

Psychology Faculty Articles and Research

Psychology

2012

# A Complex Systems Science Perspective for Whole Systems of Complementary and Alternative Medicine Research

Mary Koithan University of Arizona

Iris R. Bell University of Arizona

Kathryn Niemeyer University of Arizona

David Pincus Chapman University, pincus@chapman.edu

Follow this and additional works at: https://digitalcommons.chapman.edu/psychology\_articles

Part of the Alternative and Complementary Medicine Commons

## **Recommended Citation**

Koithan, Mary, Iris R. Bell, Kathryn Niemeyer, and David Pincus. (2012). "A complex systems science perspective for whole systems of complementary and alternative medicine research." *Forschende Komplementarmedizin 19*(1) 7-14. doi: 10.1159/000335181

This Article is brought to you for free and open access by the Psychology at Chapman University Digital Commons. It has been accepted for inclusion in Psychology Faculty Articles and Research by an authorized administrator of Chapman University Digital Commons. For more information, please contact laughtin@chapman.edu.

# A Complex Systems Science Perspective for Whole Systems of Complementary and Alternative Medicine Research

# Comments

This is a pre-copy-editing, author-produced PDF of an article accepted for publication in *Forschende Komplementärmedizin / Research in Complementary Medicine*, volume 19, supplement 1, in 2012 following peer review. The definitive publisher-authenticated version is available online at DOI:10.1159/ 000335181.

Copyright <sub>Karger</sub>

### For submission to: Forschende Komplementarmedizin (updated 09/02/11)

Running Head: Complex Systems Perspective

**Keywords**: complex systems science, dynamic systems, complex adaptive systems, complementary and alternative medicine, world view, CAM metatheory

# A Complex Systems Science Perspective for Whole Systems of CAM Research Mary Koithan, PhD, RN, CNS-BC, <sup>1,2</sup> Iris R. Bell, MD PhD,<sup>1-6</sup> Kathryn Niemeyer, MSN, MSc, RN, FNP-BC<sup>1</sup> and David Pincus, PhD<sup>7</sup>

For reprints and all correspondence: Dr. Mary Koithan, The University of Arizona College of Nursing, 1305 N. Martin Ave., Tucson, AZ 85724-21203, USA. Tel. 520-626-2506; FAX 520-626-7891; Email: <u>mkoithan@nursing.arizona.edu</u>

From: The University of Arizona, College of Nursing<sup>1</sup>, Department of Family and Community Medicine, <sup>2</sup> Psychiatry, <sup>3</sup> Psychology, <sup>4</sup> Medicine (Integrative Medicine), <sup>5</sup> and Public Health, <sup>6</sup> Tucson, AZ; and the Crean School of Health and Life Sciences<sup>7</sup>, Chapman University, Orange, CA.

Funding: This work was supported in part by grant funding from the Lotte and John Hecht Foundation; the Samueli Institute; and the National Center for Complementary and Alternative Medicine/National Institutes of Health grants R13 AT005189-01, K24 AT 000057, T32 AT01287.

Conflict of Interest: Financial Disclosure -- Dr. Bell is a consultant to Standard Homeopathic/Hyland's Inc., Los Angeles, CA.

Acknowledgments: The authors thank Stephen J. Guastello, PhD, for his helpful comments on earlier versions of this manuscript.

#### Abstract

Whole systems complementary and alternative medicine (WS-CAM) approaches share a basic world view that embraces interconnectedness; emergent, non-linear outcomes to treatment that include both local and global changes in the human condition; a contextual view of human beings that are inseparable from and responsive to their environments; and interventions that are complex, synergistic, and interdependent. These fundamental beliefs and principles run counter to the assumptions of reductionism and conventional biomedical research methods that presuppose uni-dimensional simple causes and thus dismantle and individually test various interventions that comprise only single aspects of the WS-CAM system. This paper will demonstrate the superior fit and practical advantages of using Complex Adaptive Systems (CAS) and related modeling approaches to develop the scientific basis for WS-CAM. Furthermore, the details of these CAS models will be used to provide working hypotheses to explain clinical phenomena such as (a) persistence of changes for weeks to months between treatments and/or after cessation of treatment; (b) nonlocal and whole systems changes resulting from therapy; (c) Hering's Law; and (d) healing crises. Finally, complex systems science will be used to offer an alternative perspective on cause, beyond the simple reductionism of mainstream mechanistic ontology and more parsimonious than the historical vitalism of WS-CAM . Rather, Complex Systems Science provides a scientifically rigorous, yet essentially holistic ontological perspective with which to conceptualize and empirically explore the development of disease and illness experiences, as well as experiences of healing and wellness.

#### Introduction

There is a growing body of research literature in biomedicine, medical anthropology, nursing, and public health suggesting that current views of science and accompanying research methods have considerable limitations when applied to the complex and dynamical processes involved in health/illness of individual human beings, families and communities [1-2]. Whole-systems complementary and alternative medicine (WS-CAM) has been particularly vocal about these limitations, consistently suggesting that alternative world views may provide more helpful ways to conceptualize how disease/health/illness experiences manifest within individual persons and how various interventions or systems of care facilitate the process of healing and health promotion [3-7].

The National Center for Complementary and Alternative Medicine at the National Institutes for Health NIH/NCCAM defines WS-CAM as "complete systems of theory and practice that have evolved independently from or parallel to allopathic (conventional) medicine. Many are traditional systems of medicine that are practiced by individual cultures throughout the world."

(http://nccam.nih.gov/health/whatiscam/wholemedical/). WS-CAM, with hundreds to thousands of years of historical use include: classical homeopathy (Europe), traditional Chinese medicine (TCM) (China), Ayurvedic medicine (India), and naturopathy (Europe/North America), as well as many indigenous medical systems referred to as Traditional Medicine (TM) by the World Health Organization. These systems of care differ in their cultural contexts and evolution, as well as in the specific diagnostic approaches, therapeutic modalities used, and clinical goals. Nonetheless, they share variants of a vitalistic philosophy that asserts the flow of a non-material life force throughout the living person [8].

In addition, WS-CAM share a basic world view that embraces interconnectedness; emergent, non-linear outcomes to treatment that include both local and global changes in the human condition; a contextual view of the human being that is inseparable from and responsive to their environment; and interventions that are complex, synergistic, and interdependent. These fundamental beliefs and principles

run counter to the assumptions of reductionism and conventional biomedical research methods that dismantle and individually test various interventions that comprise aspects of the WS-CAM system [3-7, 9-12]. Table 1 summarizes issues with the conventional scientific paradigm identified by WS-CAM researchers as well as clinicians.

We suggest that these basic conceptual and theoretical differences form the basis for calls by the CAM practice and research communities (4-7, 13-14) for greater external validity in research studies, signaling the need for new theoretical and methodological approaches that align with a world view consistent with that of WS-CAM traditions. Complex Adaptive Systems (CAS) Theory, including its attendant theories of nonlinear dynamical systems (NDS) and fractal networks offer a meta-theoretical perspective that can be used to develop the scientific basis for WS-CAM. Further, innovative research methods arising from this perspective, such as agent-based modeling, network analysis, state space analysis, and various time-series analyses for measuring complexity and patterning can be used to reconsider some of the methodological challenges facing the WS-CAM scientific community [10,15-28]. Together, this entire field has been referred to as complex systems science (CCS) [29-32].

#### **Theoretical Tenets of Complex Systems Science**

Complex systems science studies "how the parts of a system give rise to the collective behaviors of the system and how the system interacts with its environment" (http://necsi.org/guide/study.html; last accessed Oct 31<sup>st</sup> 2011) [33]. Complex adaptive systems (CAS) are open systems, exchanging information with the environments with which they are nested. These systems are inter-dependent and self-organizing wholes with emergent properties greater than the sum of the parts [34]. Moreover, a CAS exhibits nonlinear dynamics, i.e., a small change in one aspect of an open system may produce disproportionately large effects over time in remotely related systems (the butterfly effect in weather; the princess-and-the-pea effect of childhood fairytales) [32, 35]. Because of these and other complex processes of information exchange, timing plays a much more prominent role in characterizing the

evolutionary dynamics of a CAS than it does in previous conceptualizations of mechanical or integrated systems [30-31, 33].

While the mathematical origins of CAS and NDS can be quite complex, six basic tenets summarize the systems properties that are directly applicable to the nascent science of WS-CAM. CAS are:

(1) whole systems that

(2) change over time [34]. They are characterized by

(3) **emergence, connectivity** [37], and **mutual causation** [38]; sufficiently complex interactions among system components lead to global order. Furthermore,

(4) emergence is a function of the whole system and not predictable by the properties of the parts[39]. Emergence of coherent patterns in nonlinear dynamical systems is exponential, potentiallysynergistic, and is driven by

(5) **self-organization** [40], whereby emergent order feeds back to the level of system components allowing a system to self-tune its levels of complexity for adaptive purposes. In this sense,

(6) **Stability and flexibility are critically paired** in emergent phenomena as systems naturally evolve to a state at the edge-of-chaos, where levels of coherence versus flexibility may shift rapidly in response to changes in flows of information among system components [37-38].

(1) CAS are wholes that operate within a context or environment of other CAS or nested wholes. Complex systems are self-sustaining entities that are comprised of nested networks of relationships [39]. Newtonian ontological and epistemological principles conceive systems as machines with subsystems of pieces and parts that are independent and externally controlled. Such a worldview is replaced in complex systems science by the view that systems are actually assemblies of other systems, emerging hierarchically across scales. Elements of the system at each scale co-create the larger CAS of which they are agents, with the increasingly global patterns emerging from these layered relationships and interactions. Cause is viewed, within such systems, as a complex mixture of bottom-up and top-down processes. As Goldberger [27] noted, the principle of superposition, a major tenet of linearity, is replaced within complex systems science. A CAS cannot be fully understood by simply analyzing each of its constituent parts and their relationships to each other. Neither can change or response of the system be predicted by investigating individual elements of a stimulus and "adding up" their effects. The global or supra-system does not respond in a summative manner; rather, the larger system responds as an integrating whole because of the unique time sensitive exchanges of information that occur among the systemic components and within the nesting environment.

Biology can be viewed as an exemplar of complexity in action. Liebovitch et al [41] comment: "...biology is not linear, it is a network of highly nonlinear genomic and proteomic interactions. . . Everything is connected to everything else. In this beautiful and tangled complex web, any therapeutic interaction spreads throughout the entire network of interactions. There is no single effect that can be associated with a single cause. A single therapeutic intervention does not produce a single desired effect; it produces many 'side effects'."

(2) Change in a CAS is an inherent quality of the system and is characterized as nonlinear and unpredictable. As noted by Goldberger, once the principle of superposition fails, systems behaviors are not predictable [27]. Since CASs are nested systems rather than a system comprised of independent and modular pieces and parts, change is an emergent property of the whole. Causality is circular, without beginning or end, powered by a host of feedback loops, network configurations, and points of bifurcation or system instability. Complex systems can be identified or mapped based on a series of behavioral phases, characterized as a state space or landscape that describes how the system is functioning across various possible contexts. Attractors (fixed, spiral, periodic, strange/chaotic) represent pulls toward particular behaviors, repellors represent unlikely system states, and saddle points represent a combination of an attractor and repellor. Together, the constellation of these stable aspects of a system creates a behavioral landscape or a set of possible behaviors of a system. The intrinsic dynamics of the system, as well as its initial conditions, ultimately determine the system's set of attractors, its potentially multi-stable state-space. Changes in the attractors occur at bifurcation points as the system is capable of adapting

toward new and innovative patterns that will lead to greater fitness and adaptability, thereby increasing global complexity and flexibility [29-33, 35, 40].

At points of bifurcation an abrupt change in dynamical patterns occurs, and a cascade of events unfolds across the system, manifesting in a whole system response that appears to have both local and global features. However, what is "local" may actually have its origins in a distant feedback loop; likewise what appears to be global may well be a whole systems response. As such, this calls into question labels such as "specific and non-specific treatment effects" and the common practice of testing for specific, predictable responses to a system change while dismissing the more global responses as "system noise". Complex adaptive systems may contain a variety of noisy outcomes, some random (i.e., white noise) and others deterministic (e.g., pink noise), each of which may play a role as the system selects from a variety of emergent outcomes involving co-evolving shifts with their environmental fields to find their "best-fit" [31-32].

(3) Change occurs across both local and global scales. Since system component effects are not additive and may lead to emergent properties, complex systems scientists anticipate change to be at both global and local levels of behavior. Further, local perturbations in the system can produce distant change. In a given ecosystem, for example, eradicating a specific insect could make it harder for the natural predator of that insect to find enough food to survive, which might lead, indirectly to reduced survival of the insect's predator. It may also lead to an overgrowth of the first insect's food source (perhaps plant material) which will eradicate competing plants.

This tenet also calls into question the concepts of "specific" and "non-specific effects". As complex webs of relationships, with infinite varieties of possible feedback loops and responses to a system perturbation, CAS can be expected to have responses across levels of scale that are unpredictable and emergent. Thus, it could be argued that all effects are specific within complex systems science [30-32]. The practical outcome of such a view is to minimize the focus on the specifics of a particular intervention, and to increase the emphasis on where and when the intervention is applied within the CAS. (4) The CAS self-organizes, seeking greater efficiency and sustainability. A self-organizing system is one that does not require outside agents to foster adaptive change. Kauffman [42] and Guastello & Liebovitch [40] characterize self-organization as "order for free," wherein internal systems dynamics seek the "best-fit," the most efficient, or the optimal conditions for the system in environmental context. Distributed control within the system enables learning and adaptive strategies of the whole. Therefore, outcomes occur as a process of ongoing system re-configuration, increasingly complex relationships, and evolution information transfer within the system to maximize the changes of success. Flexibility or nimbleness signals a robust system, a system that is able to adapt to potentially abrupt changes and to learn within complex fitness landscapes [40].

(5) *Change is emergent and occurs as a function of the whole; it is not additive in nature.* Change in a CAS is emergent, a function of the entire system with all of its nested systems and complexities. Emergence and self-organization may occur through a variety of processes such as synergetics (e.g., multicomponent global coherence such as lasers), rugged landscapes (complex adaptive organization in tune with a shifting environment), multiple basin (interactive multi-stability among a variety of attractors), and the sandpile/avalanche models (complex systemic outputs in response to distributed information build-up across the system) [32, 40]. Taken together, these models focus on (a) information flow between subsystems and agents and (b) bi-directional feedback across scales, explaining how small stimuli often result in large effects and how seemingly catastrophic events can, at times, result in merely a ripple effect across the system [32, 40].

Lorenz [43] first coined the metaphorical description of the "butterfly effect" to capture how small changes in atmospheric conditions can greatly alter global weather patterns. This hypothesis demonstrates the sensitivity of dynamical systems to the timing of intervention or change. Thus, change in a CAS defies proportionality, a central principle in linear systems thinking. Output in a complex system does not necessarily occur in a linear proportion to the magnitude of the input because of the influence intrinsic dynamics have within a system co-evolving with an ever-changing context [44]. (6) Emergent, self-organizing CAS display both stability and flexibility in dynamic dance. Emergence of complex behaviors or phenomena is a product of system integration and is dependent on connectivity within the CAS. Emergence represents criticality that is not dependent on specific elements at lower levels within a system but rather the processes of their complex interactions. Therefore, emergence is a function of the whole and not reducible to parts. Adaptive, self-organization tends to occur when a system is at a complex region referred to as the edge-of-chaos [34] where there is an ideal mix of stability and flexibility. Within this complex region, a system also is poised to become either more or less coherent, depending upon adaptive demands from within or from the nesting environment. [37-38]. Table 2 summarizes complex systems science terminology.

#### Explanatory Power of the Complex Systems Science and NDS for WS-CAM

Theories are only as useful as their explanatory power or applicability within a particular discipline [46]. Therefore, to determine if complex systems science is useful in conceptualizing WS-CAM, we examine exemplars from clinical theories and practice observations that have historically been identified as problematic when applying the traditional science paradigm.

Constitutionally-oriented WS-CAM therapies strive to alter the whole-person process underlying susceptibility to the environmental allergens and irritants gradually over time, rather than directly preventing expression of symptoms. In classical homeopathy, for instance, contemporary homeopath Jeremy Sherr [47] has written: "The fixed verb is a constant factor in any proving or case, repeating on every level…In pathology, a person will tend to excel at performing their main verb while failing at everything else...As pathology advances it becomes progressively more static, just as all verbs flow into nouns. Nouns (arthritis, tumor, neurosis) are the end result of a pathological process that began dynamically and ended as a fixed entity...The 'verb' of a case or remedy is its most dynamic expression...Western physiology and pathology focuses on nouns. In homeopathy, these nouns are termed affinities. Systems of analysis such as the four elements (or Chinese five elements) focus on adjectives – color, taste, temperature, etc. Verbs run silently behind these components, lending them

motion and life." Sherr [47] also notes: "This restricted verb pervades the whole organism. As a stuck repetitive action, people often express this verb as 'must', 'have to', 'should', and 'need to.'" In this analysis of Eastern versus Western languages of healing, connections to NDS are apparent in the central health-related factors of dynamical change involving rigidity versus flexibility.

Moreover, homeopaths and naturopaths assess clinical progress during treatment in terms of Hering's Law of Cure, a clinical principle that is consistent with the principles of self-organization and non-specific response to change [48-49]. Practice theory postulates that the center of gravity or deepest level of symptomatology shifts within the person from above downward (head towards toes), from inside outward (more important to less important organs, e.g., from lungs to skin), and in reverse order of time of original symptom appearance (newer symptoms resolve sooner than long-standing symptoms). Practitioners also monitor patients for global improvements such as an increased sense of overall wellbeing, even when specific local organ symptoms temporarily worsen [49-51]. Therefore, when treating a patient with joint pain, a WS-CAM practitioner would conclude a patient experiencing less depression and more energy but more joint pain for a few days or weeks was showing a good treatment response. By contrast, a conventional health care provider would rate the same patient as "worse".

WS-CAM practitioners utilize information about emergent person-environmental patterns as indicators of the patient's condition, their diagnosis and their requisite treatment. Thus, effects of hot or cold external temperatures, ingested foods and beverages, dryness or dampness, environmental odors, seasonal changes, and circadian times of day all make a difference in the diagnosis, treatment plan, and patient outcomes [50-56]. Interventions by practitioners of WS-CAM can be conceptualized to (a) manipulate the balance of the person as an integrated functional network (changing the interaction rules for the body parts or subsystems that comprise the person, e.g., with Traditional Chinese Medicine (TCM) or Ayurveda) or (b) alter the control parameters of the whole person, thereby driving changes of function at the global level and local subsystem levels hierarchically across levels of organizational scale (e.g., with an individualized homeopathic remedy) [59].

When observing for responses to treatment, practitioners observe and monitor emergent patterns as evidence of what the person as an indivisible system does in his/her world context over time. WS-CAM clinicians anticipate abrupt worsenings and improvements during the course of therapy. Homeopathy, TCM and Ayurveda all report healing crises (aggravations) or a worsening of both local and global symptoms in response to initiation of treatment and prior to system improvement. [51, 52, 58-60]. WS-CAM researchers have termed the sudden events as "unsticking" and the periods of transitional instability as "unstuckness" [61-62]. Each of these processes is consistent with complex systems science principles involving rigidity and flexibility as well as bi-directional transitions across scales. These "bifurcations" in dynamics can lead to transitional periods that create new patterns of adaptation that better fit the fitness landscape of the environment. Phase transitions in NDS, consistent with the periods of unsticking that have been observed following WS-CAM interventions in themselves do not necessarily result in clinically improved system dynamics; however these periods do offer opportunities for a complex system to transition into patterns that are more efficient and effective for the organism overall. Thus, a complex systems science perspective would justify improving WS-CAM clinical trials by adding better baseline measures to assess the dynamical processes underlying unique patient illnesses prior to intervention, assessment of a variety of potentially relevant clinical parameters across biopsychosial scales during the trial, and longer trial durations [6, 28, 63-65].

#### Conclusions

Complex systems science offers a theory-driven perspective that maps onto observed phenomena from clinical practice. At the very least, there is face validity supporting the use of Complex Adaptive Systems (CAS) Theory, Nonlinear Dynamical Systems (NDS) theory, and Networked Systems Theory/Agent Based Modeling. More likely, such models are the only truly adequate conceptual background for WS-CAM. These models provide working hypotheses that suggest explanatory mechanisms of action for such clinical phenomena as (a) persistence of changes for weeks to months between treatments and/or after cessation of treatment; (b) nonlocal and whole systems changes resulting from therapy; (c) Hering's Law; and (d) healing crises.

Further, complex systems science offers a way to move beyond the more limited, simple causal models of both mainstream mechanistic ontology and the historical perspective of WS-CAM vitalism (Figure 1).

#### [INSERT FIGURE 1 HERE]

As Langton, an early leader in complex systems science observed, the "real world" involves multidirectional interactions of parts and wholes to generate emergent outcomes of increasing complexity [8]. Complex systems science provides a holistic ontological perspective with which to conceptualize the development of disease and illness experiences, as well as experiences of healing and wellness [10].

#### References

- 1. Anderson RA, Crabtree BF, Steele DJ, McDaniel RR Jr.: Case study research: the view from complexity science. *Qual Health Res 2005 May*;15(5):669-85 2005; 15(4):669-685.
- 2. West B: Where Medicine Went Wrong: *Rediscovering the Path to Complexity (Studies of Nonlinear Phenomena in Life Science)*: World Scientific Publishing Company; 2006.
- 3. Ritenbaugh C, Verhoef M, Fleishman S, Boon H, Leis A: Whole systems research: a discipline for studying complementary and alternative medicine. *Altern Ther Health Med* 2003; 9(4):32-36.
- 4. Verhoef M, Lewith G, Ritenbaugh C, Thomas K, Boon H, Fonnebo V: Whole systems research: moving forward. *Focus on Alternative and Complementary Therapies* 2004; 9(2):87-90.
- 5. Verhoef MJ, Lewith G, Ritenbaugh C, Boon H, Fleishman S, Leis A: Complementary and alternative medicine whole systems research: Beyond identification of inadequacies of the RCT. *Complement Ther Med* 2005; 13(3):206-212.
- Fønnebø V, Grimsgaard S, Walach H, Ritenbaugh C, Norheim AJ, MacPherson H, Lewith G, Launsø L, Koithan M, Falkenberg T, Boon H, Aickin M.: Researching complementary and alternative treatments--the gatekeepers are not at home. *BMC Med Res Methodol* 2007; 7:7.
- 7. Walach H: The efficacy paradox in randomized controlled trials of CAM and elsewhere: beware of the placebo trap. *Journal of Alternative & Complementary Medicine* 2001; 7(3):213-218.
- 8. Lewin R. Complexity Life at the Edge of Chaos. 2nd edition. University of Chicago Press, 2000.
- 9. Walach H, Jonas WB.: Homeopathy. In Lewith G, Jonas WB, Walach H. (eds). Clinical Research in Complementary Therapies. Edinburgh: Churchill, Livingstone; 2002, pp. 229-246.
- 10. Bell IR, Koithan M. Models for the study of whole systems. *Integrative Cancer Therapies.* 2006; 5(4), 293-307.
- 11. Verhoef MJ, Lewith G, Ritenbaugh C, Boon H, Fleishman S, Leis A. Complementary and alternative medicine whole systems research: beyond identification of inadequacies of the RCT. Complement Ther Med. 2005 Sep;13(3):206-12.
- 12. Boon H, Macpherson H, Fleishman S, Grimsgaard S, Koithan M, Norheim AJ, Walach H: Evaluating Complex Healthcare Systems: A Critique of Four Approaches. *Evidence-based Complement Alternative Medicine*. 2007; 4(3):279-285.
- 13. Langevin HM, Wayne PM, Macpherson H, Schnyer R, Milley RM, Napadow V, et al: Paradoxes in acupuncture research: Strategies for moving forward. *Evidence-based Complementary and Alternative Medicine* 2011; 2011: 180805.
- 14. Sarmukkaddam S, Chopra A, Tillu G. Efficacy and safety of Ayurvedic medicine: Recommending equivalence trial design and proposing safety index. *International Journal of Ayurveda Research* 2010; 1(3): 175-180.
- Bell IR, Caspi O, Schwartz GE, Grant KL, Gaudet TW, Rychener D, Maizes V, Weil A: Integrative medicine and systemic outcomes research: issues in the emergence of a new model for primary health care. *Archives of Internal Medicine* 2002; 162(2):133-140.

- Bell IR, Baldwin CM, Schwartz GE: Translating a nonlinear systems theory model for homeopathy into empirical tests. *Alternative Therapies in Health & Medicine* 2002; 8(3):58-66.
- Bellavite P, Signorini, A.: The Emerging Science of Homeopathy. Complexity, Biodynamics, and Nanopharmacology, 2nd edn. Berkeley: North Atlantic Books; 2002.
- 18. Bellavite P: Complexity science and homeopathy: a synthetic overview. *Homeopathy: the Journal of the Faculty of Homeopathy* 2003; 92(4):203-212.
- 19. Torres JL: Homeopathic effect: a network perspective. *Homeopathy: the Journal of the Faculty of Homeopathy* 2002; 91(2):89-94.
- 20. Ruiz-Vega G, Poitevin, B., Pérez-Ordaz, L.: Histamine at high dilution reduces spectral density in delta band in sleeping rats. *Homeopathy* 2005; 94(2):86-91.
- 21. Shepperd J: Chaos theory: implications for homeopathy. *Journal of the American Institute of Homeopathy* 1994; 87(4):22.
- 22. Hyland ME, Lewith GT: Oscillatory effects in a homeopathic clinical trial: an explanation using complexity theory, and implications for clinical practice. *Homeopathy* 2002; 91(3):145-149.
- 23. Hyland M: Extended network generalized entanglement theory: therapeutic mechanisms, empirical predictions, and investigations. *Journal of Alternative & Complementary Medicine* 2003; 9(6):919-936.
- 24. Kang GL, Li S, Zhang JF.: Entropy-based model for interpreting life systems in Traditional Chinese Medicine. *Evid Based Complement Alternat Med* 2008; 5(3):273-279.
- Bellavite P, Ortolani R, Pontarollo F, Pitari G, Conforti A: Immunology and Homeopathy. 5. The Rationale of the 'Simile'. *Evid Based Complement Alternat Med* 2007; 4(2):149-163.
- 26. Coffey DS: Self-organization, complexity, and chaos: the new biology for medicine. *Nature Medicine* 1998; 4(8):882-885.
- 27. Goldberger AL: Non-linear dynamics for clinicians: chaos theory, fractals, and complexity at the bedside. *Lancet* 1996; 347:1312-1314.
- Pincus D, Metten, AM. Nonlinear dynamics in biopsychosocial resilience. Nonlinear Dynamics, Psychol Life Sci. 2010; 14:353-380.
- 29. Zimmerman B, Lindberg C, & Plesk P. Edgeware: Insights from Complexity Science for Health Care Leaders. VHA, Inc; 2001.
- 30. Miller JH & Page SE. Complex Adaptive Systems: An Introduction to Computational Models of Social Life. Princeton University Press; 2007.
- 31. Erdi P. Complexity Explained. Springer Publishing; 2008.
- 32. Guastello SJ, Koopmans M & Pincus D. (eds). *Chaos and Complexity in Psychology: The Theory of Nonlinear Dynamical Systems*. Cambridge Press; 2009.
- 33. Bar-Yam Y: *Making Things Work: Solving Complex Problems in a Complex World.* Knowledge Press; 2004.
- 34. Kauffman S: At Home in the Universe. *The Search for the Laws of Self-Organization and Complexity*. Oxford University Press; 1995.
- 35. Bar-Yam Y: Dynamics of Complex Systems. Perseus Books; 1997.

- Granic, I., & Hollenstein, T. A survey of dynamic systems methods for developmental psychopathology. In D. Cicchetti & D. J. Cohen (Eds.), *Developmental Psychopathology*. New York: Plenum Press, 2006, pp 889-930.
- 37. Newell D. Concepts in the study of complexity and their possible relation to chiropractic health care: a scientific rationale for a holistic approach. *Clinical Chiropractic* 2003; 6:15-33.
- 38. Morin E. On Complexity (R. Postel, Trans.). Hampton Press, Inc; 2008.
- 39. Gilbert S F, & Sarkar S. (2000). Embracing complexity: Organicism for the 21st century. *Developmental Dynamics* 2000; 219, 1-9.
- 40. Guastello SJ & Liebovitch LS. Introduction to Nonlinear dynamics and complexity. In *Chaos and Complexity in Psychology: The Theory of Nonlinear Dynamical Systems*. Cambridge Press; 2009, pp. 1-40.
- 41. Liebovitch LS, Tsinoremas, N., Pandya, A.: Developing combinatorial multi-component therapies (CMCT) of drugs that are more specific and have fewer side effects than traditional one drug therapies. *Nonlinear Biomed Phys* 2007; 1(1):11.
- 42. Kauffman S. Origins of Order: Self-organization and Selection in Evolution. Oxford Press; 1993.
- 43. Lorenz, Edward N. (March 1963). Deterministic nonperiodic flow. *Journal of the Atmospheric Sciences*; 1963; 20(2): 130–141.
- 44. Goldberger A. Complex systems. *Proceedings of the American Thoracic Society;* 2006; 3: 467-472.
- 45. Goldstein, J. (2001). A nonlinear dynamics and complexity glossary. In B. Zimmerman, C. Lindberg, & P. Plsek (Eds.), *Edgeware: Insights from Complexity Science for Healthcare Leaders*. (pp. 239-271). Irving: VHA Inc.
- 46. Fawcett J. Criteria for evaluation of theory. *Nursing Science Quarterly*; 2005; 18(2): 131-135
- 47. Sherr J: Dynamic Materia Medica. Syphilis: A Study of Syphilitic Miasm through Remedies. Great Malvern Worcestershire, England: Dynamis Books; 2002.
- 48. Oberbaum M, Singer SR, Vithoulkas G. The colour of the homeopathic improvement: the multidimensional nature of the response to homeopathic therapy. *Homeopathy* 2005; 94(3):196-199.
- 49. Zeff J, Snider P, Myers S. The hierarchy of healing: The therapeutic order. In *The Textbook of Natural Medicine (3<sup>rd</sup> edition)*. Elsevier Publishing; 2006.
- 50. Rowe T. *Homeopathic Methodology: Repertory, Case Taking, and Case Analysis.* Berkeley: North Atlantic Books; 1998.
- 51. Lansky AL: Impossible Cure: The Promise of Homeopathy. Portola Valley, CA: R.L. Ranch Press; 2003.
- 52. Lad V: Textbook of Ayurveda, Volume One (Fundamental Principles): Ayurvedic Press; 2001.
- 53. Lad V: Textbook of Ayurveda, Volume Two (A Complete Guide to Clinical Assessment): Ayurvedic Press; 2007.
- 54. Owen D: Principles and Practice of Homeopathy: The Therapeutic and Healing Process.: Churchill Livingstone; 2007.
- 55. Tsang P: Optimal Healing: A Guide to Traditional Chinese Medicine: Balance for Health Publishing; 2008.
- 56. Yanchi L: The Essential Book of Traditional Chinese Medicine: Columbia University Press; 1988.

- 57. Vasquez A, Dobrin R, Sergi D, Eckmann JP, Oltvai ZN, Barabasi AL: The topological relationship between the large-scale attributes and local interaction patterns of complex networks. *Proceedings of the National Academy of Sciences of the United States of America* 2004; 101(52):17940-17945.
- 58. MacPherson H, Thomas, K., Walters, S.: The York acupuncture safety study: prospective survey of 34 000 treatments by traditional acupuncturists. *BMJ* 2001; 323:486-487.
- 59. Oberbaum M, Singer SR, Vithoulkas G: The colour of the homeopathic improvement: the multidimensional nature of the response to homeopathic therapy. *Homeopathy: the Journal of the Faculty of Homeopathy* 2005; 94(3):196-199.
- 60. Vithoulkas G: *The Science of Homeopathy*. N.Y.: Grove Weidenfeld; 1980.
- 61. Koithan M, Verhoef, M., Bell, I.R., Ritenbaugh, C., White, M., Mulkins, A.: The process of whole person healing: "unstuckness" and beyond. *J Altern Complement Med* 2007; 13(6):659-668.
- 62. Bell IR, Koithan M, Gorman MM, Baldwin CM: Homeopathic practitioner views of changes in patients undergoing constitutional treatment for chronic disease. *Journal of Alternative & Complementary Medicine* 2003; 9(1):39-50.
- 63. Witt CM, Ludtke R, Mengler N, Willich SN: How healthy are chronically ill patients after eight years of homeopathic treatment? Results from a long term observational study. *BMC Public Health* 2008; 8(1):413.
- 64. Elder C, Aickin M, Bell IR, Fønnebø V, Lewith GT, Ritenbaugh C, Verhoef M.: Methodological challenges in whole systems research. *J Altern Complement Med* 2006; 12(9):843-850.
- 65. Miller E, Maimon Y, Rosenblatt Y, Mendler A, Hasner A, Barad A, Amir H, Dekel S, Lev-Ari S.: Delayed Effect of Acupuncture Treatment in OA of the Knee: A Blinded, Randomized, Controlled Trial. *Evid Based Complement Alternat Med* 2009.