525 EAST 68th STREET, NEW YORK, N.Y. 10021

THE NEW YORK HOSPITAL-CORNELL MEDICAL CENTER

DEPARTMENT OF NEUROLOGY

March 5, 1979

Dr. Joshua Lederberg
President, The Rockefeller University
1230 York Ave.
New York, NY 10021

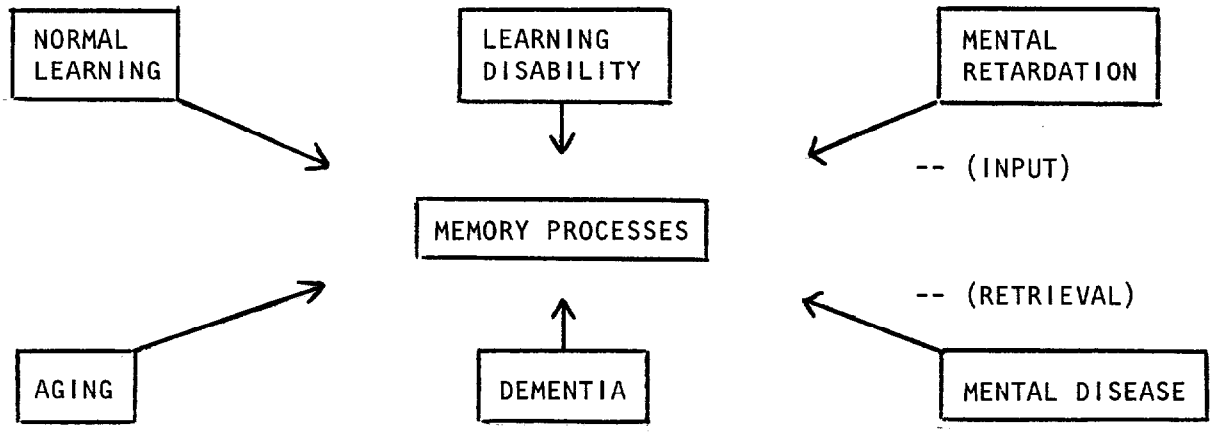
CONFIDENTIAL

Dear Dr. Lederberg:

I have thought about some of the issues you outlined in our conversation on February 14 and would like to pass along some suggestions that I think would make sense for Rockefeller in both the areas of basic neurosciences and the ongoing program in Cognitive Neuroscience. With the several faculty changes occurring at Rockefeller and with the fact that behavioral science on the 68th Street corner ought to grow out of a biomedical model, planning the future of these two major disciplines in a coordinated manner would be most productive. In general terms the scheme builds on the assumption that the proper program for the 80's is to arrange an intellectual environment where basic scientists in biology and the cognitive sciences come to know and understand in great detail the advances, insights and styles of scientific inquiry in the other fields. The students of this union in the 90's will be the first to integrate successfully brain and behavioral principles.

General Background

Of the many subjects of intellectual concern in both neurobiology and human behavior, the most prominent and promising at the present time is the understanding of memory. I believe that the problem of understanding memory processes can serve as a focal issue for basic research in the areas of biology, psychology and medicine. Memory mechanisms and their normal operation are pivotal in a wide variety of medical and social problems. If one considers only a couple of the issues in understanding memory such as the mechanisms of establishing memory traces as opposed to the problem of retrieving stored information, we can see the importance of understanding these processes in detail. Consider the following diagram:



At the input stage, the normal process of storing information in the central nervous system occurs. When these processes are disrupted, mild to severe impairments are seen in behavior which move from the usually transient learning disabilities syndromes into severe mental retardation. Although, a variety of other problems are usually associated with these syndromes, memory disorder is almost always present.

Conversely, accessing old memories as well as grasping the relationships between older, stored information and giving that information its appropriate value are processes that become disrupted in aging and also in two of mankind's most devastating diseases, dementia and mental disorders. Understanding at both cognitive and biologic levels how these rational processes work remains one of the life sciences' most outstanding and important problems.

This brief outline, of course, only draws attention to problems that are well known. While there are other problems that could possibly serve as an integrating theme, the appeal of memory lies not only in its inherent intriguing nature but also that it is beginning to be amenable to analysis with present techniques. Other topics such as the biology and psychology of visual processes are also appealing but these more traditional problem areas are being well attacked at other already established programs at other major universities. Lastly, a build-up in the key areas outlined below would find Rockefeller University (RU) hiring in disciplines of basic research that are presently recognized as vital and important in contemporary life science. If the programatic theme on memory does not congeal, the individual endeavors will all stand alone on their high quality. In the following, I will outline the issues that are most widely discussed in the three interest areas I have described.

Neuroscience

When one scrapes away hyperbole and bad thinking, the central assumption in neurobiology has been that synaptic modification is in some way involved in memory formation. While contrary views such as pattern changes in electrophysiologic responses, biochemical encoding schemes, and the like are not ruled

out, they have given way in recent times to the studies of the mechanism of synaptic formation and maintenance. This later approach is centrally placed in the study of the mechanism of information storage in the central nervous system. In contemporary terms this translates as people involved in developmental neurobiology. Even though Sperry laid out the problem 35 years ago and also suggested a biochemical model, most work on the problem is still anatomic in nature. While it can be compelling as well as highly sophisticated in technique, it is Mendelian in its nature. Yet it is solid ground to build on and such an area must be strongly represented in a good neuroscience program. Both cognitive scientists and neurochemists do and will continue to feed on such information. At present, Rockefeller is not represented in this area. Coming at it from another angle, this area has been identified by your own faculty as needing attention.

Attacking the problem on a cell to cell specificity basis, in terms of a biochemical mechanism, is only now beginning. Approaches to the problems at this level are a key to future directions of the field and there are several young investigators who are doing good work in this area. For example, exciting work by David Gottlieb at Washington University is being carried out on the membrane properties of the growing nerve. Other work on the neuromuscular junction by Denburg at Iowa is also beginning to point toward some biochemical clues on cell to cell specificity.

Cognitive Science

Since the turn of the century, memory has been one of the main problems of experimental psychology. Today, the subject is being vigorously explored with respect to such issues as how the organism apprehends information in discrete time periods, how kinds of erroneous intrusions and confusions occur in long term memory, how fast-access to old information varies, etc. These key parameters plus literally dozens more are being carefully studied today in cognitive science and are yielding rich insights as to how man best stores and accesses information under a variety of circumstances. Yet few of these theories, although properly explaining data arrived at in experimental psychological situations, can be validated in a biologic framework. It was this kind of a situation that generated the joint program that was started between Cornell and Rockefeller in Cognitive Neuroscience. Specifically, one of our goals was to determine how various models of memory mechanisms could be validated and one answer seems to be through looking at cases of patients with particular kinds of focal and diffuse brain disease. That enterprise is ongoing and actively being carried out now through our joint program. With George Miller's departure what is needed here are one or two young biologically sophisticated psychologists. I must emphasize that it is the cognitively trained scientists that lay out the framework for the biologist in this area. They are the ones that are delineating the operational rules of the memory systems and as such are crucial to the overall success of such a program. Of course, the best man in the world for this position is George Miller and if you are interested I have a specific idea on how to salvage the events of last month.

Medical Science

I need only mention here the staggering and well known facts of the problems of dementia and mental disease, learning disabilities and mental retardation. They make clear the motivation and need to come to a fundamental understanding of memory mechanisms.

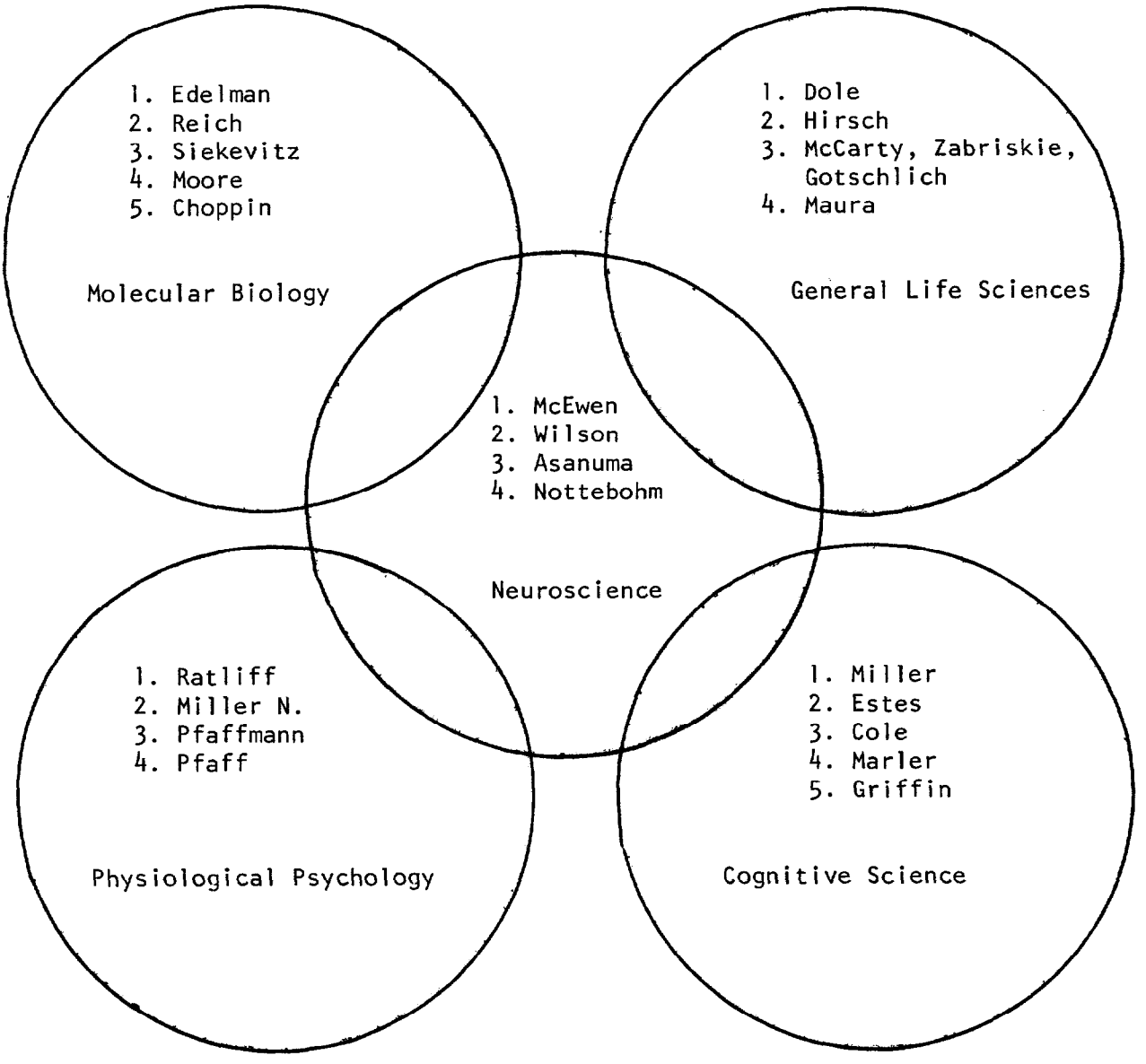
For Cornell and Rockefeller to join forces in this area is especially productive. The New York Hospital has one of the most active Neurology and Neurosurgery units in the world. I monitor the patient flow daily, directly and through my staff. In the acute care setting here we study the patients of particular interest to us. At the Rockefeller Hospital we have carried out special studies on patients who are medically stable yet behaviorally interesting. The medical aspects of these patients are cared for by one of the Fellows of our Cognitive Neurosciences program, Dr. Bruce T. Volpe, M.D., who is both an outstanding neurologist as well as an internist.

In short, on 68th Street there are unique opportunities for interaction between cognitive science, neuroscience and medical science.

Personnel

Present Rockefeller Staff:

In one sense, anyone who deals with the nervous system is a neuroscientist, and there are several faculty members at Rockefeller involved in this general area. More realistically, however, many of the Rockefeller faculty who have been listed as involved in the Neurosciences are actually peripheral to the central problems of the field. This is especially true when one considers the upcoming personnel changes most heavily affecting the behavioral physiology and cognitive sciences areas. Additionally, one could not find in the present Rockefeller staff a theme or a general strategy emerging from the varied interests of the present staff if all of those listed in the following diagram are called neuroscientists:



I have tried to break down the faculty into more appropriate categories. When this is carried out, the number of people in neuroscience as it is more generally defined is small, and some have interests that reflect past advances in the field rather than future directions. In other words, while essentially every member of the Rockefeller faculty is a distinguished scientist who has made major contributions to a particular field of interest over the years, it becomes difficult to imagine how their interests might mesh into a coherent future plan.

Present Cornell Staff

There are a variety of excellent neuroscientists here at Cornell as at Rockefeller. They are mostly part of the Neurology Department. These would include the Chairman, Dr. Fred Plum who works on stroke and cerebral metabolism; Dr. Donald Reis who is an authority on catecholamine systems, brain mechanisms in hypertension, etc.; Dr. Ira Black who is a developmental neurobiologist (and also neurologist) who studies the development of the autonomic CNS; Dr.John Blass who studies genetic error in human disease, and who is initiating a program on the metabolic aspects of dementia. In the physiology department, Dr. Bernice Grafstein studies axonal transport mechanisms. There are less inspired research activities within the anatomy department.

This leaves as the Cornell staff that are most relevant to the Cornell-Rockefeller joint projects, the people of my Division of Cognitive Neuroscience. We study problems of brain and behavioral relationships in both animal models and the special Neurologic patient.

Memorial Hospital

Dr. Jerry Posner who is also a Professor of Neurology here at Cornell is the Chief of Neurology at Memorial and will be the PI on the Pet Scanner Project. They have gone ahead and ordered the scanner which will arrive in October. It will be a few months before they hear whether or not they will be one of the 6 Centers awarded funds for its operation. Dr. Posner is first class and a helpful liaison with our joint interests. He also runs an excellent department which includes many fine young scientists including Dr. Pasternak who has just come from Dr. Snyder's lab. He will be studying opiate systems in the human brain.

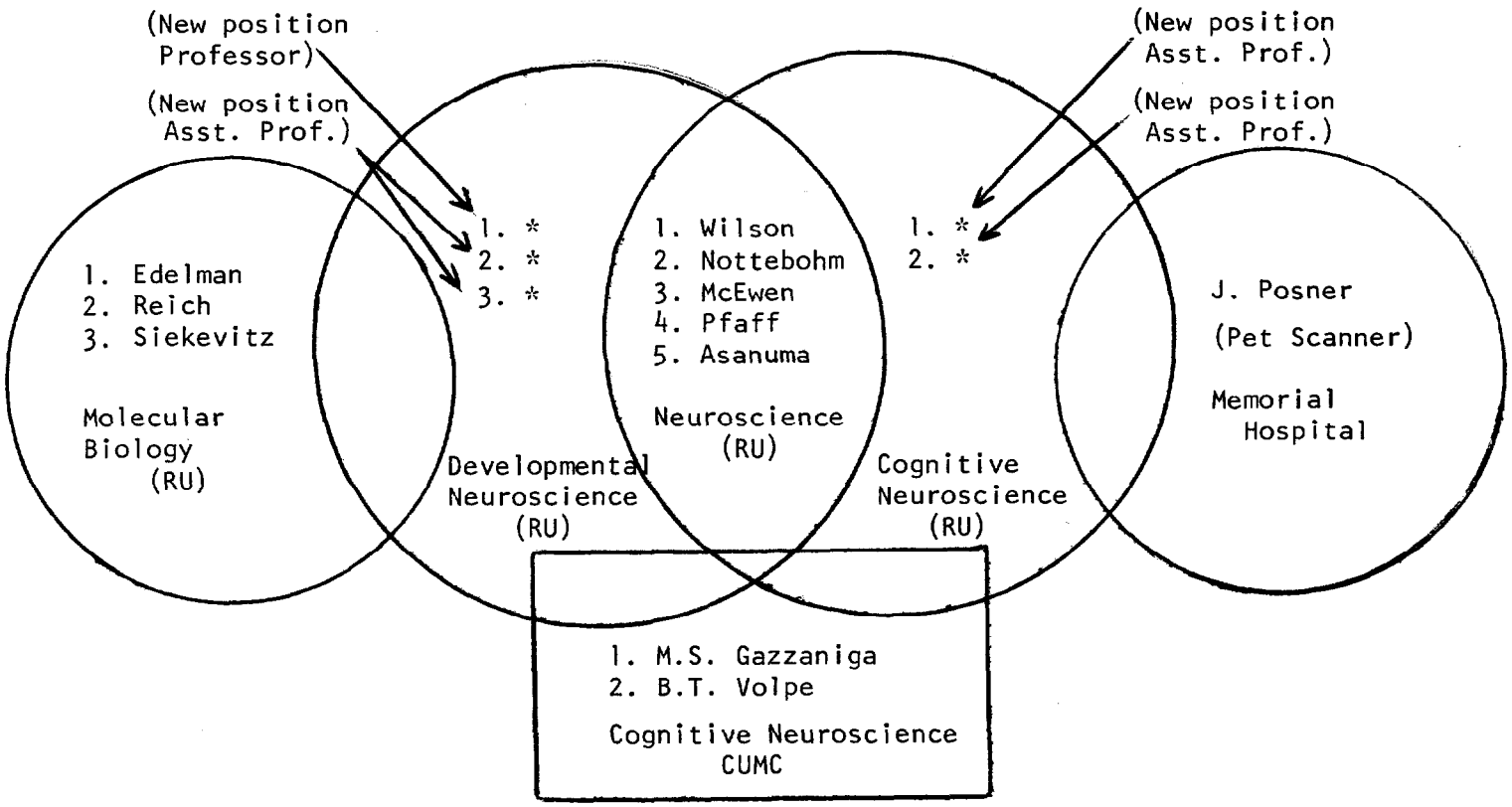
Future Organizational Possibilities:

As already outlined, one of the major growth areas in neuroscience is to merge towards cell biology on the one hand and cognitive science on the other. It is that kind of organization which I think leads to a different characterization of what the program might look like and the possibility exists for a more rational approach to problems in the area of brain and behavior. In the following, I present yet another diagram which takes note of the impending changes in personnel that are known to me. With this plan, new appointments in the Developmental Neurosciences and Cognitive Neurosciences would be cast as already described as working on memory mechanisms, while its existing neuroscience staff as well as other life scientists would serve mainly as interested parties. How this effort would interact with Cornell and Memorial Hospital is indicated below:

logic
computer sc.

JOINT PROGRAM IN MEMORY

(Personnel Profile)
(1980-81)



I think I can say with some confidence that CUMC and Dean Cooper would support this kind of joint project. Dr. Posner of Memorial would also be an enthusiastic supporter.

If the foregoing framework seems reasonable, I would like to proceed with the process of identifying specific candidates for RU's consideration in the areas of developmental neurobiology and cognitive science. One way to

accomplish this would be to organize a seminar series next year at RU. To that end I also submit two different schedule ideas--one for neurobiology and one for cognitive neuroscience. My Sloan grant could underwrite the latter effort.

It goes without saying that I would appreciate this memo to be considered for you personally. I see nothing to gain by having antibodies form to perhaps the wrong antigens! At the same time, if you think the idea is not realistic perhaps we could meet again and further identify what might be viewed as a more viable plan.

Cordially,

Michael S. Gazzaniga, Ph.D.
Director, Division of Cognitive Neuroscience

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