

Molecular psychobiology of memory: Its appearance, contributions, and decline

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The development of molecular psychobiology in its concern with memory aspects is traced over four periods from its inception about 1950 to the present time. There was tremendous excitement during the second period (about 1958-1964) with the expectation that outstanding contributions concerning the molecular basis for memory would be provided. Unfortunately, little was produced of substantial nature; one of the main reasons was the extensive use of methodologies which emphasized quantitative aspects of RNA and protein, rather than methods which might indicate the presence of qualitatively different molecules and their role during learning and memory events. Only three procedures appear to have been suitable in handling these important aspects: DNA-RNA hybridization methods, polyacrylamide gel electrophoresis experiments, and the transfer paradigm. The latter is the only worthwhile one which is in extensive use today.

With the rapid development of molecular biology during the 50s and 60s, producing important basic contributions, it was inevitable that the ideas and methods of molecular biology would permeate the behavioral sciences as well. Thus it was that during the late 50s and early 60s a new area of research and theory gradually developed. This domain has been labeled molecular psychology (Gaito, Note 1), molecular psychobiology (Gaito, 1966, 1971), or molecular neurobiology (Schmitt, 1967). This area of endeavor had as its main concern the uncovering of the molecular mechanisms of memory. Now, however, it appears that molecular psychobiology as a separate and unique entity is rapidly disappearing. The purpose of this paper is to trace the development and decline of this area and to evaluate its contributions. The overall conclusion is that although the approach was a tremendously exciting one, with the expectation that important contributions would be forthcoming, and although much data were generated, *little of an outstanding nature was accomplished.*

BACKGROUND

Molecular psychobiology, as an area of research and theory, was concerned with the relationship between gene and gene products (the nucleic acids—DNA, RNA—and proteins) and behavior (mainly memory aspects). As the name indicates, it involved an integration of the ideas and methods of psychology with those from molecular biology. However, it included subject matter from a number of scientific disciplines, viz, biochemistry, physical chemistry, biophysics, virology, bacteriology, genetics, cytology, psychology, neurology, neurobiology, neurophysiology, neurochemistry, and neurohistology.

Because molecular biology had made rapid progress, it was assumed by many of the early workers in the area

that similar contributions would be provided relative to behavior. Although behavior in general was of some concern, the major effort of most investigators was relative to the molecular basis of learning and memory. Thus many individuals assumed that molecular psychobiology would determine the molecular basis of memory within a few years. The optimism and enthusiasm generated during the early days among a number of researchers was tremendous.

Many researchers in molecular psychobiology assumed that there were one or more specific DNA sites that were quiescent (or relatively so) during nonlearning periods. During learning events, these sites would become active in the synthesis of a specific RNA (presumably messenger RNA) (Bonner, 1964, 1966; Briggs & Kitto, 1962; Gaito, 1964a, b, 1966). This RNA was then to be translated into specific proteins or polypeptides which performed some important function, possibly at the synapse. There were variations of this theme. However, the important assumption was that there were unique RNA and/or protein molecules present during learning which were not present during nonlearning situations. Furthermore, these unique species of RNA and/or proteins were assumed to form the basis for memory events.

In attempting to determine the relationship between learning and the nucleic acids and proteins, there were two types of procedures utilized: the direct and the indirect procedures.

The direct approach used behavior as the independent variable and neurochemical aspects as the dependent variable. For example, Hyden and Egyhazi (1962) trained rats to climb a wire to obtain food and analyzed the RNA base ratios to determine if these ratios differed in trained and untrained animals; Gaito (Note 2) contrasted the amounts, and specific activities, of RNA and protein in avoidance conditioned and control rats.

The direct approach has a molecular biology empha-

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Table of Contents Molecular Psychobiology

1. Understanding the eBook Molecular Psychobiology
 - The Rise of Digital Reading Molecular Psychobiology
 - Advantages of eBooks Over Traditional Books
2. Identifying Molecular Psychobiology
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Molecular Psychobiology
 - User-Friendly Interface
4. Exploring eBook Recommendations from Molecular Psychobiology
 - Personalized Recommendations

- Molecular Psychobiology User Reviews and Ratings
- Molecular Psychobiology and Bestseller Lists
- 5. Accessing Molecular Psychobiology Free and Paid eBooks
 - Molecular Psychobiology Public Domain eBooks
 - Molecular Psychobiology eBook Subscription Services
 - Molecular Psychobiology Budget-Friendly Options
- 6. Navigating Molecular Psychobiology eBook Formats
 - ePub, PDF, MOBI, and More
 - Molecular Psychobiology Compatibility with Devices
 - Molecular Psychobiology Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Molecular Psychobiology
 - Highlighting and Note-Taking Molecular Psychobiology
 - Interactive Elements Molecular Psychobiology
- 8. Staying Engaged with Molecular Psychobiology
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Molecular Psychobiology
- 9. Balancing eBooks and Physical Books Molecular Psychobiology
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Molecular Psychobiology
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Molecular Psychobiology
 - Setting Reading Goals Molecular Psychobiology
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Molecular Psychobiology
 - Fact-Checking eBook Content of Molecular Psychobiology

- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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