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Swedish contributions to the understanding of amphibian embryogenesis – A phenomenon of the past?

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Developmental biology of today is in many ways a different scientific discipline than the one pursued merely a decade ago, not to mention the 'pre-historic' periods of the 1950´s-1970´s. Nevertheless, many aspects remain more or less unchanged. We are still busy trying to understand fundamental developmental phenomena such as the generation of multicellularity, early embryonic induction and subsequent cell differentiation, and the processes of morphogenesis. Furthermore, we still employ the same vertebrate model systems for these studies, with the exception of the recent appearance of the zebrafish, *Danio rerio*. So, although the technical advances and the understanding of many molecular interactions enable a more sophisticated design and analysis of experiments, we essentially struggle with the same problems as did our predecessors.

The Swedish history of developmental biology includes only a few scientists who worked with the amphibian embryo as their model. In recent years, only two major labs can be identified that have consistently employed amphibians. Some of the accomplishments of Søren Løvtrup in the field of amphibian embryology are outlined in more detail in the following paragraphs. Professor Løvtrup has been a very versatile scientist, with interest in fields such as cellular and developmental biology, evolution, biomathematics, and philosophy and history of science. Furthermore, the studies of Professor Jan Löfberg and his collaborators are worth mentioning. Their work has furthered our understanding of the factors needed for chromatophore development. Using embryos of the urodele *Ambystoma mexicanum* (the axolotl), they have elegantly shown the importance of components in the extracellular matrix, both for pigment cell migration and differentiation. Presently, Jan Löfberg is active in experimental research, whereas very few others in Sweden use the advantages of the amphibian embryo for studies on development. How the future will turn out is, of course, hard to predict, but there is certainly a gap to be filled by young and ambitious investigators.

Now, over to Professor Søren Løvtrup. After training and researching in microbiology and biochemistry, which took place in his native and beloved Copenhagen, he turned his attention towards developmental biology in general, and amphibian development in particular, in the 1950ies. Using *Xenopus*, *Rana*, and *Ambystoma*, he wanted to find the principles governing embryonic cell differentiation and morphogenesis. His analyses and compilation of results from many other laboratories besides his own, led to a great scholarly achievement, the monograph *Epigenetics* (1974), which has become widely read, especially by theoretical biologists who want to elucidate principles rather than details. The main theme of the book is that the cell, rather than the genome or the tissue, is the principal player. As the cell develops it expresses its potential, determined on the genome level, after encountering environmental factors, be they physical or biological. An extension of these ideas is found in two of the probably last reviews on experimental embryology that Søren Løvtrup has written, where especially the concept of polarities, and also cell-cell and cell-matrix interactions and their importance for early differentiation and for generating the vertebrate body plan, are discussed (Løvtrup, 1983, 1986). Such critical reviews of several subjects, not only amphibian embryogenesis, have been somewhat of a trademark of Professor Løvtrup.

Another important contribution of Søren Løvtrup's is the elucidation of the origin of the mesodermal cells in the amphibian blastula stage embryo. By experimental approaches, he showed that the classical so-called "fate map" of the amphibian embryo

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Fig. 1. Professor Søren Løvtrup as always sitting close to pen and paper in his laboratory at the Department of Zoophysiology, Umeå University.

was only partly correct (Løvtrup, 1975; Landström and Løvtrup, 1979). The accepted view up to the mid 1970ies was that all three germ layers (ectoderm, mesoderm, endoderm) are located on the surface of the embryo prior to gastrulation (Fig. 2A). Vital dye staining and explant culture from the late-blastula stage of the axolotl embryo, and culture of these small aggregates (around 15 cells) in the absence of additives like serum, made it possible to morphologically identify the cells that differentiated *in vitro*. Compilation of these data generated the modified fate map which can be seen in Figure 2B,C. The majority of mesodermal precursors were found to reside in the deep layer of cells in the embryo, a finding which later was shown by others to hold for the *Xenopus* embryo as well. The prospective notochord cells are however both superficially and deeply located in the early urodele embryo. These differences between anurans and urodeles might have implications for how mesoderm induction is fulfilled in each order. These thoughts were not pursued experimentally, probably much to Professor Løvtrup's discontent.

These contributions of Søren Løvtrup's are, of course, only fragments from a long and successful scientific career. They also show that it was possible for a dedicated researcher much on his own to make long-lasting impressions on the scientific map. Today a critical mass of scientists is needed before a tradition and a school of thought can be established, which generates the kind of scientific impact that we all want to have. Whether such school of students of amphibian developmental biology will ever blossom in Sweden remains to be seen.

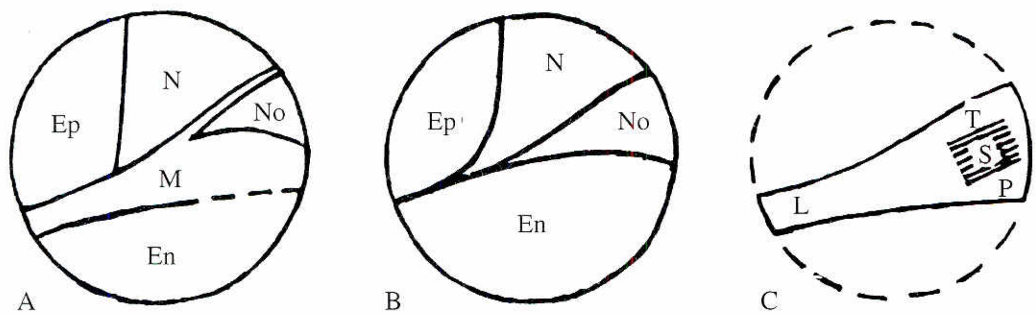

Fig. 2. Fate maps of the urodelan blastula. (A) *Vogt's fate map.* **(B,C)** *Revised fate map according to Søren Løvtrup. Ectodermal and endodermal derivatives are shown in* **B,** *mesoderm in* **C.** *Ep, epidermis; N, neural plate; No, notochord; En, endoderm; L, lateral plate mesoderm; T, tail mesoderm; S, somites; P, prechordal mesoderm (from J. Embryol. Exp. Morphol. 54, pp. 113-130, 1979, with the Publisher's permission).*

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