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The macro, meso, and micro dimensions of Yin-Yang theory in traditional Chinese medicine: a three-level analysis of Yin and Yang

Miao Ouyang[a], Gedi Zhang[b], Mengdan Yu[c], Hongning Liu[b*]

a. Student Affairs Office, Jiangxi University of Chinese Medicine, Nanchang, Jiangxi 330004, China

b. Institute of Advanced Studies, Jiangxi University of Chinese Medicine, Nanchang, Jiangxi 330004, China

c. Research Center for the Differentiation and Development of TCM Basic Theories, Jiangxi University of Chinese Medicine, Nanchang, Jiangxi 330004, China

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ABSTRACT

Yin-Yang theory is one of the core components of the foundational theory of traditional Chinese medicine (TCM), yet its classification as philosophical or scientific has long been controversial. To move beyond the longstanding either-philosophy-or-science debate surrounding Yin-Yang theory in TCM, this article, for the first time, proposes a three-level framework spanning macro, meso, and micro perspectives. At the macro level, Yin and Yang are a theoretical achievement of ancient Chinese natural philosophy, used to explain universal laws governing how the cosmos operates, which constitutes Yin-Yang theory in philosophy; at the meso level, *Huangdi Neijing* (《黄帝内经》, *Inner Canon of Huangdi*) translated Yin-Yang from a cosmological framework into medical discourse, making it a core methodological basis for clinical pattern differentiation and treatment, which constitutes Yin-Yang theory in medicine; at the micro level, Yin-Yang theory in TCM has increasingly converged with modern science, showing scientific features that are testable and reproducible, which constitutes Yin-Yang theory in science. The article further demonstrates that Yin-Yang theory in TCM differs markedly from Yin-Yang as a general philosophical doctrine in core application and practical orientation: in the course of its medical transformation, elements related to life phenomena were selectively incorporated, while, within a medical context, abstract propositions such as cosmological speculation were bracketed and rendered concrete, thereby achieving a practice-oriented transition from philosophy to medicine. Based on this, the present study conducts analyses from four aspects, namely philosophical roots, clinical application, modern scientific interpretation, and implications for life sciences; it substantiates the logical basis for Yin-Yang theory in TCM as the overarching framework for clinical pattern differentiation and treatment, reviews modern research progress from perspectives such as systems science and network regulation, and explores its potential value in advancing a new paradigm of state-based medicine. The study suggests that an accurate understanding of Yin-Yang theory in TCM requires moving beyond the either-philosophy-or-science binary and analyzing specific issues on a case-by-case basis. Across different perspectives, Yin-Yang theory in TCM has philosophical, medical, and scientific attributes. Only by grounding the theory in actual clinical efficacy and engaging with modern science can the innovative development of Yin-Yang theory in TCM be promoted, thereby providing valuable Eastern insights for building a life science system with original Chinese contributions.

*Corresponding author: Hongning Liu, E-mail: lhn0791@139.com.

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1 Introduction

The Yin-Yang theory in traditional Chinese medicine (TCM) is one of the core theoretical constructs of Chinese medicine. From ancient times to the present, it has not only helped people understand human life activities, but has also consistently guided clinical diagnosis, treatment, and health preservation. Accordingly, Yin-Yang theory is indispensable to a truly comprehensive understanding of TCM [1]. However, a longstanding debate has persisted in academia around this theory: is Yin-Yang theory in TCM essentially ancient philosophical speculation [2], or does it have a scientific basis [3]?

The complexity of this issue lies in the fact that Yin-Yang theory in TCM is not a single, uniform concept. Much of the longstanding debate stems from the fact that different scholars are not discussing it at the same level; the examples they cite tend to support only their own positions, making a unified conclusion difficult. To move beyond this binary, this article, for the first time, proposes a three-level framework spanning macro, meso, and micro perspectives. At the macro level, it is a product of traditional Chinese natural philosophy and addresses universal laws governing the operation of the cosmos [4]; at the meso level, through the transformation in classics such as *Huangdi Neijing* (《黄帝内经》, *Inner Canon of Huangdi*), it became a medical approach for understanding life and disease and for guiding clinical practice [5]; at the micro level, it is increasingly converging with modern science and the life sciences, showing scientific features that are testable and verifiable [6]. Yin-Yang theory thus presents a coherent trajectory from philosophy toward science, while continuing to develop through medical practice. Accordingly, classifying Yin-Yang theory in TCM simply as either philosophy or science is not sufficiently accurate and does not facilitate the modern development of TCM theory.

This article adopts a hierarchical analysis approach and conducts analyses from four aspects, namely philosophical roots and medical transformation, clinical practice, modern scientific interpretation, and implications for life sciences, moving beyond the either-philosophy-or-science binary and presenting more systematically the theoretical structure and contemporary value of Yin-Yang theory in TCM, thereby providing a reference for the inheritance, innovation, and modern transformation of TCM theory.

2 The origins and hierarchical structure of Yin-Yang theory in TCM

2.1 Macro level: Yin-Yang is the sublimation of natural philosophy

Yin-Yang theory in TCM originated from the observations of nature and philosophical reflection by ancestors. The concept initially arose from the highly concrete notion of "sunlight exposure and shade", referring to the intuitive spatial relationship between the sunny side and the shaded side [7]. It was later abstracted from natural phenomena such as day and night, cold and heat, and the sun and the moon into a philosophical category characterized by the unity of opposites. In the late Western Zhou period, Boyangfu explained earthquakes with the statement that "when Yang is concealed and cannot emerge, and Yin is constrained and cannot ascend", marking the beginning of the use of Yin-Yang to account for the laws of nature [8]. By the Warring States period, the *Yizhuan* (《易传》, *The Commentary on the Changes*) proposed that "the interplay of Yin and Yang is the essence of the Dao", regarding the opposition, interdependence, waxing and waning, and transformation of Yin and Yang as the fundamental law governing the generation, development, and change of all things in the universe [9]. Xunzi also proposed that "when Yin and Yang interact, transformation arises", further emphasizing that the interaction between Yin and Yang is the driving force of change [10]. By this stage, Yin and Yang had evolved from a descriptive concept into a cosmological model for explaining the order underlying the operation of the world.

2.2 Meso level: the medical transformation of Yin-Yang theory in TCM

The application of the philosophical view of Yin and Yang in TCM to the understanding of human life activities and disease processes marked a crucial transformation from natural philosophy to life medicine. *Huangdi Neijing* states that "human life has form and cannot be separated from Yin and Yang", incorporating bodily structure, physiological function, and pathological change into the overarching framework of Yin-Yang analysis [11]. The body surface, the six Fu-organs, Qi, and functional activities belong to Yang, whereas the interior of the body, the five Zang-organs, blood, and the material basis belong to Yin. This is not merely a matter of classification, but also embodies an understanding of the dynamic balance between function and material basis.

In incorporating Yin-Yang theory in philosophy, *Huangdi Neijing* carried out targeted selection and creative transformation, focusing its attention on human physiology and pathology and developing a set of operational language suited to clinical practice. In this way, Yin and Yang were transformed from abstract categories into a medical method that could be used for diagnosis and intervention. At the same time, while preserving the core spirit of Yin-Yang theory in philosophy, it reinterpreted certain concepts in accordance with the needs of medical practice. This was precisely the key to the transformation from philosophy at the macro level to a clinical medical method at the meso level, marking a practical leap in

Yin-Yang thought from explaining the world to safeguarding health and endowing TCM theory with a solid philosophical foundation.

After being introduced into medicine, Yin-Yang theory was continuously reconstructed in clinical practice. During the Jin-Yuan period, Danxi Zhu proposed that "Yang is often in excess while Yin is often insufficient" and strongly advocated nourishing Yin and subduing fire [12]; in the Qing dynasty, the Warm Disease School developed defensive-Qi-nutritive-blood pattern differentiation, offering a refined account of the waxing and waning of Yin and Yang in warm-heat diseases [13]. This shows that Yin-Yang theory in TCM is a living theoretical system that has been continuously activated and reconstructed in clinical practice, thereby forming a theory capable of guiding clinical practice.

2.3 Micro level: the emergence of the scientific connotations of Yin-Yang theory in TCM

At the micro level, Yin-Yang theory exhibits verifiable scientific connotations. The "micro" referred to here includes not only matter at microscopic scales in the natural sciences, such as molecules and quanta, but also micro-systems. At the micro level, Yin and Yang refer to increasingly specific phenomena as investigation becomes more fine-grained, and the scientific features of Yin-Yang theory in TCM become increasingly evident, particularly in terms of falsifiability, testability, reproducibility, and revisability. A typical example is Academician Ziyin Shen's research on kidney Yang deficiency. Through systematic investigation, he found a regular association between kidney Yang deficiency syndrome and hypofunction of the hypothalamic-pituitary-adrenal/thyroid/gonadal axes, thereby providing this traditional pattern with an objective physiological and pathological basis [14-18].

Therefore, Yin-Yang theory in TCM encompasses philosophical, medical, and scientific dimensions, with distinct meanings at different levels. This differentiation helps to further advance the development of Yin-Yang theory in TCM.

3 The essential difference between Yin-Yang theory in TCM and in philosophy

At the macro level, Yin-Yang theory originated from ancient Chinese natural philosophy and possesses universality in a cosmological sense. However, in its incorporation into TCM, this philosophical category was not adopted in its entirety, but was selectively appropriated in accordance with the needs of medical practice, while certain elements were necessarily set aside. This process was, in essence, a creative transformation.

3.1 TCM's appropriation of Yin-Yang theory in philosophy

Although Yin-Yang theory, at the macro level, originated from the sublimation of ancient Chinese natural philosophy, in its incorporation into TCM, those core principles of Yin-Yang theory in philosophy most closely related to life phenomena were selectively appropriated in accordance with the needs of medical practice and rendered into instrumental concepts for medical analysis.

3.1.1 Opposition and unity: from universal law to pathomechanism analysis In TCM, Yin-Yang theory in philosophy was applied to the analysis of pathomechanism, thereby laying the foundation for the pattern differentiation by the Eight Principles. Exterior and interior, cold and heat, deficiency and excess can ultimately all be subsumed under the categories of Yin and Yang [15]. Take fever and aversion to cold as an example: these are a typical pair of opposing symptoms. When they appear simultaneously, they often indicate a state of struggle between Yin and Yang within the body, rather than simply being regarded as manifestations of a single pathological process. This mode of thinking in terms of the unity of opposites makes it possible to grasp the essence of disease within seemingly contradictory symptoms.

3.1.2 Dynamic balance: from cosmic rhythm to the maintenance of homeostasis Yin-Yang theory in philosophy emphasizes that the waxing and waning of Yin and Yang constitute the basic rhythm of cosmic operation, and in TCM, this was transformed into a view of health centered on "balance between Yin and Yang". *Suwen* (《素问》, *Plain Questions*), in the chapter On Generative Qi Communicating with Nature, states: "only when balance is achieved between Yin and Yang can essence-spirit be normal; if Yin and Yang separate from each other, essential Qi will be exhausted" [16]. Health is not a static state of Yin-Yang balance, but a relative equilibrium maintained through dynamic waxing and waning. This view of balance is highly consistent with the modern physiological concept of homeostasis, but places greater emphasis on the dynamic and regulable nature of balance [17].

3.1.3 Mutual rooting and mutual use: from interdependence to the function-structure relationship Yin-Yang theory in philosophy holds that each side of Yin and Yang is the precondition for the existence of the other: without Yin, Yang has no basis for generation; without Yang, Yin has no basis for transformation. In TCM, this was transformed into an understanding of the relationship between function (Yang) and material basis (Yin): the functional activities of the human body cannot be separated from material foundations such as Qi and blood, body fluids, and Zang-Fu organs structures, while the generation and distribution of these material foundations also depend on the driving force of functional activities.

3.1.4 Ascending, descending, exiting, and entering: from cyclical movement to the theory of Qi movement On the basis of Yin-Yang theory in philosophy, "ascending, descending, exiting, and entering" was further distilled in TCM as forms of movement specific to life. *Suwen,* in the chapter Great Theory on Movement of Six-Qi, states: "if exiting and entering cease, the mechanism of spirit transformation is extinguished; if ascending and descending stop, Qi stands isolated and endangered". Ascending and descending, exiting and entering are the concrete manifestations of Yin-Yang movement within the human body [18]. The Qi of the heart and lung should descend, whereas the Qi of the liver and kidney should ascend, and the spleen and stomach serve as the pivot of ascent and descent. This mode of thinking, which explains the coordinated functions of the Zang-Fu organs in terms of Yin-Yang ascent and descent, has become an important tool in TCM for understanding physiology and pathology.

3.2 Selective bracketing and bounded inheritance of Yin-Yang theory in philosophy

Yin-Yang theory in TCM neither mechanically reproduces Yin-Yang as a philosophical concept nor departs from its core mode of thought. With medical practice as the criterion, Yin-Yang theory in philosophy underwent a process of creative selection in its incorporation into TCM: on one hand, metaphysical speculation and mechanical deduction not directly related to human life were bracketed; on the other hand, its core modes of thought were fully retained, such as the correlation between heaven and humanity at the cosmological level and abstract universality at the categorical level, while being strictly delimited to the domain of life sciences and transformed through processes of concretization and operationalization, ultimately giving rise to a theoretical system that combines philosophical grounding with medical specificity.

3.2.1 Bracketing ultimate cosmological inquiry while preserving the core logic of the correlation between heaven and humanity Yin-Yang theory in philosophy often extends to ultimate questions such as cosmogenesis and the origin of all things [19], as expressed in *Taiji Tushuo* (《太极图说》, *Explanation of the Taiji Diagram*): "from Wuji arises Taiji, Taiji in movement gives rise to Yang, and when movement reaches its limit, stillness emerges, from which Yin arises". The cosmological framework was not denied in the medical transformation of Yin-Yang theory; rather, ultimate inquiries that could not directly guide clinical practice were consciously bracketed, and the focus was shifted from how the cosmos came into being to how cosmic laws influence human life activities. Yin-Yang theory in TCM has always been rooted in the cosmological mode of thought of "the unity of heaven and humanity", and the statement in *Huangdi Neijing* that "human beings are born from the Qi of heaven and earth and are brought to completion by the laws of the four seasons" is clear evidence of this. This correlation between heaven and humanity runs through the entire process of etiology, pathomechanism, treatment, and health preservation, and constitutes an indispensable philosophical underpinning of Yin-Yang theory in TCM. What was bracketed in TCM was only pure speculation detached from life phenomena.

3.2.2 Delimiting the boundaries of abstract universality within the domain of life Yin-Yang theory in philosophy is characterized by a high degree of abstraction and universal applicability, extending Yin and Yang to many domains such as nature, society, and human affairs [20]. This mode of thinking in terms of abstract universality was retained in TCM, where "Yin-Yang" is used to subsume all physiologic and pathologic phenomena of opposition and unity within the human body, from structure to function, and from cold and heat to deficiency and excess. It is precisely for this reason that Yin-Yang could become the overarching framework for clinical pattern differentiation and treatment. Unlike Yin-Yang theory in philosophy, however, the scope of this abstract universality was strictly delimited in TCM. Rather than being generalized to non-life domains such as society and politics, it was focused on human life activities and transformed into specific concepts such as "Yin deficiency" and "Yang deficiency" that are diagnosable and amenable to intervention, thereby turning abstract principles into clinical tools.

3.2.3 Setting aside the excessive application of image-number deduction Yin-Yang theory in philosophy is often combined with the image-number system of *Yijing* (《易经》, *The Book of Changes*), forming a mode that uses hexagrams, line symbols, and numerological deduction to explain all things, some of which developed into mechanical analogy [21]. Although in TCM the principle of "following the laws of Yin-Yang and adopting appropriate methods and techniques of health preservation" was preserved, and image-number thinking was also used to explain the correspondence between the Zang-Fu organs and nature, clinical practice remained the fundamental criterion. The scope of image-number deduction was therefore strictly delimited, and mechanical deduction detached from the combination of the four diagnostic methods was rejected. Theories such as the mutual generation and mutual restraint of the five elements have been transformed into practical tools for explaining relationships among the Zang-Fu organs, and their rationality is tested through clinical efficacy; excessive deductions that cannot be verified have been cautiously excluded.

3.3 The practical transformation from philosophy to medicine: the dialectical unity of inheritance and bracketing

The selective bracketing and bounded inheritance discussed above constitute the key mechanism through which Yin-Yang theory in philosophy at the macro level was transformed into Yin-Yang theory in medicine at the meso level. The distinctiveness of Yin-Yang theory in TCM lies in the fact that it not only inherited the core logic of Yin-Yang theory in philosophy, including opposition and unity, dynamic balance, and the correlation between heaven and humanity, but also, through bracketing ultimate inquiries, delimiting the boundaries of application, and stripping away mechanical deduction, removed those elements irrelevant to medical practice and transformed abstract categories into an operable medical method. Without inheritance, Yin-Yang theory in TCM would lose its foundation; without bracketing, it would lapse into metaphysical speculation. It is this dialectical unity that enabled Yin-Yang theory to accomplish a practical leap from explaining the world to safeguarding health, thereby giving rise to a TCM theoretical system of Yin-Yang that combines philosophical depth with clinical efficacy.

4 The construction of a medical system through the clinical application of Yin-Yang theory in TCM

Through its sustained application in clinical practice, Yin-Yang theory was refined from a philosophical concept into a rigorous medical methodology, comprehensively guiding diagnosis, treatment, medication, and health preservation in TCM, and thereby constructing a medical system in which theory, principles, prescriptions, and medicinals are closely interconnected.

4.1 Yin-Yang as the overarching framework for clinical pattern differentiation and treatment

Yin-Yang theory in TCM is the overarching framework for clinical pattern differentiation and treatment. The principle established in *Suwen*, in the chapter Great Treatise on the Correspondences of Yin and Yang, that "a skilled diagnostician, in observing the complexion and palpating the pulse, first distinguishes Yin and Yang" has become an unshakable core rule in TCM diagnosis and treatment [22]. After collecting information on the condition through the four diagnostic methods of inspection, auscultation and olfaction, inquiry, and palpation, the physician's primary task is to determine whether Yin and Yang in the body are in a state of relative excess, relative deficiency, or disharmony in their mutual relationship. This differentiation not only determines the basic nature of the disease, but also provides the basis on which the Eight Principles, including exterior and interior, cold and heat, and deficiency and excess, can ultimately be subsumed under Yin and Yang, while directly indicating the fundamental direction of treatment, such as nourishing Yin, warming Yang, draining fire, or dispersing cold. In this way, Yin-Yang theory in TCM became a theoretically rigorous system of medicine.

4.2 Specific guidance for diagnosis, treatment, medication, and health preservation

In diagnosis, TCM follows the principle of "first distinguishing Yin and Yang", classifying symptoms and signs in terms of Yin and Yang. For example, fever, facial redness, irritability, and a rapid and forceful pulse are generally classified as Yang manifestations, whereas aversion to cold, a pale complexion, fatigue, and a slow and weak pulse are classified as Yin manifestations. Through this method of classification that grasps the essential points, TCM physicians are able to identify the essence of the disease pattern amid complex and diverse symptoms.

In treatment, the fundamental therapeutic principle of "carefully examining where Yin and Yang are located and regulating them, with restoring balance as the aim" was established [23]. At the core of TCM treatment lies the regulation of the dynamic balance of Yin and Yang. For example, in hypertension characterized by Yin deficiency with Yang hyperactivity, clinical manifestations often include facial flushing, red eyes, irritability, and proneness to anger, indicating hyperactivity of Yang, together with dry mouth and soreness and weakness of the lower back and knees, indicating deficiency of Yin. In such cases, the method of nourishing Yin and subduing Yang should be adopted in order to restore the balance between Yin and Yang.

In medication and prescription composition, the four properties of Chinese medicinals, namely cold, hot, warm, and cool, and the five flavors, namely sour, bitter, sweet, acrid, and salty, are classifications based on Yin-Yang properties. Cold belongs to Yin and hot belongs to Yang; sour has a Yin nature of astringing, whereas acrid has a Yang nature of dispersing. In TCM, compatibility among medicinals based on their Yin-Yang properties creates a synergistic corrective force against the patient's disorder.

In prevention and health preservation, TCM advocates the principle of "following the laws of Yin and Yang and harmonizing with appropriate methods and techniques", coordinating daily life, emotional regulation, diet, work, and rest with the waxing and waning of Yin and Yang in nature, thereby serving as the highest principle for maintaining internal harmony between Yin and Yang and preventing disease.

4.3 Clinical efficacy determining theoretical value

Through centuries of clinical practice, Yin-Yang theory in TCM has developed from a philosophical concept into a

mature form of medical practice. Its scientific character is not determined by its similarity to modern theories, but by its effectiveness in guiding clinical practice. Over the centuries, the diagnosis and treatment of disease, prognostic judgment, and the guidance of medication on the basis of Yin-Yang theory have given rise to reproducible clinical experience, which constitutes important evidence of scientific validity.

Mechanistic research cannot replace clinical efficacy; the two are complementary rather than opposed. The validity of a theory lies first in its ability to guide practice and produce predictable results, and only then in explaining why it works. Equating scientific validity with already known mechanisms is consistent neither with the consensus in the philosophy of science nor with the experience of medical history. Many treatments that proved effective over the long term, such as aspirin, had their mechanisms elucidated only decades after they had already been in use [24].

4.4 The manifestation of Yin-Yang theory in TCM regarding specific diseases

In clinical practice, Yin-Yang theory in TCM is not an abstract concept, but a concrete clinical issue. When confronting a patient, the physician seeks to determine whether the patient's condition is characterized by Yin deficiency or Yang deficiency, excess Yin or hyperactivity of Yang, whether a Yin disorder affects Yang or Yang deficiency affects Yin, and whether the appropriate approach is to nourish Yin, warm Yang, drain fire, or disperse cold. This series of inquiries transforms Yin-Yang theory from philosophical speculation into clinical operation.

The reason why "in observing the complexion and palpating the pulse, first distinguishing Yin and Yang" has become a core rule in TCM diagnosis and treatment is precisely that classification in terms of Yin and Yang directly determines the direction of treatment. Even when the same symptom of fever is present, treatment varies according to the judgment of Yin and Yang. If it is classified as an excess-heat pattern (Yang), cool-property medicines are used to clear heat and drain fire; if it is classified as a deficiency-heat pattern characterized by Yin deficiency with Yang hyperactivity, Yin-nourishing medicinals are used to subdue Yang and reduce fire; if it is classified as a pattern of true cold with false heat due to excessive Yin rejecting Yang, heat-property medicines should instead be used to guide fire back to its origin. Thus, the same symptom may require entirely opposite treatments because of different judgments of Yin and Yang. This is a typical manifestation of treating the same disease with different methods in TCM, and the significance of Yin-Yang theory in TCM lies in its ability to guide effective clinical decision-making.

The principal form in which Yin-Yang theory is applied at the level of disease in TCM is the pattern. A pattern is not a single symptom, but a cluster of internally related symptoms, constituting a functional summary of the overall state of a disease at a particular stage. Patterns such as kidney Yang deficiency, heart Yin deficiency, and hyperactivity of liver Yang are, in essence, manifestations of Yin-Yang imbalance in specific Zang-Fu organs and specific diseases.

Take kidney Yang deficiency pattern as an example: this pattern does not refer to a localized lesion in a single organ, but rather to a comprehensive summary of the functional state underlying a cluster of symptoms including aversion to cold, cold limbs, soreness and weakness of the lower back and knees, fatigue and lassitude, profuse clear urination, frequent nocturia, a pale and enlarged tongue with white coating, and a deep, slow, and weak pulse. Although these symptoms appear to involve multiple systems, their internal unity lies in the pathological essence that "Yang deficiency leads to cold". Research by Academician Ziyin Shen et al. [25] has shown that this pattern is regularly associated with hypofunction of the hypothalamic-pituitary-adrenal/thyroid/gonadal axes, confirming that Yin-Yang theory in TCM has an objective physiological and pathological basis at the level of disease.

The formation of a pattern follows the logic of "inferring the viscera state from the manifestations": internal Yin-Yang imbalance necessarily reveals itself through external symptoms [26]. By collecting these "manifestations" through the four diagnostic methods and then conducting an integrated analysis on the basis of Yin-Yang theory, the physician can infer the underlying pathomechanism. This cognitive path, proceeding from manifestations to the viscera state, bears a striking resemblance to the way contemporary systems biology infers network states from phenotypes.

5 The modern scientific connotations of Yin-Yang theory in TCM

With the advancement of modern science, especially the rapid development of systems science, complexity science, and molecular biology, the modern scientific connotations of Yin-Yang theory in TCM have increasingly become a focus of research. Scholars have attempted to reinterpret the contemporary value of this ancient theory through multiple approaches, including systems biology [27], mathematical modeling [28], and physical measurement [29].

5.1 Predictability at the micro level

At the micro level, Yin-Yang theory in TCM can be translated into concrete hypotheses subject to empirical

testing, and such predictive power is an important marker of scientificity. On the basis of the principle that "Yang deficiency leads to cold", it can be predicted that patients with kidney Yang deficiency exhibit hypofunction in energy metabolism pathways. Academician Ziyin Shen et al. [30] found regular associations between kidney Yang deficiency pattern and reduced function of the hypothalamic-pituitary-adrenal axis, thyroid axis, and gonadal axis, thereby confirming the predictive validity of the theory. On the basis of the principle that "Yin deficiency leads to heat", it can likewise be reasonably predicted that patients with Yin deficiency pattern should exhibit manifestations of metabolic hyperactivity, such as an elevated basal metabolic rate and enhanced sympathetic excitability [31].

More importantly, the principle of opposition and mutual restraint between Yin and Yang provides a distinctive guide for micro level discovery. According to this logic, once the function of one molecule is clearly identified, it can be inferred that there may exist a corresponding molecule with an opposite and mutually restraining function. For example, upon identifying oncogenes that promote cell proliferation, one may predict the existence of tumor suppressor genes that inhibit cell proliferation; the two mutually restrain one another to maintain the normal operation of the cell cycle [32]. On the basis of the principle of mutual rooting between Yin and Yang, it may further be inferred that two molecules may have corresponding structural relationships or form mutually restraining regulatory circuits within signaling pathways. This predictive capacity grounded in Yin-Yang theory gives it a forward-looking character at the micro level that goes beyond ex post explanation, and provides a distinctive theoretical tool for discovering new molecular targets and elucidating the regulatory mechanisms of signaling pathways.

5.2 Falsifiability and scientific testing

Falsifiability is a core criterion in modern philosophy of science. The scientific value of a theory lies not in being eternally correct, but in being open to testing and allowing itself to be falsified. At the micro level, research on Yin-Yang in TCM is advancing precisely along this line of logic. The correlation between kidney Yang deficiency and hypofunction of the hypothalamic-pituitary-target gland axes is a proposition that can be tested experimentally. If subsequent studies are to show that such a correlation does not exist, exists only in certain subtypes, or is inconsistent across different populations, the original understanding will need to be revised and refined. It is precisely this process of continuous testing and constant improvement that drives research on patterns in TCM toward greater depth. Falsifiability is also reflected in the delineation of the boundaries of Yin-Yang theory in TCM, for it is not universally applicable. For example, in the early stage of acute infectious diseases, the imbalance of Yin and Yang often manifests as exuberance of Yang, whereas with disease progression it may transform into Yang deficiency. This pattern of transformation can itself be tested through empirical research. It is precisely this openness to testing and refutation that has enabled Yin-Yang theory in TCM to move beyond metaphysical speculation and gradually acquire the characteristics of modern science at the micro level.

5.3 The unique value beyond reductionism

Predictability and falsifiability provide the basis for relating Yin-Yang theory in TCM to modern science, while its value beyond reductionist approaches reveals its distinctive methodological significance. This is also the aspect in which Yin-Yang theory in TCM is most illuminating for modern life sciences [33]. Reductionism has achieved remarkable results in the life sciences by revealing the molecular basis of life phenomena. Yet when faced with the human body as a complex giant system, an excessive focus on isolated elements can easily lead to the predicament of "seeing the trees but not the forest". Yin-Yang theory in TCM offers precisely a mode of thought complementary to reductionism, and this distinctive value is manifested in the following four dimensions.

5.3.1 A holistic orientation toward quantifiability The quantification of Yin-Yang theory in TCM does not aim to identify a single gold-standard molecule, but rather to reflect the overall functional state of the system through the integration of multiple indicators. Take kidney Yang deficiency as an example: rather than searching for a single biomarker of kidney Yang deficiency, Academician Ziyin Shen's team examined multi-level hormonal profiles across the hypothalamic-pituitary-adrenal axis, thyroid axis, and gonadal axis, and combined these with parameters such as energy metabolism and immune function to construct a multidimensional evaluation system [34]. This form of quantification seeks a comprehensive characterization of systemic state, rather than the precise identification of a single causal chain. At the level of mathematical modeling, scholars have attempted to model TCM systems through a complex-valued five-agent network, using complex variables to represent Yin-Yang properties and network coupling to characterize the generating and restraining relationships of the five elements. Here again, the logic of quantification is grounded in holistic systems analysis rather than in reducing complex physiological and pathological processes to a few isolated variables [35].

5.3.2 Nonlinear thinking The reductionist paradigm is accustomed to linear causal explanations and tends to seek simple correspondences such as gene-disease and

target-drug relationships. Life systems, however, are nonlinear in nature: small perturbations may trigger enormous responses, whereas strong interventions may sometimes produce only limited effects. Yin-Yang theory in TCM embodies a mode of nonlinear thinking. The waxing and waning of Yin and Yang proceed in cyclical fluctuations [36], and transformation occurs at critical points, so that once a threshold is crossed, a qualitative change takes place, as expressed in the proposition that "extreme Yin transforms to Yang, and extreme Yang transforms to Yin". Yin and Yang mutually constrain one another and serve as each other's precondition, forming a typical nonlinear coupling relationship. This nonlinear mode of thinking is widely reflected at the micro level. Phenomena such as switch-like behavior in cellular signaling pathways [37], bistability in gene regulatory networks [38], and cytokine storms in immune responses [39] can all be viewed anew from the perspective of Yin-Yang transformation, thereby providing a cognitive framework for understanding biological complexity that differs from linear reductionism.

5.3.3 A view of network regulation The opposition and mutual restraint, as well as the mutual rooting and mutual use, of Yin and Yang correspond to such relationships in biological networks as positive and negative feedback, activation and inhibition, and synergy and antagonism [40]. On this basis, therapeutic strategies in TCM do not rely on precise targeting of a single molecular target, but seek to restore the overall homeostasis of the network through the synergistic intervention of multiple targets in compound prescriptions. This is highly consistent with recent developments in systems biology and network pharmacology. Study has shown that complex diseases such as hypertension, diabetes mellitus, and tumors are frequently associated with dysregulation across multiple signaling pathways [41]. Under such conditions, simply blocking a single target often fails to produce satisfactory therapeutic effects and may readily give rise to compensatory activation or drug resistance. Through the synergistic action of multiple components on multiple targets, Chinese medicinal compound prescriptions regulate multiple nodes within the network and restore homeostasis, thereby providing a new therapeutic approach to complex diseases that differs from single-target intervention.

5.3.4 The clinical grounding of operability The scientific connotations revealed by Yin-Yang theory in TCM at the micro level are always oriented toward clinical translation, and therefore need to be transformed into diagnostic biomarkers, therapeutic targets, or indicators for evaluating therapeutic efficacy. Academician Ziyin Shen's research on kidney Yang deficiency pattern not only verified the association between Yang deficiency and hypofunction of endocrine axes, but also promoted the standardized clinical application of warming Yang methods, thereby endowing warming Yang and kidney tonifying prescriptions with clearly defined indications and efficacy criteria [42]. Differences in the Yin-Yang attributes of mitophagy across different diseases provide a basis for formulating therapeutic strategies aimed at enhancing or inhibiting mitophagy, thereby directly guiding clinical decision-making. Likewise, understanding the association between the state of Yin deficiency-induced internal heat and sympathetic excitability provides a modern scientific explanation for the use of Yin-nourishing and fire-subduing methods in the treatment of diseases such as hypertension and insomnia. This capacity for translation from micro level discovery to clinical application is precisely an important characteristic of Yin-Yang theory in TCM as a medical theory, and also the source of its value beyond purely reductionist research.

5.4 Digital representation and scientific testing

The deep integration of artificial intelligence and multiomics technologies is driving Yin-Yang theory in TCM from qualitative description toward a digital paradigm that is quantifiable, computable, and falsifiable. At the core of this process is the mapping of abstract Yin-Yang states onto multidimensional measurable datasets, followed by empirical testing through large-sample statistical analysis.

Information derived from the four diagnostic methods has been among the first to be objectively collected and quantified. In tongue diagnosis, automated tongue image analysis systems based on convolutional neural networks (CNNs) are capable of performing pixel-level analysis of tongue images and transforming phenotypic features such as tongue color and coating characteristics into standardized digital vectors, thereby completing the transition from experience to data [43]. In pulse diagnosis, the combination of piezoresistive sensor arrays with mobile platforms enables real-time capture of radial artery pulse waves, while deep learning is used to extract time-frequency features, thereby achieving objective classification of fundamental pulse qualities such as floating, deep, slow, and rapid. On the basis of a dataset comprising 2 127 pulse records, the CNN model achieved a classification accuracy of over 95%, and denoising through autoencoders further laid the signal foundation for the digitalization of pulse diagnosis [44].

At the micro level, bioinformatics has strengthened the falsifiability of the theory. Using public datasets, one study identified 217 differentially expressed genes associated with Yin deficiency patterns and 189 differentially expressed genes associated with Yang deficiency patterns. Combined with weighted gene co-expression network analysis (WGCNA), six core gene modules strongly associated with Yin deficiency and five functional

modules significantly associated with Yang deficiency were identified. A pattern classification model was then constructed using a random forest algorithm implemented in R software, achieving a predictive accuracy of 89.7%. This analysis elucidated the spatial gene expression characteristics of Yin deficiency and Yang deficiency patterns, and provided quantifiable genetic evidence for the molecular classification of states of Yin-Yang imbalance [45]. Digital representation and scientific testing provide an objective and reproducible path for validating Yin-Yang theory in TCM, thereby promoting the transformation and upgrading of traditional theory toward a modern scientific paradigm.

6 Implications of Yin-Yang theory in TCM for life sciences

6.1 Giving rise to a new paradigm of state-based medicine research

Driven by the reductionist paradigm, modern medicine has developed a disease-centered model of diagnosis and treatment, whose core lies in identifying clearly defined pathological targets and then implementing precise intervention. This model has achieved remarkable success in the treatment of acute diseases and monogenic disorders.

However, when confronted with complex chronic diseases such as hypertension, diabetes mellitus, and autoimmune disorders, its limitations have gradually become apparent. Such diseases often cannot be adequately explained by a single molecular abnormality, and even when interventions are directed at specific targets, the therapeutic response may be characterized by temporary improvement in certain indicators followed by rebound after treatment discontinuation. The key issue is that disease may not simply reflect dysfunction in isolated components, but rather a systemic imbalance in the body's overall functional state, and TCM patterns describe such global states.

Modern research on patterns, namely pattern biology, has become an important bridge connecting traditional theory with modern science [46]. Take kidney Yang deficiency as an example. Some scholars have found that this pattern does not correspond to an abnormality in a single endocrine axis, but rather manifests as generalized hypofunction across multiple target gland axes, including the hypothalamic-pituitary-adrenal, thyroid, and gonadal axes. This reveals a key fact: as a complex giant system, the maintenance of homeostasis in the human body depends on coordination and antagonism across multiple systems and multiple levels. When this network coordination fails, it manifests as a specific pattern. This finding provides an important example for investigating the systemic mechanisms of complex diseases.

The possible "state-based medicine" paradigm that may arise from this has as its central proposition that disease is essentially an imbalance in the body's overall state rather than a functional abnormality of isolated targets [47]. The future development of medicine should lie in the complementary integration of disease-based medicine and state-based medicine, with the former emphasizing precise intervention and the latter focusing on overall coordination. Together, they constitute a more complete medical landscape.

6.2 New approaches to the treatment of complex chronic diseases

To make this paradigm more clinically actionable, type 2 diabetes mellitus can be taken as an example. Modern medicine emphasizes precise intervention with glucose-lowering drugs, yet the same therapeutic regimen may produce markedly different effects in different patients. From the perspective of state-based medicine, such differences may reflect variation in patients' overall functional states. Some patients present with deficiency of both Qi and Yin, as in populations characterized by insulin resistance together with relatively insufficient insulin secretion [48]; some present with damp-heat encumbering the spleen, as in obese populations accompanied by chronic inflammatory states [49]; and some present with deficiency of both Yin and Yang, as in patients at later stages of the disease accompanied by multisystem functional decline [50]. The combination of precise glucose-lowering intervention with overall regulation may be more effective in restoring the body's network homeostasis, and may thus provide a more comprehensive basis for individualized treatment.

6.3 Building a life science system with Chinese originality

In summary, predictability and falsifiability give Yin-Yang theory in TCM a testable empirical basis at the micro level, allowing it to engage with modern science in a verifiable way. Meanwhile, its value beyond reductionism reveals its deeper significance as a distinctive methodological resource: it seeks to quantify overall states rather than precisely identify single targets, to grasp patterns of nonlinear transformation rather than linear causal chains, to focus on the regulation of network homeostasis rather than intervention in isolated components, and to orient itself toward clinical applicability rather than stopping at the discovery of mechanisms.

The three levels support one another and together constitute a complete picture of how Yin-Yang theory in TCM moves from traditional speculation toward modern science. The significance of this transformation lies in the fact that Yin-Yang theory in TCM is no longer merely a form of traditional knowledge to be explained or verified, but a living theoretical system that can engage with modern science and offer distinctive methodological resources for life science research. It meets the basic

requirements of modern science in terms of predictability and falsifiability, while retaining its distinctive character beyond reductionism, thereby demonstrating enduring vitality in the dialogue between tradition and modernity and in exchanges between Chinese and Western knowledge systems.

7 Conclusion

The Yin-Yang theory in TCM has undergone a layered evolution from philosophy at the macro level to medicine at the meso level and ultimately to science at the micro level. While appropriating the core principles of Yin-Yang theory in philosophy, it has bracketed and transformed abstract propositions such as cosmological speculation within a medical context, thereby achieving a practical leap from philosophy to medicine.

The value of this theory ultimately depends on its clinical efficacy. Over the centuries, it has run through every stage of diagnosis, treatment, medication, and health preservation, forming a medical system centered on "achieving balance". Future research should respect its philosophical origins, remain grounded in clinical practice, and integrate modern science so as to promote innovative development in the life sciences.

Accordingly, Yin-Yang theory in TCM is not only links between ancient wisdom and modern science, but also offers distinctive Eastern insights for building a life science system with Chinese originality.

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Author contributions

Miao Ouyang: data curation, conceptualization, writing – original draft, and writing – review & editing. Gedi Zhang: investigation and validation. Mengdan Yu: data curation. Hongning Liu: methodology, supervision, project administration, and formal analysis. All authors approved the submission and take responsibility for this manuscript.

Competing interests

The authors declare no conflict of interest.

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中医阴阳理论的宏观、中观与微观：一阴一阳，三层意蕴

欧阳苗[a], 张格第[b], 喻梦丹[c], 刘红宁[b*]

a. 江西中医药大学学生工作处, 江西 南昌 330004, 中国
b. 江西中医药大学高等研究院, 江西 南昌 330004, 中国
c. 江西中医药大学中医基础理论分化发展研究中心, 江西 南昌 330004, 中国

【摘要】阴阳理论是中医基础理论的核心内容之一，但其哲学或科学属性的归类历来争论不休。针对中医阴阳理论哲学属性与科学属性的长期争议，本文首次提出宏观、中观、微观三层次划分，用以化解非哲即科的二元对立。在宏观维度，阴阳为中国古代自然哲学的成果，阐述的是宇宙运行的普适规律，此为哲学阴阳；在中观维度，经《黄帝内经》的转化，阴阳成为指导临床辨证论治的医学方法，此即医学阴阳；在微观维度，中医阴阳理论与现代科学逐渐融合，展现出可检验、可重复的科学特性，此即科学阴阳。中医阴阳与一般阴阳哲学存在核心应用与实践属性的显著差异：其在医学转化进程中，有选择性地汲取了与生命现象相关的内容，同时将宇宙论思辨等抽象命题在医学语境中加以悬置与具体化，进而实现了从哲学到医学的实践性跨越。基于此，本研究从哲学根源、临床应用、现代科学阐释及其对生命科学的启示四个方面展开分析，论证了中医阴阳理论作为辨证论治总纲的逻辑依据，梳理了其在系统科学、网络调控等视角下的现代研究进展，并探讨了其在推动状态医学新范式方面的潜在价值。研究认为，对中医阴阳理论的准确认知应突破非哲学即科学的二元思维框架，具体问题具体分析。在不同维度上，该理论兼具哲学、医学和科学属性。唯有立足临床实际疗效、面向现代科学，方能推动中医阴阳理论的创新发展，为构建具有中国原创性的生命科学体系提供有益的东方智慧。

【关键词】中医阴阳理论；层级分析；生命科学；系统科学；复杂科学