BIOGRAPHICAL
MEMOIRS

Dorothy Mary Moyle Needham. 22 September 1896 – 22 December 1987

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Biogr. Mems Fell. R. Soc. 2003 **49**, 351-365, published 1 December 2003

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Biogr. Mems Fell. R. Soc. Lond. **49**, 351–365 (2003)

D. M. Needham

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Elected FRS 1948

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Biographical memoirs have their fortunes too[1]

In July 1994 I was approached by The Royal Society asking whether I would be willing to help in putting together a biographical memoir for Dr Dorothy Moyle Needham, who died in December 1987. For a variety of reasons, the Fellow of The Royal Society who originally undertook to write the memoir had been unable to deliver it before his death. After responding that I would be happy to assist, I was informed that I would, no doubt, be contacted by the writer who undertook to complete the task. As it turned out, I heard nothing more and, while occasionally wondering at the unusual delay in the publication of the memoir, I left it at that. That is, until in the spring of 2000 when I noticed that there was still no memoir on 'Dophi', as she was known to friends and colleagues. I found this very strange in view of the fact that almost $11\frac{1}{2}$ years had elapsed since her death and that she was among the first 10 elected female Fellows of The Royal Society.[2]

After some hesitation, I wrote on 7 May 2000 to The Lord Lewis of Newnham FRS (then Warden of Robinson College, Cambridge), alerting him to the situation. He was more than surprised and, following his enquiries, in July 2000 I became the third author invited to prepare Dr D.M. Needham's biographical memoir.

As in private duty bound, I accepted the invitation, although not without anxiety over predicaments perceived beforehand. For one thing, though I had been collaborating with Dorothy Needham since 1972, the subject was history of biochemistry. Usually a biographical memoir is prepared by a person acquainted at first hand with the experimental/theoretical features of the work of the deceased Fellow. For another thing, I realized that I would be able to work on the memoir only intermittently because of other commitments, including prolonged stays abroad. All this has something to do with the delay in preparing this memoir, including the format.

Dorothy Mary Moyle Needham was born in London on 22 September 1896. Her father, John Moyle, was a civil clerk in the Patent Office. According to Dorothy's husband, Joseph Needham (FRS 1941), John Moyle 'became more and more revolutionary as he became older—a great contrast with the many people who become more conservative as they get older … he was a man of the type of William Morris and Keir Hardie who wanted to build Jerusalem in England's green and pleasant land'.[3] No doubt, this was formative to how she came to embrace lastingly socialist ideas in combination with deep-felt Christianity. These beliefs go some way to illumine Dorothy Needham's lifelong multifarious involvements in humanitarian actions and progressive politics.

It was her mother's sister, Miss Agnes Daves, the headmistress of Claremont College, Stockport (which Dorothy attended), who became aware that her niece would benefit from a university education. She was behind Dorothy's taking the entrance examination at Girton College, Cambridge, where she lived as a student from 1915 to 1919. Autobiographical material dealing with this period indicates that, although she had some grounding in science, mainly botany, before she arrived at Girton, it was here that she came to learn her chemistry. This was due to Miss M.B. Thomas who devised practical work in the College laboratory which, in Dorothy's judgement, was then superior to that offered by the University Department of Chemistry. As to university lectures, 'it was ordained (I do not recall by whom)', writes Dorothy Needham, 'that we should all sit together in the front row of the lecture halls. Girton being a long way out of town, hansoms or four-wheeled cabs were provided for those students who were not bicycling.'[4]

> *The justification for considering muscle tissue out of all the active tissues of the organism, lies in the fact that only in muscle can we come near to comparing the chemical changes going on with the simultaneous work done or energy set free as heat.*
> D.M. Needham (1932)[5]

Dorothy Needham became a leading authority on the biochemistry of muscle. The beginnings of her interest in chemical processes in biological systems can be traced to her attendance of lectures by Sir Frederick Gowland Hopkins FRS, who held the Chair of Biochemistry (founded in 1914). Apart from Joseph Needham (they were married in 1924), the future joint recipient of the Nobel Prize for Physiology or Medicine in 1929 'for his discovery of growth-promoting vitamins' and President of The Royal Society (1930–35) was the single greatest influence in her life. She retained her boundless admiration for 'Hoppy' into her old age, having shared it with pupils and collaborators from some 30 countries, who held 100 chairs or so throughout the world, including some 30 Fellows of The Royal Society and five Nobel laureates. Joseph and Dorothy Needham expressed memorably the affection, gratitude and respect in which the doyen of British biochemistry was held worldwide when they wrote, shortly after his death, 'One never came across anybody at all like him, and now one is sure one never will.'[6]

Hopkins certainly seems to have been an exception among heads of scientific departments in Cambridge to offer opportunities to women to do research at the time when Dorothy Moyle had completed her university studies. Then women in Cambridge could not receive a degree in a formal ceremony. They were given a diploma 'entitling' them to a degree. Dorothy took her MA in 1923 and her PhD in 1930. She got her DSc in a proper ceremony only after the war in 1945.

When she started research under Hopkins in 1920 there were apparently nine men and nine women working in the department. Soon after Dorothy joined it, the seed of her love affair with muscle biochemistry was planted. Then Hopkins asked her and another research worker, Dorothy L. Foster, to translate papers on frog muscle by Otto Meyerhof (ForMemRS 1937) that appeared in *Archiv für die gesamte Physiologie des Menschen und der Tiere* (1919–20). Moreover, he suggested that they should reinvestigate the interconversion of glycogen and lactic acid that the work of Meyerhof stipulated.

That is, Meyerhof confirmed much of what Walter (later Sir Walter) Morley Fletcher (FRS 1915) and Hopkins had presented regarding the formation of lactic acid on anaerobic contraction of muscle and its removal on recovery in oxygen in a seminal paper (1907), followed by a review of the state of the art (1915).[7] But Meyerhof went further. He found, by simultaneous estimations of lactic acid and glycogen in excised muscles, before and after recovery in oxygen from previous fatigue, that one is reconverted into the other. Because some workers in the field doubted the resynthesis of glycogen, Hopkins asked Foster and Moyle to re-examine the problem. Their joint work, employing Hopkins's method of estimation, confirmed the interconversion of glycogen and lactic acid.[8]

Between 1924 and 1930 Dorothy published several studies on the metabolism of succinic, fumaric and malic acids in muscle, including their formation from glutamic and aspartic acids. They can be viewed as contribution to the then unfolding discussion of the extent to which the pathways of anaerobic and aerobic breakdown of carbohydrate coincide.

In the course of her work Dorothy found that the two amino acids, when added to minced muscle under anaerobic conditions, gave rise to an increased amount of succinic, fumaric and malic acids. Their formation was not accompanied by the production of ammonia nor by any increase of soluble nitrogen fractions (urea, uric acid, amide-nitrogen). Under aerobic conditions an increased oxygen uptake was observed, again without any change in the soluble fractions but it was found that the aspartic acid had disappeared. She suggested, 'the possibility of the linkage of the NH_2 group of the glutamic acid with some reactive carbohydrate in the muscle, when oxidation and splitting off of the nitrogen with production of succinic acid occurs, the nitrogen is left in combination with this carbon chain, a new α-amino-acid thus being formed.'[9] This was perhaps the earliest intimation of the existence of the metabolic group-transfer reaction, later to be referred to as 'transamination'.

Ever since Arthur (later Sir Arthur) Harden (FRS 1909) and William John Young had pointed out, in 1906, that the rate of alcoholic fermentation related to the presence or absence of inorganic phosphate, it was acknowledged to be a key discovery.[10] It became the starting point for looking upon the phosphorylation of carbohydrate as the way and means of splitting it to obtain energy *and* to transfer it for biological purposes.

Until the mid-1930s or so, little if any consideration was given to the enzymic activity underlying the oxidative generation of biochemical energy. In fact what was gradually emerging was that the phosphorylation of carbohydrate could be perceived as a metabolic cycle, ostensibly involving a sequence of reversible enzymic reactions ('phosphate cycle').

The idea of cyclic phosphate transfer in muscle contraction was explicitly discussed by Dorothy Needham in 1937:[11]

> There is little doubt that in appropriately prepared [muscle] extracts … reactions can take place with little if any formation or disappearance of free phosphate—the organic phosphate functioning in practically closed cycles.
>
> The presence in muscle extracts of this beautifully co-ordinated series of enzymes—such that circulating phosphate can be kept always in the organic form, its transfer ensuring economical transfer also of energy—might tempt one to assume that, in the intact muscle itself, such cycles are used to the full.

Then Dorothy was studying phosphate esterification in muscle. She was familiar with the work of Meyerhof and his collaborator Wilhelm Kiessling, who drew attention to the oxido-reduction mechanism involving the oxidation of triosephosphoric acid to phosphoglyceric acid and the reduction of pyruvic acid to lactic acid.[12] Bearing on this, she postulated for muscle[13]

> an endothermic reaction coupled with an exothermic one—the formation of adenylpyrosphophate from adenylic acid and free phosphate, coupled with the oxido-reduction between pyruvic acid and triosephosphate:
>
> Pyruvic acid + triosephosphate → lactic acid + phosphoglyceric acid
> (+ about 8000 gm.cals.).

At the time of her writing this passage, there was no direct evidence for the postulated mechanism. But while in press, she and her colleague Raman Kochukrishna Pillai were able to demonstrate the existence of such a relationship and thus to make a distinguished contribution to the understanding of anaerobic carbohydrate metabolism.[14]

In 1939 the biochemical world was startled by the discovery by Vladimir Aleksandrovich Engelhardt and Militsa Nikolaevna Lyubimova that myosin, the contractile protein of muscle, behaved as the enzyme adenosine triphosphatase (ATPase).[15] Among the first to enlarge the subject on lines similar to those of the Soviet investigators was a group of researchers in Cambridge, headed by Joseph and Dorothy Needham. The elaborate experimental technique involved measurements of the changes in the double refraction of flow and viscosity of myosin solutions. As Sir Andrew Huxley FRS (PRS 1980–85) noted in 1977:[16]

> In the 1930s there was more interest in birefringence and its quantitative analysis, both in cellular structures and in solution, than there has been since the second world war, probably because it was then the only index of structural organization below the limit of resolution of the light microscope.

Without going into detail, it can be said that the findings of the group of the Needhams confirmed the contractile enzyme hypothesis of the Soviet investigators, in so far as adenosine triphosphate caused a reversible decrease in the axial ratio of the myosin particles; they considered several possible explanations for this, e.g. an actual contraction of the molecule, or a sliding effect of complex micelles.[17]

At that time actin, a new protein discovered in muscle contemporaneously by Albert Szent-Györgyi[18] and his school in Szeged, Hungary, was not known in Britain. In the light of this finding, it was later understood that the solutions in the Cambridge coaxial viscosimeter must have consisted of actomyosin. Reviewing the 'state of the art' in 1950, Dorothy Needham reaffirmed that 'the conception of energy provision by the splitting off of the terminal phosphate group of ATP, under the influence of myosin or actomyosin acting as ATPase, is central in current hypotheses of muscle contraction'. At the same time she was pointing to gaps in knowledge, such as the difficulty in specifying the optimal pH conditions for the adenosine triphosphatase activity.[19]

The discovery of the enzymic property of myosin was a landmark in the history of muscle chemistry. For the first time in the history of biochemistry and physiology a direct relation between microstructure and chemical action was experimentally established. A further impetus to an understanding of the link between these two worlds came from examinations of the fine structure of the muscle fibre by X-ray diffraction and the use of light and electron microscopies. What these techniques revealed was the existence of two sets of filaments in the myofibril: the thick filaments composed of myosin and the thin filaments composed of actin. Initiated in 1953 by Hugh E. Huxley (FRS 1960),[20] these observations led him and Sir Andrew Huxley to suggest the sliding-filament hypothesis. That is, the contraction of vertebrate striated muscle involves sliding the thick and thin filaments past each other.

Dorothy Needham followed these developments very keenly although her interest had shifted to the study of contraction of vertebrate smooth muscle, with Jennifer M. Williams and Catherine F. Shoenberg. With the latter, who explored the relevance of the sliding mechanism for the mechanism of contraction of vertebrate smooth muscle, she kept in close touch even after retiring from experimental work in 1963. In 1972, appropriately, she organized with Professor Edith Bülbring FRS a Royal Society Discussion Meeting on 'Recent developments in vertebrate smooth muscle physiology'.

A year beforehand, in 1971, *Machina carnis*, her exhaustive historical account of the biochemistry of muscular contraction, was published. Therefore her concluding characterization of the contemporaneous situation is of interest: 'yet still the keystone may be said to be lacking, the full explanation of exactly how the sliding occurs'.[21]

It was in recognition of her researches on the biochemistry of muscle that Dorothy was elected a Fellow of The Royal Society. But she was active, from time to time, also in other areas. Thus she collaborated with J. Needham on intracellular pH and rH (oxidation–reduction potential) in the 1920s, with J. Needham and Conrad H. Waddington (FRS 1947) on the chemical nature of amphibian organizer, and mainly with Ernest Baldwin on the comparative biochemistry of phosphagen in the 1930s.

To determine intracellular pH and rH the Needhams microinjected amoebae and sea-urchin eggs, which induced their brilliant colleague John Burdon Sanderson Haldane (FRS 1932) (then Reader in Biochemistry in Cambridge) to compose the following verse:[22]

> Next door N.J.T. and D.M. Needham
> Transfix amoebae, yes, and bleed 'em,
> Besides determining their buffering,
> And so decreasing human suffering.

As Joseph Needham explained, 'the point of this last remark was that Sir William Dunn, who had given the money for the erection of the Biochemical Laboratory in 1922, hoped that it would conduce to the amelioration of human suffering. It was always said that he had been looking for something to endow, and that Fletcher (then Secretary of the Medical Research Council) had told him "Cambridge is the place, and Hopkins is the man".'

(Sir) Walter Morley Fletcher, Hopkins's former collaborator, left Cambridge to serve, during 1914–33, a new established body—the Medical Research Committee (later to become the Medical Research Council)—as Secretary. In this function he tried to influence Hopkins to develop the study of vitamins. Thus, two years before Hopkins was awarded the Nobel Prize, Fletcher famously wrote to A.V. Hill FRS:[23]

> I told Hopkins that, having somehow bagged the credit for inventing vitamins, he spends all his times collecting gold medals on the strength of it, and yet in the past ten years has neither done, nor got others to do, a hand's turn of work in the subject. His place bristles with clever young Jews and talkative women, who are frightfully learned about protein molecules and oxidation–reduction potentials and all that. But they all seem to run away from biology. The vitamin story is clamouring for analysis … yet not a soul at Cambridge will look at it.

A light-hearted private throwaway remark? An indication of prevalent aversion to Jews and women in academe? Be that as it may, Fletcher's observation corroborates that Hopkin's department at Cambridge was free of anti-Semitism and misogyny.

> *[I] belong to the generation for whom it was calmly assumed that married women would be supported financially by their husbands, and if they chose to work in the laboratory all day and half the night, it was their own concern.*
> D. Needham (1982)[24]

Indeed, Dorothy Needham spent long hours working hard in the laboratory. In her dealings with academic and non-academics, friends and colleagues, she was unfailingly helpful and kind. She was extremely modest and self-effacing. In the anonymous obituary in *The Times* (26 December 1987) it is stated that 'throughout her life she retained a certain innocence and freedom from wordliness'. True, already during Dorothy's lifetime her behavioural and mental characteristics were looked upon as well-nigh saint-like. But there was another side to her that her one-time assistant Jennifer Williams in the obituary in *The Independent* (11 January 1988) portrays as follows: 'She had a very gentle manner, which belied her strength of mind'.

To be sure, without possessing it, it would have been hard for a woman scientist to reach the top rung of her profession as Dorothy did. Of course, there had to be other ingredients, such as ability, opportunity and material security. Clearly, Dorothy displayed an early aptitude for scientific research that she was capable of realizing within the sympathetic and inspirational environment of the Cambridge Biochemical Laboratory. But materially and mentally she must have been under ongoing stress because she had depended on temporary grants throughout her working life. Although she had researched and taught in Cambridge France, Germany, Belgium and the USA, she had never enjoyed the security of a tenured research or teaching post.

When Dorothy Moyle started research, her first grant came from the Food Investigation Board.[25] From 1925 to 1928 she was a Beit Memorial Research Fellow. It seems that in the 1930s, when Dorothy was producing her most important contributions to knowledge of the biochemistry of muscle, she was financially on her own. During 1940–43 she worked for the Ministry of Supply on the metabolism of skin and bone marrow as member of a chemical research group, led by a Cambridge colleague, Malcolm Dixon (FRS 1942) (later Professor of Enzyme Biochemistry). Between 1944 and 1946 she was a member of a group of British and Chinese scientists and engineers organized by Joseph Needham into the Sino-British Science Co-operation Office at the British Embassy in Chunking. She functioned as Chemical Advisor and for a time as Associate Director.

After the war, when Dorothy Needham returned to research in Cambridge, the quest for its funding reappeared. Her election as a Fellow of The Royal Society in 1948 notwithstanding, there was no royal road to get it. The problem was to secure a long-term personal stipend. This was the basis of Medical Research Council's refusal in 1952 to renew a short-term grant for the third time. Between 1952 and 1955 she was supported by the Broodbank Fund of the university. In 1955 Dorothy's married status subverted her overture to The Royal Society. Apparently, the President (Lord Adrian) held that married women, Fellows or not, had no need to be salaried.[26] Afterwards, she was funded mainly by the Agricultural Research Council. In 1961–62 she benefited from The Royal Society's Foulerton Gift Donation. On her retirement in 1963 she received a Leverhulme Award.

It is no wonder when years later, as she surveyed her career in science, she had this to say:[27]

> Looking back over my 45 years in research I find it remarkable, especially from the point of view of contemporary practice, that although a fully qualified and full-time investigator, I never received, or even applied for any substantive post. I simply existed on one research grant after another, devoid of position, rank, or assured

> emolument .… Moral support I also received consistently from Joseph, but it was never in his power to give me the self-respect, which comes from a recognised and established position. I am glad that the young women in science today are not expected to observe this discouraging system of dependence.

By the time these words were published, Dorothy Needham had been one of the founding Fellows of Lucy Cavendish College, the first women's graduate foundation in the University of Cambridge (1965), of which she was made Honorary Fellow a year later. She was elected to Honorary Membership of the Biochemical Society in 1974. She was made Honorary Fellow of Girton College in 1976 and, as the first woman, Honorary of Fellow of Gonville and Caius College in 1979. This was a historic event indeed in view of the fact that the college was founded in 1348 and even in these days 'it is not normal practice to invite members of your own family' to dinner at High Table.

Although the situation of women scientists has improved, there are problems that do not go away, such as how to combine work in the laboratory with having a family. According to a recent appraisal by Christiane Nüsslein-Volhard ForMemRS (she shared the 1995 Nobel Prize in Physiology or Medicine) this is almost impossible to achieve.[28] True, she is discussing the situation in Germany but this does not really differ from the one experienced by women scientists in Britain or elsewhere.

Dorothy and Joseph Needham were the first married couple to be elected Fellows of The Royal Society in acknowledgement of their scientific achievements. They were married for 63 years. 'The fact that there were no children of their marriage', we read in the *The Times* obituary, 'served only to deepen her relationship with her husband'. I suspect that this observation originated with Joseph, as indeed did the obituary itself. In any case, in view of the place that Joseph and Dorothy occupied in each other's existence, it is imperative to give their bond its due in any serious account of their individual life stories,

Some of the collaborative work with Joseph, referred to previously, originated during 1925–28 when they stayed in marine biological stations, such as Roscoff in Brittany, Cumbray on the Clyde, and Monterey and Woods Hole in the USA.

At about this time, Joseph and Dorothy, ardent Christian socialists as they were, started an association of many years with the Church of Thaxted in Essex:[29]

> [f]orty years the clerks of Thaxted, first under Conrad Noel and then under Jack Putterill, have formed a group of friends drawn from all walks of life devoted to the coming of the Kingdom on earth, the celebration of the holy liturgy, and one another.

Dorothy Needham participated in meetings, during 1932–38, of a small group of biologists, physical scientists and philosophers interested in philosophical and methodological problems of biology. The Theoretical Biology Club, as the group became known, constituted itself in 1932 in the wake of the Second International Congress for the History of Science held in London in 1931. Its prime movers were Joseph Needham and the embryologist Joseph Henry Woodger searching, as they were, for answers to questions, such as what is the relation of form to function or organic part to whole.[30]

As already pointed out, the Needhams were not only philosophically oriented but also socially and politically so. This they demonstrated in a telling manner through their association with the liaison office in Chunking referred to earlier. Dorothy kept a diary from which some entries were published in 1948. They illustrate clearly her international and social consciousness and critical attitude to the way in which the West treated the East in scientific–technical and nutritional fields immediately after the hostilities of World War II ended.[31]

24th Nov. [1945] Heard the news of the destruction of the Japanese cyclotrons by MacArthur's orders. Chinese colleagues very upset—took it as a blow against Asiatic science that the cyclotrons were not sent to China. Only two days before, Hu Chien-Shan had attended a meeting of physicists and Government which decided on a project of Chinese research in nuclear physics. They were expecting that the large cyclotron would come to Nanking. J. [Joseph] wrote off to the scientific weeklies in the West informing them of this quite justified reaction, and suggesting strong protests.

1st Dec [1945] Tea at Lady Seymour's. Gwei-Djen[32] talked about international difficulties in the nutritional field. For example, the case of defatted soyabean meal-firms wanted to sell it to China in large quantities, but this could not be accepted. It contains only 0.8% fat and could not therefore be made up into any of the characteristic Chinese soyabean dishes (such as *doufu*) which they are accustomed to eat. Indeed, it would be indigestible and of little use even for pig food or fertilizer. It was also made of the wrong variety of soyabean, or rather of a mixture of the right and wrong varieties.

Another case was the 'parboiled rice'; firms in the West make this, which they call 'converted rice', by heating unhusked rice under pressure in steam for a few hours; this dextrinizes the starch and causes the vitamins to diffuse into the grain from the pericarp, so that when it is afterwards fried and husked, the rice is much more nutritious. But this process is already widely used in China and India, mainly for invalids. Since the taste differs from normal rice, parboiled rice is not popular. It is not clear why firms in the West should make a big profit on a process which any family in China and India can carry out in the home.

Mr. Aldous Huxley, writing in just praise of the literary, as distinct from the scientific, work of his grandfather, remarks that Thomas Henry Huxley was a hero of science; but is, and will remain a hero of literature. He develops the theme that individual scientific accomplishment, unlike literary accomplishment, is fated to be forgotten because it is always but a step in progress, and loses its importance as knowledge grows and widens. The truth of this view is, I think, but limited. Great personal accomplishment in science is not forgotten, even if for obvious reasons it is stored in fewer memories than is great literature. Yet I think the historians of science should meet with all encouragement, and not alone because of their piety towards past labours. The perspective of history is illuminating and a corrective at all times. It is especially valuable in maintaining sound judgements in times of revolution; and science to-day is revolutionary. I hope that you will agree with me that Chairs in the History of Science are among the needs of our time.

Sir Frederick Gowland Hopkins (1932)[33]

If one embarks on such a field one usually does not know where to begin. There is one thing one can always do, and this I did: repeat the work of old masters. I repeated what W. Kühne did a hundred years earlier. I extracted myosin with strong potassium chloride (KCl) and kept my eyes open.

Albert (von) Szent-Györgyi (1963)[34]

Those ignorant of the historical development of science are not likely ever to understand fully the nature of science and scientific research.

Sir Hans Adolf Krebs (1970)[35]

These are remarkable observations on the value of historical approach by three Nobel Prize biochemists. Hopkins was known to have paid attention to the historical side of biochemistry, especially in his lectures to the advanced class. Recalling the 1930s Norman Wingate Pirie FRS, one of Hopkins's most independent-minded students, wrote that '[they] were fascinating accounts of the early history of Biochemistry and Physiology, and of Biochemistry during the period in which he had watched it develop'.[36]

It may well be that Hopkins's approach influenced Dorothy to see in the acquaintance with the history of biochemistry a useful adjunct to the study of biochemistry. In her first book, *The biochemistry of muscle*, the oldest bibliographical reference is to T.W. Engelmann's suggestion 'as long ago as 1875 that the doubly refracting portions were specially associated with contractility'. But when it comes to the history of muscle biochemistry, she writes decisively:[37]

> In considering the history of muscle biochemistry, there is no need to look farther back than 1898, when Fletcher[38] published his first paper on the survival respiration of excised muscle. Fletcher came fresh and with an open mind to a subject the growth of which was being stifled by theorisation. He had a new, rapid and comparatively 'micro' method for carbon dioxide estimation, and he understood the dangers of bacterial infection, as his predecessors had not.
>
> At that time, muscular energy, or any kind of cell-activity was supposed to depend on the sudden splitting up of an unstable compound, the inogen molecule, which contained oxygen stored ready for the combustion of the rest of the molecule. The breakdown of this molecule was supposed to yield both lactic acid and carbon dioxide, and, as the oxygen was provided in the molecule, it should make no difference whether or not there was a contemporary external supply.
>
> With his improved technique Fletcher now found the curve for carbon dioxide output in nitrogen; it showed a fall, then a steady plateau, and stimulation to contraction had little or no effect on this plateau, unless fatigue was so great that the muscle became markedly acid. Fletcher had a new explanation for these facts. He suggested that the early fall in the curve, from its shape, was due to diffusion out of carbon dioxide already present in the muscle, and that during the steady part carbon dioxide was being displaced from carbonates by slow production of acid; on contraction, no oxidation took place, but more rapid acid production, resulting finally in increased carbon dioxide displacement.
>
> In oxygen he found that the muscle at rest gave three times as much carbon dioxide as in nitrogen, and when stimulated gave a great outburst of carbon dioxide. A contemporary oxygen supply, then, had great effect on the course of events, both in rest and in contraction.[39]

It would be difficult to better this summary of the knowledge of muscle biochemistry in about 1900. Moreover, it is remarkable for the full credit given to the pioneering studies by Fletcher on muscular contraction before his joint research with Hopkins. The small format of the book of merely 155 pages disguises its richness. In fact, it is a treasure of information to be mined by historians and scientists alike, interested in 'the increase of our knowledge … of the chemical changes providing the energy for contraction in muscle' within a period of time meticulously circumscribed by the author: 'during the last 35 years'.[40]

The above quoted text from Dorothy's monograph from 1932 will be comprehensible to the present-day reader, apart from the reference to 'inogen molecule'. It relates to the so-called inogen concept of muscular contraction, worked out by the German investigator Ludimar Hermann (ForMemRS 1905) in the later 1860s and earlier 1870s, whose influence extended into the first decade of the twentieth century.

By 1850 it was recognized that muscle could contract in the absence of oxygen, which led to studies of contraction under vacuum conditions. Hermann must have been one of the first physiologists to make use of the Geissler mercury air-pump to investigate the chemical processes taking place in resting and active muscle *in vacuo*.

Apart from drawing on his own results, Hermann took into account contemporary experimental achievements and theoretical discussions. Willy Kühne (ForMemRS 1892) had discovered the muscle protein myosin; Hermann had applied Moritz Traube's idea of the oxygen carrying ferment to myosin; and it was generally recognized that the criticisms and results produced by Traube, Adolf Fick, Johannes Wislicenus (ForMemRS 1897) and others tended to invalidate the supposition of Justus Liebig ForMemRS that proteins were metabolized during muscular exertion.

Among others, Hermann found that the resting muscle exposed to vacuum and deprived of oxygen produced a hardly noticeable amount of carbonic acid, which increased on contraction.

Hermann concluded that, in muscle respiration, the taking up of oxygen and the giving off of carbonic acids were not essentially interdependent. He imagined that oxygen passed from the flowing blood to the muscle fibre and became bound to myosin. As for carbonic acid, he suggested that its formation resulted not from an oxidative process but from the decomposition of a complex substance called 'inogen'. Myosin acted as an organic catalyst in a cycle of chemical changes that involved the restitution of the inogen but not the contraction of the muscle. Inogen was the first in a series of 'giant' molecules that just at the turn of the century were thought of fundamental components of protoplasm, responsible for life itself.

The inogen hypothesis was condemned outright as an example of unproductive speculative thinking ever since Fletcher and Hopkins demonstrated that there could be no common precursor for carbon dioxide and lactic acid and that it depended on conditions whether they were produced simultaneously in the absence of oxygen supply. However, the hard fact remains that the validity of the inogen hypothesis was accepted for more than 30 years, and this makes it difficult to ignore, at least from a historian's point of view.

All this and much else is discussed by Dorothy Needham in her monumental historical survey *Machina carnis*. With the authority of over 40 years' research experience and with a fine sense of historical detail she produced a *magnum opus*, which scientists and historians have every reason to be grateful for.

The distinguished biochemists-cum-historians Joseph Fruton and Marcel Florkin can be singled out as authors who found the book invaluable for the all-inclusiveness on its subject. Before these two with another eminent biochemist, John T. Edsall, became productive as historians, the only comprehensive work on the history of biochemistry was Fritz Lieben's *Die Geschichte der physiologischen Chemie*, first published in 1935 and reprinted in 1970.

In the material that Joseph Needham handed over to me after Dorothy's death I found a pencil-written draft note addressed to me, from which I quote:

> As I believe Joseph mentioned to you, I have been thinking over the possibility of trying to prepare a translation of Fritz Lieben's Geschichte der Physiologischen Chemie. It would be a great task but this is a unique and very useful book; I think I could manage the work, with help from German friends sometimes concerning language difficulties, and also from yourself, if you would be kind enough to advise on historical matters. I don't know whether you would feel like a collaboration? If so, this would be very welcome to me.

The note carries no date but I believe it to have been written in the spring of 1972. In its time Lieben's book was a magnificent achievement and its reprint was worthwhile. But I advised against a translation because it was virtually out of date.

Instead, I proposed that Harvard University Press, running a series of source books in various sciences, should be approached. The idea was to prepare a *Source book in biochemistry*, encompassing broadly the period 1800–1940. Harvard University Press accepted the proposal and, by October 1972, when I joined Gonville and Caius College as Visiting Scholar, the work on the project had begun.

What was hoped to be concluded in three years took much longer. Early in January 1985[41] I sent the manuscript *A source book in biochemistry c. 1770–1940* to Harvard University Press, which did not publish it, objecting to its length. Cambridge University Press declined to publish the book because the referees' reports indicated 'neither biochemists nor historians of science would find the volume useful for their work'.[42] Oxford University Press would have considered an 'up-to-date' work, that is, taking account of developments in molecular biology up to the 1970s. Those who asked going beyond 1940 did not seem to have realized that a serious full-scale analysis of this aspect of history could not be produced at the drop of a hat.

The book was eventually published in 1992 by the now defunct Leicester University Press, with an altered title and the following acknowledgement:[43]

> Next, my warmest thoughts go to the memory of Dr Dorothy Moyle Needham, FRS, whose name appears on the title page; she sadly died on 22 December 1987 at the age of 91. Her knowledge of the inter-war developments of biochemistry, in which she participated with great distinction as an active researcher, has been invaluable in preparation of the volume in draft form. Moreover, she has made a vital contribution to this volume by translating the selected German and French texts.

With regards to the title, the highly respected historian of science William H. Brock, reviewing the book, noted that

> Teich's volume, intriguingly described as a 'documentary history' rather than as a 'source book' has been long in the making. Conceived (chastely) with the Cambridge biochemist, Dorothy Needham, in 1972, the work has been twenty years in the making, fraught by her death in 1987 at the age of 91 as well as by his own precarious position within British academe.
>
> The result, however is a masterpiece that works both as a series of reprints, translations and extracts from books and papers concerned with 'the chemistry of life' between the 1770s and 1940s, but also, through its generously-conceived editorial narratives, glosses and documentation, as a history of biochemistry.[44]

Habent sua fata libelli.

Acknowledgements

I thank Karen Peters, Head of The Royal Society's Library and Information Services, for helping me in the preparation of this memoir with material, including the catalogue of papers and correspondence of D.M.M. Needham FRS. This was compiled by T.E. Powell and P. Harper of the National Cataloguing Unit for the Archives of Contemporary Scientists, University of Bath.

The frontispiece photograph was taken by Walter Stoneman, Godfrey Argent Studio, and is reproduced with permission.

Notes

1 Allusion to *Habent sua fata libelli* ('Books have their fortunes') by Terentius Maurus, *De litteris etc.* (*ca.* A.D. 200).

2 Joan Mason, 'The admission of the first women to The Royal Society of London', *Notes Rec. R. Soc. Lond.* **46**, 279 (1992) provides a most instructive account of the subject. See also Joan Mason, 'The women Fellows' jubilee', *Notes Rec. R. Soc. Lond.* **49**, 125 (1995).

3 'Dorothy Needham', An Address by Joseph Needham, *The Caian* (November 1988), p. 128.

4 D. Needham, 'Women in Cambridge biochemistry', in *Women scientists: the road to liberation* (ed. D. Richter), pp. 158–159 (Macmillan, London, 1982).

5 D.M. Needham, *The biochemistry of muscle* (Methuen, London, 1932), p. 1.

6 Joseph and Dorothy Needham, 'Sir Frederick Gowland Hopkins, O.M., P.R.S.', *Br. Med. Bull.* **5**, 301 (1948). Reprinted in *Hopkins & biochemistry* (ed. J. Needham and E. Baldwin), p. 119 (Heffer, Cambridge, 1949).

7 W.M. Fletcher and F.G. Hopkins, 'Lactic acid in amphibian muscle', *J. Physiol.* **35**, 247 (1907); 'Croonian Lecture of 1915: the respiratory process in muscle and the nature of muscular motion', *Proc. R. Soc. Lond.* B **89**, 444 (1917). Theirs were the first reliable quantitative data on lactic acid in muscle obtained by a novel but simple method. It involved cooling the muscle to 0 °C then crushing it quickly in ice-cold ethanol and grinding it with sand. The lactic acid that dissolved out was given as percentages of anhydrous zinc lactate. This procedure avoided the stimulation of muscle, accompanied by lactic acid production, which would thus have vitiated the quantitative relations.

8 D.L. Foster and D.M. Moyle, 'A contribution to the study of the interconversion of carbohydrate and lactic acid in muscle', *Biochem. J.* **15**, 672 (1921). For his work on muscular contraction Meyerhof received the 1922 Nobel Prize in Physiology or Medicine, which he shared with Archibald Vivian Hill (Biological Secretary of The Royal Society 1935–45; Foreign Secretary, 1945–46).

9 D.M. Needham, 'A quantitative study of succinic acid in muscle. III. Glutamic and aspartic acids as precursors', *Biochem. J.* **24**, 224 (1930).

10 A. Harden and W.J. Young, 'The alcoholic ferment of yeast-juice. Part II. The co-ferment of yeast-juice', *Proc. R. Soc. Lond.* B **78**, 369 (1906). For this work Harden was awarded the Nobel Prize in Chemistry in 1929, which he shared with Hans v. Euler-Chelpin.

11 D.M. Needham, 'Chemical cycles in muscle contraction', in *Perspectives in biochemistry* (ed. J. Needham and D.E. Green), p. 203 (Cambridge University Press, 1937). This was a highly acclaimed volume—it went into three editions—written by 32 students and associates of Sir Frederick Gowland Hopkins to celebrate his 75th birthday.

12 O. Meyerhof and W. Kiessling, 'Über den Hauptweg der Milchsäurebildung in der Muskulatur', *Biochem. Z.* **283**, 83 (1935–36).

13 D.M. Needham (note 11), p. 204.

14 D.M. Needham and R.K. Pillai, 'Coupling of dismutations with esterification of phosphate in muscle', *Nature* **140**, 64 (1937). The communication appeared independently and very shortly after Meyerhof had shown that this phosphate uptake depends on the presence of the adenylic system. The presence of a phosphate acceptor was necessary for rapid response, and for this Meyerhof used creatine. See O. Meyerhof, 'Über die Synthese der Kreatinphosphorsäure im Muskel und die „Reaktionsform" des Zuckers', *Naturwissenschaften* **25**, 443 (1937).

15 W.A. Engelhardt and M.N. Ljubimowa, 'Myosine and adenosuntriphosphatase', *Nature* **144**, 668 (1939).

16 A.F. Huxley, 'Looking back on muscle', in *The pursuit of nature: informal essays on the history of physiology*, p. 49 (Cambridge University Press, 1977).

17 The group included: M. Dainty, A. Kleinzeller, A.S.C. Lawrence, M. Miall and C.-S. Shen. For an account of their efforts to study interaction of adenosine triphosphate with myosin, see D.M. Needham, *Machina carnis: the biochemistry of muscular contraction in its historical development* (Cambridge University Press, 1971), pp. 147–148.

18 Albert (von) Szent-Györgyi received the Nobel Prize for Physiology or Medicine in 1937 'in recognition of his discoveries concerning the biological oxidation processes with special reference to vitamin C and the fumaric acid catalyst'.

19 D.M. Needham, 'Myosin adenosintriphosphate in relation to muscle contraction', in *Metabolism and function in honor of Otto Meyerhof* (ed. D. Nachmansohn), p. 42 (Amsterdam: Elsevier, 1950). The original of this book appeared as an issue of *Biochim. Biophys. Acta* **4**, 1–348 (1950).

20 H.E. Huxley, 'Electron microscope studies of the organisation of the filaments in striated muscle', *Biochim. Biophys. Acta* **12**, 387 (1953)

21 D.M. Needham (note 17), p. 602.

22 J. Needham, (note 3), p. 130.

23 R.E. Kohler, *From medical chemistry to biochemistry: the making of a biomedical discipline* (Cambridge University Press, 1982), p. 85.

24 D. Needham (note 4), p. 161.

25 The Food Investigation Board was part of the Department of Scientific and Industrial Research, established by the government in 1917.

26 Cf. *Catalogue of papers and correspondence of Dorothy Mary Moyle Needham FRS (1896–1987)* deposited in the Library, Girton College, Cambridge. Compiled by T.E. Powell and P. Harper (University of Bath, 1990), p. 5.

27 D. Needham (note 4), p. 161.

28 Cf. Christiane Nüsslein-Volhard, 'Mehr Frauen an die Forschungsfront', *Die Zeit*, 23 May 2002.

29 H. Holorenshaw [J. Needham], 'The making of an Honorary Taoist', in *Changing perspectives in history of science: essays in honour of Joseph Needham* (ed. M. Teich and R. Young), p. 9 (Heinemann, London, 1972).

30 For a discussion of the Theoretical Biology Club, see Pnina G. Abir-Am, 'The Biotheoretical Gathering, transdisciplinary authority and the incipient legitimation of molecular biology in the 1930s: new perspective on the historical sociology of science', *Hist. Sci.* **25**, 1 (1987).

31 J. Needham and D. Needham (eds.), *Science Outpost Papers of the Sino-British Science Co-operation Office (British Council Scientific Office in China) 1942–1946*, pp. 244–245 (The Pilot Press Ltd, London, 1948).

32 Lu Gwei-Djen came to Cambridge Biochemical Laboratory in the 1930s, she worked with Dorothy on pyruvic acid, and eventually became Joseph's closest collaborator in his work on the history of science and technology in China. After Dorothy's death she became Joseph's second wife in 1989.

33 F.G. Hopkins, 'Address of the President, Anniversary Meeting, 30 November 1932', *Proc. R. Soc. Lond.* B **112**, 167 (1932–33).

34 A. Szent-Györgyi, 'Lost in the twentieth century', *A. Rev. Biochem.* **32**, 9 (1963). This refers to historically significant efforts by the great Willy Kühne, between 1859 and 1864, to find out something more specific about protoplasmatic contractility which, it was believed, could be usefully studied in muscle. Employing a 10% NaCl solution he obtained from muscle a protein compound that he named myosin. As it turned out, the discovery of this substance became of signal consequence in the history of knowledge of muscle contraction.

35 H.A. Krebs, 'The history of the tricarboxylic acid cycle', *Perspect. Biol. Med.* **14**, 168 (1970).

36 N.W. Pirie, 'Sir Frederick Gowland Hopkins (1861–1947)' in *A history of biochemistry: selected topics in the history of biochemistry personal recollections* (ed. G. Semenza), vol. 1, p. 106 (Elsevier, Amsterdam, 1983).

37 D.M. Needham (note 5), pp. 2 and 128 (T.W. Engelmann. 'Contractilität und Doppelbrechung', *Arch. Ges. Physiol.* **11**, 411 (1875)].

38 W.M. Fletcher, 'The survival respiration of muscle', *J. Physiol.* **23,** 10 (1898–99).

39 W.M. Fletcher, 'The influence of oxygen upon the survival respiration of muscle', *J. Physiol.* **28**, 354 (1902); 'The relation of oxygen to the survival metabolism of muscle', *J. Physiol.* **28**, 474 (1902).

40 D.M. Needham (note 5), p. v.

41 By then Dorothy had been affected with what was later diagnosed as Alzheimer's disease. In a 'Memorandum on the health of Dr Dorothy Needham, F R S' Joseph Needham states: 'She is rather deaf, very forgetful, and liable to become confused, though often lucid in conversation; and she cannot organise papers or do any of her usual work. (Copy of typescript dated 29 Feb 84.)

42 Letter by Biological Sciences Editor, Cambridge University Press, 16 January 1987.

43 M. Teich with Dorothy M. Needham, *A documentary history of biochemistry 1770-1940* (Leicester University Press, 1992), p. xxvii. Puzzlingly, *Who Was Who* vol. VIII (1981–90) lists among Dorothy Mary Moyle Needham's publications a book called *Source book in the history of biochemistry 1740 to 1940* as published in 1987.

44 W.H. Brock, 'A biochemical ferment', *Hist. Sci.* **30**, 325 (1992).

Bibliography

A full bibliography appears on the accompanying microfiche, a photocopy of which is available from The Royal Society's Library at cost.