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Quantum-Holographic Hopfield-like Biomolecular Recognition

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Abstract—**A possible decoherence-based quantum-holographic Hopfield-like approach to biomolecular recognition is considered. This might be of fundamental importance in understanding underlying macroscopic quantum-holographic Hopfield-like control mechanisms of morphogenesis, with significant potential holistic psychosomatic implications.**

Keywords—**Biomolecular recognition, conformational transitions, quantum biophysics, quantum bioinformatics.**

I. Introduction

Conformational properties of enzymes are essentially important for understanding of enzymic catalytic activity. The *conformational lability of a protein* makes possible its *specific interaction* with *substrates*. As the substrate is (most frequently) low-molecular, and the enzyme is (high-molecular) protein, then the substrate directly interact with particular small part of the enzyme molecule – its *active site* (group and distribution of amino acid residues and cofactors (coenzymes, vitamins, metalo-organic complexes, hormones)).

In the *enzyme-substrate complex* (ESC) the *induced structural correspondence* of the enzyme and substrate is dynamically established, thus providing the optimal value of the free energy of interaction. The *conformational transformations* involved lead to a structural fit between the enzyme and the substrate, i.e. *biomolecular recognition*. The enzyme-substrate interaction is a *weak chemical bond* (Van der Waals, hydrogen, hydrophobic, ...), which is, however, very *enhanced* due to *hydrophobic active site of the enzyme*: namely, relative dielectric permittivity ε_r of the cavity of active site of the enzyme is much less ($\varepsilon_r \sim 3$–4) compared to water environment ($\varepsilon_r \sim 81$), which significantly facilitates the occurrence of electric interactions ($F \sim q_1 q_2 / 4\pi\varepsilon_o\varepsilon_r r^2$) between the substrate and the active site of the enzyme. Practically, *electrostatic* interactions within *hydrophobic cavity* (active site) *of the enzyme* provide main contribution to bioenergetics of enzymic catalysis, i.e. *to reduction of the activation barrier* in the enzyme-substrate complex. The energy necessary for conformational changes of the enzyme structure is liberated upon binding of the substrate to the enzyme.

During enzyme-substrate interaction and formation of the enzyme-substrate complex, the states of the electronic shells of the substrate and of the atomic groups of the active site of the enzyme are excited. In the enzyme-substrate complex the energy of electronic excitation is converted to the work of *displacement of atomic nuclei*. Among the movements of atomic nuclei the *lowest energy* is demanded by *low-frequency deformational vibrations* and *rotations around single bonds*, i.e. *conformational changes*! Hence, for *enzymic catalysis* the most significant are interactions of electronic and conformational degrees of freedom – *Electronic-Conformational Interactions* [1,2].

However, two *unresolved issues* of the (semi)classically addressed problems in molecular biophysics are *unreasonably long time* necessary for *change* of biopolymer conformations (Levinthal paradox [3]) and *long-range directedness* of selective biomolecular recognition processes – implying their essential *quantum origin* [4-6].

The *quantum* nature of *biomolecular conformational transitions* might be supported by experimentally *observed* poorly dimensionally-sensitive dispersion laws (which is generally the case of any internal more or less delocalized quasiparticle excitations in any condensed-state quantum system: electrons, optical phonons, conformones etc. [7,8]). On the contrary, *(semi)classical* kinetic (nonstationary) predictions imply the continuous map/conformation change ($k_i \rightarrow k_f$) which *requires* a sequence of n local *non-commuting* successive elementary transformations (local rotations of characteristic time τ_o), with the time necessary for the net transformation much longer than characteristic time necessary for a local rotation ($\tau_n \sim n\tau_o \gg \tau_o$) and the frequency of corresponding global transition much lower than the frequency of a local rotation ($f_n \sim 1/n\tau_o \sim f_o/n \ll f_o$) – strongly dependent on a degree of polymerization n (in *contra-distinction* with experiments).

The quantum nature of *biomolecular recognition* might be supported by *Resonant Recognition Model* (RRM) [9-11], confirmed on more than 1000 proteins from more than 30 functional groups – with numerous potential practical advantages in the fields of molecular biology, biotechnology, medicine, agriculture and nano-technology. It is based on findings that there is significant correlation between spectra of the numerical presentation of constitutive elements of primary sequences (amino acids, nucleotides) and their biological activity or interaction in corresponding bio-molecules (proteins, DNAs). The RRM model interprets this linear information by assigning the electron-ion interaction potential (EIIP) value to each constitutive element of primary sequence thus describing their average energy states of valence electrons, with subsequent using signal analysis methods in fast Fourier transform transforming this numerical series into single-electron wavenumber/RRM frequency domain and determining the common frequency components as peak frequencies in the multiple cross-spectral function for a group of primary sequences. The presence of peak with significant signal-to-noise ratio in a multiple cross-spectral function of a group of sequences with the same biological function means that all of the analysed sequences within the group have this single-electron RRM frequency component in common, with the following

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general conclusions [9]: (i) such a peak exists only for the group of biomolecules with the same function; (ii) no significant peak exists for biologically unrelated biomolecules; (iii) peak frequencies are different for different biological function; (iv) ligand-proteins and their biomolecular target-receptors have the same characteristic frequency in common but almost opposite phase – providing also novel theoretical possibilities for protein *de novo* design with desired functions.

Considered in the framework of Hückel-like theory of molecular orbits, quantum approach to the RRM-model shows that discrete Fourier transform in the RRM model is basically related to sequential contributions to the first order correction of energy (i.e. *primary sequence of amino-residues*, but not to (single-electron) energy of the periodic part of protein's chain) [11]. So, results of the RRM model imply that on the biomolecular level an information processing is going on in the *inverse space* of Fourier spectra of the primary sequences of biomolecules, bearing resemblance to quantum-holographic ideas that cognitive information processing is going in the *inverse space* of the Fourier spectra of the perceptive stimuli [12], thus tentatively supporting picture of *quantum-holographic fractal coupling* of various hierarchical levels in biological species, with significant potential psychosomatic implications.

On the other hand, the proposal of the *selectivity of protein-target EM interactions* based on *RRM resonant energy transfer between interacting biomolecules* involved in key-lock *biomolecular recognitions*, suggests appearance of corresponding macromolecular *resonant non-radiative electronic-vibrational isomeric transitions of the protein-target complex* [11] within the *Theory of Non-Radiative Resonant Structural Transitions* [13], cf. Fig. 1. These transitions are *induced by external EM excitation energy*, RRM theoretically predicted and experimentally observed in the frequency range of 10^{13} to 10^{15} Hz [14] – which incorporates infrared radiation (when vibrational excitations of ground many-electron hypersurface should be involved), but also visible and a small portion of the ultraviolet radiation (when higher electronic-vibrational excitations of many-electron hypersurface should be involved).

II. Quantum-Holographic Hopfield-like Model of Electronic-Conformational Interactions and Biomolecular Recognition

The quantum nature of *conformational transitions* and *biomolecular recognition* might be also supported by the *Model of Quantum Decoherence* [15-17], which is in agreement with the *Theory of Non-Radiative Resonant Structural Transitions* [13], achieved via intermediate quantum-coherent superposition of the externally activated electronic-vibrational states of the participating biomolecules, cf. Fig. 1. The model generally allows reproduction of both *existence and stability* of the (stationary) ligand-proteins/target-receptors key/lock mismatching and matching conformations, and the *short time scales* for the quantum-mechanical processes resulting effectively in (nonstationary) mismatching-to-matching 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 cyto-plasmatic environment.

Dynamic modification of many-electron energy-state hyper-surface $E_e(\phi_e)$, of the *cell's quantum-ensemble* protein/substrate biomolecular macroscopic open quantum system (via changes in operator of density of states $\hat{\rho}_e(t)$, cf. Fig. 2), is a natural consequence of coupled electronic-conformational processes – which implies potential possibility to consider cell's biomolecular recognition as *Hopfield's quantum-holographic associative neural network*. This approach assumes *standard cell's local treatment of quantum ensemble of non-interacting dynamically non-coupled N distinguishable* quantum biomolecular proteins of the same type (and their corresponding biomolecular classes of substrates) [4,5,15-17].

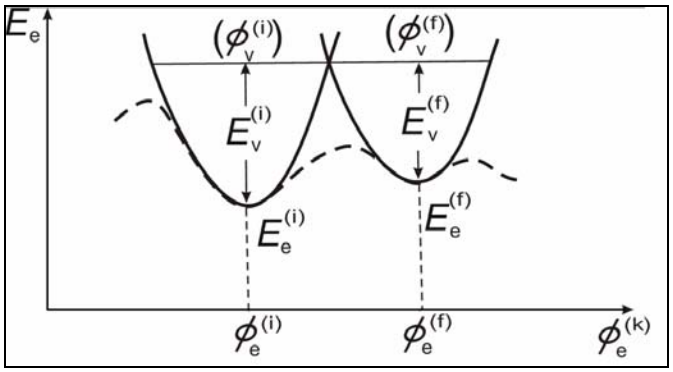

Fig. 1 The (semi)classical problem of the ground many-electron hypersurface $E_e(\phi_e^{(k)})$ as a potential energy for adiabatically decoupled Q1D vibrational and conformational system (with local minima as semi-classical 'positions', i.e. many-atomic isomer configurations on many-electron hypersurface (broken line in the figure) – not adiabatically well-defined when traversing between two adjacent local minima – is replaced in the framework of theory of non-radiative resonant transitions by better defined problem of two (virtually intersecting) isomeric many-electron hyper-surfaces (hyperparaboloids) serving as potential hypersurfaces for two vibrational (isomeric) problems (full line in the figure); adopted from ref. [5]. In this approach, by external perturbation of the isomers, at this very intersection the conditions for electronic-vibrational non-radiative resonant transitions between the two isomers (*i, f*) are achieved: in the first approximation, the matrix element of dipole transition from *i*-th to *f*-th isomer is given by $\boldsymbol{\mu}^{(i,f)} \approx \boldsymbol{\mu}_e^{(i,f)} \mathrm{S}_v^{(i,f)} + \boldsymbol{\mu}_v^{(i,f)} \mathrm{S}_e^{(i,f)}$, and it is obvious that transition between two isomers will be allowed when components of corresponding electronic and vibrational dipole moments, $\boldsymbol{\mu}_e^{(i,f)}$ and $\boldsymbol{\mu}_v^{(i,f)}$, and electronic and vibrational overlap integrals, $\mathrm{S}_v^{(i,f)}$ and $\mathrm{S}_e^{(i,f)}$, do not vanish. Also, during these resonant transitions the perturbed biomolecular system is shortly described by quantum-coherent superposition $(\phi_e^{(i)} \phi_v^{(i)} \pm \phi_e^{(f)} \phi_v^{(f)})/\sqrt{2}$, before its decoherence into final electronic state $\phi_e^{(f)}$ or into initial electronic state $\phi_e^{(i)}$ (with subsequent de-excitations into lower vibrational states).

However, there is an alternative possibility of *holistic cell's non-local treatment of quantum system of non-interacting dynamically coupled N in-distinguishable* quantum biomolecular proteins of the same type (and their corresponding biomolecular classes of substrates) [4,5,18,19]. Then dynamical modification of many-electron energy-state hypersurface of cell's biomolecular protein macroscopic open quantum system (and analogously their corresponding biomolecular classes of substrates), can be best represented in the formalism of *second quantization*, which treats *all biomolecules of the same atomic configuration* as *in-distinguishable quantum particles* which *occupy different isomeric-conformational states*, and considers such cell's *N-particle protein quantum state* in quantum-mechanical

occupational basis which describes *number of proteins that occupy* subsequently all states *of complete basis set of single-particle isomeric-conformational protein states*.

The both approaches provide a *plausible quantum-holistic* picture of biological cell (while experiments will decide in favour of one of them!) – and especially *phenomenologically approved quantum-holographic (fractal) coupling of various* hierarchical quantum levels – from biological cell to acupuncture system/ consciousness. This implies Hopfield-like quantum-holographic feedback influence of the EM field of acupuncture system on cells' conformational protein changes and genes' expression (so called macroscopic 'downward causation'), and not only reversed (microscopic 'upward causation'), with mutual quantum-informational control of ontogenesis/embryogenesis and morphogenesis, starting from the first division of the fertilized cell when differentiation of the acupuncture system begins – with significant *psychosomatic and cognitive bioinformational implications* [4,5,18-20].

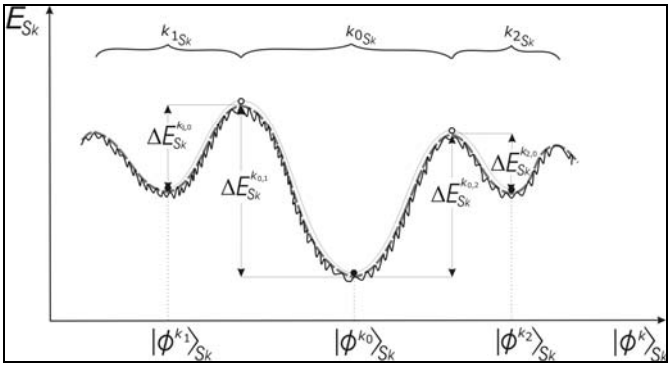

Fig. 2 Schematic presentation of the memory attractors in the energy-state ($E_{S_k}(\phi^k)$) hypersurface of the quantum-holographic memory/propagator of the open macroscopic quantum system S_k (cell's protein/target biomolecular one); adopted from ref. [5]:

$$G^{(k)}(\boldsymbol{r}_2,t_2,\boldsymbol{r}_1,t_1) = \sum_i \phi^{(k_i)}(\boldsymbol{r}_2,t_2)\,\phi^{(k_i)}(\boldsymbol{r}_1,t_1)^* = \sum_i A_{k_i}(\boldsymbol{r}_2,t_2)\,A_{k_i}(\boldsymbol{r}_1,t_1)\,e^{\frac{i}{\hbar}(\alpha_{k_i}(r_2,t_2)-\alpha_{k_i}(r_1,t_1))}.$$

It should be pointed out that quantum decoherence presumably plays fundamental role in biological quantum-holographic neural networks, through presented energy hypersurface shape adaptation (in contrast to low-temperature artificial qubit quantum processors where it must be avoided until the very read-out act of quantum computation) – which implies that Nature presumably has chosen elegant room-temperature solution for biological quantum-holographic information processing, permanently fluctuating between quantum-coherent states $\left|\phi^k(t)\right\rangle_{S_k} = \sum_i c_{k_i}(t)\left|\phi^{k_i}\right\rangle_{S_k}$ and classically-reduced states $\widehat{\rho}^k_{S_k}(t) = \sum_i \left|c_{k_i}(t)\right|^2 \left|\phi^{k_i}\right\rangle_{S_kS_k}\left\langle\phi^{k_i}\right|$ of cell's biomolecular open macroscopic quantum system S_k, through nonstationary interactions with farther bodily environment and through decoherence by bodily closer environment. The same might be related to higher hierarchical quantum-holographic macroscopic open acupuncture system/consciousness level, thus providing natural framework for quantum-holographic coupling with lower cellular level, thus changing the expression of genes.

To be more specific [5], in the formalism of second quantization – the mentioned cell's *N*-particle protein quantum state is considered in quantum-mechanical *occupational basis* (generally bosonic, because of protein-substrate integer spin due to even number of their covalent bonded electrons!), describing number of proteins which occupy complete set of *single-particle protein-substrate isomeric/conformational states*: $\left|n_0n_1n_2...\right\rangle_e$, with conditions $N = n_0 + n_1 + n_2 + ...$ and $E_{S_e} = n_0E_e^{(0)} + n_1E_e^{(1)} + n_2E_e^{(2)} + ...$ (where E_{S_e} is the many-electron energy of the total cell's *N*-particle-protein quantum state, while $E_e^{(0)}$, $E_e^{(1)}$, $E_e^{(2)}$... are the many-electron energies of the protein single-particle quantum isomeric/conformational states 0, 1, 2, ...). An many-electron energy-state hypersurface (dynamically modified via changes in corresponding operator of density of states $\widehat{\rho}_e(t)$) of such protein *N*-particle-isomeric/conformational state has a schematic representation of Fig. 2, where internal surface of every minimum is proportional to the partial energy ($n_iE_e^{(i)}$) of the *i*-th protein single-particle-isomeric/conformational state occupied by n_i isomers of the same form (i = 0, 1, 2, ...), so that total energy ($E_{S_{ke}}$) of the cell's protein *N*-particle-isomeric/conformational state is proportional to the sum of internal surfaces of the all minima of the many-electron hypersurface.

On the same line [5], ragarding multi-phonon energy-state hypersurface (dynamically modified via changes in corresponding operator of density of states $\widehat{\rho}_v(t)$) of the all possible protein-substrate isomeric/conformational states, requires their consideration in quantum-mechanical *occupational basis* (also bosonic, because of phonon's integer spin!) – describing number of phonons occupying complete set of single-particle *phonon states* of the all protein-substrate isomers/ conformations: $\left|n_1^{(0)}n_2^{(0)}...n_{3N-6}^{(0)}n_1^{(1)}n_2^{(1)}...n_{3N-6}^{(1)}n_1^{(2)}n_2^{(2)}...n_{3N-6}^{(2)}...\right\rangle_v$ where every isomeric protein-substrate complex composed of *N* atoms has generally 3*N*-6 vibrational degrees of freedom (phonon types), out of which every phonon state can be occupied by unlimitted number of phonons (which is characteristic of all bosons, i.e. particles of integer spin). It should be pointed out that an energy hypersuface of multy-dimensional phonon quantum state has also a schematic representation of Fig. 2, with potentially unlimitted number of phonons in every single-phonon state. This energy hypersuface of multi-phonon quantum state might also include low-energy long-range coherent microwave Fröhlich excitations [21] (created as a result of interaction of electronic and phonon isomeric subsystems – of particular significance in microwave resonance therapy (MRT) [22-24] of a dynamic modification of the EM multi-phonon (and related many-electron) acupuncture macroscopic quantum subsystem [4,5,20]!).

For instance, in two-isomeric protein-substrate transitions $\phi_e^{(i)} \rightarrow \phi_e^{(f)}$ there appear *dynamic modification* of both *many electron N-particle-isomeric/conformational state* and corresponding *EM multi-phonon hypersurface* $E_v(\phi_v^{(k)})$ of the cell's *N*-particle *protein-substrate macroscopic quantum system* – in full analogy with training in Hopfild's associative neural networks.

So, on the cellular level of the *N*-particle *protein-substrate* macroscopic quantum system, there would exist *two* (interacting) cell's *protein-substrate* macroscopic quantum subsystems – first with *modifying many-electron protein-substrate hypersurface* $E_e(\phi_e^{(k)})$ and second with *modifying EM multi-phonon* protein-substrate *hypersurface* $E_v(\phi_v^{(k)})$, described by the second quantization Hamiltonian [5]:

$$\widehat{H} = \widehat{H}_{is}^{(0)} + \widehat{H}_{ph}^{(0)} + \hat{H}_{\text{int}}^{is-E} + \hat{H}_{\text{int}}^{ph-E} + \widehat{H}_{\text{int}}^{is-ph}$$

$$= \sum_i E_{is}^{(i)} a_i^+ a_i + \sum_i \sum_{j=1}^{3N-6} E_{ph}^{(i,j)} b_{i,j}^+ b_{i,j} + H_{\text{int}}^{is-E} + H_{\text{int}}^{ph-E} + \widehat{H}_{\text{int}}^{is-ph}$$

in which a_i^+, a_i are creation and annihilation operators of the various many-electron protein-substrate isomeric/conformational states, $b_{i,j}^+, b_{i,j}$ are creation and annihilation operators of the various phonon states in all many-electron protein-substrate isomeric/conformational states, and $\hat{H}_{\text{int}}^{is-E}$ is a model-dependent Hamiltonian of the many-electron protein-substrate isomeric-environment interactions, $\hat{H}_{\text{int}}^{ph-E}$ is a model-dependent Hamiltonian of the many-electron protein-substrate isomeric phonon-environment interactions, and $\widehat{H}_{\text{int}}^{is-ph}$ is a model-dependent Hamiltonian of the many-electron protein-substrate isomeric-phonon interactions.

III. CONCLUSIONS

Two unresolved issues of the (semi)classically addressed problems in molecular biophysics are unreasonably long time necessary for change of biopolymer conformations and long-range directedness of selective biomolecular recognition processes – implying their essential quantum origin. In this paper a possible decoherence-based quantum-holographic Hopfield-like approach to biomolecular recognition is considered. It is shown that on the cellular level of the *N*-particle *protein-substrate* macroscopic quantum system, there would exist *two* (interacting) cell's *protein-substrate* macroscopic quantum subsystems – first with *modifying many-electron protein-substrate hypersurface* and second with *modifying EM multi-phonon* protein-substrate *hypersurface*. This approach might be of fundamental importance in understanding possible underlying macroscopic quantum-holographic Hopfield-like control mechanisms of morphogenesis, and their backward influence on the expression of genes, with significant potential holistic psychosomatic implications.

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