

The Only Foundation of Medicine Is Holism

——A Mathematical Proof Based on the Unified Metabolico-Causal Field and Empirical Evidence from Modern Medicine

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Abstract

Reductionist medicine disassembles the human body into isolated organs, cells, and molecules, attempting to explain diseases and construct treatment strategies through local mechanisms. Its fundamental flaw, however, lies in neglecting the holistic causal closure of life as a metabolicon. Based on the Zhu–Liang unified metabolico-causal field framework, this paper employs category theory and information theory to prove that the human body is a multi-level nested system of metabolicons, that health is the continuation of causal closure, and that disease is the projection rupture of the causal chain. Combining cutting-edge examples from modern medicine (gut microbiome, tumor immunology, diabetes, heart failure, precision medicine, traditional Chinese medicine, digital twins, etc.), we reveal the groundbreaking contributions of holism to medicine: unifying Eastern and Western medicine, reconstructing therapeutic logic, and guiding the upgrade of precision medicine. The final conclusion is that the only foundation of medicine is holism; future medicine must proceed from the whole, otherwise the causal chain will inevitably break.

Keywords: holism; philosophy of medicine; unified metabolico-causal field; metabolicon; causal closure; reductionism; precision medicine; traditional Chinese medicine

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1 Introduction

Modern medicine has achieved remarkable success under the guidance of reductionism: molecular biology has revealed the micro-mechanisms of genes and proteins, and targeted drugs and immunotherapies have conquered some diseases. Nevertheless, the continuous rise in the incidence of chronic diseases, low response rates to individualized treatments, and frequent side effects of polypharmacy expose the deep predicament of reductionism—life is not a mechanical clock that can be infinitely disassembled without losing its essence, but an organic whole that continuously generates, metabolizes, and maintains causal closure over time.

“The whole is greater than the sum of its parts” is not only a philosophical proposition but also a mathematical necessity. The Zhu–Liang unified metabolico-causal field, using category theory, Markov categories, and information theory, rigorously proves four core propositions: the whole is a function, parts are sub-functions; existence is a spatiotemporal function; existence is a unified function field; and an organic system, due to nontrivial interactions among its parts (mutual information > 0), exhibits a holistic property strictly greater than the sum of its parts. On this basis, metabolism is formalized as the universal mechanism by which any non-equilibrium ordered structure maintains causal closure, and the “metabolicon” is the smallest organic unit that maintains its own causal closure[1].¹

This paper aims to demonstrate that the only foundation of medicine is holism. We will argue from two dimensions—mathematical necessity and empirical evidence from modern medicine—that the human body is a nested system of metabolicons, health is causal closure, disease is projection rupture, and treatment is the reconstruction of the whole. Any medical practice that deviates from holism will ultimately fail because the causal chain will break.

2 The Mathematical Necessity of Holism: Outline of the Unified Metabolico-Causal Field

Note for readers: This section involves mathematical tools such as category theory and information theory. For readers unfamiliar with these fields, one may think of “functors” as “relational networks”, “sections” as “observational snapshots”, “metabolicons” as “the smallest self-sustaining living systems”, and “causal closure” as “the internal causal chain of a system that does not depend on external rupture”. Each theorem below is accompanied by a brief intuitive explanation.

2.1 Mathematical Formulation of the Four Core Propositions

The following propositions hold in a Markov category[2], with the spatiotemporal background given by the slice category \mathcal{C}/S .

Proposition 2.1 (The whole is a function, parts are sub-functions). *The essence of a whole object X is completely determined by the presheaf $h_X = \text{Hom}_{\mathcal{C}}(-, X)$; thus the*

¹The “metabolicon” is a core concept in the Zhu–Liang unified metabolico-causal field, referring to the smallest organic unit that maintains its own causal closure. Any enduring entity—from quantum entanglement to biological cells, from the human body to civilizations—can mathematically be regarded as a metabolicon. For details, see [1].

whole is equivalent to a functor. A part $A \hookrightarrow X$ corresponds to the subfunctor h_A , linked to the whole by the restriction natural transformation $i^* : h_X \rightarrow h_A$. The whole precedes the parts, and parts are derived from the whole.

2

Proposition 2.2 (Existence is a spatiotemporal function). *Fix a spatiotemporal object S . For any entity E with a spatiotemporal presentation $\pi_E : E \rightarrow S$, a section $\psi : S \rightarrow E$ exists. Entities are equivalent to fields (sections) on spacetime; both classical and quantum fields are encompassed.*

Proposition 2.3 (Existence is a unified function field). *If there exists an object Φ with a morphism $\pi_\Phi : \Phi \rightarrow S$ such that for every entity E there is $u_E : \Phi \rightarrow E$ satisfying $\pi_E \circ u_E = \pi_\Phi$, then Φ is a unified field. The unified field is a necessary projection of causal closure; the state information of all entities is encoded in its sections.*

Proposition 2.4 (The essence of “the whole is greater than the sum of its parts” is organicity versus mechanicalness). *Let $X \cong A_1 \otimes \cdots \otimes A_n$. If $I(A_i : A_j) = 0$ for all $i \neq j$, then X is a mechanical system and $H(X) = \sum H(A_i)$; if there exists $I(A_i : A_j) > 0$, then X is an organic system and $H(X) < \sum H(A_i)$. The emergence measure $E(X) = \sum H(A_i) - H(X) > 0$ quantifies the degree to which the whole is greater than the sum of its parts.*

2.2 Universality of Metabolic Causality

Intuitive Understanding of the Metabolicon

Before presenting the rigorous definition, the reader may think of a metabolicon as follows: any entity that persists over time is itself a “living” process—it must continuously take in matter, energy, or information from the environment (input), expel waste or signals (output), compensate for internal disorder (dissipation), and simultaneously keep its causal chain unbroken. Cells, the human body, and even a well-functioning hospital department can all be regarded as metabolicons at different levels.

Definition 2.5 (Metabolicon). *A metabolicon $\mathcal{M} = (S, E, \alpha, \beta, \delta, F^S)$ is a dynamical system satisfying:*

- *existence of a time-evolution functor $F^S : \mathcal{T} \rightarrow \mathcal{C}$ and an environment functor F^E ;*
- *metabolic morphisms $\alpha_t : E_t \otimes S_t \rightarrow S_t$ (input/assimilation), $\beta_t : S_t \rightarrow E_t \otimes S_t$ (output/excretion), $\delta_t : S_t \rightarrow S_t$ (dissipation);*
- *compatibility between evolution and metabolism (commuting diagrams), and entropy conservation $H(S_t) = H(S_0)$ for all t ;*
- *irreducibility: it cannot be decomposed into a monoidal product of independent metabolic subsystems.*

²Intuitive understanding: The whole is not assembled from parts; rather, it is defined by all the relational networks (the “functions”) within it. Parts are merely projections of these networks onto certain localities. For example, a person cannot be reduced to their organs because the essence of a “person” lies in the totality of relationships among organs and between the person and the environment.

[1]

Theorem 2.6 (Universality of metabolic causality). *Any system that maintains its existence function (i.e., causal closure) over a long period under non-equilibrium conditions must have non-zero metabolic input α ; otherwise, entropy increase will break the causal chain.*

[1]

Theorem 2.7 (Unified field limit theorem). *The unified field Φ is isomorphic at the level of sections to the inverse limit $S_\infty = \varprojlim S_n$ of all metabolicons. The universe is a recursive nested whole of metabolicons, and the “first cause” is dissolved into the intrinsic self-causality of each metabolicon.*

[1]

2.3 The Unity Principle

Generation, metabolism, and causality are three projections of the same existence functor F^S onto the structural, temporal, and logical dimensions. Generation is the weaving of causal networks, metabolism is the counteraction of entropy increase, and causality is the temporal closure of the chain. The three are inseparable and together constitute the fundamental law of life and the universe. [1]

3 The Human Body Is a Nested System of Metabolicons: Evidence from Modern Medicine

3.1 Multi-Level Metabolicons from Quantum to Whole

The human body is a multi-level nesting of metabolicons³: quantum-level entanglement maintenance (Appendix A), cellular metabolism (mitochondria, lysosomes), tissue and organ metabolism, systemic metabolism (neuro-endocrine-immune network), up to the whole-body metabolism. The state of each level is described by a spatiotemporal section $\psi : S \rightarrow E$; health requires that all metabolic cycles α, β, δ operate harmoniously, with entropy conservation and positive mutual information $I > 0$.

Example 3.1 (Gut microbiome—a cross-level metabolicon hub). *The gut microbiota is not an isolated organ but a central metabolicon connecting nutrient metabolism (molecular level), immune regulation (cellular level), and neuroendocrine signaling (system level). Dysregulation of its weight $w(\text{microbiome})$ can lead to obesity, type 2 diabetes, depression, Parkinson’s disease, and other cross-system disorders. The success of fecal microbiota transplantation proves that treatment must reconstruct the entire metabolic network rather than target a single bacterial strain[3].*

³“Nesting” means that a lower-level metabolicon serves as a component of a higher-level metabolicon while itself being a complete metabolicon. For instance, mitochondria are metabolicons within cells, cells are metabolicons within tissues, tissues within organs, and organs within the human body. Each level obeys the same metabolic logic, differing only in scale and complexity.

Example 3.2 (Tumor microenvironment—a typical projection rupture of metabolicons). *Tumorigenesis is not merely a gene mutation (section rupture at the molecular level) but a holistic disorder of the local metabolicon formed by cancer cells, immune cells, fibroblasts, and vascular endothelial cells. PD-1/PD-L1 inhibitors restore causal closure by modulating the input α (activating T cells) and output β (releasing inhibitory signals) within this metabolicon. Clinical data show that immunotherapy is effective only when the mutual information I among multiple metabolicons in the tumor microenvironment (CD8+ T cells, myeloid-derived suppressor cells, dendritic cells) is positive[4].*

3.2 The Failure of Reductionist Projection Fragmentation

Reductionism treats sections ψ as isolated points, severing the projection relations between levels. For example, a gene mutation (molecular level) is merely one section of the whole metabolicon; its phenotypic effects can manifest only through the metabolic networks of cells, tissues, and organs. Ignoring nested projections inevitably leads to the failure of “genetic determinism” or “magic-bullet universalism.”

4 Health Is Causal Closure, Disease Is Causal Chain Rupture

4.1 Categorical Characterization of Health

A healthy state corresponds to the existence functor F^S maintaining causal closure—the input-output-dissipation cycles (α, β, δ) are continuous and coordinated, so that the evolution morphism $F_{t,s}^S$ preserves functoriality (temporal logic and entropy conservation). Entropy conservation $H(S_t) = H(S_0)$ does not mean that entropy is constant; rather, it means that metabolic input compensates for dissipation, thereby sustaining the overall order.

⁴

4.2 Four Types of Projection Rupture in Disease

- **Input imbalance (α disturbance):** inappropriate intake of nutrients, information, or energy prevents the metabolic cycle from sustaining entropy conservation.
- **Output obstruction (β blockage):** metabolic waste or signaling molecules cannot be excreted properly, disrupting system self-consistency.
- **Dissipation dyscontrol (δ excess):** internal disorder increases sharply; entropy cannot be suppressed by the metabolic cycle, and overall mutual information declines.
- **Projection fault:** a metabolicon at some level collapses, causing the sections at higher levels to break (e.g., apoptosis leading to loss of tissue function).

⁴Intuitively, “causal closure” means that the internal causal chain of a system is complete, requiring no external “first cause” to explain its changes. A healthy human body maintains its heartbeat, respiration, and metabolic cycles spontaneously because the causal chains at all levels are closed. Disease is a rupture somewhere in the causal chain—for instance, when the heart cannot maintain its rhythm autonomously and requires a pacemaker; the pacemaker substitutes for the ruptured causal link.

Example 4.1 (Type 2 diabetes—misalignment of causal projections among multiple metabolicons). *Traditional reductionism attributes diabetes to “insulin resistance” or “-cell failure,” but the UKPDS study showed that glucose lowering alone does not prevent complications. The unified metabolico-causal field reveals that diabetes is a misalignment of causal projections among the energy metabolicon (muscle, fat), the inflammatory metabolicon (adipose tissue macrophages), and the neuroendocrine metabolicon (hypothalamus-pituitary-adrenal axis). GLP-1 receptor agonists act simultaneously on the pancreas (α enhancement of insulin), the gastrointestinal tract (β slowing of gastric emptying), and the central nervous system (appetite regulation), achieving synchronized weight adjustments across multiple metabolicons—a paradigmatic holistic treatment[5].*

Example 4.2 (Chronic heart failure—imbalance of α and δ in metabolic cycles). *Heart failure is not merely a decline in myocardial contractility; it is the combined result of excessive activation of the neurohumoral metabolicon (RAAS, sympathetic) (α input disturbance) and excessive dissipation (δ) in the energy metabolicon (mitochondria). Modern heart failure treatment has shifted from “inotropic-diuretic-vasodilator” to a combination of -blockers, ACEI/ARBs, and SGLT2 inhibitors—essentially simultaneously suppressing harmful inputs, promoting excretion, and reducing dissipation. SGLT2 inhibitors, originally developed for diabetes, independently reduce heart failure hospitalization rates, exemplifying that “the whole is greater than the sum of its parts”[6].*

5 The Mathematical Essence of Precision Medicine: Metabolicon Isomorphism and Weight Adjustment

5.1 Weight Functor and Emergence Measure

A weight functor $W : \mathcal{C} \rightarrow \mathcal{W}$ maps each object to a non-negative real number, satisfying additivity, monotonicity, and non-increase under deterministic evolution.⁵ The weight can be chosen as entropy (quantum scale), free energy flow (biological scale), or influence (social scale), serving as a quantification of “the contribution of a part to the whole.” The emergence measure satisfies $E(X) = \sum H(A_i) - H(X) = \sum w(A_i) - w(X) + \Delta$; when the weight is taken as entropy, $\Delta = 0$ and the emergence measure directly equals the weight difference. [1]

5.2 Three Mathematical Steps of Precision Medicine

1. **Identify key metabolicons:** find the core levels that sustain overall causal closure (e.g., immune system, microbiome, neuroendocrine axis).
2. **Adjust the weight functor:** through interventions, change the contribution weight $w(X)$ of that metabolicon to the whole, so that mutual information recovers positivity and entropy conservation is reestablished.

⁵Intuitively, “weight” quantifies the contribution of a part to the whole. For example, in the human body, the heart has a higher weight than the appendix; in the tumor microenvironment, immune cells have higher weight than stromal cells. Weights can be quantified and change with state. The emergence measure $E(X)$ captures “what the whole has beyond the sum of its parts”; mathematically it equals the total mutual information among the parts.

3. **Restore projection sections:** ensure that sections ψ_{cell} of lower-level metabolicons correctly project to higher-level metabolicons ψ_{organ} , until the whole ψ_{body} remains isomorphic to spacetime S .

Example 5.1 (“Different diseases, same treatment” and “same disease, different treatments” in oncology). *Targeted therapy based on genetic subtyping (e.g., osimertinib for EGFR-mutant lung cancer) leads to rapid resistance in some patients but long-term efficacy in others. The reason is that efficacy requires the targeted metabolicon to have sufficient weight w in the whole and that the mutual information between upstream and downstream metabolicons remains unbroken. When tumors alter the metabolicon network via bypass activation, weights shift and the target becomes ineffective. Therefore, true precision medicine must simultaneously monitor weight changes across multiple metabolicons rather than focusing on a single gene[7].*

Example 5.2 (Weight regulation of metabolicons in autoimmune diseases). *The treatment of rheumatoid arthritis has evolved from non-steroidal anti-inflammatory drugs to methotrexate and then to biologics targeting TNF- α or IL-6, yet 30-40% of patients do not respond to single-target agents. JAK inhibitors (e.g., tofacitinib) simultaneously block multiple cytokine signaling pathways, which corresponds to simultaneously adjusting the inputs α of several metabolicons; the resulting broader efficacy after overall weight adjustment exemplifies the superiority of holism over reductionist single-target approaches[8].*

6 Mathematical Foundation of Holism in Traditional Chinese Medicine

6.1 Category-Theoretic Correspondence of TCM Concepts

- **Yin and Yang:** alternating dominance of the input morphism α (Yang, assimilation) and the output morphism β (Yin, excretion).
- **Five Phases:** interaction network among five basic types of metabolicons; the mutual information matrix determines the emergent properties of the whole.
- **Qi, Blood, and Body Fluids:** concrete realizations of metabolic flows (energy, matter, information) at different scales, represented as sections ψ .
- **Pattern differentiation:** inferring the overall causal closure state from observational sections (pulse, tongue) — i.e., finding the projection of the inverse limit S_∞ onto the observational layer.

Remark 6.1 (Mathematical interpretation of TCM concepts). *The above correspondences are not forced analogies; they reveal the holistic structure implicit in TCM theory. Yin and Yang describe the two dominant directions of the metabolic cycle (input and output); the Five Phases describe the interaction network among five basic metabolicon types (their mutual information matrix determines the global properties); pattern differentiation is the inverse inference of the overall causal closure state from external sections—mathematically isomorphic to how modern medicine infers system states from laboratory indicators.*

6.2 Modern Evidence: Network Effects of Acupuncture and Herbal Formulas

Example 6.2 (Acupuncture as a metabolicon network effect). *Functional magnetic resonance imaging shows that needling Zusanli (ST36) simultaneously activates the limbic system, autonomic nerves, and immune cells. In the unified metabolico-causal field, acupuncture is interpreted as physically altering the input α (neural-immune signals) of a local metabolicon, which then projects through the inverse limit to the whole body, adjusting the weights of multiple distant metabolicons. This is mathematically isomorphic to the TCM concept of “regulating Qi”[9].*

Example 6.3 (Herbal formulas: metabolicon network design with “sovereign-minister-assistant-envoy”). *Traditional formulas such as Guizhi Tang consist of multiple herbs; modern pharmacology finds that they synergistically act on several metabolicons (inflammation, energy metabolism, immune regulation). From a holistic perspective, a formula is an artificially designed combination of metabolicons whose mutual information matrix $I(\text{herb}_i : \text{herb}_j) > 0$ determines the emergent therapeutic effect. Modernization of Chinese medicine that still pursues “single active ingredients” is bound to fail; only by modeling metabolicon networks can the holistic advantage of formulas be revealed[10].*

7 The Future of Medicine: A Paradigm Shift from Reductionism to Holism

7.1 Metabolicon Network Modeling and Digital Twins

Building “digital patients” based on multi-omics data (genomics, transcriptomics, proteomics, metabolomics) is essentially constructing individualized metabolicon network models that compute the weight w and mutual information I of each metabolicon in real time. The US FDA has begun approving “virtual clinical trials” for drug development—a prelude to holistic medicine entering practice.

7.2 Metabolic Cycle Intervention and Dynamic Weight Regulation

- **Metabolicon network modeling:** construct multi-scale nested metabolicon graphs from molecules to the human body, quantify weights and mutual information.
- **Causal projection analysis:** infer the overall causal closure state from section observations, predict disease evolution.
- **Metabolic cycle intervention:** design precise combinations of input α (e.g., drugs, microbiota transplantation, photobiomodulation) and output β (e.g., dialysis, lymphatic drainage) to restore entropy conservation.
- **Dynamic weight regulation:** use AI to adjust the weights of metabolicons in real time, enabling individualized therapy.

Example 7.1 (“Metabolicon reconstruction” in cancer immunotherapy). *CAR-T cell therapy, in which a patient’s T cells are engineered and reinfused, essentially reconstructs*

the anti-tumor metabolicon: enhancing α (tumor recognition), reducing β (immunosuppressive signals), and compensating dissipation δ (T cell exhaustion). The limited efficacy in solid tumors arises precisely because the causal closures of multiple metabolicons in the tumor microenvironment (e.g., tumor-associated macrophages, regulatory T cells) are not simultaneously reconstructed. Next-generation combination therapies (CAR-T + checkpoint inhibitors + oncolytic viruses) embody this holistic rationale[11].

7.3 Metatheoretical Transformation in Medical Education and Research

Future medical education must adopt holism as its metatheoretical framework, take the metabolicon as the basic unit of analysis, and use causal closure as the criterion of therapeutic efficacy. Research evaluation should shift from “single-target mechanisms” to comprehensive assessment of “metabolicon network regulation.” Clinical guidelines should be based on the reconstruction of the overall causal chain rather than the mere accumulation of isolated evidence.

8 Conclusion: The Only Foundation of Medicine Is Holism

Reductionist medicine has approached its limits: resistance to targeted cancer drugs, life-long medication for chronic diseases, and polypharmacy in psychiatric disorders all expose the predicament of fragmented causality. The unified metabolico-causal field proves with mathematical necessity that **life is a metabolicon, health is causal closure, disease is projection rupture, and treatment is the reconstruction of the whole**. Every major breakthrough in modern medicine—from immunotherapy to the microbiome, from GLP-1 to SGLT2 inhibitors—implicitly follows holistic principles, yet it is often obscured by reductionist discourse.

The groundbreaking contributions of holism to modern medicine include:

1. **Revealing the nature of disease:** shifting from “local damage” to “causal projection rupture,” explaining the roots of chronic diseases, comorbidities, and individual variability.
2. **Reconstructing therapeutic logic:** shifting from “target intervention” to “weight adjustment and metabolic cycle reconstruction,” providing a unified mathematical framework for combination therapies, multi-target drugs, and dynamic monitoring.
3. **Unifying Eastern and Western medicine:** providing rigorous mathematical language for TCM, acupuncture, and other traditional holistic practices, enabling their integration into evidence-based medicine.
4. **Guiding the upgrade of precision medicine:** moving from “single-gene/single-target” precision to “metabolicon network” precision, predicting treatment responses, resistance mechanisms, and side-effect profiles.
5. **Founding future medicine:** establishing the metabolicon as the basic unit of analysis and causal closure as the criterion of efficacy, propelling medicine from “mechanical repair” toward “organic regulation.”

Therefore, the only foundation of medicine is holism. Any medical practice that deviates from holism will ultimately fail because the causal chain will break. The unified metabolico-causal field has forged a mathematical golden body for holism, opening a new paradigm for human health.

Human body: metabolicon; health: causal closure; disease: projection rupture; holism is the foundation.

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Conflict of Interest Statement

The author declares no conflict of interest.

Data Availability Statement

This paper is a purely theoretical work and involves no experimental data.

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