March 1, 1968

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Dear Jane:

At last I found an evening to go over your MS. I'll offer some suggestions, although I cannot go deeply into the matter.

I don't think Holtfreter is right about "diffuse organization." The organization is quite clear, as you put it down on the yellow sheet. I think what disappoints the reader is the negative outcome of your historical analysis. Perhaps Hanes comes closer to pinpointing the shortcoming when he asks for a "firmer backbone of leading thoughts" and more meat. I have the feeling that you point at one of the fundamental problems but don't come to grips with it. The organized induction and related phenomena, such as the influence of surrounding mesoderm on the shape of the neural tube, and morphogenetic movements are, by their nature, supercellular phenomena. In the 20s and 30s, tools were available for handling them (Spemann, Harrison) and the conceptualization (fields, inductors, etc.) was self-contained on the supercellular level. What Wilson's contemporary cell approach could do was to handle blastomeres and localization in eggs. He had no access to the above-mentioned problems.

Now the crucial point; Holtfreter was one of the few who was aware that eventually the supercellular phenomena had to be explained in terms of cell properties. In the 40s, he spent a great deal of time and effort on studies of embryonic cells in isolation (gastrulation papers '43; motility '46; inclusions '46, kinetics '47, etc.). Perhaps it is a meaningful question to ask why this did not pan out; why his findings could not be related to supercellular processes at that time. And what is germinative in these ideas? E.G. modern studies of gastrulation movements go back to his emphasis on flask cells (see Tinkaus in "Organogenesis" and 25th Growth Symposium). We certainly have to put strong emphasis on the cell membrane, as he did in the '48 paper in the N. Y. Academy of Science. He may be wrong factually, due to primitive knowledge of the membrane properties; but he saw the lights. One could probably find similar insights in the dissociation and affinity papers. Perhaps it would improve the MS if you would handle your subject more around his contributions and ideas. I see nothing wrong in this; on the contrary, why should a symposium in his honor not be slanted in this direction, if it comes natural?
But you can say that what all this adds up to is still negative: an unsuccessful effort, because the time was not ripe in the 40s. One can then ask: Do we come closer now? Apparently by a detour, by way of behavior of determined cells and their group behavior (Grobstein, Moscona, Bonner, Lash, Konigsberger, etc.). Information on the sorting out in these systems should eventually help to understand self-organization in the chorda-mesoderm field or the limb field. What seems to me appropriate would be to emphasize more in detail how these people go back to Holtfreter and Townes and Holtfreter. The success of the latter was that they used (for the first time?) cells that had already acquired initial determination, or to put it differently; membrane properties that permit recognition.

One small detail: I think you should mention Hiroko specifically on p. 10. I don't see much point in expanding on genetics.

Baltzer was very anxious to read this MS. You would do him a great favor if you would send him a Xerox copy. At the moment, he is in the hospital for a cataract operation.

All good wishes,

Viktor Hamburger
Professor of Biology

VH:1q