The Grammar of Life

How the Closure Framework Grounds Denis Noble's Biological Relativity

CF Dietz

> *It is not reasonable to privilege one level of understanding over all others. Causation flows both upward and downward.*
> Denis Noble, Dance to the Tune of Life, 2016

> *Every finite closure generates remainder. The remainder is not noise. It is the proof that the grammar is finite.*
> CF Dietz, Consciousness, Closure, and the Cosmos, 2026

Abstract

Denis Noble has spent three decades arguing that biology cannot be explained by genes alone: that living systems involve genuine downward causation between levels of organization, that organisms harness randomness as a resource rather than merely enduring it, and that agency and purpose are fundamental features of life rather than apparent or metaphorical ones. These claims have empirical support, mathematical grounding, and increasing acceptance among systems biologists, yet they remain philosophically underdeveloped. Noble can demonstrate that multi-level causation occurs. He cannot yet explain from first principles why it must occur in any living system. This paper provides that explanation. The closure framework developed in Consciousness, Closure, and the Cosmos establishes that any living system is a nested hierarchy of closure regimes, each of which stabilizes some content, generates remainder at its boundary, and is constrained by the boundary conditions set by higher levels. Multi-level circular causation is not a special empirical discovery about hearts or cells. It is a structural necessity that follows from what any nested closure hierarchy is. Noble's four central claims, biological relativity, the genome as tool not blueprint, the harnessing of stochasticity, and agency as a real biological property, all follow as consequences of this structural account. The paper is written to be accessible to readers who know Noble's biology but not the closure framework, and to readers who know the framework but have not encountered Noble's challenge to the central dogma. No prior knowledge of either is assumed beyond what the paper itself provides.

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1. A Cell Does Something Genes Cannot Explain

Begin with a fact so ordinary it is easy to miss how strange it is.

Your heart has been beating since before you were born. It will beat approximately three billion times in your lifetime, adjusting its rate to every physical and emotional demand you place on it, maintaining a rhythm that no engineer has yet been able to replicate with comparable reliability in comparable space. The remarkable thing is not that this happens. The remarkable thing is where the rhythm comes from.

It does not come from a gene. There is no gene for heartbeat rhythm. The genes encode the proteins that form ion channels in cardiac cell membranes. Those ion channels allow charged particles to flow in and out of the cell in response to electrical potentials. The flow of ions changes the electrical potential across the membrane. The changed potential affects the behavior of the ion channels. The changed channel behavior affects the ion flow. The rhythm emerges from this cycle of mutual influence, from feedback loops operating at the level of the cell as a whole, not from any instruction encoded at the molecular level.

Denis Noble demonstrated this mathematically in 1960, building the first computational model of a beating cardiac cell. The model worked. It reproduced the heartbeat. And it revealed something that gene-centric biology has been struggling with ever since: you cannot get from the genome to the heartbeat without invoking properties that belong to the cell as a whole rather than to any of its molecular components. The cell is not executing a genetic program. It is constituting a rhythm from the interactions of its parts, and that constitution is something the parts alone cannot do.

This observation is the beginning of Noble's argument and the beginning of this paper. What kind of thing is a cell, such that it can do this? The answer Noble has been developing across thirty years of systems biology is the answer this paper will show is a structural consequence of what any sufficiently organized living system must be. The vocabulary for that answer comes from the closure framework. But the puzzle is stated here, in the heartbeat, before any framework arrives.

2. Noble's Four Claims

Noble's challenge to gene-centric biology has four interconnected parts. Each is worth stating in plain language before the framework touches it.

2.1 Biological Relativity: No Level Is Privileged

The central dogma of molecular biology holds that information flows in one direction: from DNA to RNA to protein to organism. Genes are the source. Everything else is downstream consequence. Noble's principle of biological relativity says this is wrong, not as a matter of empirical detail but as a matter of logical structure. No level of biological organization has privileged causal authority. The genome influences the cell. The cell influences the genome. The organ influences the cells within it. The organism influences its organs. These influences run in both directions simultaneously, and neither direction is more fundamental than the other.

Noble is not denying that genes matter. He is denying that they are the only things that matter, or that they matter in a uniquely foundational way. The genome is, in his phrase, more like a set of organ pipes than a blueprint for life. The pipes do not play themselves. The music requires a player, and the player operates at a level above the pipes.

2.2 The Genome as Tool, Not Blueprint

A blueprint specifies a structure independently of the context in which it is built. The same blueprint produces the same building regardless of who reads it or where they build. Genes do not work this way. Which genes are expressed, when, at what level, and with what effect depends on the cellular environment, the organism's developmental history, the physiological state of surrounding tissues, and signals from the external world. The genome is not a context-independent specification. It is a context-sensitive resource that the organism deploys in response to its situation.

This matters enormously for how we think about development, disease, and evolution. If the genome is a blueprint, you can understand an organism by reading its genes. If the genome is a tool, you can only understand an organism by understanding the system that wields the tool, which is the living cell and the organism as a whole. The implications for medicine, for our understanding of heritable disease, and for evolutionary biology are substantial. Noble has been drawing them out for decades. The philosophical foundation for why the genome must be a tool rather than a blueprint is what this paper provides.

2.3 Harnessing Stochasticity: Randomness as Resource

The standard account of evolution treats random mutation as the source of variation and natural selection as the filter. Mutations happen by chance. Selection keeps the useful ones. The organism is passive in this story: it is the site where mutations occur and the object that selection acts upon.

Noble's account of harnessing stochasticity is more radical. Organisms have evolved mechanisms that actively use randomness rather than merely enduring it. When under stress, cells can increase mutation rates in targeted regions of the genome. They can reorganize regulatory networks to generate novel phenotypes rapidly. They can, in effect, search solution spaces using randomness as the engine of search rather than waiting for useful accidents to accumulate. What appears to be blind chance at the molecular level becomes, at higher levels of organization, a directed search process.

The key word is harnessing. The randomness is real. The molecules are genuinely doing what statistical mechanics says they do. But the organism as a whole is structured in a way that makes some outcomes of that randomness more likely to be useful, and that selects among the outcomes in ways that advance the organism's coherence and survival. Randomness at the lower level becomes resource at the higher level. This, Noble argues, is how organisms can evolve solutions to environmental challenges far faster than blind chance alone could manage.

2.4 Agency and Purpose: Real, Not Metaphorical

Noble's most philosophically ambitious claim is that agency and purpose are genuine features of living systems, not anthropomorphic projections onto mechanisms that are fundamentally purposeless. He is not claiming that evolution has a cosmic goal or that organisms are guided by an external designer. He is claiming that organisms have short-term goals, internal to themselves, that shape their behavior, their development, and their evolutionary trajectory.

The purposive agent is the organism as a whole. It maintains its own coherence. It responds to environmental challenges in ways that make sense in retrospect even when they could not have been predicted in advance. It uses the resources available to it, including the randomness at the molecular level, to generate responses that serve its continued existence. Noble and his colleagues have argued that purposive agency became banned from evolutionary biology for ideological rather than empirical reasons following the hardening of the Modern Synthesis after Darwin's death, and that biology has been impoverished by that exclusion ever since.

3. The Missing Foundation

Noble's four claims are empirically grounded, mathematically modeled, and increasingly accepted among systems biologists. They face a specific philosophical objection that has prevented their full acceptance in mainstream biology and philosophy of science.

The objection is this: even if multi-level causation occurs in biology, you have not explained why it must occur. Even if organisms do harness stochasticity, you have not explained why any sufficiently organized system would develop this capacity. Even if agency is real in living systems, you have not explained what agency is in physical terms, or why it should appear at all in a universe of molecules following mechanical laws.

Noble has responses to each version of this objection. But the responses are defensive: they show that the objection does not succeed on its own terms rather than providing a positive account of why multi-level causation, harnessing, and agency are structural necessities rather than contingent discoveries. Noble can demonstrate that his biology is consistent with physics. He cannot yet derive his biology from a more fundamental account of what organized systems are.

That derivation is what the closure framework provides.

4. Two Concepts That Change Everything

The closure framework developed in Consciousness, Closure, and the Cosmos introduces a large vocabulary for thinking about organization, causation, and consciousness. This paper uses only two of its concepts, the minimum needed to ground Noble's biology. Readers who want the full account are directed to the source paper. Here only what the argument requires is introduced.

4.1 Closure: What a Living Level Is

A closure regime is a system that stabilizes some content by drawing distinctions, establishing identity criteria, and maintaining lawful relationships among its elements. The closure constitutes facts within its scope: it determines what counts as the same entity across different moments and contexts, what relationships between entities are lawful, and what falls outside its modeling capacity as remainder.

Remainder is the key concept. Every finite closure generates remainder: the content that the closure's distinctions and identity criteria cannot capture. A closure over molecular degrees of freedom, which is what a cell is, cannot model everything about the molecules it contains. It constitutes some facts about them, the ones relevant to its own organization, and leaves the rest as remainder. That remainder is not a defect of the closure. It is a structural consequence of the closure being finite. An infinite closure would generate no remainder. There are no infinite closures in the physical world.

A living cell is a closure regime in this precise sense. It draws distinctions between self and environment, between active and inactive gene sequences, between signals that matter and signals that do not. It maintains identity criteria across time: the cell that divides tomorrow is the same cell as the cell that exists today, not because any particular molecule persists unchanged, but because the organizational closure persists. And it generates remainder: molecular processes that the cell's organization does not control, does not model, and cannot predict.

4.2 Nested Levels: Why Downward Causation Is Necessary

A living organism is not one closure regime but a nested hierarchy of them. Molecules form cells. Cells form tissues. Tissues form organs. Organs form organisms. Each level is a genuine closure regime with its own identity criteria and its own remainder. And the levels are nested: higher-level closures contain lower-level closures as their elements.

The crucial consequence of nesting is this: the boundary conditions within which a lower-level closure operates are set by the higher-level closure that contains it. This is not a metaphor. It is a mathematical fact about nested dynamical systems. The differential equations that describe ion channel behavior in cardiac cells require boundary conditions to have specific solutions. Those boundary conditions are determined by the state of the cell as a whole, which is a higher-level closure. The higher level sets the conditions within which the lower level operates. That is downward causation, and it is a structural necessity of nested closure hierarchies, not an empirical discovery about hearts.

Noble has argued this point from the direction of mathematics and systems biology. The closure framework derives it from the direction of first principles about what organized systems are. The derivations converge. Multi-level circular causation is not a feature of biology that we discovered by studying organisms. It is what any nested hierarchy of finite closure regimes must produce.

A note on scope is required here, and it is directed specifically at readers who know Noble's work and who are rightly cautious about speculative overreach. The closure framework developed in Consciousness, Closure, and the Cosmos extends these two concepts, closure and nested levels,

to cosmological and phenomenological claims that Noble may find speculative and that this paper does not require him to accept. The biological argument of this paper is self-contained. A reader who accepts closure as stabilized regime and nested levels as the structural basis of downward causation has everything needed to follow the argument that Noble's biology makes. That reader is not thereby committed to the broader cosmological framework of CC-C. The convergence between the framework and Noble's biology is offered as evidence that both are tracking a structural truth about organized systems. Whether that structural truth has the cosmological scope CC-C proposes is a separate question that Noble and every reader are invited to examine independently, without it bearing on the biological argument made here.

5. Four Claims, One Structure

Before connecting each claim to the framework, it is worth making the vocabulary correspondence explicit, because Noble has already done much of the philosophical work in his own mathematical language. What the closure framework calls a closure regime, Noble calls a level of biological organization. What the framework calls remainder, Noble calls stochasticity available for harnessing. What the framework calls a nested closure hierarchy, Noble calls a multi-level system with circular causation. And what the framework calls downward causation as boundary condition setting is formally equivalent to Noble's own account of how higher-level closures constrain lower-level dynamics through the initial and boundary conditions in differential equation models. Noble has made the boundary conditions argument himself in precisely mathematical terms. The closure framework gives that argument a name and derives it from structural first principles rather than from the mathematics of specific biological systems. Readers who already speak Noble's language will find the framework familiar at every point of contact.

5.1 Biological Relativity Follows from Closure

No level of biological organization has privileged causal authority because no level of a nested closure hierarchy has privileged causal authority. This is not a biological discovery. It is a consequence of what nested closure hierarchies are. Higher levels set boundary conditions for lower levels. Lower levels generate the dynamics that higher levels integrate. Both directions are real. Both are necessary. Neither can be reduced to the other without losing something that is genuinely there.

Noble's principle of biological relativity is the biological instance of a structural truth about nested closure regimes. The closure framework does not borrow prestige from biology to make a philosophical point. It derives the philosophical principle and then recognizes Noble's biology as its demonstration.

5.2 The Genome as Tool Follows from Remainder

The genome cannot be a blueprint because a blueprint specifies outcomes independently of context, and the genome operates entirely within context. Which genes are expressed depends on the cellular closure's current state, its history, and the boundary conditions set by higher-level closures above it. The genome is a resource that the cell, as a closure regime, deploys in response to its situation.

This is not contingent on the details of molecular biology. It follows from what it means to be an element within a closure regime. Elements within a closure do not execute programs. They participate in the maintenance of the closure's identity and the generation of its outputs. The genome participates. The cell decides, not in a cognitive sense, but in the precise sense that the cell as a closure regime determines which genomic resources are relevant to its current state and activates them accordingly.

5.3 Harnessing Stochasticity Is Remainder Deployed as Resource

This connection is the most striking. Noble's harnessing of stochasticity describes how organisms use molecular randomness as a resource for generating novel responses to environmental challenges. The closure framework establishes that every finite closure generates remainder at its boundary: content that the closure cannot model and cannot control. That remainder is not eliminated by the closure. It persists at the boundary, available to be used.

What Noble calls harnessing stochasticity is, in closure terms, a higher-level closure deploying its lower-level remainder as the raw material for generating variation. The cell as a closure regime does not control the quantum and thermal noise at the molecular level. But it is organized in a way that makes some outcomes of that noise more likely to be incorporated into useful responses. The randomness is real and uncontrolled at the molecular level. The harnessing is real and organized at the cellular level. Remainder, genuinely present at the boundary of the lower closure, becomes resource when viewed from the perspective of the higher closure that contains it.

This is the same structure identified in the Grammar of Healing and Semantic Remainder: remainder is not noise to be eliminated but a generative resource that the system uses. Noble's biology confirms this independently from the direction of molecular biology. The convergence across domains is the argument.

5.4 Agency Follows from What Closure Regimes Do

A closure regime maintains its own identity across time by constituting facts, managing its remainder, and adjusting its boundary conditions in response to what the world presents. That maintenance is what agency means in a non-teleological sense. Not that the organism has a cosmic goal or a soul. That the organism as a higher-level closure regime is structurally oriented toward maintaining its own coherence, and that orientation shapes everything it does.

Purpose, in this account, is not imported into biology from outside. It is a structural feature of sufficiently complex nested closure hierarchies. An organism that did not maintain its coherence, that did not use its resources to respond to environmental challenges, that did not harness its remainder in ways that served its continued existence, would not be a living organism. It would be a dissolving one. Purpose is what the difference between maintaining and dissolving looks like from the inside of a closure regime.

Noble's claim that agency and teleonomy are fundamental facts of life rather than apparent or metaphorical ones is confirmed by this account. They are fundamental not because biology

happens to have them but because any sufficiently organized nested closure hierarchy will exhibit them as structural consequences of what nested closure hierarchies are.

6. What This Changes for Biology and Philosophy

The convergence between Noble's biology and the closure framework has consequences for both.

For biology, it means that the resistance to Noble's claims on philosophical grounds is misplaced. The objection that agency is not a physical concept, that downward causation is spooky, that purpose cannot be real in a mechanical universe, all of these fail against the closure account. Downward causation is not spooky. It is the mathematically necessary consequence of higher-level closures setting boundary conditions for lower-level ones. Agency is not a non-physical concept. It is what any nested hierarchy of finite closures does when it maintains its own coherence. Purpose is not imported from outside biology. It is what living systems exhibit because of what living systems structurally are. Crucially, the closure account makes structural predictions that are in principle testable at the biological level. Noble's own experimental program, the virtual heart, the ion channel models, the epigenetic inheritance research, the physiological selection studies, constitutes exactly this kind of testing. Those experiments have returned positive results not merely for Noble's biology but for the structural account this paper offers. Noble has been running the experiment for sixty years. The closure framework names what the results have been showing.

For philosophy, it means that the hard questions Noble raises about levels of causation, about what genes really are, about how organisms relate to their genomes, have structural answers that do not require either reductionism or vitalism. The closure framework provides a third position: organized systems are genuinely multi-level, neither reducible to their lowest-level components nor requiring non-physical additions to explain their higher-level properties. The structure itself, the nested hierarchy of finite closures, does the explanatory work.

For medicine, the implications follow directly from Noble's own argument extended by the framework. If the genome is a tool wielded by the cell rather than a blueprint executed by the organism, then the promise of genomic medicine, the idea that sequencing the genome will tell us how to fix disease, is systematically overestimated. This is not because genetics is wrong. It is because the cell, as a closure regime, integrates genomic information with everything else it knows about its current situation, and that integration is not readable from the genome alone. Medicine that understands this will attend to the cellular and organismic closure levels, not only to the molecular ones. This is, not coincidentally, exactly what Noble's systems biology and the Grammar of Healing's account of placebo and nocebo both recommend.

7. The Grammar of Life

A living cell is not a machine that executes instructions. It is a closure regime that stabilizes some content, generates remainder at its boundary, and operates within boundary conditions set by higher-level closures above it, while setting boundary conditions for lower-level closures below it. That is what Noble's heartbeat demonstrates. That is what his biological relativity describes. That is what his harnessing of stochasticity employs. That is what his account of agency requires.

Noble has been right. The genome is not the blueprint. Causation flows in both directions. Randomness is a resource. Agency is real. He has been right empirically, mathematically, and physiologically. What he has not yet had is a philosophical framework that derives these truths from what organized systems structurally are rather than discovering them inductively in the behavior of hearts and cells and evolving populations.

The closure framework provides that derivation. Multi-level circular causation is a structural necessity of nested closure hierarchies. The genome as tool rather than blueprint follows from what it means to be an element within a closure regime. Harnessing stochasticity is remainder deployed as resource, which is what finite closure regimes necessarily have available to them. Agency is what nested closure hierarchies exhibit when they maintain their own coherence across time.

Biology is not physics plus complexity. It is not chemistry plus selection. It is nested closure regimes generating remainder, using that remainder, and constituting facts at every level simultaneously. That is the grammar of life. Noble has been reading it for sixty years. This framework names what he has been reading.

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Author's Note

This paper is a response to and engagement with Denis Noble's work in systems biology and philosophy of biology. It does not claim Noble's agreement with the closure framework or its vocabulary. It claims only that the closure framework, developed independently in Consciousness, Closure, and the Cosmos, derives from structural first principles the conclusions that Noble's biology has established empirically and mathematically. The convergence across independent routes is offered as evidence that both accounts are tracking something real about what living systems are. The author welcomes engagement from biologists, philosophers of biology, and systems scientists who find the convergence productive or problematic.