Article

Mechanism of Xenon Anesthetic Action in Spin-mediated Consciousness Theory & Its Experimental Support

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ABSTRACT

In this paper, we discuss the mechanism of xenon anesthetic action in spin-mediated consciousness theory in light of the recent experimental findings of Li, *et.al.* on nuclear spins of xenon isotopes, xenon 131 and xenon 129, attenuating their anesthetic potency in mice. In the spin-mediated consciousness theory put forward in 2002, molecules containing unpaired electron spins, such as oxygen (O_2) and nitric oxide (NO), interact with the mind pixels comprised of various nuclear spins in neural membranes and proteins and activate the latter as one of the steps generating conscious experience. Therefore, general anesthetics such as xenon produce anesthesia by perturbing O_2 and/or NO pathways in neural membranes and proteins thus blocking and/or distorting their activation functions in consciousness. Naturally, the nuclear spins of xenon 131 and xenon 129 may partially play the activating roles of displaced O_2 and/or NO among other possibilities to be briefly discussed and, thus attenuate the anesthetic potency of nuclear-spin-carrying xenon isotopes.

Keywords: Spin-mediated, consciousness, mind pixel, xenon isotopes, xenon 131, xenon 129, mechanism of anesthetic action.

1. Introduction

It is believed that the anesthetic functions of xenon is associated with its binding to NMDA receptor (See, *e.g.*, [1-2]). However, there is no commonly accepted theory on how general anesthetics work even after more than 160 years since their discovery. There are two schools of thoughts on the subject. The first and oldest is the "lipid theory" which proposes that anesthetics dissolve into cell membranes and produce common structural perturbation resulting in depressed function of ion channels and receptors that are involved in brain functions (See, e.g., [3, 7]). The second, more popular and recent theory is the "protein theory" which suggests that anesthetics directly interact with membrane proteins such as ion channels and receptors that are involved in brain functions. But the protein theory doesn't seem to square well with the low affinity and diversity of the general anesthetics. There is no direct experimental evidence to support either theory (See, e.g., [4, 7]).

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Both theoretical and experimental studies have shown that many general anesthetics cause changes in membrane structures and properties at or just above the clinical concentrations required for anesthesia (See, e.g., [5-6]). Since both O_2 and general anesthetics are hydrophobic, we proposed in 2001 within the framework of conventional neuroscience that general anesthetic may cause unconsciousness by perturbing O_2 pathway in neural membranes and O_2-utilizing proteins, such that the availability of O_2 to its sites of utilization is reduced, which in turn triggers cascading cellular responses through O_2-sensing mechanisms, resulting in general anesthesia [7].

Further, in the spin-mediated consciousness theory of 2002 [8], we hypothesized that anesthetic perturbations of oxygen pathways in neural membranes and proteins themselves are the direct cause of unconsciousness within the framework of quantum biology/brain. This hypothesis requires that O_2 be directly involved in consciousness such as awareness. Indeed, the low affinity, diversity and pervasiveness of general anesthetics point to this direction [8].

The spin-mediated consciousness theory says that quantum spin is the seat of consciousness and the linchpin between mind and the brain, that is, spin is the “mind-pixel”, and the unity of mind is achieved by quantum entanglement of these mind-pixels [8]. The theory is based on the fact that quantum spin is the most basic quantum bit ("qubit") for encoding information and neural membranes and proteins are saturated with quantum spin carrying nuclei and these nuclear spins have relatively long quantum coherence time [8]. There is also a version of spin-mediated consciousness theory based on unpaired electron spin (See additional refs in [8]).

Since spin-mediated consciousness theory was put forth in 2002 [8], the idea that nuclear spins and/or unpaired electron spins in the brain may play some roles in consciousness has gains traction recently (See, e.g., [9-13]).

Importantly, Li, *et.al.* have found experimentally that nuclear spins of xenon isotopes, xenon 131 and xenon 129, attenuate their anesthetic potency in mice [11]. The authors therein suggest that "the quantum property of nuclear spin in the monoatomic anesthetic xenon promotes conscious processes at the xenon site of action, consistent with theories proposing quantum mechanisms in consciousness" and speculate that quantum entanglement of nuclear spins may be involved in consciousness [11]. However, for whatever reason (hopefully benign such as oversight), the authors therein did not cite or mention [8], which was the first, to the best knowledge of the herein first author, to propose nuclear/electron spin mediated/based consciousness theory back in 2002.

In this paper, we discuss the mechanism of xenon anesthetic action in spin-mediated consciousness theory [8] in light of Li *et al.*’s finding [11]. In the spin-mediated consciousness theory, molecules containing unpaired electron spins, such as oxygen (O_2) and nitric oxide (NO), interact with the mind pixels comprised of various nuclear spins in neural membranes and proteins and activate the latter as one of the steps generating conscious experience (8). Therefore, general anesthetics such as xenon produce anesthesia by perturbing O_2 and/or NO pathways in neural membranes and proteins thus distorting and/or blocking their activation functions in consciousness such as awareness [8]. Naturally, the nuclear spins of xenon 131 and xenon 129

may partially play the activating roles of displaced O_2 and/or NO among other possibilities and, thus attenuate the anesthetic potency of nuclear-spin-carrying xenon isotopes as shown in [11].

2. Brief Comparisons of Oxygen, Nitric Oxide, Nitrous Oxide & Xenon

Each O_2 contains two unpaired valence electrons thus is strongly paramagnetic and at the same time chemically reactive as a bi-radical [8]. It is capable of producing a large fluctuating magnetic field along its diffusing pathway thus serves as a natural contrast agent in MRI (See, e.g., [14]). The existence of unpaired electrons in stable molecules is very rare indeed. O_2 are the only paramagnetic specie to be found in large quantities in the brain besides enzyme-produced nitric oxide (NO) [8]. In addition, O_2 is an essential component for energy production in the central nervous system.

O_2 and NO are hydrophobic small molecules so their concentrations in neural membranes are much higher than in aqueous solutions such as cytoplasma (See, e.g., [15]). Both O_2 and NO, the latter being an unstable free radical with one unpaired electron and a small neural transmitter (See, e.g., [21]), are well known in spin chemistry - a field focused on the study of free-radical mediated chemical reactions where very small magnetic energies can change non-equilibrium spin conversion process (See, e.g., [16]).

In contrast, nitrous oxide (N_2O) and xenon (Xe) contain no unpaired electrons and are general anesthetics. They are also hydrophobic small molecules so their concentrations in neural membranes are much higher than in aqueous solutions such as cytoplasma (See, e.g., [8]). Xenon has 9 stable isotopes among which xenon 129 has a nuclear spin of 1/2, xenon 131 has nuclear spin of 3/2, and the other seven isotopes have no nuclear spin (See, e.g., [11]).

3. Postulates of Spin-mediated Consciousness Theory

Within the context of brain-based consciousness, the spin-mediated consciousness theory says that quantum spin is the seat of consciousness and the linchpin between mind and the brain, that is, spin is the “mind-pixel”, and the unity of mind is achieved by quantum entanglement of these mind-pixels [8]. The theory is based on the fact that quantum spin is the most basic quantum bit ("qubit") for encoding information and a fundamental quantum process associated with the structure of neural membranes and proteins that are saturated with quantum spin carrying nuclei and these nuclear spins have relatively long quantum coherence time (8, also see [22]).

Spin-mediated consciousness theory of 2002 [8] postulates that: (a) Consciousness is intrinsically connected to quantum spin; (b) The mind-pixels of the brain are comprised of the nuclear spins distributed in the neural membranes and proteins, the pixel-activating agents are comprised of biologically available paramagnetic species such as O_2 and NO, and the neural memories are comprised of all possible entangled quantum states of the mind-pixels; (c) Action potential modulations of nuclear spin interactions input information to the mind pixels and spin chemistry is the output circuit to classical neural activities; and (d) Consciousness emerges from the collapses of those entangled quantum states which are able to survive decoherence, said

collapses are contextual, irreversible and non-computable and the unity of consciousness is achieved through quantum entanglement of the mind-pixels.

As mind-pixel activating agents, the unpaired electrons of the paramagnetic species such as O_2 and NO can interact with nuclear spins through their large magnetic dipoles and collision-induced Fermi-contact mechanism thus activating the neural nuclear spin ensembles [8]. Indeed, because the magnetic dipole moment of an unpaired electron is 658 times larger than that of the ^{1}H nucleus, O_2 and NO can respectively produce magnetic fields 1,316 and 658 times larger than ^{1}H (See, e.g., [17]). In addition, O_2 and NO are hydrophobic small molecules so their concentrations in neural membranes are much higher than in aqueous solutions such as cytoplasma (See, e.g., [15]). Thus, as they rapidly tumble and diffuse, they produce microscopically strong and fluctuating magnetic fields. O_2 are the predominant sources of internal magnetic fields in neural membranes and proteins, as evidenced by the strong effect of O_2 on spin-spin and spin-lattice relaxation rates (See, e.g., [18]).

In additions, nuclear spin networks in neural membranes and proteins are modulated by action potentials through *J*-coupling, dipolar coupling and chemical shielding tensors and perturbed by microscopically strong and fluctuating internal magnetic fields produced largely by paramagnetic oxygen [19-20].

Further, both nuclear spin in neural membranes and proteins as mind-pixels and unpaired electron spins of O_2 and NO as mind-pixel activating agents are also modulated by action potentials through relativistic effect of moving spin in strong electric field [20, 22] and, in turn, said modulation of the activating agents influence the nuclear spins in the brain as shown below.

Thus, action-potential modulations of both nuclear and unpaired electron spins synchronize their collective dynamics to the neural firings [19-20].

The decoherence effect which causes a quantum system to lose quantum coherence through interactions with its environment has been a major concern for any quantum theory of the brain (See, *e.g.*, [23]). However, nuclear spins only have weak interactions with their environments thus long relaxation time after excitation (See, *e.g.*, [14]). Indeed, there are both theoretical and experimental studies indicating the possibility of large-scale quantum coherence with entanglement in the nuclear spin ensembles distributed in the neural membranes and proteins (See, e.g., [24-32]). Further, studies show that decoherence-free subspaces can exist within the Hilbert space of a complex quantum system (See, *e.g.*, [33-34]).

4. Action Potential Modulations of Nuclear Spins & Unpaired Electron Spins

The range of electric field strength E_m inside the neural membranes during a typical action potential as calculated from $E_m = V_m/d$ where V_m and d are respectively the membrane voltage and thickness is shown in Figure1. It oscillates between -9 to +6 million volts per meter during the course of each action potential [19-20]. These strengths are comparable to those causing

electroporation of cell membranes and dielectric breakdown of many materials at which the covalent bonds of the constituent molecules are torn apart (See, *e.g.*, [35]). So it significantly affects the conformations and collective dynamics of the neural membrane components such as phospholipids, cholesterols and proteins. Indeed, voltage-dependent ion channels perform their functions through electric field induced conformation changes of the constituent protein (See, *e.g.*, [36]) and studies on the effects of electric fields on lipids support the above conclusion (See, *e.g.*, [37-38]).

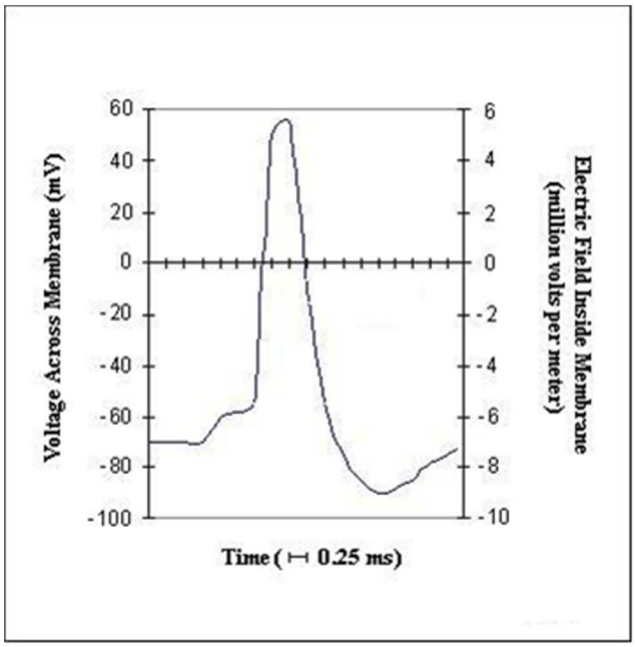

Figure 1. Electric field strength inside neural membrane during the course of an action potential. The calculation is down by assuming a typical membrane thickness of about 10 nm and the results are shown in the unit of one million volts per meter with "-" and "+" indicating that the direction of electric field is respectively pointing outward or inward inside the neural membrane.

The nuclear spins carried by the nuclei such as ^{1}H, ^{13}C and ^{31}P inside the neural membranes and proteins form complex intra- and inter-molecular spin networks through various intra-molecular J- and dipolar couplings and both short- and long-range intermolecular dipolar couplings [19] and even through-space J-couplings (See, e.g. [39]). Since J-coupling is the indirect interaction between two nuclear spins through covalent bonds and dipolar coupling is the direct interaction of two nuclear spins through space, their strengths and anisotropies strongly depend on the conformations of the neural membrane components (See, *e.g.*, [40-41]). Further, the chemical shielding of each nuclear spin also depends on the conformations of surrounding covalent bonds (See, *e.g.*, [42]). Thus, when these spin networks are subjected to the enormous changing electric field produced during each action potential, the J-coupling, dipolar coupling and chemical shielding tensors oscillate with it [19]. Studies on the effects of electric fields on these tensors (See, *e.g.*, [40-42]) also support this conclusion.

Further, nuclear and electron spins interact with electric field through relativistic effect due to their motion in electric field [20, 22] – This is also the cause of spin-orbital couplings and can be vigorously derived from Dirac equation as will be shown in a separate paper. The motion producing the relativistic effect of moving nuclear spin or electron spin seeing/experiencing a magnetic field in its rest frame includes molecule motion such as rotation, electron orbital motion in an atom, rotation of multi-nucleon nucleus and motion a sub-nuclear particle such as quark inside a nucleon (proton or neutron) as illustrated below.

In special relativity, a moving particle in an electric field $\boldsymbol{E}$ sees a magnetic field $\boldsymbol{B'}$ in its own rest frame (See, e.g., [43]):

$$\boldsymbol{B'} = \frac{\boldsymbol{E}\times\boldsymbol{v}/c^2}{\sqrt{1-v^2/c^2}} \approx \frac{\boldsymbol{E}\times\boldsymbol{v}}{c^2} \tag{1}$$

However, due to Thomas precession [44], the magnetic field $\boldsymbol{B'}$ seen by the nuclear spin **I** is:

$$\boldsymbol{B'} \approx \frac{\boldsymbol{E}\times\boldsymbol{v}}{2c^2} \tag{2}$$

Thus, $\boldsymbol{E}$ exerts a torque (twisting force) on moving proton spin **I** at speed $\boldsymbol{v}$ as illustrated below in Figure 2:

$$\boldsymbol{f} = \boldsymbol{m}_I \times \boldsymbol{B'} = \mathrm{g}_I \mu_I \boldsymbol{I} \times \frac{\boldsymbol{E}\times\boldsymbol{v}}{2c^2} \tag{3}$$

Similarly, $\boldsymbol{E}$ exerts a torque (twisting force) on moving electron spin **S** at speed $\boldsymbol{v}$ as illustrated in Figure 2:

$$\boldsymbol{f} = \boldsymbol{m}_e \times \boldsymbol{B'} = -\mathrm{g}_e \mu_e \boldsymbol{S} \times \frac{\boldsymbol{E}\times\boldsymbol{v}}{2c^2} \tag{4}$$

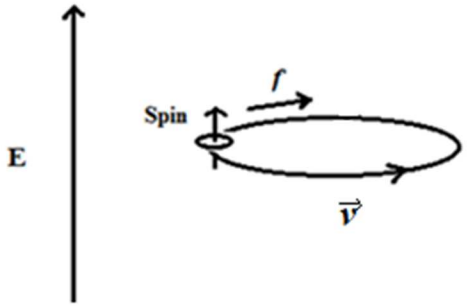

Figure 2. Illustration of spin transverse torque/force $\boldsymbol{f}$ exerted on moving nuclear spin inside the neural membranes and proteins due to molecular rotation, nucleus rotation or sub-nucleon motion, or moving unpaired electron spin inside the neural membranes and proteins due to molecular rotation or atomic electron orbital motion.

Therefore, the interactions between the moving nuclear/electronic spins in neural membranes and proteins and the varying high-voltage electric fields inside neural membranes and proteins driven by action potentials are capable of directly feeding information into the neurons [20].

We now estimate the strengths of $\boldsymbol{B'}$ seen by nuclear spin and electron spin carried by various molecules in neural membranes and proteins using the formula:

$$B' = Ev/(2c^2) \quad (5)$$

and the estimated $E \sim 9x10^6$ *V/m* as the maximal electric field strength in neural membranes or proteins of a thickness/length $\sim 10x10^{-9}m$.

(1) Strength of $\boldsymbol{B'}$ seen in the rest frame of rotating lipid molecule by a nuclear-spin-carrying proton/hydrogen

For a lipid molecule with a diameter $\sim 0.9x10^{-9}m$ and rotation frequency along the chain $\sim 1x10^7$/s (See, e.g., [45]), the estimated molecular rotation speed of a spin ½ proton/hydrogen on the lipid molecule is $2 \times 3.14 \times 0.45x10^{-9}m \times 1x10^7/s = 0.0283$ *m/s*.

Thus, B' seen on lipid molecule rest frame by a proton/hydrogen atom due to rotation along the chain is $\sim (9x10^6$ *V/m* x 0.0283 *m/s*$)/(2x(2.99x10^8 m/s)^2 = 7.122 \times 10^{-13}$ *Vs/m*^{2} (Tesla) , that is, 0.7122 pico-Tesla.

(2) Strength of $\boldsymbol{B'}$ seen in the rest frame of rotating nucleus of multiple nucleons such as deuteron, C^{13}, P^{31} and Xe^{129} by a nuclear-spin-carrying proton/neutron

For a nucleus of multiple nucleons with diameter $\sim 4.2 \times 10^{-15}m$ (e.g., deuteron) and rotation frequency $\sim 4.74 \times 10^{21}/s$ (See, e.g., [46]), the estimated rotation speed of the nucleus is $\sim 2 \times 3.14 \times 2.1 \times 10^{-15}m \times 4.74 \times 10^{21}/s = 58.95 \times 10^6 m/s$.

Thus, B' seen in the nucleus rest frame by a spin ½ nucleon (proton or neutron) due to rotation of nucleus of multiple nucleons is $\sim (9x10^6$ *V/m* x 58.95 x $10^6 m/s)/(2x(2.99x10^8 m/s)^2 = 14.836 \times 10^{-4}$ *Vs/m*^{2} (Tesla), that is, 14.836 Gauss or 1.484 milli-Tesla.

(3) Strength of $\boldsymbol{B'}$ seen in the rest frame of rotating sub-nucleon particle such as a spin-carrying quark inside a nucleon

For a nucleon with rotating sub-nuclear particle with orbital diameter $\sim 0.8 \times 10^{-15}m$ (e.g., the size of a proton) and rotation frequency $\sim 4.74 \times 10^{21}/s$ (a pure guess based on [46]), the estimated

orbital speed of a sub-nuclear particle inside a nucleon is ~ 2 x 3.14 x 0.4 x $10^{-15}m$ x 4.74 x $10^{21}/s$ = 11.907 x $10^{6}m/s$.

Thus, B' seen in the sub-nucleon rest frame by a spin ½ sub-nucleon particle due to sub-nucleon rotation is ~ (9x10^{6} V/m x 11.907 x $10^{6}m/s$)/(2x(2.99x$10^{8}m/s$)^2 = 2.997 x 10^{-4} Vs/m^2 (Tesla), that is, 2.997 Gauss or 0.300 milli-Tesla.

(4) **Strength of B' seen in the rest frame of rotating oxygen molecule by an unpaired electron spin**

For an oxygen molecule with size/diameter ~ 3.46x$10^{-11}m$ and rotation frequency ~ 1.07x10^{12}/s (See, e.g., [47]), the estimated rotation speed of a spin-carrying unpaired electron on the oxygen molecule in neural membranes or proteins is 2 x 3.14 x 1.73 x $10^{-11}m$ x 1.07 x10^{12}/s = 1.162 x 10^{2} m/s.

Thus, B' seen in the rest frame of oxygen molecule by a spin-carrying unpaired electron due to rotation of oxygen molecule is ~ (9x10^{6} V/m x 1.162 x 10^{2} m/s)/(2x(2.99x$10^{8}m/s$)^2 = 2.924 x 10^{-9} Vs/m^2 (Tesla), that is, 2.924 nano-Tesla.

(5) **Strength of B' seen in the rest frame of electron orbital in oxygen molecule by an unpaired electron spin**

The estimated electron orbital speed in a Bohr atom is ~c/137 (See, e.g., [48]). Using this speed as an estimate of the electron orbital speed in oxygen molecule, B' seen in the rest frame of electron orbital by a spin-carrying unpaired electron due to electron orbital motion is ~ (9x10^{6} V/m x (1/137 x 2.99x$10^{8}m/s$)/(2x(2.99x$10^{8}m/s$)^2 = 54.93 x$10^{-6}Vs/m^2$ (Tesla), that is, 54.93 micro-Tesla or 0.549 Gauss.

We now illustrate action potential modulations of two intra- or inter-molecular nuclear-spin system $\mathbf{I_1}$ and $\mathbf{I_2}$ inside neural membranes or proteins by the following heuristic Hamiltonian:

$$\hat{H} = -\hbar\gamma_1\hat{\mathbf{I}}_1\cdot\left(\mathbf{1}-\boldsymbol{\sigma}_{1R}-\boldsymbol{\sigma}_{1A}\right)\cdot\left(\mathbf{B}_{1i}+\mathbf{B}_{1e}+\mathbf{B}'_1\right)-\hbar\gamma_2\hat{\mathbf{I}}_2\cdot\left(\mathbf{1}-\boldsymbol{\sigma}_{2R}-\boldsymbol{\sigma}_{2A}\right)\cdot\left(\mathbf{B}_{2i}+\mathbf{B}_{2e}+\mathbf{B}'_2\right)+ h\hat{\mathbf{I}}_1\cdot\left(\mathbf{J}_R+\mathbf{J}_A\right)\cdot\hat{\mathbf{I}}_2+h\hat{\mathbf{I}}_1\cdot\left(\mathbf{D}_R+\mathbf{D}_A\right)\cdot\hat{\mathbf{I}}_2 \quad (6)$$

where $\mathbf{B}_{1i}, \mathbf{B}_{1e}, \mathbf{B}'_1, \mathbf{B}_{2i}, \mathbf{B}_{2e}$ and $\mathbf{B}'_2$ are respectively the internal, external and relativistic-effect magnetic fields at the locations of first and second spins, γ_1 and γ_2 are respectively the gyromagnetic ratios of the said first and second spins, and other terms are explained below.

In the above equation (6), the two nuclear spins are coupled to each other through J-coupling tensor (including "through space" J-coupling, see, e.g., [39]) $\mathbf{J} = \mathbf{J}_R + \mathbf{J}_A$, where $\mathbf{J}_R$ is for resting potential and $\mathbf{J}_A$ accounts for contribution from action potential modulation, and dipolar coupling

tensor $\mathbf{D} = \mathbf{D}_R + \mathbf{D}_A$, where $\mathbf{D}_R$ is for resting potential and $\mathbf{D}_A$ accounts for contribution from action potential modulation (19). Second, chemical shielding tensor of each nuclear spin which also contains contribution from action potential modulation of its surrounding covalent bonds are taken into account - For the first spin $\boldsymbol{\sigma}_1 = \boldsymbol{\sigma}_{1R} + \boldsymbol{\sigma}_{1A}$ and for the second spin $\boldsymbol{\sigma}_2 = \boldsymbol{\sigma}_{2R} + \boldsymbol{\sigma}_{2A}$ where $\boldsymbol{\sigma}_{1R}$ and $\boldsymbol{\sigma}_{2R}$ are the chemical shielding tensors at resting potential and $\boldsymbol{\sigma}_{1A}$ and $\boldsymbol{\sigma}_{2A}$ are the first-order contribution to $\boldsymbol{\sigma}_1$ and $\boldsymbol{\sigma}_2$ respectively from action potential modulations. Third, the effects of internal magnetic field $\mathbf{B}_i$ from other spins, external magnetic field $\mathbf{B}_e$ and the magnetic field $\mathbf{B}'$ due to relativistic effect on moving nuclear spin in the electric field of action potentials are also taken into accounts (20).

In the above equation (6), $\mathbf{J}_A$, $\mathbf{D}_A$, $\boldsymbol{\sigma}_{1A}, \boldsymbol{\sigma}_{2A}$, $\mathbf{B}_{1i}, \mathbf{B}'_1, \mathbf{B}_{2i}$ and $\mathbf{B}'_2$ are all functions of membrane voltage V_m which is driven by action potentials. Thus, the above Hamiltonian of interaction allows the action potentials to modulate nuclear spin dynamics through J-coupling, dipolar coupling, chemical shift, internal magnetic field and relativistic effect of moving spin in electric field of the action potential. Importantly, the spin-spin interaction in the above Hamiltonian causes the two nuclear spins in the two-spin system to form entangled quantum states known as Bell States.

We further illustrate the action potential modulations of one nuclear-spin system **I** and one unpaired electron spin **S** inside neural membranes or proteins by the following heuristic Hamiltonian:

$$\hat{H} = -\hbar\gamma_I \hat{\mathbf{I}} \cdot \left(\mathbf{1} - \boldsymbol{\sigma}_R - \boldsymbol{\sigma}_A\right) \cdot \left(\mathbf{B}_{Ii} + \mathbf{B}_{Ie} + \mathbf{B}'_I\right) + \hbar\gamma_S \hat{\mathbf{S}} \cdot \left(\mathbf{B}_{Si} + \mathbf{B}_{Se} + \mathbf{B}'_S\right) + h\hat{\mathbf{I}} \cdot \left(\mathbf{A}_R + \mathbf{A}_A\right) \cdot \hat{\mathbf{S}} \qquad (7)$$

where $\mathbf{B}_{Ii}, \mathbf{B}_{Ie}, \mathbf{B}'_I, \mathbf{B}_{Si}, \mathbf{B}_{Se}$ and $\mathbf{B}'_S$ are respectively the internal, external and relativistic-effect magnetic fields at the locations of nuclear-spin system **I** and unpaired electron spin **S**, γ_I and γ_S are respectively the gyromagnetic ratios of the said nuclear spin and unpaired electron spin, and other terms are explained below.

In the above equation (7), the nuclear spin and unpaired electron spin are coupled to each other through dipolar coupling tensor $\mathbf{A} = \mathbf{A}_R + \mathbf{A}_A$, where $\mathbf{A}_r$ is for resting potential and $\mathbf{A}_a$ accounts for contribution from action potential modulation. Second, chemical shielding tensor $\boldsymbol{\sigma}$ of the nuclear spin which also contains contribution from action potential modulation of its surrounding covalent bonds are taken into account, That is, $\boldsymbol{\sigma} = \boldsymbol{\sigma}_R + \boldsymbol{\sigma}_A$ where $\boldsymbol{\sigma}_A$ is the first-order contribution to $\boldsymbol{\sigma}$ from action potential modulations. Third, the effects of internal magnetic field magnetic field $\mathbf{B}_i$

from other spins, external magnetic field $\mathbf{B}_e$ and the magnetic field $\mathbf{B}'$ due to relativistic effect of moving spin in the electric field of action potential are taken into accounts.

In equation (7), $\mathbf{A}_a$, $\boldsymbol{\sigma}_A$, $\mathbf{B}_{Ii}, \mathbf{B}'_I$, $\mathbf{B}_{Si}$ and $\mathbf{B}'_S$ are all functions of membrane voltage V_m which is driven by action potential. The above Hamiltonian of interactions allows unpaired electron spin **S** of O_2 and/or NO to activate/polarize/interact with nuclear spin **I** and the action potentials to modulate nuclear-electronic two-spin system dynamics through dipolar coupling, chemical shift, internal magnetic field and relativistic effect of moving spin in electric field of the action potential. Importantly, the nuclear spin and electron spin interaction in the above Hamiltonian cause the two spins to form entangled quantum states known as Bell States.

The above considerations of simple two-spin systems in neural membranes and/or protein illustrate that the neural spin networks inside the membranes are capable to form complex modulated structures through action potential driven oscillations of *J*-coupling, dipolar coupling and chemical shielding tensors plus oscillations of internal magnetic field and relativistic effect of moving spin in electric field of the action potentials [8, 19-20]. Thus, the neural spike trains of various frequencies can directly input information carried by them into these spin networks [8, 19-20].

The fluctuating internal magnetic fields are produced by the paramagnetic species such as O_2 and NO and spin-carrying nuclei themselves such as ^{1}H, ^{13}C and ^{31}P. Table 1 shows the maximal magnetic field strengths produced by the magnetic dipoles of the unpaired electrons of O_2 and NO and the nucleus of ^{1}H along the axes of said dipoles at given distances [19]. Because the magnetic dipole moment of an unpaired electron is 658 times larger than that of the ^{1}H nucleus, O_2 and NO can respectively produce magnetic fields 1,316 and 658 times larger than ^{1}H [19].

As distance r increases, the strength of the magnetic dipole field quickly attenuate according to

$$B_i = \frac{\mu_0 m}{4\pi r^3} \tag{8}$$

where μ_0 is the permeability of free space and m is the magnetic dipole moment. As mentioned earlier, O_2 and NO are hydrophobic small molecules so their concentrations in neural membranes are much higher than in aqueous solutions such as cytoplasma (See, e.g., [15]). As they rapidly tumble and diffuse, they produce microscopically strong and fluctuating magnetic fields. Indeed, O_2 are the predominant sources of internal magnetic fields in neural membranes as evidenced by the strong effect of O_2 on spin-spin and spin-lattice relaxation rates (See, e.g., [15, 18]).

Table 1. Magnetic Fields Produced by O_2, NO and ^1H			
Distance (Å)	O_2 (Tesla)	NO (Tesla)	^1H (Tesla)
1.0	3.713940	1.856970	0.002821
2.0	0.464243	0.232122	0.000353
3.0	0.137553	0.068777	0.000104
4.0	0.058030	0.029015	0.000044
5.0	0.029712	0.014856	0.000023
10.0	0.003714	0.001857	0.000003

Again, these fluctuating internal magnetic fields are modulated by action potentials through relativistic effects on nuclear/electronic spins moving in electric field and continuously perturb the neural spin networks. The intensities of said perturbations depend on the concentrations of O_2 and NO that are highly regulated in the brain. Thus, these modulated perturbations not only activate various neural spin networks but also are likely capable of enhancing the synchronization of these dynamics to the neural spike trains through non-linear processes such as stochastic resonance that is known to occur in the brain (See, e.g., [49-51]).

The collective dynamics of the neural spin networks under modulations by action potentials and perturbations by fluctuating internal magnetic fields which are also modulated by action potentials represent meaningful information to the brain [19-20, 22]. An analogy is the mechanism of liquid crystal display (LCD) where information-carrying electric voltages applied to the pixel cells change the optical properties of the constituent molecules such that when lights pass through these cells their phases get rotated differently which in turn represent different information to the viewer of the LCD screen (See, e.g., [52]). Accordingly, the cause of unconsciousness by general anesthetics can be explained as the direct consequence of their effects the O_2 and/or NO pathways inside neural membranes and proteins and/or the neural membrane structures themselves [7-8, 19-20].

However, how can one explains that cognitive functions seem in general insensitive to environmental and even medical strength external magnetic fields such as those generated by the power lines and the ones used in MRI? It is argued that most of these disturbances do not represent meaningful information to the brain and, further, the brain likely have developed other mechanisms through evolution to counter the effects of external magnetic fields. In the cases where external magnetic disturbances were reported to have observable effects on cognition, the above discussions provide a basis for interpreting these effects as said disturbances contain meaningful information to the brain [7-8, 19-20].

4. Mechanism of Xenon Anesthetic Action in Spin-mediated Consciousness Theory

We describe here mechanism of anesthetic action in accordance with the spin-mediated theory as put forward in 2002 [8]. Figure 3(a) schematically shows the normal diffusion of O_2 and NO without anesthetics dissolved into the neural membranes and proteins. As these molecules rapidly diffuse through the membranes, they interact with the neural membrane components and generate strong and fluctuating internal magnetic fields which are modulated by action potentials thus activating the nuclear spin ensembles inside these membranes. Figure 3(b) schematically shows anesthetic perturbations of O_2 and NO pathways and neural membranes themselves by anesthetic molecules and xenon atoms and the resulting distortion and/or obstruction of these pathways. Such perturbations render O_2 and NO not able to perform their normal activation functions thus resulting in unconsciousness.

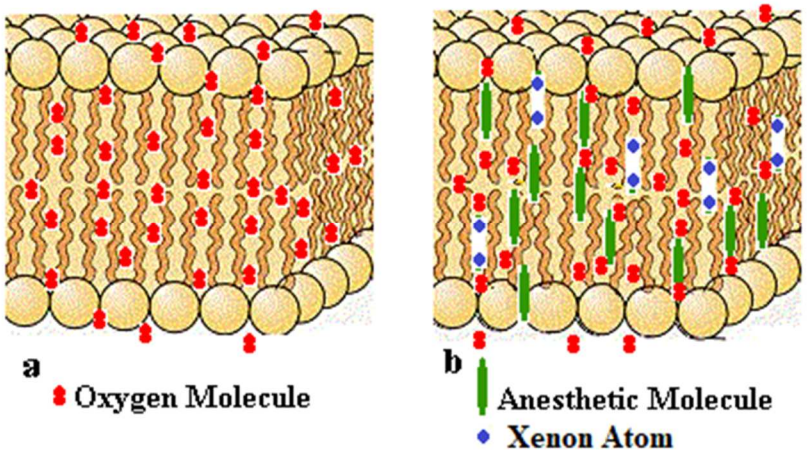

Figure 3. Illustration of anesthetic action. **a** shows the normal diffusion of O_2 without anesthetics dissolved into neural membranes. **b** shows xenon and anesthetic molecule perturbations of O_2 pathways and neural membranes themselves.

Further, as illustrated in Figure 4 below, anesthetic molecules and xenon atoms perturb not only oxygen transport across cell membranes but also its lateral movement within the membrane and the movement within a hydrophobic pocket of the protein.

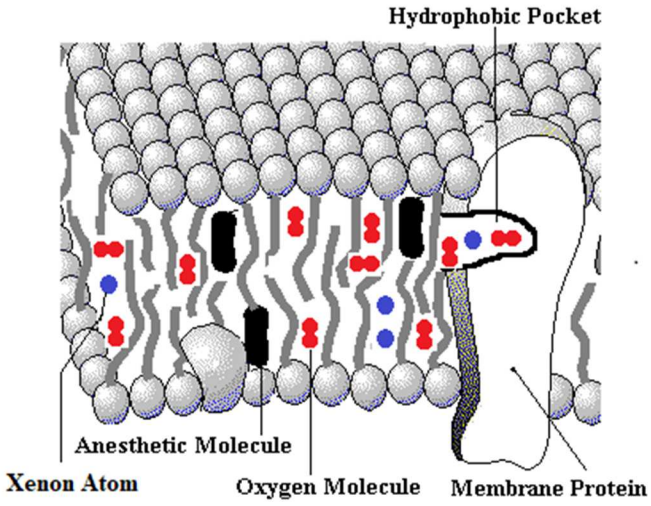

Figure 4. Perturbation of oxygen pathways in membranes and proteins by anesthetic molecules and xenon atoms. According to spin-mediated consciousness theory, anesthetic molecules and xenon atoms block, dislocate, distort or otherwise interfere with O_2 and/or NO pathways in both membranes and proteins. They perturb not only oxygen transport across cell membranes but also its lateral movement within the membrane and the movement within a hydrophobic pocket of the protein.

Using the above system of one nuclear-spin **I** and one (or two) unpaired electron spin **S** inside neural membranes or proteins under the action potential modulation as an illustration, one may write a heuristic Hamiltonian for the two-spin system as:

$$\hat{H} = -\hbar\gamma_I \hat{\mathbf{I}} \cdot (\mathbf{1} - \boldsymbol{\sigma}_R - \boldsymbol{\sigma}_A) \cdot (\mathbf{B}_{Ii} + \mathbf{B}_{Ie} + \mathbf{B}'_I) + \hbar\gamma_S \hat{\mathbf{S}} \cdot (\mathbf{B}_{Si} + \mathbf{B}_{Se} + \mathbf{B}'_S) + h\hat{\mathbf{I}} \cdot (\mathbf{A}_R + \mathbf{A}_A) \cdot \hat{\mathbf{S}} \qquad (9)$$

After the unpaired-electron-carrying molecule such as O_2 or NO is displaced by an anesthetic such as xenon 132 or xenon 134 which has no unpaired electron spin and nuclear spin, the Hamiltonian becomes:

$$\hat{H} = -\hbar\gamma_I \hat{\mathbf{I}} \cdot (\mathbf{1} - \boldsymbol{\sigma}_R - \boldsymbol{\sigma}_A) \cdot (\mathbf{B}_{Ii} + \mathbf{B}_{Ie} + \mathbf{B}'_I) \qquad (10)$$

which contains no interaction between nuclear spin **I** and the activating agent O_2 or NO.

On the other hand, if the unpaired-electron-carrying molecule such as O_2 or NO is displaced by an anesthetic such as xenon 129 or xenon 131 which has no unpaired electron spin but has nuclear spin $\mathbf{I}_2$, the Hamiltonian (9) becomes:

$$\hat{H} = -\hbar\gamma_I \hat{\mathbf{I}} \cdot \left(\mathbf{1} - \boldsymbol{\sigma}_R - \boldsymbol{\sigma}_A\right) \cdot \left(\mathbf{B}_{Ii} + \mathbf{B}_{Ie} + \mathbf{B}'_I\right) - \hbar\gamma_2 \hat{\mathbf{I}}_2 \cdot \left(\mathbf{1} - \boldsymbol{\sigma}_{2R} - \boldsymbol{\sigma}_{2A}\right) \cdot \left(\mathbf{B}_{2i} + \mathbf{B}_{2e} + \mathbf{B}'_2\right) + h\hat{\mathbf{I}} \cdot \left(\mathbf{J}_R + \mathbf{J}_A\right) \cdot \hat{\mathbf{I}}_2 + h\hat{\mathbf{I}} \cdot \left(\mathbf{D}_R + \mathbf{D}_A\right) \cdot \hat{\mathbf{I}}_2 \quad (11)$$

which contains both intermolecular ('through space") J-coupling (See, e.g., [39]) and dipolar coupling between nuclear spin $\mathbf{I}$ and xenon 129 or xenon 131's nuclear spin $\mathbf{I}_2$ modulated by action potentials – These modulated couplings may then attenuate the anesthetic potency of nuclear-spin-carrying xenon 129 and xenon 131.

5. The Experimental Results by Li *et. el.* with Xenon Isotopes Applied to Mice

Recently, Li *et. al.* postulated that xenon isotopes might have different anesthetic potencies and experimentally tested the postulates in mice [11]. They found that "[t]he potency of two xenon isotopes with nuclear spin, xenon 129 and xenon 131, is less than the potency of two xenon isotopes, xenon 132 and xenon 134, that do not have nuclear spin[; t]his difference in potency cannot be explained, either by differences in outer electron shells (there are none) or the variations in atomic mass "[11] .

The conclusion by Li *et. al.* is that "[x]enon isotopes with nuclear spin are less potent than those without, and polarizability cannot account for the difference[; t]he lower anesthetic potency of ^{129}Xe may be the result of it participating in conscious processing and therefore partially antagonizing its own anesthetic potency" [11] .

Li *et. al.* suggest that "the quantum property of nuclear spin in the monoatomic anesthetic xenon promotes conscious processes at the xenon site of action, consistent with theories proposing quantum mechanisms in consciousness" and speculate that quantum entanglement of nuclear spins may be involved in consciousness [11].

6. Discussions & Conclusions

As shown and discussed above, spin-mediated consciousness theory [8, 19-20, 22] naturally explains the attenuation of the anesthetic potency of nuclear-spin-carrying xenon 129 and xenon 131 found by Li *et. al.*[11].

Therefore, the important results of Li *et. al.* [11], if replicable, provide direct and strong support to the spin-mediated consciousness theory put forward in 2002 [8] by the herein authors and its later developments [19-20, 22].

Li *et. al.* [11] did not provide a detailed mechanism of their own to explain their results but cites some work done recently on possible role of nuclear spin in consciousness or cognition in order to offer a plausible explanation. However, it is herein authors' views that the work cited by Li *et. al.* on the subject may be largely without merits to be discussed in the future if the circumstances call for such discussions.

For whatever reason (hopefully benign such as oversight), Li *et. al.* [11] did not cite or mention [8] which was the first, to the best knowledge of the herein first author, to propose nuclear/electron spin mediated/based consciousness theory back in 2002.

Among other plausible explanations of Li *et. al.*'s results [11], one is the different quantum behaviors of some xenon isotopes being fermions and some of them being bosons. Xenon 129 and xenon 131 are fermions but xenon 132 and xenon 134 are bosons (see, e.g., [53]). Thus, besides the difference in formation of quantum entanglement, their roles in spin chemistry and/or quantum dynamics of the brain, if not negligible, may be different.

In summary, we have discussed in this paper the mechanism of xenon anesthetic action in spin-mediated consciousness theory [8, 19-20, 22] in light of the recent experimental findings of Li, *et.al.* [11] on nuclear spins of xenon isotopes, xenon 131 and xenon 129, attenuating their anesthetic potency in mice. In the spin-mediated consciousness theory put forward in 2002 [8], molecules containing unpaired electron spins, such as oxygen (O_2) and nitric oxide (NO), interact with the mind pixels comprised of various nuclear spins in the brain and activate the latter as one of the steps generating conscious experience. Therefore, general anesthetics such as xenon produce anesthesia by perturbing O_2 and/or NO pathways thus distorting and/or blocking their activation functions in consciousness. Naturally, the nuclear spins of xenon 131 and xenon 129 may partially play the activating roles of displaced O_2 and/or NO among other possibilities and, thus attenuate the anesthetic potency of nuclear-spin-carrying xenon isotopes found by Li, *et.al.* [11].

References

1. Franks, N.P., Dickinson, R., de Sousa, S.L.M., Hall, A.C., Lieb, W.R. (1998): How does xenon produce anaesthesia? Nature, 396: pp. 324–324.
2. Andrijchenko, *et. al.* (2015): Andrijchenko, N.N., Ermilov, A.Y., Khriachtchev, L., Räsänen, M., Nemukhin A.V. (2015): Toward molecular mechanism of xenon anesthesia. J. Phys. Chem. A., 119(11): 2517-21.
3. Cantor, R. S. (1997): The lateral pressure profile in membranes: a physical mechanism of general anesthesia. Biochem. 36: 2339-2344.
4. Cameron J.W. (2006): The molecular mechanisms of general anaesthesia: dissecting the GABAA receptor. Continuing Education in Anaesthesia. Critical Care & Pain. 6 (2): 49–53.
5. Tu, K. (1998): Effect of anesthetics on the structure of a phospholipid bilayer. Biophys. J. 75: 2123-2134.
6. Koubi, L. (2000): Distribution of halothane in a dipalmitoylphosphatidylcholine bilayer from molecular dynamics calculations. Biophys. J. 78: 800-811.
7. Hu, H., Wu, M. (2001): Mechanism of anesthetic action: oxygen pathway perturbation hypothesis. Med. Hypotheses 57, 619-627.
8. Hu, H., Wu, M. (2002): Spin-mediated consciousness theory. arXiv:quant-ph/0208068v1; Med. Hypotheses (2004): 63: 633-646. For spin-mediated consciousness theory based on unpaired electron spins, see http://cogprints.org/3544 or http://cds.cern.ch/record/728255 .
9. Turin, L., Skoulakis, E. M. C., Horsfield, A. P. (2014): Electron Spin Changes during General Anesthesia in Drosophila. Proc. Natl. Acad. Sci. U. S. A. 111, E3524–E3533.
10. Fisher M.P.A. (2015): Quantum cognition: The possibility of processing with nuclear spins in the brain. Ann. Phys. 362:593–602.
11. Li, N., Lu, D., Yang, L., Tao, H., Xu, Y., Wang, C., et al. (2018): Nuclear spin attenuates the anesthetic potency of xenon isotopes in mice: implications for the mechanisms of anesthesia and consciousness. Anesthesiology 129, 271–277.
12. Chen, Z.B., Quantum neural network and soft quantum computing, arXiv:1810.05025v1 [quant-ph].
13. Simon, C. (2019): Can quantum physics help solve the hard problem of consciousness? J. Consciousness Studies, 26(5-6): 204-218.
14. Morris, P. G. (1986): Nuclear Magnetic Resonance Imaging in Medicine and Biology (Oxford: Clarendon Press).
15. Marsh, D. (2001): Polarity and permeation profiles in lipid membranes. Proc. Natl. Acad. Sci. USA 98: 7777–7782.
16. Hayashi, H. (2002): Advent of spin chemistry. RIKEN Review 44: 7-10.
17. Wertz, J. E., Bolton J. R. (1972): Electron Spin Resonance: Elementary theory and practical application (New York: McGraw-Hill Book Company).
18. Prosser, R. S., Luchette, P. A., Weterman, P. W., Rozek, A., Hancock, R. E. W. (2001): Determination of membrane immersion depth with O2: A high-pressure 19F NMR study. Biophys. J. 80:1406–1416
19. Hu, H., Wu, M. (2004): Action potential modulation of neural spin networks suggests possible role of spin in memory and consciousness. NeuroQuantology 2: 309-316.

20. Hu, H., Wu, M. (2008): Concerning spin as mind-pixel: how mind interacts with the brain through electric spin effects. NeuroQuantology 6: 26-31.
21. Bult, H., Boeckxstaens, G.E., Pelckmans, P.A., Jordaens, F.H., Van Maercke, Y.M. & Herman, A.G. (1990): Nitric oxide as an inhibitory non-adrenergic non-cholinergic neurotransmitter. Nature 345: 346–347.
22. Hu, H. & Wu, M. (2016): Quantum spin formulism of consciousness, in Biophysics of Consciousness (pp. 415-458), Poznanski, R. R., Tuszynski, J. A. & Feinberg, T. E. Eds (World Scientific Publishing Co., Singapore).
23. Tegmark, M. (2000): The importance of quantum decoherence in brain processes. Phys. Rev. E 61: 4194–4206.
24. Khitrin, A. K. & Ermakov, V. L. (2002): Spin Processor. arXiv:quant-ph/0205040
25. Khitrin, A. K., Ermakov, V. L. & Fung, B. M. (2002): Information storage using a cluster of dipolar-coupled spins. Chem. Phys. Lett. 360: 161-166.
26. Khitrin, A. K., Ermakov, V. L. & Fung, B. M. (2002): NMR molecular photography. J. Chem. Phys. 117: 6903-6906.
27. Warren, W. S. et al. (1993): Generation of impossible correlation peaks between bulk water and biomolecules in solution NMR. Science 262: 2005-2009.
28. Warren, W. S. et al. (1998): MR imaging contrast based on intermolecular zero-quantum coherence. Science 281: 274-250.
29. Julsgaard, B., Kozhekin, A. & Polzik, E. S. (2001): Experimentally long-lived entanglement of two macroscopic objects. Nature 413, 400–403.
30. Saeedi, K., Simmons, S., Salvail, J. Z., et. al. (2013): Room-temperature quantum bit storage exceeding 39 minutes using ionized donors in silicon-28.Science 342: 830–833.
31. Turanov, A. & Khitrin, A.K. (2013): Suspended long-lived NMR echo in solids. arXiv:1306.3485 [cond-mat.mes-hall].
32. Klimov, P. V., Falk, A. L., Christle, D. J., Dobrovitski,V. V. & Awschalom, D. D. (2015): Quantum entanglement atambient conditions in a macroscopic solid-state spin en-semble. Science Advances 1: 1-7
33. Lidar, D. A. & Whaley, K. B. (2003): Decoherence-free subspaces and subsystems. In: Irreversible Quantum Dynamics (Benatti , F., Floreanini, R. Eds.): 83-120 (Berlin: Springer Lecture Notes in Physics vol. 622).
34. Altepeter, J.P., Hadley, P.G., Wendelken, S.M., Berglund, A.J. & Kwiat, P.G. (2004): Experimental investigation of a two-qubit decoherence-free subspace. Phys. Rev. Lett. 92: 147901-1-4.
35. Barnet, A. & Weaver, J. C. (1991): Electroporation: a unified, quantitative theory of reversible electrical breakdown and mechanical rupture in artificial planar bilayer membranes. Bioelectrochem. Bioenerg.. 25: 163–182.
36. Morais-Cabral, J. H., Zhou, Y. & MacKinnon, R. (2001): Energy optimisation of ion conduction rate by the K selectivity filter. Nature 414, 37–42.
37. Sargent, D. F. (1975): Voltage jump/capacitance relaxation studies of bilayer structure and dynamics. J. Membr. Biol. 23: 227–247.

38. Saux, A. L., Ruysschaert, J. M. & Goormaghtigh, E. (2001): Membrane molecule reorientation in an electric field recorded by attenuated total reflection Fourier-transform infrared spectroscopy. Biophys. J. 80: 324-330–125.
39. Camacho, P.S., McKay, D., Dawson, D.M. et. al. (2016): Investigating unusual homonuclear intermolecular "through-space" J couplings in organochalcogen systems. Inorg. Chem. 55: 10881−10887.
40. Peshkovsky, A. & McDermott, A. E. (2000): Dipolar interactions in molecules aligned by strong AC electric fields. J. Magn. Reson. 147: 104–109.
41. Grayson, M. (2003): Electric field effects on 2JHH spin-spin coupling constants. Int'l J. Mol. Sci. 4: 218–230.
42. Buckingham, A. D. (1960): Chemical shifts in the nuclear magnetic resonance spectra of molecules containing polar groups. Can. J. Chem. 38: 300–307.
43. Sun, Q. F., Guo, H. & Wang, J. (2004): Spin-current-induced electric field. Phys. Rev. B 69: 054409.
44. Thomas, L.H. (1927): The kinematics of an electron with an axis, Phil. Mag. 7: 1-23.
45. Klauda, J.B., Roberts, M.F., Redfield, A.G., Brooks, B.R., Pastor, R.W. (2008): Rotation of lipids in membranes: molecular dynamics simulation, 31P spin-lattice relaxation, and rigid-body dynamics. Biophys J. 94(8): 3074-83.
46. Thayer Watkins, http://www.sjsu.edu/faculty/watkins/nuclearrot2.htm
47. https://wikieducator.org/images/d/d4/Mec0004.pdf
48. https://www2.chemistry.msu.edu/faculty/harrison/cem483/bohr_model.pdf
49. Bezrukov, S. M. & Vodyanoy, I. (1955): Noise-induced enhancement of signal transduction across voltage-dependent ion channels. Nature 378: 362–364.
50. Simonotto, E., Riani, M., Seife, C., Roberts, M., Twitty, J. & Moss, F. (1997): Visual perception of stochastic resonance. Phys. Rev. Lett. 78, 1186–1189.
51. Viola, L., Fortunato, E. M., Lloyd, S., Tseng, C. H. & Cory, D. G. (2000): Stochastic resonance and nonlinear response using NMR spectroscopy. Phys. Rev. Lett. 84: 5466–5469.
52. Bryan-Brown, G. P., Brown, C. V., Sage, I. C. & Hui, V. C. (1998): Voltage-dependent anchoring of a nematic liquid crystal on a grating surface. Nature 392: 365–367.
53. https://periodictable.com/Isotopes/054.129/index.html