



Will Nanocarbon Onion-Like Fullerenes (NOLFs) Play a Decisive Role in the Future of Molecular Medicine? Part 1. Foundation in Fullerenes: Theoretical Application of NOLFs in the Quantum Cell

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Abstract

Mitochondria are central to the defense, bioenergetics, biosynthesis, replication, and other metabolic activities of the cell. Mitochondrial perturbation triggers a cascade of cellular defenses that affect the entire organism. Unabated, this perturbation can cause impairment of whole body systems resulting in chronic, degenerative diseases and aging. Molecular substances that improve or restore the quantum mechanics and electrostatics of mitochondria (and, thus, the cell) may become the medicines of the future. Due to their unique structure and properties, fullerenes may have significant beneficial effects in humans.

Keywords: Allotrope; Aromatic Ring; C₆₀; Cyclic Native Aggregation; Dielectric Property; Fullerene; Hormesis; Mitochondria; Mitochondrial QED; Nanocarbon; Oxphos; Pharmacophore; Pi Clouds; Raman Band; Shungite; Thermodynamic; Quantum Electrodynamic

Abbreviations

CDR	:	cell danger response
CNO	:	carbon nano-onion
MitoQED	:	mitochondrial QED
MWCNO	:	multi-walled (shelled) carbon nano-onion
NOLF	:	nanocarbon onion-like fullerene
NOLF-M	:	nanocarbon onion-like fullerene material
OLC	:	onion-like carbon
OXPHOS	:	oxidative phosphorylation
PCa	:	prostate cancer
PDT	:	photodynamic therapy
QED	:	quantum electrodynamics
PLTR	:	purinergic life-threat response
ROS	:	reactive oxygen species

Preface

The biology underlying medicine is undergoing a subtle but radical paradigm shift. Investigations into the quantum cell have been gaining acceptance; and one can envision that, at some point, there must also be a paradigm shift in medicine to reconcile with the emerging realization that life's cellular machinery teeters on quantum criticality between order and chaos. Thus, an understanding of the detailed mechanisms behind this apparent self-organized criticality [1] becomes necessary in the prevention and treatment of disease.

Biology, based on classical physics, has failed to explain how the highly organized molecular machinery (taking care of myriads of complex processes such as DNA replication, protein synthesis, cell division, and metabolism) can operate with perfect timing and precision in a healthy cell. The electrodynamics of the quantum cell provides the required perpetual and precise transfer of charges throughout the system for perfect execution of biochemical tasks [2]. To more fully fathom the following exploration, it is helpful to be acquainted with concepts of the quantum cell, quantum electrodynamics, and electromagnetic fields in biologic systems as well as protein conformational change, structured cell water, and alternative cell physiology.

Introduction

Structure, Discovery, and Characteristics of Fullerene

The 3rd allotrope of crystalline carbon is a fullerene. Fullerenes are molecules composed entirely of carbon in the form of an enclosed caged polytope with one to several shells that are sometimes linked (catenated) together. Fullerenes were recognized more than a century before they were “newly discovered” by modern science from mineraloid carbonaceous deposits called shungite found in the Republic of Karelia, Russia near the town of Shun'ga, and where Peter the Great built a spa known for its health benefits [3]. Shungite is a carbon-rich Precambrian age rock with non-crystalline and non-graphitized nanocarbon content between 5% and up to 95%. Modern investigation has revealed that shungite is formed with well-ordered sp²-hybridized carbon nanoclusters of about 10nm. Graphite-like layers are skewed allowing for a hexagonal symmetry and fullerene-like structure to the nanocarbon clusters.

The properties of the shungite have long been used to include water purification, metallurgy, and other practical uses, as well as

being recognized for its medicinal effects. However, science has yet to make a connection between the microstructure of shungite and its physical properties, i.e., electron structure, conductivity, dimagnetic properties, and appearance of different defects [4]. The most stable fullerene is a 60 vertex, truncated icosahedral single shell C₆₀ polytope. C₆₀ is composed of 20 hexagonal rings of (near) equal length carbon-carbon bonds that are joined together forming 12 pentagonal rings [5]. The 1985 publication of the discovery of C₆₀ began the era of nanotechnology and with it a flurry of research into nanocarbon and fullerenes (Figure 1).

Figure 1. A representation of fullerene C₆₀.

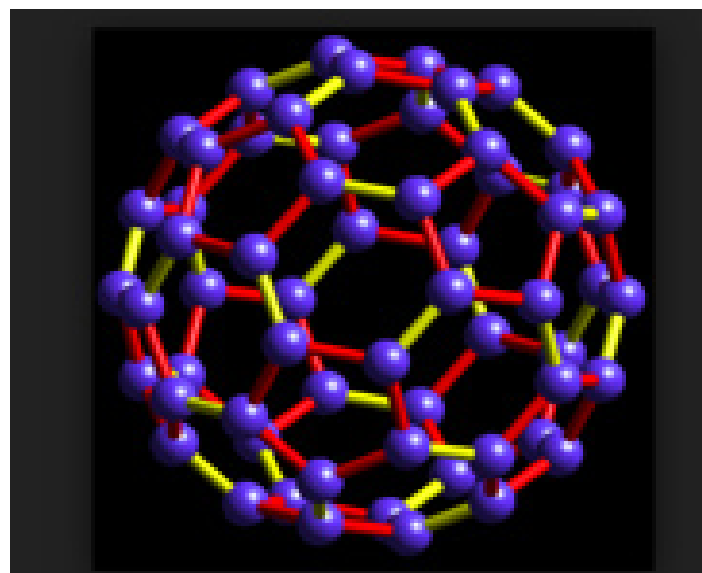


Image in Public Domain.

Although the molecule had been proposed in work by Japanese researchers in 1970, and the calculations for it were published (only in the Russian language) by Soviet scientists in 1973; the formal “Discovery” of C₆₀ had to wait until 1985 when Harold Kroto, James R. Heath, Sean O’Brien, Robert Curl, and Richard Smalley at Rice University first published their findings. After some initial confusion regarding the C₆₀ structure, the accepted symmetry and “soccer ball” shape reminded Kroto of the geodesic dome created by Buckminster Fuller, a prominent architect at that time; and C₆₀ was named, Buckminsterfullerene, or “buckyball” (Figure 2). Confirmation of the actual C₆₀ structure had to wait until 1990, and the determination of bond lengths until the following year [6].

Figure 2. Richard Buckminster Fuller and his Montreal World Fair's Dome, 1967. Architect Buckminster Fuller with a geodesic dome; the basis of the descriptive term for fullerene-the "buckyball" or "buckyfullerene".



Courtesy of Magnum Photos.

The discovery of C_{60} structure was novel as the expectation of scientists to that point was of planar carbon structures. Carbon bonding in fullerenes also turned out to be more involved. In the C_{60} buckyball, each carbon had two single bonds and one double bond to satisfy carbon's valence of four. The truncated icosahedral C_{60} structure came close, but did not have the perfect symmetry of a sphere. The carbons had to adjust to a non-planar environment resulting in three σ -bonds with its $Sp^{2.3}$ hybrid orbitals and one π -bond with the remaining p-orbital.

The C_{60} molecule has excellent stability due to the high number of double carbon-carbon bonds. It is hydrophobic, diamagnetic, and electrically non-conductive. Since three of each of the 60 carbon atoms valence electrons form σ -bonds, the remaining 60 electrons are delocalized into a pi cloud over the surface of the C_{60} molecule. The valence positions available result in 12,500 resonance structures [7]. Kekule valence structures (bonded electron pairs in covalent bonds) contain meaningful structural information on conjugated polycyclic systems, but have been generally overlooked or not fully appreciated for their contribution to fullerene characteristics; 5,828 of these resonant structures have been shown to result in 99.82% of the molecular energy of C_{60} [8].

The nonsymmetry of the C_{60} structure also alters the expected electron distribution between the high- and low-lying energy orbitals of C_{60} resulting in C_{60} having no unpaired outer orbital electrons allowing for its diamagnetic and electrically non-conductive properties. Yet, C_{60} has a reasonably high affinity for electrons and has low-lying unoccupied energy levels that can accept up to six electrons [9].

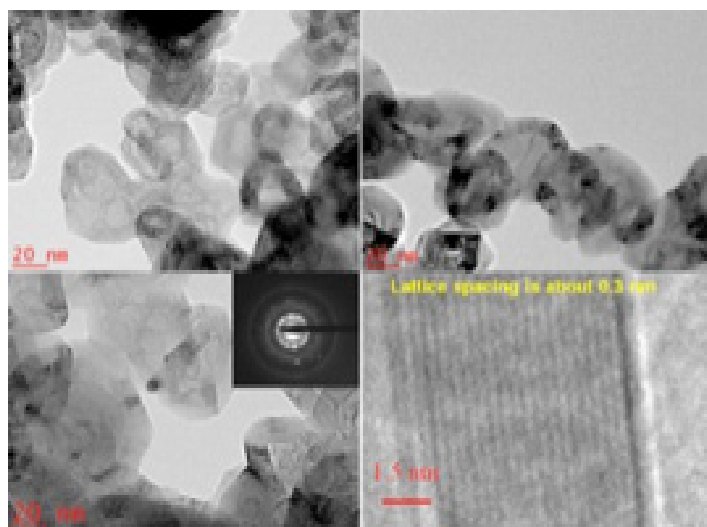
Soon after the discovery of C_{60} , a variety of shapes and sizes

of six- and five-membered rings were observed to exist including shapes never before known to science [10]. Onion-like carbon structures were first observed in 1980 by Sumio Iijima looking at carbon black through an electron microscope. Daniel Ugarte discovered a method to make nanocarbon onion-like fullerene (NOLF) in 1992 [11-13]. As previously mentioned, many isomeric NOLFs exist with similar energies; however, in their most electrically stable configuration, they are composed of concentric shells based on carbon arrangements of $C_{60} n^2$ ($n = 2, 3, 4, \dots$) [10].

Historically, multi-shelled fullerenes have been referred to as carbon nano-onions (CNOs), onion-like carbon (OLC), nanocarbon onion-like fullerenes (NOLFs) or multi-walled carbon nano-onions (MWCNOs). However, shungite also contains a multi-layered highly graphitic fullerene structure with known health benefits. For simplicity, these materials will subsequently be referred to as nanocarbon onion-like fullerenes (NOLFs) or nanocarbon onion-like fullerene-containing material (NOLF-M).

Each shell layer is separated by 3.4 - 3.5 Å which closely approximates the sum of the van der Waals radii between carbon atoms. The reason for such a fortuitous relation between structure and energy is unknown [10]. Their morphology can be roughly spherical or polyhedral depending on the temperature to which they are annealed. There are different methods to prepare NOLF-M, and each method produces NOLF-M with its characteristics and size. However, most methods produce limited quantities of NOLF-M and require purification methods to remove other occurring carbonaceous material, such as amorphous carbon.

Figure 3. TEM images of Graphonyx. Transmission electron microscope (TEM) images of the high-purity NOLF (Graphonyx) used in Dr. Desantis' work.



Courtesy of Graphitic Nano Onions, LLC.

All pristine fullerenes are hydrophobic and, essentially, insoluble in polar and H-bonding solvents. However, most multi-shelled fullerenes have defective shells resulting in Sp^3 orbitals. The reactivity of NOLF occurs on its surface that becomes increasingly resistant as the diameter increases. Both single-shelled and multi-shelled fullerene material can be functionalized. The chemical covalent functionalization of carbon nano-onions, CNOs-NOLFs, has been investigated, and several synthetic pathways were found to be applicable for the introduction of a variety of functional groups. Covalent functionalization of NOLF increases solubility and expands the potential for a future medical application [12,14]. Fullerenes are “functionalized” with chemical groups that provide water solubility and biological targeting ability. Tissue targeting is generally warranted; thus, molecular groups, such as folic acid or monoclonal antibodies, are attached. For photodynamic therapy (PDT), photosensitizers might be attached.

Investigations into Fullerene Toxicity

Since the discovery of fullerenes, there have been extensive investigations into their toxicity and characterization for applications of both single- and multi-shelled fullerenes. Significant among these investigations was the so-called Baati rat study. This study investigated beneficial protection of hepatocytes exposed to CCl_4 and credible longevity gains with C_{60} in olive oil. Of particular interest was the lack of expected cancer in the long-lived experimental animals [15]. Perhaps these observations should not have been so unexpected given the long medicinal history of shungite; however, since the Baati rat study, several authors have concluded there is a favorable cellular and biological interaction with fullerene materials [16,17]. Some authors have expressed concern regarding possible environmental and cellular toxicity from nanocarbon given the known toxicity of other nanomaterials [18]. Yet, the consensus supports not only good biocompatibility but also numerous advantageous effects of pristine and functionalized fullerenes with little or no toxicity.

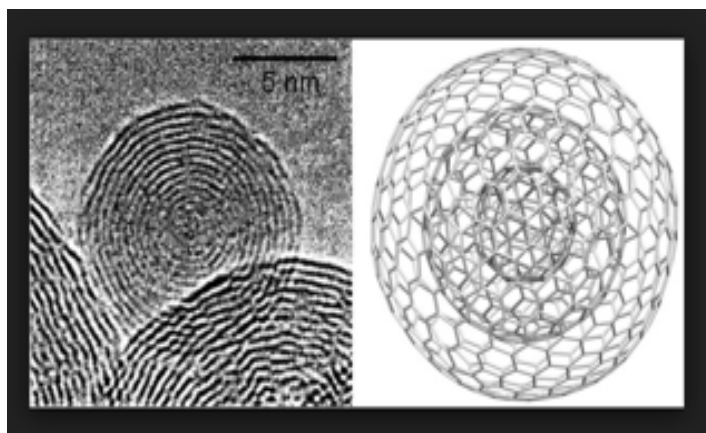
Properties of Shungite and Functionalized Nanocarbon Fullerenes

The natural mineraloid shungite, long used in folk medicine, and recently “discovered” single-shelled and multi-shelled fullerenes all share nonplanar hexagonal carbon ring patterning that induces rich delocalized electron pi clouds in these molecules. These carbon allotropes display similar physical and dielectric properties and a high degree of commonality in their complementary interactions within cells and tissues with little or no toxicity. With the prospect of excellent biocompatibility, nanocarbon fullerene materials and their functionalized derivatives are increasingly being studied for their promising use in several areas of medicine; but, surprisingly, nanocarbon fullerenes’ biological effects and metabolism have gone mostly unexplained and unexplored.

Potential Medical Applications of Fullerenes

One of the most intriguing peculiarities of fullerenes as pharmacophores is their ability to intervene into the structural domains of functional proteins including enzyme- and organelle-linked receptors; also, they play a role of intercalators interacting with DNA double helix. These characteristics may lead to various compelling corollaries impacting cell signaling pathways; such as biopolymer conformational flexibility shifts, catalytic activity changes, and ligand docking affinity [19].

Figure 4. Carbon nano-onions. TEM Imaging and graphic representation of NOLF [20].



NOLF and Athymic Nude Mice Unintended Results

Significant, but unintended and unexpected, results were observed after injection of 292molar concentration of NOLF in castor oil into human DU-145 prostate cancer (PCa) tumors on nine of ten athymic nude mice. The original intent of the research (as reported in the *Journal of Vascular and Interventional Radiology*, 2013 [21]; Radiological Society of North America, 2014; and *The Journal of Nuclear Medicine*, 2014) was to investigate the thermal properties of NOLF in the treatment of tumors, primarily with microwave, and evaluate the toxic burden of nanocarbon used during treatment.

The findings demonstrated that 62.5% of the NOLF-treated mice were alive at 18 months with no signs of toxicity or tumor recurrence. The surviving mice were not euthanized but observed for signs of toxicity, a return of tumors, and general long-term effects of a high dose injection of NOLF. To date, the observations of conceivable mechanisms of NOLF on the vitality, longevity, improved immune function of all the NOLF-treated mice, and anticancer/antitumor effects have neither been explored nor explained. While mice are as susceptible to cancer as humans, mice tend to form more sarcomas and lymphomas and fewer carcinomas. Although the Nude mouse model has been developed for the study of human PCa, no mouse model fully reproduces

all the characteristics of human PCa [22]. Perhaps the lack of recurrence of PCa can be explained by factors such as differences in histopathology and timeframe of PCa development between humans and mice. Also, cancer metastases in mice, especially to bone, have a propensity to originate from mesenchymal cells; whereas human metastases, generally, originate from epithelial cells in PCa [22].

The absence of development of any tumor well into senescence, the absence of expected disease susceptibility, and the expressed vitality and longevity in this immune-compromised mouse model were not readily explained nor expected. What was observed was the absence of toxicity given the large bolus of the carbon material injected into each mouse [23]. The demonstrated lack of apparent adverse effects combined with the longevity, vitality, absence of tumors well into senescence, and possible immune enhancement has yet to be explained.

The “Baati rat study” created an uproar regarding the biological potential of the single-shelled fullerene C₆₀ [15]. Mouse #9 demonstrated a probable anticancer effect of multi-shelled NOLF [21]. Prylutska (2011) demonstrated pristine hydrated C₆₀ fullerenes inhibited the rate of tumor growth and metastasis with a modest increase in lifespan at a low, single therapeutic dose of 5 mg/kg with no toxicity [24]. However, as of the date of this research, there are no definitive justifications or inclusive models to explain these observations.

Limitations of Fullerene Research

There are unavoidable and considerable limitations in NOLF research. This lack of NOLF research is primarily due to insufficient access to NOLF which has been limited in quantity and quality. Obtaining high-quality and ultra-pure NOLF routinely requires chemical purification. Research grade materials of sufficient purity are expensive, with no guarantee of uniformity between samples. Distinct sizes of NOLF with disparate shell numbers and shell defects are derived by differing production methods that can produce contrasting properties, i.e., electrodynamic and resonance properties. In many instances, batch samples vary, even when obtained from the same source, which produces mixed experimental results. Instrumentation to adequately study and assess nanocarbon fullerene and NOLF is expensive, and such instrumentation is constrained mainly to universities. With most instrumentation acquired under federal grants in the United States. As a result, research into NOLF's influences on mitochondria is limited, necessitating comparison to other fullerene material, predominantly C₆₀.

The most consequential research limitation in the biological effects of fullerenes and NOLFs is the failure to address their plausible involvement in quantum cell phenomena. This limitation is not surprising since the quantum cell concept has been largely ignored in biology since Schrödinger proffered a related hypothesis in his 1944 book, *What is Life?* He and others suggested quantum mechanics could be applied to biological issues. Ling challenged the Cell Membrane (Pump) Theory in 1952 paving the way for coherence and entanglement and multilayered structured water as necessary for living cells [25,26]. The discoveries in the mid-2000s that photosynthesis, bird migration, and even sense of smell involved quantum processes renewed an interest to look beyond classical concepts to explain discrepancies in current biological theory. Fortunately, interest in the quantum cell has been gaining respectability among a growing number of researchers.

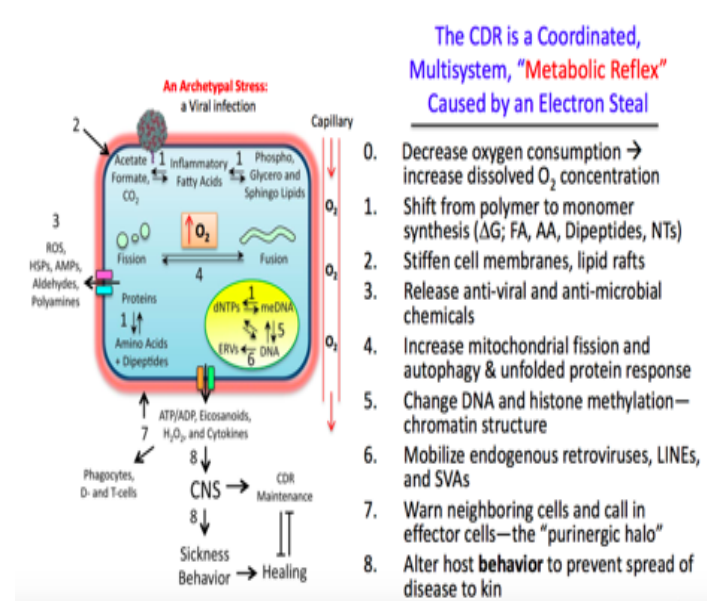
Discussion

Mitochondria and Homeostasis

Living cells are spatially bounded, low entropy systems that, although far from thermodynamic equilibrium, have persisted for billions of years [27]. Living systems are fundamentally unstable as they exist far from thermodynamic equilibrium. However, this seemingly precarious state allows for the following critical responses: 1) *Feedback* so that loss of order, due to environmental perturbations, initiates a corresponding response to restore a baseline state; 2) *Death* due to a return to thermodynamic equilibrium to rapidly eliminate systems that cannot maintain order in local conditions; and 3) *Mitosis* that rewards successful systems, even when they attain order that is too high to be sustained by environmental energy, by dividing so that each daughter cell has a much smaller energy requirement than the parent cell [27]. Mitochondria are central to the bioenergetics, defense, biosynthesis, replication, and other metabolic activities of the cell. They are cellular organelles at the boundary between chemical-genetic and physical processes in living cells [2]. Together with microtubules, they establish, regulate, and balance the electrodynamics of the cell [28].

Mitochondria monitor threats by sensing electron flow being diverted from the usual energy needs of the cell. These diversions may be caused by injuries, invaders (such as viruses), or substances (like reactive oxygen species [ROS], heavy metals, or chemicals) that induce electron steal (Figure 5). The resultant mitochondrial perturbation triggers a cascade of cellular defenses, collectively referred to as the Cell Danger Response (CDR). The CDR affects the entire organism [29] (Figure 5).

Figure 5. The archetypal Cell Danger Response [29].



When the CDR persists abnormally, the systemic form is termed the Purinergic Life-Threat Response (PLTR). PLTR produces impairment of whole body systems, i.e., the gut and multiple organ systems; subsequently, chronic, degenerative diseases and aging result [29]. This more precise understanding of the role of mitochondrial perturbation implies that the development of specific small molecules targeting aberrant mitochondrial function could provide therapeutic benefits [30].

Mitochondria and NOLF

With this foundational understanding of PLTR, there is a path forward to address cellular dysfunction, chronic degenerative diseases, aging, and cancer. Mitochondrial quantum electrodynamics comprises a central role in cell function and, ultimately, health and disease. Molecular substances and modalities that enhance or restore the quantum mechanics and electrodynamics of mitochondria and, subsequently, the cell are poised to become the medicines and therapies of a new healthcare paradigm. One such class of molecules may already be accessible: fullerenes and, markedly, multi-shelled fullerenes.

Structure and Characteristics of Fullerenes

Fullerenes are composed of periodic hexagonal carbon rings resembling graphene. The six carbon hexagonal ring is among the most electrodynamically stable carbon structures, and is essential to the known biochemistry of life due to its dense, delocalized pi cloud properties. Fullerenes comprise a class of pure carbon molecules composed of a highly graphitic single-layer or concentric multi-layered shells. The most uncomplicated and most isoelectrically stable fullerene is C₆₀.

C₆₀ is the best known, most researched, and perhaps the most stable of all fullerenes. It has 20 hexagon rings proposed to be joined in a semi-spherical icosahedron resulting in 12 five-member rings that are thought to relieve curvature stress. Electron pi clouds delocalize around the C₆₀ structure and contribute to the unique properties of C₆₀. Multi-shelled fullerenes are comprised of highly graphitic, concentric layered carbon shells of varying designs including polyhedral to nearly spherical forms, often surrounding a C₆₀ core. They frequently have defective shells as evidenced by two broad Raman bands between 1300 - 1600 cm⁻¹ representing sp³ carbon bonds of disordered structural defects and sp²-hybridized carbon respectively [12]. The higher number of periodic hexagonal carbon rings, and their arrangement in layers available in multi-walled fullerenes, suggests greater biological benefit potential.

Although speculative at this point, it is proposed that greater benefits could be derived from a larger, more diffuse pi cloud and multiple layers of available double carbon-carbon bonds becoming exposed with cleavage of successive shells during metabolic degradation. Current research seems to bear out this hypothesis, but further research in this area is needed. Since their discovery in 1992, NOLFs have not been as extensively studied as C₆₀ mainly due to limited availability. Despite a number of structural differences, many of the beneficial biological effects seem to be shared between all spherical fullerenes. Currently, there is heightened interest in developing fullerene materials as pharmacophores and in photodynamic therapy, diagnostic imaging, and other medical applications. The neutral electrophilic nature of fullerene material and its free radical scavenging properties may help explain some reports of increased energy, anti-inflammatory effects, life extension gains, anticancer effects, and perhaps differences in experimental findings. Since more dramatic effects are observed in injured, dysfunctional or hypoxic metabolic states, theoretical fullerene-mitochondrial interaction as a key mechanism is considered.

The interaction of nanocarbon onion-like fullerene material (NOLF-M) with the dynamics of mitochondrial perturbation and its effect on cellular function may be better defined in combined quantum and classic cellular terms than in purely biochemical terms. The classic electron charge transfers and free radical scavenging properties of fullerenes alone cannot account for the diversity of advantages observed in vivo. The unique fullerene structure and dense delocalized pi cloud contribute to electrodynamic characteristics that seem to fit the quantum conductor/insulator criticality exhibited by all biomolecules involved in the bioenergetics of the cell. Along with fullerene's ability to absorb, store, and release energy and enhance structured cell water, its pi cloud characteristic may have a profound impact on normalizing mitochondrial bioenergetics in perturbed states. Therefore, NOLF's application in disease, aging, and cancer warrant investigation.

Fullerene and Disruptive Mitochondrial Perturbation

Although NOLF-M research is relatively new and limited in scope, NOLF-M has been studied in many of the same applications as simple single-walled fullerenes, such as C_{60} . Fullerenes, including NOLFs, have been proposed to impact cellular and mitochondrial function advantageously. Studies support their role in enhancing ROS protection, anti-inflammatory action, and HIV protease inhibition, and in promoting apoptosis in cancer cells as well as increasing longevity. Fullerene materials are progressively being modified as transporter molecules, and are being considered for primary treatment options in a wide array of diseases, including cancer [20]. However, fullerene's role in medicine is still unsettled science.

Fullerene's functional role has been limited mainly to and by a Newtonian physics-based investigative perspective; there has been relatively little consideration from a quantum cellular perspective. It is posited and proposed, herein, that—due to their repetitive, non-linear, six-carbon ring structure—NOLFs are capable of enhancing mitochondrial-cellular coherence and quantum processes. All NOLFs have large, dense, delocalized electron pi clouds that have resonance and phonons; they absorb and release photons when stimulated, respond to electromagnetic fields, and have an affinity for electrons. These characteristics suggest ways in which NOLFs might interact with mitochondria, microtubules, enzymes, proteins, and nucleotides that also have aromatic rings with pi clouds. NOLFs and other fullerenes may also interact to preserve, restore or increase the polarized multilayered water around cellular structures. Their impact on mitochondrial enzymes/chromophores alone could produce profound effects on the electrodynamics of the cell.

Ordered systems, such as mitochondria, may respond, modify, and adapt or become chaotic or disordered in response to various stimuli; this is termed, perturbation. Mitochondrial perturbations are normal and necessary for health and mitochondrial adaptation. Mild perturbations (small deviations from homeostasis) result in adaptation to better resist homeostatic stressors; this process is essential and known as hormesis. This process may underlie the evolution of intelligence and might play a role in maintaining it [31]. Perturbations that are too large or too small can lead to an abrupt or a progressive decline of the system and chaos if order cannot be restored. Correspondingly, mitochondrial perturbations are critical to cell function. Mitochondria have been traditionally recognized for their central role in cell bioenergetics and biosynthesis [32,33] and their non-energetic roles as regulators of the CDR [29], apoptosis, intracellular messengers, and nuclear gene expression, as well as their role in disease and cancer states [34].

Mitochondrial dysfunction, resulting from excessive or chronic perturbation, leads to metabolic, immunologic, and degenerative disease, and cancer and aging [35]. Optimum cellular

function requires health status feedback from mitochondria that acts as a checkpoint before cellular action and dictates commands or provides signals to alter biological outcomes [32].

Misconceptions and Clarifications on the Role of Fullerenes

Fullerenes, and especially C_{60} , are being considered, principally, for pharmaceutical roles as carriers and photosensitizers in imaging. Their biological roles are limited mainly to toxicology studies despite evidence of diverse beneficial biological effects. The current hypothesis is that fullerene material, in its various forms, acts as an antioxidant and that it is in this role as a super antioxidant that it can influence positive changes in biological systems. The alternative hypothesis is that fullerene, while a paradoxical free radical scavenging electrophile, is not chiefly an antioxidant; but that it is through other mechanisms that it extends its greatest benefits to biological systems.

In pursuing an explanation for fullerene material's observed effects on systemic health and disease states and in evaluating the hypothetical choices, the question must be put forth: *How does fullerene material affect disruptive mitochondrial perturbation?* If fullerenes and NOLFs continue to prove biocompatible and involved in promoting homeostatic effects on mitochondrial electrodynamics and function (through both classical and quantum mechanisms) in both health and disease states, strategies can be developed to exploit fullerene material's potential in medical treatment and in maintaining health and preventing disease.

Proposed NOLF-M Mediation of Mitochondrial Perturbative Pathology

Excessive or chronic progressive oxidative stress-induced mitochondrial perturbation results in progressive dysregulation, decreased structured cell water environment, disorganization, and dysfunctional cell processes. The presence of these sequelae represents the pathological state of a diseased cell. Based on all available evidence, fullerene material's structural properties preclude it from being, fundamentally, a "Super Antioxidant". The principal oxidative stress benefit may be through fullerene-protein and fullerene-cell water interaction with subsequent improvement in mitochondrial quantum electrodynamics (QED).

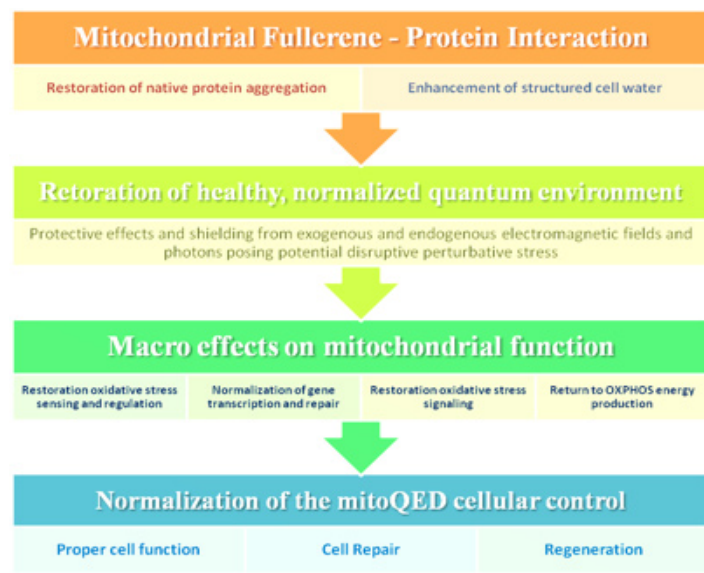
NOLF-Ms, with their periodic, curved, six-carbon ring structure and sizable, delocalized pi clouds, may decidedly impact the state of the cell. They may contribute through the restoration of mitochondrial protein mechanisms, quantum processes, mediation of disruptive perturbative effects and damage, and restoration and maintenance of OXPHOS (OxPhos) energy production. These contributions can, ultimately, restore homeostatic mitochondrial QED in cellular function. These advantages can be explored through three interconnected effects.

The first of these interconnected effects involves structured water. Under fullerene influence, structured water within the cell and mitochondrial structures (as well as in the exclusionary zone surrounding its proteins) is restored, maintained, and enhanced via fullerene's diamagnetic properties.

The second interconnected effect occurs as fullerene assists ATP with cyclic native aggregation and unfolding of mitochondrial proteins, and also promotes the formation of structured cell water by exposing dipolar charge sites on unfolded proteins (Figure 6).

The third interconnected effect supports the protection and restoration of the endogenous electromagnetic field and specific resonance patterns of coherent cellular systems. Fullerene's rich and diffuse electron cloud, under the influence of this endogenous electromagnetic field, provides for the absorption, storage, and coherent release of excessive or destabilizing electromagnetic energy and photons; thereby, augmenting mitigation of excessive or prolonged disruptive perturbative stress in the cell and restoration of coherency necessary for cellular self-organization and complex dynamics of cellular and systemic activities.

Figure 6. Mitochondrial perturbation mediation by NOLF/ Fullerene Material. NOLF effects on proteins, structured cell water, and the mitochondrial QED. Enhance and preserve oxidative regulating, sensing, and signaling enzymes helping restore and regulate oxidative stress in excessive or prolonged mitochondrial perturbation [36].



Conclusion

Mitochondria are central to the defense, bioenergetics, biosynthesis, replication, and other metabolic activities of the cell. Mitochondrial perturbation triggers a cascade of cellular defenses that affect the entire organism. These perturbation, left unchecked,

can cause irreparable damage to the host, and may result in disease and death. Molecular substances that improve or restore the quantum mechanics and electrostatics of the cell could become the medicines of the future. In this regard, and due to their unique structure and properties, fullerenes may have favorable and profound effects in humans. Fullerenes have demonstrated positive and potentially life-extension effects as demonstrated by the Baati rat study [12]; however, fullerene's "healing" effects are, currently, misunderstood as they are not limited to or caused solely by antioxidant properties or participation with ROS. Instead, fullerene's potential lies in its effect on cellular and mitochondrial proteins and quantum electrostatics [13]; thus, impacting cellular function (in particular, disruptive mitochondrial perturbations) and inducing cell function towards homeostasis.

As promising as fullerenes, and specifically NOLFs, seem to be in theory, research into their effectiveness and biocompatibility has been limited due to the specificity required for their manufacture, the cost of their production, and the lack of available instrumentation to evaluate them. Fullerenes and their potential medicinal benefits have been known for decades, but they have remained on the fringe of medical research. If NOLFs, and fullerenes in general, can live up to their theoretical promise, early researchers and contemporary proponents stand to forge their place in the history of experimental and molecular medicine, biochemical technology, pharmacological science, clinical oncology, and nanomedicine; a new paradigm in medical treatment will be spawned, and patients and humankind will benefit for generations to come.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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