Social History of Medicine Vol. 27, No. 3 pp. 577–593

Contesting the Animal Model: Axel Holst and the Controversy over Scurvy and Beriberi

Kristin Asdal*

Summary. In contemporary writing Axel Holst and Theodor Frølich are being celebrated as the first to produce an animal model for the experimental production of scurvy. But in their time their research was contested by their peers, most vocally by the polar hero and zoologist Fridtjof Nansen. This paper explores how Axel Holst initially started out as a microbe hunter and worked within a bacteriological framework, before he shifted to performing feeding experiments and came to understand scurvy as a deficiency disease. This radical shift in framework may take part in explaining the controversy around their research. But most importantly, this paper argues, we must understand this in light of the contested status of animal models and modelling work in medical science. In order to analyse this, the paper suggests that we attend to a broad set of approaching and defining 'models'. Moreover, the paper suggests that we extend our discussion from 'the animal model' and what an animal model *is*, to modelling practices and what models can do, and sometimes fail to do. The paper concludes with arguing that Holst and Frølich in fact did not develop an animal model, i.e. a shared example upon which scientists base their work.

Keywords: animal models; modelling; scurvy; bacteriology; nutrition; Axel Holst; Theodor Frølich; Fridtjof Nansen; deficiency diseases; vitamines

In 1907 the Norwegian professor Axel Holst, together with his colleague the paediatrician Theodor Frølich, published an article in the journal *Hygiene* which has been characterized as ground-breaking.[1] Indeed, it is said to be the single most important publication in the history of scurvy.[2] This importance has not been ascribed to its immediate practical results as there were few, if any. Its importance has been linked to the fact that Holst and Frølich provided an animal model for the further study of scurvy and consequently deficiency

* Center for Technology, Innovation and Culture (TIK), University of Oslo. Postbox 1108 Blindern, 0317, Oslo, Norway. E-mail: Kristin.Asdal@tik.uio.no.
Kristin Asdal is historian and professor at the Centre for Technology, Innovation and Culture at the University of Oslo. She works at the intersection of history and science and technology studies (STS). She recently published 'Contexts in Action—and the future of the past in STS' as part of a special issue she edited with Ingunn Moser on 'Context' (*Science, Technology & Human Values*, July 2012). She is currently guest editor, with Christoph Gradmann, of a special issue of *Science in Context: Science, Technology, Medicine—and the State: The Science-State Nexus in Scandinavia, 1850–1980* (forthcoming 2014).

[1] Axel Holst and Theodor Frölich, 'Experimental studies relating to ship-beri-beir and scurvy. II. On the etiology of scurvy', *Journal of Hygiene*, 1907, 7, 634–71; Axel Holst, 'Experimental Studies Relating to "Ship-beri-beri" and Scurvy. I. Introduction. On polyneuritis of poultry (polyneuritis gallinarum Eijkman)', *Journal of Hygiene*, 1907, 7, 619–33. [The correct spelling of Holst's co-author is Frølich, but in English publications this was altered to Frölich. Except when referring to his publications I will spell his name 'Frølich' throughout this paper.]

[2] Kenneth J. Carpenter, *The History of Scurvy and Vitamin C* (Cambridge: Cambridge University Press, 1986). See also Kaare R. Norum and Hans J. Grav, 'Axel Holst og Theodor Frølich—pionerer i bekjempelsen av skjørbuk', *Tidsskrift for Den Norske Legeforening*, 2002, 1686–87.

 doi:10.1093/shm/hku007
Advance Access published 7 April 2014

diseases, and the later concept of vitamins.[3] Hence, Holst's reputation has been linked to the newer science of nutrition; and this by way of a specific achievement, the fact that he, together with his colleague, developed an 'animal model'. As Simon Schaffer has pointed out, one of the things models can do is take on political work: models can establish rights over works of art and nature.[4] Thus, we may not only think about what models *are*, but also what models can do. According to Schaffer, models may enable a form of ownership of the world.

This gives immediate meaning to the way in which Holst and Frølich in contemporary writing are written into the history of science as pioneers in nutrition research. The experimentally produced disease (scurvy) is associated with their names by way of the specific model they selected and used (the guinea pig). Because of the chosen animal model, 'scurvy' has come to belong to them as a form of intellectual property. In the academic logic of competition, they were 'the first' to experimentally produce scurvy and then link this to a deficiency in the diet. However, becoming 'the first' is a social process and a process the relevant scientific community must agree on and be convinced of. This is related to another aspect of models that others have pointed to, namely that they are used for mobilizing: to train new practitioners; to gain funding; to win public support; and to convince colleagues.[5] In other words, what we might say is that models are objects of persuasion.

Attempts to persuade do not always succeed. Holst and Frølich may well have been published and are today feted as 'the first'. In their time, however, their research was not really recognised and even heavily contested by their peers in the Norwegian academic community. This included Norway's most famous and celebrated scientist at the time, the zoologist and polar hero Fridtjof Nansen. This paper demonstrates how this controversy was intimately linked to the model issue.

The paper is organized as follows: The first part narrates the research process and the shift from a bacteriological to a nutritional context, leading up to the famous publication of 1907 and the ensuing controversy. This is a part of the history of scurvy (and beriberi) that has so far not been thoroughly investigated. Unpublished letters from the main investigator Holst and his applications for research funding, together with the professional as well as public debates on beriberi and scurvy, constitute the basis for this analysis. The second part re-visits the controversy, analysing it more closely in light of the model issue. It proposes that in order to fully grasp the controversy, we need to expand our understanding of animal models from definitions of what models *are* to what models can do—and sometimes fail to do. It also suggests that rather than opting for one given definition of what an animal model *is* it might be fruitful to draw on many, even conflicting definitions—including expanding the notion of

[3] Carpenter, *The History of Scurvy and Vitamin C*. See also Kenneth J. Carpenter, 'Nutritional Diseases' under the subtitle 'Animal Models and the Vitamin Concept', in W. F. Bynum and R. Porter, eds, *Companion Encyclopedia of the History of Medicine, Vol. 1* (London: Routledge, 1993), 463–83. For 'vitamin history' in general, see also Leonard G. Wilson, 'The Clinical Definition of Scurvy and the Discovery of Vitamin C', *Journal of the History of Medicine and Allied Sciences*, 1975, 30, 40–60, and Robyn Smith, 'The Emergence of Vitamins as Bio-Political Objects During World War I', *Studies in History and Philosophy of Biological and Biomedical Sciences*, 2009, 40, 179–89.

[4] Simon Schaffer, 'Fish and Ships: Models in the Age of Reason', in N. Hopwood and S. de Chadarevian, eds, *Models. The Third Dimension of Science* (Stanford: Stanford University Press, 2004), 71–105.

[5] Nick Hopwood and Soraya de Chadarevian, 'Dimensions of Modelling', in Hopwood and de Chadarevian, eds, *Models. The Third Dimension of Science*, 1–15.

'the animal model' to the model assemblage and the layers of modelling practices that need to be accepted for an experiment to be seen as a relevant, valid and generalizable result. The paper argues that the scurvy controversy may illustrate how, in the early twentieth century, the model assemblage was still a contested object and how the relative independence models need in order to perform as tools was being questioned. Drawing on Thomas Kuhn's work and the notion of 'the exemplar', the paper ends by concluding that, contrary to what has been argued, Holst and his colleague did not develop an animal model. The animal they used, the guinea pig, was not in their own time and in their local research community accepted as a model in the form of a shared exemplar that could enable generalisation beyond the single example. This means that the guinea pig did not perform as a model.

A Nutritional versus a Bacteriological Framework: Holst as a Microbe Hunter

The subject matter of the research conducted by Holst and his then junior colleague Frølich is related to what is often characterised as a major shift in the scientific approach to nutrition from the late nineteenth century to the inter-war period. This concerns the shift from a largely quantitative framework, in which the focus was on sufficient amounts of food, to a qualitative one. Research went from being directed predominantly towards enough nutrition to the properties of food and the ways in which the diet was composed. A number of diseases, such as scurvy and beriberi, rickets and pellagra, became linked to dietary deficiencies. The content of 'vitamines', a concept developed around 1911–12 (then with an 'e' and often linked to the name of Casimir Funk), came to be seen as essential to a qualitatively good diet. However, this represented a transformation in the way diseases and nutrition were understood, which did not occur smoothly, and Holst's point of departure in pursuing this research was quite different from what has so far been acknowledged.

Just as Robert Koch has become inextricably linked to medical bacteriology, so Axel Holst has become inextricably linked to another era and another approach, namely that of the sciences of nutrition.[6] He is said to have laid the foundation for what came to be understood as deficiency diseases. But as I will show, it is only in hindsight that it really makes sense to place Holst within a nutritional framework. Indeed, Holst had a much different starting point.

In 1901 the Norwegian government appointed the 'Beriberi Committee' to explore the problem of beriberi on Norwegian sailing vessels and, if possible, to suggest remedies to improve the conditions.[7] It was this practical as well as scientific question of beriberi, not scurvy, that Holst initially set out to solve, hence the title of the first of his two papers: 'Experimental Studies Relating to "Ship Beriberi" and Scurvy: I. Introduction'.[8] Holst himself was not appointed as a member of the committee, which was chaired by the professor of ear,

[6]Christoph Gradmann, *Laboratory Disease: Robert Koch's Medical Bacteriology* (Baltimore: Johns Hopkins University Press, 2009).

[7]Beri-Beri-Committee, *Report of The Beri-Beri Committee [Beri-Beri-Komiteen, Indstilling fra den af Departementet for det Indre nedsatte Komite for 'at tage under Overveielse og fremkomme med Forslag til Midler til Bekjæmpelse og Forebyggelse af Sygdommen Beri-Beri ombord i norske Skibe, samt at undersøge Spørgsmaalet om og i Tilfælde afgive Forslag til en Reduktion i den for vore Skibe for Tiden paabudte Forsyning med Medikamenter, Instrumenter og Bandager.']* (Kristiania: Marius Stamnes Bogtrykkeri, 1902). Appointed 15 July 1901, Recommendation 15 May 1902. Members: Professor Vilhelm Uchermann (head of committee), member of Parliament Lars Abrahamsen and medical doctor P. C. Kreyberg. Professor Torup attended one of the meetings.

[8]Holst, 'Experimental Studies Relating to "Ship-beri-beri" and Scurvy. I. Introduction'.

nose and throat medicine at the University of Christiania, Vilhelm Uchermann. Uchermann had already worked on related subjects and was the author of the *Medical Book for Sailors* [*Lægebog for sømænd*] (1889). This did not stop Holst from taking a serious interest in the issue and Holst travelled abroad to study the phenomenon for himself in a tropical climate. The letters he wrote back home after having arrived in Burma clearly demonstrate his reasoning in dealing with the disease, as he complained about the lack of a bacteriological approach and principles:[9]

> So far I have never met anyone as uncritical as the English physicians in Burma. Either they are firmly rooted in the view of the 50s when the so-called 'filth' was sufficient to explain all diseases. They never seem to have heard of the concept 'specific', even less thought about it. When I arrived, I was constantly being told that 'rotten' rice was the cause of beriberi. 'Rotten rice?' I asked. 'All rotten rice?' 'Yes, all rotten rice.' 'But,' I said then, 'we happen to eat rotten rice in Europe as well, and there we hardly have beriberi.' Then the answer was, 'What we are thinking of is rotten rice in the tropics.' … '[A]s this rottenness is caused by microbes, one needs a specific microbe, then?' I asked. 'Specific microbe? Why microbe?' used to be the answer. 'Nowadays everything is ascribed to microbes—We don't care; name it whatever you like. We don't know anything about this disease. So there must a specific microbe?'[10]

Holst, for his part, was not at all in doubt when it came to beriberi: '[I] will soon be able to write a whole book on this topic. If this is not an infectious disease of a specific type, contagious like typhoid fever, that would be strange indeed. I could have given 100 Rs [Riksdaler, Norwegian currency] if I could only hunt down that microbe.'[11] Hence, Holst was a microbe hunter. And he continued on to Kuala Lumpur (the capital of Malaysia) to hunt them down:

> … have found a strange bacteria … will see if there might be more fresh cases to get hold of … in Kuala Lumpur [there are] just as many of them as there are lice in the head of an ordinary Hindu … I immediately got access [with the English physicians] with my working hypothesis about 'the intestines' as the hiding place for the damned—I damn it!—Ecoutes—contagion.[12]

Holst had become convinced that beriberi was a toxin disease caused by a contagion which was only visible at the early stage of the disease. In Kuala Lumpur he thought he had found what he was after:[13]

> Quite fresh cases of beriberi, as well as the same peculiar bacteria in the intestines. But is it the right one? You may guess that I'm rather excited and impatient to get home to have it worked out. Let's only hope it will not die on the way home.[14]

The fact that Holst was working from a bacteriological framework in his attempt to grasp the cause of beriberi should come as no surprise. After all, Holst was a professor of bacteriology

[9] Axel Holst, Letter to Ustvedt, 11 April 1902, Batavia. All the letters to Ustvedt referred to in the following are from the National Archives of Norway, F 0037, PA 1248, Hans Jacob/Ustvedt family. Box: Private matters and letters 1846–1938.
[10] *Ibid*.
[11] *Ibid*.
[12] Axel Holst, Letter to Ustvedt, 16 May 1902, Galle Face Hotel, Colombo.
[13] Axel Holst, Letter to Ustvedt, 16 May 1902.
[14] *Ibid*.

at the University of Christiania, appointed in 1893. He was truly internationally oriented when it came to the newer practices of bacteriology, and had been in Berlin with Robert Koch when he announced his tuberculin.[15] The fact that he was in Berlin with Koch and experienced the glory and fame that was attributed to him may well have been a source of inspiration for trying to find other bacteria causing yet another disease.

For a long time after returning home, Holst maintained the bacteriological approach and applied for additional funding in order to be able to pursue his ideas. After having studied beriberi clinically and epidemiologically in the East Indies and having 'started a bacteriological study of it', Holst explained, he had continued in this bacteriological direction when he returned home.[16] Apparently, the research material he had been so excited about and impatient to bring back home with him had not died out. One of the animal species he used to test his hypothesis that beriberi was caused by a particular bacteria was the cat. In a letter to a colleague, the director of the botanical garden at the university, he asked for assistance in reproducing the tropical climate back home in Norway—thus being able to further pursue this research. 'Dear colleague!' the letter began:

> I allow myself to ask if it could be possible to place a few animals in a somewhere hidden place in one of the greenhouses at Tøyen [the universitýs botanical garden]. You see, I have a bacteria 'going,' the effect of which I would like to study in a few cats, possibly also in pigeons in a 'tropical environment,' preferably in a humid one, and in order to do this I think that a greenhouse would be very well suited. The cats will be placed in proper cages and the experiments cannot be linked to any risk to humans … The experiments would not be possible to pursue if the animals were placed somewhere open to the public. The experiments will go on for about a month, from the beginning to the end of August. I apologize for asking, but have no one else to turn to, and acknowledge your sincere interest in *sancta scientia* and its progress. But if you cannot answer my plea, I do understand the difficulty …[17]

The material he had brought back home had 'peculiar effects' on the animals, giving him reason to believe that bacteria probably were the cause of the disease.[18] And the year after, in the spring of 1904, his research continued within the same bacteriological framework in his study of the causes of beriberi.[19]

From Microbe Hunting to Feeding-experiments

Holst was a well-known and vocal researcher who publicly advocated his bacteriological approach to the beriberi question. He was not at all pleased with the fact that the Beriberi Committee had no bacteriologist among its members and wrote a letter to the

[15] B. Connor Johnson, 'Axel Holst', *The Journal of Nutrition*, 1954, 53, 1–16.

[16] Axel Holst, Letter of Application for Research Funding from Axel Holst to 'Nansenfondets bestyrelse' [The board of directors of The Nansen Fund], 7 or 1 March 1903, Box: Journalsaker, 1897–1908, The National Archives of Norway, Oslo. The Nansen Fund was the most important funding agency for scientific research at the time, established in 1896 as a direct result of the happy return of the polar expedition *Fram*. All the following references to letters of application are from the archive of the Nansen Fund.

[17] Axel Holst, Letter to Wille, 22 June 1903, Håndskriftsamlingen [Handwritten Records], The National Library of Norway, Oslo. Nordal Wille was professor of botany at the University of Kristiania and director of the botanical garden.

[18] Axel Holst, Letter to the Nansen Fund, 7 or 1 March 1903.

[19] Axel Holst, Letter to The Nansen Fund, 9 March 1904.

government's chief medical officer to argue in favour of his own bacteriological approach. He also seemed rather eager to criticise and undermine the position of his colleague and chairman of the committee, Uchermann. As Holst had written to another colleague, close friend and assistant in 1902:

> In my opinion it would be good if you, as a little start, would kick colleague Uchermann just a little bit on the leg in the Magazine [*Norsk Magazin for Lægevidenskaben* (author's note)]. Take care, for instance, to shoot a little arrow in the next issue. You see, I have just written a small note to the chief medical officer of the government …[20]

The journal *Morgenbladet* published anonymous articles criticising the government for not having appointed a bacteriologist as the chairman.[21] The author might well have been Holst, who thought there was every reason to believe that the disease was caused by a 'living contagion'.[22] However, the experimental results in animals were not conclusive nor did Holst find them completely convincing. In 1904 Holst therefore argued that he needed a large series of experiments to clarify whether the bacteria he was studying really were the cause of the disease.[23] This was the background for the application for more funding that year, 1904.

Holst was successful in his applications and was granted the funding needed to continue his research activities.[24] Three years later, in the spring of 1907, his research had changed direction. For the first time, when explaining his research activities, research on scurvy was included with what was no longer simply called beriberi, but 'ship beriberi' as opposed to 'tropical beriberi'.[25] As mentioned, Holst had been researching beriberi up to that point. Now, in the spring of 1907, it was clear to him that he had not succeeded. The results had been 'promising', but despite huge efforts the experiments had not given sufficiently convincing results. That was the reason why Holst, two years earlier, had put a different focus on his research and to a larger degree had sought to study the 'so-called ship beriberi'.[26] According to Holst's understanding, ship beriberi was a disease that could be likened in some cases to tropical beriberi, but which probably was 'a form of scurvy or a closely related disease.'[27] Holst does not explain in detail how he came to change the direction of his research or the conclusion he reached. However, the major shift must be seen in relation to what his colleague and co-author, the paediatrician Frølich, added to the research. Frølich had been concerned for a long time with the so-called Barlow's disease, or infantile scurvy. According to their 1907 paper, by comparing the characteristic alterations of the bones in patients suffering from infantile scurvy and the alterations of the bones in guinea pigs, they were able to posit that scurvy was the cause: 'We have seen … that guinea pigs fed on different sorts of unpeeled grains, groats or bread … develop the

[20] Axel Holst, Letter to Ustvedt, 15 August 1902, Oslo.

[21] According to Beri-Beri-Committee, *Report of The Beri-Beri Committee*.

[22] Axel Holst in a letter to the chief medical officer [Medisinaldirektøren], August 1896, as referred to in Beri-Beri-Committee, *Report of The Beri-Beri Committee*.

[23] Axel Holst, Letter to The Nansen Fund, 9 March 1904.

[24] Thus at this stage at least, the established narrative that says Holst's research was impeded due to a lack of funding, funding that was controlled by his opponents, cannot be supported. E.g. Kaare R. Norum and Hans J. Grav, 'Axel Holst og Theodor Frølich—pionerer i bekjempelsen av skjørbuk [Axel Holst and Theodor Frølich—Pioneers in the Fight Against Scurvy]', *Tidsskrift for Den Norske Legeforening [Journal of the Norwegian Medical Association]*, 2002, 1686–7.

[25] Axel Holst, Letter to The Nansen Fund, 3 March 1907.

[26] *Ibid*.

[27] *Ibid*.

same microscopical alterations of the bones which are found by numerous German pathologists to be the essential alteration in Barlow's disease, and which do not, according to the same authors, occur in any other malady common to children.'[28]

As already mentioned, the articles by Holst and Frølich were published internationally in 1907. They were also invited to present their findings at the Epidemiological Society of London. Norwegian versions of the publications came out the same year in the journal *Norsk Magazin for Lægevidenskaben*.[29] In the Norwegian research community, however, their work was not accepted at all unquestioningly. On the contrary, it was followed by thorough, lengthy and vigorous discussions in the *Norwegian Journal for Medical Science* (*Norsk Magazin for Lægevidenskaben*), in *The Medical Association (Det Medisinske Selskab)*, or 'the club' as Axel Holst used to call it, and even in a more public arena.

In an article bearing the confident title 'A correction', Holst's colleague Uchermann, scorned Holst and his contribution: 'For those of us who have followed the beriberi question in our journals and magazines, Holst's newest conviction will come as a surprise. Beriberi, a nutritional disease, a form of, or a relative to scurvy!'[30] As Uchermann formulated it:

> … there is no need to occupy ourselves with Holst's experiments on pigeons and guinea pigs which he and his followers have put so much emphasis on. … These are of no significance to the question of beriberi. He [Holst] rejects the experiments on birds … 'because one cannot transfer results obtained by experiments on birds to humans, because the human physiology is quite different from the one we find in birds' [here, Uchermann is quoting Holst]. This obvious if sad truth, which rather late was realized by the author [i.e. Holst], does not prevent him from warmly accepting the results from experiments on guinea pigs as scurvy and then applying these to the diseases we find in humans; scurvy and beriberi. What the author should have done was to consistently raise the above-mentioned objections to the experiments on birds to guinea pigs as well. From guinea pigs to humans the leap is probably neck-breaking.[31]

And he went on to argue:

> The diseases themselves are already there as the result of the experiments on diet and dietary prescriptions; what it takes is simply to study them; clinically, critically, comparatively and historically. Experiments that in an artificial way were to replace and simulate what is already laid out by nature's own laboratory are far more difficult to pursue and, moreover, quite needless.[32]

Uchermann took a radically different approach to the disease question than Holst and Frølich: 'The experimental task that lies ahead is no more feeding experiments, as Holst is asking for, but the chemical composition of those forms of poison which could be relevant,' he argued.[33] The argument was presented with reference to a colleague, Professor Sophus

[28] Holst and Fröhlich, 'Undersøkelser i anledning av skibs-beri-beri. Fortsættelse'.

[29] Holst, 'Experimental Studies Relating to "Ship-beri-beri" and Scurvy. I. Introduction'; Holst and Fröhlich, 'Undersøkelser i anledning av skibs-beri-beri. Fortsættelse'.

[30] Vilhelm Uchermann, 'Om beri-beri. En berigtigelse [On beri-beri. A correction]', *Norsk Magazin for Lægevidenskaben*, 1907, 68, 1298–316.

[31] *Ibid*.

[32] *Ibid*.

[33] *Ibid*.

Torup, whose position was that both scurvy and beriberi were a kind of intoxication developed in foodstuffs that had not been properly conserved.[34]

Nansen versus Holst

Torup had been involved in organizing and deciding the diet for the polar expedition Fram (1893–1896) with a highly successful result. No one in the expedition experienced scurvy, in stark contrast to other polar expeditions at the time.[35] Based on this experience, the reasoning was that scurvy was caused by a form of intoxication. But Uchermann and Torup were not alone in criticizing the path followed by Holst and Frølich. As late as 1910 the controversy continued in an even more public setting and included an even more prominent actor. In a series of articles in the journal *Morgenbladet*, the Norwegian polar hero Fridtjof Nansen contested Holst's research. His arguments were closely related to those raised earlier, but now directly linked and compared to Nansen's own polar field experience.

'There can be no doubt about the fact that the cause of scurvy is to be found in the diet,' Nansen argued.[36] Nansen referred to Torup, who had helped him plan the diet of the Fram expedition. Torup's position was that scurvy was caused by a chronic poisoning; small poisonous compounds that developed as nutrients slowly decomposed. According to Nansen, not a single case had arisen that could be used to argue against Torup's 'important theory'. On the contrary, a number of factors increasingly confirmed this theory which now had to be seen as 'fully proven'. The Fram expedition was not the only experience proposed as proof. None of the other expeditions in which Torup had controlled the diet (i.e. the Sverdrup expedition and Amundsen's Gjøa expedition) had experienced scurvy: 'Close to twelve years in the polar regions without a single case of scurvy' was reported.[37] According to Nansen, who was again supported by Torup, ship beriberi had almost the same causes as scurvy and had to be seen as a variant of scurvy, 'something which Torup had been arguing from the very start'. So, how to avoid scurvy? To Nansen the answer was relatively straightforward: the problem would be solved if people were provided dependable and sufficiently sterilized tinned food or, alternatively, other forms of carefully treated supplies such as dried food, fresh food from hunting or carefully treated frozen food.

The reply from Holst demonstrates how he operated from a completely different framework. As we know, Holst had also come to see the cause of the disease as hidden in the diet. However, the issue was not poisonous effects stemming from the decomposition of foodstuffs, but, in his own words: 'the variation in content of peculiar nutrients'.[38] The problem, according to Holst, was that these much-needed, peculiar nutrients could be destroyed by the thorough heating often involved in the process of tinning food. Consequently, the remedies he proposed to improve the situation and to avoid scurvy as well as beriberi were radically different than the ones put forward by Nansen. Whereas the polar hero saw the solution in preserving food, Holst saw the preservation process as part of

[34]See Sophus Torup, 'Møte den 26de Marts [Meeting the 26th of March]', *Forhandlinger i det medicinske selskab [Negotiations in the Medical Association]*, 1907, 58–72.

[35]Carpenter, *The History of Scurvy and Vitamin* C.

[36]Fridtjof Nansen, 'Skjørbuk og Skibs-Beriberi [Scurvy and Ship-Beriberi]', 23 December 1909, *Morgenbladet*.

[37]*Ibid*.

[38]Axel Holst, 'Skjørbug og Skibs-Beriberi [Scurvy and Ship-beriberi]', 21 December 1909, *Morgenbladet*.

the problem: if nutrients were heated as intensely as was required in the preservation process, then their 'antiscorbutic' effects would be lost.[39]

In his immediate reply to Holst, Nansen focused on explaining why Holst was not to be trusted: Holst was building on experiments which, as far as Nansen was aware, 'had been exclusively done on an animal very far from humans, namely the plant-eating rodent, the guinea pig'.[40] When it came to diseases in *humans*, experiments on humans were what counted. And when it came to the issue of scurvy, luckily in Nansen's view, there were already a number of experiments to draw on. To him the Fram expedition, for which he had been responsible, was the prominent example of such a controlled experiment on humans.[41]

Holst, for his part, saw this as an 'unclean experiment', claiming that it was not sufficient to build conclusions based on cases in which the disease had not emerged, such as the Fram expedition.[42] In such instances, some would give weight to *this* factor, others to another. Nansen used the Scott expedition as a counter argument. That expedition had followed the advice of the Norwegians in detail, except for one thing: The tinned food was not properly treated. Therefore 'the scurvy emerged already the first winter'.[43]

Nansen established the lived reality, or real field experiment, as a contrast to laboratory experiments on animals. The fact that the animal in question was a plant-eating rodent, as Nansen put it, did not make the matter any easier. The guinea pig was too distant from the human both 'zoologically' and in its 'eating habits and system of nutrition'. Conclusions regarding diseases related to nutrition in humans could not be drawn based on experiments on guinea pigs. 'As a zoologist I cannot think differently,' Nansen concluded.[44]

A lack of modesty and diplomacy in encounters with colleagues and those who eventually became his opponents may be part of the reason why the controversy around Holst's research was so ferocious. I have referred already to his position vis-à-vis the Beriberi Committee and its chairman. Prior to this, Holst had taken a vocal and indeed quite public stand on Nansen's research as well: when Nansen had defended his dissertation in 1887, none other than Axel Holst had been his first opponent.[45] Holst seriously criticised Nansen's work and argued, for instance, that he had been too quick to reach conclusions. In Holst's opinion there was little ground for Nansen's new theories on the nervous system. According to Holst, Nansen ought to have started from scratch, without theory, waiting until the facts he had found could be formed into a coherent whole.

Hence, Holst had taken a highly critical stand against both of his most vocal opponents. Whereas Nansen had been his junior at the time of his doctoral defence (even if they belonged to the same generation), Nansen was now the famous and celebrated hero. Moreover, Holst himself in the end came to argue for a radically different theoretical approach to scurvy than the one he had vocally and publicly defended only a few years earlier. The rhetorical situation in which Holst found himself was not an easy one.

[39] *Ibid*.

[40] Nansen, 'Skjørbuk og Skibs-Beriberi', 23 December 1909.

[41] *Ibid*. See also Fridtjof Nansen, 'Skjørbuk og Skibs-Beriberi [Scurvy and ship-beriberi]', 1 January 1910, *Morgenbladet*.

[42] Axel Holst, 'Mer om Skjørbug og Skibs-Beriberi [More on scurvy and ship-beriberi]', 26 December 1909, *Morgenbladet*.

[43] Nansen, 'Skjørbuk og Skibs-Beriberi', 1 January 1910.

[44] *Ibid*.

[45] Harald Dag Jølle, *Nansen. Oppdageren*, Vol. 1, (Oslo: Gyldendal, 2011). See also Nils Roll-Hansen, 'Ved biologiens forskningsfront', in O. Christensen and A. Skoglund, eds, *Nansen. Ved to århundreskifter* (Oslo: Aschehoug, 1996), 137–43.

If we chose to end at this point, examining the various motives and interests of Holst's opponents, we would end the story too easily and right at the point where it really starts to become interesting, as there is more to this controversy than motives, interests and social context.[46] We also must address the very content of the issue, that is, the disagreement regarding what counted as a proper research process and experiment. Hence, the whole method upon which Holst's and Frølich's research was based was at stake. This is the issue towards which the paper will now turn.

Scurvy and the Experimental Animal in Bacteriology

The bacteriological framework within which Holst had been working for a long time may be seen as part of the explanation of why, later on, having shifted his approach, he had difficulty convincing his colleagues about his new ideas. His new approach and conclusion appear to have been seen as partly that: simply a new idea. Others have already pointed out that the success of the germ theory of disease was an obstacle to finding an answer to the enigma of scurvy.[47] In other words, a bacteriological framework focused on the significance of 'positive agents, their bacteria and their products' was difficult to combine with the notion of deficiency diseases, that is, *negative* causes of disease.[48] But the bacteriological framework should not only be seen as a dead end or a failure in this respect.[49] In Holst's research it should also be seen as part of, or what he came to see as, the solution to the problem. This involves the approach to the animal.

First, and above all else, the turn to bacteriology implied a radical shift in method: the most relevant body for examination was no longer the sick or deceased patient, but an experimentally produced model of the disease.[50] Integral to this framework was the way in which the animal body was seen and used as a culturing apparatus.[51] The animal organism was transformed into a kind of tool. The challenge then was to find the right tool, or the right organism, for the job.[52] This can be linked to the bacteriological argument that a suitable animal model needed to be found for each animal disease. Thus, as Ilana Löwy has pointed out, the specificity of germs and disease claimed by bacteriology was also their specificity for particular animal species.[53] Holst's efforts to test his hypothesis on different animals (cats, dogs,

[46] For a broader discussion of this context see Kristin Asdal, 'Contexts in Action—And the future of the past in STS', *Science, Technology & Human Values*, 37, 379–403.

[47] C. P. Stewart, 'Scurvy in the Nineteenth Century and After', in C. P. Stewart and D. Guthrie, eds, *Lind's Treatise on Scurvy: A Bicentenary Volume Containing a Reprint of the First Edition of 'A treatise of the Scurvy' by James Lind, M.D., With Additional Notes* (Edinburgh: Edinburgh University Press, 1953), here cited in Carpenter, *The History of Scurvy and Vitamin* C.

[48] See R. H. Follis, Jr., 'Cellular Pathology and the Development of the Deficiency Disease Concept', *Bulletin of the History of Medicine*, 1960, 34, 291–317; Aaron J. Ihde and Stanley L. Becker, 'Conflict of Concepts in Early Vitamin Studies', *Journal of the History of Biology*, 1971, 4, 1–33.

[49] As pointed out also by Carpenter in reference to K. Codell Carter, 'The Germ Theory, Beriberi, and the Deficiency Theory of Disease', *Medical History*, 1977, 21, 119–36.

[50] Gradmann, *Laboratory Disease*. See also W. F. Bynum, '"*C'est un malade*": Animal Models and Concepts of Human Diseases', *Journal of the History of Medicine and Allied Sciences*, 1990, 3, 397–413.

[51] *Ibid*.

[52] Here I am playing on Muriel Lederman and Richard M. Burian, 'Introduction', *Journal of the History of Biology*, 1993, 26, 235–37, and A. E. Clarke and J. H. Fujimura, eds, *The Right Tools for the Job: At Work in Twentieth-century Life Sciences* (Princeton NJ: Princeton University Press, 1992).

[53] Ilana Löwy, 'From Guinea Pigs to Man. The Development of Haffkine's Anticholera Vaccine', *Journal of the History of Medicine and Allied Sciences*, 1992, 47, 270–309. See also Gradmann, *Laboratory Disease*.

pigeons and guinea pigs) in order to be able to experimentally produce the relevant disease are perfectly understandable within this framework.

But why the guinea pig? Holst does not explain in detail why the guinea pig was chosen, neither in his publications nor in his letters of application for funding. But what he *does* say is that as the guinea pig was a mammal; it was better suited than a bird because of its relative closeness to humans.[54] However, the guinea pig was already a favourite animal of bacteriologists.[55] In this respect there was a direct link between the bacteriological way of working, the path followed by Holst, and the specific animal model he, arguably, developed.

Hence, the bacteriological framework is crucial for understanding the path of Holst's research and may be seen as a much-needed tool box for Holst's research and a key to the 1907 publication. However, as is well-known by now, this bacteriological approach did not provide the convincing conclusion that he himself would be satisfied with. In the 1907 paper, the animal was used as a tool, but in a somewhat different manner than in bacteriology: The animal was still a form of culturing apparatus, but this time an apparatus, a tool, for producing the disease by way of animal feeding experiments. This was a well-established procedure, introduced by Magendie in relation to another food-related public controversy, then in France, in the nineteenth century.[56] But even if their research in this way followed a well-established—or at least not a completely new procedure—their findings were, as I have already demonstrated, heavily contested by the Norwegian research community. This disagreement hinged on the model issue.

The Model Assemblage and Modelling Practices

William Bynum pointed out in 1990 that surprisingly little had been written on the subject of animal models.[57] The literature has blossomed since then.[58] At the same time, others have pointed out that the question of the model is somewhat exaggerated. When it comes to Robert Koch for instance, Gradmann has argued that Koch was not attempting to

[54]See Axel Holst, 'I. Om beri-beri. II. Undersøgelser i anledning af skibs-beri-beri', *Norsk magazin for lægevidenskaben. 1907*, 69, 5, 569–600.

[55]See for instance Robert Koch's paper which had already become a classic by the time of Holst's research: Robert Koch, 'Die Aetiologie der Tuberkulose', *Berliner Klinische Wochenschrift*, 1882, 19, 221–30.

[56]Frederic Lawrence Holmes, *Claude Bernard and Animal Chemistry. The Emergence of a Scientist* (Cambridge, MA: Harvard University Press, 1974).

[57]W. F. Bynum, '"*C'est un malade*": Animal Models and Concepts of Human Diseases', *Journal of the History of Medicine and Allied Sciences*, 1990, 3, 397–413.

[58]In addition to the literature I refer to elsewhere in this paper, see Rachel A. Ankeny and Sabina Leonelli, 'What is So Special About Model Organisms?' *Studies in the History and the Philosophy of Science: Part A*, 2011, 2, 313–23; Cheryl A. Logan, '"[A]re norway rats … Things?": Diversity Versus Generality in the Use of Albino Rats in Experiments on Development and Sexuality', *Journal of the History of Biology*, 2001, 2, 287–314; Cheryl A. Logan, 'Before There Were Standards: The Role of Test Animals in the Production of Scientific Generality in Physiology', *Journal of the History of Biology*, 2002, 35, 329–63; Karen Rader, *Making Mice: Standardizing Animals for American Biomedical Research 1900–1955* (Princeton, NJ: Princeton University Press, 2004); Gail Davies, 'Captivating Behaviour: Mouse Models, Experimental Genetics and Reductionist Returns in the Neurosciences', *Sociological Review Monographs*, 2010, S1, 53–7; Carrie Friese and Adele E. Clarke, 'Transposing Bodies of Knowledge and Technique: Animal Models at Work in Reproductive Sciences', *Social Studies of Science*, 201242, 31–52; as well as more generally on research materials such as, Adele E. Clarke, 'Research Materials and Reproductive Science in the United States, 1910–1940', in G. L. Geison, ed, *Physiology in the American Context* (Bethesda, MD: Waverly Press, 1987), 323–350; and J. P. Gaudillière, 'Biologists at Work: Experimental Practices in the Twentieth-century Life Sciences', in J. Krige and D. Pestre, eds, *Science in the Twentieth Century* (Paris: Harwood Academic Publishers, 1997), 683–700.

develop models. Rather, his concern was imitations: To produce imitations of the relevant disease in the animal—and hence using the animal as a culturing apparatus to imitate the relevant disease in them.[59] It seems to make immediate sense to assume the same for Holst and Frølich. Interestingly, this ambition to imitate was seen as integral to the problem by one of their opponents: Experiments that in an artificial way were to replace and simulate what was already laid out by nature's own laboratory were both needless and difficult to pursue, Uchermann had argued.[60]

Neither Holst, nor Frølich, seemed to be concerned with developing an animal model. First, they did not themselves *use* the concept animal model. Secondly, rather than taking an interest in developing a particular *model* it seems as if they took whatever animals they thought could help them to make an imitation of the disease. In doing this, they were not necessarily so concerned with the specificity of the animal either (contrary to what Löwy has pointed out for bacteriology). Rather, they seem to have combined the ambition of producing and imitating the disease with a view to the extent to which the chosen animal was sufficiently close to the human. After all, it was diseases in humans they were trying to imitate. In attending to this problem, we see that models were nevertheless highly relevant to the issue. As pointed out above, the bird was judged to be too far away from the human for the results to be relevant. This was a critical point Holst had raised against his own earlier experiments. It is in this context we should also read Holst and Frølich's efforts to produce the disease in a dog; a partly unsuccessful experiment they included in their 1907 paper.

Their research then did not have so much to do with producing an animal model as such. Rather, their research raises the model question in another, quite concrete and indeed crucial manner: the animal that they put to use in order to perform the experiments had to be accepted as a model for the human. That is, an organism that was close enough to the human for the results from the animal experiments to be judged as relevant and valid for human diseases.

This was precisely what their opponents came to contest. As Uchermann had put it: 'From guinea pigs to humans the leap is probably neck-breaking'.[61] Then Nansen followed up by arguing that Holst was building his findings on experiments which 'had been exclusively done on an animal very far from humans'.[62] The implication was that results had no relevance for humans—and the animal (the guinea pig in this case) was rejected as a model for the human.

But not only was the animal rejected as a model; so was the very setting, that is, the laboratory in which the animal experiments had taken place: experiments that in an artificial way were to replace and simulate what is already laid out by nature's own laboratory were not only difficult to pursue, they were, also quite needless.[63] This argument by Uchermann was supported by Nansen who posited the lived reality, the real field experiment, in contrast to the laboratory.

The laboratory has been described as an enhanced environment, one that 'improves upon' the natural order as experienced in everyday life and that serves as a place in which

[59]Gradmann, *Laboratory Disease*; Ankeny and Leonelli, 'What is so Special About Model Organisms?'
[60]Uchermann, 'Om beri-beri. En berigtigelse'.
[61]*Ibid*.
[62]Nansen, 'Skjørbuk og Skibs-Beriberi', 23 December 1909.
[63]Uchermann, 'Om beri-beri. En berigtigelse'.

the world 'out there' is made available for intervention.[64] Precisely this setting, the laboratory as a model for nature was rejected and considered useless. The laboratory was understood to be an artificial setting which could not serve as a stand-in for nature; it was not an acceptable model for real life.

In their writing on models, Morrison and Morgan interestingly underline this aspect of models: in order to function as a model, the model has to have a certain link to an external reality.[65] Such a link is not, of course, given in nature but has to be made and accepted. In our case, the model's link to reality was rejected—for two reasons: on the one hand in the form of the tool, the animal as a proper model for the human, and on the other hand in the form of the setting, the laboratory as a proper model for nature.

According to Morgan and Morrison, models also need to have a certain link to theory if they are to function as a model. This can be likened to what Gradmann has argued, namely that a certain level of abstraction is needed for a model to be a model.[66] In our case, Holst's research in relation to the animal went from being linked with a bacteriological approach—and a theory that certain bacteria were the cause of certain diseases—to a theory about nutrition. The theory, or line of reasoning, that came to accompany the research process was that the lack of certain foodstuffs could cause diseases; hence the theory about deficiency diseases. However, at the time this theory was not generally established or accepted; it also lacked a fully developed vocabulary. Those which later came to be named *vitamines*, were now, as in Holst's newspaper articles, called 'peculiar nutrients'. Integral to this theory was the idea that not only did certain forms of food contain certain peculiar nutrients that were needed for a healthy diet, these 'peculiar nutrients could also be destroyed', through heating, for example. Thus the theory had implications for what caused the disease and what had to be done to remedy it: Food intended for polar expeditions, for example, ought not to be cooked and tinned as the food could then be devoid of its otherwise positive, or antiscorbutic, effects.

Not only was the nutritional theory not fully developed; Holst's and Frølich's opponents had their own theory that they thought could explain the same disease. Their theory was also related to diet, but seen as caused by a form of intoxication of the food. To Holst and Frølich the disease they had modelled both had a link to an outside reality (by way of the animal and its assumption of sufficient likeness to the human, as well as the laboratory setting as an acceptable replacement for nature) as well as a link to theory. Neither of these links was accepted by their opponents.

But Morgan and Morrison add another important element to the discussion and argue that the model also needs to have a certain independence, both from an external reality and a relevant theory. Integral to this independence is the capacity to perform as a tool: to do work. This links to what others have pointed out when it comes to the question of

[64]Karen Knorr-Cetina, 'Laboratory Studies. The Cultural Approach to the Study of Science', in S. Jasanoff, G. E. Markle, J. C. Petersen and T. Pinch, eds, *Handbook of Science and Technology Studies* (London: Sage, 1995), 140–66.

[65]Margaret Morrison and Mary S. Morgan, 'Models as Mediating Instruments' in M. S. Morgan and M. Morrison, eds, *Models as Mediators. Perspectives on Natural and Social Science* (Cambridge: Cambridge University Press, 1999), 10–37.

[66]Christoph Gradmann, 'Das Maß der Krankheit. Das Pathologische Tierexperiment in der medizinschen Bakteriologie Robert Kochs', in C. Borck, V. Hess and H. Schmidgen, eds, *Maß und Eigensinn. Studien im Anschluß an Georges Canguilhem* (München: Wilhelm Fink Verlag, 2005), 71–90.

what a model is, namely a simplified version of an outside reality, set up to enable a focus on what is thought to be crucial or most important for what one wants to explain, while excluding what is considered less important. This practice of *modelling* is an integral part of discussions on models. This practice—to model, elaborate on, enhance and foreground some parts of reality while others are excluded—was precisely what was contested in the debate on Holst's and Frølich's research findings. On the contrary, a so-called real field reality and real human beings were proposed as the answer to the problem. 'Models', in the sense of semi-independent tools established to enhance and work upon reality, were thought to be useless and unnecessary.

In academic contributions on the role of animals in biological research, the model organism is sometimes the preferred notion.[67] The controversy and contestation over Holst's and Frølich's research underline the need to pay close attention not only to the animal organism as such, but just as much to the setting or system in which the animal is made to take part. Drawing loosely on Hans-Jörg Rheinberger's work, Alkeny distinguishes the animal model from the model system and points out that the latter may be understood to be not only the animal organism, but also the techniques and experimental methodologies that the organism is part of.[68] This includes the experimental setting as well the procedure in which the model organism is made an integral part. This is highly fruitful and relevant for understanding the scurvy controversy. I would nevertheless like to expand on this notion of the model system.

The scurvy controversy points to three levels in a system: First, the laboratory setting that was modelled, one could say, upon the external field or the outside reality (think, for example, of Holst's efforts to imitate a tropical climate for his specimen cats in the university's botanical garden). This means that the laboratory was set up as a model of the outside reality (but then of course in a semi-independent way, as Morgan and Morrison have pointed out). Secondly, the animal organism was a model of the human organism. Thirdly, the disease was modelled within the animal body as a model of the human disease. This was a model-system, or as I would suggest, designed to emphasize that this has to do with a series of practices, a *modelling* system.

The scurvy controversy may alert us to the many layers of the research assemblage that have to be accepted before something can be recognised as valid research and a possible scientific fact. Hence, modelling is a form of practice that does not always succeed. This takes us back to the aspect of models with which I introduced this paper; namely the ways in which models are objects of persuasion.[69] The scurvy controversy is an apt example of the work involved in persuading the relevant audience, and that the process

[67] As for instance Rachel A. Ankeny, 'Wormy Logic: Model Organism as Case-Based Reasoning', in A. N. H. Creager, E. Lunbeck and M. Norton Wise, eds, *Science Without Laws: Model Systems, Cases, Exemplary Narratives* (Durham and London: Duke University Press, 2007), 46–58.

[68] *Ibid*; Hans-Jörg Rheinberger, *Toward a History of Epistemic Things. Synthesizing Proteins in the Test Tube* (Stanford: Stanford University Press, 1997). Rheinberger uses the notion of the experimental system.

[69] Thus this relates to the persuasive element of science and the role of the audience, something which various scholars have linked to material technologies, for instance Shapin and Schaffer on e.g. literary technologies and Latour on literary inscriptions. Steven Shapin and Simon Schaffer, *Leviathan and the Air-pump: Hobbes, Boyle and the Experimental Life* (Princeton, NJ: Princeton University Press, 1985). See also Bruno Latour and Steve Woolgar, *Laboratory Life: The Construction of Scientific Facts* (Princeton, NJ: Princeton University Press, 1986).

of persuasion, in this case, rested upon the acceptance of what we might call a modelling system and a model assemblage that had yet to become a fully routinised part of medicine.

Conclusion

'Life before Model Systems' was the title of Frederick B. Churchill's paper on the vast range of animals that were subjected to scrutiny within zoology at August Weismann's Institute.[70] The present case has explored, not life *before* model systems, but rather life and the *emergence* of a modelling system and a model assemblage.[71] In the early twentieth century, the modelling system was not a ready-made and stable assemblage. Rather it was *emerging* and was sought to be established as a model assemblage—partly independent, hence enabled to perform as a tool and a modelling practice.

This is not to say that those who opposed Holst and Frølich were genuinely and principally against laboratory animal research or against drawing conclusions based on research on animals. Whereas Parliament at the turn of the twentieth century raised critical voices and challenged the use, and assumed abuse, of laboratory animals, Axel Holst and Sophus Torup joined forces with colleagues to argue for the benefits of such animal experiments.[72] And even if Nansen argued against the relevance of experiments on guinea pigs for the understanding of scurvy, in his doctoral thesis he himself had defended wide-ranging conclusions regarding the central nervous system based on his research on lower animals. In working on the issue of the central nervous system, his ambition, based in research on lower animals, was to draw general conclusions applicable to all animals, humans included.[73] The zoologist Nansen may have seen the zoologist in a particular and exceptional position—having, as he saw it, life itself as the task, and the understanding of life, its origin and development as the objective.[74] Moreover, life was to be studied in its own right, for example its real environment.

In the postscript to *The Structure of Scientific Revolutions* (1962), Thomas Kuhn points not to the model but to 'the exemplar', arguing that 'the exemplar' is a shared example upon which scientists base their work at the research front. In his development of Kuhn's argument, Andrew Pickering stresses that such a shared example involves the concrete demonstration in some practical situation of the utility of a cultural product, for example a new experimental technique or a new theoretical model. It is by way of such demonstrations, through practice which involves exemplars, that new concepts are linked to the natural world and acquire their meanings. Particular research networks within a given scientific community are to be seen as engaged in the articulation, the working out in practice, of

[70] Frederick B. Churchill, 'Life Before Model Systems: General Zoology at August Weizmann's Institute', *American Zoologist*, 1997, 3, 260–8.

[71] On the establishment of such systems and standards in later periods see for instance Robert G. W. Kirk, 'A Brave New Animal for a Brave New World: The British Laboratory Animals Bureau and the Constitution of International Standards of Laboratory Animal Production and Use, circa 1947–1968', *Isis*, 2010, 101, 62–94, and Tone Druglitrø, 'Å skape en standard for velferd. Forsøksdyr i norsk biomedisin, 1953–1986' (Unpublished PhD thesis, University of Oslo, 2012).

[72] For this see Kristin Asdal, 'Subjected to Parliament: The Laboratory of Experimental Medicine and the Animal Body', *Social Studies of Science*, 2008, 38, 899–917. See also the rich literature on related controversies in a range of countries in about the same period, for instance Nicolaas A. Rupke ed., *Vivisection in Historical Perspective* (London, New York: Routledge, 1994); Susan E. Lederer, 'Hideyo Noguchi's Luetin Experiment and the Antivivisectionists', *Isis*, 1985, 76, 31–48.

[73] Jølle, *Nansen. Oppdageren,* 62.

[74] *Ibid*., 42.

particular exemplars.[75] I have tried to demonstrate that Holst and Frølich did not succeed in establishing such a shared exemplar; neither in the form of the modelling practice, the model assemblage, or in the form of a model organism.

This is not to deny that Holst and Frølich were the first to experimentally produce scurvy in an animal organism and explain this as caused by a lack of particular nutrients. However, I have argued that whereas Holst and Frølich were concerned with experimentally producing, hence modelling, a disease (scurvy), their concern was not related to developing an animal model. And it was only later that the guinea pig became what Holmes (for the frog) termed 'the old martyr of science' in relation to scurvy.[76] The guinea pig has become one of those few organisms that (together with the white mouse, the fruit fly, field corn and the zebra fish) have been the locus of biologist's endeavours and in-depth studies.[77] When it comes to scurvy, this relation has to do with the fact that the guinea pig, just like humans, has been found to be dependent upon C-vitamin supplements. Hence, without such supplements the guinea pig develops scurvy—and with such supplements outbreaks of scurvy can be cured.

But again, and what should be evident from the above controversy, this is not to say that the model issue was irrelevant in Holst's and Frølich's research and the ensuing controversy. Quite the contrary, their research was dependent upon a modelling practice and a method assemblage that was contested by their peers. Hence, the disease model they produced and the imitation they experimentally performed did not become a shared exemplar, an exemplar that stood out as enabling generalisation beyond the single example of the 'plant-eating rodent': the guinea pig.

Holst died in 1931 without having received the Nobel Prize or any other honours for his work.[78] Frølich was nominated for the Nobel Prize in medicine for 1931, but was not awarded it. Later on, as many as three Nobel Prizes were awarded to others for their contribution to the research on what came to be called C vitamins, in contrast to the antiscorbutic or 'peculiar nutrients' that the polar hero and zoologist Nansen could not believe in. In 1926, when Casimir Funk listed who he saw as the pioneers in vitamin research, neither Holst nor Frølich were included. Later, it was Sir Frederick Hopkins and Christiaan Eijkman who won a shared Nobel award, Hopkins for having proven the existence of what was called 'accessory food factors', and Eijkman for his work on human beriberi and avian polyneuritis. Holst and his colleague Frølich were 'the first', to experimentally produce scurvy by way of animal experiments and thus explain the causes of scurvy. But in its time, their work was not established as a shared exemplar within the research community, and in this sense it did not become 'a model'.

[75]Thomas S. Kuhn, *The Structure of Scientific Revolutions* (Chicago: University of Chicago Press, 1962); Andrew Pickering, 'Interests and Analogies', in B. Barnes and D. Edges, eds, *Science in Context: Readings in the Sociology of Science* (Milton Keynes: The Open University Press, 1982), 125–46. Pickering has elaborated on Kuhn on this issue. However, I do not follow Pickering in his development of this aspect of Kuhn into an interest model.

[76]Frederic L. Holmes, 'The Old Martyr of Science. The Frog in Experimental Physiology', *Journal of the History of Biology*, 1993, 2, 311–28.

[77]Churchill, 'Life Before Model Systems'.

[78]Norum and Grav 2002; Casimir Funk, 'Who Discovered Vitamines?', *Science*, 1926, 63, 455–6; Obituary signed T.M. 'Casimir Funk PhD', *The British Medical Journal*, 1967, 4, 624–5.

Acknowledgements

I am grateful to Tone Druglitrø, Christoph Gradmann, Anne Kveim Lie, Karen Rader and Liv Emma Thorsen for comments and discussions on earlier drafts of this paper. I am also grateful to the three anonymous referees and the editors of *Social History of Medicine* for helpful comments. I would also like to thank Stefan Erbs and Bård Hobæk for assistance.

Funding

The research for this paper was made possible by financial support from the Norwegian Research Council and the University History project at the University of Oslo.