The Genetic Selection (GS) Principle

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The Genetic Selection (GS) Principle states that *selection must occur at the molecular/genetic level,* not just at the fittest phenotypic/organismic level, to produce and explain life.[1] In other words, selection for *potential* biofunction must occur upon formation of the rigid 3'5' phosphodiester bonds in DNA and RNA sequences. This is the point at which functional linear digital polynucleotide syntax is prescribed. The selection of each nucleotide out of a phase space of four options constitutes the setting of a quaternary (four-way) configurable switch.[2-8] The specific setting of these configurable switches in nucleic acid primary structure (monomeric sequencing) determines not only amino acid sequencing in protein primary structure, but also translational pausing (TP).[9] TP in turn determines how translated biopolymeric strings will fold into three-dimensional molecular machines.[10]

Chaperone proteins also assist in protein folding.[11-15] But, chaperones are themselves prescribed by particular nucleotide syntax. This syntax must first be programmed into DNA and edited into mRNA. These symbolic instructions must then be processed in ribosomes. Both programming and processing require Selection *FOR (in pursuit of)* formal function, not just Selection *FROM AMONG* the fittest already-living phenotypic organisms.[16,17] No organisms would exist, let alone the fittest ones, were it not for programmed instructions, and the formal processing of those instructions. Thus, selection *FOR* must take place at the molecular/genetic level, before any phenotypic organisms can be alive to compete.[1,18] Life comes into existence only through programming, processing, and extremely sophisticated ongoing genetic and epigenetic controls.

Nucleotide sequence functions in a material symbol system (MSS).[19,20] Triplet codons are block codes. A block code of three physical

symbol vehicles (nucleotides) not only "represents," but prescribes each amino acid.[21,22] No direct physicochemical connection exists between DNA (or even edited mRNA) and amino acids. Noise-pollution-reducing redundancy is further programmed into this symbol system by virtue of multiple codons prescribing the same amino acid. Thus genetics and genomics utilize a formal representational symbol system, not simply physicodynamics (chance and necessity).[8] The exact same physicochemical bonds are used to polymerize all four nucleotide symbol vehicles. Nucleotide syntax is dynamically inert (physicodynamically indeterminant and incoherent; decoupled from physical causation).[23,24] Nucleotide syntax is an arbitrary convention represented by the codon table that obeys formal semantic and pragmatic rules, not physical laws.

Superimposed onto the triplet codon coding is another layer of sextet nucleotide block coding that prescribes translational pausing and folding.

As with any linear digital symbol system, communication of meaningful (functional) messages depends upon symbol selection from an alphabet of symbols, and the syntax of those symbol selections. These selections are made on the basis of potential function, not existing function.[5-7,25-30] In the case of DNA, these selections for potential function are "written in stone" with rigid covalent bonds in the primary structure (the sequence of the polynucleotide string). These configurable switch-settings must be made prior to the realization of any folding or biofunction. The string is complete before any syntactic genetic prescription is realized. Computational halting must be anticipated and accomplished in the programming "choices" recorded in the genetic Turing tape decision nodes and logic gates. This constitutes Selection *FOR (IN PURSUIT OF)*, not just Selection *FROM AMONG*, as is the case with evolution.

Natural selection cannot operate at the genetic level. Selection pressure favors only *existing* biofunction. Even with existing function, natural selection does not select for isolated function over nonfunction. The environment could care less whether anything functions. The environment has no preferences, values, goals or desires. Inanimate nature is blind and indifferent to *utility*. This is all the more true of *potential* utility. Utility can only be defined, appreciated, and pursued formally, not physicodynamically. Pragmatics requires an added dimension beyond those dimensions required for Chance and Necessity.[7,8,25-27,29,31-34]

Natural selection is nothing more than the differential survival and reproduction of the most successful already-living organisms.

For an organism to be alive, it must first have many hundreds of biochemical pathways and cycles already integrated into holistic, cooperative, organized metabolic schemes. Perhaps no phenomenon known to science is more purposeful and goal-oriented than metabolism. Differential survival of the fittest species offers no model of mechanism for generating the cybernetic programming of linear digital genetic prescription.[17] Biomessages provide linear digital instructions to prescribe cellular structures, specific transport and catalysis. Yet DNA is largely inert from a physicochemical standpoint. Natural selection cannot favor unrealized, not-yet-existent function represented in DNA syntax.

Polycodon-coded prescription of potential biofunction instructs the formation of each polyamino acid string. The folding of proteins is determined by DNA polynucleotide sequencing. To further compound the conceptual complexity of this linear digital prescription of three-dimensional biofunction, translational pausing (TP) and divergent transcription start site (TSS) transcriptions also occur. Regulatory RNAs are often transcribed from the negative "anti-sense" strand that unwinds from the positive sense strand of DNA that prescribes proteins.[35-37] Linear digital prescription can be bidirectional in DNA. Thus the so-called "anti-sense" strand can be full of sense and meaning. Most of what was thought to be junk DNA is highly instructive code. In addition, overlapping gene transcriptions[38] and the functional three-dimensional supercoiling of three-dimensional DNA molecules[39] contains additional layers of prescriptive information (PI) that is ultimately dependent upon the instructions found in linear digital monomeric sequencing. None of this Prescriptive Information (PI) is explainable from physicodynamics. It is purely formal, abstract, conceptual and non-physical.

How are all of these configurable switches set in DNA, in advance, so as to coordinate hundreds of three-dimensional molecular machine interactions? How are all of the biological integrated circuits and computational haltings programmed? This is not only the most fundamental question of gene emergence. It is the most fundamental question of life-origin and all of biology. Natural selection offers no model or theory to explain genetic programming.

All known life is cybernetic.[40-43] This means that the integration and regulation of biochemical pathways and cycles into homeostatic metabolism is programmatically controlled, not just physicodynamically constrained. Life crosses *The Cybernetic Cut*[5] across a one-way CS (Configurable Switch) Bridge.[5] This bridge traverses a great ravine. On the near side is found all those phenomena that can be explained by physicodynamics alone. On the far side are those phenomena than can be explained only by selection for *potential* (not-yet-existing) function. Traffic across this bridge flows only from the non-physical world of formalism into physicality through the instantiation of purposeful choices into physicality.[7] Such instantiation requires wise physical configurable switch-settings and arbitrary (dynamically-inert) selections of physical symbol vehicles in material symbol systems (See *The Cybernetic Cut* also in Scirus SciTopic pages).

Three-dimensional genomes have been suggested in theoretical protolife models (e.g., crystalline genes[44] and composomes.[45] But none of these models have fared well in peer-reviewed life-origin literature. All known life depends upon linear digital Prescriptive Information (PI), cybernetic programming, and the processing of that programming. Even most epigenetic factors are ultimately instructed and "manufactured" via transcription, editing and translation.

"The GS Principle" first appeared in peer-reviewed scientific literature in 2005.[33,3-5,21,46] But the definitive paper on The GS Principle did not appear in the literature until Jan 1 of 2009.[1]

References:

1. Abel DL. The GS (Genetic Selection) Principle. *Frontiers in Bioscience.* 2009;14(January 1):2959-2969 Open access at http://www.bioscience.org/2009/v2914/af/3426/fulltext.htm [Last Accessed Sept, 2017] Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

2. Abel DL. Is Life Reducible to Complexity? In: Palyi G, Zucchi C, Caglioti L, eds. *Fundamentals of Life*. Paris: Elsevier; 2002:57-72.

3. Abel DL. Complexity, self-organization, and emergence at the edge of chaos in life-origin models. *Journal of the Washington Academy of Sciences.* 2007;93(4):1-20 http://lifeorigin.academia.edu/DrDavidLAbel [Last accessed: Sept, 2017].

4. Abel DL. The capabilities of chaos and complexity. Society for Chaos Theory: Society for Complexity in Psychology and the Life Sciences; Aug 8-10, 2008; International Conference at Virginia Commonwealth University, Richmond, VA.

5. Abel DL. The 'Cybernetic Cut': Progressing from Description to Prescription in Systems Theory. *The Open Cybernetics and Systemics Journal.* 2008;2:252-262 Open Access Also available from http://lifeorigin.academia.edu/DrDavidLAbel [Last accessed Sept, 2017]

6. Abel DL. What is ProtoBioCybernetics? In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press-Academic: Biolog. Res. Div.; 2011:1-18 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

7. Abel DL. The Cybernetic Cut and Configurable Switch (CS) Bridge. In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press--Academic, Biol. Res. Div.; 2011:55-74 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

8. Abel DL. Linear Digital Material Symbol Systems (MSS). In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press--Academic, Biol. Res. Div.; 2011:135-160 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

9. Li G-W, Oh E, Weissman JS. The anti-Shine-Dalgarno sequence drives translational pausing and codon choice in bacteria. *Nature.* 2012;484(26 APRIL):538

10. D'onofrio DJ, Abel DL. Redundancy of the genetic code enables translational pausing. *Frontiers in Genetics.* 2014-May-20 2014;5:140 Open access at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4033003/.

11. Saibil H. Molecular chaperones: containers and surfaces for folding, stabilising or unfolding proteins. *Curr Opin Struct Biol.* 2000;10(2):251-258.

12. Elsasser SJ, D'Arcy S. Towards a mechanism for histone chaperones. *Biochim Biophys Acta.* Mar 2012; 1819 (3-4): 211-221.

13. Hoffmann A, Becker Annemarie H, Zachmann-Brand B, Deuerling E, Bukau B, Kramer G. Concerted Action of the Ribosome and the Associated Chaperone Trigger Factor Confines Nascent Polypeptide Folding. *Molecular Cell.* 2012;48(1):63-74.

14.   Taipale M, Tucker G, Peng J, et al. A quantitative chaperone interaction network reveals the architecture of cellular protein homeostasis pathways. *Cell.* Jul 17 2014;158(2):434-448.

15.   Weinstock MT, Jacobsen MT, Kay MS. Synthesis and folding of a mirror-image enzyme reveals ambidextrous chaperone activity. *Proc Natl Acad Sci U S A.* Jul 28 2014.

16.   Abel DL, ed *The First Gene: The Birth of Programming, Messaging and Formal Control.* New York, NY: LongView Press-Academic; 2011.

17.   Abel DL. *Primordial Prescription: The Most Plaguing Problem of Life Origin Science.* New York, N.Y.: LongView Press Academic; 2015.

18.   Abel DL. The Genetic Selection (GS) Principle. In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press--Academic; 2011:161-188 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

19.   Rocha LM. Evidence Sets and Contextual Genetic Algorithms: Exploring uncertainity, context, and embodiment in cognitive and biological systems. In: Computer Research Group MPLANL, ed. *Evidence Sets and Contextual Genetic Algorithms*1997.

20.   Rocha LM. The physics and evolution of symbols and codes: reflections on the work of Howard Pattee. *Biosystems.* Apr-May 2001;60:1-4.

21.   Abel DL, Trevors JT. More than metaphor: Genomes are objective sign systems. *Journal of BioSemiotics.* 2006;1(2):253-267 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

22.   Abel DL, Trevors JT. More than Metaphor: Genomes are Objective Sign Systems. In: Barbieri M, ed. *BioSemiotic Research Trends*. New York: Nova Science Publishers; 2007:1-15 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

23.   Rocha LM. Evolution with material symbol systems. *Biosystems.* 2001;60:95-121.

24.   Rocha LM, Hordijk W. Material representations: from the genetic code to the evolution of cellular automata. *Artif Life.* Winter-Spring 2005;11(1-2):189-214.

25.   Abel DL. The capabilities of chaos and complexity. *Int. J. Mol. Sci.* 2009;10(Special Issue on Life Origin):247-291 Open access at http://mdpi.com/1422-0067/1410/1421/1247 [last accessed: Sept, 2017] Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

26.   Abel DL. The biosemiosis of prescriptive information. *Semiotica.* 2009;2009(174):1-19 Also available from http://lifeorigin.academia.edu/DrDavidLAbel

27.   Abel DL. Constraints vs. Controls: Progressing from description to prescription in systems theory. *Open Cybernetics and Systemics Journal.* 2010;4:14-27 Open Access at http://benthamopen.com/contents/pdf/TOCSJ/TOCSJ-14-14.pdf [Last accessed: Sept, 2017] Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

28.   Abel DL. The Formalism > Physicality (F > P) Principle. In: Abel DL, ed. *In the First Gene: The birth of Programming, Messaging and Formal Control.* New York, New York: Ed. LongView Press-Academic, 2011: Biological Research

Division; 2011:447-492 Also available from
http://lifeorigin.academia.edu/DrDavidLAbel.

29. Abel DL. The three fundamental categories of reality. In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press-Academic: Biolog. Res. Div.; 2011:19-54 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

30. Abel DL. What utility does order, pattern or complexity prescribe? In: Abel DL, ed. *The First Gene: The Birth of Programming, Messaging and Formal Control*. New York, N.Y.: LongView Press--Academic, Biol. Res. Div.; 2011:75-116 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

31. Abel DL. Moving 'far from equilibrium' in a prebitoic environment: The role of Maxwell's Demon in life origin. In: Seckbach J, Gordon R, eds. *Genesis - In the Beginning: Precursors of Life, Chemical Models and Early Biological Evolution.* Dordrecht: Springer; 2012:219-236 Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

32. Abel DL. Is life unique? *Life.* 2012;2(1):106-134 Open access at http://www.mdpi.com/2075-1729/2072/2071/2106 [Last accessed Sept, 2017] Also available from http://lifeorigin.academia.edu/DrDavidLAbel.

33. Abel DL, Trevors JT. Three subsets of sequence complexity and their relevance to biopolymeric information. *Theoretical Biology and Medical Modeling.* 2005;2:29-45.

34. Trevors JT, Abel DL. Chance and necessity do not explain the origin of life. *Cell Biol Int.* 2004;28(11):abel729-739.

35. Beiter T, Reich E, Williams R, Simon P. Antisense transcription: A critical look in both directions. *Cellular and Molecular Life Sciences (CMLS).* 2009.

36. Dinger ME, Pang KC, Mercer TR, Mattick JS. Differentiating Protein-Coding and Noncoding RNA: Challenges and Ambiguities. *PLoS Computational Biology.* 11/28 2008;4(11):e1000176.

37. He Y, Vogelstein B, Velculescu VE, Papadopoulos N, Kinzler KW. The Antisense Transcriptomes of Human Cells. *Science.* December 19, 2008 2008;322(5909):1855-1857.

38. Sabath N, Landan G, Graur D. A method for the simultaneous estimation of selection intensities in overlapping genes. *PLoS ONE.* 2008;3(12):e3996.

39. Ohyama T. *DNA conformation and transcription.* Georgetown, Tex.
New York, NY.: Landes Bioscience ;
Springer Science Business Media; 2005.

40. de Silva AP, Uchiyama S. Molecular logic and computing. *Nat Nano.* 2007;2(7):399-410.

41. Korzeniewski B. Cybernetic Formulation of the Definition of Life. *Journal of Theoretical Biology.* 2001;209(3):275-286.

42. Korzeniewski B. Confrontation of the cybernetic definition of a living individual with the real world. *Acta Biotheor.* 2005;53(1):1-28.

43. Nurse P. Life, logic and information. *Nature.* 2008;454(7203):424-426.

44. Cairns-Smith AG. *Seven Clues to the Origin of Life.* Canto ed. Cambridge: Cambridge University Press; 1990.