Original Article

Quantum biological considerations on the mechanism of SUNGOiD water (CCMNS solution) dissociating Aβ aggregates in nerve cells

[1)] Institute of Environmental Microbiology, Tadao 2-15-5, Machida, Tokyo 194-0035, Japan
[2)]Mineral Activation Technical Research Center, Omuta, Fukuoka 836-0041, Japan

Yasuhiro Yoshikawa[1)] , Koichi Furusaki[2)]

Summary The mesoscopic nanosized structures with calcium carbonates ($CaCO_3$/$Ca(HCO_3)_2$) as the main component exist during the formation of plant growth points, coral skeletons, and layered shells. When a solution is made by applying ultrasonic waves, high voltage and infrared rays to a water extract of dried plant groups and mixing it with the permeated water of a mixture of coral, shells and lime of different capacities, a mesoscopic nanosized structure of calcium carbonates (CCMNS) is regenerated.

This aqueous solution is named SUNGOiD water (CCMNS solution). This mesoscopic structure emits terahertz (THz) pulse waves. Recently, these THz pulse waves dissociated abnormal prion proteins (prions) with beta-sheet structures, making them non-infectious. The SUNGOiD water also inhibited the aggregation of Aβ and Tau proteins and dissociated the aggregated proteins, which were thought to be the cause of Alzheimer's disease, at the molecular, cellular and model animal (Drosophila) levels. There is, however, no clear explanation of how THz waves inhibit the aggregation of these proteins, or dissociation of abnormal protein aggregation.

We thought that quantum mechanics would be necessary to understand. The nano-level phenomenon may be occurred in which THz waves emitted from mesoscopic structure created by living organisms themselves induces vibration of aggregated proteins within cells. In this study, we investigated the dissociation of intracellular Aβ aggregate using a quantum biological perspective and discuss the possibility that this phenomenon can occur quantum mechanically interactions.

Key words: SUNGOiD water (CCMNS solution), terahertz pulse wave, mesoscopic structure, Prion, Aβ and Tau proteins, Alzheimer disease, CCMNS (previous name: CAC717)

*Correspondence to: Yoshikawa, Y. : y-yoshikawa@ous.ac.jp
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Introduction

Research for terahertz (THz) waves is said to have begun in the 1890s. Despite being researched for over 100 years, they have not been put to practical use. The reason is that THz waves are a "difficult frequency band" to handle[1].

THz waves are electromagnetic waves that fall between radio waves and light, and in general, the technology used to handle radio waves and light differs each other. THz waves have too low an energy level to be measured as light, and their frequency is too high to be measured as radio waves. In addition, since THz waves have properties of both light and radio waves, they have the characteristics of being straight going, penetrative and permeable. In normal systems, the generation efficiency of THz waves is poor, and the detection sensitivity is extremely poor. To advance research, it is necessary to have an oscillator and detector (biologically, a receptor) that match the characteristics of THz waves. It can be said that THz waves are electromagnetic waves in a region that is difficult to approach from a traditional physics perspective.

On the other hand, in recent years, with the rapid development of THz wave technology, there has been a lot of attention paid to basic research on THz waves and their application in biomedicine. Since the rotation and vibration energy levels of hydrated macromolecules fall within the energy range of THz waves, there is a high possibility that THz waves shake macromolecules. The actual effects of THz waves on macromolecules are, however, largely unknown. To clarify the relationship between THz waves and macromolecules and to achieve accurate control of biological macromolecules using THz waves, there are still many technical barriers that need to be overcome[2].

Research using biological reactions as a detection system for THz wave has recently begun to be conducted in the medical field. For example, the effectiveness of non-drug, non-invasive THz waves in inhibiting telomerase activity and suppressing cancer cells has been reported. In vitro experiments have shown that regular irradiation with 33 THz waves for 21 days significantly reduces telomerase activity in 4T1 cells (mouse-derived breast cancer cells) and MCF-7 cells (human breast cancer cells) by 77% and 80%, respectively. It has also been reported that the tumorigenicity of 4T1 cells in mice irradiated with 33THz wave for 21 days was reduced by 70%[3].

However, there have been no attempts to use THz waves radiated from biologically generated micro emitters to evaluate their effects on macromolecules. The SUNGOiD water which has been used for our previous experiments was made as follows. Extract of chrysanthemum, rose, raspberry, and other plants can be slowly degraded by exposing to ultrasonic vibrations. When high voltage DC (8300 V, 100 mA) is applied, followed by irradiation of the resulting solution with far infrared radiation (18.8- 50 THz) and then mixed with coral, shell, and lime permeate, mesoscopic nanostructure of calcium carbonates (CCMNS) is formed. These structures are assembled calcium carbonates; $CaCO_3$ and $Ca(HCO_3)_2$, with the size ranging from approximately 50-500 nm. They generate a wide ranges of THz waves (it may be overall 0.8μm-200μm; 1.5-375 THz)[4].

Until now, it has been thought that the effect of SUNGOiD water on pathogens such as viruses and bacteria *in vitro* is mainly due to its high pH. However, we demonstrated that SUNGOiD water dissociates scrapie prions *in vitro* (PrPsc; aggregates of abnormal prion protein with β-sheet structure and highly resistant for heat, acid, alkali and disinfectants) and abolishes their pathogenic properties in mice[5]. Prions are known to cause transmissible spongiform encephalopathy, incurable progressive neurological diseases.

Furthermore, it was suggested that SUNGOiD water may be effective in the prevention and treatment of Alzheimer's disease, the most common human age-related neurological disease. In our study, it was shown that SUNGOiD water inhibits the aggregation of Aβ protein and dissociate the aggregated Aβ protein[6], which is thought to be one of the causes of Alzheimer's disease. We also showed that SUNGOiD water acts to inhibit the formation

of aggregated Tau protein, which plays a major role in the neurodegeneration of Alzheimer's disease. Our studies have revealed that it inhibits the aggregation of abnormal tau proteins expressed in cultured nerve cells and causes the dissociation of aggregates. Furthermore, when genetically modified Drosophila for the AD model were allowed to lick SUNGOiD water diluted with sugar water absorbed in filter paper, prevention of a shortening of lifespan, loss of motor function and destruction of photoreceptor cells, and a decrease in aggregated tau protein in the brain of the Drosophila were observed[7,8].

In general, 1N (4%) NaOH (pH 14) at room temperature for 1 hour is recommended for inactivation of prions. However, pH of SUNGOiD water is extremely rapidly neutralized upon contact with skin (pH12.39→pH8.84 in one min.)[12], suggesting that the above-mentioned phenomena are likely mediated by mechanisms other than the conventional high alkalinity. In addition to the high pH of SUNGOiD water, it has been confirmed that fixed samples exhibit a radiation ratio of over 90% relative to a blackbody in the 12-60 THz waves (5–25 μm) range[4]. Therefore, in this paper, we attempted to consider the possibility of A β aggregate dissociation occurring due to the activation of water molecule motion by middle-infrared waves and the vibration of the A β peptides.

Since it is impossible to measure the state in which nano-level peptides receive minute energy emitted from nano-level emitters derived from living organisms, we considered and examined a thought experiment in quantum mechanically interactions.

In this paper, we try to conduct an analysis from a quantum mechanical perspective, using a simulation model of a normally performed cellular-level experiment. It suggests that A β aggregation in nerve cells may be able to dissociate by THz waves. The CCMNS with the core of $CaCO_3$ lattice has the potential to exhibit quantum electromagnetic behavior due to its mesoscopic structure, which is composed of interconnected dendritic nanostructures[9]. For example, the frequency of the emitted THz waves can be shifted by changing the coupling distance between the CCMNS due to the branched structures. This is related to the report that CCMNS may emit a wide range of electromagnetic waves. When biominerals ($CaCO_3$, Ca $(HCO_3)_2$) or nanostructures derived from living organisms are used *in vivo*, they can easily interact with macromolecules in the body, unlike artificial external irradiation devices.

Furthermore, the following points can be considered as characteristics of the mesoscopic structure. (1) Amplification of THz waves through resonance enhancement. When the mesoscopic structure is present, a local resonance cascade effect occurs, and there is a possibility that the radiation intensity of THz waves will increase. (2) Nanostructures with branching structures can function as waveguides for phonon-polaritons. This improves the efficiency of THz wave generation and propagation. (3) The formation of a dendrite-like nanostructure at the mesoscale has the potential to create a stable oscillation source using self-assembly. In addition, the radiation efficiency of THz waves is improved by having a structure larger than the nanoscale. (4) The branched structure has a natural antenna effect, enabling directional THz radiation in a specific frequency range. This allows the THz wave spectrum distribution and radiation pattern to be controlled. In this way, mesoscopic structures of CCMNS that emit THz waves produced by living organisms are probably the most suitable for affecting macromolecules inside living organisms.

Materials and Method

Overview of the method for producing SUNGOiD water (CCMNS solution)

The method of making CCMNS raw water is disclosed in Japan patent No. 5778328 and is synthesized in the following steps. Solution A is made by mixing materials A1 and A2 in a 1:3 ratio and then immersing them in distilled water as concentration of 12.5% (w/v) and put in a reaction vessel. Material A1 is a dry powder made by mixing equal quantities of A11 and A12. A11 is a dried powder

made by mixing *Artemisia indica var. maximowiczii*, *Farfugium japonicum* and *Cirsium japonicum* in the ratio 6:3:1(w/w). A12 is a powder made by mixing raspberry, *Rosa multiflora* and *Geum japonicum* in the ratio 7:2:1(w/w). Material A2 is a dried mixture of powdered cedar, maple and *Betula platyphylla* var. *japonica* in the ratio 5:2.5:2.5.

The reaction vessel contains distilled water, and a conductor covered with a Teflon insulating layer, and direct current (8300V, 100mA) is passed through the conductor. This current causes a water flow in the same direction as the direct current, which promotes the dissolution of minerals. To ensure uniform mixing, a pump-driven water circulation device is attached to maintain the water flow around the conductor. Next, ultrasonic vibrations are added to the water to further promote the dissolution of minerals. The ultrasonic generator stirs the water molecules at a frequency of 50 kHz, a wavelength of 29.64 mm, and an amplitude of 1.5/1000 mm. Ultrasound generates longitudinal waves that repeatedly compress and expand as they travel through the water. Therefore, the water molecules vibrate within a range of 1.5 μm, causing them to move back and forth 50,000 times per second. This stirring promotes the decomposition of raw material A. After the minerals have sufficiently dissolved, solution A is exposed to far-infrared radiation. Far-infrared radiation with a wavelength of 6 to 14 μm (21.4 to 50 THz) gives energy to the dissolved mineral particles, further promoting the stabilization of the solution.

Solution B is permeating distilled water by passing through six containers. These containers are filled with different mineral-imparting materials (B1 to B6) as follows. B1: A mixture of lime ($CaCO_3$), fossil coral and seashells in a weight ratio (W/W) of 7: 1.5:1.5. B2: A mixture of lime, seashells, fossil coral and activated carbon in a weight ratio (W/W) of 4:4:1.5:0.5. B3: A mixture of lime, fossil coral and shells in a mixture of 8:1.5:0.5. B4: A mixture of lime, fossil coral and shells in a ratio of 9:0.5:0.5. B5: A mixture of lime, fossil coral and shells in a ratio of 8:1:1. B6: A mixture of lime, fossil coral and shells in a ratio of 6:3:1. When distilled water passes through each container in order from B1 to B6, different minerals dissolve in the water at each stage due to the specific composition of the mineral-imparting material, and solution B is formed. Solution A and so-

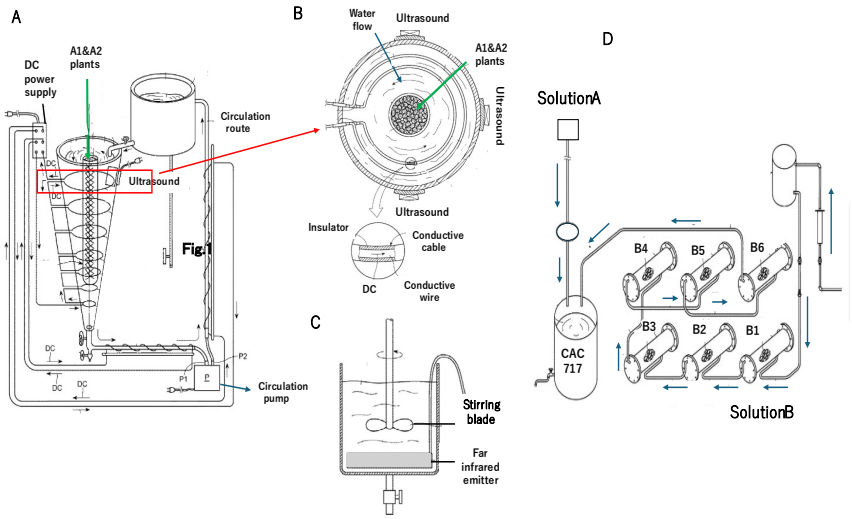

Fig. 1 CCMNS solution manufacturing process
(A) Overall diagram of the solution A manufacturing device. The center contains various plant-derived powders. (B) Cross-section of diagram (A). Water flows around the conductive circle with the ultrasonic device attached, extracting minerals from the plant. (C) Stirring of the extracted water and application of energy through far-infrared rays. (D) The CCMNS solution is created by mixing the A solution, and the B solution which is through the permeate water manufacturing device.

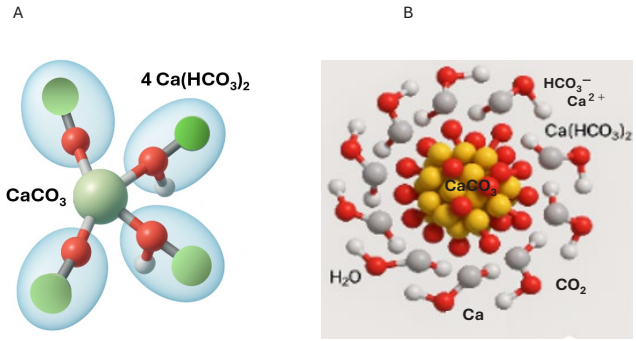

Fig 2. Basic unit of $CaCO_3$+$Ca^{2+}HCO_3^-$ shell and ACC(amorphous $CaCO_3$) clusters
(A)Basic unit of $CaCO_3$ and Ca $(HCO_3)_2$ molecules. (B) Structure of ACC cluster

lution B are mixed in a ratio of 1:10. This optimal ratio produces a solution (CCMNS raw solution) with a pH of 12.3 that contains mesoscopic structure of calcium carbonates. CCMNS solution producing process is shown in Fig. 1 modified from Japan patent No. 5778328.

Formation process of calcium carbonate mesoscopic nanosized structures (CCMNS)

In coral calcification, $CaCO_3$ primarily precipitates as an aragonite-type insulator and forms the skeleton (macroscopic structure). On the other hand, $Ca(HCO_3)_2$ exists in a hydrated state in which Ca^{2+} is coordinated with multiple HCO_3^- and H_2O molecules. However, during the calcification process, the initially formed small ACC (amorphous $CaCO_3$) clusters are surrounded by hydrated Ca^{2+} and HCO_3^- ions present in the surrounding environment, forming an ion shell and resulting in the formation of stable clusters. The entire cluster exists in a hydrated state, with ions dynamically moving in and out, and Ca^{2+} and HCO_3^- being incorporated toward the ACC core, resulting in the progression of ossification[10,11].

In the case of CCMNS, the basic structure (microscopic) consists of an $CaCO^3$ core surrounded by an ion shell, which aggregates into amorphous microparticles (quantum dots, 6 nm in size), and these further aggregate into larger structures (50–500 nm) as mesoscopic nanostructures (CCMNS). Thus, CCMNS is such as mesoscopic composite mineral-based electrically active microparticles. In the CCMNS, around the $CaCO_3$ core, water molecules and ions are adsorbed and coordinated through electrostatic interactions, forming an electric double layer, which stabilizes the dispersion in water. This is consistent with the zeta potential measurement results of CCMNS (zeta potential of -77 mV at pH 12.5).

Regarding the ratio of Ca in the core to Ca in the shell, CO_3^{2-} forms a planar triangle, and when arranged three-dimensionally, a 4-point (tetrahedral) configuration exhibits superior symmetry and stability. In addition, since each $Ca(HCO_3)_2$ has Ca^{2+} – $HCO_3^- \times 2$, it is suitable for surrounding the CO_3^{2-} plane through electrostatic interactions and hydrogen bonding. Therefore, considering that a structure in which $Ca(HCO_3)_2$ molecules are arranged in four directions forms the basis for the formation of aragonite-type clusters, a ratio of 1 Ca molecule to 4 shells seems appropriate (basic unit, Fig. 2).

Size and 3D conformation model of CCMNS

The CCMNS is composed of brick-like nanostructures, which are the basic units of THz wave radiation, in a branched, dendrite arrangement, as evidenced by the scanning electron micrograph [12]. The size of the CCMNS is close to that of the pox virus, which belongs to a large-scale virus of the nucleocytoplasmic large DNA viruses (Fig. 3). The size of the pox virus is approximately 200 nm x 300 nm x 250 nm, close a brick-like structure[13,] and its volume is Vpox = 4/3 x π x a x b x c ; a = 100 nm (semi-major axis 1), b = 150 nm (semi-major axis 2), c = 125 nm (semi-major axis 3), which gives approximately Vpox = 7.85 x 10^6 nm^3. This is approx-

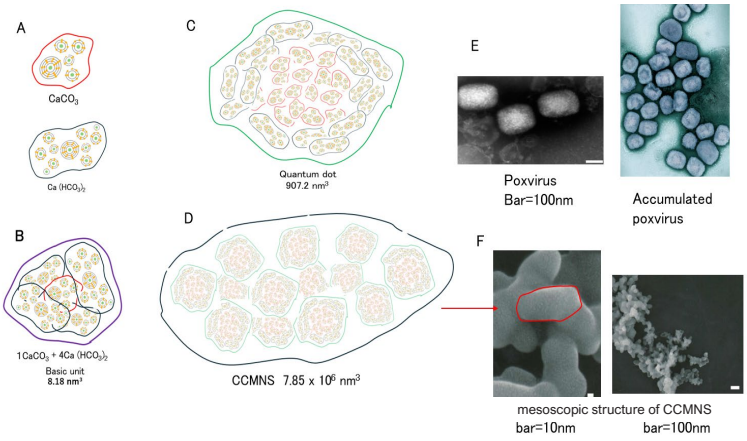

Fig. 3 Scheme of calcium carbonate, basic unit, quantum dot, CCMNS and poxvirus.
(A)Atomic structure of calcium carbonate molecules ($CaCO_3$ and Ca $(HCO_3)_2$). (B) Basic unit, with a molecular ratio of $CaCO_3$ and Ca $(HCO_3)_2$ of approximately 1:4 and its size. (C) Quantum dot-size, containing approximately 110 basic units. Ca^{2+} and HCO_3^- surround the core of the ACC (Amorphous Calcium Carbonate) cluster as a shell . (D) CCMNS, containing approximately $1x10^6$ basic units or 8650 quantum dots. It is about the similar size to a pox virus. (E) Pox virus and its aggregates for comparison. Scanning electron microscope image. (F) CCMNS make branching and dendrite-like arrangement of the nanostructure can be seen. Scanning electron microscope image[12]. The process from the basic unit to CCMNS is as follows. Basic unit → ACC cluster (quantum dot) → CCMNS (forming mesoscopic dendritic structure).

imately the similar size to a CCMNS.

As mentioned earlier, the core of the basic unit forms a spherical shape (e.g., diameter 1.5 nm). The shell is composed of 4–6 Ca^{2+} and HCO_3^- ions coordinated around the core, forming a spherical shell (thickness≈ 0.3–0.5 nm). Assuming interatomic distances of Ca–O≈ 0.24 nm and HCO_3^-length ≈ 0.3–0.35 nm, the diameter including the outer shell is≈ 2.1–2.5 nm. Assuming the radius of this basic unit to be approximately 1.25 nm, the volume is $4/3 \times \pi \times (1.25)^3 = 8.18$ nm³ (basic unit: Fig 2 A).

Assuming a structure where Ca^{2+} and HCO_3^- surround the core of the ACC (Amorphous Calcium Carbonate) cluster as a shell (Fig 2 B), if the cluster size is considered a quantum dot, its radius is approximately 6 nm. In this case, the volume is $4/3 \times \pi \times 6^3$ nm³ (907.2 nm³), containing approximately 110.9 basic units. Considering that the size of CCMNS is nearly the same as that of a poxvirus, Vpox = 7.85×10^6 nm³, so the CCMNS contains approximately 0.96×10^6 basic units and 8653 quantum dots.

In summary, approximately 110 basic units form amorphous clusters of quantum dot size, and approximately 8,650 quantum dots form CCMNS (containing approximately 1×10^6 basic units). As the pH of the CCMNS aqueous solution approaches neutral from alkaline, the zeta potential of CCMNS increases, leading to instability in stable dispersion. This may result in the formation of a mesoscopic structure resembling the branched dendritic aggregate arrangement shown in Fig. 3 (micro-particle aggregation and floc formation of CCMNS). Furthermore, during the crystallization, aggregation, and reconfiguration of the $CaCO_3$ core, it is possible that THz waves are emitted more strongly due to lattice vibrations (phonon).

THz waves and energy emitted from CCMNS

Measurements of blackbody radiation from CCMNS immobilized samples indicate that mid-infrared electromagnetic waves in the 12–60 THz (5–25 μm) range are likely to be emitted[4]. However, in the rotation and contraction of complex molecules with hydrated structures involving hydrated ACC, etc., far-infrared THz waves of 3 THz or less (100 μm or more) are thought to be the mainstream. On the other hand, electromagnetic waves emitted by lattice vibrations (phonons) of $CaCO_3$ caused by collective vibrations of ACC or during the initial crystallization stage are reported to have a wavelength range of 1.5–12 THz (25–200 μm). Furthermore, regarding the phonon-derived electromagnetic wave

response (infrared activity transverse optical (TO) and longitudinal optical (LO) modes) of aragonite, it has been reported that peaks concentrated between 4.5 THz and 8 THz[14]. Another paper states that the phonons of aragonite are in the 25–43 THz (7–12 μm) range[15]. Based on the above data, in this conceptual experiment, the peak wavelength of electromagnetic waves emitted from CCMNS was provisionally set at 12 THz (25 μm) as medium value of every data and the result of blackbody radiation from CCMNS immobilized samples.

The theoretical basis for calculating the energy of radiation and its acceptance of target receptor molecules, from the molar amount of an emitter substance and the wavelength emitted by that substance is based on Max Planck's quantum theory and Albert Einstein's light quantum hypothesis. The procedure of calculation is as follows: 1) Calculate the photon energy from the wavelength emitted. 2) Calculate the energy of one mole of photons (including Avogadro's number of photons). 3) Correct for the molar equivalent of the sample. For the energy of the THz waves emitted by CCMNS, the molar equivalent value per 1 mL of SUNGOiD water (CCMNS solution) used in the simulation experiment is first determined, and then the energy amount is calculated. The calcium concentration in the raw water of SUNGOiD water containing CCMNS is reported to be 2.5 mg/mL, but the measured value was 720 mg/L. Since the atomic mass of calcium is 40, the molar concentration is 0.72/40 = 0.018 mol/L. For the simulation experiment, a 10% diluted solution was used instead of the raw water, and the experiment was conducted on a 1 mL scale, resulting in a molar quantity of 1.8×10^{-6} moles.

The number of Ca atoms (nCa) constituting CCMNS in 1 mL of SUNGOiD water is calculated as $nCa = 1.8 \times 10^{-6}$ mol. The total number is calculated using Avogadro's number as $NCa = n \times NA = 1.8 \times 10^{-6} \times 6.022 \times 10^{23} \approx 1.08 \times 10^{18}$ particles. Each CCMNS contains 1×10^6 basic units, and each basic unit contains 5 Ca atoms. Therefore, the number of CCMNS in 1 mL is $1.08 \times 10^{18} / (5 \times 10^6) = 2.16 \times 10^{11}$.

As mentioned earlier, CCMNS contains approximately 1×10^6 basic units consisting of a $CaCO_3$ core and a $Ca^{2+} \cdot HCO_3^-$ shell. As an electrically active microparticle, CCMNS has a zeta potential of -77 mV at pH 12.5, but at pH 7.0, its stable dispersion in water becomes unstable, and CCMNS undergoes mesoscopic-sized dendritic growth or amorphous $CaCO_3$ promotes aragonite-type crystallization. Crystallized $CaCO_3$ lattice vibrations (aragonite type, phonons) primarily emit electromagnetic waves at approximately 12 THz. As described later, it is estimated that these waves are mainly emitted for approximately at least 300 seconds.

On the other hand, since the Ca content in the core of CCMNS accounts for approximately 1/5 of the total (core 1: shell 4), the number of $CaCO_3$ molecules capable of causing lattice vibrations (phonons) in total CCMNS is $1.08 \times 10^{18}/5 = 2.16 \times 10^{17}$. If electromagnetic waves at 12 THz are emitted from the $CaCO_3$ in the core of CCMNS, the phonon frequency is 12 THz (855 cm^{-1}) in the aragonite main mode. The energy per phonon is E_1 phonon $= h \times \nu = 6.626 \times 10^{-34} \times 12 \times 10^{12} = 7.9512 \times 10^{-21}$J. If the energy released per $CaCO_3$ is averaged to 10 phonons based on atomic rearrangement during crystallization and known vibration data of nano materials, the total energy released is 7.9512×10^{-20} J. The total energy released in 300 seconds is $Etotal = 2.16 \times 10^{17} \times 7.9512 \times 10^{-20} = 1.72 \times 10^{-2}$ J/mL. The energy release decreases exponentially, but the average value over 300 seconds is 5.72×10^{-5} J/mL per second.

Simulation for an experiment model

We examined whether the phenomenon of dissociation of prions[5], Aβ[6] and Tau[7,8] proteins that aggregate in nerve cells, etc. can be explained by the THz waves emitted by CCMNS with quantum mechanically. The frequency of the THz waves was 12 THz, and the wavelength was 25 μm. As a model, we mixed 0.5 mL of a 5-fold diluted raw solution of CCMNS with 0.5 mL of a culture medium containing $1x10^6$ nerve cells with Aβ aggregates and set up a situation in which 10^6 nerve cells

with Aβ molecule aggregates were suspended in 1 mL of SUNGOiD water (a 10-fold dilution of the CCMNS raw solution).

Results

Relationship between No. of nerve cells and No. of CCMNS in SUNGOiD water

In the simulation model experiment, $1x10^6$ nerve cells are suspended in 1mL of SUNGOiD water (CCMNS solution). The nerve cells were transfected with a plasmid carrying amyloid precursor protein (APP) that contained a mutant form of Aβ that is easily cleaved (Swedish mutation)[16] or a mutant form of Aβ that is easily aggregated (E22K; Italian mutation etc.)[17,18]. Therefore, aggregation of Aβ easily occurs within the nerve cells.

The number of CCMNS in 1mL of SUNGOiD water is calculated before ($2.16x10^{11}$). 1mL of SUNGOiD water is 1cc, and is equivalent to $1x10^{-6}m^3$. If you now put 1cc of SUNGOiD water into an imaginary small pool that is 10cm long, 10cm wide and 0.1mm deep (10^{-1} x 10^{-1} x 10^{-4}=$10^{-6}m^3$), 1mL will be able to fill the pool exactly. If we assume summing the four CCMNS wavelength ranges (25 μm x 4 = 100 μm) which generate a wave of 100μm evenly, then a wave of 10^3 in length and 10^3 in width (a total of 10^6 waves) will be formed. There are 10^6 nerve cells in 1mL, so the calculation for the model is that there is one nerve cell at the bottom of each 100 μm wave. There are $2.16x10^{11}$ CCMNS in 1mL, therefore each nerve cell is surrounded by $2.16x10^5$ CCMNS in each 100μm wave (Fig. 4).

Energy given to nerve cells by THz waves of CCMNS

As mentioned above, the energy released by CCMNS in 1 mL of SUNGOiD water is Etotal=$1.72x10^{-2}$ J. This amount of energy can be considered at the macro level as follows. The energy required to raise 1 g of water by 1℃ is 4.186 J. Therefore, for SUNGOiD water, (4.186 J/mL)/($1.72x10^{-2}$ J/mL) = 243.4 to raise water by 1℃ , which means that about 240 mL of SUNGOiD water energy is required for 1mL of water.

However, the effect of energy of THz waves on the nano-sized molecules is somewhat different. In our time-course experiment done before on the dissociation of aggregate Aβ, we found that the dissociation was almost complete within about 5 minutes[6] (Fig. 5). The calculated time to dissociate aggregate Aβ into oligomers or monomers was 284.6 seconds. Thus, the energy released by the CCMNS is Esec=$1.72x10^{-2}$ /284.6=$6.033x10^{-5}$ J/

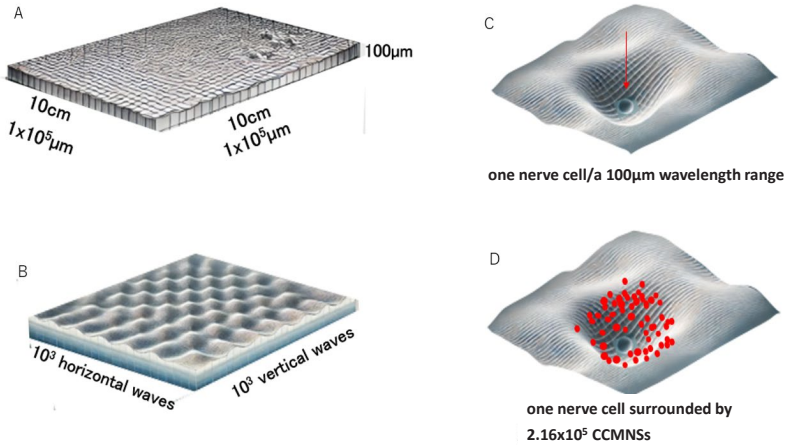

Fig. 4 A nerve cell in a 100μm wavelength range surrounded by many CCMNSs
(A)One mL of SUNGOiD water is placed in an imaginary pool 10cm ($1x10^5$μm) long and 10cm ($1x10^5$μm) wide and 0.1mm (100μm) deep. (B) A wave range 100μm in diameter is created in this pool. The number of longitudinal and lateral waves is 10^3 each, for a total of 10^6 waves. (C) The figure shows one representative nerve cell (red arrow) of total $1x10^6$ nerve cells at the bottom of a wave. (D) The nerve cell is surrounded by approximately $2.16x10^5$ CCMNSs, indicated by the red dots.

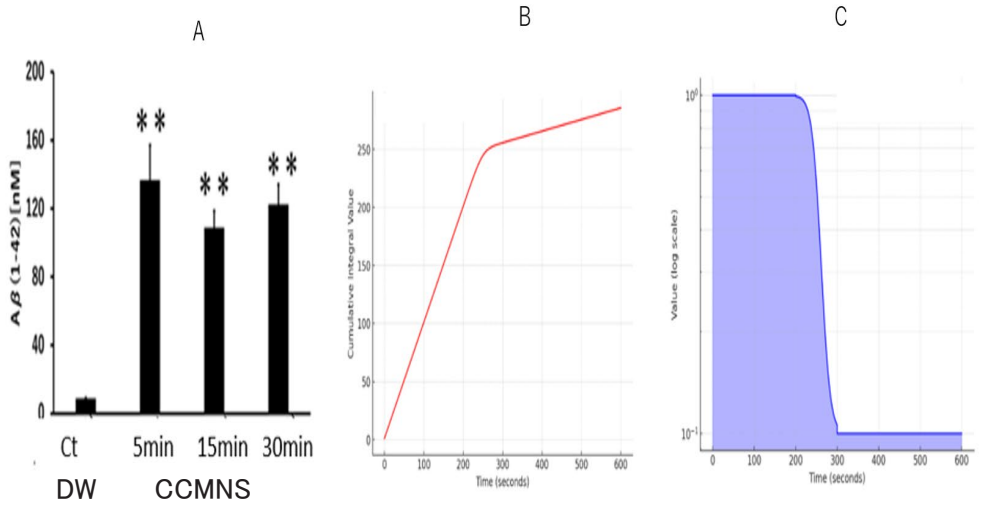

Fig. 5 Dissociation of A β aggregates by CCMNS over time.
(A)Dissociation of A β aggregate was measured with a monoclonal antibody recognizing monomers/oligomers of A β. (B) Cumulative integral curve of the dissociation of A β by CCMNS. (C) Integral of the A β dissociation function over time by CCMNS (284.6 seconds).

sec. In this way, one nerve cell received total energy from 2.16×10^{5} CCMNS is 1.72×10^{-2}J/(1×10^{-6}) $=1.72 \times 10^{-8}$ J and then for one nerve cell per second is 6.033×10^{-11}J/sec.

Energy of CCMNS given to aggregated A β

Fig 6A shows the mid-infrared rays emitted by CCMNS, with a wavelength of 25μm, indicated by the red circles, and a nerve cell placed in the center, viewed from above. The nerve cell, with an average diameter of 14μm, is seen floating in the 25μm wave emitted by 2.16×10^{5} CCMNSs. If we assume that

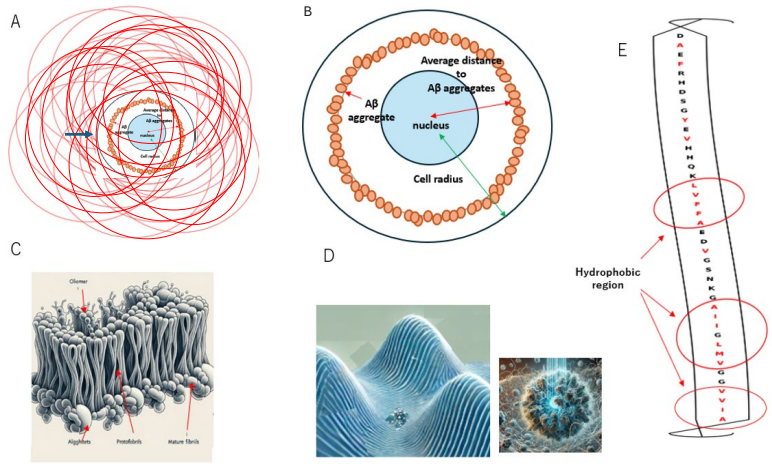

Fig. 6 Scheme of the effect of THz wave on A β aggregate
(A)Top view of a nerve cell (arrow) surrounded by THz waves (red circles, 25μm) from many (2.16×10^{5}) CCMNSs. (B) This is a schematic diagram of the structure of a nerve cell. A β aggregates are arranged in an average distribution in the middle (radius 5μm, brown dots) between the nucleus (radius 3μm, light blue) and the cell membrane (radius 7μm). (C) Aggregate image of spherical and fibrous A β proteins. (D) On the left is an image of a nerve cell (14 μm in diameter) floating in electromagnetic wave of the CCMNS. On the right is an image of A β aggregates receiving 12 THz photons. (E) The amino acid sequence of A β 1-42 and the sequence region of hydrophobic amino acids. It is thought that these regions are involved in hydrophobic interactions that cause aggregation.

the diameter of the nerve cell is 14μm (radius 7μm), then its surface area is $4\pi R^2=4x3.14x7^2=615.4\mu m^2$. And if we assume that the average distribution of Aβ aggregates formed in the cytoplasm is in the zone roughly halfway between the nucleus and the cell membrane, the radius will be 5μm, so the area will be $4\pi r^2=4 \times 3.14 \times 5^2=314\mu m^2$.

We suppose that the radiated energy is an isotropic distribution and the CCMNS (emitter) radiates isotropically on the cell surface. Then the energy diffuses from a sphere with a radius of 7μm (cell membrane surface) to a sphere with a radius of 5μm (Aβ aggregate). We also assume that the energy is distributed in proportion to the ratio of the sphere surface areas. As a result, the energy received by the Aβ aggregates is calculated using the ratio of the sphere surface areas, as follows. $E_{A\beta}$ = E x (Aβ aggregate sphere / cell surface sphere), and when the total energy of 1.72×10^{-8} received by one nerve cell is substituted, $E_{A\beta} = (1.72 \times 10^{-8} \times 314)/615.4=8.78 \times 10^{-9}$ J.

The energy received by a single Aβ molecule and dissociation of aggregated Aβ protein

To calculate the average area of a single molecule of Aβ 1-42, it is necessary to estimate the area based on the shape and structure of the protein. Aβ 1-42 is a peptide composed of 42 amino acids, and when it is extended in a straight line, it is thought to be approximately 14.7 nm in length[19]. In the monomer state in solution, Aβ 1-42 often takes on a spherical shape (approximately 7 nm^2). However, in Aβ aggregates, the β-sheet structure stacks up to form a fibrous structure. The average width of an amino acid is estimated to be 0.72 nm and Aβ 1-42 length 14.7 nm. Thus, Aβ square is $0.72 \times 14.7 = 10.6$ nm^2. In addition, the area of an Aβ aggregate is 314 μm^2, and the area of a single molecule of Aβ is 10.6 nm^2. Therefore, the surface of an Aβ aggregate sphere contains 314×10^6 nm^2 / 10.6 nm^2 = 2.96×10^7 Aβ molecules. The energy received by a single Aβ molecule is 8.78×10^{-9} / $2.96 \times 10^7 = 2.97 \times 10^{-16}$ J.

The vibrational modes of proteins are mainly excited in the infrared and terahertz regions. The number of photons (N) when 2.97×10^{-16} J of energy (E) from a 12 THz wave of CCMNS is irradiated on a single molecule of Aβ protein is as follows. $N = E/h\nu$, it becomes $2.97 \times 10^{-16}/ (6.626 \times 10^{-34} \times 12 \times 10^{12}) = 3.74 \times 10^4$ photons. Since the main radiation time of 12THz wave was calculated 284.6 seconds, one molecule of Aβ protein is exposed to $(3.74 \times 10^4)/284.6 = 131.25$ photons per second.

We investigated whether the molecules of hydrophobic aggregation proteins dissociate when they receive 12 THz, 3.74×10^4 photons (or 131 photons/sec). Protein aggregation due to hydrophobic interactions is formed mainly by the following factors: interactions between hydrophobic amino acids (non-polar interactions), hydrophobic effects due to water molecules (entropy-driven), stabilization of secondary structures (such as β-sheet structures), and van der Waals forces and electrostatic interactions between molecules. The energy of hydrophobic interactions is generally 2-10 kJ/mol (in the case of intermolecular interactions), and when converted to per molecule, it is a maximum value of 10×10^3 J / $(6.022 \times 10^{23}) = 1.66 \times 10^{-20}$ J. The energy of a single photon of electromagnetic waves at 12THz is $E_{photon} = h\nu$, so $E_{photon} = 6.626 \times 10^{-34}$ Js $\times$ 12×10^{12} /s = 7.951×10^{-21} J. Since the maximum energy required to dissociate a hydrophobic bonding molecule is 1.66×10^{-20} J, the number of photons required is 1.66×10^{-20} / 7.951×10^{-21} = 2.09 (about 2.09 photons by 12THz wave).

This photon value (2.09) is much smaller (3.74×10^4 total photons or 131.4 photons per second) than the energy received from CCMNS. Thus, the photon energy received by a single Aβ molecule is more than 10^4 or 62.9 times ($3.47 \times 10^4/2.09=1.66 \times 10^4$ or 131.4/2.09=62.9 times, total or per second, respectively) greater than the hydrophobic interaction energy, so hydrophobic aggregation is highly likely to dissociate. Since THz waves easily affect hydrogen bonds and intermolecular interactions, it is thought that local vibrations and hydration changes caused by photons induce the aggregation structure to collapse.

Discussion

In the middle of the 20th century [20], senile plagues were found in a dog brain. Subsequently, reports were published in dogs and monkeys. We also found senile plaques in the brains of old primates (Asian macaque monkeys: crab-eating macaques) for the first time[21,22,23]. Currently, there are reports of senile plaques and tau protein aggregation in the brains of many aged animals, including wild animals. Many genetically engineered animal models have also been created and studied. However, not truly effective, preventive or therapeutic agents for Alzheimer's disease have yet been found.

In 2001, bovine spongiform encephalopathy (BSE), a prion disease of cattle, entered Japan and caused panic[24]. Prisons, which have not an alfa-helix structure but a beta-sheet structure, cannot be inactivated by ordinary heating or disinfectants. They can infect humans and animals and, if transmitted, cause progressive central nervous system damage and death in 100% of cases. No effective preventive or therapeutic agents have been found for prion diseases either. Both nationally and internationally, administrative measures have been taken to control this infectious disease[25,26].

Fortunately, however, it has been shown that CCMNS has the effect of degrading and inactivating not only many bacteria and viruses, but also prions. Furthermore, it has been shown that it is possible to inhibit the formation of aggregates of Aβ and Tau proteins and cause them to dissociate[27]. It is thought that the high alkalinity (pH 12.3~12.5) of the CCMNS aqueous solution is the main factor in inactivating microorganisms. On the other hand, it is thought that the THz waves emitted from the CCMNS are important for dissociating aggregates such as prions, Aβ and Tau proteins.

CCMNS has the potential to exhibit both quantum effects and classical electromagnetic wave behavior due to its mesoscale structure, which is formed by linking together nanostructures in the shape of dendrite-like structure. For example, the frequency of the emitted THz waves can be shifted by changing the bonding distance between nanostructures using branching structures and dendrite-like links. This is related to the fact that CCMNS emits a wide range of electromagnetic waves from 0.8 to 200 μm. When nanostructures or biominerals ($CaCO_3$, Ca $(HCO_3)_2$) derived from living organisms are involved, they can easily interact with biological macromolecules in the body, unlike artificial external irradiation devices.

Mesoscopic structures may have some characteristics as follows. The dendritic nanostructures are likely to induce plasmon resonance and phonon-polariton resonance, and it is expected that local electric field enhancement will occur. And there is the possibility that the radiation intensity of THz waves will increase. A nanoscale structure with a branching structure can function as a waveguide for phonon–polaritons. This improves the efficiency of THz wave generation and propagation. The formation of a dendrite-like nanostructure at the mesoscale has the potential to create a stable oscillation source using self-organization. Having a structure larger than the nanoscale improves the radiation efficiency of THz waves. The branched structure has a natural antenna effect, enabling directional THz radiation in a specific frequency range.

In the simulation experiment model used in this study, THz wave of nano-sized emitters (CCMNS) produced by living organisms interact with nano-sized macromolecules. However, this energy level is ignored by the macroscopic perspective. On the other hand, number of photons with a single Aβ molecule receives is, at the nanoscale, more than 10^4 times (or 64 times per sec) greater than the photon number required in hydrophobic interaction energy. This paper may be the first quantum biology report to assess the biological energy effect produced by living organism itself at the nanoscale level using quantum mechanics. Fig. 7 shows an overview of the process assumed in this simulation experiment in which CCMNS can dissociate Aβ molecule aggregates.

SUNGOiD water uses a variety of natural ingredients as raw materials. Therefore, depending on the origin of the raw materials, there may be slight differences in effectiveness. However, when three

lots were tested, a 1:1 to 1:4 dilution was found to be effective for dissociation against A β and tau aggregates compared to the control. To develop this product into a pharmaceutical drug, further improvements are needed in terms of raw materials and manufacturing processes.

Conflicts of Interest: Y. Y. is employed by Kyowa Kako Co. Ltd. and K.F. is employed by the Mineral Activation Technical Research Center and has a patent (Japan patent No. 5778328). Both researchers have no conflicts of interest with the content of this article.

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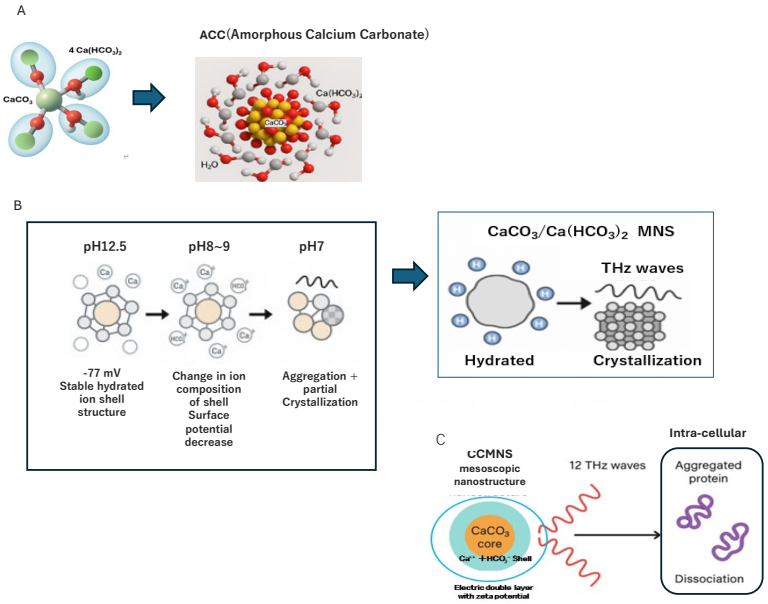

Fig 7. A simulation of the process by which CCMNS dissociates aggregated A β molecules.
(A)The basic unit on the upper right is a structure in which one $CaCO_3$ molecule is surrounded by four Ca^{2+} and HCO_3^- ions. The upper left shows a quantum dot-sized amorphous calcium carbonate (ACC) structure, which is an amorphous structure in which the $CaCO_3$ molecule core is surrounded by a shell of Ca^{2+} and HCO_3^- ions, and develops into an aragonite-type skeleton. (B) In the middle, the CCMNS is an electromagnetic wave nano-emitting unit with size of a poxvirus, containing approximately 8,600 quantum dots. The CCMNS in SUNGOiD water encounters a target, causing a change in the pH of the field. At pH 12.3–12.5, CCMNS exists as a stable, dispersed structure. However, as pH decreases, CCMNS may aggregate and coagulate into dendritic mesoscopic bodies, aragonite formation may progress rapidly, and the vibration (phonons) of the $CaCO_3$ lattice in the core is enhanced, resulting in the emission of more strong electromagnetic waves at 12 THz. (C) In the lower region, the electromagnetic waves (photons) emitted from CCMNS interact with A β molecule aggregates, causing them to dissociate.

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