Introduction

Doctors and therapists on a daily basis report large numbers of people with medically unexplained symptoms. That’s a problem, because it concerns people who often feel that they are not being taken seriously, but also for many doctors and therapists it is unsatisfactory that they cannot provide an adequate diagnosis or intervention.

The problem is that a human being is a huge, complex creature, in an equally complex world. It’s hard to understand the complexity in all its aspects. Besides, we do not yet know the answers to the questions: what is disease and what is health. Obviously, there are still many problems in combating diseases. Hans Westerhoff (2013), professor of systems biology in Amsterdam, notes: "People get medication prescribed, but an individual patient has in only 30% of the cases benefited from the medication first supplied to him. The other 70% goes home with non-working medication and will in all likelihood report again to the doctor after some time for another 30% chance, if the disease has not resolved itself in the meantime, as often happens in most cases happily." A probability of 30% is not very impressive, especially when one considers that with placebos similar outcomes can be obtained.

Certainly, progress is being made. For instance, the death rate for cancer drops slowly but steadily, thanks to the huge amount of money being pumped into cancer research. But it should be noted that the decline is largely due to prevention and education and - in particular - the decline in the number of smokers (Westerhoff, 2013).

Of course, the treatment of cancer is not simple because cancer is not a sitting duck. Cancers are moving targets, in that cancer cells can change during therapy and have the capacity for self-renewal. Research has focussed on the differences between cancerous cells and healthy cells. The emerging picture is overwhelmingly complex. Molecules out of many parallel signal pathways are involved, while their activities are controlled by multiple factors. Non-linear aspects of involved biochemical processes complicate the understanding and prediction of outcomes of intracellular signalling (Homberg, et al, 2006).

In general, health problems are difficult to solve for doctors and therapists, in part because in many disorders multiple factors play a role. They are disorders of the network, that is to say, they are system disorders. Thus, it is important to look at the system as a whole, especially since errors deep in the system can manifest in unexpected ways.
It should be noted that it is also wise to shift the focus to a significant extension from disease to health. The current WHO definition of health, formulated in 1948, describes health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.” A fine definition, but it is clear that the WHO definition has certain limitations. In the BMJ, one of the most influential medical journals, one can read a proposal for a new definition. That is, health is the ability to adapt and to self manage in the face of social, physical and emotional challenges (Huber, et al, 2011). Health occurs within a homeostatic/homeokinetic range allowing “normal functioning” (Que, et al., 2001; Nicolini, et al., 2012).

Healthcare is slowly evolving from reactive disease care to medicine that is predictive, preventive, personalized and participatory (P4). Flores (2014) and colleagues wrote about P4: “Systems approaches to biology and medicine are now beginning to provide patients, consumers and physicians with personalized information about each individual’s unique health experience of both health and disease at the molecular, cellular and organ levels. This information will make disease care radically more cost effective by personalizing care to each person’s unique biology and by treating the causes rather than the symptoms of disease. It will also provide the basis for concrete action by consumers to improve their health as they observe the impact of lifestyle decisions.”

**Systems medicine**

Paul Smiths (2013), professor of pharmacology in Nijmegen, noticed therefore that the time has come to focus on systems medicine. He notices that for a proper understanding of diseases and health, all steps from molecule through organ and the entire human being to a complete population is a must. Such “bigger-picture” research perspectives lead to a higher level of understanding in terms for health and for complex and multifactorial disease conditions (Ayers & Day, 2015).

Systems medicine is an approach that looks at the systems of the human body as part of an integrated whole, incorporating and combining biochemical, physiological, and environmental interactions (Walter, 2013). It is the application of systems biology approaches to medical research and practice, with the aim to enable understanding of human functioning and the physiological mechanisms and with that prognosis, diagnosis and treatment of diseases (Kyriakopoulou & Mulligan, 2010).

Systems medicine is therefore based on systems science and systems biology, the science that seeks to understand how the parts of biological systems are integrated to produce the impressive cells, organisms, and ecosystems that exist in our world. Systems medicine is focused on disease, health and ultimately life, and underlying inter-cellular and intra-cellular networks, with attention for relationships, information, communication, and in general for system-oriented approaches (Cosentino, 2008).
**Systems thinking**

Systems medicine is a field for specialists and not for the average doctor or therapist. But it is certainly important that doctors and therapists can view health and disease from the perspective of systems theory. It will lead to better diagnoses and therapy recommendations. According to the Health Foundation (2010) in the UK the advantages of systems thinking are that it: challenges existing assumptions, focusses on relationships and interaction rather than simple cause and effects models, and provides a more complete picture and a framework for categorising and analysing knowledge.

In other words, systems thinking, or better, complex adaptive systems thinking, is a way of thinking by identifying complexity, patterns, relationships, information and communication. The term ‘complex adaptive system’ was coined at the Santa Fe Institute, and defined by John Holland (1999) as dynamic network of agents acting in parallel, constantly reacting to what other agents are doing, which in turn influences behaviour and the network as a whole. A complex adaptive system has a number of specific characteristics and properties, which will be described shortly.

**Complex.** A complex system consists of various autonomous but interrelated and interdependent constituents, like the birds in a flock, the cells in an organ, or the players of a soccer team.

**Dynamic.** A complex adaptive system is as a rule built up from a large number of elements which interact dynamically. Related to that is systems thinking aimed at understanding the behaviour of complex systems over time.

**Non-linear.** The interactions in a complex adaptive system are non-linear; small changes in inputs may lead to relatively large outputs.

**Adaptive.** Complex adaptive systems are dynamic systems that are able to adapt in and evolve with a changing environment (Chan, 2001). Adaptability also has to do with continuous fluctuations of lots of homeostatically-controlled physiological parameters (Oosten, 1996). Life and health is about homeostasis, or better homeokinesis, that is “the ability of an organism … to maintain a highly organized internal environment fluctuating within acceptable limits …” (Que, et al., 2001; Macklem & Seely, 2010).

**Co-evolution.** Co-evolution is the change of elements in a system based on their interactions with one another and with the environment. So change needs to be seen in terms of co-evolution with all other related systems (Chan, 2001).

**Connectivity.** The ways in which the constituents in a system connect and relate to one another is critical to the system’s survival and so the relationships between the constituents are usually seen as more important than the constituents themselves in complex adaptive systems thinking (Dekkers, 2015).

**Open.** A complex adaptive system is an open system, which means that the system can interact with its surroundings by an exchange of information, energy and matter.
Nested. Most systems are nested within other systems and many systems contain smaller systems. For instance, a human being contains a number of organs, while an organ is built up from cells.

Local. The elements, also indicated as the agents, in a complex adaptive system are not aware of the behaviour of the system as a whole and respond only to what is available or known locally (Hass, 2009).

Emergence. Properties of a complex system are said to be emergent if they arise out of the properties of simpler constituents, but are neither predictable from, nor reducible to, these lower-level characteristics (van Belle, 2014). An emergent property can be seen as unexpected behaviour arising from interaction between the constituents and the environment (Johnson, 2006). Many biological systems have emergent properties or emergent behaviour. Think of the complex behaviour of colonies of ants, or the behaviour of swarms of bees. Or think of the pumping of the heart, keeping in mind that the individual cells of the heart cannot pump blood. In relation to emergence, it is often said that the whole is more than the sum of its parts. But actually, the whole is not merely more, but the whole is very different from the sum of its parts.

Simple rules. Often, complex adaptive systems are governed by simple rules and not very complicated. The rules could be simple, but their effects intricate and are unexpected because of the interaction of the constituents. Complex and intelligent behaviour can result from a set of simple rules.

Iteration. Complex adaptive systems evolve iteratively. They rely on processes that are executed repeatedly.

Sub-optimal. A complex adaptive system does not have to be perfect to flourish in its environment (Hass, 2009).

Self-organising. There is no hierarchy of command and control in a complex adaptive system. There is no planning or managing, but there is a constant re-organising to find the best fit with the surroundings (Janssen & Kuk, 2006).

Sensitivity to initial conditions. Complex systems show sensitivity to initial conditions. As a consequence slight differences in initial conditions can lead to very different outcomes (Lewin, 1999). It is therefore problematic to predict the long-term behaviour of such systems.

Order and chaos. Systems can behave in an orderly way, but also in a chaotic way, that is in a way without any order. A mobile phone is an example of a highly-orderly system, which means that a mobile phone usually behaves in a predictable way. Natural systems often can be classified as chaotic. For instance, it is hard to make an accurate prediction of the weather. Well-known is the phrase: "When a butterfly flaps its wings in one part of the world, it can cause a storm in another part of the world". This aspect of chaotic systems is known as the “butterfly effect." Chaotic systems have extraordinary sensitivity to internal conditions which makes them inherently unpredictable in the long term (Ives, 2011).
Edge of Chaos. In 1993, mathematician Ian Malcolm gives a college at the Santa Fe Institute in the United States over “Life at the edge of chaos”. He asserts that a system with too much order will not cross rigid borders, and cannot evolve. On the other hand, too much chaos will cause a system to lose its organization. Complex adaptive systems must maintain themselves between this randomness and order where they can somehow use both in order to configure and reconfigure themselves, going through both integration and differentiation in evolving to become more complex. Malcolm said: “… complex systems seem to strike a balance between the need for order and the imperative to change. Complex systems tend to locate themselves at a place we call 'the edge of chaos.' We imagine the edge of chaos as a place where there is enough innovation to keep a living system vibrant, and enough stability to keep it from collapsing into anarchy. It is a zone of conflict and upheaval, where the old and the new are constantly at war. Finding the balance point must be a delicate matter--if a living system drifts too close, it risks falling over into incoherence and dissolution; but if the system moves too far from the edge, it becomes rigid, frozen, totalitarian. Both conditions lead to extinction. Too much change is as destructive as too little. Only at the edge of chaos can complex systems flourish.”

Systems modelling

A system is often much too complex to be understood in all its aspects. In general we have in our minds an idea of the reality in which we live. But that idea is inevitably an interpretation of that reality. It is an interpretation based on what we have learned, what we have done and what we have felt during our lives. It is fundamentally impossible to create a complete and consistent picture of the reality (Oosten, 2013).

If people want to communicate on a system on a scientific way, they have to make explicit their interpretations. Not the complete interpretations of the system, but the elements that are important for communication only. This is necessary, because the interpretations of people generally are very comprehensive, with all kinds of personal details, but also because they are usually not consistent (Oosten, 2004).

It also should be noted that people with different backgrounds and interests look at a system in different ways. A specialist for internal diseases will examine people in a different way than a surgeon. And an osteopath has other ideas about the human body than a physiotherapist. So, depending on their interests people have different views on man, or in general, on a system.

For fruitful communication it is therefore important to determine from which viewpoint one will look at a system. A viewpoint must be specified so that all interested parties can speak the same language. A viewpoint is specified by describing the stakeholders, the concerns, the conceptual structure and the notation.

Stakeholders are the people with involvement or interests in a system, as for example specialists, scientists or osteopaths. Concerns are aspects of the system that by a stakeholder are seen as important or essential. The conceptual structure is a list of all relevant concepts and their meaning, possibly supplemented by a description of the relationships between the concepts. Finally, a notation is a language that enables people to describe a system.
The description of a system from a specific viewpoint is called a view. For an osteopath one can think of a view of the respiratory and circulatory system, or the view of the neurological system.

A view is made up from one or more models. We are trying to get a grip on the phenomena of the reality by formulating models. A model is a representation of the reality for a specific purpose. It is an abstraction of a coherent part of a system. A matching set of models is thus a view, so one can speak of a view of the neurological system, made up from a number of models.

There lots and lots of types of models. Frequently used are pictures. Everybody knows the pictures of a liver or the lungs of a human being. Pictures are literally very illustrative.


Pictures are attractive in some respects, but they give hardly any information on the functioning of complex adaptive systems. As said, systems thinking has to do with thinking about complexity, patterns, relationships, information and communication. As a consequence, a complex adaptive system is an assembly of an information system and a processing system. Information systems and processing systems operate on the basis of a rule, which enables a complex adaptive system to also be seen as a rule-based system (or knowledge system).

Three types of models that are important for thinking about systems are therefore, data models for the description of information systems, process models for the description of processing systems, and rule-based models for capturing the knowledge. These three model types will be introduced in a subsequent paper, and of course one can read about the three types in literature (Oosten, 2004; Elmasri, et al., 2007; Maus, et al., 2011).
**Literature**


**Burton C. (2003).** ‘Beyond somatisation: a review of the understanding and treatment of medically unexplained physical symptoms (MUPS)’. *British Journal of General Practise. 53(488). 231-239*


**Cosentino, C. (2008).** ‘Introduction to System Biology’. [https://users.ece.cmu.edu/~brunos/Lecture1.pdf](https://users.ece.cmu.edu/~brunos/Lecture1.pdf)


**Huber, M., L.W. Green, H.E. van der Horst, M.I. Loureiro (2010).** How should we define health? *BMJ (online), July.*


**Johnson, C. W. (2006).** ‘What are Emergent Properties and How Do They Affect the Engineering of Complex Systems?’ *Reliability Engineering; System Safety 91(12).*


