

Difficult Concepts in Systems Biology III

Function & Purpose at the molecular level

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Motivation. System Biology is very much in the vogue, but is also a reality in that full modelling of biological systems is now a possibility. The literature of systems biology have elements that are very well defined, such as different forms of high throughput data, knowledge of biological structures and dynamical modelling. However, the literature is also dominated by concepts that can only be describes as elusive and in many contexts unnecessary. Such concepts are “Life”, “Function”, “Emergence”, “Purpose”, “Modularity”, “Level”, “Reduction”, “Interpretation”, “Analyzability”, “Explanation”, “Understanding”, “Cause”, “Disease/Dysfunction” and “Machine as metaphor in biology”. There are most likely others. These concepts are problematic since they are easily used by the majority of the bio-science community, but there are no consensus about their definition or even the necessity of these concepts. We will define a series of projects that hopefully will clarify these concepts. (Cautionary note: The literature on the topic is extensive and the articles often appear in philosophical journals. So the articles read, should be chosen with serious care to avoid being overwhelmed.) Again there are other concepts like “robustness”, “complexity”, “redundancy” and “evolvability” that can be used in a sloppy fashion, but can be defined properly with a little effort.

Background. The overall motivation for the present project is the rise of integrative genomics and systems biology in the biosciences which use the concept of function on a large scale. Molecules and genes are often labelled by their “function”, where function has been defined by a different person than the one doing the annotation. Additionally, this is being done on such a large scale that there is a move towards automation of this process. Clearly, this necessitates clarity and convention around the concept of function.

The concept of function can be defined in a variety of ways. In engineering machines are conceived by a designer and components will typically have planned functions. Biologist are often tempted to used analogous descriptions as in engineering, despite the setup is being very different as biological machines are evolved and not designed. This implies that that the decomposition of organisms into components with different functions cannot be taken for granted, but need to be argued for in advance.

The definition of life entails that it must reproduce and have inheritance with error (mutation). The necessity of metabolism comes from fundamental thermodynamic consideration. One could imagine an organism/machine, where only the whole does something and it was very hard to decompose such individual parts had roles, but still was life according the general definition. It would be a worthwhile challenge to design such an organism. There are formal model of life such as Ganti’s Chemoton (Ganti, 1997), but they have a division of labour into genetic material, metabolism and membrane with some overlap.

Are functions only associated components (physically connected objects) or could they be associated more generally to traits, were trait is defined as any mapping from a total description of the organism? Gould and Lewontin (1979) had a scathing criticism of the way biologists construct adaptive history of traits. This does not directly impinge on our discussion of function, but underlines the problems associated the concepts of traits.

Some uses of biomolecular function are unproblematic and is just a description of a well defined action. This will be the case for the majority of descriptions found in for instance Gene Ontology (Bodenreicher and Stevens, 2006) or Enzyme Classification (EC). Function only becomes contentious when function is defined via a purpose for the whole. One could call the first local definition of function, while the second could be called global or holistic.

Lewens (2004,2006) discusses a variety of definitions of function.

Project.

The overall purpose is to survey and discuss the concepts of function/purpose in relationship to systems biology resulting a good report on the topic. At least two aspects of function must be covered:

- i. Action aspect. A natural starting point for this could be the gene ontology project and enzyme classification – see links below.
- ii. Definitions and use of function when referring the purposeful role within the organism or some subsystem. Discuss how a variety of definitions of function translate and apply at the molecular level?

A main challenge of this project will be to both be molecular and specific, while provide clarity and overview with abstract concepts relating to function.

Work schedule

- Read key literature. The reference list below is larger than necessary, but should be helpful in literature search.
- Find examples of functions. Find and discuss specific examples of functions and the size of the systems necessary to them to appear. Are functions uniquely defined or are there alternatives? This will imply independent critical literature search.
- What are the simplest examples of function? Minimal systems where function could arise?
- Computational aspects of function. Formulate simple dynamical models and investigate the probability of a function arising. This could for instance be done by sampling linear dynamical systems (Hirsch et al., 2004) and ask what is the probability that a random dynamical system?
- Automatic search for function. Given a full description of a system, how would one define components and then attach functions to the components?
- Is the concept of function necessary and useful?

Comments: For an earlier report on difficult concepts in systems biology, please see: <http://www.stats.ox.ac.uk/research/genome/projects>

A large part of these “difficult concepts..” projects have been written by Jotun Hein, although in maximal consultation with others. JH is not a philosopher, although he had an interest in the topic when younger. The projects descriptions are thus meant as motivator for philosophers of science to be interested in these topics and make no claim to dealing professionally with metascientific concepts.

References

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 Schaffner, K (1993) Discovery and Explanation in Biology and Medicine chapter 8 p362-410 Chicago University Press

Links

- <http://www.hps.cam.ac.uk/research/philofbio.html>
<http://www.geneontology.org/>
<http://www.chem.qmul.ac.uk/iubmb/enzyme/rules.html>
<http://huss.exeter.ac.uk/sociology/staff/dupre/index.php>
<http://plato.stanford.edu/entries/teleology-biology/>
<http://fds.duke.edu/db/aas/Philosophy/faculty/alexrose>