Marcello Malpighi and the difficult birth of modern life sciences

Marco Piccolino

All his life, Marcello Malpighi (1628–1694), the founder of modern microscopic anatomy, was unwillingly involved in difficult debates within a reactionary medical milieu that questioned the significance of modern science and its utility to medicine. Malpighi's responses to his detractors, included in posthumous works first published in 1697 by the Royal Society, offer an important insight into a critical phase of scientific progress in the 17th century and help to reveal the prevailing conception of science. In some ways, Malpighi's views predate important ideas in modern biology.

I never had believed, and never would, the vulgar notion that some men are condemned by some concatenation and series of unknown causes to perpetual troubles and annoyances not only in their domestic affairs but also in more important ones, such as literary matters, and yet this seems indeed proved and verified in my life. Soon after becoming a physician I began to see sharp written attacks against the doctrine I was professing ... Then as time went on I have read books published against me, books with humiliating titles and full of raillery: and finally there was an epistle against my studies entitled *De Recentiorum Medicorum Studio Dissertatio Epistolaris ad Amicum* in which the author execrates and impugns rational medicine and, embracing empiricism, tries hard to prove that anatomy is useless.[1]

Marcello Malpighi

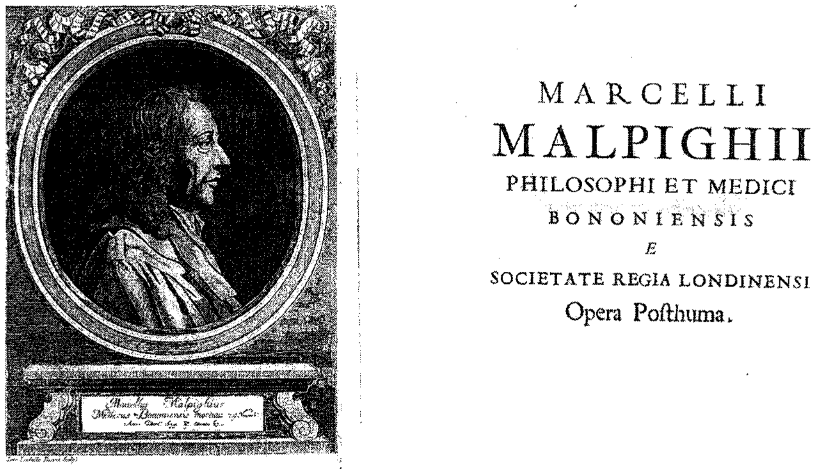

Figure 1 The initial pages of the *Opera Posthuma* (from the 1698 Venetian *in folio* edition), courtesy of the Accademia delle Scienze of Ferrara.

This passage is contained in the response that Marcello Malpighi, Professor at Bologna University, wrote in defence against the anonymous author of a pamphlet that appeared in Bologna around 1689. This latter document contested the utility of modern science for medical practice (see Ref. 1). Malpighi, who did not wish to inflame the polemics that had accompanied his scientific life, instructed that his response was to be published after his death. The Royal Society of London elected Malpighi as an honorary member in 1669 and systematically published his works (Figure 1); accordingly, his response to *De Recentiorum Medicorum* was included in the *Opera Posthuma* first published by the Royal Society in 1797. This volume also contained a response written by Malpighi, in 1665, against *Galenistarum Triumphus*, a violent pamphlet[2] issued by the traditionalist medical community of Messina, where he was Professor of Medicine from 1662 to 1666.

It seems ironic that a man, who longed for a life dedicated exclusively to his studies in the retirement of his country home, 'to mitigate the irksomeness of a life of poor health'[3], should devote a considerable part of his time to polemical writings against his detractors.

Malpighi's scientific contributions

Malpighi's achievements in several scientific fields cannot be overstated[4–6]: he provided fundamental contributions to anatomy, embryology, entomology, botany and pathology. Importantly, Malpighi discovered blood capillaries, thus filling the 'gap' in blood circulation left by Harvey[7] (and contributing to the acceptance of the 'new physiology' initiated by the Harvey's discovery[8]) and he was also first to detect the red blood corpuscles (*atoma rubra*). Moreover, he showed that lung parenchyma, far from being a homogeneous structure as the name implied ('parenchyma' meaning effused blood), was composed of microscopic alveoli, closely associated with capillaries (Figure 2). In the kidney, he identified (Malpighi's) corpuscles, key elements of the microscopic filtration system, whose description was completed about two centuries later by William Bowman[9]. Importantly, Malpighi contributed to understanding the structure of the skin and its accessory formations (with a clear recognition of its sensory structures associated with nerve terminations), and first described the microscopic structure of the gustatory papillae of tongue (Figure 3).

In embryology, Malpighi worked along the path initiated by Harvey, in aiming to examine the individual parts that Nature produces in the construction of complex organisms, probably acting similarly to 'craftsmen who, in the construction of machines, ... prepare preliminarily the single parts so

Marco Piccolino

is at the Dipartimento di Biologia dell'Università di Ferrara, 44100 Ferrara, Italy.
e-mail: pic@dns.unife.it

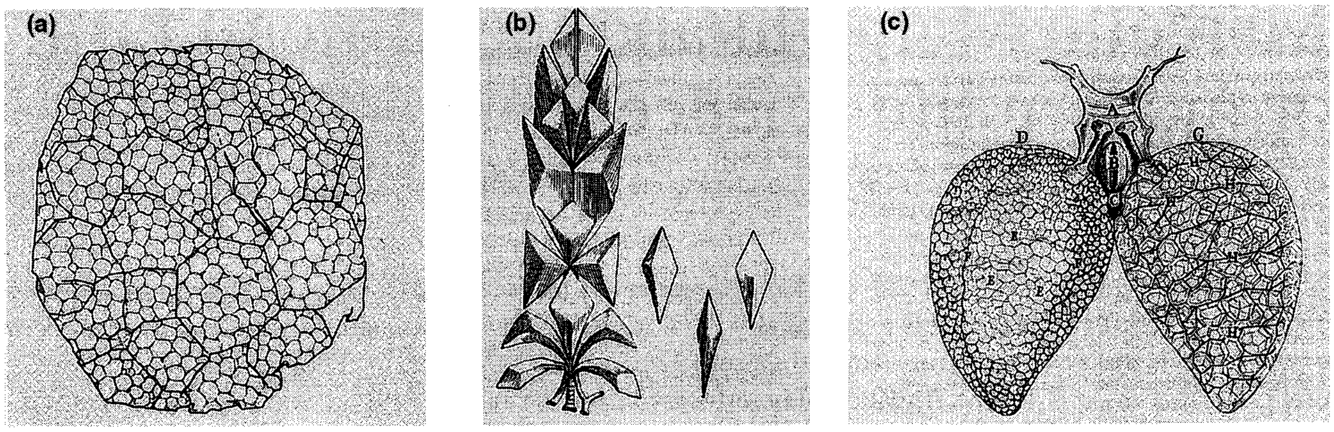

Figure 2 Images from Malpighi's works on frog lung. Desiccated lung scrap (a) with clearly visible alveolar design. Different insertion modalities of lung lobules to trachea and blood vessels (b). Notice the diamond design reminiscent of the mathematical characters of the 'Book of Universe' according to Galileo (see text). Frog lung (c) with the alveolar design on the left (E) and pulmonary artery branching on the right (H). Courtesy of the Library 'G. Romiti' of the Anatomical Institute of the University of Pisa.

that one could see separately the pieces which must afterwards be assembled'[10]. In *De Formatione Pulli in Ovo*, Malpighi followed the developmental stages of the chicken and, among other things, detected the vascular area with the terminal sinus, the cardiac tube and aortic arcs, the somites, the neural plicae and the neural tube, and the cerebral and optic vesicles (Figure 3).

Malpighi also made a fundamental contribution to entomology with *De Bombyce*, the first systematic treatment of the microscopic anatomy of an insect – the silkworm[11]. The treatise contained detailed descriptions of the different developmental phases (larva, pupa and moth) by which an amazing animal machine develops that is capable of producing silk threads. It also illustrated the respiratory channels (the famous *tracheae*), the pulsating vessels of the circulatory system (the 'tiny hearts' or *corcula*) and a variety of other original observations. This work was later considered as '... a tissue of discoveries, a treatise from which one can learn more about the wonderful internal structure of insects than from all earlier works combined'[12].

Along with the contemporary works of Nehemiah Grew[13], Malpighi also laid down the foundation for the microscopic anatomy of plants. In particular, he recognized the importance of leaves in plant physiology, envisioning them as laboratories producing the substances necessary for plant growth. Moreover, Malpighi inaugurated modern botanical pathology, recognizing that galls – the abnormal outgrowths of some plants – are caused by the deposition of insect eggs, and he thereby came closer to recognizing the role of infection in some diseases[14].

Rather than continuing to survey Malpighi's achievements, where even a simple list could fill several pages, we should ask how a single man could make so many discoveries in so many different fields. There are several possible reasons, which I discuss below.

The experimenter and his influences

Notwithstanding his apparently poor health, Malpighi was an indefatigable experimenter. His daily activities can be readily assessed from his systematic record of experimental activity. For a single day, there are records of a prodigious number of experimental observations made on tens of different vertebrates and invertebrates, and plants (see Ref. 5). Moreover, Malpighi was very talented as an experimenter and he profited from the technical advancements of his epoch, especially from the microscope that Galileo had started using for the observation of living organisms[5,6].

> To the knowledge of nature one arrives more easily with the sense aided by the art, by means of the valuable instruments discovered in the present century, which with two glances of the immortal Galileo has discovered more than all the past millenniums have beheld: and with the microscopes applied to the view of the smallest parts of the animated body, has seen in the smallest animals, marvellous machines, bizzarries and pranks, in the perfect ones, it has revealed the structure of many viscera and the contexture of many machines: anatomy can consequently hope for a great progress from the magnification that this instrument makes possible.[1]

This passage, from Malpighi's response to the Galenists of Messina, contains important hints about his scientific program and the revolutionary climate in which his endeavour flourished.

Although Malpighi had no direct contact with Galileo (1564–1642), the great physicist of Pisa was nevertheless a fundamental reference for him. Malpighi taught theoretical medicine in the University of Pisa from 1656 to 1659, and was indirectly influenced by Galileo's work via Giovanni Alfonso Borelli (1609–1679), an eminent mathematician and physicist, who was professor in the same University. Borelli's lifelong scientific program was to found a new animal physiology based on physical laws, which culminated in the publication *De Motu Animalium*, the manifesto of a new science that we would now call biomechanics[15].

According to Galileo, we should try to interpret the immense 'Book of Universe' by learning the language and the characters in which it is written: 'It is written in a mathematical language and the characters are triangles, circles and geometric figures'[16] (see Figure 2). But what language did the scientists in Borelli's laboratory use to interpret the internal organization of living beings? Without doubt they drew analogies with man-made mechanisms and used the language of machines (see Ref. 17), as Malpighi indicates in his response to the *De Recentiorum*. His adversaries considered modern anatomy and modern science generally useless for practical medicine, but Malpighi notes that by examining body parts by means of dissection, philosophy and mechanics, their structure and use could be learnt and *a priori* models formed. From a series of such models, aided by reasoning, physiology, pathology and medicine were founded. Nevertheless, Malpighi thought that:

> The way our soul uses the body in operating is ineffable, yet it is certain that in the operations of growth, sensation, and motion the soul is forced in conformity with the machine on which it is acting, just as a clock or a mill is moved in the same way by a pendulum or lead or stone, or by an animal or by a man; indeed if an angel moved it, he would produce the same motion with changes of positions as the animals or agents do. Hence, even though I did not know how the angel operates, if on the other hand I did know the precise structure of the mill, I would understand this motion and action, and if the mill were out of order, I would try to repair the wheels or the damage to their structure without bothering to investigate how the angel moving them operated.[1]

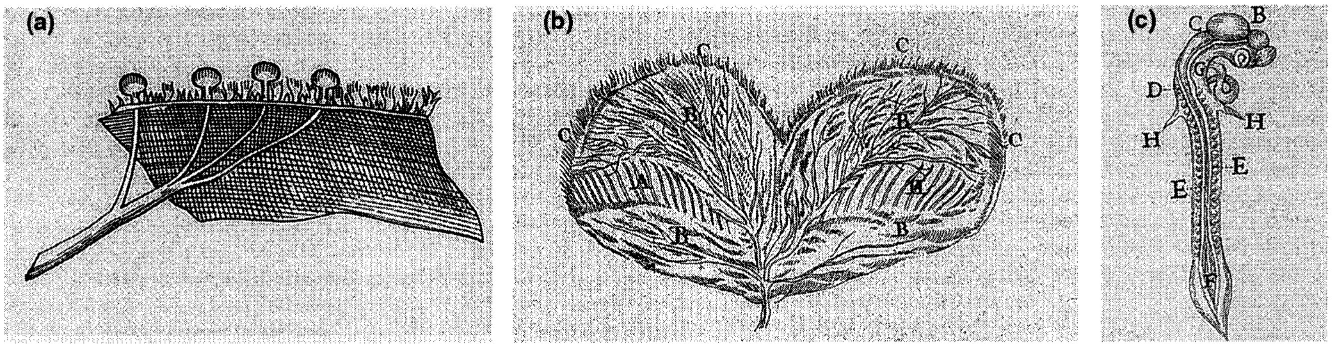

Figure 3 Images from Malpighi's works that are of neuroscience interest. Tongue scrap (a) showing the continuity between nervous fibres and gustatory papillae. Preparation of fish brain (b) with blood vessels and nervous fibres particularly visible (A and C). This is possibly the first published image of brain microscopic anatomy (year 1665). Malpighi assumed that the brain had a glandular structure, but he did not publish any image of his 'brain glands', which were probably preparation artefacts[6,25]. Developing nervous system of chick embryo (c) with clearly visible spinal cord, encephalic vesicles and optic vesicles. Courtesy of the Library 'G. Romiti' of the Anatomical Institute of the University of Pisa.

Responses to detractors

Malpighi spent much of his life systematically investigating the composition of the body machine and how it works, interrupted only because he was obliged to take up his quill and write in defence of 'his science'. From Malpighi's polemical writings we can vividly appreciate the difficulties that marked the emergence of modern life sciences and, moreover, we can gain important insight into the methodological attitude of a protagonist of the scientific revolution of the 17th century.

Although the two polemical responses published in the *Opera Posthuma* are a defence against the attacks of the traditional medical community, they implied a different defensive attitude on Malpighi's side. The main argument of detractors was somewhat contradictory in the two circumstances. In the first case, the criticism of modern science was based on the idea that the foundations of medicine had been established forever by the studies of classics, in particular by Galen, and thus there was no need for further research. According to the Galenists of Messina, medicine was, like mathematics, an axiomatic science that proceeds by deductions and, since the principles established by the Ancients are absolute truth, medical knowledge is not open to revision.

To undermine this antagonistic thesis, Malpighi analysed classical texts and showed that, even in Greek and Alexandrine science, medicine was subject to revisions and there were disagreements between authors about fundamental physiological aspects; for instance, in the doctrine of the 'four body humours' (blood, phlegm, choler and melancholy). Differences also existed in the writings of a given author, for instance Hippocrates or Galen, during various periods of their life. Malpighi proceeded by asserting that medical science was far from being a closed book with the last word already written. He pointed out that many problems had been left by the Ancients that could only be solved through experimental investigation based on anatomy, particularly microscopic anatomy. However, he contended, an exaggerated respect for the Ancients might be harmful, as exemplified by the French anatomist who, having noticed in his animal dissections that some things did not correspond to Galen's teaching, concluded that animal bodies had changed since Galen's time.

In opposition to a dogmatic and retrograde vision of medicine, Malpighi praised the scientific discoveries of his times, and particularly the experimental character of modern science, which did not base validity exclusively on *a priori* reasoning as Galenists did:

> human concepts are so fallacious when they are not derived from the teaching of Nature that we should better investigate by ourselves the body of animals or men, instead of being confident on what is written in books.[1]

By alluding to one of Borelli's classical experiments, Malpighi showed how the classical notion of medicine that places the source of 'vital heat' in the heart can easily be dismissed simply by measuring the temperature in various body parts with a thermometer, and noting that the temperature in the intestines and muscles is no less than that in the heart[15]. Even the precepts of practical medicine, Malpighi said, 'depend not on discourses and rational progresses but on the observation, frequently experimented, even without giving reason of it'[15].

Malpighi was thus giving particular emphasis to the experimental character of scientific endeavour, and the last passage seems to be inspired by an empiricist creed. Knowledge is based on observation, both direct and aided 'by the new mechanisms, which have served to help our weak senses', and on experimentation with its artifices, which helps us to reveal the 'smallest components, structures and organisations' of living organisms. The controversy with the Galenists could easily be discounted as a result of the difficulty that a conservative cultural milieu had in accepting a science that was drastically undermining an apparently immutable body of knowledge.

It proved to be more complicated for Malpighi to reply to the publication of *De Recentiorum*. The author of the latter can easily be identified as Giovanni Girolamo Sbaraglia, Malpighi's colleague. Sbaraglia also invoked the authority of the Ancients, but his criticism was more subtle and based on the contention that, notwithstanding its great progress, modern science had provided no significant contributions to practical medicine (see Ref. 18). According to Sbaraglia, medicine was eminently empirical. It was based on the ability to recognize certain symptoms, to evaluate the efficacy of treatments and to predict the course of diseases – abilities that a medical practitioner acquires from his everyday activity and from records of medical histories. The conclusion therefore was that there is no need to study the structural and functional organization of the human body to be able to practise medicine: a knowledge of human anatomy would only be needed for wound healing, but for this purpose medical students need not spend a long time in practising dissections. In particular, there is no need to study minute anatomy (*subtilior anatome*) or to carry out dissection of animals (*anatome comparata*) and plants (*dendranatome*). Sbaraglia noticed that, in his time, the introduction of a medicament like cinchona bark resulted from empirical observations, and not from the modern study of organisms. Even Harvey's discovery of blood circulation had not changed the treatment of heart diseases to a significant degree. According to Sbaraglia, far from being useful for medical practice, a theoretical attitude might potentially limit the freedom of observation, the real base of knowledge acquisition.

Sbaraglia had as his main reference the 'empirical sect' of classical medicine, and in particular its principal member, Aulus Celsus, who maintained that Nature is essentially incomprehensible and thus knowledge can be exclusively pragmatic. Sbaraglia was not an isolated and out-dated voice, but reflected a general reaction against 'rational medicine' that had important supporters in Gideon Harvey, Thomas Sydenham and John Locke (see Refs 18,19).

Malpighi responded to Sbaraglia by a careful analysis of texts, and showed that classical medicine was based on a rational study of Nature and gave anatomy prominent importance. Galen had praised the importance of anatomy and had studied it in various animals to understand the organization of the human body and he also investigated plants. He did not study very small animals because he could not trust himself in the absence of adequate observational instruments.

A rational life science

In spite of the empiricist confidence in the power of personal observation Malpighi knew rational medical practice could not be established using only simple observation, a description of symptoms and records of medical histories. He argued that it is impossible for a given practitioner to come into contact with an unlimited variety of diseases in the course of his practice and, moreover, new and more complicated diseases can emerge – diseases that nobody had encountered previously – which would require an approach that did not derive exclusively from empirical observation.

Sbaraglia's criticism of modern science was not without grounds. Since Harvey's discovery of the circulation of the blood, life sciences had made more progress in a few decades than during the past millennia; however, the advances in practical medicine had been deceptive. Therapy had not changed considerably, and mankind still depended on old-fashioned medicaments and out-dated treatments. Indeed, when Malpighi tried to exemplify the utility of new discoveries for rational therapy, there was still the question of revulsives, vesicatories, diaphoretics, lenitives, blood-letting and treatments aimed at rendering internal humours more or less fluid or more or less acid.

But what then? Were *subtilior anatome*, *anatome comparata*, *dendranatome*, and the whole modern science, really useless for practical medicine, as Malpighi's adversary was asserting? Certainly not. In the 17th century, confidence in the practical usefulness of science maintained by Malpighi, and by the various scientists who contributed to the revolution in life sciences in Europe, was in many respects utopian; but to faith in this utopia we owe much of modern medical progress. The notion advocated by Malpighi, that medicine should be a 'rational science', has guided its progress in western culture through the past three centuries. In Malpighi's understanding of the word, 'rational' meant based on a system derived, through logical deductions, from the achievements of the experimental study of organisms and, more generally, from any relevant scientific progress.

A strong aversion for empiricism from a scientist who, far from being a speculative philosopher, was an extremely hard-working experimenter and one who trusted experimentation as the necessary basis of scientific progress, might appear difficult to understand. For Malpighi and other great experimental scientists of the 17th century, 'rationality' both implied an internal coherence of knowledge and also a guarantee of the truthfulness of scientific assertions. Pure empiricism is open to charlatanism, because, owing to the limits of individual experience, one must necessarily depend on what one hears from others. Thus, in the absence of a critical method of evaluation, one must necessarily trust some of the stories that fill printed pages. Old medical literature is full of absurd stories, on which authors pretend to base the value of their scientific conceptions: women that burn spontaneously, owing to an excess of internal fire (or of electricity), men that emit light and produce electrical shocks (like electric fish) during sexual intercourse[20], and so on. Although less gullible than in ancient times, more recent medical practice may not be immune to charlatanism; as witnessed by the miraculous effects of empirical treatments seen in the mass media.

But apart from the practical implications of a 'rational' life science, where Malpighi was more farsighted than his adversaries, he contributed significantly to other important notions largely verified by modern science. 'In its things', Malpighi said, 'Nature operates by necessity always in a uniform way ... Even though they appear disparate, the things of Nature are not so disconnected that one cannot observe a concatenation and uniformity in operating'[1]. The vastness of Malpighi's interests was surely a result of a belief in the uniformity of Nature's plan: by enlarging the field of our studies, we can hope to penetrate the secrets of Nature because we can see how it, by starting from a single model, creates somewhat different structures or machines according to the particular necessities of animal economy.

Malpighi passed easily from the study of one animal to another in the aim of elucidating a particular problem, extending the analogy from animals to plants and vice versa. Possibly only Harvey before him held a similarly clear notion that one needs to find suitable experimental preparations, and that, by studying the variations of a given structure among different species, or in a given species throughout its embryological development, is it possible to obtain important hints as to its function. After studying mammals unsuccessfully, Malpighi turned to the frog in which he could detect capillaries and clearly see how blood passes from arteries to veins in the frog lung, an ideal preparation because of its transparency and the fact that it does not collapse when the chest is opened. To establish whether there is a continuity between the nerve fibres observed in the medullar (white) matter of brain and the similar fibres of the spinal cord, Malpighi studied the nervous system of fish, whose structure appeared more suited to direct observation than that of mammals.

In his second epistle on lungs, Malpighi remarks that we should investigate both lower ('imperfect') and higher ('perfect') animals because 'Nature is wont to undertake its great works only after a series of attempts at the lowest level, and to place in imperfect the rudiments of perfect'[21]. And elsewhere he notes that 'the study of insects, fish and of the first and rough sketches of animals in the course of their development, has taught to this present century more than did past ages which limited themselves to the study of perfect animals'[22]. For Malpighi, even 'monsters or all other errors of Nature teaches to our ignorance in a more easy and sure way compared to the wonderful and perfect machines of Nature'[22]. He knew that the study of varieties in all their aspects was the way to penetrate the intimate design of Nature and could never be a purely descriptive search. The rationale for extending the limits of scientific inquiry appears clearly in Malpighi's first work on plant anatomy:

> The nature of things is enveloped in darkness and it manifests itself only through analogy. Thus we must investigate Nature in its totality, so that we can resolve the most complicated machines through those more simple and more accessible to sensible experience.[23]

In his second work on plants[14], Malpighi considered the growth of vegetal tissues by subsequent increments and discussed the similar plan Nature uses in the growth of bones and of dental tissues, whose structure and development Malpighi could study particularly well in young animals or foetuses.

According to the life scientists following the path traced by Galileo, one of the salient aspects of the way Nature operates in building up wonderful organic machines is by using minute structures (*minima* or *atoma*), so small that they can be perceived only through the microscope. But, 'if with the microscope you may discern many subtle structures, you must conclude that there are others, even smaller ones, such that they can escape any acuteness of the instruments made by us'[23]. The discovery of minute machines in organic tissues, previously supposed as unstructured, was thus the announcement of more minute ones, as the vision through the telescope of thousands of stars in galaxies was the announcement of even a greater multitude of celestial bodies. The old atomism of Democritus was thus rising again in the *zootomia democritaea*, as the new fine dissection of organisms was called in the 17th century[6,24].

Concluding remarks

This is an epoch in which biology has rediscovered the uniformity of Nature's plan: how it is sustained throughout evolution; how the function of 'perfect' structures can be made different by small readjustments; and how small the 'molecular machines' are on which life's designs are based. It is abundantly clear, therefore, just how insightful Malpighi and his generation of biologists were who contributed to the scientific revolution of the 17th century. We can perhaps rejoice in recognizing that we belong to the epoch prophesied by Malpighi when he wrote: 'the operative industry of Nature is so prolific that machines will be eventually found not only unknown to us but also unimaginable by our mind'[22].

Acknowledgements

This article is largely inspired by the fundamental works on Malpighi written by Luigi Belloni and Howard B. Adelmann (most of the English translations of Malpighi's texts were derived from Adelmann). I thank Lucia Galli-Resta and Adriana Fiorentini for critically reading the manuscript. Moreover, I express my gratitude to Maria Grieco, Laura Padovan and Vincenzo Reale of the University of Pisa, and to Carlo Alberto Segnini of the 'Domus Galileiana' of Pisa for help in accessing old scientific literature.

Selected references

1 Malpighi, M. (1697) *Opera Posthuma*, Churchill
2 Lipari, M. (1665) *Galenistarum Triumphus, Novatorum Medicorum Insanias Funditùs Eradicans*, Ruffo
3 Malpighi, M. (1675) *Anatome Plantarum Idea*, Martyn
4 Malpighi, M. (1686) *Opera Omnia*, Scott & Wells
5 Adelmann, H.B. (1966) *Marcello Malpighi and the Evolution of Embryology*, Cornell
6 Belloni, L. (1967) *Opere Scelte di Marcello Malpighi*, UTET
7 Harvey, W. (1628) *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*, Fitzeri
8 Bertoloni Meli, D. (1997) in *Marcello Malpighi, Anatomist and Physician* (Bertoloni Meli, D., ed.), pp. 21–62, Olschki
9 Bowman, W. (1842) *Philos. Trans. R. Soc. London* 132, 57–80
10 Malpighi, M. (1673) *Dissertatio Epistolica de Formatione Pulli in Ovo*, Martyn
11 Malpighi, M. (1669) *Dissertatio Epistolica de Bombyce*, Martyn & Allestry
12 Réaumur, R.A.F. (1736) *Mémoires pour Servir à l'Histoire des Insectes*, Imprimerie Royale
13 Grew, N. (1672) *The Anatomy of Vegetables Begun*, Hickman
14 Malpighi, M. (1679) *Anatome Plantarum – Pars Altera*, Martyn
15 Borelli, G.A. (1680) *De Motu Animalium*, Bernabò
16 Galilei, G. (1623) *Il Saggiatore*, Mascardi
17 Giglioni, G. (1997) in *Marcello Malpighi, Anatomist and Physician* (Bertoloni Meli, D., ed.), pp. 149–174, Olschki
18 Cavazza, M. (1997) in *Marcello Malpighi, Anatomist and Physician* (Bertoloni Meli, D., ed.), pp. 129–145, Olschki
19 Wolfe, D.E. (1961) *Bull. Hist. Med.* 35, 193–220
20 Bertholon, P. (1786) *De l'Electricité du Corps Humain*, Croulbois
21 Malpighi, M. (1661) *De Pulmonibus Epistola Altera*, Ferroni
22 Malpighi, M. (1666) *De Viscerum Structura*, Montii
23 Cesi, F. (1625) *Apiarum*, Mascardi
24 Severino, M.A. (1645) *Zootomia Democritea*, Endterianis
25 Clarke, E. and Bearn, J.G. (1968) *J. Hist. Med. Allied Sci.* 23, 309–330