

PERSPECTIVE ARTICLE

Immunity as an evolutionary stabilizer: Microbial competition, biological complexity, and thermodynamic organization

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Abstract

Life operates within thermodynamic constraints requiring continuous energy acquisition, utilization, and dissipation. Among evolution's most consequential innovations is immunity, which stabilizes increasingly complex organisms against continual microbial challenge. Microbial competition, pathogen–host interactions, and immune regulation are dynamic processes sustaining biological homeostasis under changing selective conditions. As life diversified, mechanisms that distinguish self from non-self became essential for preserving internal stability—thereby positioning immunity as an evolutionary gatekeeper enabling the transition from simple microbial systems to complex multicellular organisms capable of cognition. Advances in immunometabolism, trained immunity, and microbiome research confirm that immune processes are fundamentally linked to energy allocation, information exchange, and metabolic regulation. Collectively, microbial competition and immune stabilization represent central manifestations of thermodynamic organization, enabling biological persistence, diversification, and increasing complexity.

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1. Introduction

The question of how life emerged and diversified within a universe governed by thermodynamic principles has long engaged evolutionary biologists, physiologists, and theoretical scientists.^{1–3} This perspective advances the argument that immunity—far from functioning solely as a defensive mechanism—is a fundamental evolutionary stabilizer enabling the transition from simple microbial communities to complex multicellular organisms capable of cognition and adaptive behavior.^{4,5} Drawing on converging evidence from immunometabolism, trained immunity, microbiome biology, and pathogen–host interactions, we propose that microbial competition and immune regulation are central biological manifestations of thermodynamic organization in living systems. The sections that follow develop this framework from its thermodynamic foundations through microbial evolution, immune stabilization, pathogen–host competition, and the emergence of cognition, concluding with an integrative view of biological complexity and evolutionary persistence.

2. Thermodynamic organization and the emergence of life

The universe evolved from an early dense state toward increasing structural complexity in a manner consistent with the second law of thermodynamics: although entropy increases globally, local order can arise within open systems sustained by continuous energy flow, producing the dissipative structures classically described by non-equilibrium thermodynamics.^{1–3,6} Within favorable planetary environments, this principle extended into chemistry: increasingly complex molecular assemblies capable of replication, compartmentalization, and information storage emerged within lipid membranes and catalytic networks, giving rise to protocellular systems capable of persistence and adaptation.^{7–9} The transition from chemistry to biology therefore represents an extension of thermodynamic principles rather than an exception to them, with living systems functioning as organized, energy-processing entities that exploit environmental gradients to maintain internal order.^{3,9} As these systems grew more sophisticated, competition for resources, survival, and replication emerged as a fundamental evolutionary pressure.

Importantly, the persistence of biological systems required more than mere acquisition of energy. As microbial diversity expanded, organisms faced continual challenges from competing biological entities. The ability to maintain internal stability while interacting with an increasingly complex microbial environment became a prerequisite for evolutionary success. This requirement ultimately contributed to the emergence of mechanisms that would later evolve into immune recognition and host-defense systems.^{4,5}

3. Microbial evolution and adaptive competition

Microorganisms represent the earliest and most enduring biological inhabitants of Earth. For billions of years, microbial communities have shaped planetary chemistry, nutrient cycling, ecological interactions, and the biological conditions necessary for multicellular life.^{5,10} Throughout this evolutionary history, microorganisms have engaged in continual competition for energy resources, environmental niches, and reproductive success (Figure 1).

Microbial adaptation is characterized by remarkable flexibility. Microbial populations can rapidly acquire beneficial traits through mutation, horizontal gene transfer, plasmid exchange, transduction, and transformation.¹¹ These mechanisms facilitate the dissemination of genetic information, enabling microbial communities to adapt

to changing environmental conditions and selective pressures. Consequently, microbial evolution is not solely a process of vertical inheritance but also a dynamic network of genetic exchange (Figure 1).

Bacteriophage–host interactions further illustrate the complexity of microbial competition. Bacteriophages exert strong selective pressures on bacterial populations, driving the evolution of defense mechanisms, including restriction-modification systems and clustered regularly interspaced short palindromic repeats (CRISPR)–CRISPR-associated protein immunity.^{12,13} Conversely, phages continuously evolve countermeasures that permit successful infection and replication. These interactions exemplify an ongoing evolutionary arms race in which competing biological systems gain selective advantages by exploiting energy, resources, and genetic information.

From a thermodynamic perspective, microbial ecosystems may be viewed as highly dynamic networks that continuously dissipate energy while maintaining local organization.³ Competition, cooperation, symbiosis, and predation all contribute to the redistribution of energy and information within microbial communities. The persistence of these systems depends upon their ability to adapt while maintaining sufficient stability to survive environmental fluctuations. Microbial evolution also provided the foundation upon which later biological complexity emerged (Figure 1). Many cellular processes central to modern organisms, including energy metabolism, genetic regulation, membrane transport, and signal transduction, have deep microbial origins.^{10,14} Thus, microbial adaptation represents not only the earliest phase of biological evolution but also the continuing substrate upon which higher-order biological complexity depends.

4. Immunity as an evolutionary stabilizer

The emergence of immunity represents one of evolution's most significant stabilizing innovations. As biological systems increased in complexity, they required mechanisms capable of distinguishing self from non-self, preserving tissue integrity, and maintaining internal stability despite continual exposure to microbial challenge.^{4,15} Without such mechanisms, increasingly complex organisms would remain vulnerable to uncontrolled infection, resource exploitation, and structural disruption. From an evolutionary perspective, immunity may therefore be regarded as a biological stabilization strategy that permits increasingly complex forms of organization to persist despite continual microbial and environmental perturbation (Figure 1).

From this perspective, immunity may be viewed as an evolutionary stabilizer. Rather than functioning

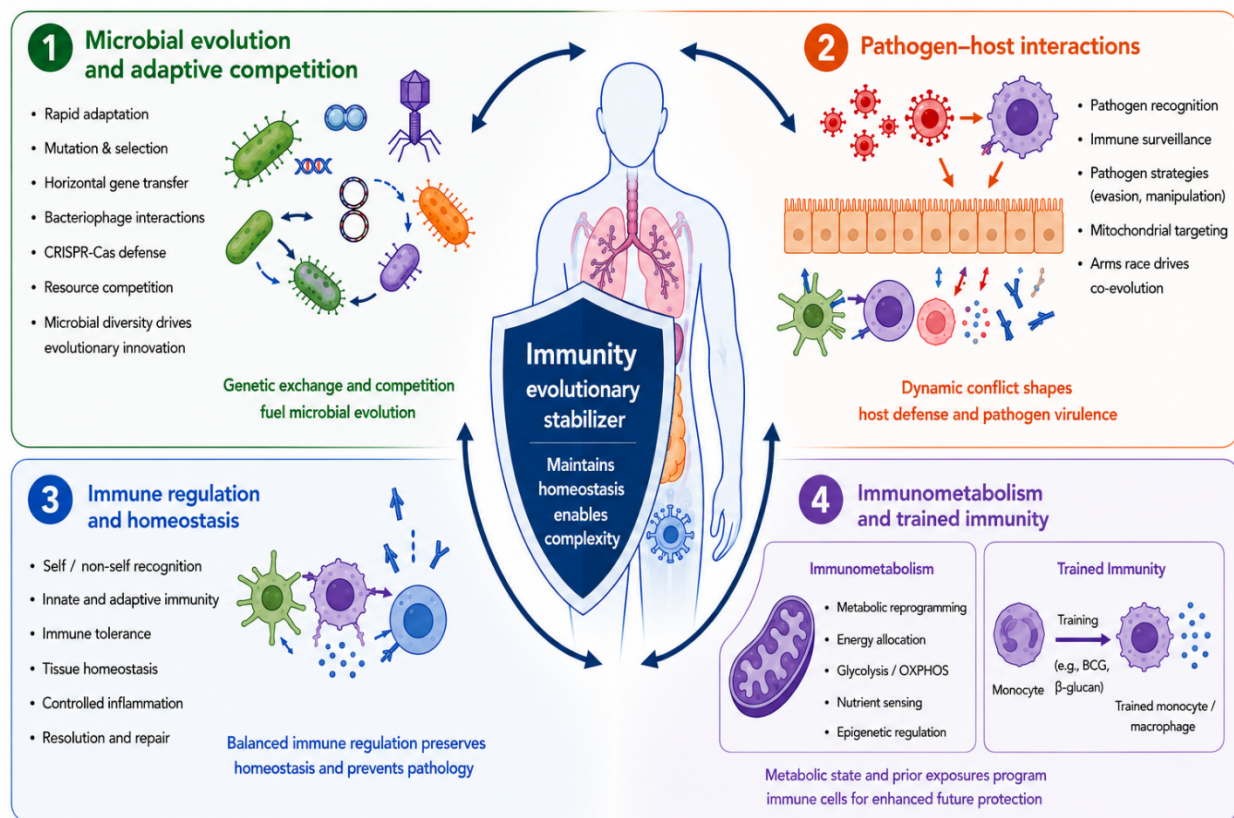


Figure 1. Immunity as an evolutionary stabilizer: integration of microbial evolution, pathogen–host interactions, immunometabolism, and trained immunity. This conceptual illustration depicts immunity as a central evolutionary stabilizing mechanism emerging from continual microbial competition and pathogen–host interactions. (1) Microbial adaptation, including mutation, selection, horizontal gene transfer, bacteriophage interactions, and CRISPR–Cas defense systems, drives evolutionary innovation, while pathogen–host interactions generate selective pressures through immune surveillance, pathogen evasion strategies, mitochondrial targeting, and co-evolutionary “arms races.” (2) Pathogen–host interactions illustrate co-evolutionary competition over energy and regulatory control: pathogens deploy immune evasion strategies, mitochondrial targeting, and manipulation of host metabolism to support replication, while hosts counter through immune surveillance, antiviral signaling, and metabolic restriction. These reciprocal pressures constitute an ongoing molecular arms race that has shaped both pathogen diversity and host immune architecture across evolutionary time. (3) Immune regulation maintains homeostasis through self/non-self recognition, innate and adaptive immune responses, immune tolerance, controlled inflammation, and tissue repair. (4) Immunometabolism and trained immunity further enhance host resilience through metabolic reprogramming, energy allocation, epigenetic regulation, and heightened innate immune responsiveness following prior microbial exposure. Collectively, these integrated processes position immunity as a key evolutionary stabilizer that preserves biological integrity, supports increasing complexity, facilitates cognition and adaptive behavior, and promotes the long-term persistence and diversification of life.

Abbreviations: BCG: Bacillus Calmette–Guérin; CRISPR–Cas: Clustered regularly interspaced short palindromic repeats–CRISPR-associated proteins; OXPHOS: Oxidative phosphorylation.

solely as a defensive system, immunity contributes to the preservation of biological organization by continuously monitoring, regulating, and responding to internal and external perturbations.^{4,15} Immune systems therefore support the persistence of complex biological structures within environments characterized by continual microbial interaction.

It should be clarified that natural selection acts directly on reproductive fitness rather than on stability per se;

immune-mediated stability is therefore best understood as one mechanism among several through which fitness is enhanced, rather than as the primary outcome of evolution itself. Because immune surveillance corrects replication errors, limits the propagation of deleterious mutations, and curtails pathogen-driven damage to the soma and germline, it preserves the physiological conditions under which reproduction can proceed normally. Immune-mediated stability and reproductive fitness are therefore complementary rather than competing explanatory

frameworks: stability is the proximate mechanism, and enhanced fitness is the ultimate evolutionary consequence.

It is also worth emphasizing that increasing biological complexity is the product of multiple convergent evolutionary factors, including expanded energy supply, genome and gene-regulatory network expansion, and the transition to multicellularity, and immunity is not proposed here as a replacement for these processes. Rather, immunity occupies a distinct and necessary role among them: whereas energetic, genomic, and multicellular innovations expand the scope and scale of biological organization, immunity preserves the organismal conditions under which those innovations can be expressed correctly, allowing the “correct” developmental, physiological, and reproductive processes to proceed at the high level of functional and physiological selectivity that increasingly complex life requires.

This framework does not imply that immune function is uniformly beneficial. Autoimmune disorders, immunosenescence, chronic low-grade inflammation, and other immune-mediated pathological states demonstrate that immune responses can themselves compromise physiological stability, representing genuine evolutionary trade-offs rather than incidental side effects. These negative outcomes, however, do not contradict the stabilizer framework; rather, they illustrate why relative immune stability—calibrated activation balanced against tolerance and resolution—is itself a critical and actively regulated ancillary function. Excessive, misdirected, or prolonged immune activation is, in effect, a failure of the very stabilizing function this perspective describes, underscoring that immune regulation, not immune activation alone, is the evolutionarily significant trait.

The evolutionary roots of immunity extend far beyond vertebrate adaptive immune systems. Primitive forms of self-recognition and defense are observed throughout biology, including microbial restriction systems, CRISPR-mediated defense mechanisms, innate immune recognition pathways, and conserved stress-response networks.^{12,13} These systems demonstrate that the capacity to identify and respond to biological threats emerged early in evolutionary history and likely contributed to the long-term stability of living systems.

Modern immunology further reveals that immunity is intimately linked to homeostasis. Immune cells participate not only in pathogen elimination but also in tissue repair, metabolic regulation, developmental processes, and interactions with commensal microorganisms.^{5,15,16} The immune system continuously negotiates a balance between activation and tolerance, ensuring effective defense while minimizing collateral damage to host

tissues. In this regard, advances in the field of trained immunity have further expanded this view (Figure 1). Innate immune cells can undergo metabolic and epigenetic reprogramming following microbial exposure, producing enhanced responses to subsequent challenges.^{17–19} These findings suggest that immune adaptation extends beyond classical adaptive immunity and represents a broader biological strategy for maintaining resilience in changing environments. Immunity can therefore be interpreted as a regulatory system that promotes biological persistence by preserving organizational stability amid continual ecological and microbial perturbation. This stabilizing function may have been essential for the evolution of increasingly complex multicellular organisms and the eventual emergence of advanced biological functions, including cognition.

5. Pathogen–host interactions and immunometabolic competition

Pathogen–host interactions provide one of the clearest biological examples of competition over energy, information, and regulatory control (Figure 1). Viruses, bacteria, fungi, and parasites depend upon host-derived resources to support survival and replication. Hosts, in turn, deploy immune mechanisms designed to limit pathogen proliferation while preserving tissue function and metabolic integrity.^{4,15}

Recent advances in immunometabolism demonstrate that immune responses are fundamentally linked to cellular energy management. Activation of immune cells requires substantial metabolic reprogramming involving glycolysis, oxidative phosphorylation, amino acid metabolism, and lipid utilization.^{16,20,21} Consequently, immune defense is not simply a signaling phenomenon but an energetically demanding biological process requiring careful allocation of metabolic resources. Pathogens frequently target these same metabolic pathways. Numerous viruses manipulate mitochondrial function, alter cellular bioenergetics, suppress antiviral signaling pathways, and redirect host metabolism to favor replication.^{22–24} Because mitochondria play central roles in energy production, innate immunity, apoptosis, and cellular stress responses, they represent critical targets during infection. Such interactions illustrate how microbial survival strategies often converge upon the energetic foundations of host physiology.

This field continues to advance rapidly: single-cell metabolic profiling and *in vivo* metabolic tracing have refined the understanding of how individual immune cell subsets dynamically rewire glycolytic, oxidative, and lipid metabolism in a context- and tissue-specific manner, and how this metabolic plasticity in turn dictates

T-cell differentiation, effector function, and memory formation.^{25,26} These more recent findings reinforce, with greater mechanistic resolution, the central premise that immune competence is inseparable from cellular bioenergetics.

The evolutionary relationship between pathogens and hosts extends over immense timescales. Horizontal gene transfer, endosymbiotic events, viral genetic incorporation, and co-evolutionary pressures have collectively shaped modern biological systems.^{11,14} Indeed, the bacterial origins of mitochondria and chloroplasts demonstrate that interactions initially characterized by competition may ultimately give rise to new forms of biological organization and complexity.

It is therefore reasonable to speculate that the earliest forms of biological self-preservation emerged from the need to distinguish and stabilize self from competing biological entities. Primitive mechanisms of self-recognition may have functioned as ancestral precursors of immunity, promoting persistence within thermodynamically feasible environments long before the emergence of sophisticated immune systems. In this sense, immunity can be viewed not merely as a defensive adaptation but as a fundamental organizational principle that enabled increasingly complex forms of life to survive, diversify, and evolve.

6. Cognition as a consequence of biological stabilization

Cognition represents one of the most sophisticated outcomes of biological evolution. Although often considered independently of immunity and microbial biology, the emergence of advanced nervous systems depended upon the prior evolution of mechanisms capable of maintaining physiological stability within increasingly complex organisms.^{27,28} Without effective host defense, metabolic regulation, and homeostatic control, the energetic demands required for neural development and cognitive processing would be difficult to sustain. In this regard, growing evidence demonstrates that immune, metabolic, and neural systems are deeply interconnected. Immune mediators influence neurodevelopment, synaptic plasticity, learning, memory, and behavioral responses.^{29,30} Likewise, the microbiome contributes to neural function through immune regulation, metabolite production, endocrine signaling, and neural communication pathways linking the gut and the central nervous system.^{31,32} These observations suggest that cognition did not emerge independently of microbial and immune processes but rather evolved within biological systems already shaped by continual host–microbe interactions.

The link proposed here rests on two converging lines

of evidence beyond neuroimmune signaling alone: the integration of neural function with cellular bioenergetics, and the direct modulation of learning, memory, and neuroplasticity by immune mediators. Mitochondrial energy production is rate-limiting for neural development, synaptic maintenance, and the high metabolic demands of cognitive processing; therefore, immune regulation of metabolic and mitochondrial function constrains the energetic substrate available for neural computation.³³ Independently, immune mediators have been shown to directly shape learning, memory, neurogenesis, and synaptic plasticity, indicating that immune signaling does not merely accompany neural function but actively participates in it.^{29,34} Taken together, these findings support the conclusion that the energetic and regulatory foundations laid by immune stabilization represent a fundamental precondition for, rather than a coincidental correlate of, the evolutionary emergence of cognition.

The concept that cognition represents “matter becoming aware of itself” remains philosophical rather than experimentally testable. Cognition may be more appropriately defined scientifically as the capacity of biological systems to acquire, process, store, and utilize information to guide adaptive behavior.³⁵ Within this framework, cognition represents an advanced extension of biological information management that evolved upon earlier foundations of metabolic regulation, immune stabilization, and environmental adaptation.

From a thermodynamic perspective, neural activity is energetically expensive. The human brain consumes a disproportionate fraction of total metabolic energy relative to its mass, emphasizing the intimate relationship between cognition and energy availability.³³ Consequently, advanced cognition may be viewed as a specialized biological strategy that improves prediction, adaptation, social coordination, resource acquisition, and ultimately survival. Importantly, numerous pathogens target neural and metabolic systems, illustrating the continuing evolutionary interplay between microbial competition and cognitive function. Viral manipulation of mitochondrial activity, neuroinflammation, and immune signaling demonstrates that cognition remains linked to the same biological and energetic constraints that shaped earlier evolutionary processes.^{22,36,37}

7. Biological complexity, energy dissipation, and evolutionary persistence

The evolution of biological complexity does not contradict thermodynamic principles. Rather, increasing complexity may emerge when energy flow through open systems supports the formation of increasingly organized structures

capable of maintaining themselves far from equilibrium.^{3,38} Local order can therefore arise while overall entropy continues to increase. Microbial communities, immune systems, multicellular organisms, and nervous systems each represent progressively more sophisticated examples of biological organization sustained through continuous energy exchange with the environment. The persistence of these systems depends upon their ability to acquire resources, regulate internal states, repair damage, and adapt to changing conditions.^{38,39}

Within this broader framework, immunity occupies a unique position. Unlike many biological processes that serve specialized functions, immunity directly contributes to the preservation of organizational stability across multiple biological scales. By identifying threats, regulating inflammation, coordinating tissue repair, maintaining tolerance, and interacting with resident microbial communities, immune systems help preserve the conditions necessary for continued biological complexity.^{4,15,17} This perspective does not imply that evolution possesses predetermined goals or directionality. Rather, it suggests that biological systems capable of maintaining stability under environmental challenge are more likely to persist and diversify. Immunity, therefore, represents a fundamental adaptive strategy through which living systems resist disruption while remaining capable of evolutionary innovation.

Microbial competition, pathogen–host interactions, and immune adaptation may thus be interpreted as interconnected manifestations of biological organization operating within thermodynamic constraints. Although the specific mechanisms have evolved over billions of years, the underlying requirement remains constant: living systems must continuously balance energy acquisition, information processing, adaptation, and self-preservation.

8. Limitations and future considerations

While the evolutionary stabilizer framework developed in this perspective offers a coherent synthesis of microbial competition, immune regulation, and biological complexity, several limitations merit acknowledgment. First, the causal relationships proposed between immune stabilization and the emergence of complex multicellular life remain necessarily inferential; direct experimental evidence linking immune-mediated stability to the specific evolutionary transitions described is inherently difficult to obtain from deep evolutionary history. The framework should therefore be understood as a conceptual synthesis generating testable predictions rather than as an established mechanistic account. Second, while the thermodynamic framing provides a

powerful heuristic, it does not fully account for other major drivers of biological complexity, including niche construction, developmental plasticity, ecological network dynamics, and stochastic evolutionary events. Third, the proposed link between immune stabilization and the emergence of cognition, while supported by convergent neuroimmune and immunometabolic evidence, remains the most speculative component of this perspective and will require further empirical support from comparative genomics, evolutionary developmental biology, and longitudinal immunological modeling. Acknowledging these constraints situates the stabilizer framework within an appropriate level of scientific caution and identifies productive directions for future investigation, including cross-species analyses of immune complexity and cognitive capacity, experimental models of trained immunity under ecologically realistic conditions, and computational modeling of immune–metabolic–neural networks across evolutionary timescales.

9. Conclusion

The evolution of life can be viewed as a thermodynamic process in which increasing biological complexity emerged within systems capable of exploiting environmental energy gradients while maintaining organizational stability. Although the physical foundations of this process extend to the earliest stages of cosmic evolution, microbial adaptation and immune regulation represent the more immediate biological mechanisms responsible for the persistence and diversification of life.

Microorganisms established the earliest ecological and evolutionary frameworks through which competition, cooperation, genetic exchange, and metabolic innovation emerged. As biological complexity increased, immunity evolved as a critical stabilizing mechanism capable of distinguishing self from non-self, regulating homeostasis, and preserving organismal integrity in the face of continual microbial challenge. Contemporary discoveries in immunometabolism, trained immunity, microbiome biology, and pathogen–host interactions increasingly support the view that immune processes are intimately connected to energy utilization, information exchange, and adaptive regulation. Therefore, immunity may be regarded as one of evolution's most important organizational innovations. By promoting biological persistence amid continual ecological and thermodynamic perturbation, immune systems enabled the emergence of increasingly complex multicellular organisms and ultimately cognition itself. Thus, while life remains constrained by the universal principles of energy flow and dissipation, immunity may be viewed as a fundamental evolutionary stabilizer that enabled the persistence, diversification, and increasing

complexity of life within the thermodynamic constraints imposed by continual energy dissipation.

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Further disclosure

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