

The chemical factory that fabricates itself: a systems biological view of the living cell.

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The realisation in the last few years that DNA (or genomics) is only one of the keys to understanding life and that epigenetic processes are equally if not more important has catapulted the discipline of systems biology to the forefront of science. Systems biology aims to develop an understanding of how the parts of a living organism and their properties are related to each other in order to produce those emergent properties that are only apparent when considering the intact system. The most important of these emergent properties is of course that of a material system being alive. In this lecture I would like to describe the first results of a project which I call Living Cell Theory, the aim of which is to develop a formal theory of living organisms that explains what distinguishes living from non-living systems and which, together with the theory of evolution by natural selection, can form the basis for a complete systems biological view of life. As a starting point the living cell is defined as a material system that is organised in such a way that it can autonomously and continuously fabricate itself, i.e., the lifetime of the cell far exceeds the functional lifetimes of any of its parts. This definition and way of thinking about living organisms has a distinguished history from which Living Cell Theory pulls together four strands of thought: (i) The theory of metabolism-repair systems as developed by the theoretical biologist Robert Rosen [1], (ii) the theory of self-reproducing automata developed by the polymath John von Neumann [2], (iii) the ribotype theory of Marcello Barbieri [3], and (iv) metabolic supply-demand analysis developed by Hofmeyr and Cornish-Bowden [4], which allows quantification of control and regulation in cellular systems and provides a way of studying functional organisation, thereby bridging the gap between relational descriptions and quantitative behaviour.

¹ Rosen, R. (1991) *Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life*. Columbia University Press, New York.

² Von Neumann, J. (1966) *Theory of Self-Reproducing Automata* (Burks, A.W., ed.) University of Illinois Press, Urbana.

³ Barbieri, M. (1981) The ribotype theory of the origin of life. *J. theor. Biol.* 91, 545–601.

⁴ Hofmeyr, J.-H.S. and Cornish-Bowden, A. (2000) Regulating the cellular economy of supply and demand. *FEBS Lett.* 467, 47–51.