Use of Formal Diagramming Techniques to Build a Systems Understanding of Complex Biological Processes

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ABSTRACT

A system, any system, no matter how simple or how complex, has structure and organization oriented towards fulfilling its purpose and/or accomplishing its function. Whether designed by man or nature, large systems tend towards modularity and hierarchical structure to manage the complexity. In man-made systems, such design is documented by the charts and diagrams used to initially develop, then build, maintain, and modify the system. These charts and diagrams, whether blueprints, design specifications, or numerical descriptions, provide a means of representing the design concepts and of documenting and communicating them.

In drug development, researchers are faced with the interesting problem of coming up with a "fix" to a system for which there are no such blueprints or other design documents. Historically, much scientific innovation has occurred through a process whereby researchers form, manipulate, and develop mental models of the phenomenon they observe. Externally, such mental images and models are represented as physical entities at some level of abstraction, such as diagrams, graphics, computer simulations, or physical models [5]. These external representations have been used extensively in many scientific and engineering disciplines, but not to as large an extent in biology. In today's drug development environment, the use of such external methods for representing and communicating models will help to develop the necessary systems understanding of biology that is required in order to make the breakthroughs for the next generation of drug development.

This poster describes and illustrates a systematic knowledge acquisition and diagramming technique that has been used successfully many times to develop an external model, or blueprint, of a specified biological process in the context of drug development. The diagramming methodology provides the ability to collect, organize, structure, and integrate vast amounts of data and information from a variety of sources, and assemble it into useable, systems-level knowledge. Such diagrams provide hierarchical and modular organization, as well as a view on the complex interrelationships among system components, including the extensive feedback loops found in any biological system. In addition, they have *emergent properties* [4], such that their construction leads to new inferences and insights. The poster will also illustrate how these diagrams can be used as a foundation for building *in silico* models of the biological processes they represent [3], consequently providing further power in developing insight and driving drug discovery.

Use of knowledge diagrams has numerous advantages, including 1) supporting, extending, and making explicit the mental models that scientists already use, 2) integrating data and information from various sources into a single view, or theory, and making explicit what is and is not known, 3) serving as a mechanism for communicating among individuals with disparate backgrounds [1], 4) providing a new platform from which to interpret research data that exploits the human's natural ability to perform perceptual reasoning [2], and 5) forming the foundation from which *in silico* models can be developed. Sample diagrams and actual computer models will be available for demonstration.

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