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Aging Diseases Beyond Quantum Medicine

Pedro Bullon
Chairman Oral Medicine and Periodontology, Universidad de Sevilla
ORCID ID: https://orcid.org/0000-0003-4873-4196
Corresponding author:
pbullon@us.es
Departamento de Estomatologia, Facultad de Odontologia, Universidad de Sevilla
c/Avicena s/n 41009 Sevilla
Spain
Phone number 0034954481120

ABSTRACT
Aging is the main characteristic of our society with a markedly increase of diseases producing people needing high level of care. The leading cause and foremost reason for mortality and morbidity in aging is a group known as Noncommunicable Diseases. The best approach to treat them is to evaluate and control the risk factors. There are shared by all these diseases leading to the existence of some meeting points behind all of them. There should be some key to acquire conditions that modify the cells homeostasis and impaired the cell physiology developing different diseases. Physics try to explain the nature of the phenomena that surround us, at first, at the level of our macroscopic perception. Quantum physics studied the atomic and subatomic particles and revolutionized the reality perception with paradoxical and weird concepts. Heisenberg's uncertainty principle established that it is not possible to determine the two characteristic properties of particles with accuracy; measurement affects the system and change it. Subatomic particles have a wave-particle duality that could be in a coherence statement, also can pass through high-energy barriers. Two subatomic particles are entangled, something happening over here can have an instantaneous effect over there, no matter how far away there are. All these concepts have tried to apply to biology and life sciences, especially when classical physics fails to give an accurate description. Quantum biology is behind photosynthesis, mitochondrial respiration, enzyme activity, the sense of smell, animal migration, heredity's fidelity, and consciousness. We can apply all these concepts to diseases pathogeny. So, we describe quantum phenomena in oxidative stress, calcification, signal transduction, vitamin D production, cancer mutations, and microbiome induced pathology. I want to propose that aging diseases also can be explained by applying quantum physics concepts. It is a new, hard to believe, and an incredible path to be built, but we need to open the treatment options to our patients with new perspectives.

Key words: oxidative stress, calcification, signal transduction, vitamin D, cancer mutations, microbiota, quantum phenomena

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1) INTRODUCTION

We know that aging is the most important characteristic of our current population, but is a double edge sword. All of us like to live as much as possible but aging involves an impairment in physiology and an increase vulnerability to diseases. We have to recognize that nowadays we have a considerable amount of information about the biology and physiology´ knowledge applied to diseases. Researchers supply us these data thanks to the fact that more and more they have a high level of capacity in a specific field and use the newest, sophisticated, and accurate tools. All these data applied to the treatment of diseases are very successful. They produce a high life expectancy but providing an aging population that needs high-cost care creating a society issue. The leading cause and foremost reason for mortality and morbidity in aging is a group known as Noncommunicable Diseases. These are namely, heart disease, stroke, cancer, chronic respiratory diseases, and diabetes. Two of them, cardiovascular diseases and cancer, are the world's biggest killers ([1]). Almost all the treatments are symptomatic due to the abundant pending questions about the pathogeny. Therefore, the best approach to treat them is to evaluate and control the risk factors. They are related to age, aging present specific physiological modifications, which in essence are produced by metabolic wear. The most remarkable aspect is that all these diseases are interconnected; they share numerous pathogenic mechanisms. To improve our treatment results, we should gather the different knowledge contributed by the different disciplines. WHO considers Noncommunicable Diseases as an invisible epidemy and the cause of poverty, which hinders the economic development of many countries. Also, the Global Action Plan Objectives was established, for the prevention and control some targets, the main is to reduce the modifiable risk factors. ([2]). The main risk factors for Non-communicable diseases globally include high blood pressure, smoking, obesity, high blood sugar, alcohol, insufficient physical activity, and environmental factors such as air pollution ([3]). Different diseases share most of them. For instance, in cancer patients, we have increased survival' success; nevertheless, the recurrence with the same type of tumor or a new one is frequent. It seems that the patient has a predisposition to developing cancer cells related to risk factors. All these data show us that Noncommunicable Diseases have some types of predisposition status to develop those diseases. We want to highlight some aspects of the existing medical research landscape, propose a new approach that can explain the risk or predisposition to suffer those diseases, and provide further clues to offer new treatment perspectives. Specifically, we would like to apply physic concepts. It has been accepted that aging is characterized by increasing entropy ([4]). Entropy can be defined as a lack of order or predictability that measures the dispersal of energy. The second law of thermodynamics says that entropy always increases with time. In the biological systems results in the random loss of molecular fidelity, the strength of chemical bonds is absolutely essential for life. Repair and replacement processes suffer the same fate, since their substrate are biomolecules, thereby increasing vulnerability to pathologies or diseases associated with age ([5]).

We propose to deepen in aging applying the concepts of another part of the physic such as Quantum Physics.

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2) QUANTUM PHYSICS

Up to a certain time, physics only described the world of what our senses perceived, the macroscopic world. This phase of physics was based on the belief that atoms were the constituent unit of the smallest possible matter. Furthermore, thinking was necessarily based on the possibilities that technology made available to scientists at any given time. Thanks to new techniques invented at the end of the nineteenth century, subatomic particles began to be described, the first being the electron. Today up to 25 particles have been described, the last one discovered being the Higgs boson ([6]). The analysis of the physics of these particles is what gave rise to quantum physics. The first proponent of this idea was Max Planck. His main contribution was to establish that energy can only be absorbed or produced, not continuously, but at certain moments and in small quantities called quanta. Einstein took this idea and applied it to all electromagnetic radiations, including light, establishing that it is constituted by discrete packets or particles called photons. Later, Bohr proposed in his atomic model that electrons occupy precise orbits around the nucleus and only pass from one to another emitting or capturing electromagnetic energy in the form of a photon. All the concepts of quantum physics that have been developed have produced a revolution in the thoughts of how we conceive different physical phenomena. The main problem is that they can be paradoxical and difficult to assimilate. But we have to think that they describe a world in a different dimension from the one we see or perceive. Al-Khalili and McFadden ([7]) characterized that reality as having three layers: that of Newton's mechanics describing the behavior of the macroscopic world; that of thermodynamics describing the world of molecules and atoms in the generation of energy; and the world of quantum mechanics describing the behavior of subatomic particles. We also need to highlight the complicating condition that each separate observer irreducibly modifies all the quantum phenomena. According to the Copenhagen interpretation, Quantum Physics does not describe physical reality as it is (ontic phenomena), but one that is the result of measurements performed by macroscopic measurement devices ([8]). This exciting, strange, and often incomprehensible, but real, the quantum world must influence the two upper layers. These ideas may sound odd but are considered correct today and make the concepts of quantum physics hard to comprehend. These ideas must necessarily be the basis of the phenomena that we notice because all of them influence in some way the macroscopic world that we can perceive. More specifically, they affect the field of biology and, therefore, can be applied to medicine. Next, and in the following sections, we will briefly explain some of the basic concepts of quantum physics:

a) Heisenberg's uncertainty principle

This principle states that it is not possible to establish with perfect accuracy both of two crucial factors which determine the movement of one of the smallest particles—its position and its velocity. Both cannot be determined accurately and is, in general, not possible to predict the value of a quantity with arbitrary certainty, even if all initial conditions are specified. Heisenberg explains it with the observer effect, in which measurements of specific systems cannot be made without affecting the system and changing it. It is inherent in the properties of all wave-like systems that do not have a particular location, and we can only establish a probability. So, the atom is a ghostly and insubstantial place that is defined with the measurement and every quantum

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state can be represented as a sum of two or more other distinct states, which is called quantum superposition ([9]).

b) Wave–particle duality

This was first postulated to describe the nature of light and based on Young's Double Slit Experiment. In quantum mechanics, every particle or quantum entity may be described as either a particle or a wave. This phenomenon has been verified not only for elementary particles but also for compound particles like atoms and even molecules. Also, the fact of observing or measuring is capable of altering and making a pass from one state to another ([10]).

c) Quantum coherence

The association of an electron with a wave is unique to quantum theory. Coherence phenomena arise from interference or the addition of wave -like amplitudes with fixed phase differences. But coherence develops in decoherence which is the physical process whereby the coherence is lost, and the quantum becomes classical. Usually, it is expected to be fragile and very short-lived unless the quantum system can be isolated and/or cooled. However, recent data show coherence in chemical and biological systems are robust and can survive in the face of disorder and noise ([11]).

d) Quantum tunneling

Chemical reactions suppose a high-level barrier that delays it. Quantum tunneling is the phenomenon where an object passes through this barrier, higher than its kinetic energy. It plays an essential role in the nuclear fusion that occurs in main sequence stars like the Sun and is applied in the transistors used in microprocessors. It is explained as a consequence of the Heisenberg uncertainty principle and the wave - particle duality´s characteristic of subatomic particles, that allow moving in space without passing over the potential energy barrier ([12]).

e) Entanglement

It refers to the idea that something happening over here can have an instantaneous effect over there, no matter how far away there are ([13]). It is described for the spin angular momentum, it is the movement of a subatomic particle in a circular motion, just as the earth spins on its axis as it orbits the sun. This spin is quantized, can have two directions clockwise or anticlockwise, and according to the quantum world, when not being watched, both directions exist at the same time. Every electron spin in this peculiar way, and obey the Pauli Exclusion Principle. It states that two or more identical fermions cannot simultaneously occupy the same quantum state within a quantum system. In the case of electrons shared between atoms, they have to have opposite spin, and this is named spin-singlet state. When we separate two electrons in the same atom, being in a singlet state, they have to have an opposite spin at all times. When two entanglement electrons are separated and measured, both must have the opposite spin, one of an entangled pair immediately collapses the superposition of the other. It does no matter how far away they are; it is the entanglement property. If one electron from a singlet pair sitting in the same atom jumps across into a neighboring atom, its spin can flip over so that it is now spinning in the same direction as the twin is left behind, creating a triplet spin state. Also, according to the quantum

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superposition concept, both can be in singlet or triplet state simultaneously, spinning in the same and in the opposite directions at once.

3) QUANTUM BIOLOGY

All these concepts have tried to apply to biology and life sciences, especially when classical physics fails to give an accurate description ([14]). Biological systems are built with matter and must also comply with physical laws. Biology is, after all, a kind of applied chemistry, and chemistry is a kind of applied physics. Since the beginning, the physics pioneers have attempted to implicate quantum physics in biology. Niels Bohr was first when he described life as intrinsically a quantum phenomenon ([15]). This made Erwin Schrödinger ([16]) ask in his lecture series "What is life" about the influence of quantum mechanics in biology. He predicted that all the quantum definition must determine the mechanisms of life, but life is so complicated that in those days was very difficult to apply and understand. Also, he pointed out that life is structured and orderly at a molecular level, and the quantum events that take place can have consequences for an entire organism. We can assume that quantum theory is a strikingly accurate representation of physical reality but at the subatomic level. Biomolecules such as DNA or enzymes are made of fundamental particles like protons and electrons whose interactions are governed by quantum mechanics. All systems sufficiently well isolated behave according to quantum principles, and life is a sum of multiple systems. Moreover, life is tough to be precisely defined, but one main point is that it includes complex chemical reactions involving the transfer of electrons from one atom to another. Therefore, quantum mechanics can contribute to explaining the role of energy transmission and conversion in a cell.

Another problem that intrigued Schrödinger was the mysterious process of heredity and how same copies of genes pass with almost 100% of precision from generation to the next. He knew that the accuracy of thermodynamics laws could be applied to a large number of particles interacting, but not to a little amount, as could be this case. He quantified the decline in accuracy, like the magnitude of deviations that is inversely proportional to the square root of the number of particles involved. He proposed that each biological machine that is involved in life is so tiny that it cannot be governed by classical laws but as by the quantum-level laws ([14]). Later, this concept was questioned ([17]) based on that quantum states could not possibly survive in the warm, wet, and busy molecular environments that distinguish the living organisms. But nowadays, it remains a conceptually challenging model of nature as new advances have raised a new awareness and sketch a more optimistic picture. New technologies of working with micro-particles, individual electrons, atoms, and molecules have been developed and have given a new impulse to quantum biology ([18]). There are some successful applications of quantum theory to biology that we would like to summarize.

a) Photosynthesis

It is the process used by plants and other organisms to convert light energy into chemical energy and producing carbohydrate molecules; they are synthesized from carbon dioxide and water and release oxygen. The absorption of a photon of solar energy, develop in the magnesium atom of the chlorophyll an exciton. This is an

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electron that has been knocked out of its orbit together with the hole it leaves behind. It is very unstable and has to transport to a more stable chemical battery called NADPH, which similarly produce ATP as the mitochondrial respiratory chain, and then to the reaction centers. But they are quite distant, in molecular terms, and need to be led to a specific route in a hundred percent efficient way. Experiments performed in photosynthetic bacteria show that exciton follows multiple paths simultaneously, acting as a quantum computer to find the quickest route, denominate a quantum walk ([19]). Then the most abundant enzyme on earth, called RuBisCo, captures the carbon atoms from carbon dioxide and produces ribulose-1,5-biphosphate to make a six-carbon sugar.

b) Mitochondrial respiration

In the mitochondria the aerobic respiration take place: the most potent biological method to produce energy. It is mediated by the oxidation that consists of an electron transfer from a donor, the nutrients, to an acceptor molecule, ATP. At first, the electrons in the outer orbits of carbon atoms are transferred to the NADH, the first step in the respiratory chain. Then pass through the electron transport chain and produced a membrane proton gradient and a rotation of the ATPase which makes the transition from ADP to ATP, this ATP is considered the molecular unit of currency of intracellular energy transfer ([20]). ADP and ATP are nucleoside phosphates; this contain a nitrogenous base bound to a 5-carbon sugar, with two or three phosphate groups bound to the sugar. The enigma of respiration is how these enzymes can shift electrons so quickly and efficiently, considering that proteins are poor conductors of electricity. The explanation comes when we apply the tunneling quantum concepts ([21]). We have to remember that the wavy feature of electrons allows them to pass through proteins and between them in the respiratory chain. The electron bifurcation, define as the uphill and downhill electron transfer reactions, using two-electron donor cofactors with different potentials, has been described in the mitochondrial charge transfer chain of NADH dehydrogenase (complex I) and cytochrome c – oxidoreductase (complex III) ([22]). Also, electron exchange between redox partners, separated by molecular bridges, have been demonstrated in a so-called “hopping,” that is a multiple tunneling steps reactions ([23]).

c) Enzymes

Enzymes are the molecules that catalyze all sorts of biochemical reactions that would otherwise proceed far too slowly. They are responsible for digestion, respiration, photosynthesis, and metabolism. The way catalysts operate is through the denominated Transition State Theory ([24]). For instance, in the case of proteinases, they attack the peptide bond that connects the carbon atom from an amino acid to the nitrogen of the next. It is a very stable covalent bond, consisting of sharing a pair of electrons that attract both positive atomic nuclei. To break, it needs a process known as hydrolysis; a molecule of water donates its electrons forming a new weak bond as an intermediate state and generate a hydrogen water proton. This positively charged proton is no longer held firmly in place within the water molecule and become delocalized in the quantum mechanical sense. The proteinases promote this transition

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state and broke the peptide bonds, which is explained through the tunneling quantum concept. Electrons have a wave-like nature, and the different shells that surround the nucleus can be described as a wavy cloud of "electroness". The proteinases facilitate these electrons and protons transfer because they can pass through the energy barriers that could suppose the peptide bond ([25], [26]).
On the other hand, we have to think that enzymes are proteins. Over 40 years ago, Fröhlich predicted that vibrational modes within proteins could condense, leading to macroscopic coherence, this appears to have now been observed. Experiments show a micro- to a milli-second lifetime of the vibration that can only be explained by Fröhlich condensation, the authors conclude long-range quantum coherent states could exist in biological systems ([27]).

d) The sense of smell
The smell is essential for dogs, bears, snakes, moths, sharks, rats, and anemonefish but less for humans. The olfactory epithelium can identify thousands of different types of smells, but very few receptor genes have been identified. There is not a one-to-one mapping between types of odor receptors and types of odors. Also, every single olfactory neuron responds to several different odorants that have the same chemical structure and identical Raman spectra but are mirror images of each other. A speculative molecular mechanism by which biomolecules could detect the vibrations of chemical bonds via quantum inelastic tunneling of electrons have been proposed; by this property, an electron vanishes from one point in space and instantly materialize in another ([28], [29]).

e) Animal migration
Marine and terrestrial mammals, birds, and insects use magnetoreception to travel. They can notice the earth's magnetic field and be oriented, but to explain how this tiny energy can produce a biological effect, we need to use the quantum entanglement concept. Atoms that share a pair of electrons are always entangled, even when the bond between the atoms is broken. The separated atoms, called free radicals, find in a superposition of both singlet and triplet states. This quantum superposition is not balanced and can be sensitive to any external magnetic field ([30], [31]). The place in which the magnetic sense might indeed lie is within photoreceptors in the eye ([32]). It involves the cryptochrome, a protein responsible for the light-driven entrainment of their circadian rhythms ([33]). The molecule cryptochrome is wrapped around a pigment molecule, called FAD (flavin adenine dinucleotide), that absorbs the blue light. Similarly, to photosynthesis, the light absorption knocks an electron out of the pigment. The ejected electron leaves behind an electron vacancy that can be filled by another one donated from an entangled pair of electrons coming from tryptophan that is part of cryptochrome protein. Then the pair of entangled electrons form a superposition of singlet/triplet states that is sensitive to a magnetic field ([34]).

f) Heredity´s fidelity
We know that the double structure of DNA permits the copy mechanism that maintains the life on the earth. The specific pairing between the bases on opposite

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strands is provided by a weak hydrogen bond sharing a proton. The two DNA strands are separated, and DNA or RNA polymerase slides along and reads with unerring accuracy. Schrödinger proposed in 1944 that the fidelity of these copies is based on considering the genes are some aperiodic crystal ([14]). This means crystals with a similar repeated molecular structure to standard crystal with different periods. These are encoded at a quantum level, since each hydrogen bonds to a specific base, depending on the position of protons along its DNA strands. When the position of the protons moves to the opposite base, it is formed an alternative form of each base, called tautomer. The effects are that thymine bonds to the incorrect partner the guanosine, instead adenine, and cytosine bonds to adenine instead of thymine. If this happens in the moment of copying the newly formed DNA will carry mutations and the RNA produce modified proteins ([35]). To explain the production of the alternative proton positions that define the tautomer, we have to use the quantum tunneling concept. The indeterminacy in the area of any particle allows it to leak through an energy barrier ([36]). Also, the generated errors have to escape the correction machinery that helps to remove it.

g) Consciousness

One of the main unknown aspects of physiology that maintain a lot of open questions is how the brain can produce our mind or consciousness. Some authors try to explain that can function as a quantum computer and propose that the neuron´s microtubules are the qubits of quantum brains ([37]). They think that the entire microtubule protein, the tubulins, is in quantum superposition and entangled all over the brain. But other authors do not agree because quantum effects do not have the temporal properties required for neural information processing ([38]). Also, it highlighted the fundamental role played by the ion channels in nerve physiology and think that quantum coherence plays an indispensable role in the conduction of ions through nerve ion channels ([39]), but this idea has the same difficulties as with microtubules. To solve this problem the electromagnetic field, that we can explore with an electroencephalogram, could influence and coordinate the nerve firing patterns that are behind our consciousness ([40]). Some authors suggest that the nuclear spins, in the wet environment of the brain, form various entangled quantum states, some of which survive decoherence. Specifically, nuclear spins of hydrogen, nitrogen, and phosphorus in neuronal cellular components and electron spins of diffusible oxygen and nitric oxide in the brain might mediate consciousness ([41]). The quantum fluctuations could be functionally negligible but in complex systems may be amplified and lead the neuronal dynamics ([42]).

4) QUANTUM MEDICINE

All the quantum concepts that explain the biological processes try to give new perspectives to physiological reactions that can take place in each living organism. But the experiments of quantum physic phenomena take place in isolated circumstances. On the contrary, quantum biology phenomena take place inside a multitude of reactions, influenced by the environment. The main question that should be highlighted is that in our world, we are not alone. Around us are vast amounts of living

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entities in a specific environment. As a principle, all of us establish a relationship with our environment. We share our life with a vast number of bacteria, archaea, fungi, protozoa, and viruses. We have to consider ourselves that we are a holobiont. Our survival possibilities depend on the way we establish a relationship with other living forms. Biological interaction between two different biological organisms can be mutualistic, commensalism, or parasitic. There are a lot of examples of these processes; for instance, we need gut bacteria to produce essential metabolic components such as vitamin K. Another example of these interactions is that the relationship between environment and life forms is the stimulation of species differentiation. Darwin proposed this concept with the evolution theory, all the organisms need to obtain food from the environment to survive, and if this is scarce, the competition lead that just the most efficient and adaptable survive . In some cases, nutrients come from organic or inorganic matters, but more often from other forms of life, that could be the leading cause of the source of illness. We propose that some quantum concepts can be applied to medicine and offer a new perspective in the treatment of diseases. The aim is to go more in-depth at the next level, from the molecular level to the atomic and subatomic level, and apply the quantum physics concepts to medicine. So, all the quantum biology phenomena, described above, are produced in a very complex environment that is surrounded by a considerable number of different molecules and different types of organisms. In some aspects, we appl ied the principles of process philosophy defined by Whitehead & Russel ([43]). They proposed that reality consists of processes rather than material objects and that the relationship with other processes is what defines it. The basic principle of quantum physics is that a measurement modifies the particles´ properties, and we can consider the environment and surrounding organisms itself as observers with the similar effects of that of measurements ([44]). The interaction of large systems with their uncontrollable environment will suppress the characteristic features of the quantum mechanical description but not wholly to render its behavior 'classical' ([45]). This is the so-called 'decoherence' concept, that explains why the macroscopic world around us is manifestly classical. The environment produces interference through the molecular noise/vibrations that could inhibit the quantum coherence. Still, the quantum wo rld can only take place if decoherence can be kept at bay. But some data show the opposite, and it can happen in a coordinate way, so facilitating the coherence. For instance, in photosynthesis, the molecular noise is used to nudge an electron in a superposition of two energy states at the same time and in collaboration with the quantum coherence tunes it to improve the efficiency ([46], [47]). Also, the ability to make a quantum virtue out of a molecular vice-noise- is demonstrated in the proton tunneling produced in enzymes ([48], [49]). Therefore, we have to assume that every form of life can influence the neighbor, we are the result, not only of our metabolism but with the interactions between our living partners. The main question is how this relationship could be beneficial or harmful and, therefore, if quantum mechanics can explain some aspects of diseases. We tried to highlight the data supporting this statement and applied it to Aging diseases/Noncommunicable diseases. As was stated above, all of them are related to each other and share several risk factors. Those will be reviewed according to the data that the quantum phenomena provide us.

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a) Quantum phenomena in oxidative stress

It has been known that CVD is related to risk factors, especially metabolic diseases, such as obesity, insulin resistance, and diabetes mellitus, and infections such as periodontitis. These metabolic diseases present a dysregulated vascular redox state leading its vascular complications ([50]). Other data show that obesity, diabetes mellitus, atherosclerosis, and periodontitis share oxidative stress injury ([51]). It seems to sound clear that the high production of oxidants, such as radical oxygen species (ROS), is behind some diseases. But on the contrary, the treatment with antioxidants was proposed and have shown no benefit or even increase mortality ([52]). We have to think that oxidative stress is the result of the balance between free radicals' production, primarily reactive oxygen species, and the antioxidants mechanisms. Also, ROS at moderate concentrations has essential signaling roles in physiological functions ([53]). ROS act as a beneficial tool stimulating chloroplast-nucleus communication, a process called retrograde signaling that participates in a broad spectrum of plant physiology, such as acclimation, resistance, programmed cell death, and growth ([54]). The oxidative stress is the consequence of altered cell metabolism that modify molecular biomarkers, and even these can predict mortality with more accuracy as the conventional risk factors ([55]).

But what is the mechanism of oxidative energy production? The most crucial requirement of every living organism is the need to produce energy. The matter combustion produces energy in a high-temperature exothermic redox chemical reaction between a fuel (the reductant) and an oxidant, usually atmospheric oxygen. It is produced in an uncontrolled way, but inside a cell need to be generated in a precise, well-controlled process, and without damage. Oxygen is the main molecules involved in the reduction-oxidation reaction consists of the transfer of electrons between chemical species, one reducing agent, the nutrients that lose electrons, and other oxidizing agents, the oxygen that gains it. This reaction is due to the electrons' characteristics of the oxygen molecule; it is composed of two atoms with two electrons in unpaired orbitals and the same spin quantum number in a called triplet state condition. Molecular oxygen usually undergoes one-electron reduction at a time, so the species formed is a superoxide anion. This reduction occurs in the mitochondria cellular respiration, in photosynthesis, and at the membrane-bound enzyme complex NADPH oxidase during the oxidative burst ([56]).

If we analyze all these reactions, these involve a transfer of electrons between different atoms. But, according to quantum mechanics, all the subatomic particles have the superposition and entanglement conditions. There can be in two places at the same time and entangled, meaning that both atoms share electrons with original features. So, these properties could explain the fact that oxidative stress statement could be a consequence of metabolic conditions more than the cause of its alterations. To support this statement is the fact that the oxidative metabolic processes produce an electronic transition from the excited state to the ground state. As a consequence, all biological systems emit an ultra-weak photon emission, but at the moment that suffer the interference of various biotic (herbivores and pathogens) or abiotic (adverse environmental conditions) stresses, the intensity of ultra-weak photon emission

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increase to several hundred photons ([57]). This ultra-weak photon emission has been related to metabolic changes, particularly the methionine pathway ([58]). Also, the increases ultra-weak photon emission is strongly linked to metabolic processes, which may be associated with lipid oxidation that related to inflammatory and/or ROS-mediated processes as was demonstrated in a mouse model of collagen-induced arthritis ([59]).

The primary source of ROS is the mitochondrial electron transport chain (ETC). Mitochondrion was originated in an endosymbiont process, and part of its genome was transferred to the nucleus. The reason for the mitochondrial genes retention is explained in the colocation of gene and gene product for redox regulation of gene expression (CoRR) hypothesis. They argue that the expression of genes for protein subunits of energy-transducing enzymes must respond to change in the redox state ([60]). Electron flow through the ETC is essential to be productive, and an entanglement quantum phenomenon is described. For instance, the semiquinone -Rieske cluster can exist in a triplet state in complex III involving a spin–spin exchange ([61]).

b) Quantum phenomena in calcification

Atherosclerosis, the central lesion behind CVD, is considered as an inflammatory disease. Inflammation is an essential process in the development and complications of atherosclerosis. There is an impairment of endothelial function, oxidized lipid deposition, proliferation and migration to macrophage activation and stimulation of vascular smooth muscle cell (VSMC) ([62]). The result is the alterations of the vascular layers, its calcification and developing of a plaque, that narrowed the vessel lumen or produced a rupture and impedes the blood circulation. These processes are related to an oxidative mechanism ([63]).

The main course of biological evolution included two critical steps, nucleosides as the elementary units of genetic code and ATP as the universal energy substrate, both containing phosphate group. The first living cells that appeared on earth were prokaryotes: bacteria, and archaea, in an anaerobic environment, about 3.5 billion years ago. When life began, the concentration of free Ca^{2+} and O^2 surrounding the first cells was much lower than it is today. But oxygen production increased as a metabolism waste product, and the primordial living organisms were required to develop defense mechanisms against chemical attack from oxygen radicals. Then the microorganisms survived using oxygen to improve energy production, evolving to aerobic metabolism. Also, the marine Ca^{2+} concentration of the Precambrian era increased and was the crucial force that leads multicellularity, photosynthesis, the origin of eukaryotes, the source of metazoans, biomineralization and bone genesis ([64]). Ca^{2+} is essential outside cells since cell-cell adhesion is mediated by a Ca^{2+}-dependent cadherin protein ([65]); and as an intracellular messenger, that is behind cellular events such as movement, secretion, transformation, and division, but an intracellular prolonged high level is harmful and leads to the disintegration of cells ([66]). Therefore, cell physiology needs an appropriate concentration achieved through the intracellular organelles isolating different metabolic reactions, the calcium-binding proteins, and the ion channels controlling the flux located inside membranes ([67]). Also, the adverse effects of calcium come from the mineralization that is the precipitation of calcium

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phosphate inside the cell, with a high negative impact. But biomineralization is an essential physiological process in multicellular organisms. It is defined as the process by which living organisms produce mineralized tissues, and enabled the growth of multicellular organisms to huger size. In one step of evolution, calcium carbonate provided a skeletal and a shell to the invertebrate but is heavy. Later, calcium phosphate supplied consistency to produce teeth, that crush foods and improve digestion, and bones with a lighter weight that allows moving the body more efficiently, so calcium and phosphate have a closely related metabolism ([68]). Calcium is also involved in other organelles' physiology, such as in mitochondria. These accumulate a large amount of Ca^{2+} coming from the cytosol to prevent cellular damage, then precipitate with phosphate forming hydroxyapatite and whitlockite with ribose and ATP/ADP ([69]). It has been known that Ca^{2+} and ATP are an inseparable tandem, they control each other, and in the biological evolution they appeared at the same time ([70]).

This calcification process is similar to the bone calcification that first produce s the amorphous tricalcium phosphate, then the crystalline hydroxyapatite ([71], [72], [73]), and the tooth enamel developing ([74]). The bone needs a scaffold to crystalize that is provided by collagen with an active behavior. Mineral droplets bind to the collagen fibers, then solidifies into an amorphous phase and finally transforms into oriented apatite crystals directed by the collagen ([75]), even the location of the earliest mineralization was detected in the a1–a3 bands from the collagen fibrils ([76]). Both phases differ in atomic structure, particle morphology, and stoichiometry, and the formation pathway of Ca-P phases include a cluster growth model. The first noncrystalline phase is a hydrated calcium phosphate consisting of roughly spherical $Ca_9(PO_4)6$ so-called ''Posner's clusters'' ([77], [78]). This Posner´s cluster was identified as the transition step between amorphous calcium phosphate and the crystalline form of hydroxyapatite and named as Posner molecules. The Posner molecules are present in extracellular fluids and inside mitochondria modulated by H^+ and ATP ([79]). It has been assigned quantum properties because it provides an ideal environment for the six constituent ^{31}P nuclear spins to obtain very long spin coherence times. Since the most abundant isotopes of both calcium and oxygen have zero nuclear spin, it has been predicted that the six ^{31}P nuclear spins with S = 1/2 in a Posner molecule are especially long lived, protected from environmental decoherence ([80]).

This aspect is similar to what we have shown above that spin in neurons could give some clues to explain consciousness, as it needs to maintain quantum coherence enough time. Wherli ([81]) demonstrated that $^6Li^+$ isotope has a spin magnitude I = 1/2 with a coherence time as long as 5 minutes. Among the most common biochemical elements, just phosphorus has a nucleus with this magnitude and could be a putative neural qubit. So can act as a neural qubit allowing quantum processing to occur in the brain, and that this quantumness is protected by so-called Posner molecules, which bind phosphate ions with calcium ions. Entangled Posner molecules then trigger non-local quantum correlations of neuron firing rates ([82]). Phosphorus is bound to oxygen as organophosphate, which is an ester of orthophosphoric acid, and is a crucial biomolecule in DNA, RNA, and ATP. It is bonded to calcium as calcium phosphate in the form of hydroxyapatite, the structural material of bone and teeth, and to lipids in the

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phospholipids of the cellular membranes. Some authors argue that calcium bind to phosphate ions that allow long spin coherence time suggesting a new quantum cognition model, based on entangled calcium phosphate molecules in neurons ([83]).
On the other hand, external bone calcification is a frequent phenomenon in soft tissues such as kidneys, gallbladder, blood vessels, and gingiva. The pathogenesis is multifactorial and not fully understood, but unlike bone calcification, no collagen scaffolding is present. Inside the mitochondria, there is no collagen because it is produced outside the fibroblasts. Outside the cells, the reason could be derived from the fact that external bone calcification is related to inflammation, which includes collagen destruction and high ROS production. Other mechanisms have been described, and for instance, vascular calcification presents a transition of vascular smooth muscle cells into osteogenic cells that are mediated by oxidant stress and endoplasmic reticulum stress ([84]). It has been related with some factors: BMP-2 ([85]), impaired autophagy ([86]), osteocalcin and mitochondrial dynamics ([87]), PGC-1α by SIRT3-mediated mtROS reduction ([88]), and phosphate and fibroblast growth factor (FGF)-23 ([89]). The gingival calculus is presented in almost all the people above 30 years in two different oral environments that are namely supragingival and subgingival. The mineral composition shows four different types of calcium phosphate crystals: brushite, octacalcium phosphate, hydroxyapatite, and whitlockite. Hydroxyapatite and octacalcium phosphate, coming from the saliva, are predominant in supragingival calculus and whitlockite in the subgingival calculus, coming from gingival crevicular fluid ([90]). The concentration of calcium, magnesium, and fluoride is greater in subgingival calculus, reflecting higher levels of these ions in the gingival crevicular fluid than in saliva ([91]). Gingival calculus development involves oral biofilm bacterial calcification, and associated with specific bacteria, for instance, *Aggregatibacter Actynomicetencomitans* with the non-calculus site and *Black-Pigmented Anaerobic Rods* with calculus site ([92]). The mechanism involves the calcium binds to the phosphate of the membrane acidic phospholipids and form a Ca-phospholipid-phosphate complex ([93]). The subgingival calculus is related to periodontitis, it is a chronic inflammatory disease that produces alveolar bone loss and the consequent teeth loss, and caused by the bacterial biofilm ([94]). Severe periodontitis has a global age-standardized prevalence in the entire population of 11.2% and is considered the sixth-most prevalent condition in the world ([95]). The pathogeny involves a modified inflammation process with a mitochondria function impairment that could facilitate the intra-mitochondrial calcification ([96]).
As we mentioned above, CVD, as the central Non-communicable disease, is related to different risk factors such as diabetes and periodontitis ([97]). Periodontal disease and incident stroke risk, particularly cardioembolic and thrombotic stroke subtype, show an independent association ([98]). All of them share important inflammatory pathogenic mechanisms related to oxidative stress and mitochondrial dysfunction ([99]). But quantum phenomena could explain some features behind these relationships, and we propose that we have to explore some common pathogenic risk factor in the quantum field. There may be new clues in the level of the subatomic modifications of calcium and phosphate.

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c) Quantum Phenomena in Signal Transduction

We have exposed that calcium and phosphates could be the way to relate quantum phenomena with diseases in the calcification process. In the case of CVD, there is a relationship with insulin resistance characterized by an impaired function of receptors. Also, a neurological disorder such as Alzheimer's disease shows an insulin signal dysregulation and impaired insulin–PI3K–AKT signaling sharing common pathogenic elements with T2DM, so that is considered a 'type 3 diabetes.' ([100]). Signaling receptors are proteins embedded inside membranes that are activated by an external signal, in this case, insulin hormone, or other extracellular molecules. They allow communication between the outer space and internal space through the membrane barrier. Membranes consist of a lipid bilayer of phospholipid acting as a solvent, so proteins and lipid molecules are then free to diffuse laterally, sometimes as lipid rafts ([101], [102]). The stimulation of the receptors induces signal transduction, a second messenger such as calcium and redox signaling, enter the cytoplasm. A series of molecular events begin; the most common is protein phosphorylation catalyzed by protein kinases, which ultimately results in a cellular response. So, we propose two steps in which quantum phenomena can give new clues: the phospholipid membranes and the phosphorylation.

- Phospholipids

  These constitute the major components of membranes. The structure consists of two hydrophobic fatty acid tails and a hydrophilic head containing a phosphate group, that are negatively charged. The tails face the inside of the membrane, and the head faces the extracellular space or the cytosol. The phosphoinositide phosphates (PIPs), is one phospholipid, interact electrostatically with peripheral membrane proteins, define membrane spaces and direct it to specific locations. The Ca^{2+} hormones activate their cell surface receptors with signal transduction utilizing PIPs ([103]). It is utilized as a scaffold to generate by phosphorylation a variety of compounds that control a whole range of cellular functions. Some of them are: 1) signaling from the inner leaflet of the plasma membrane that activates several essential protein kinases; 2) regulating the activity of ion channels and transporters, controlling ion distribution; 3) help hydrophobic molecules to traverse the aqueous phase separating the membranes; 4) control the budding and fission process between membranes and regulate the vesicular trafficking; 5) mediate innate immunity inducing the pyroptotic cell death with the protein gasdermin D ([104]); activate NLRP3 inflammasome ([105]).The lipids membrane can suffer the aggression of free radicals and cause lipid peroxidation, capable of mediating inflammation in absence of infection and activation of inflammasome ([106], [107]). They are prevented by antioxidants defense, one of them is the Glutathione Peroxidase group, one of them is the GPX4 (PHGPx) that act as a phospholipid hydroperoxidase to reduce lipid peroxides to lipid alcohols ([108]). Membranes act as gatekeeper and modulator to the extracellular world and intracellular organelles relationships ([109]). These processes have been carried out by membranes lipids that integrate calcium, phosphate, and oxygen metabolism to define the identity of the cells. The innate immune system starts in the membranes, and it is also likely subject to regulation by lipid-binding factors, as an

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increasing body of literature has implicated PIP kinases and phosphatases. But all these metabolic pathways can be altered and explain some pathogeny aspects of some diseases. So, dysregulation of phosphoinositide 3-kinases (PI3K) -dependent pathways are directly involved in the etiology of cancers and thrombosis ([110]), and in cardiovascular disease ([111]). Moreover, PI3K is mediated by insulin resistance statement, that express receptor insulin activity, and also by mTOR ([112]).

- Phosphorylation

  Another step in the molecular activation mechanisms is the phosphorylation, by which a phosphoryl group is attached to sugar, lipids, proteins and ADP. In cellular regulation and signaling one essential aspect is the phosphorylation (e.g. by protein kinases) that catalyze the transfer of phosphate groups and dephosphorylation (by phosphatases) that remove phosphate group. Both processes are mediated by the presence of reactive oxygens species (ROS) that influence on cellular signal-transduction processes and, therefore, in normal and pathophysiological states ([113]). Protein phosphorylation can occur with some types of bonding one of them through a phosphoester bond formation on serine, threonine and tyrosine side chains, this is the same bonding present in nucleotides DNA, RNA and ATP. It is essential for normal cellular metabolism while abnormal phosphorylation is involved in disease conditions. Deregulation of phosphorylation leads to cancer ([114]), cardiovascular disease ([115]), diabetes ([116]), inflammatory and infectious diseases ([117]). In the last twenty years, mTOR, a PI3K-related protein kinases, has been identified as the central node in a network that controls metabolism by modulating vital cellular processes, including protein, lipids, nucleotides and ATP synthesis while limiting autophagic breakdown of cellular components. Impaired function of mTOR signaling has been implicated in metabolic disorders, neurodegeneration, cancer, and ageing ([118]).

d) Quantum Phenomena in Vitamin D synthesis

We have described the importance of calcium and phosphate in some biological processes and diseases, highlighting some quantum aspects. Still, these elements have to be incorporated into the organisms coming from the environment. One of the critical molecules that regulate the entrance and the body distribution is vitamin D. Vitamin D is one of the oldest hormones that have been made by phytoplankton for over 750 million years. These microorganisms obtain energy through the process of photosynthesis and in a similar way produce vitamin D ([119]). In photosynthesis, one molecule of the pigment chlorophyll absorbs one photon loses one electron, starting the flow of electrons down an electron transport chain, which leads to the reduction of NADP to NADPH and creates a proton gradient and synthesis of ATP. Vitamin D endocrinology started 550 million years ago when the first species developed a vitamin D receptor, controlling metabolic genes supporting cellular processes, such as innate and adaptive immunity and bone metabolism ([120]).

We know that is a vitamin that mediates the intestinal absorption of calcium, magnesium, and phosphorus that is essential to bone metabolism ([121]), and relate to oxidative stress and energy metabolism ([122]). Vitamin D is a group of fat-soluble

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secosteroids included in the organic steroid compounds. Production of vitamin D starts in the skin with the absorption of ultraviolet B photons, with a wavelength of 280-315nm, by 7-dehydrocholesterol that forms the secosteroid (split steroid) previtamin D_3. An absorbed photon produces a breakdown of the double bond between C7 and C8, and an open B ring between C9 and C10 ([123]). This previtamin D_3 presents two conformeric forms. One is the most thermodynamically stable form, but cannot isomerize to vitamin D_3. The other one is less thermodynamically stable, but cause rearrangement of the double bonds to form vitamin D_3. This reaction is an antarafacial sigmatropic [1,7] hydride shift, this mean that the covalent bond is changed to another bond around as a reaction center. As a result, the reaction can take several days to convert to vitamin D_3. The solution comes from the fact that 7-dehydrocholesterol is part of the plasma membrane of the skin cells and is incorporated within the fatty acid hydrocarbon side chain and polar head group of the triglycerides ([124], [125]). The polar head has phosphorus that, as in Posner molecule have a nuclear spin with S = ½ and can maintain the quantum coherence and facilitate the conversion in vitamin D_3. Later the bloodstream carries vitamin D_3 to the hepatocytes where is hydroxylated, forming 25-hydroxycholecalciferol (calcifediol). Then in the proximal tubules of the kidneys, take place the second hydroxylation to form calcitriol (1,25-dihydroxycholecalciferol), and finally activate the nuclear vitamin D receptor (VDR). The hydroxylation process involves the conversion of a CH group into a COH group, so it is an oxidative process that could be influenced by the oxidative stress status of the cell. We have to highlight that vitamin D regulates the low resting levels of Ca^{2+} and ROS ([126]).

But not all the sun absorbed produces vitamin D, just 15% of the energy, and also other secosteroids have been created such as lumisterol and tachysterol, that has not endocrine function; also, the reaction can revert back to 7-dehydrocholesterol, so a photoequilibrium is established ([127]).

Vitamin D deficiency has been associated with chronic illnesses, such as some cancers, cardiovascular disease, neurological disorder, autoimmune diseases, infectious diseases, type 2 diabetes mellitus, neurocognitive disorders, and aging ([128]). Also, have effects on fetal programming epigenetics and gene regulation, oxidative stress, and mitochondrial function ([129], [130]). Phosphorus and vitamin D are intimately related, so that hyperphosphatemia and vitamin D has been associated with tumorigenesis, and reduced phosphorus content and availability in tropical and subtropical soil with reduced cancer risk ([131]).

Tamulis and Grigalavicius ([132]) describe in vitamin D synthesis quantum physics phenomena. For instance, the absorbance of light by provitamin D3 and its next reorganization. The formation of supramolecular provitamin D3 as quantum phenomena such as entanglement.

e) Quantum phenomena in cancer mutations

Human cancer is now the second cause of mortality, but in the next few years, it can raise the first cause ([133]), mainly due to the increasing age of the population ([134]). All the efforts that improve cancer survival need to be made with better and specific treatments so that we can offer to our patients' better hope of survival. The main question is how a cell or group of cells that are fine controlled by multiple

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physiological mechanisms can avoid them and produce the destruction of its host. This macroscopic or histological level of the disease is now explained with the idea that somatic mutations cause cancers ([135]). But why these mutations are produced at such a high level, it seems that the organism has a mechanism that facilitates these anomalies and cannot detect and remove them. It can be the reason for the second cancer and family cancer syndrome. In the first, patients get another new cancer, as a side effect of radiotherapy or the use of genotoxic drugs that produce chromosome aberrations and genome chaos ([136], [137], [138]). Family cancer syndrome defines families suffering a high level of cancers, occurring in young ages or sustained in the sex not usually affected ([139]). It represents cases where afflicted members inherit a defective copy of one of the many different genes needed to maintain genomic integrity ([140], [141]). We can think that the organism has a trend to develop cancer due to mechanisms cellular malignancies. Therefore, we can deduce that the somatic mutations keep at a high production level as the patient´s cancer characteristic.

The possible role of quantum mechanics in adaptive mutations (Q-gene) has been studied previously ([142], [143]). The Darwinian evolution concept is based on biological mutations that are defined as random, independent of selection pressure and adaptative mutations, in which the genetic changes do not exist before the environmental pressure. Adaptive mutations are involved in the evolution of microbial pathogenesis, cancer, and drug resistance, and should be taken into account in therapeutics ([144]). Cancer can be considered as an adaptation process that could be explained by multiple mutations contributing to its development ([145]). Colorectal cancer, related to well-characterized mutations in defined cell signaling pathways, is one example of adaptive mutation-cancer paradigm ([146]). New technical advances, appeared in the last 20 years, allows us to study with high precision at a molecular level. For instance, it can describe which of the large numbers of somatic mutations that appear in tumor cells drive tumor development ([147]). The relationship between cancer and DNA was not only described for nuclear mutations. Recent data provide new keys for the mitochondrial DNA (mtDNA). In 21 different types of cancer, substantially complete catalogs of somatic mtDNA alterations, including substitutions, indels, copy-number alterations, and structural variants, were provided. These data highlight the function of mitochondrial genes in oxidative phosphorylation, DNA repair and the cell cycle with clinical applications ([148]).

The way the environment can influence the cell mutation is explained by the entanglement of the DNA protons (hydrogen atoms) that bind the DNA´s nucleotides and the shift from one site to an adjacent one. The process of decoherence will destroy the quantum state of the genome that is in a coherent linear superposition of states. It has been proposed that this decoherence is accelerated and significantly increase the rate of production of the mutated state ([149]). Quantum entanglement of protons and other components of the genome can explain the epigenetic, and some authors involve a process of decoherence in the epigenetic evolution ([150]). They argue that one of the main distinguishing features of the quantum description of composite systems is that, in general, the state of a compound system cannot be reconstructed from the rules of its subsystems, and this is the essence of quantum entanglement.

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f) Quantum phenomena in microbiota induced pathology

As we have earlier explained above, all of us are holobiont, we share our lives with our partners; all of them contributing in some way to the function of the whole. Bordernstein and Theis ([151]) proposed the hologenome´s concept as the entire gene system of the holobiont, including elements of the nuclear genome, organelles, and microbiome that posits the beneficial, deleterious, and neutral mutations in any of these genomic subunits. The bacteria and archaea that share with us our lives were the first types of living entities that appeared in the world but developed in an anaerobic environment. The transition to a multicellular organism needs a better generation of energy in the metabolism. The best way to reach improvement is with aerobic conditions. The living´s evolution in our world solved this issue with episodes of infectious endocytosis. Some archaea engulfed other bacteria and originated intracellular organelles: plastids and mitochondria. Plastids could, using light energy, metabolize carbon dioxide with water, and produce oxygen in photosynthesis. Mitochondria, burn the nutrients with oxygen in the electron transport chain. The collaboration was so positive that part of the genome was transferred to the cell nucleus. So, the genomic control of metabolism is shared by the nuclear and organelles DNA ([152]). We can conclude that we are the consequence of an intimately and productive relationship with our partners. To develop a multicellular organism is essential to establish a connection between the individuals. But this kind of productivity relationship also happens between bacteria, and the bacteria tend to develop complex surface-associated communities named biofilms. They can adapt to the presence of other bacteria, communicate between them, in a quorum sensing phenomenon, and change their metabolism and gen regulation ([153]). Simple mutations in the genome of one species caused it to adapt to the presence of the other, forming an intimate and specialized association ([154]). Another mechanism has been proposed in the microorganism co-aggregation process in the well-known environmental example consortia of methane-oxidizing archaea and sulphate-reducing bacteria. The coupling mechanism demonstrates redox-dependent staining of the matrix between cells that provide evidence for syntrophic coupling through direct electron transfer between them ([155]). Also, another example is provided by marine sediments. The oxygen consumption in the surface´s bacteria are connected with the sulfide oxidation in the subsurface´s bacteria, are coupled by interspecies electron transfer mediated by bacterial pili ([156], [157]).

If we function as holobiont there needs to be some mechanisms that relate all the elements. As in biofilm´s quorum sensing some bacterial metabolites act as interkingdom signaling messengers via penetration into the host blood circulation and tissues ([158]). Miller proposes a hologenomic entanglement model with cognition at its center and conceptualized as Pervasive Information Fields within a quantum framework ([159]). Now it has been accepted that the gut microbiota is related with metabolic and neurological diseases ([160], [161]). Also, with inflammatory diseases such as rheumatic diseases ([162]). We have to highlight that periodontitis is originated from a dysbiotic biofilm enriched in pathobionts and virulence factors that significantly

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increased the inflammatory response ([163]) and take place in the upper portion of the gastrointestinal tract and is related to metabolic and cardiovascular diseases.
The result of the relationship between bacteria and organism cells could be the induction of some types of cancer. This one could be produced by the modificati on of the genome expression with a possible quantum mechanism behind it. It is estimated that 20% of tumors worldwide are microbially driven ([164]). The mechanisms include the promotion of inflammation, impaired immune response, modification of proliferative signaling and genome instability and mutations ([165]). Two bacteria *Helicobacter pylori* and *Fusobacterium nucleatum* produce protumourigenic inflammation and nuclear factor-κB (NF-κB) activation and genotoxic compounds ([166]). Gut microbiome from patients suffering colon carcinoma harbored higher abundance of *Fusobacterium*, *Porphyromonas*, *Bacteroides*, *Phascolarctobacterium* ([167]). It has to be pointed out that *Fusobacterium nucleatum* and *Porphyromonas* are related to periodontitis that produce bone resorption and hydroxyapatite subgingival calcification. A recent metanalysis demonstrates that periodontitis may be a risk factor for gastrointestinal cancers ([168]). Some data suggest that microbiota-derived LPS, the primary ligand of TLR4 activation, potentiates tumorigenesis ([169]). Bacterial LPS can produce in fibroblasts impaired autophagy caused by insufficient lysosomal function and mitochondrial dysfunction ([170], [171], [172]). New data show that DNA mutations are directly induced by the genotoxic *E. coli* strain attacking closely spaced adenine residues; it is a direct link with genetic alterations that drive cancer development and is preserved in metastases ([173]).
Evidence now suggests not only that these microbes may confer susceptibility to certain cancers, but they can also influence the response to therapeutics ([174]). Promising cancer therapeutic is the immune system´s stimulation due to its potential to specifically target tumor cells and limit harm to healthy tissue. The gut microbiota can modulate T cell infiltration of solid tumors. The gut microbiota can modulate T cell infiltration of solid tumors. For instance, oral administration of *Bifidobacterium* stimulates the natural antitumor immunity and therapeutic effects of antibodies targeting the PD-1/PD-L1 axis. Also, the anti-PD-1-based immunotherapy, which benefits to just a subset of patients, is related to the commensal microbiome having a mechanistic impact on antitumor immunity in human cancer patients ([175]). Antitumor effects of CTLA-4 blockade, a major negative regulator of T cell activation, depend on distinct *Bacteroides* species ([176]). All these data support that the composition of gut microbes could be manipulated for therapeutic benefit. However, the mechanism that could explain these effects is still unclear ([177]), maybe quantum phenomena could improve our knowledge.

PROPOSAL

We try to give new clues to explain why aging is characterize by increasing diseases. When we analyze the description of the pathogenesis of the Noncommunicable diseases, one point that is repeated is the relationship between them, and that most are related to the aging process. We suppose that there are some meeting points behind all the diseases that are shared

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between them. Based on this fact we propose to deepen in the knowledge of all these items with a new perspective and hand in hand with quantum physic.

Life continues to show more questions than certainties. From a thermodynamic perspective, we can affirm life can be described as a 'dissipative structure.' It is driven by an energy gradient that increases the entropy of its surroundings. Death is the opposite of life in which entropy invades our organism due to Non-communicable Diseases. Biology makes sense in the light of evolution and quantum physics. I want to propose that aging also can be explained by applying quantum physics concepts. It is a new, hard to believe, and an incredible path to be built, but we need to open the treatment options to our patients with new perspectives.

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