

NEWS AND VIEWS

q-bio 2007: a watershed moment in modern biology

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The mean is often nearer to one extreme than the other, or seems nearer because of our natural tendencies.

Aristotle, *Ethics*

Cells continually use information from external signals to sense and respond to environmental changes. One of the key questions facing biology is how can we better understand the systems of cellular regulation underlying this behavior? Can cellular responses in complex environments be predicted? How are the response mechanisms tuned when a cell adapts to environmental changes? Are a cell's sensory mechanisms—in Aristotelian terms, its *natural tendencies* for perception—well-matched to its information processing tasks? Recently, researchers gathered in Santa Fe, New Mexico and addressed these questions quantitatively.

In opening comments, David H Sharp (Chief Scientist, Los Alamos National Laboratory) dedicated The First q-bio Conference on Cellular Information Processing to green fluorescent protein (GFP)—a tool that has paved the way for numerous advances in quantitative biology. In subsequent days, participants were treated to one example after another of cellular phenomena characterized using fluorescent probes, including GFP, its variants, and quantum dots. Single-cell assays of fluorescently labeled proteins, in many cases, were an essential research tool, facilitated by commercially available microscopes with advanced optics and digital image capture. In some cases, the techniques were refined to image subcellular spatial dynamics of single fluorescently labeled proteins. Of note was the increasing use of microfluidic devices, which are providing an unprecedented degree of control over the cellular environment, enabling experimental designs that are precisely tailored either to elucidate mechanisms and enable construction and testing of quantitative models of cellular behavior or to provide reproducible conditions that mimic a natural environment. Important advances were also reported in the application of high-throughput methods based on chromatin immunoprecipitation and mass spectrometry. Combined, the talks created an impression that technical barriers are vanishing, and that

systems-biology has reached a turning point in which our ability to observe is mainly limited by one's imagination and resources.

In his opening banquet talk, William Bialek (Princeton University) argued that, constrained by the physical nature of the world, biological systems inhabit a region of design space that is nearly optimal for performance of many behaviorally important tasks—in particular, information processing. For example, the input–output relation of fly photoreceptors optimizes their information throughput for the distribution of light intensities encountered in natural settings; and the response of motion-sensitive neurons is nearly optimal for the visual field dynamics encountered during acrobatic flights. Significantly, the nearly optimal information-processing performance (within the physical constraints of inevitable stochasticity in biochemical reactions) is now seen even at the molecular level, such as in the response of hunchback gene expression to the levels of its regulator, bicoid, in fruit fly early embryonic development. The talk presented strong motivation for investigating the possibility that mechanisms of other cellular systems might have evolved to maximize information-processing performance and raised the question of how this might occur in the context of other requirements such as energy efficiency, low latency, and other criteria that inform the search for biological design principles.

The wonderful thing about science is that it's alive.

Richard P Feynman

Probably no single word can characterize the q-bio conference better than *exciting*. Michael Savageau (University of California, Davis) noted that the meeting captured the best of the field, and Dale Kaiser (Stanford University) remarked he had not seen so much energy at a conference in several years. This youthful energy and excitement were expressed in two lively poster sessions that lasted well past midnight. Results reported in the main sessions also fueled the fire. For example, a movie of single molecules in motion revealed that corraling by the

cytoskeleton causes anomalous diffusion of the cell-surface receptor for IgE antibody. Another reported study confirmed that one-dimensional diffusion along DNA enables *lac* repressor to find its binding site orders of magnitude faster than that in a three-dimensional search. An elegant cell-sorting experiment demonstrated a strong correlation between phage λ infection outcomes and *Escherichia coli* cell volume, calling into question the significance of random behavior in the lysis/lysogeny decision circuitry. A synthesis of bioinformatics tools was shown to enable the construction of a large portion of the human protein phosphorylation network, highlighting the role of protein–protein interactions in determining the substrate specificity of kinases. Elementary signal-processing principles were used to design an experiment in which oscillatory chemical signals were delivered to yeast cells, leading to a mathematical model of osmotic pressure regulation.

One recurring theme was adaptation. Unexpectedly, rapid (~ 10 generations) recovery of galactose-utilization capabilities was observed in mutant yeast chemostat cultures, involving global changes in gene expression that defy explanation by known mechanisms. An intuitive model of adaptation in *E. coli* chemotaxis successfully predicted the trend in *E. coli* CheY activity at extreme attractant concentrations, perhaps at last explaining how receptor methylation enables *E. coli* to follow spatial gradients over five orders of magnitude in attractant levels. A simple theoretical model enabled the experimental demonstration of integral feedback control in the regulation of osmotic pressure in yeast.

Taken together, the talks highlighted an important gap in understanding cellular systems. Some talks emphasized development of detailed models that integrate information about a large number of components and interactions. Others focused on coarse-grained models designed to yield insight into specific mechanisms. Still others explored the input–output relations irrespective of the underlying mechanisms. How should the coarse-grained, phenomenological models be linked to the detailed models, grounding the former on solid

theoretical principles and generalizing the latter? This question begs further inquiry.

At the closing banquet, John Doyle (California Institute of Technology) observed that the meeting seemed to capture a watershed moment in modern biology, in which a large number of ongoing research projects had reached a new level of maturity, and in which biologists, physicists, and engineers had begun to share the same language. Indeed, participants witnessed a blurring of traditional scientific boundaries, with theoretical and experimental approaches being integrated in interdisciplinary teams, often under the direction of a single investigator. We are left with the impression that an emerging core set of common methods and tools has brought quantitative biology, or *q-bio science*, to the brink of a revolution in our understanding of cellular information processing systems. Much remains to be discovered, and we are eagerly looking forward to seeing stories of progress unfold at future q-bio meetings.

The First q-bio Conference on Cellular Information Processing (<http://q-bio.org>) was held August 8–11, 2007 at St John's College in Santa Fe, New Mexico and was sponsored by the Center for Nonlinear Studies at Los Alamos National Laboratory, with additional support from the New Mexico Consortium's Institute for Advanced Studies, the Molecular Sciences Institute, the Center for Spatiotemporal Modeling of Cell Signaling, the Cancer Center at the University of New Mexico, and *IET Systems Biology*, which will publish a special issue dedicated to work presented at the conference.

The Second q-bio Conference on Cellular Information Processing will be held August 6–9, 2008 in Santa Fe.



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