Research Article

The Common Denominator of All Known Lifeforms

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Abstract

All lifeforms are invariably mediated by Formal Controls. Controls direct physicodynamic events toward integrated biofunction and successful computation. Constraints and laws have no perception of, interest in, or ability to pursue function. Physicodynamic boundary conditions do not steer physicality toward "usefulness." Neither does irreversible nonequilibrium thermodynamics or quantum mechanics. All aspects of Chance and Necessity are blind to utility. To achieve Function, Controls must be chosen from among real physical options. Life is universally programmed at bona fide "decision nodes," not mere "bifurcation points." Programming is a form of Prescriptive Information (PI). The latter cannot be reduced to probabilism. Life's formal functions depend squarely upon *active* programming selections made prior to computational "halting." Secondary *passive* selection (natural selection) plays no role in molecular evolution. Even the protocellular metabolomic models of ProtoBioCybernetics require the steering of purposeful Choice Causation rather than mere Chance and Necessity. Life values, pursues and maintains being alive. Atomic theory offers no explanation for life's Controls or Function. Choice Causation is the third fundamental category of reality that comprises the common denominator of all lifeforms at the subcellular and intercellular level. All Sustained Functional Systems (SFS) require Maxwell's demon's desire, intent and choices to temporarily circumvent the 2nd Law. The science of biology cannot be crammed into purely physicalistic fanaticism.

Keywords: Life Definition*;* Biosystems; Biophysics; Molecular Biology; Protocells; Abiogenesis; Life Origin; Molecular Evolution; Chemical Evolution; Pre-Darwinian Evolution; Self-Organization; Emergence; Protometabolism; Protocellular Metabolomics; ProtoBioCybernetics.

Introduction

Controls uniquely steer physicodynamic and biochemical interactions and reactions toward utility [1-11]. Constraints and boundary conditions have never been observed to do this. Neither has irreversible nonequilibrium thermodynamics [12-15]. Cybernetics addresses and utilizes the phenomenon of formal control [7,16]. The effects of Choice Causation are unique from the effects of physicodynamic causation [12,15,17,18]. The difference lies in the area of production of nontrivial utility [12,13,19-21]. In cybernetics, recorded commands are issued to generate controls. Commands usually take the form of chosen configurable switch-settings. They can also be issued within programming strings using representational symbols, usually within a programming language [11,20,22-27]. The symbols clearly represent specific efficacious choice causation.

Life is blatantly controlled at every level [1,2,5,8]. The definition of "death" should certainly include the cessation of active, ongoing, formal control implementation. In fact, even cell death is often formally programmed [28-32]. Energy transduction, storage and calling up of usable energy when needed depends upon controls. Also manifest are innumerable controls of all manner of additional peripheral sophisticated biofunctions. Active selective membrane transport is a classic example of formal control [33-36]. These directives are instructed by formally steered commands instantiated primarily into both genetic and epigenetic configurable switch settings. Linear digital prescription controls the secondary and tertiary structure of thousands of proteins and RNA's. Programming uses the symbolization of a coding scheme and language to issue commands [37-40]. The commands, when processed, execute controls. The processing is also controlled. Symbolization is formal, not physical. If some sort of message is to be sent through a machine, the source and destination of the message within the machine must share the same linguistic rules of interpretation of the message. Otherwise, the execution of each command, and the programming string of commands, will fail to compute ("halt" and produce the desired function). Subcellular homeostatic metabolism is impossible without formal controls.

The Oxford Languages' definition of Cybernetics is: "the science of communications and automatic control systems in both machines and living things." It is rare that the role of communications and automatic control systems are attributed to subcellular or cellular life. Oxford's inclusion of "living things" is insightful, honest and refreshing. But attributing the success of biosystems to various forms of programming and control is now becoming quite routine in the literature. What other choice is there in the age of genetic engineering using ZNF, CRISPR-Cas12 and TALEN ~~CR~~ systems [41-45]? It is indisputable that all known life is programmed, cybernetically processed, and is formally computed [2]. Ada Lovelace (Babbage's cohort) pointed out in 1843 [46] that computation is fundamentally non-numeric. Controls do not necessarily have to crunch numbers. Biological commands and controls, for example, are non-numeric. Controls can be digital or analog. Even in human-generated "artificial" cybernetics, numbers are just sometimes used to symbolize whatever non-numeric command is being represented. Commands emanate from an active selection from among real options at a true decision nodes. A "bifurcation point" is not synonymous with a "decision node." A bifurcation point is nothing more than a fork-in-the-road. A fork-in-the-road does nothing useful until one of the forks is chosen with intent. Only then does the bifurcation point become a decision node through purposeful choice of which path to take. The motive of such active selection is to improve the efficiency of one's journey. In cybernetics, the point of control is to improve the efficiency of algorithmic computation. Algorithms are step-wise processes or procedures that accomplish some useful task. Life is all about accomplishing highly sophisticated useful tasks.

Unfortunately, the true nature and initial source of controls within nature continues to be swept under the investigative rug. The only reason for this is a purely metaphysical imperative that precludes quality research. Physico-chemical constraints are not controls [10]. Life is controlled, not constrained. Life is an orchestrated symphony, not just the self-ordered "dissipative structures" of chaos theory [47-52] [15]. The dissipative structures of Prigogine typically destroy organization, not produce it. What about "Complexity Theory" [53-56]? All kinds of complexity exist that do nothing useful. Mere complexity is blind to utility. No empirical evidence exists of mere complexity steering or controlling toward functionality. Maximum complexity is randomness, not order. But mere order is no better. Neither self-ordering [15,57] nor nonconceptual complexity [13,14,17,19,21,58,59] steer physicality toward non-trivial usefulness. Ask any programmer. Randomness does not compute. Neither do the laws of physics and chemistry, or the four known forces, or thermodynamic "uncertainty" or possibility."

What are formal controls?

- Directives and commands that steer events toward utility;

- The choice of how to set each dynamically-inert configurable switch;

- The programming of successful computation;

- The cybernetic processing of that programming;

- The design and engineering of the necessary *formal equipment* (nanocomputers, sophisticated molecular machines, ribosomes, chaperones) needed to process that programming into tertiary structure;

- Algorithmic optimization;

- The functional integration of circuits;

- Instructive semiosis of efficacious messages using rules, not laws;

- Orchestration of otherwise independent events and players into a holistic symphony of sophisticated homeostatic metabolism;

Sustained Functional Systems (SFS) [24] maintaining themselves far from equilibrium against the 2nd Law propensities.

Why Must Controls be Regarded as "formal" ?

Physicodynamic interactions have no awareness of "usefulness." They do not and cannot perceive, value or pursue utility. Physico-chemical reactions are utterly dumb when it comes to pragmatism. Neither laws nor constraints appreciate the value of "function." Directives that steer

and control events towards utility are always Formal, not physical. Formalisms always involve choice contingency. The achievement of sophisticated function has universally required the application of purposeful choice causation, not just raw physicodynamics.

Nothing in physicodynamics can

- steer physicality toward usefulness
- make purposeful choices
- set configurable switches to achieve desired function
- improve efficiency
- integrate circuits
- program
- compute existing programming

How are controls normally generated?

"Controls" are almost synonymous with "purposeful choices." Inanimate "constraints" don't even come close to the capabilities of controlling purposeful choices. Life is not constrained. Life is controlled at every level. Life could not exist without purposeful steering choices [15]. Purposeful choices always emanate from the far side of the Cybernetic Cut [10,16,60]. They enter physicality only across the narrow one-way Configurable Switch Bridge. Efficacious choices have never been observed in the history of science to emanate from raw mass/energy interactions [6-11,16,19,57,60,61]. Raw physicodynamics cannot even explain the existence of a metal alloy with the right tensile strength and malleability to make a simple piece of wire. How did that piece of wire get to be so long with constant diameter? Not by chance and necessity. If not even a simple piece of wire can "self-organize" or "emerge" from iron ore in the ground, why would any scientist seriously think for one second that homeostatic metabolism could self-organize and emerge?

Examples of the BioControls of BioSystems

Life and the science of biology is replete with such examples: subcellular; cellular; intercellular; organ systems; hormones, hypothalamic/pituitary axis, etc. Any philosophic naturalist is hard put to deny the reality of both genetic and epigenetic controls at just the subcellular level alone. The most primitive lifeforms display exquisite formal controls. Then there are the extremely sophisticated protein enzymes and the long noncoding yet controlling RNA's. Three-dimensional shapes are mostly prescribed by primary linear digital prescription. Appealing to chaperones only compounds the problem, since their primary, secondary and tertiary structures also have to be independently prescribed. And it's not just exons we have to explain. It's how those exons get pieced together into a singular prescriptive function at a certain time when those exons are located on multiple disparate genes [62,63].

We have to explain the exons on the negative strands, too, not just the positive strands. And it's those nasty long non-coding RNAs that control the genes and gene products. If that weren't enough, we also have to explain what caused the uniquely-set methylations and acetylations—epigenetic configurable switch-settings. Chance and Necessity can do none of these things to produce sophisticated function. Shared operons and enhancer elements simultaneously control multiple different gene functions [64,65]. If life is characterized by anything, it is by CONTROLS rather than mere constraints.

We could provide literally thousands of examples of formal biological controls. Zhou et al's paper [66], for example, shows how Nesprin-2 coordinates opposing microtubule motors during nuclear migration in neurons. Bidirectional microtubule motors are required for nuclear transport. Nesprin-2 serves as a nucleus-motor adaptor, coordinating the interplay of kinesin-1 and dynein. The Nesprin-2 fragment encompassing the motor binding sites generates persistent movements toward both microtubule minus and plus ends. Nesprin-2 drives bidirectional cargo movements over a prolonged period along perinuclear microtubules, which advance during the migration of neurons. Nesprin-2 keeps the nucleus mobile by coordinating opposing motors, enabling continuous nuclear transport along advancing microtubules in migrating cells. This is not a picture of physicodynamic constraints. It is a picture of formal BioSystem controls producing very sophisticated biofunction.

In another example of formal biocontrols, Caillier et al [67] show that immune cell amoeboid-like migration through difficult spaces is mediated through small and dynamic focal adhesions that are composed of the same proteins associated with canonical mesenchymal cell focal adhesions, such as integrins, talin, and vinculin. These focal adhesions localize to sites of contractile traction stresses, enabling T cells to pull themselves through confined spaces. They show that Th1 T cells preferentially follow tracks of other T cells, suggesting that these adhesions modify the extracellular matrix to provide additional environmental guidance cues. Integrin-mediated focal adhesions play a key role in T cell motility. T cells ability to pull themselves through confined spaces is just another example of the formal controls of BioSystems that cannot be addressed by ordinary physics and chemistry.

Probabilism is not a cause of any effect

Probabilism is merely descriptive, not causative of real effects. "Possibility theory" is not a satisfactory scientific model of causation, especially when the Universal Plausibility Metric of that model measures out with a ξ of < 1.0 [68,69] Peer- reviewers and editors are required to reject such manuscripts. Irreversible nonequilibrium thermodynamics has never been observed to produce a single nontrivial function, algorithm, program or cybernetic programming execution. Thermodynamics cannot process cybernetic halting.

How were the first controls generated in an inanimate, prebiotic environment?

What in atomic mass/energy conversions could possibly cause steering of interactions and reactions toward usefulness? "Physidocynamically inert" configurable switches had to be designed and engineered to be *un*responsive to physical causation. They had to be "physicodynamically incoherent." In other words, the switches could not be set by any law, constraint or force of physicality. The switch could only be set by formal Choice Contingency. Choice causation alone could set the switches to achieve nontrivial, multi-step formal functions. Our wall light switches are an example. The switch is designed and engineered *not* to be turned off by the force of gravity, electromagnetism, strong or weak nuclear force. Only one force can turn the light switch off: Active selection—the unique force of Choice Causation: the third fundamental category of reality besides Chance and Necessity [6].

Natural selection can't turn configurable programming switches on or off. Natural selection is passive and secondary, never active. Evolution never selects for function. It only selects for superior organisms. Evolution is nothing more than the differential survival and reproduction of the fittest already-programmed, already-cybernetically-processed, already-living *organisms.* Evolution is worthless in explaining the origin of Prescriptive information (PI) or abiogenesis. No organisms exist yet to differentially survive. Cont rols never emanate from the near side of the Cybernetic Cut [6,8-10,15,16]. They influence physicodynamics only via the one-way Configurable Switch Bridge crossing the great ravine from the far side to the near side of the Cybernetic Cut [12,16].

Discussion

Controls achieve steering toward formal success. Steering requires intent in making efficacious active selections, not just secondary passive selections. The pursuit of function must begin before the function exists to "favor." Efficacious commands must be made in advance to produce algorithmic optimization. Commands consisting of nucleoside selections are made prior to the existence of secondarily selectable function. Life is not just self-ordered [15]. Life is not self-organized, either. Nothing can organize itself into existence. It would have to already exist to do any organizing of anything, let alone of its own birth. "Self-organization" is a nonsense term that has no place in scientific literature. "Emergence" is equally vacuous. They are terms created out of desperation stemming from beginning biological thought with a faulty axiom: "mass and energy raw interactions are sufficient." They are clearly not.

Life is undeniably *orchestrated.* Life is a symphony that puts Beethoven to shame!

No programmer generates computation randomly or by law [7]. Law would produce a program of all "1's," or a program of all "0's," by law! "Does not compute!". Programs result from one thing only: a succession of wise integrated active selections made at true decision nodes in pursuit of utility. This alone is what generates and maintains life. Useful paths have to be chosen over non-useful ones. Many independent such choices have to be made in advance of life being orchestrated. It is statistically prohibitive for all of these correlated functions to be generated at the same time and place by chance and necessity.

Nothing brings this reality to a head better than the helpful reductionism of life-origin studies and the science of ProtoBioCybernetics [7]. What was the cause of the effect of "active selection" in pursuit of biofunction in an inanimate environment? Can the physical laws cause active selection at bona fide decision nodes? Which of the four known forces accomplished this feat? Whatever generated Choice Causation generated the effect we call "Life." Neither Chance nor Necessity logically could have generated Active Selection and purposeful Choice Causation. This fact is what forces acknowledgement of the third fundamental category of reality beside Chance and Necessity: Choice Causation. It is real. It can and should be fully investigated by science. To selectively ignore this phenomenon is completely disingenuous and scientifically irresponsible.

It may well be that science will not be able to determine the origin of Choice Causation. Science hasn't done very well elucidating the origin of the mathematical physical laws, either. There's no shame in metaphysics, or in the admission that science cannot address all aspects of reality. What is utterly shameful is our persistent obfuscation in admitting that Chance and Necessity cannot possibly explain life's controls. The science of biology cannot possibly be properly investigated starting with metaphysical naturalism as its starting axiom. The only hope of avoiding naturalism's demise is to redefine "natural." We are hard put to deny that the life we observe everywhere in so many different forms is natural. If philosophic naturalism expects to include biology within the natural sciences, it is going to have to redefine "natural." Only then can naturalism remain the starting axiom of the natural sciences. But if science stubbornly refuses to include the common denominator of all lifeforms (formal controls) in its investigation, then one of two things must happen. Either

1. The science of biology must be excluded from the natural sciences

2. Philosophic naturalism must be rejected as science's starting metaphysical axiom.

The Kuhnian paradigm rut of the current concept of naturalism does not and cannot include all of the pieces of the cosmic puzzle within the perimeter defined by its narrow-minded worldview. When it comes to the science of biology, the

current philosophic naturalism is utterly bankrupt. Life is a major aspect of nature. Life is as natural as any other aspect of nature. We set out correctly wanting to include biology within the natural sciences. But the facts of life expose the fallacy of the current starting axiom. If life is natural, the common denominator of all known life forms is natural. We must abandon the current Kuhnian paradigm rut in favor of redefining our concept of "natural" to include the reality of life's *controls*. This is what this author is calling, "The New Naturalism."

Conclusions

The most fundamental questions of abiogenesis are not physicochemical. They are *formal* queries:

- How did a prebiotic environment perceive or value biofunction?

- What do laws and constraints know of utility?

- What *caused* the first active selection for "usefulness" in an inanimate environment?

- What motivated nature to prefer and choose function over nonfunction?

- Can Chance and Necessity make purposeful choices?

Naturalistic science is utterly negligent in failing to address these perfectly justifiable and essential scientific questions. All biological understanding depends upon elucidating the cause of the above phenomena. The subject of the natural science of biology must include exploration of these very real phenomena. To do so, we must expand our prior definition of what we have always called "natural" to include the reality of "natural formal controls." Astrobiologists and abiogenists continue to argue that life-origin was inevitable given eons of time and a huge phase space. This contention corresponds to arguing that life origin and life are perfectly "natural." If we disagree with this argument, biology must immediately be excluded from the natural sciences. Life must be addressed in a field all its own, similar to the Engineering field. But if we do that, we are admitting that the current Science-wide axiom of philosophic naturalism is a grossly inadequate worldview for an all-encompassing science. We will be admitting that science cannot be fully pursued naturalistically as always claimed. A far better option is to redefine the "natural" in naturalism to acknowledge that life and its formal controls are a part of the natural world. We must then fairly investigate the origin of formal controls in the natural world. This constitutes pursuit of "The New Naturalism."

References

1. Abel DL. "Assembly Theory" in life-origin models: A critical review. *Biosystems* 247 (2025): 105378.

2. Abel DL. Life is Programmed Computation. *Journal of Bioinformatics and Systems Biology* 8 (2025): 1-16.

3. Abel DL. Why is Abiogenesis Such a Tough Nut to Crack? *Archives of Microbiology and Immunology* 8 (2024): 338-364.

4. Abel DL. Selection in molecular evolution. *Studies in History and Philosophy of Science* 107 (2024): 54-63.

5. Abel DL. What is Life? *Archives of Microbiology and Immunology* 8 (2024):428-443.

6. Abel DL. The three fundamental categories of reality In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel, D.L, Ed.; LongView Press-Academic: Biolog. Res. Div.: New York, NY (2011): 19-54.

7. Abel DL. What is ProtoBioCybernetics?. In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel, D.L, Ed.; LongView Press-Academic: Biolog. Res. Div.: New York NY (2011): 1-18.

8. Abel DL. Is life unique? *Life* 2 (2011): 106-134.

9. Abel DL. (Ed.) *The First Gene: The Birth of Programming, Messaging and Formal Control*. LongView Press-Academic: Biolog Res. Div.: New York NY (2011): 389.

10. Abel DL. Constraints vs. Controls: Progressing from description to prescription in systems theory *Open Cybernetics and Systemics Journal* 4 (2010): 14-27.

11. Abel DL. The biosemiosis of prescriptive information *Semiotica* (2009): 1-19.

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

13. Durston KK, Chiu DK, Abel DL, Trevors JT. Measuring the functional sequence complexity of proteins *Theoretical biology & medical modelling* 4 (2007): 1-14.

14. Abel DL. Complexity, self-organization, and emergence at the edge of chaos in life-origin models *Journal of the Washington Academy of Sciences* 93 (2007): 1-20.

15. Abel DL. Trevors, J.T. Self-Organization vs. Self-Ordering events in life-origin models *Physics of Life Reviews* 3 (2006): 211-228.

16. Abel DL. The 'Cybernetic Cut': Progressing from Description to Prescription in Systems Theory *The Open Cybernetics and Systemics Journal* 2 (2008): 252-262.

17. Abel DL. Life origin: The role of complexity at the edge of chaos In Proceedings of the Washington Academy of Science 2006, Lecture delivered at the Headquarters of the National Science Foundation, Arlington VA (2006).

18. Trevors JT, Abel DL. Chance and necessity do not explain the origin of life *Cell Biol Int* 28 (2004): 729-739.

19. Abel DL. The capabilities of chaos and complexity *Int. J. Mol. Sci* 10 (2009): 247-291.

20. Abel DL, Trevors JT. More than Metaphor: Genomes are Objective Sign Systems. In *BioSemiotic Research Trends*, Barbieri, M, Ed.; Nova Science Publishers: New York (2007): 1-15.

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

22. Abel DL. *Primordial Prescription: The Most Plaguing Problem of Life Origin Science* Long View Press Academic: New York, NY (2015).

23. D'Onofrio DJ, Abel DL. Johnson, D.E. Dichotomy in the definition of prescriptive information suggests both prescribed data and prescribed algorithms: biosemiotics applications in genomic systems *Theor Biol Med Model* 9 (2012): 8.

24. Abel DL. Moving 'far from equilibrium' in a prebiotic environment: The role of Maxwell's Demon in life origin In *Genesis - In the Beginning: Precursors of Life, Chemical Models and Early Biological Evolution*, Seckbach, J, Gordon, R, Eds.Seckbach, J, Ed.; Springer: Dordrecht (2012): 219-236.

25. Abel DL. The Formalism > Physicality (F > P) Principle In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel DL, Ed, Long View Press Academic: NY (2011): 325-351.

26. Abel DL. Linear Digital Material Symbol Systems (MSS) In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel DL, Ed, Long View Press-- Academic, Biol. Res. Div, New York, (2011): 135-160.

27. Abel DL, Trevors JT. More than metaphor: Genomes are objective sign systems *Journal of BioSemiotics* 1 (2006): 253-267.

28. Xu S, Wang Q, Qin Y, Yang Q, Xu Y, Zhou Z. Dl-3-n-butylphthalein inhibits neuronal apoptosis and ferroptosis after cerebral ischemia-reperfusion injury in rats by regulating CXCR4. *Neurotoxicol Teratol* (2025): 107434.

29. Xing X, Zhang M, Tan S, Zhu J, Li J, et al. The IRF2-INPP4B pathway is activated in CD4+ T cells and aggravates acute myeloid leukemia development by inhibiting apoptosis. *Turk J Haematol* (2025).

30. Li X, Wu Y, Peng J, Li B, Li X, Yan Z, et al. Porcine epidemic diarrhea virus induces mitophagy to inhibit the apoptosis and activation of JAK/STAT1 pathway. *Vet Microbiol* 303 (2025): 110427.

31. Li M, Chen J, Meng R, Ji X. Rhythmic deep-brain magnetic stimulation promotes angiogenesis and inhibits apoptosis by regulating the JAK2/STAT3 pathway in rats with superior sagittal sinus thrombosis. *Brain Res* (2025): 149509.

32. He G, Liu M, Chen TC, Huang LF, Ke YQ. SBFI-26 enhances apoptosis in docetaxel-treated triple-negative breast cancer cells by increasing ROS levels. *Bioimpacts* 15 (2025): 30137.

33. Singla MK, Muhammed Ali SA, Kumar R, Jangir P, Khishe M, Gulothungan G, et al. Revolutionizing proton exchange membrane fuel cell modeling through hybrid aquila optimizer and arithmetic algorithm optimization. *Sci Rep* 15 (2025): 5122

34. Samir A, Maowwad MS, Farahat MA, Talaat M. Numerical investigation of high-temperature proton exchange membrane fuel cell conductivity at different parameters. *Sci Rep* 15 (2025): 5318.

35. Samanta R, Haldar N, Pamecha A, Gajbhiye V. Cell membrane-camouflaged nanocarriers: A cutting-edge biomimetic technology to develop cancer immunotherapy. *Int J Pharm* 672 (2025): 125336.

36. Aljaidi M, Agrawal SP, Jangir P, Pandya SB, Parmar A, et al. A two stage differential evolution algorithm for parameter estimation of proton exchange membrane fuel cell. *Sci Rep* 15 (2025): 5354.

37. Kull K. The aim of extended synthesis is to include semiosis. *Theor Biol Forum* 115 (2022): 119-132.

38. Alexander VN, Bacigalupi JA, Garcia OC. Living systems are smarter bots: Slime mold semiosis versus AI symbol manipulation. *Biosystems* 206 (2021): 104430.

39. Nomura N, Muranaka T, Tomita J, Matsuno K. Time from Semiosis: E-series Time for Living Systems. *Biosemiotics* 11 (2018): 65-83

40. Affifi R. The Semiosis of "Side Effects" in Genetic Interventions. *Biosemiotics* 9 (2016): 345-364.

41. van Dongen JE, Segerink LI. Building the Future of Clinical Diagnostics: An Analysis of Potential Benefits and Current Barriers in CRISPR/Cas Diagnostics. *ACS synthetic biology* (2025).

42. Talat A, Khan AU. From supplements to superbugs: how probiotic patent gaps drive antimicrobial resistance and the CRISPR-Cas solutions. *Pharm Pat Anal* (2025): 1-3.

43. Singh S, Raj D, Mathur A, Mani N, Kumar D. Current approaches in CRISPR-Cas systems for hereditary diseases. *Prog Mol Biol Transl Sci* 210 (2025): 205-229.

44. Munshi ID, Acharya M, Mukherjee S, Mani I. Recent development in CRISPR-Cas systems for cardiac disease. *Prog Mol Biol Transl Sci* 210 (2025): 47-93.

45. Mittas DM, Gavrilov Z, Ucambarlic E, Gandor C, Otify DY, et al. CRISPR/Cas-Mediated Gene Activation as a Versatile Tool for Treatment of Inherited Retinal Dystrophies. *Adv Exp Med Biol* 1468 (2025): 95-99.

46. Fuegi JFJ. Lovelace & Babbage and the creation of the 1843 'notes' (PDF). *Annals of the History of Computing* 25 (2003): 16–26.

47. Prigogine I. *The End of Certainty*; The Free Press: New York (1997): 161-162.

48. Nicolis G, Prigogine, I. *Exploring Complexity*; Freeman: New York (1989).

49. Prigogine I, Stengers I. *Order Out of Chaos*; Heinemann: London (1984): 285-287, 297-301.

50. Prigogine I. *From Being to Becoming*; W. H. Freeman and Co: San Francisco (1980).

51. Prigogine I, Mayne F, George C, de Haan M. Microscopic theory of irreversible processes. *PNAS USA* 74 (1977): 4152-4156.

52. Nicolis G, Prigogine I. *Self-Organization in Nonequilibirum Systems: From Dissipative Structures to Order Through Fluctuations.*; Wiley-Interscience: New York (1977).

53. Gordon BL. Biological Information and Self-Organizational Complexity Theory: Introductory Comments. In *Biological Information: New Perspectives*, Marks II RJ, Behe MJ, Dembski WA, Gordon BL, Sanford JC, Eds, World Scientific: Cornell Conference Proceedings (2013): 509-512.

54. Sarmento MA, Cordoba-Camacho WY, Shanenko AA, Vagov A, Albino Aguiar J, et al. Emerging complexity in the self-dual theory of superconductivity. *J Phys Condens Matter* 36 (2024).

55. Jirasek M, Sharma A, Bame JR, Mehr SHM, Bell N, et al. Investigating and Quantifying Molecular Complexity Using Assembly Theory and Spectroscopy. *ACS Cent Sci* 10 (2024): 1054-1064.

56. Franco JP, Murawski C. Harnessing Computational Complexity Theory to Model Human Decision-making and Cognition. *Cogn Sci* 47 (2023): e13304.

57. Abel DL. What utility does order, pattern or complexity prescribe?. In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel, D.L, Ed.; LongView Press--Academic, Biol. Res. Div.: New York, (2011): 75-116.

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

59. Abel DL. Is Life Reducible to Complexity? In Proceedings of the Workshop on Life: a satellite meeting before the Millennial World Meeting of University Professors, Modena, Italy (2000): 3-4.

60. Abel DL. The Cybernetic Cut and Configurable Switch (CS) Bridge In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel, D.L, Ed.; LongView Press--Academic, Biol (2011): 55-74.

61. Abel DL. The GS (Genetic Selection) Principle. *Frontiers in Bioscience* 14 (2009): 2959-2969.

62. Ottesen EW, Singh NN, Seo J, Singh RN. U1 snRNA interactions with deep intronic sequences regulate splicing of multiple exons of spinal muscular atrophy genes. *Front Neurosci* 18 (2024): 1412893.

63. Borner S, Ragg H. Bioinformatic approaches for the identification of serpin genes with multiple reactive site loop coding exons. *Methods Enzymol* 501 (2011): 209-222.

64. Goransson M, Forsman P, Nilsson P, Uhlin BE. Upstream activating sequences that are shared by two divergently transcribed operons mediate cAMP-CRP regulation of pilus-adhesin in Escherichia coli. *Mol Microbiol* 3 (1989): 1557-1565.

65. Liebke H, Hatfull G. The sequence of the distal end of the E. coli ribosomal RNA rrnE operon indicates conserved features are shared by rrn operons. *Nucleic Acids Res* 13 (1985): 5515-5525.

66. Zhou C, Wu YK, Ishidate F, Fujiwara TK, Kengaku M. Nesprin-2 coordinates opposing microtubule motors during nuclear migration in neurons. *J Cell Biol* 223 (2024).

67. Caillier AO, David, Fowell, Deborah J. T cells use focal adhesions to pull themselves through confined environments. *J Cell Biol* 223 (2024): e202310067.

68. Abel DL. The Universal Plausibility Metric and Principle In *The First Gene: The Birth of Programming, Messaging and Formal Control*, Abel, D.L, Ed.; LongView Press-Academic: New York (2011): 305-324.

69. Abel DL. The Universal Plausibility Metric (UPM) & Principle (UPP) *Theor Biol Med Model* 6 (2009).