Research Article

On Macroscopic Quantum Phenomena in Biomolecules and Cells: From Levinthal to Hopfield

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In the context of the macroscopic quantum phenomena of the second kind, we hereby seek for a solution-in-principle of the long standing problem of the polymer folding, which was considered by Levinthal as (semi)classically intractable. To illuminate it, we applied quantum-chemical and quantum decoherence approaches to conformational transitions. Our analyses imply the existence of novel macroscopic quantum biomolecular phenomena, with biomolecular chain folding in an open environment considered as a subtle interplay between energy and conformation eigenstates of this biomolecule, governed by quantum-chemical and quantum decoherence laws. On the other hand, within an open biological cell, a system of all identical (noninteracting and dynamically noncoupled) biomolecular proteins might be considered as corresponding spatial quantum ensemble of these identical biomolecular processors, providing spatially distributed quantum solution to a single corresponding biomolecular chain folding, whose density of conformational states might be represented as Hopfield-like quantum-holographic associative neural network too (providing an equivalent global quantum-informational alternative to standard molecular-biology local biochemical approach in biomolecules and cells and higher hierarchical levels of organism, as well).

1. Introduction

On Macroscopic Quantum Phenomena. Initially, quantum mechanics appeared as a theory of microscopic physical systems (elementary particles, atoms, and molecules) and phenomena at small space-time scales; typically, quantum phenomena are manifested at dimensions smaller than 1 nm and time intervals shorter than 1 μs. However, from the very beginning of the quantum mechanical founding the question of its universality was raised, that is, the question of general validity of the quantum-physical laws for macroscopic phenomena, usually treated by the methods of classical physics. In the history of quantum physics, and especially quantum mechanics, this question has been temporarily put aside for very different reasons, being considered as a difficult scientific problem. The situation is additionally complicated by the existence of different schools of quantum mechanics, arguing about physical-epistemological status of the so-called collapse (reduction) of the wave function. In this respect the situation is not much better today, and it can be said freely that the problem of universal validity of quantum mechanics is still open [1–15]. To this end, Primas [16] emphasizes the following.

"If we consider quantum mechanics as universally valid in the atomic, molecular, mesoscopic and engineering domain,
then we have to require that a proper mathematical codifica-
tion of this theory must be capable to describe all phenomena
of molecular and engineering science. Already rather small
molecules can have classical properties, so that a classical
behavior is not a characteristic property of large systems. The
existence of molecular superselection rules and of molecular
classical observables is an empirically well-known fact in
chemistry and molecular biology. The chirality of some
molecules, the knot type of circular DNA-molecules, and the
temperature of chemical substances are three rather different
examples of molecular classical observables. Such empirical
facts can be described in an ad hoc phenomenological
manner, but it is not so easy to explain these phenomena
from the first principles of quantum mechanics. A universally
valid theory of matter has not only to describe but also to
explain why the chirality of biomolecules (like the L-amino
acids, the D-sugars, lipids or steroids) is a classical observable.
The reality of this breakdown of the superposition principle
of traditional quantum mechanics on the molecular level is
dramatically demonstrated by the terrible Vontergan tragedy
which caused many severe birth defects."

Starting from the 1980s, mainly in the papers of Leggett
[1, 2], a new period of investigation of quantum mechanical
phenomena on the macroscopic level began. Namely, a
clarification of the notions and planning of experimental
situations for observing some physical effects started. The
central problem in this respect is a notion of macroscopic
differentiation of the states of quantum system whose quan-
tum mechanical behavior is explored. More precisely, Leggett
argues that the term macroscopic quantum mechanical effect
must be related to macroscopically different states, that is, the
system states (and observables) that carry macroscopic prop-
erties (and behaviors) of the system as a whole. These states
(i.e., observables) must carry classical-physical behavior of
the system as well; this poses a task for choosing physical
conditions giving rise to observation of typical quantum
effects related to these states.\(^1\)

Hence different kinds of macroscopic quantum phenom-
enas: (i) the ones usually explored by the methods of (quan-
tum) statistical physics and not related to macroscopically
differentiated states (being classified as macroscopic quantum
phenomena of the first kind, like solid state phenomena), and
(ii) those ones regarding macroscopically different (dif-
ferrented) states (being classified as macroscopic quantum
phenomena of the second kind and being interesting to us). Numerous
different macroscopic quantum phenomena of the second
kind, some of them belonging to the fast developing
field of the quantum computing and information, unequiv-
ocally sharpen the overall problem of universal validity of
quantum mechanics.

In the context of the macroscopic quantum phenomena
of the second kind, we shall present a solution-in-principle
of the long standing problem of the polymer folding (which
was considered by Levinthal as (semi)classically intractable
[17], as shortly reviewed below)—implying the existence of
novel macroscopic quantum biomolecular phenomena, with
far reaching implications.

**Levinthal Paradox Revisited.** Contemporary methods for
calculation of conformational dependent chain properties
are based on thermodynamic aspect of the problem, which
explores (semi)classically the folding free energy landscape
for protein with several successful attempts to model these
processes in silico using molecular dynamics simulations
with full atomic representation of both protein and solvent
[18–22], producing continuous (semi)classical trajectories
with the potential to connect static structural snapshots
generated from experimental data. This is incorporated into
the (semi)classical viewpoint that conformational changes of
proteins, due to solvent, thermal, optical, and other influences
of the environment, do not occur in a random way (e.g.,
movements of gas particles) but fold to their native confor-
manation of deep global minimum in some (semi)classical funnel
of low-energy conformations leading toward it [23]. Even in
recently reported implementation of quantum annealing
(on the programmable superconducting quantum device)
for lattice protein folding problems, nothing quantum mechan-
ical is implied about principles that govern the folding of
protein chains [24] (rather quantum fluctuations are a tool
used for solving the optimization problem of protein folding,
considered classically intractable [25–27]).

Hence, these (semi)classical calculational methods do
not describe properly transitions from one conformation
to another, which is the kinetic aspect of the problem,
exploring the conformation change of long flexible chain.
This has been illustrated by Levinthal, who considered the
probability of folding a protein molecule from coiled to native
conformation [17]. Assume \(2n\) torsional angles of an \(n\)-residue
protein, each having three stable rotational states; this yields
\(3^{2n} = 10^n\) possible conformations for the chain; if a protein
can explore new conformations in a random way at the rate
that single bond can rotate, it can find approximately \(10^{13}\)
conformations per seconds; then the time \(t\) (s) required for
a protein to explore all the conformations available to it is
\(t = 10^n/10^{13}\); for a rather small protein of \(n = 100\) residues,
one obtains \(t = 10^{87}\) s, which is immensely more than
the apparent age of the universe ("Levinthal paradox"). Yet,
according to experiments, proteins can fold to their native
conformation in less than a few seconds [28].

It should be added that (semi)classical kinetic (nonst-
ationary) predictions imply the continuous map/con-
formation change \(k_i \rightarrow k_f\), which requires a sequence of \(n\)
local noncommuting successive elementary transformations
(local rotations of characteristic time \(\tau_o\)), with the time
necessary for the net transformation much longer than characteristic
time necessary for a local rotation \((\tau_o \sim n \tau_o \gg \tau_o)\) and the frequency of corresponding global
transition much lower than the frequency of a local rotation
\((f_o \sim 1/\tau_o \sim f_o/n \ll f_o)\)—strongly dependent on a
degree of polymerization \(n\) (in clear contradistinction with
the experimentally observed poorly dimensionally sensitive
dispersion laws of the internal more or less delocalized
quasiparticle excitations in any condensed state quantum
system: electrons, phonons, and etc. [29]). Thus, chain
folding based on (semi)classical (nonstationary) predictions
cannot be considered kinetically understood; the same
applies to biomolecular recognition processes based on (semi) classical selective ligand-proteins/target-receptors key/lock interactions.

2. Conformational Transitions in Biomolecules and Cells as Macroscopic Quantum Effects

2.1. Quantum-Chemical Approach to Conformational Transitions in Biomolecules. Within the framework of standard quantum-chemical Hamiltonian (including kinetic energies and Coulomb interactions of all biomolecular electrons and nuclei) and Born-Oppenheimer adiabatic approximation (of separated biomolecular electronic and vibrational degrees of freedom), the (semi)classical problem of many-electron hypersurface \( E_c(\Phi) \) is replaced by better-defined problem of two (virtually intersecting) isomeric many-electron hypersurfaces (hyper-paraboloids) serving as potential hypersurfaces for two vibrational (isomeric) problems—within the theory of nonradiative resonant structural transitions [30]. In this approach, the conditions for electronic-vibrational nonradiative resonant transitions between the \( i \)th and \( j \)th isomeric states are possible only for close states with nonvanishing electronic and vibrational dipole moments and nonvanishing electronic and vibrational overlap integrals (cf. Figure 1 and its caption for further explanation).

2.2. Quantum Decoherence Approach to Conformational Transitions in Biomolecules and Cells: From Levinthal to Hopfield. Quantum decoherence approach to conformational transitions [34–42] (cf. the Appendix) generally allows reproduction of both existence and stability of the (stationary) conformations and the short time scales for the quantum mechanical processes resulting effectively in (nonstationary) conformational transitions under external influences on the complementary environmental solution. This approach might also be applied to (nonstationary) mismatching-to-matching quantum mechanical conformational transitions in selective ligand-proteins/target-receptors key/lock biomolecular recognition processes under external (e.g., compositional/chemical, thermal/optical...) influences on the cell's complementary cytoplasmatic environment [36, 37, 41, 42].

In the context of existence and changes of conformations of biomolecules, it should be particularly pointed out that quantum-chemical approach to conformational transitions [34–42] (cf. the Appendix) generally allows reproduction of both existence and stability of the (stationary) conformations and the short time scales for the quantum mechanical processes resulting effectively in (nonstationary) conformational transitions under external influences on the complementary environmental solution. This approach might also be applied to (nonstationary) mismatching-to-matching quantum mechanical conformational transitions in selective ligand-proteins/target-receptors key/lock biomolecular recognition processes under external (e.g., compositional/chemical, thermal/optical...) influences on the cell's complementary cytoplasmatic environment [36, 37, 41, 42].

In the context of existence and changes of conformations of biomolecules, it should be particularly pointed out that biomolecular operators of Hamiltonian \( \hat{H} \) (electronic-vibrational Hamiltonian, which includes operators of kinetic energies and all Coulomb interactions between the biomolecule electrons and nuclei in the center-of-mass coordinate system) and conformations \( \hat{K} \) (so-called “reaction (conformational)” coordinates of the nuclei, defining the biomolecule conformations) do not commute, \([\hat{H},\hat{K}] \neq 0\)!

Hence, quantum-chemical approach described in the previous section (with simultaneously defined energies and conformations of biomolecules) is essentially (semi)classical, and it is only quantum decoherence that enables appearance of biomolecular conformational eigenstates (labeled by upper index \( K \) in (1)) from the biomolecular energy eigenstate of the isolated biomolecule (labeled by upper index \( E \) in (1)) via nonpotential interaction of the biomolecular quantum system (QS) with its quantum environment (QE), when one of the biomolecular conformational \( K \) eigenstates is stochastically selected via quantum decoherence (QD)\(^2\) from the biomolecular initial many-electronic energy \( E_c^{(i)} \) eigenstate of the isolated biomolecule (as only self-Hamiltonian of the biomolecule was switched-on initially, like a proper approximation when interaction with quantum environment might be accounted for via potential term of the self-Hamiltonian)\(^3\). It should be noted that the most probable biomolecular conformational eigenstate is the one labeled by \( K_i \), corresponding to biomolecular initial many-electronic energy \( E_c^{(i)} \) (with the same index \( i \), especially if it corresponds to biomolecular many-electronic ground state, in accordance with the usually adopted quantum-chemical computations within the framework of adiabatic approximation).

Subsequently, one of the stochastically QD-selected biomolecular conformational \( K_i \) eigenstates (\( K_i \), in Figure 1) might be excited by nonstationary external perturbations (photons...) into some resonant electronic-vibrational energy eigenstate \( (E_c^{(i)} + E_e^{(i)}) = E_c^{(f)} + E_e^{(f)} \), in Figure 1), when self-Hamiltonian of the biomolecule is again a proper approximation (and interaction with quantum environment might be again accounted for via potential term of the self-Hamiltonian). Then, in subsequent quantum deexcitation/decoherence\(^3\) there are finally at least two possible biomolecular conformational eigenstates (as depicted in Figure 1): \( K_f \) related to biomolecular deexcitation back into initial many-electronic state \( i \) or \( K_f \) related to biomolecular deexcitation into final many-electronic state \( f \).

And such fluctuations between eigenstates of energy and conformation of biomolecules are repeating

\[
\begin{align*}
|\Phi_i^{(E)\, QS}\rangle & = \sum_j c_j |\Phi_j^{(K)\, QS}\rangle |\Psi_j^{(E)\, QE}\rangle \\
\rightarrow & \text{QD} |\Phi_i^{(K)\, QS}\rangle |\Psi_i^{(E)\, QE}\rangle \quad \mapsto \rho_{\Phi\Psi}^{(E)} \quad +\Delta E_{\text{exc}} \\
= & \sum_f c_f |\Phi_f^{(E)\, QS}\rangle |\Psi_f^{(E)\, QE}\rangle \\
\rightarrow & \text{QD} |\Phi_f^{(E)\, QS}\rangle |\Psi_f^{(E)\, QE}\rangle \quad \mapsto \rho_{\Phi\Psi}^{(E)} = \cdots
\end{align*}
\]

and might be observed by applying methods of experimental macromolecular biophysics [43]—thus becoming a paradigm of macroscopic quantum phenomena of the second kind.

So, biomolecular chain folding in an open environmental solution might be considered as a subtle interplay between energy and conformation eigenstates of a biomolecule, governed by local quantum-chemical and quantum decoherence laws, and in this scenario the Levinthal’s paradox disappears (cf. the Appendix for some aspects of quantum decoherence scenario of conformational transitions; also cf. footnote 5
therein for revealing \textit{(semi)classical meaning} of the harmonic-like vibrating macromolecule conformations in the vicinity of local minimums of many-electron hypersurfaces.

On the other hand, within an open biological cell, a system of (noninteracting and dynamically noncoupled) \( N_k \) proteins identical in their primary chemical structure (and their biomolecular targets) might be considered as corresponding \textit{global} spatial quantum ensemble of \( N_k \) identical biomolecular processors, providing a spatially distributed quantum solution to corresponding single local biomolecular chain folding (and key-lock recognition process)—whose \textit{time-adapting} density of conformational states \( \rho_{S_k}(t) \) might be represented as \textit{global} cell’s \textit{Hopfield-like quantum-holographic associative neural network} too [41, 42] (cf. Figure 2 and its figure caption for further explanation). We hereby silently assumed \textit{ergodic hypothesis}, that is, near \textit{thermodynamic equilibrium} of the \( N_k \) proteins in their decoherence-selected (stationary) \textit{conformations}, which is \textit{not fulfilled} in \textit{(nonstationary)} \textit{conformational transitions} induced by strong \textit{environmental interactions} (cf. the Appendix for more details on our decoherence scenario) which might occur \textit{far from thermodynamic equilibrium} (as is the case in metabolic processes in biological cells [43]).

Or to generalize, a series of all \( k \) intracellular and extracellular environmentally driven (compositonally/chemically or thermally/optically) \textit{local} biochemically coupled reactions might be \textit{equivalently} considered as a series of all \( k \) corresponding intracellular and extracellular \textit{global} \textit{Hopfield-like quantum holographically coupled associative neural network layers}—providing an equivalent \textit{global} \textit{quantum-informational alternative} to standard molecular-biology local biochemical approach in biomolecules and cells (and higher hierarchical levels of organism, as well).[^4]

3. Discussion and Conclusion

\textit{Biomolecules} in a living biological cell are subjected to \textit{nonequilibrium} processes of huge complexity. Elaborate quantum mechanical descriptions of such processes are only a matter of recent considerations [45–47]. In this regard, the physical methods are a matter of intense current research [48, 49]. A fully developed quantitatively elaborate quantum mechanical background for such biological processes is yet a remote goal.
In the context of the macroscopic quantum phenomena of the second kind we hereby proposed quantum-chemical and quantum decoherence approaches to biomolecular conformational transitions, which cannot be considered kinetically understood based on (semi)classical predictions. Our qualitative proposal has a solid quantum mechanical basis of wide applicability: there are not any particular assumptions on the chemical kind, structure, or the initial state of the molecule or any assumptions on the chemical kind or on the initial state of the molecule's environment.

It seems that our matter-of-principle solution to the long standing Levinthal paradox offers a natural physical picture of a number of the important processes with biomolecules, including chain folding and biomolecular recognition. This offers a basis for some (semi)classical descriptions, such as the recent (also qualitative) proposal of Dill and Chan [23]. Actually, quantum decoherences assumed to provide (quasi)classical behavior of the biomolecules conformation degrees of freedom, which can be further (semi)classically described to provide more details of the biomolecule's conformation dynamics in molecular biology and biochemistry.

Our model, (A.2), is stochastic, not deterministic, and is sensitive to all allowed final conformations. Depending on the details of the physical model (initial state of the molecule, the kind and strengths of interactions with the solvent molecules, and the form of the energy landscape etc.), there is more than one possible final conformation in the sum equation (A.2) that in principle includes the initial conformation. Regarding the funnel landscape of Dill and Chan [23], a few scenarios are possible. For example, if the particle is in a thin local minimum, quantum tunneling can cause the highly semiclassical dynamic that is essentially described by Leggett [1] and qualitatively agrees with Dill and Chan [23]: the particle is expected quickly to go down the slope. On the other hand, for sufficiently deep local minimum, the particle can be trapped (e.g., in a metastable state), in which case the related conformation appears in the sum in (A.2). If such local minimum is in the vicinity of the absolute minimum and the related conformations are practically indistinguishable, then our model predicts redefinition of the very concept of “native state (conformation).” In this case, “native state” does not refer to a single but to a set of close conformations of the molecule—again in accordance with the qualitative considerations of Dill and Chan [23] (and the references therein).

As another virtue of our decoherence model, we emphasize existence of a few different mechanisms for the externally induced conformational transitions. Those mechanisms (“channels”) are defined by local influence on certain subsystem without yet influencing the other subsystems (degrees of freedom) of the molecule. The subsystems of interest are conformational system, vibrational system (vibrational modes), the electrons system, and the local rotational degrees of freedom of the molecule. Realistic transitions can be assumed to be combinations of those local “channels” for conformational transitions. In principle, high precision and control of the molecular degrees of freedom can experimentally partially distinguish between the different channels. For instance, illuminating the molecule by the microwaves of the characteristic frequency \( \sim 10^9 \) Hz should influence the local rotations in a molecule (with nonnegligible quantum tunneling between the allowed structural rotamers) without affecting the other degrees of freedom, while the infrared light of the frequency \( \sim 10^{13} \) Hz should influence the vibrations in a molecule with possible nonradiative resonant structural isomeric transitions (like in Figure I, for transitions within the electronic ground state hypersurface). To this end, some basic details on the conformation-transitions mechanisms can be found in [32, 33, 39], respectively, while research is still in progress. Direct influence on the conformation, which is typically considered in the statistical (e.g., thermal equilibrium) approach, is rather subtle and is often described as a net effect mainly originating from a change of physicochemical characteristics of the solution (in the manner described by Anfinsen [24]) without resorting to an elaborate model yet; see, for example, [14, equation (3.164)].

Regarding the quantum ensemble prediction of our decoherence model (DM), (A.2) and the resembling Hopfield-like quantum-holographic neural network (HQHNN) bioinformational framework of the environmentally driven biochemical reactions on the level of open biological cell (Figure 2), there are several notes that might be added in proof: (i) biochemical reactions involve enzymatic processes, and enzyme's function is the DM conformational-adaptive one (so fundamentally every single biochemical reaction has bioinformational structure of HQHNN within the occupational basis of enzyme's conformational states, as an indicator of DM enzyme-mediated biochemical reactions); (ii) regarding all biochemical reactions of the particular type in the cell, a higher percentage of the functionally appropriate enzymes take their native conformation (usually the lowest energy state...) influenced by the proximity of the corresponding biomolecular substrate (key-lock enzyme-to-substrate DM conformational adjustments), but not the remaining percentage of those enzymes that are not yet in close interaction with their biomolecular substrates (which then occupy the remaining possible conformations as well, according to DM); (iii) in accordance with the previous point, all biochemical reactions of the particular type in the cell have bioinformational structure of HQHNN within the occupational basis of the corresponding enzyme's conformational states; (iv) taking into account other successive intracellular and extracellular environmentally driven biochemical reactions that are functionally interconnected with preceding biochemical reactions in the cell, they can also be successively presented in the bioinformational framework of HQHNNs within the occupational bases of conformational states of the corresponding enzymes involved; (v) since all these successive biochemical reactions are functionally interconnected, so are the successive HQHNNs in bioinformational framework within the corresponding enzymes' occupational bases (which may be presented in the form of Haken's multilevel synergetic neural network, composed of layers of the successive HQHNNs); and (vi) in such bioinformational framework of Haken's multilevel synergetic neural network, each of the successive HQHNNs layers representing corresponding
intracellular and extracellular biochemical reactions has a formal Hopfield-like mathematical structure in the form of (nonmorphological/abstract) "formal neurons" massively interconnected by "formal connections" while the layers of HQHNNs would be mutually quantum holographically coupled via their "memory attractors" (i.e., their quantum-holographic memory states, within the occupational bases of conformational states of the corresponding enzymes involved).

Such a generalized bioinformational framework of Haken’s multilevel synergetic neural network representing corresponding intracellular and extracellular biochemical reactions is in line with trends of modeling hierarchical information processing in higher cognitive processes [44] and might also provide possible missing downward causation control mechanism of morphogenesis and psychosomatics [41, 42, 50–52]. However, it should be noted that conditions for the above resemblance between quantum ensemble prediction of our DM and HQHNN frameworks are fulfilled near thermodynamic equilibrium (while predicted very strong nonstationary conformational transitions, induced by strong environmental interactions within the decoherence model (cf. the Appendix), might occur far from thermodynamic equilibrium).

Appendix

On General Quantum Decoherence Framework for Macromolecular Conformations and Transitions

We assume that the macromolecule’s environment selects the molecule conformation as the “pointer observable.” Following the general phenomenological results and understanding, we assume that decoherence takes place for virtually all kinds of macromolecules and the solvent environment while the composite system “macromolecule + environment” is not externally disturbed. This we call “stationary state,” for which we stipulate occurrence of decoherence, that is, the environment-induced classicality of the macromolecule conformation. Typically, the conformational transitions occur due to a severe external influence exerted on the macromolecular degrees of freedom and/or to the molecule environment. In effect, this external influence redefines the macromolecule environment and thereby also the influence exerted by the new environment to the macromolecule degrees of freedom. Such physical situations, which may take some time, we describe as “nonstationary state.” For the nonstationary state, no particular assumption is made. Rather, one may expect that the change in physical characteristics and state of the environment would typically violate the conditions assumed for the occurrence of decoherence.

In formal terms, the stationary state is defined by the conformation system “mixed” state,

\[ \rho_K = \sum_i w_i \left| k_i \right \rangle \langle k_i \right| , \quad \sum_i w_i = 1, \quad (A.1) \]

where states \( \left| k_i \right \rangle \) represent the different conformational states. These (approximately orthogonal) states, \( \left| k_i \right \rangle \), represent the preferred (semi)classical “pointer basis” states for the macromolecule conformation system. Therefore, we stipulate the occurrence of decoherence as the fundamental quantum mechanical basis for the phenomenologically observed (semi)classical behavior of the macromolecules conformation stability.

On the other hand, as emphasized above, the conformational transitions occur due to a severe external influence. The related nonstationary state is defined by nonvalidity of (A.1) for the duration of the external influence. Intuitively, one may say that the external influence redefines the physical situation, the macromolecule is subjected to. In effect, the stationary state is disturbed, and there is not any semiclassical conformation state for the macromolecule. Formally, the conformation system is in state \( \rho_K' \), which cannot be presented by (A.1).

Of course, every external influence terminates and leaves the (redefined) system “molecule + environment” to relax, that is, to reach another stationary state with the final conformation state \( \rho''_K \), which is representable in the form of (A.2). The point strongly to be emphasized is that it is highly unexpected that \( \rho_K = \rho''_K \). That is, the final set of conformations need not be the same as the initial one, while for the conformations (i.e., states \( \left| k_i \right \rangle \)) common for \( \rho_K \) and \( \rho''_K \), their statistical weights need not equal each other; \( w_i \neq w''_i \). In effect, the following transition of the conformation state occurred:

\[ \rho_K = \sum_i w_i \left| k_i \right \rangle \langle k_i \right| \xrightarrow{\text{nonstationary}} \rho_K' \xrightarrow{\text{stationary}} \rho''_K \]

\[ = \sum_m w''_m \left| k_m \right \rangle \langle k_m \right| , \quad \sum_i w_i = 1 = \sum_m w''_m. \quad (A.2) \]

Duration of the whole dynamics presented by (A.2) is of the order of the time needed for the nonstationary state to terminate (note that decoherence, present for both stationary states, the most left hand and the most right hand sides of (A.2), is among the fastest physical processes known to date). So, in this scenario, the Levinthal’s paradox disappears. Furthermore, as the concept of “trajectory” (in configuration space) is not well-defined quantum mechanically, the very basis of the Levinthal’s paradox (i.e., sampling of trajectories in the configuration space) is absent in this quantum mechanical picture.

This general scenario has been analysed [46, 47] and a few possible scenarios of the external influence (i.e., of the nonstationary state) have been distinguished (see Figure 3 for a possible one).

Disclosure

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Endnotes

1. The Paradigm of the macroscopically differentiated states are the Gaussian states of the center of mass degrees of freedom of many-particle system. On the contrary, so-called relative coordinates (as observables) neither define macroscopically differentiated states nor carry classical behavior of the system, in any known physical theory or experimental situation.

2. In general, the stipulated decoherence-preferred degrees of freedom (biomolecular conformations in our case) are considered to be accessible (directly measurable) and therefore objective for an environmental observer (which is thus a part of the structure he observes). Are there some general rules and/or limitations for all possible bi-partitions QS_k + QE_k in the universe? It is not generally answered in QD theory and still needs additional fenomenological assumptions [13]. So, in the manner of quantum chemistry [29, 30] it might be plausibly proposed that many-atomic quantum systems QS_k are fenomenologically limited to the structures with dynamically coupled electrons considered as identical fermions, described by permutationally antisymmetric many-electronic eigenstates, which encompasses all existing molecules and electronic condensed state objects described by general quantum-chemical electronic self-Hamiltonian; in the case of the structures with dynamically coupled identical bosons, they are described by permutationally symmetric many-bosonic eigenstates and corresponding self-Hamiltonian.

3. In general, only closed composite system QS + QE is subject to the Schrödinger law (although this does not hold true separately for neither QS nor QE, as open quantum systems), with Hamiltonian $\hat{H} = \hat{H}_{QS} + \hat{F}_{QE} + \hat{H}_{int}$, where interaction Hamiltonian $\hat{H}_{int}$ depends on observables of both QS and QE. However, when $\hat{H}_{int}$ can be reduced to the "external field" its potential term $V$ can be added to $\hat{H}_{QS}$, providing new self-Hamiltonian of the QS, dynamically decoupled from the observables of the QE, and then QS can be treated as the closed quantum system. This is the case in most situations in quantum chemistry, with Schrödinger's equation applied to the explored closed many-atomic quantum system with appropriate boundary conditions and adopted computational approximations (giving rise to stationary ground and excited electronic-vibrational energy eigenstates of all possible many-atomic isomers, corresponding to the minimum of the electronic potential hypersurface, depicted in Figure 1, for ground electronic and corresponding excited vibrational energy eigenstates) [29, 30]. It should be noted that Schrödinger's equation cannot apply to nonstationary excitations and relaxations of the many-atomic quantum system, not only in between different isomers but also within the same isomer—when quantum deexcitation/decoherence must apply to nonpotential interaction of the open many-atomic quantum system (nondescribable fully by its self-Hamiltonian) with its quantum environment (generally field-related, including vacuum) [12, 13].

4. The similar Hopfield-like quantum-holographic picture might also be applied to individual acupuncture system [41, 42] (with quantum-like macroscopic resonances, fenomenologically observed in microwave resonance therapy [50, 51], which implies corresponding bipartition QS_acu + QE_acu, i.e., that acupuncture system has macroscopic open quantum structure with dynamically coupled electrons all along macroscopic network of acupuncture channels [41, 42, 50]). This then provides natural quantum-informational framework for psychosomatic medicine, that is, quantum-holographic downward coupling of the higher macroscopic quantum levels of acupuncture system and its projection zones (and presumably closely related consciousness [10, 41, 42]) with lower macroscopic quantum cell's biomolecular level.
changing the expression of genes (starting from the first fertilized cell division which initializes differentiation of the acupuncture system of nonthreshold electrical GJ-synapses ("gap-junctions")) [41, 42, 52].

5. Normalized “pointer basis” states $|k⟩_{\mathcal{K}}$ for the macromolecule conformation system of (A.1) are shown to be almost-classical one-dimensional harmonic oscillation “coherent states” $|\Psi_{k}(t),p_{k}(t)⟩$ [40]. Then (A.1) physically means that each macromolecule in a solution oscillates with probability $ω_i$ along classical harmonic trajectories $(q_i(t), p_i(t))$ of the mean position of values and momentum where the time change of $q_i(t)$ and $p_i(t)$ is the classical law for the harmonic oscillator position and momentum:

$$q_i(t) = q_{0i} \cos ω_it + \left(\frac{P_{0i}}{mω_i}\right) \sin ω_it, \tag{1}$$

$$p_i(t) = p_{0i} \cos ω_it - mω_iq_{0i} \sin ω_it$$

in the vicinity of the $k_i$th local minimum (which can be locally approximated by the harmonic potential, cf. Figure 3), that is, in the vicinity of the $k_i$th conformation. Bearing in mind that the “coherent states” do not change their Gaussian shape ($\Delta K_i = \text{const}$, $\Delta P_i = \text{const}$, $\Delta K_i \Delta P_i = h/2$) in the course of time [53–55], (1) has the clear (semi)classical meaning: defining the conformations as the harmonic oscillation equilibrium positions (cf. the local minimums $k_i$ in Figure 3) one obtains the semiclassical vibration of a macromolecule conformation in the vicinity of a local minimum $k_i$.

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