A Molecular Marriage: A Metaphorical Look at DNA Structure and Function.

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Introduction

Scientific investigators work constantly to increase our understanding of nature, and their efforts bear fruit. Subtle mysteries of natural existence now fall into human hands routinely, exposing a world formerly hidden from our view. The field of molecular genetics must be one of the most exciting new areas available to us now. With enthusiasm we incorporate new information from this area into applications in genetic engineering. The pharmaceutical industry is driving toward better treatments for congenital ailments based on gene therapy, and medical researchers are finding many diagnostic uses for genetic screening. Potential practical benefits from this area stagger many, and keep scientists working at mind-numbing paces to extract these benefits as soon as possible.

Could we use these discoveries in other ways? Do our inspired information gatherers bind us to a world of external opportunity, or could their work serve a more metaphysical purpose as well? The level of sophistication we enjoy in the natural world today is not matched with a commensurate level of spiritual sophistication. Our soul's kingdom is mostly ignored. Yet in 1757, Emanuel Swedenborg witnessed the coming of a new age (LJ 45),[1] in which a new revelation given from God enables beneficial explorations of spiritual frontiers (and perhaps even natural ones). Because of this revelation we enjoy a more lucid concept of God's desires for us than has ever been seen in the Western world. Some people have dedicated their lives to bringing God's revelation into our minds with even more clarity. Despite their efforts, however, we have not come far this century.

A task before us now is to join our spiritual and natural revelations,[2] animating the first and enriching the latter. Like water beads coalescing, tension disperses with happy ripples of insight as we realize new connections between these presently-segregated sources of knowledge. Some thoughtful workers have bridged both fields,[3] but we have a lot more to do. Based on the philosophical satisfaction gained from accomplishments so far, further conjunction promises more joy.

A New Frontier

The discovery of molecular mechanisms in biological processes such as photosynthesis, metabolism, and protein synthesis captivates us as we realize both the abilities of nature, and our own capabilities of observation, comprehension, and manipulation. Life unfolds before us as a complex, elegant, adaptive, and efficient set of chemical reactions. Like the first moon walk, the new experience is so extraordinary that wider meanings and implications escape attention. This has been the situation in the fields of molecular biology and biochemistry over the last several decades. But our new information is providing us with a steady supply of natural ultimates as never before. We can experience a new and more fulfilling thrill when we fit these fresh pieces with what we believe to be true about creation as revealed to us by God.

Swedenborg's theological work, *Divine Love and Wisdom*, teaches that everything in creation, both natural and spiritual, stems from the marriage of Divine good and Divine truth in God (DLW 55), and that all things represent this union in some way (DLW 56, 409). Therefore, a thinker who accepts the teachings of Swedenborg may assume that the manner in which life is organized and directed at the molecular level must also reflect, in some way, the marriage of good and truth.

Today we know of a chemical substance that serves as the directive genetic material within our cells, and we do indeed find an obvious metaphor. In addition, we find that this metaphor extends beyond the molecules involved to suggest a picture the Lord may be giving us about how men and women might function together according to His plan. The heading to *Divine Love and Wisdom* 61, "All created things have, in a certain image, relation to man," encourages the extension of thought about physical things to their relationship with humankind.

The purpose of this essay is to break from the breathless world of chemical research and traverse this new frontier with an aim toward appreciating some metaphysical models present there. Perhaps molecular genetics can find a home in our common joys such as appreciating rainbows, sunsets, exquisite music, fine stories, inspired paintings, and the like. The late English professor, E. Bruce Glenn, summed up the arts as resulting from "an affectional ordering of experience" (E.B. Glenn, 1993). Like the arts, science also involves ordering experience. Science excels at providing new experiences, and art is particularly good at ordering the same experience in many different, and often aesthetically pleasing ways. Once ordered, an experience can provide joy and satisfaction. This foray attempts to order the experience of molecular genetics.

Life at the Molecular Level

For any of the chemical processes of life to occur, some guiding mechanism must be at work that constructs the necessary molecular tools and building blocks as needed. The shaping elements (tools) of life are proteins, which are constantly being constructed and destroyed by the living cell under the direction of its genetic material. The genetic material in every living cell is DNA—deoxyribonucleic acid. A cell's genetic material determines the limits of its structural and

physiological responses to its environment. To gain an appreciation for the role DNA plays in the synthesis of proteins, a short overview of the process is provided below.

Protein synthesis occurs at the ribosome, a small, subcellular particle. Ribosomes are factories that polymerize[4] amino acids into long, linear polypeptide chains. These polypeptide chains are protein molecules, which fold into compact, roughly spherical shapes. All proteins are composed of amino acids joined with covalent bonds.[5] What distinguishes one protein from another is the length of the polypeptide chain (number of amino acids incorporated), and the *sequence* of amino acid residues along the chain. The ribosome uses molecular "blueprints" to build proteins. This "blueprint" is another long, linear, polymeric molecule known as ribonucleic acid (RNA) (Fig. 1). Since the function of RNA here is to deliver information for protein construction, these RNA molecules are called "messenger" RNAs (mRNA). mRNA has four different kinds of monomeric[6] units, distinguished from each other by cyclic side-chain structures known as "nitrogenous bases" (Figs. 2-3). The *sequence* of nitrogenous bases along an mRNA molecule determines the *sequence* of amino acid residues along the synthesized protein. Ribosomes "translate" the nucleic acid message into a protein.

mRNA molecules guide protein synthesis, but what directs RNA synthesis? mRNA molecules are short-lived in the cell, lasting just minutes in a bacterial cell (Brenner, et al. 1960), and up to a few days in a human cell (Maniatis, et al. 1987). DNA, a more permanent molecule, guides the synthesis of the messenger molecule. While DNA is very similar in molecular structure to RNA, one obvious and important difference is that complementary[7] molecules of DNA pair up into double-stranded, helical assemblies, and mRNA molecules do not (see Figs. 4-5; helical structure not shown).[8] Like RNA, the *sequence* of nitrogenous bases in DNA contains information for building

proteins. Therefore, we can read the encoded sequences of every protein made in living cells by reading the sequence of nitrogenous bases in the cell's DNA! A tremendous library of masters for blueprints!

The process of protein synthesis begins with opening and unwinding double-stranded DNA. Then, with assistance from a host of protein molecules, monomeric units of RNA align and polymerize along *one* strand of a two-stranded DNA assembly, which temporarily separates over a short distance for this purpose. As it forms, the RNA molecule copies the sequence information present intrinsically in DNA. This process is termed "transcription," because coded information in DNA is *transcribed* into the growing RNA molecule (specifically called mRNA because of its role as a messenger). Once made, the mRNA molecule relocates and binds to a ribosome, where the encoded message is used to synthesize the corresponding protein molecule. After RNA polymerization, the separated strands of DNA re-anneal, forming, once again, double-stranded, helical DNA.

Since the cell's structure and biochemical activities depend upon which proteins are present, the genetic information in the DNA determines what the cell will look like and what it will do.[9] Like a scroll in a player piano, the *sequence* of nitrogenous bases along a DNA molecule determines what song the containing living cell will sing.

A Molecular Marriage

How can we see the structure and function of DNA as a metaphor for the marriage of good and truth? The Heavenly Doctrines advise looking to the *use* of a form to understand it. *Divine Love and Wisdom* states that:

> Uses are from life alone, and their series and order from wisdom and love, while forms are containants of uses. Consequently, if forms alone are regarded, nothing of life, still less of love and wisdom, and thus nothing of God can be seen in nature (DLW 46).

When the function (use) of DNA is born in mind, a metaphor comes alive. Swedenborg's theological writings teach that good and truth, united in marriage, do uses (CL 83, 68). This is the cornerstone of creation (DLW 55-60). If the two strands of DNA are seen as married partners, it follows that their functioning together produces uses, and life depends upon these uses. Human uses are impossible without human marriage, and cellular uses are impossible without a molecular marriage. Just as children come to be through their parents, proteins take form via DNA.

Viewed another way, everything depends on the ultimate conjunction of pure good and pure truth in God. God, the Infinite marriage of good and truth, produces all creation (CL 84-85, 516), and life cannot continue without this Infinite marriage (DLW 52). Analogously, the creative force transmitted by DNA endures generation after generation, and the cell takes all direction from this source, including information about how to respond to its environment. Like a sophisticated mold, the two strands of complementary DNA "form" proteins through an intermediary mRNA molecule. This molecular molding apparatus not only determines the shape and chemical properties of the proteins it forms (and thereby the structure and function of the cell), but also controls when they are produced, and the level of production.[9] On a molecular level, DNA plays a god-like role.

DNA is neither consumed nor produced as it functions in the cell. This is also true of angelic marriages where the offspring are not children, *per se* (CL 52). Heavenly marriages produce good and truth in the form of uses as offspring (HH 382b). Similarly, the marriage of two complementary

DNA molecules does not produce DNA. Rather, DNA produces RNA and proteins—and proteins, like good and truth, sustain life by doing uses.

But when a cell divides into two cells, all the DNA present in the original cell must be copied so that the new cell can direct *its* biochemical life as well. The process in which DNA is produced is called "replication," and is accomplished through a mechanism significantly different than when DNA directs RNA synthesis. When DNA serves as a template for RNA synthesis, the two strands of DNA separate temporarily—over a small, localized area. The localized separation is necessary so that the growing RNA polymer can pair with one of the two DNA strands. After RNA synthesis the DNA strands re-conjoin. When DNA serves as a template for *DNA* synthesis (in the replication process), double strands separate into single strands, and *each* encodes another complementary strand of *DNA*. The differences are that *both* strands serve as template at the same time, and the separation is not temporary because the newly-synthesized strand of DNA remains in conjunction with its template strand.[10] This separation and replication occurs at every cell division.

Contrary to what we might assume given the analogy to marriage, the conjoining of the same two DNA strands is not eternal. This apparent anomaly serves as a warning not to take metaphorical images of physical things too far. If we do not tread lightly we might either "disprove" the Word of God through scientific observations, or we might not accept facts that science uncovers because they seem to contradict our spiritual understanding.

The anomaly suggests looking at DNA replication in another way. Since DNA is a chemical substance it cannot be eternal, but the information present in DNA lasts much longer than one generation. DNA replication passes the information from one generation to the next, so the information present in DNA is more eternal than any given DNA molecule. An appropriate analogy

seems to be the Lord's Word, which is eternal, but the natural form It takes changes over time and must be reproduced. In the replication process, therefore, we can see a representation of God's Word transmitted to different peoples at different times. This introduces the subject of molecular evolution, which will wait for another essay.

Looking again at the form of DNA, with its function in mind, we can see that DNA in a living cell is a beautiful structural representation of marriage on the molecular scale. In the cell, DNA is a two-stranded molecule, and the strands contain both obvious and subtle symmetry and complementarity. Each strand is chemically distinct, meaning that no covalent bonds link the two together. (That the strands are chemically distinct entities is reinforced by the fact that they separate in the replication process.) Yet, in double-stranded DNA, the strands are in intimate contact, interlocking and writhing about each other. For every indentation in one, the other offers a protrusion. This complementarity in structure is what allows DNA to do its function.

As in RNA, the monomeric units of DNA are distinguished from each other by four cyclic side-chains (Fig. 2). We separate these side-chains into two groups—the purines (adenine and guanine), and the pyrimidines (thymine and cytosine). Notice that the purines are larger than the pyrimidines. The purines have a bi-cyclic structure, while the pyrimidines have just one hexagonal ring. In complementary, double-stranded DNA, non-bonding chemical forces hold the nitrogenous bases from each strand in edge-on contact, forming "base pairs" (Fig. 4). Wherever we see a purine in one strand, we find a pyrimidine in the other. We never find two bulky purine residues together, pushing into each other. Similarly, we do not find two pyrimidine residues in edge-on contact, but always matched with a purine. These indentations and protrusions have clear analogies to human marriages.

Double-stranded DNA interlocks using chemical complementarity. While in edge-on contact, guanine and cytosine donate and receive specific hydrogen atoms (Fig. 4). Thymine and adenine do likewise (Fig. 4). This sharing of hydrogen atoms creates a special kind of *intermolecular* bond known as a "hydrogen bond." These bonds are about twenty-five times weaker than a covalent bond, but they are the strongest type of associative force holding two molecules together.[11] (Hydrogen bonds in water give this chemical its strange physical properties such as expansion upon freezing, and high melting and boiling temperatures.) The specificity of the hydrogen bonding is enough to ensure that opposite an adenine residue is a thymine residue, and opposite a guanine residue is a cytosine residue. As a result of this matching, *the sequence of nitrogenous bases along one strand of DNA complements the sequence of nitrogenous bases along its pair.*

In addition to edge-on contact, each base-pair is sandwiched between two other base pairs. A weak, associative force stacks one pair of nitrogenous bases on top of another pair. The flat surfaces of the bases associate with each other in a way that is similar to oil sticking to itself when floating on the surface of water.[12] Favorable interactions of these flat surfaces serve to knit the two strands together.

A still greater metaphor rewards our connection of DNA structure to how it performs its function. If we look closely at the sugar-phosphate backbone structure of double-stranded DNA (Fig. 5), we see a rotational symmetry. The sugar-phosphate linkages run in opposite directions on each strand. The oxygen atom inside the sugar ring points in one direction in one strand and in the other direction in the other strand. The opposite orientation of paired DNA strands has significant implications because, among other things, the cell reads genetic information (encoded by the

sequence of nitrogenous bases in DNA) in one direction. Furthermore, RNA polymerizes unidirectionally.[13] This means that genetic information contained by double-stranded DNA is transcribed from *one* strand, moving in *one* direction. However, the sequence of nitrogenous bases in the transcribed RNA molecule exactly matches the sequence of the *unused* DNA strand.[14] Also, the orientation of the RNA molecule matches the unused strand of DNA. This is so because the template strand of DNA directs the synthesis of its *complementary* sequence and orientation.

Relating Human and Molecular Marriages

Good and truth unite to do uses. Human marriage is an example of that—and so is DNA. Perhaps the functioning of DNA is a model the Lord has given us, showing how men and women can work together. When we extend the cooperative pattern discerned in the form and functioning of DNA into human relationships a wonderful picture emerges of good and truth interacting. DNA represents a marriage of good and truth where cooperation supersedes any form of dominance. We do not see rule and submission. We see cooperative, synergetic behavior. A question of which strand is more important in the functioning of DNA is simply dull when faced with the exquisite solidarity we find in that relationship.

In transcription both strands of DNA are necessary. The template strand directs the RNA sequence, but the other strand holds the coded message. Furthermore, both strands *together* preserve the genetic information by complementing each nitrogenous base with its pair; if one base should become damaged, the gene can be repaired by referring to the other strand.

Genetic regulation, alluded to earlier,[9] depends on signal sequences found in DNA before, after, and even within genes. Certain proteins read these signal sequences and increase or decrease

transcription levels depending on the chemical environment. These regulatory sequences are completely unreadable in single-stranded DNA. Therefore, genetic regulation depends on joined DNA strands. In other words, expression of uses requires agreement and cooperation between married partners.

Cooperation goes even further because each strand is used as template DNA for different genes. Sometimes one strand serves as template, and sometimes the other does. In either case, both strands *together* do the *use* of directing protein synthesis, but their *roles* are different. The *use* is accomplished only when *both* roles are done. There is no competition; the roles interlock perfectly in doing the use. This is a beautiful image of a true human marriage.

Human reproduction is clearly analogous to a marriage of good and truth where two distinct roles combine to engender new life. The *use* of bringing forth new life is accomplished by combining the female *role* and the male *role*. Inside one person, the role of the heart and the role of the lungs *together* do the use of supporting life. Inside any human cell the roles of each strand of DNA direct molecular life. Within any human use we can probably find two roles working together to accomplish the task at hand. With the Lord's help, the models of this conjunction in the world around us can help us find ways to conjoin these roles within ourselves and within human relationships. If this is true, investigation of natural mechanisms, colored and enlightened by God's teachings, can lead us to clearer perceptions for life at our level.

Conclusion

Within the field of structural biochemistry DNA is a classic example of structure and function united. In a wider view this "form-following-function" principle parallels what is said in

Divine Love and Wisdom 46, quoted above, and *Arcana Caelestia*, concerning the Grand Man, quoted below:

> It is the functions . . . to which heavenly communities correspond primarily, and then because they correspond to the functions they correspond to the organic forms too; for the one is indivisible from the other and inseparable, so much so that it makes no difference whether you speak about the function or about the organic form through which and from which that function exists (AC 4223.1).

The containing form of DNA reflects good and truth conjoined, and, mirrored in DNA function we see that marriage engendering and sustaining life.

We are very fortunate we can "see" DNA molecules, and understand their significance. Rather than threatening our spirituality, discernment of DNA structure and function provides us with an elegant, natural example of our spiritual beliefs. Just as the Heavenly Doctrines predicted, nature (even to its least things) reflects the marriage of good and truth. On three levels we can be aware of the operation of good and truth performing uses together: By the Lord's revelations we know that He creates and sustains the universe through the marriage of Divine Love and Divine Wisdom; in the structure and function of DNA we see, in form and function, an example of created entities reflecting the Divine marriage; and in human relationships we see, at least through extrapolation if not always in actuality, that we do uses through conjoining good and truth, faith and charity, will and understanding, female and male, or husband and wife.

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NOTES

1. Swedenborg authored a series of theological books as a result of the revelations he received from God. Swedenborgians understand these works to be the Lord's Second Coming, and refer to them as the "*Heavenly Doctrines*." These books have been published in a variety of editions, the standard English one being a thirty-volume set published by the Swedenborg Foundation. Swedenborg's theological works are cited parenthetically in the body of this essay, using the standard abbreviations.

2. Similar remarks have been made by E. Sandström, Sr. in an address published recently in *The New Philosophy* (Sandström 1989), and by R.W. Gladish in his Foreword to G.L. Baker's latest book, *Religion and Science* (Baker 1992).

3. Some recent examples from Swedenborgian authors include Odhner, 1985; Brock, 1986; Odhner, 1987; and Baker, 1992.

4. A *polymer* is a large molecule constructed by joining together many smaller molecules. Proteins and nucleic acids (both DNA and RNA) are polymers consisting of repeated subunits assembled in a head-to-tail fashion. The chemical process of joining subunits is called "*polymerization*."

5. A molecule is an assembly of atoms held together with *covalent* bonds. Covalent bonds are strong, forcing a molecule into a particular geometric configuration. As a general rule, covalently bonded atoms do not separate when a molecule reaches its boiling point.

6. *Monomers* are the smaller molecules from which polymers are synthesized. Once a monomeric molecule has been incorporated into a polymeric chain, it is often referred to as a "residue."

7. *Complementarity* between two paired strands of DNA is described further on. In short, each sequence of nitrogenous bases along any strand of DNA has one *complementary* sequence of nitrogenous bases possible along another strand of DNA. When two complementary strands of DNA meet, they pair up.

8. A single-stranded (ss) mRNA molecule also has one complementary sequence of nitrogenous bases possible along another strand of mRNA. However, under normal cellular conditions, double-stranded (ds) RNA is not as thermodynamically stable as ds DNA—due to the extra hydroxyl group present in RNA (see Fig. 3). Furthermore, the complementary mRNA strand is not present in the cell, whereas the complementary DNA strand is.

9. DNA is more than a genomic library of the cell's proteins. DNA also contains coded regions that interact with various proteins to switch transcription on and off, or to upscale or

downscale the level of transcription. This *regulatory* function is crucial to cell viability, and is not as well understood as the *encoding* function.

10. This is known as the "semiconservative" mode of DNA replication, a hypothesis formed by James Watson and Francis Crick (Watson and Crick 1953) and confirmed by a classic experiment performed by Matthew Meselson and Franklin Stahl (Meselson and Stahl 1958).

11. The strength and importance of hydrogen bonding is a matter still under considerable debate. While all agree that this electrostatic interaction is stronger than any other type of intermolecular bonding, some believe that the contribution of hydrogen bonding to structural stability is minimal. This is because whenever a hydrogen bond is made between two macromolecules, a hydrogen bond is lost to water, obviating any stability gained (Eberhardt and Raines 1994). Others maintain that the strength of a hydrogen bond depends upon the chemical nature and structure of the donor and receptor pair. In this view, it is believed that the hydrogen bonds between two strands of DNA, or between an acceptor and donor in a protein molecule, is stronger than hydrogen bonds found with or between water molecules (Loh and Markley 1994). The measured strengths of hydrogen bonds between various types of oxygen-hydrogen and nitrogen-hydrogen molecules has ranged from as low as 8 kJ/mole to as high as 21 kJ/mole (Rodham, et al. 1993). The strength of typical covalent bonds in organic molecules ranges from about 380 to 426 kJ/mole (Morrison and Boyd 1983).

12. More than the hydrophobic effect is at work here. Heterocyclic, aromatic molecules can interact with each other through their π-electron clouds (Hunter and Sanders 1990). This effect can be considerably stronger than the classic hydrophobic effect. The charge density over the flat portions of these molecules is not homogenous, and depends upon the identity of the atoms in the heterocycle. Although each nitrogenous base has characteristic electrical configurations, guanine has a particularly noticeable electronic signature (Hunter 1993) because two electronegative atoms, aromatic nitrogen in the heterocycle and the amine group, are in close proximity. This situation causes a high negative charge density along one portion of the surface. A compensating positive charge density is found over the heterocycle's hydrogen atoms. Whenever two or more guanine residues are adjacent to each other, noticeably different conformational restraints are found in X-ray structures, NMR solution structures, and molecular modeling studies (Chuprina, et al. 1993). Each sequence of adjacent nitrogenous bases has preferred conformations which, conditions allowing, maximize alignment between the negative and positive areas of adjacent nitrogenous bases.

13. Unidirectional polymerization of RNA and DNA is a consequence of the chemical structure of the monomeric triphosphate-nucleotides from which RNA and DNA are built. Before polymerization, three phosphate groups, linked to each other through linear, phosphodiester bonds, are attached to the 5' carbon atom of the ribose ring (see Fig. 3). Polymerization of RNA and DNA is an energy-consuming process, driven by the hydrolysis of two phosphodiester bonds. A DNA or RNA polymer grows by connecting the 5'-phosphate group of the in-coming monomer to the 3'-OH group of the growing polymer. In the process the other two phosphate groups present on the monomer are lost as inorganic pyrophosphate, hydrolyzing one phosphodiester bond. The second

phosphodiester bond hydrolyses when pyrophosphate is cleaved into two phosphate groups by the enzyme *pyrophosphatase.*

An important biological reason exists for supplying the chemical potential energy (phosphodiester bonds) with the in-coming monomers, rather than with the growing polymer chain. If a mismatched nitrogenous base incorporates into the growing polymer chain it can be removed by hydrolysis, leaving the original 3'-OH group ready for linkage to the correct nucleotide. If the polymer grew in the other direction, the triphosphate group present on the 5'-end of the polymer would be lost with the incorporation of the first monomer. If the incorporated monomer were consequently removed because of mismatch, the required triphosphate groups would be gone, making it impossible to incorporate the next monomeric unit.

The author is unaware of a convincing explanation for why the nucleotides are charged with phosphate groups on the 5'-OH and not the 3'-OH group. One possibility may be that phosphoryl transfer reactions occur more readily onto primary alcohol groups (as the 5'-OH group is) than secondary alcohol groups (as the 3'-OH is).

14. The RNA sequence is slightly different than the DNA sequence because thymine is not used in RNA. Uracil is used in its place. Uracil base-pairs with adenine just as thymine does. The only difference between thymine and uracil is that thymine has a methyl group added to the 5-carbon of the pyrimidine ring, and uracil does not (see Fig. 2).

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