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**Patient-Centered Research on Whole Systems of Complementary and Alternative
Medicine: A Complex Systems Science Perspective (Part I: Concepts)**

Iris R. Bell, MD PhD^{1,3-6} and Mary Koithan, RN PhD^{1,2}

For reprints and all correspondence: Dr. Iris Bell, Dept. of Family and Community Medicine, The University of Arizona College of Medicine, 1450 N. Cherry Ave., Tucson, AZ 85719-5052, USA. Tel. 520-626-5219; FAX 520-626-2030; Email: ibell@u.arizona.edu.

From: The Department of Family and Community Medicine,^{1,2} Psychiatry,³ Psychology,⁴ Medicine (Integrative Medicine),⁵ and Public Health,⁶ and the College of Nursing,² The University of Arizona, Tucson, AZ.

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Abstract

This is the first of two papers intended to provide an interdisciplinary bridge between the research worlds of whole systems of complementary and alternative medicine (WS-CAM), e.g., traditional Chinese medicine and homeopathy, and nonlinear dynamical complex systems (NDS) science. NDS science offers concepts, postulates, and methods that can inform thinking about the process of healing associated with WS-CAM. NDS studies of WS-CAM can address the limitations of current theoretical and methodological approaches grounded in world views that lead to the use of reductionistic and linear scientific models of human health and health care to study holistic interventions. Holistic, non-linear, dynamically-based study designs show greater external validity for (a) clinical theories and practices used in WS-CAM, e.g., constitutional types interacting with the natural environment; (b) “non-specific” multi-level and sometimes abrupt bidirectional changes in patients during treatment, e.g., healing crises and hierarchical, self-similar healing patterns across bodily subsystems; and (c) persistence of improvements between treatments and/or after the end of WS-CAM treatment, in contrast with drug-based interventions that require the ongoing presence of the drug. Previous work on NDS in childhood development, psychotherapeutic processes, and group dynamics provide useful precedents for patient-centered WS-CAM research. NDS studies on WS-CAM can open new perspectives on dynamical mechanisms to understand the evolution of disease and effects of various treatments. We posit that NDS theory and methods will stimulate ground-breaking research on the processes and trajectory of individualized healing from chronic illness during WS-CAM treatment.

Keywords: whole systems of complementary and alternative medicine, nonlinear dynamical systems, attractor patterns, bifurcation, healing, process, individualized treatment outcomes

*It is much more important to know what sort of a patient has a disease than
what sort of a disease a patient has.*

– William Osler, MD

Introduction

There is a growing body of research literature in biomedicine, medical anthropology, nursing, and public health suggesting that historical 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). One discipline from the biomedical world, complementary and alternative medicine (CAM), has been particularly vocal about these limitations, consistently suggesting that alternative world views and research frameworks may provide more helpful ways to investigate how disease and illness experiences manifest within individual persons and how various interventions or systems of care facilitate the process of healing and health promotion (3-7). These concerns follow from the use of the Western pharmaceutical randomized controlled trial (RCT) model to study whole systems of complementary and alternative medicine (WS-CAM) and the resultant mixed and contradictory findings that have fueled debates over the most appropriate theoretical and methodological approaches for testing CAM interventions and evaluating patient outcomes (<http://www.WholeSystemsResearch.org>) (6, 8-14).

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) (Table 1). These systems of care differ in their cultural contexts and evolution, as well as in the specific

therapeutic modalities used. Nonetheless, they share variants of a vitalistic philosophy that asserts the flow of a non-material life force throughout the living person.

[Insert Table 1 About Here]

Interconnectedness. Each WS-CAM employs its own diagnostic approach, identifying patterns of bio-psycho-social symptoms. Yet all WS-CAM approaches treat these symptoms as multiple manifestations of an emergent, unitary, patient-centered, rather than disease-based, disorder in an environmental context. For example, a patient with gallstones and a behavioral style linked to anger suppression/expression while working with other people, may find improvement over time in both the physical condition and behavioral pattern, using one single, therapeutically coordinated patient-centered treatment package in a WS-CAM such as TCM or classical homeopathy. Thus, WS-CAM providers view mind and body as interlinked, and they would not apply separate diagnoses or multiple isolated treatments for these two seemingly very different symptoms from the perspective of Western medicine.

Global and Local Effects. The objective of WS-CAM interventions is treating the overall disease process of the person as an integrated whole organism, rather than seeking separate magic bullets for each symptom (Figure 1). In short, WS-CAM embrace beliefs that posit (a) a global person-level-of-scale emergent and (b) local (subsystem) level-of-scale behaviors that interact, shape each other's expression, and share fundamental properties and change collectively with treatment..(15) "Side-effect" is a less relevant term for WS-CAM therapies, as these therapies intend to produce broad, "non-specific," rather than narrow, "specific" effects at the outset, in contrast with most pharmaceutical drugs (8, 12, 16, 17).

[Insert Figure 1 About Here]

The Role of Environmental Context. In contrast with endogenous mechanistic, local disease-focused diagnoses of mainstream Western medicine, many WS-CAM also utilize information about environmental contextual factors as intrinsic aspects of the patient's diagnosis and invoke modifications of the person's lifestyle within the environment as part of the treatment

plan. Thus, effects of hot or cold external temperatures, ingested foods and beverages, dryness or dampness, environmental odors, seasonal changes, and circadian times of day make a difference in the diagnosis, treatment plan, and patient outcomes (18-23). In many WS-CAM, the social environment is also relevant to the diagnosis and treatment of the person. For example, homeopaths consider whether symptoms are exacerbated or alleviated when the person is alone or when with other people. Many CAM clinicians consider lessening or resolution of such environmental reactivity as one aspect of overall therapeutic benefit. Therefore, while each WS-CAM has distinct characteristics and treatment models, they also converge conceptually to suggest the need for new theoretical and philosophical approaches to health/illness that account for the complex, ever-changing dynamics of a person in transaction with their internal and external environments (24) (Table 2).

[Insert Table 2 About Here]

General Research Implications. The recent research literature in WS-CAM highlights this need for greater external validity in research studies to capture the full clinical process and outcomes (Figures 2a, 2b). One factor in the inconsistencies between studies and the frequent divergence between RCT findings and clinical claims is that the underlying world view assumptions of the scientific methodology (reductionism and materialism/mechanism) are a mismatch for those of the clinical WS-CAM field under study (e.g., holism) (25). Western medicine assumes linear, local direct causality of disease and of healing, whereas WS-CAM assume constitutional (person-level) diagnoses encompassing biopsychosocial clinical patterns of presentations and predict complex, often indirect processes of change in time and space (body parts), as inherent to a good therapeutic response (19-26).

[Insert Figure 2a, 2b About Here]

A second factor in the clinical observation-research findings schism is the WS-CAM belief that the biopsychosocial environmental context affects the individual's constitution and plays a central role in their diagnoses and treatments. That is, certain constitutions are better or

worse under particular environmental circumstances. Western medical practice may separately acknowledge these influences, but they are not intrinsic to the diagnosis or choice of drug as they are in WS-CAM. Conventional observational/effectiveness study designs may offer some advantage for capturing real-world contexts and dealing with the differences between WS-CAM and pharmaceutical drugs (6), but they can still fall short methodologically.

Various investigators have proposed that complex systems theory, involving nonlinear dynamical systems and network models and their various methodological approaches offer a holistic and modern research framework for reconsidering some of the challenges that WS-CAM studies pose within a reductionistic design framework (13, 25-35). Complexity is a holistic science that studies systemic processes and patterns within and between levels of organizational scale in systems evolving over time in environmental context, whereas conventional medicine is a reductionist science that studies reproducible local content and single-agent effects (specific mechanisms, specific symptoms in specific structures) at points in time (36-43). As a result, complex systems science has a greater capacity than does reductionist conventional medical science for enabling studies to accommodate the theories and capture the clinical practices and observations of WS-CAM with greater external validity (13, 25, 26, 44). The current papers go beyond previous theoretical reviews in a given WS-CAM to (a) synthesize the case for applications of complexity science and NDS research approaches to practice theories of WS-CAM and (b) propose a concrete program of possible studies for operationalizing the conceptual argument.

Conceptualizing Clinical Conditions and Change with Complex Systems Science: Prior Research in Conventional Medicine and Psychotherapy

Complex systems science is a relatively new field that 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>) (41). The parts of a complex system are inter-

dependent and self-organize to generate a whole with emergent properties greater than the sum of the parts (45). Moreover, complex systems exhibit nonlinear dynamics, i.e., change over time in which the nature and magnitude of the change is disproportionate to the nature and size of the perturbation that mobilized the change (the butterfly effect in weather; the princess-and-the-pea effect of childhood fairytales) (39, 46). Time plays a much more prominent role in characterizing the real-time dynamical and evolutionary time features of a complex system than it does in mainstream mechanistic science.

Living systems are open systems, adaptive to their environment, with which they interact. Several authors have pointed out the potential relevance of complexity science to certain “dynamical diseases” such as epilepsy, cardiac arrhythmias, diabetes, cancer, and depression (36, 37, 47-52) and to conventional medical interventions overall (2, 53). Tschacher and Junghan (54) summarize the NDS view that “disease is thus equivalent to a significant change of a system’s dynamical engine, such that pathological behavior evolves out of healthy behavior by way of a phase transition between two dynamical regimes. The expectation is that rather than the system per se, it is only the dynamics which is [*sic*] pathologically altered.”

Causality in complex systems is typically indirect and nonlinear because of the emergence of distant physical effects that are remote in time from the original point of action of the initiating stimulus (e.g., disease agent, or therapeutic intervention(s)). As Liebovitch et al. (55) 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’.”

What Liebovitch et al. say about interdependent networks in biology (genes, proteins, cells, organs) is also valid for many other types of networks at higher levels of organizational scale, such as those studied in individual and interpersonal psychology, and social systems

research. A key point about complexity science is the self-similarity (fractality) of structural patterns and functional dynamical processes across levels of scale for both space and time (<http://www.SocietyForChaosTheory.org/>) (37, 56). A common example of fractality in its branching structure is the self-similarity of the components of the lungs across levels of scale. Several review papers and texts provide excellent introductions to the theories and methods of the field (36, 37, 39, 41, 42, 46, 57). The website <http://www.WholeSystemsResearch.org> also provides glossaries with definitions of complex systems, NDS, and WS-CAM concepts for readers unfamiliar with one or the other field.

Conceptualizing Disease as Stuckness in Repetitive Dysfunctional Patterns. In an individual patient, clinicians routinely observe complexity and dynamics in action (36, 37, 57-61). Psychotherapy patients, for instance, often present as stuck in repetitive dysfunctional behaviors or relationships (62). Week to week, they come to sessions, describing events and interactions that play out with similar responses by them to similar events, ending with the same emotions, such as fear, anxiety, anger, sadness, and/or frustration. That is, their process is similar week to week, even though the specific content of the event details differs. If the identified patient tries to change his/her behaviors, the people in their dysfunctional social network environment expect and require “business-as-usual” from the person. In fact, they say and do things to push the patient back into and elicit the more familiar and usual behaviors, e.g., being the victim of abuse or taking addictive drugs (63). Without effective therapy, even if patients manage to extricate themselves from one negative or abusive relationship, they seem remarkably able to find another abuser in an entirely different person for their next relationship.

In complexity terms, this patient is a system with a stable, unhealthy, and rigid attractor pattern of individual and interpersonal dynamics that manifests as a limited range of behaviors that he/she knows how to emit in response to external events (62, 64-68). An attractor is defined as “a box of space in which movement (of system dynamics) could take place or not”(46). More rigid attractor patterns include fixed point attractors and limit cycles (and correspond with less

healthy, i.e., less complex, dynamics), whereas more flexible attractors are certain chaotic attractors or complexors (and correspond with more healthy, optimally complex dynamics) (Table 3) (68-70).

Living systems self-organize in a dynamic balance between excessive order (e.g., death) and complete chaos (e.g., ventricular fibrillation). Lipsitz and Goldberger proposed that aging and disease lead to a loss of complexity – and hence, loss of adaptability to environmental challenges -- in physiological and behavioral systems (61, 71). Subsequent studies support their contention across a wide range of conventional clinical diagnoses, including unipolar and bipolar depression, bipolar disorder, posttraumatic stress disorder, Alzheimer’s disease, epilepsy, Parkinson’s disease, multiple sclerosis, diabetes mellitus, and various cardiac diseases (36, 37, 47, 72-79).

[Insert Table 3 About Here]

Understanding Treatment in Complex Systems Terms. During most types of psychotherapy, the deeper therapeutic goal is not merely to give the patient support and solace for the emotional pain of each adverse event. Rather, the goal is to help him/her recognize the process that generates the same undesirable outcomes, change the process to a more resilient and adaptive process, and maintain those changes despite subsequent environmental challenges. In complexity terms, the therapeutic goal is to destabilize the system out of his/her usual behavioral patterns (disrupt usual dynamics – see bifurcation dynamics, Figure 2e), thus fostering transition from a rigid attractor pattern into a healthier, more flexible behavioral pattern (i.e., more complex and adaptive attractor pattern) (62, 68).

The concept of individual differences in nonlinear dynamics of treatment responders versus non-responders also argues for evaluating patient dynamics at baseline and at follow-up visits in the course of prospective, long-term observational trials, whose duration can span years rather than a few months. Individuals who do and do not report clinical improvements in such observational studies should have already completed any treatment-initiated phase transitions and re-stabilized into post-treatment attractor patterns. Together with other methodological issues,

these points could help account for the consistently positive findings in favor of WS-CAM in observational studies, (80-83) as contrasted with the mixed conclusions of RCTs (84-87).

Sudden Change in Clinical Course: NDS Implications. The transition process towards recovery (healing) in psychotherapy sometimes parallels the healing crises reported during WS-CAM treatment. For instance, Pincus (46, 62) notes that previous psychotherapy researchers (88) have observed sudden transitions in patients with successful outcomes. Some depressed patients abruptly experience transient worsening of symptoms prior to improvement (potentially a bifurcation of system dynamics). Other psychotherapy patients with depression, perhaps as many as 42%, undergo sudden gains, especially early in treatment, that lead to sustained positive outcomes (89). In a two-year follow-up study, patients with sudden gains during cognitive therapy had a 74% lower relapse risk than responders without a history of sudden gains during treatment (90). Studying the actual process of therapy with qualitative and quantitative tools, rather than merely assessing the outcome endpoints, is emerging as a strategy for psychotherapy research that may inform parallel considerations for WS-CAM (91-93). Process-outcome studies, including evaluation of session by session events, for instance, may help document the nature of the therapy actually delivered and the patient's trajectory of response.

The patterns and processes of the individual – good and bad -- travel through life with him/her unless persistently modified. There is a body of conventional research on psychotherapy versus psychopharmacology treatment that suggests that even though panic disorder or depression patients treated with cognitive-behavioral therapy (CBT) versus psychopharmacological drugs have comparable short-term benefits in RCTs, it is the CBT-treated individuals who show better maintenance of improvements over time after cessation of the intervention (90). Drug-treated patients relapse sooner, potentially because they only temporarily experienced externally-forced changes in their brain chemistry, but had not learned to modify their intrinsic process of interacting with the world. The psychotherapy-treated patients learned new and healthier ways of interacting with their environment that allow them to draw on those tools even after therapy ends.

Complexity concepts also can apply to treating medical pathology. Experimental studies have shown the ability to re-set apneic episodes to normal breathing patterns by administering low-level vibratory stimulation to preterm sleeping infants (94). Cardiology researchers have aborted heart arrhythmias and normalized heart function by giving small, irregularly timed electrical stimuli to the heart based on nonlinear dynamical modeling (95). Again, the nonlinear effects of the intervention are carried forward in time by changes in dynamics of the system, not by the intervention itself.

In the medical setting, conventional medical providers see many patients with chronic conditions who return over and over with flares of the condition under the same types of environmental factors or stressors. The usual intervention is to suppress the symptoms, not to alter the dynamics of the system generating the symptoms. A common example is asthmatics who have attacks from pollens during spring allergy season, aerobic exercise, a spike in outdoor air pollution, and/or eating peanuts (albeit individually-salient factors on an individual basis). Conventional drug treatments strive to block the local tissue and cellular mechanisms for the expression of the asthmatic symptoms in the moment. When the asthma drugs are stopped, however, symptoms rebound and relapse quickly. In contrast, studies suggest that certain CAM interventions act less like symptom-suppressing drugs and, instead, more like nonlinear agents of change to trigger the person as a system to change course in his/her dynamics (32, 96).

Conceptualizing WS-CAM Therapies in Complex Systems Terms.

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 (Figure 1). In classical homeopathy, for instance, Sherr (97) 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 (97) also notes: “This restricted verb pervades the whole organism. As a stuck repetitive action [cf. rigid attractor dynamics?], people often express this verb as ‘must’, ‘have to’, ‘should’, ‘need to’ etc.”

When patients finish successful WS-CAM treatments, they reportedly maintain improvements for extended periods of months or even years (96, 98-100). Thus, although the levels of scale, the nature of the interventions, and outcome variables may differ, successful psychotherapy and WS-CAM interventions may have more in common with one another for their dynamical system process effects than they do with drug-based treatments. Adapting theories, knowledge, and techniques from dynamical systems-related studies of psychotherapy could accelerate advances in research on WS-CAM.

As do complexity researchers, WS-CAM clinicians and scientists look for emergent patterns as evidence of what the person as an indivisible system does in his/her world context. To intervene in the person’s dynamics, an NDS-based model is that practitioners of WS-CAM are either (a) manipulating 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 TCM or Ayurveda) or (b) altering 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).

Consequently, the time course and patterns of change across multiple levels of scale in the person may be seemingly dilatory and lengthy, requiring longer study durations more typical of observational trials than of RCTs to document (6, 99, 101, 102). A complex systems

framework for understanding the healing process in WS-CAM suggests the likelihood of greater variability of outcomes early in treatment rather than, necessarily, rapid resolution of any given specific symptom(s) in a local body part. Viewing even local symptoms as behavioral manifestations of dysfunction of the person as a whole system means that healing is a person-wide nonlinear dynamical process involving changes at global and multiple lower levels of scale in a hierarchically self-organized complex adaptive system.

The abrupt worsenings and improvements reported in psychotherapy patients (88) or abrupt shifts in clinical trajectory of medical patients treated with small, specially-timed interventions (36) sound parallel to the healing crises (aggravations) and clinical course of symptoms reported in many WS-CAM. For instance, WS-CAM clinicians variably estimate the incidence of healing crises and aggravations, as well as intervening sudden onset colds and flu, early in treatment of patients with a variety of chronic illnesses at a range of 3-40% of their cases with a variety of conventional diagnoses (20, 98, 103-105). WS-CAM researchers have termed the sudden events as “unsticking” and the periods of transitional instability as “unstuckness” (24, 100). Retrospective chart review and prospective studies of outcomes in WS-CAM patients with and without histories of sudden early changes for better and/or worse could yield novel ways to identify individuals who will eventually become optimal treatment responders and facilitate triage of likely non-responders to other treatment programs.

As noted above, in dynamical systems, abrupt bi-directional transitions are labeled “bifurcations” and can lead to transitional periods and then, to new, more stable patterns. Phase transitions in themselves do not necessarily resolve with stabilization into clinically improved system dynamics. Patients could undergo a phase transition and end up in a new, stable, but still relatively rigid dynamical pattern (Figure 4). Data from the Lewith et al. (106) study of homeopathically-prepared dust mite in asthmatics are consistent with this hypothesis. Verum patients oscillated up and down in direction for all three of their outcome measures over 16 weeks, but showed no net clinical benefit from the intervention (which was isopathy, not

homeopathy in its clinical approach) (32). The ability to assess individual differences at different points in time in the process of change and healing during WS-CAM treatment could lead to innovative N-of-1 dynamical study designs.

A testable hypothesis is time-based. That is, certain WS-CAM therapies, notably those that target root disturbance, serve as nonlinear agents of change in triggering persistent changes in individual dynamics at a system level of the person that *outlast the duration of treatment*, in contrast with conventional drugs that cause specific biochemical effects only while present in the system.

Examples of Methodological Approaches from Complex Systems Science with Implications for WS-CAM Research

In Part II, we will discuss a wide range of methods in complexity science and NDS that offer innovative approaches to studying patients as complex adaptive systems and the healing process as longitudinal non-linear dynamical change. One of the areas of health and healing in which preventive medicine and WS-CAM converge in terms of goals is health promotion and optimizing wellness and well-being. The World Health Organization's definition of health, for instance, is: "Health is not only the absence of infirmity and disease, but also a state of physical, mental, and social well-being."

NDS researchers may have operationalized the WHO definition of multi-scale well-being in terms of human flourishing. For instance, Fredrickson and Losada (68) used a set of differential equations to model the dynamics of human flourishing from judges' ratings of, e.g., (videotaped) behaviors. Optimal complexity and adaptability in the behavioral attractor pattern of the person corresponds to the flexible type of complexor seen in Table 3d (68-70). Languishers exhibited behavioral dynamics more like limit cycle attractors (Table 3b).

Furthermore, the mathematical models for conditions under which systems manifest well-being revealed that ratios of positive to negative (P/N) system behaviors of at least 2.9:1 as a cut-

off for bifurcation (then, up to a limit of 11.6:1) occur in systems that generate the healthier, optimally complex dynamics in the short-term and greater objectively-measured success in the long-term. In contrast, positivity-negativity ratios below 2.9 correlate with more dysfunctional, rigid dynamics and poorer outcomes. Ratios around 5-6:1 appear predictive of the highest productivity in business teams or the long-term survival of marriages. We posit that the dynamics of human flourishing may hold great relevance for studying the positive dimensions of clinical outcomes, including positive life-altering transformative changes, reported in a subset of patients treated with various WS-CAM, beyond absence of disease (16, 98, 107, 108).

Using a mathematically less-intensive method, Hollenstein, Granic, and colleagues have published several studies using a graphical technique called state-space grids (SSG) to document system dynamics within one individual or between two people (66, 67, 109). They have assessed the real-time patterns of interactional behaviors between mother and child or between adolescents in flexible versus rigid relationships from coded videotapes of conversations (Table 3) (65-67, 93). Repeated measurement of real-time dynamics, sampled longitudinally during therapeutic intervention, revealed the impact of treatment via changes in the system's behavior patterns. Individuals who responded well clinically exhibited more flexible (less rigid) dynamical patterns in their behavioral attractors on SSGs, whereas poor responders remained measurably stuck in their rigid attractors. Thus, real-time dynamical patterns can predict future clinical outcomes, e.g., which adolescent goes on to exhibit delinquent behaviors (110).

[Insert Figure 3 About Here]

Figure 3 provides a visualization of a natural transitional process during human development from a given behavioral attractor pattern of a child who enters adolescence and undergoes an abrupt disruption into a bifurcation (two stable dynamical states, e.g., clinical worsening and clinical improvement) and, ultimately, a phase transition (one stable dynamical state), re-stabilizing over a period of years into a new and different attractor pattern of behavioral dynamics (65). As Hollenstein notes, state space grids can reveal bifurcations and phase

transitions in the individual by showing (a) greater variability of real-time patterns during transitional periods as compared with previous status; and (b) lack of consistency across measurement occasions (67).

[Insert Figure 4 About here]

Researchers have applied SSG methods to study the evolution of pathological behavior and/or the process of recovery during treatment of a person or social system. The potential application of SSGs to research on the evolution of the healing process during treatment with WS-CAM is obvious. During treatment, patients with clinical favorable outcomes should show changes in their dynamics from rigid attractors to more flexible attractors that analysis of their videotaped behaviors (65, 66, 93, 111, 112) (including use of language patterns) (78, 113, 114) and/or physiology (56) over time could capture. Graphing an individual behavior on one axis and time-locked physiological activity on the other axis would allow dynamical studies across levels of organizational scale within the individual person (66, 67, 93, 115). Non-responders will exhibit little or no dynamical alteration from their stably rigid attractor patterns at baseline. These methods could also apply to research on therapeutic relationships emerging from WS-CAM patient-provider-environment interactions.

We propose that some of the problems in reproducibility between different RCTs of WS-CAM derive from the ability of these therapies to de-stabilize patient dynamics and cause bifurcations and phase transitions that begin at various times and run through the end of the short study durations typical of RCTs, e.g., 12-16 weeks. Thus, average outcomes in verum treatment groups could reflect differential status of individual patients in various phases of dynamical oscillation during the process of change. Averaging outcomes over a group would risk canceling one patient's ups with another's downs on a given variable, much as sine waves 180 degrees out of phase cancel each other (25). The averaging procedure thereby yields an apparent lack of net group effect, even though the individual dynamics under verum are markedly different from those of placebo patients (who are truly dynamically unchanged over time as a group) (32).

The SSG technique also could facilitate capturing individual healing crises as sudden-onset destabilized periods (bifurcations, phase transitions) in true healing processes followed by re-stabilization into more flexible attractor patterns, as compared with the persistently more rigid dynamical attractors of ineffective verum- and placebo-or sham-treated individuals. Mere psychological shifts in response set such as a re-calibration of current perceived status compared with baseline status should manifest with minimal change in actual dynamical patterns over time.

Conclusions – Part I.

The NDS approach for studying individual patient outcomes in WS-CAM research offers theory-driven models that map with at least face validity onto phenomena that practitioners report in evaluating and treating their patients within the real-world. Over long-term treatment, the persistence of changes for weeks to months between treatments and/or after cessation of treatment is one clinical indicator of effective WS-CAM therapies. The persistence of effects may be a unique feature of dynamical therapies and runs in distinction to conventional drug-like mechanisms requiring the ongoing presence of the treatment agent.

Complexity/NDS empirical and computer simulation techniques permit a more holistic assessment of the person's dynamics without dissecting the system into separate subsystems isolated from each other and from their environmental context. These NDS approaches use the patient's own words and behaviors in real time as the raw data, (116-118) avoiding methodological pitfalls from relying on subjective self-assessments by questionnaire summary ratings of symptoms or states. Self-ratings are prone to distortions as a function of high levels of social desirability or trait defensiveness or response shifts over time with recalibration of recall of baseline status, as well as lack of awareness of one's own recurrent, dysfunctional patterns of behavior while in the middle of expressing these behaviors (12).

As starting points for NDS studies of patient dynamics during WS-CAM treatment, constitutionally-oriented homeopathy and TCM offer the most promising model interventions that

could alter control parameters in the person-system (Table 2). Their practice theories involve concepts that appear to translate in heuristically useful ways into modern concepts of NDS/complexity/network science. Furthermore, the homeopathic simillimum remedy translates into a motif (a recurring element that symbolizes the theme) (119) for potentially shifting the dynamics of the disease attractor into a bifurcation or phase transition at global and local levels (cf. Vasquez) (Figure 2a).

The typically multi-modal/multi-component, but still coordinated, set of treatments in TCM translate into potential dynamical modulators for optimizing connectivity across the network organization of the person as a system (Figure 2b) (55). Moreover, homeopathy and TCM as exemplar whole systems of CAM provide an opportunity to compare and contrast interventional approaches that differ markedly in the number of treatment agents utilized to bring about therapeutic shifts in the dynamics of the individual, that is, one provider plus one homeopathic remedy versus one provider plus a multi-modal package of TCM care (acupuncture, moxibustion, Chinese herbs, qi gong, etc) (16, 107, 120, 121). Complexity/NDS methods offer novel approaches for documenting individual short-term responses and the trajectory of long-term outcomes in response to interventions. As a result, NDS methods can facilitate studying the treatment and healing process – including when and where they may go well or badly. In Part II, we will outline a proposed research agenda for studying WS-CAM from the perspective of complexity science and NDS.

Table 1. Leading Whole Systems of CAM and Therapeutic Components. All WS-CAM**Individualize Selection of Treatment Program for Each Patient.**

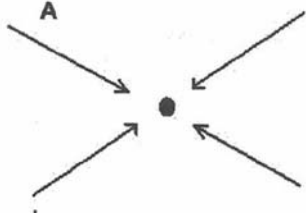
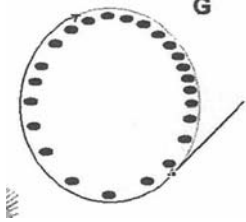
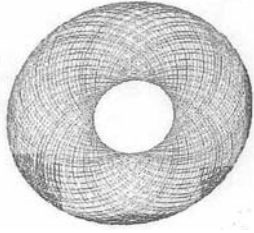

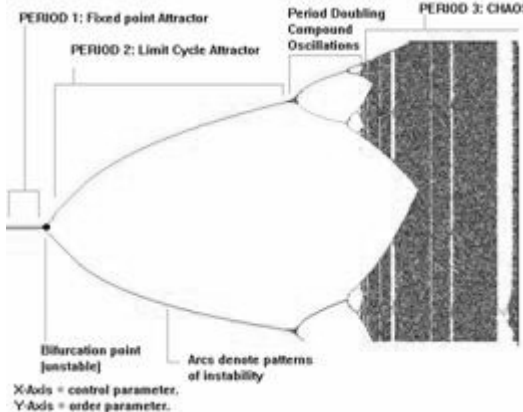
	Homeopathy	TCM	Ayurveda	Naturopathy
Trained Provider	Yes	Yes	Yes	Yes
Homeopathic Remedy	Yes	No	No	Yes, varies
Acupuncture	No	Yes	No	Yes, varies
Herbs & Supplements	No	Yes	Yes	Yes
Detoxification Procedures	Yes, in terms of removing “obstacles to cure” (but no specific therapies given)	Yes	Yes	Yes
Dietary Changes	Yes, in terms of removing “obstacles to cure” (but no specific diets or nutrients advised)	Yes	Yes	Yes
Specialized Exercise/Movement Therapy	No	Yes (Tai Chi, Qi Gong)	Yoga	Yes (aerobic)
Massage/Structural Therapies	No	Yes (Tui Na)	Yes	Yes, varies
Patient Self-Care Education	Yes, but lesser component of care	Yes	Yes	Yes, major component of care

Table 2. Intersection of Primary Therapeutic Strategies with Complexity Concepts

	Homeopathy*	TCM*	Ayurveda	Naturopathy
Therapy acts as a nonlinear change agent in the person by directly manipulating the multi-scale control parameters of the person as a network	++++ (Remedy triggers change in accord with Hering's Law of Cure – hierarchical endogenous healing process from above downward, from inside out, in reverse order of time of appearance)	++++ (Acupuncture meridian and point network regulating qi to create endogenous harmony, balance, and flow of energy throughout the person-system and in relationship to the environment)	++ (Ayurvedic therapies focus a great deal on improving the environmental context or fitness landscape of the patient working with the limitations of the constitution)	+/- (Varies, depending on therapist's use of homeopathy and/or acupuncture in treatment plan)
Therapy acts on the individual's environmental context (e.g., specific diet, avoidance of damp or dry climates)	+ (Remove obstacles to cure by the remedy)	+++ (Diet)	++++ (Detoxification & Diet)	++++/- (Varies, depending on therapist's use of diets, herbal and nutritional supplements, other modalities external to individual.)

* See Figures 1a and 1b for additional descriptive diagrams reflecting clinical practice theories of homeopathy and TCM.

Table 3. Different Types of Attractor Patterns and Changes in Nonlinear Dynamical Systems *

<p>(a) Fixed Point Attractor (Associated with dysfunctional behaviors and/or physiology) (122)</p>	
<p>(b) Limit Cycle (Periodic) Attractor (Associated with intermediate levels of behavioral and physiological function) (122)</p>	
<p>(c) Toroidal Attractor (Nonperiodic) (122)</p>	
<p>(d) Chaotic Attractor (Complexor) (Associated with healthier functioning behaviorally and physiologically) (http://www.societyforchaostheory.org/tutorials/)</p>	
<p>(e) Change through Bifurcation Points from One Attractor Pattern to Another (Note the discontinuous shifts in dynamics at each bifurcation point) (http://www.societyforchaostheory.org/tutorials/)</p>	 <p>PERIOD 1: Fixed point Attractor Period Doubling Compound Oscillations PERIOD 3: CHAOS</p> <p>PERIOD 2: Limit Cycle Attractor</p> <p>Bifurcation point [unstable]</p> <p>Arcs denote patterns of instability</p> <p>X-Axis = control parameter. Y-Axis = order parameter.</p>

NOTE: Sources identified in body of table

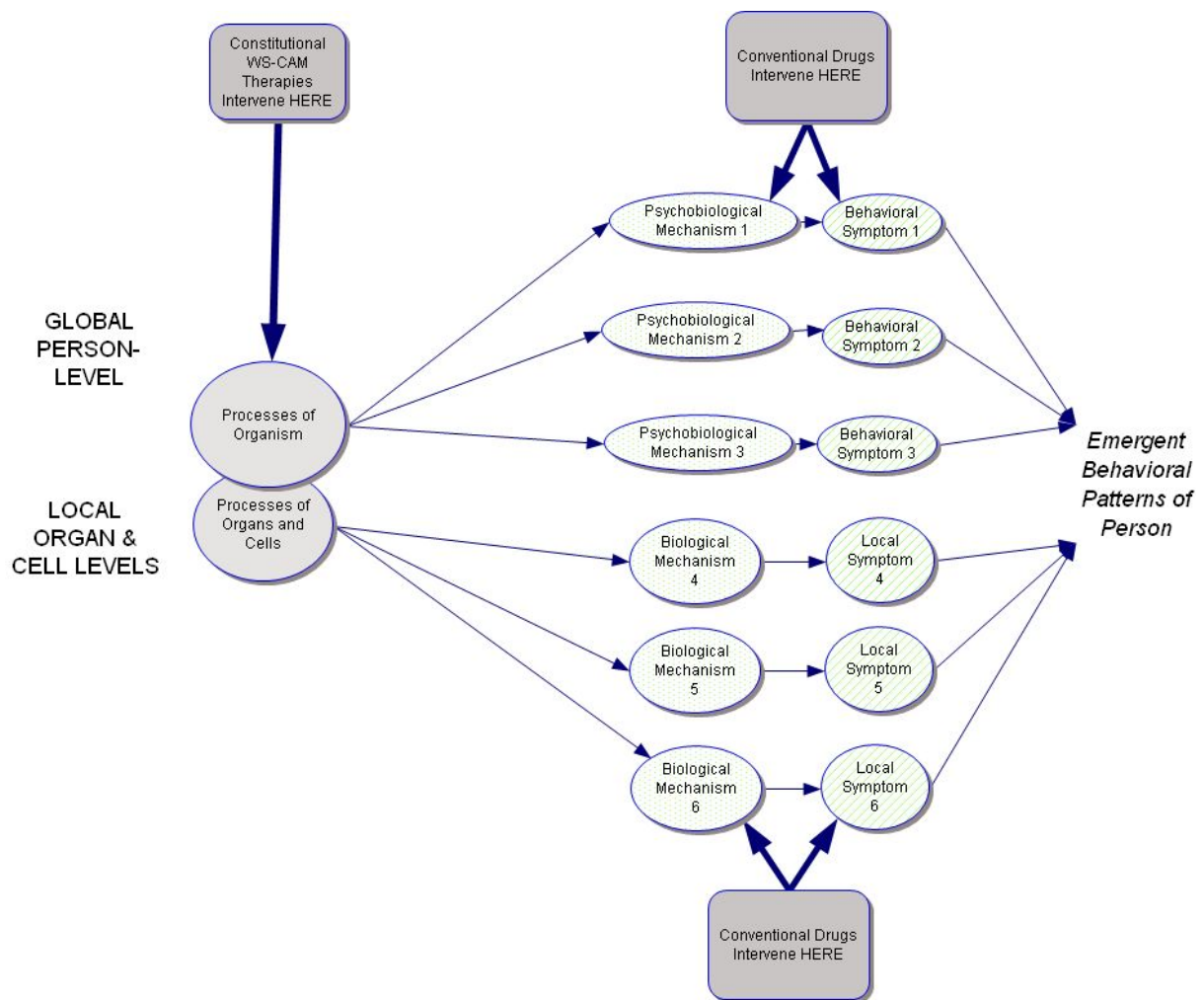


Figure 1. Conceptual Model for Points of Intervention in WS-CAM versus Drug Clinical Interventions and for Research in Complexity Science versus Reductionist/Mechanistic Science. *WS-CAM therapies (targeting the individual's constitution) and complexity scientists (studying the systems/network phenomena) manipulate the initial conditions (rules by which the parts interact with one another) for the processes of the system at whatever level of scale is under investigation (organism, organ, cell, genes/proteins, etc.) and then evaluate the emergent behavioral patterns of the person as the dynamics unfold over time. Conventional medical reductionists intervene at and evaluate manifestations of specific mechanisms and their associated local symptoms.*

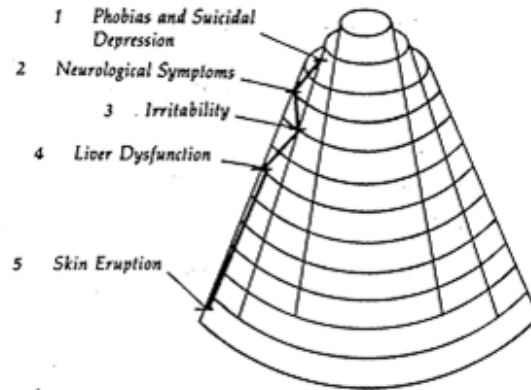


Figure 2a. Example of Hierarchical Healing in Phases, From Above Downward and From Inside Outward over Time during Constitutional Homeopathic Treatment with the Simillimum Remedy, in accord with Hering’s Law of Cure in Homeopathic Practice Theory (Source: Vithoulkas 1980) (105). *Homeopathic remedies are prepared from any of over 3,000 different natural animal, mineral, and plant sources, serially diluted in ratios of 1/10 or 1/100 in alcohol-water solvent, and vigorous shaken multiple times after each dilution step. Basic science studies suggest that the turbulence introduced by the succussion process is essential to generating a therapeutic agent with properties different from those of plain solvent (123-130).*

Practitioners choose the simillimum, the single homeopathic remedy from a specific animal, mineral, or plant source chosen to match the recurring and repetitive pattern of symptom manifestations or motif that runs across levels of scale through the patient’s complete biopsychosocial case history and that occurred during drug development testing when healthy individuals took the same remedy (Law of Similars: Like Cures Like). A remedy that is not the simillimum for the individual can exert a disruptive but non-therapeutic effect on the person.

A simillimum remedy's information carries a healthier dynamical template for systemic organization and function than does the disease attractor in which the person is stuck. The remedy itself appears to function as a momentary exogenously-derived control parameter for the endogenous dynamics of the person-system, carrying environmental information from animal, mineral, or plant kingdoms that is somehow similar to but not identical with the disease attractor (cf., sensitivity to initial conditions) and that initiates dynamical change .

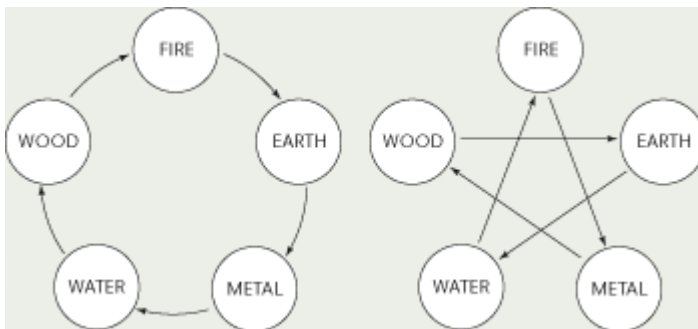
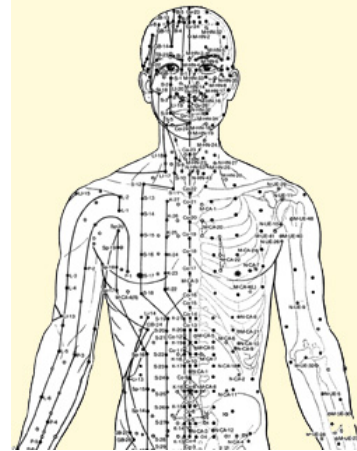


Figure 2b. Relationship of Microcosmic Elements in Chinese Medicine Practice Theory that are Interdependent and Interactive; Network Character of Meridians and Acupuncture Points (Sources: <http://www.clairebattersby.co.uk/tcm/diagnosis>;

<http://marinorientalmedicine.com/acupuncture.html>, accessed 3/5/09). : *In Chinese Medicine, the human body is a microcosm of the larger macrocosm of the natural world (environment). Health involves a harmonious balance between yin and yang (potentially translated into optimal connectivity, flow, and coherence of subsystems within the larger network system that is the person) in each of the 12 organs (as defined in Chinese medicine, not necessarily identical to Western organs), as well as global factors of qi (vital life force) and blood/body fluids. Disease occurs when the dynamic balance of yin and yang is disrupted by excess or deficiency. Strong internal states such as anger or fear and external factors (infectious agents, trauma, toxins, heat,*

cold, damp, dryness, fire; change of seasons, weather events) can cause disharmony and lead to disease. The five elements of fire, earth, metal, water, and wood interact and interregulate one another in a cycle (potentially nexi for information flow across the nodes and hubs/subsystems of the person). For diagnosis, Chinese medicine practitioners use patient symptom patterns and physical examination (taking specialized pulses and evaluating specific tongue properties such as shape, color, coating). Treatments to re-balance and harmonize often include individualized multi-modal packages of care, e.g., acupuncture, Chinese herbs, qi gong.

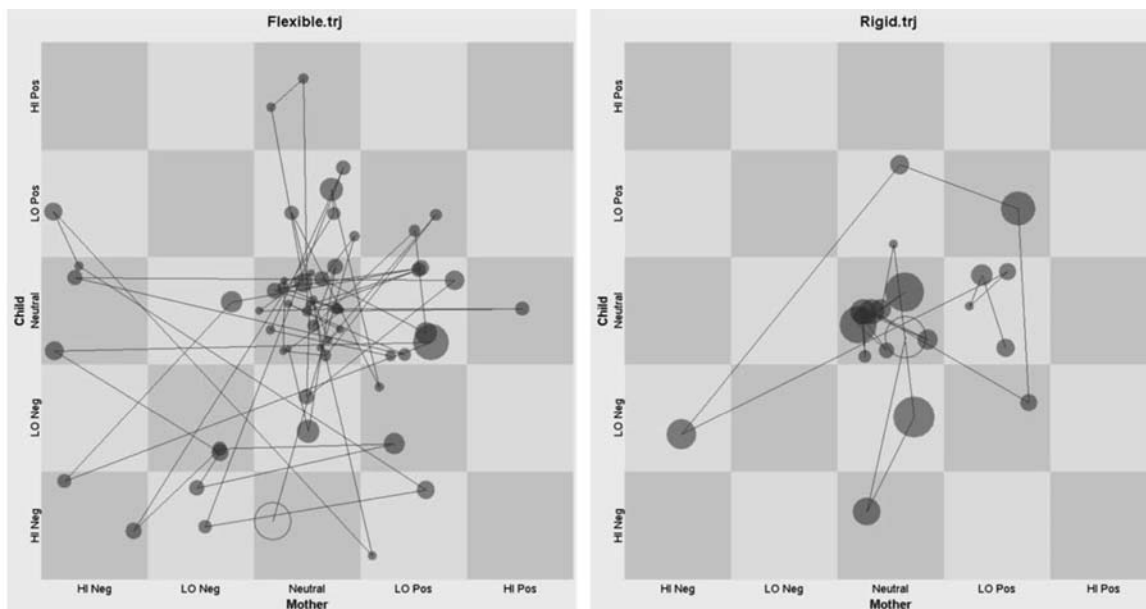


Figure 3. State Space Grid Plots of Relatively Flexible versus Rigid Mother-Child Interactions Based on Ratings of Videotaped Behaviors during Discussions of Neutral or Conflictual Topics (67). Hollenstein operationalizes flexibility in State Space Grid measures by (1) the range or number of different behavioral states (count of cells occupied); (2) number of transitions between states in terms of trajectories (dispersion); (3) tendency to get stuck in a small number of states (perseveration=average of all of the individual cell mean durations).

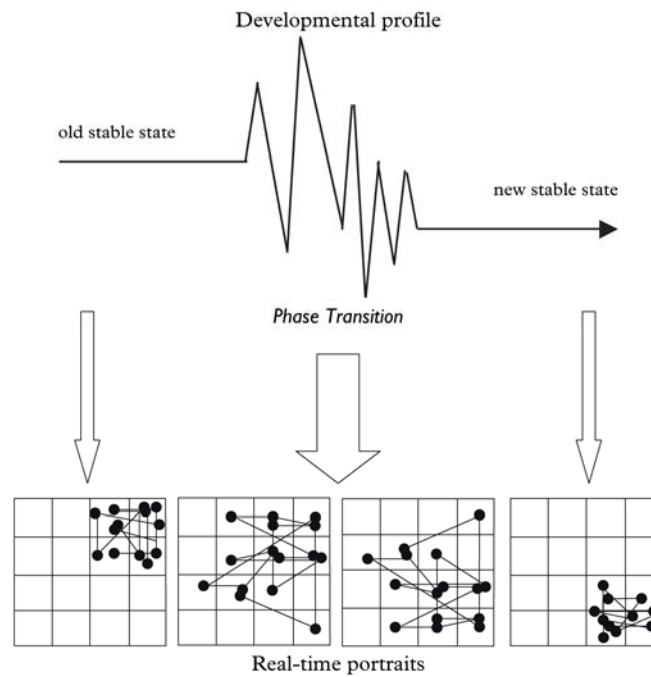


Figure 4. Diagram of a Behavioral Phase Transition. Example of a Child (stable attractor pattern) Entering Adolescence (phase transition with increased dynamical instability) and then Young Adulthood (new but different stable attractor pattern) - Source: Hollenstein 2007) (67) *The phenomena of “unsticking” and “unstuckness” described in the qualitative literature on patient change during CAM therapies may correspond respectively to a catastrophe or bifurcation point at the beginning of a phase transition, respectively in the individual’s dynamics. The dynamics may restabilize during effective WS-CAM treatment into a more adaptive and flexible attractor pattern, i.e., “transformation”, whereas ineffective treatment would leave the individual either in the original disease attractor or in a different, but still maladaptive disease attractor dynamical pattern. The real-time portraits in this Figure represent state space grid plots of two behaviors (either behavioral states of two different people or two different behaviors of the same person) on the x and y axes.*

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