EVIDENCE FOR THE EXISTENCE OF AN INTELLIGIBLE GENETIC CODE

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Research results are presented that strongly support the Creationist viewpoint. The genetic code, which evolutionists consider to be the highly degenerate product of random mutations, has been shown to function as the blueprint for the three-dimensional structure of proteins. This code is generally accepted to be universal, and the way it is translated into proteins by ribosomes is basically identical from the most "primitive" microorganisms to man. Scientific evidence is reviewed for a self-correcting genetic code which edits out mutational errors under normal conditions.

The genetic code has been shown, by scale model building of antigen and antibody reactive sites, to be capable of distinguishing between "self" and "not-self" protein conformations.

This demonstrated orderliness in the genetic code indicates that it was formulated as an intelligible code by the Creator.

Introduction

One of the best candidates for the most exciting biological discovery of all time was the first breakthrough in "cracking" the genetic code, first reported in 1961, by Nobel prize winner Nirenberg.[1] Nothing else in the history of science has aroused so many thousands of investigators to such urgent efforts for such a continuous period of time, and the race to decipher the genetic messages is accelerating with each passing year.

Motivation for this kind of dedication to just one tiny aspect of biological research is the conviction that genetic messages present on the genes hold the key to understanding the life processes of all living cells and organisms, from microorganisms to man. To mention only a single example of the many exciting possibilities that could follow comprehension of genetic messages, the more than 300 inherited human diseases might be eliminated through genetic engineering.

Progress in reading genetic messages has been very slow for many technical reasons. The principle problem is that, in most cells, literally thousands of different genetic messages are being transcribed simultaneously, and the chemical separation of a single message is extremely difficult. A second problem is that the genetic messages in different types of cells in an organism, such as the human, differ somewhat, and messenger ribonucleic acids (mRNA) extracts prepared from biopsied tissue usually contain mRNA from a wide variety of cell types present in such tissue.

Still another complication is introduced because mRNA extracts may contain other types of nucleic acid, such as deoxyribonucleic acid (DNA), ribosomal ribonucleic acid (rRNA), amino acid transfer ribonucleic acid (tRNA), and other, less well-defined nucleic acids, all of which interfere with chemical isolation and characterization of the mRNAs. Last, and by no means least in importance, the long mRNA strands tend to be snipped into small lengths by a family of enzymes, the ribonucleases (RNAses), when the organization within the cell is disrupted by extraction processes.

Chemical methods of isolation of a single mRNA message are necessary, since the submicroscopic size of the individual mRNA strands precludes physical isolation by even the most expert microscopist. The size of the task involved in trying to read the entire genetic code for the human has been illustrated by Frair.[2] The human body contains at least ten trillion cells, and each of these cells contains about three million genes, each of which may be producing a specific pattern of mRNA messages.

Molecular geneticists appreciate this diversity and, accordingly, have studied the simplest genetic systems, namely, (1) cells of microscopic size, and viruses, that contain very few genes, and (2) highly differentiated cells that express only a very few of the myriads of genes present.

An example of the first type is MS2 bacteriophage (phage), which is a virus infecting the host bacterium, *Escherichia coli*. This phage has only three genes, and all three are always expressed in the same order, as three consecutive messages carried by a single long strand of mRNA. Translation within *E. coli* of this "polycistronic" mRNA into three different phage proteins proceeds from left to right along the mRNA strand; these proteins differ enough in chemical properties and functions to make their separation and chemical characterization possible. The single strand of MS2 mRNA also makes it possible to determine the sequence of mRNA codons (genetic words) used to code for the three phage proteins.

Three examples of highly differentiated cells that express only a few of the many possible genes are:

(a) The human multiple myeloma cell, which proliferates into a population of millions of circulating abnormal plasma cells or myeloma cells,

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each of which forms and secretes identical molecules of a specific myeloma protein that resembles the antibody or immunoglobulin (Ig) molecule in general structure.

(b) The normal plasma cell or immunocyte which is the end-product of differentiation of a lymphocyte that has become immunized against an antigenic determinant (epitope). An immunocyte expresses only those genes required for synthesis of the specific immunoglobulin required to react specifically against the epitope.

(c) Non-nucleated red blood cells (RBC), such as those of the human, seem to have lost or destroyed nearly all genes except those required for production of hemoglobin (Hb); as a result, each of the five billion RBC per ml of blood is packed with about 280 million Hb molecules. The amino acid sequence (primary structure) of Hb from many species, including the human, has been determined. Study of the corresponding mRNA codon sequences, however, has just begun.

Most of the current concepts of genetic function are based on studies of these simpler genetic systems, with the accepted operating model being that described in the following section. (A wealth of background material is available in the *Cold Spring Harbor Symposia on Quantitative Biology*.[3,4])

Overview of Cellular Genetic Apparatus

In the 1940's and 1950's, molecular geneticists were teaching that the newly discovered DNA molecule had the remarkable ability to reproduce itself from simpler components in a direct process similar to crystallization, as for example, precipitation of salt crystals from saturated brine. DNA was hailed as the long sought life-force and the obvious first viable form to appear in biological "evolution," perhaps three billion years ago.[5]

Evolutionists anticipated that a strand of DNA would spontaneously generate life when the right variety of "primordial soup" was poured over it in the test tube, just as it was assumed to have generated the first living cell on earth. These simplest of single-celled microorganisms were expected to reflect their "primitive" natures with an unsophisticated reproductive and control mechanism that did not depend on genes; each step upward on the phylogenetic ladder was expected to show emergence of a better genetic language and a more elegant genetic mechanism, as a demonstration of the principle of "survival of the fittest."

Bacteria became the favorite organisms for research on the so-called evolutionary process, since their generation time was about 20 minutes. Many kinds of bacteria were observed to divide three times each hour, endlessly, under suitable conditions. Millions of descendents of a single ancestral cell could accumulate in only 20 generations, and a million generations of bacteria required only 30 to 50 years. Many biologists claimed, if evolution could arise from random mutations that were assumed to occur in each generation, then natural selection would produce superior new species of bacteria, and higher forms would begin to arise in a laboratory recapitulation of the evolutionary process.

Although only 20 additional years of research in molecular genetics have passed since such predictions were made, most scientists know already how naive, even ridiculous, most of these evolutionary speculations were. Invariably, in every species of organism examined, ranging from viruses to man, at least one gene is present, and the genetic messages on this gene are written in the "universal genetic code" that uses the four-letter genetic alphabet to form a 64-word genetic "dictionary," which is the same in every organism.

Far from finding evidence of the evolution of more effective genetic machinery as increasingly more differentiated species were examined, biologists discovered that the same basic mechanism of inheritance and genetic control was in operation in all known species. This mechanism may be outlined as follows:

DNA acts as the master blueprint for constructon of major cellular components, including DNA, itself: DNA functions as the reference or template for replication of DNA needed for progeny, and it also functions as a template for transcription of expendable copies formed of a slightly different nucleic acid, ribonucleic acid (RNA).

Ribonucleic acid appears in three principal forms, messenger RNA (mRNA), ribosomal RNA (rRNA), and amino acid transfer RNA (tRNA), all of which are used in the parallel translation of the sequence of words or codons in a gene into the corresponding sequence of amino acids in a polypeptide chain. The four-letter RNA alphabet differs by only one letter from the DNA alphabet, and the 64 codons in the RNA language have the same three-letter-word format as the DNA language. The rRNA appears in ribosomes, which serve as the "reading head" for mRNA messages that are being translated into polypeptides, composed of amino acids that are presented to the ribosome by tRNAs.

Although hundreds of different amino acids occur in nature, and each of these amino acids can assume both a right-handed and a left-handed form with regard to the location of the side chain which gives individuality to the different amino acids, only 20 different amino acids, **all of the L-form,** are ever used in translation of mRNA messages.

Amino acids all have the same "backbone" structure, with an alpha-carbon (C_α) forming the "body," the amino-group forming two "arms," and the carboxyl group forming two "legs"; the side-chain, then, could be considered the "head." Amino acids are linked by peptide bond formation to give the polypeptide molecule: during translation, one of the amino-group arms joins to one of the carboxyl-group legs of the preceding amino acid, and the components of water are lost from the union, so that the amino acids are "residues" after the peptide bond has formed.

Peptide bonds are not formed each time between arms and legs on the same side of the amino acid molecules, but the use of arms and legs is alternated in successive peptide bonds, giving a "staggered" or *trans* pattern to the linkage. Polypeptide chains most commonly are assembled into biologically active proteins such as enzymes, hormones, and immunoglobulins. The enzymes comprise the principle machinery of the cell, forming cellular components of wide variety, generating energy required for life processes, and participating as moving parts in many cellular activities.

The DNA-RNA team does not act independently to translate genes into proteins but is supported by more than one hundred other kinds of molecules which interact in precise order and in intricate relationships to insure the fidelity and balance of translation.

The complex relationships between genes that lead to differentiation of cells in multicellular organisms, control behavioral patterns such as instincts, and even operate "biological clocks" are all still far above the present level of comprehension of molecular biologists.

Built-in Safeguards Against Evolution

DNA is such a fragile, unstable molecule that it is truly remarkable for it to survive even five minutes without complete disintegration, not to mention loss, addition, or alteration of an occasional nucleotide somewhere in that very long flexible chain of deoxyribonucleotides that comprise DNA. How, then, can DNA be transcribed and replicated millions of times in fast-growing microorganisms without alteration of species characteristics? The answer lies in built-in safeguards provided by the Creator to keep DNA in its original "wild type." Some of these mechanisms have been discovered by scientists, and more will undoubtedly be disclosed, in time; the following then, are incomplete examples:

(1) Although only a single template strand of DNA is needed for expression of the genetic message of a given gene, invariably, in all complete forms of life, the template strand—when not being copied—is stabilized by being "zipped" together with a "complementary" strand of DNA that is the genetic mirror-image of the template strand. Attraction between the template and complementary DNA strands is dependent on the strong affinity between certain pairs of purine and pyrimidine bases which are present in nucleic acids: the purine, adenine (A) strongly binds to the pyrimidine, uracil (U) in RNA and to the pyrimidine, thymine (T) in DNA; the purine, guanine (G) strongly binds to the pyrimidine, cytosine (C) in both RNA and DNA.

The Nobel Prize for 1961 was awarded to the scientic team of Watson and Crick[6] for describing the interaction of A:U and G:C "homologous base pairs" in the production of the "Double Helix" by the DNA template and complementary strands, cross-linked position by position along the DNAs. These workers also showed that when the template DNA strand was transcribed, each A bound T, T bound A, G bound C, and C bound G; DNA polymerase enzyme then attached these homologous bases, like a string of beads, to a "thread" of deoxyribosephosphate, thus producing a strand of complementary DNA.

This process is reversible, so that the complementary strand can act as the genetic mirror-image or template for transcription of template DNA copies. White[7] has presented a helpful description of some of the chemistry involved in these genetic processes.

Not only is the double helix of DNA much more stable than single-stranded DNA, but for about 99 percent of the life cycle of a growing cell, the DNA double helix is "condensed" or tightly coiled and is embedded in layers of protective proteins and other types of macromolecules which reduce still further the possibility of mutational injury to DNA. Only when copies of DNA are needed for progeny or for use in cell control does DNA uncoil briefly for the replication and transcription processes.

Template and complementary DNAs forming the same gene in identical individuals of the same species are completely homologous, as shown by template DNA strands being interchanged without loss of homology appearing. The same compatibility between template and complementary DNA strands does not exist when the same gene from two different species is considered.

Template DNA coding for human hemoglobin (Hb) is not homologous for long stretches of mouse complementary DNA for Hb, and if they are paired in vitro they zip together incompletely. The unpaired, single-stranded regions of DNA are quickly attacked by DNAse enzymes found normally with DNA and are split into inactive

fragments. This is one reason why artificial hybrids formed in the laboratory between mouse and human cell cultures eliminate the human genes and revert to normal mouse cells after three to four cell divisions.

(2) Template and complementary strands of DNA act as mutually cross-checking genetic systems through a process that has been called "editing": a variety of enzymes surrounding the template strand of DNA detect missing or injured portions in the template strand and use the mirror-image complementary strand as a reference or mold to fill in the gaps or to replace injured DNA sections with the proper DNA. This process works, in reverse, to edit the complementary strand of DNA, using the template strand as the genetic reference. This self-editing process is credited with elimination of many mutations before they can be expressed in mutant organisms.

(3) All living species, including bacteria, spend at least some of their life cycle in the diploid state, in which the body or somatic cells each carry two complete sets of genes; with rare exception, one set of genes comes from each of the two parent organisms. These sets of genes pair off on chromosomes, with corresponding genes forming a pair of alleles: either, neither, or both allelic genes may be expressed in a given cell, depending on how the DNA has been "programmed" during differentiation of this cell. Frequently, one of the two allelic genes will be "dominant" over its allelic partner, which then becomes "recessive."

Fortunately, most lethal mutations are found in recessive genes, so that a heterozygous individual, bearing a lethal recessive gene from only one parent, merely shows a sickly "trait," because the normal dominant gene partially counteracts the effects of the recessive gene. Homozygous recessive individuals with a double dose of a lethal recessive gene mutation do not survive long under natural conditions, and their defective DNA is eliminated from the "gene pool" of that species.

(4) In the nucleus of cells of higher animals, there are as many as a thousand copies of the same gene; how many different genes are present in this multiplicity has not yet been established. This finding is too recent to evaluate, but it, too, can be expected to contribute to the "fail-safe" design of the genetic blueprints.

In summary, mutations tend to disappear, except under unusual circumstances, usually man made; such as, selective inbreeding, or laboratory isolation of artificial mutants.

The Translation Process

Nirenberg received the 1968 Nobel prize for identifying the 64 mRNA codons in terms of the amino acids they represent. For some time after mRNA codons were identified, it was thought that mRNA messages were merely a string of codons which the ribosome translated directly into a corresponding sequence of amino acid residues comprising a polypeptide.

Recent research results have shown that mRNA is not the simple string of codons first visualized, but is a highly structured macromolecule containing some sequences of untranslatable codons that seem to act as punctuation and formatting devices, controlling such variables as when, where, how much, and in what order, the multiple messages on a long strand of mRNA are to be translated.

So, too, the structure and function of ribosomes has recently been found to be vastly more elaborate than the original model of a bead of pure rRNA that slid along the mRNA, catalyzing polypeptide synthesis as it rolled along. Especially in animal cells, it is obvious that from 5 to 20 ribosomes are organized into chains and packets called polysomes, with each polysome acting as the organelle for reading and translating a mRNA message. Polysomes, in turn, assume an organizational pattern which seems to determine the arrangement of polypeptide chains in the quaternary structure of a multi-chain protein.

Polysomes may contain smaller-sized ribosomes for translation of smaller polypeptides, and larger ribosomes for synthesis of larger polypeptides, when the protein being assembled contains polypeptide chains of two different lengths. Each ribosome in a polysome is itself an aggregate of several subtypes of rRNA, plus about 75 specialized ribosomal proteins that interact to make translation of mRNA possible.

When first discovered, tRNAs were considered to be pliable loops of RNA with an "anticodon" at one side and the amino-acid-binding-site at the other. There were supposedly only 20 different varieties of isoaccepting tRNA, each capable of transferring only one of the 20 common amino acids, and each having a different anticodon.

An isoaccepting tRNA did not seem, at first, to be able to recognize the homologous base pairing mRNA codon with any marked fidelity. Some of the anticodons could manage a "wobble fit" with six different mRNA codon synonyms for the same amino acid, and some workers felt that a single mRNA codon synonym could be recognized by more than one tRNA anticodon. Now, however, these responses are considered artifacts: in vivo, tRNA anticodons recognize only their completely homologous codons.

The structure and function of tRNAs soon became highly controversial with regard to molecular shape, chemical composition, and specificity of transfer function. Since tRNA contains only 60 to 90 nucleotides per molecule, stabilized by base-pairing between the two sides of the folded chain, it has been relatively easy to isolate from cells. Also the sequence of bases has been determined for at least 60 different tRNAs obtained from various organisms and, in some cases, from various tissues of the same multicellular organism. Under physiological conditions, all tRNAs assume a three-dimensional structure that resembles a clover-leaf with an L-shaped handle, although the precise conformation of the iso-accepting tRNAs may depend on the amino acids to which they are bound by the coupling enzyme, aminoacyl tRNA synthetase.

Changing Concepts About mRNA

One of the cherished beliefs of molecular evolutionists has been that the genetic code, as reflected in mRNA codons, is highly defective (also called redundant, degenerate, anomolous, and ambiguous) because of accumulated mutations, as indicated by the fact that as many as six different codons may all code for the same amino acid during the translation process.

Messenger RNA was assumed, therefore, to be composed of random selections of codon synonyms for a given amino acid, as only the sequence of amino acids in a polypeptide was deemed of consequence: the hydrophobic side-chains of a polypeptide were supposedly endowed with the ability to interact with each other to give instantaneous secondary structures that represented the most stable state, and simultaneously conferred the specific biological activity on the protein.

Only in recent months has evidence for non-random (ambiguous) use of codons been suggested, as in the report of Friers[8] that in a group of related phages which had "coat proteins" that differed by only a single amino acid at a single position, the corresponding coat protein mRNAs used identical codon sequences except for the selection of appropriate codons for the different amino acid at its position in the coat protein.

This was interpreted to mean that the selection of codons probably was essential for control of the secondary structure of coat proteins in phages. Geneticists have found such a concept appealing, for it would explain how the cell can form nearly two million peptide bonds per second and complete 2,000 multi-chain protein molecules each second without an error, no matter how many mRNA messages are present. This smooth and rapid process seems all the more remarkable when compared to the slow and inefficient chemosynthesis of protein.

The first laboratory synthesis of natural proteins, such as the enzyme ribonuclease and the hormone insulin, required remarkable patience and dedication by an army of specialists who spent millions of man-hours and billions of dollars, in a 50-year program that overcame tremendous technical obstacles. The vast majority of proteins are very readily irreversibly denatured, with loss of biological activity, by exposure to nonphysiological conditions.

Some of the smaller, less complex, proteins may be renatured to their normal conformation and function following gentle, partial denaturation. However, the renaturation step occurs slowly and seldom is complete, because polypeptide chains that have been unfolded and uncoiled during denaturation tend to refold and recoil in random patterns during renaturation. Before chemosynthesis could be attempted in a rational manner, it was essential that the exact composition and shape of a protein molecule be determined; accordingly, protein chemists worked first on development of techniques for preserving the native structure of a protein during X-ray analysis of the relative location of each amino acid residue in the polypeptide chains.

"Ground Rules" for Protein Synthesis

From these early studies came the "ground rules" for synthesis of a normal protein molecule, namely:

(1) Only the L-form of the following 20 amino acids may be used: Alanine (Ala), arginine (Arg), asparagine (Asn), aspartic acid (Asp), cysteine (Cys), glutamic acid (Glu), glutamine (Gln), glycine (Gly), histidine (His), isoleucine (Ilu), leucine (Leu), lysine (Lys), methionine (Met), phenylalanine (Phe), proline (Pro), serine (Ser), threonine (Thr), tryptophane (Trp), tyrosine (Tyr), and valine (Val).

(2) Peptide bonds are formed in trans configuration, with respect to the C_α carbons of amino acid residues, and the distance between nearest neighbor C_α's is very near 3.8 A.

(3) Those amino acids with hydrophobic (oily) side chains almost always are oriented away from the aqueous environment, and those side chains tend to bind each other through many weak "hydrogen bonds." The hydrophobic amino acids are Ilu, Leu, Met, Phe, Pro, and Val.

Conversely, amino acids with hydrophilic side chains are most commonly found on the surface of the protein molecule, with their side chains oriented outward toward the aqueous environment. These hydrophilic amino acids are Asp, Arg, Glu, His, and Lys.

The remaining amino acids are neutral or ambivalent and may be inserted anywhere in the polypeptide chain; this group is made up of Ala, Asn, Cys, Gly, Gln, Ser, Thr, Trp, and Tyr.

(4) Cross linkage between side chains can only be permitted between half-cysteine residues; the disulfide-interchange enzyme forms disulfide bonds at the proper locations to produce closed loops along the polypeptide chains and link two polypeptide chains in the assembly of proteins into quaternary structure. These disulfide bonds keep the molecular structure from spontaneously denaturing.

(5) Only those spatial orientations of residues are permitted that avoid "steric hindrance" within the protein molecule between the often bulky side chains. The preferred orientations of residues usually were those giving the lowest free energy or least strain, although some of the "active sites" on proteins seemed to require a less stable configuration that tended to denature to a more stable state, with loss of the protein's specific activity.

Unless all these ground rules were rigorously followed, the attempted synthesis produced "tar" or plastic, rather than the normal polypeptide chain. Years of brilliant research were required to develop multi-step procedures that have been automated to produce, per day, six consecutive peptide bonds in a known amino acid sequence of a protein such as lysozyme; the native protein molecule could be chemosynthesized completely and demonstrated to have normal biological activity. Success in chemosynthesis of proteins was largely dependent on the selection of procedures that restricted the amino acid residues to the correct orientation.

It seemed logical to assume that biosynthesis of the same chemosynthesized protein utilized some kind of control over orientation of the residues, also. This viewpoint had some scientific support in the report by Galizzi[9] that the unknown mRNA codon for leucine at position 48 of the α-chain of rabbit Hb would be recognized by only one of five leucine isoacceptor tRNAs.

It was possible to visualize, then, a mechanism for genetic control of the secondary structure of proteins involving a fixed codon sequence in mRNA being recognized during translation by only those tRNAs which presented the appropriate amino acids in correct orientation.

This was the kind of intelligible code that the Creator alone could have devised, I believed, but I saw no way to demonstrate its operation, scientifically. Just how the four codon-synonyms for glycine, GGG, GGA, GGC, and GGU determined the orientation of a glycine residue was baffling, and I needed an inspiration to comprehend what approach to take in solving this mystery.

Research on Operation of an Intelligible Genetic Code

I started my research with a prayer for a clue, and an answer came in the form of a question: "Why don't you write the codons in digital arithmetic?" The first four numbers of digital arithmetic 00, 01, 10, and 11 (0, 1, 2, 3 of the familiar decimal arithmetic) could be set equal to G, A, U, and C: since 0 and 1 are complementary numbers, the digital codons gave a valid representation of the complementarity between A:U and G:C. Since the highest six place (six bit) digital number is 111111, or 64, there were just enough numbers available for representing the 64 triplet nucleotide codons in the genetic dictionary.

When the amino acid sequence of a polypeptide was represented by certain sequences of corresponding digital codons, it was sometimes possible to predict the selection of an amino acid for the next position by summing the digital codons for the preceding residues. It also could be shown that the location of α-helical bonded regions along the polypeptide chain represented in digital codons required residues whose bit patterns of "0" and "1" in corresponding bits were complementary. These observations indicated that genetic control operated with mathematical precision, but did not indicate how this precision was achieved. Again, I needed inspiration, and my appeal was quickly answered by the positive suggestion: "Transform the digital codons into magnetic codons."

It was not until I chanced upon a collection of small arrow-shaped magnets that I could visualize this conversion; all I had to do was represent digital "1's" by the arrow of the magnets pointing upward and "0's" by the arrow pointing downward. When holes were drilled through midpoints of magnets and the magnetic codons were assembled on a wire to keep them in linear array, the 000000 digital codon for Glycine became SSSSSS in magnetic codon format.

All these magnets stayed inertly in place for this magnetic codon, but when the next magnetic codon, SSSSSN, was assembled, an unexpected pattern developed: each of the six magnets was deflected to a new position by rotating around its midpoint. The deflection of each of these magnets was measured as a clockwise rotation from the vertical and recorded. Table 1 shows the various forms for expression of mRNA codons.

The mRNA codons each gave a different pattern of rotational angles when they were represented as magnetic codons. Had there been only two angles, they might have been considered as

Table 1. Steps in Conversion of Codons into Conformers

Amino Acid Conformer	Trinucleotide Codon Acronym	Binary Codon	Magnetic Codon	Rotational Angles for Amino and Carboxyl Groups in x, y, z planes					
Gly-1	GGG	000000	SSSSSS	0	0	0	0	0	0
Gly-2	GGA	000001	SSSSSN	300	300	300	300	300	60
Gly-3	GGU	000010	SSSSNS	0	0	0	0	270	0
Gly-4	GGC	000011	SSSSNN	340	340	340	340	70	70

the "phi" positive clockwise rotation of the C_a-N axis, and the "psi" positive clockwise rotation of the C_a-C axis of the backbone of the amino acids, respectively (these being the only two rotational parameters required to describe the twists present in the ribbonlike polypeptide chain which generate its coils and folds).

These two angles are insufficient, however, to describe the orientation of the amino acid residues in three-dimensional (3-D) space; for this description the rotation angle of each residue's amino and carboxyl groups in each of three mutually perpendicular planes would be required, a total of six angles. These 3-D orientations were determined by placing a Kendrew wire model on the stage of a "universal stage" and actually performing the indicated angular rotations, leading to a spatial orientation of the model that has been called its "conformer."* The four conformers of Gly that correspond to the four Gly codons are pictured in Figure 1.

Concept Tested by Kendrew Wire Models

The validity of conformers as a basis for genetic control of secondary structure could best be proved by building scale models of polypeptides, using known mRNA codon sequences to specify the order of conformers: production of the known secondary and tertiary structure of a polypeptide chain would constitute definitive proof.

At present, the "state of the art" in molecular genetics and protein chemistry has not reached the point where this information is available; in fact, a very few mRNA messages have been fully sequenced, such as that for the terminal 45 amino acid residues of the A-protein of phage MS2. The A-protein, in intact form, contains about 300 amino acid residues and is thought to serve as the attachment site for the host bacterium, *Escherichia coli*, although the conformation has not been determined. Proteins whose complete structures have been well-defined are numerous, but the corresponding mRNAs have not been isolated and "mapped."

Despite the limited available information about the relationships of mRNA codons and protein structure, it was decided to test the ability of conformers to assemble in "best fit" fashion to produce the known structures of polypeptides of known amino acid sequence. When this approach was taken, the conformers specified by the mRNA codons in the message for the termi-

*Some workers prefer the term, "configuron."

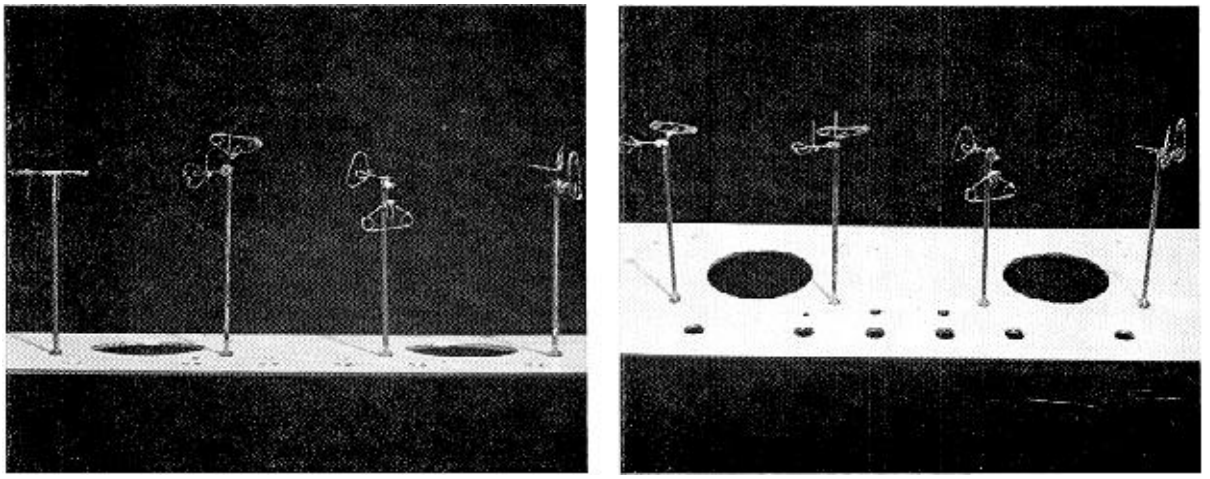

Figure 1. (a) Front view (left), and (b) Top view (right). These show the four conformers of Glycine, as Kendrew wire scale models.

In the *Scientific American,* December 1961, pp. 1-6, J. C. Kendrew popularized the use in protein structural research of scale models of amino acids whose structures had been derived from x-ray diffraction data. These "Kendrew models" have been constructed of many materials, and the scale of enlargement from the Angstrom range has also varied at the convenience of the researcher. In this study, the amino acids were built on the scale of 1 to 100 million, and No. 18 gauge copper wire was the selected construction material.

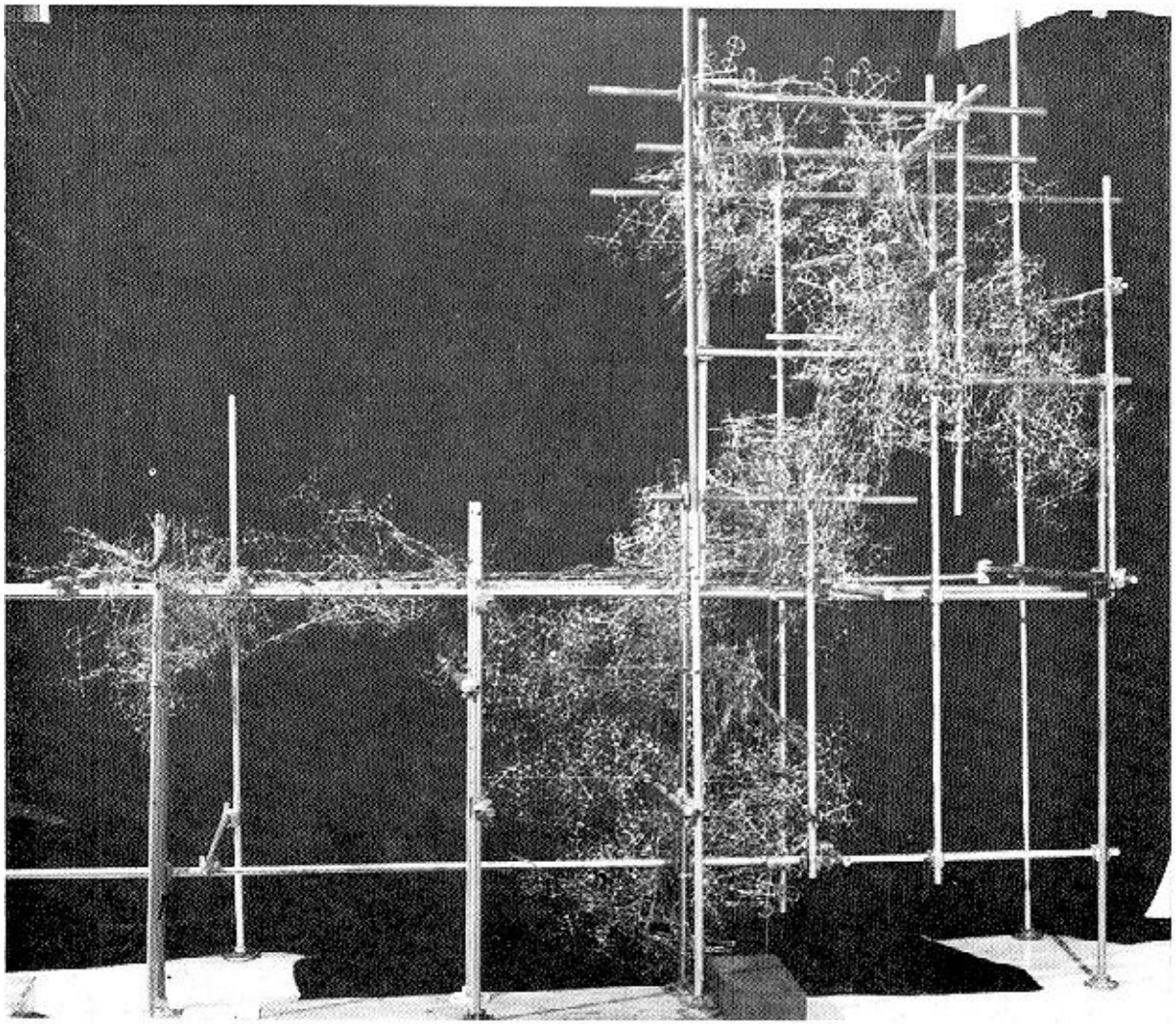

Figure 2. Kendrew wire model of Human G1(Eu) Immunoglobulin Light Chain produced by best fit conformers.

nal 45 amino acid residues of the A-protein fit together according to the ground rules of protein synthesis and generated an elongated filament in the process, not unlike the predicted shape of an attachment spike.

Even more significant, none of the other codon synonyms for amino acids could be substituted without introducing steric hindrance among the conformers. The same results were obtained when the primary amino acid sequences of well-characterized proteins were assembled by "best-fit" conformers; only one conformer satisfied all the ground rules, although several different conformers of a given amino acid sometimes could temporarily seem to fit. The models produced closely resembled the accepted protein conformations.

To an immunologist, the assembly of the L-chain of the Eu immunoglobulin from "best fit" conformers was intriguing, not only because of the unique shape of the molecule, but because the "variable" half of the chain generated half of an antibody-combining-site. When the known sequence of 214 amino acids was assembled as the corresponding sequence of "best fit" conformers, the conformation was as pictured in Figure 2.

Biophysical measurements reveal that the L-chain forms a shallow trough at the location of the antibody-combining-site at the left (amino terminal) side of the molecule, after which the chain forms a densely-packed cylindric shape extending to the right.[10,11]

Not only did conformers give the overall shape that is considered valid for the L-chain, but hydrophobic side chains were located "in" and hydrophilic side chains were oriented "out" in this Kendrew wire model, as may be noted. From this best fit selection of conformer sequences, the corresponding mRNA codon sequences automatically appear, so that one may predict the mRNA message required to form a given polypeptide. The logical deduction follows from these results that the template DNA carries a blueprint for the exact conformation of "self" proteins.

Immunologists have puzzled over the mechanisms of the well-known immunological phenomenon involved in the recognition of "self" and "not-self" antigenic determinants which is the basis for production of specific immunoglobulins (antibodies) directed against not-self determinants. Although more than a hundred different classes of cells comprise the animal body, only one class, the lymphocytes, are able to show immune recognition, as reflected in their differentiation into immunocytes capable of showing specific immune responses against the inducing not-self antigenic determinant. Lymphocytes can recognize only epitopes, or short peptides of no more than ten residues length, as this seems to be the maximum size of peptide that can be fitted into the antibody-combining-site of immunoglobulins.

This is no real limitation to the immune recognition system, however, as a leading immunologist, Jerne,[12] has pointed out: the human body contains about one trillion lymphocytes, among which are possibly 10 million "clonal type" lymphocytes; each clonal type can respond immunologically only against a specific epitope. This clonal response seems to depend on the binding of a specific epitope to a lymphocyte that bears about 100,000 identical antibody-like receptors for this epitope.

Differentiation of this "enlightened" lymphocyte leads first to rapid proliferation, which could produce 20 million progeny within one week. Then most of these cells become immunocytes (plasma cells) which synthesize a specific immunoglobulin at the rate of 2,000 molecules per second until half the dry weight of each immunocyte is pure immunoglobulin. The basic question behind this immune recognition system is concerned with the location of the genetic processor that sorts epitopes into self and not-self markers, for normal lymphocytes never become immune against self epitopes.

Fortuitous mutations of astronomical proportions give rise to this highly complex system, according to Darwinian evolutionists, but a direct, and far more plausible, mechanism for self and not-self recognition resides in the DNA double helix, with the template strand defining self, and the complementary strand defining not-self. This creationistic concept may be tested by model building, as outlined below.

A Role for Conformers in Immune Recognition System

Transcription of mRNA from the template strand of the gene for the L-chain of antibody active against the epitope at the amino-terminal end of the A-protein fragment and the subsequent translation of this mRNA message leads to formation of the L-chain component of the antibody-combining-site.

Now, if the corresponding complementary DNA strand is a mirror-image in genetic function of the template strand, then the mRNA transcribed from it should translate into the A-protein epitope. Lymphocytes may very well use these two DNA strands as discriminators of self and not-self during differentiation into clonal types; a clonal type of lymphocyte has the blueprint for production of antibody-combining-site in the template DNA against the not-self epitope coded for in the corresponding site on the complementary DNA strand.

The mRNA codon sequence for antibody-combining site against the A-protein epitope is not available, but the mRNA codon sequence for the A-protein epitope is, so the reverse relationship may be tested, in the following manner: translation of mRNA for the amino-terminal pentapeptide of the A-protein fragment into conformers should produce the epitope structure; the complementary mRNA is predicted to translate into the corresponding antibody-combining site. The mRNA for the epitope is GCU.AAG.GCC.CAA.AUC., which translates into the conformer sequence ala15.Lys21.Ala16.Gln54.Ilu28 that is shown assembled in Figure 3. It may be noted that this peptide forms two clockwise turns of a helix.

The complement of this mRNA codon sequence is CGA.UUC.CGC.GUU.UAC. When this mRNA is translated, the conformer sequence produced is Arg50.Phe44.Arg49.Val11.Amb37, which gives the structure shown in Figure 4. Only four conformers are assembled because the last conformer, "Amb," is a recognized "Stop" signal that terminates translation, in vivo.

The goodness-of-fit of these two peptides, when they are brought together, as shown in Figure 5, is compatible with the accepted "lock and key" relation between antibody and antigen.

Discussion

Darwinian evolutionists have used the observed differences in mRNA codon-synonyms as the basis for claims that the genetic code is the degenerate product of random mutations; accord-

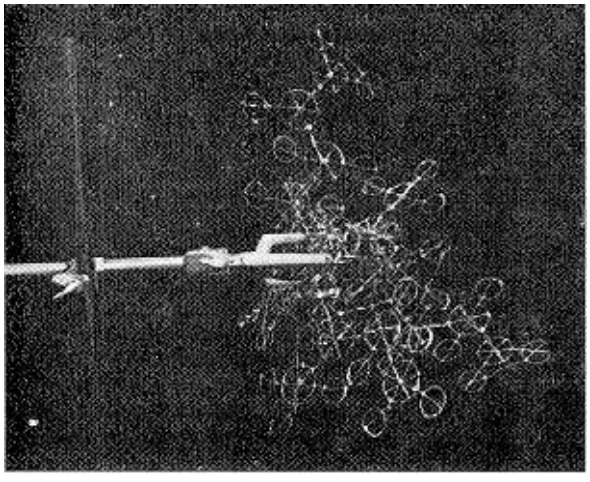

Figure 3. Kendrew wire model of Epitope of MS2 Phage-A Protein, produced by translation of corresponding mRNA Codon sequences into conformers. This mRNA codes for the Amino-Terminal Pentapeptide of the last 45 amino acid residues of A-Protein (Carboxyl-Terminal Fragment).

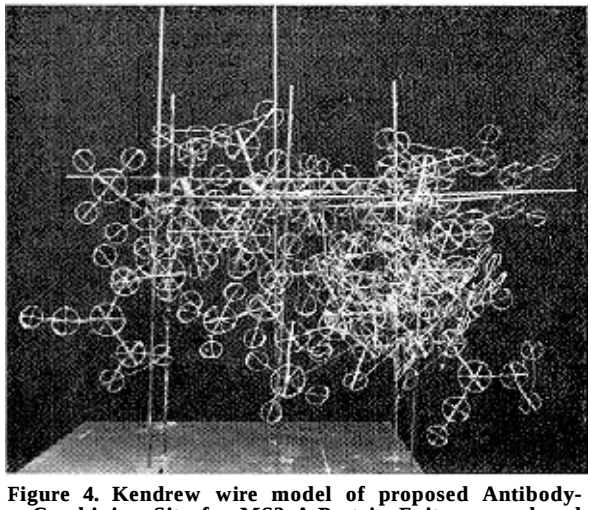

Figure 4. Kendrew wire model of proposed Antibody-Combining Site for MS2 A-Protein Epitope, produced by translation of complementary mRNA into conformers.

ingly, all scientific reports supporting orderliness in translation of genetic messages are branded as "ambiguous."

In the research reported here, a case is made for existence of a highly-ordered genetic control system that expresses itself in messages written in the form of intelligible codons. These codons are intelligent in the sense of being able to recognize each other and anticipate 'how they will interact upon translation into corresponding polypeptide chains, in vivo.

Model building experiments have been described here which support the view that 64 intelligible mRNA codons are used to control the

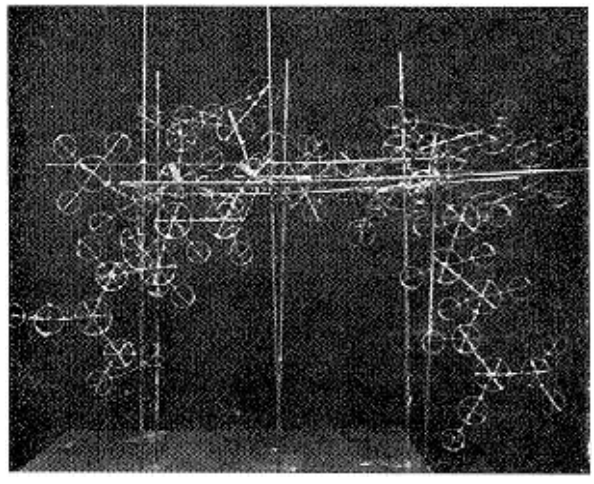

Figure 5. Kendrew wire model of MS2 A-Protein Epitope paired with proposed Antibody-Combining Site for this epitope.

three-dimensional orientation of amino acids in a polypeptide chain that is produced by in vivo translation of a specific sequence of codons.

Not only does every living cell have genes whose template DNAs control the formation of "self" proteins, but within each gene there is a genetic mirror-image copy of template DNA, in the form of complementary DNA, that forms a stable homologous base-paired double helix with the template DNA.

Evidence has been presented here that indicates lymphocytes use this genetic mirror-image relationship between template and complementary DNAs to distinguish self from not-self epitopes; mRNA transcribed from the template (sense) DNA strand is translated into the antibody-combining-site for the mirror-image epitope coded for by the DNA of the corresponding region of the complementary strand. In other words, the self epitope serves as antibody-combining-site against the antigenic not-self epitope.

Obviously, this line of research needs to be pursued much farther, but even at this point the handiwork of an intelligent Creator is clearly evident.

EDITOR'S NOTE

Already, while this article was being prepared for printing, interest in certain points has been expressed; such as, the details and interpretation of the use of the magnets. Thus it is hoped soon to have a sequel, dealing with some of these matters.

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PERPETUATION OF THE RECAPITULATION MYTH*

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Recapitulation, or the biogenetic "law" is shown to be held in disrepute by many biologists. Evidences from embryology as well as logical implications of the "law" if it were true are used to show that recapitulation cannot be a valid biological principle. Quotations from several modern textbooks are given to illustrate that some biologists are unwilling to reject ***in toto*** *the views of Haeckel, in spite of evidence to the contrary. In fact, many authors continue to refer to fishlike gill slits in mammalian embryos, thereby perpetuating the myth of recapitulation.*

Introduction

Occasionally a grossly mistaken concept is perpetuated as "evidence" for macro-evolution, especially in popular literature and even in some textbooks and journals. While many individuals may be aware of the situation, little effort is directed toward purging the literature of the misconception. Such seems to be the case with the myth of recapitulation.

Also known as the biogenetic "law,"[1] the theory of recapitulation was promulgated in the late 1800's by the biologist Haeckel. The essence of his concept was that ontogeny recapitulates phylogeny. That is, "each embryo in its development passes through abbreviated stages that more or less resemble some developmental stage of its evolutionary ancestors, both remote and immediate."[2]

Haeckel's views amounted to an adulteration of the concepts proposed by von Baer in 1824. von Baer's first two conclusions indicated that in the development of a vertebrate embryo, there is an early stage at which it could be recognized as a vertebrate, but it was impossible to distinguish what kind of a vertebrate it was (e.g., reptile, bird or mammal).[3] At a later stage it may be recognized supposedly as a bird, for instance, but it cannot be determined what kind of a bird it is. von Baer's last two conclusions express the concept that animals are more similar at early stages of development than when they are fully grown, and these similarities are diminished as the animals mature.[3]

Oppenheimer, a well-known embryologist, stated that the work of Haeckel was the "culmination" of the "extremes of exaggeration" which followed Darwin.[4] She further declared that Haeckel's influence was "damaging to science."[5] Later she continued:

> The investigators [e.g., Haeckel] who have derived their ideas from the philosophical side, and examined their embryos to fit their observations into philosophical patterns already set and rigid . . . were the minds whose philosophical patterns delayed rather than accelerated the course of embryological progress.[6]

A few contemporaries of Haeckel refused to accept the biogenetic "law." von Baer himself warned against comparing "embryos of 'higher' forms to adults of 'lower' forms."[7] Rádl mentioned that "everything important that has ever been cited against the recapitulation theory was known when the theory was first put forward; nevertheless it was widely accepted."[8]

According to Oppenheimer, "Haeckel's doctrines" were blindly and uncritically accepted not only by workers in the many related fields of biology, but aso by "professional embryologists."[9] She then categorized Haeckel as a "fanatic" who never could be considered to have been a "professional embrylogist."[10]

*A condensed version of this paper has appeared eslewhere.

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