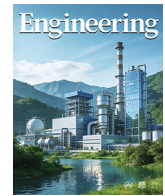




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XiangShu Omics: A Framework Based on the Spatio–Temporal Field Rhythms of Human Life and Systems Intelligence Methodology

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ABSTRACT

This review is the first to systematically propose and construct XiangShu (image–number) omics (XSO) that inherits the ecological values, epistemology, and methodology of traditional Chinese medicine (TCM), and absorbs modern mathematical sciences. We reposition XSO as a “promising research paradigm” rather than a definitive solution, serving as an exploratory computational bridge to address the epistemological chasm. By integrating the four diagnostic methods of TCM with cutting-edge multimodal technologies spanning acoustics, optics, thermodynamics, mechanics, electromagnetism, and magnetism, Xiang omics is established based on multiscale phenotypic data ranging from astronomical and geographical parameters to human macro-, meso-, and micro-level physiological characteristics. The Xiang data are then computed into Shu (number) Omics using classical TCM numerology and modern artificial intelligence. Shu omics contains two tiers of models. The small model aims to elucidate Yin–Yang dynamics conceptualized as a mathematical classification model; the progression from pre-disease to disease to recovery modeled via Shannon entropy-based predictive frameworks; the five-element relationships represented through complex functional equations. The large model integrates large language models (LLMs) based on the classical therapeutic logic of principle–method–formula–medicine, such as the Shu-Zhi Qihuang large model. Both models work together to support intelligent reasoning and system-level knowledge synthesis. Driven by the dual engines of data-intensive and experience-driven “blind computation” and “directed inference,” XSO enables a panoramic decoding of human life rhythms across temporal, spatial, and field dimensions, thereby inform clinical decision-making and precision-oriented interventions in TCM.

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1. XiangShu omics (XSO) to decode the temporal–spatial–field rhythms (TSFRs) of life

1.1. TSFRs in the life cycle

Life is a cycle of dynamic coupling and evolution across three dimensions of time, space, and field (TSF). In analyzing a disease,

therefore, we should move beyond the view of a reductionist, which regards a disease as something isolated within a specific organ or associated with a single molecular target, to a dynamic, holistic, and network-oriented perspective that deepens into the rhythms of life. A precise decoding of such multi-dimensional and nonlinear TSFRs is essential to addressing the pressing challenges in modern medicine, namely, chronic illnesses, complex systemic disorders, and population aging.

As life sciences keep opening their new chapters, genomics and subsequent phenomics have been established, marking that scientific exploration has stepped up from the molecular level to the system level. Phenomics also provides a pathway for the

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modernization of traditional Chinese medicine (TCM) theories [1]. Through quantifying TCM expressions on clinical diseases, modern technologies can be employed to standardize the phenotypes of syndromes, constitutions, and others. Then, the phenomic data are based on for constructing medical models. In the present study, we make a step forward by proposing XSO, a new paradigm in TCM research that integrates the methodologies of phenomics and systemic biology.

As suggested in TCM theories, a disease has its own temporal rhythm. Wu Yun Liu Qi can elucidate the patterns of climatic changes in nature and their influences on human physiology and pathology, thereby guiding disease prevention and treatment [2]. Wu Yun refers to the five fundamental elements, including wood, fire, earth, metal, and water that show cyclical transformations in the cosmos; Liu Qi denotes six climatic or energetic states, including wind, cold, summer heat, dampness, dryness, and fire, which reflect the influences of the dynamic environment on the human body. Tian Gan Di Zhi, an ancient Chinese calendrical framework to denote years, months, days, and hours [3], can predict how macro-environmental periodicity regulates human physiological functions over time. This regulatory effect is not a simple linear causality, but a nonlinear, resonance-based periodic interaction. At the macroscopic level, the temporal rhythm manifests the macro-cyclic regulation of Wu Yun Liu Qi over regional climate and phenological patterns. At the mesoscopic level, it reflects the periodic activities of physiological processes, including hormonal synthesis and secretion, immune modulation, and the traditional concept of organ-time coordination (Zang-Fu Zhushi) in TCM. At the microscopic level, the temporal rhythm can be implicated in periodic biochemical oscillations, such as circadian gene expression, signal transduction, and other cell-level regulatory pathways [4–8]. Temporal rhythms can be modeled with an array of techniques, such as multi-periodic Fourier decomposition and transformer-based algorithms, that can encode macroscopic temporal features as external periodic drivers, and then embed them into coupled differential equations (CDEs) that describe the dynamic interactions among Zang-Fu organs. A successful modeling enables to predict the time point of disease onset, guide the practice of chronopharmacology, and optimize therapeutic dosing windows [9–12]. Chi-square tests have confirmed that an individual's innate constitution is significantly associated with the risk of later coronary heart disease [13–16], providing a robust evidence for quantifying the temporal features of diseases.

As to the spatial rhythm, a life involves the complex coupling between internal bodily space and external geographical space. The internal space refers to the human body's intrinsic network of Zang-Xiang and meridians, which embodies multi-organ interactions, heterogeneous aging, and disease transmission and transformation [17]. Conventional linear statistical methods are inadequate for capturing the high-dimensional, non-Euclidean topologies inherent in such spatial structures. Therefore, a successful modeling should incorporate algebraic topology and graph neural networks (GNNs) [18,19]. In this framework, Zang-Fu organs can be abstracted as nodes within a graph, while the generative and restrictive relationships among the five elements (Wuxing Shengke), a foundational theory in ancient Chinese philosophy that explains the composition and interactions of things in the universe through the five elements metal, wood, water, fire, and earth [20], along with meridian linkages, are modeled as edges. This allows for quantitative prediction of the optimal pathways and temporal delays of disease transmission [21]. A model has been constructed to predict the spatiotemporal dynamic propagation of tau protein in the context of neurodegenerative diseases. This model is trained using longitudinal Tau positron emission tomography imaging data, and reports a high performance, with an error rate of less than 5% in predicting node-wise propagation delay and a Pearson

correlation coefficient exceeding 0.9 ($r > 0.9$) for predicted versus observed trajectories [22]. These results prove the capability of GNNs in predicting disease transmission pathways, and model the multi-dimensional topological structures of complex biological systems. The impact of external geographical factors, such as altitude and climatic zones, on TCM syndromes may also be analyzed using geographic information systems (GISs) that can provide region-specific strategies [23]. For example, a cross-sectional study involving 22 081 residents across seven distinct regions of China revealed that the prevalence of osteoporosis was significantly higher ($P < 0.05$) in inland regions, such as the southeast, southwest, northwest, and northeast, compared to eastern coastal regions [24]. Among 1602 patients with rheumatoid arthritis from 18 research centers across China, another syndrome differentiation analysis reveals that the distribution of TCM syndromes varies significantly ($P < 0.05$) across these geographical regions characterized by distinct temperature, barometric pressure, and humidity profiles [25].

At the field level, the rhythm reflects the interactions between the body's internal energy fields and the external physical fields. The dynamic changes in the “field” can be quantified with modern non-contact sensing acoustic, optical, thermal, mechanical, electrical, and magnetic technologies [26]. For instance, high-resolution infrared thermography can acquire surface temperature field distributions, enabling the quantitative assessment of disease natures, such as coldness/heat and deficiency/excess [27]. In parallel, bioelectromagnetic sensors can measure bioelectrical impedance along meridian pathways, thereby capturing Qi dynamics (Qi Ji) [28]. Physical signals can be converted into tensor structures, and algorithms such as tensor decomposition can be used to analyze their field features. The goal of field rhythm analysis is to provide physics-based evidence for the regulatory mechanisms of meridian-acupoint systems, thereby providing guidance for interventions such as acupuncture and Tuina (Chinese therapeutic massage).

XSO can be employed to construct high-dimensional, dynamic, and network-based predictive models that provide a time window for proactive interventions [29,30]. For instance, the BianqueNet model has been constructed to quantify the imaging data during the latent phase of spinal degeneration, thereby providing an early warning of critical transition points in disease progression [31]. According to TCM theory, kidney essence (Shen Jing), the vital substance stored in the kidneys, underpins the occurrence, rise, and maintenance of life. A model has simulated the dynamic curve of Shen Jing over the full life cycle, and predicted the time point of its decline, typically sharply after the age of 40, during which timely, system-level interventions should be taken to mitigate frailty and reduce fall risks [32]. In addition, XSO models can detect the high-profile signals during the pre-onset stage, thus allowing earlier warning than traditional molecular biomarkers, especially in the prevention and control of chronic and complex diseases [33]. In summary, XSO represents a major step forward in the translation of the TCM theories into a modern scientific paradigm that is modelable, computable, and verifiable.

1.2. Limitations of current computational paradigms

Current computational paradigms exhibit ontological and methodological limitations in bridging TCM and modern medicine. Both reductionism and purely data-intensive frameworks fall short in capturing the logic that underpins TCM theory. Reductionists tend to attribute the etiology of a diseases to certain molecules, and rely on simple models to simulate disease processes. Such methods are fundamentally incompatible with the TCM theory that regards a disease as a result from the synergy of multiple factors, targets, and systems [34]. The digital transformation of TCM

faces a box of challenges, including low data quality, lack of standard protocols, and poor data utilization efficiency [35,36]. Traditional medical records often consist of handwritten notes, inconsistent terms, and four diagnostic methods data that lack objective quantifiable standards, all of which hinder the construction of high-quality, interoperable databases. Furthermore, computational models based solely on data-driven “blind computation” may uncover statistical correlations, but their black-box nature results in a limited explainability and a poor capacity for mechanistic interpretation [37].

Rooted in the ancient cosmological systems of the HeTu and LuoShu, XiangShu (image–number) represents an ontology that unifies the width of “image” (Xiang) and the precision of “number” (Shu) [38–40]. XiangShu methodologies can transform obscure information of TCM into “soft constraints” [41]. Besides, systemic intelligence, centering on explainable artificial intelligence (XAI), can be employed to ensure that every step in TCM knowledge computation is quantitative and can be traced back to a theory (Li) (Fig. 1, Table S1 in Appendix A).

1.3. XSO: A model based on system intelligence (SI)

Here we propose XSO as an SI-based methodology for computation in the context of TCM. At its core is a bidirectional computational engine, coordinated by an integrated dialectical hub. This engine operates through the synergistic coupling of two layers: data acquisition and symbolic abstraction layer, and the computational modeling and algorithmic reasoning layer. The former acquires TSF phenotypic features to construct a Xiang omics database. The latter is dedicated to building Shu omics, an integrated computational architecture that combines both small models and large models to analyze and predict TSFRs. Specifically, we formalize the operational distinction between the two layers: ① Xiang omics is defined as the “perception and representation layer”, responsible for data acquisition and the standardization of phenotypic features to answer “What is the state?” As the digitization of phenotypes, feature vectors (e.g., tongue geometric features) are generated on this layer. ② In contrast, Shu omics is the “algorithmic and reasoning layer”, responsible for abstract reasoning, dynamic prediction, and systemic control to answer “How do relationships evolve?” (Table S2 in Appendix A).

The integrated dialectical hub, as the core responsible for logic reasoning, resolves conflicts, ensures coherence between the two layers, and validates initial decisions. In the Xiang layer, various technologies, such as hyperspectral imaging, sensor arrays, and tensor decomposition, collectively generate multimodal fusion feature vectors and construct a high signal-to-noise ratio (SNR) database. In the Shu layer, an architecture is constructed through technologies including symbolic regression (SR) for uncovering interpretable functional relationships, GNNs for modeling the topology of physiological systems and syndrome networks, and large language models (LLMs) for semantic representation and reasoning over TCM knowledge. In the theoretical layer, TSFRs are decoded to inform clinical decision-making through techniques including criticality theory, chronopharmacological algorithms, and prospective clinical trial validation.

An innovation of XSO lies in its ability to translate experiential knowledge in TCM into computable basic units, termed TCM knowledge units (TCM-KUs). A TCM-KU is mathematically formalized using fuzzy set theory and manifold learning as [42,43]:

$$\text{TCM-KU} = \Phi \left(\sum_i \omega_i \cdot \text{Phenotype}_i \right)$$

where Phenotype_i represents quantitative features from Xiang omics, ω_i is a Gaussian membership function (e.g.,

$\omega_{\text{Heat}}(p_i) = \exp \left(-\frac{(p_i - c_{\text{Heat}})^2}{2\sigma_{\text{Heat}}^2} \right)$, where p_i denotes the observed value of the i th phenotype feature, c_{Heat} represents the center parameter reflecting the prototypical state, and σ_{Heat} signifies the width parameter determining the range of fuzzy boundaries) that quantifies the fuzzy degree of a syndrome (e.g., heat), and Φ is a non-linear mapping operator (implemented via variational autoencoder (VAE) or spectral embedding) that projects features into a low-dimensional latent space of TCM semantics. This mechanism fulfills a threefold function: ① structured expression of fuzziness in TCM, ② computable modeling of complexity in TCM, and ③ modern interpretation of TCM philosophy. The XSO aims to achieve a panoramic, high-precision, and explainable analysis of TSFRs in human life (Fig. 2).

2. Xiang omics

2.1. Xiang data acquired with the four diagnostic methods

As the perception layer within the XSO, Xiang omics transforms the information obtained through traditional four diagnostic methods into objective, standardized, and quantifiable data through high-precision sensing and codified operational protocols.

Inspection (Wang Zhen) results can provide a source of data for Xiang omics. Tongue features can reflect the status of the Zang–Fu organs, Qi and blood, and body fluids. A hyperspectral imaging system (HIS) can allow the capture and extreme quantification of tongue features with a spectral resolution far beyond the that of naked eyes [44]. HIS can capture the reflectance and absorbance of narrow wavebands (e.g., 400–1000 nm), allowing an extreme quantification of water content in the tongue fur (reflecting moisture and dryness) and hemoglobin absorption rates (reflecting blood stasis) [45]. Through this system, information of “yellow or white tongue fur” and “red or crimson tongue body” can be acquired and built into a spectral reflectance matrix [46]. Then, deep convolutional neural networks (CNNs) or U-Net architectures are employed to perform high-precision semantic segmentation, enabling automated delineation of regions such as the tongue body, fur, marks, and cracks. Geometric features are then transformed into feature vectors in Xiang omics. For instance, the topological complexity of surface cracks serves as a geometric quantification index for “deficiency in body fluids” (Jin Ye Kui Xu) [47–49]. To ensure data consistency, stringent standards should be established to specify ambient lighting, camera angles, and image preprocessing to eliminate environmental and operator-related variability [50,51].

For inquiry (Wen Zhen) and auscultation/olfaction (Wen Zhen), natural language processing (NLP) techniques, particularly transformer and bidirectional encoder representations from transformers (BERT), can be employed to extract semantic labels and perform entity recognition (e.g., diseases, syndromes, and prescriptions) from unstructured medical records and consultation transcripts. These entities are subsequently encoded using standardized ontologies. Furthermore, sentiment analysis techniques (a subset of NLP for detecting and extracting emotional information from the text) are applied to objectively quantify the patient’s subjective psychological state from a transcript written in classical Chinese expressions and inconsistent terms [52–54]. For auscultation/olfaction, high-fidelity microphone arrays and acoustic feature extraction technologies are employed to capture and analyze vocal and respiratory sounds. These data are then systematically correlated with traditional syndrome patterns such as Qi deficiency, often manifested as low and feeble voice, and phlegm-dampness, typically associated with heavy and turbid coughing sounds [55,56]. In palpation (Qie Zhen) or pulse diagnosis (Mai Zhen), Xiang omics leverages high-resolution pressure sensor arrays, with sub-millimeter spatial resolution, to precisely capture subtle

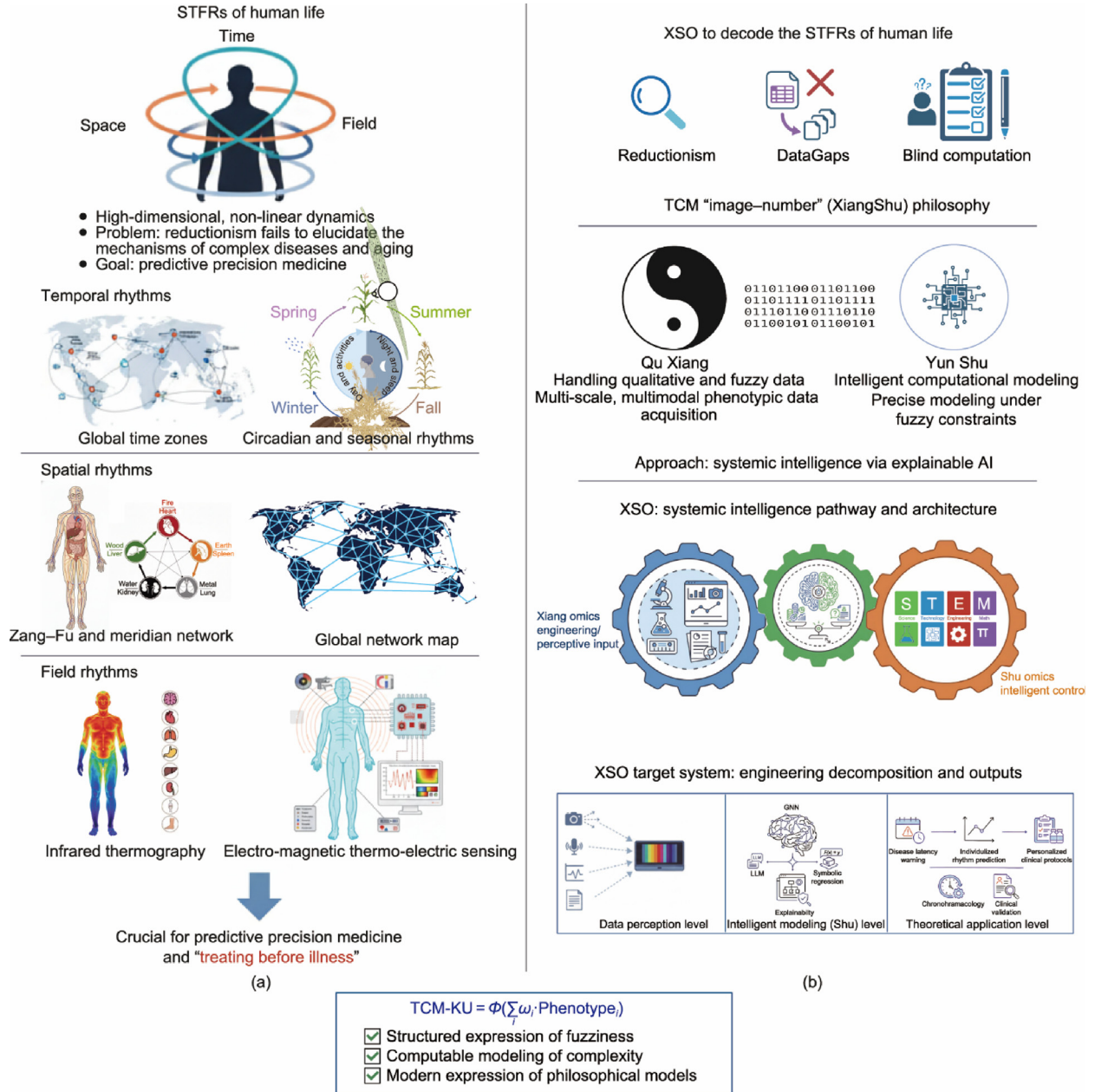


Fig. 1. XSO to decode the TSFRs of human life. (a) The TSFRs of human life. The figure shows the temporal (circadian/seasonal), spatial (Zang-Fu/geographic), and field (physical energy) rhythms that may be employed to realize the goal of precision medicine and "treat diseases before onset." (b) The philosophy to develop XSO. XSO is based on an architecture derived from TCM "image (Xiang)-number (Shu)" philosophy and operated by a systemic intelligence framework. Rather than simply through reductionism and blind computation, XSO utilizes explainable AI to generate standardized TCM knowledge unit (TCM-KU). AI: artificial intelligence; LLM: large language model; Phenotype_i: quantitative features from Xiang omics; ω_i : a Gaussian membership function that quantifies the fuzzy degree of a syndrome; Φ : a non-linear mapping operator that projects features into a low-dimensional latent space of TCM semantics.

waveforms and multi-point positional features of pulses from the radial artery. The sensors are integrated with adaptive pressurization and torque calibration modules to eliminate variability introduced by the practitioner's finger pressure, thereby ensuring reproducibility and standardization of acquired data. Subsequently, the acquired temporal mechanical signals are processed through wavelet transformation and fast Fourier transform (FFT) to extract harmonic components of the pulse waveform. Macro-level descriptors traditionally used in pulse diagnosis, such as pulse rate (Mai Lü), pulse amplitude (Mai Fu), and pulse tension (Jin Zhang), are systematically translated into quantitative mathematical parameters, including dominant frequency, harmonic coefficient, energy distribution, and pulse wave propagation velocity.

For instance, dual-pathway deep learning networks, such as B-Net, have been employed to extract prototype features from pulse waveforms, like energy distribution and propagation velocity, with a high accuracy in both simulated and experimental datasets [57]. Intelligent algorithms can autonomously identify multidimensional pulse signals (e.g., six-dimensional parameter spaces), achieving a recognition accuracy up to 97.8%, which has enabled their integration into wearable health devices for disease prediction and real-time physiological monitoring [58,59].

Despite the significant advancements in the quantification of the four diagnostic methods, the Xiang-based acquisition system still faces critical challenges on its path toward large-scale, multicenter clinical implementation. Firstly, the substantial

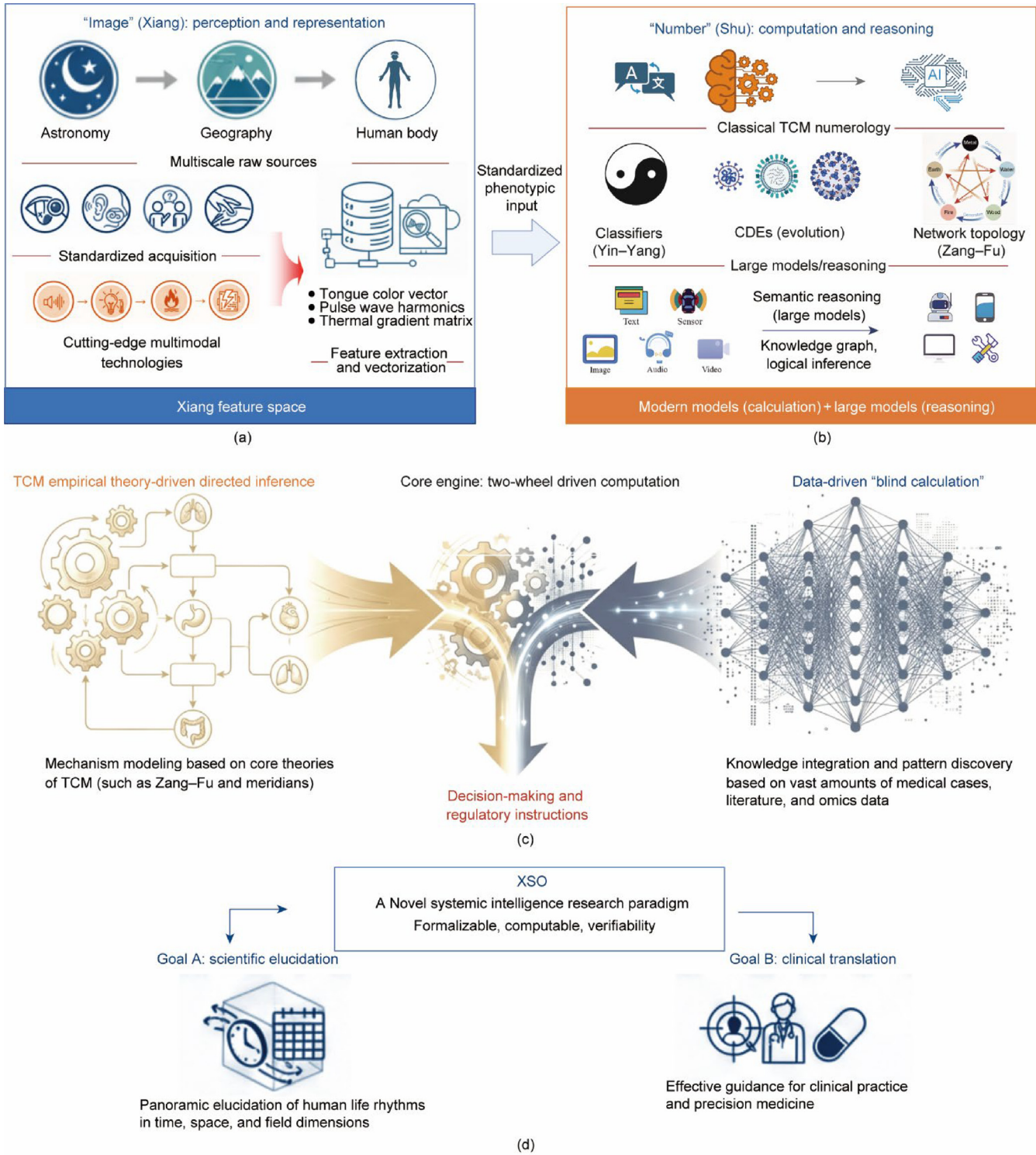


Fig. 2. The architecture and SI in XSO. (a) Xiang (image) data system is established through the information acquired through TCM diagnostics and standardized through multimodal sensing. (b) Shu (number) algorithmic system combines TCM numerology with modern AI (incorporating small and large language models). (c) The core engine operates via a "two-wheel" mechanism welding data-driven "blind computation" with theory-guided "directed computation". (d) Goals include scientific elucidation of rhythms and clinical translation.

inter-individual differences in physiological structures and baseline statuses represent a primary obstacle. Inherent physiological factors, such as vascular anatomy, subcutaneous fat thickness, and skin pigmentation, can directly lead to significant baseline drift and domain discrepancy in the raw signals acquired, including pulse pressure waveforms and tongue spectral images [60]. If such

heterogeneous data are directly used for training, the model may exhibit a poor generalizability and fail to adapt to new individuals. To address this challenge, it is essential to introduce advanced domain adaptation algorithms and adversarial training strategies [61]. By explicitly learning and disentangling non-discriminative features associated with individual identity during model training,

the system can be forced to focus on invariant patterns that are universally related to syndromic representations, thus constructing a stable and comparable Xiang omics feature space involving different devices, operators, and even data collection centers [62,63]. Secondly, the synchronization and fusion of multimodal and heterogeneous data streams represent another major challenge. Xiang omics does not merely collect static images, but also high-frequency temporal pulse signals (even at the kilohertz level), voice streams, and potentially synchronous thermal imaging video streams. These data streams differ significantly in temporal scales, formats, and physical semantics. Aligning them along the time axis (for instance, associating a specific cardiac beat with the micro-changes in the tongue image and vocal cord vibrations) requires a nanosecond-level high-precision synchronization clock protocol at the hardware level. At the software and algorithmic levels, it is necessary to construct a unified TSF tensor data structure. Multimodal transformers- or tensor decomposition-based fusion algorithms are then employed to uncover the latent and deeply coupled relationships among these heterogeneous modalities. For example, to explore the correlation between features of pulse harmonic energy (e.g., P-wave and T-wave morphology) and temperature distributions in specific tongue regions (such as tongue edge/tip), a Xiang-omics model has yielded a high discriminative performance (area under the curve (AUC) = 0.95, $P < 0.01$), elucidating the synergistic manifestation of Qi stagnation and blood stasis within the force and thermal fields [47,64].

To address these challenges while ensuring system efficiency, a hierarchical computational architecture integrating edge intelligence and cloud computing has been invented. For instance, a cloud-based system integrates deep-learning models to analyze temporal features of pulse wave harmonic energy in conjunction with the spatiotemporal patterns of tongue temperature fluctuations, thereby generating a personalized cardiovascular risk score (hazard ratio (HR) index). In a clinical trial involving 20 volunteers, this system achieves a mean absolute error of 2.1 mmHg (1 mmHg = 133.3 Pa) in predicting blood pressure variability, significantly outperforming traditional methods (5.3 mmHg) [65]. High-performance edge computing modules can also be embedded into data acquisition terminals (such as TCM Health Assessment Bio-Cabin). These modules are responsible for real-time, online signal preprocessing and feature extraction from high-frequency, large-volume raw data streams. For instance, filtering, denoising, baseline correction, and preliminary waveform recognition (e.g., P-wave and T-wave identification) can be applied to raw pulse voltage signals [57]. These modules significantly alleviate the bandwidth pressure and storage burden associated with transmitting raw data to the cloud, and simultaneously enable low-latency responses for real-time clinical decision support, such as critical value alerts, by performing preliminary data normalization and structuring on the spot. Therefore, an XSO system can be built into a closed-loop from “perception” to “decision-making.”

The feasibility of synchronized multimodal acquisition is supported by existing prototypes, such as the “TCM Health Status Identification Bio-Cabin” developed by Wang and Li [66], which achieves millisecond-level synchronization of physiological signals. While acknowledging the challenges in large-scale deployment, these prototypes demonstrate an obvious viability in processing the data from “macro-four diagnostics.”

2.2. Xiang data in physical fields

XSO leverages modern physical technologies, including acoustic, optical, thermal, mechanical, electrical, and magnetic techniques, to enable non-contact, multimodal, and temporally synchronized perception of human STFRs. For capturing field rhythms, the XSO relies on the TCM Health Assessment Bio-

Cabin, a platform comprising multi-channel sensors, signal processing units, and edge computing modules. This platform enables synchronized, high-frequency, and multimodal acquisition of physiological phenotypes, such as pulse signals (Mai Xiang), tongue images (She Xiang), surface thermal fields, and bioelectrical fields. Temporal alignment across heterogeneous sensors is ensured via high-precision synchronous clock protocols. In subsequent STF coupling analysis, the edge computing module can be used to perform denoising, feature extraction, and preliminary analysis of high-frequency, high-volume raw signals.

The acquisition and quantification of thermal field rhythms rely on high-sensitivity, high-resolution infrared thermography [67]. By analyzing the dynamic distribution of surface temperature fields and computing thermal gradients and asymmetries, the platform enables objective quantification of TCM-defined cold (Han Zheng) and heat (Re Zheng) syndromes. Cold syndromes typically exhibit minimal thermal gradients and local hypothermia, whereas heat syndromes present with focal hyperthermal regions or steep temperature gradients [68]. Furthermore, by quantitatively calculating the thermal flux density at specific acupoints and meridians, and analyzing their circadian variations, thermal field data can serve as input for analyzing temporal rhythmicity, which can reflect the dynamics of Yin–Yang waxing and waning [69].

The acquisition of bioelectrical field rhythms and mapping of meridians can be achieved through high-density bioelectrical impedance analysis (BIA) and electrophysiological techniques [28]. Meridians are conceptualized as low-impedance channels for the transmission of information and energy. By employing multi-channel and multi-frequency BIA measurements, a three-dimensional bioimpedance tensor can be constructed for noninvasive mapping of the meridian field [70]. Subsequently, a TSF coupling analysis between the bioelectrical field tensor and the thermal field feature matrix can be performed to decode the rhythmic characteristics of Qi dynamics [28,71,72]. Furthermore, the force field and motor rhythms can be caught through a module integrating inertial measurement units (IMUs), force sensors, and high-speed motion capture systems. Gait characteristics, balance capacity, and fall risk parameters can be obtained, and can directly reflect the “balance of sinews and bones,” a TCM theory pertaining to the coordinated interaction between tendons (including fascia, tendons, ligaments, and joint capsules) and bones to jointly maintain joint functionality and stability [73]. In parallel, Xiang omics also acquires the data about the STF in the macroscopic environment, including geographical location, altitude, atmospheric pressure, humidity, geomagnetic field intensity, and solar sunspot activity index. Such data are transformed into exogenous TSF driving feature vectors, serving as periodic driving terms in SR models, to construct a complete “correspondence between heaven and man” (Tian–Ren Xiangying) data chain.

The data from those fields present different dimensionality, data formats, sampling frequencies, and spatiotemporal resolutions. For instance, infrared thermography provides a two-dimensional spatial distribution of thermal radiation, whereas BIA yields a three-dimensional distribution of internal electrical impedance. How to accurately register the superficial thermal field with the internal bioelectrical characteristics within a coherent anatomical system presents a challenge in multimodal spatial alignment [74]. The Bio-Cabin serves not merely as a sensor array, but as a metrologically rigorous, system-level calibrated scientific instrument—ensuring that measurements across disparate physical domains can be meaningfully compared and computed within a unified spatiotemporal reference frame.

Secondly, data fusion, with an extent far beyond data superposition, can uncover the intrinsic correlations and synergistic patterns across multiple physical domains. By conducting STF coupling analysis among bioelectric field tensors, surface thermal

field matrices, and kinematic time-series data, composite indicators can be extracted to characterize the state of Qi dynamics. For example, it speculates that electrical impedance, local heat flux density, and subcutaneous micro-vibrations in the region of a specific acupoint may exhibit coupled variations in response to acupuncture stimulation, and that the propagation of such changes may align with the pathways of meridian circulation [75]. To prove them, advanced multi-way tensor decomposition and causal discovery algorithms can be taken to disentangle co-varying latent factors, thereby constructing a quantifiable multi-physics evidence chain for TCM concepts such as “De Qi” (referring to the sensing of soreness, numbness, distention, heaviness, or warmth at the acupoint during acupuncture stimulation [76]) and “Qi Zhi Bing Suo” (Qi reaching the diseased site) [77].

Even minimal temporal misalignments can critically compromise multimodal coupling analyses. Therefore, high-precision synchronous clock protocols serve as the cornerstone for maintaining temporal consistency across modalities. The edge computing modules can concurrently handle diverse computational loads ranging from images and time-series signals to three-dimensional tensors, thus enabling real-time feature extraction and integration and laying the foundation for immediate clinical feedback (Fig. 3).

2.3. Xiang data about microscopic molecular phenotypes

At the microscopic level, XSO seeks to provide quantitative molecular mechanisms and network-based interpretations for the TCM concept of syndromes, and establish cross-scale linkages at macro- to meso- to microscopic levels, thereby offering a robust biological foundation for the modernization of TCM theory.

The microbiota ecosystem offers a lens for elucidating the TCM concepts of spleen–stomach transportation and transformation of food and water. Netagenomics and metatranscriptomics on tongue fur samples verified that tongue microbiome reflects the functional states of the spleen and stomach, as well as syndrome patterns such as “damp-heat” arising in the middle jiao [78,79], suggesting that the microbial characteristics link with the macroscopic features of tongue fur (such as color, thickness, and moisture). Thereafter, quantifiable molecular network signatures can be constructed for mapping syndrome patterns like “damp-heat” and “spleen–stomach transport and transformation deficiency.” Consequently, vague descriptions such as “greasy fur” (Tai Ni), referring to an abnormal state in which the tongue fur appears fine-grained, dense, tightly adherent to the tongue surface, and difficult to be scraped off, can be translated into specific indices of microbiota dysbiosis or threshold concentrations of metabolites [80,81].

XSO is also expected to elucidate the neuro–endocrine–immune (NEI) network and its mechanistic correspondence with central TCM constructs, such as kidney essence (Shen Jing). Leveraging high-frequency sampling of NEI-related indicators—such as cortisol circadian rhythms, cytokine profiles, and heart rate variability (HRV)—alongside dynamic network biomarker (DNB) analysis and network-based modeling, XSO can uncover the nonlinear evolutionary trajectories of Shen Jing across the stages of life: birth, growth, maturity, aging, and decline [82]. Simultaneously, based on transcriptomic, metabolomic, and proteomic data, XSO establishes a molecular feature set for each of the five Zang organs [83]. For example, the liver is analogized to the element wood in the five elements, embodying the attributes of a tree, like growth, expansion, and plasticity [84]. Through approaches such as network pharmacology, XSO identifies core molecular targets and biomarkers associated with TCM syndromes in the liver, like “Gan Yu” (the stagnation of Qi and blood stream in the liver) [19,85]. Furthermore, the integration of “temporal omics” allows the acquisition of time-series dynamic data, rather than just static

data, enabling systematic capture of molecular oscillation patterns aligned with circadian rhythms and seasonal fluctuations (Jie Qi). By applying network models and multivariate analyses, XSO quantitatively characterizes molecular dynamics under multi-periodic superimposition, thereby validating the dynamic data that can be trained for elucidating the evolution of TCM syndromes and the interactive mechanisms within the NEI network [86].

All XSO data are organized into a tensor structure denoted as data tensor, $D \in R^{I \times J \times K}$, where R represents the set of real numbers, I denotes the number of individuals, J corresponds to time points or circadian intervals, and K encompasses phenotypic dimensions across macro-level tongue and pulse images, mesoscopic medical images, and micro-level omics profiles [87]. Tensor decomposition algorithms such as Tucker decomposition are employed to extract latent factors that span across scales and temporal sequences from high-dimensional tensors [88]. These latent factors are used as standardized inputs for array-based computational models, ultimately generating multimodal and fused feature vectors suitable for further computational inference. However, how to embed micro-level omics data into the theoretical framework of TCM and achieving cross-scale integration remains a tough challenge, as shown by the “curse of dimensionality” and interpretive ambiguity introduced by biological complexity. Omics technologies generate massive amounts of molecular features, the vast majority of which represent biological noise or inter-individual heterogeneity unrelated to TCM syndromes [89,90]. As false correlations may arise, analytical strategies should shift from hypothesis-free exploratory to theory-constrained precise mining [91]. In other words, it is essential to leverage aprioristic TCM theories to formulate biologically plausible hypotheses. A classical theory is “The kidney governs the bones and generates the marrow,” which implies a direct regulatory relationship between the renal and the skeletal systems. The molecular underpinnings may involve stem cell differentiation and the bone marrow microenvironment. Extending from those hypotheses, one can narrow the focus to specific molecular modules and pathways for in-depth exploration, thereby achieving dimensionality reduction, while enhancing biological interpretability [92].

Secondly, there exists a substantial spatiotemporal gap and causal indeterminacy between microscopic molecular events and macroscopic functional phenotypes. Transcriptomic alterations typically reflect the cumulative effects of cellular processes over several hours or even days, whereas pulse waveforms can show capture millisecond-level fluctuations in cardiovascular hemodynamics. Naively associated, both levels of data may yield biologically meaningless correlations. A potential solution lies in the integration of multiscale dynamic modeling and mediation analysis. It is essential to construct dynamic models that simulate how perturbations at the molecular network level propagate upward across cellular, tissue, and organ levels. Specifically, models have emerged to characterize how chronic stress, corresponding to the psychosocial dimension of “liver Qi stagnation” in TCM, induces sustained activation of the hypothalamic–pituitary–adrenal (HPA) axis [93], leading to dysregulation of glucocorticoid rhythmicity within the NEI network [94]. This, in turn, alters hepatic lipid metabolic programming via the glucocorticoid receptor signaling pathway (at the metabolomic level) [82], eventually culminating in the pulse feature known as Xian Mai (“wiry” pulse), which is biomechanically associated with sympathetic overactivation and high vascular tone under chronic stress.

Although algorithms, such as tensor decomposition, can technically integrate multi-omics data, a critical issue remains unresolved: how to ensure that the resulting mathematical components produce meaningful TCM connotations, rather than abstract statistical significances? This dilemma calls for the development of interpretable tensor decomposition methods, in which

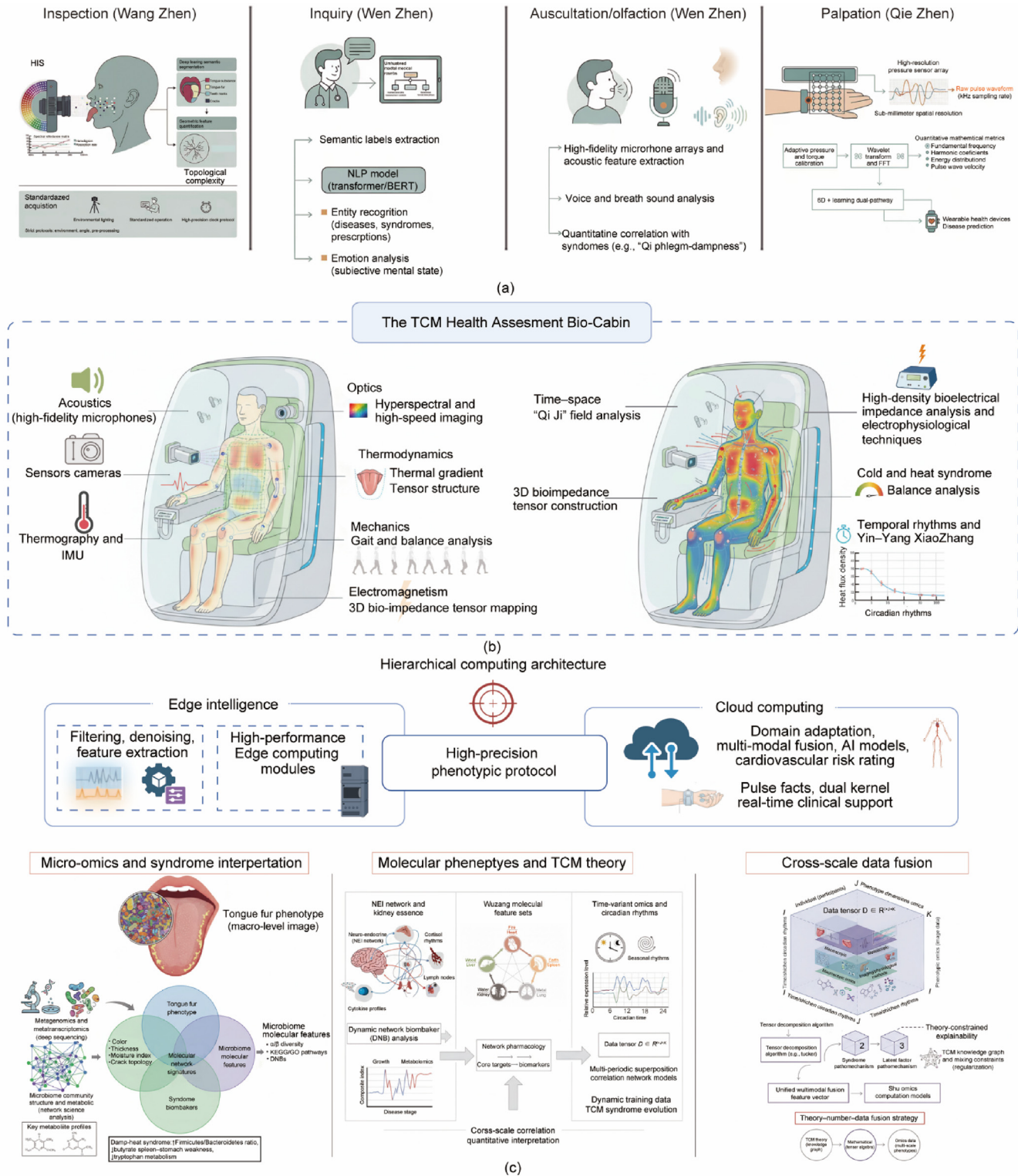


Fig. 3. Establishment of Xiang omics. The data are acquired from digital diagnostics and fused across scales. (a) Standardization of the Xiang data obtained through four TCM diagnostics. Inspection data are obtained using hyperspectral imaging; inquiry data using NLP models (transformer/BERT) for semantic extraction; auscultation/olfaction data using high-fidelity microphone arrays; palpation data using high-resolution pressure sensors to quantify pulse waveforms. (b) The TCM Health Assessment Bio-Cabin. This system captures "Qi Ji" (Qi dynamics) field rhythms through multimodal technologies spanning acoustics, optics, thermodynamics, mechanics, electromagnetics, and magnetism, supported by edge intelligence (feature extraction) and cloud computing (multimodal fusion). (c) Micro-mechanism and data fusion. The left panel shows molecular interpretation of TCM syndromes diagnosed based on tongue microbiota and metabolic profiles; the middle panel illustrates the integration of molecular phenotypes with TCM theory, incorporating the neuro-endocrine-immune (NEI) network (related to kidney essence), Wuzang molecular feature sets, and time-variant omics with circadian rhythms to construct quantitative correlation models for TCM syndrome evolution via network pharmacology; the right panel outlines the multi-modal data fusion strategy, employing tensor decomposition algorithms to integrate individual, phenotypic, and multi-omics data across different scales.

theoretical constraints from classical TCM are embedded as regularization terms within the decomposition process, thus guiding the algorithm to extract latent factors that are not only consistent with the intrinsic structure of the data, but also the core principles of TCM.

3. Shu omics

3.1. Shu in Yin–Yang

As the most fundamental concept in TCM, Yin–Yang is transformed into high-precision, explainable classifiers and adaptive control systems to construct Shu omics. To clear away the ambiguity in TCM terms for syndrome description, Shu omics employs fuzzy set theory for quantification [95]. By constructing membership functions, qualitative data describing features of pulses, tongues, or others are converted into continuous numerical values. For example, pulse features can be quantified using non-linear functions based on such parameters as power spectrum fundamental frequency F0 (the basic frequency of the pulse beat), cepstrum wave feature RC (the type of pulse cepstrum wave), and cepstrum zero component Cx0 (the intensity of the pulse) [96]. Through the analysis of the red, green, blue (RGB) color space of tongue images and physiological indicators, a diagnosis can be automatically made [97].

Deep neural network (DNN) classifiers are constructed for discriminating cold/heat and deficiency/excess, and XSO provide multimodal fusion feature vectors as inputs. To ensure the explainability of the model's decisions, an attribution analysis using tools like Shapley additive explanation (SHAP) is essential. SHAP can reveal the contribution of tongue substance spectral features. For instance, when judging a heat syndrome, high reflectance bands may correspond to changes in the tongue substance, thereby mapping artificial intelligence (AI) decisions to TCM connotations [27]. One model, by fusing tongue images with partial basic physiological indicators, achieves an F1 score (a single metric that combines precision and recall to evaluate the model's overall accuracy in correctly identifying fatty liver cases) of 0.797, a recall of 0.847, and an AUC of 0.924 in predicting fatty liver in the population [47]. Using infrared thermography, another study compares the heating and cooling loads on the tongue tip and laterals between coronary heart disease patients and normal populations, finding a higher infrared thermal radiation in the patient group ($P < 0.05$) [98].

However, the concepts and terms in Yin–Yang theory are difficult to be fused into computable classification models. Yin and Yang do not always exist in a dichotomous, but a dynamic state [99]. In clinical practice, a mixture of cold and heat syndromes (Han Re Cuo Za) is common [100]. A simple binary classification may fail to capture a continuous spectrum of pathological states, and distinguish syndromes with fuzzy boundaries and in dynamic transitions. DNNs possess a powerful capability to classify, but their “black box” nature inherently conflicts with the logical transparency advocated in TCM. To resolve this limitation, XAI models can reveal which features influence the decision and how these features reflect TCM pathomechanisms. For example, the model can map the thermal images with specific acupoint areas like Mingmen and Guanyuan, achieving a semantic explanation of TCM theory. Furthermore, recurrent neural networks or state-space models to capture the dynamic features of Yin–Yang transitions with circadian rhythms and solar terms [101].

3.2. Shu in the five elements

The theory of five elements describes the complex, non-linear feedback regulatory network among Zang and Fu organs. To con-

structs Shu omics, tools such as SR and GNNs can be employed to transform this theory into solvable mathematical equations. SR is a directed inference algorithm that does not presuppose a function form, but directly searches for the optimal functional expression from the time-series dynamic data of XSO [102]. Using the functional state $x_i(t)$ of the Wu Zang Liu Fu (five Zang organs and six Fu organs) as variables—where x represents the functional state, subscript i denotes the index of the specific organ, and t represents time—SR can deduce the CDEs to transform their interactions into structural constraints or regularization terms, guiding the model to learn dynamic laws that conform to TCM principles [103,104]. One study showed that patients with liver (wood) depression and spleen (earth) deficiency syndrome demonstrated significant [105] and beneficial changes in splenic function indicators after TCM interventions: serum hyaluronic acid (mean difference = -61.15 ; 95% confidence interval (CI): -92.71 , -29.58 ; $P < 0.00001$), procollagen type III, and laminin reduced (both $P < 0.00001$) [106]. This indicates that liver dysfunction can exert an inhibitory effect on spleen function (transformation and transportation) [107], providing both statistical and theoretical support for setting a negative coupling term “wood $\rightarrow$ earth” in the model. “Wood overacting on earth,” a condition common in TCM literature, can be mathematized with a threshold-activated Hill function within the CDEs: $f_{\text{Cheng}}(x_1) = c_{31}^{\text{base}} + \delta_{\text{patho}} \cdot \frac{(x_1)^n}{(x_1)^n + (\theta_{\text{thresh}})^n}$, where x_1 represents the liver Qi tension, c_{31}^{base} is the baseline physiological restraint, δ_{patho} denotes the maximum intensity of the pathological overacting effect, θ_{thresh} is the critical threshold that triggers the dysfunction, and n is the Hill coefficient governing the steepness of this non-linear transition. This transforms the literary description into a predictable mathematical process where liver Qi tension (x_1) exceeding a critical threshold (θ_{thresh}) forces the spleen into a state of deficiency [108].

GNNs are used for dynamic learning and prediction on the Zang–Fu topological structure. This method abstracts Zang and Fu as nodes in a graph, five-element relationships and meridian connections as edges. A message-passing mechanism can simulate the dynamic evolution of the Zang–Fu states on the Zang–Xiang topological structure. GNNs demonstrate the potential to drive a system (e.g., brain networks) that describes disease transmission and quantify the optimal path and time constant, as suggested by their AUC values between 0.80 and 0.95 [109]. To verify the five elements principle, Shu omics utilizes the Lyapunov function to analyze the stability of derived CDEs, and determines whether the system can return to a dynamic equilibrium through its internal generation-restriction mechanisms under external perturbations (pathogenic factors). In a model for the coronavirus disease 2019 (COVID-19) Omicron transmission [110], the Lyapunov function is used to analyze the stability of the infectious disease. Combined with model fitting and parameter sensitivity verification, it can predict the point to reach the global disease-free equilibrium, and provide the basic reproduction number (R_0) and the system stability threshold, suggesting that the “Zhi Hua” principle can be mathematically transformed.

The five-element relationships are inherently non-linear, time-varying, and context-dependent, and simple linear differential equations can hardly capture their rich dynamics [111]. For example, for modeling the transmission of Qi from the mother to her baby, the GNN should be capable of handling asymmetric and conditional interactions. Although SR methods can automatically discover equation forms, their search space grows exponentially with the number of variables, and finally, these methods become extremely sensitive to data quality and noise [112]. The solution is to introduce constraint optimization based on prior TCM knowledge, using the intensity of five-element relationships described in classical texts, like the *Huangdi Neijing* (Yellow Emperor's Canon of

Internal Medicine), as constraints on the search space, thereby achieving a balance between mathematical rigor and the theoretical fidelity to TCM. Furthermore, considering the high dependency of GNNs on network topology, a dual anatomical-functional TCM network should be constructed first, followed by fusion of multi-source evidence.

3.3. Shu in calendars and solar terms

At the macroscopic level, one's temporal rhythms correspond to calendars and solar terms. Shu omics adopts a multi-period modeling approach based on spatiotemporal convolution to capture these non-linear correspondences, providing a pathway to compute the theory of "Tian Ren Xiang Ying" (correspondence between nature and man). One study has shown that the Temporal Pattern Activation Module can effectively extract the dependencies of sequences on multiple time scales through a two-layer convolution [113]. First, adaptive signal processing methods, such as empirical mode decomposition (EMD) or ensemble EMD, are used to decompose the time-series data of physiological indicators, teasing out their intrinsic diurnal, monthly, and annual rhythms. Simultaneously, the Wu Yun Liu Qi in the 60-year cycle and the 24 solar terms are transformed into high-dimensional periodic feature vectors, serving as the external driving term Φ_{Time} (the continuous tensor encoding temporal environmental dynamics) for the CDEs. Deep learning architectures, such as spatiotemporal graph convolutional networks, are employed to process these multi-variable, long-dependency time series [114]. Through its core attention mechanism, the model can learn the contribution weights of different periodic signals to an individual's physiological state. Furthermore, by utilizing the Hilbert-Huang Transform, the model can calculate the risk of "resonance" between an individual's internal rhythm and the external cycle, thus quantify the effects of time and place on diseases.

To map traditional calendrical cycles with modern physiological time-series, data collection and algorithm selection are challengeable. The 60-year cycle of Wu Yun Liu Qi far exceeds the span of an individual's life [115], making model training almost impossible based on the data from individuals, but populations or cohorts. An intergenerational "time-constitution-disease" model can be established by integrating meteorological data, epidemiological data, and modern omics data. Rhythmic signals vary greatly in amplitude, frequency, and phase. Traditional Fourier transformation assumes signal stationarity; however, physiological signals are inherently non-stationary [116,117]. Although adaptive methods, like EMD, can handle non-stationary signals, their end-effect and mode-mixing can reduce the accuracy of rhythm extraction [118]. Therefore, TCM-specific time-series algorithms should be developed, incorporating prior TCM knowledge about the association between Shi Chen (hours), solar terms, and Zang-Fu functions as regularization terms for decomposition. In this way, the algorithms can extract rhythmic features with TCM significance more accurately. Additionally, the resonance between individual rhythms and cosmic rhythms requires a mathematical definition, potentially involving non-linear calculations, such as phase synchronization and frequency locking.

3.4. Shu in pre-disease

Pre-disease is a critical point where the body shifts from a healthy to a pathological state [119]. Shu omics equipped with DNB can provide an early warning for this critical point [120]. The DNB can monitor the dynamic correlations within the molecular network and identify key sub-network signals indicating the transition of disease stage ($\text{AUC} > 0.85$, $P < 0.01$) [121]. In the "pre-disease" stage, the molecular network exhibits critical fea-

tures with meaningful fluctuations and correlations in models of various cancers and metabolic diseases [120,122]. Shu omics utilizes the DNB algorithm to warn the progression of TCM syndromes [123]. Shannon entropy is used to measure the degree of information disorder in the XSO feature space [122]. Monitoring the sudden increase in Shannon entropy over time, the rise in DNB indicators, and the decrease in the Lyapunov exponent, the CDEs model can constitute a multi-indicator, high-confidence system for warning a pre-disease state [124]. The BianqueNet model, through the quantification of imaging data during the latent phase of spinal degeneration (Dice coefficient > 0.90), shows an ability to predict the point turning to the pre-disease state.

3.5. Fusion of small with large models through SI

LLMs can realize a logical reasoning of "principle-method-for mula-medicine." This model can serve as the knowledge shell and interpreter for various TCM small models. For example, the Shu-Zhi Qihuang large model, jointly developed by East China Normal University, Shanghai University of TCM, and others, has successfully passed the simulated TCM physician licensing examination [125,126]. Through knowledge graph embedding technology, TCM symbols are mapped into a low-dimensional vector space to achieve numerical computation and logical reasoning. In this model, a specialized LLM is customized using the transformer architecture [127]. An LLM has shown capabilities to fuse multiple models and directly process unstructured inputs from XSO, thus realizing syndrome differentiation based on four diagnostics [128,129]. However, simple statistical learning based on token co-occurrence is hard to capture their deep meanings. For example, "Yang Qi" may refer to warming, mobility, or immune activation in different contexts [130]. The "hallucination" is also inherent in current LLMs that generate the content that does not conform to the theory-treatment principle-prescription-medical logic [131].

Shu omics is a computational system integrating small models with large models hierarchically through SI. The mechanism in the Shu omics is as follows: The quantitative, high-precision outputs of small models (e.g., CDEs, GNNs, and classifiers), such as "kidney essence index below threshold" or "DNB alert triggered," are fed as structured prompts into the large model [132]. These quantitative constraints provide a limited space for the reasoning in the large model, preventing it from generating logical errors. Conversely, techniques such as semantic loss functions are used to transform TCM symbolic knowledge into mathematical losses for training small models, ensuring that the quantitative output of the small models conform to TCM logics. Ultimately, through XAI and ethical norms, all conclusions provided by the LLM can be traced back to TCM theories.

To deeply integrate small and large models, interaction protocols and conflict resolution mechanisms should be designed [133]. When a contradiction arises between the small model and the large model, the system should be able to make decisions intelligently. Therefore, a hierarchical confidence assessment system should be established to dynamically assign weights to task performance, data quality, and conformation to TCM theory in the model. A challenge is how to feed new knowledge gained from clinical practice back into the model. The small model can learn new data through updating its parameters, while the large model needs to absorb new TCM theories and clinical experience through renewing knowledge graphs. This necessitates the design of a pipeline that can continuously and consistently carry out knowledge absorption and conflict detection. Moreover, this SI system is rooted in the deep mining and intelligent computation of massive, multimodal TCM data. Then, the other core driver of XSO—the data-intensive computing engine—should be designed (Fig. 4).

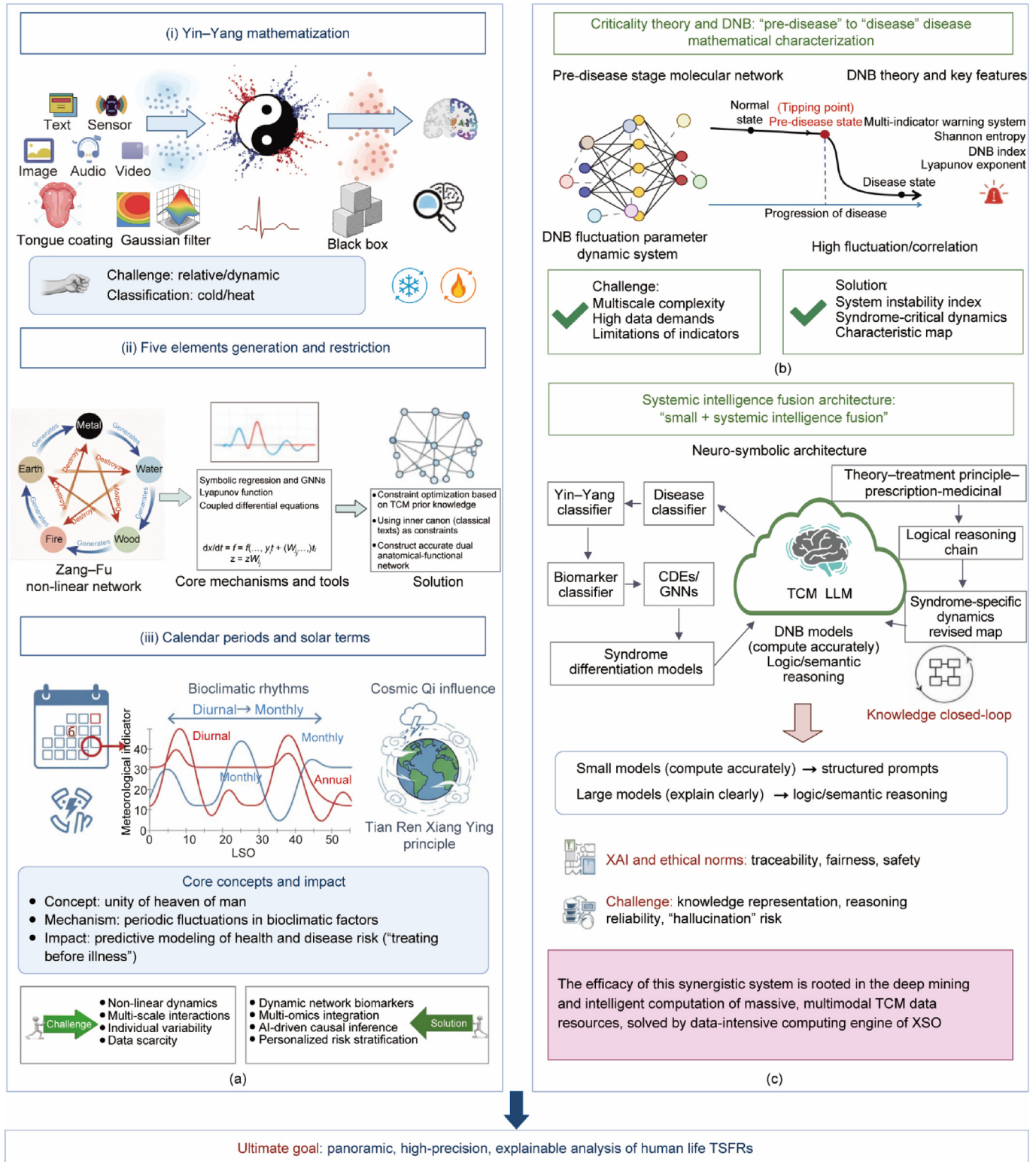


Fig. 4. Establishment of Shu omics. Traditional numerology is integrated with modern mathematical algorithms. (a) Modeling of core theories. (i) Yin–Yang theory is transformed into high-precision classification models; (ii) five elements generation-restriction theory is characterized dynamically via CDEs and GNNs; (iii) calendars and solar terms are constructed into predictive periodic models. (b) Criticality theory and DNB. DNBs are used to quantify the phase transition critical point of the "pre-disease" stage. (c) Systemic intelligence fusion architecture. Adopting a "neuro-symbolic" synergistic mode, it integrates "small models" (providing precise quantitative computation) with TCM LLMs (providing logical reasoning and semantic explanation) to build a closed-loop knowledge system. LSO: local solar time.

4. XSO driven by data and theory

4.1. Data-driven blind calculation in XSO

Data-driven blind calculation hinges on the quality, dimensionality, and SNR of the data provided by Xiang omics. A high SNR of input data can be ensured through strict signal processing, denoising algorithms, and standardized protocols. The blind calculation engine receives multimodal fusion feature vectors processed by dimensionality reduction techniques, such as tensor decomposition, and can analyze both macroscopic and microscopic data to discover latent, cross-scale patterns [134].

The blind calculation engine uses unsupervised or weakly supervised learning methods to mine features and recognize patterns without pre-set assumptions. For instance, by analyzing the patient's Xiang omics feature space with algorithms like deep clustering or variational autoencoders, potential syndromes can be differentiated, and new disease subtypes revealed [135]. Utilizing deep association rule mining, the algorithm can discover the complex relationships hidden within massive clinical data. For example, using the IDentif.AI platform, a study has found that potential combinations such as levofloxacin/rifabutin show significant synergistic effects in combating *Mycobacterium* abscesses, with an inhibition rate reaching $(58.33 \pm 4.99)\%$ [136]. Through blind calculation using spatio-temporal graph convolutional networks, the propagation dynamics of diseases in a population can be predicted to prevent regional epidemics. For example, a GNN not only effectively extracts the spatiotemporal joint features of multivariate time series, but also achieves an accuracy 36.54% to 161.47% higher than baseline models [137].

Purely data-driven approaches may fall short in processing TCM data. Firstly, a correlation does not equal a causation, which is more prominent in TCM. Blind calculation may discover a statistical correlation between the tongue fur microbiome and the pulse condition, but whether this correlation reflects the pathomechanism of "damp-heat in the spleen and stomach" or is merely a co-existence requires a further explanation based on TCM theory. Secondly, when massive Xiang omics features are analyzed simultaneously, even after rigorous correction, statistically significant but TCM theory-unexplainable spurious correlations still emerge. In this light, a blind calculation engine is needed to filter mechanism based on TCM pathomechanism theory, such as retaining only those associations that bridge macro and micro scales and conform to the Zang-Fu theory [138]. For instance, the discriminative dimensionality reduction tree has once identified five metabolic phenotypes in obese patients, which further helps to individualize diagnosis and treatment [139].

4.2. Theory-driven directed inference in XSO

Theory-driven directed inference ensures that XSO does not deviate from TCM ontology and epistemology. Through directed inference, principles such as five elements and Zang-Fu are transformed into regularization terms within the objective function for optimization. For example, when training a Zang-Xiang GNN, a penalty term is added to the loss function to force the learned Shengke relationship weight matrix in the framework of classical TCM theories. The state-aware GNN not only improves processing efficiency but also the accuracy by 18.8% [140]. Prior knowledge graphs are used for initializing the weights and designing the network structure in deep learning models, thereby accelerating convergence and enhancing generalization. A knowledge-driven multi-modal graph convolutional network (KMGCN) model based on a prior knowledge graph achieved classification accuracies of 86.87% and 86.40% on the Alzheimer's disease neuroimaging initia-

tive (ADNI) and autism brain imaging data exchange (ABIDE) datasets, respectively [141].

Directed inference can also ensure mandatory explainability. AI tools are used to perform attribution analysis on model decisions [142]. For example, when the model recommends a certain kidney-tonifying prescription, it means that the CDEs-predicted value of the kidney essence index is below the critical threshold, and the molecules in the prescription can regulate mitochondrial function (one of the potential molecular mechanisms of kidney essence). The CDEs are derived through SR which itself constitutes a mathematical expression of TCM pathomechanism. By analyzing its functional form and parameter stability, a mechanism-based reduction from phenomenon to model and then to principle is achieved [143,144].

The blurry and seemingly contradictory statements within TCM theory are difficult to be mathematized. A cross-sectional study common medical phrases finds that the public can understand non-technical phrases more accurately than comparative terms [145]. Directed inference, potentially through multi-version knowledge graphs and evidence-weighted theoretical confidence assessments, allows the model to perform comparative inferences from different theoretical perspectives, ultimately forming a comprehensive judgment [146]. Furthermore, overly strong theoretical constraints may prevent the model from breaking existing theoretical frameworks, thus a balance between theoretical fidelity and scientific openness should be maintained.

4.3. Syndrome Differentiation Hub as a digital twin system

The Syndrome Differentiation Hub, the core of XSO, can coordinate data-driven and theory-driven approaches, resolve potential conflicts, and form a closed-loop feedback. The Hub continuously receives Xiang omics data streams and simultaneously monitors the outputs of the blind calculation engine (e.g., DNB alerts) and the directed inference in small models (e.g., CDEs system state). Crucially, the Hub is not a "black box" but a modular decision system based on multi-objective optimization. It functions through three key mechanisms:

- (1) Confidence evaluation: Calculating the prediction entropy of data-driven models versus the parameter sensitivity of theory-driven models.
- (2) Conflict resolution: When "blind calculation" diverges from "directed inference," the Hub initiates attribution analysis to determine if the mismatch stems from data noise or theoretical inapplicability.
- (3) Falsifiability testing: To avoid "self-fulfilling prophecies," XSO employs a rigorous testing strategy. Theory-constrained models (e.g., GNNs with fixed five element edges) can be used in comparison to theory-neutral baselines (GNNs learning edges purely from data). If the neutral model significantly outperforms the constrained one, the specific theoretical assumption is considered false or locally inapplicable, prompting an iterative refinement of the theory.

Based on these evaluations, the Hub dynamically allocates the weights of the two computations in decision-making. For clear, classical syndromes, a larger weight is assigned onto directed inference; for a disease at the critical point or with complex syndromes, the weight on blind calculation is increased.

The Hub also constitutes a closed-loop feedback and knowledge iteration project. During a model-guided treatment, the real-time Xiang omics data are fed back to the Syndrome Differentiation Hub to optimize the parameters of the small model and update the knowledge graph of the large model. Ultimately, XSO constructs a digital twin system to virtually map an individual or a typical constitution, and can dynamically simulate and infer his

or her life rhythms and disease progression. To construct the Hub, conflict resolution mechanisms are necessary to transcend simple weight allocation to deep decision logic based on TCM epistemology. To compare the confidences of two models, a multi-level evidence fusion framework is needed, involving factors such as the quality of evidence sources, the strength of TCM theoretical support, and clinical urgency. In a study aiming to resolve diagnostic bias caused by “confounding factors” in AI models due to imaging, a causal intervention strategy is introduced to decouple causal and non-causal factors, achieving an average accuracy of 87% across three independent test sets of 782 subjects [147].

An overly complex Syndrome Differentiation Hub may become a “black box within a black box,” and its decision-making process is difficult for even experts to understand and trust. Therefore, hierarchical explainability interfaces should be designed. Furthermore, an ethical question arises: when a treatment plan recommended by the XSO model leads to an adverse outcome, how is responsibility assigned? Therefore, ethical constraints and human oversight nodes should be embedded in the system design, ensuring that physicians have always the right to make the final decision, and the system only serves as an intelligent tool. Ultimately, the success of the Syndrome Differentiation Hub depends not only on its technical competence, but more on a perfect human-machine collaboration (Fig. 5).

5. Application of XSO in life sciences

5.1. Interpreting the life cycle

XSO provides a research framework for analyzing the life cycle. From the perspective of TCM, the birth, growth, prime, and senescence are regulated by kidney essence, peaking between 28 and 32 years and exponentially declining 40 years later [148]. A model of Shu omics, through its CDEs, predicts an individual's physiological reserve and risk resistance capacity. The model can precisely predict the critical age when an individual's kidney essence begins to decline. For example, for an individual with a specific constitution, the model may predict that the bone density accelerates to decline at as old as 45 years. Then, a preemptive anti-aging intervention can be taken before this time window.

Mechanistically, Shu omics utilizes GNNs to predict the aging of the multi-organ systems, such as the kidney–bone–spleen–brain. GNNs can identify the critical hub nodes where coupling relationships undergo abrupt changes during the aging process [149]. By analyzing the changes in the edge weights of the GNN, the intrinsic mechanisms of heterogeneous aging can be uncovered, and the most vulnerable organs can be identified [150,151]. For instance, even if the disease is manifested as bone disorders, the aging cascade may start from the spleen or stomach, and the intervention strategy should aim to tonify the spleen and nourish the kidney. CDEs can reveal the interaction strength and feedback time delay between kidney function and other Zang–Fu variables, proving that the aging process is determined by the kidney essence.

A reliable full life cycle mathematical model should be established on appropriate data integration and methodological selection. During a longtime life, modern technologies are rapidly iterating. For example, using a 15-second kidney fingerprinting technology, a study found that parameter definitions in traditional models differ from those in new models, thus failing data integration [152]. Therefore, technology baseline drift may undermine the accuracy of long-term predictions. At the methodological level, transforming the abstract concept of kidney essence into a measurable indicator system is an epistemological challenge. We indirectly quantify kidney essence through surrogate indicators like the NEI network and metabolomics, but the extent to which these

surrogates truly explain the meaning of kidney essence still requires rigorous validation. Furthermore, an individual life cycle is influenced by multiple factors, such as genetics, environment, lifestyle; simple differential equation models may fail to capture these high-order interactions [153]. Therefore, new multi-scale, high-precision modeling frameworks are needed to perform fine-grained modeling during data-rich stages, while maintaining the robustness in sparse, long-term prediction.

5.2. Explaining the theory of kidney essence

For diseases related to kidney essence, XSO enables an objective syndrome diagnosis and a dynamic function prediction. Targeting kidney Yin deficiency (Shen Yin Xu) and kidney Yang deficiency (Shen Yang Xu), a deep classifier can be constructed for high-precision differentiation between the two sets of hyperspectral tongue image data (quantifying tongue fur moisture/dryness and tongue substance redness) and infrared thermography (quantifying body surface cold/heat distribution) [154]. Concurrently, Xiang omics of microscopic data, such as metabolomics and transcriptomics, can be used to identify core molecular network features associated with kidney essence deficiency, such as mitochondrial dysfunction and activation of oxidative stress pathways [155]. Furthermore, a digital twin model can be constructed through integrating the CDEs dynamics, node features within the Zang–Xiang GNN, and microscopic molecular networks. Based on the real-time data about an individual's pulse wave time-series, estimated kidney essence index, and serum molecular markers, this model can dynamically simulate the abundance or depletion of kidney essence and predict the functional compensation limit of the kidney under different physiological or psychological loads.

A digital twin system should overcome model complexity and present verification feasibility. The kidney in TCM has a meaning scope far exceeding that of the anatomical kidney, and functions on multiple systems responsible for reproduction, growth, and mobility [156]. Therefore, the digital twin, as a “functional system model” rather than an “organ entity model,” should be established based on a hierarchical structure, fine-grained models at data-rich scales, simple representations at data-sparse scales, and data acquisition strategies through active learning [157,158]. Concurrently, a virtual clinical trial platform, encompassing numerous simulated interventions *in silico*, needs to be established to progressively validate and optimize the digital twin's predictive capability, ultimately achieving a paradigm shift from empirical “kidney tonification” to precise “kidney regulation” [159].

5.3. Elucidating the functional mechanisms of meridians

XSO provides a pathway to explore the functional mechanisms of meridians in TCM. Firstly, high-density BIA and ultra-high-sensitivity electrophysiological techniques can be utilized for non-contact quantification of the bio-impedance and potential signals in the meridians, thus constructing a meridian electrical field model [160]. Subsequently, algebraic topology and GNNs can model the meridian network transmitting the information and energy within the human body [161]. GNNs can explore the dynamic characteristics of meridians as a functional network in space and time. Furthermore, the finite element analysis (FEA) or system dynamics models can simulate the effect of interventions, like acupuncture and moxibustion, on the field rhythms of acupoints. FEA can calculate the conduction velocity, attenuation rate, and time delay of biophysical signals (such as stress and electrical fields) generated by physical stimuli transmitting along the meridian topological structure to downstream Zang–Fu nodes [162]. For example, Xiang omics can calculate the optimal stimulation

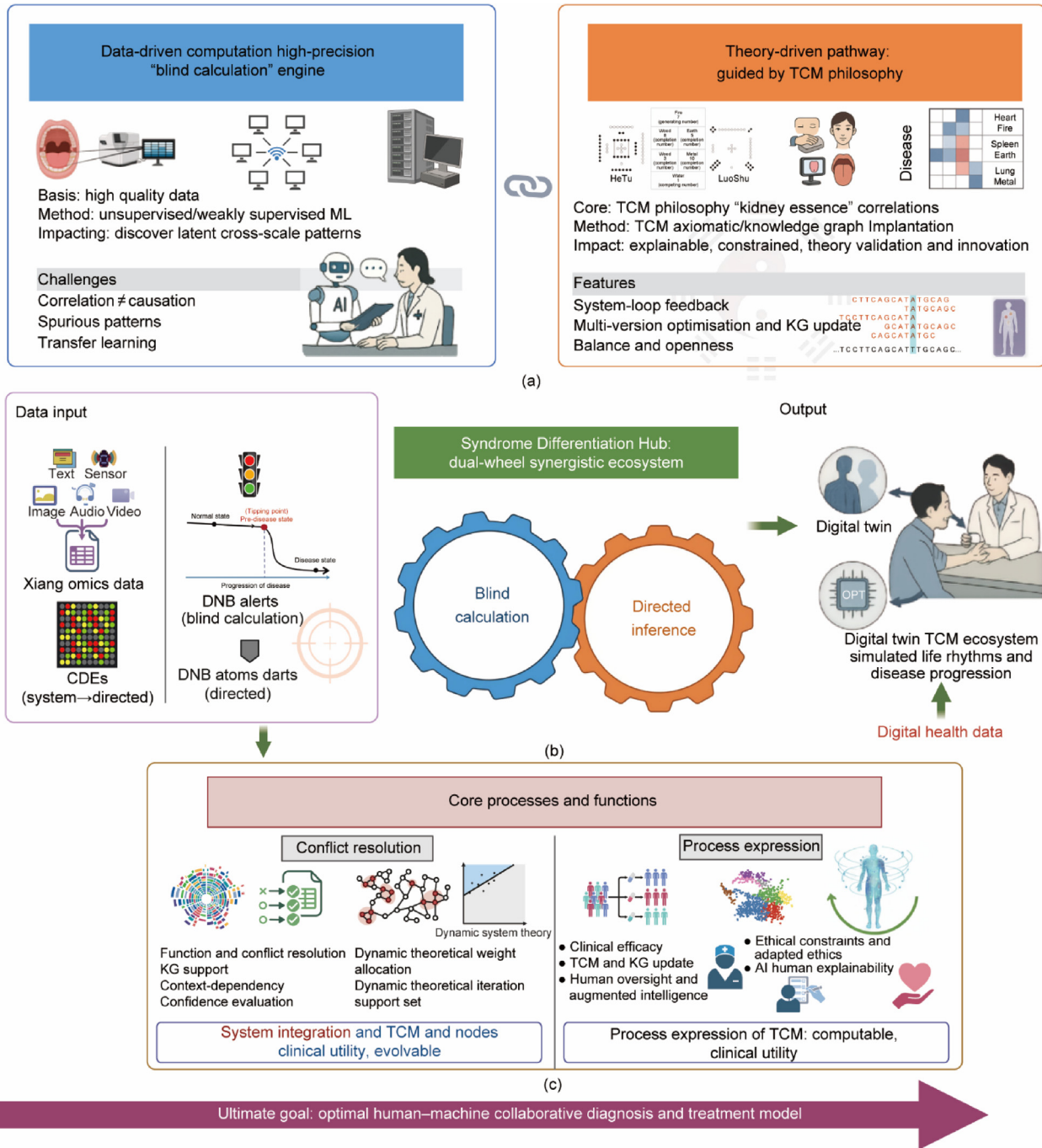


Fig. 5. Data-driven blind calculation and theory-driven directed inference in XSO. A dual-wheel engine in XSO. (a) The data-driven "blind calculation" engine utilizes unsupervised machine learning (ML) to discover latent cross-scale patterns, while the TCM theory-guided "directed inference" engine uses prior knowledge graphs (KGs) to provide explainable constraints. (b) The Syndrome Differentiation Hub ecosystem. The dual-wheel engine of "blind calculation" and "directed inference" integrates Xiang omics data, DNB alerts, and CDE inputs to construct digital twin diagnostic and treatment models. (c) Core processes and functions, including conflict resolution mechanisms, dynamic weight allocation, and ethical constraints, to achieve an optimal human-machine collaboration in diagnosis and treatment.

intensity, depth, and duration of acupuncture that stimulates Zusanli to regulate the "spleen and stomach."

The digital research of meridians should transit from phenomenal description to mechanistic exploration. Current measurements based on BIA and electrophysiology primarily capture the electrical properties of the meridians, and these properties only represent partial multi-dimensional physical characteristics of meridians [163]. As channels for information and energy transmission, meridians may also involve the synergy of multiple physical signals, such as sound, light, and heat [164]. Even if the physical characteristics

of meridians can be precisely quantified, how to prove that these physical signals actually carry Qi? The answer requires a causal evidence chain of biophysical signal-physiological function regulation-clinical efficacy, experimentally demonstrating that the physical changes in meridians can predict corresponding physiological changes. Additionally, a meridian model should be validated based on empirical acupoint selection, and then used to optimize empirical acupoint selection. Breaking this cycle requires a methodological independence of traditional experience, such as randomized controlled trials comparing new stimulation protocols

predicted by the model against traditional ones, or observing whether the functional response to specific meridian physical parameters is consistent with model predictions. For example, using independent samples, a clinical study reported an AI model that assists in interpreting syphilis test results, with an accuracy of 82.67% for reactive rings and 84.44% for non-reactive rings [165], proving the model's predictive capability, reliability, and generalizability (Fig. 6).

6. Application of XSO in clinical settings

6.1. Orthopedic diseases

In the field of orthopedics, particularly in preventing bone fractures among the elderly, XSO can construct a multimodal, dynamic fall risk index (FRI). FRI integrates quantitative features from three dimensions: time, space, and field. Time-related indicators involve

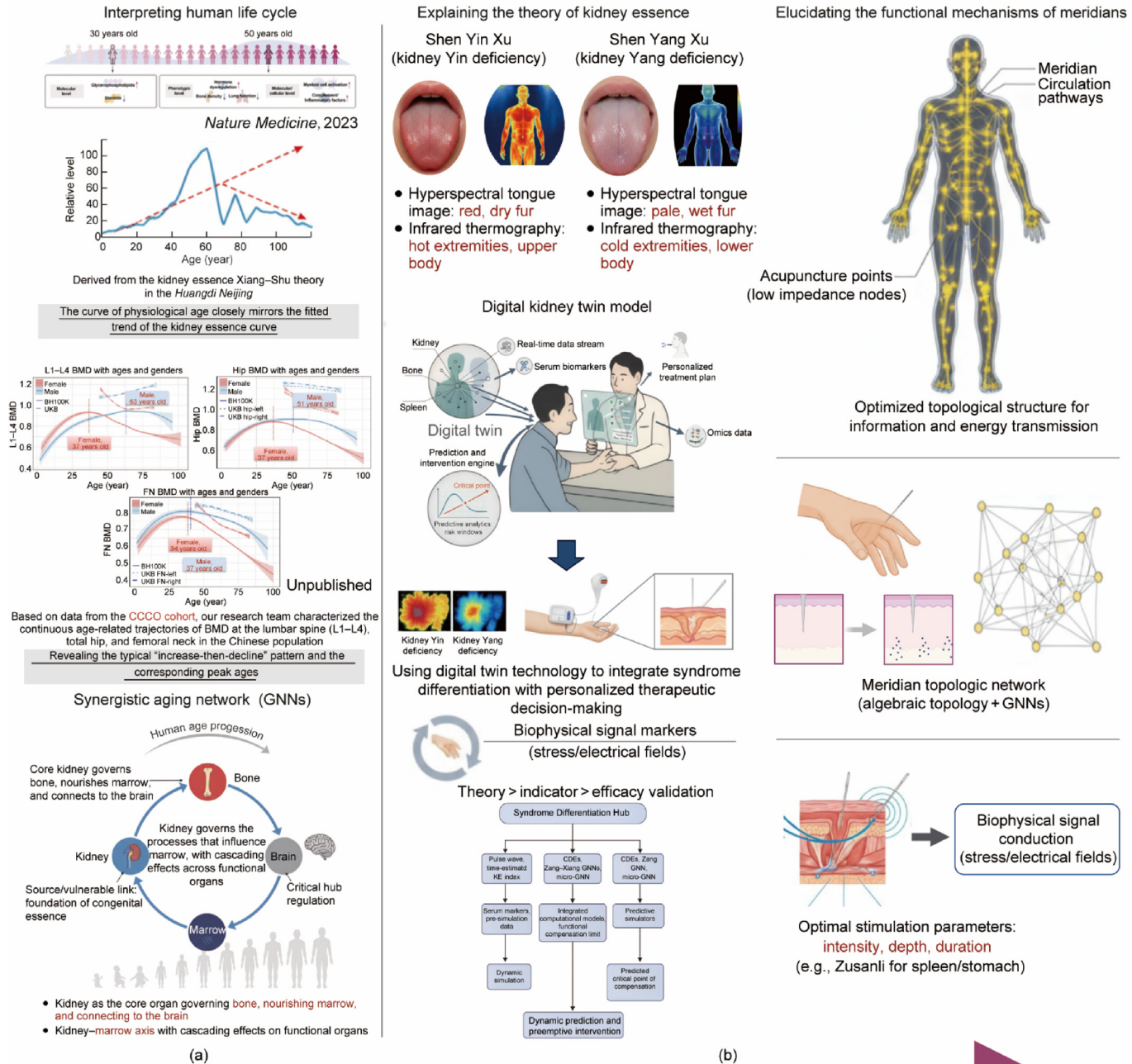


Fig. 6. Applications of XSO in life sciences. (a) Interpreting life cycle. Construction of the "kidney-bone-marrow-brain" network using GNNs and fitting of the kidney essence curve. (b) Explaining the theory of kidney essence. Differentiation of kidney Yin/Yang deficiency via hyperspectral and infrared thermal imaging to construct digital twin models for dynamic prediction and precision intervention. (c) Elucidating the functional mechanisms of meridians. Algebraic topology and GNNs are used to quantify optimal acupuncture stimulation parameters (intensity, depth, and duration). CCCO: China community-based cohort of osteoporosis; KE: kidney essence.

circadian rhythm disorders, such as the coefficient of variation of daily HRV and the chronopharmacological effect of drugs (differences in drug efficacy at different times) [166]. In the dimension of space and field, FRI incorporates the kidney essence index (related to bone density and muscle strength), gait parameters (stride length, posture stability collected via inertial measurement unit (IMU) sensors), and fluid distribution measured by BIA (reflecting the state of “water-dampness” [167,168]. The quantitative results from the BianqueNet model are integrated as a long-term, slow-changing feature reflecting the baseline status of the skeleton, which can be assessed along with bone mineral density (BMD) to predict the fracture risk.

A one standard deviation increase in BMD can significantly reduce the fracture risk by 17%–28% [169]. The Syndrome Differentiation Hub monitors all variables of the FRI in real time, especially the high-frequency collected pulse, HRV, and IMU data. Shu omics models (such as dynamic Bayesian networks) predict the periods during the next 24 h in which the patient has a high risk to fall. When the predicted risk exceeds a pre-set critical threshold, the system immediately releases a warning. The Hub then formulates a personalized intervention based on the cause of the fall (muscle weakness due to Qi deficiency or skeletal fragility due to kidney essence deficiency). The final decision support system automatically generates a comprehensive intervention plan: at the chronopharmacology level, it tells the time to take in sedatives or antihypertensives, avoiding the rhythmic peak of their side effects [170]; at the field level, it guides the patient to receive biofeedback-based somatosensory training, and monitor BIA signals in real time to restore the balance between normal fluid distribution and force field; at the Zang–Fu level, based on the decay rate of the kidney essence index, it recommends the use of kidney-tonifying herbal prescriptions and time-specific acupressure.

In constructing such a fall-warning model, cross-scale data should be fused via multi-resolution assimilation algorithms, such as the Bayesian analytics for spatial segmentation (BASS) algorithm proposed in spatial transcriptomics research [171,172]. Another challenge is the generality of the predictive model in real-world environments. Since models are often trained in controlled laboratory settings, their performance may significantly decline in other environments (e.g., home) due to factors like incorrect sensor placement. To render the model with a strong online self-adaptive learning capability, parameters based on individual feedback should be adjusted using AI methods. A study showed that such as model achieved an accuracy of at least 75% and an average precision of 0.93 in testing 6283 images [173].

6.2. Precision health management

XSO can transform the rationale of “Yin Shi Zhi Yi” (manage one’s health according to time) into health management plans. At the macroscopic level, by embedding Wu Yun Liu Qi and the 24 solar terms as external periodic driving terms, the Zang–Fu CDEs model can calculate the functional trough or imbalance risk during a specific period. The Syndrome Differentiation Hub provides seasonal, population-wide warnings for individuals with different constitutions to take preventive measures. Circadian rhythm data, continuously collected by wearable devices, can be used as signals [174], to calibrate macroscopic rhythms, ultimately generating a spatiotemporal rhythm curve at the hour level. Based on this curve, the decision support system can automatically generate personalized and precise intervention plans for exercise type, intensity, rest times, and dietary structure, meeting the principle of “Zang–Fu Zhushi” [175]. Based on the CDEs, the model calculates the optimal chronotherapy window and dynamic dosage curve for medicinal intervention. For example, the classical TCM text *Pi Wei Lun* (*Treatise on the Spleen and Stomach*) advocates that the lung and large

intestine are interior–exterior related, and medications spleen–stomach diseases should be taken at 3–5 a.m. (Yin Shi), a time for the lung meridian, to achieve a better efficacy [176]. BIA biofeedback-based electrical field conditioning or magnetic therapy at specific acupoints should also be conducted during specific hours to facilitate the smooth flow of meridian Qi [177].

However, there are significant differences among the climates of different regions and individual sensitivities to these changes. A simple periodic driving model may fail to capture this spatial heterogeneity and individual specificity [178]. Therefore, geographically weighted TCM climate-physiology association models should be constructed, combining local historical meteorological data and health records. One’s rhythms should be monitored over a long time and the complexity of data should be interpreted. To reduce the effect of minor fluctuations in rhythm data, miniaturized, multi-parameter integrated smart wearable devices should be designed, and intelligent algorithms constructed to automatically identify abnormal rhythmic changes with clinical significances [179,180] (Fig. 7).

7. Conclusion and outlook

SI-driven XSO represents a deep integration of the qualitative Xiang (images/phenomena) of TCM with the quantitative Shu (numbers/computation) of modern sciences, including hyperspectral sensing, sensor arrays, GNNs, SR, and TCM LLMs. XSO serves as a reliable tool for the dynamic, precise quantification of macroscopic, mesoscopic, and microscopic TSFR phenotypes in TCM, providing new insights into the Wu Yun Liu Qi temporality, Yin–Yang dynamics, Zang–Fu network, and life cycle. XSO emphasizes the dual-wheel synergy of data-driven (blind calculation) and theory-driven (directed inference) approaches, with a Syndrome Differentiation Hub responsible for conflict resolution and closed-loop feedback. At the microscopic level, XSO achieves the molecular mechanism reduction of syndrome phenotypes through metagenomics and NEI network analysis; at the mathematical level, it transforms Yin–Yang duality into high-precision classifiers, five-element relationships into CDEs, and introduces DNB theory to predict the critical points in the pre-disease stage. In clinical practice, XSO employs the FRI to realize precise health management based on solar terms and individual microscopic rhythms.

Based on XSO, causal inference models should be established in the future to offer a causal bridge between TCM concepts and modern biological indicators. Simultaneously, the next generation of XSO should be self-adaptive, self-evolving, capable of autonomously discovering new treatment regularities while maintaining theoretical consistency. XSO provides a research methodology that transcends reductionism and a Chinese-style systemic solution to address public health issues.

CRedit authorship contribution statement

Hongyu Wang: Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. **Chunchun Yuan:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Conceptualization. **Haitao Zhang:** Writing – original draft, Validation, Resources, Methodology. **Xiaoyun Wang:** Writing – review & editing, Validation, Resources. **Haifeng Jia:** Writing – review & editing, Formal analysis. **Furui Fu:** Writing – review & editing, Validation, Software. **Xichen Tang:** Writing – review & editing, Resources. **Jiarui Cui:** Writing – review & editing, Validation. **Jiangxun Ji:** Writing – review & editing, Formal analysis. **Senjie Shi:** Writing – review & editing, Visualization. **Hongbin Xu:** Writing – review & editing, Resources. **Jinni Hong:** Writing – review & editing, Validation.

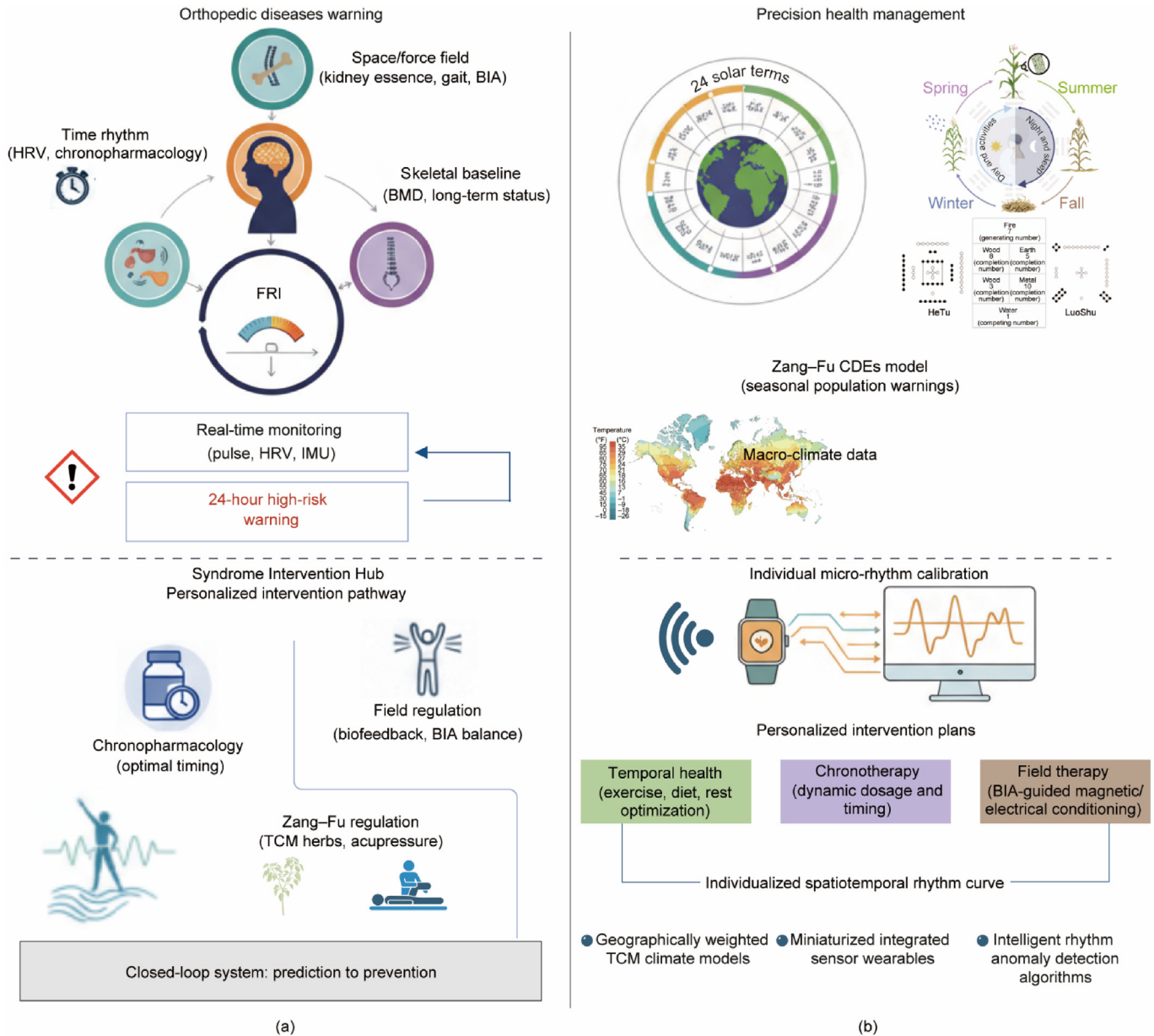


Fig. 7. Applications of XSO in clinical settings. (a) Construction and intervention of the dynamic FRI. Temporal rhythm (HRV), space/force field (gait, BIA), and skeletal baseline (BMD) data are integrated into an XSO model to enable 24-h high-risk warnings and personalized interventions. (b) Precision health management guided by solar terms. Macro-climate data of the 24 solar terms are combined with individual micro-rhythm data to construct Zang-Fu CDEs models that can generate precision intervention plans.

Tianpeng Liu: Writing – review & editing, Software. **Junhao Liang:** Writing – review & editing, Formal analysis. **Mengting Yuan:** Writing – review & editing, Validation. **Xiaomei Liu:** Writing – review & editing, Resources. **Qianqian Liang:** Writing – review & editing, Methodology. **Dezhi Tang:** Writing – review & editing, Validation. **Qi Shi:** Writing – review & editing, Supervision, Project administration, Funding acquisition. **Yongjun Wang:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eng.2026.02.018>.

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