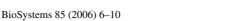


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### Mini-review

# Maps, books and other metaphors for systems biology

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#### Abstract

We briefly review the use of metaphors in science and progressively focus on fields from biology and molecular biology to genomics and bioinformatics. We discuss how metaphors are both a tool for scientific exploration and a medium for public communication of complex subjects, by various short examples. Finally, we propose a metaphor for systems biology that provides an illuminating perspective for the ambitious goals of this field and delimits its current agenda.

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#### 1. Prologue

Professor Ray Paton has pioneered multiple research threads, including representational issues and the use of metaphors in the context of molecular biology and genomics, with particular emphasis on genome function and protein interactions (Paton, 1996, 1997, 2002, 1993). Thus, we feel it is both our honour and duty to explore the issue of metaphors in computational genomics in a short critical review article, dedicated to Ray's memory.

#### 2. Metaphors in science

Metaphors in science are used widely and they vary significantly in their scope and intensity. Despite their utmost importance in shaping our cognitive processes and the scientific discourse, metaphors are not always sufficiently appreciated (Draaisma, 2001). Most scientists might unconsciously adopt a metaphor at an early

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stage of their career and without necessarily questioning further this conceptual framework within their research. Popular science authors and the news media are using metaphors more extensively in order to communicate complex scientific subjects, sometimes very eloquently.

Some metaphors have been loosely (and somewhat unsuccessfully) used to map new domains to familiar concepts, while others have been so pervasive and powerful that we often forget that they are nothing but useful metaphors. In biology, an example of the former category is "the cell as a factory", a somewhat vague term mapping biotechnology to the concept of an industrial (perhaps chemical?) processing plant (Westers et al., 2004). An example of the latter category is "the DNA as a message" (Searls, 1997)—all the way to "the genome as the book of life" (Copland, 2005). This has been such a strong metaphor, that methods developed within its framework have further influenced the development of string theory in computer science (Ouzounis, 2002).

In fact, even this powerful, omnipresent metaphor in biology has its limitations (Copland, 2005), and it has been argued that its origins could be attributed to the socio-political context of the post-WWII and the Cold War eras (Kay, 1995).

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#### 3. Metaphors in biology

Despite the fact that we are not attempting to comprehensively review the use of metaphors in biology, it is worth remembering that they have a long history. The first metaphor in biology can be traced back to classical times: around 500 B.C., Alcmaeon of Croton, philosopher, scientist and possibly the first anatomist, used a political metaphor about health and disease. The equality of powers (isonomia) maintains health, while an extreme form of political structure, namely monarchy, results in disease (Vlastos, 1953). Darwin used the Malthusian metaphor for limited resources (Todes, 1987), the development of bacteriology in Europe explicitly borrowed a language from politics in imperial Germany (Gradmann, 2000), and the metaphor of a 'ladder' has been used in various fields, from eugenics to bioethics (Cooke, 1998).

In linguistics, languages have been treated as 'families' and genealogical family trees connected them (Cavalli-Sforza et al., 1992), while other metaphors such as 'waves' have been explored in this context (Nadasdy, 1993). Even in management science, businesses have been seen as biological systems (Rose, 2001), and in behavioral genetics, multiple metaphors for the role of genes in human behavior have been rigorously analyzed (Nordgren, 2003).

### 4. Metaphors in molecular biology

Progressively narrowing our scope, it is worth examining in some detail the use of metaphors in modern molecular biology. The 'absence' of molecules in specific processes has been deemed as an important analytical tool (Marijuan, 1996), the 'tree of life' has been questioned and occasionally represented as a web or a net (Doolittle, 1999), structural versus functional models in developmental biology have been assessed (McLachlan, 1999) and adaptive landscapes have been considered as models for developmental genetics, and more specifically the issue of phenotypic plasticity (Price et al., 2003).

It is worth noting that the language metaphor has continued to be used extensively at various levels of biological organization, from cells to societies (Wallace and Wallace, 1999). Apparently esoteric endeavors from semiotics and ontology, for example the definition of 'self' in different social and linguistic backgrounds, might have very important implications in fields such as immunobiology (Spiess, 2001). Even laboratory animals (and more specifically mice) did not escape from this process, considered from 'saviors' to 'tools' (Birke, 2003).

More extreme examples reflect the richness of the biological domain to provide metaphors for microscopic, not directly observable, systems. For instance, ant communities as clonal populations have been likened to cellular populations that are able to attain diversified roles within different environmental conditions, where specialized units might emerge (Sachs, 2003).

#### 5. Metaphors in genomics

In the field of genomics, there is a long and colorful history of metaphors (Avise, 2001; Konopka, 2002), from the 'selfish gene' concept (Dawkins, 2001) to the human genome project (Petsko, 2001). This 'mapping' project has been likened to the Rosetta Stone (Petsko, 2001), the mission to the Moon, the discovery of nuclear fission (Schrader, 2001) or a map of an unknown world (Hall, 2003), in order to secure financial, political and social support. Indeed, the 'space exploration' story has been very common in the literature (Vukmirovic and Tilghman, 2000).

There have been vocal criticisms for the adoption of some of these concepts, with fears that this 'branding' campaign "leads to restricted conceptions of health and illness, reinforces inequities in the distribution of health and, by privatizing and individualizing responsibility for health, creates and legitimizes a new arena for social control" (Lippman, 1992).

The news media have explored the "cultural images of genetics and its medical possibilities, and [...] the mechanisms by which these images are (re) produced and sustained" (Petersen, 2001). It is typical that the therapeutic applications of genomics are always at the forefront, from media content to grant applications. Less attention is usually paid to the motives or methods of genomics (Petersen, 2001). Various metaphors have been reported, both in the popular media and scientific articles (Bubela and Caulfield, 2004) as well as shifting trends within this media and social landscape (Nerlich and Hellsten, 2004).

Criticisms on the lack of continuity of the human genome project metaphors with traditional cultures and the study of heredity have also been raised (Davis, 2004), with specific concerns about issues of collaborating with indigenous tribes for the discovery of pharmaceutical compounds within their rich natural heritage or the concept of 'biopiracy' by biotechnology corporations (Davis, 2004).

At the other end of the spectrum, novel metaphors are being sought, e.g. "the genome as an ecosystem" (Mauricio, 2005) and "the proteome as a signalling process" (Rose, 2003), or old metaphors criticized, e.g. "the

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