Consider Context

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The amount of data being produced to study biological systems at various scales, from molecules to ecosystems, is growing exponentially, and handling this data from local production to its storage in publicly accessible and integratable depositories poses technical challenges that some areas of biology are already confronting. But the conceptual challenges ahead may be even more daunting. A major one is quantifying the impact of context, that is, experimental constraints and environmental factors that influence results. Internal and environmental properties together characterize biological systems, exemplified by human diseases, which are affected by complex genetic and environmental components, the latter being barely understood and still frequently neglected in current studies. Another challenge is how much we can abstract from observations derived from cultivated cell lines, given the absence of a native tissue context? Many current technologies impose noise onto real biological signals (for instance, studying cell populations rather than individual cells is frequently unavoidable), and given the complexity of biological systems in terms of their many interacting elements and confounding variables, how are we to estimate which aspects of a finding remain valid in other settings? Thus, there is an urgent need for generalized formal descriptions of the state and the environmental context of biological systems (metadata), which would not only improve the reproducibility and comparability of observations, but would also enable strategies for quantifying the impact of environmental conditions. Such efforts will help to minimize data overinterpretation (as can easily occur with indirect correlations) and reduce the accumulation of misleading results.

Systems Pharmacology

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It is in pharmacology that systems biology may face its most practical challenge and opportunity. Although everyone might grant that drug action is both a quantitative and multicomponent problem, the targets of drugs are not pathways, but individual proteins. Hence, the question naturally arises: If the ultimate targets of drugs are products of individual genes, are the qualitative pictures that we currently derive from biochemistry and genetics sufficiently informative to allow those targets to be identified effectively? Or could the process be facilitated by a quantitative understanding of the dynamics of the pathways at a high level of integration? We can all grant that high-level integration exists without agreeing that analyzing it quantitatively will dramatically increase efficiency in the high-stakes search for new and better medicines. We should soon know the answer, however, because approaches for understanding pathways derived from systems biology will certainly merge with more traditional areas of pharmacology, if for no other reason than that present approaches are often unproductive. But it would be wrong to think of systems biology just as a set of tools to bring to pharmacology. Systems biology is invading virgin intellectual territory, much as molecular biology and cell biology did before. And this brash invasion has already begun to raise new questions, pose testable hypotheses, and question long-held beliefs. It will transform how we understand biological behavior. Quantitative and broad knowledge from systems biology, more than just its new tools, could soon bring major new insights to physiology and pharmacology.