N-methyl-d-aspartate channel and consciousness: from signal coincidence detection to quantum computing

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Abstract

Research on Blindsight, Neglect/Extinction and Phantom limb syndromes, as well as electrical measurements of mammalian brain activity, have suggested the dependence of vivid perception on both incoming sensory information at primary sensory cortex and reentrant information from associative cortex. Coherence between incoming and reentrant signals seems to be a necessary condition for (conscious) perception. General reticular activating system and local electrical synchronization are some of the tools used by the brain to establish coarse coherence at the sensory cortex, upon which biochemical processes are coordinated. Besides electrical synchrony and chemical modulation at the synapse, a central mechanism supporting such a coherence is the N-methyl-D-aspartate channel, working as a ‘coincidence detector’ for an incoming signal causing the depolarization necessary to remove Mg$^{2+}$, and reentrant information releasing the glutamate that finally prompts Ca$^{2+}$ entry. We propose that a signal transduction pathway activated by Ca$^{2+}$ entry into cortical neurons is in charge of triggering a quantum computational process that accelerates inter-neuronal communication, thus solving systemic conflict and supporting the unity of consciousness. © 2001 Elsevier Science Ltd. All rights reserved.
1. Introduction

Investigation on the neuronal correlates of consciousness has become a major area in brain and cognitive sciences (Frith et al., 1999; Metzinger, 2000). Large efforts have been directed to show that one or other aspect of neuronal function (electrical, magnetic, chemical, quantum) is closely related to the phenomenon of consciousness. Here, we make a systematic attempt to develop a complete (as possible) model where such correlates, the evidences supporting them, as well as a general mechanism, are described and discussed.

This review practices a comprehensive strategy, beginning with the general assumption of consciousness as a conflict-solving process (Section 2). In the sequence, we discuss results from lesion neuropsychology, neuroimaging and electroencephalogram (EEG) (Section 3), relating them with the N-methyl-D-aspartate (NMDA) mechanism and evidences from neuropharmacology about related cognitive phenomena (Section 4). We review models of electrical activity in the thalamo-cortical system and their possible limitation in solving systemic conflict (Section 5), and suggest a signal transduction pathway (STP) controlled by Ca²⁺ entry that would be able to trigger quantum conscious processing (Section 6), then describing how classical network processes could prepare a quantum computational system (Section 7) that accelerates inter-neuronal communication, solving conflict and providing the unity of consciousness (Section 8). In the conclusion, we make suggestions about how our hypothesis could be tested.

2. Consciousness as a conflict-solving process

Our analysis relies on a general assumption about the nature of consciousness. We assume that consciousness emerged in evolution as a powerful way of solving conflict in a highly distributed, non-linear system submitted to adaptive pressure, the central nervous system (CNS). The existence of thresholds for conscious processing (Young, 1994) suggests that all kinds of problems below a (relative and species-variable) degree of difficulty are likely to be unconsciously processed by the CNS. Therefore, a large range of problems studied by artificial intelligence and computational neuroscience are examples of processes, which can be unconsciously performed.

The central subject of distributed intelligent processing systems (DIPS’s) theory is the study of intelligent communities, which comprise collections of interacting, coordinated and specialized agents. Agents specialize in data collecting (sensors), problem solving (experts), data communication (channels), acting upon the surrounding environment (effectors), etc. Intelligence is approached in terms of a society of communicating specialized experts and the brain is considered an example of natural DIPS (Hewitt, 1977; Chandrasekaran, 1981; Fox, 1981; Lesser and Corkill, 1981; Davis and Smith, 1983; Hewitt and Inman, 1991; Lesser, 1991; Ornstein, 1991; Rocha, 1992; Luck, 1995; Maunsell, 1995; Singer, 1995; Ungerleider, 1995; Rocha, 1997).

DIPS reasoning is the cooperative activity among as much as possible decentralized and loosely coupled collection of experts that may provide the solution of a given problem. Decentralized means that both control and data are logically and often geographically distributed; there is neither global control nor global data storage. The reasoning (or programming) intends to build models in which the control structure emerges (and is learned) as a pattern of passing messages among the agents being modeled. Task distribution is an interactive process between an agent with a task to be executed and a group of agents that may be able to execute the task.

Central to the notion of using a set of agents to obtain an intelligent solution for a given problem are the concepts of conflict, consensus and negotiation. As agents are able to independently solve the tasks they are specialized for, and different agents may be assigned to handle the same task, conflicting (inconsistent) information may be available. Consensus may be used as a way to solve conflict if opposing pieces of information exhibit at least different degrees of confidence and/or relevance such that consensus may be achieved for the task solution, otherwise negotiation has to be used to change agent confidence and/or relevance (Rocha, 1992). Hierarchy is another process to be used in conflict solving and negotiation. However, hierarchy must
be kept within boundaries, otherwise the system intelligence is reduced to that (if any) of the highest agent in power. The best solution is some sort of hierarchical democracy, where each agent is assigned a degree of freedom while being rewarded by using this freedom in benefit of the entire system. DIPS intelligence derives, therefore, from combining distinct factors as agent specialization, communication, conflict, negotiation, hierarchy, autonomy, etc. in a suitable form for a problem-solving task (Rocha, 1997).

Digital computers based on Turing architectures, although having only one central processor, frequently suffer a breakdown when two conflicting instructions are read. A distributed system as the brain, where each of a billion of neurons may be regarded as a central processing unit, should undergo all sorts of computational conflict that cannot be always solved by adding more instructions and memory, because of size, heating and other biological adaptive constraints. Conscious processing, along with plasticity, could be considered a solution found by evolution for a large class of conflict in the CNS — conflict between information from different sensors (even in the same modality), different connections between central receptors and effectors, and different patterns of effector activation that are not amenable to be solved by Hebbian-Boolean-like mechanisms.

Therefore, we regard the investigation on the neuronal correlates of consciousness as the search for large-scale processes responsible for an integration of information, extending beyond well-known synaptic mechanisms and classical computation. Such an approach rejects a popular strategy, the search for brain ‘modules’ that when activated could be considered sufficient for the production of one or other kind of conscious representation (for a criticism of such strategy, Lamme et al., 2000). Since conflict involves many parts of the brain responsible for perception, executive processing and action, the solution of conflict must functionally integrate all areas, which are taking part on it. Alternatively, we suggest that the solution of conflict would depend on a quantum-like mechanism, prepared by electrochemical processes and triggered by a specific kind of signal transduction processes, to be discovered by experimental research in molecular neurobiology (possible studies are proposed in the conclusion of this paper).

3. Experimental evidences about neuronal networks involved in conscious perception

Knowledge obtained from lesion studies in neuropsychology, neuroimaging and electroencephalographic studies in the last four decades has brought converging evidence about brain networks involved in conscious perception. Among such evidences, Blindsight, Neglect/Extinction and Phantom limb syndromes have helped to reveal the necessity of activation of a recurrent neuronal network to generate consciousness of a stimulus.

Studies on the Blindsight syndrome have revealed that human patients with an extensive lesion at the primary visual cortex could behaviorally respond to a visual stimulus without being conscious of it. One patient (Weiskrantz, 1997) reported having a dimmer consciousness of the stimulus, presumably generated by a remaining part of the primary visual cortex and/or by an alternative network involving the superior colliculus and the prefrontal cortex. However, a series of experiments with monkeys (Cowey and Stoerig, 1995; Stoerig and Cowey, 1995, 1997) demonstrated that a complete lesion in primary visual areas invariably generates blindness (i.e., absence of vivid visual consciousness).

An interesting result, relating activity in primary visual cortex of primates and perceptual consciousness, was obtained by Macknik and Haglund (1999). They optically imaged VI activity of rhesus monkeys during a visual task known to generate a masking illusion, and found that VI activity was correlated with the illusory percept but not with the stimulus. Their interpretation was that ‘neurons in the early visual system do not seem to solely reconstruct the visual scene… but instead seem to, in addition, reflect a stage in the construction of the perception itself’. A partial conclusion to be drawn from this and Cowey/Stoerig studies on blindsight is that some kind of activity in primary sensory areas should be necessary for vivid perceptual consciousness and possibly for imagery (Miyashita, 1995).

However, it seems to be equally true that the activation of primary sensory areas by afferent stimulation, e.g., when the subject is under anesthesia but still able to process sensory input is not sufficient for the generation of perceptual consciousness. Lamme et al. (2000) suggest that only a percentage of VI activity correlates with awareness, a fact that would require a broad model of consciousness generation to be correctly interpreted (see also a discussion of VI coding in Vinje and Gallant, 2000). An important clue comes from studies of hemineglect in human subjects, pointing to the role of feedback from other cortical areas. Such studies have led to the conclusion that neglect is ‘a higher-order disorder’ that preserves primary sensory processes but impairs attentional modulation by associative areas as the parietal cortex (Vallar and Perani, 1986; Vallar, 1993). The generation of perceptual consciousness would depend on both primary sensory activation and recurrent (or ‘reentrant’, as proposed by Edelman, 1989) signals from higher cortical areas.

Studies on perceptual rivalry (Lumer et al., 1998) have shown that competing stimuli to conscious perception involves the activation of distinct associative areas.
For instance, in the case of competing stimuli of faces and houses, the former are recognized if the fusiform face area is activated, and the latter are perceived if the parahippocampal place area is activated (Tong et al., 1998). The results may be understood as showing that reentrant signals from these different areas over the primary visual cortex are required to produce the final conscious result. It seems, therefore, that important information reentrance over the primary sensory cortex occurs at variable time intervals after the cortical sensory neuron being primed by the incoming sensory data. This may imply different instruction writing and result reading of a sequential processing that may take up to seconds depending on the complexity of the task being solved. The times for these writing and readings may be set by attentional control (signalizing from associative to sensory areas) and synchronizing neurons (see discussion below).

A recent functional magnetic resonance imaging (fMRI) study on visual extinction (Rees et al., 2000), with a right inferior parietal patient, showed that when different stimuli (faces, houses) are presented to right and left visual fields, only the ipsilesional stimulus (projected to the left hemisphere) is consciously seen, although occipital activation is measured in both hemispheres. The authors conclude that ‘activation of primary visual cortex (and early extrastriate cortex) by a visual stimulus is not sufficient to evoke awareness. But the synchrony of neural firing in such areas and/or their interaction with other areas (such as the damaged inferior parietal lobule) normally plays a critical role in awareness’.

A question that arises in the discussion of concurrent activation of cortical areas to generate consciousness is: could feedback between layers of a cortical area alone be sufficient to generate perceptual consciousness? Electrode measurements of the somatosensory cortex (Cauller and Kulics, 1991; discussion in Cauller, 1995) have led to the suggestion that feedback between layers in a single sensory area (McComas and Cupido, 1999) could be sufficient to generate conscious sensation. However, the negative component in Cauller and Kulics’ (1991) experiment associated to conscious perception was assumed to come from ‘backward’ cortico-cortical projections from secondary somatosensory areas to S1’. Electrophysiological studies seem to point to a dependence of sensory qualia upon the reentrance of information from associative cortex around 100 ms after the arrival of the original sensory activation of the primary pyramidal neuron (Rocha, 1997).

A similar interpretation comes from the fact that many processes at S1, as those involving egocentric space (Vallar’s studies, op.cit., relative to patients with right hemisphere lesions) would always depend on recurrent signaling from higher cortical areas. Moreover, our initial assumption about the nature of consciousness rules out the possibility that the activation of a cortical region alone would be sufficient to produce any kind of perception. In the case of direct stimulation of a cortical site (as performed during some kinds of epilepsy and/or brain tumors surgery), a temporal delay for the production of a sensation or perception (as the proposed delay of 500 ms — Libet, 1999) would be necessary, because communication with a larger neuronal network is required to generate conscious experience, and such a communication surely requires a time to be triggered (of course, the delay may be smaller than Libet’s hypothesis predicts).

An analysis of Phantom limb phenomena (Ramachandran and Rogers-Ramachandran, 2000) also reveals the necessity of both afferent and reentrant signaling to generate perceptual consciousness. Once the original source of afferent signaling to a neuronal population at the somatosensory cortex is lost, the same population (that still receives reentrant signaling from associative areas) will generate conscious sensation (referred to the lost limb) only if it receives afferent stimulation from other sources. What makes the change possible is that afferent sensors in the somatosensory system have divergent connections to cortical neurons. The phenomena also reveals the importance of neural plasticity in the generation of perception. Why is the sensation referred to the lost limb, and not to the sensor where the afferent signal comes from? The answer to this question should involve a variety of factors, from genetic dispositions to previous neuronal learning, and the present origin of the reentrant signal necessary to generate the conscious sensation, suggesting a dependence of consciousness generation on internal (inherited and learned) models, mostly supported by associative areas. Internal models shared by a large neuronal population seem to be able to drive perceptual processes and undermine informational patterns held by a smaller population.

The same kind of concurrent activity supporting consciousness has been observed in EEG studies of linguistic performance. Event-related potentials (ERPs) are changes in electrical voltage, recorded from many sites over the surface of the scalp, which are time-locked to the occurrence of a particular stimulus. These electrical potentials reflect underlying neural activity, and components of the resulting waveform can be used to differentiate different cognitive conditions (Coull, 1998). Several ERP components are modulated by attention; their amplitude seem to increase to stimuli which are conscious, compared to stimuli which are not. Attention modulates components that have already been elicited by visual (P100 and N100), auditory stimuli (N100), somatic stimulation (N100 and P100), infrequent stimuli (P300) or semantic incongruent stimuli (N400). Also, late positive components are associated to conscious word memory (Olichay et al., 2000).
The N100 component of the ERP waveform was enhanced compared to the unattended ear, suggesting that unattended stimuli dampen the N100 response because they are not selected for later (conscious) processing. In the case of visual stimuli, the P100 amplitude was similar for valid and neutral cues, but attenuated for invalid trials. On the other hand, the N100 amplitude was similar for invalid cues and neutral cues and larger for valid cues. Therefore, it seems that P100 component reflects the cost of being cued to the wrong target (may be induced by some sort of conflict). On the other hand, the N100 amplitude was similar for invalid cues and neutral cues and larger for valid cues, and possibly reflects the benefit of being validly cued to the correct target location (Coull, 1998).

One of the most prominent theories regarding the cognitive basis of the P300 is that it indexes on-line updating of working memory, but it can also be interpreted as an index of attentional function (Knight, 1997) because, as with the N100/P100 effects described above, the amplitude of P300 seems to be modulated by attention in the case of conflict solving. Also the N400 component is proposed to be modulated by attention (Coull, 1998) as a way to solve an existing conflict. It is elicited in response to semantically deviant stimuli: the more unrelated the target word is in the context, the larger the amplitude of N400.

Besides the diversity of cognitive phenomena and methodologies, studies of the above syndromes, fMRI of normal subjects and EEG/invasive electrode measurement results all indicate that conscious perception depends on systemic coherence between primary and associative areas of the brain. In this regard, Smythies (1999) pointed that ‘it could be argued that consciousness depends on the general level of activity of the whole cortex via a wide range of cortico-thalamic relays as determined by a proper balance between glutamatergic activation and GABAergic (gamma-aminobutyric acid) inhibition, plus modulation by other factors, such as local cholinergic neurotransmission, as much as on the activity of strategically placed brain stem nuclei.’ This ‘general activation’ view doesn’t rule out the existence of specific mechanisms which may be regarded as central to the generation of consciousness, as the NMDA channel function. According to Rocha (1997), ‘worth noting is the dependence of sensory consciousness upon the reentrance of information from secondary cortical areas around 100 ms after the arrival of the original sensory activation of the primary pyramidal cortical neurons (PCN), that may be associated with a Ca$$^{2+}$$ entrance… Consciousness at the primitive level of qualia may be thought to be supported by unstable energy states triggered by reproducible and specific activation of defined signal pathways’. In the next sections, we discuss possible mechanisms controlling informational coherence in the CNS.

4. The ‘coincidence detection’ function of the NMDA channel and evidences about related cognitive phenomena

There are different kinds of ‘coincidence detection’ mechanisms studied in neuroscience and other scientific areas; for instance, in the study of serial computational processes in the visual system a neuron is called a ‘coincidence detector’ if activated only when two other preceding parallel neurons are simultaneously activated. In a classical review about long-term potentiation (LTP) in the hippocampus, Bliss and Collingridge (1993) compared the NMDA receptor function to a Hebbian (Hebb, 1949) ‘coincidence-detection’ mechanism, regarding three aspects: (a) cooperativity: unblocking the NMDA channel require cooperative excitatory input to promote depolarization of the cell and reduction of Mg$$^{2+}$$ levels, (b) associativity: ‘the required depolarization is provided by a different set of afferent fibers’, and (c) input-specificity: ‘the need for the presynaptic terminal to provide a sufficient concentration of L-glutamate to activate adequate number of NMDA receptors’.

In this paper, we use the term ‘coincidence detection’ in a narrower sense, referring to a mechanism that detects concurrent activation between different layers of perceptual systems in the CNS (here, we will not consider cortical microlayers, because of the above discussed reasons). In the visual system, for example, such layers basically are: (a) the lateral geniculate nucleus at the thalamus, (b) the striate cortex, (c) early extrastriate visual cortex, (d) ‘what’/temporal and ‘where’/parietal associative areas, and finally (e) areas of the prefrontal cortex that connect with the preceding ones.

One of the ways that a multi-layered neuronal network can self-organize is by developing a specific mechanism to detect the coincidence of activation of assemblies in lower and higher layers (similar to the matching mechanism in the adaptive resonance theory proposed by Grossberg, 1999). Such a coincidence should occur in a precise (although variable, in different perceptual systems) time window to be detected, thus assuring that the input patterns (from the stimulus) and the reentrant signal (shaped by memory) could participate in the generation of the same perception. Two of the possible adaptive functions of this mechanism are to avoid hallucinatory phenomena-generated by endogenous patterns alone and the driving of behavior by non-voluntary processing alone, this would be the case if afferent patterns could directly control motor and endocrine efferents (e.g. the mechanism of a simple mechanical robot). For the reasons raised by Bliss and Collingridge (op.cit.), the physiology of the NMDA channel seems to be perfectly adequate to this kind of coincidence detection function.
Glutamate and aspartate are known to be major excitatory transmitters in the cerebral cortex. Glutamate is also released by the sensory terminals in thalamus and it is assumed to be the transmitter in charge to convey sensory information to the thalamic relay neuron (TRN). Glutamate binds to three different classes of membrane receptors:

1. Metabotropic receptors: glutamate binding to these receptors promotes the activation of G-proteins in charge of controlling different types of STPs;
2. $\alpha$-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors: glutamate binding to these receptors opens ionic channels and depolarizes the membrane (Fig. 1);
3. NMDA receptors: the effect of glutamate binding on this receptor depends on the electrical state of the membrane. In hyperpolarized states, $\text{Mg}^{2+}$ ions bind to the inner core of the channel controlled by the receptor and block any other ion movement through the channel. Depolarization reduces the NMDA channel affinity for the $\text{Mg}^{2+}$, such that these ions may leave the channel. In this condition, glutamate binding opens the NMDA channel to $\text{Ca}^{2+}$ ion entrance (Fig. 1).

A coincidence detector system is provided whenever both types of channel coexist in the same membrane. A first signal arriving over the AMPA/kainate depolarizes the membrane and removes $\text{Mg}^{2+}$ from the NMDA channel, such that if another signal arrives over this latter channel while the membrane is still depolarized, it may trigger the $\text{Ca}^{2+}$ entrance. Therefore, this $\text{Ca}^{2+}$ movement may encode any coherence among both signals. The $\text{Ca}^{2+}$ moved into the cell (Ghosh and Greenberg, 1995; Alkon et al., 1998) activates many different STPs binding to calmodulin (CaM) (Fig. 4) to activate certain types of kinases, like the calmodulin kinase II (CaMKII). This kinase, in turn, may control the action of many other types of molecules. Ca-activated CaM may also control phosphodiesterase, which may be in charge of modulating different types of STPs (for a detailed discussion about possible models of this NMDA/Ca control, see Rocha, 1997).

The importance of the NMDA function in the neocortex for consciousness was initially proposed by Flohr (1995), who also suggested a central role to nitric oxide (NO) in the formation of neuronal assemblies supporting conscious processes. The second part of his model doesn’t apply our proposal, because NO couldn’t directly trigger a specific intra-cellular process covering several primary sensory and associative areas. Alternatively, one of us (Rocha, 1997) proposed the NMDA coincidence detector property to be an important issue for consciousness and $\text{Ca}^{2+}$ as the key modulating signal linked to it. The integrative mechanism, in our present model, would rather depend on a quantum computing process triggered by NMDA-coordinated $\text{Ca}^{2+}$, entry and a signaling pathway different from NO retrograde messenger function. Such quantum process would be able to produce non-local communication between larger areas of the brain, and only this kind of communication would be able to solve computational conflict between different sensory and associative networks.

Strong evidence for the relation between NMDA function at the neocortex and conscious processing has recently emerged from a series of studies in humans, by blocking the NMDA channel with a subanesthetic dose of ketamine (Lahti et al., 1999; Newcomer et al., 1999; Oranje et al., 2000). Evidence also comes from studies of epilepsy in experimental models; e.g. Kochan et al. (2000) observed that ‘Status Epilepticus induced a significant inhibition of calcium and CaMKII activity that involves NMDA receptor activation’. As epilepsy frequently has strong effects on consciousness in humans (amplitude increase of EEG is related to conscious impairment leading to coma), the observed alterations of NMDA activity would probably be related to conscious dysfunction.

Although the results in such studies seem to be conclusive regarding the relation between NMDA dysfunction and alterations of consciousness, we note that they can be given different interpretations. Antagonists to non-NMDA receptors seems to produce effects that interact with NMDA function (Sato et al., 1999). Ketamine also affects non-neocortical regions, as peripheral nociceptor sensors (Davidson and Carlton, 1998) and the limbic system (Duncan et al., 1998), possibly disrupting LTP at the hippocampus (Mills et al., 1998). At the neocortex, it possibly interacts with the muscarinic acetylcholine (Ach) receptor (Durieux, 1995), which may be coproducing the observed cognitive effects. Therefore, it would be useful to distinguish, in our model, between a central mechanism involved in the triggering of conscious processing, the NMDA channel and other mechanisms that modulate it. For example, Keverne (1999) proposed a model of psychosis based on the role of GABAergic inter-neurons controlled by serotonin and dopamine innervations. In our view, such a mechanism isn’t the central one that triggers conscious processing, but one that directly modulates the former.
Since the opening of the NMDA channel to calcium entry into the cell depends on a previous depolarization of the membrane, a variety of transmitters and modulators, which are able to depolarize or hyperpolarize the membrane may produce effects on consciousness. For example, attention is modulated by midbrain cholinergic and noradrenergic system and limbic emotional circuits recruiting both 5-HT and histamine (HA) neurons. These transmitters are able to change the electrical encoding at both TRN and PCN from rhythmic burst firing toward a tonic spike firing (see below). These transmitters may facilitate the depolarization triggered by the activation of the AMPA channel induced by the incoming sensory information. In this condition, cholinergic, noradrenergic, serotoninergic and histaminergic systems may enhance or inhibit the capacity of the NMDA channel to act as a coincidence detector.

Our model can, therefore, provide a useful framework to interpret the mechanisms of mental dysfunction and pharmacological drugs. For instance, Krystal et al. (1999) argued that ‘recent studies question the centrality of D2-receptor stimulation to the NMDA-antagonist psychosis… to the extent that NMDA antagonists effects provide insight into the pathophysiology of schizophrenia, these novel pharmacological strategies and others may provide a rationale for the exploration of new treatments that do not involve D2-receptor blockade’ (Javitt et al., 1996; for a review on this subject, Jentsch and Roth, 1999). In other words, longer lasting and more efficacious treatments may emerge, when we focus on the central mechanism itself (NMDA function) rather than only on modulating mechanisms.

The same kind of reasoning applies to the discussion of theories of general anesthesia. Since the opening of the NMDA channel is a complex operation that is influenced by several factors, including the action of ionotropic receptors to depolarize the membrane and the availability of calcium ions at the extracellular milieu, the putative effects of all known anesthetics relate in some extent to controlling NMDA function. As Flohr et al. (1998) claimed, ‘modification of NMDA-dependent computational processes is the final common pathway of anesthetic action. Agents that directly inactivate the NMDA synapse necessarily have anesthetic properties; agents that do not directly affect the NMDA synapse will exert an anesthetic action, if they inhibit NMDA-dependent processes’.

5. Electrical modeling of thalamic and pyramidal cortical neurons

Before discussing the proposed key role of the NMDA channel in triggering quantum computations, it is necessary to describe the kind of thalamic and cortical neurons, which may be involved at the neural network level. The TRN and PCN neurons have two basic modes of action potential generation: tonic firing and rhythmic burst generation (Fig. 2). Tonic firing is prevalent during ‘brain activated’ states, characterized by EEG desynchronization, such as in awake and attentive animals or rapid eye movement (REM) sleep. Rhythmic burst firing is prevalent during periods of synchronized slow waves in the EEG, such as during slow wave sleep and deep anesthesia (Steriade, 1996; Rocha, 1997).
McCormick (1992) proposed an original model of spike generation modes, where burst firing is due to the activation of low threshold Ca$^{2+}$ spikes, which are generated by the low-threshold Ca$^{2+}$ current or T-current ($I_T$). This T-current is, in turn, activated by depolarization of the membranes up to approximately −80 mV and becomes progressively inactivated by depolarization such that inactivation is complete around −60 mV. Owing to this, it is proposed that $I_T$ is dependent on both activating (m) and inactivating (h) gates: the m gates begin to open at a membrane potential around of −80 mV and reach the full opened state at a potential around of −40 mV, and the h gates change from a full opened state at −100 mV to a closed one at membrane potentials near −60 mV. Tonic firing is assumed to be supported by the classical Na/K system, such that depolarization of the membrane to adequate levels results in the generation of spike trains.

Ach inhibits the rhythmic burst firing by promoting the membrane depolarization due to the activation of both nicotinic and muscarinic receptors. While the nicotinic response seems to be due to an increase in membrane cation conductance, the muscarinic effect results from the blocking of a resting K$^+$ conductance, which substantially contributes to the resting ‘leak’ conductance and, therefore, has been termed $I_{K_{L}}$. (Rocha, 1997). HA also promotes a membrane depolarization due to a reduction of $I_{K_{L}}$, induced in this case by the activation of a G-protein. Another effect of HA is to increase $I_{KL}$, a depolarizing current carried by both Na$^+$ and K$^+$. The above effects allow both Ach and HA to switch the TRN and PCN firing from the rhythmic burst mode to the tonic spiking.

Norepinephrine (NE) results in a prolonged enhancement of both TRN and PCN activity due to a decrease of $I_{K_{L}}$, induced by the activation of a G-protein promoted by $z_2$ adrenoceptors. The $\beta$ adrenoceptors, in turn, are shown to enhance $I_{KL}$ in a similar way to HA. Finally, 5-HT seems to promote a small membrane depolarization associated with an enhancement of $I_{KL}$.

The functional consequence of the chemical control of the TRN and PCN spike firing by Ach, NE, HA and 5-HT is that sensory information from periphery is encoded in a dependent manner on the emotional and arousal/sleep conditions of the animal. These states are determined by the activity of the cholinergic, noradrenergic, histaminergic and serotonergic functional systems arising from the brain stem and hypothalamus. For instance, the low activity of these systems during synchronized slow wave sleep switch the TRN and PCN encoding to the rhythmic burst firing. On the contrary, the enhanced activity of the cholinergic system in awake and REM states sets the encoding at these neurons to a generation of spike trains. NE, HA and 5-HT systems also contribute to the selection of this type of encoding during the awake/attentive states.

The TRN may exhibit two other rhythmic activities in the range of 7–12 and 30–50 Hz, which are consequences of the intra-thalamic circuitry and cortico-thalamic connections, respectively. Intra-cellular recordings in TRN during the generation of EEG spindle oscillations reveal barrages of inhibitory postsynaptic potentials arriving at a frequency of approximately 7–12 Hz, while recording in the nucleus reticularis cells reveal a sequence of depolarizations in the same frequency. The precise origin of these higher frequency oscillations is not fully understood, and it has been assumed to arise not from activity of thalamic neurons, but as a result of a descending cortical control upon the thalamic activity (Nicolelis et al., 1995; Contreras et al., 1996; Steriade, 1996).

Singer (1990) and Munk et al. (1996) showed that gamma range activity can be enhanced by stimulation of the midbrain reticular formation. Llinàs et al. (1991) recorded in vitro the single neuron and field activities of the frontal cortex in guinea-pigs. These authors detected subthreshold oscillations in the range 35–50 Hz in layer IV (which contains inter-neurons). Llinàs (1992) hypothesized that such inter-neurons would influence the activity of other cortical neurons involved in a cortico–thalamo-cortical loop to produce gamma oscillations: ‘the descending 40 Hz rhythmic volley, by activating thalamic projection neurons and the thalamic reticularis neurons, would result in the generation of 40 Hz excitatory postsynaptic potential sequence in the thalamus’. During waking, the regular neuron firing of the thalamic reticular nucleus, which contrasts with the bursting mode of discharge during slow wave, is more likely to generate the short-lasting inhibitory synaptic potentials conductive to 40 Hz bursting in thalamic projection neurons (Llinàs, 1991). Steriade et al. (1991) confirmed in anesthetized cats the ability to record gamma range activities in thalamo-cortical neurons, and found that stimulation of the mesopontine cholinergic nuclei (mimicking waking process) potentiated the 40 Hz activity in the thalamo-cortical neurons.

Neocortical oscillatory synchrony at the gamma (30–50 Hz) has been suggested to be a central component of a ‘binding’ mechanism responsible for intra- and intermodal integration of information, forming unitary perceptions (Gray and Singer, 1989; Llinàs and Ribary, 1992; Singer, 1993; Llinàs and Ribary, 1994; Roelfsema et al., 1996; Pulvermüller et al., 1997; Rodriguez et al., 1999) and also for associative learning (Wolfgang et al., 1999). Engel et al. (1992) propose that ‘synchrony may be the ‘glue’ that binds distributed neuronal activity into unique representations’. But how does synchrony work as a ‘glue’? The authors say that ‘in this conceptual framework… synchrony among distributed groups is the relevant code for binding, whereas the intrinsic temporal structure of the responses is, as such, not assumed to represent particular aspects of the visual
A possible interpretation of synchrony as ‘code for binding’, proposed by the authors, is that ‘ oscillatory signals may be well suited as carrier signals for a temporal code’. In other words, evoked potentials could ‘encode’ properties of stimuli using the synchronous wave as a ‘carrier’ that broadcasts the signals processed by each responsive neuron to the whole assembly.

A second interpretation of the role of oscillatory synchrony is the idea of a ‘pacemaker’ coordinating the activity of large neuronal assemblies. Such a coordination would putatively contribute to produce a state corresponding to a unit of perception. Poppel et al. (1990) developed the hypothesis that perception is ‘temporally segmented by sequential processing units of 30–40 ms (more conservative: 20–50 ms) duration’, reflecting states ‘brought about by neuronal oscillations… Successive system states can be linked together by an integration mechanism. Such temporal integration has an upper limit of a few (approximately 3) seconds’. This view implies that all modalities are integrated into 20–50 ms ‘chunks’, which are temporally linked into meaningful sequences with larger duration. But could the minimal unit be the same for all modalities? Comparing the visual and auditory modalities, Poppel et al. (1990) say that the ‘leading sense’ sets off a relaxation oscillation, defining ‘a system state for both sensory modalities’ (p. 146). However, if different modalities entrain different oscillatory periods, there would not exist a common unit of perception. In this case, inter-modal integration would occur in larger temporal intervals, where the synchronizing peaks entrained by the dominant modality would work as reference pulses to coordinate all modalities. Therefore, the timing of the whole perception would be defined by the timing of the dominant modality.

A third possibility is that synchronous electric oscillations could have no critical role in perceptual binding. In some cases reported by Pulvermüller et al. (1997), gamma oscillations appear 300 ms after the onset of stimuli, while the perception of the stimulus may have occurred between 100 and 300 ms. Their function would be related to sensorimotor functions, one of the possibilities suggested by Roelfsema et al. (1996) and Miltner et al. (1999). More to the point, Roelfsema et al., op. cit., suggest that ‘multiple stimuli may induce responses in pools of neurons that are related to incompatible movements, and which engage in competitive interactions’. In order to avoid excessive conflict ‘neurons that are related to compatible movement components should be linked together with synchronizing connections’.

The measurement of synchronous oscillations has surely brought new possibilities to model cognitive functions in the brain. Other frequencies have also been measured, as the theta (4–7 Hz) coherence between prefrontal and posterior association cortex in humans (Sarnthein et al., 1998). The view that synchrony has a role of reducing conflict is attractive; combining synchrony and asynchrony the brain could solve some (but not all) kinds of conflict. In our view, synchrony per se doesn’t promote conscious integration, yet it does have a role in supporting the mechanism of integration. Synchrony is well suited to the role of ‘temporally gluing’ neuronal assemblies to participate in a quantum entangled state; it could be a necessary step in the preparation of macro-entangled states that cover diverse parts of the brain. The macro-entangled states are assumed to occur between internal proteins activated by signal transduction processes in the cells participating in an assembly, generating a supplementary interneuronal communication that would effectively integrate the spatially distributed processes that participate in the composition of a unitary conscious perception.

6. The triggering of conscious perception

The distributed character of brain processing is a well-established theory. According to this approach (Fuster, 1995; LeDoux, 1996; Fuster, 1997; Bartels and Zeki, 1998; Tononi et al., 1998), cognition may be eventually supported by activity in each and all of the areas of the cerebral cortex and several subcortical structures. Perception depends on neural activity in multiple regions simultaneously activated (Gevins et al., 1994; Fuster, 1995, 1997; Knight, 1997; Roy John et al., 1994; Fuster, 1995; LeDoux, 1996; Fuster, 1997; Bartels and Zeki, 1998; Kastner et al., 1998; Ojemann et al., 1998; Uningerleider et al., 1998), rather than in a single region. The same idea holds for memory: during free recall or recall generated by perception in a recognition task, the multiple region activity necessary for the retrieval occurs near the sensory portals and motor output sites (Damasio, 1990), hence the recall of experiences is assumed to be supported by centrally guided reactivation of those input and output sites, and not by central or peripheral areas alone. The distributed theory of brain processing has been also supported by studies on neuronal plasticity. Although inherited information plays an important role in the specification of cerebral connectivity, the networks are shaped by experience as a result of the concurrent activation of neuronal ensembles responding to diverse aspects of the environment and controlling motor and endocrine action. The variety of potential connections allowed by the mechanisms of plasticity confirms the idea that each neuronal ensemble may be part of multiple networks and thus take part in multiple cognitive processes.

The major cortical neuronal ensembles (Edelman, 1989; Fuster, 1995; LeDoux, 1996; Schmahmann and Sherman, 1998) are organized into:
1. ‘primary and early association cortices (both sensory and motor), which constitute the substrate for feature-based records’ (Damasio, 1990);
2. ‘association cortices of different orders (both sensory and motor), some limbic structures, and the neostriatum/cerebellum, which constitute the substrate for convergence zones’ (Damasio, 1990), and
3. frontal cortices and their connections with other convergence zones, which constitute the substrate for executive functions.

Feed-forward and feedback connectivity interrelates (1), (2) and (3) at multiple hierarchical levels, with reciprocal patterns, and provides the substrate for some synchronized action among their neuronal ensembles (Damasio, 1990). This and a loosely hierarchical processing provide the main strategies to keep conflict among neural subsystems between acceptable boundaries. They are also the key elements providing two sort of coherent signals – sensory and central reentrant pieces of information, to be detected by the NMDA channel at the sensory cortical areas, in charge of triggering the conscious processing when systemic conflict reaches a critical threshold (Fig. 3).

Rhythmic activity in the brain may be both a local subject as well as a coordinated action promoted by specific systems. Asynchrony enables each DIPS’ agent to operate as quickly as possible given local circumstances (Hewitt and Inman, 1991; Bartels and Zeki, 1998; Zeki and Bartels, 1998), but it also favors conflict, because new information can generate new commitments conflicting with pre-existing not yet updated local commitments. Local authority enables participants to react immediately to changing circumstances (Hewitt, 1977; Hewitt and Inman, 1991), but they may have to consult (or be consulted by) more centrally decision makers when conflicts arise. Synchronous activity enforces agents to import and export data at more or less defined epochs to reduce any possible measure disagreement in a changing environment. Any central coordination by executive agents certainly reduces conflict in distributed processing, but it may also reduce the computational capacity of the distributed system proportionally to the computational capacity of the central schedulers. Self-reliance is the agent’s capability to act using the resources available locally, whereas interdependence refers to its capacity to obtain resources elsewhere in order to act. The balance among self-reliance and interdependence is the key issue for any DIPS to keep conflict within acceptable boundaries and to allow intelligence to emerge from the coherent activity of a team of loosely connected agents.

Whenever consensus, negotiation, synchronization and loose hierarchies fall short to reduce conflict among different agents, any weakly spatially constrained process, following the model of non-local effects in the quantum domain may be of interest to guarantee a global information distribution among conflicting agents, which may provide a way of reducing conflict and helping to guide the system’s adaptive behavior. Consciousness is proposed to be supported by this kind of weakly constrained computations in charge of reducing conflict among different cerebral agents. Current research on cognitive neuroscience has mainly attempted to identify neural correlates of consciousness at

![Fig. 3. The proposed reentrant circuit.](image-url)
the level of network electrical activity and chemical types at the synapse (Taylor, 1998; Frith et al., 1999; Perry et al., 1999), recently focusing on molecular changes in protein conformation related to the (presumably conscious) retrieval of information about a painful experience (Nader et al., 2000). The logical consequence of our assumption is that continuously solving systemic conflict in the brain and generating an unitary consciousness would require a supplementary mechanism, allowing communication between STP processes in large neuronal populations. Contemporary science and technology give us a suitable model of what such a supplementary mechanism would be, the model of quantum computing theory and experimentation.

Proposals of a quantum basis of consciousness may be surprising at first sight, because of the brain is a macroscopic system and scientists in many areas are accustomed to avoid mixing different scales in the study of the same system. However, besides recent attempts to build multiscale models in science (Glimm and Sharp, 1997), biological evidence also indicates that the brain simultaneously works at different scales: peripheral sensors are sensible to photons, electrons and microscopic particles; neurons at the CNS receive electrochemical information and transduce it to the molecular level, activating ion currents, STPs and other microscopic phenomena in biological molecules. Therefore, an adequate discussion of the biophysical basis of consciousness must refer to different scales of brain activity and to possible interactions between phenomena occurring in each one. The core idea of our proposal is the following (Fig. 4):

1. The sensory signal arriving at the PCN is responsible, among others, for promoting a membrane depolarization that may displace Mg$^{2+}$ from the NMDA channel. The degree of this depolarization is dependent on the actual membrane encoding properties. It is supposed to be greater in the case of the tonic spiking state associated to wakefulness than in the case of the rhythmic burst firing observed in the case of the slow wave sleep.

2. The sensory terminals contact the proximal dendritic membrane of the pyramidal neuron and then, besides controlling Mg$^{2+}$ at the NMDA channel, they provide electrical activation serving the sensory processing. This activation may result in a spike volley at the axon encoding the result of such processing, to be distributed to other high-order neurons. The thalamic incoming information utilizes mainly AMPA channels to promote such effects.

3. The tonic spiking state at TRN is responsible for better signal-to-noise ratio encoding of the sensory information to be transmitted to the primary sensory cortical areas. On the contrary, the rhythmic burst firing will be associated to a low rate of information transmission.

4. The cortico-thalamo-cortical loop is in charge both of synchronizing the different sensory volleys that must reach the cortex, as of defining the structure and size of the codewords used to convey the possible highest amount of information. This is assured by the tonic spiking code.

5. Reentrant information from high-order cortical neurons is distributed over the distal sites of the dendritic tree of the pyramidal sensory cortical neuron. The glutamate released by this reentrant signal is proposed to bind to NMDA channels.

6. If both the sensory information and the reentrant signal are coherently associated then Ca$^{2+}$ entrance is favored, due to the properties of NMDA channel acting as a coincidence detector discussed above. This Ca$^{2+}$ entrance in normal circumstances is likely to occur in the tonic spiking state, and it is likely to be blocked in the case of rhythmic burst state.

7. The Ca$^{2+}$ entrance now activates several STPs inside the PCN, through, e.g., its binding to CaM (Fig. 4) and phosphorylation of kinases (Alkon et al., 1998; Shen and Meyer, 1999). Among these pathways, one will be of interest. CaM may bind to a CamKII or other phosphorylated protein anchored near the NMDA channel. This activated protein is assumed to be in charge of generating the required non-local transactions supporting the conscious process. For example, it could take place at the protons $^1$H or $^{13}$C of the protein or at the atom of a cation linked to it (see discussion below).

8. The above quantum effects are proposed to trigger threshold transitions at other proteins of the same
kind, previously entangled and simultaneously activated at the high-order cortical neurons involved in generating the reentrant signal. This is a key step in order to guarantee that the conscious event is not a mere epiphenomenon, because it allows that the quantum computation triggered by the above Ca\(^2+\) entrance will change the activity of all neurons experiencing such threshold changes of state.

9. This highly efficient communication between entangled and simultaneously activated molecules convey information for conflict solution. Cycles of quantum computation may be repeated until the conflict is finally resolved. This hypothesis is supported by ERP data showing that conflict may be identified as latter as 400–700 ms, and that its solution may be attained up to 1 s after the initial stimulus was presented.

10. This conscious computation is available during wakefulness and inhibited during the slow wave sleep. In the case of REM sleep it may be activated if pontogeniculocipital spikes are assumed to play the same role of the sensory stimuli in modulating the state of the NMDA channel.

7. Quantum computing and macro-entanglement

Let Q be a device having at least two possible states, e.g. activated/not activated, phosphorylated/not phosphorylated, conducting/not conducting, etc., respectively denoted as \( |1\rangle \) and \( |0\rangle \). If both states can coexist at the same time in any arbitrary condition, Q is defined as a quantum device (Fig. 5).

An important rule in the quantum domain is: what is not forbidden is compulsory (Gilmore, 1995). Therefore, state superposition is the expected condition for Q unless a restriction is given. Coherence is the property that allows state superposition. Decoherence brings quantum states back to classic behavior. Both processes may be controlled by adequate energy transactions. Quantum computing is supported by quantum devices, Q. Classic bits can take either value 0 or 1, but quantum bits (qubits) can be in a linear superposition of the two classical states. If classical bits are denoted \( |1\rangle \) and \( |0\rangle \), a quantum bit can be in any state (Brassard, 1997; Brassard et al., 1998)

\[
|\psi\rangle = x|1\rangle + \beta|0\rangle,
\]

where \( x \) and \( \beta \) are complex numbers called amplitudes, subject to

\[
|x|^2 + |\beta|^2 = 1.
\]

Any attempt at measuring qubits induces an irreversible disturbance. Direct measurements on \( x|1\rangle + \beta|0\rangle \) results in the qubit making a probabilistic decision: with probability \( |x|^2 \), it becomes \( |0\rangle \) and with complementary probability \( |\beta|^2 \), it becomes \( |1\rangle \) (Brassard et al., 1998).

Unlike classical bits, where a single string of \( n \) zeros and ones suffices to describe the state of \( n \) bits, a physical system of \( n \) qubits requires \( 2^n \) complex numbers to describe its state. For example, two qubits can be in the state

\[
x|00\rangle + \beta|01\rangle + \gamma|10\rangle + \delta|11\rangle,
\]

subject only to the constraint that

\[
|x|^2 + |\beta|^2 + |\gamma|^2 + |\delta|^2 = 1.
\]

Four complex numbers are required to describe the above state superposition.

Let a quantum computer (QC) be defined by Eq. (3), subject to the condition stated by Eq. (4). A given instruction \( I_i \) may be written on it by, e.g. changing its state to

\[
x|00\rangle + \beta|01\rangle + \gamma|10\rangle - \delta|11\rangle,
\]

that is, by modifying the condition of qubit \( |11\rangle \). Experimentally, this operation corresponds, e.g., to a phase shift in spin orientation. Now, it is possible to ask the following question as the solution of the quantum computation:

\[
x < 00| + \beta < 01| + \gamma < 10| - \delta < 11|
\]

subject to the constraint that

\[
|x|^2 + |\beta|^2 + |\gamma|^2 + |\delta|^2 = 1.
\]

What makes QC programmable is the phenomenon of amplitude interference among quantum states. Interference is a classical property of waves. It happens when amplitudes or disturbances from different sources come together, since they may add in some places and subtract or cancel in others. This will result in regions of intense or low activity respectively (Fig. 6). Interference requires extended, overlapping distributions. Particles, which may take different paths (states) exist as superposition of amplitudes. Each possible path contributes an amplitude, or option, for the particles’ behavior, and the amplitudes are all present together. Further, if these amplitudes are in some way brought together then they can add or subtract and the overall probability distribution is changed. This effect is seen in practice wherever it might be expected. Quantum com-

![Fig. 5. State superposition of a quantum device.](image-url)
computing takes advantage of interference to change state amplitudes for both writing and reading instructions (Gilmore, 1995; Ahn et al., 2000). Interference is also responsible for the collapse of a quantum state into a classic one.

Nuclear magnetic resonance (NMR) is being used to implement a QC (Warren, 1997). From the perspective of the NMR chemist, the primary purpose is to elucidate molecular structure and chemical dynamics, and great efforts are made to enhance the desired signal and render the detected spectra into a form that reflects properties of the system under study. From the perspective of the QC scientist, the main purpose is to change molecule spin orientation, by means of radiofrequency pulses (rfps) (Gershenfeld and Chuang, 1997). Sequence of rfps, which manipulate spin orientations and couplings constitute quantum logic gates and perform unitary transformations on the state, because it may control interference.

The first step in NMR quantum computing is to create coherence, by using rfps in order to create state superposition. The second step also uses rfps, to modify spin orientations in order to write the desired instruction. Finally, rfps are used to change state probabilities to enhance the probability (i.e., to cause the collapse) of the desired answer.

Given a QC defined by the following superposition (Brassard et al., 1998; Chuang et al., 1998):

$$\left| \psi_0 \right> = (|00\rangle + |01\rangle + |10\rangle + |11\rangle)/\sqrt{2}, \quad (8)$$

$$\alpha = \beta = \gamma = \delta = \sqrt{2},$$

equation numbers (1) to (2)

rfps may be used to flip the phase of the adequate element in order to change it to

$$\left| \psi_0 \right> = (|00\rangle + |01\rangle + |10\rangle - |11\rangle)/\sqrt{2}. \quad (9)$$

Measurement of this state is not useful because each answer occurs with equal probability $\sqrt{2}$. Grover’s algorithm (Grover, 1998) amplifies the correct answer by following the conditional flip with a second operation that inverts each state about the mean. Applied to the superposition $\Sigma_k x_k|k\rangle$, this step gives a new state $\Sigma_k \beta_k|k\rangle$, with

$$\beta_k = -x_k + 2(z), \quad (10)$$

where $z$ is the mean value of $x_k$ (Chuang et al., 1998). For the QC defined by Eq. (8) and the flip for $k = 4$, the inversion about the mean is the state $|\psi_1\rangle = |11\rangle$, that provides the desired answer, because

$$z = (1/2 + 1/2 + 1/2 + 1/2)/4 = 1/4. \quad (11)$$

$$\beta_1 = -1/2 + 2(z) = 0,$$

$$\beta_2 = -1/2 + 2(z) = 0,$$

$$\beta_3 = -1/2 + 2(z) = 0,$$

$$\beta_4 = -1/2 - 2(z) = -1.$$ But the probability of any state $|\psi_k\rangle$ is given by $\beta_k^2$, that results in a probability equal to 1 for $|11\rangle$ and equal to zero to all other states.

Quantum parallelism arises because a quantum operation acting on a superposition of inputs (Eq. (12)) produces a superposition of outputs (Eq. (13)). For example, consider some function $f$ and a quantum logic circuit $U$ that computes it by mapping quantum register $|x, 0\rangle$ to output $|x, f(x)\rangle$. Let $x$ and $y$ be two distinct inputs, and prepare the superposition (Brassard et al., 1998)

$$\left( |x, 0\rangle + |y, 0\rangle \right)/\sqrt{2}. \quad (12)$$

Applying $U$ produces

$$\left( |x, f(x)\rangle + |y, f(y)\rangle \right)/\sqrt{2}. \quad (13)$$

The value of function $f$ is computed on both inputs $x$ and $y$ even though circuit $U$ is used once only. This works for even larger superpositions. For example, applying $U$ to

$$\Sigma \epsilon |x, 0\rangle, \quad \epsilon = 2^{-n/2} \quad \text{as normalization factor} \quad (14)$$
gives

$$\Sigma \epsilon |x, f(x)\rangle \quad (15)$$
an equal superposition of all input–output pairs. An exponential amount of computation has been achieved in the time it takes to compute the function on a single input. Quantum parallelism is a key issue in conflict solving because it reduces the spatial constraining over information distribution.

NMR QCs have been built based on $^1$H and $^{13}$C nuclei in isotopically labeled chloroform (Chuang et al., 1998), on $^{2}$Ce atom (Ahn et al., 2000), using two $^1$H nuclei in cytosine (Jones, 1998), and on the molecules of alanine and trichloroethylene. These results clearly
show that quantum computing may be implemented in organic molecules, mainly on aminoacids. Another technique being proposed to implement quantum computing is that of ions in a array of microtraps (Cirac and Zoller, 2000). In this approach, a set of N ions confined in independent harmonic potential wells, which are separated by some constant distance $d$ is used to implement the QC. This can be done if $d$ is large enough to prevent Coulomb repulsion to excite the vibrational state of the ions and to allow the ions to be individually addressed.

Following the above evidences, we assume that state superposition may be achieved on specific proteins associated to the STP governed by Ca$^{2+}$ entrance through NMDA channels (Fig. 7). Coherence of protein states may be achieved by means of energy pulses furnished by CamKs-controlled phosphorylations. In other words, coherence may be built by means of metabolic energy pulses (meps). Also, meps may write sensory instructions as well as other information provided by supplementary reentrant signals on these QCs. Instruction writing may also be executed by meps delivery by STPs controlled by other associated (e.g. intra-collen-) incoming signals. Interference is proposed to be responsible for finally provoking the decoherence associated to the reading of the resultant quantum computation. Decoherence will be triggered by energy pulses delivered by other STPs, perhaps activated by signals arriving from high frequency synchronizing neurons.

Entanglement of two or more quantum objects is a process whereby the quantum mechanical wave functions describing these individual objects are manipulated to create a new, interwoven state comprising a superposition of the individual wave functions (Fig. 9). In this entangled system, all objects are correlated, and measuring the state of just one of them gives information on all of the others. This is the same to say that entanglement allows instantaneous information transmission among all entangled objects. This is what is sufficient to solve any class of conflict in DIPS.

Consider the two qubit state
\[
|\psi^+\rangle = \frac{1}{\sqrt{2}} (|00\rangle - |11\rangle).
\]
\[
|\psi^-\rangle = \frac{1}{\sqrt{2}} (|00\rangle + |11\rangle).
\]
\[
|\phi^+\rangle = \frac{1}{\sqrt{2}} (|00\rangle + |11\rangle).
\]
\[
|\phi^-\rangle = \frac{1}{\sqrt{2}} (|00\rangle - |11\rangle).
\]

This state is less complicated than it actually looks, because it can be factored into the product of two one qubits states, each of which is
\[
(0\rangle - |1\rangle)/\sqrt{2}.
\]
cannot be factored. When these two qubits are measured, they yield either 0 and 1 or 1 and 0, with equal probability \(1/\sqrt{2}^2 = 1/2\) (Brassard et al., 1998; Bennett and DiVincenzo, 2000), but which of these two outcomes will occur is not determined until the measurements is actually performed. These entangled states are called Bell states or EPR (Enstein-Podolsky-Rosen) pairs.

Entanglement supports quantum teleportation and quantum superdense coding (QSC). These involve an initial stage (Bennett and DiVincenzo, 2000) in which a EPR pair is shared between two parties with an amplitude \(x = 1/\sqrt{2}\), followed by a second stage in which this shared entanglement is used to achieve, respectively, transmission of a qubit via two classical bits, or transmission of two classical bit via one qubit. The problem QSC solves is to enable two protagonists, Alice and Bob, who share no secret information initially, to transmit a secret message \(x\), for example, a cryptographic key, under the nose of an adversary Eve, who is free to eavesdrop on all their communications (Fig. 10).

If Alice and Bob are limited to classical communication, they cannot detect eavesdropping, or can they prevent Eve from overhearing enough information to recover their entire secret. The best they can hope for is to make it computationally difficult for her to do so. Now, if Alice and Bob's classical public communication is supplemented by a quantum channel, the fragile nature of quantum information will prevent Eve to eavesdrop on. Any eavesdropping disturbs the quantum transmission in a way likely to be detected by Alice and Bob (Bennett and Shor, 1999). But channel noise may also cause code corruption in quantum transmission. If the quantum channel is not too noisy, Alice can encode the input qubit into several qubits using a quantum error-correcting code, send these through the noisy channel, and have Bob decode them. However, for very noisy channels this will not work. In this case, the best known strategy (Bennett and DiVincenzo, 2000) is for Alice not to send the input qubit through the channel at all, but instead prepare a number of pure EPR pairs, and share them through the noisy channel with Bob, resulting in noisy EPR pairs. Then, using their ability to communicate classically, Alice and Bob distil a smaller number of good EPR pairs, and additional classical communication, to teleport the input qubit safely to Bob.

Quantum cryptography may be required to explain how one single sensory (e.g., visual, auditory, etc.) quantum computation could be prevented to be influenced (or corrupted) by simultaneous computations carried on each other of these sensory modalities. It may be proposed that entanglement in the brain is created and maintained by meps provided by a specific STP, activated by reentrant information over sensory and associative areas. Now, information transmission via classical spiking code may be used to teleport qubits associated to one task safely from other concomitant but dissociated quantum processing (Fig. 11).

In summary, we propose that conscious 'binding', as a solution to computational conflict in the brain, is supported by ensembles of quantum enzyme computers. Such ensembles cover large brain areas activated by afferent and reentrant signals pertaining to the same unitary perception (Fig. 11). Decoherence of quantum states generated in such an ensemble is required for consciousness to be not an epiphenomenon, since it provides the way for conscious processing to alter enzyme action, and in this way to control membrane electrical activity and influence behavior.

8. Conscious quantum computing — a workable hypothesis

The diverse pieces of theory and evidence reviewed in the preceding sections form a picture of how the brain works to generate perceptual consciousness. Conscious processing is, in our model, a multiscale mechanism that encompasses quantum, molecular, cellular and network processes in different time windows.

1. QCs may be prepared in the brain by setting distinct NMDA-coordinated temporally coherent ensembles. This is the task of both the midbrain and limbic attention control circuits, called here general purpose attention system (GPAS), and the more specific attention (frontal and parietal) cortical areas -called here task specific attention system (TSAS).

2. GPAS is in charge of changing the spike code from bursting toward tonic spiking, which enables QC building because tonic spike firing favors the mem-
brane depolarization required to set the NMDA coincidence detector systems. Therefore, GPAS has the central role of enabling QC building in the awake and REM states, and disabling it during synchronized sleep. GPAS controls the spike code by modulating the Ach, NE, HA and 5-HT neurons, that are able to control $I_{KL}$, $I_t$ and $I_H$ at TRNs and PCNs, and in this way to change the membrane from a hyperpolarized toward a depolarized state.

3. TSAS has the capacity to modulate the GPAS action, and in this way it may set different QCs in operation to solve specific tasks, by modulating attention over these specific tasks. TSAS is expected to act mainly by locally increasing Ach, NE, HA and 5-HT action over defined sets of TRNs and PCNs, associated to a given task execution, and also modulating GPAS neurons at the midbrain and hypothalamus. In this way, TSAS may enhance the action of these neurons over specific TRNs and PCNs, while decreasing it over other sets of competing or distracting neurons.

4. Local synchronizing cortico-thalamic systems (LCTS) have the function of setting the quantum computing epochs (qces), and adjusting the codeword length of the spike firing to the selected qces. LCTS are also responsible for determining when instruction writing and result reading on QC is to be performed.

5. Since QC supporting consciousness is assumed to be loosely and weakly spatially constrained, any complex quantum computing must be performed as a series of writings and readings until the proposed problem is solved. LCTS are, therefore, in charge of temporally organizing the qces required by the solution of the conflict in solving an existing problem. This is the role played by executive memory circuits: they are in charge of determining the best sequences of writing and readings over the distinct neural subcircuits supporting different jobs to solve a problem. Initially, conflict must be solved in each sensory system providing information about the task to be performed. In the sequence, each piece of sensory information must be integrated and the conflicts arising from such integration must be solved. Finally, an action must be selected among those possible outcomes as the best way to perform the task.

6. The complex sequence of qces required to solve a task may not in many instances be serially executed since some constraints on the availability of information for conflict solving may require a delay of some computations. Another aspect of the function of executive memory circuits is to keep the record of previously set qces and their results, as well as to track the opportunities of obtaining information to finish the remaining computations.
9. Conclusion

The hypothesis proposed here can be experimentally tested. Some examples of such experiments are briefly discussed.

1. It may be assumed that Ca$^{2+}$-activated proteins would have $^1$H and/or $^{13}$C of at least one of its aminoacids entangled (Figs. 7 and 8). A possible candidate would be tyrosine, a frequent and important component of many STPs (Rocha, 1997). Tyrosine would be used to build a NRM QC using the same techniques described (Warren, 1997 and Jones, 1998). In the case of a successful experiment, the dynamics of the used rfps should be carefully studied. Once this dynamics is specified, it would be possible to verify if it could be replicated by means of a sequence of meps. In the negative case, the hypothesis would be refused, otherwise it would receive strong experimental support.

2. Once some putative aminoacid is identified, enzymes from the STPs containing this aminoacid could be searched. A very short transduction pathway (VSTP; Pereira and Rocha, 2000) consistent with the timing of conscious perception would have to operate in the range of milliseconds, and for this reason the quantum computing enzyme is supposed to be located very near the NMDA channel. Also, this VSTP has to be constituted by a very few elements supporting a short cascade of enzymatic transactions.

3. Different VSTPs may eventually identified associated to the different primary sensory cortices. If this is the case, their similarities and differences should shed some light on how different 'qualia' may arise from quantum computing.

4. Once any quantum computing enzyme of these VSTPs is identified, the genes encoding them may be searched for. In the case of successful results, knockout gene technology should be used to produce animals deprived of specific conscious sensory processing. For example, genetic blindsight would be technically produced.

5. If such animals become available, the electrophysiology of conscious events would be amenable to experimental scrutiny by comparing the electrical activity of normal and animals deprived of some conscious capacity. Also, the physiology of VSTPs would be studied in details by comparing the enzymatic transactions of normal and such genetic-engineered cells.

Many other kinds of experiments would be thought if some of the above propositions are tested successfully. The most important consequence from the above is to help bringing the study of consciousness to the laboratory and turning it an empirically testable subject, other than a matter for thought experiments and/or armchair speculation.