Design and Development of Novel Compounds Aimed at Optimizing the Function of Microtubules and Tubulin in the Immune System and the Brain

Marco Ruggiero

National Coalition of Independent Scholars, United States of America; marco.ruggiero@ncis.org

Abstract: This study describes the design and development of novel compounds aimed at optimizing the function of microtubules and tubulin in the immune system and the brain as they relate to the Orch OR theory of consciousness. These compounds are defined by the following molecular formulas: $C_{65}H_{100}CoN_{15}O_{22}P(C_6H_{12}O_5)$; $C_{65}H_{100}CoN_{15}O_{22}P(C_5H_{10}NO_4)$; $(C_{65}H_{100}CoN_{15}O_{22}P)(C_6H_{12}N_2O)_n$; $(C_{65}H_{100}CoN_{15}O_{22}P)(C_6H_{12}O_5)(C_6H_{12}N_2O)_n$; $(C_6H_{12}N_2O)_n(C_6H_{12}O_5)_m$; $Zn(C_6H_{12}O_5)_2$; These molecules, formulated under the form of drugs, health functional foods, or food supplements, have the potential to positively affect a number of areas ranging from prevention and therapy of neurological diseases to supporting the immune system.

Keywords: tubulin; microtubules; immune system; brain; consciousness; Orch OR

Introduction

The Orch OR (Orchestrated Objective Reduction) theory of consciousness postulates that consciousness arises from quantum computations in microtubules inside brain neurons. The theory was first proposed by Sir Roger Penrose and Professor Stuart Hameroff in the early 1990s. Microtubules are hollow, cylindrical structures that are found in all eukaryotic cells. They play a role in a variety of cellular processes, including cell division, cell shape, and intracellular transport. Tubulin proteins (alpha- and beta-tubulin), which make up the building blocks of microtubules, can exist in different conformational states. These conformational states are thought to be involved in the quantum computations that underlie consciousness. The Orch OR theory proposes that tubulin proteins in microtubules can exist in a superposition of states, meaning that they can be in multiple states at the same time. This superposition of states is thought to be necessary for quantum computations. The Orch OR theory also proposes that tubulin proteins can interact with each other in a way that allows them to entangle with each other. Entanglement is a phenomenon in which two entities are linked together in such a way that they share the same fate, even if they are separated by a large distance. The Orch OR theory proposes that the entanglement of tubulin proteins allows them to perform quantum computations that are thought to underlie the subjective experience of consciousness. The Orch OR theory has a number of important ramifications. For example, it suggests that consciousness is a fundamental property of the universe and not simply a product of the brain. It also suggests that consciousness is not limited to humans and other animals, but that it may be present in all quantum systems. This might implicate, for example, that consciousness may be present in subatomic particles, stars, and galaxies. It also means that consciousness may be present in computers and other artificial intelligence systems [García-Aguilar et al. 2023; Gardiner 2012; Hameroff 2021; Hameroff and Penrose 2014; Hameroff 2023; Ichikawa and Bui 2018; Lamme 2018; Reddy and Pereira 2017; Ruggiero 2023a; Ruggiero2023b].

The Orch OR theory could lead to new ways to diagnose and treat neurological diseases as well as disorders of consciousness. For example, it could lead to the development of new approaches that target microtubules and tubulin. Here, a novel approach targeting microtubules and tubulin is described; this approach is based on novel compounds deriving from the self-assembly of two types of information-containing aperiodic crystals. The first type of crystals consists of poly-lysine and

glutamic acid; the second type consists of sulfated polysaccharides containing fucose, galactose, xylose, arabinose and rhamnose, and lysine, alanine, tyrosine and cyanocobalamin. In addition, a novel compound that is based on the self-assembly of Zinc and fucose is described; this compound has the goal of targeting microtubules and tubulin in the context of the immune system.

Description of self-assembling information-containing aperiodic crystals

The rationale for designing and developing self-assembling information-containing aperiodic crystals is to use the potential of molecules such as cyanocobalamin, fucose or tyrosine to improve consciousness. As far as aperiodic crystals are concerned, in 1992 the International Union of Crystallography (IUCr) Commission on Aperiodic Structures proposed a new definition of aperiodic crystal by expanding the original definition of crystal. The new definition states that an aperiodic crystal is any solid that has a diffraction pattern that is essentially discrete, but in which three-dimensional lattice periodicity is absent. This means that the arrangement of atoms in the crystal is not perfectly repeating, but rather has a specific but non-periodic pattern. The IUCr definition also includes crystals in which three-dimensional periodicity is too weak to describe significant correlations in the atomic configuration, but which can be properly described by crystallographic methods developed for actual aperiodic crystals. In the context of biology, the term aperiodic crystal is used to describe genetic material, such as DNA or RNA. In other words, aperiodic crystals are solid materials with a specific but non-periodic arrangement of atoms. The self-assembling aperiodic crystals described here are based on the prescient intuition of Erwin Schroedinger. In 1944, the Austrian physicist published a book called "What is Life?" In this book, Schrödinger proposed a number of hypotheses about the nature of life, including the hypothesis that the genetic material containing the information for life is an aperiodic crystal [Ogryzko 2008]. Schrödinger's hypothesis was based on the idea that genetic information must be encoded in a physical structure that is stable and can be copied accurately. He argued that a periodic crystal would not be suitable for this purpose, because it would be too rigid and would not be able to accommodate all of the possible variations in genetic information. In contrast, an aperiodic crystal would be able to encode a wide variety of information in a stable and reproducible way. The key point here is that Schrödinger also argued that aperiodic crystals would be able to self-assemble and this is the peculiarity of the crystals described in this study.

The first type of crystals here described consists of poly-lysine and glutamic acid; the second type consists of crystals of sulfated polysaccharides containing fucose, galactose, xylose, arabinose and rhamnose, and lysine, alanine, tyrosine and cyanocobalamin. In the first type of crystals, poly-lysine constitutes the backbone for the establishment of non-covalent bonds between the positively charged amino groups of poly-lysine and the negatively charged acidic moiety of glutamic acid. In the second type of crystals, the mixture of lysine, alanine, tyrosine and cyanocobalamin is complexed, through formation of non-covalent bonds, with the acidic backbone constituted by the sulfated polysaccharides where the negatively charged sulfate ester and carboxylic groups of the polysaccharides interact with the positively charged moieties of the amino acids and cyanocobalamin. The two types of aperiodic crystals interact in a CO_2-enriched hydrophilic medium with the resulting self-assembly of complex structures composed of random-sized aperiodic crystals of [poly-lysine/glutamic acid], and [sulfated polysaccharides /lysine/alanine/tyrosine/cyanocobalamin]. The composition of the CO_2-enriched hydrophilic medium is the following:

Sodium (mg/L)   1.8
Magnesium (mg/L)   1.5
Calcium (mg/L)   8.4
Sulfates (mg/L)   7.8
Nitrates (mg/L)   6
pH   6.65
Resistivity (Ω)   18,000
Fixed residue as 180 °C (mg/L)   39

The aqueous medium contains dissolved CO_2.

These crystals, because of their random-size and, therefore, random distribution of electrical charges on their molecular surface, contain an elevated degree of information according to Shannon's

entropy equation. The Shannon entropy equation is a formula used to quantify the uncertainty or randomness of a probability distribution. It is named after Claude Shannon, the American mathematician and electrical engineer who is considered to be the father of information theory. The Shannon entropy equation is as follows:

$$H(X) = -\sum_i p(x\_i) \log_2(p(x\_i))$$

where:

H(X) is the entropy of the probability distribution X

p(x_i) is the probability of the event x_i occurring

An additional level of information can be found in the molecular structure of tyrosine, an amino acid taking part in the formation of the aperiodic crystals and also a key constituent of tubulin proteins. In the context of microtubules, tyrosine residues are involved in a number of important functions, including microtubule assembly and stability [Peris et al. 2006]. For example, tyrosine residues are involved in the formation of hydrogen bonds between alpha- and beta-tubulin subunits. These hydrogen bonds are essential for the stability of microtubules. Tyrosine residues are also involved in the interactions of microtubules with other proteins, such as motor proteins and microtubule-associated proteins. These interactions are essential for the many functions of microtubules in the cell. The main point here, however, is that tyrosine has pi resonance clouds that are deemed essential for consciousness [Hameroff, 2022]. Pi resonance clouds are delocalized electron clouds that are found in aromatic amino acids such as tryptophan, phenylalanine, and tyrosine. In order to have pi resonance, a molecule must have a flat ring structure with alternating single and double bonds. This is because the delocalized electrons are able to move freely around the ring, which allows them to form pi bonds. Orch OR proposes that the pi resonance clouds in microtubules can form quantum superpositions. This means that they can exist in multiple states at the same time. When the brain is processing information, these quantum superpositions are thought to collapse into specific states, giving rise to conscious experience [Hameroff 2022].

Role of cyanocobalamin in the self-assembling information-containing aperiodic crystals

Cyanocobalamin is a key component of one of the crystals; also known as vitamin B_{12}, it is an essential nutrient that plays a vital role in many bodily functions, including red blood cell formation, DNA synthesis, and nerve function. In the context of this study, however, the main reason for its integration in the crystal is that it plays a role in consciousness. Cyanocobalamin deficiency can lead to a variety of cognitive impairments, including impaired memory, attention, and executive function, whereas cyanocobalamin supplementation can improve cognitive function in people with cyanocobalamin deficiency [Pavlov et al. 2019]. One possible way that cyanocobalamin could influence consciousness is by affecting microtubule dynamics and stability since it is a cofactor for the enzyme methionine synthase, which is involved in the genesis of microtubules [Wu et al. 2019]. Therefore, cyanocobalamin deficiency could lead to impaired microtubule assembly and function, which could, in turn, affect consciousness. Another possible way that cyanocobalamin could influence consciousness is by affecting the production of neurotransmitters. Cyanocobalamin is involved in the synthesis of serotonin [Sangle et al. 2020] a neurotransmitter that plays a role in a variety of cognitive functions, including attention, memory, and mood. Therefore, cyanocobalamin deficiency could lead to impaired serotonin production, which could, in turn, affect consciousness. The relationship between cyanocobalamin and consciousness has a number of important implications. For example, it could lead to new treatments for disorders of consciousness, such as coma and Alzheimer's disease. Additionally, it could lead to new ways to improve cognitive function in healthy individuals. One of the most interesting aspects of the relationship between cyanocobalamin and consciousness is that it suggests that consciousness is influenced by food or food supplements. For example, eating a diet that is supplemented with cyanocobalamin may help to improve cognitive function and consciousness; and cyanocobalamin supplementation could be used to improve cognitive function in people with cyanocobalamin deficiency [Shipton and Thachil 2015; Wu et al. 2019; Li et al. 2021].

The effects of cyanocobalamin on microtubule dynamics and stability are also thought to be important for axonal transport that is the process by which nutrients and other molecules are transported along axons. In addition to its effects on microtubules, cyanocobalamin has also been shown to have a number of other functions in the nervous system. For example, cyanocobalamin is essential for the synthesis of myelin [Miller et al. 2005] and protects neurons from damage. All these effects of cyanocobalamin on the central nervous system led to suggestions that it may be used to prevent or treat neurodegenerative diseases such as Alzheimer's [Lauer et al. 2022] and Parkinson's disease [Dietiker et al. 2019].

Although cyanocobalamin is present in a number of commercially available supplements for oral use, its absorption when administered orally is relatively poor, with only about 1-2% of the ingested dose being absorbed. Therefore, in order to overcome this obstacle, the novel approach to oral supplementation of cyanocobalamin here described was developed; in this approach, the vitamin is complexed in the information-containing aperiodic crystals mentioned above.

Molecular interactions of cyanocobalamin with other constituents of the self-assembling information-containing aperiodic crystals

This section describes some notable interactions of cyanocobalamin with other constituents of the self-assembling information-containing aperiodic crystals in the aqueous carbonated medium specified above.

Interaction of cyanocobalamin with fucose

Cyanocobalamin and fucose are two very different molecules. Cyanocobalamin is a large, complex molecule that contains a cobalt atom at its center. Fucose is a small, simple sugar molecule that, in the context of the crystals described in this article, is the main component of a sulfated polysaccharide that is composed of fucose and sulfate groups, in addition to other minor components such as mannose, glucose, xylose, and uronic acid. Cyanocobalamin and fucose interact with each other through hydrogen bonding. Hydrogen bonding is a weak chemical bond that forms between two molecules that have hydrogen atoms bonded to electronegative atoms, such as oxygen or nitrogen. In addition, cyanocobalamin and fucose interact with each other through electrostatic interactions. Electrostatic interactions are forces of attraction or repulsion between two molecules that have opposite or similar charges.

Following is the molecular formula for a novel compound that contains both cyanocobalamin and fucose:

$C_{65}H_{100}\mathbf{Co}N_{15}O_{22}P(C_6H_{12}O_5)$

This compound is formed by linking a cyanocobalamin molecule to a fucose molecule through a hydrogen bond. The hydrogen bond is formed between the hydroxyl group (-OH) on the fucose molecule and the amide nitrogen ($-NH_2$) on the cyanocobalamin molecule.

Interactions of cyanocobalamin with glutamic acid

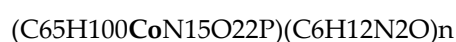
Following is the molecular formula for a novel compound where cyanocobalamin interacts with glutamic acid in water:

$C_{65}H_{100}\mathbf{Co}N_{15}O_{22}P(C_5H_{10}NO_4)$

This compound is formed by linking a cyanocobalamin molecule to a glutamic acid molecule through a hydrogen bond. The hydrogen bond is formed between the carboxyl group (-COOH) on the glutamic acid molecule and the amide nitrogen ($-NH_2$) on the cyanocobalamin molecule.

Interactions of cyanocobalamin with poly-lysine

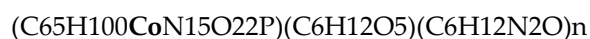
Following is the molecular formula for a novel compound where cyanocobalamin interacts with poly-lysine in water:

$(C_{65}H_{100}\mathbf{Co}N_{15}O_{22}P)(C_6H_{12}N_2O)n$

This compound is formed by linking a cyanocobalamin molecule to a poly-lysine molecule through electrostatic interactions. The positive charges on the amino groups of the poly-lysine

molecule are attracted to the negative charges on the phosphate group of the cyanocobalamin molecule. The value of n in the chemical formula depends on the length of the poly-lysine molecule.

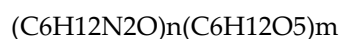
As it is evident from the interactions briefly described above, cyanocobalamin interacts with the two backbones of the aperiodic crystals, the basic backbone constituted by poly-lysine, and the acidic backbone constituted by the sulfated polysaccharide that is mainly composed of fucose and sulfate groups.

The interaction between cyanocobalamin and the two backbones is described by the following molecular formula:

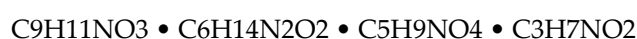
$(C_{65}H_{100}\textbf{Co}N_{15}O_{22}P)(C_6H_{12}O_5)(C_6H_{12}N_2O)n$

This novel compound is formed by linking a cyanocobalamin molecule to a fucose molecule and a poly-lysine molecule through electrostatic interactions and hydrogen bonds. The positive charges on the amino groups of the poly-lysine molecule are attracted to the negative charges on the phosphate group of the cyanocobalamin molecule. The hydroxyl group on the fucose molecule is attracted to the amide nitrogen on the cyanocobalamin molecule.

Interactions of poly-lysine with fucose

Following is the molecular formula for a novel compound where poly-lysine interacts with fucose:

$(C_6H_{12}N_2O)n(C_6H_{12}O_5)m$

This compound is formed by linking poly-lysine molecules to fucose molecules through hydrogen bonds. The amino groups on the poly-lysine molecules are attracted to the hydroxyl groups on the fucose molecules. The values of n and m in the chemical formula depend on the length of the poly-lysine molecule and the number of fucose molecules that are attached to it. Poly-lysine can be composed of anywhere from a few to hundreds of lysine molecules, and each lysine molecule can have up to six fucose molecules attached to it.

It will not have escaped the attention of the reader that the structure of the two aperiodic crystals are reminiscent of copolymer-1, a synthetic polypeptide composed of four amino acids found in myelin basic protein (MBP): L-Alanine, L-Glutamic acid, L-Lysine, and L-Tyrosine. Copolymer 1 has a random amino acid sequence and an average molecular mass of 6.4 kDa and its chemical composition is as follows:

$C_9H_{11}NO_3 \bullet C_6H_{14}N_2O_2 \bullet C_5H_9NO_4 \bullet C_3H_7NO_2$

The significant difference here is that in copolimer-1 the four amino acids are bound by peptide bonds, whereas in the aperiodic crystals hydrogen bonds and electrostatic forces are responsible for the self-assembly. Other significant differences are that copolymer-1 is not absorbed orally and does not contain cyanocobalamin [Arnon and Aharoni 2004].

An approach to microtubules and tubulin as they relate to the immune system

Microtubules and tubulin play an essential role in the immune system as they are involved in the following functions:

Cell migration: Microtubules are involved in the migration of immune cells, such as neutrophils, macrophages, and lymphocytes, to sites of infection or inflammation.

Cell adhesion: Microtubules are involved in the adhesion of immune cells to other cells or to the extracellular matrix. This is important for the formation of the immune synapse, which is a specialized structure that allows immune cells to communicate with each other and with other cells in the body.

Cytokine secretion: Microtubules are involved in the secretion of cytokines, which are signaling molecules that play a key role in the immune response.

Antigen presentation: Microtubules are involved in the presentation of antigens to T cells. This is an essential step in the activation of the adaptive immune response [for review on microtubules in the immune system, please see Kopf and Kiermaier 2021].

Here, an approach to support and optimize tubulin function in the immune system is described. This approach is based on the self-assembly of Zinc, a micronutrient, with fucose according to the following molecular formula:

Zn(C6H12O5)2

This novel compound is formed by the coordination of two fucose molecules to a zinc ion. The hydroxyl groups on the fucose molecules coordinate to the zinc ion through dative bonds. A dative bond, also known as a coordinate covalent bond, is a type of covalent bond in which both of the shared electrons come from the same atom. This is in contrast to a regular covalent bond, in which each atom contributes one electron to the bond. Dative bonds are typically formed when one atom has a lone pair of electrons and another atom has an empty electron orbital. The atom with the lone pair donates the electron pair to the atom with the empty orbital, and the two atoms share the electrons equally. Interestingly, dative bonds can exist in superposition states. A superposition state is a quantum mechanical state in which a system is in multiple states at the same time. For example, an electron can be in a superposition state of spin up and spin down. Superposition states of dative bonds are important for many biological processes. For example, photosynthesis involves the transfer of electrons between different molecules. These electron transfers are often mediated by dative bonds in superposition states. Superposition states of dative bonds are also important for quantum computing. Quantum computers use superposition states to perform calculations that are impossible for classical computers. Therefore, it can be hypothesized that the superposition states of the dative bonds pertaining to the Zinc-containing novel compound described above contribute to the quantum computations typical of Orch OR.

The novel compound described above is soluble in water, as the fucose molecules are hydrophilic. It is also stable in water, as the Zinc ion is tightly coordinated to the fucose molecules.

The rationale for choosing Zinc consists in the fact that it is an essential mineral that plays a role in many cellular processes, including those pertaining to the central nervous system [Frederickson et al. 2000]. In particular, Zinc is an important regulator of tubulin function and Zinc deficiency may play a role in the development of a number of diseases that are characterized by tubulin dysfunction [Drewes et al. 1992; Hesketh 1982; Eagle et al. 1983; Gower-Winter and Levenson 2012; Li et al. 2022; Wang et al. 1999;]. Therefore, Zinc supplementation has been shown to have beneficial effects in a number of animal models of diseases that are characterized by tubulin dysfunction, such as Alzheimer's and Parkinson's disease [Sikora and Ouagazzal 2021].

In the approach here described, Zinc is self-assembled with fucose from Fucoidan. Fucoidan is a sulfated polysaccharide that is found in brown seaweed [Abdel-Latif e al. 2022]. It has been shown to have a number of health-supporting properties, including:

Anti-cancer: Fucoidan has been shown to inhibit the growth and spread of cancer cells in a variety of studies. It is thought to work by targeting multiple pathways involved in cancer development and progression [Atashrazm et al. 2015].

Anti-inflammatory: Fucoidan has anti-inflammatory properties and can help to reduce inflammation throughout the body. This may be beneficial for a variety of conditions, including arthritis, inflammatory bowel disease, and asthma [Apostolova et al. 2020].

Antioxidant: Fucoidan is a powerful antioxidant that can help to protect cells from damage caused by free radicals. Free radicals are unstable molecules that can damage cells and contribute to a variety of diseases, including cancer, heart disease, and Alzheimer's disease [Husni et al. 2022].

Immune-boosting: Fucoidan can help to boost the immune system and fight off infection. It is thought to work by increasing the production of white blood cells and other immune cells [Zhang et al. 2015]. In addition, Fucoidan shows GcMAF-like activity as it reduces the expression of nagalase in human colon cancer cells [Bakunina et al. 2018].

Antiviral: Fucoidan has antiviral properties and can help to protect against a variety of viruses, including HIV, influenza, and herpes simplex virus [Krylova et al. 2020]. As far as viral diseases are concerned, Fucoidan has been shown to inhibit the replication of SARS-CoV-2 [Kwon et al. 2020]. It is thought to work by binding to the viral spike protein and preventing it from attaching to host cells. Fucoidan has also been shown to inhibit the activity of the viral main protease, which is an essential enzyme for viral replication. In addition to its antiviral properties, Fucoidan also has anti-

inflammatory and immunomodulatory properties. These properties may also be beneficial in the treatment of COVID-19 [Pradhan et al. 2022].

Anticoagulant: Fucoidan has anticoagulant properties and can help to prevent blood clots [Ushakova et al. 2008]. This may be beneficial for people with a high risk of blood clots, such as those with atrial fibrillation or deep vein thrombosis. In addition to these health-supporting properties, Fucoidan has also been shown to improve blood sugar control, reduce cholesterol levels, and protect against liver damage [Li et al. 2016].

Orch OR, the immune system and the rhyzome

The approaches described in this article are based, on one side, on the Orch OR theory of consciousness and its ramifications as far as the immune system is concerned, and, on the other side, on the concept of the rhyzome. The rhizome is a concept in philosophy developed by Gilles Deleuze and Félix Guattary [Roberts 2007; Ruggiero 2017; Ruggiero 2021]. It is a way of thinking about the world that is non-hierarchical and non-linear. The rhizome is a network of connections that can be extended in any direction. It is not bound by any central authority or structure. Orch OR is a theory of consciousness that proposes that consciousness arises from quantum computations in microtubules inside brain neurons. One relationship between the concept of the rhizome and Orch OR is that they both suggest that consciousness is not a centralized phenomenon. The rhizome is a network of connections that is not bound by any central authority or structure. Orch OR suggests that consciousness arises from quantum computations in microtubules, which are interconnected throughout the brain. This suggests that consciousness is a distributed phenomenon that is not localized to any specific part of the brain. Another relationship between the concept of the rhizome and Orch OR is that they both suggest that consciousness is dynamic and constantly changing. The rhizome is a network of connections that is constantly expanding and evolving. Orch OR suggests that consciousness arises from quantum computations, which are inherently dynamic and unpredictable. This suggests that consciousness is not a static state, but rather a dynamic process that is constantly changing. The relationship between the concept of the rhizome and Orch OR extends to the basic quantum features of Orch OR, that are represented by pi resonance clouds. Pi resonance clouds are often used to represent the uncertainty and ambiguity of the quantum world. The rhizome is a concept that embraces uncertainty and ambiguity. A rhizome can be envisioned as a network of roots that spread out underground. The roots are interconnected and nomadic, and they can grow in any direction. The rhizome is constantly shifting and changing, and it is impossible to predict where it will go next. Pi resonance clouds are like the rhizome in that they represent the uncertainty and ambiguity of the quantum world. The electrons in a pi resonance cloud are not bound to any one atom, and they can move in any direction. The pi resonance cloud is constantly shifting and changing, and it is impossible to predict where the electrons will go next. The connection between pi resonance clouds and the rhizome is a reminder that the world is a dynamic and unpredictable place. It is a place where new possibilities are constantly emerging. More in general, the relationship between the concept of the rhizome and Orch OR suggests that there may be a deeper connection between consciousness and the nature of reality than we currently understand.

Here, it is proposed that there is also a relationship between the rhizome and the immune system since the immune system can also be seen as a rhizome. It is a complex and interconnected system that is constantly adapting to new threats. The immune system is made up of a variety of different cells and molecules, all of which work together to protect the body from infection. There is no central hierarchy in the immune system; instead, the different cells and molecules communicate with each other and work together in a decentralized way [Farmer et al. 1986].

Here are some specific analogies between the concept of the rhizome and the immune system:

Interconnectedness: The rhizome is a decentralized system that is made up of interconnected parts. The immune system is also a decentralized system that is made up of interconnected cells and molecules.

Adaptability: The rhizome is constantly adapting to new conditions. The immune system is also constantly adapting to new threats.

Resilience: The rhizome is resilient to damage. The immune system is also resilient to damage.

Creativity: The rhizome is a creative system that is capable of generating new forms. The immune system is also a creative system that is capable of generating new antibodies and other immune cells to fight off new threats.

In the context of this article, the concept of the rhizome has been instrumental for designing ways to optimize the function of the immune system, for example, through the self-assembly of Zinc with fucose. One way to think about the relationship between Zinc and the concept of the rhizome is that Zinc is essential for the interconnectedness, creativity and adaptability of the immune system. The interconnectedness of the immune system is essential for its ability to function effectively. Zinc is essential for maintaining this interconnectedness by supporting the development and function of many of the different cells and molecules involved in the coordinated immune response. Zinc is also essential for the creativity of the immune system. Zinc is involved in the production of antibodies, which are "creatively" synthesized in response to antigens whose occurrence is unpredictable. Finally, the adaptability of the immune system is also essential for its ability to protect the body from new threats. Zinc is essential for maintaining this adaptability by supporting the development and function of dendritic cells, which are responsible for detecting and presenting new antigens to the immune system.

Likewise, cyanocobalamin, the constituent of the approach targeting microtubules and tubulin in the context of consciousness, has a functional connection with the concept of the rhyzome. One relationship between the concept of the rhizome and cyanocobalamin is that they both suggest that the body and mind are interconnected. The rhizome is a metaphor for the way that different parts of the body and mind are interconnected. Cyanocobalamin is a nutrient that is essential for the proper functioning of both the body and mind. Another relationship between the concept of the rhizome and cyanocobalamin is that they both suggest that the body and mind are constantly changing. The rhizome is a dynamic network of connections that is constantly evolving. Cyanocobalamin is a nutrient that is essential for the growth and repair of cells. This suggests that cyanocobalamin may play a role in the dynamic and ever-changing nature of the body and mind. Both the rhizome and cyanocobalamin suggest that the body and mind are interconnected and constantly changing.

Conclusions

This article describes novel compounds defined by the following molecular formulas:
$C_{65}H_{100}\textbf{Co}N_{15}O_{22}P(C_6H_{12}O_5)$
$C_{65}H_{100}\textbf{Co}N_{15}O_{22}P(C_5H_{10}NO_4)$
$(C_{65}H_{100}\textbf{Co}N_{15}O_{22}P)(C_6H_{12}N_2O)_n$
$(C_{65}H_{100}\textbf{Co}N_{15}O_{22}P)(C_6H_{12}O_5)(C_6H_{12}N_2O)_n$
$(C_6H_{12}N_2O)_n(C_6H_{12}O_5)_m$
$\textbf{Zn}(C_6H_{12}O_5)_2$

These compounds are able to support and optimize the function of microtubules and tubulin in the context of Orch OR as well as in the context of their role in the immune system. These formulas, once integrated in drugs, health functional foods, or food supplements, have the potential to prevent and treat a number of conditions, ranging from neurological diseases to immune deficiencies, cancer, and diseases caused by viruses.

Corresponding Author: Marco Ruggiero, MD, PhD, National Coalition of Independent Scholars. 125 Putney Rd Battleboro, VT 05301, United States of America. email: marco.ruggiero@ncis.org.

Author Contributions: The author contributed solely to the work.

Funding: The author did not receive any funding for this study.

Acknowledgments: The author wishes to thank Mr. Choi Hyuk of Dana Biologics for encouragement in pursuing this line of research as well as for inspiring discussion.

Conflicts of interest: The formulas described in this study are incorporated in health functional foods and food supplements that are commercially available. However, these products are not mentioned in this study, neither the author receives any benefit from the sales of these products.

Ethical approval: Not applicable. This article does not report experiments performed on humans or animals.

Consent to participate: Not applicable.

References

1. Abdel-Latif HMR, Dawood MAO, Alagawany M, Faggio C, Nowosad J, Kucharczyk D. Health benefits and potential applications of fucoidan (FCD) extracted from brown seaweeds in aquaculture: An updated review. Fish Shellfish Immunol. 2022 Mar;122:115-130. doi: 10.1016/j.fsi.2022.01.039. https://pubmed.ncbi.nlm.nih.gov/35093524/

2. Apostolova E, Lukova P, Baldzhieva A, Katsarov P, Nikolova M, Iliev I, Peychev L, Trica B, Oancea F, Delattre C, Kokova V. Immunomodulatory and Anti-Inflammatory Effects of Fucoidan: A Review. Polymers (Basel). 2020 Oct 13;12(10):2338. doi: 10.3390/polym12102338. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7602053/

3. Arnon R, Aharoni R. Mechanism of action of glatiramer acetate in multiple sclerosis and its potential for the development of new applications. Proc Natl Acad Sci U S A. 2004 Oct 5;101 Suppl 2(Suppl 2):14593-8. doi: 10.1073/pnas.0404887101. https://pubmed.ncbi.nlm.nih.gov/15371592/

4. Atashrazm F, Lowenthal RM, Woods GM, Holloway AF, Dickinson JL. Fucoidan and cancer: a multifunctional molecule with anti-tumor potential. Mar Drugs. 2015 Apr 14;13(4):2327-46. doi: 10.3390/md13042327. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4413214/

5. Bakunina I, Chadova O, Malyarenko O, Ermakova S. The Effect of Fucoidan from the Brown Alga Fucus evanescence on the Activity of α-N-Acetylgalactosaminidase of Human Colon Carcinoma Cells. Mar Drugs. 2018 May 10;16(5):155. doi: 10.3390/md16050155. https://pubmed.ncbi.nlm.nih.gov/29748462/

6. Dietiker C, Kim S, Zhang Y, Christine CW. Characterization of Vitamin B12 Supplementation and Correlation with Clinical Outcomes in a Large Longitudinal Study of Early Parkinson's Disease. J Mov Disord. 2019 May;12(2):91-96. doi: 10.14802/jmd.18049. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6547038/

7. Drewes G, Lichtenberg-Kraag B, Döring F, Mandelkow EM, Biernat J, Goris J, Dorée M, Mandelkow E. Mitogen activated protein (MAP) kinase transforms tau protein into an Alzheimer-like state. EMBO J. 1992 Jun;11(6):2131-8. doi: 10.1002/j.1460-2075.1992.tb05272.x. https://pubmed.ncbi.nlm.nih.gov/1376245/

8. Eagle GR, Zombola RR, Himes RH. Tubulin-zinc interactions: binding and polymerization studies. Biochemistry. 1983 Jan 4;22(1):221-8. doi: 10.1021/bi00270a032. M https://pubmed.ncbi.nlm.nih.gov/6403030/

9. Farmer JD, Packard NH, Perelson AS.The immune system, adaptation, and machine learning. Physica D: Nonlinear Phenomena. 1986 Vol 22(1–3):187-204. https://doi.org/10.1016/0167-2789(86)90240-X

10. Frederickson CJ, Suh SW, Silva D, Frederickson CJ, Thompson RB. Importance of zinc in the central nervous system: the zinc-containing neuron. J Nutr. 2000 May;130(5S Suppl):1471S-83S. doi: 10.1093/jn/130.5.1471S. https://pubmed.ncbi.nlm.nih.gov/10801962/

11. García-Aguilar I, Zwaan S, Giomi L. Polymorphism in tubulin assemblies: A mechanical model. Phys. Rev. Research 5, 023093 doi:https://doi.org/10.1103/PhysRevResearch.5.023093

12. Gardiner J. Insights into plant consciousness from neuroscience, physics and mathematics: a role for quasicrystals? Plant Signal Behav. 2012 Sep 1;7(9):1049-55. doi: 10.4161/psb.21325. https://pubmed.ncbi.nlm.nih.gov/22899055/

13. Gower-Winter SD, Levenson CW. Zinc in the central nervous system: From molecules to behavior. Biofactors. 2012 May-Jun;38(3):186-93. doi: 10.1002/biof.1012. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3757551/

14. Hameroff S. 'Orch OR' is the most complete, and most easily falsifiable theory of consciousness. Cogn Neurosci. 2021 Jan-Jan;12(2):74-76. doi: 10.1080/17588928.2020.1839037. https://pubmed.ncbi.nlm.nih.gov/33232193/

15. Hameroff S, Penrose R. Consciousness in the universe: a review of the 'Orch OR' theory. Phys Life Rev. 2014 Mar;11(1):39-78. doi: 10.1016/j.plrev.2013.08.002.https://pubmed.ncbi.nlm.nih.gov/24070914/

16. Hameroff S. Consciousness, Cognition and the Neuronal Cytoskeleton - A New Paradigm Needed in Neuroscience. Front Mol Neurosci. 2022 Jun 16;15:869935. doi: 10.3389/fnmol.2022.869935. https://pubmed.ncbi.nlm.nih.gov/35782391/

17. Hameroff S. 'Smear campaign' at the crossroad of consciousness and spacetime geometry -: Comment on "At the crossroad of the search for spontaneous radiation and the Orch OR consciousness theory" by Derakhshani et al. Phys Life Rev. 2023 Mar;44:173-175. doi: 10.1016/j.plrev.2023.01.006. https://pubmed.ncbi.nlm.nih.gov/36764151/

18. Hesketh JE. Zinc-stimulated microtubule assembly and evidence for zinc binding to tubulin. Int J Biochem. 1982;14(11):983-90. doi: 10.1016/0020-711x(82)90059-3. https://pubmed.ncbi.nlm.nih.gov/7141075/

19. Husni A, Izmi N, Ayunani FZ, Kartini A, Husnayain N, Isnansetyo A. Characteristics and Antioxidant Activity of Fucoidan from Sargassum hystrix: Effect of Extraction Method. Int J Food Sci. 2022 Apr 13;2022:3689724. doi: 10.1155/2022/3689724. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9020993/

20. Ichikawa M, Bui KH. Microtubule Inner Proteins: A Meshwork of Luminal Proteins Stabilizing the Doublet Microtubule. Bioessays. 2018 Mar;40(3). doi: 10.1002/bies.201700209. https://pubmed.ncbi.nlm.nih.gov/29430673/

21. Kopf A, Kiermaier E. Dynamic Microtubule Arrays in Leukocytes and Their Role in Cell Migration and Immune Synapse Formation. Front Cell Dev Biol. 2021 Feb 9;9:635511. doi: 10.3389/fcell.2021.635511. https://pubmed.ncbi.nlm.nih.gov/33634136/

22. Krylova NV, Ermakova SP, Lavrov VF, Leneva IA, Kompanets GG, Iunikhina OV, Nosik MN, Ebralidze LK, Falynskova IN, Silchenko AS, Zaporozhets TS. The Comparative Analysis of Antiviral Activity of Native and Modified Fucoidans from Brown Algae Fucus evanescens In Vitro and In Vivo. Mar Drugs. 2020 Apr 22;18(4):224. doi: 10.3390/md18040224. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7230360/

23. Kwon PS, Oh H, Kwon SJ, Jin W, Zhang F, Fraser K, Hong JJ, Linhardt RJ, Dordick JS. Sulfated polysaccharides effectively inhibit SARS-CoV-2 in vitro. Cell Discov. 2020 Jul 24;6(1):50. doi: 10.1038/s41421-020-00192-8. https://pubmed.ncbi.nlm.nih.gov/32714563/

24. Lamme VAF. Challenges for theories of consciousness: seeing or knowing, the missing ingredient and how to deal with panpsychism. Philos Trans R Soc Lond B Biol Sci. 2018 Sep 19;373(1755):20170344. doi: 10.1098/rstb.2017.0344. https://pubmed.ncbi.nlm.nih.gov/30061458/

25. Lauer AA, Grimm HS, Apel B, Golobrodska N, Kruse L, Ratanski E, Schulten N, Schwarze L, Slawik T, Sperlich S, Vohla A, Grimm MOW. Mechanistic Link between Vitamin B12 and Alzheimer's Disease. Biomolecules. 2022 Jan 14;12(1):129. doi: 10.3390/biom12010129. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8774227/

26. Li J, Chen K, Li S, Feng J, Liu T, Wang F, Zhang R, Xu S, Zhou Y, Zhou S, Xia Y, Lu J, Zhou Y, Guo C. Protective effect of fucoidan from Fucus vesiculosus on liver fibrosis via the TGF-β1/Smad pathway-mediated inhibition of extracellular matrix and autophagy. Drug Des Devel Ther. 2016 Feb 12;10:619-30. doi: 10.2147/DDDT.S98740. https://pubmed.ncbi.nlm.nih.gov/26929597/

27. Li, S., Guo, Y., Men, J. et al. The preventive efficacy of vitamin B supplements on the cognitive decline of elderly adults: a systematic review and meta-analysis. BMC Geriatr 21, 367 (2021). https://doi.org/10.1186/s12877-021-02253-3 https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-021-02253-3

28. Li Z, Liu Y, Wei R, Yong VW, Xue M. The Important Role of Zinc in Neurological Diseases. Biomolecules. 2022 Dec 23;13(1):28. doi: 10.3390/biom13010028. https://www.mdpi.com/2218-273X/13/1/28

29. Miller A, Korem M, Almog R, Galboiz Y. Vitamin B12, demyelination, remyelination and repair in multiple sclerosis. J Neurol Sci. 2005 Jun 15;233(1-2):93-7. doi: 10.1016/j.jns.2005.03.009. https://pubmed.ncbi.nlm.nih.gov/15896807/

30. Ogryzko VV. Erwin Schroedinger, Francis Crick and epigenetic stability. Biol Direct. 2008 Apr 17;3:15. doi: 10.1186/1745-6150-3-15. https://pubmed.ncbi.nlm.nih.gov/18419815/

31. Pavlov CS, Damulin IV, Shulpekova YO, Andreev EA. Neurological disorders in vitamin B12 deficiency. Ter Arkh. 2019 May 16;91(4):122-129. doi: 10.26442/00403660.2019.04.000116. https://pubmed.ncbi.nlm.nih.gov/31094486/

32. Peris L, Thery M, Fauré J, Saoudi Y, Lafanechère L, Chilton JK, Gordon-Weeks P, Galjart N, Bornens M, Wordeman L, Wehland J, Andrieux A, Job D. Tubulin tyrosination is a major factor affecting the recruitment of CAP-Gly proteins at microtubule plus ends. J Cell Biol. 2006 Sep 11;174(6):839-49. doi: 10.1083/jcb.200512058. https://pubmed.ncbi.nlm.nih.gov/16954346/

33. Pradhan B, Nayak R, Patra S, Bhuyan PP, Behera PK, Mandal AK, Behera C, Ki JS, Adhikary SP, MubarakAli D, Jena M. A state-of-the-art review on fucoidan as an antiviral agent to combat viral infections. Carbohydr Polym. 2022 Sep 1;291:119551. doi: 10.1016/j.carbpol.2022.119551. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9057937/

34. Reddy JSK, Pereira C. Understanding the emergence of microbial consciousness: From a perspective of the Subject-Object Model (SOM). J Integr Neurosci. 2017;16(s1):S27-S36. doi: 10.3233/JIN-170064. https://pubmed.ncbi.nlm.nih.gov/29254105/

35. Roberts M. Capitalism, psychiatry, and schizophrenia: a critical introduction to Deleuze and Guattari's Anti-Oedipus. Nurs Philos. 2007 Apr;8(2):114-27. doi: 10.1111/j.1466-769X.2007.00306.x. https://pubmed.ncbi.nlm.nih.gov/17374072/

36. Ruggiero M The Human Microbiota and the Immune System; Reflections on Immortality. Madridge J Immunol. 2017; 1(1): 18-22. doi: 10.18689/mjim-1000106 https://madridge.org/journal-of-immunology/mjim-1000106.php

37. Ruggiero M The brain microbiota as it relates to the orch or theory of consciousness. J Neurol Stroke. 2021;11(5):131–133. doi: 10.15406/jnsk.2021.11.00471 https://medcraveonline.com/JNSK/JNSK-11-00471.pdf

38. Ruggiero M (a). Study of structural similarities between tubulin, TMC1, AND FTSZ proteins as they relate to mechanosensory transduction in the context of the orch or theory of consciousness. Int J Radiol Radiat Ther. 2023;10(3):65–72. doi: 10.15406/ijrrt.2023.10.00358. https://medcraveonline.com/IJRRT/IJRRT-10-00358.pdf

39. Ruggiero, M (b). On the Natural Intelligence and Consciousness of the Immune System and Its Relationship with the Brain. Preprints 2023, 2023081335. https://doi.org/10.20944/preprints202308.1335.v1

40. Sangle P, Sandhu O, Aftab Z, Anthony AT, Khan S. Vitamin B12 Supplementation: Preventing Onset and Improving Prognosis of Depression. Cureus. 2020 Oct 26;12(10):e11169. doi: 10.7759/cureus.11169. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7688056/

41. Shipton MJ, Thachil J. Vitamin B12 deficiency - A 21st century perspective. Clin Med (Lond). 2015 Apr;15(2):145-50. doi: 10.7861/clinmedicine.15-2-145. https://pubmed.ncbi.nlm.nih.gov/25824066/

42. Sikora J, Ouagazzal AM. Synaptic Zinc: An Emerging Player in Parkinson's Disease. Int J Mol Sci. 2021 Apr 29;22(9):4724. doi: 10.3390/ijms22094724. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8125092/

43. Ushakova NA, Morozevich GE, Ustiuzhanina NE, Bilan MI, Usov AI, Nifant'ev NE, Preobrazhenskaia ME. [Anticoagulant activity of fucoidans from brown algae]. Biomed Khim. 2008 Sep-Oct;54(5):597-606. Russian. PMID: 19105402. https://pubmed.ncbi.nlm.nih.gov/19105402/

44. Wang FD, Zhao FJ, Jing NH. [Effect of dietary zinc on microtubule-associated protein 2 expression in the brain of mice]. Sheng Li Xue Bao. 1999 Oct;51(5):495-500. Chinese. PMID: 11498945. https://pubmed.ncbi.nlm.nih.gov/11498945/

45. Wu F, Xu K, Liu L, Zhang K, Xia L, Zhang M, Teng C, Tong H, He Y, Xue Y, Zhang H, Chen D, Hu A. Vitamin B$_{12}$ Enhances Nerve Repair and Improves Functional Recovery After Traumatic Brain Injury by Inhibiting ER Stress-Induced Neuron Injury. Front Pharmacol. 2019 Apr 24;10:406. doi: 10.3389/fphar.2019.00406. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6491933/

46. Zhang W, Oda T, Yu Q, Jin JO. Fucoidan from Macrocystis pyrifera has powerful immune-modulatory effects compared to three other fucoidans. Mar Drugs. 2015 Feb 19;13(3):1084-104. doi: 10.3390/md13031084. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4377974/