It is impossible to believe that neuronal connectivity is fixed and identical in every individual. Accidents of cell destruction would be inevitable, even if we could believe that the life-long development of a brain was immutable. The variation in the mere size of brain parts and cell number among individuals tells us the same story. Therefore, variation in connection pattern must be taken as an inevitable component of the developmental pattern of a brain. Since this morphological development is concurrent with learning, it must play some part in it; if nothing else, the memory mechanism must accommodate itself to the immense variety of patterns of channels. Even if there were some alternative mechanism of information storage the operating behavior of the system would surely depend on variations in the connection pattern, and to that extent, the latter must inevitably play a substantial part in the behavioral development, i.e. the memory of the organism. We have now only to ask whether this interconnection pattern is influenced by the life-long experience of the animal. It is important to remember that the individual does not actually remember any part of the real world. We are entitled to infer only that what is remembered is a pattern of effective behavior which, hopefully, may be an adaptive response to past or anticipated sensory data, and which may include the regeneration of simulations of past experience. A glance at a shelf of books may enable us later to utter, be it silent or public, a fragmentary reconstruction of a few bits of description of that bookshelf. No conceivable technique of information storage would enable the books themselves to be accurately reproduced. ${ }^{1}$

1 Some remark along these lines may be absolutely essential, because $I$ sometimes feel that the people who insist on much larger dimensions of information storage have completely missed some elementary aspects of the physiological psychology of perception. I don't know whether I have stated it very well here.

If we adopt the second approach to this manuscript I would try to put together a couple of paragraphs that would relate the problem of the development of the interconnection system, since we have now placed the burden of memory on this, to the general problem of development and how this would then suggest the kind of analytical tools that would be most appropriate to further progress.
J. Lederberg 1/14/65

One motive that has impelled speculation on more complex mechanisms than neuronal interconnection has been the concern whether this could generate a high enough level of information storage. With neither a precise quantitative estimate of the requirements nor explicit model of the cerebral system, it is not easy to pass judgment on their correspondence with one another. However, we can make the following rough and ready calculations.
(1) A crude model of interconnection. Let a typical neurone have a domain of 10,000 neighbors with which it can potentially interact. If,in fact, it establishes 100 synapses, the choice of audience corresponds to about 800 bits of information per neurone, i.e. about $8 \times 10^{12}$ bits for the entire brain. The calculation follows: each synapse represents a choice of one among $10^{4}$ or $2^{13.3}$ possibilities, i.e. carries 13.3 bits. However, the 100 synapses might be arranged in 100! alternative combinations, corresponding to 525 bits ( $2525=100$ !). We have then $1330-525=805$ bits as the information content of the unordered set of synapses from a single neurone.

This calculation may be, if anything, conservative in its postulate of the richness of synapses with which it will vary in proportion. The domain of potential audience doubtless varies even more widely throughout the brain. The information value of a neurone will go roughly as a logarithm of the size of the domain.
(2) To estimate the information-storage requirement, we note that the human sensory channels can hardly sustain a continued average rate of 50 bits per second. A century is $3.15 \times 10^{9}$ seconds, giving a generous figure of $1.6 \times 10^{11}$ bits of information input per lifetime, but still this is only a fiftieth of the calculated capacity. On the most demanding assumptions of retention and infallibility of memory this still leaves ample room for redundant

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representation for storage of instinctual programs and for the computing
elements which must process this information. Further, it takes no account
of additional morphological dimensions of information, e.g. the length,
diameter and speed of each conductor, not to mention any specific qualities of
their terminations.
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$1 / 14 / 65$

Concerning the Woodfow analogy, this is perfectly appropriate in the context of this lecture. I don't think $I$ would give quite so much currency to those developments in a more studious presentation. The memistor is of course an intriguing example of an analog device with memory, but if only because it is an analog device, I think it is not the most appropriate example to give a great deal of stress to. In fact, it seems to me that a latching relay with a tired spring, or subject to a noisy environment, would be just as apt an example.

While the neurone must be regarded as a digital device, I suppose there is an analog aspect in view of its asynchrony. We could very well imagine that a good deal of information is enabled by variations in conductor length and speed with consequent variations in the synchrony of firing of the synapses at the target. This would then be added, of course, to the very familiar cell-to-cell interrelationships in the nets. We certainly still need a clearer picture, and I suspect it will be asimple one, of the way in which a bit of information is actually stored, and more particularly the way in which this bit is appropriately related to the sensory experience. From this point of view, $I$ found traz the other way of looking at it, that is the question of how to store the effector pattern makes the job appear somewhat simpler, but we still have the problem of how to match an effector subroutine(e.g. a simulation of a past impression) to the original sensation. This would obviously entail an enormous amount of computation, and it has been my hunch for a long time that sleep, and especially dreaming, were the incidents of this process. If this is true, and if several other elements of the general theory presented here are true, there should be some definite biosynthetic correlates of sleep, which as far as $I$ know, have never been looked at and which we are now discussing as the next order of business here.

