TIMELINE

# Exorcizing the animal spirits: Jan Swammerdam on nerve function

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For more than 1,500 years, nerves were thought to function through the action of 'animal spirits'. In the seventeenth century, René Descartes conceived of these 'spirits' as liquids or gases, and used the idea to explain reflex action. But he was rapidly proven wrong by a young Dutchman, Jan Swammerdam. Swammerdam's elegant experiments pioneered the frog nerve–muscle preparation and laid the foundation of our modern understanding of nerve function.

The seventeenth-century scientific revolution, which established the foundations of much of modern science, is generally associated with physics and astronomy, and the work of giants such as Galileo and Newton. However, remarkable and decisive discoveries were also made in biology (or 'natural history'), although most modern scientists know little of this work and even less of the researchers who pioneered important aspects of today's knowledge.

In both the physical sciences and natural history, the key objective of the scientific revolution was to discover new facts and to test previous knowledge of the natural world using the new techniques of experimentation, materialism and mathematical or mechanical models. The particular episode in the scientific revolution described here — the abandonment of the hypothesis of 'animal spirits' to explain nerve function — not only reveals how some familiar concepts and experiments were first developed, but also casts a fascinating light on how we interpret our own experimental findings. In particular, it shows us that the hypotheses we put forward to explain the natural world are often heavily influenced by the social world. For example, computers are now the most advanced form of our ability to manipulate nature, and concepts such as information, programming and feedback loops are used to model and explain biological phenomena. Today, it is literally impossible to imagine anything richer or more powerful than this model. Eventually, this approach will no doubt seem quaint and limited, but will nevertheless be respected for the insights it has provided. This salutary and exciting truth can be appreciated by studying the power of a more limited analogy, which dominated the scientific revolution in the middle of the seventeenth century.

### A clockwork universe

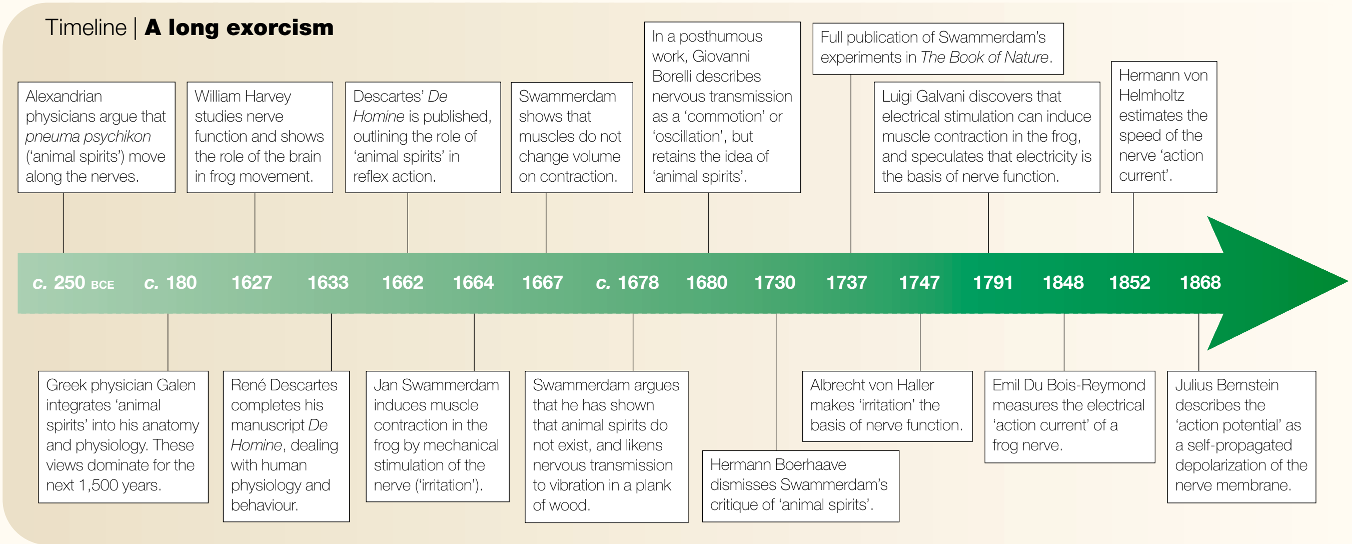
Mechanics were at the cutting edge of human technology 350 years ago. By harnessing various sources of power — mainly springs, water or wind — machines could be made to measure time, to process food or to pump water. The mechanisms involved in such machines were relatively easy to understand, but the nature of the forces that powered them (pressure, kinetic potential and so on) remained obscure. Just as the analogy of a clock was used by astronomers to explain the movement of the stars — to the extent of building celestial clockwork models, or orreries — so, too, natural historians looked to the most advanced contemporary technology for inspiration, and considered living organisms as divine machines, worked by the types of force that were involved in human-built mechanisms.

The most important advocate of this view was the philosopher René Descartes (1596–1650), who lived and worked in the newly founded Dutch Republic, which was more tolerant of his radical views than his native France. In the early 1630s, Descartes set out his view of animal and human behaviour in *De Homine* (Treatise of Man)[1] (TIMELINE). However, he apparently abandoned plans for publication when he saw how another scientific revolutionary, Galileo, was being treated at the hands of the Catholic Church. *De Homine* was eventually published posthumously in 1662.

Descartes explained behaviour and its underlying physiological bases by using the model of the hydraulic-powered mechanical statues or automata that could be found in many royal gardens, and which would move, strike poses and even sing. A few years earlier, William Harvey (1578–1657) had toyed with a similar analogy in his unpublished and unfinished work *De Motu Locali Animalium* (On the Local Movement of Animals)[2], but he did not fully develop his ideas. Descartes' breakthrough was that he argued that the only difference between machines and animals was the intricacy of the underlying mechanisms. As far as humans were concerned, the difference lay in our possession of a soul, which Descartes helpfully localized to the pineal gland, a structure that he claimed was unique to humans.

The implication of this brave and powerful analogy was twofold. First, the vast majority of human behaviours (all except those involving the soul) had analogies in the activities of animals and could therefore be studied through the investigation of animal behaviour. And second, because behaviour was fundamentally mechanical, it could be understood and its causes should be rational and lawful.

By placing behaviour and its underlying anatomical elements on the level of mechanics, and by implicitly validating the use of animal models, Descartes outlined a powerful research strategy for understanding the




biological bases of behaviour. This was in marked contrast to the established view, which went back to the concept codified by the Greek physician Galen of Pergamum (AD 129 to *c.* 216). For Galen, movement was produced by 'moving spirits'[3] that travelled down nerves, which were hollow. However, neither Galen nor any of his followers ever clarified what the 'spirits' were made of, nor how they contributed to movement. This idea had been around for more than 1,500 years without leading to any important discoveries. Indeed, when scientists such as Harvey did use Galen's concept of 'spirits of motion' to try to develop their understanding of movement, the result was confused speculation rather than precise results[2]. Descartes effectively blew away the confusion and allowed behaviour to be studied using scientific methods. For that alone, today's neuroscientists owe him a great debt.

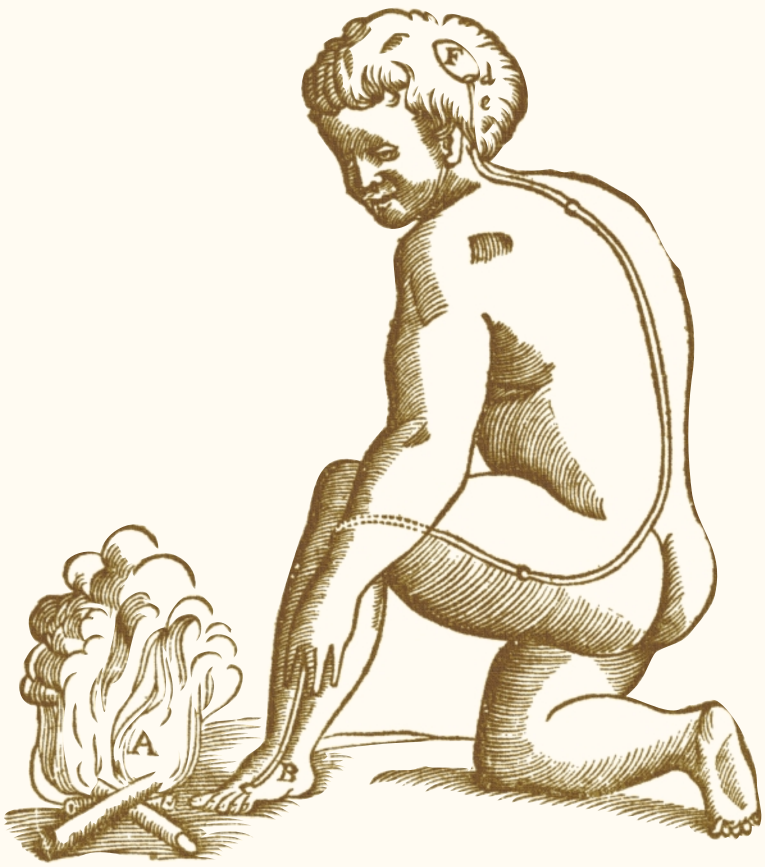



Figure 1 | **Descartes' illustration of his hypothesis of the movement of the 'animal spirits' in response to burning.** A, fire; B, foot; C,C, "small thread"; d,e, "pore"; F, "concavity" containing "animal spirits". For a full description, see the main text. Reproduced from REF. 1 © Bibliothèque Inter-Universitaire de Médicine, Paris.

### From theory to experiment

But Descartes was a philosopher, not an experimental biologist. However striking and stimulating his ideas, they had to be put to the test of empirical study. To make matters easier, his model was extremely precise: for Descartes, the mechanisms involved in movement and nervous transmission functioned on literally the same basis as the hydraulic systems that made automats move. This was made quite explicit in his description of reflex movement in reaction to a heat source (FIG. 1):

> "if the fire A is close to the foot B, the small parts of this fire, which, as you know, move very quickly, have the force to move the part of the skin of the foot that they touch, and by this means pull the small thread C,C, which you can see is attached, simultaneously opening the entrance of the pore d,e, where this small thread ends … The entrance of the pore or small passage d,e, being thus opened, the animal spirits in the concavity F enter the thread and are carried by it to the muscles that are used to withdraw the foot from the fire"[1].

This was the first clear discussion of reflex action in the history of science[4]. Using strictly mechanical concepts, Descartes put forward an explanation of how movement can take place without conscious intervention, focusing on the action of the nerves in a primitive form of reflex arc. Much of modern neuroscience can trace its roots back to this brilliant inspiration. However, Descartes was profoundly mistaken in virtually every other respect. Proving this turned out to be remarkably simple, because of two logical consequences of this view. First, the 'animal spirits' invoked by Descartes to explain nerve action, far from being his invention, were part of the common legacy of nearly 2,000 years of physiology and medicine[5], which had been codified by Galen. In Descartes' hands, and with the model of the hydraulic automats in mind, 'animal spirits' progressed from something unknowable to a substance that was analogous to a liquid, "a wind" or "a very fine flame" [1]. Through a precise mechanical analogy, the original vague vitalism was transformed into a modern mechanistic conception. Second, the movement of the 'animal spirits' from the brain ventricles through the nerve to the muscles, which was at the heart of Descartes' model, implied that the muscles had to be connected to the brains for movement to take place. Furthermore, because of Descartes' mechanical vision of the nature of the 'animal spirits', their movement from the nerves to the muscles should cause the muscles to increase in volume on contraction.

This was a huge step forward from Galen's view, but within three years of publication, Descartes' fundamental hypothesis of the bases of behaviour lay in tatters. This was due to the decisive experimental work of a young Dutchman, Jan Swammerdam (1637–1680). While he debunked Descartes' ideas, Swammerdam provided science with a key preparation for studying nerve function, as well as providing the basis of our modern understanding of nerve action and its role in more complex behaviours.

**Enter the frog**

Swammerdam is, sadly, largely forgotten by today's scientists, although his work on insect development and anatomy, using dissection and microscopy, had a fundamental role in the emergence of biology[6–8]. On 8 December 1664, while on a visit to Paris, Swammerdam carried out a gruesome but intriguing experiment in front of Olaf Borch (1626–1690), a Danish botanist who left a clear account of the study in his diary[9]. Swammerdam cut the heart out of a living, unanaesthetized frog and showed that this had no effect on its ability to move: the severely damaged animal would carry on swimming about. On the other hand, if the brain was removed, movement ceased. (Unknown to Swammerdam, or to anyone else, Harvey had discovered the same thing 40 years earlier[2].)

Swammerdam concluded that the circulatory system was not necessary for movement

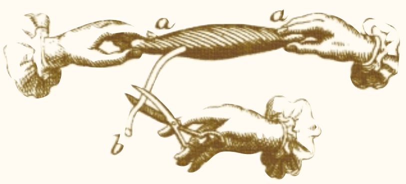



Figure 2 | **Swammerdam's frog nerve–muscle preparation.** *aa*, tendons; *b*, propending nerve. For a full description, see the main text. Reproduced from REF. 10 © Bibliothèque Inter-Universitaire de Médicine, Paris.

— at least in a frog — and that the brain was required for coordinated movements such as swimming. So far, so good for Descartes.

But Swammerdam then took the dying frog, its body bloody and gaping, and showed that if he stroked his scalpel on the severed nerve ends around the wound, the muscles contracted. This result, which he had observed informally in 1662 when dissecting dogs, showed that movement could occur without any connection between the muscle and the brain, thus putting paid to the part of Descartes' theory that involved the movement of 'animal spirits' from the brain to the muscles. Furthermore, the fact that what Swammerdam called 'irritation' could lead to movement strongly indicated that 'animal spirits' were not involved in nervous transmission and muscle movement at all.

Over the next three years, Swammerdam perfected his experiment and his vision of its implications, aware that the frog was particularly appropriate for such studies because "the nerves are very conspicuous in these animals, and may be easily discovered and laid bare."[10] He made a brief description of the effects of 'irritating' a nerve, in his anonymous 1665 article *In Ranis* (On the Frog)[11]. Furthermore, in his 1667 doctoral thesis[12], he publicly showed that movement of the dog's diaphragm could also be produced by stimulating the cut nerve.

He tried to see whether the same effect could be observed in an isolated nerve–muscle preparation: "Another very delicate and useful experiment may be made, if one of the largest muscles be separated from the thigh of a Frog, and, together with its adherent nerve, prepared in such a manner as to remain unhurt."[10]

This instantly recognizable procedure, which has been described as "one of the most important experiments of the century"[13], has since become a classic[14], being widely used in neurobiological studies and repeated in high schools the world over.

The initial demonstration simply involved holding the muscle then stimulating the nerve (FIG. 2):

> "if … you take hold, *aa*, of each tendon with your hand, and then irritate *b* the propending nerve with scissors, or any other instrument, the muscle will recover its former motion, which it had lost. You will see that it is immediately contracted, and draws together, as it were, both the hands, which hold the tendons."[10]

Not satisfied with demonstrating the effect only to the person holding the muscle, Swammerdam then proposed a more precise version of the same experiment (FIG. 3):

> "If we have a mind to observe, very exactly, in what degree the muscle thickens in its contraction, and how far its tendons approach towards each other, we must put the muscle into a glass tube, *a*, and run two fine needles *bb* through its tendons, where they had been before held by the fingers; and then fix the points of those needles, neither too loose nor too firmly, in a piece of cork. If afterwards you irritate, *c*, the nerves, you will see the muscle drawing *dd* the heads of the needles together out of the paces; and that the belly of the muscle itself becomes considerably thicker *e* in the cavity of the glass tube, and stops up the whole tube, after expelling the air. This continues till the contraction ceases, and the needles then move back into their former places"[10].

In principle, this procedure could have transduced the contractile power of the muscle onto a measurable scale — one of the key features of the scientific revolution was the mathematization of natural phenomena. Swammerdam then went on to put the final

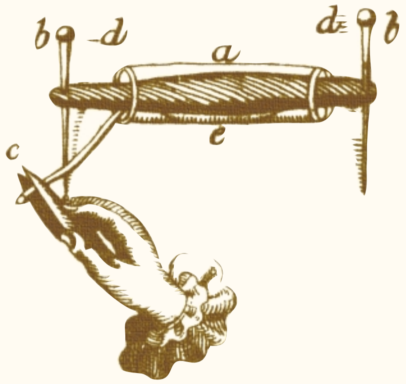
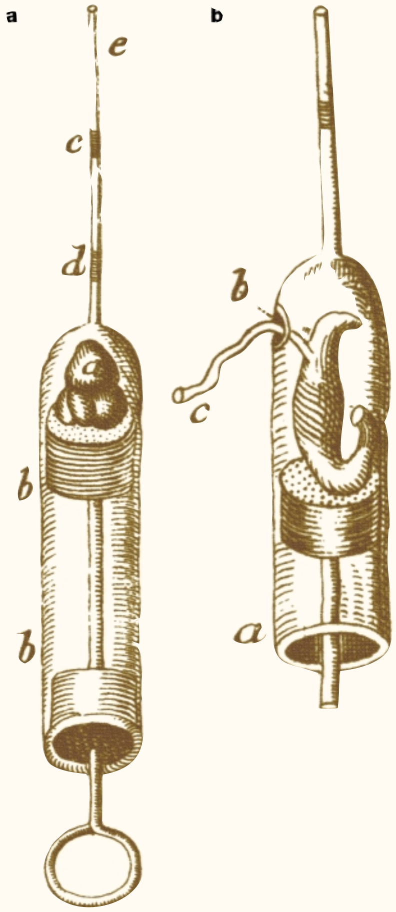



Figure 3 | **Swammerdam's demonstration of the contractile power of a frog muscle.** The nerve is 'irritated', and the distance between the two needles holding the muscle is reduced when the muscle contracts. *a*, glass tube; *bb*, needles through tendons; *c*, nerves; *dd*, movement of muscle draws heads of needles together; *e*, belly of muscle thickens. For a full description, see the main text. Reproduced from REF. 10 © Bibliothèque Inter-Universitaire de Médicine, Paris.

Box 1 | **Swammerdam on muscles: right without realizing it**




**Physiology textbooks often credit Swammerdam with being the first person to have shown that muscles do not increase in volume on contraction. The little-known and intriguing truth is that although he did indeed show this, he literally did not believe his own eyes.**

**To test Descartes' hypothesis that the influx of 'animal spirits' increased muscle volume on contraction, Swammerdam placed a frog muscle in an air-tight syringe, and measured the volume of the muscle in its contracted and relaxed state by observing the movement of a bubble of water in the end of the syringe (in doing so, he incidentally invented the plethymograph).**

**Swammerdam first did the experiment with a whole frog heart that had been dissected out (see panel a of the accompanying figure). The result was incontrovertible: when the heart spontaneously contracted "the drop of water adhering near the extremity of the tube, *c*, descends in a very remarkable and surprizing manner … the drop thus fallen down, *d*, will, on the heart's dilating itself again, rise to its former situation, *c*."[10] This completely contradicted Descartes' hypothesis.**

**He then altered the procedure slightly, using a frog's thigh muscle with the nerve protruding through a small hole in the side of the glass siphon (panel b of the figure). The results were disappointing: "In this experiment, the sinking of the drop is so inconsiderable, that it can scarce be perceived"[10].**

**Most of us will recognize his next, fatal, step. Swammerdam explained away the results from the thigh muscle experiment, arguing that "this experiment is very difficulty sensible, and requires so many conditions to be exactly performed, that it must be tedious to make it"[10] and pointing out that because the thigh muscle had neither blood supply nor antagonistic attached to it, it could not be expected to function normally, concluding "for this reason, the heart is fitter for this experiment than any other muscle"[10].**

**But in fact, the thigh muscle preparation gave the right result. Muscles do not change their volume. Although he can be commended for not hiding problematic results, Swammerdam was wrong. Convinced that the big effect was what counted, he dismissed the thigh muscle results. His mistake came because when the heart contracted, it probably compressed some of the air trapped in the ventricles, reducing the total volume in the syringe. Swammerdam decisively proved Descartes wrong, but unwittingly he provided us all with a salient lesson in how to interpret experiments and the need to exclude artefacts.**

nail in the coffin of Descartes' vision of nerve function when he used the same frog nerve–muscle preparation to show that, against Descartes' fundamental prediction, muscles do not increase in volume when they contract (BOX 1).

Swammerdam was acutely aware that he had discovered something vitally important. He had shown that 'animal spirits', whether they were like water, fire or air, were not involved in movement:

> "From these experiments, therefore, it may, I think, be fairly concluded, that a simple and natural motion or irritation of the nerve alone is necessary to produce muscular motion, whether it has its origin in the brain, or in the marrow, or elsewhere."[10]

And, as he made quite clear in his later presentation of the results, this was not something that was specific to the frog or to its thigh muscle: these were "Experiments on the particular motion of the muscles in the Frog; which may be also, in General, applied to all the motions of the muscles in Men and Brutes"[10].

Although the full details of these experiments were not published until more than 50 years after his death[8], they were widely known in the early modern European scientific community. Swammerdam would show them to the rich and influential visitors who came to see him at work, such as the future Grand Duke Cosimo III of Tuscany, who visited him in Amsterdam in 1668. Furthermore, Swammerdam was in close contact with some of the most influential figures in science, such as his student friend the Danish anatomist Nicolas Steno[15], and two of the driving forces behind early modern science, the Frenchman Melchisedec Thévenot[16], who was behind the foundation of the Académie des Sciences, and the first secretary of the Royal Society, Henry Oldenburg[17]. By a network of letters, visits and discussions[18], such contacts ensured that knowledge of Swammerdam's findings spread rapidly, even in the absence of detailed experimental descriptions.

### Revolutionary implications

Swammerdam's experiment was typical of the scientific revolution — not only did it lead to an important discovery, it also showed what was new and powerful about science itself. First, it dealt with a phenomenon that was completely unsuspected and went against the grain of centuries of ideas about the natural world. The clinging cobwebs of tradition and authority were blown away by experimental audacity. By turning to the study of the novel, rather than re-hashing the accepted, science provided itself with a vital tool to create a new vision of the world and, ultimately, to change that world. Second, it showed the power of the reductionist method. Swammerdam literally reduced the frog to its component parts, in this case a nerve and a muscle, and suggested that something could be learned about the behaviour and organization of the whole frog — indeed of all animals — on the basis of this example. Third, it showed the relationship between biological and mechanical phenomena. Swammerdam effectively transformed the nerve–muscle preparation into an instrument that, in principle, could provide quantitative information. And within this instrument, the biological component had a simple mechanical role, implying that, in natural movement also, muscles and nerves could be compared to mechanical components. Fourth, it was backed up by a detailed description that showed the reader how the experiment could be carried out. This was a hallmark of the development of science and its ability to spread across the globe and through subsequent generations of scientists down the centuries.

Swammerdam's research also set the intellectual stage for the development of more complex theories of behaviour and nerve function, based not on Cartesian hydraulics, but on mechanics. For neuroscience, the most important thing about this series of experiments was that Swammerdam had shown that movement was due to the external stimulation ('irritation') of the nerve.

The decisive connection between stimulus and response that was conceived of by Swammerdam was part of a revolutionary mechanistic view of the organization of the body and behaviour. Abandoning all talk of 'spirits', this view stated simply that when something happened to the animal (or to part of it), it responded, much as releasing a brake would set a machine in motion. Descartes' view of the body as a machine was applied thoroughly, down to its smallest components.

This view was not only revolutionary in its immediate context, it had continuing reverberations down the centuries: without this view triumphing somewhere and at some time, modern neuroscience would look very different. Swammerdam's discovery was the basis of all that followed: it led directly to the conception that an organism's behaviour could be understood in terms of the sum of the stimuli that it received, which was in turn the basis of all the theories of learning that appeared in the twentieth century and, in particular, of Ivan Pavlov's conception of conditioned reflexes and J. B. Watson's behaviourism. All that from a simple experiment on a frog nerve.

### Swammerdam's speculations

The final phase of Swammerdam's work on nerve function came in the 1670s, as he sought to understand his results. He had clearly shown that nerves did not function through 'animal spirits', but he had not found any explanation of how 'irritation' might lead to movement. Although he felt that the true answer lay "buried in impenetrable darkness", he nevertheless rose to the challenge and outlined both a strategy for studying the phenomenon and an analogy. First, he reiterated why the traditional view was wrong:

> "I would have it seriously considered, that it cannot be demonstrated by any experiments, that any matter of sensible or comprehensible bulk flows through the nerves into the muscles. Nor does any thing else pass through the nerves to the muscles: all is a very quick kind of motion, which is indeed so rapid, that it may be properly called instantaneous."[10]

He then put forward the following analogy:

> "Therefore the spirit, as it is called, or that subtile [sic] matter, which flies in an instant through the nerves into the muscles, may with the greatest propriety be compared to that most swift motion, which, when one extremity of a long beam or board is struck with the finger, runs with such velocity along the wood, that it is perceived almost at the same instant at the other end"[10].

This statement provided an explanation of nervous transmission that was in keeping with the most radical mechanistic conceptions of the time. In itself, the use of such an analogy is a striking confirmation of Swammerdam's status as one of the foremost thinkers of the scientific revolution with regard to physiology and anatomy — it is far more novel than Descartes' idea of fluid 'animal spirits'. And tantalizingly, he was not so wide of the mark — the transmission of the action potential down the axon is based on a cascade of biochemical phenomena, just as a vibration travels down a plank by a cascade of interactions between molecules. However, it is not clear what contemporary experiments might have flowed from this analogy, and it is hardly surprising that neither Swammerdam nor anybody else followed up this insight.

> "… a simple and natural motion or irritation of the nerve alone is necessary to produce muscular motion"

He then went on to suggest that, because it was so difficult to investigate nerve action in animals, a useful approach would be to make a comparative study of movement in plants such as the sensitive plant. Although it is unlikely that any further insights into nerve function would have arisen from such a study, considering the different bases of movement in plants and animals, this suggestion was nevertheless important, because it formed part of the comparative method that was a key aspect of the development of science.

Swammerdam also developed his ideas of the specificity of nervous function. In his 1667 doctoral thesis, he noted that nerves that were involved in conscious movement were connected to antagonistic pairs of muscles, whereas those that were linked to single or multiple sets of muscles were not under conscious control. Later on, his many dissections of a wide range of animals, both vertebrates and invertebrates, led him to notice a decisive difference in the organization of sensory and motor nerves[19]:

> "the motion produced in the muscle by irritating the nerve, is always propagated out of the larger into the smaller branches, and goes outwards continually descending. The nerves designed for the senses are circumstanced in a quite different manner; for in these, the sensitive motions, doubtless, tend upwards."[10]

Whatever its limits, this is a huge advance over contemporary views of nerve function. Descartes' vision (FIG. 1) was typical of the widely held view that the same nerve served sensory and motor functions. Although Harvey for one had realized that this posed several major problems[20], Swammerdam was the first to clearly outline the different functions of different nerves.

Finally, Swammerdam took his innovative idea of 'irritation' producing a response in the nerve, which was adopted at around the same time by the English physician Francis Glisson (1597–1677), and tried to apply it to perception. He described the pupil reflex response in humans, noting "the contraction of the pupil of the eye, which instantaneously expands and dilates itself, by means of its muscles, as the eye is more or less irritated by the particles of light."[10] Later on, as part of his pioneering work on comparative insect anatomy, he described the organization of the visual system in the brain of the bee, suggesting that the "great number of pyramidal fibres are excited by the light falling on them"[10].

Again, these are perceptive speculations, based on the most developed contemporary knowledge and the most powerful analogies available at the time. Their immediate impact, however, was relatively limited: the gulf between the knowledge that would be required to fully investigate and exploit them and that which was available to contemporary investigators was too great. They remain as brilliant but inevitably fruitless insights.

### From irritation to action potential

Despite Swammerdam's clear demonstration, the 'animal spirits' had a long life ahead of them[5,21]. A few years after Swammerdam resolved the problem, Giovanni Borelli (1608–1680), a pupil of Galileo who had been Professor of Mathematics at Pisa and Messina before going to work in the court of Queen Christina of Sweden, began to work on the nature of animal movement, focusing on a mathematical interpretation of muscle function. In his posthumous work *De Motu Animali* (On the Movement of Animals; 1680–1681), Borelli followed Swammerdam's insight by arguing that what moved down the nerve was a 'commotion' or 'oscillation', but like Descartes, he maintained that there was a

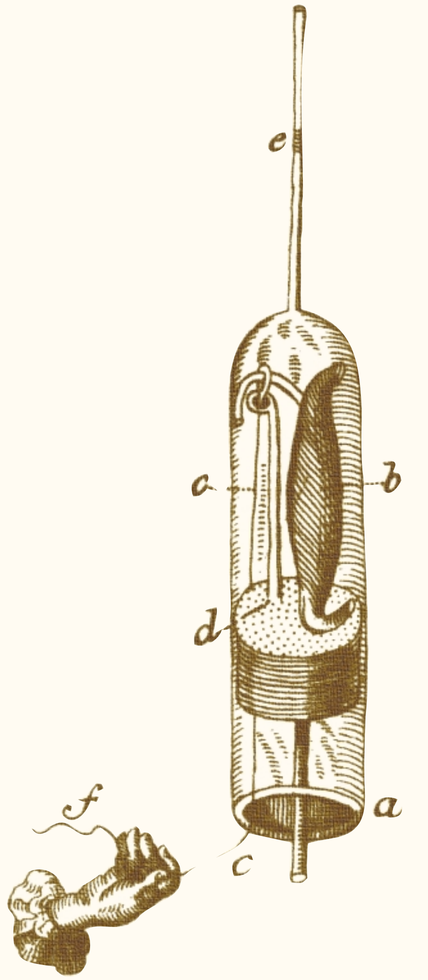



Figure 4 | **Possible electrical stimulation of the frog nerve by Jan Swammerdam.** The nerve runs through a brass eye and is stimulated with a silver thread, perhaps inducing an electrical current. "a) The glas [sic] tube, or syphon. b) The muscle. c) A silver wire with a ring in it, through which the nerve passes. d) A brass wire … through which the silver wire passes. e) A drop of water in the glass tube. f) The hand that irritates the nerve, in consequence of which irritation the drop on the muscle, contracting itself, descends a little." Reproduced from REF. 10 © Bibliothèque Inter-Universitaire de Médicine, Paris.

fluid within the nerves — a *succus nerveus spirituosus* — that contributed to the inflation of muscles on contraction[22].

In the first part of the eighteenth century, thinkers continued to invoke 'animal spirits' to explain nerve function, even those who were well aware of Swammerdam's work, such as his editor, the great Dutch physician Herman Boerhaave (1668–1738)[23]. For some scientists, and especially for physicians, it was better to pursue a vague but wrong explanation that could at least lead to a spurious diagnosis and treatment than to admit that there was no satisfactory explanation of what the 'commotion', 'irritation' or 'vibration' was, nor how it moved down the nerve. In 1751, Albrecht von Haller (1708–1777), who knew of Swammerdam's work and was extremely admiring of it[6], tried to define and study nervous 'irritability', but was unable to come to any precise explanation, although he did rule out explicitly the role of electricity[24].

The decisive breakthrough came at the end of the eighteenth century, when Luigi Galvani (1737–1798) dissected a frog on the same bench as an 'electric machine' and discovered, by chance, that muscles responded to external electrical stimuli[25]. He went on to reason that it was probable that the internal factor responsible for movement was also electrical. Even on this point, it is possible that Swammerdam unwittingly got there first[26]. One of Galvani's decisive experiments was to show that movement could be induced by stroking an iron plate against a brass hook inserted into the frog's spinal column, which generated a small electrical current. In one version of Swammerdam's nerve–muscle experiment (FIG. 4), the nerve was suspended by a brass hook, which was then stroked with a silver wire — it is possible that this induced a small electrical current that gave rise to the subsequent muscular contraction.

In 1848, the young Emil Du Bois-Reymond (1818–1896) took Galvani's conception a whole stage further when he used a sensitive galvanometer to measure a nerve's 'action current'[27]. He too used a version of Swammerdam's frog nerve–muscle preparation. Four years later, Hermann von Helmholtz (1821–1894) measured the speed of the nerve impulse that led to muscular contraction, estimating it at ~27 m $s^{-1}$ (REF. 28). At the end of the 1860s, Julius Bernstein (1839–1917), who had studied under both Du Bois-Reymond and von Helmholtz, found that what he called the 'action potential' also moved at ~27 m $s^{-1}$, and argued that it consists of a self-propagated depolarization of the nerve membrane[29].

The 'animal spirits' were finally exorcized, and mechanical analogies began to give way to a higher reality that incorporated their most important insights, but which took the science of nerve function far from its initial insights into 'irritation', 'vibrations' or 'commotions'. Swammerdam's work had served science in two ways: by helping to show the falsity of the hypothesis of 'animal spirits', and by providing an extremely powerful way of investigating the true nature of nerve function — the frog nerve–muscle preparation.

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DOI: 10.1038/nrn806

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