
Palade GE, Palay SL. Electron microscope observations of interneuronal and neuromuscular synapses. Anat Rec 1954; 118: 335-336.
Pribram KH. Brain and perception, holonomy and structure in figural processing. Lawrence Erlbaum Associates (Pub), 1991, Hillsdale, USA.
Ramon y Cajal S. The structure and connections of neurons – Nobel lecture December 12, 1906. Nobel lectures – Physiology or Medicine 1901-1921, 1967, Elsevier (Pub.), Amsterdam.
Raviola E, Mazzarello P. The diffuse nervous network of Camillo Golgi: Facts and fiction. Brain Res Rev 2011; 66: 75-82.
Robertson JD. The ultrastructure of a reptilian myoneuronal junction. J Biophys Biochem Cytol 1956; 2: 381-394.
Segrè E. From X rays to quarks: modern physicists and their discoveries. Dover Publications, 2007, Mineola, USA, 352p.
Slinger C, Cameron C, Stanley M. Computer-generated holography as a generic display technology. IEEE Computer Society, August 2005; 46-53.
Stapp HP. Attention, intention, and will in quantum physics. J Consci Stud 1999; 6: 143-164.
Tarlaci S. Quantum physics in living matter: from quantum biology to quantum neurobiology. NeuroQuantology 2011; 4: 692-701.
Trimmer PA, Schwartz KM, Borland MK, De Taboada L, Streeter J, Oron U. Reduced axonal transport in Parkinson's disease cybrid neurites is restored by light therapy. Mol Neurodegener 2009; 4: 26.
Warren JJ, Ener ME, Vlček Jr. A, Winkler JR, Gray HB. Electron hopping through proteins. Coord Chem Rev 2012; 256: 2478-2487.
Winkler JR. Long-range electron transfer in biology. Encyclopedia of inorganic chemistry, Wiley J. and Sons (copyright), 2006.