EDITORIAL

System, Crowd, and Communal Innovation: Can the Monks Solve the Elephant?

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A systems approach reveals emergent group behavior of an assembly of interacting elements, networks, and subgroups, using modeling and simulation analyses that are capable of handling massive data and complex structures. As system complexity and data sizes increase, efficient collaboration becomes crucial to construct, refine, and analyze the model in a timely manner. A solution may be "crowd sourcing," which provides a platform for communal innovation.

> *"What has changed over the decades is that instead of innovation being seen simply as the domain of particular groups, companies or governments, it has become a highly collaborative, cumulative and social activity, in which people with different skills, points of view and insights share and develop ideas around them."*
> —Lynda Gratton[1]

The image on the cover of this issue is an *Ukiyo-e* woodblock print of an elephant being scrutinized by blind monks, who disagree about the characteristics of the elephant because each is touching and examining a different part of the animal. When we see this print by Hanabusa Itchō, an eighteenth-century Japanese artist and poet, we immediately understand its metaphor. I chose the cover art for two reasons that perhaps deviate from the artist's intention. First, the implied metaphor remains relevant to current biomedical science, including our own field of clinical pharmacology. Second, as Lynda Gratton[1] writes, the image of the blind monks exploring the elephant can also signify the cognitive leap collectively achieved by many individuals or groups of individuals with different views and skills—a leap that would be difficult, if not impossible, for a single person or a group of people with similar thinking. I call it "communal innovation."

Systems approaches for drug discovery, development, and toxicity prevention

How is the metaphor of blind monks examining an elephant relevant to clinical pharmacology? Simply put, after each of the monks has learned about a different part of the elephant, it is time to combine their knowledge so as to arrive at a better understanding of the whole to determine what the elephant looks like and what it does. These blind monks could be seen as representing the highly successful reductionist approach, and our viewpoint with regard to the elephant is a "systems

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doi:10.1038/clpt.2013.42

approach" integrating all key information; both strategies are indispensable components of our efforts in disease mechanism discovery as well as in drug target identification and development. In their State of the Art article in this issue, Lesko *et al.*[2] explain the current understanding of this approach, focusing on drug toxicity risk assessment. The term "systems approach" denotes a methodology applicable to a wide range of science fields. Although systems approaches in our discipline of clinical pharmacology range from systems biology to systems pharmacology (including systems toxicology), a feature common to all the approaches is their ability to handle data-rich structures of their respective models.

The key properties of a system, compared with each of its elements or parts, are its emerging patterns and behavior. In other words, as Helikar *et al.*[3] explain in their article on whole-cell modeling, a system's behavior often cannot be intuitively predicted by either observing each of its components separately or simply summing them up. These unexpected patterns and behaviors of a system are said to be "emergent." Their unpredictability, along with the massive data involved, explain the need for simulation-based analyses of models in systems approaches.

What is a model in systems approaches? Although there are many ways to define and categorize models, in our discipline a model can be defined as a simplified and quantitative representation of an object or a process, such as a signaling pathway, a whole cell, an organ, or a person. A model is amenable to interrogation, manipulation, and intervention to characterize its behavior; such experimentation would be difficult if we were to use the object or process itself. Because the often complex structures and data richness involved in systems approaches defy intuitive prediction, computational and statistical tool kits are important for modeling analyses. As Arrel and Terzic[4] explain in this issue, network analyses are particularly important in the context of complex systems that stretch the limits of our intuitive comprehension. For example, we may fully understand and intuitively explain the behavior of one- or two-compartment models without the help of a computer, but, as far as I am concerned, it is difficult to intuitively understand the behavior of a system described in three (or more) compartment models with various input and output processes, let alone a network.

Systems approaches in our discipline can be categorized into systems biology, systems toxicology, and systems pharmacology, depending on the goals for which the method is used. Vicini and van der Graaf[5] correctly position systems pharmacology within the confines of translational medicine, distinguishing it from systems biology, which at present focuses largely on cellular and subcellular networks and on systems in the domain of molecular medicine. Although these two approaches differ in many respects, they are not mutually exclusive and will eventually merge.

Crowd to improve on systems approaches: communal innovation

As Gratton[1] articulates in her book about the working lives of future generations, large-scale collaboration such as "crowd sourcing" is becoming a de facto norm for innovation in many commercial sectors and research areas. Crowd sourcing to improve on a product has been particularly valued in information-technology sectors, where it has proven to be effective and successful. As Costello and Stolovitzky[6] point out, landscape changes in the biomedical research world,

including massive data generation, open data access, and the need for data mining tools, have also made crowd sourcing a viable option for addressing systems-approach questions.

The concept of crowd or open sourcing to address a scientific question is not new. In fact, it has been embedded in the field of science as a rule of engagement. For example, scientific discovery and translational development are based on sharing knowledge and ideas among peers through publication and presentation, which then become an incubator for newer knowledge and innovative application. However, this is a protracted process that is limited by slowness of information transfer and a behind-the-scenes style of innovation. By contrast, crowd sourcing as presently understood can be viewed as an accelerated and transparent version of the traditional collaboration approach; speed and transparency are key to the success of communal innovation.

However, communal innovation in systems approaches—or in any domain of science—faces a challenge posed by the traditional academic and industrial environment, namely, maintaining a fine balance between the secrecy demanded by academic or commercial interests and the transparency necessary to maximize the speed and effectiveness of communal innovation. In other words, academics believe they must protect their data to win a publication race while industry considers it necessary to defend intellectual property—and both goals are fundamentally incompatible with the concept of communal innovation. In fact, the need for a new reward and recognition scheme for scientists has been recognized.[7] Despite the challenges, open-source precompetitive collaboration is already happening in industry.[8] So, what is 2025 going to look like? Unfortunately, I do not have a valid model to predict the future. However, given an increasing demand for social accountability, I boldly predict that someday academic and industrial secrecy in the domain of medicine and drug development will evaporate into historical obscurity.

CONFLICT OF INTEREST

The author declared no conflict of interest.

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