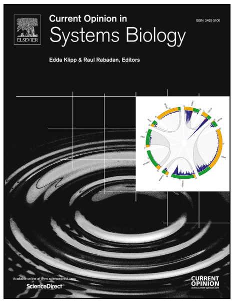
Accepted Manuscript



Cross-hierarchy systems principles

Lea Goentoro

PII: S2452-3100(16)30026-9
DOI: 10.1016/j.coisb.2016.12.006
Reference: COISB 6

To appear in: *Current Opinion in Systems Biology*

Please cite this article as: Goentoro L, Cross-hierarchy systems principles, *Current Opinion in Systems Biology* (2017), doi: 10.1016/j.coisb.2016.12.006.

Cross-hierarchy systems principles

Lea Goentoro
California Institute of Technology

Corresponding author:
goentoro@caltech.edu
1200 East California Boulevard
Pasadena, CA 91125
626-395-2841

Abstract. One driving motivation of systems biology is the search for general principles that govern the design of biological systems. But questions often arise as to what kind of general principles biology could have. Concepts from engineering such as robustness and modularity are indeed becoming a regular way of describing biological systems. Another source of potential general principles is the emerging similarities found in processes across biological hierarchies. In this piece, I describe several emerging cross-hierarchy similarities. Identification of more cross-hierarchy principles, and understanding the implications these convergence have on the construction of biological systems, I believe, present exciting challenges for systems biology in the decades to come.

Introduction

Systems biology is often defined by the tools it uses, *e.g.*, mathematical modeling, high-throughput measurements, large statistical analysis. Apart from the tools, systems biology may also be defined as a way of thinking, in the kinds of questions the students ask, and the kinds of answers the students search for (1). Systems thinking is a consideration of the behavior that a biological process gives rise to as a whole. An apt demonstration of what systems thinking is came from the systems scientist Donella Meadows, who sadly died too young. Meadows described how in the beginning of her class, she would bring a slinky (2). She would hold one end of the slinky, and then with the most dramatic gesture she could muster, she would flip it so the slinky ended up hanging from her hand and oscillating up and down. She would then ask the class what caused the slinky to oscillate. Some students would say, *e.g.*, ‘you hold it upside down’ or ‘gravity’. She would then take the box that the slinky came in, and performed a similar ritual. This time, of course, nothing happened, just the box hanging upside down. This demonstration illustrates a different view of causation: The slinky oscillated up and down not because it was held upside down or experienced gravitational force. In systems view, the slinky is constructed in such a manner and from such a material that it responds to those external factors by oscillating. Similarly, for example, we do not catch a cold because of a virus; our body provides the conditions that allow the virus to flourish.

A system is, in Meadows’ words, “an interconnected set of elements that is coherently organized in a way that achieves something” (3). A system may be a circuit of two