rays, and alpha particles. In recent years of the 20th century, the *direct* conversion of the energies of these invisible particles into light, at operating temperatures near room temperature, has become a major commercial function of phosphors which are now produced at the rate of over 200,000 kilograms a year. Meanwhile, phosphors are finding increasing scientific use in detecting these invisible particles and others, including infrared and gamma-ray photons, fast-moving ions, and even neutrons, by converting their energies into radiations which the human eye may detect directly, or indirectly through other photosensitive devices, such as multiplier phototubes (usually coupled with oscilloscopes or meters), photographic films, or other phosphors used in cascade.

In addition to the practical progress already made by empirical phosphor research, some progress has been made toward developing a qualitative theory of luminescence of solids, although a useful quantitative theory is not yet available. Luminescence is such a convenient and sensitive indicator of changes of composition, structure, and atomic interactions in solids that it has contributed much to our improved understanding of the solid state of matter. In the future, the practical consequences of this broad aspect of luminescence research may well overshadow the tangible results already obtained.

References

1. FONDA, G. R., and SEITZ, F. (Eds.) *Preparation and characteristics of solid luminescent materials.* New York: John Wiley, 1948.
2. FORSYTHE, W. E., and ADAMS, E. Q. *Fluorescent and other gaseous discharge lamps.* New York: Murray Hill, 1948.
3. KRÖGER, F. A. *Some aspects of the luminescence of solids.* New York: Elsevier, 1948.
4. LEVERENZ, H. W. *Introduction to the luminescence of solids.* New York: John Wiley, in press.

The Nature of the Organizer

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APPROXIMATELY TWENTY-FIVE YEARS AGO, Spemann and Hilde Mangold demonstrated that the dorsal lip of the blastopore acts as the primary organizer of the amphibian embryo after it is carried inside the gastrula to form a layer of chordamesoderm beneath the ectoderm. The contact thus established between these two layers results in an induction by the chordamesoderm (organizer) of nervous tissue in the overlying ectoderm. Since this discovery was made, an intensive search has been conducted for an explanation of both the stimulus and the response in this reaction. In terms of biochemistry and cellular physiology, however, the precise nature of embryonic induction still eludes us. It may be useful, nevertheless, to summarize the current ideas on the nature of the organizer.

First, let us consider the question of specificity of organizer action. Many studies have suggested that the inducing stimulus is nonspecific. It has been shown that amphibian ectoderm capable of response (competent) can be induced to form neural tissue by an array of inductors, some of which are: 1) living organizers from other vertebrate embryos; 2) extracts from whole embryos or parts of embryos; 3) tissues from the embryonic or adult bodies of many kinds of animals, providing the tissues are first killed by heat, drying, freezing, or treatment with organic solvents; 4) certain chemical compounds, such as cephalin, digitonin, and various polycyclic hydrocarbons; and 5) chemical or physical conditions that cytolyze some of the ectodermal cells with the release of toxic products evoking a neuralizing response in the surviving cells. Actually there may be no distinction between the last two categories.

Spemann (*11*) himself was finally inclined to the conclusion that the inducing stimulus is nonspecific and Holtfreter (*8*, p. 34) has recently taken this position, pointing out that neuralization of competent ectoderm "can be achieved by the application of various agents which have not more in common than the faculty of increasing the permeability of the cell membrane, and of causing cytolysis if applied in excess." If this interpretation is correct it follows that the factors for specificity of the reaction lie within the ectoderm.

On the other hand, there are studies which suggest that inductors are not qualitatively alike and that the specificity of induction does not reside entirely within the reacting system. Evidence supporting this interpretation includes the following points. 1) The results of experiments on regional determination indicate differences in the action of the organizer along the primary axis of the embryo. Thus, anteriormost mesoderm induces brain and sense organs, whereas more posterior levels induce spinal cord. 2) Dead

inductors differ from living organizers in that the response to the former lacks the organization and completeness of anatomical pattern (individuation) which characterize the secondary embryo developing in response to a living organizer. Holtfreter (*8*, p. 33) refutes this point, however, as follows: explants of competent ectoderm stimulated by cytolyzing agents "differentiate not merely into a heap of neural cells, but the previously nonorganized cells become integrated into anatomical patterns which can be identified as brain diverticula. If these formations are covered by a mantle of epidermis the latter frequently forms nasal pits and frontal glands . . . . the original concept of the organizer as an all-powerful individuating agent should be revised. Furthermore, the data available leave little doubt that it is futile to make a distinction between living inductors and artificial 'evocators.'" Holtfreter admits, however, that "posterocephalic" inductions were not obtained by the action of cytolyzing agents and that, furthermore, mesodermal structures have never been observed in the explants. 3) Living inductors can evocate mesodermal structures; dead ones usually do not. Chuang (*5*), for example, observed the induction of muscle, notochord, pronephros, and other mesodermal structures by fresh mouse kidney. Induction of notochord and pronephros failed if the kidney had been boiled for five minutes and no mesodermal structures were obtained if it had been boiled for fifteen minutes. Moreover, boiling for varying periods changed the relative frequency with which the several ectodermal organs were formed. Holtfreter (*7*) had observed earlier that prolonged boiling of a tissue or heating to 135° C reduced the activity of the inductor, and a temperature of 172° completely abolished it. 4) It was observed by Waddington (*12*) that boiled nuclei were better inductors than boiled cytoplasm with respect to percentage of inductions obtained and volume of induced structures. Chuang found also that newt liver and mouse kidney were unlike in their inductive actions.

These examples are sufficient, I think, to indicate the type of evidence supporting the contention, on the one hand, that inductors are nonspecific and, on the other hand, that they are different in their action and that some measure of the specificity in response is a function of the stimulus. Unfortunately, as Needham (*9*) has so clearly stated, we have no adequate test for induction. A response by competent ectoderm is unsatisfactory because ectoderm itself may possess the inducing agent in a bound or masked form. Ventral ectoderm which cannot induce when living will stimulate neuralization if killed. We lack a reacting system which will respond to a neuralizing stimulus but which is incapable of acting as an inductor alive or dead.

We may proceed further in our analysis, however, if we assume that the critical agent in induction is the same irrespective of whether the stimulus comes from *without* the ectoderm or whether it is released *within* the ectoderm. According to the first concept (lefthand side of Fig. 1) a nonspecific stimulus produces a change in permeability of the inner membranes of the ectodermal cells which somehow sets off

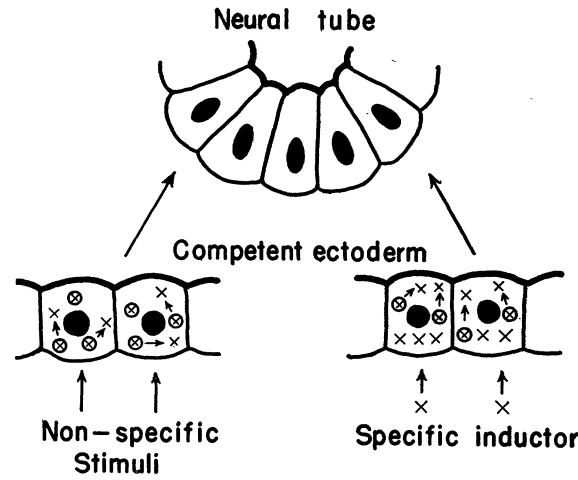

FIG. 1.

the chain of reactions leading to the formation of a neural tube. Maybe a bound substance (encircled x) is released, or perhaps it is synthesized and then, like a virus, is self-duplicated within the cells. In any event, free x is the critical inducing agent. According to the second concept (righthand side of Fig. 1), free x of specific qualities is provided by an inductor—in the living embryo by the mesoderm—which diffuses into the ectoderm and initiates neuralization. Release of bound x or its synthesis and self-duplication might follow secondarily. In both schemes x is the same. What is x?

Two principal suggestions as to the chemical nature of the inducing agent have been proposed: Needham's sterol theory and Brachet's nucleoprotein theory. Needham (*9*) postulated that the cells of the dorsal lip possess the inducing steroid substance in a bound form—perhaps in a polysaccharide-protein-sterol complex. In the course of gastrulation the characteristic metabolism of the organizer breaks down the complex, releasing the sterol which induces the overlying ectoderm to form a neural tube. Evidence presented by Needham, Waddington, and their collaborators includes the following points. 1) The inducing activity of ethereal extracts of embryonic and adult tissues was traced to the digitonin precipitate of the unsaponifiable fraction. Later Barth (*2*) showed that the protein fraction exhibited a greater inducing power. 2) Pure sterols or sterol-like compounds

acted as evocators of a neural response in competent ectoderm. 3) Lastly, the dosage of an active steroid required for induction was very low. In connection with the last point, the work of Shen is cited by Needham as being a strategic piece of evidence. Shen (*10*) recorded induction with a water-soluble carcinogenic hydrocarbon, dibenzanthracene, in very small concentrations. A maximal response of 41 percent induction of neural tube was obtained with a dose of .0125 γ per embryo. This dosage was much smaller than those of nonsteroid substances required to evoke a neural response and was in the same general range of concentration as that shown by other biologically active substances, such as hormones and vitamins.

Brachet, on the other hand, has extended the earlier suggestion of Barth that the organizer may be a protein, by his studies on the relation of ribonucleic acids to induction. According to Brachet (*4*) the inducing substance may be a nucleoprotein released from the mesoderm in the form of granules which probably include other substances, possibly enzymes. These granules are then engulfed by the ectoderm within which neuralization is initiated. Another possibility is that the metabolism of the mesoderm splits the nucleoprotein into mononucleotides, which become the activitating agents when transferred to the ectoderm. Very briefly, some of the evidence presented by Brachet for a relationship between induction and ribonucleic acid is as follows. 1) Grafts show a decrease in cytoplasmic basophilia in those instances in which they act as an inductor but not in the absence of a response by the ectoderm overlying the graft. Cytoplasmic basophilia is indicative of the presence of ribonucleic acid. 2) Ectoderm which becomes induced to form a neural tube exhibits increased cytoplasmic basophilia, but not if neuralization fails. 3) The inducing power of a variety of nucleoproteins, including plant and virus nucleoproteins, is proportional to their ribonucleic acid content. 4) Crushed eggs or tissues from the early embryo exhibit basophilic granules which after centrifugation are accumulated in the clear layer. This layer, when grafted in a coagulated state, is the only one which exhibits considerable inducing power. 5) Breakdown of the nucleoprotein by thermal or enzymatic methods abolishes its inducing power.

Brachet's suggestion thus far described is in terms of a specific inductor from outside the ectoderm. He points out, however, that ribonucleic acids may be involved in substance x, which is released within the ectodermal cell in response to some nonspecific cytolyzing agent. He has observed that in cytolysis there are changes in cytoplasmic basophilia, namely, a rise at first, followed by a decline—changes suggestive of synthesis and then release or breakdown of ribonucleic acids.

For further analysis of the problem of induction, certain lines of research on the metabolism of the embryo may be rewarding. The researches of Needham, Boell, Barth, Brachet and others (see Boell, *3*) are providing data on respiration, enzymatic activities, et cetera. One line of investigation may be especially useful, namely, a study of protein synthesis in the amphibian gastrula and neurula. Using radioactive tracers, Abrams, *et al.* (*1*) have shown recently that the amino acid glycine is a probable precursor of the purines adenine and guanine, the purines in nucleic acids. Friedberg and Eakin (*6*) have studied the uptake of radioactive glycine by the amphibian gastrula and neurula and have obtained evidence of a greater incorporation by the dorsal half of the embryo and probably by the dorsal lip than by ventral regions. Brachet had shown earlier that dorsal halves of gastrulae and neurulae contained more ribonucleic acid than the ventral halves. Such physiological investigations may eventually prove to be decisive in elucidating the chemical nature of the organizer.

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References

1. ABRAMS, R., HAMMARSTEN, E., and SHEMIN, D. *J. biol. Chem.*, 1948, **173**, 429.
2. BARTH, L. G., and GRAFF, S. *Cold Spr. Harb. Sympos. quant. Biol.*, 1938, **6**, 385.
3. BOELL, E. J. *Ann. N. Y. Acad. Sci.*, 1948, **49**, 773.
4. BRACHET, J. *Cold Spr. Harb. Sympos. quant. Biol.*, 1947, **12**, 18.
5. CHUANG, H. *Arch. EntwMech. Org.*, 1939, **139**, 556.
6. FRIEDBERG, F., and EAKIN, R. M. *J. exp. Zool.*, in press.
7. HOLTFRETER, J. *Arch. Entw. Mech. Org.*, 1934, **132**, 225.
8. HOLTFRETER, J. *Sympos. Soc. exp. Biol.*, 1948, **2**, 17.
9. NEEDHAM, J. *Biochemistry and morphogenesis.* Cambridge, Engl.: at the Univ. Press, 1942.
10. SHEN, S. C. *J. exp. Biol.*, 1939, **16**, 143.
11. SPEMANN, H. *Embryonic development and induction.* New Haven: Yale Univ. Press, 1938.
12. WADDINGTON, C. H. *J. exp. Biol.*, 1938, **15**, 382.