The Complexity of the Homeopathic Healing Response Part 1: The Role of the Body as a Complex Adaptive System in Simillimum-Initiated Recovery from Disease

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Abstract	 Background The concepts of complex systems science enhance the understanding of how people develop and recover from disease. Living systems (human beings, animals, and plants) are self-organizing complex adaptive systems (CAS): that is, interconnected networks. CAS maintain life by initiating and carrying out non-linear dynamical changes to optimize survival fitness and function in the context of an ever-changing environment. Aims In Part 1 of this two-part paper, we relate concepts from complex systems science to homeopathic healing. The systemic changes of homeopathic healing involve <i>adaptive patterns</i> of responses to salient signals (similia) for reversing disease patterns and generating emergent multi-symptom healing over time. Methods and Results This narrative review relates homeopathic clinical practice theory to complex systems and network research. Homeopathic medicines communicate individually salient environmental information to the organism, with effects that are multi-system and indirect. The body's defense mechanisms recognize the self-similar information that the correctly chosen simillimum medicine at low dose conveys as a weak external/internal environmental stressor or danger signal (hormetin) to mobilize neural and cellular defenses.
Keywords	The body networks then use endogenous cell to cell signaling and amplify the small magnitude signal information. The results are disproportionately large: that is, non-linear,
► homeopathy	adaptive, modifications across the inter-connected self-organized biological networks/sub-
 self-organization 	systems of the body. CAS amplification mechanisms for small or weak signals include
 complex adaptive 	stochastic resonance, time-dependent sensitization, and hormesis.
systems	Conclusions The body as a complex system has the capacity for self-organization,
 biological signaling networks 	emergence and self-similarity over global (overall health and wellbeing) and local
 self-similarity 	(organ) levels of organization. These features are key for future research on the systemic healing that evolves over time during individualized homeopathic treatment.
- Self-Similarity	systemic nearing that evolves over time during individualized noneopathic treatment.

This two-part paper focuses on the integrative model for the

complex, self-organizing nature of both (1) recipient living

systems¹⁻⁴ and (2) homeopathic medicines⁵⁻¹⁰ as the basis

for homeopathic healing. In Part 1, we review how complex

Introduction

systems science applies to homeopathic clinical concepts and the non-linear, system-wide healing response that simillimum treatment initiates.

Homeopathy is historically one of several whole systems of care in complementary and alternative medicine (CAM).^{11–14} Classical homeopathy focuses on treating the

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patient as an indivisible whole (living system).^{11–13} For homeopathy, the "diagnosis" is determination of the one medicine that best matches (is most similar to) the whole, integrated, bio-psychosocial symptom picture or pattern (state) of the patient at the time of treatment.

As a whole system of CAM, classical homeopathy requires one unified diagnosis (the medicine picture [state of the patient] in the present time), and treatment with the single medicine treatment that best captures the *information pattern* of a similar, multi-subsystem pattern of symptoms. Homeopathic symptoms are manifestations of a singular, pervasive, emergent disturbance of the state of the individual as a whole system or network of networks, not of a specific body part or biological mechanism in isolation.

Homeopathic clinical practice theory provides a framework for understanding and studying the whole-system nature of homeopathic healing from disease. In fact, clinical practice theory steers research thinking toward the modern science of complex systems (complexity).^{1–3,12,15–20} Complexity science involves the study of systems that comprise many separate but inter-connected, inter-dependent, and interactive parts.

Complexity, Complex Systems, and Networks

Complex adaptive systems (CAS) are living systems or networks adapting and optimizing their fitness to survive over time within the context of an ever-changing environment. In a complex adaptive system, the global, that is, emergent, whole is greater than the sum of the parts (\sim **Table 1**).^{1,2,15,21–27}

From a complexity perspective, changes in the external and/or internal environment trigger interactive non-linear dynamical adaptive changes in a biological system across different levels of self-organized scale. Change in one part leads to change in other parts because of the network physiological and biochemical linkages between the parts.²⁸ Disease evolves over time when the "adaptive" changes to environmental stressors lead to undesirable alterations in functional set-points and emergence of disease symptoms.²⁶ The body is doing the best it can to cope with and survive the

 Table 1 Complex adaptive system at different levels of selforganized scale

Parts —————>	Emergents
Genes	Cells
Cells	Organs
Organs	Body network functions
Organisms	Individual behaviors
Groups, societies	Social behaviors
Chemical, biological, physical Environments	Planetary ecosystem

Note: Non-linear dynamical adaptive interactions of the parts at a given level of organizational scale generate collective properties that in turn emerge at the next level of organizational scale (e.g., cells to organs to organism to behavior of the organism within its environment). [Content is original to the author] impact of its surrounding adverse bio-psychosocial and/or physical environmental stressors/conditions.

At different levels of scale, patterns of weather, societies, individual organisms (e.g., a human body or a yeast cell's biochemical network),²⁸ an organ, or a mammalian cell each reflect their inherent nature as a type of complex adaptive system at a particular level of organizational scale^{25,28,29}. **Table 1** lists self-organizing CAS at different levels of organizational scale, as well as their emergents (collective properties). Self-organization is a hallmark feature of CAS.^{25,30}

Several key clinical observations reveal the importance of a complexity model for homeopathic healing. These observations include:

- (a) the diagnostic goal of identifying patterns of symptoms, not an isolated symptom, to match to the individually correct medicine symptom picture (simillimum): for example, generalities such as location, quality, timing, pace of the clinical course, improvement or worsening under specific environmental conditions such as temperature, weather, altitude (overall, patterns of system behavior across different levels of organizational scale-sensitivity to initial conditions; self-similarity-see - Table 2);
- (b) observing the ability of an *individually salient*, *quantita-tively low*, *dose of* the correct medicine (simillimum) to trigger disproportionately large-magnitude system-wide reversal of multiple symptoms (disease) (non-linearity; self-organized criticality; emergence—see **-Table 2**);
- (c) noting systemic change in healing that follows a *self-organized* hierarchical course from above downward, inside out, from more important to less important organs, and in reverse order of time of symptom appearance: that is, Hering's Law of Cure³¹ (*self-organization—see*-Table 2). Symptom suppression by conventional drugs, in contrast, prevents disease manifestation at a less important organ and redirects the disease process back to more important organs within the body network.

Table 2 lists properties of CAS. Among the properties is self-similarity across multiple levels of organizational scale. This property can be *structural and/or temporal* in nature.
 Figure 1 illustrates an example of a natural complex system in which the sub-unit structure resembles the structure of the whole unit: for example, a snowflake. As a snowflake forms, cold water freezes on to dust particles and self-organizes into a repeating pattern of structural growth from its smallest component part to its overall global ice crystal shape. Physiological functions can take on temporal self-similarity in their emergent signals: for example, electroencephalography (EEG), heart rate beat-to-beat variability.

In the present model, once initiated, the adaptive changes evolve over time across the biological network that is the body, without requiring continued presence of a medicine or drug in the body. Emergent properties, that is, altered system behaviors (e.g., symptom patterns [system behavior]), are one feature of any complex adaptive system.^{1–3,15,17,18} The parts of a living system are in continuous interaction with one another and with the emergent global whole over time.³²

Property	Definition
Sensitivity to initial conditions	State-dependency in which the nature and direction of change depend on the initial conditions of the complex system (including but not limited to past history) at the time of an environmental change that evokes adaptation. ²⁷
Emergence	The properties (behaviors) of the global whole are greater than the sum of the parts of the system. ²⁵
Self-organization	A process whereby local interactions between parts lead to <i>spontaneous order</i> patterns of the larger whole (global) open system. There is no external hierarchical or controlling agent that predetermines the emergent order. ^{28,30,40}
Self-organized criticality	A property of far-from-equilibrium, non-linear, dynamical systems (such as the brain) in which the system attains a critical state and spontaneously shifts into a new state space (attractor) with self-similar behavior patterns in space and/or time. Examples in nature include avalanches and landslides. Homeopathic healing may involve this type of shift in the body. ^{37,45}
Adaptive ability (evolution)	Capacity to change the functioning and linkages within the system/network itself to optimize its fitness in interaction with changes in its environment over time. ^{25,28}
Self-similarity (frac- tality— - Fig. 1)	Similarity of <i>geometric structure</i> (spatial) or <i>processes in time</i> (temporal) at every level of scale as in a shape or a signal (e.g., a shape comprising parts that are similar to the whole—in nature, a snowflake, a landscape, a bronchial tree; a physiological signal such as an electroencephalogram or heart rate variability)—also observed in chaotic phenomena such as <i>crystal growth</i> and <i>fluid turbulence</i> : patterns or images of dynamic systems in space and time. ^{12,17,21,45} Clinically, consider a <i>Bryonia</i> patient with self-similar modalities for symptoms throughout the body, such as worse from movement during ankle pain from a sprain or from coughing during a flu; or consider an <i>Aconite</i> patient with sudden violent fear or sudden violent headache. Researchers also use fractal dimension and related analyses to quantify complexity of physiological signals ^{17,41} as well as examine blood samples of patients with specific diseases. ¹⁰³
Non-linear dynam- ical system	CAS function as non-linear dynamical systems. Non-linear means that small changes in inputs can lead to disproportionately large changes in system outputs. Dynamical is a term for the <i>role of time and timing</i> in the relationship between inputs and outputs of a system. ⁴⁵

 Table 2 Properties and definitions in complex adaptive systems (CAS) science^{13,25,32,33} [Content is original to the author]

Another relevant fact is that the medicine sources in classical homeopathy are typically natural plants (e.g., herbal), animals, and/or mineral materials. As such, the medicine information derives from what Csermely et al term "multitarget drugs" in the research literature on complex networks and health.^{33,34} That is, the simillimum medicine as a complex natural product can induce multiple changes in different directions at multiple different levels of the body networks, involving a variety of biological mechanisms.

In a complex system such as the human body, a multisymptom response evolves over time across multiple biological sub-systems or sub-networks (different levels of organizational scale) as the interactive information flows from different parts of the overall network change. As in homeopathic practice, the CAS response depends on the initial state of the recipient organism and then evolves over time.³⁵ Consequently, the emergent outcomes are indirect rather than direct results of homeopathic simillimum treatment.

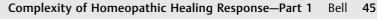
A classical homeopath selects each medicine with *similar* properties to best match the current *symptom pattern of an individual patient*, rather than a given symptom in isolation. Classical homeopathy thus treats disease as an emergent behavior pattern of the individual patient as an indivisible complex adaptive system, not as isolated local symptom mechanisms. In contrast, most conventional drugs typically target only one specific receptor type, thereby suppressing specific symptoms without treating the person as an integrated whole system/network.

Applying Complexity Concepts to Health and Disease

CAS include inter-dependent, inter-connected, and interactive parts at lower levels of organizational scale that signal and modulate each other's activity, as well as collectively^{22,36-38} generate an emergent global whole in a nonlinear manner. In turn, the emergent global whole modulates function at the parts. **– Figure 2** illustrates the ways in which the information flows both in and out of, as well as within, a CAS. "Parts" can be physical structures such as organs in a body or different mediators and signaling molecules in biochemical pathway networks.

The global level of scale within the system interacts with and modulates the functioning of the parts (where each part is a semi-autonomous agent: for example, an organ or a biochemical pathway). As noted above, in a complex system, the whole is greater than the sum of the parts (emergence).

Thus, the living body is a complex adaptive system evolving over time for optimal functional fitness to survive as it interacts with constant changes in its internal and external environment.^{13,21,25,39} The evolution of health or disease in the body over time emerges as a result of the non-linear dynamics underlying inter-connections, inter-relationships, and interactions of the parts that make up the whole.³⁷ Functional links between the parts can change in directionality and linkage strength during adaptation.^{28,40}



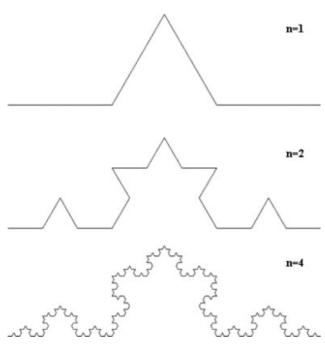


Fig. 1 Self-similarity of fractal structures in a snowflake at different levels of scale. [Used with license: Panther [CC BY-SA 3.0 (http://creativecommons.org/licenses/by-sa/3.0/)].

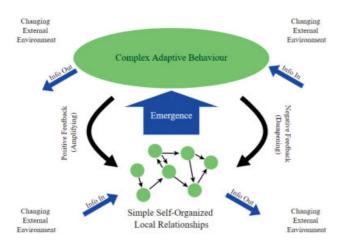


Fig. 2 Complex adaptive system interactivity diagram. [Used with Creative Commons license: https://commons.wikimedia.org/wiki/File:Complex_adaptive_system.svg]

Disease and aging can reduce systemic complexity of an organism.⁴¹ In developing diseases such as cancer, the process engages the complex signaling networks or inter-connected intracellular and extracellular pathways of the body as a complex adaptive system/network.^{28,34,42–44} In disease, the body is an open, self-organized complex adaptive system that is out of equilibrium as a consequence of its responses to environmental stressors. Consequently, the body generates patterns of symptoms that are emergent, indirect results of the overall disease process.^{25,45,46}

Restoration of healthier complexity and resilience to stressors is a therapeutic goal in this context.^{25,47} It is important to intervene in the non-linear dynamics of CAS at just the right time. That is, the well-timed intervention can interrupt the disease dynamics and trigger a self-organized criticality shift

in the state of CAS functioning, allowing the system to restabilize over time into a healthier complex dynamical state.⁴⁵

Initial complexity treatment studies in conventional medical research focused on *carefully timing* certain electrophysiological interventions to interrupt the dysfunctional nonlinear dynamics of epileptic or cardiac disease in the body.^{25,48,49} Similarly, in homeopathy, properly timing each simillimum medicine dose is also important.^{35,50} It is counterproductive to repeat a medicine too early or too late in shaping the homeopathic healing response of the organism as a whole⁵¹ back toward health.⁵⁰

In homeopathy, timing matters. For example, in clinical practice, practitioners space out repeat doses of a medicine in time by waiting until symptom improvements from the last dose plateau or begin to relapse.^{50,52} Re-dosing too soon may imprint unwanted medicine-relevant symptoms on the state of the organism for an extended period of time.⁵⁰

The Interface between the Homeopathic Medicine and the Body: Endogenous Signal Amplification Processes

In a complexity model for homeopathic healing, bodily sensory nervous systems for olfaction, taste or touch detect the signal,^{53–56} and endogenous non-linear amplification mechanisms,¹⁸ including stochastic resonance, time-dependent sensitization (TDS) in the brain, and hormesis heighten medicine information as a discrete signal and propagate a growing multi-system response.^{18,56–58}

All of these non-linear amplification processes require interaction of the treatment with a complex adaptive system to occur. The "treatment" medicine in homeopathy would constitute a biologically detectable, low-intensity discrete input of environmental information that conveys an individually salient danger or damage signal similar to the preexisting disease and triggers endogenous adaptive defense responses in biological networks.

For example, stochastic resonance⁵⁹ is the amplification of a weak signal (cf., medicine information as a small magnitude stressor signal) by a larger band of noise that contains within it the frequency of the stressor signal (cf., emergent disease pattern from the internal environment⁶⁰). In animals from rodents to crayfish, sensory systems use stochastic resonance to detect, amplify, and distinguish salient but weak predator danger stimuli (olfactory receptors in rodents or mechano-receptors in crayfish) from random noise in the external environment. Torres and Ruiz first suggested that stochastic resonance might help amplify an individual's response to a correctly matched homeopathic medicine.⁵⁷

Time-dependent sensitization is another endogenous amplification mechanism observed in CAS. TDS involves the progressive increase in the size of the response within the same recipient to repeated, intermittent "dosing" of small or weak stimuli (i.e., electrical, biochemical, immune, pharmacological, or stressful in nature), simply by the passage of time between exposures.⁶¹ The signal input magnitude *per se* can remain small. It is the endogenous adaptive response that grows over time. As a result, in TDS, any stimulus perceived or experienced by the organism as a warning of future or past danger or threat will later elicit a much larger bio-behavioral response than it did on first exposure. Thus, if a simillimum medicine captures a small complex informational pattern that resonates in frequency with the emergent body electromagnetic "noise" in the system from the cumulative history and current state of the organism,⁵⁶ the response could be amplified, up to biological limits.⁶²

At physiological limits in TDS, however, the direction of change within the same system reverses itself and shifts in the opposite direction: that is, it oscillates from the direction of the original response or current state.⁶² Different classes of stimuli/stressors can cross-sensitize with one another.^{63,64} Once initiated, TDS causes a persistent underlying reactive state of the organism, even a year before the next encounter with the same or a cross-sensitized stimulus/stressor.

TDS occurs with repeated homeopathic medicine dosing. In homeopathy, Bell et al demonstrated that repeated intermittent dose sniffs of individualized medicine versus placebo initiate TDS of spectral EEG responses to subsequent exposures, even when (1) every dose is placed below—not in—the nose and (2) the next dose is more dilute (but also homeopathically more succussed).⁵⁴ Dependent upon the history and state of the organism, repeated subsequent placebocontrolled sniffs of the "same" verum medicine can also *evoke directional reversals and/or variations in direction and magnitude* of the spectral EEG response patterns.^{53,65}

Finally, hormesis is a non-linear (bi-directional) adaptive dose–response phenomenon in a complex adaptive system to interact with a low intensity (weak) or low-dose environmental agent or stressor (including biological, chemical, physical, electromagnetic, and/or psychosocial types of stressors). Hormesis involves low-dose stimulation versus high-dose inhibition or toxicity of physiological and biochemical functions.^{66–69} Consistent with the phenomenology of hormesis, at least three different research groups have shown that various homeopathically prepared medicines at different potencies can stimulate hormetic responses in living cells.^{70–75}

With hormesis, the adaptive processes manifest as a complex non-linear dynamical evolving *pattern* of multisystem and global symptom changes, occurring across the network biology and behavior of the individual recipient.^{50,52} In living systems, these endogenous amplification mechanisms all require interaction of the salient weak (low level) medicine signal information with a complex adaptive system.^{59,61,68,69,76}

Summary and Discussion

Complexity is a dynamical state poised between excessive order and chaos. Adaptations in a living system are all in the service of optimizing the individual's fitness as CAS to survive in an environment that includes encounters with ever-changing larger and smaller stressors. When the adaptations are successful, healing from disease emerges and evolves over time. Resilience to future environmental stressors results. The potential disease damage/danger signal properties of the correct medicine serve as a salient environmental stressor (see Part 2). The danger signal properties of the simillimum emerge from signaling sensory and/or immune systems to activate body defenses against the low-dose homeopathic medicine information (i.e., an individualized, quantitatively low-dose form of the current disease state of the person—see Part 2 for more detailed discussion).

The implication is that advanced treatment strategies, such as homeopathic simillimum medicine dosing, will also modulate the inter-relationships and interactions of endogenous biological signaling networks and gene expression, a hypothesis supported by studies of certain homeopathic medicines in animal or cellular models for cancer.^{44,51,77-79}

If the system is already diseased in some way, it is at or close to its physiological limits (cf., TDS and oscillation).^{61,62,80,81} The body will potentially exhibit transient aggravation up to its physiological limits and then reverse its direction of change back from disease toward a healthier degree of complexity, following the arrival of a low-dose, hormetic salient stimulus to do so.^{17,35}

Additional considerations include evidence that (1) endogenous non-linear amplification processes include stochastic resonance, hormesis, and/or TDS; (2) nanostructures, including but not limited to DNA^{82,83} or miRNA,⁸⁴ can generate weak electromagnetic and/or nano-scale biological signals that stimulate changes in nearby bystander cell biological systems.^{83,85–87} Biological systems are capable of amplifying signals from weak electromagnetic fields.⁸⁸

The correct medicine and living system recipient require communication of an individually relevant "message"²⁵ or information pattern at their interface. Sensory detection, ^{53,56,65} endogenous non-linear cell-to-cell communication, ^{77,87,89–95} and non-linear amplification processes^{18,54} in the body engage the inter-connected cells and sub-systems that comprise the body.⁴⁵ The body as an inter-connected emergent network of cells and sub-systems—not the direct effects of the medicine—generates the healing response.^{19,20,96,97} **Figure 3** summarizes the proposed flow of events.

In homeopathy, the recipient complex adaptive system manifests symptoms as a reflection of the cumulative and interactive emergent effects that past stressors of all categories (biological, chemical, physical, and psychosocial) and intensities have induced in the individual.^{26,98–101} Given a low dose of the correctly chosen homeopathic medicine similar to the current state (i.e., individual's emergent symptom pattern with its associated biology),⁴⁶ systemic healing evolves to strengthen the network and its inter-connected parts against similar existing and future stressors.⁴⁵ The system may alter the links and/or the strength of links between different parts of its network during its stress-adaptive process.^{19,20,28,34,40} Improved systemic resilience to current and future stressors is the overall result.⁴⁵

Future research should involve borrowing from existing and emerging methods for the study of (1) non-linear dynamics, (2) self-organization and emergence, and (3) self-similarity. In clinical trials, evaluating both global (overall health ratings) and local (expression of symptoms in specific

From Homeopathic Manufacturing to Hormetic Healing

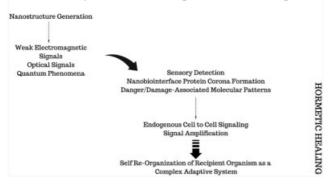


Fig. 3 Overall complexity-based model for homeopathic healing. In this model, once the quantitatively low dose of the homeopathic simillimum medicine in potency interacts with the recipient's sensory and/or immune systems (including the cell danger/damage defense response pathways), the endogenous biology of the organism takes over the healing process as a type of hormesis. The events bring about non-linear adaptive changes that amplify the response to the information of the simillimum and reverse the current disease state that was present at the time of medicine administration (hormesis). Systemic healing further evolves over time via non-linear adaptive changes in biological function across the functional interactive networks of the living system. [Content is original to the author]

organs) states with appropriate outcome measures is important to capture systemic outcomes.¹⁰²

This also means adopting research technologies and analytical methods that can objectively document existence of and changes in the complexity of non-linear modulation of patient physiology: for example, in sleep and waking EEG¹⁷ and/or heart rate variability and/or spectroscopy of blood patterns in health and disease.^{103,104}

Conclusions

The body as a complex adaptive system has the capacity for functional self-reorganization, emergence, and multi-scale self-similarity over global (overall health and wellbeing) and local (organ) levels of organization. These features are the key for future biological research on the systemic healing that evolves over time during individualized homeopathic treatment. Complexity is a relevant scientific perspective for understanding the nature of the non-linear healing processes that the homeopathic simillimum can initiate.

In Part 2 of this paper synthesizing available evidence, we shall explore the complex-system nature of homeopathic medicines themselves, during manufacturing and upon administration, in generating the individually salient signal to trigger adaptive healing responses in the biology of a complex adaptive system.

Highlights

- Living systems are self-organized complex adaptive systems (CAS): that is, networks of inter-connected and interactive parts that manifest healthy or diseased states.
- The simillimum medicine conveys a low-intensity, individually salient environmental danger signal (infor-

mation that captures a low-dose version of the preexisting disease pattern) to the sensory and cell defense response networks of the body and thereby initiates the adaptive systemic phenomenon of hormesis.

- In turn, endogenous cell-to-cell signaling pathways transduce and amplify the low-intensity homeopathic information throughout the overall CAS, mobilizing adaptive self-organized changes to improve stress resistance, resilience, and fitness for survival.
- Endogenous signal amplification mechanisms include stochastic resonance, time-dependent sensitization and hormesis.
- The latter two mechanisms can generate directional reversal of symptom pattern expression as a function, respectively, of the initial state of the individual recipient and of the quantitatively low dose of the medicine as a hormetin.
- Consequently, the correct medicine (simillimum) initiates a system-wide non-linear homeopathic healing process carried through the internal dynamics of the body sub-systems/networks, rather than by a direct local pharmacological mechanism of the homeopathic medicine.

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Conflict of Interest

Dr. Bell is a consultant to Standard Homeopathic/Hyland's Inc., a US-based manufacturer of homeopathic medicines. The company did not provide financial support for this paper.

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