Perturbation, Integration, Possibility Space

Why Highly Adaptive Phenomena Occur and Why Neo-Darwinism Cannot Explain Them

Abstract. Neo-Darwinism describes the filter, not the structure of what gets filtered. It does not explain why highly adaptive phenomena occur: coherent, rapid adaptations across multiple traits simultaneously, which random search in the entire possibility space could not achieve. This paper develops an alternative framework. The central thesis is that autocatalytic systems generate, through their history of perturbations, a structured, non-uniformly distributed variation space whose topology makes certain variations more probable than others. When this pre-structured space is congruent with current selective pressure, the result appears highly adaptive. This congruence is neither guaranteed nor random, but itself a product of system history. The thesis is developed at the cell-biological, epigenetic, and evolutionary-biological levels, empirically anchored, and precisely demarcated from Jablonka's four-dimensions model and from neo-Darwinism. Recent findings on epigenetically driven mutational bias, stress-induced transposon mobilization, cryptic genetic variation, and the G-matrix framework provide converging empirical support.

1. The Explanandum: Highly Adaptive Phenomena

When observing evolutionary adaptation processes, one finding stands out that remains in need of explanation within the neo-Darwinian standard model: in some cases, organisms adapt precisely, coherently across multiple traits simultaneously, and with a speed that would require many times the actual elapsed time if variation were uniformly randomly distributed across the possibility space.

Before addressing this finding theoretically, a methodological caution is required: we observe only surviving lineages. All lineages that responded maladaptively are no longer visible. What we describe as the high adaptivity of evolution has already been filtered through a massive survivorship bias. Evolution is not per se highly adaptive. But highly adaptive phenomena do occur, and they require explanation.

The precise question is therefore: why do highly adaptive phenomena occur? Not: why is evolution efficient. The more precise formulation of the explanandum also changes the requirements for an explanation.

2. What Neo-Darwinism Explains and What It Does Not

Neo-Darwinism explains adaptation through three mechanisms: random mutation, recombination, and natural selection. The model is accurate for many phenomena and empirically well supported. Its explanatory gap lies precisely where highly adaptive phenomena occur.

First: neo-Darwinism has, strictly speaking, no feedback channel. Selection is not an information transmission process but an elimination process. The environment does not send information back to the organism. It simply does not allow certain genotypes to survive. What remains is the result of a filter, not a communication. A genotype is not selected because it received feedback, it is selected because it is the only one still there.

Second: recombination shifts the randomness problem only one level up. Which units get recombined is itself randomly distributed. That is the same randomness principle in different form, not a new explanatory mechanism.

Third: the model begins its explanation at variation and asks what happens to it. It does not explain how the structure of variation arises, why certain variations are available in certain populations at certain moments, and why they can appear coherently across multiple traits simultaneously. Selection presupposes variation. The origin of variation's structure remains in neo-Darwinism essentially left to chance.

3. Jablonka's Extension and Its Category Error

Eva Jablonka and Marion Lamb argued in *Evolution in Four Dimensions* (2005) that four inheritance systems operate in parallel: the genetic, epigenetic, behavioral, and symbolic. This is the most elaborated attempt to extend neo-Darwinism. It contains a category error, however, that must be explicitly named here.

Inheritance in the biological sense is a causal mechanism that transfers structures from one generation to the next, independently of the interpretive capacity of the receiving system. Genetic inheritance through DNA replication, epigenetic inheritance through methylation patterns and histone modifications, and behavioral transmission through imitation and learning are all causal mechanisms in this sense, albeit at different levels.

Symbolic transmission is categorically different. A symbol has no causal force without an interpreter. The transmission of symbolic content presupposes already interpretation-capable organisms and operates at the level of meaning and intentionality, not at the level of physical-chemical causality. Jablonka thus conflates two fundamentally different levels: the level of causal inheritance mechanisms and the level of meaning-dependent transmission.

This is precisely the type of category error that a reconstructivist methodology uncovers: one takes a phenomenon at a higher level, calls it inheritance, and treats it as if it belonged to the same causal class as methylation patterns or gene expression. The theory developed here does not need this fourth dimension. It remains consistently at the level of causal mechanisms, thereby avoiding the error.

4. The Central Thesis: Perturbation and Topological Change of the Possibility Space

The central claim is: autocatalytic systems generate, through their history of perturbations, a structured, non-uniformly distributed variation space whose topology makes certain variations more probable than others. Environmental feedback does not merely filter, it changes the grammar according to which new variations are generated. This is neither Darwinism nor Lamarckism, but categorially a third thing.

Darwinism knows an elimination process. Lamarckism claims the direct inheritance of acquired traits. The present thesis claims: perturbations do not change the content of inheritance, but the topology of the space from which future variations are drawn. That is a meta-level above selection.

Topology here means: which regions of the variation space are connected to each other, which are separated, where barriers lie, where attractors are. A perturbation does not necessarily change the current phenotype, it changes the probability distribution of future variations. The result can be

adaptive, maladaptive, or neutral. Maladaptation is not an objection to the thesis but part of it: the changed possibility space does not always align with subsequent selective pressure. Congruence between a pre-structured variation space and selective pressure is the necessary condition for the occurrence of highly adaptive phenomena. It is neither guaranteed nor random, but itself a product of system history.

5. Cell-Biological Foundations: The Autocatalytic System as Carrier

5.1 Autocatalysis as an Organizational Principle

Autocatalytic systems are defined by recursive feedback loops: products catalyze their own emergence. Kauffman showed that intermediary metabolism is invariantly autocatalytic for ATP, and that coenzymes such as NAD+, Coenzyme A, and tetrahydrofolate occur as obligate autocatalytic metabolites in various organisms (Kun et al., 2008). Autocatalytic sets emerge spontaneously in chemical networks and are potentially evolvable (Hordijk, 2022).

Crucially: an autocatalytic system cannot be adequately described as a computer. It does not operate on discrete symbols with fixed content, but in continuous, recursive state trajectories. External stimuli do not function as inputs in the sense of data; they function as perturbations. They do not initiate computations but modulate ongoing processes. There is no clearly demarcated transition from input to processing to output, but a continuous self-execution.

5.2 Attractor Dynamics and Stability Gradients

Autocatalytic networks have multiple attractors: stable states to which the system returns after perturbations or into which it permanently transitions. Waddington's epigenetic landscape metaphor, formalized in the language of Boolean networks, describes cell states as attractors in a dynamic system. More recent analyses show that biological systems operate near a critical regime that optimizes the trade-off between robustness and adaptability (Balleza et al., 2008).

A perturbation strong enough can permanently shift the system into a different attractor. This new attractor has a different internal structure, thus different transition probabilities between states. This is grammar change in the precise sense: not what the system currently does, but which state transitions become more or less probable in the future.

5.3 The Stability Gradient of the Genome

The genome is not a static information store but a historically layered archive with a stability gradient from old to new, from fixed to flexible. Highly conserved genomic regions, which have barely changed over hundreds of millions of years, encode basic cellular processes. Mutations there are almost invariably lethal. Less conserved regions, regulatory elements, non-coding RNAs, transposon-rich areas, are more plastic and respond more strongly to environmental conditions.

This gradient is not accidental but is itself the result of the system's integration history. What has proven robust across many generations under many different conditions is deeply anchored. What emerged under more specific or more recent conditions remains more flexible. What is inherited is therefore not a program and not a blueprint, but a historically layered stability gradient that determines in which regions variation is probable and in which it is almost excluded.

In this model, chance is not uniformly distributed across the genome, but itself gradually structured. In the fixed part, variation is almost excluded. In the flexible part, variation is permitted and

functional, because there mutation does not endanger basic processes. The scope for chance is itself a product of integration history.

5.4 Three Cell-Biological Levels of Grammar Change

At the epigenetic level, methylation patterns and histone modifications determine which genes are expressible at all. Perturbations can permanently shift these patterns. The stimulus then does not merely trigger a current reaction, but changes the space of possible future reactions. This is structural change, not merely functional.

At the level of signal transduction, receptor networks are not static. Chronic stimulus patterns alter receptor densities, thresholds, and coupling efficiencies between signaling cascades. This changes how perturbations are categorized and routed at all. The system changes not only its answer, but its internal classification of the stimulus.

At the metabolic level, autocatalytic networks have bifurcation points at which perturbations can permanently shift the system into different attractors. More recent work shows that mutations alter the topology of metabolic correlation networks, generating emergent phenotypes that cannot be derived directly from individual mutations, but arise from the complexity of the network as a whole (Lloréns-Rico et al., 2025).

6. The Mutation Spectrum as Signature, and Molecular Grammar Generators

6.1 Epigenetically Driven Mutational Bias

If the thesis is correct, the pre-structured variation space should leave empirical signatures. One such signature would be the mutation spectrum: the distribution of which mutations actually occur, not merely how frequently.

Maharjan and Ferenci showed in *Escherichia coli* that different nutrient stresses only partially increase the overall mutation rate, but each stress generates a unique mutation spectrum, suggesting that specific stresses shape evolutionary dynamics by changing the quality, not merely the quantity, of variation (PLOS Biology, 2017). Shewaramani et al. found that mutation rates evolve rapidly in response to demographic and environmental changes, with substantial bidirectional shifts after only 59 generations (Nature Communications, 2022).

A decisive mechanistic underpinning comes from Monroe et al. (Nature, 2022), who showed in *Arabidopsis thaliana* that mutation rates in essential genes, those under strong epigenomic protection, are more than halved compared to less-protected regions. Mutation is therefore not uniformly distributed chance, but is actively steered by the epigenome. The mechanism is physicochemical: methylated cytosine (5mC) spontaneously deaminates to thymine, making hypermethylated regions mutation hotspots. When a parental perturbation stably de-methylates or hypermethylates specific germline regions through heritable small RNAs, it physically shifts the local mutation risk in the next generation. This is the field of epigenetic mutational bias, and it shows that the epigenome dictates the physical landscape for the mutation machinery.

Jiang et al. (2014) provided direct evidence at the germline level: salt stress in *Arabidopsis* not only increased mutation rates but changed their type, with a rise in transversions and indels, preferentially in gene regions, and many of these changes were heritably transmitted to offspring. This is strong evidence that environmental factors can directly influence the quality of the genetic raw material for evolution.

The EDGE hypothesis (Epigenetically Directed Genetic Errors) builds a theoretical bridge: environmentally induced epigenetic changes can, across generations, lead to permanent mutations at specific contingency genes. What begins as flexible epigenetic adaptation may be evolutionarily consolidated through genetic mutation.

6.2 Transposon Mobilization as Topological Shifter

Barbara McClintock's concept of the genome under stress is experiencing a renaissance. Transposable elements (TEs) are normally epigenetically silenced through piRNAs and methylation. Environmental perturbations can lift this epigenetic control in the germline. Crucially, when TEs jump, they do not do so completely randomly, they have preferred insertion sites in A/T-rich regions and regulatory elements. A parental perturbation thus leads to a specific pattern of TE deregulation in germ cells; offspring inherit a genome in which mutations are induced at specific regulatory network nodes. This is grammar change at the molecular level: the topology of the genomic possibility space is restructured, not by accumulating random point mutations, but by the mobilization of genomic elements at structurally relevant positions.

6.3 DRT3 as a Molecular Grammar Generator

A recent biochemical finding illustrates the principle with unusual clarity. Deng et al. (Science, 2026) showed that the antiphage system DRT3 synthesizes sequence-specific DNA entirely without a nucleic acid template. The enzyme Drt3b generates a defined DNA sequence based solely on the geometry of its catalytic center, the protein itself serves as the template. Selection history has been encoded directly into protein structure, which now determines what DNA is produced.

This is not autocatalysis in the strict sense, but it is a molecular example of what this paper calls a grammar generator: a system in which the history of selective pressure has shaped the structure of a molecular machine such that it produces specific variation, not randomly, not freely, but according to a structurally embedded logic. The finding shows that the boundary between information carrier and catalyst is more fluid than the central dogma suggests, and that selection history can be inscribed into the production of new genetic material in ways that bypass classical template-based inheritance.

7. Transgenerational Epigenetic Inheritance: Bridge Between Levels

The crucial question is whether the grammar change described at the cell-biological level is transmitted across generations. Research on transgenerational epigenetic inheritance provides differentiated findings here.

At the mechanistic level, the following is established: parents exposed to changed environmental conditions alter the epigenetic state of their chromatin in both somatic tissues and the germline. These changes are transmitted to offspring. Studies in rodents show that paternal stress acts transgenerationally through small non-coding RNAs in sperm, and first human studies confirm analogous patterns (Bale, 2014; Gapp et al., 2021).

At the functional level, the picture is more differentiated. A study on *Daphnia* clones shows that transgenerational epigenetic inheritance increases trait variance without being consistently adaptive: epigenetic exposure to a stressor led to reduced survival and growth rates in offspring (Munoz et al., 2025). A study in *Drosophila melanogaster* showed that epigenetic inheritance can even reverse phenotypic direction across generations, what was adaptive in one generation can become maladaptive in the next (Bhalla & Sharma, 2023). Both findings are not refutations but confirmations at a deeper level: the topology of the variation space has changed, but whether this change is

adaptive depends entirely on whether the new structure is congruent with subsequent selective pressure.

Crucially: existing research has almost invariably asked whether transgenerational epigenetic inheritance is adaptive. That is the wrong question for the present thesis. The right question is: does the perturbation history change the topology of the variation space of offspring, regardless of whether this change is adaptive? And as a follow-up: under which conditions is this change adaptive, under which maladaptive, and under which neutral?

8. Chance and Its Location

Chance in neo-Darwinism is a property of mutation: mutations are undirected and independent of selective pressure. This is correct as a description of the biochemical process of replication errors. But it does not describe the structure of the variation space from which these mutations are drawn.

In the present framework, chance is contextual and relational. It lives at the interface between system structure and environment. The same organism type in a different environment generates different chance, because different possibilities are open or closed. The same environment with a differently structured organism likewise generates different chance. What we call chance is the not fully predictable actualization of the system's potential under concrete conditions.

This is more precise than Gould's concept of contingency, which describes chance as historical path-dependence without naming the mechanism. And it differs from genetic determinism: not genes as program, but system structure as possibility space, which comes into contact with an environment anew in each generation. Chance is thus not a primary feature of biological processes, but a relational property, a function of the encounter between a structured system and a structured world.

9. Why Highly Adaptive Phenomena Occur: A Synthesis

Highly adaptive phenomena occur when three conditions are simultaneously fulfilled. First, the autocatalytic system must have generated, through its perturbation history, a variation space whose topology is pre-structured in the direction of current selective pressure. Second, this pre-structuring must be transmittable to the next generation through epigenetic germline mechanisms. Third, the environment of the successor generation must be sufficiently similar to the environment in which the pre-structuring arose, so that congruence between variation space topology and selective pressure is realized.

When these three conditions are fulfilled, the result appears highly adaptive: fast, coherent across multiple traits, and exceeding what random search could achieve. The mechanism is neither teleological nor Lamarckist. It is the emergent result of the self-organization of autocatalytic systems under perturbation, combined with epigenetic germline inheritance as transmission channel.

When conditions are not fulfilled, the result appears maladaptive or neutral. Same mechanism, different context conditions. This is theoretical economy: a single mechanism explains both highly adaptive and maladaptive phenomena without requiring different explanations for each.

10. Demarcation, Empirical Anchoring, and Open Questions

The present theory differs from neo-Darwinism in its level of explanation: it does not begin at variation, but at the emergence of variation structure. Selection remains necessary, but it is no longer the primary explanatory mechanism, it is the secondary filter of a process primarily structured by system dynamics.

From Jablonka it differs through categorical clarity: it remains at the level of causal mechanisms and avoids the category error of symbolic inheritance. It does not need a fourth dimension, because the causal continuity between cell-biological grammar change, epigenetic germline inheritance, and population-biological variation structure suffices to explain the explanandum.

10.1 The First Open Question: Epigenetic Mutational Bias

The first open question, whether epigenetic germline changes specifically shift the mutation spectrum toward the direction of parental selective pressure, is empirically closer to resolution than previously recognized. Monroe et al. (2022) show that the epigenome actively steers where mutation is permitted. Jiang et al. (2014) show that stress changes the type of mutation in a heritable way. Transposon mobilization under stress produces structurally non-random variation at regulatory nodes. The EDGE hypothesis provides a theoretical framework for how epigenetic flexibility consolidates into genetic change. Together, these findings constitute converging evidence for epigenetic mutational bias as a real phenomenon. What remains to be shown is its directional specificity, that germline epigenetic changes preferentially shift mutation probability toward regions relevant for coping with the parental stressor. That experiment has not yet been conducted with full methodological rigor, but its design is now formulable.

10.2 The Second Open Question: Causal Continuity and System-Level Signatures

The second open question, causal continuity between levels without reduction to individual mechanisms, has also received substantial formal and empirical support.

The CIPHER framework (Kuznets-Speck et al., 2025) demonstrates that the covariance structure of single-cell data, the off-diagonal elements of the covariance matrix, that is, gene-gene correlations, carries the majority of predictive information about genome-wide perturbation responses. This is precisely the system-level signature sought: not individual genes, but the structure of fluctuations encodes the response capacity.

Fluctuation-response theorems from statistical physics (Onsager, Kubo), increasingly applied in systems biology, provide the formal framework: the response of a system to small perturbations is encoded in its spontaneous fluctuations. This means the perturbation history of a system is readable from its unperturbed fluctuation structure, without requiring reductionist analysis of individual mechanisms.

In evolutionary biology, the concept of cryptic genetic variation (CGV) and the breaking of canalization (Waddington) provide the macroscopic evidence. The Hsp90 system (Rutherford & Lindquist) is the classical empirical anchor: Hsp90 is a chaperone that stabilizes proteins across the proteome. Under environmental stress, Hsp90 is overwhelmed. The result: large quantities of previously hidden mutations across the entire network simultaneously break through phenotypically, coherently and across multiple traits at once. This is the macroscopic signature of exactly what the present thesis predicts: a system history that channeled variation now releases it coherently under perturbation. The system does not mutate more, the network permits variations that were previously suppressed.

The G-matrix framework from quantitative genetics offers the formal measurement tool: the genetic variance-covariance matrix describes how traits are genetically coupled. A perturbation history that changes the topology of the possibility space means, in this language, a change in the orientation and shape of the G-matrix, a change in the directions in which a population can vary at all. Studies on the evolution of the G-matrix under different environmental regimes could test directly whether perturbation history leaves heritable signatures in variance structure.

10.3 What Remains to Be Done

Both open questions are no longer vague desiderata but precisely formulable, methodologically approachable hypotheses. What is missing is their systematic experimental prosecution: multi-generational variance structure analysis in populations with different perturbation histories, combined with epigenomic profiling of germline cells, mutation spectrum sequencing, and G-matrix measurement across generations and environmental conditions. These experiments are technically feasible with current methods. They have not yet been conducted with the theoretical framework presented here as an explicit guiding hypothesis.

References (Selected)

Bale, T.L. (2014). Lifetime stress experience: transgenerational epigenetics and germ cell programming. *Dialogues in Clinical Neuroscience* 16(3).

Bhalla, N., Sharma, A. (2023). Epigenetic inheritance and phenotypic reversal across generations in *Drosophila melanogaster*. [Cited in feedback compilation.]

Bons, E. et al. (2020). Shifts in mutation spectra enhance access to beneficial mutations. *biorXiv*.

Deng, P., Lee, H., Armijo, C., Wang, H., Gao, A. (2026). Protein-templated synthesis of dinucleotide repeat DNA by an antiphage reverse transcriptase. *Science* aed1656.

Gapp, K. et al. (2021). Sperm epigenetic alterations contribute to inter- and transgenerational effects of paternal exposure to long-term psychological stress via evading offspring embryonic reprogramming. *Cell Discovery*.

Hordijk, W. (2022). Autocatalytic Sets: Complexity at the Interface. The Evolution Institute.

Jablonka, E., Lamb, M. (2005). *Evolution in Four Dimensions*. MIT Press.

Jiang, C. et al. (2014). Environmentally responsive genome-wide accumulation of de novo Arabidopsis thaliana mutations and epigenetic variation. *Molecular Plant* 7(3).

Kun, Á. et al. (2008). Computational identification of obligatorily autocatalytic replicators embedded in metabolic networks. *Genome Biology*.

Kuznets-Speck, B. et al. (2025). CIPHER: Predicting genome-wide perturbation responses from covariance structure. *biorXiv*.

Lloréns-Rico, V. et al. (2025). Metabolite correlation networks reveal complex phenotypes of adaptation-driving mutations. *biorXiv*.

Maharjan, R., Ferenci, T. (2017). A shifting mutational landscape in 6 nutritional states. *PLOS Biology*.

Monroe, J.G. et al. (2022). Mutation bias reflects natural selection in *Arabidopsis thaliana*. *Nature* 602.

Munoz, N. et al. (2025). Transgenerational epigenetic inheritance increases trait variation but is not adaptive. *Evolution*.

Rutherford, S.L., Lindquist, S. (1998). Hsp90 as a capacitor for morphological evolution. *Nature* 396.

Shewaramani, S. et al. (2022). Rapid evolution of mutation rate and spectrum in response to environmental and population-genetic challenges. *Nature Communications*.

Stegemann, W. (2026). Beyond Representation: Why the Brain Does Not Map the World. Unpublished manuscript.