FINAL REPORT

GRANT AF-AFOSR 9-66

April 1, 1966 - March 31, 1967

# Investigations in the Field of Relational Biology

The scientific work carried out under the previous grants (AF-AFOSR 9-64, AF-AFOSR 9-65), as reported in the Final Reports for those grants, was performed under difficult circumstances, owing to increasing administrative harrassment of the Committee on Mathematical Biology at the University of Chicago. This harrassment had existed for some time, but sharpened considerably and increasingly following the appointment of a new Associate Dean in 1965. By the beginning of the grant period of the present grant, the situation had become intolerable. Accordingly I requested a leave of absence from the University of Chicago, and spent most of the grant period as Visiting Professor of Biophysics and Mathematics at the State University of New York at Buffalo. Most of the work described in this report was carried out at Buffalo, and it is a pleasure for me to acknowledge with thanks the kind hospitality of the above-named departments, and of the Center for Theoretical Biology.

As mentioned in last year's Final Report, the main problem to which we addressed ourselves during the present grant period was the construction of a unified formalism for a relational theory of cellular regulation and control, incorporating in particular the insights obtained by our extensive studies of the (M,R)-systems. Partly to assist in this endeavor, and partly for its own sake, we prepared a detailed review of all theoretical work bearing on cellular control mechanisms, which will appear shortly in the International Reviews of Cytology (see Bibliography below). This review was aimed at extracting the underlying system-theoretic homologies and unities common to all these theoretical developments, diverse as they may appear at first sight, and placing them in a framework from which the unified relational formalism can be seen. Certain aspects of this unified framework are treated in greater detail in the paper on two-factor networks.

It was felt important to find a specific experimental system on which the theoretical developments could be tested. A suitable system was found in the circle of phenomena associated with cell sorting and pattern generation in cultures of dissociated embryonic cells. Accordingly, we have begun a detailed relational investigation of cell sorting phenomena, aimed at applying our theoretical formalism directly to this experimental situation, and based in part on the experimental work of Malcolm Steinberg (cf. for example M. Steinberg, "Reconstruction of Tissues by Dissociated Cells", Science 141 (1963), 401-411). This work is of considerable independent interest, and will enable us to determine among other things, (a) under what conditions the information obtained from cell sorting experiments can be directly applied to morphogenetic problems in the intact embryo, and (b) the class of algorithms which will serve to generate patterns corresponding to particular histological structures (e.g., tubules). What we called the Central Problem in the theory of (M, R)-systems has a direct analog in the cell sorting situation, so that a direct interplay between theoretical and experimental work is here possible. Although we have obtained a number of significant results in this direction, most of them were obtained after the expiration of the grant, and will not be reported here.

Mr. L. M. Demetrius, who was appointed Research Assistant on the grant, continued his investigations into the relation between the theory of (M, R)-systems and the theory of automata. Most of this work was incorporated into his Ph.D. dissertation, and will be published in three parts in the Bulletin of Mathematical Biophysics.

## PAPERS ARISING FROM GRANT

Demetrius, L. M. "Cellular Systems as Graphs". Bull. Math. Biophysics, in press (to appear 3/68).

_____ "Cellular Systems as Sequential Machines". ibid., in press (to appear 3/68)

_____ "Cellular Systems as Dynamical Systems and Finite Automata". ibid., in press.

Rosen, R. 1967. "Further Comments on Replication in (M, R)-Systems". ibid. 29, 91-94.

Rosen, R. 1966. "Biological and Physical Realizations of Abstract Metabolic Models". Proceedings of Second Annual Helgoländer Wiss. Meeresunt. 14, 25-31.

_____ 1967. "Two-Factor Models, Neural Nets and Biochemical Automata". J. Theoretical Biology, 15, 282-297.

_____ 1967. "Recent Developments in the Theory of Control and Regulation of Cellular Processes". International Reviews of Cytology, in press (to appear 12/67).

Robert Rosen
Principal Investigator

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13. ABSTRACT

A variety of further results dealing with questions arising in the relational theory of cellular systems are briefly described. They bear on the construction of a general theoretical formalism encompassing all aspects of regulation and control of cellular processes in a unified fashion, and on the testing of this formalism on a specific experimental system (namely, on pattern generation and cell sorting in cultures of dissociated embryonic cells).

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