Response or explanation to two questions on MRET:

1. How is enhanced ingestion or hydration of MRET Water achieved?

2. How does MRET Water mutate RNA?

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1. Specifically, what happens once the water is ingested into the body? How is it specifically alleviating particular disease symptoms? And what is known specifically about the pharmacology and toxicology of the water?

Water is the foundation for all life processes. Although even today most of people still assume that water is only H_2O. It has been proven that water has a very complicated structure which was only recently begun to be researched. It is not surprising, therefore, that when judging the quality of water, its structure (molecular orientation and juxtaposition) is seldom considered. Modern research in biophysics proved that even slight change in molecular structure of water could dramatically change physical and physiological properties of water. In the past years, extensive terahertz laser vibration-rotationtunneling spectra and mid-IR laser spectra were used for water structure research. As a dipole, water would constitute a series of clusters such as micro-clustered water (e.g., stable hexamer) and macro-clustered water (e.g., icosahedral water or buckey balls). Water is also a key component of bio-clusters with protein and DNA which form biological hydrogen networks. The Lawrence Berkeley National Laboratory was the first institution to obtain the photo of water hexamers, a particularly stable form of water cluster, using scanning tunneling microscopy. Water is one of the most polar molecules known in nature. The polarity of water underlines its chemistry and thus the chemistry of life. Polar molecules interact with one another through attraction. This weak attraction is called a hydrogen bond. In regular water polar molecules form short-range, unstable associations of different crystal shapes (unstable clusters of water molecules). Untreated water is able to form cluster's associations that have only 5 to 10% of the strength of covalent bonds. The process of water MRET activation induces the formation of long-range water molecular domains (stable clusters) similar to water molecular structures found in living cells.

When untreated water is ingested into the body the water molecules have tendency to go through the specific process that leads to formation of water bio-clusters since water molecules are attracted to molecules of proteins, lipids, etc (Wan der Walls attractive forces) of the body tissues. These attractions change the dipole momentum of water molecules and leads to formation of relatively stable water clusters. This type of water is named structured water, another word it is water with highly organized molecular structure. Based on the recent discoveries in biophysics and biochemistry it is know that only structured water can be assimilated and metabolized in biological systems. It is generally known that all metabolic reactions in living organisms take place within colloidal solutions. In colloidal solutions substances are dispersed in such a fine manner that they can no longer be differentiated from the liquid. Important examples are blood, plant juices, etc. Disturbances of these colloidal systems, or even worse, their total disruption, are synonymous with degenerative conditions of diseases. There is a relationship between the health of living organisms and the colloidal state in their tissues. The stability of colloidal solutions stands in a direct physical relationship to the

molecular structure of water. It is important for the stability of colloidal systems that the structure of water exerts a great degree of organization upon the colloidal particles. The extent and propagation of such an ordered state throughout the water could be described as its information content. Another word the more organized the molecular structure of water the more stable is colloidal system.

MRET water has a highly organized molecular structure to compare with regular water. For example, Bioelectrical Impedance Analyzer test (currently approved by FDA, BIA) designed to measure phase angle, hydration, and cellular water movement showed that MRET water can affect intracellular/extracellular water exchange in the human body 3 times faster comparing with regular water (for regular water it requires 50-60 minutes; for MRET water it requires 15-20 minutes). Another word MRET water can go inside the cells and go outside the cells 3 times faster comparing with regular non-structured water.

Pure water has no particular pharmacological and/or toxicological effect on human body. Water is considered to be a basis of biochemistry in the body since human body is composed of about 70% of water. Water is essential factor in order to support normal homeostasis of the body. In this case we can talk only about pharmacology and toxicology of foreign substances that are dissolved in water. In this case water plays role of the solvent and agent for transportation of foreign substances in the body. There are no foreign substances introduced to the body of water during MRET treatment. We require to use chemically pure drinking water for MRET treatment. MRET technology is based on the concept of the treatment of water with subtle low frequency electromagnetic oscillations (frequency range is below 10 Hz). The intensity and range of frequencies generated by MRET device is out of scope of FCC and NIEHS standards in regards to the human health risk from EMF exposure (frequency range from 10 KHz to 3-5 GHz). The subtle low frequency oscillations generated by MRET device can only induce formation of water molecular clusters since it requires application of EMF of extremely low intensity. There is no scientific evidence that such type of EMF can be a source of the potential human health risk. This statement can be also proved by some experimental data. Test in vitro conducted at Engene Biotechnologies Corp. showed that MRET water has ability to inhibit the growth of tumor cells while the simultaneous observation on normal cells did not show any effect of inhibition, they grew normally. Test in vivo conducted at University of Toronto on Transgenic mice also provide evidence that animals on MRET water lived longer and did not show any abnormality in behavioral pattern (in case of MRET water toxicity they supposed to die faster and mortality rate should be higher …).

We provide a scientific explanation of the mechanism of MRET water effect in regards to alleviation of disease symptoms in our book “Introduction to the Biophysics of Activated Water”. All systems of a living organism are subject to constant external and internal influence from many physical and chemical factors of natural and man-made origin. The development of diseases symptoms is a direct result of such type if influences on human body. Without going deep into discussion of mechanisms, by which water affects these processes note, that interaction of biological molecules in a water-salt environment is one of the main instruments of maintaining of normal homeostasis and development of an organism’s protection against effects of ionizing and non-ionizing radiation, as well as influence of free radicals. The anomalous electrodynamic

characteristics of MRET Activated water provide some evidence regarding its possible effect on electrical activity of the cells. The relationship between such electrodynamic characteristic of water as dielectric permittivity and biochemical activity of cells can be explained with the analysis of dispersion characteristics of deoxyribonucleids (DNA). Deoxyribonucleic acid (DNA) is a high molecular biopolymer with a linear chain consisting of alternating monomeric units – deoxyribonucleotides (shortly – nucleotides). Four types of monomers are normally found in natural DNA: deoxyadenosine monophosphate (adenine), deoxyguanozin monophosphate (guanine), deoxytimidin monophosphat (timine) and deoxycitidin monophosphate (cytosine). The basis of an informational structure of a DNA macromolecule is alteration of sequences of four basics – A, G, T and C. This sequence determines the code of hereditary information. In a double DNA spiral there is, on average, about the same quantity of four main nucleotides, provided that naturally the quantity of nucleotides included in their respective complimentary pairs AT and GC is matched exactly. The mole ratio of different pairs changes only slightly (by not more than 2-5%) in different organisms and also from molecule to molecule in same cells. In the process of forming DNA spiral structure water surrounding a DNA spiral, plays a very important role. In the absence of water (for example, on the surface of covering glass) cross section of a molecule of DNA assumes the ellipsoid shape. The distance between adjacent pairs of nucleotides equals 3.4 A° and each turn of the spiral contains 10 nucleotide pairs. A spiral with such parameters represents the so-called "stretched" B-form of DNA, which is an unstable meta stable form of a molecule, distinguished from the stable "compressed" A-form with eleven nucleotides by one full turn of the spiral and spiral step of 28 A°.

The DNA spiral with step 28A° (A-form) corresponds well with the quasi-crystalline water structure. DNA is capable of bringing water into order on the distance of up to 1000 A° from its surface. Transfers between forms A and B in the result of dehydration of DNA is a non-specific reaction on very different forms of external influence (radiation, heat, pH, etc.) conditional upon breaks of hydrogen links, neutralization of phosphorus groups as well as suppression of their dissociation. Regulation of protein synthesis and the process of self-reproduction is accomplished by a DNA free of protein casing, activated in the result of protein depravation and the A$\rightarrow$B transfer. The character of interaction of fragments of biological molecules largely depends on their dispersion characteristics.

It is a well known fact that none of the enzymatic methods of reparation of damages to DNA can fully restore ruptures of complementary chains of a DNA spiral. It happens because in order for an enzyme to fulfill its "repairs" it needs a special platform, on which such restoration of DNA integrity is performed. In case of single breaks, an undamaged complimentary DNA string serves as such a platform.

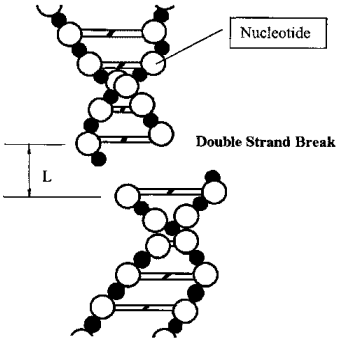

Fig.4 Spatial structure of a DNA spiral in the area of a double break

In case of double breaks, such possibility is no longer feasible. This, at a first glance, must lead to an irreversible destruction of DNA with a loss of genetic information. The only possibility of restoring DNA in this case is by using the method of non-enzymatic self-reparation mechanism. The efficiency of implementing the mechanism of non-enzymatic reparation depends on the features of long-distance force interaction between ruptured parts of a double-string DNA spiral in liquid inner molecular environment. Since dispersion parameters of the nucleotides are stable and they cannot be controlled, the only possibility of regulating the process of self-reparation of DNA is through controlling the dispersion parameters of water in liquid inner molecular environment. These dispersion parameters directly depend on dielectric permittivity and conductivity characteristics of water. Thus, by introducing to the biological system water with highly organized molecular structure (MRET water) it is possible to control the mechanism of DNA development and reparation. This mechanism leads to alleviation of diseases symptoms.

2. Dr. Inouye also brought up some other important questions when you discussed how MRET affects the RNA. I know you have some information from Dr. Smirnov that MRET water can selectively attack or mutate RNA, but what is the exact mechanism? Could you ask Dr. Smirnov how MRET water specifically attacks RNA? What is the first destructive force on the molecular structure of the RNA? Does MRET water inhibit some enzyme? Also, does it penetrate the viral capsid? And what are the structural changes that inhibit RNA replication and transcription, and how does the RNA of viruses differ from normal cells?

We have to discuss a proposed mechanism of water clusters dissociation/association in protein cavities in order to explain of possible MRET water effect on RNA (DNA) structure. The ”flickering water clusters” means excitation of librational and translational primary water clathrates (initial organized formations of water molecules that further form clusters, proposed by Dr. Pauling, 1959, Nobel prize laureate), accompanied by [association/dissociation] of coherent water formations. The water cluster association and dissociation in protein cavities in terms of mesoscopic model represent the *ac* - clathrate or *bc* - clathrate. These excitations stimulate the large scale (LS) - librations of domains in composition of clusters. The frequencies of (ac) and (bc) clathrates, has the order of about 10^8 s^{-1}. This value correlates well with experimental characteristic times for protein domains librations. The geometrical deformation of the inter-subunits large central cavity of

oligomeric proteins and the destabilization of the water cluster located in it, lead to relaxational change of (A - B) equilibrium constant, providing their cooperative properties. At the temperature interval (0-100C0) the frequencies of translational and librational macroclusters are in the interval of (1.3-2.8) 10^9 s^{-1} and (0.2-13)10^6 s^{-1} correspondingly. It is obvious, that between the dynamics/function of proteins, membranes, etc. and dynamics of their aqueous environment exists the strong correlation (Fig.3.3).

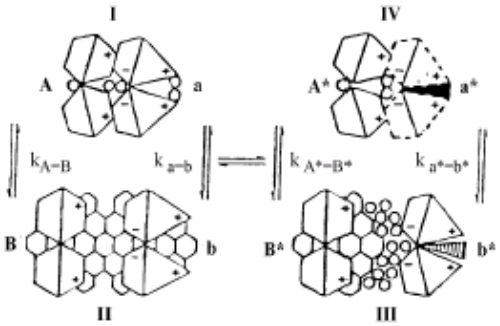

Figure 3.3. The schematic picture of the protein association (Fab subunits of antibody with a ligand), which is accompanied by destabilization of water clusters in cavities, according to dynamic model (Kaivarainen, 1985). The dotted line denotes the perturbation of the tertiary structure of the domains forming the active site. Antibodies of IgG type contain usually two such Fab subunit and one Fc subunit, conjugated with 2Fab by flexible hinge, forming the general

According to this model of specific complexes formation the following order of events is
assumed:

1. Ligand (L) collides with the active site (AS), formed usually by two domains, in its open
(b) state: the structure of water cluster in AS is being perturbed and water is forced out of AS
cavity totally or partially;
2. Transition of AS from the open (b) to the closed (a) state occurs due to strong shift of *a* - *b* equilibrium to the left, i.e. to the AS domains large scale dynamics;
3. A process of dynamic adaptation of complex [L-AS] begins, accompanied by the directed
ligand diffusion in AS cavity due to its domains small-scale dynamics and deformation of their tertiary structure;
4. If the protein is oligomeric with few AS, then the above events cause
changes in the geometry of the central cavity between subunits in the open state leading to the destabilization of the large central water cluster and the shift of the *A- B*, corresponding to *R - T* equilibrium of quaternary structure leftward. Water is partially forced out from central cavity. Due to the feedback mechanism this shift can influence the *a - b* equilibrium of the remaining free AS and promotes its reaction with the next ligand. Every new ligand stimulates this process, promoting the positive cooperation. The negative cooperativity also could be resulted from the interaction between central cavity and active sites;
5. The terminal *protein - ligand* complex is formed as a consequence of the relaxation process, representing deformation of domains and subunits tertiary structure. This stage could be much slower than the initial ones. As a result of it, the stability of the complex grows up.

The proposed mechanism suggest that within millions years of organic evolution the interaction of water clusters with protein structures developed specific dynamic cooperation and as a result certain stability of protein complex necessary for survival of normal cells. This stability is necessary to support normal development of cells without any mutation and it is governed by the allowance of possible correct interactions between water clusters and protein cavities. This allowance is guaranteed by specific geometry of water clusters which includes size and juxtaposition of water molecules in the cluster. MRET treatment of water leads to the formation of optimum stable clathrate-cluster structures in water that may play role of "controllers" of correct assembling of proteins segments. The discussed above mechanism provides a conclusion that structured water in nature may play role of "controller" of the normal development of living cells and prevent cells to go through unstop continues mutations.

RNA molecules are single stranded except in some viruses however it is possible for RNA molecules to fold on themselves to form short regions of double helix by forming a hair-pin loop. In these regions binding is A=U and G=C. G can also form a base pair with U to give G=U, but is a very weak pair. Base pairing in RNA hairpin loops is frequently imperfect, often opposite bases cannot base pair, and one or more bases along a strand may be looped out in order for base pairing to occur by proper base pairing. The RNA structure of various types of viruses (as well as normal cells) may differ from each other because of different geometry of protein segments in RNA structure. Chemically these segments are the same but their juxtaposition relative to helix is different.

RNA viruses, comprising 70% of all viruses, vary remarkably in genome structure. Because of the error rate of the enzymes involved in RNA replication, these viruses usually show much higher mutation rates than do the DNA viruses. Mutation rates lead to the continuous generation of virus variants which show great adaptability to new hosts. A variety of mechanisms enable viral genomes to replicate in balance with host cell multiplication. Most of the well-studied mechanisms of persistence of RNA viruses in primary cell cultures or established cell lines involve genetic variation of the virus, the cell, or both. A classic example is provided by defective interfering (DI) particles of vesicular stomatitis virus (VSV), and related viruses. During serial passage of VSV at high multiplicity of infection, DI particles accumulate in a cyclic pattern. Standard VSV and DI particles alternate in their dominance in a continuous process of mutant generation, competition, and selection. For RNA and possibly some DNA viruses, increasing evidence suggests that genetic variation (mutation, recombination, and genome segment reassortment in the case of multipartite genomes) affects adaptability to environmental changes. The consideration of the mechanism of the interaction between water clusters and protein cavities and the following conclusion of the ability of structured MRET water to prevent cells to go through multi-mutation processes it is possible for MRET water to arrest the genetic variation of the virus. As a result, it allows immune system of the body to identify and attack viruses which leads to recovery of the body.

The microbiology experiments conducted at Institute of Microbiology of Ukraine Academy of Science provide some evidence that MRET water can affect

microorganisms (E.coli experiment) on genetic level. The introduction of E.coli to MRET treated agar-meat bullion under Aerobic condition led to dramatic change of their normal color, form, and cellular division. Technically, the "coliform group" is defined to be all the aerobic and facultative anaerobic, non-spore-forming, rod-shaped bacteria. It can vary the pore diameter of its outer membrane porins to accommodate larger molecules (nutrients) or to exclude inhibitory substances. The described effect of MRET water on E.coli morphology can be possible only in the case of the penetration of MRET water molecules through the outer membrane. Based on this result it is possible to assume that MRET water molecules can penetrate the viral capsid as well.

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