# Time-Irreversible Quantum-Classical Dynamics of Molecular Models in the Brain

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# Abstract

This manuscript aims to illustrate a quantum-classical dissipative theory (suited to be converted to effective algorithms for numerical simulations) within the long-term project of studying molecular processes in the brain. Other approaches, briefly sketched in the text, have advocated the need to deal with both quantum and classical dynamic variables when studying the brain. At variance with these other frameworks, the manuscript's formalism allows us to explicitly treat the classical dynamical variables. The theory must be dissipative not because of formal requirements but because brain processes appear to be dissipative at the molecular, physiological, and high functional levels. We discuss theoretically that using Brownian dynamics or the Nosè-Hoover-Chain thermostat to perform computer simulations provides an effective way to introduce an arrow of time for open quantum systems in a classical environment. In the future, We plan to study classical models of neurons and astrocytes, as well as their networks, coupled to quantum dynamical variables describing, e.g., nuclear and electron spins, HOMO and LUMO orbitals of phenyl and indole rings, ion channels, and tunneling protons.

**Keywords:** quantum-classical dynamics; quantum brain; open quantum systems; neuroscience

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#### I. INTRODUCTION

Recent years have witnessed the coming of age of quantum biology [1–6]. This has led to attempts at modeling some molecular and cell phenomena happening in the brain in terms of quantum mechanics [7–9]. Quantum models are expected to explain not only local effects, such as charge transfer or tunneling (important at both the cellular and the sub-cellular scales), but also non-local mechanisms, invoking, for example, quantum synchronization and entanglement [10–12].

The diameter of the soma of neurons ranges to be between 4 and 100  $\mu$ m while thier lengths are about 10 to 25  $\mu$ m. However, human motor neurons can be longer than one meter. The hot (in healthy subjects, the average brain temperature is 38.5 °C and deeper brain regions frequently even exceed 40 °C) and the watery environment of the brain make quantum mechanical treatments of all the brain coordinates unrealistic.

We do not believe that the coherence of large domains can be the physically relevant property for quantum effects in the brain. Decoherence [13-15] suggests that quantum coherence cannot play a role in the brain. However, nuclear and electron spins, HOMO and LUMO orbitals of phenyl and indole rings, ion channels, and tunneling protons, for example, could be treated quantum mechanically even at room temperature. Pascual Jordan proposed a mechanism to amplify information from the quantum to the classical level [4–6], and he considered it as key to quantum biology. This process is akin to any measurement, where a quantum state is reduced and registered irreversibly into a specific state of the environment (i.e., a state of the measuring apparatus). In other words, the nonlinear quantum reduction process controls the environment, determining its state. Jordan used the term 'amplification' because in such a process the physical information is transferred from the atomic/molecular level to the macroscopic scale of the environment. When devising explanations of quantum biological phenomena, we think that Jordan's amplification must be considered together with the environment backreaction onto the quantum subsystem [9]. The quantum-classical (QC) formalism of Refs. [16–36] naturally complies with this physical requirement.

We consider microscopic (quantum) phenomena taking place on the scale between petaHz and teraHz. For example, the HOMO/LUMO frequency of oscillations in carbon rings is of the order of petaHz. We expect proton tunneling to also unfold in the brain on the scale of petaHz. Another example of a quantum process is given by the variation of both the magnitude and direction of the dipole magnetic field at the nucleus of a Posner molecule, with a frequency around about ten teraHertz [7, 8]. From teraHz upward, a classical description can often suffice. Mesoscopic dynamics can be represented by oscillations of biomembranes. Their thermal fluctuations can occur in the interval between teraHertz and gigaHertz. The frequency of biomembranes' dynamical response to stimuli, such as ion channels' flow, can vary between Hz and kHz, while perturbations arising from, e.g., the application of biosensors can cause oscillations in the interval between kHz to MHz. Such frequency values lead to resonances and nonadiabatic dynamics. Considering the frequencies associated with quantum and classical coordinates' dynamics, the resonance mechanism suggests that such dynamics are coupled.

Hence, we are led to consider brain models requiring the simultaneous presence of classical dynamical variables as well as quantum coordinates shielded from decoherence. To this end, we introduced an abstract model [9], based on a quasi-Lie bracket (QLB) [22–25], for studying molecular processes in the brain. The formalism described in Ref. [9] treats quantum and classical dynamical variables on an equal footing, entailing the occurrence of both quantum [37–39] and classical [40] phase transitions. From this perspective, the brain is a complex emergent nested system that supports both quantum and classical complexity [41]. Numerical algorithms are already available for performing computer simulations of such models [26–33].

An example of the type of model we would like to simulate in the future is given by a Hodgkin–Huxley model [42, 43] coupled with suitable quantum dynamical variables, such as those above listed. In fact, despite its success, some weaknesses of this model have already been discussed [44–46]. A significant one is the description of ion channels [47, 48]. This is particularly relevant to our endeavor because studies suggest the relevance of quantum mechanical effects in ion channels [49– 51]. As we have already discussed above, such studies invoke quantum mechanics based on shielding the confinement of quantum dynamical variables.

Besides devising abstract models, and adopting the ideas of complex systems biology [52] in the study of the brain, it would also be important to first look for observables carrying information from the quantum to the classical level, and only afterward developing the theoretical model. In this respect, in agreement with our thought, it has been suggested that the brain is both a (classical) neurocomputer and a quantum computer [53]. One way to elaborate quantum information would arise from the coupling between HOMO/LUMO quantum coherent dynamics and the orientation of carbon rings in microtubules [54]. Another example is given by cytoskeletal signaling, where it has been suggested that memory could be encoded in microtubule lattices by CaMKII phosphorylation [55–57], offering far better stability than that of synapsis.

We deem our theoretical efforts particularly useful in searching for such QC observables that are relevant to brain dynamics. Given the current limitations of experimental techniques, devising measurements with a high signal-to-noise ratio is difficult. The hope is that the development of quantum metrology [58–66] could also help in this endeavor. As the authors of Ref. [67] state, "Experimental methods, which could distinguish classical from quantum correlations in the living brain, have not yet been established." Nevertheless, their NMR measurements suggest that proton spins in bulk water act as an entanglement mediator between quantum dynamical variables in the brain [67].

Quantum effects based on the tryptophan molecule were observed in Ref. [68]. Tryptophan organizes spatially in various cellular structures. The cooperative effects induced by the ultraviolet excitation of tryptophan network structures, which are of interest for biological systems, were theoretically and experimentally investigated. The theory predicted a superradiant response of the tryptophan networks to the ultraviolet excitation. In turn, this determines an enhancement of the fluorescence quantum yield that was experimentally confirmed [68].

Entanglement in the brain may also be generated by oscillations in C-H bonds in the myelin sheath [69]. Using Cavity QED [70], the C-H bonds in the tails of lipid molecules were observed to radiate entangled photon pairs [69]. The authors suggested that the confining myelin sheath could play a similar role to the cavity of the experiment, facilitating the emission of entangled photons by vibrating bonds. In turn, such entangled photons would be responsible for the synchronization between far regions in the brain.

The systems of Refs. [67–69] can be analyzed through QC toy models on which one can perform numerical experiments with the aid of a computer. The target would be to trace the qualitative aspects of the observed behavior of the brain in the numerical response exhibited by the toy models. This numerical approach has no quantitative ambitions for the prediction of aspects of brain activity. Rather, this investigative strategy could help us make progress in improving the selection of the QC model to adopt.

In this paper, we highlight how quantum-classical models, when applied to the dynamics of brain molecules, must necessarily be dissipative so that the direction of time flow can be fixed. The formalism of Ref. [9] can simulate dissipation (and, thus, the direction of time) using two methods, both based on embedding the quantum subsystem in a dissipative classical bath [32]. The first method uses Langevin-like dynamics for the classical variables [35]. The second one applies a deterministic NHC thermostat [71, 72] to the classical variables [22, 23]. We must note that there are other approaches, see Refs. [54, 73–82], to brain modeling that entail dissipation and a fixed direction for the arrow of time. These approaches, however, treat classical coordinates only implicitly, given that they do not appear in the Hamiltonian.

The idea that theoretical models of the dynamics of brain molecules must possess a fixed direction for the arrow of time has been derived from psychology and neuroscience. In a deeply anesthetized subject, without self-awareness, there is no feeling of the passage of time. From this perspective, we can say that self-awareness is the necessary status of the mind making us capable of understanding the difference between the future and the past. The breaking of time-reversal symmetry is associated with the second law of thermodynamics [83], and neuroscientists have been interested in the details of how such a law applies to the brain; see, e.g., Refs. [84–88].

The paper is structured as follows. In Section II, we introduce the theory of open quantum systems embedded in classical environments (also more simply called quantum-classical systems). In Section III, we discuss an open quantum subsystem in a dissipative classical bath that is subject to Langevin dynamics [35]. A different method of simulating dissipation, which uses the NHC thermostat, is presented in Section IV. These three theoretical sections are followed by Section V. In this section, we illustrate how nontrivial molecular processes and higher brain functions of interest for our research projects display time asymmetry: the diffusion molecular process [84] is involved in synaptic transmission, action potential propagation, and ion flow in cellular channels [85], while the response of different regions of the cerebral cortex to visual stimuli [86, 87], the time scale of irreversibility in obsessive-compulsive disorder (OCD) [88], and spatial neglect with temporal asymmetry [89–92] are examples of phenomena in higher brain functions. We expect that these phenomena can ultimately constitute a field of research for our theory. Our conclusions are given in Section VI. Appendices VI and VI sketch the Dissipative Quantum Model of the Brain (DQMB) [73–78] and the Orchestrated Objective Reduction (Orch-OR) approach, respectively.

### **II. QUANTUM SYSTEMS IN CLASSICAL ENVIRONMENTS**

The formalism of Refs. [16–25] can be expressed in a way that is suitable for studying the dynamics of brain molecules [9]. The fundamental object of the theory is the Wigner function operator depending on the classical degrees of freedom (DOF) of the system S + B, pictorially represented in Figure 1. When studying open systems, the rigorous approach is based on the use of the density matrix, which in this case reads  $\hat{\rho}(\hat{r}, \hat{R}, t)$ , where  $\hat{r}$  are the position operators of system S and  $\hat{R}$  are the position operators of system B. The equation dictating the dynamics of the total system S + B is the quantum Liouville equation  $\partial \hat{\rho}(t)/\partial t = -i/\hbar[\hat{H}, \hat{\rho}(t)]$  [93], where  $\hat{H}$  is the total Hamiltonian operator of the interacting system S + B. Upon performing a partial Wigner transform of the density matrix over the operators  $\hat{R}$  [21], the density matrix transforms into the Wigner operator  $\tilde{\mathcal{F}}_{W}(X;t)$ , where X = (R, P), and the quantum Liouville equation transforms into

$$\frac{\partial \tilde{\mathcal{F}}_{\mathrm{W}}(\hat{r}, X; t)}{\partial t} = \tilde{\mathcal{F}}_{\mathrm{W}}(\hat{r}, R; t) e^{\frac{\hbar}{2i} \overleftarrow{\nabla}\Omega \overrightarrow{\nabla}} \tilde{H} - \tilde{H} e^{\frac{\hbar}{2i} \overleftarrow{\nabla}\Omega \overrightarrow{\nabla}} \tilde{\mathcal{F}}_{\mathrm{W}}(\hat{r}, X; t) .$$
(1)

Variables R and P in Equation (1) are c-numbers and can be interpreted as phase space coordinates. Accordingly,  $\nabla = ((\partial/\partial R), (\partial/\partial P))$  is the phase space gradient and  $\Omega$  is the symplectic matrix

$$\mathbf{\Omega} = \begin{bmatrix} 0 & 1 \\ -1 & 0 \end{bmatrix} \,. \tag{2}$$

The symbol  $\hat{H}$  denotes the partial Wigner transform of the Hamiltonian operator  $\hat{H}$ . Also, note that from here onwards purely quantum operators will be denoted by  $\hat{\mathcal{O}}$ , phase-space-dependent operators will be denoted as  $\tilde{\mathcal{O}}_j$ ,  $j = 1, \ldots, n$ , and purely classical variables will be denoted as  $\mathcal{O}_J(X)$ ,  $J = 1, \ldots, N$ . The definition of X,  $\tilde{\mathcal{O}}_j$ , and  $\mathcal{O}_J(X)$  is determined by the system to be studied. We want to remark that Equation (1) is exact and that, at this stage, we have not simplified

the formulation concerning the quantum Liouville equation. However, if the de Broglie wavelength  $\lambda$  associated with the dynamics variables  $\hat{r}$  is much larger than the de Broglie wavelength  $\Lambda$  associated with the dynamical variables  $\hat{R}$ ,  $\lambda \gg \Lambda$ , Equation (1) can be linearized, obtaining a QC approximation of the dynamics of the system S + B:

$$\frac{\partial}{\partial t}\tilde{\mathcal{F}}_{W}(t) = -\frac{i}{\hbar} \begin{bmatrix} \tilde{H} & \tilde{\mathcal{F}}_{W}(t) \end{bmatrix} \mathcal{D} \begin{bmatrix} \tilde{H} \\ \\ \\ \\ \tilde{\mathcal{F}}_{W}(t) \end{bmatrix}, \qquad (3)$$

$$= -\frac{i}{\hbar} \left( \tilde{H}, \tilde{\mathcal{F}}_{W}(t) \right) . \tag{4}$$

In Equation (4), we have defined the antisymmetric matrix operator  $\boldsymbol{\mathcal{D}}$  as

$$\boldsymbol{\mathcal{D}} = \begin{bmatrix} 0 & \left(1 + \frac{\hbar}{2i} \overleftarrow{\boldsymbol{\nabla}} \Omega \overrightarrow{\boldsymbol{\nabla}}\right) \\ - \left(1 + \frac{\hbar}{2i} \overleftarrow{\boldsymbol{\nabla}} \Omega \overrightarrow{\boldsymbol{\nabla}}\right) & 0 \end{bmatrix} .$$
(5)

Such an approach naturally leads to emergent complex nested systems [41].

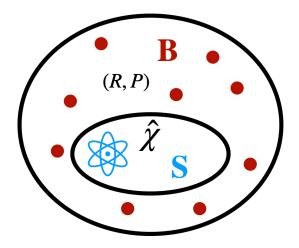


FIG. 1: Pictorial representation of a quantum subsystem S in its classical environment B. The quantum system is specified by quantum operators  $\hat{\mathcal{O}}$  that interact with the classical DOF of system B, whose phase space coordinates are (R, P). The transformation of the description from  $\hat{S} + \hat{B}$  to  $\hat{S} + B$  defines a complex emergent nested system [41].

The second equality in the r.h.s of Equation (4) defines the QLB  $(\ldots,\ldots)$ . When Equation (4) is written in its explicit form,

$$\frac{\partial}{\partial t}\tilde{\mathcal{F}}_{\mathrm{W}}(t) = -\frac{i}{\hbar}\left[\tilde{H},\tilde{\mathcal{F}}_{\mathrm{W}}(t)\right] + \frac{\left\{\tilde{H},\tilde{\mathcal{F}}_{\mathrm{W}}(t)\right\} - \left\{\tilde{\mathcal{F}}_{\mathrm{W}}(t),\tilde{H}\right\}}{2} = -i\hat{\hat{\mathcal{L}}}\tilde{\mathcal{F}}_{\mathrm{W}}(t), (6)$$

it is known as the QC Liouville equation, where the QC Liouville operator  $\hat{\mathcal{L}}$  is

$$\hat{\mathcal{L}} = \frac{1}{\hbar} \left( \tilde{H}, \ldots \right) = \frac{1}{\hbar} \left[ \tilde{H}, \ldots \right] + i \frac{\left\{ \tilde{H}, \ldots \right\} - \left\{ \ldots, \tilde{H} \right\}}{2} \,. \tag{7}$$

The QLB is defined as  $(\ldots,\ldots) = \hbar \hat{\mathcal{L}}$ . In a previous paper [9], we compared transcranial direct current stimulation [94–98] to the compression of specific areas of the brain cortex. Here, we would like to note that a modification of  $\Omega$  in Equation (4), according to what is explained in Ref. [72], can simulate the action of a barostat on a computer. This could be used to devise compressible models of the brain, the responses of which can be compared to experiments [94–98]. Suppose self-awareness is related to an asymmetric time flow. In that case, the QC picture of the brain should also describe an irreversible motion in time of the dynamical variables. However, although the primitive form of the QLB formalism breaks time-translation invariance, it is still formally time reversible. To achieve time irreversibility, a second, larger environment including the first classical bath must be included [83]. The QLB confers to QC dynamics peculiar time properties. The QLB [24] obeys the same algebraic rules of Lie brackets, such as Poisson brackets and commutators, except the Jacobi relation that is not valid in general:

$$\sum_{\text{even perm } j,k,m} \left( \left( \tilde{\mathcal{O}}_j(X), \tilde{\mathcal{O}}_k(X) \right), \tilde{\mathcal{O}}_m \right) \neq 0 , \qquad (8)$$

where  $\tilde{\mathcal{O}}_j$ , j = 1, 2, 3 are arbitrary operators. and we sum over the even permutations of (j, k, m). One important consequence of Equation (8) is that the QLB (and thus the whole theory) violates time translation invariance:

$$e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)}\left(\tilde{\mathcal{O}}_{j}(0),\tilde{\mathcal{O}}_{k}(0)\right)\neq\left(e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)}\tilde{\mathcal{O}}_{j}(0),e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)}\tilde{\mathcal{O}}_{k}(0)\right)=\left(\tilde{\mathcal{O}}_{j}(t),\tilde{\mathcal{O}}_{k}(t)\right)$$
(9)

where we have introduced the operator  $(\ldots, \tilde{H})\tilde{\mathcal{O}} = (\tilde{\mathcal{O}}, \tilde{H})$ . In other words, the algebraic expressions built with the QLB, such as those arising in the definition of correlation functions, have an internal 'clock', which singles out the time origin. Nevertheless, microscopic dynamics is formally time-reversible:

$$e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)} \left(e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)}\right)^{\dagger} = e^{\frac{it}{\hbar}\left(\dots,\tilde{H}\right)} e^{\frac{-it}{\hbar}\left(\dots,\tilde{H}\right)} = 1.$$
(10)

In practice, QC dynamics is represented as a piece-wise deterministic process, i.e., a process where deterministic trajectories of the classical-like DOF are interspersed by stochastic events. The interplay of quantum effects and classical statistical fluctuations can be numerically simulated by means of state-of-the-art algorithms [26–33]. There is ample proof of the effectiveness of such algorithms for numerically simulating the dynamics of non-trivial models of condensed matter systems (see, for example, [26–33]).

## III. DISSIPATIVE QC DYNAMICS

Although the time-evolution of a QC system is conservative and time-reversible, one can imagine situations in which it can be viewed as the dissipative dynamics of the QC system included in a stochastic bath. A dissipative QC formalism is suited to describe brain phenomena lacking time-reversal symmetry [32, 33]. We can imagine that the system S + B, represented in Figure 2, is included in a larger bath, U, of very fast classical DOF, Y = (Q, Z); see Figure 2. The embedding bath U interacts only with the small bath B and does not directly couple to the quantum subsystem S. The Y DOF act as a thermal bath and lead to the dissipative dynamics of the S + B system [34]. The total system S + B + U provides an example of a complex emergent nested system [41]. Using projection operator methods, the equation of motion for the QC system S + B has been derived in Ref. [34]. It takes the form of

$$\frac{\partial \tilde{\mathcal{F}}_{W}(t)}{\partial t} = -\frac{i}{\hbar} \begin{bmatrix} \tilde{H} & \tilde{\mathcal{F}}_{W}(t) \end{bmatrix} \mathcal{D} \begin{bmatrix} \tilde{H} \\ \\ \\ \\ \tilde{\mathcal{F}}_{W}(t) \end{bmatrix} + \eta \frac{\partial}{\partial P} \left( \frac{P}{M} + \frac{\partial}{\partial(\beta P)} \right) \tilde{\mathcal{F}}_{W}(t) ,$$
(11)

$$= -i\hat{\mathcal{L}}^{\mathrm{D}}\tilde{\mathcal{F}}_{\mathrm{W}}(t) , \qquad (12)$$

where  $\beta = 1/k_{\rm B}T$ ,  $\eta$  is the friction constant, and  $\hat{\mathcal{L}}^{\rm D}$  is the dissipative QC Liouville operator. Equation (11) is derived under the assumption that the coordinates X' = (R', P') of system U describe harmonic oscillators and they are weakly coupled to the X coordinates of system B. The specific way to integrate over coordinate X' is chosen in order to obtain a correct description of the multiparticle Brownian motion of system S. Without quantum dynamical variables, Equation (11) describes a Markov process. However, when both quantum and classical variables are present, the presence of memory terms depends on whether the total dynamics are adiabatic or nonadiabatic. When the dynamics are nonadiabatic, quantum transitions between the different energy surfaces occur. Moreover, the backreaction of the classical onto the quantum subsystem is expected to generate memory effects for S + B, even if B is affected by memoryless white noise.

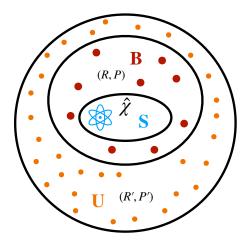


FIG. 2: Pictorial representation of a quantum subsystem S included in a dissipative classical bath B. The B DOF, (R, P), have dissipative dynamics because they are coupled to a larger classical system U with classical DOF (R', P'). The total system S + B + U provides an example of a complex emergent nested system [41]. Whenever the dynamics of U are not considered explicitly, the equations of motion in the Markovian approximation for subsystem B can take a Langevin form.

Upon writing Equation (12) in the adiabatic basis and invoking the theory of random processes [99], one can show that the propagation of the Wigner operator can be calculated in terms of piecewise trajectories on adiabatic trajectories or their coherent superposition, the accumulation of phase factors, and quantum transitions between such trajectories. Here, we sketch this derivation, and more details are found in Refs. [34, 35].

The typical partially phase-space-dependent Hamiltonian operator found in statistical mechanics has the form of

$$\tilde{H} = \frac{P^2}{2M} + \tilde{\eta}(R) .$$
(13)

The adiabatic basis is defined by the eigenvectors  $|\Phi_{\alpha}\rangle$  of the phase-spacedependent Hamiltonian operator  $\tilde{\eta}(R)$  of subsystem S:

$$\tilde{\eta}(R)|\Phi_{\alpha}\rangle = E_{\alpha}(R)|\Phi_{\alpha}\rangle , \qquad (14)$$

where  $E_{\alpha}(R)$  are the adiabatic eigenvalues. The adiabatic representation of  $\tilde{\tilde{\mathcal{L}}}^{D}$  is given by

$$i\mathcal{L}^{\mathrm{D}}_{\alpha\alpha',\nu\nu'}(t) = \left(i\phi_{\alpha\alpha'}(R') + i\Gamma^{\mathrm{K}}_{\alpha\alpha'}(t)\right)\delta_{\alpha\nu}\delta_{\alpha'\nu'} - \mathcal{J}_{\alpha\alpha',\nu\nu'},\qquad(15)$$

where  $\phi_{\alpha\alpha'}(R')$  are the Bohr frequencies and  $\mathcal{J}_{\alpha\alpha',\nu\nu'}$  are the quantum transition operators. The detailed expressions of both  $\phi_{\alpha\alpha'}(R')$  and  $\mathcal{J}_{\alpha\alpha'\nu\nu'}$  have already been reported many times in the literature [26–29, 32–35]. For the sake of the present discussion, it is enough to know what the different terms represent conceptuality. The Bohr frequencies determine a non-holonomic phase factor that must be integrated along the phase space trajectory when the propagation is coherent, i.e.,  $\alpha \neq \alpha'$ . The symbol  $\mathcal{J}_{\alpha\alpha'\nu\nu'}$  denotes the quantum transitions operator that is responsible for quantum jumps between the adiabatic energy surfaces.

Instead, it is useful to write the explicit expression of the Kramers operator [34, 35]:

$$i\Gamma_{\alpha\alpha'}^{\rm K}(t) = \left[\frac{P}{M}\frac{\partial}{\partial R} + \frac{F_{\alpha}(R) + F_{\alpha'}(R)}{2}\frac{\partial}{\partial P} - \eta\frac{\partial}{\partial P}\left(\frac{P}{M} + \frac{\partial}{\partial(\beta P)}\right)\right]\frac{\partial}{\partial P},\quad(16)$$

where  $F_{\alpha}(R) = -\partial E_{\alpha}(R)/\partial R$  is the Hellmann–Feynman force on adiabatic surface  $\alpha$ .

Now, considering any phase-space-dependent operator  $\tilde{\mathcal{O}}(X)$ , its QC average is calculated as

$$\begin{split} \langle \tilde{\mathcal{O}} \rangle(t) &= \sum_{\alpha \alpha', \nu \nu'} \int dX \mathcal{O}_{\alpha \alpha'}(X) \exp\left[-it \mathcal{L}^{\mathrm{D}}\right]_{\alpha \alpha', \nu \nu'} \mathcal{F}_{\mathrm{W}}^{\nu \nu'}(X) \\ &= \sum_{\alpha \alpha', \nu \nu'} \int dX \mathcal{F}_{\mathrm{W}}^{\nu \nu'}(X) \exp\left[it \mathcal{L}^{\mathrm{DB}}\right]_{\nu \nu', \alpha \alpha'} \mathcal{O}_{\alpha \alpha'}(X) , \end{split}$$
(17)

where  $i\mathcal{L}_{\nu\nu',\alpha\alpha'}^{\text{DB}}$  is the backward QC dissipative Liouville operator:

$$i\mathcal{L}_{\nu\nu',\alpha\alpha'}^{\mathrm{DB}} = \left[i\phi_{\nu\nu'} + i\Gamma_{\nu\nu'}^{\mathrm{KB}}\right]\delta_{\nu\alpha}\delta_{\nu'\alpha'} - \mathcal{J}_{\nu\nu',\alpha\alpha'},\qquad(18)$$

where the backward Kramers operator  $i\Gamma^{\rm KB}_{\nu\nu'}$  is

$$i\Gamma_{\nu\nu'}^{\rm KB} = \left[\frac{P}{M}\frac{\partial}{\partial R} + \frac{F_{\alpha}(R) + F_{\alpha'}(R)}{2}\frac{\partial}{\partial P} - \eta\left(\frac{P}{M} - \frac{\partial}{\partial(\beta P)}\right)\frac{\partial}{\partial(\beta P)}\right]\delta_{\nu\alpha}\delta_{\nu'\alpha'}.$$
(19)

In agreement with the theory of random processes [99], the evolution determined by the backward QC Kramers operator can be substituted by an average over swarms of Langevin trajectories [35] defined by the equations of motion:

$$\dot{R} = \frac{P}{M} \tag{20}$$

$$\dot{P} = -\eta \frac{P}{M} + \frac{F_{\alpha}(R) + F_{\alpha'}(R)}{2} + \mathcal{N}(t) ,$$
 (21)

where  $\mathcal{N}(t)$  is a Gaussian white noise process with the properties

$$\langle \mathcal{N}(t) \rangle = 0 , \qquad (22)$$

$$\langle \mathcal{N}(t)\mathcal{N}(t')\rangle = 2k_B T \eta \delta(t-t')$$
 (23)

With Equations (20) and (21), we can associate a classical-like time-dependent Liouville operator:

$$i\Gamma^{\rm L}_{\nu\nu\prime}(t) = \frac{P}{M}\frac{\partial}{\partial R} + \left(\frac{F_{\nu}(R) + F_{\nu\prime}(R)}{2} - \eta\frac{P}{M} + \mathcal{N}(t)\right)\frac{\partial}{\partial P}.$$
 (24)

Considering the possibility of nonadiabatic transitions, the complete QC Langevin Liouville operator reads [34, 35]:

$$i\mathcal{L}^{\mathrm{L}}_{\nu\nu',\alpha\alpha'}(t) = \left[i\phi_{\nu\nu'} + i\Gamma^{\mathrm{L}}_{\nu\nu'}(t)\right]\delta\nu\alpha\delta_{\nu'\alpha'} - \mathcal{J}_{\nu\nu',\alpha\alpha'}.$$
 (25)

We can now define a QC Langevin time-dependent propagator as

$$\mathcal{U}_{\alpha\alpha'\beta\beta'}^{\mathrm{L}}(t,0) = \mathcal{T} \exp\left[\int_{0}^{t} dt' i \mathcal{L}_{\alpha\alpha'\beta\beta'}^{\mathrm{L}}(t')\right] , \qquad (26)$$

where  $\mathcal{T}$  is the time-ordering operator. In this Langevin theory, the QC average of a dynamical variable  $\tilde{\mathcal{O}}$  is

$$<\tilde{\mathcal{O}}>(t) = \sum_{\alpha\alpha'\nu\nu'} \overline{\int dX \mathcal{F}_{W}^{\nu\nu'}(X) \mathcal{U}_{\nu\nu'\alpha\alpha'}^{L}(t) \mathcal{O}_{\alpha'\alpha}'(X)}$$
, (27)

where the over-line stands for an average over the different realizations of the Langevin stochastic process. Equation (27) expresses dissipative QC averages as weighted sums over different Langevin trajectories with phase factors, interspersed with quantum transitions. Its form is convenient for numerical simulations.

The dynamics of the bath B, defined by the propagator in Equation (26), are derived under certain assumptions concerning the larger bath U [34, 35], including the absence of memory effects and the lack of direct interaction between U and S. Hence, when S is not present, it is legitimate to state that the evolution of B is Markovian. However, this is no longer true when S is present and interacts with B. The QC formalism of this paper [9, 21–36] is derived from the full quantum description invoking neither the Markovian nor the rotating-wave approximation [36]. Non-Markovian effects are particularly important in the photon blockade [100–102].

## IV. NHC CONSTANT-TEMPERATURE QC DYNAMICS

Temperature control can be imposed on computer models of QC systems by the deterministic NHC thermostat [71]. A simple NHC of length two can produce ergodicity even for high-frequency dynamics [71, 72]. The phase space coordinates X and the coordinates of the thermostat define an augmented phase space. The augmented phase space coordinates are written as  $X^{e} = (R, \xi_{1}, \xi_{2}, P, \zeta_{1}, \zeta_{2})$ . Consequently, the augmented gradient is  $\nabla^{e} =$  $((\partial/\partial R), (\partial/\partial \xi_{1}), (\partial/\partial \xi_{2}), (\partial/\partial P), (\partial/\partial \zeta_{1}), (\partial/\partial \zeta_{2}))$ . The matrix  $\mathcal{R} = -\mathcal{R}^{-1}$  can now be defined:

$$\boldsymbol{\mathcal{R}} = \begin{bmatrix} 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ -1 & 0 & 0 & 0 & -P & 0 \\ 0 & -1 & 0 & P & 0 & -\zeta_1 \\ 0 & 0 & -1 & 0 & \zeta_1 & 0 \end{bmatrix},$$
(28)

together with the Wigner function operator of the augmented Hamiltonian,

$$\tilde{\mathcal{H}}^{\rm e}(X^{\rm e}) = \hat{\mathcal{H}}_{\rm S} + \mathcal{H}_{\rm B}(X) + \tilde{\mathcal{V}}_{\rm SB}(R) + \sum_{K=1}^{2} \frac{\zeta_{K}^{2}}{2\mu_{K}} + gk_{\rm B}T\xi_{1} + k_{\rm B}T\xi_{2} , \qquad (29)$$

where  $\mu_K$ , K = 1, 2 are the fictitious masses associated with the NHC coordinates,  $k_{\rm B}$  represents the Boltzmann constant, and T represents the temperature of the classical bath. The Hamiltonian  $\hat{\mathcal{H}}_{\rm S}$  describes the quantum subsystem S,  $\mathcal{H}_{\rm B}(X)$ models the bath B, and  $\mathcal{H}_{\rm B}(X)$  describes the interaction between S and B. The remaining terms of the total energy of the augmented model are  $\sum_{K=1}^{2} \frac{\zeta_{K}^{2}}{2\mu_{K}} + gk_{\rm B}T\xi_{1} + k_{\rm B}T\xi_{2}$ , where g is the number of DOF whose temperature must be kept constant. Such a QC model constitutes an example of a complex emergent nested system [41]. The isothermal QC dynamics are defined by the following compact equation [24]:

$$\partial_{t}\tilde{\mathcal{O}}^{e}(t) = \frac{i}{\hbar} \left[ \tilde{\mathcal{H}}^{e} \; \tilde{\mathcal{O}}^{e}(t) \right] \mathbf{\Omega} \left[ \begin{array}{c} \tilde{\mathcal{H}}^{e} \\ \tilde{\mathcal{O}}^{e}(t) \end{array} \right] - \frac{1}{2} \tilde{\mathcal{H}}^{e} \overleftarrow{\nabla}^{e} \mathcal{R} \overrightarrow{\nabla}^{e} \tilde{\mathcal{O}}^{e}(t) \\ + \frac{1}{2} \tilde{\mathcal{O}}^{e}(t) \overleftarrow{\nabla}^{e} \mathcal{R} \overrightarrow{\nabla}^{e} \tilde{\mathcal{H}}^{e} , \qquad (30)$$

where  $\tilde{\mathcal{O}}^{e}(t) = \tilde{\mathcal{O}}^{e}(X^{e}, t)$ . In Figure 3, one can see a pictorial representation of the action of the NHC thermostat, where the forces

$$G_0(P;T_{\rm B}) = \frac{P^2}{M} - gk_{\rm B}T_{\rm B} , \qquad (31)$$

$$G_1(\zeta_1; T_{\rm B}) = \frac{\zeta_1^2}{\mu_1} - k_{\rm B} T_{\rm B} . \qquad (32)$$

The thermostat forces in Equations (31) and (32) enter the equations of motion

$$\dot{\zeta}_1 = G_0(P; T_{\rm B}) ,$$
 (33)

$$\dot{\zeta}_2 = G_1(\zeta_1; T_{\rm B}) , \qquad (34)$$

where  $\zeta_J = \mu_J \dot{\xi}_J$ , with J = 1, 2.

Isothermal averages and correlation functions can be calculated by choosing the Wigner function operator  $\tilde{\mathcal{F}}_{W}^{e}(X^{e})$  in augmented space as

$$\tilde{\mathcal{F}}_{W,\alpha\alpha'}^{e,T}(X^e) = \hat{w}_{S}\tilde{\mathcal{F}}_{rmW,\alpha\alpha'}^{T}(X)\prod_{I=1}^{2}\prod_{L=1}^{2}\delta\left(\eta_{L}^{(I)}\right)\delta\left(P_{\eta_{L}}^{(I)}\right) , \qquad (35)$$

where  $\hat{w}_{\rm S}$  is the density matrix of the quantum subsystem while  $\mathcal{F}_{{\rm W},\alpha\alpha'}^{\rm T}(X)$  is the thermal Wigner function operator of the physical system with phase space coordinates X. Because we want to calculate isothermal averages and correlation functions of physical QC quantities, we must consider QC operators  $\tilde{\mathcal{O}}(X)$  that at t = 0 only depend on the physical phase space point X. Hence, the isothermal QC averages are defined as

$$\langle \tilde{\mathcal{O}}(X,t) \rangle_{\mathrm{e}} = \mathrm{Tr}' \int dX^{\mathrm{e}} \,\mathcal{F}_{\mathrm{W}}^{\mathrm{e}}(X^{\mathrm{e}}) \tilde{\mathcal{O}}(X,t) ,$$
 (36)

$$\langle \tilde{\mathcal{O}}_1(X,t)\tilde{\mathcal{O}}_2(X)\rangle_{\mathrm{e}} = \mathrm{Tr}' \int dX^{\mathrm{e}} \mathcal{F}^{\mathrm{e}}_{\mathrm{W}}(X^{\mathrm{e}})\tilde{\mathcal{O}}_1(X,t)\tilde{\mathcal{O}}_2(X) .$$
 (37)

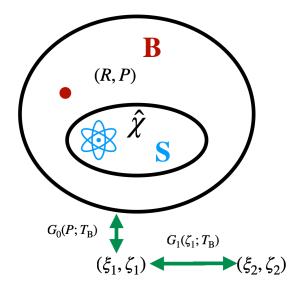


FIG. 3: Pictorial representation of an open quantum system coupled to a dissipative environment at constant temperature. The subsystem S is nested into bath B, whose temperature is controlled by the NHC thermostat. For simplicity, we have considered only two virtual phase space coordinates  $(\xi_1, \xi_2)$  and two virtual momenta  $(\zeta_1, \zeta_2)$ . The thermostat forces  $G_0(P; T_B)$  and  $G_1(\zeta_1; T_B)$  are defined as equal to  $\frac{P^2}{M} - gk_BT_B$  and  $\frac{\zeta_1^2}{\mu_1} - k_BT_B$ , respectively. In the expression of  $G_1$ , g is the number of DOF that the coordinates  $(\xi_1, \zeta_1)$  must thermostat. The coupling of system B to the NHC thermostat takes place through the equations of motion  $\dot{\zeta}_J = G_{J-1}$ , with J = 1, 2. The link between the coordinates and the momenta of the NHC thermostat is given by  $\zeta_J = \mu_J \dot{\xi}_J$ , with J = 1, 2.

The dynamics generated by the NHC thermostat are non-Markovian. The time evolution of  $(\zeta_1, \zeta_2)$  contains all the frequencies of the DOF of B. As a result, the dynamics of P [22, 23], given by the equation

$$\dot{P} = \frac{F_{\alpha} + F_{\alpha'}(R)}{2} - \frac{\zeta_1}{\mu_1} P , \qquad (38)$$

also contain all frequencies of the system, given that

$$\dot{\zeta}_1 = \frac{P^2}{M} - gk_{\rm B}T - \frac{\zeta_2}{\mu_2}\zeta_1 , \qquad (39)$$

$$\dot{\zeta}_2 = \frac{\zeta_1^2}{\mu_1} - k_{\rm B}T \ .$$
(40)

The use of longer chains, i.e.,  $(\zeta_1, \zeta_2, \ldots, \zeta_n)$ , each having associated a different inertial parameter  $(\mu_1, \mu_2, \ldots, \mu_n)$ , can also easily produce coloured noise.

## V. INDICATIONS OF TIME-ASYMMETRY IN THE BRAIN

In the previous sections, the methods describing brain molecular phenomena affirm that models must lack time-reversal symmetry. The models we plan to construct, e.g., comprising suitable quantum dynamical variables coupled to classical nonlinear networks akin to the Hodgkin–Huxley model [42, 43], are ultimately meant to study higher brain functions. The final computer simulation algorithm will be based on a multiscale theory, going from the quantum to the classical level of neuron models. In this section, we want to provide some examples of the macroscopic phenomena and higher functions in the brain that manifest an arrow of time. Indeed, many specific mechanisms that characterize mesoscopic brain activity, e.g., memory, show a well-defined and non-reversible direction of time. Time asymmetry and irreversibility naturally emerge in the brain on the mesoscopic scale because of the second law of thermodynamics. Figure 4 provides a representation of the breaking of time-reversal symmetry in the brain. We discuss the importance of such a symmetry breaking at the macroscopic level in the following. The QC theory we adopt predicts the backreaction of the classical variables on the quantum coordinates. Such a backreaction causes the irreversible dynamics of the quantum subsystem. This implies the quantum irreversible dynamics of both molecular brain structures and quantum coordinates.

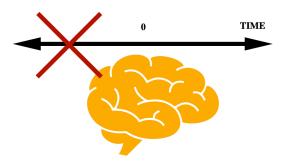


FIG. 4: Pictorial representation of the breaking of time-reversal symmetry in the brain.

The approaches of Sections III and IV describe diffusive dynamics in classical phase space coupled to the dynamics of a quantum subsystem. The diffusion process is found everywhere in living systems and also plays an important part in the brain. Smith takes diffusion as a paradigm to discuss how time asymmetry arises in the brain [84]. For example, diffusion plays a key role in both synaptic transmission and action potential propagation [85]. For action potentials and a given voltage gradient, both calcium and sodium passive channels are opened and ions flow irreversibly into the cell because of intracellular/extracellular concentration difference. In synaptic transmission, diffusion involves the motion of neurotransmitter molecules. Neurotransmitters diffuse from the vesicles to the receptor also for gradient concentration. Finally, the reception of the ion is also based on diffusion driven by gradient concentration. One must also note that action potential generation is caused by the sufficient depolarization of the target neuronal membrane via the sum of incoming depolarizations originating from various sources, including synaptically driven depolarizations, and traveling action potentials from the neuron, which crosses the threshold for action potential generation. The sum (or integration) of incoming depolarization causes a loss of information, i.e., a production of entropy. In this way, action potential generation also depends on transmembrane concentration gradients of sodium and potassium. For example,

a minimal QC model of the action potential generation could be constructed in terms of a chain of quantum spins coupled to the nonlinear electrical and mechanical oscillations representing neuronal dynamics. As discussed before, the quantum dynamics of the spin chain can steer the classical mechanics of the nonlinear model thanks to the amplification mechanism introduced by Pascual Jordan [5, 6].

The time arrow is not only expected to appear in complex emergent nested systems [41] on conceptual grounds. It manifests itself, and indeed, it has been studied experimentally in higher brain functions. For example, the response of different regions of the cerebral cortex to visual stimuli, provided by silent movies, has been studied by functional magnetic resonance tomography [86, 87]. The authors adopted the usual conventional activation analysis [87] to look for the different brain responses to stimulations relative to the dynamics of the movie in the time domain. Such stimuli were directed in time in three different ways: Uniformly forward, uniformly backward, and randomly forward-backward in time. The researchers observed time arrow-independent effects in primary visual areas. However, more complex regions displayed time-dependent effects, relevant to "making" sense of a scene, occurring only for forward-played movies. Complex brain areas also require that the movie's information be accumulated over a longer time than primary visual areas before a response can be registered. Particularly, for primary sensory areas, these encode something one can think about visual pictures, but not a pattern evolving with time. Thus, time is not a relevant factor, because the pictures will be the same, wherever these are shown in time. The more complex areas encode for scenarios that develop in time. Thus, the temporal succession contains critical information, which cannot be decoded similarly if movies are shown backward. We are not aware of any model addressing these behaviors. It would be interesting to study QC models where the quantum levels display quantum resonances and Jordan amplification.

OCD also offers a case study for investigating the brain's time arrow. A method

that can be followed to determine the presence of a time asymmetry is to analyze brain dynamics in terms of stationary stochastic processes. Since linear Gaussian random processes and static non-linear transformations of such processes are timereversible, time irreversibility cannot be present when Gaussian linear models are detected. Bernardi et al. compared the magnetoencephalographic [88] recordings of brain activity in the resting state in two groups of people. One group was composed of patients with OCD and the other was composed of control individuals matched according to sex and age. The recordings showed that time directionality was more prominent at faster time scales in the case of patients with OCD [88], who also displayed a more uniform distribution of time asymmetry in their brain hemispheres than healthy controls [88]. This could be because patients with OCD may have more uniform thoughts, e.g., obsessive thoughts, whereas there is more randomness in healthy controls.

From our perspective, the phenomenon of spatial neglect is much more complex, requiring the understanding of how the brain weaves time and space within perceptions. Physicists are used to thinking of a spatiotemporal continuum, where space and time are inextricably interleaved. A recent study showed how this is naturally engrained in the brain and relates to spatiotemporal attention [103]. Spatial neglect (or hemispatial neglect) is defined as missing visual perception in the left or the right visual field [89–92]. It was shown that beyond anatomy-based foundations of damaged/disturbed visual areas, spatial neglect also involves asymmetric spatial attention. This spatial attention deficit also has an anatomical foundation. Spatial neglect has space components, but also temporal dynamics because attention takes place in the time domain. This displays a space-time connection in such an impaired perceptual function. This knowledge was accompanied by the conjecture that left spatial neglect is caused (at least in part) by non-spatial attention disorders associated with dysfunctions of the right side of the frontoparietal brain area [89–92]. Recent tests focused on the comparison of foveal perception (the fovea is the area of maximum visual acuity and color discrimination in the eye) in patients with right-hemispheric damage and no spatial neglect, both compared to healthy patients [103]. The result of the study was that the impairment of temporal attention caused left spatial neglect [103].

The examples presented in this section exemplify the brain functions for which we believe a QC approach could prove most useful. We leave checking these ideas to both our future efforts and time.

### VI. CONCLUSIONS

This manuscript has introduced, without conceptual uncertainties or veiled conjectures, an approach to capture some aspects of the physical processes that regulate brain dynamics. Based on both physical and physiological considerations, we have proposed that a complex emergent nested system [41], such as the one provided by QC systems, is suitable for modeling brain processes at various spatiotemporal scales. Attention has been focused on which essential features QC systems must have to be viable models of the dynamics of brain molecules. Such models are meant to be studied through computer simulation methods. We have concluded that there is no need to invoke an improbable quantum coherence of large domains in the brain to have quantum mechanics play an important role. The reduction of the state vector of a few quantum dynamical variables coupled to even many classical coordinates can control their classical dynamics. This is Pascual Jordan's [5, 6] amplification process. State reduction is an irreversible process; equivalently, the backreaction of the environment dynamics on the subsystem forces its dynamics to become dissipative on general grounds. This can be realized by enclosing the quantum subsystem in a classical isothermal bath. We have shown explicitly how this can be theoretically achieved using Brownian dynamics or the NHC thermostat. We can conclude that the lack of time-reversal symmetry

is essential for modeling the brain. The unfolding of higher brain functions also witnesses the importance of the arrow of time in brain processes [84–88].

Other quantum descriptions of brain dynamics invoke the use of QC dynamical variables [75–78]. However, in these alternative approaches, the classical variables are somewhat hidden, and their effective role does not appear to be easily analyzable. Instead, our mathematical formalism (defined through the qLB) treats QC dynamical variables explicitly [9, 24, 25]. Statistical properties can be calculated by taking the appropriate QC average, tracing it over quantum coordinates, and integrating it over phase space DOF. Within such an approach, classical DOF can be treated with atomistic detail.

Future works will be devoted to two different lines of research. The first is to apply our description to specific processes in the brain, compare our results to what is already available in the literature, and try to understand the general qualitative features of a given brain process. The second is to further develop the theory by defining a non-Hermitian dynamics for the quantum subsystem and/or driven non-equilibrium dynamics of the classical bath.

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Umezawa's and Vitiello's Quantum Field Theories of the Brain]Umezawa's and Vitiello's Quantum Field Theories of the Brain

The Quantum Model of the Brain [73, 74] and the DQMB [75] introduce some key ideas, agreeing with Karl Lashley's proposal concerning the direct relation between memory formation and the mass of both neuropil and the connectome [104, 105]. Nowadays, Lashley's ideas [104, 105] are somewhat outdated, depending on specific functions, and very small lesions to the appropriate target area can have critical effects. However, Lashley's hypothesis was supported by a set of experiments in which surgical ablation of brain tissue alters memories only in proportion to the mass of the cortex (Principle of Mass Action [104, 105]). Unless the brain suffers serious damage, it can also happen that different parts of the cortex can overtake memory functions when other parts are damaged (Principle of Equipotentiality [104, 105]). To the Principle of Mass Action and the Principle of Equipotentiality, one must also add evidence that memory is only momentarily impaired by electric shock or drug administration. For such reasons, at the time of its inception, the predictions of the DQMB were compared to those of Lashley's proposal [104, 105].

Despite other data regarding the functional differentiation of disparate areas of the cerebral cortex, the idea that non-local quantum effects [10–12, 67, 69] are responsible for information processing in biological organs [106–112] is worth investigating. Such non-local effects are described within the QMB [73, 74] and DQMB [75] through quantum bosonic fields. These bosonic fields provide the coarse-grained description of a number of microscopic variables of the order  $10^{23}$ . Long-range, non-local effects are described through quantum wave excitations [106–112].

The excitations of the quantum fields are called Corticons. Corticons are distinct from neurons and, e.g., astrocytes, other brain cells' excitations, in the model, are considered classical because of their very short de Broglie wavelength. Thus, one should think of the brain as a QC system [9, 16–21, 24, 25] where, according to the QMB, the dynamics of macromolecules is classical and the dynamics of other collective variables is quantum mechanical. However, in the QMB [73, 74] and DQMB [75], the classical dynamical variables are not explicitly treated: the neuron is a classical object but it is somewhat awkwardly described by quantum Corticons. At the same time, the interaction between neurons and Corticons [73, 74] is not specified, as acknowledged by the authors themselves [74].

According to the QMB and DQMB, spontaneous symmetry breaking generates a code for memory storage, producing multiple ground states with their

associated quantum numbers. A model Hamiltonian is introduced in Ref. [74] to illustrate that a spin-boson model can give rise to a degenerate ground state through symmetry-breaking. Even if the multiple ground states are isoenergetic, they are separated by very high entropic barriers. Collective oscillatory modes, known as Nambu–Goldstone bosons [113–115], emerge as perturbations of each degenerate ground state. Nambu–Goldstone bosons are the sources of long-range correlations within the infinite number of ground states. In the QMB and DQMB, such Nambu–Goldstone bosons are responsible for memorizing and remembering, and synchronization between distant brain areas. The Nambu–Goldstone bosons emerging in the QMB and DQMB are called Symmetrons [73, 74]. The DQMB identifies the Corticons with the excitations of the polarization field of water and the Symmetrons with dipolar wave quanta. Hence, only the rotational symmetry of the polarization field is present in the DQMB. The choice for a special role of the water polarization field is supported by the brain composition, which is 1%carbohydrates and inorganic salts, 2% soluble organic substances, 8% proteins, 10 to 12% lipids, and 77 to 78% water [116]. This identification is phenomenologically consistent with the fact that dehydration strongly impacts cognitive functions of the brain |117-123|.

Vitiello generalized the QMB [73, 74] to solve the problem with memory storage [75]. Given that in the QMB, different ground states cannot be superimposed, because of the entropic barrier, every ground state can code only one memory. In other words, a new memory overwrites the preceding one. If one does not perform the thermodynamic limit but still considers very big systems, the degenerate ground states are no longer entropically separated from each other and can be superimposed. However, the memory storage problem is still not solved because the code could be continuously scrambled by random transitions (caused by external perturbations) between the degenerate ground states. A completely different physical situation emerges if one takes the coding ground state as a coherent superposition of all the infinite ground states corresponding to a single value of the order parameter. Adopting Umezawa's finite temperature quantum field theory [124–126], known as thermo field dynamics, Vitiello developed the DQMB [75]. In this approach, the brain is coupled to the environment, which acts as a thermostat.

Within thermo field dynamics [124–126], the duality between the polarization field and the dipolar wave quanta determines the appearance of a non-Hermitian energy-non-conserving Hamiltonian. This Hamiltonian, comprising both physical and fictitious fields, conserves the energy of the total system to keep the temperature constant. Physical and fictitious quanta populate the dynamical states of the total system. Because of such a trick, thermal averages can be calculated on a ground state defined on a doubled Fock space. Since the energy of the total system is conserved, the energy of the physical system is not: the physical system is dissipative and breaks time reversal invariance. The fictitious DOF provide a virtual representation of the environment.

## Orch-OR

The Orch-OR theory [54, 79–82] suggests that quantum effect tubulin lattices, found in the cytoplasm of brain cells, can operate on physical information in a noncomputational way. Time evolution of electronic wave function of decoherenceshielded carboxyl groups inside tubulin's hollow region, the spinorial dynamics of the nuclei, various forms of information communication between microtubules, followed by the spontaneous reduction of microtubules' quantum state vectors are the pillars of the theory. The unpredictable reduction of the state vector is an irreversible process that introduces the direction of the flow of time. The idea that the inside of the cell could work as an information-processing unit was developed by Hameroff after considering the reaction of microtubule lattices to anesthetics. Penrose's spontaneous collapse process provides the means to overcome the limited efficiency that classical diffusion dynamics has for transferring physical information over long distances.

In Orch-OR, quantum gravity makes the superposition of states associated with different masses unstable. Past a determined time interval, such superpositions collapse spontaneously. The superposition lifetime can be estimated considering the Bohr frequency associated with the superimposed eigenstates:

$$\omega_{\rm Bohr} = \Delta E/\hbar \ . \tag{41}$$

Hence, the estimated lifetime is

$$\tau \approx \frac{h}{\Delta E}$$
 (42)

Brain dynamics is then interspersed with discrete events associated with state vector reductions. Each reduction introduces a time direction because the probabilistic collapse acts as a wall between the states before and after the collapse.

The Orch-OR hypothesizes that inside each tubulin there are coordinates supporting quantum dynamics between wave function collapses. Carbon rings and delocalized molecular orbitals provide one example. Coherent dynamics can be sustained by carboxyl groups found inside the microtubulin's hollow space, where they are protected from decoherence [13–15]. The correlated orientation of carboxyl groups in the microtubule lattice form preferred pathways along which energy can be transported without dissipation [54, 82]. For example, Orch-OR can affect the feedback [53] between quantum effects in microtubule lattices and the classical time-evolution of microtubule-associated proteins [56, 57].

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