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COORDINATION MECHANISM IN DOPAMINE NEURONS OF THE *SUBSTANTIA NIGRA PARS COMPACTA* AND NOREPINEPHRINE NEURONS OF THE *LOCUS COERULEUS*

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ABBREVIATIONS

LC = *locus coeruleus*; QD = quantum dot; SNc = *substantia nigra pars compacta*; MPTP = 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine

ABSTRACT

In this review, the author shows that ferritin has documented quantum dot material properties that have been reported in numerous independent studies and can generate coherent electron conduction bands over substantial distances, using quantum coherence. In addition, neuromelanin is a conjugated polymer, and quantum dot/conjugated polymer combinations have been reported in numerous independent studies to generate coherent electron conduction bands for solar photovoltaic applications. Both ferritin and neuromelanin are present in large quantities in the dopamine neurons of the *substantia nigra pars compacta* and the norepinephrine neurons of the *locus coeruleus*. The unique structure of subgroups of these neurons that have a large number of axon branches and synapses appears to have evolved to take advantage of these coherent electron conduction bands to coordinate conscious action. Independent clinical and laboratory studies are also reviewed that corroborate this theory of coordinated action in these neuron groups. Proposed research to validate the theory using an existing fluorescent probe material is proposed.

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Keywords – neuromelanin, ferritin, quantum dot, *substantia nigra pars compacta*, *locus coeruleus*, quantum biology

1.0 INTRODUCTION

Neuromelanin and ferritin are found in certain groups of catecholaminergic neurons, such as those of the *substantia nigra pars compacta* (SNc) and the *locus coeruleus* (LC). In this review, extensive evidence from independent research is discussed that shows that neuromelanin and ferritin have physical characteristics of quantum dots (QDs) and form a random array of QDs that could support the formation of electron conductance bands and the transfer of electrons between neurons. This transfer would be facilitated by ferritin in the intercellular fluid between those neurons, in combination with the generation of internal cell voltages and possibly pressures. These electron conductance bands would cause electrons to be transferred to/localize in the neuron having an axon that presents the lowest impedance path to ground, in part as a function of the extracellular field of downstream neurons. This configuration would effectively form a gate circuit that senses the impedance of each of the available axon paths to ground and conducts energy to the neuron that is best situated to activate, to facilitate formation of the action potential for that neuron. The neurological function of this gate circuit would enable multiple parallel processes to be performed by the brain and allow for selection of the "best" of those processes, which correlates to the experience of conscious selection of an action. Clinical and laboratory evidence corroborates this theory of function.

2.0 REVIEW

2.1 Ferritin QD properties

The technical literature clearly shows that ferritin has the physical properties of a QD. QDs were discovered in 1981 by Ekimov and Onushchenko, who studied color formation in semiconductor doped glass and observed that the absorption frequency of light in such doped glass was lower than expected. This effect was subsequently found to be caused by the quantum confinement of electron-hole pairs, also called "excitons," in small semiconductor crystals. QDs can be spherical and are usually 50 nm in diameter or smaller, although the size requirements for

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a specific QD are related to the Bohr radius of the excitons associated with the QD (Hennequin, 2008).

Ferritin is a spherical molecule with a diameter of approximately 12 nm and has an inner core of ferrihydrite that is approximately 8 nm (Kell and Pretorius, 2014). It was recognized as early as 1992 as having measurable quantum mechanical effects that are representative of QDs (Awschalom et al., 1992)—an observation that has been subsequently confirmed (Tejada et al., 1997; Schäfer-Nolte et al., 2014; He and Marles-Wright, 2015). Ferritin is a magnetic nanoparticle (Fittipaldi et al., 2011) and includes iron in a form that is antiferromagnetic at room temperature (Kaur, 2009). Antiferromagnetism has been shown to extend coherence lifetimes in QDs under certain conditions (Tackeuchi et al., 2006; Papaefthymiou, 2010; Cole and Hollenberg, 2009; Moro et al., 2015; Caram et al., 2015). Ferritin has both direct and indirect electron band gaps, meaning that it can generate excitons either due only to an electric field and in the absence of photons or as a function of photon energy. Measured band gaps range from approximately 2.1 eV to 3.07 eV and vary as a function of the number of iron atoms stored and the presence of different anionic elements or compounds (Colton et al., 2014; Smith, 2015). This prior work has thus established that the properties of naturally occurring ferritin can be used to generate quantum mechanical effects similar to those of man-made QDs; it has also established that ferritin can generate excitons due to an applied electric field. Electron flux, coherent tunneling, sequential tunneling, and hopping by changing the iron content inside the ferritin molecules are quantum effects that have been observed under laboratory conditions and are attributable to coherent electron transfer (Axford and Davis, 2007; Rakshit and Mukhopadhyay, 2012; Bostick et al., 2018; Kumar et al., 2016).

2.2 Neuromelanin QD properties

Although the technical literature does not appear to have addressed whether neuromelanin is a QD, melanin in sheet form has been studied for its semiconducting properties and for possible use as an organic semiconductor. Neuromelanin is a molecule that is approximately 30 nm in diameter and is found in certain catecholaminergic neurons, including dopamine neurons of the SNc and norepinephrine neurons of the LC (Schwartz and Roth, 2008; Oades and Halliday, 1987; Margolis et al., 2006; Damier et al., 1999). Neuromelanin has been extensively studied, but no consensus has been reached on its function or even its properties.

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Some observers have suggested that it is detritus that accumulates with age (Haining and Achat-Mendes, 2017). Others have suggested that it might function to collect heavy metals and other material that might otherwise damage the neuron (Zecca et al., 2008). Some studies have estimated the band gap of melanin to range from 2.5 eV to 3.4 eV (Crippa et al., 1978; Obeid and Hussain, 2013), but at least one study concluded that the electrical behavior of melanin can be explained as an electronic-ionic hybrid conductor. (Mostert et al., 2012). These observations are consistent with the pi-conjugated structure of melanin, because conjugated polymers can have conductive or semiconductive properties (Haining and Achat-Mendes, 2017; Ito, 2006). In addition, one documented function of neuromelanin is its ability to attract ferritin, as ferritin has been demonstrated to be present in proximity to the neuromelanin of the SNc (Tribl et al., 2009). Neuromelanin is formed by the reaction of iron with excess cytosolic catecholamines not accumulated in synaptic vesicles (Zecca et al., 2001).

2.3 Concentration of ferritin and neuromelanin in catecholaminergic neurons

Neuromelanin is found in organelles in catecholaminergic neurons, and it is found in the SNc and LC in greater proportion than in any other areas of the brain (Kumar et al., 2016). One study reported that neuromelanin organelles make up 50% of the image area of dorsal SN neurons, where the density of SN neurons is lower, and 25% of the image area of ventral SN neurons, where the density is greater. These observations suggest that neuromelanin content is lower in dopamine neurons in areas where they have greater density, where a lower density of neuromelanin and ferritin would be required to support the creation of electron conduction bands, and greater in areas where the neurons have lower density (Halliday et al., 2005; Gibb and Lees, 1991). Based on an average estimated number of 1000 neuromelanin organelles per neuron, 100 neuromelanin molecules per neuromelanin organelle and a cell body diameter of 25 μm, the average distance between neuromelanin molecules within the SNc and LC cell bodies is 50 nm, although it is noted that neuromelanin molecules aggregate in neuromelanin organelles and are not evenly distributed throughout the cell body.

Ferritin has been observed in large quantities in SNc cell bodies, adjacent to neuromelanin organelles, using immunogold markers, and with an estimated density on the same order of magnitude as neuromelanin (Tribl et al., 2009). Serum ferritin has a low normal concentration in men (350 ng mL^{-1}) and women (150 ng mL^{-1}), which equates to a concentration

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of approximately 5 x 10^{11}/2.2 x 10^{11} molecules per mL, or a separation distance of approximately 2 μm between molecules, but the concentration of ferritin is higher in the intercellular fluid of the SNc and LC. For example, one study estimated that the concentration of ferritin molecules in the SNc in healthy subjects is approximately 3 ferritin cores per 0.003 μm^3, which works out to a spacing of approximately 100 nm between ferritin cores, on average (Bertini et al., 2012). This is similar to the spacing of ferritin molecules as studied for application in the qubit-structured QD array, reported by Choi et al. (2005), and would support the formation of quantum mechanical effects between these molecules.

2.4 QD electron conductance band formation

Quantum mechanical effects have been shown to drive biological functions that were previously impossible to explain using non-quantum analysis (Brookes, 2017). The quantum mechanical characteristics of QDs are physical characteristics and have been tested in materials that are similar to the in vivo environment, such as celluloid hydrogels (Khabibullin et al., 2017). The effects of QDs formed from different materials and sizes on the quantum mechanical properties of structures formed from those QDs have been extensively studied, as have systems of multiple similar QDs (Dolde et al., 2013; Burkard et al., 1999). The effect of random variations in size and spacing of QDs has also been studied (Mahler and Wawer, 1998; Gomez et al., 2002; Nozik et al., 2010). These studies demonstrated the existence of quantum mechanical effects in random/non-regimented QD arrays that are observed more prominently in regimented QD arrays but which are still present at functional levels in such disordered arrays. One of these quantum effects is the creation of electron conductance bands, also referred to as mini-bands (Sun et al., 2008; Lazarenkova and Balandin, 2002). This effect was first demonstrated in a quantum well structure (which is a structure that constrains electron movement in two dimensions, instead of three dimensions, like a QD). A spatially extended electron wave function was demonstrated to exist when there was no applied electric field, which formed an electron conductance band (Bradshaw and Leavitt, 1998). As the electric field surrounding the quantum well structure was increased, the electron wave function reduced in extent (known as the Wannier-Stark regime) until it became fully localized into a single quantum well at a high electric field. This effect occurs when the low-energy electrons gain energy and decrease their wavelength.

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Electron conductance band formation has also been observed in both ordered and random three-dimensional arrays (Khituna et al., 2001; Jongen, 2013). Coupling between QDs modifies the energy level spacing of one QD depending on the state of its neighbors, such that neighboring QDs would positively influence the formation of electron conductance bands (Jaskolski et al., 2004).

Furthermore, the synergistic interaction of QDs (like ferritin) and conjugated polymers (like neuromelanin) has been demonstrated to facilitate exciton diffusion and non-radiative energy transfer between those materials (Guzelturk et al., 2014; Su et al., 2014). These studies indicated that such systems can cooperate to create persistent free electrons by disassociation of electrons from excitons formed by exposure of ferritin to electric fields or ions and the subsequent migration of the electrons into the conjugated polymer (Lattante, 2014; Ruizhi et al., 2017; Konstantatos and Sargent, 2009). These disassociated electrons facilitate the formation of electron conduction bands and may have lifetimes of more than 10 ms (Ruizhi et al., 2017). Quantum gating effects at room temperature have also been shown to facilitate the formation of electron conduction bands and other quantum effects in random arrays (Burkard et al., 1999).

Combined force vectors, such as simultaneously applied electric and strain fields, can be used to control the creation of quantum effects in QDs of different size, such as to generate entangled photons at room temperature “on demand” in asymmetric QDs (Zallo et al., 2014). This behavior is also referred to as “strain-tunable” (Zhang et al., 2015). The combination of such strain/stress field vectors has thus been demonstrated to result in controllable generation of quantum mechanical effects, even where the dimensional characteristics of the QDs are not matched. This suggests that such combined stress fields may be useful in the generation of other quantum effects at room temperature, such as formation of electron conduction bands and localization of electrons in those electron conduction bands (Wilmer et al., 2016).

2.5 Electric and pressure fields in SNc and LC neurons

To form electron conductance bands and cause the electrons to transport/localize between neuromelanin and/or ferritin in different neurons, it is necessary to have time-varying electric fields and possibly strain fields. Dynamic electric fields and strain fields exist in neurons. For example, a biophysical model for a mechanical action wave that accompanies the electrical component of the action potential has been reported and has been used to model predictions for a

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giant squid axon, garfish olfactory neurons, crab motor neurons, and rat hippocampal neurons (El Hady and Machta, 2015).

SNc dopamine neurons exhibit different electrical behaviors as a function of the extent of axonal branching. Neurons that have fewer branches exhibit autonomous firing of action potentials that invade the entire axonal arbor, but synaptic stimulation was required for neurons with a large number of branches (Pissadaki and Bolam, 2013; Matsuda et al., 2009). This difference in behavior of SNc dopamine neurons as a function of axonal branches shows that there are two classes of dopamine neurons in the SNc. The first class is associated with autonomous neuronal activity, such as the pacemaker functionality that has been observed in the SNc (Colpan and Slavin, 2010). The second class is associated with non-autonomous neuronal activity, such as reflexive or conscious action (Joensson et al., 2015; Parvizi and Damasio, 2001). The number of branches in the first class of SNc neurons is less than or equal to a transition point (9 branches), whereas the number of branches in the second class is greater than that transition point. Similar pacemaker activity and axonal branching has also been observed in the norepinephrine neurons of the LC. However, the function and structure of the LC neurons are varied and substantially different from the dopamine neurons of the SNc (Shirokawa et al., 2000; Alreja and Aghajanian, 1991).

2.6 Effect of efferent dendritic extracellular field on electrotonic axon impedance

The non-propagated electrical behavior of neurons can be modelled using electrotonic modelling (Buzsáki et al., 2012; Auerbach and Bennett, 1969). To cause electron localization in a disordered array of neuromelanin and ferritin molecules formed from the distribution of neuron cell bodies in the SNc and LC, it would be necessary for the electrons to have a low impedance path to ground. Otherwise, the electrons would simply localize at the initial position of each electron within the electron conductance bands (Freed, 1971). For electron conductance bands extending through neuromelanin and ferritin in an array of neuron cell bodies in the SNc and LC, the neuron with the lowest axonic impedance from the cell body to the common reference voltage of the intercellular fluid will present the lowest impedance path (Buzsáki et al., 2012; Svirskis et al., 2001; Schwindt and Crill, 1977). The extracellular field associated with the dendritic voltages at the synapse of each axon branch is seen as a negative resistance and functions to lower the instantaneous impedance seen from the cell body for that axon (Buzsáki et

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al., 2012). Such antidromic electrotonic behavior has been observed in the LC and elsewhere (Marzo et al., 2014; Auerbach and Bennett, 1969).

In the SNc, extensive axonal arborization is associated with the second class of dopamine neurons and involves hundreds of thousands of synaptic connections to the striatum (Pissadaki and Bolam, 2013). These efferent connections provide a large number of antidromic negative impedances when the associated efferent neural structures are activated but have not yet reached an action potential. The anatomy of the LC is different from the SNc in this regard. It includes four different classes of neurons, one of which has a large number of branches and is associated with efferent forebrain connections (Aston-Jones and Cohen, 2005; Schwarz and Luo, 2015; Samuels and Szabadi, 2008; Brightwell and Taylor, 2009). This class of neurons is associated with antidromic signal generation at efferent connections and may be involved in the hypothesized switching mechanism in the LC (Marzo et al., 2014). However, because of the anatomy of the LC, it is more difficult to identify a class of neurons that would likely have the lowest axonic impedance as seen from the cell body.

2.7 Intracellular voltage measurements

Intracellular voltages provide a source of energy to both generate excitons from ferritin and potentially neuromelanin and drive electron localization. Intracellular voltages have been measured using 30-nm “photonic voltmeters” and indicate that the cytoplasm of neurons forms distinct microdomains, where electric fields in excess of 1.0×10^6 volts/meter magnitude can be generated (Tyner et al., 2007). These field strengths are sufficient to create a high probability (>10%) of electron disassociation from an exciton at the interface to a conjugated polymer (Nenashev et al., 2012). Pacemaker activity of SNc and LC neurons helps to coordinate the generation of these voltages between neurons and could further facilitate localization (Guzman et al., 2009; Joensson et al., 2015; Parvizi and Damasio, 2001; Shirokawa et al., 2000; Alreja and Aghajanian, 1991).

2.8 Generation of Fe2+ ions from transferred electrons

The 8-nm diameter internal cavity of ferritin can hold up to 4500 iron atoms (Kell and Pretorius, 2014). The protein shell structure of ferritin allows ferrous ions to diffuse in and out of the core, through eight hydrophilic channels located at a three-fold symmetry axis (Theil, 2011;

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Theil, 2011; Bou-Abdallah et al., 2008; Tosha et al., 2010; Turano et al., 2010; Bertini et al., 2012). Ferritin stores iron in the form of ferrihydrite ($[Fe^{3+}]_2O_3 \bullet 0.5H_2O$), which is water insoluble, by using ferroxidase of the ferritin heavy chain protein to remove excess Fe^{2+} by oxidizing it to water-insoluble Fe^{3+}. The stored Fe^{3+} is reduced to water soluble Fe^{2+} iron by receipt of a free electron.

2.9 Calcium release due to Fe2+ ion release

Neural mechanisms that use Ca2+ ions are also activated by Fe2+ (Lopin et al., 2012), and Fe2+ may assist in the generation of action potentials in a manner similar to that of Ca2+ ions (Riegel and Williams, 2008). It has also been reported that Fe2+ generates Ca2+ signals through reactive oxygen species mediated ryanodine receptor stimulation (Hidalgo and Núñez, 2007). This effect has also been proposed to function as a cellular redox sensor (Hidalgo et al., 2005). Labile Fe2+ can be detected in cells using a reaction-based fluorescent probe, although this does not appear to have tried on dopamine neurons of the SNc or norepinephrine neurons of the LC (Xuan et al, 2016).

2.10 Iron in SNc and LC neurons

High levels of iron appear to either contribute or correlate to neuron damage in Parkinson's disease for dopamine neurons in the SNc and norepinephrine neurons of the LC to a greater extent than for other dopamine and norepinephrine neurons. These high levels of iron are also an indicator not only of higher levels of iron in those regions of the brain but also of an associated functional difference relating to iron between those areas and other areas with catecholaminergic neurons and neuromelanin (Zucca et al., 2006). This damage does not appear to be related only to iron content, since other regions of the brain with higher iron content, like the red nucleus, do not atrophy due to Parkinson's disease and may actually increase in size, possibly because of iron storage in lipofuscin instead of neuromelanin and ferritin (Colpan and Slavin, 2010).

2.11 Clinical and laboratory studies of damage to SNc and LC neurons

Selective damage to the SNc dopamine neurons can be caused by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and results in akinesia (Davis et al., 1979; Langston, 2017).

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This damage is unlike the damage caused by Parkinson's disease, which also causes damage to norepinephrine neurons of the LC (Zucca et al., 2006; Gesi et al., 2000). It is similar, though, in that such damage results in a loss of the ability to initiate conscious action, a loss that can be relieved by levodopa (Langston and Ballard, 1984). Damage to dopamine neurons caused by MPTP does not immediately result in cell death, and replacement of dopamine by treatment with levodopa may mitigate disruption of the Ca2+-mediated signaling pathways (Mattson 2012), which may be involved with Fe2+ mediated action potential generation, as discussed above. The damaged dopamine neurons are able to respond to dendritic inputs, such as to generate reflex actions (Morris 2000).

Clinical studies have shown that a decrement in LC function affects specific components of cognition in healthy older adults (Hämmerer et al., 2018). Laboratory studies on animals have also shown that loss of locus coeruleus neurons contributes to motor dysfunction (Rommelfanger et al., 2007). However, the reported complete destruction of the LC does not result in a loss of cognitive function in animals (Korf et al., 1973).

2.12 Relationship between dopamine neurons and movement

The relationship between dopamine neuron function and movement is demonstrated at a simple level by *Caenorhabditis elegans*, which has eight dopamine neurons. It has been observed that normal specimens with functioning dopamine neurons are able to make small adjustments to their speed to maintain constant rates of locomotion. However, mutant specimens with a defective gene for controlling dopamine synthesis made larger adjustments to their speeds, resulting in large fluctuations in their rates of locomotion. These mutant specimens also frequently exhibited both abnormally high and abnormally low average speeds (Omura et al., 2012). Replacement of dopamine was found to correct the movement abnormality in the mutant specimens, such that the correlation between more competitive movement and dopamine is clear. *C. elegans* also lacks neuromelanin, although ferritin is present (Anderson and Leibold, 2014), and could provide the basis for electron conductance band formation in the eight dopamine neurons of *C. elegans*.

The lifespan of *C. elegans* is only several weeks, which might not be long enough for neuromelanin to develop. For example, it takes several years for neuromelanin to accumulate in human infants, who are not born with substantial levels of neuromelanin in the SNc or LC (Itzev

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et al., 2002). However, earthworms have longer lifespans of up to several years. They have a neuromelanin-like substance in their dopamine neurons, which suggests that development of neuromelanin in dopamine neurons may have been guided by evolutionary vectors (Fyffe et al., 1999).

3.0 THEORY AND DISCUSSION

Numerous studies in the technical literature have established that ferritin is a QD and can generate excitons, either under normal conditions at room temperature or when exposed to a chemical and electrical environment that would be present within the cell bodies of dopamine and norepinephrine neurons. In addition, numerous studies have shown that ferritin or other QDs having concentrations similar to those found in the SNc and LC can generate coherent electron bands. Neuromelanin also has properties of QDs and is at least a conjugated polymer that can interact with QDs like ferritin to separate electrons from QD excitons and to extend the lifetime of those separated electrons. This would facilitate the creation of electron conductance bands in an array of ferritin and neuromelanin. Although the specific combination of ferritin and neuromelanin does not appear to have been studied, there is no reason why these materials would not exhibit quantum properties in combination that ferritin exhibits alone.

The dopamine neurons of the SNc and the norepinephrine neurons of the LC contain a substantial number of neuromelanin organelles. Ferritin molecules are attracted to those neuromelanin organelles and are present in large quantities inside of those neurons. Ferritin is also present in substantial concentrations in the intercellular fluid between neurons, at concentrations that support the formation of electron conductance bands that extend through the associated neurons. The spacing of these molecules within these neurons and in the inter cellular fluid (100 nm or less) is within one order of magnitude of spacings that have been demonstrated to result in the formation of electron conductance bands (20 nm), as shown in Figure 1.

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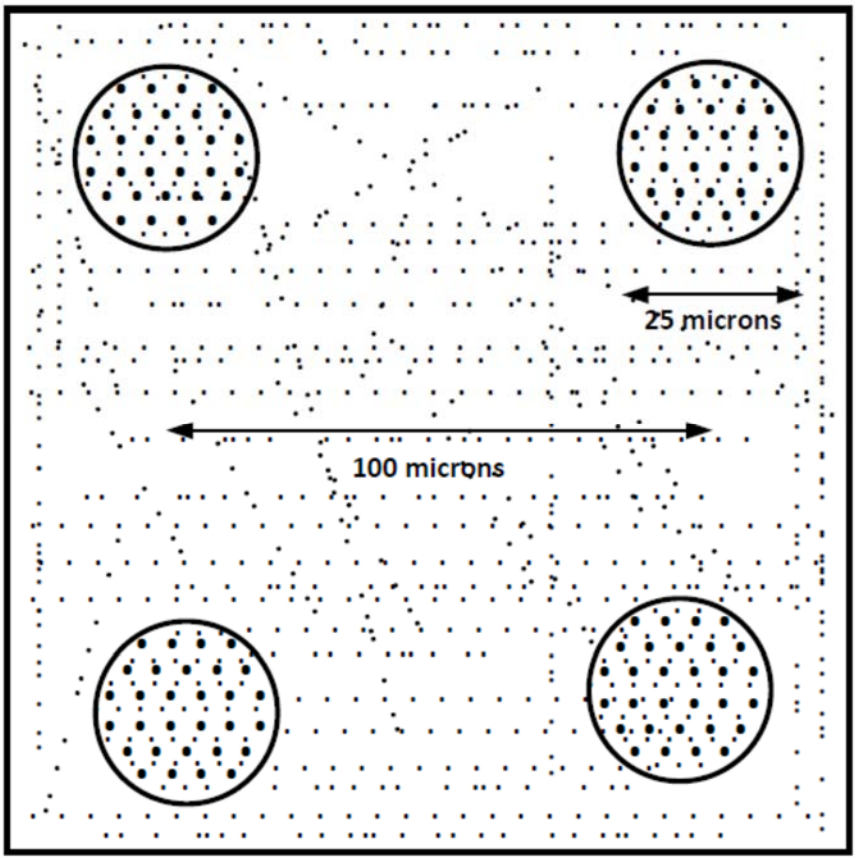

FIGURE 1 Simplified model of spacing of neuromelanin/ferritin molecules in SNc and LC neurons

Ferritin should also operate in a synergistic manner with neuromelanin, at least because neuromelanin is a conjugated polymer, but also because neuromelanin itself might exhibit the quantum mechanical properties of a QD. Numerous studies indicate that room temperature quantum mechanical effects are possible, at least for periods of hundreds of femtoseconds, and possibly for periods longer than a millisecond. These include studies involving different material types of QDs operating as quantum gates, and studies involving QDs that incorporate magnetic materials. Based on these studies, the combination of ferritin and neuromelanin at densities found in the SNc and LC neurons could support the formation of coherent electron bands for energy transfer (other regions of the brain also have neuromelanin organelles at lower concentrations but could potentially use the hypothesized energy transfer mechanism).

The unusual structures of the SNc and LC neurons that provide the ferritin and neuromelanin disordered arrays also provide synchronized electric fields in a manner that could facilitate exciton formation and subsequent localization of electrons in one of those neurons at a

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time. As a preliminary matter, a substantial electric field might not even be required to generate excitons. This is because the measured electron band gaps of ferritin could allow thermal excitons to form without an associated electric field. It has also been shown that anionic components of the intracellular environment, such as cl- ions, can cause excitons to form. However, low-level fields are also present in the intracellular environment. Although peak field strengths of greater than 3.5 x 10^6 volts/meter magnitude have been measured, those peak fields would not be sustained indefinitely and would vary as a function of cellular dynamics. As such, while a specific mechanism for exciton generation has not been conclusively identified, many mechanisms that have been shown to generate excitons in QDs are present in SNc and LC neuron cell bodies.

In addition, the SNc and LC regions include at least two different classes of catecholaminergic neurons, with a large number of neurons of a first class that have a small number of branches and a small number of neurons of a second class that have a very large number of branches (SNc) or antidromic signals (LC) . All these neurons express autonomous pacemaker activity, but that activity is only sufficient to generate an action potential in the first class of neurons. The axonal arbors associated with the second class of neurons in the SNc include hundreds of thousands of synapses and have substantially greater energy requirements associated with both action potential generation and axon arbor energization. The amount of energy associated with firing of these neurons suggests that they do not fire as frequently as the first class of neurons. Although dendritic inputs could generate action potentials, such dendritic inputs would normally be associated with reflex-type reactions, in response to strong neural stimuli from afferent neurons. Generation of non-reflex action potentials in the SNc, such as when associated physical actions are not reflexive but are rather the result of contemplation, would appear to require a different physical mechanism than dendritic inputs. Although this axonal arborization is not present in the LC, at least one mechanism (antidromic currents) would facilitate the impedance-based switching mechanism in a class of the norepinephrine neurons of the LC.

The extracellular electric fields associated with the dendrites of the efferent neurons of this second class of SNc and possibly LC neurons will result in an associated lower apparent impedance from the cell body for the associated axon. This lower impedance would cause electrons from the neurons that form the electron conductance bands to localize in the associated

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neuron with a lower axonal impedance, because it is best situated to conduct those electrons to the ground potential of the intercellular fluid. Consider a simple four-neuron example, as shown in Figure 2.

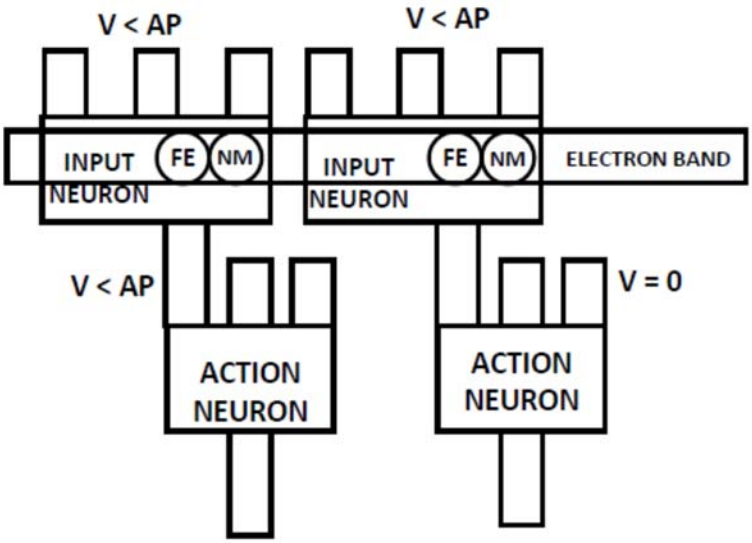

FIGURE 2 Simplified model of input neurons with neuromelanin/ferritin electron coherence bands

This structure has two "input" neurons that have afferent connections that are both stimulated, but where neither has reached the action potential. Each "input" neuron also has efferent connections to an "action" neuron. One "action" neuron is near its action potential due to dendritic potential, whereas the second "action" neuron is receiving no stimulation. If this organism had no electron conductance function, no action will occur unless something else happens—either another stimulus to the "input" neurons or another stimulus to the "action" neuron. If the organism has an electron conductance function for switching energy to the "input" neuron that is better situated to actuate an "action" neuron, it will be able to act without any additional inputs. Conversely, a similar organism without the electron conductance function would not be able to act without additional inputs, and thus be able to obtain food, avoid danger, or otherwise improve its odds for survival.

As seen in Figure 3, a neuron with a large number of axonal branches has an effective impedance that is lower than a neuron with a small number of axonal branches. This is because the impedances of each parallel branch (shown in Figure 1 as a resistance for simplicity) generally add as the inverse of the sum of the inverses (1/[1/R1 + 1/R2 + . . . 1/Rn]), in

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accordance with Ohms law (capacitances add directly, but capacitive impedances are small relative to resistance).

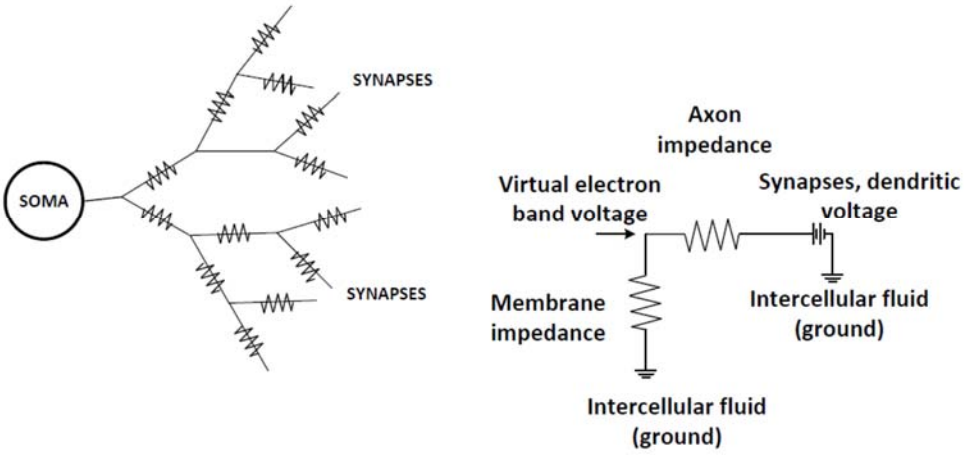

FIGURE 3 Simplified electrotonic model of axonal branches and virtual electron band voltage, relative to intercellular fluid ground

The energy delivered by the electron conductance function through the transfer of electrons to ferritin molecules of a single neuron would not flow to ground. Instead, the electron conductance function would operate to reduce the water-insoluble stored Fe3+ ions of the ferritin molecules to water-soluble Fe2+ ions. These Fe2+ ions would enter into solution in the intercellular fluid, and could either directly increase in the positive charge internal to the neuron, or trigger Ca2+ ion release through reactive oxygen species mediated ryanodine receptor stimulation, either of which would activate an action potential.

Prior to electron localization, the electrons in the electron conductance band are probabilistically extended over a large number of axons. As shown below in the simplified example of Figure 4 (Rougier), as the electron conductance function selects the axon path with the lowest impedance (which corresponds to the axon having the most synapses with dendrites that are at high dendritic voltages), it also electrically couples the parallel neural structures that are also connected to the associated efferent neurons.

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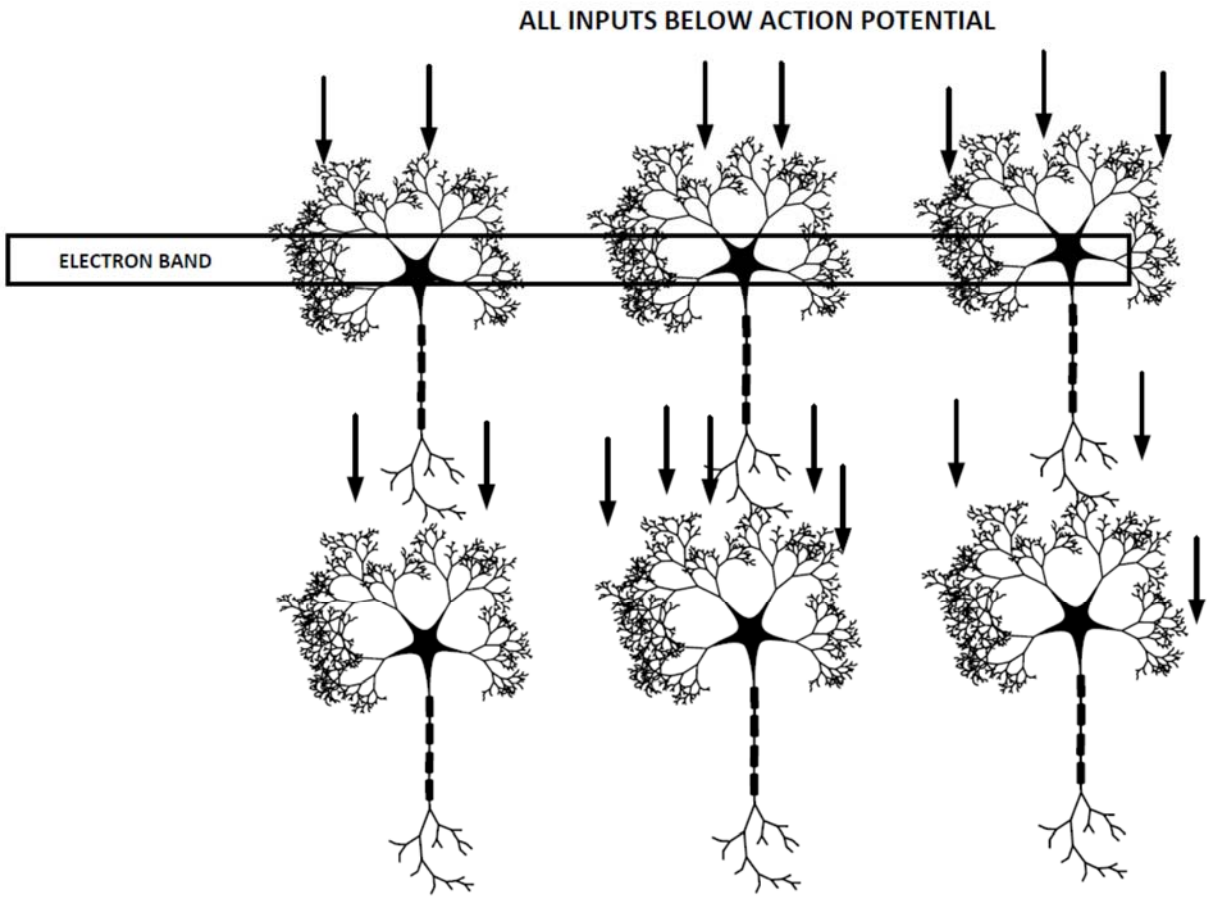

FIGURE 4 Simplified model of input neurons with electron conductance bands and associated action neurons

For an SNc neuron, most axonic connections are to the striatum; for LC neurons, axonic connections include several different areas, such as the cerebral cortex, the thalamus, and the spinal cord. However, axons with the lowest axonic impedance as seen from the cell body may be the ones that project to the cerebral cortex, which have a large number of branches and also have associated antidromic signals. The striatum controls movement, and the SNc is associated with neural signals that are associated with conscious movement, whereas the LC is associated with neural signals that are associated with conscious thought, as well as other functions. Based on this distinction, damage to SNc neurons that is sufficient to eliminate the electron conductance band formation, without associated damage to LC neurons, should result in a condition similar to locked-in syndrome. However, while non-reflexive conscious action would be incapacitated, reflexive action based on dendritic stimulation should still be capable of generating an action potential, if it is present and if the associated neurons are still functional at a

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reduced level that supports the generation of action potentials from dendritic inputs. The observations of akinesia in MPTP-injured patients and ability of these patients to perform reflexive actions, and to recover the ability to perform conscious action when treated with levodopa, appear to corroborate this theory of function. In particular, levodopa is believed to mitigate disruption of the Ca2+-mediated signaling pathways that would be involved in action potential generation in response to Fe2+ generation and reactive oxygen species mediated ryanodine receptor stimulation. In contrast, a similar level of damage to the LC without associated damage to the SNc should not result in loss of any kind of consciousness. Instead, it should only impair higher-level cognitive functions associated with the cerebral cortex. Observed loss of LC neurons appears to correlate with such impairment in reported studies. While these clinical studies are not conclusive evidence that ferritin and neuromelanin in the SNc and LC form electron conductance bands that assist with the generation of action potentials, they are not inconsistent with that theory. Additional work could be performed to verify this theory using fluorescent probes that have been used to detect the presence of Fe2+ ions in cells, which might be detected in *C. elegans* or earthworms, although testing on more complex neural structures of small mammals might ultimately be needed if the release of Fe2+ associated with action potentials in dopamine or norepinephrine neurons cannot be conclusively determined in simpler specimens.

4.0 CONCLUSION

The postulated electron conductance mechanism might seem unlikely, but other electron conductance mechanisms are widely accepted to exist and to regulate heartbeat, breathing, or even individual neurons themselves (Tyson et al., 2008). Such routing mechanisms are among known practical applications for QD arrays in semiconductor device applications. Therefore, it is at least possible that the SNc, LC, or possibly other regions of the brain have evolved to use the disordered arrays of neuromelanin and ferritin and that physical conductance mechanism, as hypothesized. Additional research to investigate this proposed physical mechanism could be conducted.

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