Quantum biology: Harnessing nano-technology's last frontier with modified excipients and food ingredients.

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Editor, Journal of Excipients and Food Chemicals

Received: December 1, 2014; *Accepted:* December 15, 2014

Review Article

ABSTRACT

Emerging evidence indicates that quantum phenomena may be operational in biological systems despite unfavorable temperatures and environmental noise. It is possible that protein quaternary architecture may be conducive to sustaining quantum entanglement and coherence. Models ranging from quantum resonant recognition, proton tunneling in DNA, radiation wave therapy and the magnetic isotope effect have been proposed that validate the importance of the wave-particle duality of matter in persisting in and modulating biological processes. The ability of food ingredients and pharmaceutical excipients to manipulate bioeffector mechanisms *via* quantum effects is discussed. It is hoped that this new perspective will provide impetus for further research in this field.

KEY WORDS: Quantum biology, nano-technology, food ingredients, excipients, magnetic isotope effect, resonance recognition model, proton tunneling, quantum dots

> *"…It was true that .. he had made up his mind, but it was only what was left of his mind. That small and active fragment now dominated; the rest comprised an absence hardly to be endured. He was a wanderer between two worlds and must ever wander…."* James Hilton in 'Lost Horizon'.

INTRODUCTION

Not unlike the conundrum, and its solution encountered by Hilton's protagonist quoted above, quantum entanglement, coherence and collapse may provide the answers to many biological puzzles that evade explanation using 'diffusive' Newtonian mechanics. These phenomena assume increasing significance at sub-nanoscale dimensions but may be able to 'evade' the collapse to 'classicality' at the quasi-classical nanometer scale and ambient temperature due to 'quantum-friendly' bio-molecular architecture. The ability of the 'wave function' of an electron in biological processes to sample multiple eigenstates simultaneously, to 'tunnel' through seemingly unsurmountable energetic barriers, to alter reaction kinetics and product ratios depending on externally applied electromagnetic fields or to avoid decoherence in the presence of environmental interference has, so far, remained immune to unequivocal falsification. In fact, emerging evidence supports the view that life may have deliberately harnessed quantum phenomena for various ends and purposes (1, 2).

The statement 'Folded proteins and enzymes preserve quantum coherence' has, to the

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author's knowledge, not been explicitly so stated or inferred as yet in/from the literature. While this inductive assertion seems speculative in the absence of data, the phenomenon may be eminently possible, given that quaternary protein architecture is conducive to quantum sampling, 'classical' diffusive explanations are not convincing and evidence to the contrary does not exist. The exclusion of water and ions from the interior 'hydrophobic' cavity of the folded protein helix acts to impose physical boundary conditions and to consequently serve as a decoherence shield, thus preserving and maintaining 'decoherence free subspaces' (3), quantized states, for a considerable period of time even in the presence of biological thermal noise and environmental electromagnetic interference. The simultaneous cutting of two spatially distinct phosphodiester bonds has been proposed as being caused by the non-local role of quantum entanglement in synchronizing the catalytic centers of several type II restriction endonucleases (4). Quantum coherence has been calculated to contribute significantly to electron transfer within the intramolecular chain of seven iron-sulfur clusters that exist within the NADH : ubiquinone oxidoreductase respiratory complex I, despite persisting for only a fraction of the typical timescale of quinone reduction (10-100 μs) (5). The orchestrated objective reduction of quantum coherence (the Orch OR) in brain microtubules has been proposed as a model for consciousness (6). In the Orch-OR model, this 'self-collapse' of superposed quantum states is hypothesized to be different (7) from the Copenhagen interpretation of the 'collapse to classicality' that occurs due to environmental entanglement, measurement or conscious observation. A conclusion of quantum simultaneous sampling of phosphorylated and non-phosphorylated states can be drawn from the suggestion of Ca^{+2} calmodulin dependent kinase II spatial interactions with microtubule hexagonal lattices to encode long term memory (8).

It may be that the conventional 'ball and stick' classical physics paradigm of medicinal chemistry has encountered a sufficient enough impasse so as to explore the seemingly improbable 'hot and wet' regime of quantum biology, or it may be that that technology and events are in place for the coming of age of this sub-nanometer missing ingredient in life's dynamics.

Radiation wave therapy

Targeted nanotech will kill only cancer cells while sparing normal cells, but relapse can still occur due to metastasis. Approaches based on magnetoreception, quantum coherence is expected to kill non-localized tumor cells as well, unless specifically targeted to location. An intriguing, yet hypothetical idea is to convert ionizing radiation (consisting primarily of electrons released from a β decaying isotope) from particle to wave, allowing for greater depth of penetration *via* quantum tunneling than would be possible with 'conventional' radiotherapy (9, 10). The conversion to a quantum electron wave would be achieved using nano-magnets in the vicinity of the cancer cells. Such quantum tunneling of magnetization has been achieved at low temperatures under controlled conditions inhibiting decoherence (11), and for distances spanning nanometers on biologically relevant timescales (12).

The presence of an externally applied magnetic field in conjunction with radiation produces the singlet spin quantum state S_1 and the triplet spin quantum states T_{-1}, T_0 and T_{+1} with equal probability (see the section on the Magnetic isotope effect below). Since the T states are non-degenerate and distinct, there is a 75% increase in free radical concentration due to the external magnetic field. This phenomenon could therefore be used to inhibit the recombination of free radicals in the tumor vicinity thereby increasing tumor cell apoptosis and consequently, increase the therapeutic ratio of the radiation treatment (13).

Functionalized Quantum Dot (QD) bioconjugates have the potential to act as photosensitizers (14). Decreasing the size of a QD results in a greater degree of quantum confinement, which produces an exciton of greater energy. The consequent greater bandgap energy induces greater frequency narrow emission band radiation. Therefore, different sizes of QD probes can be used to image and track multiple molecular targets and biomarkers simultaneously with very little overlap (15).A peptide formed from as few as two phenylalanine amino acids has been shown to associate in methanol into 2.1 nm QDs' consisting of two peptides (16).

The magnetic isotope effect

Free-radical reactions show different reaction rates and different yields of products depending on whether the reagents contain magnetic or nonmagnetic isotopes and on the presence of electromagnetic (EM) fields or radiation respectively (17). The first phenomenon is known as the 'magnetic isotope effect' (MIE), a kinetic phenomenon which manifests itself as the dependence of the reaction rate on the nuclear spins of the reactants. MIE is a well characterized feature of chemical transformations that have radical pairs as transient reaction intermediates. The second phenomenon determines the relative product yields of multiple products in a reaction based on the orientation of the reactants in the EM field. Because radical pair reactions must conserve electron spin, the radical pair is produced in a singlet (S) state with antiparallel electron spins (↓↑), one in each radical. When a magnetic isotope is used, its nuclear magnetic moment couples to the magnetic moment of the valence electron of its cation radical, converting the singlet radical pair into its triplet form (T) in which the electron spins are parallel (↑↑). This process is coherent and quantum mechanical. It follows that for both these phenomena to alter the rates or the ratio of products to any appreciable extent, the electron spins of the radical pairs (in the form of T or S) must be protected from an irreversible loss of quantum coherence. It has been calculated that superposition and entanglement are sustained in such radical pairs for at least tens of microseconds (18), exceeding the time required for decoherent kinetic reaction rate perturbations or for susceptibility to externally applied (or to the Earth's) magnetic or EM fields.

Evidence is mounting in favor of a MIE on phosphorylation processes (19-22), although findings to the contrary are not uncommon (23). Because phosphorylation plays a ubiquitous role in enzymatic ATP synthesis, enzymatic phosphorylation of proteins and DNA replication, the incorporation of magnetic metal isotopes into catalytic metalloenzymes can change the kinetics of these reactions as well as their end products (24). Creatinine kinases loaded with ^{25}Mg, ^{67}Zn or ^{43}Ca showed an increased rate of ATP synthesis over their non-magnetic metal isotope loaded counterparts. When magnetic metal nuclei are present in the catalytic site of DNA synthesis, the S-T spin conversion competes with the reverse electron transfer reaction and increases the ratio of the T-T pair relative to the S-S radical pair. The increased lifetime of the T-T pair makes the addition of the ribose oxy-radical to the P-O bond more favorable, in turn forming the secondary oxy-radical which suppresses DNA synthesis. As a result, both ^{25}Mg and ^{67}Zn ions suppress DNA synthesis. Protein kinases phosphorylate proteins in a nuclear spin dependent manner, as exemplified by the increased phosphorylation of prothrombin by ^{25}Mg Prothrombin kinase.

It has been proposed that the MIE could be used to stimulate ATP synthesis in cardiac diseases. Magnetic isotope ions could be used to alleviate hypoxia and cardiac insufficiency. In instances where mitochondrial ATP synthase and apoptotic cytosolic enzymes are functional, magnetic isotopes can be used to deter the cellular switch from oxidative phosphorylation to glycolysis (25), thus providing a means for controlling cell proliferation and to stimulate apoptosis of transformed cells. Food supplements or processed food could incorporate stable magnetic isotope ions instead of those with natural isotope abundance, as could metal containing excipients used in medicines meant for chronic administration.

Quantum resonance frequencies

Interactions between biological molecules are proposed to occur within the framework of a mechanistic 'lock-and-key' model of molecular recognition. Molecular structure and free energy considerations give credence to this model and it has been used to successfully design small molecule enzyme inhibitors. However, this model does not fully explain how different proteins or peptides may 'recognize' and interact *selectively* and *specifically* with each other, function in concert and in the vicinity of each other or exchange signaling information amid thousands of other molecules packed in the cellular milieu. An alternative model, the resonant recognition model (RRM) proposes that resonant wave energy transfer between interacting biomolecules underpins the selectivity and 'homing' of protein-target reactions (26). Converting the electron excitation energies of each amino acid in a protein into a Fourier spectrum leads to the conclusion that there is significant correlation between the spectra of proteins and their biological activity, which is further semi-empirically correlated

to a particular electromagnetic (EM) peak in the ultraviolet (UV), visible (VIS) or infrared (IR) domain (27). The characteristic frequencies of proteins could represent the oscillations of a physical field which, in turn, could be interpreted as the time-frequency dependent coherence-decoherence events unfolding in its quaternary structure.

The utility of this model lies in the fact that de-novo design of peptides possessing any desired pharmacological effect becomes possible using only computational input. Because a unique peak exists for a group of protein sequences sharing the same biological function, an iterative inverse Fourier transform can identify different amino acid sequences that produce specific spectral characteristics, and hence, the desired biological activity. As a corollary, short chain peptides (capable of absorption through the gastrointestinal tract (GIT)) could be identified in protein containing food products and/or excipients with pre-defined biological properties. A variety of probiotics type foods could be envisaged, containing different encapsulated 'restriction enzymes' that would breakdown proteinaceous food into pre-defined GIT absorbable amino acid sequences, in turn capable of modulating specific biological processes *via* their calculated resonant recognition energy signatures. As proof-of-concept examples, an 18-mer peptide was identified with a similar RRM spectra as that of the 3.5 kDa human glucagon protein (28), peptides of 20 amino acids were designed capable of mimicking the HIV envelope gp160 protein immunorecognition function (29) and peptides with lengths of 10-24 amino acids were identified as FGF antagonists based on the (> 7 kDa) protein's receptor recognition frequency (30).

As in the case of the coherent entanglement of magnetic spins enabling external EM fields to influence biological reaction rate kinetics and product yield ratios (see the section on the Magnetic isotope effect), the correlation between the resonant energy of bio-peptides and (UV, VIS and IR) light frequencies turns out to be more than just mathematical coincidence. Incident light frequency dependent effects on biological processes have been observed which are correlated to the calculated quantum-mechanical resonant recognition frequencies of participating photosensitive biomolecules (31, 32). It should theoretically be possible to select indoor lighting frequencies so as to modulate specific enzymes. For example, light of different frequency may be used to induce/increase collagenase, caspases (in conjunction with curcumin) (33), IL-10 mRNA expression and CD4(+) cell counts (34) and cytochrome C oxidase (35) to modulate wound healing, melanoma, neuronal cell recovery after stroke and redox mitochondrial status respectively. The wide gamut of biological targets that can be potentially modulated by visible radiation attests to the significance of quantum-mechanical resonance.

The literature is replete with empirical studies of the influence of EM fields on biological processes (36-39), often with disparate, conflicting and inconclusive results. As a result, skepticism about such 'action-at-a-distance' non-classical biological phenomena has been difficult to dissipate. The emerging field of quantum biology provides the conceptual framework for evaluating and measuring such phenomena. Carefully controlled experiments can be envisaged for quantitatively and mechanistically studying the effects on biological processes of 'low energy' radiation, ranging from wi-fi, FM radio, cell phones, to airport X-ray scanners and power generating substations.

QDs' could potentially be designed to produce EM radiation at a single (or several) frequency(ies) that matche(s) the proto(oncogene) protein products frequencies using the RRM model. Multiple narrow band frequency emitters can be designed by using QDs' of different particle sizes. In this model, the QDs' actually would function as homing and therapeutic devices instead of only as facile substrates on which therapeutic entities are anchored. Although not explicitly invoked by the authors, the RRM model may be used to explain the inhibitory effect of CdSe QDs' on Rho-associated kinase (ROCK) activity in cervical carcinoma HeLa cells associated with the attenuation of ROCK-c-Myc signaling (40). In this context, researching and building an RRM library of proteins and enzymes would represent a major addition toward designing 'therapeutic quantum modulators' and should be pursued.

Proton tunneling in DNA

Proton tunneling between base pairs of DNA has been proposed to cause spontaneous mutations (41). If decoherence (loss of entanglement of a 'proton wave' between two base pairs) caused by

DNA strand splitting during a replication event 'collapses' the proton so that it is now chemically bound to the lone pair of electrons of its complementary base (42), the canonical structure of both bases would effectively be changed to their tautomeric structures, which would not bind to their initial base pair partners. Subsequent base pairing orchestrated by DNA polymerase would err in 'reading' the base, causing a universal spontaneous point mutation bias with respect to transitions of the base pairs C:G to A:T and A:T to C:G.

The genetic code has been proposed to be optimized for quantum searching (43). Per Grover's algorithm (44) of quantum computation, for one and three sampling operations, optimal improvement over a classical search is obtained when the number of objects is 4 and 20.2 respectively. It has been pointed out that the fact that the genetic code is based on triplets of nucleotides of four molecules that code for 21 amino acids, is either a numerical coincidence or evidence that life is optimized for quantum computing at the molecular level. It has been suggested that the genetic code should be regarded as a quantum code, allowing superpositions of coding states to occur, leading to spontaneous mutations (45).

Quantum coherence and quantum entanglement must have processes and means to decohere to enable evolutionary modification and genetic recombination of the genome to occur. Perhaps this is why DNA possesses the structure and scaffold that it does, to deliberately ensure a (greater than) certain degree of decoherence and discontinuous random changes in the code to occur *via* proton tunneling between the hydrogen bonded base pairs (46, 47) and to enable or disable genetic transcription determined by histone architecture. The rate of quantum decoherence (and thus the chance of random mutations) may reasonably be assumed to be modulated by how loosely (or tightly) the DNA is wound around the histone protein (48), which therefore directly implicates histone deacetylase (HDAC) inhibitors (49) as upstream epigenetic effectors in the quantum control of carcinogenesis. Foods and food ingredients that modulate HDAC (50) would therefore seem to modulate quantum decoherence as their end-mechanism to exercise their anti-carcinogenic effect. To label these as 'Quantum foods', however kitsch sounding, may indeed be justified. It may turn out that the often, caricatured as pseudo-scientific, concepts in Chinese medicine in the form of *chi* or *qi*, and in Ayurvedic medicine in the form of *prana*, which presumably refer to these 'last mile' quantum effects, are ubiquitously pertinent, cogent and capable of being manipulated pharmacologically, and have, in fact, epistemologically been the ultimate pharmacological targets all along.

Just as the isotope spin is a determinant in quantum coherence, the hydrogen isotope mass is conducive to mutation bias in DNA by the phenomenon of quantum tunneling. The spontaneous mutation rate of deuterated *Bacillus cereus* spores was significantly reduced when compared with that of its natural hydrogen (protium) counterpart (51). Heavy water (D_2O) has been shown to be cytotoxic to several cancer cell lines both *in vivo* and *in vitro* (52, 53). This is in conformity with the proton tunneling theory since tunneling probability is directly proportional to the mass of the particle.

CONCLUSIONS

If quantum phenomena underlie the 'last mile' (a phrase used in logistics to refer to the final leg of connectivity to the consumer, of information, goods and services) of aberrant biological processes to various degrees, then the ghost of Ehrlich's elusive 'magic bullet' theory may yet be capable of exorcism. In fact, it may be that pharmacologically manipulative substances, including food ingredients and electromagnetic radiation, have been modulating this 'last mile' all along, *sans* our knowledge, so that the mechanism conventionally (and erroneously) attributed to the 'lock and key' formalism should actually be attributed to the wave nature of matter. The good news is that there are still other avenues and opportunities of therapeutic intervention that have not yet been utilized which can explicitly exploit the wave-particle duality of matter in decoherence shielded biological targets.

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