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The Spemann-Mangold organiser and the dissemination of its discovery in interwar Finland

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ABSTRACT A century has passed since the publication of the discovery of the Spemann-Mangold organiser, most visibly celebrated by the Festschrift *Spemann and Mangold centennial special issue* in *Cells & Development* and the conference *Self-Organization in Biology: Freiburg Spemann-Mangold Centennial Symposium* in September 2024. In honour of the anniversary, the Festschrift commemorates and reviews the history of the Spemann school of embryology and the later developments in the quest to understand the mechanistic underpinnings of the organiser. Here, I share a few new and untold insights from the Finnish archives on how the discovery of the organiser was communicated to and within Finland in the 1920s and '30s. The Finnish zoologists Alexander Luther and Gunnar Ekman had been visiting scholars in Spemann's laboratory, brought the field of experimental embryology to their home country, and incorporated it into the curriculum. Especially Ekman taught embryology to a generation of students in both tertiary and secondary education, created the Finnish terminology of the field, and actively popularised the latest discoveries in various books and journals. Intriguingly, the archives reveal that Ekman published a synopsis of the organiser experiment in Finnish in the spring of 1924 prior to the publication of the original article in September, and invited Spemann to visit Finland in September 1925. These efforts consolidated the popularity of the Spemann school of experimental embryology in Finnish academia, and shed light on "how experimental embryology was transplanted to Finland".

KEYWORDS: Spemann-Mangold organiser, Gunnar Ekman, history of embryology, developmental biology in Finland, experimental embryology

Introduction

The discovery of the Spemann-Mangold organiser in 1924 marked a turning point in the history of embryology by providing a definitive demonstration of the epigenetic viewpoint of development (i.e. cell-cell communication directs development) at the expense of preformationist perceptions (Nakamura and Toivonen, 1978; De Robertis *et al.,* 2024). The discovery of the organiser was the culmination of the Spemann school of experimental embryology, which had started with Spemann's constriction experiments on newt embryos resulting in axial duplications (1901–1904) and grew into an international "induction research network" of scholars throughout Europe, USA, and Asia (Hamburger, 1988; Fäßler, 1996; Dietrich, 2019). After the discovery of the organiser, the following breakthrough was the realisation that the organising factor is "devitalised" or a "dead" chemical (Bautzmann *et al.,* 1932; Hamburger, 1988). This finding sparked a "gold rush" of efforts to isolate and characterise the molecular nature of the organiser (Nakamura and Toivonen, 1978). However, significant progress had to wait until advances in molecular biology in the 1980s and '90s led to the identification of the now well-known signalling pathways (De Robertis, 2009; Slack, 2023; Asashima and Satou-Kobayashi 2024). However, the chapter on the organiser is far from closed, and ongoing investigations into its regulatory logic have recently uncovered, for example, the maternal factor Huluwa in zebrafish and frog embryos (Yan *et al.,* 2018).

As De Robertis recalls, it was widely considered in the 1970s that "Spemann-Mangold had slowed down developmental biology by forty years" (Williamson, 2023). Meanwhile, Asashima and Satou-Kobayashi (2024) note that the publication of the monograph (Nakamura and Toivonen, 1978) commemorating the 50th anniversary "received a cold reception". In contrast, Hamburger (1988) succeeded in revitalising interest in the organiser with his influential monograph and inspired the field to apply modern

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techniques to an old problem (De Robertis, 2009; Williamson, 2023). Alongside a contemporary review, both Nakamura and Toivonen (1978) and Hamburger (1988) presented the history of the Spemann school, complementing some earlier recollections (Mangold, 1953; Oppenheimer, 1970a, 1970b; Hamburger, 1968). Their work evidently inspired others to share their insights in the subsequent years (Arechaga, 1989; Leikola, 1989; Holtfreter, 1991; Waelsch, 1992). Similarly, Fäßler (1996, 1997) and Fäßler and Sander (1996) delved into the archives to decipher events in Spemann's laboratory, while Lenhoff (1991) called to mind Ethel Browne Harvey's grafting experiments in *Hydra* as a precursor to the Spemann-Mangold transplantation. For the 75th anniversary, a Special Issue of the *International Journal of Developmental Biology (Int. J. Dev. Biol.)* provided an international perspective and reviews on the organiser experiment (Sander and Fäßler, 2001), as well as its influence on the history of developmental biology in Germany (Grunz, 2001), Finland (Saxén, 2001), Japan (Asashima and Okada, 2001), Belgium (Alexandre, 2001), France (Beetschen and Duprat, 2001), Russia (Mikhailov and Gorgolyuk, 2001), and the UK and the USA (Horder, 2001).

Although Leikola (1989), Saxén (2001) and most recently Gilbert (2024) have reviewed Spemann's legacy in the history of developmental biology in Finland, the recently digitised archives unravel some new insights. Like most other reviews, both Leikola (1989) and Saxén (2001) focus on the role of the Spemann-Mangold experiment in the history of science, while the associated educational and societal history of the discovery has been less explored. Recently, von Bubnoff (2024) has analysed the societal impact of the discovery but has mainly focused on trends in Germany, the UK, and the USA. Here, I provide a complementary Finnish perspective and examine the dissemination of the discovery of the organiser in interwar Finland, including communication within the scientific community, teaching in tertiary and secondary education, and outreach to the wider society.

Two Finnish zoologists under the guidance of German embryologists

Experimental embryology was brought to Finland by two early-career zoologists, Alexander Luther (1877–1970) and Gunnar Ekman (1883–1937) (Fig. 1A) (Leikola, 1989; Saxén, 2001). After completing his doctoral thesis on the morphology and taxonomy of certain Turbellarians (phylum Platyhelminthes, flatworms), Luther moved to Heidelberg, Germany, in 1909 to be trained in comparative anatomy of vertebrates (Leikola, 2011). By the end of his time in Germany, Luther had developed an interest in embryology and spent a year in Spemann's laboratory from 1913 to 1914 as the first foreign scholar of the group (Leikola, 1989). However, Luther had to leave Germany at the onset of the First World War in the summer of 1914, and most of his experimental material was left behind (Hufvudstadsbladet 17th Feb 1927). Nonetheless, Luther managed to save his most precious amphibians and bring them to Finland after "several adventures and difficulties" (Hufvudstadsbladet 17th Feb 1927). Back home, Luther was able to continue with his embryological experiments, concentrating on the development of sensory organs and limbs along with the hormonal regulation of metamorphosis (Luther, 1916, 1917, 1925). However, he abandoned the field in the 1920s and returned to the study of Turbellarians, a subject he pursued for the remainder of his career (Leikola, 2011). Despite leaving the field of experimental embryology, Luther maintained a friendship with Spemann, inviting him to become a Foreign Member of the Finnish Society of Sciences and Letters in February 1922 (Hufvudstadsbladet 23rd Feb 1922; Leikola, 1989). As late as 1937, Spemann reciprocated this friendship by writing the introduction to the *Festschrift* commemorating Luther's 60th birthday in *Acta Societatis pro Fauna et Flora Fennica* (Hufvudstadsbladet 18th Feb 1937).

In contrast, Ekman was to make a career as an experimental embryologist, and he firmly established the field in Finland (Fig. 1A) (Leikola, 1989, 2011). For his doctoral degree, Ekman visited the laboratory of anatomist and embryologist Hermann Braus in Heidelberg from 1911 to 1913, studying the development of gill pouches in frogs (Fig. 1B) (Ekman, 1913; Leikola, 1989). After completing his thesis, Ekman continued to study lens development and gastrulation before specialising in the mechanisms of cardiac development during the 1920s (Leikola, 1989, 2011). Appointed as Extraordinary Professor of Experimental Zoology in 1928, Ekman became increasingly interested in primary embryonic induction. He successfully passed on the necessary experimental techniques to Sulo Toivonen before his untimely death in October 1937 (Arechaga, 1989; Leikola, 1989). Following investigations into the chemical nature of the organiser by Holtfreter and others, Ekman had proposed "heterogenous inductors" as a PhD project for Toivonen (Arechaga, 1989; Leikola, 1989). Toivonen continued this line of research throughout his career, formulating the dual gradient model with Lauri Saxén in the 1950s and training a new generation of Finnish developmental biologists (Leikola, 1989; Gilbert, 2024).

In addition to his scientific contributions, Ekman was an active educator and populariser of his field. Before Ekman, embryology and its terminology did not exist in Finnish, leaving him with the unique challenge of creating a vocabulary for the field from virtually nothing. To address this, he described mammalian and vertebrate development for the first time in Finnish in the journal *Luonnon Ystävä* in 1910 (Fig. 1C). He subsequently published articles in Finnish on the experimental embryology of limbs and eyes in amphibians in 1912 and 1913 (Fig. 1D) (Ekman, 1910, 1912, 1913). In 1914, Ekman wrote the first comprehensive Finnish treatise on concepts and theories in embryology (Fig. 1E) (Ekman, 1914). This work summarised the history of the field, outlined the debate on preformation and epigenesis, explained the concepts of mosaic and regulative development alongside relevant experimental evidence, reviewed the regenerative abilities of for example *Hydra* and Urodela, and discussed the significance of cell biology for the future of embryology (Fig. 1E) (Ekman, 1914).

Five years later, Ekman published *Biologian peruskysymyksiä* (*Fundamental Questions in Biology*), a general textbook on biology intended for both students and a lay audience. It included a 48-page comprehensive section on embryology, which constituted the first chapter on embryology in a Finnish schoolbook (Fig. 1F) (Ekman, 1919). In this section, Ekman described vertebrate development from fertilisation to birth, outlined the latest techniques and findings of experimental embryology, and briefly summarised regeneration in different metazoans (Fig. 1F) (Ekman, 1919). As a testament to Ekman's embryological endeavours, the front cover of the book illustrated conjoined twins in newts following partial constriction of the embryo (Fig. 1F) (Ekman, 1919). Furthermore, the choice of the conjoined newts for the

Fig. 1. Developmental biology in interwar Finland. (A) Developmental biologists Alexander Luther (1877–1970) in 1911 and Gunnar Ekman (1883–1937) in 1916 (Carpelan and Tudeer, 1925a, 1925b). **(B)** Title page of Ekman's doctoral thesis on the development of amphibian gill pouches (in German; Ekman, 1913). **(C)** The first figure on developmental biology in Finnish, depicting cross-sections of chicken eggs at different stages (Ekman, 1910). **(D)** Tadpole of the frog *Bombinator* (*Bombina*) with ectopic hindlimbs after transplantation of forelimb primordia into the posterior (Ekman, 1912). **(E)** The first page of the article *Yksilökehitystä käsittävistä teorioista*, the earliest coherent article in Finnish on concepts and theories in developmental biology (Ekman, 1914). **(F)** Front cover of *Biologian peruskysymyksiä*, the first Finnish textbook with a comprehensive section on embryology (Ekman, 1919). The cover features an anterior axial duplication in a newt embryo following partial constriction (Ekman, 1919).

cover could reflect Ekman's increasing interest in Spemann's work. Spemann had performed partial constriction experiments leading to anterior axial duplications from 1901 to 1903, but he revisited the problem of duplications from 1914 to 1919, fusing two half-gastrulae in different constellations to generate different axial duplicates (Spemann, 1918; Hamburger, 1988). These findings appeared in print in February 1918 (Spemann, 1918), and Ekman likely had access to Spemann's article at the Zoological Station of Tvärminne, where he claims to have written *Biologian peruskysymyksiä* over the summer of 1918, after the Finnish Civil War ended in May 1918 (Ekman, 1919). Altogether, Ekman had begun his independent career as an experimental embryologist and laid the foundation for teaching the subject in Finnish by the early 1920s.

Ekman presented and popularised Spemann's findings in the early 1920s

Interestingly, both Leikola (1989) and Saxén (2001) mention that Ekman visited Spemann's laboratory in Freiburg "several times in the 1920s", leaving it ambiguous whether these visits took place before or after the publication of the organiser discovery. Additionally, Gilbert (2024) notes that "after Braus' death in 1924, Ekman worked in Spemann's laboratory in Freiburg", most likely referring to Hamburger (1988), who states that "after the death of Braus in 1924, Ekman spent some time in Spemann's laboratory in Freiburg, where I made his acquaintance". Meanwhile, Arechaga (1989) reports in his interview with Toivonen that Ekman "had worked with Professor Herman Braus and Professor Hans Spemann in Germany

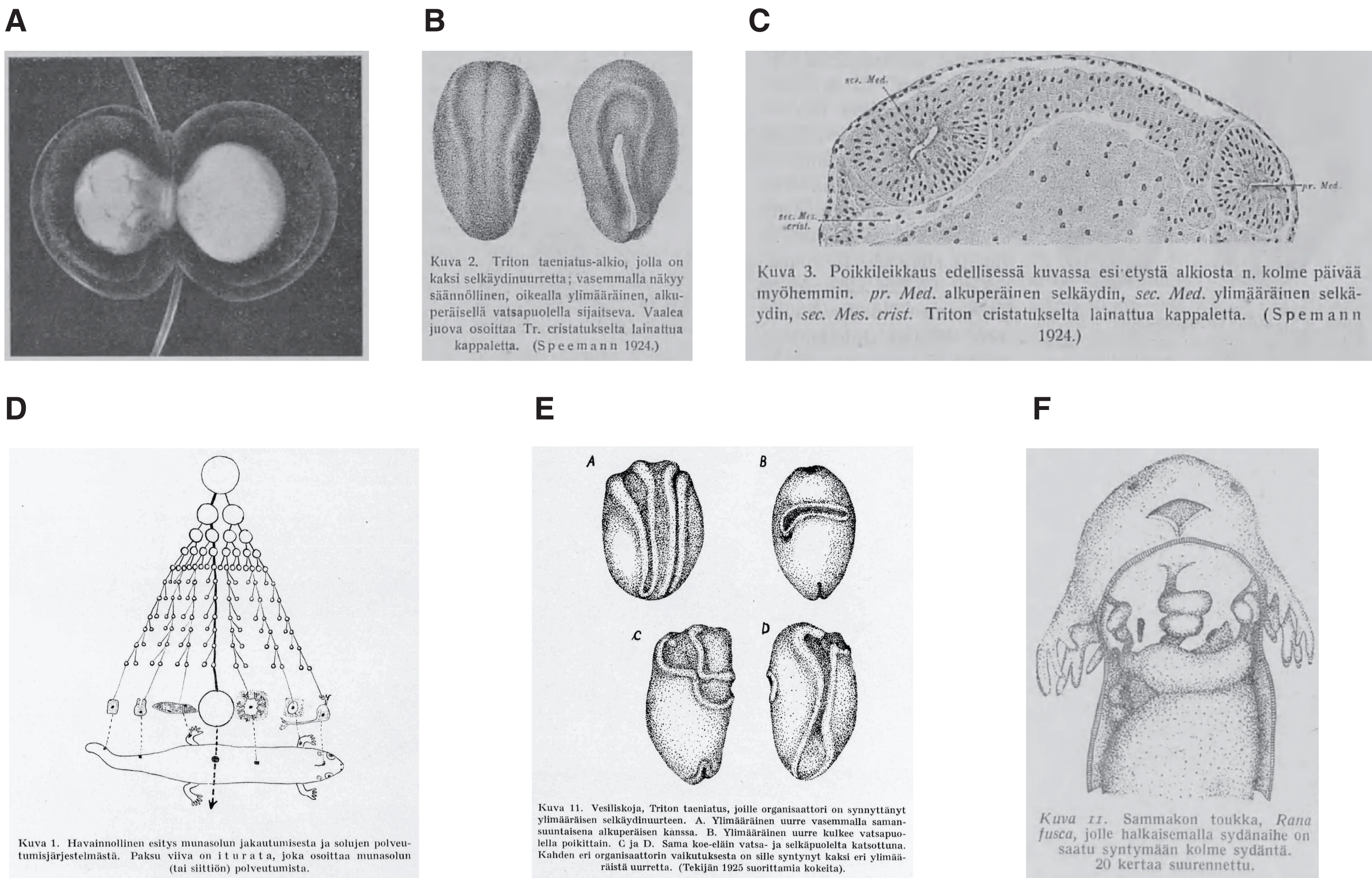


Fig. 2. Experimental embryology in Finnish journals and books in the 1920s. (A) Fig. 1 in the Finnish article *Uusimpia kokeellisia tutkimuksia sammakkoeläinten sikiön kehityksestä* that reports Spemann's constriction experiments on zygotes (Ekman, 1922). **(B)** Fig. 2 in the Finnish article (Ekman, 1924) entitled *Uusia saavutuksia determinatiokysymyksen alalla,* which reproduces Figs. 2,3 in Spemann and Mangold (1924a). The figure legend in Finnish is: "Figure 2. An embryo of *Triton taeniatus* with two neural grooves; the normal one is on the left, while an ectopic groove is on the right, located on the original ventral side. The light stripe corresponds to a transplant from Tr. cristatus. (Spemann, 1924.)" **(C)** Fig. 3 in Ekman (1924) reproducing Fig. 4 in Spemann and Mangold (1924a). The figure legend in Finnish: "Figure 3. Cross-section of the embryo shown in the previous figure, about three days later, *pr. Med.* the primary spinal cord, *sec. Med.* the ectopic spinal cord, *sec. Mes. crist.* the transplant from Triton cristatus." **(D)** A visualisation of the cell lineage concept by Ekman (1928). The thick line represents the germline (Ekman, 1928). **(E)** Illustrations of the grafting experiments performed by Ekman in 1925 in Spemann's laboratory in Freiburg (Ekman, 1928). In the experiments, Ekman transplanted the organiser and generated ectopic secondary axes in different constellations. **(F)** An illustration of Ekman's own scientific work on the experimental embryology of cardiac development popularised in Finnish (Ekman, 1927). In his experiments, Ekman separated the heart tube and demonstrated that the separated tubes are able to develop autonomously. In the figure, the heart tube has been separated into three (Ekman, 1927).

during the twenties and thirties". However, both Suomalainen (1937) and Välikangas (1937) provide clarity in their obituaries of Ekman, stating that Ekman visited Germany twice in the 1920s: in 1920 in Heidelberg and in 1925 in Freiburg, most likely meeting Spemann both times.

A first visit in 1920 is further supported by the fact that Ekman lectured in March 1921 on the formation of conjoined twins at the meeting of *Societas pro Fauna et Flora Fennica*, "dwelling particularly on the latest research of Spemann and Mangold" (Uusi Suomi 11th March 1921). Similarly, Ekman presented "some of the remarkable experimental techniques, which the German Spemann and his students have recently invented" at a symposium in August 1922, and he reviewed Spemann's constriction experiments on zygotes (Spemann, 1914) in the journal *Luonnon Ystävä* (Fig. 2A) (Ekman, 1922; Hufvudstadsbladet 22nd Aug 1922). In a series of lesser-known experiments, Spemann constricted zygotes so that the nucleus remained in one half, while the other half was enucleated (Spemann, 1914; Brandt, 2022a). The nucleus divided, and when one of the daughter nuclei migrated to the enucleated half, it had the potential to give rise to a normal embryo, providing preliminary support for nuclear equivalence (Spemann, 1914; Brandt, 2022a). In the same article, Ekman (1922) reported Spemann's fusion experiments on embryos, reproducing figures 6 and 7 from the original article (Spemann, 1918). Therefore, Ekman appears to have become acquainted with Spemann in 1920 and become greatly inspired by the work of the group, as he actively popularised their findings alongside his own scientific work on cardiac development (Fig. 2F) (Ekman, 1922, 1927).

As is well known, the organiser was discovered when Hilde Mangold (née Pröscholdt) in Spemann's laboratory transplanted the dorsal lip of the blastopore from a gastrula of *Triturus (Triton) cristatus* (unpigmented) to the ventrolateral ectoderm of the gastrula of *T. taeniatus* (pigmented), and observed the formation of an ectopic secondary body axis (Spemann and Mangold, 1924a). Apparently, Ekman was aware of the experiment before its publication in September 1924, as he gave a presentation on the "great organising and determining effect of the blastopore" on 18th March 1924 for the *society Suomalaisen Eläin- ja Kasvitieteellinen Seura Vanamo* (currently *Suomen Biologian Seura Vanamo*) (Luonnon Ystävä 1924). Remarkably, he also published the article *Uusia saavutuksia determinatiokysymyksen alalla* (*New achievements in the Determination Problem*) in *Luonnon Ystävä* in late spring 1924 (Ekman, 1924). The fourth issue of the year is not dated, but it reports an announcement signed on 4th May and advertises a meeting in June, suggesting that it was published at the end of May 1924. In the article, Ekman first introduces gastrulation, and then details how Spemann transplanted the blastopore lip from *T. cristatus* to the ventral side of *T. taeniatus* and observed the formation of a secondary body axis.

*"Spemann has now conducted his latest experiments in such a way that two embryos were used, one from Triton taeniatus and one from Triton cristatus, in which the upper blastopore lip has just appeared. From the former embryo, a small tissue fragment (*Fig. 1A*) was dissected from the blastopore and transplanted to the ventral side of the former (*Fig. 1B*) in exchange of a removed fragment of similar size. This transplant attached well to its new environment and continued to develop there. From an experimental perspective, it is significant that the transplant has been taken from a fully different species, since it is distinguishable from its surroundings for a long time by its colour and cell structure. According to Spemann, I report a few of such operations below.* Fig. 2 *shows the embryo of Triton taeniatus about two days after the treatment, in which a small fragment of the dorsal blastopore lip has been transplanted to the ventral side slightly to the right. The left image shows the regular dorsal side of the animal, in which the neural groove is clearly visible, while the right image shows the original ventral side of the same specimen, where the transplant appears as a light stripe. Initially, the transplant was circular, but has elongated together with its surroundings into a long and narrow stripe. Its environment most clearly resembles the regular neural groove. The animal was kept alive for a few more days, during which both neural grooves fused, after which it was fixed and processed into a series of cross-sections for microscopic examination."*

At the end of the article, Ekman summarises the significance of the discovery and discusses unanswered questions.

"The experiments described above display very clearly that even the minuscule part of the dorsal blastopore lip has a remarkable ability to affect its surrounding tissues. Therefore, it can be called a determinant or an organiser. And its organising capacity is truly miraculous. When placed in a fully foreign environment, in the middle of the ventral side of even another species, this small group of cells dorsalises that side almost at the rate of normal development. In this event, it participates as building material only partially, in different ways in different cases, as the majority of the ectopic dorsal side develops from ventrally fated cells. One could almost say that this organiser creates another individual alongside the original, as the dorsal side, apart from the heart, harbours all the vital organs of the embryo.

Yet, we do not know how this small organiser functions in detail, or what type of "force" might emanate from it. However, it has been observed that it has the tendency to invaginate, as if initiating gastrulation and forming another blastopore. After all, also normal development proceeds from the blastopore, but how, we do not know either."

To illustrate the article, Ekman (1924) first provides a general schematic illustration of the anatomy of the amphibian embryo, but then reproduces figures 2 and 3 from Spemann and Mangold (1924a) as figure 2 (Fig. 2B), figure 4 as figure 3 (Fig. 2C), figures 19 and 20 as figure 4, figure 21 as figure 5, and figure 22 as figure 6. In the figure legends, Ekman (1924) cites "(Spemann 1924.)", but the article does not provide a list of references.

Hilde Mangold performed the transplantations in the springs of 1921 and 1922 and wrote her thesis in the autumn of 1922 (Hamburger, 1988; Fäßler, 1996). Her thesis was graded by Spemann in February 1923, and the manuscript for the article was prepared in the spring of 1923 (Fäßler, 1996). The original article by Spemann and Mangold (1924a) states that it was received on the 1st of June 1923, and Hamburger (1984, 1988) also recalls that the manuscript was submitted in June 1923 and appeared in print in September 1924. At the same time, Hilde Mangold tragically died from burns after a kitchen stove explosion in September 1924, and she never saw the impact of her experiments (Hamburger, 1988; Fäßler, 1996).

Therefore, it appears that Ekman had access to the submitted manuscript before its publication in September 1924. Spemann gave a lecture tour in the Netherlands in March 1924, sharing some information on the organiser experiment (Brandt, 2022b). The journal *Archiv für mikroskopische Anatomie und Entwicklungsmechanik* published corrections to the article in March 1924 (Spemann and Mangold, 1924b), suggesting that an earlier version of the article was in circulation before September 1924. Most likely, Ekman used this version to write a synopsis and share the results of the experiment, rapidly disseminating the discovery within Finnish academia.

Spemann visited Finland in September 1925

After the publication of the organiser experiment, Ekman evidently visited Spemann's laboratory in 1925 (Ekman, 1928; Välikangas, 1937; Hamburger, 1988). In the laboratory, Ekman repeated and modified the organiser experiment, later reporting his transplants with secondary axes in Finnish in the journal *Valvoja-Aika* (Ekman, 1928). During his visit, Ekman likely encouraged Spemann to visit Finland, as Spemann travelled to Helsinki later that year. In early September 1925, Finnish newspapers announced that the famous zoologist Hans Spemann would visit Helsinki and deliver a "significant lecture" in the Great Hall of the University of Helsinki in two weeks' time (Uusi Suomi 9th September 1925; Hufvudstadsbladet 10th September 1925). The newspapers did not hesitate to point out that professor Spemann "had always shown a great interest in our country" (Uusi Suomi 9th September 1925; Hufvudstadsbladet 10th September 1925).

On the 21st of September 1925, Spemann presented his findings on the organiser in a lecture entitled *On some methods, results, and objectives of experimental biology*, which was free and open to the public (Hufvudstadsbladet 22nd September 1925; Uusi Suomi 22nd September 1925). According to newspaper reports, the lecture was well attended and began with a presentation on Spemann's lens induction experiments before a description of the organiser experiment (Hufvudstadsbladet 22nd September 1925; Uusi Suomi 22nd September 1925). Later that same week, Spemann continued to give a talk entitled *On organisers in animal development* at a meeting of the Finnish Society of Sciences and Letters (Hufvudstadsbladet 22nd September 1925; Uusi Suomi 22nd September 1925). Furthermore, Spemann may have visited the Tvärminne Zoological Station on the southern coast of Finland during the same tour, as his name appears in the guestbook in 1936 (Uusi Suomi 12th Jan 1936). In 1929, Spemann was also elected a member of *Societas pro Fauna et Flora Fennica* (Helsingin Sanomat 22th May 1929).

Interestingly, Spemann declined an invitation from the British scientist William Bateson in January 1925 due to the occupation of the Ruhr area. It was not until November 1927 that Spemann visited London, Cambridge, and Oxford, where he gave several presentations, including the prestigious Croonian Lecture, the Royal Society of London's lecture in biological sciences (Brandt 2022a, 2022b). However, Spemann accepted the invitation to visit Finland that same year, suggesting that he may also have decided on his lecture tour destinations on political grounds. Additionally, Finnish students and zoologists were highly proficient in German at the time, as they published almost all their scientific work in this language until the Second World War (Klinge, 1993; Leikola, 2011). Spemann also attended the International Congress of Zoology in Budapest in September 1927, and his Silliman lectures at Yale University in 1933 famously inspired him to write *Embryonic Development and Induction* (Spemann 1936, 1938; Hamburger, 1988). Therefore, the lectures at the University of Helsinki and in other Finnish academic circles add another noteworthy foreign visit to Spemann's résumé; this visit seemingly contributed to the status and popularity of experimental zoology in interwar Finnish academia.

Ekman reported and speculated on the chemical nature of the organiser

After Spemann's visit, Ekman continued to popularise both his own and Spemann's work (Ekman, 1927, 1928, 1934). In 1928, Ekman once again summarised the organiser experiment for the journal *Valvoja-Aika* (Ekman, 1928). This time, he also cited "H. Mangold" and reported on Otto Mangold's and Spemann's recent transplantation experiments published the previous year (Mangold and Spemann, 1927; Ekman, 1928). Mangold and Spemann had asked how an age difference between the donor and recipient affects induction, leading to their discovery of what they termed homeogenetic induction: the medullary plate from a neurula could induce a medullary plate from the epidermis of a gastrula, i.e. a tissue induces a tissue of its own kind (Mangold and Spemann, 1927; Hamburger, 1988; Rinard, 1988). This discovery was surprising, as it was the first report of an inductive event that does not occur normally during development (Hamburger, 1988). However, neither Mangold nor Spemann pursued the project further (Hamburger, 1988). Interestingly, Ekman (1928) continues to discuss the likelihood of a chemical inductive mechanism, and even speculates about the existence of multiple different chemical agents in primary induction.

"Still, it needs to be clarified how the organiser functions. For now, we can only provide assumptions, but a chemical mechanism is the most likely. Among other things, this is supported by the contribution of the organiser itself to the structure of the ectopic dorsal side which can vary greatly.

We can imagine that the cells of the organisational field contain some type of a substance, perhaps an enzyme, which is not present in other parts of the blastula. If a fragment with such a substance is transplanted to a new environment "empty" in this regard, the substance spreads there according to the general laws of osmosis. This creates a larger area with a similar chemical state as in the original dorsal primordium. Dependent on these chemical conditions, the cells in the ectoderm divide, arrange, and differentiate in a specific manner, resulting in the formation of a more or less complete and uniform dorsal side. However, as previously mentioned, the extent of the result depends somewhat on which part of the organisational field the transplant is taken from, and where it is let to exert its influence. Therefore, it is likely that different parts of the organisational field contain slightly different substances."

According to Hamburger (1988), Spemann had "come close to a realistic consideration of the chemical nature of induction" in the late 1920s, given that he had raised the possibility of the chemical nature of the neural-inducing agent in the article describing homeogenetic induction in 1927 (Mangold and Spemann, 1927). However, Spemann postponed experiments to identify the chemical agent until 1929 and delayed reporting until 1931. Hamburger (1988) attributes this to a lack of suitable experimental equipment and Spemann's personal preference for "the living embryo". Instead, the main driver of the project was Johannes Holtfreter. After hearing Spemann's preliminary findings at the meeting of the German Zoological Society in 1931 in Utrecht, he began experiments to determine the inductive capacity of the devitalised organiser (Hamburger, 1988). Following correspondence between Bautzmann, Holtfreter, Otto Mangold and Spemann, whose experiments were carried out by his student Else Wehmeier, four independent studies were published together as a single article in December 1932 (Bautzmann *et al*., 1932). Against this background, it appears that Ekman was already convinced of the possibility of a chemical inducing agent in 1928. However, he did not conduct experiments to demonstrate this, for which Holtfreter's solution turned out to be crucial in improving the viability of experimental embryos (Hamburger, 1988).

In early 1934, Ekman wrote about the devitalisation experiment for the journal *Luonnon Ystävä* (Ekman, 1934), also reporting Holtfreter's follow-up experiments, which demonstrated that a range of different animal tissues possess inductive properties (Holtfreter, 1933). Ekman (1934) further discusses the nature of the chemical, reporting Woerdeman's recent finding that glycogen is present in the same region as the organiser but gradually disappears during development (Woerdeman, 1933a, 1933b). Ekman (1934) concludes that, even if the chemical were identified, the problems of the "formation of a harmonious entity" and "cellular cooperation" would still remain unsolved. Thus, Ekman's description closely resembles the modern formulation of the problem of pattern formation. Lastly, Ekman (1934) draws rather optimistic parallels between the embryological or morphogenetic field and electromagnetic fields.

"Even if we were to identify the substance that performs the same function as the living, natural organiser, we would still need to clarify how an ectopic dorsal side forms a harmonious entity. It is understandable that a certain substance may accelerate cellular development, and that the faster developing part of the embryo develops in a different manner from the part developing more slowly. Yet, it remains an enigma how the cooperation between cells arises, which ultimately forms the symmetrical entity.

Even in this matter a solution is in sight, since the physical concept of a field has been started to be applied to biological phenomena. It is well known how e.g. an electric current or a magnet affects small, separate particles, such as iron filings, organising them into a field pattern corresponding to specific field lines. Thus, such a physical field is an orderly entity, where parts obey a common directive. Now, it appears rather probable that something similar occurs in organisms, that there are biological fields. For example, one might speculate that development of the dorsal side of an embryo is organised by a specific dorsal field, under the direction of which all the involved cells are. If two such fields arise in the embryo, then also two patterned dorsal sides may develop. In turn, the formation of the field may depend on the type and differentiation rate of cells."

In March 1924, Julian Huxley connected Child's gradient concept with the organiser, and he elaborated on the concepts of fields and gradients together with Gavin de Beer in their book *The Elements of Experimental Embryology*, published in 1934 (Huxley and de Beer, 1934; Brandt, 2022b). In their treatise, Huxley and de Beer (1934) define fields as "a region throughout which some agency is at work in a co-ordinated way" but refrain from examining the explanatory mechanism further, stating that gradients may arise through metabolic processes or chemical diffusion. As Wolpert (1991) notes, Spemann was likely the first to use the field concept in the early 1920s, borrowing the term from physics. Thus, Ekman elaborated on the field metaphor to explain the function of the organiser, suggesting that he had become increasingly intrigued by the mechanism of the organiser in the early 1930s.

A journalist called Spemann before the Nobel Committee

In 1935, Spemann received the Nobel Prize in Physiology or Medicine "for his discovery of the organiser effect in embryonic development". The Nobel Committee is usually the first to inform the laureate of the award via a phone call. However, a correspondent for the Finnish newspaper *Hufvudstadsbladet* (in the Swedish language) appears to have been the first to notify Spemann of his receiving the Nobel Prize in Physiology or Medicine on Thursday 24th October 1935 (Fig. 3A) (Hufvudstadsbladet 25th Oct 1935). The newspaper reports the following interview:

When Spemann received the news (from the correspondent of Hufvudstadsbladet), Stockholm Thursday. - Am Freiburg in Breisgau, Professor Hans Spemann has been called. - We wish to convey our congratulations. I assume that you have already heard the news. - No.. What news? - That you have received the Nobel Prize in Medicine. - Oh, really.. - Does the news come as a complete surprise? - Completely unexpected. The voice on the phone does not sound like that of a sixty-year-old. On the contrary, it is full of youthful energy. We ask our scientist to tell a little bit about his work. - My research subject is experimental embryology. I have always worked with the same simple model system, namely amphibians. I have come to the conclusion that the development of different parts of the organism are dependent on each other. From this starting point, we have conducted research in various directions. Lastly, I have studied the chemical factors of development. In my studies, I have discovered interesting facts regarding the embryos of various organisms. - Are you professor emeritus, or do you continue with your research at the university? - Despite having reached the retirement age, I have been encouraged to continue in my position for another year. I do not feel old at all, and the message I have now received is especially well suited to rejuvenate a professor in his sixties. What will I do with the Nobel Prize? Well, I have not had time to think about that. When will the official confirmation come? Oh, already this evening. Thank you for the message, and see you in Stockholm.

As independent evidence, Spemann shares in his letter to Hamburger on 20th November 1935 that "already the first telephone message, even before the passing of the announcement of the decision. My complete surprise; then, after 2 minutes, the question: 'What are you going to do with the money?'" (MBLWHOI Library, 2024). However, the *Hufvudstadsbladet* reporter does not reveal how he gained access to the identity of that year's laureate.

A day after the announcement, Ekman gave a televised presentation on the year's Nobel Prize for the Finnish national broadcaster Yleisradio (Ilta-Sanomat 25th Oct 1935). A month later, he wrote an article for the newspaper *Uusi Suomi* (Fig. 3B), briefly providing a background to embryology, introducing the concept of embryonic induction by summarising Spemann's experiments on the vertebrate lens, and then explaining the organiser experiment (Uusi Suomi 24th Nov 1935). Lastly, he mentioned the experiments on the devitalised organiser, and noted that the chemical nature of the organiser was being actively investigated worldwide (Uusi Suomi 24th Nov 1935). Interestingly, Ekman used "teaching" as a metaphor for the inductive effect of the organiser; the organiser is a "teacher" that "teaches" surrounding tissues to become competent for certain developmental fates (Uusi Suomi 24th Nov 1935).

Interestingly, although von Bubnoff (2024) finds that the holistic or organistic viewpoint resonated with both the right and left on the political spectrum, the organiser or its metaphors were not widely discussed in a political context in interwar Finland. The only political metaphor I could find in the archives is a column by Hilja Vilkemaa, a former Member of Parliament for the National Progressive Party, who advocated for the temperance movement using the organiser as a supportive argument following the announcement of the Nobel Prize (Vilkemaa, 1935). In her column, Vilkemaa (1935) argues that societal organisation can be compared to biological organisation and that, as in biological systems, society has a "great teacher" or a "great organiser" in the form of the intelligentsia. Consequently, she contends that it is the responsibility of the intelligentsia to fight against the intoxicating effect of alcohol to maintain harmonious order in society (Vilkemaa, 1935). In the realm of art, the worldview of the Nobel laureate in literature Frans Emil Sillanpää was influenced by Ekman, who had taught him during his time as a medical student at the University of Helsinki (Enäjärvi-Haavio, 1937).

Ekman established the Finnish education of experimental embryology

At the University of Helsinki, Ekman's teaching of experimental embryology was limited by the short breeding season, as amphibian embryos were available only for a few weeks each year (Suomalainen, 1937). As his student Paavo Suomalainen (1937) recalled from the late 1920s, this limitation made experimental embryology accessible to pretrained scientists like Ekman, but posed significant difficulties for beginners and students. To mitigate this issue, Ekman prepared an extensive collection of microscopy slides representing different embryonic stages to better visualise his subject (Suomalainen, 1937). Additionally, he used a plasticine ball to demonstrate developmental anatomy, including gastrulation, neurulation, and segmentation (Suomalainen, 1937). Before his death, Ekman succeeded in incorporating the Spemann-Mangold organiser into upper secondary school textbooks (Fig. 3C) (Ekman, 1938). In his textbook *Yleisbiologia*, he introduced embryology by first describing the development of various mammalian organ systems, followed by a primer on experimental embryology (Ekman, 1938). In this primer, Ekman (1938) outlined the organiser experiment and referenced devitalisation experiments, as well as the chemical nature of the organiser, ensuring that the latest research was taught in Finnish upper secondary schools in the 1930s.

At a Nordic conference in Helsinki in August 1936, Ekman presented the latest findings on "organisers in embryonic development" from the Spemann school, as well as some of his own unpublished results (Svenska pressen 13th Aug 1936). Later, in December 1936, he gave a presentation on organisers for the *Finnish Society of Sciences and Letters* (Hufvudstadsbladet 20th Dec 1936). In this presentation, Ekman discussed how "the organiser gives rise to a determination field", and demonstrated cases "in which different determination fields have come into conflict with each other, whereby the stronger field solely determines development" (Hufvudstadsbladet 20th Dec 1936). He continued by discussing heterogenous organisers, i.e. the inductive capacity of non-embryonic tissues such as hepatic and renal tissue samples (Hufvudstadsbladet 20th Dec 1936). Lastly, he speculated that there are multiple inducing chemical agents, and their quality but also quantity is crucial for primary embryonic induction (Hufvudstadsbladet 20th Dec 1936).

A


HUFVUDSTADSBLADET

Italiens krav för förlikning ha preciserats.

Hans Spemann fick Nobelpriset

När Spemann mottog budet.

När „Esbo" havererade vid engelska kusten.

Smugglarbatalj får efterspel.

Äro nu de skyldiga spårade?

B


SUNNUNTAILIITE UUSI SUOMI

"... ja huumaavalla ryskeellä hän hajoitti vihollisen rivit."

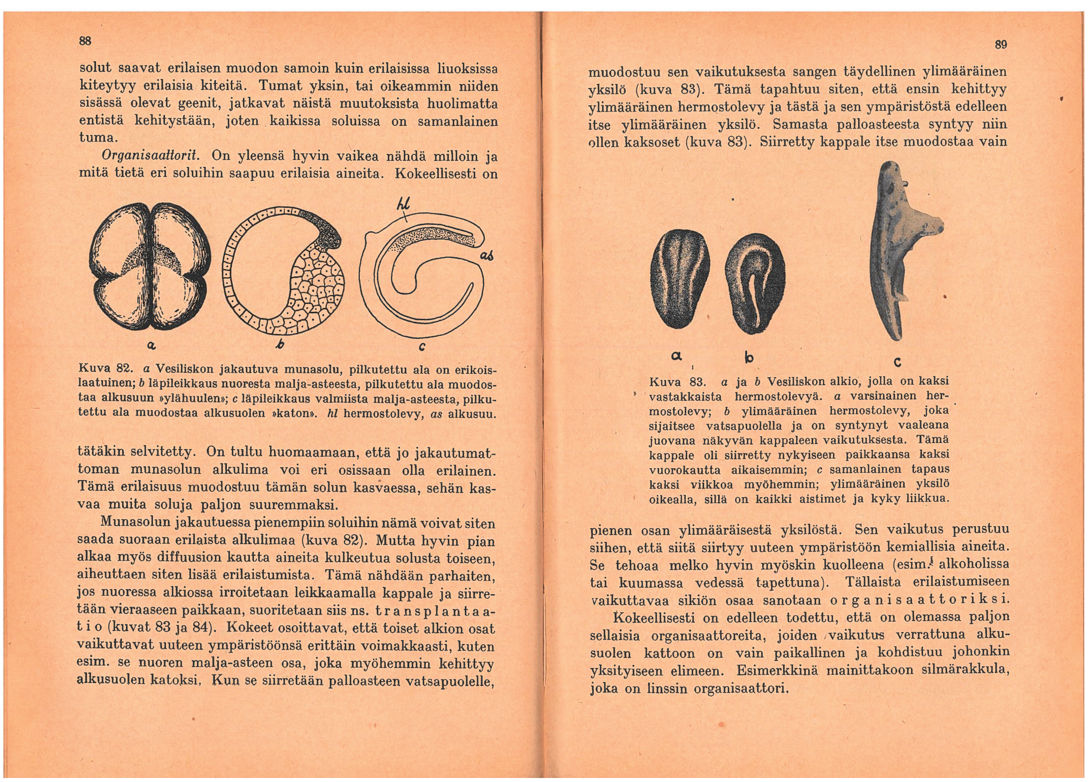
ELI MIKSI CROMWELL OLI SUURI MIES.

HANS SPEMANN

SIKIÖKEHITYKSEN ONGELMAN SELVITTÄJÄNÄ.

HANS SPEMANN...

C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solut saavat erilaisen muodon samoin kuin erilaisissa liuoksissa kiteytyy erilaisia kiteitä. Tumat yksin, tai oikeammin niiden sisässä olevat geenit, jatkavat näistä muutoksista huolimatta entistä kehitystään, joten kaikissa soluissa on samanlainen tuma.

Organisaattorit. On yleensä hyvin vaikea nähdä milloin ja mitä tietä eri soluihin saapuu erilaisia aineita. Kokeellisesti on

Kuva 82. *a* Vesiliskon jakautuva munasolu, pilkutettu ala on erikoislaatuinen; *b* läpileikkaus nuoresta malja-asteesta, pilkutettu ala muodostaa alkusuuen »ylähuulen»; *c* läpileikkaus valmiista malja-asteesta, pilkutettu ala muodostaa alkusuolen »katon». *hl* hermostolevy, *as* alkusuu.

tätäkin selvitetty. On tultu huomaamaan, että jo jakautumattoman munasolun alkulima voi eri osissaan olla erilainen. Tämä erilaisuus muodostuu tämän solun kasvaessa, sehän kasvaa muita soluja paljon suuremmaksi.

Munasolun jakautuessa pienempiin soluihin nämä voivat siten saada suoraan erilaista alkulimaa (kuva 82). Mutta hyvin pian alkaa myös diffuusion kautta aineita kulkeutua solusta toiseen, aiheuttaen siten lisää erilaistumista. Tämä nähdään parhaiten, jos nuoressa alkiossa irroitetaan leikkaamalla kappale ja siirretään vieraaseen paikkaan, suoritetaan siis ns. t r a n s p l a n t a a t i o (kuvat 83 ja 84). Kokeet osoittavat, että toiset alkion osat vaikuttavat uuteen ympäristöönsä erittäin voimakkaasti, kuten esim. se nuoren malja-asteen osa, joka myöhemmin kehittyy alkusuolen katoksi. Kun se siirretään palloasteen vatsapuolelle,

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muodostuu sen vaikutuksesta sangen täydellinen ylimääräinen yksilö (kuva 83). Tämä tapahtuu siten, että ensin kehittyy ylimääräinen hermostolevy ja tästä ja sen ympäristöstä edelleen itse ylimääräinen yksilö. Samasta palloasteesta syntyy niin ollen kaksoset (kuva 83). Siirretty kappale itse muodostaa vain

Kuva 83. *a* ja *b* Vesiliskon alkio, jolla on kaksi vastakkaista hermostolevyä. *a* varsinainen hermostolevy; *b* ylimääräinen hermostolevy, joka sijaitsee vatsapuolella ja on syntynyt vaaleana juovana näkyvän kappaleen vaikutuksesta. Tämä kappale oli siirretty nykyiseen paikkaansa kaksi vuorokautta aikaisemmin; *c* samanlainen tapaus kaksi viikkoa myöhemmin; ylimääräinen yksilö oikealla, sillä on kaikki aistimet ja kyky liikkua.

pienen osan ylimääräisestä yksilöstä. Sen vaikutus perustuu siihen, että siitä siirtyy uuteen ympäristöön kemiallisia aineita. Se tehoaa melko hyvin myöskin kuolleena (esim. alkoholissa tai kuumassa vedessä tapettuna). Tällaista erilaistumiseen vaikuttavaa sikiön osaa sanotaan o r g a n i s a a t t o r i k s i.

Kokeellisesti on edelleen todettu, että on olemassa paljon sellaisia organisaattoreita, joiden vaikutus verrattuna alkusuolen kattoon on vain paikallinen ja kohdistuu johonkin yksityiseen elimeen. Esimerkkinä mainittakoon silmärakkula, joka on linssin organisaattori.

Fig. 3. Spemann received the Nobel Prize and the organiser was taught in Finnish school books. (A) The third page of *Hufvudstadsbladet* (Helsinki, Finland) on the 25th of October, 1935. The interview with Spemann, suggesting that the newspaper's journalist called him before the Nobel Committee, is highlighted with a box (Hufvudstadsbladet, 25th Oct 1935). **(B)** The special issue of *Uusi Suomi* featuring Ekman's article on that year's Nobel Prize (Uusi Suomi, 24th Nov 1935). **(C)** One of the earliest descriptions of the Spemann-Mangold organiser in a Finnish secondary school textbook (Ekman, 1938).

As a result, Ekman had become increasingly interested in the organiser and heterogenous inductors towards the end of the 1930s, inspired by Holtfreter's extensive experiments in the recent years (Arechaga, 1989). In pursuit of this interest, he began to work on the project with his new graduate student, Sulo Toivonen, in the spring of 1936 (Leikola, 1989). Their work continued into the spring of 1937, but was interrupted by Ekman's sudden death in October 1937 (Leikola, 1989). In November 1937, Toivonen gave a talk on "Latest milestones in experimental embryology" at the meeting of the society *Vanamo*, emphasising the importance of aseptic techniques in handling amphibian embryos as an introduction. Then, he presented his and Ekman's work from the last two years; Ekman had attempted to induce as complete an ectopic secondary body axis as possible, while Toivonen had succeeded in using heterogenous inductors in almost 600 embryos, with microscopic examination ongoing at the time (Uusi Suomi 6th Nov 1937). Nonetheless, Toivonen was already able to share his preliminary observations on the regional specificity of heterogenous inductors and the existence of a mesodermalising and a neuralising factor (Uusi Suomi 6th Nov 1937). The following year, Toivonen published his preliminary results (1938b), but he continued to expand his sample size to 2,000 embryos between 1938 and 1939, before publishing his work in December 1940 (Toivonen, 1940). Additionally, Toivonen upheld Ekman's tradition of popularising experimental embryology in Finnish, beginning with an article on current experimental techniques in the field for *Luonnon Ystävä* (1938a). In his article, Toivonen (1938a) summarised his presentation on aseptic principles in modern research, and outlined briefly transplantations, implantation or the Einsteck method, and explantation according to Ekman (Toivonen, 1938a). Taken together, Ekman's educational efforts ensured that the Spemann school of experimental embryology and the research program investigating the mechanism of the organiser were firmly anchored in Finland.

Conclusion

Following the discovery of the organiser, the Spemann school of experimental embryology developed into an international "induction research network" with connections across Europe, North America, and Asia (Dietrich, 2019). Although several scholars visited Spemann's laboratory after 1924, the history of the organiser has mainly been told by his most famous students, Viktor Hamburger and Johannes Holtfreter (Hamburger, 1988; Dietrich, 2019). In light of this, gaining a more detailed understanding of the events and trajectories of the other branches of this network reveals how developmental biology became truly international. Here, I have studied the Finnish branch, aiming to shed more light on the question posed by Hamburger (1988): "How was experimental embryology transplanted to Finland?".

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