Lazzaro Spallanzani: At the Roots of Modern Biology

ERNESTO CAPANNA*
Dipartimento di Biologia Animale e dell'Uomo Universitá "La Sapienza" Roma 00161, Italy

ABSTRACT The scientific work of Lazzaro Spallanzani is outlined, with emphasis on the elements of originality in his introduction of the experimental method in biology. Particular stress is placed on Spallanzani's contribution to solving the *Theoria Generationis*, from the problems connected with the spontaneous generation of living creatures to those of natural fertilization and artificial insemination and, finally, those of regeneration. *J. Exp. Zool. (Mol. Dev. Evol.) 285:178–196, 1999.* © 1999 Wiley-Liss, Inc.

Vous passez pour le meilleur observateur de l'Europe. Toutes vos experiences ont été faites avec la plus grande sagacité. Quand un homme tel que vous nous annonce qu'il a ressuscité des morts, il faut l'en croire. […] J'en peu de jours á vivre, Monsieur, je les passerai á vous lire, á vous estimer, et á vous regarder comme le premier Naturaliste de l'Europe. Continuez, je vous prie, Monsieur, d'honorer de vos bontés et de vos instructions le vieux malade de Ferney. (Letter to Spallanzani from Voltaire, dated "á Ferney 6 juin 1776")

OLD AND NEW PARADIGMS

After previous centuries, especially the seventeenth, broke down the paradigms of classical science, it fell to the eighteenth century, in the history of scientific and philosophic thought, to be the cradle of modern science. Lazzaro Spallanzani (1729–1799) was one of the leading figures in this scientific renaissance.

In the sixteenth century, the rigorous theoretical and experimental foundation of the Copernican system put in crisis the Aristotelian-Ptolemaic concept of the cosmos. In the seventeenth century the physiology of Galen, the other great scientific paradigm of the ancient world, also suffered a crisis following the dramatic crash between theoretical philosophic constraints and the new experimental science, between deep thinkers and meticulous naturalists, between imaginative metaphysicians and the first microscopists.

Emblematic of this scientific revolution was the question of how blood circulated. In fact, the physiology revolution was enacted in the seventeenth and eighteenth centuries on the phenomena of blood circulation. Seventeenth-century science, where medicine and anatomy are concerned, was based on the system formulated by Galen (131–210) that substantially was accepted even in the new scientific climate that formed. The great Vesalius (André van Vesele, 1514–1564), reformer of the teaching of anatomy, essentially accepted the Galenic doctrine, although he admitted complete separation between the right and left sections of the heart. Galen's system, in reality, was not a true "circulation" of the blood, but a continuous production of blood by the liver that was rendered vital in the heart during the diastole by the air breathed in through the lungs. During the systolic phase, blood was impelled throughout the body, thereby transferring the *animal spirit* it derived from being mixed with air from the lungs. The vital principles of the Aristotelian basis of science are evident in this formulation.

Servetus (Miguel Serveto, 1511–1553), Matteo Realdo Colombo (1520–1599), Caesalpinus (Andrea Cesalpino, 1519–1603), and Fabricius (Girolamo Fabrizio da Acquapendente, 1537–1619) knew the anatomy of the greater and lesser circulation, but failed to realise the physiological import of the discovery and the quality of real *scientific revolution* implied by the precise definition of the circulation of the blood. However, the full understanding of this revolution did not escape William Harvey (1578–1657). The originality of this Englishman's work was in a new method of approaching the problem: experimenting by measuring the parameters of the phenomenon of the circulation.

Harvey broke down the Galenic paradigms and

*Correspondence to: Ernesto Capanna, Dipartimento di Biologia Animale e dell'Uomo Universitá "La Sapienza," Via Boreli 50, Roma 00161, Italy. E-mail: capanna@axrma.uniroma1.it

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laid the foundations of modern physiology in the 72 pages of *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (1628) (Fig. 1). He unequivocally demonstrated through experiment and mathematics that blood cannot be produced by the liver and continuously transferred to peripheral parts of the body, but that it circulates constantly in the vasal system. Based on the volume of the ventricular cavity when the heart is dilated and contracted, he calculated the quantity of blood passing through the heart at each beat, which he assessed at 2 ounces (about 50 g). Considering that the heart beats about 72 times per minute, he inferred that the quantity of blood passing through the heart in one hour would be 540 pounds (more than 200 kg). Justly, Harvey asked himself how the liver can produce a quantity of blood equal to three times the weight of a man of normal build.

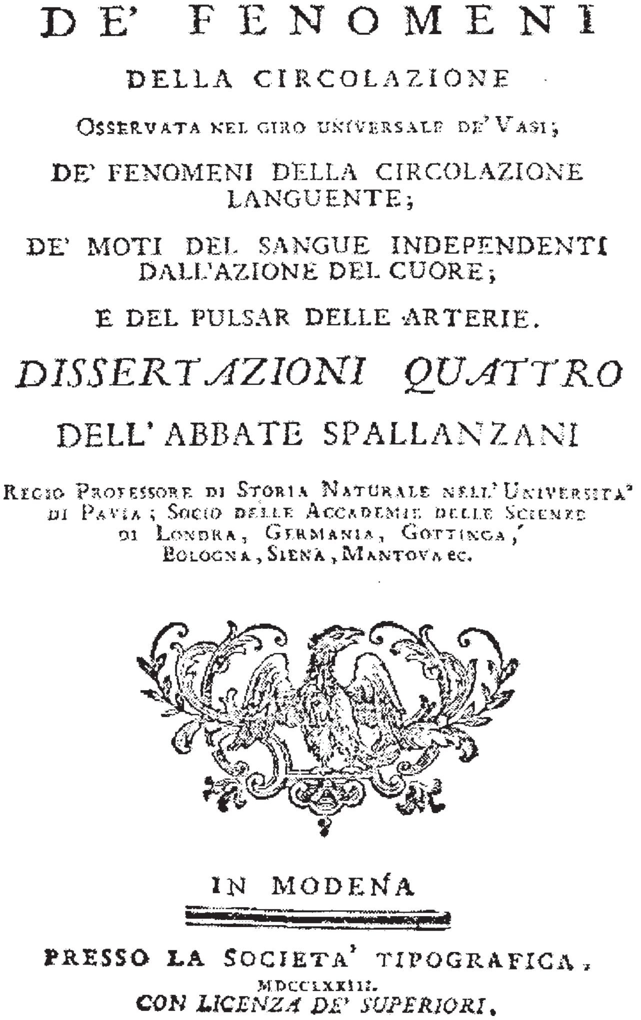
Fig. 1. Title page of the Rotterdam edition (1648) of William Harvey's *Exercitatio anatomica de motu cordis*. Corsini library of the Accademia Nazionale dei Lincei.

Only about a century later do we encounter the genial measurement experiments of blood pressure, performed by the Reverend Stephen Hales (1677–1765), and described by Spallanzani (1768a) as an "acuto ed eccellente Osservatore." Introducing a slender cannula in the arteries and veins, Hales obtained surprisingly accurate measurements of arterial and venous pressure in different animals, both in the systolic and in the diastolic phase. He verified differences of pressure in relation to different physical and psychic states and measured the speed of the circulatory flow.

This propensity to measure biological phenomena is typical of this eighteenth-century phase of science, aimed at the observance of Galileo's precept in the *Dialogo sopra i massimi sistemi* (1632): "…the book of Nature is written in the language of mathematics, and the characters are triangles, circles and other geometrical figures. Without comprehending these instruments it is not humanly possible to understand one word; without these it is like going round in circles in an obscure labyrinth."[1] The measurement and mathematical interpretation of biological processes was indeed the aim of the *iathrophysicists* and *iathrochemists*, who in the physical analysis of the processes in the nascent science of physiology were the precursors of Hermann Boerhaave (1668–1738), whose famous *Istitutiones Medicae* (1708) remained the master treatise on physiology throughout the eighteenth century.

In this climate, as new paradigms were formed based on experimentation and microscopy, Lazzaro Spallanzani came to grips in some of his first studies with a problem concerning the circulation of the blood (Fig. 2) (Spallanzani, 1768a; 1773). The circulation in the *vasa in capillamenta resoluta* had been clearly demonstrated by Marcello Malpighi (1628–1694) (Malpighi, 1661), in whose wake Spallanzani proceeded. However, his analysis had a precise aim: to verify the action of the cardiac muscle in the movement of blood in veins and arteries of different sizes, down to the detail of observing the coronary vessels. But the acuity of the meticulous observer is shown by a discovery made

[1] "…il libro della Natura è scritto in lingua matematica, e i caratteri son triangoli cerchi e altre figure geometriche, senza i quali mezzi è impossibile a intendere umanamente parola; senza questi è un aggirarsi vanamente in oscuro labirinto." (G. Galilei, Dialogo … sopra i due massimi sistemi del mondo tolemaico e copernicano. Firenze 1632)



DE' FENOMENI

DELLA CIRCOLAZIONE

OSSERVATA NEL GIRO UNIVERSALE DE' VASI;

DE' FENOMENI DELLA CIRCOLAZIONE LANGUENTE;

DE' MOTI DEL SANGUE INDEPENDENTI DALL'AZIONE DEL CUORE;

E DEL PULSAR DELLE ARTERIE.

DISSERTAZIONI QUATTRO

DELL'ABBATE SPALLANZANI

REGIO PROFESSORE DI STORIA NATURALE NELL'UNIVERSITA' DI PAVIA; SOCIO DELLE ACCADEMIE DELLE SCIENZE DI LONDRA, GERMANIA, GOTTINGA, BOLOGNA, SIENA, MANTOVA ec.

IN MODENA

PRESSO LA SOCIETA' TIPOGRAFICA,
MDCCLXXIII.
CON LICENZA DE' SUPERIORI.

Fig. 2. Title page of Spallanzani's *De' Fenomeni della Circolazione &*. Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

by Spallanzani that remained almost unknown, buried under the ponderous mass of his writings. He was the first to describe blood leukocytes. After having described with great exactitude the form of salamander red blood cells, he encountered a nucleated element clearly different in shape and size, thus his discovery of leukocytes. He preceded English microscopist William Hewson (1739–1774), whom treatises of haematology and general histology, indicate as the discoverer of this family of blood cells. Spallanzani, on the contrary, was perfectly aware of his discovery and of its novelty. In fact, he wrote: "I have *discovered* a species of globules which are smaller and present in far smaller numbers than the first ones." Then he proves his great stature as a scientist, as prudent in concluding as he is accurate in observing: "Since I myself doubted of my discovery, I wanted to make sure of it. I feared that the observation might derive from an optical effect, since the normal globules could be seen from the pointed end and thus be judged smaller and of a different nature. But after repeated, diligent and minute observations I could be certain that the two species of globule must absolutely be distinguished"[2] (Spallanzani, 1768a).

THE *THEORIA GENERATIONIS*

Certainly the fame that Spallanzani enjoys is due more to his observations on the theory of generation than to his observations on blood circulation, or his genial writings on the digestion and a thousand other things. The name *Theoria generationis*, in classical physiology and still in the eighteenth century, included all the biological phenomena whose intrinsic involvement in philosophy and theology attracted the general interest of cultured persons and the unlettered masses. It was, in fact, a matter of understanding of the fundamental phenomena of the reproduction of organisms, embryonic development, and parts regeneration of parts, along with the problem of organic life emerging from inorganic molecules.

If on the scientific plane these problems have been substantially resolved, on the philosophical and above all the ethical plane they still agitate the consciences both of the cultured and the uninformed. This symposium is a clear example of the perpetual topicality of the *Theoria generationis* and of the problems that it brings in its train.

The formulation of the problem of the generation was proposed by Aristotle (384–322 B.C.) in his *De generatione Animalium*. It bears marked traces of the metaphysical framework of the Greek philosopher: The embryo is the result of the life-giving action of the sperm infusing the incorporeal soul in the menstrual blood of the female, which is essentially inert and devoted exclusively to nourishing the embryo. Galen, on the contrary, imagined that the two seeds, masculine and feminine, participated equally in the constitution of the embryo. These two hypotheses, handed down

[2]"... ve ne ho *scoperta* una specie di più piccoli, quantunque in numero senza paragone minori. [...] Veramente pria di dare l'assenso a me stesso ho voluto dubitarne per qualche tempo: Io temeva ciò nascesse per ventura da inganno dell'occhio, potendomisi i volgari globetti presentare in punta alla vista, e quindi giudicarli più piccoli e perciò diversi di specie. Ma l'induzione di replicate, diligenti, e minute osservazioni mi ha fatto vedere, che le due specie de' menzionati globetti si debbono assolutamente distinguere." (L. Spallanzani "Dell'azione del cuore ne' vasi sanguigni, Modena 1768)

through disputes, contrapositions, and attempts at syncretism until the seventeenth century, were filtered through a fine mesh of philosophical reflections containing prohibitions that were the real hobbles on the progress of scientific knowledge. A new vision of the organisation of the natural world, which opens with the great philosopher-scientists Galileo (1564–1642), Descartes (1596–1650), Newton (1642–1727), and Leibniz (1646–1716), and in this New Science context the dramatic microscopical discoveries of Leeuwenhoeck (1632–1723) Marcello Malpighi, and then of Abraham Trembley (1710–1784), John Turberville Needham (1713–1781), and Spallanzani put an end definitively to the old Aristotelian and Galenic paradigms.

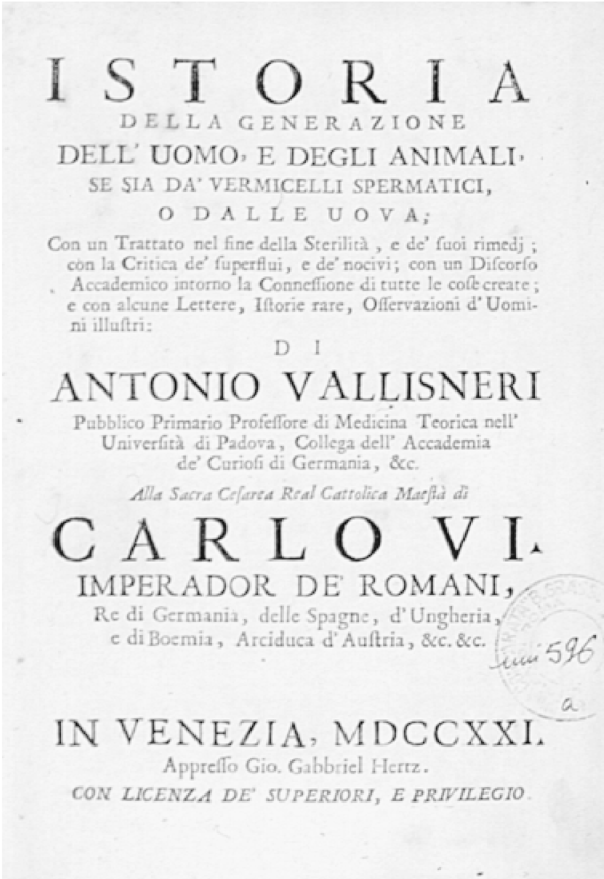
This time too, the scientific revolution springs from the work of that same great anatomist who overturned the Galenic model of the circulation of the blood: William Harvey. In 1651 he published his *Exercitationes de generatione animalium* (Fig. 3), which repeats in its title the work of Aristotle. In its construction, the work is Aristotelian, but it marks the origin of a new construction of scientific thought based on the analysis of concrete facts, not on their consistency with philosophical systems. Thus in the course of a few decades, this paradigm of the ancient world arrived at its definitive downfall. Harvey placed the origin of the new organism in the egg. The substantial correspondence between the courses of development of oviparous and viviparous creatures, well demonstrated in the works of Volcher Coiter (1534–1576) (Adelmann, 1933) and Fabricius (1621), convinced Harvey of the essential uniformity of the processes in the two categories of living creatures. Harvey, however, maintained (in this agreeing with Aristotle) that the sperm performed its fertilizing action through an immaterial principle and that the later development of the eggs, produced by the wall of the uterus, took place through subsequent additions, part by part, starting from the blood that supplies the uterine walls. In terminology formulated later, we could say that Harvey was "*ovist*" since he situated the material basis of the future organism in the egg, and "*epigenesist*" since he considered the phenomena of development extrinsic to the potentialities contained in the egg.

True ovism came later, thanks to the succession of observations of the female genital apparatus of viviparous animals conducted in Holland by Johann van Horne (1621–1670) and by the Dane, Niels Stensen (1638–1686), in Italy called Stenone, anatomist of the Grand Duke of Tuscany.

Fig. 3. Title page of the Hague edition (1680) of William Harvey's *Exercitationes de Generatione animalium*. Jupiter is shown opening an egg from which spring out many animal species: a baby, a deer, a bird, etc. Corsini library of the Accademia Nazionale dei Lincei.

But the decisive contribution is due to Renier de Graaf (1641–1673) in his *De mulierum organis generationis inservientibus* (1672). The egg, however, was still invisible and remained so until 1827, when it was discovered by Karl Ernst von Baer (1792–1876). But, as Antonio Vallisneri (1661–1730) affirmed, the egg of the mammals had to exist and to be produced by the ovary (Fig. 4) (Vallisneri, 1721).

Galen's paradigm of double seeding fell defini-



ISTORIA
DELLA GENERAZIONE
DELL' UOMO, E DEGLI ANIMALI,
SE SIA DA' VERMICELLI SPERMATICI,
O DALLE UOVA;
Con un Trattato nel fine della Sterilità, e de' suoi rimedj; con la Critica de' superflui, e de' nocivi; con un Discorso Accademico intorno la Connessione di tutte le cose create; e con alcune Lettere, Istorie rare, Osservazioni d' Uomini illustri:
DI
ANTONIO VALLISNERI
Pubblico Primario Professore di Medicina Teorica nell' Università di Padova, Collega dell' Accademia de' Curiosi di Germania, &c.
Alla Sacra Cesarea Real Cattolica Maestà di
CARLO VI.
IMPERADOR DE' ROMANI,
Re di Germania, delle Spagne, d' Ungheria, e di Boemia, Arciduca d' Austria, &c. &c.
IN VENEZIA, MDCCXXI.
Appresso Gio. Gabbriel Hertz.
CON LICENZA DE' SUPERIORI, E PRIVILEGIO.

Fig. 4. Title-page of Vallisneri's *Istoria della generazione* (Venice 1721). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

tively. The egg, then, is the origin of the new organism and, according to the canon of orthodox ovism, that new organism was perfectly pre-formed, an invisible miniature inside the egg. In the construction of the ovist system, the role of sperm remained to be clarified. Harvey had not seen sperm in the uterus of deer dissected immediately after coitus. This observation, which passed undiscussed, excluded physical action by the sperm in fertilization and led the ovists to formulate the theory of an *aura spermatica,* volatile and spiritual, very Aristotelian flavor, able to set in motion the manifestation of the miniaturized germ within the egg. We shall see hereunder Spallanzani's contribution to the confutation by experiment of this hypothesis of the *aura spermatica*.

OVISTS AND "VERMICELLAI"

But while the egg of the viviparous animals remained invisible, the spermatozoon did not. Only five years after the work of de Graaf, another Dutchman, Anton van Leeuwenhoeck, discovered in human sperm minuscule creatures, *animalculi*, endowed with active motion, not so different from the microscopical animals he had discovered in rainwater.

Thus animalculism was opposed to ovism. Let it not be thought, however, that the animalculist hypothesis derived immediately from the discovery of the spermatozoon. That hypothesis required many years and, above all, the elaboration of a strong theoretical framework so that it could sustain a dialectical confrontation with that of the ovists.

The intransigence of the discoverer of spermatic animalcules led Leeuwenhoeck to deny the very existence of the invisible *ova viviparorum* and to sustain that the animalcules were implanted directly in the uterine wall. Further, the metaphor of the spermatic "worm" transformed in the foetus in the same way as the tadpole is metamorphosed into the frog seemed impossible to propose even in animalculist circles. So that metaphor rapidly was replaced by another, no less improbable, of the pre-formation of a *homunculus*, a little man in miniature inside the animalcule, seen or imagined, and exactly drawn by imaginative microscopists such as the Frenchman Francois de la Plantade (1670–1741) (Fig. 5). This hypothesis was, with great determination, upheld by physiologists of great prestige such as Jan Swam-

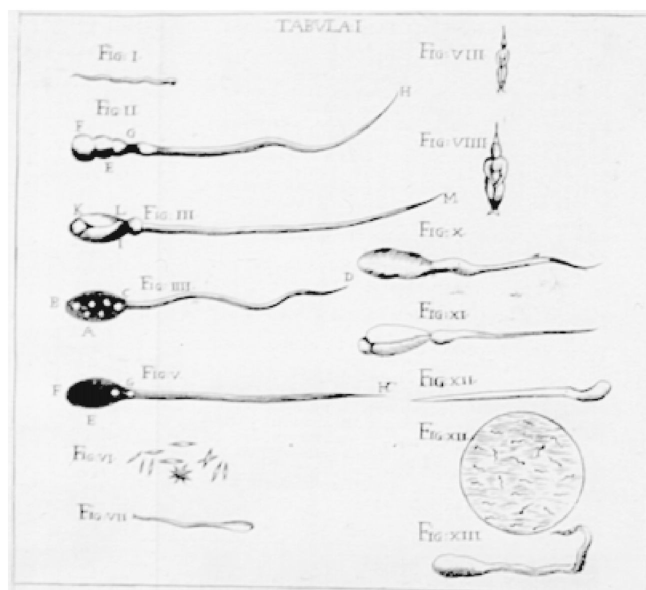


Fig. 5. Table from Vallisneri's *Istoria della generazione* where different spermatozoa are represented. Notice figures VIII and VIIII showing the "*Homunculus*" according to François de la Plantade. Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

merdam (1637–1680), author of the renowned *Bijbel der Nature*.

Such was the state of the art when Spallanzani started studying the problem of generation and tackled it experimentally. A convinced ovist, like most physiologists in the eighteenth century, he referred ironically to the animalculists as *vermicellai*, a name he derived from the *vermicelli spermatici* (little spermatic worms).

The theoretical position accepted by Spallanzani was that upheld by Charles Bonnet (1720–1793) to whom he was bound in deep friendship, and by Baron Albrecht von Haller (1707–1777). An ovist, preformist philosophical position also was acceptable theologically. A preformation of the germ envisaged even the preformation of the germs of succeeding generations, Charles Bonnet maintained in his *Palingénésie* (1770), so allowing the Creator to create with Eve all subsequent humanity.

The preformist hypothesis encountered severe criticisms on the scientific plane. A young Berliner, Caspar Fridric Wolff (1733–1794), meticulously contradicted, with detailed observations on the development of chicks, the description given by von Haller. Wolff (1759) succeeded in demolishing the preformist theory by demonstrating that chick organs proceeded to form one after another according to a decidedly epigenetic scheme.

On the basis of his frog development observations, Spallanzani thought he had corroborated Hallerian preformism. Studied at the microscope, frogspawn seemed identical before and after fertilization. Not only that, it was never possible to see the "*vermicello spermatico*" inside the egg after fertilization. Spallanzani (1768b) believed that he had demonstrated that the spermatozoon made no contribution to egg development, thus refuting the animalculist thesis. Having found no apparent transformation in the fertilized egg, he thought he also had contradicted the epigenetic thesis. On this occasion, our Spallanzani did not show great sagacity. It was easy to object, as the Abbé Felice Fontana (1730–1805) did in a letter to Spallanzani (Fontana 1768), that he repeated almost entirely in his *Lettera ad un amico sopra il sistema degli sviluppi* (Fontana 1792), that the absence of organization before fertilization was clear evidence of the absence of preformation and, therefore, demonstrated epigenesis.[3] Penetration of the egg by spermatozoon was demonstrated much later, in 1875, by Oscar Hertwig (1849–1922), in sea-urchin eggs (Hertwig, 1875), considerably more transparent than those of the frog. Hertwig used optical instruments certainly more adequate than the "Macchinetta di Lyonnet" the simple microscope used by Spallanzani (Fig. 6).

Preformism met other difficulties of a scientific nature. I shall mention only a few, those that Spallanzani tackled by experiment, including the problem of spontaneous generation of living creatures from inanimate material: irrefutable and evident proof of epigenetic development of living forms from organic material.

Another problem was whether the spermatozoon participated materially in fertilization, or whether this process was due to an immaterial *aura spermatica*. This question had an interesting corollary in the problem of hybrids: How to explain the inheritance of paternal character if the embryo develops from the egg alone.

Last, but not least in terms of theoretical importance, the problem of regeneration: How to explain the regeneration in single organisms such as the polyps described by Trembley, and that of complex organs in more highly evolved animals in the *échelle des etres vivants* like the lobster-claws of René-Antoine de Réaumur (1683–1757), or our Spallanzani's heads of snails. If the organism is preformed in the embryo, *a fortiori* it is definitively preformed in the adult. How, then, is it possible to replace a piece taken away?

NIHIL DE NIHILO

In the ancient world, the possibility that living creatures were generated from the inanimate was an accepted fact that presented no problem. Aristotle did not exclude the hypothesis of generation from mud and from the putrefying substance of animals without red blood (ἄναιμα), or even of little fishes. Also Lucretius (95–55 B.C.), for all his Epicurean materialism, writes in *De Rerum Natura:* "Nothing can be created from nothing," but a few verses further on in the same work admits "Also many animals are generated from the earth, from the rain and from the heat haze of the sun."[4]

It was only in the climate of the Galilean *Nuova*

[3] "Due sole cose non sono ben chiare per me nel vostro Prodromo, l'una risguarda la circolazione, l'altra la preesistenza del feto nell'ovo non fecondato. […] La seconda non mi par dimostrata chiaramente, almeno io non ne sento tutta la forza, perché i vermicellai e gli epigenesisti vi diranno che non veder nulla nell'ovo infecondato mostra appunto che non v'è l'animale prima della fecondazione, e che l'osservazione oculare sta tutta per essi. Che poi non veggiate nulla d'organico né ancor dopo la fecondazione seguìta da poco vuol dire che l'animale entratovi collo sperma, o i piccoli organini che si van formando successivamente, sono ancora impercettibili all'occhio anche armato di microscopio." (Letter by F. Fontana to L. Spallanzani dated Florence April 15th 1768)

[4] "Quas ob res, ubi viderimus, nihil posse creare de nihilo" (T. Lucretius Caro. De Rerum Natura I, 153–154); Multaque nunc etiam existunt animalia terris, imbribus et calido solis concreta vapore." (ib. V, 747–748)

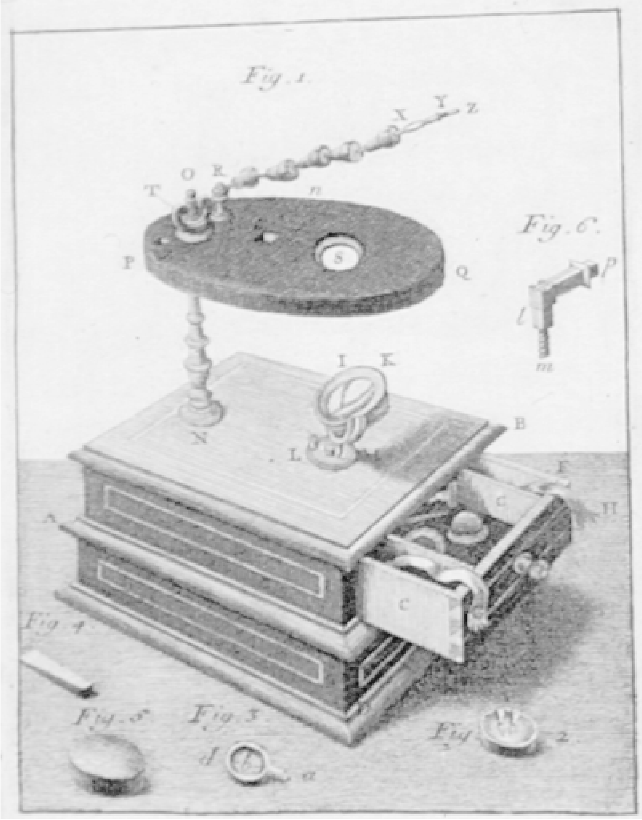


Fig. 6. The *Macchinetta del Lyonnet*, i.e., the simple microscope constructed by Lyonnet, used by Lazzaro Spallanzani for his microscopical observation. Table from Pierre Lyonnet's *Traité Anatomique de la Chenille* (The Hague, 1762), Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

Fig. 7. Portrait of Francesco Redi, from the front page of the "*Opere di Francesco Redi*" (Venice, 1742). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

scientia that the hypothesis was put to the experimental test. Francesco Redi (1626–1698) (Fig. 7) knew medicine and Greek literature well. Homer, in the canto of the Iliad in which Achilles beweeps the lifeless body of his companion Patroclus, writes "I fear that through the wounds inflicted by the bronze the flies may enter the hero's body and there give birth to worms, so that, the life spent, all the flesh will putrefy" (Iliad XIX, 23–37). So Redi recalls that he too "had always seen flies, of the same species as those that will be born, alight on the flesh before it putrefies" (Redi, 1668).[5] Hence derives the famous experiment, certainly known to all: In sealed vessels no flies were born from putrescent flesh, but many were born in those left open. No flies were born even in vessels left open to the air but protected from penetration by flies by a *sottilissimo velo di Napoli* (ultra-fine Neapolitan fabric). Today, we would say covered with gauze.

Rather than on the experiment itself, already well known, I should like to comment briefly on the process that impelled Redi to experiment, the scientific method that would later be typical of the procedure of Spallanzani, i.e., (1) bibliographical knowledge (Homer in this case), (2) critical personal observation, and (3) the bringing to perfection of an adequate experimental apparatus. Redi's experiments are authoritatively confirmed by Swammerdam, Vallisneri and Réaumur.

So we come to the period of Lazzaro Spallanzani,

[5]"Di qui io cominciai a dubitare; se per fortuna tutti i bachi della carne dal seme delle sole mosche derivassero, e non dalle carni stesse imputridite: e tanto più mi confermava nel mio dubbio, quanto che in tutte le generazioni da me fatte nascere, sempre io avea veduto sulle carni, avanti che inverminassero, posarsi mosche della stessa spezie, di quelle che poscia ne nacquero." (F. Redi Esperienze sopra la generazione degli Insetti. Firenze 1668)

when the epigenesis hypothesis of spontaneous generation, although denied at levels of complex organization, presented itself anew at the level of that minuscule world that the new science of microscopy unveiled. This time, however, a well-constructed theoretical framework gave valid enough support to experiments apparently conducted well.

We can trace this new construction back to the rationalism of Descartes. The French philosopher was very interested in the problem of regeneration and expressed his thought about it in various writings. The corpus, however, of his ideas in this sector can be found only in a late-published posthumous collection (Clerselier, 1701), *Primae Cogitationes circa Generatione Animalium.* For Descartes, the generation of the higher animals takes place through an epigenesis process that follows the mixing of the two seeds, masculine and feminine. However, the origin of the lower animal and vegetable forms, and life itself, are provoked by the action of heat on putrescent material. In the one case as in the other, the process is purely epigenetic, exclusively physical, and articulated through the addition of organic parts without the intervention of vital spirits or souls. On this Cartesian basis, Pierre-Louis Moreau de Maupertuis (1698–1759) founded this new system of generation, adding to the generative causes of living creatures in the Cartesian model, i.e., heat, motion and fermentation, the idea derived from Newtonian physics of an attraction between similar particles (Maupertuis, 1745). In his *Système de la nature* (1754) he introduces the concept of psychic attraction between organic particles based on a memory belonging to the material itself and able to direct its development. The intelligence that regulates life and its development for Maupertuis was immanent in the material and does not transcend it.

The hypothesis of generation of Needham, the first Roman Catholic clergyman to be a member of the Royal Society of London, is developed on an epigenic basis. From infusions of the most diverse nature and origins, from the very English mutton broth to the infusion of pepper or cloves, Needham obtained the spontaneous birth of those animalcules that, because of their birth from infusions, the German microscopist Ledermuller (1719–1769) had called *Infusoria*. He attempted, however, a vitalistic vision of the phenomenon, somewhat similar to that in the tradition of the Jesuit Athanasius Kircher (1601–1680). It is not a physical attraction between molecules that generates life but the exhalation of a life force possessed by every slightest fragment of living matter, even after death.

The model proposed by Count Buffon (George-Louis Leclerc, 1707–1788) is definitely mechanistic. Buffon's system of generation is certainly the best put together of all those advanced in the whole of the eighteenth century, and the most Cartesian, in the sense of being a purely rational model aimed at unifying preformism and epigenesis, along with ovism and animalculism. In fact, his intention was to demonstrate that preformism and epigenesis were not analogous concepts, but that preformism could easily find a place within an epigenetic thesis. The epigenetic aggregation of molecules is due not to psychic memories but to physical mechanisms such as internal moulds (*moulages intérieures*). The germ of the future organism is produced by the mingling of molecules coming from both progenitors. But during the lifetimes of the two parents the molecules have formed in the parental internal moulds and, so modified, are subsequently conveyed into the parents' genital organs. This theory explained perfectly both the inheritance of characteristics from both parents and the regular epigenic development toward a very precise prospective form. Preformism, then, exists at the molecular level, and not at that of the *Homunculus* curled up in the spermatic worm of the imaginative drawings of François de la Plantade. Today, when we know about the DNA template that determines the primary structure of the proteins, we might be tempted to read Buffon's hypothesis a modern interpretative key attributing to Buffon a biological prophetic spirit, which certainly is not the case.

While Buffon was an excellent theorist, he was not an equally good experimenter. Thus, when he knew of Needham's experiments and several times met him in Paris, he adopted the Englishman's experimentation and Needham put his best microscope at Buffon's disposal. In the collaboration between the two scientists, Buffon assumed the leadership but Needham did not complain of his supporting role. As an experimenter and observer, Buffon was rather a muddler; not so Needham, who was a more careful experimenter. To cut a long story short, the fundamental texts of this *Systema generationis* were published between 1745 and 1750. Needham began, with his *New microscopical discoveries* in 1745; then in 1749 Buffon published the first volume of his *Histoire naturelle générale et particulière* in which he exposed his general system of animal reproduction (chapter one) and the results of his experiments on spontaneous generation (chapter five). There immediately followed a French translation of Needham's experiments (1750).

THE CHALLENGE TO NEEDHAM AND BUFFON

In those years, Spallanzani was a law student at Bologna University. But certainly there was much discussion of Needham's marvelous experiments and of Buffon's system of generation in the scientific *salon* of Spallanzani's cousin Laura Bassi (1711–1778), mathematician and physicist of Bologna University, which the young Lazzaro frequented and where his conversion to the physical sciences was decided. When Spallanzani published the *Saggio di osservazioni microscopiche concernenti il sistema della generazione de' Signori di Needham e Buffon* (1765) (Fig. 8), he was already more than 30 years old and a Professor of Philosophy at the University of Modena, but above all he had behind him consolidated experience as a microscopist and experimenter. The publication of that essay came after nearly three years of careful experiments, each repeated several times. He did not risk preconceived judgements against Needham and Buffon as Father de Lignac did in a virulent little book (*Lettre á un Américain,* Joseph-Adrien Le Large de Lignac, 1710–1761), but he repeats the experiments of Needham, with whom he enters into correspondence. Obviously the *Saggio* immediately had great success among the preformists. Baron von Haller and, above all, Charles Bonnet were exultant. The latter, who did not know Italian, had the work translated by Trembley, his cousin, Genevan like him. On the contrary, Needham was not at all happy with the deductions that Spallanzani drew with stringent logic from the rigorous experiments that led him to conclude that it was certainly not *l'universale semenza*, i.e., the universal seed, present in the air, that generated living creatures, but the "germs" deposited by the previous generation of Infusoria. Flying in the air there were, if anything, *volanti ovetti*, i.e., little flying eggs, an ovist and preformist conclusion that contradicted the epigenetic hypothesis. The relationship, however, between the two Roman Catholic priests was friendly, and Needham himself attended to the French translation of the *Saggio* printed in Paris and London,

SAGGIO
DI OSSERVAZIONI
MICROSCOPICHE
CONCERNENTI IL SISTEMA
DELLA GENERAZIONE
DE' SIGNORI
DI NEEDHAM,
E BUFFON.

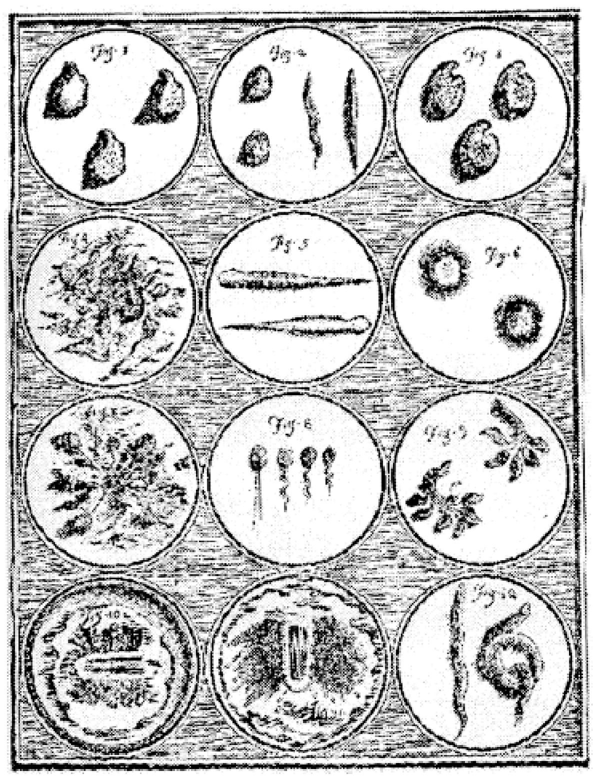


Fig. 8. Table from Spallanzani's *Saggio di osservazioni microscopiche concernenti il sistema della generazione de'Signori di Needham e Buffon* (Modena 1765). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

to which he appended some notes in defence of his own theories.

Spallanzani sent Charles Bonnet (Fig. 9) a copy of the *Saggio*, hot from the press, which initiated an intense correspondence and a profound friendship that lasted throughout the lives of the two great scientists. The complete works of Spallanzani, recently published on the initiative of Modena University, devote to the correspondence between Spallanzani and Bonnet (Di Pietro, 1984–1990) an entire volume of more than 500 pages: 193 letters, equally divided between the two. In the letters written between 1757 and 1765, we can follow the development of the controversy, the counter-deductions of Needham and the arguments of Spallanzani. Some letters from Spallanzani are so long and detailed in their contents, often illustrated with drawings in his own hand, as to be considered real treatises. Bonnet in reply to one of those long letters writes: "I thank you, Sir, for the letter you sent me, I should say indeed the book, which I shall keep as such in my library."

Fig. 9. Portrait of Charles Bonnet. From the *Edizione Nazionale delle opere di Lazzaro Spallanzani*. Carteggi, Vol. 2. Mucchi, Modena, 1984–1990.

In 1769 Spallanzani moved to the University of Pavia, which was becoming one of the major European universities thanks to a wise plan of the Emperor Joseph II of Austria. It was obligatory for a professor called to a new university to deliver a solemn inaugural lecture to the teaching body and all the students. Spallanzani chose as the subject of his inaugural lecture the generation of the organisms in infusions. Also in this text, written in faultless Latin, Spallanzani was prodigal of praise for Buffon and Needham. He wrote: "I have not discussed these things attempting to diminish the fame of Buffon (who am I to contradict such an authority?), nor in order that you, my dear young men, reading and meditating on this, should abandon him" (Spallanzani, 1770).[6] His precise duty, however, being responsible for the scientific development of those adolescents, was to form a critical spirit able to withstand the authority of the famous. In fact, his criticism is sharp of the exhumation he defines as gathered from the science of the ancients, immaterial shaping forces that the new post-Galilean science had definitively banished.

The enthusiasm of Bonnet for that lecture was uncontainable. "Your inaugural lecture seemed to me well thought and well written. It is a pity that the great Francesco Redi was not present, he would hence been enthusiastic. With what great pleasure Malpighi and Vallisnieri would have listened to you."[7]

Spallanzani's *Opuscoli di Fisica Animale e vegetabile* appeared in 1776 (Figs. 10 and 11). The first of them bears the subtitle *Osservazioni ed Esperienze intorno agni Animalucci delle infusioni, in occasione di un esame della nuova Opera del Sig. di Needham*. The English priest had published *Nouvelles recherches sur les découvertes microscopiques et de la génération des corps organisés* (Needham, 1769) in which he tried to

[6]"Neque vero haec a me ita disputantur, ut contendam vel Buffonii auctoritate munuire (quis ego sum, qui cum tanto Homine congredi audeam?) aut vos dilectissimi Adolescentes ab eo legendo, meditatoque amovere." (Lazari Spallanzani in Regio Ticinensis Gymnasio publici naturalis historiae professoris prolusio &. Modena 1770)

[7]"Votre Prolusion m'a paru assez bien pensée que bien écrite. Je vous fais le remerciements. Pourquoi le célèbre Redi n'etoit pas la? Il ne vous auroit pas résisté. Avec quel plaisir encore les Malpighi et les Vallisneri ne vous auroient-ils écouté!" (Letter of Bonnet to Spallanzani, dated "de ma Retraite, le 20 d'Avril 1771")

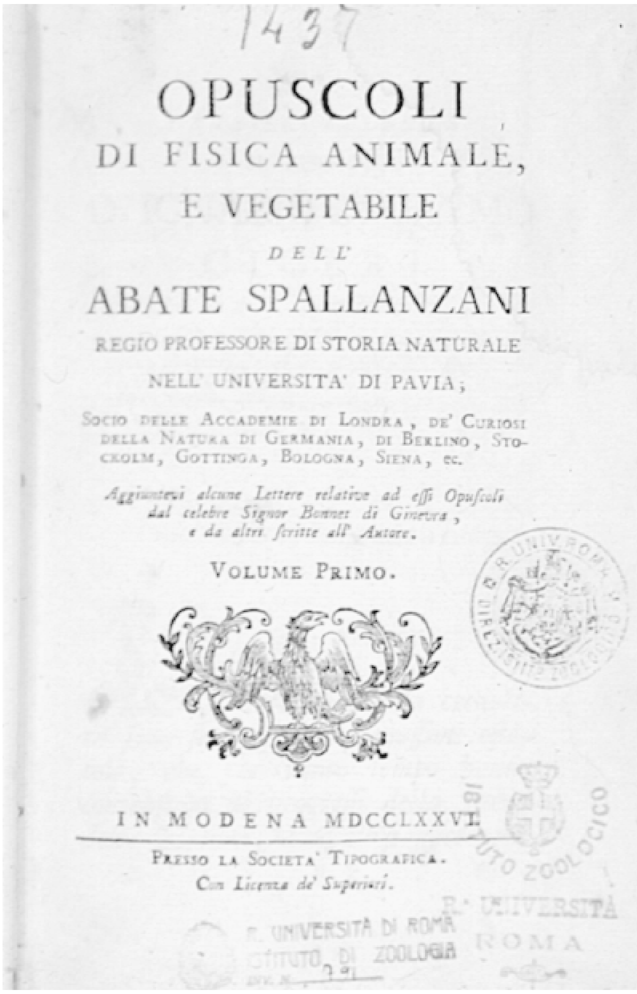

OPUSCOLI
DI FISICA ANIMALE,
E VEGETABILE
DELL'
ABATE SPALLANZANI
REGIO PROFESSORE DI STORIA NATURALE
NELL' UNIVERSITA' DI PAVIA;
SOCIO DELLE ACCADEMIE DI LONDRA, DE' CURIOSI DELLA NATURA DI GERMANIA, DI BERLINO, STOCKOLM, GOTTINGA, BOLOGNA, SIENA, ec.
Aggiuntevi alcune Lettere relative ad essi Opuscoli dal celebre Signor Bonnet di Ginevra, e da altri scritte all' Autore.
VOLUME PRIMO.
IN MODENA MDCCLXXVI.
PRESSO LA SOCIETA' TIPOGRAFICA.
Con Licenza de' Superiori.
R. UNIVERSITÀ DI ROMA
ISTITUTO DI ZOOLOGIA
ISTITUTO ZOOLOGICO
R. UNIVERSITÀ ROMA

Fig. 10. Title page of Spallanzani's *Opuscoli di Fisica Animale e Vegetabile* (Modena, 1776). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

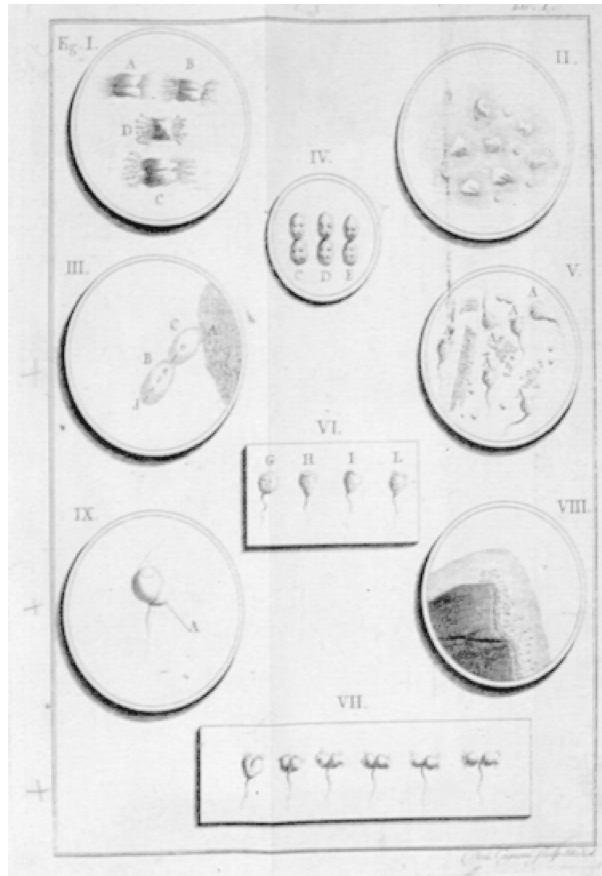


Fig. 11. Table from the first volume of the *Opuscoli* of Lazzaro Spallanzani. Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

bring his system back into favor. Spallanzani's patience was by now at an end, and in his *Opuscolo* his tone became harsh. Spallanzani challenged Buffon and Needham not so much on preformism or epigenesis, as on experimental method and the rigor of experimental protocols: "He who proposes to investigate Nature with his mind cluttered with some preconceived idea does not perform an experiment,"[8] and again "in physics, he errs who instead of questioning Nature tries to intuit her."[9] Spallanzani aims these lapidary phrases as those who "have not too good a mastery of the difficult art of observing well," that is to say, in his opinion, Needham and Buffon. We too, who have made biological experiment our profession should always feel this epistemological concern so well expressed in Spallanzani's text.

Voltaire (Francois-Marie Arouet, 1694–1778) also entered the dispute with all the irony of which he was capable. Having received from Spallanzani a copy of the *Opuscoli di Fisica Animale e Vegetabile*, he wrote in a letter to the Marquis of Villevieille, dated from Ferney, August 26, 1776, "Would you believe that an Irish Jesuit has finished by putting weapons in the hands of atheistic philosophy, sustaining that animals form themselves. In brief, it has been necessary for Spallanzani, the best observer in Europe, to demonstrate unequivocally the fallaciousness of the experiments of that imbecile, Needham. Believe me, my dear Marquis, there is nothing good in atheism." Voltaire was mistaken: Needham was

[8] "Chi discende ad interrogar la natura col capo preoccupato per qualche preferita sua ipotesi non fa Esperimento." (L. Spallanzani, Opuscoli di Fisica Animale e Vegetabile, Tomo I)

[9] "…nella cose Fisiche per lo più sgarra, quando in vece di interrogar la Natura presumiamo d'indovinarla." (L. Spallanzani, Ibidem)

neither a Jesuit nor Irish and, above all, he was not an imbecile. Two things, however, in Voltaire's judgement are exact: Spallanzani was the keenest observer in Europe, and there is nothing good in atheism.

NATURAL FERTILIZATION AND ARTIFICIAL INSEMINATION

After studying the organisms in infusions for 14 years, Spallanzani was convinced that he had terminated definitively the chapter on spontaneous generation. As early as 1771 Spallanzani had begun to interest himself in the phenomenon of fertilization. He had published some first observations in the *Prodromo di un'opera da imprimersi sulle riproduzioni animali* (Spallanzani, 1768b), but he went into the problem in some detail in the second of his *Opuscoli di Fisica Animale e Vegetabile* (Spallanzani, 1776). As a good, convinced ovist he interpreted the *little spermatic worms* as parasites in the seed, perhaps transmitted from one generation to the next, as Vallisnieri thought happened with intestinal worms. Spallanzani was sure that they played no part in fertilization, a function he attributed to the seminal fluid.

With these theoretical assumptions, but without preconceptions, Spallanzani set to work experimentally. He had observed spermatic animalcules in many animals: various mammals, including man, fish and amphibians. Thus equipped with direct personal experience, not basing his words on descriptions by previous authors, he could write: "For many years I had no longer read their discoveries about spermatic worms, therefore, I had only general ideas about them. I should have liked even to cancel those general ideas from my memory in order to approach the research as a *Tabula rasa*, myself open only to the sense of sight, without concerning myself about the discoveries of others."[10] For his first experiment he chose amphibians.

Réaumur (Fig. 12), or rather his collaborator Mademoiselle Moustiers, the fine draughtswoman who executed the illustrations for his *Mémoires pour servir á l'Histoire des insectes* had observed that during the act of mating there issued from the cloaca of the male frog a jet of liquid "like the puff of smoke from a pipe." In 1736 Réaumur, together with the Abbé Jean-Antoine Nollet (1700–1770), put into effect an experimental stratagem (Torlais, '39a,b). He tried to enclose the "posterior" of the male in drawers made of various materials, pig's bladder, taffeta, etc. The two naturalists intended on the one hand to collect the sperm and on the other to verify whether this strange garment could prevent the fertilization of the eggs. Unfortunately Réaumur met with no success because the frogs did not tolerate the unaccustomed garb and freed themselves of it. Spallanzani was more careful in experimenting, more patient in observing, or perhaps, only luckier. Repeating Réaumur's experimental set-up he succeeded in collecting a few drops of sperm inside the drawers with which he had clothed some green toads. To verify the real nature of this liquid, in subsequent experiments he wetted with it some virgin eggs and obtained their complete development. Spallanzani repeated this experiment several times using different amphibian species, taking the sperm directly from the testis or from the vas deferens. He always obtained complete development of the eggs.

It must, however, be recalled that in artificial insemination Spallanzani was preceded, perhaps by a year, by the Baron Weltheim von Harbke, who practiced it in trout and salmon. It was Bonnet who gave the news of this to his Italian friend.[11]

In the article "Fecondazione Artificiale" (Artificial Fertilization) he wrote for the *Enciclopedia Italiana*, Spallanzani wondered whether the practice could be applied to viviparous creatures. It seems that in reality the Arabs already practiced artificial insemination in horses in the Middle Ages (about A.H. 700), but this was not known in Spallanzani's day. Our biologist made the experiment on a little dog, to be precise a female poodle. More than the audacity of the experiment, especially performed by a priest, is the scientific correctness with which it was conducted. The bitch was not primiparous, therefore, her fecundity was certain. She was kept segregated in a place to which only Spallanzani possessed the key and from behavioral signs well-known to breeders, the phase was awaited when the bitch would be on heat and seeking the male, the phase most propitious for insemination. The seed spontaneously

[10]"Era da molti anni ch'io non aveva rivedute le loro scoperte sui vermicelli spermatici e conseguentemente non mi restavano dei pensamenti di questi naturalisti che le nozioni più generiche, le quali avrei anche voluto cancellare dalla memoria, e così trovarmi come tavola rasa in queste ricerche per essere più adattato nel ricever le immagini che mi venivano dal senso dell'occhio, senza preoccupazione delle altrui invenzioni." (L. Spallanzani, Opuscoli di Fisica Animale e Vegetabile, Tomo II)

[11]"Je viens de lire dans la seconde partie du tome XXXV de la Bibliothèque des Sciences un extrait du tome XX des Mémoires de l'Academie de Prusse, où se trouve un fait que nous intéresse tous deux. Le voici. 'Exposition abrégée d'une fécondation artificielle des truites et de saumons, qui est appuyée sur des expériences certaines, faites par un habile Naturaliste' par M.r. Gleditsch, traduit de l'Alemand." (C. Bonnet, letter to L. Spallanzanini, dated "de ma Retraite le 13 Janvier 1781")

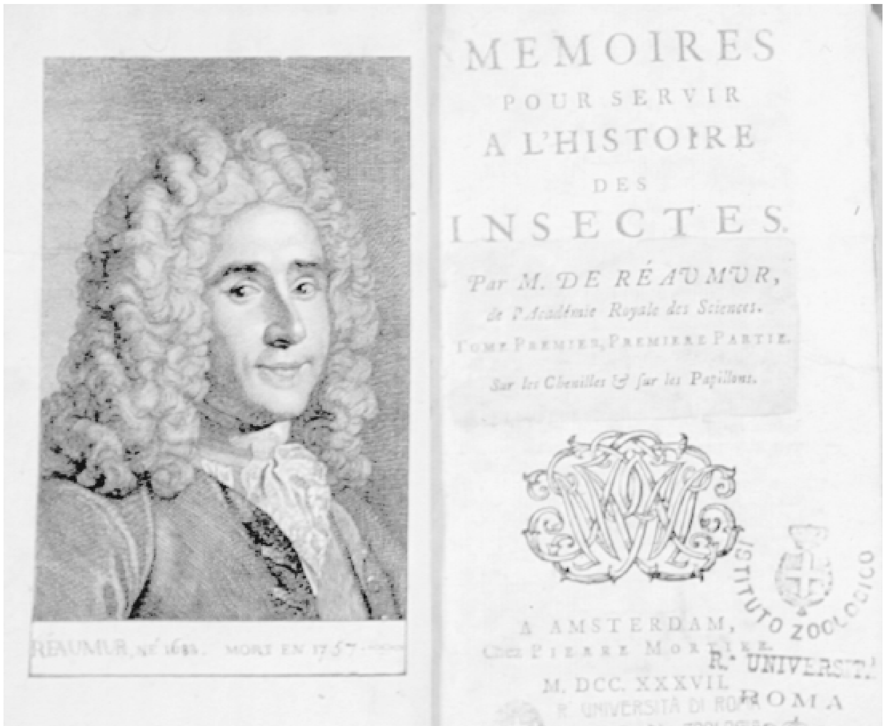


Fig. 12. Portrait of René-Antoine de Réaumur and the title page of his *Mémoires pour servir á l'Histoire des Insects* (Amsterdam, 1737). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

emitted was collected and conserved at 30° Réaumur. After injection of the seed into the vagina, the poodle was again kept sequestered until the signs of pregnancy became unmistakable. Sixty-two days after injection of the seed, the animal littered three pups; two males and one female.

I have some doubts about the spontaneity of the sperm emission affirmed by Spallanzani. He is forgiven the fib because it would have been embarrassing to admit that a priest had masturbated a dog! Our incomparable Abbé is at the zenith of felicity: "I have succeeded in fecundating a quadruped. The happiness I have had from this is among the greatest of my life, since I dedicated myself to experiment."[12] Bonnet, promptly informed of the event, wrote to his friend: "This is one of the most interesting new novelties that have ever been offered for the consideration of naturalists and philosophers since the Creation.... There is nothing finer or more original than this experiment. You have in your hands a precious thread that will lead you to the most important and un-thought of discoveries. And it is not impossible that one day your discovery will find applications in the human species of which we dare not think, the consequences of which would certainly not be slight. You understand me...." (Bonnet, 1781).[13] What would Bonnet, the strict Calvinist theologian, have thought about the present-day practices of assisted fertilization in man?

Probably this prospect did not interest Spallanzani. For him, artificial insemination was an experimental tool for investigating the intimate nature of the problem of generation. What is the nature of the "fertilizing virtue" of the sperm?

EXPERIMENT ON FILTRATION OF SPERM: A MISSED OCCASION

In the second of his *Opuscoli di Fisica Animale e Vegetabile* (1776), Spallanzani reports some tens

[12]"Così a me riuscì di fecondar questo Quadrupede, e la contentezza ch'io n'ebbi posso dire con veritá che è stata una delle maggiori che provato abbia in mia vita, dopodiché mi esercito nella sperimentale Filosofia."

[13]"C'est lá une des plus grandes et des plus intéressantes nouveautés qui se soient offrtes aux yeux des naturalistes et des philosophes dépuis la Création du monde. [...] Vous tenéz un fil précieux qui vous conduira aux découvertes les plus importantes et les plus imprévues. Je ne sais même si ce que vous venez de découvrir n'aura pas quelque jour dans l'espèce humaine des applications auxquelles nous ne songeons et dont les suites ne seront pas légères. Vous pénétrez assez ma pensée." (Letter of C. Bonnet to L. Spallanzani dated "de ma Solitude, le 13 Janvier 1781")


DISSERTAZIONI

DI FISICA ANIMALE, E VEGETABILE

DELL'

ABATE SPALLANZANI

REGIO PROFESSORE DI STORIA NATURALE
NELL' UNIVERSITA' DI PAVIA,

E SOPRANTENDENTE AL PUBBLICO MUSEO
DELLA MEDESIMA;

SOCIO DELLE ACCADEMIE DI LONDRA, DI PRUSSIA, STOCKOLM, GOTTINGA, BOLOGNA, SIENA, DE' CURIOSI DELLA NATURA DI GERMANIA, E BERLINO, CORRISPONDENTE DELLA SOCIETA' REALE DELLE SCIENZE DI MONTPELLIER, EC.

Aggiuntevi due Lettere relative ad esse Dissertazioni dal celebre Signor Bonnet di Ginevra scritte all' Autore.

TOMO I.

IN MODENA. MDCCLXXX.

PRESSO LA SOCIETA' TIPOGRAFICA.

Fig. 13. Front page of the *Dissertazioni di Fisica Animale e Vegetabile* by Lazzaro Spallanzani (Modena 1780). Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

of experiments on amphibians regarding the fertilizing power of the sperm. He detected the sperm, cooled it, heated it, and tried even to measure the unitary dimension to be attributed to the sperm for it to fertilize an egg. Through complicated calculations based on assumptions unrelated to the reality we know today, he arrived at the determination that the dimensional ratio between the "spermatic particle" and the egg had to be about one to 1 billion. For the eggs and spermatozoa of amphibians this value is not so far from being correct.

The most important experiments, for their intrinsic epistemological significance, were those on the nature of the fertilizing power. The accepted doctrine at that time was that of the *aura seminalis* or *aura spermatica*, a sort of vapor emanating from the sperm. Spallanzani, therefore, placed a certain quantity of toad sperm on a watch glass. In the bottom of another glass that he turned upside down to cover the first, he stuck a dozen eggs of the same species. The eggs, however, remained a few millimeters apart from the sperm. After five hours the eggs were covered "as if by a dew," from the condensation of the evaporated seminal fluid, but the eggs did not develop. He repeated the experiment several times, reducing the distance between the sperm and the eggs, joining the two glasses together with putty, or allowing air to circulate freely inside the system. The result was always the same.

So, the spermatic aura did not exist. Fertilization took place by physical contact between the eggs and the sperm. It remained to be clarified which fraction of the sperm was the active part in fertilization. With this aim, from 1781 onwards Spallanzani conducted a series of experiments in the filtration of spermatized water, that is, sperm much diluted with water. The fertilizing power of this water diminished progressively in proportion to the thickness and the number of the filters used, finally disappearing altogether. The fraction active in fertilization remained trapped in the filters, and so was material. Spallanzani counterchecked: He washed the filters with water and this water used for filter washing then acquired the fertilizing property. It would have been enough to examine this water under the microscope. He would have seen in it the abhorred "little spermatic worms," and resolved an old dispute. He did not do it.

Nearly 40 years later, the sperm filtration experiment was repeated by two young French biologists, Jean-Louis Prévost (1790–1850) and Jean-Baptiste-André Dumas (1800–1884). They, however, studied at the microscope the water in which the filters had been washed and saw in it the spermatozoa, which they observed also in the gelatinous coats of amphibian eggs (Dumas, 1825).

THE *JUMARTS*, OR THE PROBLEM OF HYBRIDIZATION

Maupertuis (1745) wrote: "If all the animals of a single species were already formed and contained within one father or one mother, respectively in the form of worms or eggs, would these similarities be observed with both parents? If the foetus were the worm that swims in the seminal liquid of the father, why should it sometimes resemble the mother? Would a foal already formed in the mare's egg develop a donkey's ears because a donkey had set in motion the parts of the egg?"

The preformist physiologists' answers to this objection were never convincing. It must be said that in the eighteenth century hybridization between different species was an accepted possibility; not only between horse and ass, but also in imagination between mare and bull and between stallion and cow. This hypothetical cross-breeding would have given birth to the *Jumarts* in whose existence Spallanzani (1775) believed unreservedly on the strength of the report by Claude Bourgelat, Inspector General of the School of Veterinary Science of France, who affirmed that he had produced them several times. Buffon showed himself more cautious, and biologically less inexpert. In Volume XIV of his *Histoire naturelle*, Buffon reports that he had had occasion to observe and to dissect one of these *Jumarts* and to have come to the conclusion that it was a common hinny.

Spallanzani had long been interested in the problem of hybridization. He began to concern himself with it in a short bibliographical publication (Spallanzani, 1768c), *Memorie sopra i muli di vari autori* in which he set out the state of the art in the question. But when he obtained the artificial insemination of the poodle, he thought that he had the right instrument for proceeding to experimentation. Bonnet, in the letter already quoted (Bonnet, 1781) is prodigal of advice: "Now you possess a sure and easy mean of determine whether this or that species and this or that other can procreate together […] you could try, by introducing through your syringe the sperm of a poodle into the uterus of a cat or a rabbit, or by introducing the sperm of a cat or a rabbit into the uterus of your poodle."[14]

Today it is difficult not to smile at these projected experiments. It seems absurd to us to think that biologists of the quality of Bonnet and Spallanzani could think of producing a hybrid between dog and rabbit. But in that bizarre, contradictory eighteenth century, the possibility of crossing a mare with a bull was accepted without discussion. Some even considered it possible to cross a rabbit with a hen. The great Réaumur (1749) discussed this in all seriousness, reporting that the experiment had been attempted by a certain Abbé Fontenue.

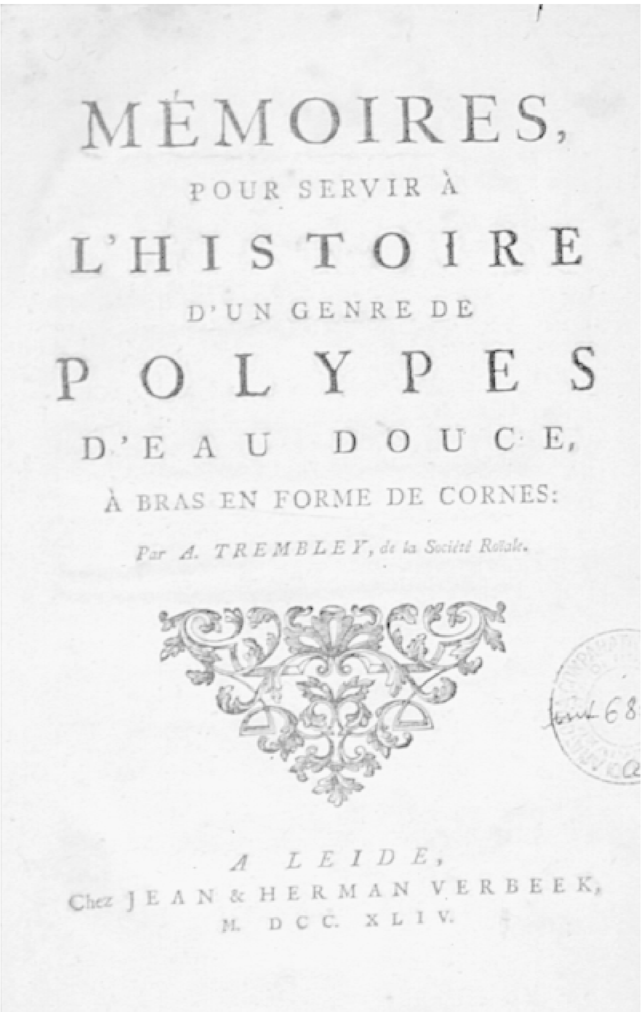
In the wake of his success with dogs, Spallanzani (1783) attempted to cross dog with cat, and obviously failed. He had a project of crossbreeding a she-ass with a bull, to obtain the mythical *Jumart,* but never carried it out. He was more occupied (Spallanzani, 1780) with his experiments on the amphibia, more easily handled and which he already had used in experiments in fertilization. He attempted hybridization between urodeles and anurans, and between anurans of different families, Hylidae, Ranidae, Bufonidae, and Pelobatidae, without achieving any success. He concluded that crossbreeding between "batrachians" of different species was not possible. The error in Spallanzani's experimental approach was to attempt crosses between species systematically remote from each other, as was pointed out by Arthur de l'Isle (1873), who a century after Spallanzani's experimentation succeeded in crossbreeding various congeneric anuran species. Spallanzani worked with species whose gametes matured in the same period of the year, and could not have done otherwise.

LES COLIMAÇONS DU RÉVÉREND PÈRE L'ESCARBOTIER

We come now to the problem of the regeneration of parts of animals, which, as we said at the beginning, is situated in the context between preformism and epigenesis.

One may well say that the problem of regeneration, or "animal reproduction" as it was called then, was among the first that Spallanzani investigated experimentally, starting in 1765. He published his first results of these experiments in his *Prodromo di un opera da imprimersi sopra le riproduzioni animali* (Spallanzani, 1768b). This theme in experimental biology was opened in scientific terms by Réaumur (1712), who described the regeneration of claws, nippers, and antenna in various crustacean species. But if the claws of crustaceans did not present excessive philosophical problems, the regeneration of an entire hydra from a fragment of it, described by Trembley (1744) (Fig. 14), unleashed a succession of disputes on the naturalistic plane—for example, if the little creatures were animals or plants—and also on the metaphysical and theological plane. What happens to the soul of the polyp? In which of the two fragments does the soul remains? If it remains in one to animate the process of regeneration, how does the other fragment, in which it must be lacking,

[14]"Vous possedez á present un moyen bien sûr et bien facile de vous assurer si telle ou telle espèces peuvent procréer ensemble et les espériences que vous-vous proposés […] ne vaudront pas celles que vous tenteriez entroduissant avec votre seringue le sperme de ce barbet dans la matrice d'une lapine ou d'une chatte, et introduissant le sperme du lapin ou du chat dans la matrice de la chienne. " (Letter of C. Bonnet to L. Spallanzani dated "de ma Solitude, le 13 Janvier 1781")



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. 14. Front page of the *Mémoires pour servir à l'Histoire du Polypes d'eau douce* (Genéve, 1744), by Abraham Trembley. Library of the Department of Animal and Human Biology, Rome University "La Sapienza."

manage to regenerate? One must, then, admit that the soul is not indivisible, but that it may be divided in two to make the two fragments regenerate. In this argument, which today seems ridiculous, intervened the most famous naturalists of the time: von Haller, Bonnet, Réaumur, and even, as was only to be expected, Voltaire. Voltaire upheld the vegetable nature of the hydra and so resolved the problem simplicistatically. Bonnet and Réaumur directed their studies to the regeneration of the heartworm, of which the animal nature could not be doubted, and of which the regenerative capacities were well known. Spallanzani too devoted himself to this experimental analysis, but according to very precise experimental protocols he sectioned the body of the earthworm at different distances from the head and succeeded in determining what today is called a gradient of regenerative capacity. He divided the animal into several parts and noted that not only the part with the head regenerates, but also the caudal part and intermediate fragments between the two. He even described the regeneration of regenerated parts. Where, then, is the seat of the earthworm's soul? But as Bonnet wrote in his *Palingénésie* "In physics, souls are very convenient things. They are always available for any eventuality, since they are invisible, untouchable and unknowable, and we can attribute to them whatever one wishes."

Even before publishing his discoveries in the *Prodromo*, Spallanzani communicated them by letter to Bonnet (Spallanzani, 1778). The naturalist of Geneva was enthusiastic. He compared his Italian friend to Redi and Malpighi (Bonnet, 1776).[15]

In that same year that the *Prodromo di un opera da imprimersi sopra le riproduzioni animali* was published, Spallanzani was elected a member of the Institut de France. Then this veritable box of wonders, "une petite boite toute pleine de prodiges," as Bonnet put it (1768) was opened among the academicians of France, revealing its portentous contents. One gem in this collection was the phenomenon of the regeneration of snails' heads. The discovery was communicated to the *Académie des Sciences de Paris* and propagated immediately to the general public by an article in the newspaper *Avant-Coureur* of May 20. The sensation aroused by the news was due to the fact that it was not the leg of salamander or the claws of crab that were regenerated, but the heads of complex organisms. The time had not yet arrived when in Paris crowned heads fell under the guillotine without any hope of regeneration, but to think of heads that could be re-grown from the neck was certainly not bad! Opposing parties were formed. On one side were aligned those who, having attempted it unsuccessfully, did not believe in regeneration, and on the other those who did. Among the latter was the great Lavoisier (1743–1794), who although destined to lose his own head under the guillotine of the Revolution, managed to see a snail's regenerated. Between 1768 and 1770, a great number of snails lost their heads,

[15]"Toutes vos observations, toutes vos expériences, toutes vos réfléxions prouvent également vôtre patience, vôtre sacacité et vôtre sagesse, Continués comme vous avés commencé. Je puis facilement prédire que vôtre nom sera placé a côté de celui des Redi et des Malpighi, vos illustres compatriottes." (Letter of C. Bonnet to L. Spallanzani dated Genève, le 9 Octobre [et 1 Novembre] 1766)

and only a small percentage of them developed a new one.

Spallanzani's experiment was correctly set up on the basis of an exact knowledge of the animal's anatomy. He described precisely how to cut it, noted himself that whenever the cerebral ganglion, which he called the brain, was compromised the regeneration did not occur, and so on. Thus he anticipated the criticisms of those who did not obtain regeneration. The cut Spallanzani made was oblique, not vertical, and others objected that operating in this way he cut off the skullcaps, not the heads. Today we know that the phenomenon is considerably more complex than Spallanzani or the other naturalists of the eighteenth century could imagine. The process involves factors of induction and of territorial competence with regeneration dependent on what species is chosen for the experiment, since in some *Helix*, e.g., *H. nemoralis*, the regenerative capacity is good, while in others, e.g., *H. ericetorum*, it is rather limited.

Voltaire, too, began to cut off snails' heads to obtain, in some cases, regeneration and in others the animal's death, when the cut removed the anterior ganglion of the periosophageal cingulum. The fantasy and sagacity of the great French philosopher are fully shown in his publication on this subject (Voltaire 1768). The title alone exemplifies the irony of which he was capable: *Les Colimaçons du Révérend Père L'Escarbotier, par la grace de Dieu capucin indigne, Prédicateur ordinaire et Cuisinier du gran Convent de la Ville de Clermont en Auvergne. Au Révérend Père Elia, Carme Chaussé, Docteur en Théologie*. The allusion to the Reverend Father Spallanzani is obvious.

Bonnet, who harbored some resentment against Voltaire, who had reproved him for the mysticism with which he filled his scientific analysis, alerted Spallanzani: "He is making fun of you!… The poet plays at being a Naturalist"[16] (Bonnet, 1768). But Spallanzani was not of this opinion. In fact, Voltaire did not deny the possibility demonstrated by Spallanzani of regeneration of the head of those molluscs: In a letter to Bonnet, Spallanzani (1768d) minimized the episode and concluded: "Voltaire's book has made the same impression on me as the greater part of his work: it has amused me."[17]

The question of regeneration of snails' heads needed revision and a final word because the sensation it created had been too great. Spallanzani took the subject up again in two texts (Spallanzani 1782, 1784) that focused exclusively on this problem. In the first, he intended to close the question with a phrase that expressed well his scientific personality: proud, intolerant of criticism by others, and absolutely convinced of the merits of his ideas and of his experimental tests. "Lo sperimentare comunque è mestiere di tutti, lo sperimentare a dovere è sempre stato, e sará sempre, di pochi," i.e., "To experiment whatever is work for everybody, to experiment as one should is, and always will be, work for few."

THE INHERITANCE OF SPALLANZANI

The inheritance that Spallanzani left us stands written in the phrase: the experimental method as the fundamental instrument for investigating biological processes. Certainly in this approach he followed the line traced by the physicists of the Florentine Accademia del Cimento, Galilean in its approach, which stated as its motto "Provando e Riprovando", i.e., try and try again. But Spallanzani succeeded in making this method an absolute discipline. In a text written in his maturity and published posthumously (Spallanzani, 1803b), he wrote almost as a spiritual testament: "This is my fundamental method, whatever I tackle, even the most disparate things, so long as they have material causes: to take no account of the opinions, however authoritative and respectable, of those who have defined them before, but to dedicate oneself to a practical examination of the facts."[18]

The need to restrict my contribution to the phenomena of reproduction and development has obliged me to neglect other fundamental works performed by Spallanzani, from fundamental ones on digestion (Spallanzani, 1780), and respiration (Spallanzani, 1803), to those on the orientation of bats (Spallanzani, 1794), on animal electricity, and on marine bioluminescence (Spallanzani, 1794).

[16]"Elle roule sur vos expériences; vous vous amuserés á voir le poëte s'ériger en garçon naturaliste, et vous reconnoîtrés qu'il disserte mieux sur un point de litterature que sur un point d'histoire naturelle." (Letter of C. Bonnet to L. Spallanzani dated Genthod, October 8th 1768)

[17]"La brochure de Voltaire a causé en moi cette impression que j'eprouve de la plus grande partie de ses ouvrages, c'est á dire elle m'a fait rire." (Letter of L. Spallanzani to C. Bonnet dated á Modene ce 15 Novembre 1768)

[18]"Tale appunto essendo l'inalterabile mio metodo nelle cose eziandio le più universalmente abbracciate, ma che dipendono dai fatti, di prescindere dall'autoritá ancorché rispettabilissima di chi le ha stabilite allorquando discendo a un pratico esame de' medesimi fatti." (Memorie sulla Respirazione, opera postuma dell'Abate Lazzaro Spallanzani, Memoria III, § XXXI)

Thus the stature of this great scientist may seem diminished in this text by comparison with this real greatness. I, however, believe that as a scientist Spallanzani is of a stature equal to that of William Harvey. In fact, when speaking of the circulation of blood one cannot fail to mention the great English physiologist, in the same way that when tackling a problem by experiment in working on the biological processes of development, in any biology laboratory whatsoever, one cannot fail to pay tribute to the memory of Lazzaro Spallazani.

ACKNOWLEDGMENTS

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