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Developmental Biology in Geneva: A Three Century-Long Tradition

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Recent books and publications dealing with the history of science and, in particular, with natural science and biology in Geneva, have profoundly changed and enriched our understanding of the scientific movement that developed in this small independent town, which became part of Switzerland as recently as in 1815 (Buscaglia *et al.,* 1994; Dawson, 1987; Dinsmore, 1991; Lenhoff and Lenhoff 1986; Montandon, 1975; Trembley, 1987). These contributions, added to more classical ones (e.g. Baker, 1952; Guyénot, 1941; Vartanian, 1950), suggest some general considerations about the birth, origin and development of this original scientific community, with a particular focus on its seminal contribution to the fields of embryology, regeneration and developmental biology at large.

It has been previously argued that no genuine scientific activity took place in Geneva before the very end of the seventeenth century. This is largely true, despite the earlier publication, by local editors, of some books dealing with either scientific or medical matters. However, this situation changed drastically around the middle of the eighteenth century when significant contributions started to emanate from the city of Calvin. This rather late occurrence of visible science in Geneva has been explained by several authors (Dawson, 1987; Trembley, 1987) and appears to be the result of mainly religious and economical reasons. But the situation changed around 1700, when science in Geneva started to develop, first on a family scale. This local network further established strong contacts with other scientific communities, especially in France, England, Holland, Germany and Italy (Montandon, 1975). During the early days, these naturalists developed a very pragmatic, utilitarian activity; they borrowed from other communities the elements of their own scientific ideology (Buscaglia, 1997), which can be tentatively summarized as: *"less theory and more experiment is best"* (see in particular the work of Sigrist, 2002).

The scientific community in Geneva was exceptionally bright and flourishing during the 18th century, but really became a recognized part of the international scene of science only after the beginning of the 19th century. However, even when considering these latter centuries, a genuine 'Geneva School' of science is difficult to define, for example in developmental biology, even though reproductive biology, descriptive embryology and experimental developmental biology have frequently been the centers of interest of many scientists from the eighteenth century up to now. Therefore, it is fair to say that, if not a school, a solid tradition in developmental biology was built up by many scientists over the centuries, which contributed to the long-lasting reputation of Geneva in this discipline.

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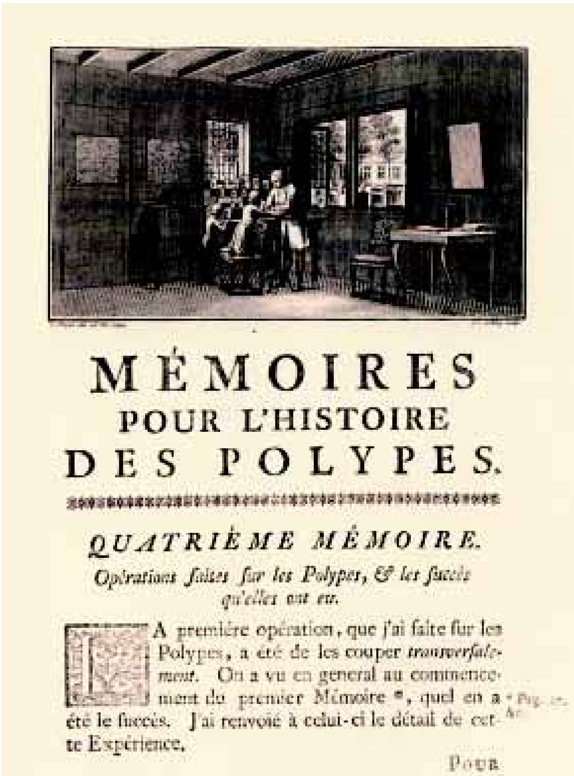


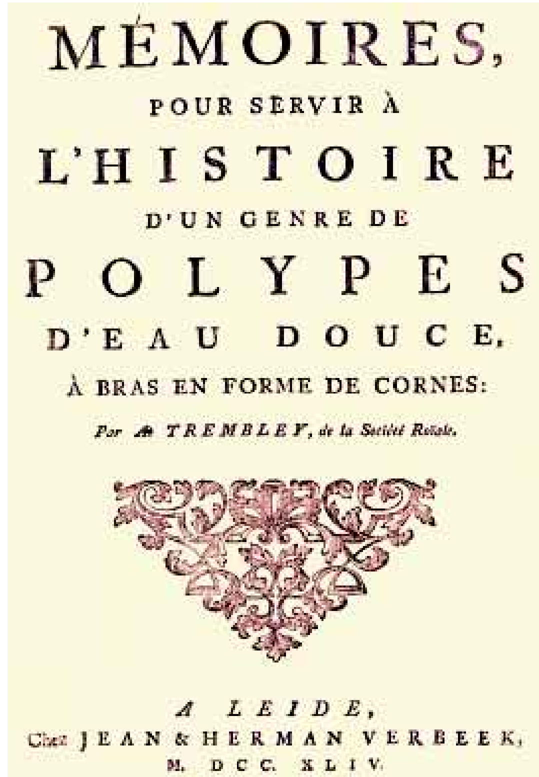
MÉMOIRES
POUR L'HISTOIRE
DES POLYPES.

QUATRIÈME MÉMOIRE.

Opérations faites sur les Polypes, & les succès qu'elles ont eu.

LA première opération, que j'ai faite sur les Polypes, a été de les couper *transversalement*. On a vu en general au commencement du premier Mémoire *, quel en a été le succès. J'ai renvoié à celui-ci le détail de cette Expérience.

POUR



MÉMOIRES,
POUR SERVIR À
L'HISTOIRE
D'UN GENRE DE
POLYPES
D'EAU DOUCE,
À BRAS EN FORME DE CORNES:
Par A. TREMBLEY, de la Société Royale.

A LEIDE,
Chez JEAN & HERMAN VERBEEK,
M. DCC. XLIV.

Fig. 1. (Left) Abraham Trembley and his two pupils studying polyps at the Bentinck mansion in Sorgvliet *(This picture heads the fourth Memoir, Leiden, 1744). The text reads "Treatise on the history of polyps. Fourth Memorandum. Manipulations carried out on polyps, and how successful they were. The first operation which I performed on polyps, was to cut them transversally. We have seen before, in the first Memoir, how successful this operation was. Here I reproduce the details of this experiment."*

Fig. 2. (Right) Title page from the 1744 edition of Trembley's *Mémoires*. *(Leiden). The text reads: "Treatise to serve the natural history of a fresh-water polyp, with horn-like arms: From A. Trembley, of the Royal Society." Translation, Denis Duboule (DD).*

In this short paper, we would like to illustrate this tradition by presenting some examples of observations and experiments performed in the field of reproductive and developmental biology, either carried out in Geneva, or by scientists from this city. We shall focus on major methodological and conceptual contributions, as well as on some novel theories and facts brought to light by this community. To start with, one has to realize that from Fabricius d'Aquapendente to Marcello Malpighi, via William Harvey and many others, the 17^{th} and 18^{th} centuries were dominated by the biology of reproduction and its many contradictory theories such as ovism, animalculism, preformationism or the theory of epigenesis (Bernardi, 1986; Roger, 1971). It is within this particular context that natural science emerged and developed in Geneva.

Abraham Trembley - An Admired Experimenter

Two prominent scientists, at the origin of life sciences in Geneva, made an impact on the future of developmental biology: Abraham Trembley (1710-1784) and Charles Bonnet (1720-1793). Both worked on a private scale and contributed to reproductive and developmental biology in a spectacular way. They set up the standard of scientific endeavor in Geneva for more than half a century.

The work of Trembley has been extensively analyzed by many scholars, including Trembley's own cousin and early biographer, Jean Trembley (Trembley, 1787), as well as by modern historians and epistemologists (Baker, 1952; Buscaglia, 1985, 1998; Dawson, 1987; Lenhoff and Lenhoff, 1986). All these different analyses converge towards the description of a very gifted experimenter. While not very inspired by systematics and classification, Trembley showed great interest in doing experiments and trying to convince others about his views. Both his strong methodological instinct and his technical gifts were recognized by Thomas H. Morgan himself. These latter authors have emphasized a few remarkable methodological ideas proposed by Trembley, who discovered novel, important, aquatic, microscopic organisms including the cniderian hydra. He understood many aspects of both budding and sexual reproduction in this fresh water polyp. However, it is his subsequent discovery of animal regeneration that made him famous.

Trembley was born in Geneva, but exerted his talents as naturalist during the Summer, in the house of the Count of Bentinck, in Sugvliet near The Hague (Netherlands). He was also active as a diplomat and as a teacher. He dedicated nine years of his life to biology and four years only to the experimental approach of reproductive biology and regeneration in hydra. It was in fact while being the mentor of the two children of the Count of Bentinck (Fig. 1), that he discovered the green polyps *(hydra viridis)*. On November the 25th 1740, while trying to discriminate between the animal or vegetal nature of this recently discovered organism, he undertook his first series of experiments (Trembley, 1743). These very logical and remarkable experiments carried out on polyps were described in the influential '*Mémoires pour servir l'histoire d'un genre de polypes d'eau douce à bras en forme de corne*' *(Treatise to serve the natural history of a kind of fresh water polyp, with horn-*

like arms) (Fig. 2), published in 1744 and translated into English by Lenhoff and Lenhoff in 1986 . Despite his rather short active period, this set of famous experiments on hydra regeneration remains as a major contribution to eighteenth century experimental biology (Trembley 1743, 1744).

To address the complex issue of the biological nature of polyps, he first reasoned that should they regenerate after being sectioned, they would certainly be plants. Accordingly, he embarked on an impressive series of experiments involving the sectioning of polyps. However, after a first series of transverse sections, which were mostly followed by the complete regeneration of both halves (Fig. 3), he started to realize that in contrast to his previous preconceived idea, hydra was undoubtedly an animal for obvious reasons linked to the behavior of polyps, such that their capacity to swim, to hunt as well as to react to their environment.

At this point of the demonstration, he could as well have lost interest in these animals and stopped the experiments. Yet, on the contrary, he continued with new manipulations, such as multiple transverse, longitudinal, incomplete anterior and incomplete posterior sections. Subsequently, he even successfully carried out experiments involving grafting protocols (Lenhoff and Lenhoff 1984). Although in some instances, such as in the inversion of the crop shaped hydra, he clearly misunderstood the outcome of the experiment, his superbly designed and exceptionally well organized series of manipulations proved to be deeply inspiring for many scientists during the eighteenth century (Buscaglia, 1985, 1998). These experiments and their unexpected results impressed both fashionable members of private 'salons' as well as influential scientists. A member of several academies, he was elected to the Royal Society of London and in 1743 was awarded the prestigious Copley medal, one of the highest signs of scientific recognition at this time.

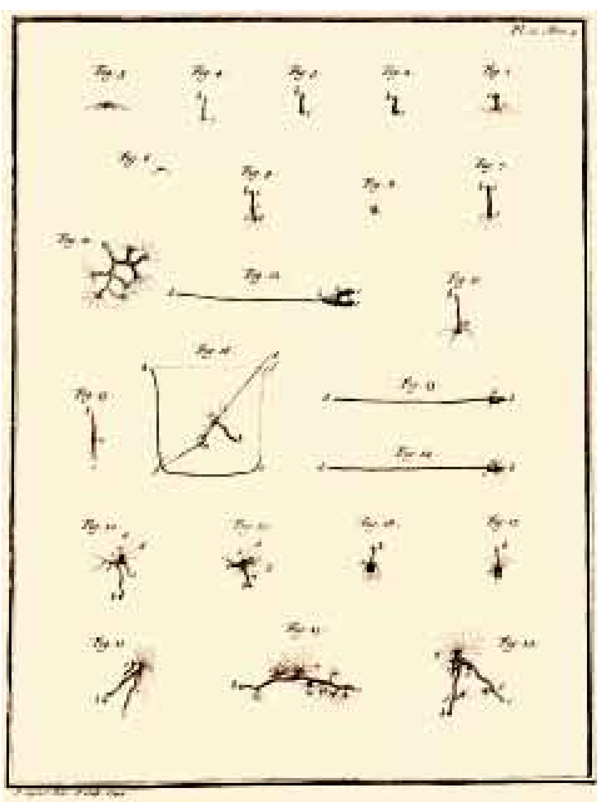


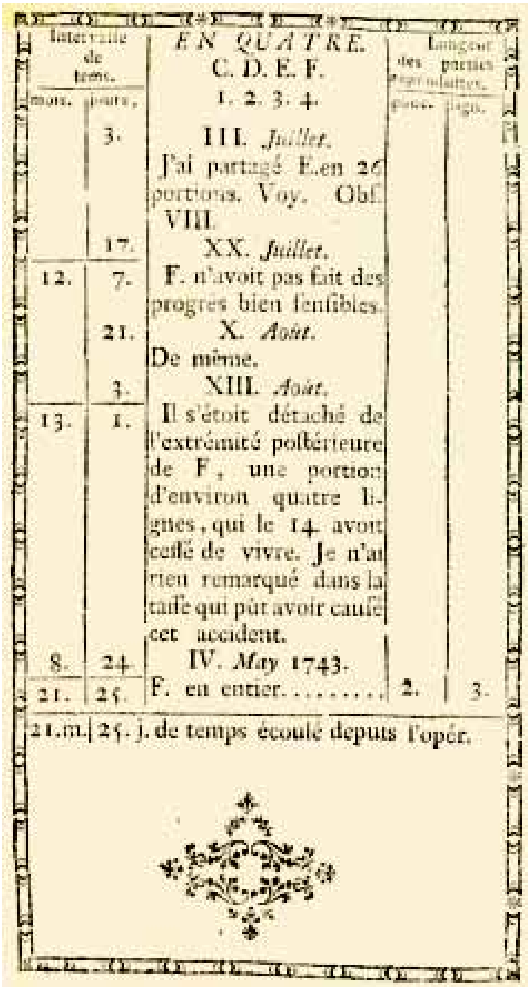
Fig. 3. Plate No. XI from the Trembley´s Fourth *Mémoire.* *It illustrates transverse and longitudinal sections of polyps, the corresponding regenerating fragments, as well as inverted polyps. Figs. 1-6 are transverse sections; Figs. 7-10 are longitudinal sections; Fig. 11 shows a hydra with seven heads and Figs. 12-23 show how to perform a polyp inversion and the fate of such inverted polyps.*

Trembley was not particularly enthusiastic about philosophical interpretations of his results. In marked contrast to Charles Bonnet, Voltaire and other contemporary figures, he never discussed the fate of the mind and the soul in regenerating polyps, a question which had been raised by his experiments. In this context, he can be seen as an example of a pragmatic experimenter, who neglected theoretical work and only believed in what he could observe. He nonetheless readily understood the general meaning of budding in animal reproduction and even stressed the *rationale* of gonad generation in hydra. His work paved the way to the experimental approach of animal reproduction and ontogenesis, mostly because the isolated working atmosphere he was working in, a private house rather than an academy, stimulated him to describe all the technical details of his experiments in order to allow others to repeat them. As a result, Trembley not only reported accurate observations and phenomena, but also introduced and popularized his strong and logical experimental organization in a scientific community whose methodology was, to say the least, not yet properly defined.

Charles Bonnet - Experimenter and Theoretician

From 1740 onwards, Geneva could count on another prominent member of the European naturalist community; Charles Bonnet. Bonnet, a relative of Trembley, had fragile health. He became almost blind soon after 1745, but with the help of servants and relatives, could nevertheless report many essential observations about insect structures and their reproduction, as well as plant physiology. In his wealthy property of Genthod, near Geneva, he also substantially contributed to the theoretical foundations of psychology (Buscaglia *et al.,* 1994; Dawson, 1987). In contrast to Trembley, he was very eager to speculate and propose theories, such as for example in the field of reproductive biology. Amongst other theoretical contributions, his ovist conception of mosaic preformism and of the *'emboitement des germes'* greatly stimulated research in the field. In his view, the egg rather than the sperm was the basis for reproduction. Even though many of his theories turned out to be wrong, they proved to have a high heuristic value. In addition, he inspired several essential experimental approaches to other great scientists such as for example Abraham Trembley, Albrecht von Haller (Monti, 2000), Horace-Bénédict de Saussure and Lazarro Spallanzani. (Savioz, 1948).

His first key contribution to the field of reproduction was suggested to him by the French naturalist René Ferchault de Réaumur; following a very simple and elegant protocol, he convincingly showed in 1740, i.e. at the age of 20, that some aphids reproduce themselves through parthenogenesis. Indeed, he reported that females, which had been isolated for weeks, could still produce offspring even after nine generations without any contact with their respective males (Bonnet, 1745, 1779). As for the sectioning approach of Trembley, these experiments were organized in a logical and coordinated series, showing beyond any doubt that



Intervalle de tems.		EN QUATRE. C. D. E. F. 1. 2. 3. 4.	Longueur des parties reproduites.	
mois.	jours.		pouc.	lign.
	3.	III. *Juillet.* J'ai partagé E. en 26 portions. Voy. Obf. VIII.		
	17.	XX. *Juillet.*		
12.	7.	F. n'avoit pas fait des progrès bien fenfibles.		
	21.	X. *Août.* De même.		
	3.	XIII. *Août.*		
13.	1.	Il s'étoit détaché de l'extrémité poftérieure de F, une portion d'environ quatre lignes, qui le 14 avoit ceffé de vivre. Je n'ai rien remarqué dans la taffe qui pût avoir caufé cet accident.		
8.	24.	IV. *May* 1743.		
21.	25.	F. en entier.	2.	3.
21.m.	25. j.	de temps écoulé depuis l'opér.		

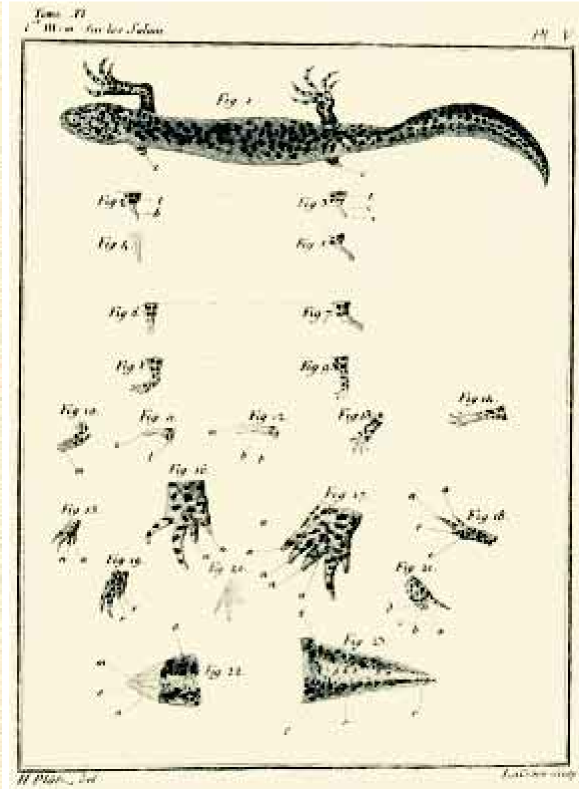


Fig. 4. (Left) Extract of C. Bonnet´s published experimental diary (1745), *which illustrates how precisely the experiments were described. In this case the regeneration of fresh water worms is documented. One can read at the top that by July the 3rd 1743, he had cut such a worm into 26 pieces. The top of the left and right columns reads:* "Time interval, month, day" *and* "Length of the reproduced parts". *In the middle column appear the daily descriptions:* "3rd July. I have separated 'E' into 26 parts. See observation VIII; 20th July. 'F' has not made any noticeable progress; 10th August, Idem.; 13th August, From the posterior extremity of 'F', a piece of about four lignes became detached, which, by the 14th, had died. I haven't noticed anything in the cup that could have induced this accident; 4th May 1743. "F" en entier..." *(likely meaning that it had regenerated). Bottom part of diary page:* "25 days spent since the operation...". *Translation, DD.*

Fig. 5. (Right) An example of the quality and precision used to describe regenerating limbs (1-21) and tails (22,23) in the newt, *emphasizing the art of observation of Charles Bonnet (1779). This experiment was performed in 1777.*

Bonnet beautifully mastered the experimental methodology, both regarding experimental processes at the bench, and with respect to the development of a genuine experimental semantic to describe the approach and results. This latter issue was (still is) of paramount importance, not only to properly communicate, but also to reinforce epistemological convergence (Buscaglia *et al.,* 1994; Ratcliff, 1995, 2001; Sigrist, 2001).

Soon after he became aware of Trembley's regenerating polyps, he decided to investigate whether other organisms could possibly exhibit a similar potentiality. As a result, he first showed in 1741 that fresh water worms were also able to regenerate (Fig. 4). Here again, the experimental strategy was properly thought over and the design of the experiments was logical and convincing. In fact, some of these protocols were even published in order to more easily convince the readers. Subsequently, during 1777 / 1778, following Spallanzani, he performed other experiments either on the newt or using snails. He confirmed and extended the observations that snails could regenerate their eyes and head, whereas newts could regenerate many parts of their body such as their limbs, the anterior part of their head, their tail and their crest (Fig. 5).

In contrast to his own belief, these results suggested that in several animals, development could be epigenetic (resulting from epigenesis), rather than resulting from a preformationist process. Therefore, in order to reconcile the results of his experiments with his conceptual framework, he created a novel theory which allowed him to keep his beloved preformationist views; he proposed that an infinity of very small *'sleeping embryos'* were permanently waiting to become active. Activation of their souls would occur whenever a part of the body was suppressed, and the awakened soul would replace the missing pieces by growing faster. Bonnet wished to write a treatise on the fundamentals of scientific methodology. However, it was his student and friend Jean Senebier who achieved this task and who wrote in 1802 an *Essais sur l'art d'observer et de faire des experiences* (Essay on the art of observation and of performing experiments) (Huta, 1997).

From Adult Morphology Backwards to The Embryo

Early in the nineteenth century, a new systematic comparative approach started to dominate the fields of anatomy and morphology, as a result of the observation and description of many novel, macroscopic, organic structures. Macroscopic observation of both adults and embryos was accompanied by an important theoretical work on the fundamentals and structural organization of several animals, as well as on the rules that could generate such organized organisms. A prominent contributor to this important movement was Etienne Geoffroy Saint Hilaire (1772-1844), whose general principles of organization were even recently revisited. Nevertheless, the need to understand in more detail the early steps of animal development in a comparative context became critical only once the Darwinian theory of evolution had been properly perceived, and, more specifically perhaps, with the recapitulation concept of Ernst H. Haeckel (1834-1919). The issue was no longer to merely understand animal development, but mostly to trace back the origins of embryos in a phylogenetic context.

In Geneva, several zoologists contributed significantly to such a systematic observation and description of ontogenetic structures, as putative illustrations of early phylogenetic organisms. These contributions usually followed a 'backward strategy', i.e. starting with the observation of adults, then of late developing embryos, to further address earlier developmental stages and fertilization. Zoologists generally focused on aquatic organisms which were easy to observe at the microscopic level due to their transparent appearance. Even though Switzerland had, and still has, no direct access to any sea or ocean, the local developmental zoologists became increasingly attracted by the diversity of salt-water invertebrates. As a consequence, they started to work in close contact with the active German school, as well as with the French school of marine zoologists. It is in this context that two such zoologists from Geneva became deeply involved in both the inspiration and the construction of marine biological laboratories in Italy and France. Thus, Carl Vogt played an important role in inspiring Anton Dohrn, at the time (1873) the young German launched the Zoological Station in Naples (Pont *et al.,* 1998; Fantini, 2000), whereas Herman Fol (see below) created the marine biology laboratory in Villefranche sur mer and spent many years in Messina.

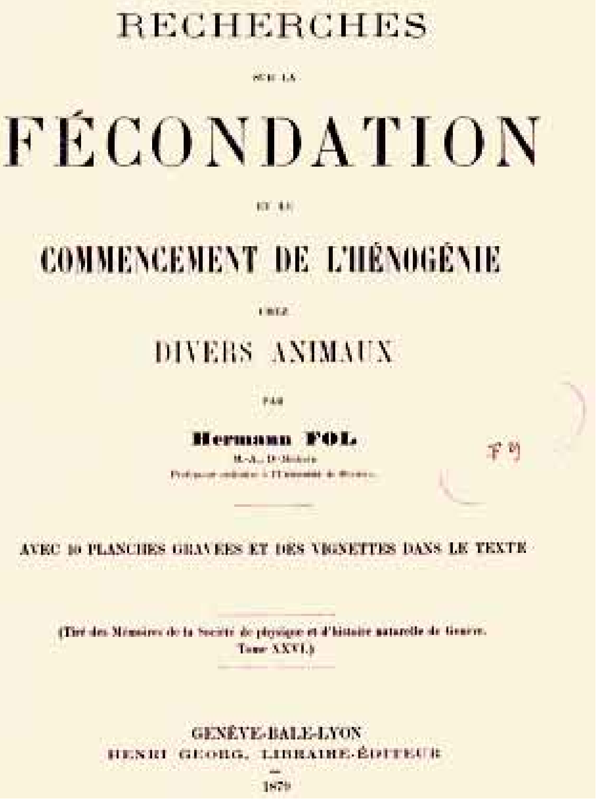
Carl Vogt and Hermann Fol

Carl Vogt (1817-1895) was the most prominent naturalist in Geneva, during this period. Born in Giessen, this German scientist had to leave his country for political reasons, acquired Swiss nationality and ended up in Geneva by 1852, where he soon became extremely influential in state affairs, as well as in university politics. He eventually represented Geneva in the federal government and became the first rector, after the old Calvinist Academy had been transformed into a modern University. This naturalist published more than 140 papers and books, and was a strong proponent of the Darwinian theory, which he helped to popularize along with his colleague Edouard Claparède (1832-1871). It is not in the scope of this short review to explain how his materialistic enthusiasm and broad knowledge of science drastically influenced the future of biology, as exemplified by his lecture at the University of Giessen in 1847, concerning the then present status of morphology, wherein he reorganized the biological corpus in an utterly convincing way (Vogt, 1847). This lesson is one of the historical masterpieces of this time regarding the thinking in biology, its methodology and the implementation of a research program (Pont *et al.,* 1998).

As a materialist philosopher, professor and politician, Vogt was a passionate polemicist. But despite all these activities, he could nevertheless describe many new marine invertebrate and vertebrate species (Vogt, 1868). He was an accurate comparative morphologist and physiologist and, as a descriptive embryologist, he published works on the development of the toad (Alytes), the salmon and of some mollusks. Being very influential, he stimulated the scientific community for almost half a century. Concomitantly and along the same lines, though with less impact, the work of his colleague E. Claparède on the histology of worms and, most importantly, on the descriptive embryology of gastropods and spiders should also not be overlooked.

Hermann Fol (1845-1892) was a student of Carl Vogt in Geneva from 1862 to 1864. He further received his scientific education in German universities, first in Iena (1865-1867), then in Heidelberg (1867-1868) and Berlin (1868). During this period, he could meet many of the greatest naturalists of this time, such as Gegenbaur, Haeckel, Helmoltz, Buchner and Bunsen. In 1878, he became professor of embryology at Geneva University. Born in Saint Mandé, France, he came from a *'famille bourgeoise'* of Choulex, near Geneva. Fol enjoyed science in the fields and thus went on scientific expeditions to Lanzarote, Morocco and Sicily. He died in the shipwreck of his laboratory boat, the 'Aster' named after his work on centrioles, during an expedition to Tunisia financed by the French government, to study sponges. Between 1886 and 1887, he had organized his own marine laboratory within a hotel in Messina.

Fol was active in the field of the descriptive embryology of invertebrates, beginning with his thesis on the anatomy and development of Ctenophores (Berlin, 1869). He published more than 140 papers, of which 49 were on embryology and 15 on fertilization. He also invested some time to study human embryology and was the first to report that humans have a (transitory) tail,


RECHERCHES

FÉCONDATION

COMMENCEMENT DE L'HÉNOGÉNIE

DIVERS ANIMAUX

Hermann FOL

AVEC 10 PLANCHES GRAVÉES ET DES VIGNETTES DANS LE TEXTE

(Tiré des Mémoires de la Société de physique et d'histoire naturelle de Genève. Tome XXVI.)

GENÈVE-BALE-LYON
HENRI GEORG, LIBRAIRE-ÉDITEUR
1879

Fig. 6. Title page of the publication of the seminal work of Hermann Fol (1879) on echinoderm fertilization and early development in sea urchins. *The text reads:* "Research on Fertilization and the Beginning of Henogenesis in Various Animals by Hermann FOL". *Translation by DD.*

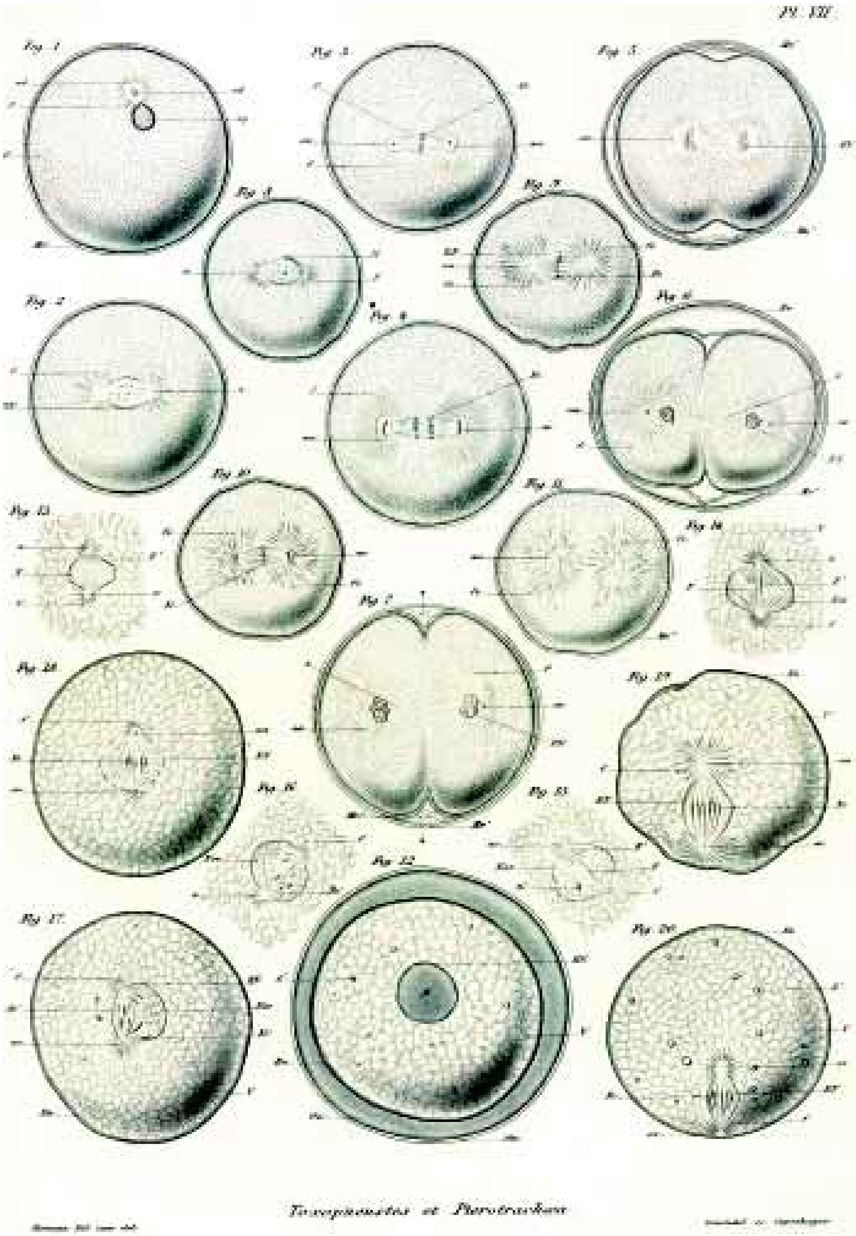


Fig. 7. Plate No. VII from the paper by Hermann Fol (1879), *showing nuclear amphimixy and the early cell divisions after fertilization in fixed material (see Fig. 6).*

an observation that had escaped the attention of his Swiss colleague from Basel and great anatomist W. His (1831-1904) (Fol, 1885). He published several papers on descriptive and comparative embryology. His work was characterized by stringent criteria of quality, to publish anatomical, histological and cytological descriptions as exactly as possible. With this objective in mind, he developed several methods of imaging, including photography. He was not very attracted by theories, hence he devoted his time and efforts to setting up imaging processes to illustrate both stable and dynamic macroscopic and microscopic structures; a precursor in this topical field, indeed. He used these technological tools in his famous work on fertilization and early blastomere division in sea urchins and starfish (Fig. 6), in what remains as a superb example of a "backward" strategy (Fol, 1879). In this case, as in other pieces of work, he went back first to early development (Fig. 7), then to fertilization (Fig. 8), to end up studying events which take place before fertilization. His pictures of fertilization were largely acknowledged and popularized, notably by Oscar Hertwig (1849-1922) (Hertwig, 1890) and others. In this context, it is important to remember that the role of spermatozoa during the fertilization process was clearly understood only in 1822, by Jean Louis Prevost (1790-1850) and Jean Batiste Dumas (1800-1884), when working in Geneva (Buscaglia 1990).

The Early Days of Experimental Embryology

Interestingly, from the epistemological viewpoint, the transition of H. Fol from the study of morphology to causal experimental embryology was dictated by his rational conclusions about the comparative development of mollusks. Indeed, comparative observations on helicoid mollusk development led him to propose a causal theory of developmental asymmetry. This theory was subsequently challenged, experimentally, in collaboration with Stanislas Warynski (Bedot, 1894; Fol and Warynski 1883, 1884, 1886). These contributions are vivid examples of very early attempts, if not the first, to embark on embryological experimentalism, a discipline (causal embryology) which later on flourished in southern Germany. However, these publications must be considered in the context of the leading work of Camille Darest (1822-1899) on monsters and causalities in teratology (Darest 1896; see Fischer, 1994). They anticipated the impressive methodology, results and concepts which would soon after characterize the German school of developmental mechanisms.

In the Fol and Warynski papers (Fig. 9), where the chicken was used as a model system for embryological manipulations, the following general conclusion is reached: any artificially induced modification of 'the cause', may select amongst different potential reactions of the embryo itself. In this context, any observed modification in development is actively produced by the organism, as an integrated response to the experimental alteration of the cause. This idea was very similar to the future concept of *'Selbstregulation'* and announced its formulation by W. Roux (Roux, 1914). Such a novel experimental approach was presented in a bright and pioneering but short paper in 1883. By analyzing the onset of developmental asymmetry during chicken embryogenesis (heterotaxy), which later on generates adult left-right asymmetry, the authors made specific attempts to experimentally induce modifications of symmetry.

The described experimental protocol was amazingly modern, as it can be considered to follow the major conceptual and

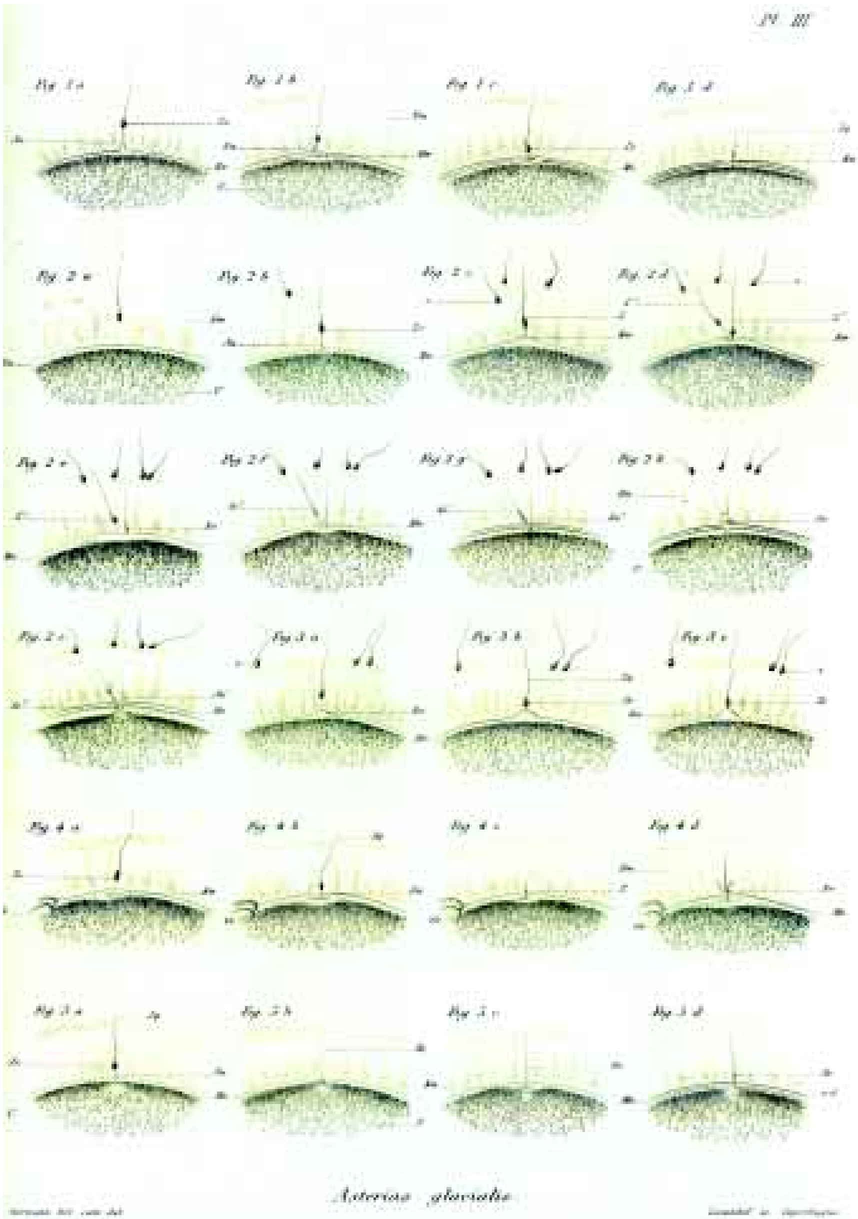


Fig. 8. Plate No III from the paper by Hermann Fol (1879) *showing* in vivo *drawings of the various steps in the fertilisation in* Asterias glacialis *(see Fig. 6).*

pragmatic rules of experimental biology. First, they explicitly proposed a causal hypothesis in order to explain asymmetry (lateral differences in the rates of cell divisions would account for lateral asymmetry). Secondly, and as a consequence of their hypothesis, they proposed to slow down cell division on one side only, an operation carried out by moderate heating of specific areas (it was not possible to increase the rate of cell division). The high quality of their surgical approach allowed them to give enough time to the embryo to properly react (over days), such that they could accurately observe the resulting modifications in more than a hundred manipulated chicken embryos. The conclusions were related to the initial hypothesis, and the authors claimed the results had validated their postulated explanation of the process.

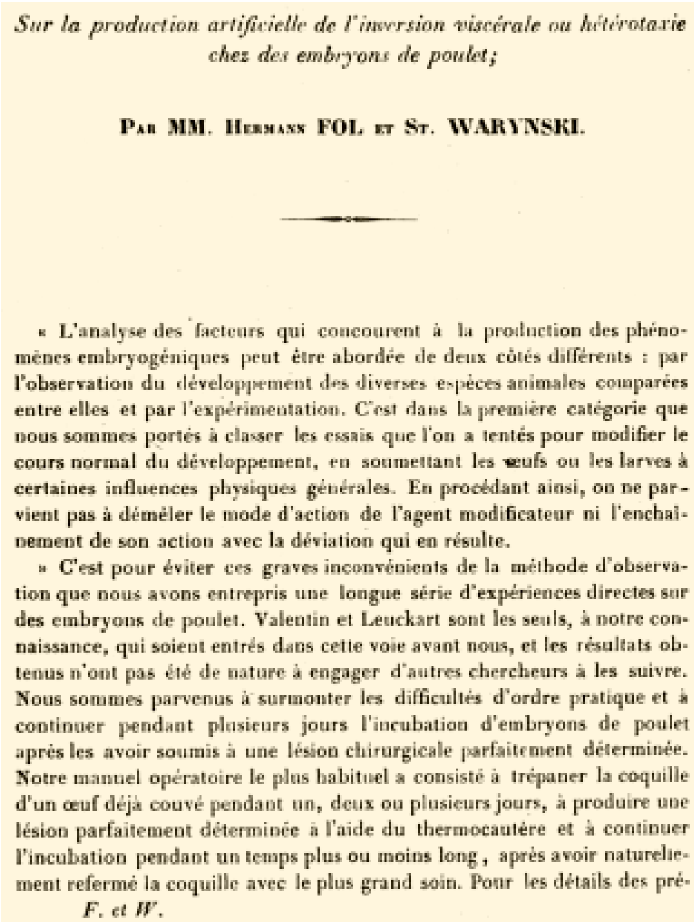
Whether it was Warynski or Fol who provided the essential contribution to what is considered by some as the birth of experimental embryology, and to the development of fundamental concepts and experimental protocols, is not yet absolutely clear. While Warynski was indeed the prominent author of the few seminal papers they wrote on this very topic, further studies will be necessary to clarify this issue. Also, unfortunately, these papers were not followed by subsequent experiments using the same methodology. They were nonetheless an essential step on the way to the elaboration of a generalized experimental embryology, which finally acquired its status with the *'Entwicklungsmechanik'* (Roux, 1914) and, subsequently, with the work of H. Spemann (1869-1941) (see Sander and Faessler, 2001; Spemann and Mangold, 1924).

The Tradition Goes On

Without discussing too much the situation in the last century, we would like to complement this short account of developmental biology in the past in Geneva, by adding a few words on the work of Emile Guyénot (1885-1963) and Kitty Ponse (1897-1982; Fig. 10), both professors at what is known today as the Department of Zoology and Animal Biology of the University of Geneva.

One century after Trembley and Bonnet, Emile Guyénot, who also published papers on his two famous predecessors, re-activated research on animal regeneration in Geneva (Guyénot, 1941). With his gifted assistants, Marco Zalocar, Daniel Bovet, Kitty Ponse, Oscar Schotté and others, they analyzed the potentialities of regenerating structures in newts and lizards, such as the head, the eyes, the limbs, the tail and the crest. Much attention was given to the non-specific stimulatory effects of the nervous system, as compared to specific differentiation induced by regeneration territories, especially when different areas were brought into contact with each other. Just before joining the faculty in Geneva where he taught zoology, he had designed a method to keep *Drosophila* in a sterile, pastorian condition (Guyénot, 1917). His idea was to prevent the effect of microbes when analyzing hereditary processes during development. This method, which opened the way to studies of environmental effects on embryological development, was subsequently popularized by T.H. Morgan.

It was in 1922 in Guyénot's laboratory, where Kitty Ponse showed how castrated male toads became fertile bidderian females. Hence she switched to developmental biology by studying the process of gonad differentiation, an important step in the study of organogenesis and an essential contribution to our knowledge of sexual differentiation (Ponse 1922, 1948). In the same department, closely associated with the *'Station de Zoologie Expérimentale'* which was created in 1933 as an outstation of the


Sur la production artificielle de l'inversion viscérale ou hétérotaxie chez des embryons de poulet;

PAR MM. HERMANN FOL ET ST. WARYNSKI.

« L'analyse des facteurs qui concourent à la production des phénomènes embryogéniques peut être abordée de deux côtés différents : par l'observation du développement des diverses espèces animales comparées entre elles et par l'expérimentation. C'est dans la première catégorie que nous sommes portés à classer les essais que l'on a tentés pour modifier le cours normal du développement, en soumettant les œufs ou les larves à certaines influences physiques générales. En procédant ainsi, on ne parvient pas à démêler le mode d'action de l'agent modificateur ni l'enchaînement de son action avec la déviation qui en résulte.

» C'est pour éviter ces graves inconvénients de la méthode d'observation que nous avons entrepris une longue série d'expériences directes sur des embryons de poulet. Valentin et Leuckart sont les seuls, à notre connaissance, qui soient entrés dans cette voie avant nous, et les résultats obtenus n'ont pas été de nature à engager d'autres chercheurs à les suivre. Nous sommes parvenus à surmonter les difficultés d'ordre pratique et à continuer pendant plusieurs jours l'incubation d'embryons de poulet après les avoir soumis à une lésion chirurgicale parfaitement déterminée. Notre manuel opératoire le plus habituel a consisté à trépaner la coquille d'un œuf déjà couvé pendant un, deux ou plusieurs jours, à produire une lésion parfaitement déterminée à l'aide du thermocautère et à continuer l'incubation pendant un temps plus ou moins long, après avoir naturellement refermé la coquille avec le plus grand soin. Pour les détails des pré-

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Fig. 9. (Left) First page of a note sent by H. Fol and S. Warynski (1883) to the French Academy of Science in Paris, reporting the experimental reversal of symmetry *(situs)* in the chicken embryo. *This report is one of the earliest, if not the earliest, examples of a systematic and rigorous use of the experimental approach in embryology. The text reads:* "On the artificial production of visceral inversion or heterotaxia in chicken embryos... *(Second paragraph)* "It was to prevent the important drawbacks of mere observation that we undertook a long series of direct experiments on chicken embryos". *(Further below)* "We managed to overcome the practical difficulties and could continue to incubate chicken embryos for several days, after a perfectly determined surgical operation." "Our usual protocol was to open the egg shell (…) and to continue the incubation for an undetermined period of time, after having closed the shell with the greatest possible care…..". *Translation, DD.*

Fig. 10. (Right) Kitty Ponse (standing behind) and Emile Guyénot *teaching* Drosophila *genetics in the 1920's in their laboratory in Geneva.*

department to support and stimulate this work (see the paper by Rungger in this volume, pp. 49-63) and which still belongs to this department, the tradition of studying development, genetics and regeneration has been maintained since then (see e.g. Rungger, this volume, pp. 49-63 and Galliot and Schmidt, this volume, pp. 39-48). The fact that five papers in this Special Issue are issued from this department demonstrates how faithful extant scientists in Geneva are to their renowned predecessors, and how eager they are to maintain the tradition of a long-standing scientific reputation of this city.

Summary

It was in the first half of the 18th century when life sciences started to flourish in the independent republic of Geneva. However, it is difficult to identify a genuine school of developmental biologists during that era. Nevertheless, several prominent scientists over the past two and a half centuries have established and maintained a strong tradition of studies in embryological development and reproduction. In this short historical account, we briefly pay tribute to these famous forerunners, by emphasizing both the originality and quality of their work, as well as the many accompanying conceptual and methodological advances. We start with Abraham Trembley (1710-1784) and the discovery of Hydra and of regeneration, and with Charles Bonnet (1720-1793) who, amongst other contributions, first observed parthenogenetic development. In the 19th century, Carl Vogt (1817-1895) and Edouard Claparède (1832-1871) were well-known scientists in this field of research, whereas Hermann Fol (1845-1892) can be considered as one of the pioneers, if not the founder, of causal embryology, through his experiments on lateral asymmetry in manipulated chicken. More recently, Emile Guyénot (1885-1963) and Kitty Ponse (1897-1982) perpetuated this tradition, which is well alive nowadays in the city of Calvin.

References

BAKER J. (1952) Abraham Trembley of Geneva, Scientist and Philosopher, 1710-1784. *Arnold, London.*

BEDOT, M. (1894) Hermann Fol, sa vie et ses travaux. *Arch. Des Sciences de la Bibliothèque Universelle*, 31.

BERNARDI, W. (1986) Le metafisiche dell'embrione. Scienze della vita e filosofia da Malpighi a Spallanzani (1672-1793) Olschki, Florence.

BUSCAGLIA M. (1985) The Rhetoric of Proof and persuasion utilized by Abraham Trembley, In H.W. Lenhoff et P. Tardent (Eds.) From Trembley's Polyps to New

Directions in Research on Hydra: Proceeding of a Symposium Honoring Abraham Trembley (1710-1784), *Archs Sci. Genève*, 38: 305-319.

BUSCAGLIA M. (1990) Etablissement de la théorie de l'hérédité et de la fécondation au XIXème siècle. Contributions présentées dans le cadre de la Sociétét de Physique et d'Histoire Naturelle de Genève. *Mémoires de la Société de Physique et d'Histoire naturelle de Genève*, 45: 81-106.

BUSCAGLIA, M., SIGRIST, R., TREMBLEY, J. and WÜEST, J. (Eds.) (1994) Charles Bonnet, savant et philosophe (1720-1793) Ed. Passé-Présent, Genève et Mém. Soc. Phys. Hist. Nat. de Genève, 47:137-154.

BUSCAGLIA, M. (1997) Comment aborder la naissance des sciences naturelles genevoises. In: C'est la faute à Voltaire, c'est la faute à Rousseau. *Recueil anniversaire pour Jean Daniel Candaux, Roger Durand ed., Librairie Droz, Genève*: 401-414.

BUSCAGLIA, M. (1998) La pratique, la figure et les mots dans les Mémoires d'Abraham Trembley sur les Polypes (1744), comme exemple de communication scientifique. In *Le forme della communicazione scientifica.* (Ed. di M. Galuzzi, G. Micheli and M.-T. Monti) Franco Angeli, Milano. pp. 313-346.

BONNET, C. (1745) Traité d'Insectologie, Durand, Paris,1745.

BONNET, C. (1779) Oeuvres d'Histoire naturelle et de philosophie de Charles Bonnet, Fauche, Neufchâtel.

DAREST, C. (1891) Recherches sur la production artificielle des monstruosités ou essais de tératogénie expérimentale. Reinwald, Paris.

DAWSON, V. (1987) Nature's Enigma. The Problem of the Polyp in the Letters of Bonnet, Trembley and Réaumur. *Mémoirs of the American Philosophical Society*, Vol 174, Philadelphia.

DINSMORE, C. E. (ed.)(1991) A History of Regeneration Research. Milestones in the Evolution of a Science. Cambridge University Press.

FANTINI, B. (2000) The "Stazione Zoologica Anton Dohrn" and the History of Embryology. *Int. J. Dev. Biol.* 44: 523-535.

FISCHER, J. L. (1994) Camille Darest, 1822-1899. *Deutschen Akademie der Naturforscher Leopoldina, Halle/Saale*, 21: 1-283.

FOL, H. (1879) Recherches sur la fécondation et le commencement de l'hénogénie chez divers animaux. Georg, Genève.

FOL, H. (1885) Sur la queue de l'embryon humain. *C.R. Acad. Sc*. (Paris).

FOL, H. and WARYNSKY, S. (1883) Sur la production artificielle de l'inversion viscérale ou hétérotaxie chez des embryons de poulet. *C.R. Acad. Sc.* (Paris), 96:1674-1676.

FOL, H. and WARYNSKY, S. (1884) Recherches expérimentales sur la cause de quelques monstruosités simples et de divers processus embryogéniques. *Recueil zool. suisse*,I:1 -25

FOL, H. and WARYNSKY, S. (1886) Sur la production artificielle de monstres à coeur double chez le poulet, Genève.

GALLIOT, B and SCHMID, V. (2002) Cnidarians as a model system for understanding evolution and regeneration. *Int. J. Dev. Biol.* 46: 39-48.

GUYÉNOT, E. (1917) Recherches expérimentales sur la vie aseptique et le développement d'un organisme en fonction du milieu. Thèse, Faculté des sciences, Université de Paris.

GUYENOT, E. (1941) Les Sciences de la vie aux XVIIe et XVIIIe siècles, Albin-Michel, Paris.

HERTWIG, O. (1890) Lehrbuch der Entwicklungsgeschichte des Menschen und der Wirbeltiere, Fischer, Jena.

HUTA, C. (1997) Jean Senebier (1742-1809) ou le dialogue de l'ombre et de la lumière. L'art d'observer à la fin du XVIIIe siècle, Thesis 2891, University of Geneva.

LENHOFF, S. G. H. M. and LENHOFF H. M. (1984) Tissue Grafting in Animals: Its Discovery in 1742 by Abraham Trembley as he experimented with Hydra. *Biol. Bull.* 166: 1-10.

LENHOFF S. G. H. M. and LENHOFF H. M. (1986) Hydra and the Birth of experimental Biology-1744. The Boxwood Press, Pacific Grove, California.

MONTANDON, C. (1975) Le développement de la science à Genève aux XVIIIe et XIXe siècles. Delta, Vevey.

MONTI, M.-T. (2000) Preface in *Commentarius de formatione cordis in ovo incubato.* (Ed. Albrecht von Haller) Maria-Teresa Monti, Studia Halleriana VI, Schwabe, Basel. pp. I-LXIX.

PONSE, K. (1922) L'organe de Bidder et le déterminisme des caractères sexuels secondaires chez le crapaud (*Bufo vulgaris*). *Rev. suisse Zool*, 31: 176-341.

PONSE, K (1948) La différenciation du sexe et l'intersexualité chez les vertébrés, Rouge Lausanne.

PONT, J.-C., BUI, D., DUBOSSON, F. and LACKI, J. (Eds.) (1998) Carl Vogt, Science, Philosophie et Politique (1817-1895). Bibliothèque d'Histoire des Sciences, Georg, Genève

RATCLIFF, M. (1995) Le lexique de la méthode dans l'oeuvre de Charles Bonnet, *Archs Sci. Genève*, 2: 197-208.

RATCLIFF, M. (2001) Europe and the microscope in the Enlightenment. Thesis, University College, London.

ROGER, J. (1971) Les sciences de la vie dans la pensée française, Colin Paris.

ROUX, W. (1914) Die Selbstregulation ein charakteristisches und nicht notwendig vitalistisches Vermögen aller Lebenwesen. *Abh. der Kaiserl. Leop.-Carol. Deutschen Akademie der Naturforscher*. 2: 1-91.

RUNGGER, D. (2002) Xenopus helveticus, an endangered species. *Int. J. Dev. Biol.* 46: 49-63.

SANDER, K. and FAESSLER, P. (2001) Introducing the Spemann-Mangold Organizer: experiments and insights that generated a key concept in developmental biology. *Int. J. Dev. Biol.* 45: 1-11.

SAUSSURE de H. (1871) Notice sur Edouard Claparède. Ramboz et Schuchardt, Genève.

SAVIOZ, R. (1948) Mémoires autobiographiques de Charles Bonnet de Genève. Vrin, Paris.

SIGRIST, R. (2001) L'expérimentation comme rhétorique de la preuve: L'exemple du traité d'insectologie de Charles Bonnet. *Rev. Hist. Sci.*, 54: 419-449.

SIGRIST, R. (2002) La République des lettres et l'essort des sciences expérimentales: exemple genevois (1670-1820). Thèse Université de Genève.

SPEMANN, H. and MANGOLD, H. (2001) Induction of Embryonic Primordia by Implantation of Organizers from a Different Species (reproduction of 1924 paper). *Int. J. Dev. Biol.* 45: 13-38.

TREMBLEY, A. (1743) Observations and experiments upon the fresh-water polyps (first published in 1743 and republished in 1743) *Phil Trans.*, 42, iii.

TREMBLEY, A. (1744) Mémoires, pour servir l'histoire naturelle d'un genre de Polypes d'eau douce, à bras en forme de corne, chez Jean et Herman Verbeek, Leide, 1744.

TREMBLEY, J. (ed.) (1987) Les savants genevois dans l'Europe intellectuelle du XVIIe au milieu du XIXe siècle. Edition du Journal de Genève, 1987.

TREMBLEY, J. (1787) Memoire historique sur la vie et les écrits de Monsieur Abraham Trembley. Fauche Neuchâtel.

TREMBLEY, M. (1943) Correspondance inédite entre Réaumur et A. Trembley. Georg, Genève.

VARTANIAN, A. (1950) Trembley's Polyps, La Mettrie, and 18th-century French Materialism. *J. of the History of Ideas*. 11: 259-280.

VOGT, C. (1847) Ueber den heutigen Stand der beschreibenden Naturwissenschaften, Giessen. Ricker ed.

VOGT, C. (1854) Recherches sur les animaux inférieurs de la Méditerranée. *Mémoires de l'Institut Genevois*,1853, later published by Georg, Geneva (1868).