

Differential and Integral Views of Gene-Phenotype Relations: A Systems Biological Insight

Denis Noble

Department of Physiology, Anatomy and Genetics,
Oxford University, UK
`denis.noble@dpag.ox.ac.uk`

Abstract. This lecture uses an integrative systems biological view of the relationship between genotypes and phenotypes to clarify some conceptual problems in biological debates about causality. The differential (gene-centric) view is incomplete in a sense analogous to using differentiation without integration in mathematics. Differences in genotype are frequently not reflected in significant differences in phenotype as they are buffered by networks of molecular interactions capable of substituting an alternative pathway to achieve a given phenotype characteristic when one pathway is removed. Those networks integrate the influences of many genes on each phenotype so that the effect of a modification in DNA depends on the context in which it occurs. Mathematical modelling of these interactions can help to understand the mechanisms of buffering and the contextual-dependence of phenotypic outcome, and so to represent correctly and quantitatively the relations between genomes and phenotypes. By incorporating all the causal factors in generating a phenotype, this approach also highlights the role of non-DNA forms of inheritance, and of the interactions at multiple levels.

References

1. Noble, D.: Differential and Integral view of genetics in computational systems biology. *Interface Focus* 1, 7–15 (2011)
2. Noble, D.: *The Music of Life; Biology Beyond the Genome*. Oxford University Press (2008)