

Systems biology, the Physiome Project and oriental medicine

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Received: 13 January 2009 / Accepted: 13 January 2009 / Published online: 5 March 2009
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Abstract Systems biology, particularly at the higher levels that are the domain of the Physiome Project, offers a more promising basis for constructive dialogue with traditional oriental medicine than does reductive molecular biology alone. However, there are major problems to be overcome before this can be achieved. First, systems biology is at an early stage of development as a fully quantitative and computational discipline. We still do not know what the higher level concepts should be that might map well to traditional oriental medical concepts. Second, there are major problems of translation and interpretation to be tackled. Exploring the full semantic frame of the oriental concepts will be necessary before mapping to concepts in western medicine can be useful.

Keywords Systems biology · Physiome Project · Oriental medicine · Sasang · Kampo

In an article in this journal, Shim et al. [1] draw attention to a possible synergy between the approach of the Physiome Project to the study of the physiology of the body and that of Korean *Sasang* constitutional medicine [2, 3]. *Sasang* (四象, literally four types) is one of the forms of the Korean oriental medicine tradition that owes its origin to Chinese Daoist medical texts that date back more than 2,000 years. The canonical text is that known as the Inner Canon of the Yellow Emperor, 黃帝內經 *Huángdì Nèijīng*, usually dated to about the second century BCE [4]. This dating and the

essence of the texts themselves are both amply confirmed by important tomb excavations made in China since 1970, in particular the texts found on silk screens and bamboo slips in the *Mawangdui* 馬王堆 excavation of a tomb that was closed in 168 BCE. These remarkable texts have been fully translated into English [5] and are the subject of active research [6–8].

Also of great historical and medical importance are the texts of *Ishimpo* 醫心方, a medical manual based on ancient Chinese medicine collated in 982 by Tamba Yasuyori 丹波康賴 and kept in the Imperial Library of Japan. The *Ishimpo* is uniquely important since it contains Chinese medical texts that had been lost in China itself. *Ishimpo* and other texts, particularly as they relate to sexual health, have been translated into English [9].

As in the case of Korea, Japan has also developed its own form of oriental medicine, known as *Kampo* 漢方 [10–12].

These developments of oriental medicine took place within a philosophical and historical context very different from that of the West [13–15].

The standard western scientific attitude to this remarkable corpus of knowledge and practice has been one of deep scepticism. One of the reasons is that western physiology developed from the work of scientists like Claude Bernard [16] who, in the nineteenth century, worked hard to distance physiology from the ideas of the vitalists [17]. The concept of ‘vital force’, against which Bernard argued, has some resemblance to some of the concepts of traditional oriental medicine, in particular the concept of *ki* 氣 (*qi*), which is often translated as ‘life energy’. The analogy is obvious. I will return to this question later in this article.

The question raised by Shim and his colleagues is whether the approach of systems biology, and in particular its form as the higher level Physiome Project, offers the

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possibility of a bridge between the traditional oriental and modern western traditions. Before I give my answer to that question, let me hasten to add that ‘western’ here refers to the system of scientific thought having its origins in the West. It is of course also practised in the East as countries like Japan, Korea and China have adopted and developed western scientific methods so effectively. In fact, they developed so well in these countries that, for some time, traditional oriental medicine became neglected. It is relatively recently that the tradition has become valued again, and not only in the East. Even the NIH in Washington has a section that deals with what it calls ‘complementary and alternative medicine’, much of which refers to traditional oriental methods such as acupuncture, reflexology, herbal medicines and meditation. There is a good reason for this development. Large numbers of patients in western countries now use these therapies. There is therefore an obligation on public organisations like funding and regulatory agencies to assess and regulate these methods.

Does systems biology offer such a bridge? This was the question addressed by a recent conference in Oxford. I introduced the meeting by referring to four of my ten ‘principles of systems biology’ [17, 18]:

1. Biological functionality is multi-level;
2. Transmission of information is NOT one-way (the ‘central dogma of biology’ was misapplied);
3. DNA is NOT the sole transmitter of inheritance;
4. There is no privileged level of causality in biological systems (theory of ‘biological relativity’).

There was general agreement in the meeting that these principles, and particularly the existence of ‘downward causation’ (i.e., higher level control of lower level processes), do open up the possibility of constructive dialogue between the western and oriental medical traditions in a way that was not possible within the dominant reductive mode of biology.

The reasons for this agreement were:

1. Since systems biology is more holistic than reductive biology and since oriental medicine is also holistic, ‘downward causation’ could be a way of linking the two traditions.
2. Systems biology can identify multiple actions as being more beneficial than single-site actions (e.g., multiple action drugs within the western medical tradition, most recently ranolazine—see, e.g., [19]). This could open the way to a better understanding of, and development of, herbal medicine, since this also depends on synergistic actions of multiple components.
3. Systems biology recognises the importance of control of the genome by higher levels (via epigenetic marking and control), including even the role of behavioural

and social factors (see, for example, the work of Weaver et al. [20] on epigenetic inheritance of stroking behaviour in rats). This could open the way to dialogue on the central role of the mind in oriental medicine.

4. Korean Sasang can be viewed as a patient-specific form of treatment. Genomics and systems biology are also looking towards the development of patient-specific medication and treatment. However, systems biology is not looking towards ancient Galenic or other interpretations of constitution. The question therefore arises whether oriental medicine could be open to investigation on this question. In agreement with Shim et al., I think it can.
5. Could oriental medicine become consistent with the need for regulation and clinical trial evidence? There are already examples of successful clinical trials of acupuncture for pain relief and of meditation therapy for depression. Oriental medicine should not be fearful of clinical trials, though it has to be admitted that there are special difficulties in establishing effective controls in such trials. The correct placebo for a treatment like acupuncture is much more difficult to arrange than is a sugary pill!
6. But perhaps the biggest problem is historical and cultural. In the West, oriental medicine is thought by many people to include many kinds of ‘magic’, mysterious effects that are perceived as anti-scientific. This raises the question whether oriental medicine could be de-mythologised.

What do I mean by demythologising? I mean whether it would be possible to map concepts like 氣 (*ki*, *qi*), that at first sight closely resemble that of ‘vital energy’, to systems-level concepts that are empirically testable and do not simply resurrect the old concept of vital energy. There are similar questions with concepts such as 精 (*jing* essence?), 神 (*shen* spirit?), 陰 (*yin*), 陽 (*yang*), and 脉 (*mai* vessel?). My proposal is that we might more profitably identify these with systems *processes*, not as separate *substances*. In this context, it is interesting that in a recent study of the practice of traditional Chinese medicine in modern China, Hsu [21] ends with the conclusion:

“It was the *process* which brought about disharmony, not the material aspects... this conception of the body in its disordered state was common to *qigong* and Chinese medicine”.

So far, in this commentary, I have been optimistic. The general answer to the question whether a systems approach offers the prospect of a more constructive dialogue with oriental medicine in its various forms in China, Japan and Korea and in the way in which it has also developed in the West is a strong ‘yes’.

There are however some major problems to be overcome. I will refer to just two of these in this article.

The first is the fact that systems biology is at a very early stage of development. It is in fact an old discipline. As I argue in [17], Claude Bernard could be regarded as the first systems biologist, and there is a long tradition of a systems approach in physiology throughout the nineteenth and twentieth centuries. However, it is relatively recently that it has developed as a fully *quantitative* discipline using mathematics and computing to achieve its goal of interpreting the interactions in complex pathways of multiple components and between multiple levels of function [22]. There is a very long way to go before we arrive at the possibility of mapping systems biological concepts to the high-level concepts used in traditional oriental medicine. We don't yet even know what those systems biological concepts will be (one of my ten principles is 'there are many more to be discovered. A theory of biology does not yet exist'). It may therefore be premature to try to conduct *scientific* projects to link the two approaches.

This takes me on to my second major problem, which is that, before we can effectively formulate what those scientific projects should be, we need to clarify the problems of translation and interpretation. This will not be easy. Hsu's study [21] lists as many as 28 possible translations of 氣, depending on the context in which the character is found. This immediately tells us that what the linguists call the semantic frame is totally different in oriental and western languages. Translating qi 氣 simply as 'breath' or 'energy' will not do. Hsu [6, 7] even suggests that in some uses in oriental medical texts it works more like a categoriser than as a word with a meaning in its own right. For English speakers, imagine trying to define what 'ness' means in words like 'redness', 'deepness' or 'righteousness'. It is a 'word' that functions to classify by the quality referred to, not to have a separate meaning in itself. We must beware of thinking that there must always be lexical equivalents in different languages.

We encounter a similar difficulty when we try to translate the characters for the various organs of the body. The characters for 'lung' 肺, 'liver' 肝, 'kidney' 腎 or 'spleen' 脾 simply do not correspond to their western anatomical equivalents since what is referred to in each case is more like a system than a single organ. This itself reinforces the view that a systems biological approach is required, but it also reminds us that we are far from having an adequate numerical understanding of the relevant systems that could be modelled in predictive ways by the standards of, say, engineering science. It is the aim of the Physiome Project to achieve that. As it does so, we may be able to explore the links with traditional oriental medicine more effectively. But we cannot prejudge the outcome, and we have only a vague idea at the present time of how the links might be achieved.

Acknowledgements Work in the author's laboratory is funded by the EU Framework 7 PreDiCT project, by the British Heart Foundation and by the Wellcome Trust.

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