

Functions of human non-coding DNA sequences

Milanko Stupar, Vitomir Vidović, Dragomir Lukač

SUMMARY

The development of string theory has opened a completely new chapter and the way of thinking. A tight connection Arch Oncol 2011;19(3-4):81-5. between DNA, water and strings, as well as their properties, lead to the idea that the soul is the shelter of our thoughts. Only 2% of the haploid human genome codes for proteins, while the rest consists of non-coding RNA genes, regulatory sequences, introns. The rest of the DNA, about 2.9 billion of base pairs, represents: cultural heredity of the person's family and a part being formed by the person during his/her lifetime, which gives the answer to what the use of the non-coding sequences is. Water molecules do not stay permanently united with DNA (the connection is not covalent), but they disconnect at every 0.5-1 nsec, forming and leaving the DNA molecule. It is well known that the DNA structure depends on water and that "water remembers thoughts", and depending on the thoughts of a person it carries them 21000 Novi Sad, Serbia to the physical structure of DNA. At the beginning of the physical organization of the water molecule there are strings. When a person dies, the DNA and water molecule are disconnected leaving only strings with an appropriate features being conditioned by three-dimensional structure of DNA shaped by water. Every person has a unique string appear- Received: 02.02.2011

ance, as it is the case with the snowflakes (the DNA print in the strings).

Key words: DNA; DNA, Intergenic; Water; Sequence Analysis, DNA; Base Sequence; Genome, Human; Models, Theoretical; Elementary Particles; Non MeSH String Theory

INTRODUCTION

We exist in a wonderfully designed world being ruled by laws of elemental particles, as it has been thought so far. The development of the string theory has opened a completely new chapter and the way of thinking. A tight connection between the DNA, water and strings, as well as their proprieties, lead to the idea that the soul is the shelter of our thoughts. Only 2% of the haploid human genome codes for proteins (about 23,000 genes), while the rest consists of non-coding RNA genes, regulatory sequences, introns. Other non-coding sequences (about 98%) have likely but as-yet undetermined function, an inference from high levels of homology and conservation seen in sequences that do not encode proteins but appear to be under heavy selective pressure. The rest of the DNA, about 2.9 billion of base pairs, represents: the cultural heredity of the person's family, and a part being formed by the person during his/her lifetime, which gives the answer of what the use of the non-coding sequences is. To each pair of nucleotides a few tent parts of water molecules are united, depending on A-T or C-G base pairs. Water molecules do not stay permanently united to DNA (the connection is not covalent), but they disconnect at every 0.5-1 nsec, forming and leaving the DNA molecule. It is well known that the DNA structure depends on water and that "water remembers thoughts". Water remembers the thoughts and depending on the thoughts of a person it carries them to the physical structure of the DNA. At the beginning of the physical organization of the water molecule there are strings. When a person dies, the DNA and a water molecule are disconnected leaving only strings with an appropriate features being conditioned by the three-dimensional structure of the DNA shaped by water. Every person has a unique string appearance, as it is the case with the snowflakes (the DNA print in the strings). Based on this, it can be concluded that the soul is the shelter and depot of the thoughts. After the spore-like cells are discovered in parenchyma tissue of the long-extinct mammals, as well as in humans, the idea of connection of these "snowflakes of thoughts" with the DNA of these cells after mundane life has been imposed.

At birth, about 500 ova are formed at female, while spermatozoids develop later starting in puberty. In order to fertilize the existing ovum, a spermatozoid should be chosen. At the moment of choice of the appropriate spermatozoid, the sex of a child is determined, genetic basis and cultural heritage of his/her ancestor has already been encoded in DNA of fertilized egg. Billions of spermatozoids wait to be chosen, but only one gets a chance, which means that life is a great gift. It is a good basis for the idea that life, once given, never ends either physically or spiritually. This idea deserves an explanation and this is one of the ways to be explained. DNA in human genome is arranged into 24 distinct chromosomes, chromosome 1 has the most genes (2968), and the Y chromosome has the least number of genes-231. The genes comprise only about 2% of the human genome; the remainder consist of non-coding regions, whose functions may include providing chromosomal structural integrity and regulation where, when and in what quantity proteins are made. Human genome is estimated to contain 20,000-25,000 genes. Human genome contains 3164.7 million base pairs. An average gene consists of 3000 bases, but the size varies greatly, with the largest known human gene being dystrophin with 2.4 million bases. Almost all, 99.9% of nucleotide bases are exactly the same in all people. The functions are unknown for over 50% of the discovered genes.

The human genome's gene-dense "urban centers" are predominantly composed of the DNA building blocks G and C. In contrast, the gene-poor "deserts" are rich in the DNA building blocks A and T. Genes appear to be concentrated in random areas along the genome, with vast spaces of non-coding DNA in-between. Stretches of up to 30,000 C and G bases repeated over and over often occur adjacent to gene-rich areas, forming a barrier between the genes and the "junk DNA". These CpG islands are believed to help regulate gene activity, which is in agreement with the idea of this article, regarding he hydration state of the DNA.

UDC: 340.64:577.212:615.07 DOI: 10.2298/A001104081S Faculty of Agriculture, Department of Animal Science, Novi Sad, Serbia Correspondence to: Milanko Stupar, Faculty of Agriculture. Department of Animal Science, Dositeia Obradovića 8

milanko.stupar@laposte.net

Provisionally accepted: 11.03. 2011 Accepted: 12.04.2011

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HYDRATION OF THE DNA

Hydration of the DNA is an important factor in determining the physical, chemical and biological properties of the different DNA regions. X-ray fiber-diffraction studies indicate a high degree of stereochemical specificity in interaction between water and the DNA double helix. Evidence for this comes from the data showing that the molecular conformations assumed by the DNA in fibers are highly reproducible and that the hydration-driven transition between these conformations are fully reversible. These conformational transitions are induced by varying the relative humidity of the fiber environment and hence its water content. Further evidence for stereochemical specificity comes from the observed dependence of the conformation assumed on the ionic content of the fiber and the nucleotide sequence of the DNA. If the biochemical processes involving the DNA have evolved to exploit the structural features observed in the DNA fibers and oligonucleotide single crystals, the challenges in developing alternatives to a water environment can be expected to be very severe.

Hydration is crucially important for the conformation and utility of nucleic acids (1). The strength of these aqueous interactions is far greater than those for proteins due to their highly ionic character (2). The DNA double helix can take up a number of conformations, for example, right handed A-DNA pitch 28.2 Å 11 bp, B-DNA pitch 34 Å 10 bp, C-DNA pitch 31 Å 9.33 bp, D-DNA pitch 24.2 Å 8 bp and left handed Z-DNA pitch 43 Å 12 bp, with different hydration. The predominant natural DNA, B-DNA, has a wide and deep major groove and a narrow and deep minor groove and requires the greatest hydration. It needs about 30% of the weight, of water to maintain its native conformation in the crystalline state. Partial dehydration converts it to A-DNA, with a narrow and deep major groove and very wide but shallow minor groove, by decreasing the free energy required for the A-DNA deformation and twisting, which is employed by encouraging supercoiling but eventually leads to denaturation (3). Further dehydration would result in the least hydrated D-DNA (favored by excess counter-ions, ions that shield the DNA phosphate charges), which has a very narrow minor groove with a string of alternating water and counterions distributed along its edge (4). Hydration is greater and more strongly held around the phosphate groups that run along the inner edges of the major grooves.



Figure 1. Hydration of the DNA base pairs. Functionality of the DNA depends on its structure, thus the hydration of the DNA influences expression of genes

Water molecules are not permanently situated however, due to the rather diffuse electron distribution of the phosphate groups. Hydration is more ordered and more persistent around the bases with their more directional hydrogen-bonding ability and restricted space. Water molecules are held relatively strongly with residence times for the first hydration shell being about 0.5-1 ns (2). Because of the regular structure of the DNA, hydrating water is held in a cooperative manner along the double helix in both the major and minor grooves. The cooperative nature of this hydration aids both the zipping (annealing) and unzipping (unwinding) of the double helix.

Nucleic acids have a number of groups that can hydrogen bond to water, with the RNA having a greater extent of hydration than the DNA due to its extra oxygen atoms (that is ribose 02') and unpaired base sites (Figure 1). These extra hydroxyl groups also create additional hydration in duplex RNA as they provide a scaffold for the minor groove hydration network (5). In the B-DNA, guanine will hydrogen bond to a water molecule from both the minor groove 2-amino and major groove 6-keto-groups with further single hydration on the free ring nitrogen atoms (minor groove N3 and major groove N7). Cytosine will hydrogen bond to a water molecule from both the major groove 4-amino- and minor groove 2-keto-groups. Adenine will hydrogen bond to a water molecule from the major groove 6-amino-group with further single hydration on the free ring nitrogen atoms (minor groove N3 and major groove N7). Thymine (and uracil, if base-paired in RNA) will hydrogen bond to a water molecule from both the minor groove 2-keto- and major groove 4-keto-groups. The total for all these hydrations, in a G-C duplex, would be about 26-27 water molecules. There are a number of ways in which these water molecules can be arranged with the B-DNA possessing 22 possible primary hydration sites per base pair in a G-C duplex but only occupying 19 of them (6). This hydration is stronger in A-T duplex, about 44 molecules per base pairing (7). In average, 35-40 molecules of water are hydrogen bond to the one base pair. 3 billions of human base pairs bond about 120 billions of water molecules, sufficiently enough to mark every second of our existence.

The DNA structure depends on how these sites are occupied; water provides the zipping, bending, twisting, looping, holding the two strands together. It should be noted that about 2% of the hydrating water molecule sites may be transiently replaced by cations. The processing of the genetic information within the DNA is facilitated by highly discriminatory and strong protein binding. It has been shown that the interfacial water molecules can serve as "hydration fingerprints" of a given DNA sequence (8). For example, about 110 water molecules are released on binding of the restriction endonuclease EcoRI to its site GAATTC leaving an essentially dry surface and firmly bound complex (with binding which is 10,000 times stronger than for nonspecific binding) (9). Highly structured water molecules, with lengthy residence times, have been found to be essential for the structural dynamics and function of the ribosomes, where water communicates structural rearrangements in an analogous manner to its action around many proteins.

Klenow fragment of *Escherichia coli* DNA Polymerase I, for example, which was co-crystallized with the duplex DNA, positioned 11 base pairs of the DNA in a groove that lies at right angles to the cleft that contains the polymerase active site and is adjacent to the 3° to 5° exonuclease

domain. When the fragment bonds the DNA, a region previously referred to as the "disordered domain" becomes more ordered and moves along with two helices toward the 3´ to 5´ exonuclease domain to form the binding groove. A single-stranded, 3´ extension of three nucleotides bound to the 3´ to 5´ exonuclease active site (10). The structure is highly symmetrical, with each monomer containing three domains of identical topology. What happens when water molecules change spatial structure of the DNA, as well as three-dimensional structure of the DNA polymerase (since the protein structure is water determined)? In that case there is no close relationship between the DNA and the polymerase. If the mistake is not corrected, the structure of the DNA changes with various consequences. The DNA concentrated in chromosomes should be monitored as an anthill with its stable and organized interlaced changes, that are delicately masterminded and each selection played badly affects biochemistry of the cells.



Figure 2. Two-step conversion of B-DNA to A-DNA by varying the two helix parameters slide and roll. (a) Initial idealized B-DNA. (b) and (c) Intermediate structure. (d) A-DNA form. Is it possible to cause this change with thoughts?

WATER AND THE GUEST MOLECULE

This idea is focused on a relationship between the DNA, water and transposal of thoughts-energy. At this point, to study psychokinetic association with the DNA, a sample of distilled water in a sealed test tube was presented to the subjects. Five individuals were used in this study (11). While holding a beaker containing the samples, subjects were asked to focus on the samples and intentionally alter their structure for five minutes. In an adjacent room, control samples were aliquoted from the original stock solution into identical test tubes. Water samples were analyzed by two different methods immediately after the treatment. The first technique involved measuring structural changes in the water using a computerized ultraviolet spectrophotometer with a kinetic program which allows sequential automated measurements (10 seconds apart). Previous experiments indicated that structural changes were most apparent in the 200 nm region of the spectrum (12). The second technique involved studying the ability of the treated water to influence a biological system. Conformational changes in human DNA were chosen as the biological target since previous research indicated that intentional heart-directed changes caused bidirectional changes in the conformation of the DNA (13). DNA conformation was measured by a UV spectrometer from 210 to 310 nm. An increased absorbance at 260 nm is known to be due to denaturation (unwinding) of the two DNA strands. Absorbance measurements were taken before and after adding of 20 μ l of treated or controlled water to a 1.0 ml aqueous solution of human placental DNA (20 μ g/ml). Three treated simples and three control samples were tested. The results were expressed as a percent change in absorbance values at 260 nm.

Preliminary results from the DNA experiments indicated that control water caused a mean decrease in absorbance by 0.46% (+/- 0.36) in contrast to treated water, which caused a 1.35% (+/- 0.61) decrease. These results suggest that water structured in the above experiments facilitated the spontaneous tendency of the DNA to rewind (decrease absorbance). These studies were an extension of previous research indicating that water structured with bioenergy alters the growth of plants and mammalian cells in culture (14) (Figure 2). So far, many such papers were presented (confirming this idea), as well as many others relating to the so called "DNA phantom effect".

At ambient pressure, water molecules form the cavities and interact specifically with encaged molecules (in this case with the DNA) (Figure 3). At an increasing pressure, water compresses leading eventually to structural changes and expulsion of the guest DNA molecules (15). After cells' function have stopped, only the water cluster remains as a model around the DNA. Out of water cluster being formed in this way, only strings remain. The speed of this reaction could be approximately one femptosecond.



Figure 3. Clusters of the water around the DNA. DNA has left imprint in the water which squeezes the DNA as a guest, the clusters of water only remain as a template around the DNA. Only strings remain out of the water clusters formed in this way

STRINGS

Further on, this article is focused on the string theory having in mind a relationship between the DNA, water and subatomic composition of the universe, especially with the strings, in order to explain spirit as a "stock of ideas".

We live in a wonderfully complex universe and it is our privilege to live in a time when enormous progress has been made towards finding some of the answers to our curiosity. Our matter is made of atoms, which are in turn

made of just three basic components: electrons, neutrons and protons. The electron is a truly fundamental particle (it is one of a family of particles known as leptons), but neutrons and protons are made of smaller particles known as quarks. Quarks are, as far as we know, truly elemental. We can find fascinating links between the characteristics of elemental particles and everyday life. Our current knowledge about the subatomic composition of the universe is summarized in what is known as the Standard Model of particle physics. It describes both the fundamental building blocks out of which the world is made, and forces through which these blocks interact. There are twelve basic building blocks. Six of these are guarks - they go by the interesting names of up, down, charm, strange, bottom and top. A proton, for instance, is made of two up guarks and one down guark. The other six are leptons - these include the electron and its two heavier siblings, the muon and the tauon, as well as three neutrinos. There are four fundamental forces in the universe: gravity, electromagnetism, and the weak and strong nuclear forces. The behavior of all of these particles and forces is described with impeccable precision by the Standard Model, with one notable exception: gravity.

In the last few decades, the string theory has emerged as the most promising candidate for a microscopic theory of gravity (16). String theory is a model of fundamental physics, whose building blocks are one-dimensional extended objects called strings, tiny vibrating strands of energy, rather than the zero-dimensional point particles that form the basis for the Standard Model. The basic idea behind all string theories is that the constituents of reality are strings of extremely small size (possibly of the order of the Planck length, about 10^{35} m) which vibrate at specific resonant frequencies. Thus, any particle should be thought of as a tiny vibrating object, rather than as a point. This object can vibrate in different models (just as a guitar string can produce different notes), with every mode appearing as a different particle (electron, photon, etc.). Strings can split and combine, which would appear as a particles emitting and absorbing other particles, presumably giving rise to the known interactions between the particles.

Based on the string theory, there are five different possibilities. It is supposed that one of string is the "graviton", i.e. the carrier of gravity. Three strings are enough to form elemental particles by their joining (association) and vibration. The hypothesis presented in this paper is based on the idea of existing of the "mislion", i.e. the basic unit that serves for "thoughts spreading" (higher level of brain activity) onto water, and through water onto the DNA, predominantly. The last one, the fifth string would be the "mislion" with the "tachyonic neutrino's" speed = 1.52 times the speed of light). This speed was calculated by Tesla who is the "father" of neutrinos. Closed string are allowed to move everywhere through the ten-dimensional space-time, while open strings have their ends attached to the D-branes, which are membranes of lower dimensionality. The bosonic string theory, as well as phenomenal, more relevant Superstring theory, has tachyonic states in its spectrum (17). So that, "stock of thoughts" (the soul), supposed to have negative mass squared, travel faster than light, bypass black holes, guasars and penetrating into the "tachyonic space", depending on the knowledge that it bears. In other words, the "mislion" can represent a cluster of closed string tachyons traveling tachyonic neutrino's speed.

CONCLUSION

During the lifetime, a person creates by her/his thoughts that part of a DNA that relates to the personal heredity. The DNA being shaped in that way is protected and marked by water molecules till the end of life of that person. The question is asked about what happens with such a compound structure after the person's death. The DNA and water are submitted to physical separation, and even to destruction of the DNA but the strings remain as a non-materialistic unit. Based on the above mentioned, water pushes out the DNA molecule and only its matrix remains. After water discomposed, only strings remain and make a unique cluster i.e. the "soul". Since every person thinks in a different way, all these soul's clusters are different, too, as the snowflakes, and they are indestructible and flutter in the Universe in the form of the "snowflakes of thoughts" (Figure 4).



Figure 4. Every snowflake has its own form, depending on the water cluster. In the same manner, depending on the water molecules, "snowflakes of thoughts" are different for everybody

About four hours after death, all cells extinct, as it has been thought so far. The Vacanti brothers (18) have found the cells that can be divided even after death and they called them the spore-like cells. The spore-like cells are cells that exhibit behavior characteristic of spores. Known spore-like cells are a specific class of stem cells in adult organisms, including humans, which are very small, very versatile, and most frequently remain in a dormant "spore-like" state as the rest of the cells of the organism divide, grow and die. Despite their dormancy, they retain the ability to grow, divide and differentiate into other cell types expressing characteristics appropriate to the tissue environment from which they were initially isolated, if some external stimulus should prompt them to do so. This capacity to continue to regenerate new cells has been shown in *in-vitro* conditions for some animals in which all other cells have died, especially if the animal died from exposure to cold elements.

This ability has led researchers to try to revitalize spore-like cells from tissue samples of frozen carcasses deposited in permafrost for decades

(frozen walrus meat more than 100 years old, and mammoth and bison in Alaska estimated to be 50,000 years old). Because the cell-size of less than 5 micrometers seems rather small to contain the entire human genome, we can speculate on the "concept of a minimal genome". The most important question is what is the reason for existence of such cells in humans after the mundane life. Therefore the "snowflakes of thoughts" (i.e. the soul) can be related to these spore-like cells.

Conflict of interest

We declare no conflicts of interest.

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