

Functions for Genomics and Philosophy

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Functions for Genomics and Philosophy

Genomic researchers in the ENCODE (Encyclopedia of DNA Elements) project, which published a mammoth series of biochemical studies of the human genome last September, have got themselves into philosophical hot water. The project's scientists claimed to have identified a function for 80 percent of human DNA, and this was widely thought to have killed the idea that "junk DNA" pervades the genome (doi:10.1038/nature11247). It was a startling result for evolutionary biologists. Now the other shoe has dropped: Biologists with a more evolutionary view have published incisive critiques of not only the methodologies employed by the ENCODE researchers but of their rationales for ascribing function to DNA.

The recent critiques by W. Ford Doolittle (doi:10.1073/pnas.1221376110) and by Dan Graur and his colleagues (doi:10.1093/gbe/evt028) are instructive (and entertaining). Doolittle and Graur find much to dispute in the main ENCODE publication, but a central objection is to ENCODE's use of the idea of a *function*. Some functions of molecular entities are inextricably bound up with the evolutionary reasons for their presence—although only a fraction of those were selected for, in the Darwinian sense (whether for the benefit of the organism or for that of some other level in the biological hierarchy). Other "functions" recognized by ENCODE, however, might have no evolutionary significance. The critics are having a field day making distinctions that were passed over in the euphoria over ENCODE's discovery of widespread biochemical activity in the human genome.

It seems that biologists' conventional understanding of *information*, since the discovery of the genetic code in the 1960s, is starting to fray. "Increasingly, genomics is expanding the boundaries of information as geneticists have usually understood it," Doolittle writes. The meaning or function of any molecule depends on its context. But contexts change with environmental conditions, over the cell cycle, over the lifetime of an individual, and over evolutionary timescales. Matter and information do not always stay in the distinct realms in which they are mentally filed.

The dustup over the functions of genes lends weight to the article by Dietmar Kultz and his colleagues that appears on p. 464 of this issue of *BioScience*. They make a welcome case for a new emphasis in research on understanding how organisms function and interact as integrated units. Genomic data will surely be important for advancing the understanding of emergent characteristics, but no less important will be studies of individual variation and the complex interactions of genomes and life histories. Huge amounts of data will be needed, and they will require a new cadre of investigators trained in handling very large data sets. Yet the techniques are known, and the technologies exist. Proteomics will have to be a large part of the effort, given the growing recognition of the importance of posttranscriptional and posttranslational mechanisms in cells. Future biologists will need to cross disciplinary boundaries every day to understand phenotypes.

Aside from the satisfaction of understanding life in a deeper way, the agenda sketched by Kultz and his coauthors will provide insights essential to predicting how organisms react to changing environmental conditions. The potential benefits for conservation, agriculture, and medicine are clear. And along the way, genomics researchers might get out of philosophical hot water.

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