Imperfection as the foundation of life, imprinting of DNA sequence on water.

Ivan V. Savelev1, Michael M. Rempel1, Oksana O. Polesskaya1, Richard Alan Miller1, and Max Myakishev-Rempel1

1 DNA Resonance Research Foundation, San Diego, CA, USA, ivan.savelyev23@gmail.com, mikerempel3@gmail.com, opolesskaya@gmail.com, rick@richardalanmiller.com, max@dnaresonance.org

*Correspondence: MM, max@dnaresonance.org

A novel model is presented of DNA-water interactions within the cell nucleus, proposing a mechanism for continuous self-reorganization of water structures around DNA. The model suggests that DNA sequences may imprint information onto water through stepwise shifting water layers. A key consequence of this model is the proposed prevalence of homologous sequence-specific adhesion of repetitive DNA elements, particularly transposons. In this, two identical double-helical DNA sequences stick to each other in head-to-head orientation via transverse water layers, without unwinding or separating their strands. This adhesion is proposed to drive perpetual dynamic chromatin refolding by pairing identical transposons to form large DNA loops and helices and thus create 30nm fibers and higher-order chromatin structures. Further, the model postulates the existence of a transposon code based on the positions of transposons in introns and intergenic sequences. This way positions of transposons are proposed to program chromatin refolding patterns. It is proposed that sequence-specific refolding dance of chromatin defined by transposons is a mechanism how the cell processes information, performs logical operations and ultimately, thinks. Predictions based on this structural model were tested using genome sequence data, revealing specific patterns in purine sequence distribution and nucleotide homology that provide preliminary support for the model. While largely theoretical, the model generates testable predictions. The potential applications of the proposed model include gene regulation, developmental biology, regenerative medicine and cancer research.

Introduction

While modern medical practice can replace heart valves and transplant kidneys, it remains unable to regrow a finger or regenerate a damaged joint. Some reptiles can regrow tails, and young frogs can regenerate limbs, yet mainstream biomedical research has failed to achieve limb and organ regeneration. This failure results from the pharma-dominated approach to understanding how body structure is created and maintained.

The scientific challenge to chemical reductionism has deep historical roots. In the late 18th century, Franz Mesmer introduced the concept of animal magnetism and used healing energy from his hands to treat patients. The methods and results of Mesmer resemble modern Reiki and QiGong energy healing techniques. A committee headed by Benjamin Franklin investigated

Mesmer's claims in 1784 and concluded that the results were due to the placebo effect. This was possibly the first description of the placebo effect (Franklin et al. 1784). In the early 19th century, vitalism emerged as a prominent theory, with proponents like Marie François Xavier Bichat (Bichat 1802) and Jöns Jacob Berzelius suggesting that life is driven by a vital force (Berzelius 1827). Johannes Peter Müller, a prominent experimental physiologist, made significant contributions to neurophysiology (Müller 1840). In 1840, he argued that the presence of a soul makes each organism an indivisible whole. He suggested that light and sound waves indicate that living organisms possess a unique life energy unexplainable by physical laws.

Hans Driesch introduced the term "biofield" in 1892 through his experimental work on sea urchin eggs (Driesch 1892; Weiss 1920). In the 1920s, Alexander Gurwitsch (A. G. Gurwitsch 1923), Hans Spemann (Spemann 1924), and Paul Alfred Weiss (Weiss 1920) independently proposed the concept of morphogenetic fields that define body structure during development. Gurwitsch's lab experimentally demonstrated mitogenetic radiation (radiation that speeds up the receiver's growth) using living biological models for sending and receiving the signal (A. Gurwitsch 1922; L. Gurwitsch 1924; A. G. Gurwitsch and Gurwitsch 1934). They used quartz prisms to analyze the spectrum of mitogenetic radiation. Gurwitsch's insight came from a fundamental problem in developmental biology - how organisms achieve and maintain their precise form. He proposed that electromagnetic fields could provide the precise spatial measurement needed to coordinate development across large distances. His concept of morphogenetic fields offered a framework for understanding how organisms create and maintain their proportions with high precision.

In the 1930s and 1940s, Harold Saxton Burr, a recognized experimentalist, developed the electrodynamic theory of life, describing "life fields" that define body structure (Burr 1935). Burr conducted numerous experiments measuring voltage gradients in living tissues and studying the bioelectrical properties of cancer cells, embryonic development, and the nervous system (Burr and Northrop 1935). In the 1940s and 1950s, Albert Szent-Györgyi, a prominent experimentalist, explored biological semiconductors and water properties in biological systems (Szabó 2014; A. G. Szent-Györgyi 2004; A. Szent-Györgyi 1957). He used muscle tissues from rabbits and conducted metabolic studies on humans. His experiments focused on muscle contraction, studying proteins like actin and myosin, and cellular respiration. Szent-Györgyi proposed that quantum processes, such as proton tunneling, facilitate bioelectrical activities within cells (A. G. Szent-Györgyi 2004).

The discovery of the DNA double helix in 1953 by Watson, Crick (Watson and Crick 1953), Franklin, and Wilkins (Wilkins and Franklin 1953) pivoted biological research towards molecular biology and led to modern genetics and genomics. Per-Olov Löwdin proposed quantum biology in 1963 (Löwdin 1966; Lindgren 1963). His work focused on the quantum-mechanical properties of DNA, such as proton tunneling and delocalized π electrons, and their biological function at the nanoscale. In 1969, Stanford Goldman introduced the concepts of biological quantum mechanics and DNA holograms. He studied the role of DNA in biological systems from an electrical engineering perspective and integrated quantum mechanics in biology (Goldman 1969).

In 1972, Richard Alan Miller and Burt Webb presented a model describing the DNA hologram as a biofield (Richard A. Miller and Webb 1972, 2002; Richard Alan Miller, Webb, and Dickson 1975; I. Miller, Miller, and Webb 2011). They proposed that DNA produces and interacts with a

holographic field. They discussed DNA's interaction with electromagnetic fields, resonance properties, nonlinear dynamics, and quantum coherence, connecting molecular biology with quantum physics (Richard A. Miller and Webb 1972, 2002).

In the early 1980s, Fritz-Albert Popp conducted experiments on biophotons and demonstrated that living organisms emit weak electromagnetic radiation, which plays a role in biological processes (F. A. Popp and Gu 1992; F.-A. Popp et al. 1976). James Oschman's work since the 1980s explored energy medicine, focusing on how weak electromagnetic fields influence biological systems. He investigated how the body's connective tissues, particularly fascia, act as a network of waveguides conducting bioelectrical signals. Oschman's research linked these fields to morphogenesis, health, and healing, providing a framework for therapies like acupuncture and Reiki (James L. Oschman 2000; J. L. Oschman 1981).

The earliest observation of high dilutions of substances having biological activity was by Hahnemann in 1842 (Hahnemann 1842). The ideas of biological active water structures and water memory were reintroduced by Jacques Benveniste in 1988, whose lab experimentally demonstrated that water could retain the biological activity of substances after their serial dilution. High degrees of dilution were used, so the original molecules of the substances were diluted out (Davenas et al., 1988). Luc Montagnier proposed in 2009-2015 that DNA sequences can imprint their structure on water. Montagnier suggested the transmission of genetic information via the propagation of DNA-imprinted structures in water (Montagnier et al., 2011).

Michael Levin's experimental work demonstrated direct evidence for bioelectrical control of development. He showed how bioelectric gradients can regulate embryonic development (Pai et al. 2015) and alter muscle patterning (Lobikin et al. 2015). His research provided concrete experimental validation for the role of bioelectric signals in morphogenesis.

Since the 1980s, molecular biology has revealed morphogenetic protein gradients that guide tissue patterning (Driever and Nüsslein-Volhard 1988). The gradients explain some of the developmental phenomena very convincingly. But when it comes to the precise forms of large organisms, such as lions, horses, and elephants, the gradient mechanism of measuring distance is not acceptable as an explanation for maintaining the exact body shape. The protein gradients cannot measure large distances - their spread depends on temperature and salt concentrations. Neuronal signals have the same problem - their speed varies with temperature and salt concentrations, making distance measurement impossible. Mechanoreceptors can detect force but not distance. The chemistry-dominated mainstream biology simply has no tools to measure distances at the scale of meters. This fundamental limitation of the chemistry-dominated science helps explain why, currently, the development of the body structure is poorly understood, and for that reason, current medicine is still unable to regenerate damaged organs and joints. Yet nature maintains precise proportions in large organisms. It makes perfect sense that nature utilizes physical fields such as electromagnetic and acoustic fields to measure and maintain structures, especially at larger scales. Therefore, we emphasize that the spatial coordination problem Gurwitsch and others identified in the 1920s can only be solved by force fields.

Various waves are perfect for positioning and structuring applications. Very impressive are cymatics videos that show the formation of structures resembling biological ones. These experiments typically use interference patterns of sound waves that are visualized by patterns of

sand or water dynamically formed and reformed by sound. Bats use sound for navigation. Ultrasound is used for imaging. We and animals use light to see and coordinate movements. We use infrared cameras to see in the dark. Microwaves and millimeter waves are used by radars for visualizing objects. These are candidate waves to consider among candidates for the morphogenetic field of Gurwitsch. In particular, the most obvious candidates are infrared and millimeter wave spectral regions (infrared: 0.75-1000 micrometers; millimeter waves: 1-10 millimeters). We suggest that our bodies maintain the warm temperature in part to harbor infrared and millimeter waves that take part in the biofield, coordinating the structure of the body and that transfer biological information. This idea is in agreement with the idea of Philip Ball that the body's heat transfers biological information via quantum entanglement (Ball 2018).

Role of DNA in Inheritance and Development

DNA plays a fundamental role in defining body shape and function, as evidenced by multiple lines of evidence. Different biological species have different DNA sequences. The evolution of species is essentially the evolution of the genome, where new functions arise through the acquisition of new sequences, and loss of functions occurs through the degradation of DNA sequences. DNA sequences that program for indispensable functions are conserved in evolution. This conservation is revealed by comparing genome sequences of various species - sequences that undergo very little change get high conservation scores, while sequences that change significantly get low scores.

Importantly, among highly conserved sequences, only 1/3 codes for proteins. The remaining 2/3 of conserved sequences are located in the non-protein-coding parts of the genome. The protein-coding sequences, called exons, comprise 4.5% of our genome, while non-protein-coding sequences comprise the remaining 95.5%, Figure [Genome]. Of these, 53% are occasionally transcribed to RNA and the rest are the intergenic sequences.

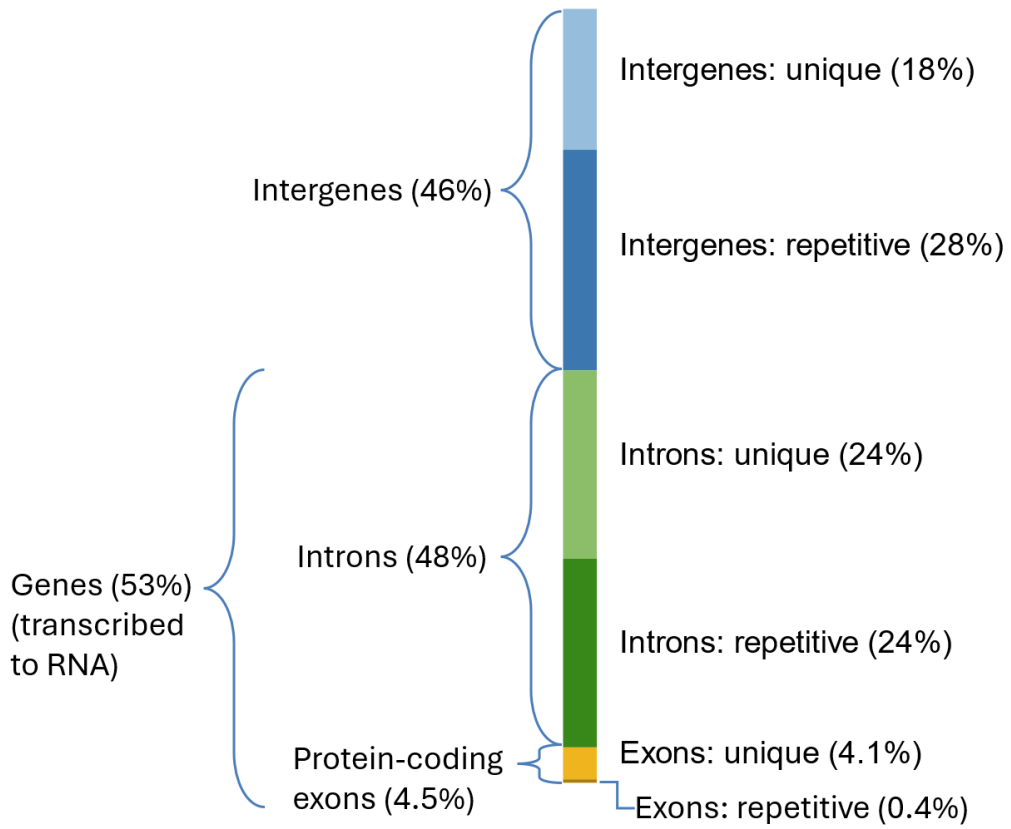

Figure [Genome]. Composition of the human genome. Intergenes - intergenic regions. Unique - unique sequences and low copy number repeats. Repetitive - as defined by the Repeat Masker (56% of the genome). Not shown: 2.7% of the genome (consisting of untranslated exons and untranslated gene ends (UTRs)). The figure was compiled by the authors based on human-curated annotations of the Ensembl genome database, release 108.

This demonstrates that both protein-coding and non-protein-coding sequences have functional roles. While protein-coding sequences define the amino acid sequence of proteins, the remaining 95.5% of the genome defines when and where, in which tissues, these proteins are produced. Additionally, non-protein-coding sequences participate in the programming of an individual's behavior. Furthermore, in this and the previous chapter, we argue that non-protein-coding sequences directly participate in cellular and organismal thinking and consciousness.

Missing Heritability Problem

While the mainstream overestimates the importance of chemistry over the fields, Rupert Sheldrake and other alternative biofield scientists argue that fields are important for body shape, function, behavior, thinking and consciousness. Specifically, Rupert Sheldrake argued that DNA is primarily important for biochemistry rather than body structure or behavior, pointing to what became known as the "missing heritability problem" (R. Sheldrake 1988). So, while mainstream overestimates the role of the DNA sequence in the body structure, function and behavior, based on the missing heritability problem, Sheldrake rejects these roles of DNA. Instead, Sheldrake proposes that body structure, behavior and thinking come from the field that he called the

"morphic field". The morphic field is defined by Sheldrake as a nonlocal informational field that defines the body structure, influences our behavior and substantially contributes to our thoughts. In the body-structure-creating aspect, the morphic field of Sheldrake is the same as the morphogenetic field of Gurwitch (note the "genetic", the "shape-creating" component of the term). In the thought- and behavior-creating aspect of the morphic field, it resembles the collective unconscious of Carl Jung. While we accept both morphogenetic and behavior- and thought-creating functions of Sheldrake's morphic field, we find that in rejecting DNA's importance, Sheldrake goes too far. We think that the truth is in the middle - between the mainstream's focus on DNA's protein-producing function and Sheldrake's underestimate of DNA's involvement in morphogenesis, behavior and thinking via various types of the biofield. To resolve this disagreement, we will first explore the missing heritability problem and then expand on the role of DNA in producing the biofields and receiving the information from them.

The missing heritability problem is a historical discrepancy between the estimates of genetic heritability between twin studies and other types of genetic studies. Genetic heritability is measured for various important traits (metrics) such as height, body mass index, height, weight, schizophrenia, intelligence, diabetes, autism, and depression. Genetic heritability is measured as what fraction of the total variation range for the specific trait in a population is contributed by genetics as opposed to nongenetic factors such as life experience, financial inheritance, environment and upbringing. Initially, the genetic heritability was measured using twin studies. Twin studies compare the variation of a specific trait between monozygotic (identical) twins to dizygotic (fraternal) twins. Identical twins have nearly 100% identical DNA (meaning their DNA sequence variations are nearly 99.99+% identical as if they were cloned or copied), while dizygotic twins share only 50% of variants, as do siblings. Therefore, it was thought that phenotype (body and behavior trait metrics) variations between the identical twins could only be caused by the nongenetic factors (environment, culture, natural divergence, etc) while the differences between fraternal twins would come from both. The genetic inheritance in twin studies is calculated by quantifying a specific trait like schizophrenia, and subtracting the average similarity in fraternal twin pairs from the average similarity in identical twin pairs, then multiplying it by a factor of 2. The factor of 2 comes from the fact that identical twins share 2 times more variants (100%) than fraternal twins (50%). The advantage of twin studies is that they don't require much genetic testing; the twins' DNA is only tested to tell whether they are identical or fraternal. Also, their environment is closely matched since they not only share the family but also develop in the same womb.

The estimates of high genetic heritability produced very high estimates in the 1970s-1990s: fingerprint patterns (95%), blood type (100%), autism (90%), bipolar (85%), schizophrenia (80, and intelligence (80%). These estimates resulted in an extensive global effort to identify the exact genetic variants responsible for the variations. For that, very different genetic methods were used. Family studies use large families of over 10 relatives or small families - 2-3 relatives to correlate the inheritance of genetic variants and traits. Genome-wide association studies (GWAS) use large numbers of individuals who are not close relatives. Adoption studies compare traits between adopted children and their genetic parents versus their adoptive (non-genetic) parents. These different approaches consistently showed much lower heritability than twin studies, revealing a large "missing heritability" gap, especially for behavior, psychiatric and

intelligence traits. Over time, genetic analysis methods expanded in their power and scope. Starting from just a few genetic markers, they progressed to examining millions of variants across the entire genome. Modern approaches, combining different methods and using haplotype reconstruction, can capture around 80% of common genetic variation. Yet, despite this technical progress, the gap between twin studies and these molecular approaches remains big, Table [Heritability].

Trait Category	Non-twin Study Genetic Heritability	Reference	Missing Heritability Gap	Twin Study Heritability
Height	40%	(Yengo et al. 2022)	50%	90%
Body Mass Index	55%	(Locke et al. 2015)	15%	70%
Type 2 Diabetes	20%	(Mahajan et al. 2018)	50%	70%
Intelligence	25%	(Savage et al. 2018)	45%	70%
Depression	10%	(Wray et al. 2018)	30%	40%
Schizophrenia	32% 44%	(Ripke et al. 2014) (Light et al. 2014)	48% 36%	80%
Autism	30%	(Grove et al. 2019)	50%	80%
Learning and Memory	15%	(Davies et al. 2018)	50%	65%

Table [Heritability]

Importantly, the missing heritability problem arises only from the twin studies. The other genetics studies, such as GWAS, show much more modest but true genetic inheritance, shown in the first column of Table [Heritability]. Therefore, the functional role of DNA in the physical and behavioral properties of the body is not disproven by the missed heritability problem; it is only deflated to real, smaller but still substantial values.

Let's now explore the possible causes of the missing heritability gap, shown in column 3 of Table [Heritability]. First, we will review possible explanations where DNA doesn't play the central role. For that, let's look more closely at the emergence of identical and fraternal twins.

Depending on when identical twins separate (days 1-3, 4-8, or 8-13 after fertilization), they can have separate amniotic sacs and placentas, separate sacs but shared placenta, or shared both sac and placenta. The most common type, split on days 4-8, results in twins with separate amniotic sacs who share one placenta. In contrast, fraternal twins always develop with separate placentas and separate amniotic sacs. So the missing heritability gap emerges from identical twins not being separated by a double-placenta wall.

The first possible non-DNA explanation relates to a known fact that placentas compete for nutrients and thus diverge into bigger and smaller fetuses (Lewis, Demmelmair, and Gaillard 2021). Since identical twins share a placenta, they don't diverge through that mechanism, while fraternal twins do diverge as their placentas compete for nutrients.

The second possible non-DNA explanation is that by sharing a placenta, identical twins synchronize through chemical, electrical, electromagnetic and acoustic signals, while siblings do

that less due to separation by a double placental wall. The identical twins originate by splitting one embryo into two. The split happens as one embryo consisting of typically 64 cells splits into two embryos of 32 cells each. The fetuses then grow to about 2 trillion cells at birth, requiring about 32 cell divisions. During this time, the cells undergo multiple waves of epigenetic differentiation via sequence-specific methylation of various locations in the genome. What specific locations are methylated in the genome and when - is essential for the development of body and mind and can be affected by chemical, electrical, and electromagnetic signals. Being in one placenta synchronizes this epigenetic development of the identical twins. Originating from the same 64-cell embryo also makes them more similar than fraternal twins.

The third possible non-DNA explanation is that identical twins synchronize through the above-mentioned biological quantum entanglement proposed by Philipp Ball (Ball 2018). Being in the same placenta, identical twins sharing fluids, chemicals, wave signals, radial and diffusive heat, become more biologically quantum entangled than fraternal twins. Again, originating from the same 32-cell embryo would increase the extent of their biological quantum entanglement.

But ultimately, there is an explanation that combines DNA similarity and Sheldrake's morphic resonance (R. Sheldrake 2012; Rupert Sheldrake 1981). In fraternal twins, the 50% shared genetic variants are scattered across the genome as 50-100 large patches of continuously identical sequences (haplotypes), interrupted by partly dissimilar sequences containing millions of dissimilar variants. In contrast, identical twins share practically 100% of their genome (99.999999% identical). While the similarity between twins increases only twofold from 50% to 100%, the dissimilarity between them drops dramatically from 50% (approximately 2 million variants) to 0.0000001% (under 80 variants). So, in identical twins, the whole chromosomes are identical and not patched as in fraternal twins. This dramatic difference in sequence patterns - scattered patches versus complete similarity - creates different conditions for morphic resonance. The scattered pattern in fraternal twins enables only partial resonance, while the complete sequence similarity in identical twins enables coherent genome-wide resonance. This genomic coherence explains their disproportionally stronger phenotypic similarity and morphic resonance, contributing to the missing heritability gap. This effect would work not only among identical twins but also among highly genetically similar relatives. Therefore, the missing heritability gap does not diminish the importance of DNA but rather demonstrates how DNA sequence similarity enables coherent genome-wide morphic resonance.

The Standish study examined brain activity between physically separated identical twins (Standish 2024). One twin viewed changing images while the other viewed a static image in soundproof rooms 20 meters apart. Brain scanning showed that activity patterns in the observing twin aligned with image presentation timing to the other twin ($p = 4\times10^{-8}$). This illustrates that 100% genetic similarity could cause remote synchronization. Based on morphic resonance between identical DNA sequences, it would be interesting to investigate whether blood tests could affect subject health outcomes. Similarly, morphic resonance could provide a mechanism explaining the therapeutic efficacy of leech therapy, since blood containing the donor's DNA sequences undergoes modification and may influence its original donor.

An interesting question remains: which part of the missing heritability is explained by the flaws in the classical genetic analysis, which part is by much higher DNA resonance between identical twins due to their identical genomes and which part is by the fact that identical twins develop in the same placenta? See Figure [Decomposition]. This could be addressed experimentally. The ideal comparison for that would be identical twins vs. clones vs. siblings. Since human clones are hard to get by, it would be sufficient to study twins vs clones in the model organisms. Clones, like twins, have identical DNA but are born separately. If clones show as high a heritability gap as twins in comparison with siblings, this would allow us to quantify the true contribution of DNA resonance as opposed to effects produced by gestation in one placenta. It is easy to produce clones and siblings in some model organisms such hydra, planarians, daphnia, and aphids. In these, the genetic clones are produced through asexual reproduction and siblings through sexual reproduction, providing an economical way to compare concordance between clones vs concordance between siblings. Yet, in these organisms, it is costly to produce twins and genetic or GWAS studies that are needed to reproduce the heritability gap. Therefore we would need a model organism with placenta or eggs, to compare all three metrics: identical twins, fraternal twins, clones and heritability based on family and population studies. Such a suitable model is zebra fish. Its genetics is pretty well studied and also there are accessible established methods to produce twins (Mizuno, Yamaha, and Wakahara 1997) and clones (Kaftanovskaya, Motosugi, and Kinoshita 2007) with reasonable effort.

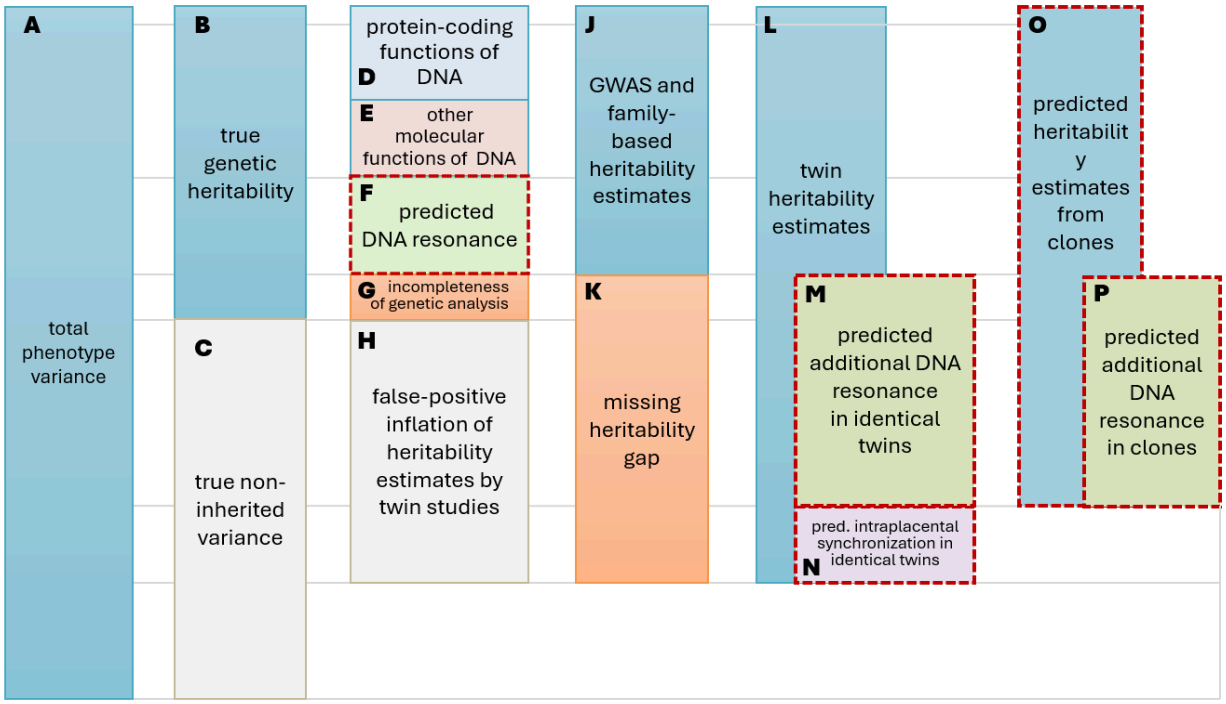

Figure [Decomposition]. Decomposition of total phenotype variance showing how the components add up. The proportions shown represent our best estimate. Dashed boxes represent novel predicted phenomena.The purple box "pred. intraplacental synchronization in identical twins" includes the proposed lack of competition, chemical, bioelectrical and epigenetic synchronization, and quantum biological entanglement in identical twins due to placenta sharing.

To summarize how the above discussed missing heritability problem can be dissected, we illustrated that in the Figure [Decomposition]. The missing heritability gap (K) arizes from the comparison of twin heritability estimates (L) and GWAS and family-based heritability estimates (J). We agree with Sheldrake that only a small part of the missing heritability gap can be explained by the incompleteness of the genetic analysis (G). The rest is false-positive inflation of heritability estimates by twin studies (H). Twin studies (we believe incorrectly) estimate heritability by comparing phenotypic concordance bwetewen identical twins to concordance between fraternal twins. Alshtough it is true that identical twins have twice as many concordant DNA variants as fraternal twins, two substantial factors are ommitted in twin heritability estimates. As we explained in detail above, we propose that inflation (H) arises from these two ommitted factors:

- (M) due to identical DNA, the identical twins have a large increase in DNA resonance as compared to fraternal twins that have over a million dissimilar genetic fariants.
- (N) due to shared placenta identical twins don't compete, do quantum entangle and do syncrhonize in chemical, bioelectrical and epigenetic development.

We suggested that studies with model organisms such as zebra fish would allow to exclude the placental effects (N) by comparing clones to twins to non-twin genetic heritability estimates (O). That would allow a more accurate estimate of effects of DNA resonance between clones and will prove that the bulk of similarity between identical twins arises from DNA resonance. That shuld take care of the mystery with the missing heritability gap (K) by explaining the inflation (H).

Without twin studies, the estimates of true genetic heritability are more modest (B). The rest of variation in population is true non-inherited vaiance (C) - individuals grow up different unless they are twins or clones. In essence we suggest that exceptional similarity in twins and clones although largely genetic can not be used to estimate the genetic inheritance in the rest of popularion since twins and clones sinchronize disproportioinally more.

Coming back to non-twin heritability J, it is composed from 3 factors: genetic inheritance of protein coding functions of DNA (D), other molecular (biochemical) funcitons of DNA (E) and proposed DNA resonance (F).

The role of DNA in morphogenesis

Two possibilities exist regarding DNA's role in development: either DNA directly contains the program for body development and shape, or (in substantial agreement with Sheldrake's theory) DNA sequence acts as a key or barcode that retrieves information from the morphic field. Most likely, both mechanisms substantially contribute to the development and function of the body and mind. However, in either case, DNA's role in morphogenesis and behavior is substantial. Below we will show specific examples of the role of DNA sequences in morphogenesis that go

beyond mere protein production but define where and when specific proteins are produced, thus affecting morphogenesis and behavior.

DNA sequence determines body structure

Until now, we reviewed the works that utilize the forward genetics approach - they start with the natural variation in the population, do genome-wide screens for variations (alleles) correlated with the phenotype and calculate genetic heritability metrics. The reverse genetics approach uses genetic engineering to manipulate specific genes. This genetic manipulation approach allows to study the influence of specific sequences on body shape or behavior in detail with proper controls.

In butterflies, scientists identified DNA sequences that control wing patterns. The WntA regulatory sequences work like switches, determining color boundaries on wings. When scientists took these sequences from a butterfly with orange stripes and inserted them into a species with white stripes, the recipient butterflies grew orange stripes in precisely the donor pattern locations. The transplanted DNA directly determined the physical pattern (Martin et al. 2012; Mazo-Vargas et al. 2017).

In vertebrates, a different DNA sequence controls limb formation. The ZPA regulatory sequence - 780 DNA letters long - directs where and when embryonic tissues produce Sonic Hedgehog protein during limb development. Scientists found that changing a single letter in this sequence causes specific limb deformities. In mice, these mutations led to extra digits. In humans, researchers discovered the same DNA changes in patients with identical finger malformations. The sequence dictates limb structure across species (Lettice et al. 2003; Sagai et al. 2009).

In mice, separate DNA sequences control how digits develop. The Hoxd enhancer sequences determine when each finger forms and where it grows. These sequences activate digit-building genes in sequence. When researchers altered these control regions, they could predictably disrupt finger timing and position. Each DNA modification led to specific changes in digit arrangement (Spitz, Gonzalez, and Duboule 2003; Montavon et al. 2011).

In fruit flies, DNA directly controls how the body is divided into segments - the distinct repeating sections you can see as stripes on the fly's abdomen. A DNA sequence called the "stripe 2" enhancer determines where the second body segment forms. When scientists deleted this sequence, the second segment vanished completely - leaving a gap in the body pattern. When they added an extra copy of this sequence, an extra segment grew. When they moved this sequence from one fruit fly species to another, the segment formed exactly where it would in the donor species (Small, Blair, and Levine 1992; Ludwig et al. 2005).

This represents direct experimental genetic manipulation, showing DNA sequences contain instructions for building biological structures. DNA does not only specify proteins. It directs the assembly of complex physical forms through precise control sequences that orchestrate development.

The role of DNA in behavior

Here are the specific examples of DNA involvement in behavior that goes beyond the production of proteins, including hormones.

Circadian Rhythms: The period (per) gene in Drosophila provides clear evidence. The perShort and perLong mutations change daily activity cycles from 24 hours to 19 or 28 hours, respectively (Konopka and Benzer 1971). A single base change in regulatory regions shifted the entire timing of daily behaviors - when flies wake up, feed, and become active. Later studies showed these mutations affect the timing of per gene's daily oscillations, and not just protein levels (Hardin, Hall, and Rosbash 1990).

Mating timing: In fruit flies, specific sequence variants in the timeless gene affect when during the day courtship behavior occurs (Tataroglu and Emery 2014). These variants influence whether flies mate in the morning versus evening, creating temporally isolated populations.

DNA sequence controls behavior not just through protein structure but through complex regulation of when and where genes are expressed. Two examples clearly demonstrate this principle. First, in fruit flies, the fruitless (fru) gene controls male courtship behavior through sex-specific splicing patterns. While both males and females have the same fru gene, different regulatory sequences determine how the gene is spliced and expressed in specific neurons during development. This controlled pattern of expression, not just protein levels, determines whether the fly displays male courtship behaviors (Demir and Dickson 2005; Manoli et al. 2005; Stockinger et al. 2005).

The second example comes from comparative studies of social behavior in voles. Prairie voles form strong pair bonds, while closely related montane voles do not. This behavioral difference stems from distinct patterns of vasopressin receptor (Avpr1a) expression in their brains, controlled by differences in regulatory DNA sequences. When these regulatory sequences are transferred between species, they carry with them their specific expression patterns and corresponding social behaviors (Young et al. 1999; Hammock and Young 2002; Lim et al. 2004).

DNA Hologram

Upon demonstrating the central role of DNA in both morphogenesis and behavior, we return to the fundamental problem discussed earlier - maintaining precise body structure at large scales. Chemical gradients and neural signals cannot reliably measure or maintain distances in large organisms due to their variability at different temperatures and salt concentrations. The field concept was suggested to be a much more suitable mechanism for spatial coordination. Now, we can explore how DNA can produce the physical fields and interact with them. The DNA hologram concept offers a mechanistic framework that unifies DNA's regulatory functions in form and behavior with the need for field-based spatial coordination. It explains how a one-dimensional DNA sequence could orchestrate three-dimensional biological structures through field effects.

We propose that DNA functions as both a source and receiver of biofield information, forming a feedback loop (Richard A. Miller and Webb 1972, 2002; Richard Alan Miller, Webb, and Dickson 1975; I. Miller, Miller, and Webb 2011). The biofield is generated by the body and regulates where and when protein-coding genes are activated. The biofield coordinates gene expression in space and time, establishing the body's symmetry and structural patterns. Since here biofield controls morphogenesis, we will also refer to is as the morphogenetic field, named so by Gurwitsch.

We propose that DNA operates holographically through several key mechanisms. Its linear sequence encodes wave-based patterns that interact via electromagnetic fields to generate three-dimensional biological structures. First, this follows the holographic principle of interference patterns, as DNA's electromagnetic oscillations create complex standing waves that contain spatial information. Second, the DNA field patterns exhibit distributed information storage, where each portion contains information about the whole organism, just as each piece of a hologram retains the complete image. Third, phase relationships and coherence between DNA oscillations coordinate biological organization across space and time, similar to how phase information enables 3D holographic reconstruction. Finally, these wave-based patterns from DNA guide morphogenesis by creating resonant structures that direct matter into coherent forms, transforming one-dimensional genetic information into complete three-dimensional organisms (Richard A. Miller and Webb 1972, 2002; Richard Alan Miller, Webb, and Dickson 1975; I. Miller, Miller, and Webb 2011).

Upon demonstrating DNA's central role in both morphogenesis and behavior, we return to the morphogenesis problem discussed earlier - maintaining precise body structure at large scales. Chemical gradients and neural signals cannot reliably measure or maintain distances in large organisms due to their variability at different temperatures and salt concentrations. To address this spatial coordination challenge, Gurwitsch proposed the concept of morphogenetic fields. In 1972, Miller and Webb extended this idea by suggesting that DNA itself could generate and interact with these fields through holographic principles (Richard A. Miller and Webb 1972, 2002; Richard Alan Miller, Webb, and Dickson 1975; I. Miller, Miller, and Webb 2011).

We propose that DNA functions as both a source and receiver of biofield information, forming a feedback loop. The biofield, equivalent to Gurwitsch's morphogenetic field, is generated by the body and regulates where and when protein-coding genes are activated. This field coordinates gene expression in space and time, establishing the body's symmetry and structural patterns.

The DNA hologram concept explains how a one-dimensional genetic sequence could guide the creation and maintenance of three-dimensional biological structures through field effects. DNA operates holographically through two key mechanisms. First, coherent wave interference patterns between DNA oscillations coordinate biological form in space, similar to how two stereo speakers create three-dimensional sound through phase interference. Second, the DNA field patterns exhibit distributed information storage, where each portion contains information about the whole organism, just as each piece of a hologram retains the complete image.

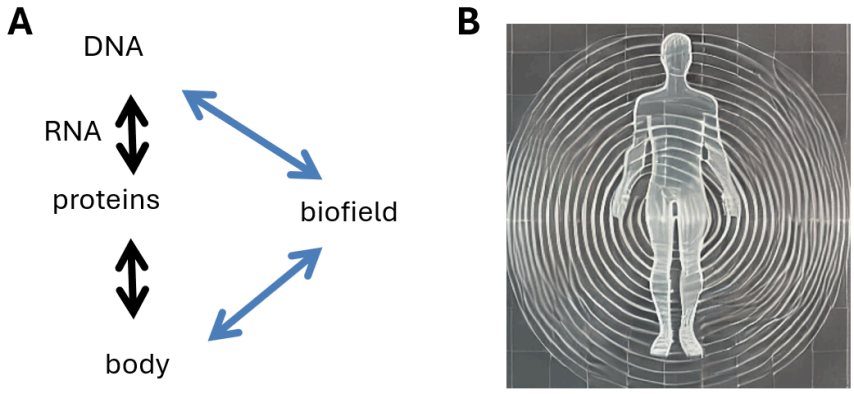

Fig. [Biofield]: Conceptual model of biofield interactions with biological systems. A. Diagram showing interconnections between DNA, RNA, proteins, body, and biofield. Black arrows represent the Central Dogma of molecular biology, while blue arrows indicate proposed biofield interactions. The bidirectional DNA-biofield arrow emphasizes genomic DNA's role in creating the biofield via the holographic principle. B. Artistic representation of a human body surrounded by concentric rings, symbolizing the morphogenetic field shaping the physical body, extending the concept of DNA-originated biofields to the organismal level.

Moreover, we proposed that DNA's holographic functions extend beyond morphogenesis to participate in consciousness. Through its sequence-specific interactions with the biofield, particularly through non-protein-coding regions, DNA plays a dual role - both in physical structure formation and in the grounding of universal consciousness. We have expanded this role of DNA in grounding universal consciousness via biofield in the previous chapter.

Chromatin structure and the field

In multicellular organisms, DNA is never naked; it is wrapped a histone core. This arrangement resembles a metal snake coiled around a napkin, Fig. [Nuc]. The double helical DNA is structured in about two turns around the nucleosome, creating a typical well-characterized structure. The tetranucleosome, depicted in Fig. [Nuc], represents the largest orderly DNA structure. Beyond this, larger structures containing nucleosomes and tetranucleosomes are arranged aperiodically, lacking an obvious order.

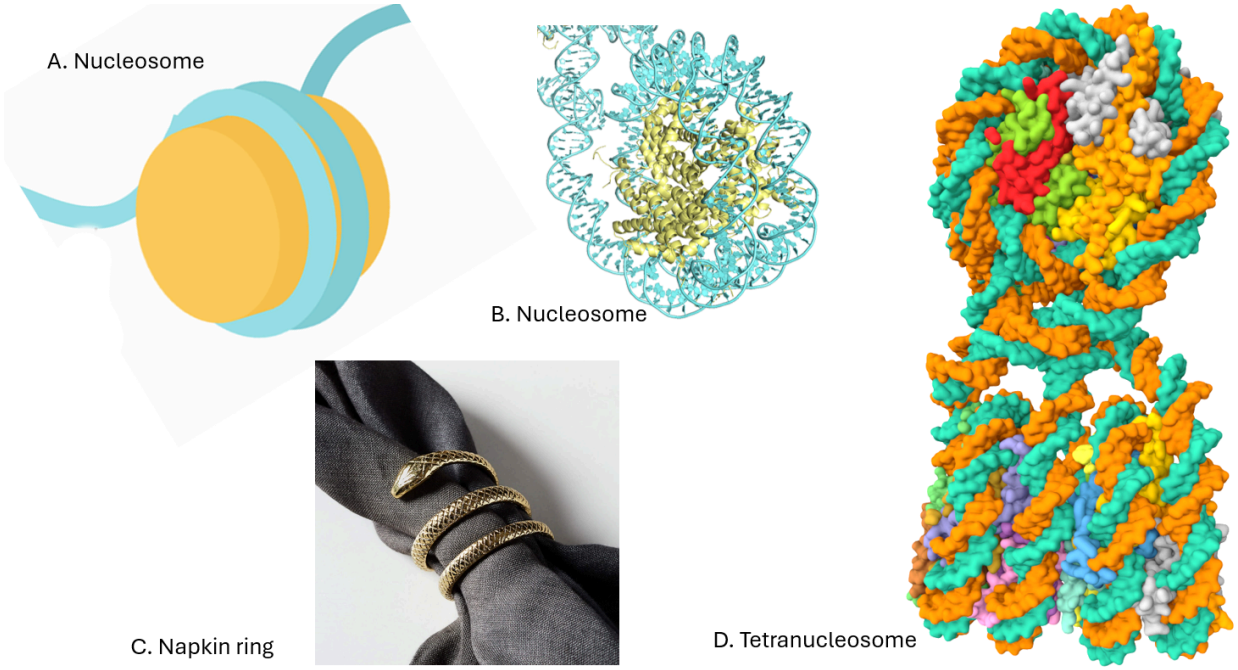

Fig. [Nuc]. Structural organization of DNA in chromatin. A. Simplified schematic of a nucleosome, showing DNA (blue) wrapped around histone protein core (yellow). B. Molecular model of a nucleosome, illustrating DNA (blue) coiled around the histone core (yellow). C. Napkin ring analogy for DNA wrapping around histones, demonstrating the coiling nature of DNA in nucleosomes as a left-handed helix. D. A typical crystallographic tetranucleosome structure, displaying four nucleosomes connected by linker DNA.

In 2003, we introduced the concept of DNA resonance at Michael Levin's seminar. We proposed that nucleosomes function as electromagnetic antennas, with DNA serving as the conductor. As alternating current flows through the DNA coiled around nucleosomes, they emit electromagnetic waves. Nucleosomes containing identical DNA sequences would have matching natural frequencies and oscillation patterns, allowing them to resonate. In this model, a DNA resonator is defined by its unique oscillation signature. When resonators interact through electromagnetic waves, they establish resonance and exchange information, amplifying their oscillations. This process requires biochemical energy, that might be supplied by ATP - one cell expends energy to generate the signal, while another cell with matching resonators receives and converts it into biochemical responses, such as RNA transcription (Figure [Res]) (Polesskaya et al. 2017).

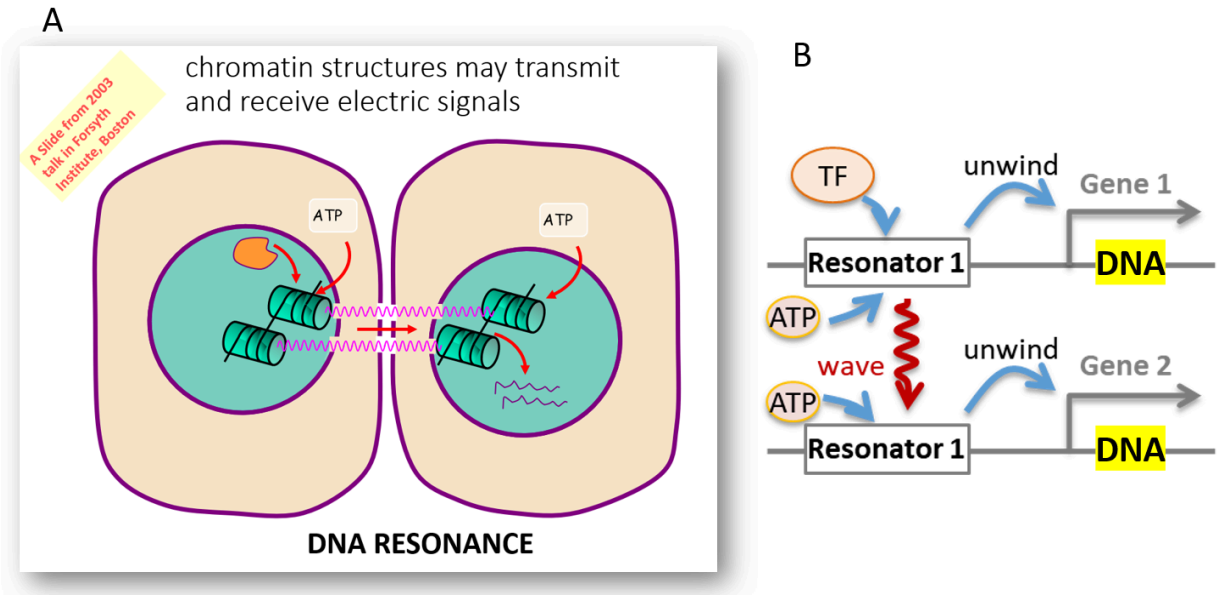

Figure [Res]: Conceptual model of DNA resonance and its potential role in gene regulation. A. Chromatin structures transmitting electric signals via ATP-driven oscillations as presented by MVM in 2003. B. Schematic of DNA resonance-mediated gene activation, showing how resonators may facilitate coordinated gene expression.

Figure [Res] visually represents the DNA resonance concept. Panel A, presented in 2003, illustrates how nucleosomes, resembling electric magnets, can emit electromagnetic waves when alternating current passes through the surrounding DNA. Panel B demonstrates how this principle might apply to gene regulation. Here, specific DNA sequences acting as resonators can be activated by transcription factors and fueled by ATP. The resulting electromagnetic waves can propagate to other resonators with matching oscillation patterns, leading to gene activation. This model provides a potential explanation for the coordinated expression of distant genes and offers insight into how resonance signaling in chromatin can contribute to gene regulation. Since identical DNA sequences should have similar structures and similar oscillation frequencies and patterns, they are primary candidate for resonating structures in DNA. In search for identical sequences in DNA we immediately stumbled upon the fact that our genomes contain extraordinary numbers of identical sequences. These are repetitive transposable elements what comprize about 50-55% of our genome, Figure [Genome]. We will further discuss the role of repetitive elements (transposons) further in this chapter.

Imprinting of DNA on water structure

For a while, our interest in water structure and in DNA resonance didn't overlap as we thought that base stack (the inner core of the double helix) is hydrophobic and is electrically insulated from water. Only thorough modeling of delocalized groups of protons of DNA brought us to the realization that it is only the inner part of the base stack is hydrophobic, while the outer part of the base stack is hydrophilic and exchanges protons with the surrounding water. Thus our modeling of electron and proton oscillations in DNA (Savelev and Myakishev-Rempel 2020a, 2020b; I. Savelyev and Myakishev-Rempel 2019; I. V. Savelyev et al. 2018; Aleksandr V. Vikhorev et al. 2024) led us to the necessity to model the structure of water surrounding DNA. We came to understanding that biological information could spread through water as a front of

new structure that reorganizes the liquid crystal of water in a new pattern. While DNA signaling through electromagnetic waves represents patterns in time, crystal propagation in water structured by DNA represents patterns in space. We hypothesized that DNA might initiate the microcrystallization of water and imprint its sequence onto the water structure, a process we termed crystal pattern propagation or snowflake signaling, Fig.[Snowflake]. In snowflakes, patterns propagate in multiple directions and change with distance from the center. Similarly, in biology, microtubules self-crystallize from monomers, often growing from one end and dissolving on another end, or alternating growth and dissolution. This is a dynamic bidirectional process. Other cellular fibers, including actin filaments and intermediate filaments, display similar dynamic self-assembly from monomers and dissolution. We proposed that in the nucleus, DNA imprints its sequence-dependent structures onto the surrounding water, creating microscopic liquid crystal structures. These water-based patterns then propagate outwards from DNA carrying sequence-specific information. This suggests that genetic information could spread through structured water.

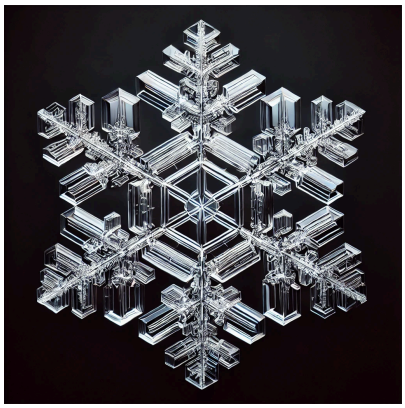

Fig.[Snowflake] Snowflake, an artificial image.

The concept of DNA imprinting on water structure resonates with experimental observations by Montagnier and colleagues (Luc Montagnier et al. 2009; L. Montagnier et al. 2011), claiming the experimental evidence that DNA solutions could embed sequence information in water structure. Similarly, Benveniste showed experimentally that water could retain biological activity after serial dilutions (Davenas et al. 1988). So the idea of water memory of drugs, proteins and DNA has been around for many years.

Gilbert Ling suggesting that cellular water is organized in multilayers around proteins and other components (Ling 1962). It has been proposed that within the cells, there are small clusters of structured water, forming liquid crystals. Experimental studies support this concept, showing that water near biopolymers can exist in ordered forms. For instance, NMR and X-ray diffraction studies have shown two structural states of water in hydrated biomolecules (Denisov et al. 1997). Gerald Pollack has advanced the notion of a "fourth phase of water" or "exclusion zone water" near hydrophilic surfaces, which he argues may play a crucial role in cellular functions (G. H. Pollack 2001). Martin Chaplin has extensively reviewed the potential structures and behaviors of water in biological systems (Chaplin 2006). Cryo-electron microscopy and neutron scattering have provided direct observations of ordered water clusters around DNA and proteins, essential for their stability and function (Ebbinghaus et al. 2007). The structuring of

water in cells is likely dynamic around biopolymers in the cells (Ball 2008). Infrared spectroscopy has demonstrated special vibrational properties of water near biological interfaces, suggesting the formation of structured water clusters (Cherkasova et al. 2020).

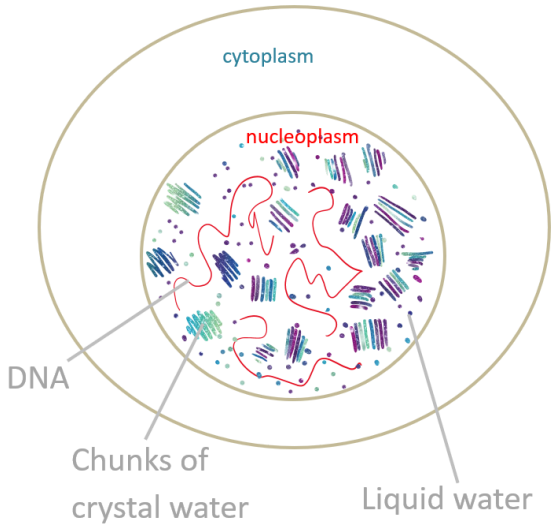

Fig. [Clusters] Clusters of structured water in the nucleoplasm

The cell nucleus contains nucleoplasm - a thick, gel-like fluid enclosed by the nuclear membrane, Table [Nucleoplasm]. Its composition consists primarily of water at 77%, with proteins making up about 19% (including histones at 11% and other nuclear proteins at 8%). DNA accounts for 1%, RNA for 3.5%, and small molecules and ions make up the remaining 0.5%.

Component	w/w %	mM
Water	77 %	43,000 mM
Proteins:		
Histones	11 %	1-2 mM
Nuclear matrix proteins (Lamins, Nuclear pore complex proteins, Actin, Spectrin-repeat proteins)	3 %	0.1-0.5 mM
Other proteins: (hnRNPs, RNA polymerase II, Topoisomerase II)	5 %	0.5-2 mM
DNA	1 %	0.01 mM
RNA	3.5 %	0.5-1 mM
Small molecules and ions (K+, Na+, Glutamate, NAD+, Cl-, ATP, Glycine, Inorganic Phosphate, etc.)	0.5 %	150-200 mM

Table [Nucleoplasm]: Estimated concentrations of nucleoplasm components. The relative concentrations of all components are variable depending on the cell type and activity. Only the absolute amount of DNA is constant.

During interphase, chromosomal DNA undergoes continuous dynamic movement throughout the nucleoplasm. This phenomenon has been well-documented through fluorescence in situ hybridization (FISH) and live-cell microscopy (Tortora, Salari, and Jost 2020). Multiple research groups have shown that chromatin mobility follows complex but measurable patterns through detailed tracking studies.

We propose that within this dynamic environment, the nucleoplasm contains organized clusters of structured water contributing to its gel-like properties. This builds directly on Pollack's work (G. H. Pollack 2001) on structured water in biological systems. Microscopy studies have demonstrated that the nucleoplasm behaves as a self-organizing gel, maintaining both fluidity and structural coherence.

Szent-Györgyi developed the concept that biological systems function optimally in states between order and chaos, suggesting this enables their response to subtle fields (Albert Szent-Györgyi 1960, 1941, 1968) . (We use the term subtle fields in a broad sense to describe non-electromagnetic informational fields that are not detectable by conventional instruments but are captured by biological systems). To illustrate the idea of sensitivity of unstable systems to weak inforces, consider these simple mechanical examples: A plate covered with sand reveals sound wave patterns when vibrated. A stuck cork requires twisting motion to reduce friction before it can be pulled out. The key idea here is that some form of perpetual random motion helps the system respond to weak forces. A radio receiver demonstrates both sensitivity and specificity - it combines a capacitor and induction coil tuned to a specific frequency, feeds energy into oscillations, and amplifies weak signals captured by the antenna.

The nucleoplasm exemplifies a responsive state. It contains highly charged DNA in constant motion, continuously self-reorganizing, within warm water that undergoes extensive Brownian motion. Accordingly, this state has the capacity to respond to and amplify weak electromagnetic, electroacoustic and subtle fields. This model builds upon Fröhlich's work (Herbert Fröhlich 1968) on coherent excitations in biological systems. We propose that the combination of chromatin remodeling and structured water dynamics generates a medium actively interacting with the biofield.

The biofield model connects nucleoplasm structure with electromagnetic fields. In this model, moving charged coils of DNA and oppositely charged histones generate electromagnetic fields in the conducting nucleoplasm. Formation of electromagnetic vortices from such charge separation has been well documented in unmagnetized systems, where charge gradients and non-conservative forces naturally create vortex patterns (Kumar 2024). At microscale, comparable to nucleoplasm dimensions, electromagnetic fields can organize moving charged particles into self-sustaining vortices, as demonstrated in experimental systems (Kokot and Snezhko 2018).

We suggest that within the nucleoplasm, these electromagnetic vortexes form through the interplay of moving charged DNA and histones, electromagnetic induction, and fluid dynamics (Savelyev et al. 2019). The circular motion of charged molecules generates magnetic fields, inducing currents that reinforce the original motion. This self-amplifying process creates stable EM vortexes at various scales. The principles of magnetohydrodynamics govern these

interactions, where the conductive nucleoplasm behaves as both a fluid and an electromagnetic medium. Lorentz forces act on moving charges, while induced currents generate additional magnetic fields, creating a complex feedback system of fluid flow and electromagnetic phenomena."

The biofield model connects nucleoplasm structure with electromagnetic fields. In this model, moving charged coils of DNA and oppositely charged histones generate electromagnetic fields in the conducting nucleoplasm. While fluid vortices are not observed in microscopy of nucleoplasm, we propose formation of purely electromagnetic vortices - patterns in electromagnetic fields that exist without visible fluid rotation. The physics of electromagnetic vortex formation from moving charges has been demonstrated in simpler systems: charge gradients create electromagnetic vortex patterns in unmagnetized plasmas (Kumar 2024), and spinning charged molecules like DNA helices and protein domains can generate vortices through the Lorentz effect. At microscale, comparable to nucleoplasm dimensions, electromagnetic fields can organize moving charged particles into self-sustaining vortices, as demonstrated in experimental non-biological systems (Kokot and Snezhko 2018).

Within the nucleoplasm, we proposed these electromagnetic vortexes could form through the interplay of moving charged particles, electromagnetic induction, and fluid dynamics (V. Savelyev et al. 2019). According to this model, movement of charged molecules generates magnetic fields, inducing currents that reinforce the original motion in a self-amplifying process that creates stable electromagnetic vortices at various scales (V. Savelyev et al. 2019).

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Structured Water Patterns in Nucleoplasm

For a long time, we viewed the base stack of DNA as hydrophobic and electrically insulated from water. Yet, as we explored proton delocalization in DNA, our modeling revealed that while the inner core of the base stack is hydrophobic, its outer surface is hydrophilic and actively exchanges protons with surrounding water. This led us to examine how DNA-water structure relates to the DNA hologram concept. Two earlier works were relevant to that. Benveniste had demonstrated that water retains biological activity after serial dilutions (Davenas et al. 1988). Later, Montagnier showed that DNA solutions could embed sequence information in water structure (L. Montagnier et al. 2011).

In our search for suitable water structure models, we first examined classical ice structures, particularly Ice IV, as these were well studied. However, we found ice structures unsuitable for sequence imprinting due to their rigid hydrogen bonding networks. We then examined Gerald Pollack's work, which showed that water forms ordered layers near hydrophilic surfaces (Pollack 2001, 2013). In a discussion following his YouTube presentation, Pollack suggested that layer shifting might provide a mechanism for water memory (G. Pollack 2019). When we inspected the molecular models of Pollack's structured water, we noticed they would be impossible without gaps, though these gaps were not explicitly included in his models.

This observation led us to Lippincott's polywater paper from 1969 (Lippincott et al. 1969). We found that his model already contained the structural gaps that would later be proposed by Pollack. Looking deeper at the Russian sources uncovered that Devyatkin, who worked directly with polywater samples, maintained that the polywater after all was not an experimental artifact - polywater was not disproven, but rather classified away from mainstream research (Дерягин and Чураев 1989; Дерягин 1990; Щукин and Русанова 1994).

The Lippincott model showed particular promise for our purposes. It describes a hexagonal water structure with well-defined gaps, maintaining electrical neutrality. Its honeycomb pattern contains incomplete hexagons and spaces for single water molecules, allowing dynamic growth and dissolution. Most importantly, we observed that the hexagonal patterns in DNA base pairs (G-C and A-T) align naturally with this honeycomb structure.

This observation led us to examine polywater, first discovered by Fedyakin in 1961 and further developed by Deryagin (Derjaguin and Churaev 1966). Lippincott's detailed structural analysis from 1969 (Lippincott et al. 1969) revealed a model that contained the structural gaps that explained how polywater maintains overall neutrality. While polywater research was repressed in both Western and Soviet scientific literature, Deryagin maintained its validity until his death in 1994, supporting his position with extensive experimental evidence (Дерягин and Чураев 1989; Дерягин 1990; Щукин and Русанова 1994).

We observed that base pairs of DNA display a hexagonal arrangement of atoms, a structural feature documented in Watson and Crick's original work (Watson and Crick 1953). This hexagonal pattern exists both in the arrangement of atoms within G-C and A-T pairs and in the gap where hydrogen bonds form between bases. Since Lippincott's polywater model forms a hexagonal honeycomb structure, we considered whether the hexagonal patterns in base pairs could align with it.

For the hexagonal patterns to align, water layers must form perpendicular to the DNA axis. This orientation makes the water layers parallel and coplanar with the base pairs, potentially allowing

them to imprint structure of the DNA double helix into water layer shifts.

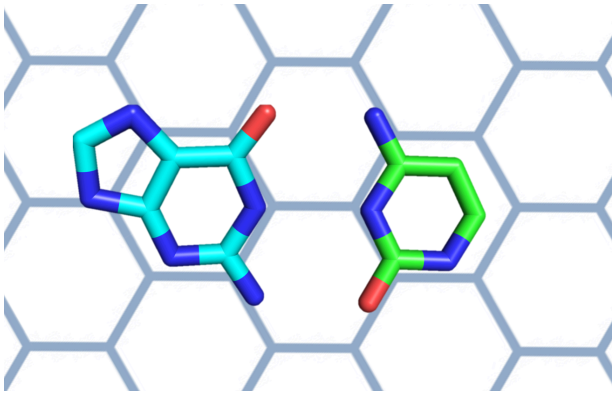
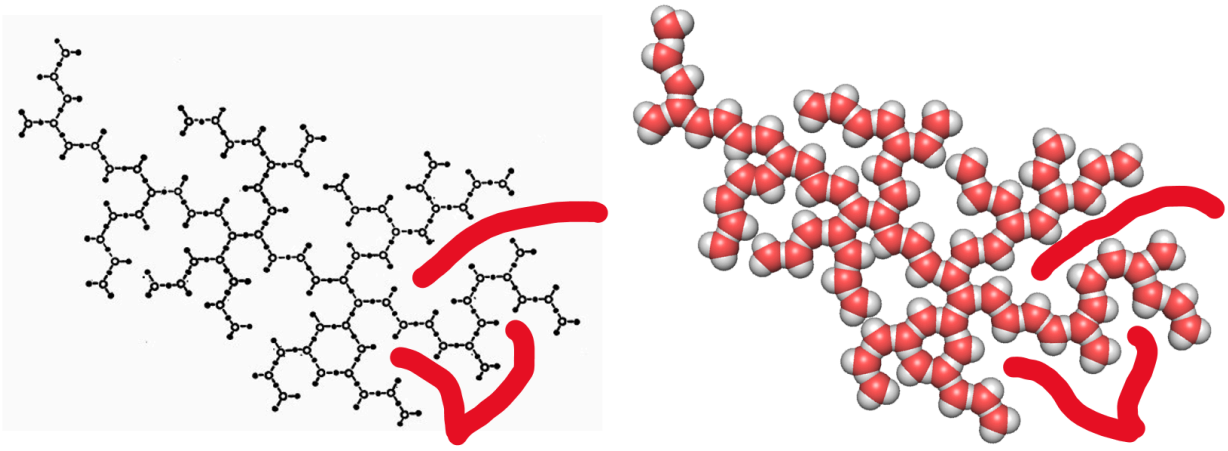


Fig.[Embedding] Proportions of the base pair GC embedded in the Lippincott's honeycomb water layer. The hexagonal geometry of DNA base pairs matches the honeycomb pattern of polywater when water layers are oriented perpendicular to the DNA axis. This perpendicular orientation allows water layers to be coplanar with base pairs and capture the double helix structure.

We believe that Lippincott's polywater has the same water structure as Pollack's EZ water, which forms near negatively charged biopolymers such as DNA. Unlike Pollack's EZ water, Lippincott's polywater structure is electrically neutral overall, featuring a honeycomb pattern with gaps (which we term "canyons") that are crucial for continuous dynamic self-reorganization of water. It contains incomplete hexagons and spaces for single water molecules, allowing for continuous dynamic growth and dissolution.



Original Lippincott's 1969 polywater structure

Same structure as a ball model

Fig.[Polywater] Lippincott's honeycomb structure of polywater (Lippincott et al. 1969). Some canyon gaps are is shown in red.

The interplay of order and chaos in polywater layers

The polywater structure (Fig. [Polywater] above) contains spaces for single water molecules,

allowing for a dynamic interplay between structured and liquid water. As the structure grows, it accumulates a negative charge. This accumulation of charge creates an inherent instability: if the structure grows too far, it becomes energetically favorable for it to begin dissolving, thereby reducing the negative charge. This results in a continuous process of growth and dissolution. The islands of polycomb water could stay in place or potentially travel by growing on one end and dissolving on another end, as do microtubules and other self-assembling biological filaments. This dynamic, imperfect nature of polywater, with its capacity for continuous reorganization and information encoding, is likely the key foundation of life.

As previously mentioned (L. Montagnier et al. 2011; Luc Montagnier et al. 2009), DNA solutions were proposed to embed sequence information in water structures. This aligns with our model of DNA and its surrounding water structure where every other layer of water is coplanar with DNA basepairs. On the other hand, as we mentioned, classical ice models, are unsuitable for imprinting DNA sequences. In classical ice, the layers are not flat and are strongly bound to each other via hydrogen bonds, prohibiting shifts between layers. This rigidity doesn't allow for the flexibility needed to imprint DNA sequences.

As we outlined above, unlike classical Ice IV, the Lippincott polywater structure (Lippincott et al. 1969) has flat layers with weaker van der Waals forces between them, allowing for shifts in multiple directions, Fig. [Shift]. This flexibility is crucial for our hypothesis of DNA imprinting its sequence onto water structures. The ability of polywater to shift and reorganize makes it a suitable structure for encoding and transmitting biological information.

We propose that when DNA moves through the nucleoplasm, its high negative charge dissolves existing water structures and initiates the crystallization of new polywater layers. These layers form perpendicular to the main axis of the DNA double helix, with the hexagonal shapes observed in DNA base pairs serving as nucleation points for the honeycomb polywater structure. Our size estimates suggest that for every basepair of DNA, there are two polywater layers.

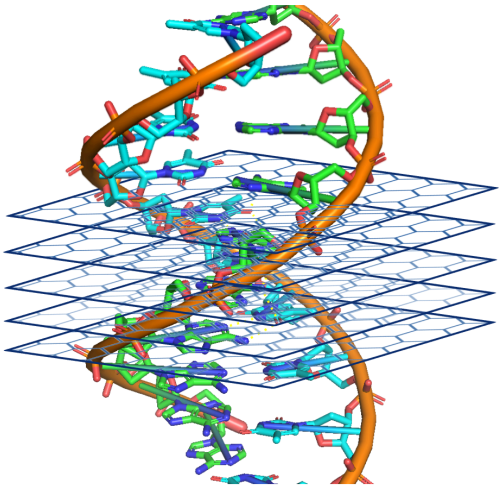


Fig. [Layers] Layers of polywater initiated by DNA and crystallized around the DNA perpendicular to the main axis of the double helix

A crucial property of this polywater model is the shifting of layers, Fig. [Shift]. Each layer can shift in one of six directions relative to the adjacent layer, potentially encoding DNA sequence information, see red dots in the center. Now, if we consider three consecutive layers, the third layer can occupy 19 different positions relative to the first layer: 12 points on the outside (blue dots), 6 points on the inside, and 1 central point, distributed across 12 possible angles of the shift direction.

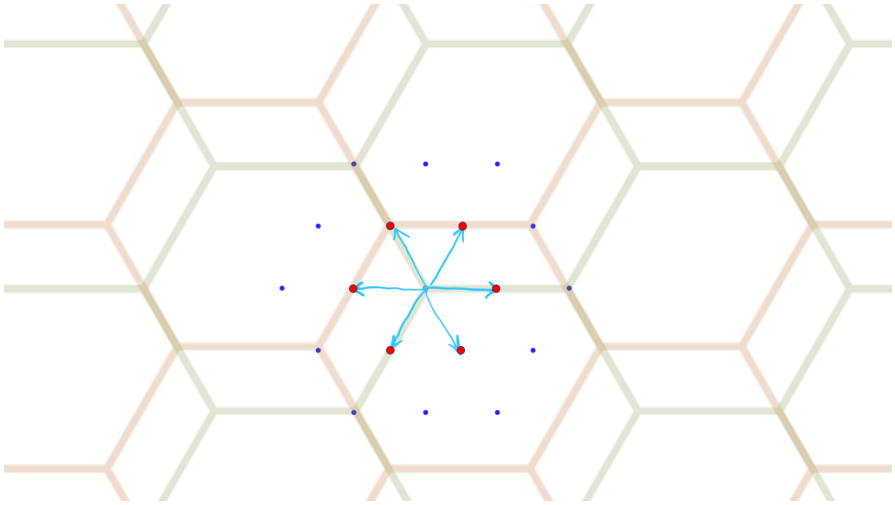


Fig. [Shift]. Multi-layer shifting patterns in polywater structures. The hexagonal lattice represents the honeycomb structure of polywater layers. Blue arrows indicate the six possible directions of shift between adjacent layers. Red dots mark the six potential positions for oxygen atoms in the next (second) layer relative to the central position. Blue dots represent the additional 12 possible positions for oxygen atoms in the third layer. Together, the 18 red and blue dots illustrate all possible positions of the third layer relative to the first. This two-step shifting mechanism allows for complex three-dimensional arrangements, potentially encoding DNA sequence in the polywater layer structure. The figure demonstrates how each layer can shift to one of six positions, and then the subsequent layer can shift again in any of the six directions again, including a shift that returns it to alignment with the first layer.

In developing our model, we made several unconventional choices that may need explanation. First, we posit that water forms planar layers. Second, we propose that these water layers are oriented perpendicular to the DNA axis, a seemingly arbitrary arrangement. Third, we suggest that these water layers consist of flat polywater honeycombs rather than corrugated ice-IV honeycombs. We acknowledge that alternative water structures may exist that do not rely on layers, have layers oriented differently relative to DNA, or consist of structures other than Lippincott's honeycomb. However, the appeal of our model lies in its being the simplest and most elegant structure that allows for both the imprinting of DNA sequences onto water and a nearly lossless propagation of this imprinted information through the water medium away from DNA.

Henceforth, we will refer to our model as the "pintumbler" model, reflecting its key feature of imprinting DNA sequences onto water through the shifting of honeycomb water layers as in pin tumbler lock, Fig. [Purines]. It is likely that the composition of nucleoplasm may have evolved to create conditions favorable for pintumbler water structure, as this would enable DNA sequences to imprint information onto water, potentially serving important biological functions. In the

following sections, we will elaborate on the structural details and potential functions of this model.

As we mentioned, 2 consecutive base pairs would align with water layers 1 and 3, so that 3rd layer could shift stepwise 19 different positions relative to the first layer. This arrangement allows for a sophisticated encoding system. We propose that the specific shifts between layers could correspond to the sequence of base pairs in the DNA. For instance, the presence of a purine (A or G) or a pyrimidine (C or T) in the DNA sequence might dictate the direction and magnitude of the shift between adjacent water layers.

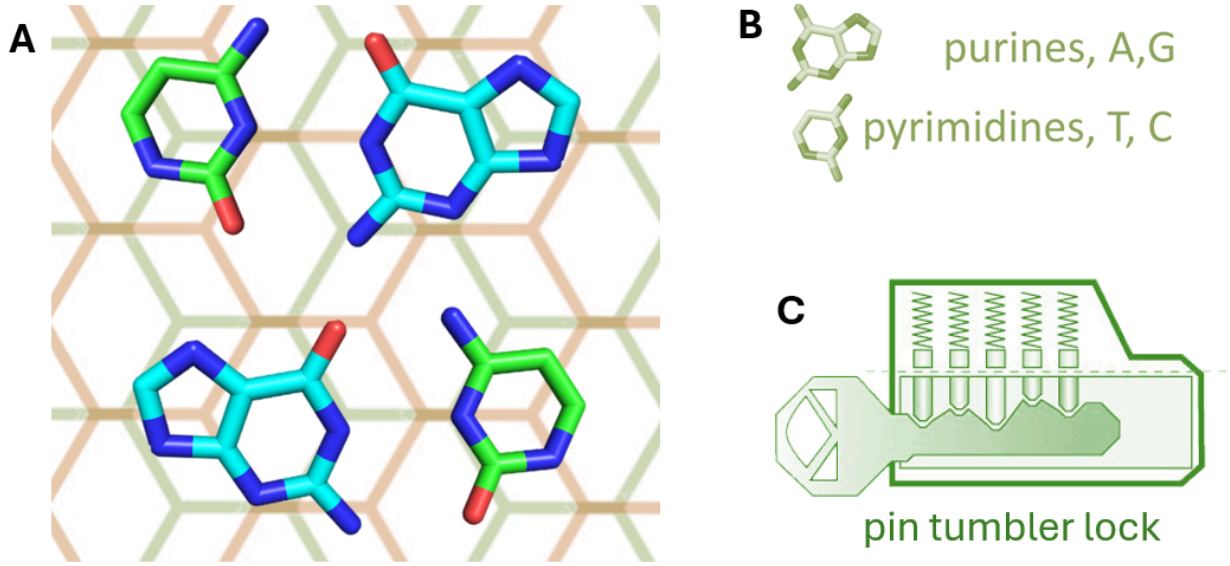


Fig. [Purines] A. The principle of imprinting purine sequences on water by shifting honeycomb layers. Basepairs CG (top) and GC (bottom) are aligned vertically to maintain their position relative to the sugar-phosphate backbone, demonstrating the horizontal shift that occurs when the basepair is flipped. B. The general structures of Purines (A, G), with their two fused rings, and pyrimidines (T, C), with one ring. C. The pins are shifted by the bumps on the key in the pin tumbler lock.

The pintumbler model proposes a mechanism for DNA to imprint its sequence information onto surrounding water structures. The key to this process lies in the structural differences between purines (A and G) and pyrimidines (T and C) and their alignment with the honeycomb water structure. Crucially, the base pairs are positioned in Fig. [Purines] to maintain their alignment with the sugar-phosphate backbone. This alignment reveals an important feature: when the basepair is flipped (for example, A≡G to G≡A), there is a horizontal shift of the hexagonal part of the basepair relative to the backbone. In this example, not all the information of the DNA sequence is imprinted on water, but only its purine-pyrimidine sequence. This partial information transfer can be referred to as degeneracy or redundancy.

Therefore, on the crude model level, only the purine-pyrimidine sequence of DNA influences the shifting pattern of the surrounding water layers, creating a unique "watermark" that reflects the underlying DNA sequence. This shifting pattern could propagate as the layers grow, potentially

allowing for medium- or long-range transmission of purine sequence information of DNA. Such water-mediated information transfer could be involved in various biological processes, including long-range DNA-DNA interactions, dynamic chromatin organization, and signaling.

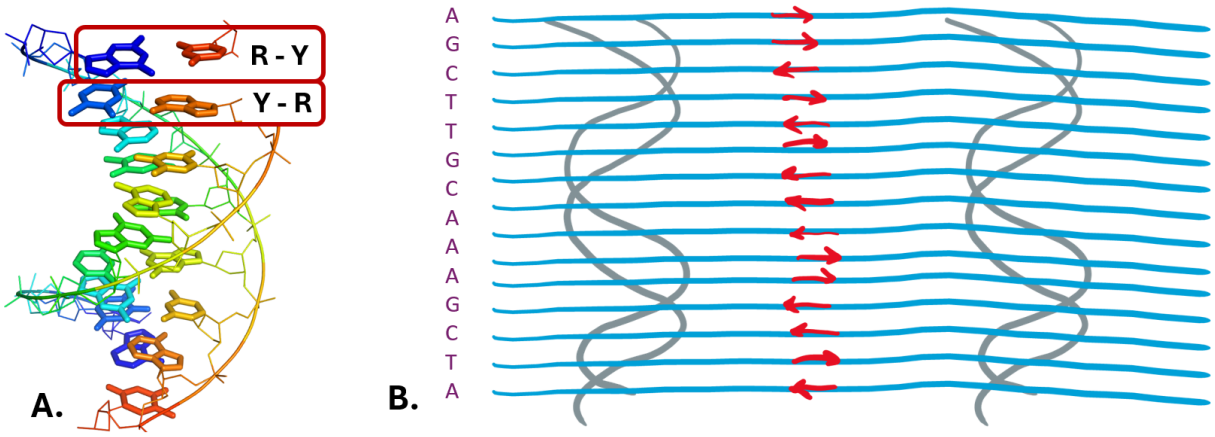


Fig. [Imprint] Imprinting of DNA sequence on water structure

Figure [Imprint] demonstrates the pintumbler model's concept of DNA sequence imprinting on surrounding water structures. The image juxtaposes a DNA double helix (A) with simplified flattened shifts of water layers (B).

In part A, two base pairs are highlighted with red boxes labeled "R-Y" and "Y-R". These labels emphasize that each base pair contains one purine (R) and one pyrimidine (Y), with their orientation flipping as dictated by the DNA sequence. This flipping of the R-Y pattern is key to understanding how DNA sequence information is imprinted onto the water structure.

Part B shows how this R-Y pattern influences water layer shifts, indicated by red arrows. The imprinting depends on the orientation of purines and pyrimidines within each pair, reflecting the alternating pattern seen in part A. In a simplified Panel B, purines A and G shift layers to the right, and pyrimidines C and T shift the layers to the left.

While this 2D representation illustrates the principle, it is a simplified representation of a more complex 3D structure where each basepair rotates 1/10.5 turns per step. The proposed honeycomb water structure accommodates these three-dimensional shifts, though our flattened illustration doesn't reflect 3D turns. Only every other water layer is shown on Panel B.

Nucleosomal packaging of DNA

All multicellular organisms are eukaryotes and have nuclei, and in all of them, DNA is packed in nucleosomal chromatin structures. Since morphogenesis and morphogenetic field relate to multicellular organisms guiding their shape formation, it is necessary to consider nucleosome packing of DNA when modeling the formation of the holographic field by DNA. Figure [Nuc] illustrates the nucleosomal structure of DNA packaging and how water layers might connect two double helices.

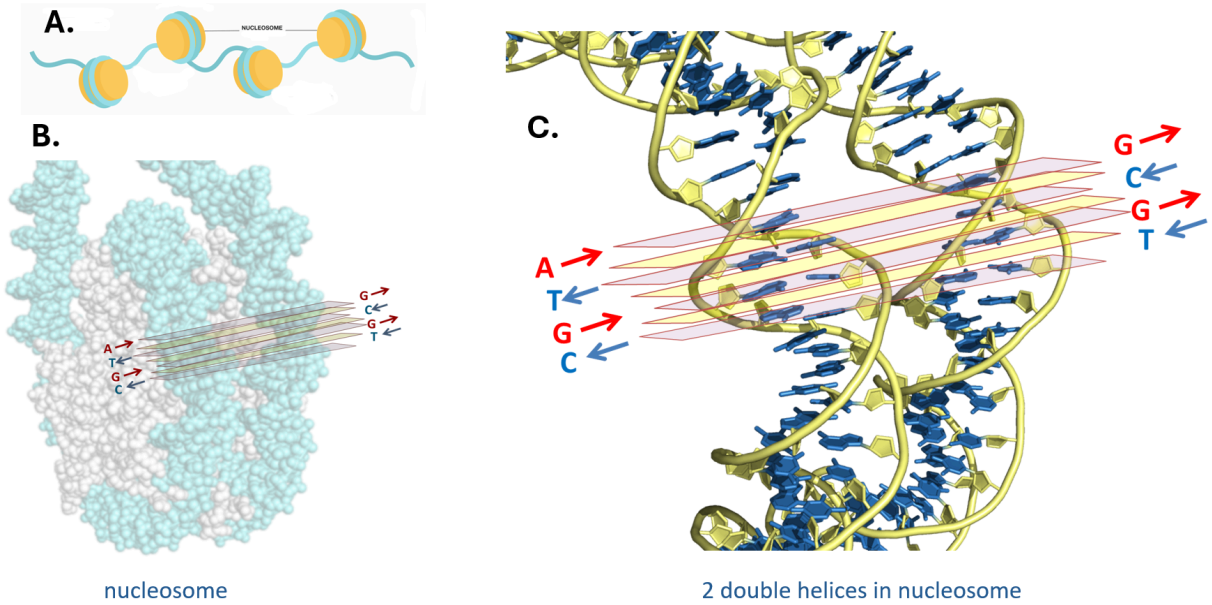


Figure [Nuc]. Proposed water structure round DNA in chromatin. A. Schematic representation of the classical "beads on a string" chromatin structure. B. A classical crystallographic molecular model of a nucleosome with DNA wrapped around the histone core. C. Detailed view of two DNA duplexes on a nucleosome surface, linked by a bridge made by honeycomb polywater sheets. The arrows indicate the shifts of the sheets guided by the purine-pyrimidine sequence of DNA. The bridge would make a more perfect structure when the purine-pyrimidine sequences of the 2 duplexes are identical.

Panel A provides a "beads on a string" structure of chromatin, where nucleosomes (depicted as yellow cylinders) are connected by linker DNA (blue line). Typically over 70% of the genome is wrapped around nucleosomes (Oberbeckmann et al. 2024) spread more or less uniformly over the genome, while under 30% are naked DNA linkers connecting nucleosomes. The mapping of nucleosome positions is reliable using chromatin conformation and accessibility assays.

Panel B illustrates a single nucleosome where the histone core (gray) has DNA (blue) wrapped around it, with approximately 147 base pairs of DNA wrapped around the histone core. A short DNA section is highlighted with red and blue arrows to show the purine-pyrimidine (R-Y) orientation of base pairs and water layer shifts in the pintumbler model.

Panel C shows two DNA double helices wrapping around a nucleosome. The DNA backbones are shown in yellow, with base pairs shown in blue. The diagram shows red and yellow water layers shifting according to the purine DNA sequence pattern. When two double helices with identical sequences align, their water layers would align with the same shifts and form a unified, coherent structure with greater stability.

Purine Jump patterns

Based on this structure, we formulated a model that makes specific predictions about DNA sequence patterns in the genome. One of the predictions is based on 2 parallel DNA loops sitting close to each other on a nucleosome, as illustrated in Figure [Loops]. When DNA wraps around a nucleosome, 2 sequential segments in linear sequence are brought into close physical

proximity. Panel A shows a 3D representation of two DNA duplex loops, which are highlighted in red in the top view (B). These loops are then depicted unwrapped into a linear sequence in panel C, emphasizing the approximately 77 base pair distance (which we call JUMP) between the corresponding start points of the red segments. Based on the potential for these loops to be connected by water layers, as illustrated in Figure [Nuc], we hypothesized that evolution might have favored similarity between purine-pyrimidine sequences in such proximal loop regions, since matching sequences would create coherent water layer patterns between the loops and thus stabilize the nucleosome structure. Moreover, this spatial arrangement would allow direct sequence comparison through water-mediated interactions, potentially creating structural interference patterns that could serve as a new mechanism by which intergenic DNA sequences are interpreted by the cell. So next, we will test whether the genome is enriched with jump patterns, Figure [Loops].

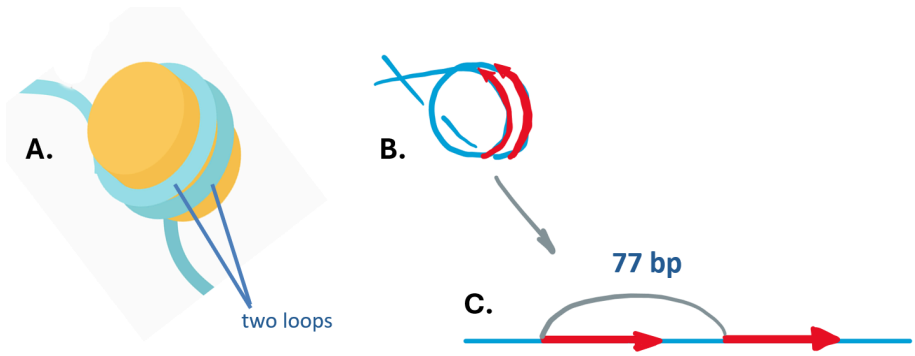


Figure [Loops]: DNA looping and nucleosome structure. A. A classical nucleosome structure uses positively charged histone proteins to twist the negatively charged double helix and bring two DNA loops together. B. The parallel parts of the loops are marked red. C. A DNA fragment with two loops is unwrapped; the two parallel red regions are shifted approximately by 77 base pairs, producing a tandem repeat pattern with a gap in between. We called this tandem repeat "Jump". The distance between the repeat starts we called Jump Distance.

Purine jump computational methods

This is the methodology for verifying the hypothesis that there is more homology between purine-pyrimidine sequence pairs separated by even-numbered jump sizes.

Data Description Chromosome sequences for analysis were downloaded from the Ensembl repository (https://ftp.ensembl.org/pub/release-109/fasta/homo_sapiens/dna/). Both unmasked chromosome sequences (e.g., Homo_sapiens.GRCh38.dna.chromosome.1.fa.gz) and masked sequences (e.g., Homo_sapiens.GRCh38.dna_rm.chromosome.1.fa.gz) were downloaded. In masked sequences, all repeats and low-complexity regions were replaced with N. Coordinates of intergenic regions were also downloaded from Ensembl (https://ftp.ensembl.org/pub/release-109/gtf/homo_sapiens/). The file with nucleosome coordinates was downloaded from https://generegulation.org/NGS/stable_nucs/hg38/ (GSE114511_70yo_Teo_stable_100bp_hg38.bed.gz). To assess conservation, chr{c}.phyloP100way.wigFix files (one file per chromosome) were downloaded from UCSC (http://hgdownload.soe.ucsc.edu/goldenPath/hg19/phyloP100way/). These files contain conservation scores for each position in the chromosome (these values were obtained based on multiple sequence alignments of hundreds of species). For each chromosome, the 20th and 80th percentiles of the conservation score were calculated. Then, all intergenic regions were divided into short fragments of 50 base pairs. Within these 50-bp fragments, the average conservation score was calculated. If this conservation score was above the 90th percentile, such a region was considered conservative. If the conservation score was below the 10th percentile, such a region was considered non-conservative. Then, conservative and non-conservative regions were merged if there were at least eight consecutive 50-bp blocks (thus, the minimum length was 400 bp). Then, purine jump analysis was performed in the resulting intergenic conservative and non-conservative regions.

During the analysis, the following designations were used to denote conditions. Repeats: RepUn = repeat masker unique, RepRe = repeat masker repeats only included, RepEv = repeat masker everything included. Nucleosomes: NuOn = Nucleosomes only, NuEv = Nucleosomes, everything included, NuEx = everything excluding nucleosomes. Conservation: ConTop90 = Conservation top 90th percentile, ConEvery = everything = any conservation, nothing excluded by conservation, ConBot10 = bottom 10th percentile.

List of terms in this chapter:

1. **Sequa**: DNA-sequence imprinted water state (from SEquence and aQUA)
2. **Kaoqua**: Water that is restructured and has chaotic arrangements (from KAOs and aQUA)
3. **Inaqua**: Water that is restructured by imprinting non-DNA order, such as primitive unidirectional shift (from INorganic AQUA)
4. **Seprinting**: DNA Sequence Imprinting on Water (from SEquence imPRINTING)
5. **Homadhesion**: Sequence-specific HOMologous adHESION between DNA duplexes
6. **Indepaction**: INtron-mediated compaction and DEcomPACTION of chromatin
7. **Unignuco** genome subset - a subset of genomic sequence which is non-repetitive (Unique), InterGenic, NUcleosome-bound and COnserved.
8. **Even-purine homology** - the homology between two sequences that matches two conditions: (1) only every other nucleotide position (odd or even) and (2) homology is measured only in the purine-pyrimidine code.
9. **Pintumbler model** - a model of DNA hydration in which every other honeycomb polywater layer is coplanar with DNA basepairs and shifted according to transverse basepair positions, thus imprinting the DNA sequence in water structure.

10. **dsDNA** - **DNA duplex -** double-stranded DNA - DNA double helix
11. **Purine code** - a simplified DNA code considering the purine-pyrimidine sequence of DNA. The primary A, G, C, T sequence of DNA is converted to a purine code sequence where R represents purines (A and G) and Y represents pyrimidines (T and C), for example, RYRRRYYY).
12. **DNA duplex**

Purine Jump results

Here, for the first time in this chapter, we introduce our typical approach to making and testing models. We often build far-reaching models with limited initial proof, then derive specific predictions that we test against public genomic data. We have successfully used this approach in previous work (Savelev and Myakishev-Rempel 2020a; Aleksandr V. Vikhorev et al. 2024; Savelev and Myakishev-Rempel 2020b). Here, we present this particular analysis of purine jumps for two reasons despite its preliminary nature. First, it introduces a Purine Jump analysis method that will be used later, and second, it illustrates how the proof can be produced in the future.

The goal of the analysis is to check whether the genome is enriched by the Jump patterns with a Jump distance of around 77 bp. Figure [Jump] presents the results of the analysis. Panel A displays a histogram of purine sequence jump frequencies across a range of Jump Distances obtained from the human genome.

Our analysis began with the entire human genome sequence, approximately 3 billion base pairs. We then applied several filters to focus on the most relevant genomic regions:

1. We selected only non-repetitive parts of the genome that had no repeats or low copy number repeats as judged by the Repeat Masker.
2. We selected only intergenic regions, which are known to comprise about 45% of the genome.
3. From these, based on MNase-seq experimental data, we extracted fragments typically bound by nucleosomes.
4. Finally, we further narrowed our focus to fragments conserved in evolution. The conservation track is obtained from the UCSC genome browser. The conservation was measured by aligning distantly related genomes to identify consistent sequence patterns conserved in evolution.
5. Therefore, this subset of sequences is non-repetitive (unique), intergenic, nucleosome-bound and conserved (abbreviated here UnIgNuCo, i.e., Unignuco genome subset). The Unignuco genome subset was divided into 3 parts: Unignuco 1, 2 and 3 to measure consistency of the signal.

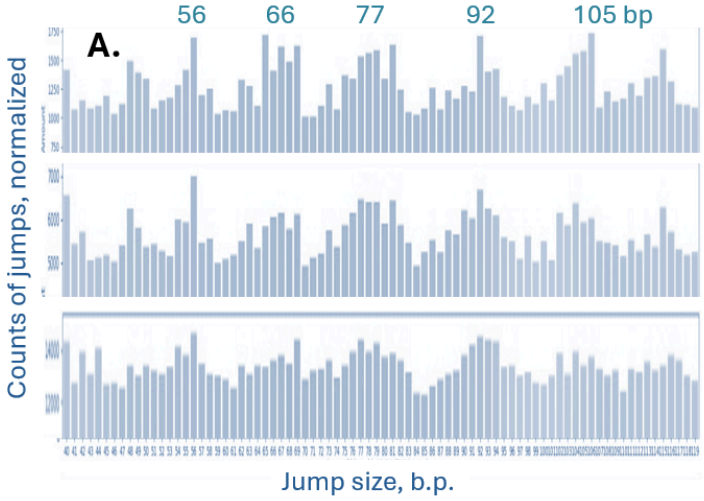
For brevity, we will call the purine-pyrimidine sequence (e.g., RYYYRRY) the "purine sequence." Within these conserved sequences, we searched for purine sequence jumps ranging from 40 to 140 base pairs in Jump Distance. The x-axis of the histogram represents the Jump Distance in base pairs, while the y-axis shows the count of these Jumps as observed in all three Unignuco genome subsets. Several peaks are visible at approximately 56, 66, 77, 92, and 105 base pair Jump Distances. The peak patterns correlate between all three Unignuco genome subsets,

indicating the non-random nature of the peaks.

If the 77 bp peak was dominant, that would be a confirmation of the hypothesis that evolution preferred 77 bp jumps - that is, that two parallel loops of DNA in nucleosomes show homology. Yet, the 77 bp jump peak is accompanied by similar size peaks corresponding to 56, 66, (77), 92, and 105 base pair Jump Distances. So, the hypothesis is neither proven nor disproven - we got intriguing results that allow for multiple interpretations. Additional analyses are needed to figure out what these peaks are. These are peaks in conserved regions of the genome typically bound by nucleosomes, so there might be a trace of something functionally important.

One possible explanation is that the peaks actually correspond to nucleosomes of various sizes (circumferences). Our search didn't locate any experimental measurements of nucleosome circumferences in cells. Apparently, scientists have focused on classical nucleosome circumference due to a tradition of modeling nucleosomes using a specific plasmid sequence. The vast majority of crystallographic studies use the same DNA sequence. It doesn't look like there were any attempts to test whether alternative nucleosome sizes coexist in cells. Our data suggest that possibly, in addition to the classical 77 bp circumference, there are alternative ones.

The loops in nucleosome are clearly coordinated inthe DNA helix phase - both double helixes are aligned in phase - so that the basepairs of the corresponding angular phase are coplanar - essentially, the double helixes are parallel with a shift to make the corresponding basepairs coplanar. So variability in circumference can come only in adding and removing the whole double helix turn which is 10.5 bp. This explains the sizes of 56, 66, 77, 92, and 105 base pairs.



B.

jump, bp	number of DNA turns (approx. 10.5 bp per turn)
56	5
66	6
77	7
92	8
105	9

Figure [Jump]: Analysis of purine sequence jumps in genomic data. A. Histogram showing the counts of purine sequence jumps at different basepair jump sizes. B. Table relating jump sizes to the number of double-helix twists that fit one circle of DNA duplex around the nucleosome.

Further experimental studies are needed to explain these multiple peaks. It would be great to modify MNase-seq and Micro-C methods to experimentally demonstrate that in live cells, nucleosomes have not only 7 DNA turns but also 5,6,7,8,9 turns. Panel B, Figure [Jump]

suggests how these peaks might relate to the number of double helical turns per nucleosome circumference.

Another possible explanation is that the DNA sequence is enriched in similar purine patterns that repeat with the periodicity of approximately 10.5 bases, and we are seeing the trace of these patterns. The emergence of such patterns would agree with out hypothesis that two DNA loops in the nucleosome have similar sequences. Further sequence analysis is needed to delineate these possibilities.

Even-purine prediction

The next testable prediction (even-purine prediction) we made was based on the comparison of angles in DNA vs water. Until now, we ignored the twists in DNA double helix. Yet, honeycomb water layers are parallel and aligned to each other. Although they shift horizontally, their angles remain aligned. Yet base pairs turn every step of the DNA ladder. This creates an imperfection of the alignment of DNA with water. This imperfection appears to arise as one of the fundamental and functionally essential principles in biology. Figure [Angles] illustrates the comparison of angular symmetry of DNA and water. Panel A presents a model of DNA intersected by transverse honeycomb water layers. Panel B shows how each next step adds a twist relative to the previous step in a medieval double-helical staircase. This is to illustrate the DNA twist angle. (skipping panel C for now). Panel D shows the hexagonal symmetry of polywater, which aligns with itself when turned 1/6 of the circle (60°).

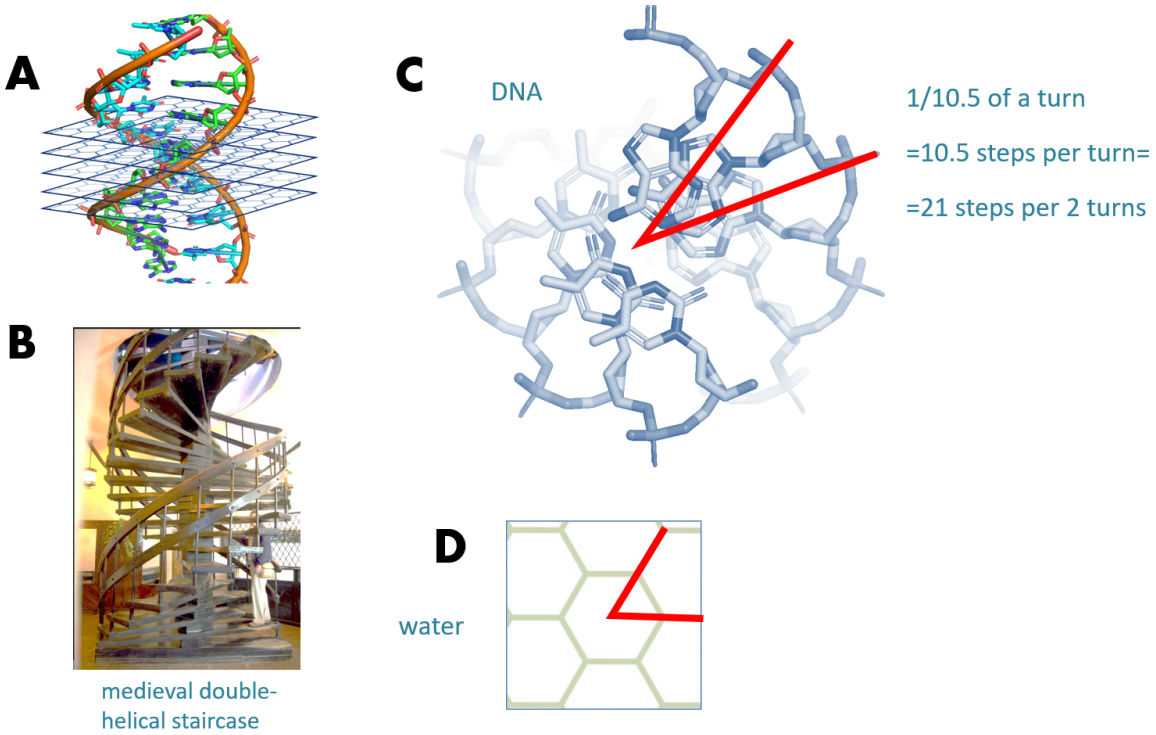


Fig. [Angles] Comparison of symmetry in DNA and water structures. Top left: DNA double helix surrounded by water layers. Top right: Hexagonal symmetry of water, repeating every 1/6 of a turn. Bottom left: Medieval double-helical staircase illustrating the helical nature of DNA. Bottom right: DNA structure, showing 1/10.5 of a

turn per step, resulting in 10.5 steps per turn or 21 steps per two full turns.

Fig. [Angles] Panel C shows a molecular model of B-form DNA. In this form, DNA completes one full turn every 10.5 base pairs, or 21 base pairs per two full turns. This means each base pair twists 34.3° degrees (360°/10.5). The difference in rotational symmetry between 34.3° (and 68.6° per two steps) of DNA and 60° of water creates a structural mismatch means that if the first basepair is aligned with water, the next base pair will be misaligned; Figure [Alternation], A and B.

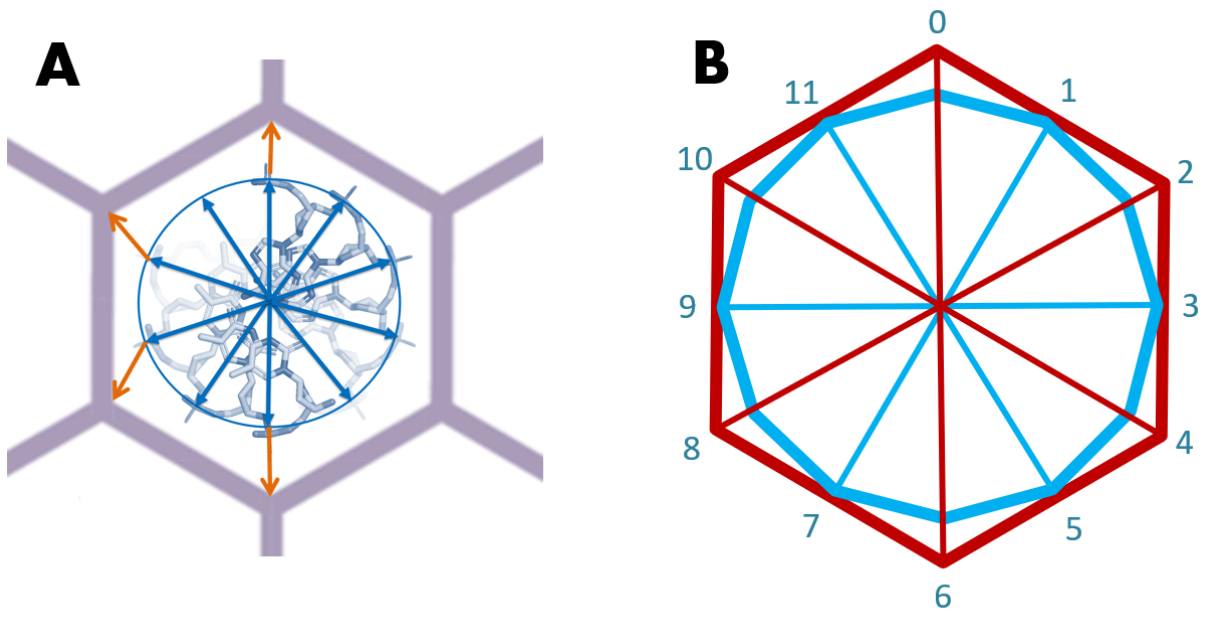


Figure [Alternation]: Alignment of DNA core and hexagonal water structures. (A) Top view of DNA double helical core (blue circle, representing 4 base pair steps) embedded in a hexagonal water structure (blue). Orange arrows indicate potential alignment points, illustrating the mismatch between DNA's natural 10.5 base pairs per turn and water's hexagonal symmetry. (B) Schematic representation of a hypothetical DNA structure with 12 base pairs per turn (blue dodecagon) relative to water's hexagonal symmetry (red hexagon). Numbers 0-11 represent DNA base pair positions. This model demonstrates how every other base pair could align with the water structure's vertices in a more tightly wound DNA configuration.

Figure [Alternation] illustrates the potential alignment between the DNA double helix core and the hexagonal symmetry of water. Panel A depicts a top view of the DNA double helical core (blue circle, representing approximately 4 base pair steps) within a hexagonal water structure (purple). The orange arrows indicate imperfect alignment points between DNA and water structures. With the natural 10.5 base pairs per turn of B-form DNA, achieving consistent alignment is challenging. The DNA core would need to constantly twist, alternately aligning different base pairs, while some would always remain misaligned with the water structure. This imperfection seems to be fundamental and functional, potentially explaining the continuous movement and energizing of DNA in living cells.

Panel B presents a hypothetical scenario where DNA is more tightly wound, with 12 base pairs per turn instead of 10.5. The red hexagon represents the hexagonal symmetry of the water structure, with its six-fold rotational symmetry. The blue dodecagon represents DNA base pair positions, numbered 0 to 11. The literature suggests that this configuration occurs only in a small percentage of genomic DNA. The structural advantage of this model is that every other basepair of DNA (positions 0, 2, 4, 6, 8, 10) aligns perfectly with the water hexagonal symmetry. On the other hand, the in-between base pairs of DNA (positions 1, 3, 5, 7, 9, 11) are misaligned with water. Therefore, there is a possibility that DNA, again, would be collectively twisting back and fort,h alternately aligning either odd or even base pairs with water.

According to our pintumbler model, since a single DNA duplex shifts layers around, two duplexes should stabilize if they shift layers around similarly. This would happen for identical sequences like those found in transposons but also between two degenerated sequences that have only partial similarity. Specifically, if only every other nucleotide aligns with water in a tightly twisted DNA (12 bp per turn), then only every other nucleotide will need to be aligned, and only in the purine-pyrimidine pattern. Therefore, we propose the "even purine" hypothesis. We predict that there will be Jumps that show homology only in either odd or even nucleotides (one of the two alternate phases) and only in purine code, which means that only the distribution of purines versus pyrimidines matters, not their specific identity. This selective pattern matching between DNA sequences through water-mediated interactions is depicted in Figure [EvenPurine].

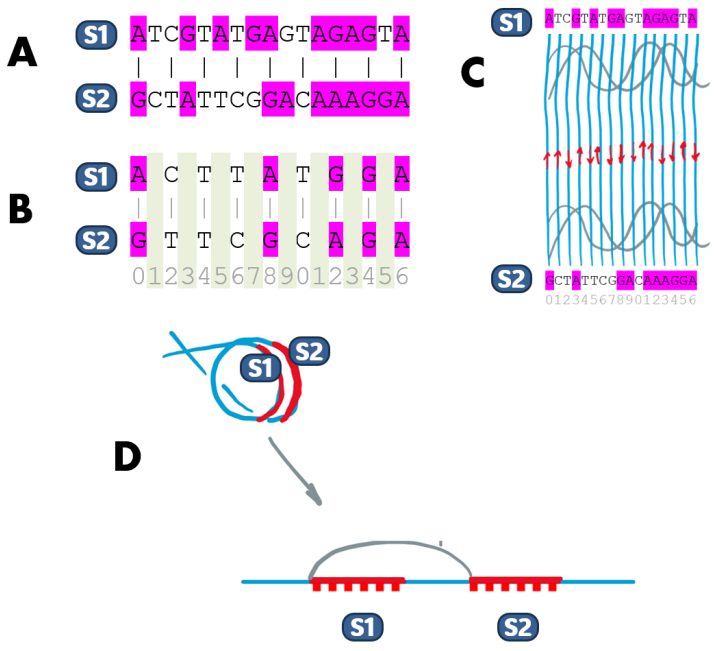


Figure [EvenPurine]: Proposed even-purine homology in DNA. (A) Primary code of DNA sequences S1 and S2

with purines highlighted in pink. (B) How even-purine code is produced from sequences S1 and S2. Only odd nucleotides are shown while even nucleotides are hidden by a grid of green bars. (C) Even-purine alignment of water layers (blue lines) between sequences S1 and S2. (D) Unwrapping two dsDNA loops of a nucleosome into a linear sequence, even nucleotides are shown with extra red teeth.

Figure [EvenPurine] illustrates how we convert a 3D model into a testable pattern enrichment prediction on a linear DNA sequence. Panel A shows two quite different DNA sequences, S1 and S2, with purines (A and G) highlighted in pink. These sequences represent potential interacting segments of DNA. In panel B, we extract what we term the "even-purine code" from these sequences. This code considers only the purine (R) or pyrimidine (Y) nature of bases at odd-numbered positions, reflecting our hypothesis that one of the two alternate phases (odd or even) evolved to align between sequences S1 and S2 in the pintumbler model. Thus, we introduced a concept of "even-purine homology," defined as the homology between two sequences when the homology occurs only between every odd or even-numbered nucleotide and occurs only in the purine-pyrimidine code. For example, in panel B, when examining only the even positions, the two seemingly different sequences, S1 and S2 appear identical in their purine code, demonstrating even-purine **homology**. Panel C shows how the two DNA duplexes, S1 and S2, could connect via shifted polywater layers. Panel D places these interactions in the context of nucleosome structure. It shows two segments of DNA (S1 and S2) potentially brought into proximity by looping around a nucleosome. Next, we show how these sequences would look on linear DNA. This scheme allows making a testable prediction - we predicted that such even-purine tandem repeats would be enriched in the genome by evolution. This structure serves a positive function by stabilizing nucleosomes and producing special interference patterns. We suggest that nucleosomes roll or slide along DNA strands looking for even-purine tandems, and once they find them, they slow down and use these tandems to produce vibrational interference patterns of the two dsDNA loops. Especially functionally strong would be the interference patterns between slightly dissimilar even-purine tandems, as they would produce overtones. Thus, nucleosomes might serve as scanning and reading devices that read DNA sequences by comparing tandem repeats spaced by approximately 77 bp.

Even-purine methods:

We analyzed unmasked human chromosome 9 (GRCh38/hg38) to test the enrichment of even-purine homological tandems in the human genome. We looked at purine/pyrimidine (RY) patterns in DNA. The sequence was converted to purine code by converting purines (A, G → R) and pyrimidines (C, T → Y). To sample enough sequence while minimizing computation, we examined eight 2Mb regions spaced 10Mb apart, starting at position 30Mb. For each tandem, we compared 40bp sequence windows that we called cp1 and cp2 (counterparts 1 and 2). The cp2 was shifted by 77 bp Jump Distance relative to cp1, as shown in Figure [EvenPurine]. Only non-overlapping tandems were tested. First, we calculated direct RY homology between cp1 and cp2 and kept only the tandems with ≥70% matching positions. For these selected tandems, we then analyzed phase divergence by separately comparing even and odd positions, calculating four homology scores: (cp1_even vs. cp2_even), (cp1_even vs. cp2_odd), (cp1_odd v.s cp2_even), and (cp1_odd vs. cp2_odd). The phase divergence was calculated as the difference between maximum and minimum phase homology scores among the 4 for each tandem. To produce randomized reference sequences, we used the same tandems in which we randomized the order of nucleotides in every 20bp bin. This method randomized fine purine structure but keeps the frequencies of purines the same per 20bp bin.

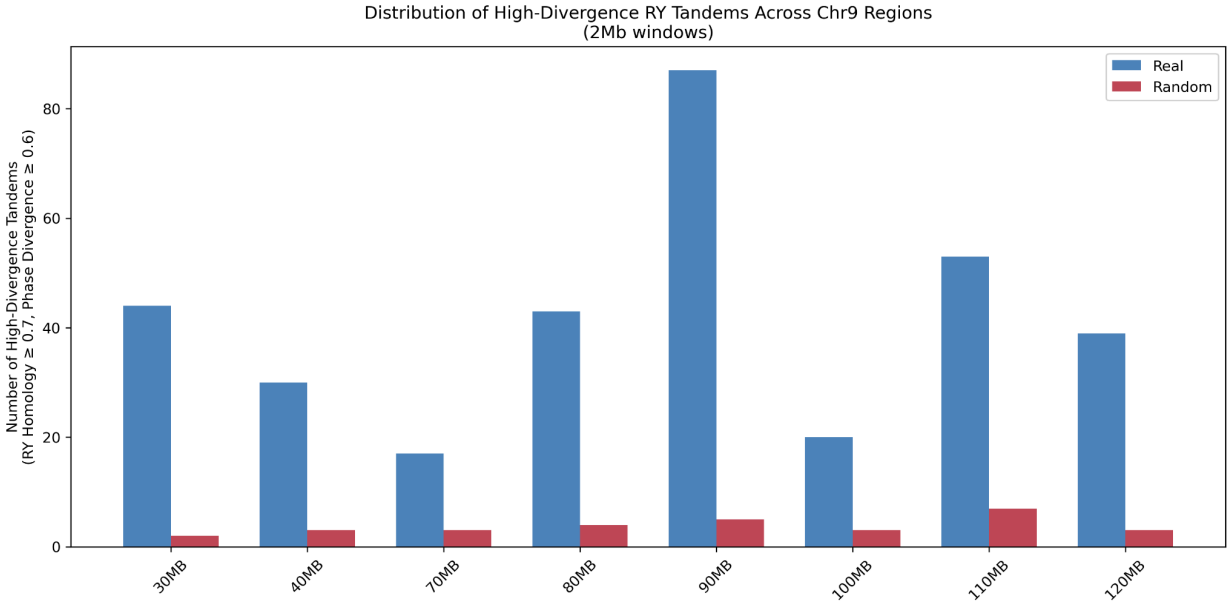


Figure [Enrichment]. Evolutionary enrichment of even-purine self-homologous tandems. The graph shows the frequency of RY tandems with >50% divergence of even and odd nucleotide phases. Compared are real sequences (blue) with randomized sequences (red). Each bar pair is calculated in a 2Mb window starting at the indicated Mb position. The consistently higher frequency in real sequences suggests the evolutionary enrichment of these patterns.

Even-purine results.

Statistical analysis revealed significant enrichment of highly phase-divergent even-purine tandems in real genomic sequence compared to the same sequence randomized

(Mann-Whitney U test, $p < 0.0005$ or 1 chance in 2000). The interpretation of this finding follows directly from our theoretical predictions. We started by formulating the idea that water bridges connect double-stranded DNA loops on nucleosomes. We then found that due to the disagreement between water and DNA symmetries, only every other basepair would align with the water structure. From this geometric constraint, we predicted that water bridges would form more stable structures when DNA loops are homologous only in every other nucleotide and only in their purine sequence pattern. Our genomic analysis confirmed this prediction by showing the enrichment of these patterns compared to randomized sequences. We searched for other possible explanations for the observed enrichment and could not find any. There is no known biological mechanism that would promote homology in even nucleotides while keeping odd nucleotides non-homologous. There are no known proteins that would be sequence-specific only in even nucleotides, particularly over the 40-nucleotide stretches we tested. Further computational analysis is needed to examine these enriched sequences in detail - their heterogeneity, positions, relations to nucleosomal binding and functional importance. Experimental studies must also test whether these even-purine tandems stabilize nucleosomes, as our model predicts.

Homadhesion

Until now, we explored even-purine patterns based on the assumption that DNA-water structural alignment would be imprecise due to geometric mismatches between DNA and the honeycomb water patterns. However, as shown in Figure [Shift], the water layer system can actually adopt 18 distinct positions per base pair step, providing sufficient complexity to encode the full primary AGCT DNA sequence information without simplification or degeneracy. Due to the relative distances between water layers and DNA basepair steps, approximately two water layers correspond to one DNA step. This arrangement allows for 18 possible positions in the three-dimensional shift of water layers, as illustrated in Figure [Shift] earlier in the chapter. These 18 positions provide sufficient variability to allow imprinting of the four possible base pairs (A-T, T-A, G-C, C-G) and potentially even DNA methylation (5mC) onto the water structure. The specific shape and chemical properties of each base pair can influence the exact shifting pattern of the surrounding water layer, in effect imprinting the precise DNA sequence information onto the water structure. This refined model explains how homadhesion can enforce exact sequence alignments rather than just purine patterns. Therefore, we will now examine this more precise water-mediated recognition. Specifically, we will explore the sequence-specific alignment of DNA duplexes through their primary nucleotide sequence.

As we explored water-DNA interactions, we turned to chromatin conformation capture data, which reveals which DNA duplexes (double helices) physically contact each other in the nucleus. While these techniques are well-established, researchers typically focus on regulatory interactions between different genomic regions. No one had considered a simple yet radical possibility: what if identical DNA duplexes preferentially stick to each other? Our water layer model suggested this could happen through water-mediated interactions. This is a directly testable hypothesis - if identical sequences adhere to each other, we should see this signature

in the data. For this phenomenon, we introduce the term homologous adhesion or homadhesion for short. Two intact DNA duplexes would adhere to each other in the nucleoplasm if they have nearly identical primary sequences without strand separation or complementary base pairing.

If identical DNA duplexes can stick to each other, what genomic sequences would participate in this process? We needed sequences that appear multiple times in the genome with high similarity. The answer was clear from our previous research - transposons perfectly fit this requirement. They exist as multiple nearly identical copies scattered throughout the genome. This insight is connected to two longstanding genomic mysteries: why do large amounts of repetitive DNA persist despite evolutionary pressure, and why do transposons are distributed aperiodically and uniformly through all eukaryotic genomes? Evolutionary processes typically remove unnecessary sequences quickly, yet 55% of the genome remains repetitive, mostly as scattered transposons. If transposons serve as sequence-specific adhesion points for chromatin organization, their persistence and distribution would make perfect sense.

The traditional view of transposons as selfish, parasitic elements is challenged by our homadhesion hypothesis. We agree that transposons behave selfishly by jumping and propagating throughout the genome. Yet, we suggest that selective evolutionary retention has created functional patterns of transposon through evolution. Our proposal builds upon earlier insights from Barbara McClintock, who discovered transposons and proposed they function as control elements for gene expression. Although initially dismissed, her view was later partially vindicated. We extend this functional perspective through our water-DNA interaction model, proposing that transposons define specific patterns and logic of chromatin folding. This makes them essential to cellular information processing - effectively how cells "think." Through homadhesion, identical transposons and other repetitive sequences throughout the genome find each other and adhere in three-dimensional space, creating the complex, dynamic architecture of the genome.

This proposed sequence-specific homadhesion is exemplified by the Alu transposon. The Alu transposon, with 1.1 million copies per haploid genome, is the highest copy number transposon in our genome, covering 10% of it. It is the highest copy number primate sequence. Out of approximately 250g of DNA contained in a human body, Alu comprises 25 g. Alu has over 30 subtypes with minor sequence variations. We predict that each Alu subtype has the ability to adhere to itself, forming codirectional duplex pairs and accordingly are responsible for sequence-specific folding and reversible sticky fastening of chromatin loops. For instance, two dsDNA fragments of the AluSx subtype might stick together, closing a chromatin loop. In this model, transverse polywater layers connecting these adhered duplexes are responsible for the sequence specificity of this adhesion.

Importantly, homadhesion differs from traditional DNA base pairing. The duplexes remain intact, adhering via transverse water layers rather than opening and forming complementary base pairs. This adhesion is likely weaker than that between complementary DNA strands, allowing for dynamic formation and dissolution at physiological temperatures.

We suggest that homadhesion-mediated dynamic chromatin folding is active in eukaryotes, particularly in multicellular species. It is known that in a typical cell during interphase, a

significant portion of chromatin is condensed as heterochromatin near the nuclear envelope, occupying about 50% of the nuclear volume. The central part contains active, unpacked euchromatin. There is a dynamic balance between chromatin compaction and decompaction. Decompaction of a specific region usually happens when a specific gene needs to be expressed. We suggest that compaction occurs through sequence-specific homadhesion of transposons. Given the numerous copies of specific transposon subfamilies, many combinations of duplex pairs are possible, leading to constant competition in partner formation. This process resembles a molecular dance with continually switching partners, in which both transposon duplexes in a pair are identical. We suggest that repetitive serial patterns of multiple transposons program for folding DNA in specific larger structures such as fibers.

Evidence for homadhesion from chromatin conformation analysis

We wanted to test our homadhesion hypothesis with real experimental genomic data, so we turned to publicly available chromatin conformation datasets. Micro-C and Hi-C are experimental techniques that capture which DNA fragments physically contact each other in the cell nucleus, essentially creating a three-dimensional map of genome folding. These methods work by chemically linking nearby DNA segments, fragmenting the genome, and sequencing the connected pieces. By analyzing these datasets, we examined how transposable elements distribute around contact points where DNA duplexes physically touch each other. The results revealed non-random density patterns that cannot be explained by chance, providing the first empirical evidence that sequence-specific adhesion occurs naturally in the genome (Alexandr V. Vikhorev et al. 2024)

Notably, each transposable element family exhibited a specific distribution pattern around contact points. These patterns showed consistency across independent datasets and biological replicates. Also, we observed strand specificity - elements on the plus strand displayed patterns distinct from those on the minus strand. This directional asymmetry indicates a chromosome-scale sequence organization. This organization resembles how European cities structure their streets radiating from a central plaza, with increasing numbers toward the periphery - a system that provides directional information without requiring a map. To our knowledge, this is the first observation that any large enough piece of a chromosome has some sequence asymmetry indicating its orientation relative to the chromosome start (short arm), Figure [Distribution].

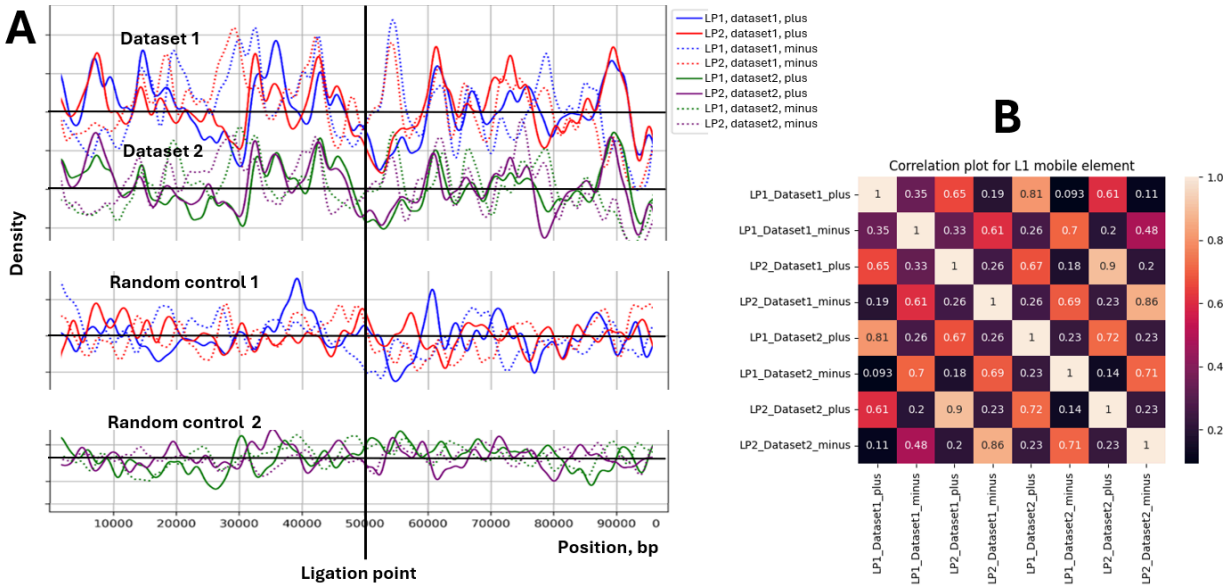


Figure [Distribution]: Distribution of L1 transposons around chromatin contact points. Panel A: Density of L1 elements (LINE1 transposons comprising 17% of the human genome) around chromatin contact points identified by Micro-C. The x-axis spans 100 kilobases centered on the contact point (vertical black line at 50,000 bp). Solid lines represent L1 elements on the plus strand; dotted lines show minus strand elements. LP1 and LP2 - are pairs of ligation points contacting each other as a pair. Note correlations in Datasets and lack of correlations in Random controls. Panel B: Correlation heatmap quantifying similarities between L1 element patterns. Lighter colors indicate stronger correlations. Note the high correlations between biological replicates for the same strand orientation (>0.6) and low correlations between opposite strands (<0.3).

Figure [Distribution] provides direct evidence for sequence-specific chromatin folding through the non-random organization of transposable elements around contact points. The reproducible patterns observed in the experimental datasets contrast sharply with random controls, which show no correlation. The consistent patterns seen across biological samples, are quantified in Panel B, confirming correlations visible in curves on Panel A. The patterns were reproducible across different cell types and chromatin conformation capture techniques, suggesting that they are part of a widespread principle of genome organization. This aperiodic yet directional organization of transposon patterns corresponds to Schrödinger's prediction that hereditary material will be an "aperiodic crystal".

The strand-specific distribution of L1 elements demonstrates that transposon distribution patterns, when averaged across the genome, have directionality. When analyzing these patterns, we were puzzled by an important question: What purpose could this asymmetry serve? The asymmetry relative to chromosome start suggests that transposon patterns of the same pattern type must be arranged codirectionally on the chromosome. This is the only arrangement that would produce the directional asymmetry we observed in the data. If transposon patterns are indeed codirectional, this means they are positioned in a head-to-tail arrangement along the chromosome, although not with strict periodicity. We observed an aperiodic yet directionally consistent organization. This head-to-tail positioning led us to consider the possible three-dimensional folding structures that would allow transposons in these

patterns to stick to each other through homadhesion. In principle, only two pairwise folding options are possible: hairpin loops or helical formations. To fold in hairpin loops, the patterns would be oriented on the chromosome in opposite directions (head to head or tail to tail). To fold in a helix, the patterns would be oriented in the same direction on a chromosome (head to tail). Since our data clearly showed codirectional arrangement of transposons, we concluded that a helical folding structure is the primary organizational pattern in chromatin, as illustrated in Figure [Helix].

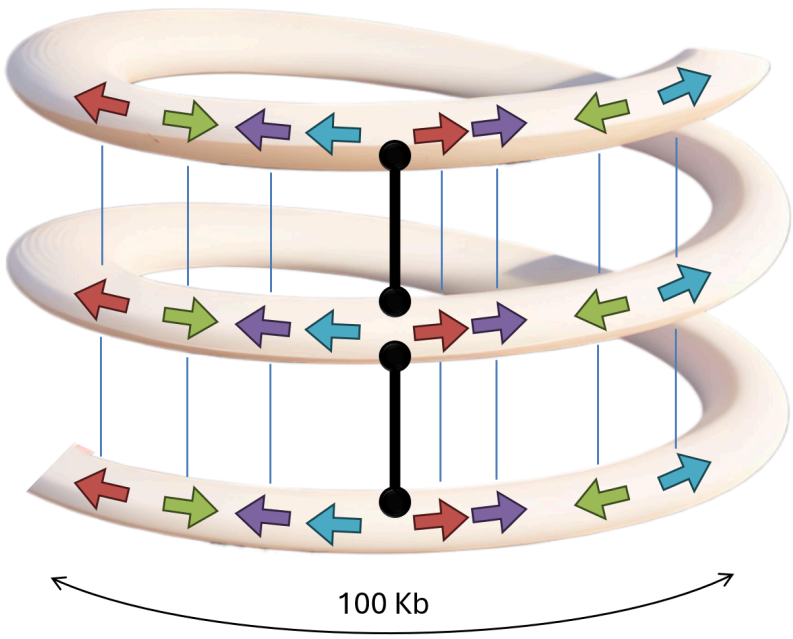


Figure [Helix]: Model of homological adhesion in chromatin folding. The schematic shows transposable elements with identical sequences forming contact points in chromatin. This model represents a higher level of DNA compaction beyond the double helix, likely involving strings of nucleosomes. The ligation points are connected by thick black lines. Gray ribbons represent chromatin fibers organized in a helical structure. Colored arrows indicate different transposon sequences, with identical colors representing identical sequences. These identical transposons adhere and hold together helical loops, creating sequence-specific contact points.

Figure [Helix] shows the proposed model for sequence-specific chromatin organization. The actual arrangement of transposons in the genome suggests that DNA sequence encodes helical folding instructions through the positioning and orientation of transposable elements. The strand-specific distribution patterns observed in Figure [Distribution] support this helical folding model.

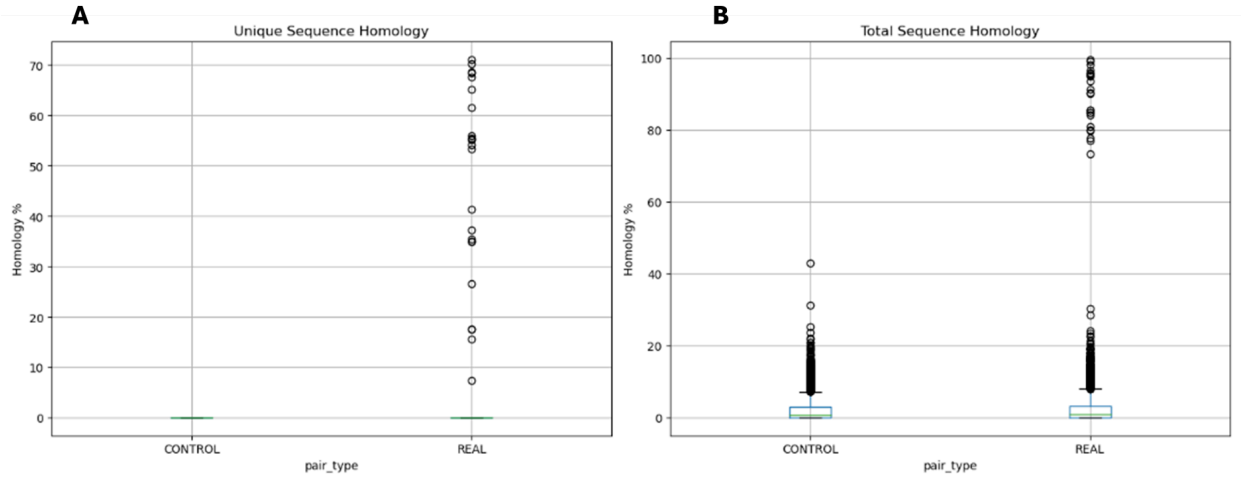


Figure 4: Distribution of sequence homology within and between chromatin contact points. Panel A: Homology percentages measured in unique and low-copy DNA sequences (after removal of repetitive elements) between paired genomic regions, using 10kb windows (±5kb) around each ligation point. REAL shows homology between two regions from the same chromatin ligation point pair. CONTROL shows homology between regions from different, unrelated ligation point pairs. Panel B: Total sequence homology percentages including all DNA sequences (unmasked, including repetitive elements) within the same 10kb windows. REAL pairs show homology between regions from the same ligation point pair, while CONTROL shows comparisons between unrelated regions.

Figure [Homology] presents quantitative evidence for sequence-specific homological adhesion in chromatin folding. We measured sequence similarity between DNA regions that physically contact each other in the nucleus (REAL pairs) compared to randomly selected non-contacting regions (CONTROL pairs). In Panel A we looked only at nonrepetitive 45% of the genome. In panel B, we looked at the whole 100% of the genome including repeats. Both panels show substantially higher homology ($p<0.001$) in pairs than randomly paired genomic sequences. These measurements support our homadhesion model by demonstrating that physically contacting DNA regions share substantial sequence similarity. The data indicate sequence-dependent interaction between intact DNA duplexes without strand separation, as predicted by our homadhesion model based on shifted polywater layers connecting DNA duplexes.

Dominant water patterns

One more interesting consequence arises from the realization that some repetitive elements are present in the genome in large numbers. Given that Alu and LINE elements together make up over 30% of our genome, the structured water formations are likely dominated by imprints from these two types of transposable sequences.

Linkers vs. nucleosomes

One of the questions to address is on possible molecular mechanisms of adhesion. Homadhesion is a combination of two components: homology and adhesion. While we already

proposed the principle which ensures the **homology** of homadhesion via the transverse layers of polywater, the mechanism of the **adhesive** component of the homadhesion should be further discussed.

For the adhesion mechanism, several forces could be considered: electrostatic, including ionic, hydrophilic-hydrophobic, hydrogen bonding, van der Waals, and other weak forces. Since we observe quick dynamic chromatin condensation and decondensation, this might hint at the mechanisms of adhesion and dissociation of duplex pairs, and for that reason, we don't think DNA duplexes are opened – we think they stay nearly intact. Although we suggest that the primary chemical responsible for adhesion is polywater, we don't exclude the possibility of other nucleoplasmic components taking an active part in homadhesion. These could include histones, other proteins, and low molecular weight chemicals abundant in the nucleoplasm.

It is also important to explain how the highly negatively charged DNA duplexes overcome electrostatic repulsion to adhere to each other. For that, they must be neutralized by positive ions. The choice of positive ions in the nucleoplasm includes proton (H+), hydronium ion (H_3O^+), histones which are positively charged, other positively charged proteins and peptides and other positively charged low molecular weight ions, such as Na^+, K^+, Mg^{2+}, and polyamines like spermine and spermidine.

Yoo et al. (2016) provided experimental evidence for sequence-dependent attractive interactions between double-stranded DNA molecules, which is highly relevant to the concept of homadhesion. Using a combination of molecular dynamics simulations and single-molecule FRET experiments, they demonstrate that DNA duplexes can attract each other over distances up to 2-3 nm in the presence of polyamines like spermine. Importantly, AT-rich sequences show stronger attraction than GC-rich sequences, and this attraction does not require sequence homology. DNA methylation enhances these interactions, making methylated GC-rich sequences interact as strongly as AT-rich ones. The mechanism involves polyamines mediating the interactions, with methyl groups on thymine or methylated cytosine affecting polyamine positioning. The Yoo study demonstrates that sequence-specific long-range attractions between DNA molecules exist and could play a role in chromosome organization and gene regulation. This work provides experimental support for homologous attraction and adhesion.

As we well know, most of the genomic DNA is wrapped on nucleosomes. Only a small fraction is unwrapped and is actively transcribed. In the nucleosome-wrapped part, about 2/3 of the sequence is wrapped onto a nucleosome and is therefore rounded, and the remaining linker sequence is free and forms a straight line. In our model, we are not sure whether it is a nucleosome-wrapped sequence or internucleosomal linear linkers that undergo homadhesion. Primarily due to charge, we think that linkers would repel a lot while nucleosomes from transposon sequence pairs would easily stick to each other. Therefore we currently prefer the idea that it is nucleosomes that undergo homadhesion. The nucleosomal core charged positively will, therefore, overcome the electrostatic repulsion of the two DNA duplexes from each other.

The structure of transverse water layers would be a bit different for nucleosomal homadhesion as opposed to linker homadhesion. In the nucleosome, the transverse water layers would be radial. This radiality requires including additional flexibility in our model. One addition is that

radial sheets of water must be separated by wedge-shaped gaps (or canyons) filled with unstructured water or wedge-shaped water structures. Another addition is that radial water layers must bend similarly to blades in a turbine rotor to maintain the approximate distance and parallelism of the radial polywater layers Fig.[Turbine]. Moreover, the necessary presence of canyon gaps in the polywater makes it quite stretchable, allowing for more complex structures such as turbine blades. These additions introduce additional imperfection mechanisms to our model: gaps and bending.

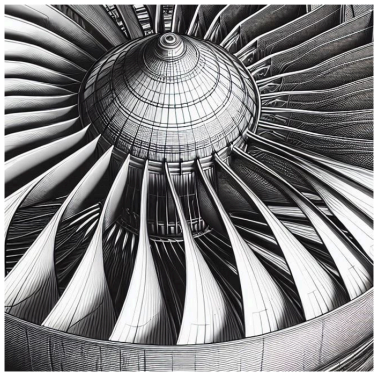


Fig.[Turbine]. Bending of polywater layers to resemble blades in a turbine rotor would allow maintenance of the approximate distance and parallelism between radial polywater layers.

Lee et al. (Lee et al. 2014) provided theoretical support for sequence-dependent interactions between intact DNA duplexes. Their model incorporated electrostatic forces and sequence-dependent DNA shape variations, predicting lower interaction energies for pairs of DNA fragments with parallel homologous sequences compared to those with uncorrelated sequences. This interaction was modeled without strand separation, considering the aqueous environment through parameters that account for electrostatic screening in solution. Their work suggests a potential mechanism for homology recognition between intact DNA duplexes prior to strand invasion.

The concept of homadhesion between intact DNA duplexes relates to questions about how similar DNA sequences interact in the genome. Barzel and Kupiec (Barzel and Kupiec 2008) reviewed models and evidence for the pairing of similar DNA sequences across different organisms. They noted an important observation in yeast: matching DNA sequences can locate each other and recombine efficiently, even when these sequences are in different genomic locations. This occurs despite the large amount of genomic DNA present. The authors presented two main hypotheses to explain this: one where the search for matching sequences is initiated by DNA damage, and another where similar sequences are paired as part of the genome's basic organization. The efficiency of this homology recognition process highlights the potential importance of mechanisms like homadhesion in facilitating DNA-DNA interactions.

Lechelon et al. (Lechelon et al. 2022) provide experimental evidence for long-range attractive forces between proteins, supporting concepts of homologous attraction from a distance. The study shows that proteins excited out of thermal equilibrium can interact over distances up to 100 nm (about 300 base pairs of DNA length). These interactions are based on a phenomenon

called Fröhlich interactions, named after physicist Herbert Fröhlich who proposed the idea in his seminal 1968 paper (H. Fröhlich 1968). The key idea is that when proteins are driven out of equilibrium (in this case by light), they can enter a state of collective oscillation. These oscillations create fluctuating electromagnetic fields that can couple with similar oscillations in other proteins. When the oscillations match in frequency, it leads to an attractive force. This force is selective (only works for matching frequencies) and long-range (works over distances much larger than typical molecular interactions). While the basic principle has been around for decades, this chapter provides some of the first clear experimental evidence for these interactions in a biological context. The authors suggest that such forces could play a role in how biomolecules find and recognize each other in the crowded environment of a cell, potentially complementing random diffusion. Accordingly, we suggest that Fröhlich interactions based on electromagnetic and electroacoustic collective vibrations are the mechanism for sequence-specific attraction and homadhesion of identical DNA fragments in chromosomal territories in the cell nucleus.

On Possible Intron Function

The concept of homadhesion introduced in this chapter may shed light on the long-standing mystery of intron function. Introns occupy a surprisingly large portion of the genome, with classical protein-coding genes transcribing into long unprocessed mRNA. This genomic sequence contains three types of sequences: exons that code for protein aminoacid chains and introns that are spliced out and not translated and untranslated terminal regions. Exons comprise 4.5% of the genome, introns 50%, and the remaining 45% is intergenic sequence.

Over 50% of both intergenic and intronic sequences are repetitive, consisting mostly of transposons. Despite this information being available since 2000, the function of introns remains largely unknown. The commonly accepted role of introns in producing splice variants is unsatisfactory, as it fails to explain their large genomic fraction. Observations of sequence evolution suggest that such a large amount of DNA would not be retained if it served only this limited function.

Building on the concept of homadhesion and the idea that perpetual chromatin refolding serves as a mechanism for cellular computation and decision-making, we propose that introns play a role in determining when and under what circumstances their associated genes should be expressed. Specifically, we suggest that introns control gene decompaction, a key mechanism of gene expression regulation alongside transcriptional complex assembly.

We introduce the concept of intron-mediated compaction and decompaction, termed "indepaction" (INtron mediated compaction and DEcomPACTION). In normal cells, the chromatin of most genes and intergenic sequences is compacted and located in the inner periphery of the nucleus, while actively transcribed genes are decompacted and centrally located. This arrangement adheres to chromosome territory rules, with each chromosome occupying a distinct 3D segment in the nucleus.

For silent genes, we propose that the repetitive parts of intronic dsDNA pair with identical repetitive DNA sequences, ensuring compaction through homadhesion. In the decompacted state, we suggest that spliced-out intronic RNA stabilizes decompaction by homologically pairing with both repetitive and non-repetitive parts of the intronic DNA. This is possible since

intronic RNA is a copy of intronic DNA. This process prevents compaction via homadhesion with homologous repetitive sequences from elsewhere in the genome.

We hypothesize that the cellular machinery switches between these two states - compacted via homadhesion and decompacted via intronic RNA-DNA pairing - by sending additional RNA sequences to regulate the process. Decompaction may be mediated by repetitive RNA sequences produced elsewhere in the genome that come to the intron, align homologically to its identical repetitive part, and this way initiate decompaction. Conversely, compaction might be induced by antisense RNA that pairs with the stabilizing intronic RNA, potentially leading to its degradation and subsequent gene compaction.

The structural basis for homological adhesion in the proposed Indepaction mechanism could potentially involve two distinct molecular configurations. One possibility is the formation of DNA-RNA heteroduplexes, where the RNA displaces one strand of the DNA, creating a localized R-loop structure (Costantino and Koshland 2015). Alternatively, the mechanism might involve the formation of triple-helical nucleic acid structures, where the RNA binds to the major groove of the DNA double helix through Hoogsteen or reverse Hoogsteen base pairing (Felsenfeld, Davies, and Rich 1957). Both of these molecular arrangements could provide sequence-specific recognition and stable binding, consistent with the proposed function in regulating chromatin compaction states.

The chromatin-opening and stabilizing RNA sequences could be medium and long (100-10000 nt), while the decompacting antisense RNAs could be short (15-30 nt). This proposed indepaction mechanism generates testable predictions using existing public genomic data. We hypothesize that co-expressed genes may stabilize each other's expression by sharing common patterns in their introns, with their intronic RNAs cross-stabilizing the introns of co-expressed genes. Similarly, we predict that gene activation pathways may include RNA copies of repetitive DNA as mediators via the proposed Indepaction mechanism.

To summarize the results, our model of DNA-water interactions proposes a "pintumbler" mechanism where DNA imprints its sequence information onto surrounding water structures, creating layered structures that shift based on the DNA sequence. Genomic analyses revealed patterns of purine jumps and even-odd nucleotide homology aligning with this model's predictions. We introduce the concept of "homadhesion" - homologous adhesion between DNA duplexes mediated by these water structures - and propose an "indepaction" mechanism for intron-mediated gene regulation. These concepts suggest a novel form of cellular information processing through dynamic chromatin reorganization. This concept of chromatin as a genome sequence-programmed 'biocomputer' extends earlier ideas proposed by Miller and Webb (Richard A. Miller and Webb 1972, 2002), who suggested that DNA functions as a quantum-holographic field. Their work, like our current model, emphasized DNA's capacity to process and transmit information beyond its linear sequence through its physical organization and interaction with electromagnetic fields.

Discussion

This study presents a novel model of DNA-water interactions and their potential role in chromatin organization. At its core, our model proposes a perpetual dynamic interplay between the tendency towards order (perfection) and the continuous disassembly of that order

(imperfection) as a fundamental principle of life.

Key aspects of the model:

1. DNA imprinting on water: We proposed that DNA may initiate microcrystallization of water, imprinting its sequence onto the water structure through a process we term "crystal pattern propagation" or "snowflake signaling."
2. Pintumbler mechanism: Our model suggests that the DNA imprints its sequence into the water of nucleoplasm by defining shifting pattern of surrounding transverse water layers, creating a unique water structure that reflects the underlying DNA sequence.
3. Dynamic competition between perfection and imperfection: The model emphasizes a constant interplay between the formation of ordered, crystal-like water structures (perfection) and their continuous dissolution and reformation (imperfection) as the basis for life.

The focus of this model is on highlighting the perpetual, self-organizing nature of living systems. It suggests that the nucleoplasm exists in a state of continuous, dynamic reorganization with three main components:

1. Recrystallization of polywater: Constant growth and dissolution of water structures around DNA.
2. Screwing oscillations: DNA's back-and-forth screwing-twisting movement within water layers due to imperfect alignment.
3. Chromatin dynamics: Sequence-specific homologous adhesion (homadhesion) of different parts of chromosomes through water-mediated structures.

This continuous state of flux, teetering between order and chaos, may provide the flexibility necessary for cellular processes while maintaining overall structure. A key insight of our model is the proposal that the refolding of chromatin in a sequence-specific manner is the primary mechanism by which cells process information - essentially, how cells "think." This dynamic reorganization of chromatin, guided by DNA-water interactions, may serve as a physical basis for cellular logic, decision making and fine-tuning. As chromatin continuously refolds in response to various inputs, it creates a dynamic, three-dimensional DNA-sequence programmed information processing system within the nucleus. This concept of chromatin as a genome sequence-programmed "biocomputer" adds a new dimension to our understanding of cellular information processing. It suggests that the genome not only stores information in its linear sequence but also actively computes and responds to cellular needs through its physical reorganization. This dynamic, sequence-specific refolding could explain how cells integrate multiple inputs and make complex decisions.

Homadhesion is guided by biofields

Consider that dynamic, continuous, perpetual, partly random self-organization processes are necessary for biofields to exert their influence. There are several self-organization levels:

1. Polywater continuously self-reorganizes.
2. Chromatin also continuously self-reorganizes.

There are waves of self-reorganization in chromatin. For example, in mammalian cells, there is a periodicity of reorganization cycles with a period of 2 minutes. This pulsation or breathing of chromatin was observed using a fluorescent LacO/LacI-GFP tandem array of repeated sequences (Nagaich et al. 2004).

The influence of biofields on biological systems may be most effective in dynamic, self-organizing processes that are in a state of partial equilibrium. While this idea hasn't been directly stated in scientific literature, we can draw parallels from other fields where similar phenomena are observed. A key aspect of systems in dynamic equilibrium is their fluidity and sensitivity to even subtle forces. In such states, small inputs can potentially shift the entire equilibrium, leading to significant changes in the system's organization. This sensitivity makes these systems particularly suitable for observing the effects of subtle fields.

Consider experiments that visualize magnetic and acoustic fields:

1. Magnetic field visualization: Magnetic particles are suspended in a fluid or placed on a low-friction surface, allowing them to move freely with minimal resistance. When a magnetic field is applied, these particles self-organize into patterns that reveal the structure of the field. The near-frictionless environment enables even weak magnetic forces to noticeably influence the particles' arrangement.
2. Cymatics: In these experiments, sand or small particles are placed on a plate that is then vibrated with sound waves. The vibration essentially creates a low-friction environment where the particles can easily move. The particles reorganize themselves into complex patterns that represent the acoustic field's interference patterns.

In both cases, the key to visualizing these invisible fields is the dynamic, self-organizing nature of the particles in a state of low friction. They're free to move and reorganize in response to even subtle influences from the field, thereby making the field's influence visible.

We suggest that biofields might operate in a similar manner within biological systems. Living organisms are in a constant state of flux, with cellular components and molecules continuously moving and reorganizing. This dynamic state, akin to a fluid system with low internal resistance, might make biological systems particularly responsive to the subtle influences of biofields.

For instance, chromatin in the cell nucleus undergoes constant reorganization. This dynamic environment could potentially allow biofields to influence gene expression or other cellular processes by guiding the self-organization of chromatin and other cellular components. This way, even small influences from subtle biofields could lead to significant shifts in cellular organization due to the system's inherent sensitivity when in a dynamic equilibrium state. This perspective suggests that to fully understand and potentially harness biofields, we should focus on studying biofields using biological systems in their dynamic, self-organizing states rather than in static or overly simplified in-vitro conditions.

The biofield concept aligns with earlier work by Miller and Webb (1972, 2002), who proposed that DNA functions as a quantum-holographic field capable of storing and transmitting information beyond its linear sequence. Our model provides a mechanism for such information transfer through the interaction of electromagnetic, electroacoustic and subtle fields with DNA-mediated water structuring and chromatin organization.

While our model presents intriguing possibilities for DNA-water interactions and chromatin

organization, it is largely theoretical at this stage. Although we observed genomic patterns that confirm our predictions, we also need to rule out alternative explanations. To build upon this initial work and rigorously test our hypotheses, we propose the following directions for future research:

1. Chromatin Conformation: Utilize chromatin conformation Micro-C and Hi-C data to search for evidence of homadhesion in chromatin structure. In these experiments a combination of experimental crosslinking with sequencing is used to map with high resolution which fragments are positioned near each other in the cells. These data can demonstrate that repeats stick to each other in live cells.
2. Co-regulation: Conduct exploratory analyses of the gene regulation networks to check whether coregulated genes or whether pairs of genes that regulate each other have similar patterns of transposons in introns more frequently than by chance. Analyze genomic sequences for patterns of homology in primary sequence, purine and even-purine codes, focusing on co-regulated genes and gene pairs where one regulates another.
3. Structural Modeling: Develop and refine the computational 3-dimensional chemical structure and dynamics models of DNA-water structures to better understand the structure and dynamics of the proposed pintumbler and homadhesion mechanisms.
4. Sequence manipulation: Use DNA sequence manipulations in cell culture to demonstrate homadhesion. That is introduce, modify or delete patterns of transposons in introns and measure how this affects gene expression. Similarly, modify patterns of transposons in intergenic regions and see how this affects DNA loop formation. These experiments should account for the need for natural nucleoplasm components, including proper 1% DNA and 20% protein concentrations. We could also measure loop formation rates when loops are closed by transposons, using FRET-based methods to measure DNA looping J-factors as we have done previously (Shoura et al. 2012, 2020; Myakishev et al. 2001).
5. Water-DNA Structure Studies: Employ a variety of techniques (NMR, optical spectroscopy, bioimpedance, acoustic spectroscopy, isotope studies, FISH with microscopic readout) to investigate water-DNA structures both *in vitro* and *in vivo*. Compare findings across different cell types (e.g., cancer vs. normal) and species. Additionally, we could employ atomic force microscopy techniques as we have done before (Vetcher et al. 2006) to directly visualize DNA conformational changes induced by water structuring and transposon-mediated looping. Importantly, we were able to achieve visualization in liquid water as opposed to traditional frozen water.
6. Comparative Water-DNA Structure Analysis: Test the hypothesis that water-DNA structures differ significantly between species, cell types, and disease states, reflecting variations in genomic organization and cellular function. Investigate these structures using both in vitro and *in vivo* models, with emphasis on live nucleoplasm or reconstituted nucleoplasm in vitro. Employ a range of methods including NMR, optical spectroscopy, bioimpedance, acoustic spectroscopy, isotope studies, and FISH with microscopic readout. Utilize fluorescent LacO/LacI-GFP tandem array of repeated sequences (Nagaich et al. 2004) inserted in live cells to visualize dynamic changes in chromatin structure. Conduct comparative analyses between cancer and normal

genomes, and across various classes of life species. We expect to find distinct water-DNA structural signatures correlating with genomic complexity, cellular differentiation states, and pathological conditions, potentially revealing the role of water-mediated DNA organization in biological information processing.

7. DNA Sequence Imprinting on Water (seprinting). This could involve imprinting various DNA sequences on reconstituted nucleoplasm, removing the DNA, and then measuring the sequence-specificity of the remaining water structure as it affects the folding of newly introduced dsDNA. To separate sequence-imprinted water from DNA we could use DNA bound to beads, or semi-permeable membranes. Structured water isolated from human cells should have an imprint of the most abundant repetitive sequences such as Alu and LINE, comprising collectively over 30% of the human genome. This structured water should affect the conformation of newly added tagged DNA constructs containing Alu and LINE sequences in a sequence-specific manner compared to other control constructs that are not homologous to human DNA. Such conformational changes can be measured by FRET or intercalation fluorescent dyes, or by circular dichroic spectrometry, or by impedance spectrometry of DNA attached to a semiconductor chip. Also LINE1 structural and vibrational signatures should be common between human and mouse chromatin, while Alu is specific to primates, so its structural and vibrational signatures should be common to human and monkey but absent in the mouse. Our DNA sequence imprinting model provides a molecular structural mechanism for the ideas of water memory proposed by Benveniste (Davenas et al. 1988) and Montagnier (L. Montagnier et al. 2011). We hypothesize that certain DNA structures may imprint on water more readily than others. Additionally, temperature and nucleoplasm content might be crucial factors in achieving proper imprinting of DNA sequence structure on water. These aspects of our model provide a framework for understanding how specific molecular information might be retained in water structures in the nucleoplasm. Therefore, *in vivo* experimentation or close reproduction of *in vivo* nucleoplasm conditions will most likely be required for proper verification of the water memory phenomenon. We suggest that for effective DNA sequence imprinting on water, any pre-existing structures would need to be randomized first. This randomization might be hard to achieve in nucleoplasm, but *in vitro* in low-molecular-weight solutions, this can be achieved using boiling and ultrasound.
8. DNA Twist Oscillations: Use polarization spectroscopy of fluorescence-labeled DNA chains to measure twist oscillations and measure the effects of homadhesion on DNA oscillations in live cells or reconstituted nucleoplasm. Check whether the addition of homologous RNA disrupts homadhesion.
9. Polywater Structure Characterization: Adapt methods from Gerald Pollack's work on the "fourth phase of water" to investigate structured water formations around DNA in reconstituted nucleoplasm (G. H. Pollack 2013). Employ techniques such as exclusion zone measurements, infrared imaging, and electrical potential recordings to characterize the properties of water layers adjacent to DNA molecules. Use DNA bound to beads or flat surfaces. Utilize microspheres, pH-sensitive dyes, and microelectrodes to map the extent and properties of these structured water regions.

10. Biofield Influence Studies: Microscopy, gene expression and chromatin conformation experiments to investigate how biofields might influence the dynamic self-organization of chromatin and water structures in the nucleus.

The use of nucleoplasm from multicellular organisms could be crucial for these experiments, as the proposed mechanisms may be more pronounced in multicellular organisms. However, when cell culture experiments are not possible (as in spectroscopic studies), reconstructing or isolating fully functional nucleoplasm is a challenging task. It is unclear whether the high protein concentration (about 20%) in the nucleus is critical for the formation of sequence-imprinted water (Sequa). If pure water, buffered solutions, or simplified imitations of nucleoplasm prove sufficient, this would greatly simplify the experiments. One might consider exploring alternatives such as typical buffers and media used in enzymatic reactions and cell culture, including PCR and restriction buffers, serum, and BSA dilutions. Additionally, commercially available kits for nucleosome reconstitution, which contain histones and other components for reconstituting chromatin, may provide a suitable approximation of the nucleoplasm. These approaches could offer practical alternatives to full nucleoplasm reconstruction while still allowing for the study of proposed DNA-water interactions.

Conclusions

In this study, we presented a novel model of DNA-water interactions within the cell nucleus. Our model suggests that DNA sequences can imprint information onto surrounding water structures, creating a unique "watermark" that reflects the underlying genetic sequence. We proposed that these water structures may mediate sequence-specific dynamic sequence-specific chromatin folding, providing the program and the mechanism for chromatin reorganization and and gene regulation.

In our model, we integrated concepts from biofield theory, polywater structure, and genomics of transposons to explain sequence-specific chromatin folding. We proposed testable mechanisms for DNA-mediated water structuring and homologous adhesion of genomic repetitive elements.

While our model was largely theoretical, our genomic analyses revealed patterns that aligned with its predictions. We proposed future research directions, including studies of chromatin structure, water-DNA interactions, and the influence of electromagnetic fields on cellular processes. This research should lead to significant advancements in our understanding of chromatin function, with potential implications for regenerative medicine, oncology and aging research.

This work offered potential explanations for several long-standing mysteries in biology. It provided a possible mechanism for how biofields influence genome function, suggested a structural mechanism for cellular thinking and decision-making, and proposed new functions for introns and intergenic sequences. We also proposed a new positive function of transposons in dynamic chromatin folding. This work not only suggests a structural basis for cellular information processing but also provides a framework for decoding the transposon code embedded in introns and intergenic "junk" DNA. By understanding this hidden transposon code, we may be able to interpret how chromosomal rearrangements in cancer disrupt normal cellular logic. As

we validate our model experimentally, we anticipate developing the ability to read and potentially manipulate this code, which could lead to breakthrough therapies in regenerative medicine and cancer treatment.

Moreover, deciphering this transposon code represents a crucial step toward understanding the vibrational code of DNA. As we previously suggested (V. Savelyev et al. 2019; Richard A. Miller and Webb 1972, 2002), there exists a fundamental vibrational code of DNA that forms the basis of the genome-wide and organism-wide DNA hologram. This hologram serves two major functions: morphogenetic regulation (responsible for body structure and function) and individual consciousness (responsible for mind). This language resides within the noncoding part of the genome, which comprises 95% of our genetic material.

The distinctive property of this code lies in its distributed and collective nature - its primary components are in the repetitive regions of the genome, particularly in the positions of transposons. The code is read holographically and expressed vibrationally through electromagnetic and electroacoustic fields and through chromatin dynamics. We can decipher this code using classical genetic approaches by examining the functions of natural and artificial variations and by analyzing the vibrational properties of DNA constructs both in vivo and spectroscopically. Once deciphered, this understanding will advance cancer therapy, regenerative medicine, psychiatry, psychology, and mind enhancement.

A key consequence of understanding the DNA hologram is its dual nature - being both local and nonlocal. The local DNA hologram is involved in forming the shape and function of the body and the work of mind. Additionally, individuals share the DNA vibrational field with each other, with Sheldrake's collective morphic field (Rupert Sheldrake 2009) and with the other life of the biosphere. This understanding emphasizes the importance of maintaining morphic field ecology and addressing factors that destabilize individual and collective morphic fields.

For example, we face a rapid increase in electromagnetic pollution, as the number of people using smartphones, GHz and THz waves has grown dramatically and continues to expand. This almost certainly exerts a strong influence on the morphic field. Additionally, extensive genetic modification of farmed plants and animals likely affects the morphic field. Human genetic modification has accelerated through genetic selection during in vitro fertilization. Moreover genetic manipulation of germlines is still legal in over 10 countries. It is likely that unauthorized genetic manipulation of germlines occurs covertly in some regions. With advancing technologies for animal genetic manipulation, the costs and accessibility of such procedures become increasingly feasible for potential misuse.

Understanding the vibrational code of DNA would reveal the nature of the DNA holographic field and underscore the necessity of global DNA field (morphic field) ecology. With the active development of brain implants by companies like Neuralink, deciphering the vibrational code of DNA would establish safe parameters for electronic implants, including those for the brain, while demonstrating methods for non-destructive brain interfacing. Understanding the mechanisms of DNA hologram formation would enable the development of computer-brain interfaces that maintain the stability of individual biofields while increasing communication bandwidth.

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