

## East is East and West is West, and never the twain shall meet?

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**W**estern medicine and Chinese medicine developed within the context of different cultures and perspectives of the natural world. The more reductionistic approach of Western biomedical sciences has generated tremendous knowledge of anatomy, physiology, histology, genetics, and biochemistry, while the phenomenological approach of Chinese medicine has produced a more holistic understanding of biology. The two concepts are complementary, and combining them to optimally balance detail and context could generate a highly rewarding step forward for medicine.

A diversity of perspectives on life and consciousness has developed across humanity's different cultures. In the Western Hemisphere, a key development was the affirmation by Greek Ionian scholars such as Thales, Pythagoras, and Archimedes that it was not gods, but rather laws of nature, that create and organize our reality. The modern concept of the laws of nature emerged in the seventeenth century through the work of scholars such as Kepler and Galileo, with the most notable contributions coming from Newton and from Descartes, who emphasized a duality between the mind and the physical body.

Philosophers have pondered whether more than one set of laws was possible. It seems that our conception of natural laws may depend on our approach to understanding reality. Hawking and Mlodinov introduced the notion of model-dependent realism, which posits that a physical theory or worldview is a model with a set of rules that connects the elements of the model to observations (1). That is, in the words of Hawking and Mlodinov, "There is no picture- or theory-independent concept of reality," and every model is only an approximation of reality.

The modern Western scientific model arose in the context of historical and cultural developments that enabled philosophical pursuits and provided fertile ground for philosophers of science. A different approach to understanding reality and the laws of nature arose in Eastern cultures, such as China. Both models can be considered valid, each with its own model-dependent realism.

### Bridging the gap

Although there are many similarities between the Greek and Chinese concepts of health and medicine, the medical systems that arose in the West and in the East are quite distinct. Most notably, a highly reductionist, detailed view dominates in the West, whereas a more phenomenological, descriptive, and systems-based view holds sway in China. In recent decades, Western systems thinkers have started to combine

theories from a variety of disciplines, developing an expanded systems view of medicine. Systems thinking, and in particular systems biology, have been recognized as the scientific bridge between Western medicine and traditional medicine models, including traditional Chinese medicine (TCM) (2, 3).

Figure 1 illustrates how systems-based theories can bridge Eastern and Western models, as well as connecting ancient and modern ideas. The left forward image shows a dynamic correlation network of interactions between various genes, proteins, and metabolites. This nodal network reflects the particularized understanding of the complexity of biochemical pathways and the dynamic organization of the body that characterize Western biomedical science. The right forward imagery is a drawing of the Taoist Inner Landscape. In keeping with ancient Taoist tradition, the drawing provides a poetic description of the complex relationships among the various organ functions of the body. The background of the figure merges two very well-known, almost archetypal, symbols of systems thinking: the Vitruvian Man (*Le proporzioni del corpo umano secondo Vitruvio*) and the *Taiji* (太极, the literal translation of which is "great pole"). The Vitruvian Man is by Leonardo da Vinci, a visionary and pioneer of the evidence-based scientific view of the universe. A man is pictured within a square, which reflects the terrestrial aspect of humanity, and a circle, which represents the spiritual realm. The *Taiji* (often called the Yin-Yang symbol in the West) represents the Eastern, Taoist tradition of systems thinking. It depicts a dynamic relationship between the two components of a duality that encompasses the known universe. Interestingly, the *Taiji*, which symbolizes humanity as part of an eternal universe, has all the properties of a fractal.

### Amalgamation in action

Figure 2 depicts an amalgamation of Western and Eastern medical systems, a process that we call systems medicine. The left side of the figure shows a simplified, hierarchical view of molecules being organized into cells, with further consolidation into tissues, organs, and, ultimately, a whole organism. This illustrates the bottom-up approach practiced in Western biomedical sciences. It has produced a tremendous amount of knowledge of anatomy, physiology, cells, genes, and biochemistry. It has also created physicians with highly specialized, albeit arguably fragmented, knowledge. In the Western scientific model, data are collected to generate information, knowledge, and, ultimately, a form of wisdom. By contrast, traditional medical systems, most prominently TCM, have focused on gaining a holistic understanding of systems, and on applying that wisdom in a top-down manner in the search for knowledge, information, and data that may increase the understanding of

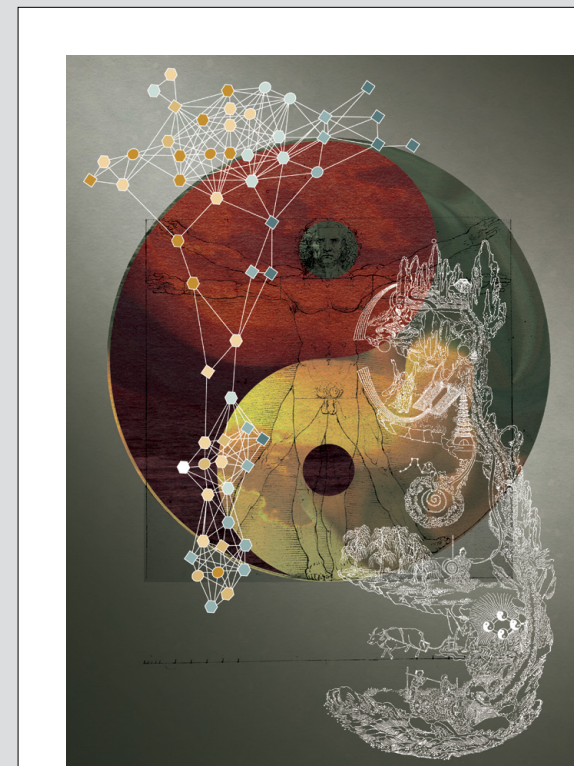
the web of life. Somewhere in the middle these two world-views meet and this nexus has the potential to yield a valuable combination in which detail and context are optimally balanced.

One way to bridge the two worldviews is through unification of diagnosis, based on an integration of the collections and arrangements of symptoms and signs. Western biomedical advances offer a plethora of biomarkers that can be detected and measured with advanced equipment, while Chinese medicine contributes knowledge about the dynamic relationships among signs and symptoms. The right side of Figure 2 provides an example of this inter-relationship for rheumatoid arthritis (RA). In Chinese culture, RA is classified as a "*Bi Zheng*," a so-called painful obstruction syndrome. In TCM diagnosis every condition is primarily distinguished according to eight basic principles: External-Internal, Heat-Cold, Excess-Deficiency, and Yin-Yang. Figure 2 focuses on the Cold-Heat differentiation.

The signs and symptoms of RA are universally represented across peoples independent of culture, although variations in concepts and emphasis can be seen. In TCM, RA patients can be subdivided based on the predominance of "hot" versus "cold" symptoms. Examples of "hot" symptoms, as illustrated in Figure 2, are thirst, fever, irritability, restlessness, warm feeling, dry mouth, and pain that is relieved by cold, while "cold" symptoms include clear urine, sharp pain, stiff joints, and pain that is relieved by warmth. This systemic approach may help biomedical researchers to distinguish biological subtypes of RA in a manner that could lead to personalization of medical care; firstly, through more personalized lifestyle advice, and in the long term, through the application of modern biomedical technology in studies of RA subtypes. Ultimately, recognizing the particular individualized presentation of RA across different patients based on a systemic approach may improve treatment choices and outcomes.

Recently, research teams have begun the process of integrating Western and Eastern notions of medicine for RA. For example, Van Wietmarschen and colleagues (4) used a questionnaire to differentiate distinct "cold" and "hot" RA subtypes. These two patient groups display differences in the regulation of apoptosis, in CD4+ T cell gene expression levels, and in plasma and urine metabolite profiles. In another study, 11 acylcarnitine metabolite variants associated with differences in muscle breakdown was used to distinguish between the "cold" and "hot" RA subtypes (5).

In similar recent work on pre-diabetes, Wei and colleagues



**FIGURE 1.** An artist impression of the ancient and modern bridge between Chinese and Western medicine.

(6) examined blood and urine samples from patients categorized by Chinese subtypes of pre-diabetes, namely *qi* and yin deficiency with or without dampness, and *qi* and yin deficiency with stagnation. Numerous sugar and amino acid level differences were recorded, indicating that the subtypes are characterized by variation in carbohydrate metabolism and renal function.

Several other studies have also shown that biological mechanisms can be correlated with TCM-based groupings in patients diagnosed in Western medical systems (7-10).

### The path ahead

In the above studies, TCM subtyping and Western diagnostic criteria coincided. This suggests that symptom pattern questionnaires could reliably standardize the segregation of patients into TCM subgroups (11). The comprehensive symptom questionnaire used in the RA study was based on the TCM perspective of arthritis as a bi-syndrome. Following completion of the question-

naire, the data was subjected to a principal component analysis, revealing one principal component related to the concepts of "internal" and "external," plus another related to "cold" and "hot" (11). These findings support the contention that TCM concepts have a basis in actual biological variation among patients. The current challenge is to uncover non-linear relationships between the diagnostic symptom clusters revealed by the questionnaire results.

We believe that Western diagnostics would benefit greatly from the integration of broader knowledge of relationships between symptoms, including consideration of TCM descriptions of syndromes. TCM descriptions offer potential directions for detailed, explanatory biomedical research, bringing us closer to a biopsychosocial model of health in which more and more relationships between diseases, psychology, and behavior are uncovered (12). Arguably, the dearth of understanding of the dynamics of systems presents the greatest opportunity for improvement in Western health care diagnostics. It is a topic that will only grow in importance as the focus in health care shifts from the treatment of acute disease to the long-term management and prevention of chronic diseases. Among the more promising developments that may improve our understanding of system dynamics are the application of nonlinear dynamic modeling techniques to the study of coherent oscillations in the brain (13), examination of the synchronization of physiological rhythms such as heart beat and breathing rhythms (14), and the study of metabolic processes that show oscillatory behavior (15). Another

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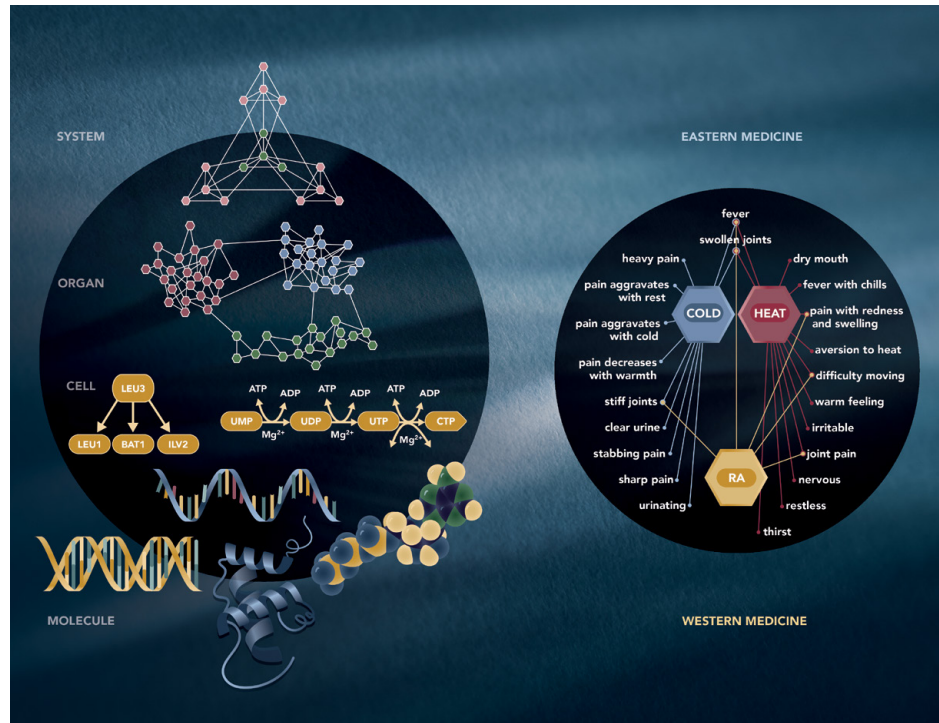
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**FIGURE 2. Systems medicine.** A hierarchical systems view on human biology (left)—scientific studies in Western medicine develop typically via a biochemistry/pathway bottom-up approach, while in Chinese medicine, a top-down dynamic symptom relationship approach is more common. The right image illustrates the diagnostic bridge between symptom relations in Chinese Medicine bi-syndrome (top) and Western medicine (bottom) for rheumatoid arthritis.



intriguing area being examined is the coherent, spontaneous ultra-weak photon emission patterns of organisms (16, 17). Recent work suggests that photon distribution dynamics may provide insights into regulatory coherence at a high systems level (18, 19). Indeed, these coherent light functions may be directly involved in communication in addition to influencing biochemical networks (20, 21).

It should also be clear that modern quantitative technologies developed in the West have a great deal to offer to Chinese diagnostics. Especially relevant are methodologies that provide information about the large-scale organization of systems as well as the dynamics of such organization (Figure 2).

Integration of Western and Chinese medicine thinking has enormous potential for synthesizing modern technological and social innovation. Although Chinese and Western medicine are perceived as wholly distinct paradigms today, they are poised to merge in the arena of personalized systems medicine, wherein patients can take a greater role in managing their own health and wellness. Human-human relationships are critical for diagnosis and intervention in a biopsychosocial context, with health care providers supporting patients through an empathic coaching role. The integration of Western and Chinese medicine can be much more than the sum of the parts: it can accelerate the shift from disease management to health promotion that is presently taking place in health care systems around the world. Although, as Kipling states in the opening lines of his famous poem, "East is East and West is West" (22), at least in the realm of diagnostic medicine, these two world cultures have met.

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## Zheng: A systems biology approach to diagnosis and treatments

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Traditional Chinese medicine (TCM) is an ancient medical practice system which emphasizes regulating the integrity of the human body and its interrelationship with natural environments. As a key concept in TCM, *Zheng* (meaning syndrome or pattern) is the overall physiological and/or pathological pattern of the human body in response to a given internal and external condition, which usually is an abstraction of internal disharmony defined by a comprehensive analysis of the clinical symptoms and signs gathered by a practitioner using inspection, auscultation, olfaction, interrogation, and palpation of the pulses (1). Correctly identifying the *Zheng* is fundamental for the diagnosis and treatment of diseases.

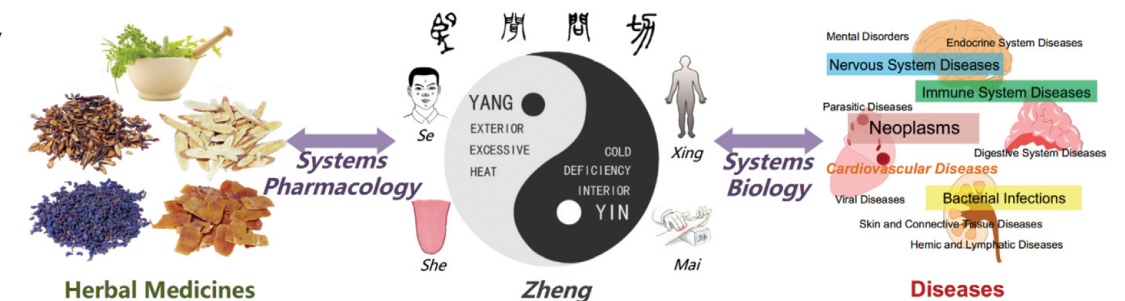
to systems level is important for advancing the identification and treatment of these syndromes, and for providing more objective and quantitative diagnostic criteria.

#### Zheng-guided disease research

In Western medicine, a disease is a particular abnormal and pathological condition that affects part or all of the human body and is often construed as a medical condition associated with specific symptoms. By contrast, *Zheng* puts forth a very different definition of a disease and encompasses all of the symptoms a patient presents.

Because of the highly interconnected nature of the human interactome, it is difficult to study different diseases at the molecular level completely independent of one another (3), and this issue also applies to *Zhenges*. Moreover, *Zhenges* are dynamic with changing boundaries, overlapping symptoms,

**FIGURE 1. Using systems pharmacology and systems biology approaches for understanding TCM Zheng can help bridge the gap between herbal medicines and diseases. Se, face color; Xing, body shape; She, tongue texture; Mai, pulse.**



Moreover, *Zheng* has been historically applied as the key pathological principle guiding the prescription of herbal formulas (Figure 1).

A lack of research on *Zheng* has left us with little understanding of its underlying biology or the relationships between different *Zhenges*, diseases, and drugs. Moreover, there have been attempts to integrate *Zheng* differentiation with modern biomedical diagnostic methods, though these efforts have not achieved the desired results (2). Many well-known herbal recipes, such as Liu Wei Di Huang Wan and Jin Kui Shen Qi Wan, have long been used for the clinical treatment of *Zheng* disorders; however, *Zheng*-guided treatments are still scarce due to the lack of evidence-based interpretations of syndromes and treatment efficacies. Thus, investigating the biological basis of *Zhenges* from a molecular

and a multiscale nature, which makes them difficult to understand at a biological and mechanistic level. Thus, we propose that a comprehensive *Zheng* map be constructed that links together all the *Zhenges* based on their molecular and cellular relationships. Further, we suggest creating the "Zhengome" as a new 'omics field, in which a network is the basic research unit used to investigate the hierarchy present in the human body, from the molecular to the systems level. A comprehensive understanding of the Zhengome requires us to bring together multiple sources of evidence, from shared genes to protein-protein interactions, shared environmental factors, common treatments, and phenotypic and clinical manifestations, in order to capture the relationships between the different *Zhenges*.

*Zheng* uses the Yin-Yang, exterior-interior, cold-heat, and deficiency-excess definitions to describe patients' conditions, which are then managed by *Zheng*-specific recipes (Figure 1). Modern 'omics techniques combined with bioinformatics and bionetwork models through a systems biology approach have

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