April 3, 1955

Dr. John von Neumann
Institute for Advanced Study
Princeton, N.J.

Dear Dr. von Neumann:

Thank you for your letter of March 14, referring me to the Hixon Symposium. By a curious coincidence, I had just then "spontaneously" stumbled on the book, and have had some chance to read your article in the interval. I also note the account by John Kemeny in the last number of the Scientific American.

Under separate cover, I did send an article of my own, "Cell Genetics and Hereditary Symbiosis" which may serve rather to illustrate perplexity than to illuminate concept.

In your treatment, I am particularly impressed by the way in which one can evade the notion of a "self-reproducing particle", for you emphasize that it is the entire assembly alone that has that property. In different language, I have been groping for the same inference, simply on the basis that genes, or even nuclei, are incapable of producing anything, much less copies of themselves, when isolated from the whole machine. But there are still some difficulties, for the geneticist would still like to abstract, from the entire organism, the least structure that will still perpetuate the genetic function. The non-germinal or somatic elements of higher organisms are generally more conspicuous than the germ, but even within the scope of a single "macromolecule", a similar differentiation can be seen, for example in the way in which terminal threonine residues have been split from tobacco mosaic virus without impairing the ability of the particle to engender further generations of typical virus. You have indicated an analogy between the genes and the "information tape", but I would be interested to know the explicit criteria by which to tell how an intracellular organelle corresponds to one or more of the elements of your assembly. I shall, in fact, be surprised if your conceptual analysis has a structural representation, or if this was intended by yourself.

As you need hardly be told, my own thoughts on this subject are still amorphous. I am still trying to see what can be salvaged of the notion of a "self-reproducing particle",if anything. I am more concerned how a system such as you postulate can have evolved, and am therefore still interested in more strictly autocatalytic processes, which may be useful in preliminary model building. I am hopeful that, once our ideas are more precisely developed, it may already be technically possible to build chemical models which may exemplify some reproductive processes.

In your article, you hint that a dozen kinds of elementary parts would suffice for a s-r machine, but I am afraid I still do not understand what you mean by a part, and would be grateful for a clarification, and for some notion how your inventory is derived.

In reviewing the whole article, I also wondered if your concluding section did not contradict the suggestion that nature has not relied on digital coding: the linear chromosome must be one of the most elegantly encoded sequences, having baffled even Gamow's cryptography. Perhaps you were referring more narrowly to neural mechanisms: the main point is obviously that a digital code needs a detailed structure on which the "tape" can be oriented, either temporally or spatially. And we have perhaps some hints of this in (some versions of) the acoustic sensory mechanism, though you are perhaps excluding codes other than those involving a single transmission line. For these, the greatest problem may be that of orientation and registration, which would have to be temporally regulated. The problem of keeping the CNS in phase with the external receptors may be biologically insuperable in view of such perturbations as result, for example, from temperature variation, whose consequences are, for the reasons you outline, far more disastrous the less the redundancy. Coding on a geometric (as opposed to temporal) scaffold is far safer, and not infrequently (indeed, in a [redacted] macromolecular chemical context, invariably) found.

Yours sincerely,

Joshua Lederberg
Professor of Genetics