CHEMISTRY AND THE TWO ORGANIC KINGDOMS OF NATURE IN THE NINETEENTH CENTURY

by

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THE CHEMICAL investigation of animals and plants had been recognized in the eighteenth century as an important area of research, which was likely to lead to a fuller understanding of the process of life.[1] But, contrary to expectation, little progress was achieved, and this remained the case during the early nineteenth century, because of the simplification of the problems involved and the continuing employment of methods of procedure that were inappropriate.

The principal way in which chemistry had been applied was in the elementary analysis of animal and vegetable substances. From the results of such experiments nitrogen had been proposed as the characteristic element of animal life, in view of its comparative abundance there, and the two organic kingdoms had been separated on this basis. Gradually in the nineteenth century, nitrogen came to be seen as an element of vegetability as well. This was due to the growing evidence of its widespread distribution in plants. For example, the whole new group of nitrogenous alkaloids were discovered in quick succession, beginning with morphine in 1805, and including caffeine,[2] which was found to have a surprisingly high nitrogen content, exceeding that of many animal substances. When in 1833 Gay-Lussac proposed the generalization that all plant seeds contained nitrogen,[3] it was hardly a risky statement resting on the evidence of a few instances.

The information which could be obtained through elementary analysis was however severely limited, since the great diversity of naturally occurring organic compounds was reduced to similar formulae, based on the percentage composition of the same few elements, chiefly carbon, hydrogen, oxygen and nitrogen. Substances with different properties gave the same elementary analyses, and their role in life remained hidden.

THE IMMEDIATE PRINCIPLES

The compounds extracted from animals and plants had been termed the 'immediate principles' in the eighteenth century, to distinguish them from the remote principles or elements. They were regarded even then as a more reliable guide to the nature of organisms, since they were extracted by a less drastic analysis, and so retained some

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[1] D. C. Goodman, 'The application of chemical criteria to biological classification in the eighteenth century', *Med. Hist.*, 1971, **15**, 23–44. I would again like to thank Professor J. Schiller for his assistance.

[2] J. B. Dumas and P. J. Pelletier, 'Recherches sur la composition élémentaire et sur quelques propriétés caractéristiques des bases salifiables organiques', *Ann. Chim. Phys.*, 1823, **24**, 182–83.

[3] J. Gay-Lussac, 'Sur la présence de l'azote dans toutes les semences', *Ann. Chim. Phys.*, 1833, **53**, 110–12.

original properties. They formed a heterogenous collection of sugars, fats, albuminous substances, acids and pigments. It was above all in the study of these, in the discovery of their origin and physiological function, that fundamental physiological problems were solved with chemical assistance in the nineteenth century, though, as will be seen, the path was not a smooth one.

Most responsible for directing inquiries along these lines was Chevreul, a pupil of Vauquelin. He said the immediate principles were compounds which had been formed in life, and that an exact determination of their nature was an essential preliminary in physiology.[4] They had to be isolated by weak solvents, such as water and alcohol, working at moderate temperatures to preserve their nature, and finally characterized by precise properties like their melting points. In this way Chevreul first demonstrated that fats were compounds of glycerol with various fatty acids.

Since a number of immediate principles were common to the two organic kingdoms, Chevreul preferred not to classify them as products of vegetation and animalization, but to put them under the mixed heading of 'products of organized bodies'.[5] Albumen was one of the common immediate principles, existing both in the organs of herbivores and in their vegetable diet.[6] He looked to chemistry to explain how food was altered in the body.

Another important step was to investigate the immediate principles *in situ* in the tissues. Raspail argued that this was the correct method to adopt. He complained that chemistry, as traditionally practised, had told us nothing about the tissues, the seat of vital reactions, because analysis mixed up substances which nature kept apart in separate organs.[7] Chemistry on the large scale, and alone, could give no indication of the original nature of the various organs. But, in association with anatomy, and particularly in conjunction with the microscope, he said, chemical tests would become valuable.

As an example of his new method, Raspail described a test which is still in use for proteins. When the ovaries of barley were treated with a drop of concentrated sulphuric acid, on the slide of a microscope, an intense purple colour resulted.[8] Further experiments showed that this was due to the combined presence of sugar and albumen. This test produced the same colouration in the membranes of the uterus during gestation. Raspail concluded that there was a remarkable analogy between embryonic animals and plants, and that this was perhaps the stage of their development when they were most alike.[9] He could find no basis for dividing organic chemistry into vegetable and animal chemistry, since this separated immediate

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[4] For typical remarks by Chevreul on the immediate principles, see his *Recherches chimiques sur les Corps gras d'Origine animale,* Paris, 1823, p. 4; also 'Quelques considérations générales et inductions relatives à la matière des êtres vivants', *J. Savants,* 1837, 663–75, and his review article, 'Recherches expérimentales sur la Végétation, par M. Georges Ville', *J. Savants,* 1858, p. 111.

[5] M. E. Chevreul, *Considérations générales sur l'Analyse organique et sur les Applications,* Paris, 1824, p. 185. Similarly he rejected the possibility of distinguishing animals and plants by their nitrogen content, ibid., pp. 232–33.

[6] Chevreul, 'Quelques considérations générales . . .', (n. 4), p. 667f.

[7] F. V. Raspail, *Nouveau Système de Chimie organique, fondé sur des Méthodes nouvelles d'Observation,* Paris, 1833, pp. 30–31.

[8] F. V. Raspail, 'Nouveau réactif destiné, dans les analyses microscopiques, à distinguer des quantités minimes de sucre, d'albumine, d'huile et de résine; et l'analogie que l'on découvre, par ce moyen, entre les ovules des plantes et les organes femelles de la génération des animaux pendant le temps de la gestation', *Bull. Sci. math. phys. chim.,* 1828, **10,** 267–72.

[9] F. V. Raspail, *Nouveau Système* (n. 7), p. 261.

principles common to the two kingdoms. No distinctive definitions could be given for animal and vegetable substances, so, like Chevreul, he classified them together as organic or organized. If a judgment had to be made on the kingdom of origin of an organic material, he said, chemistry would be useless, and only zoology or botany could decide.[10]

But the recognition of analogous immediate principles in animals and plants led to consequences which Raspail had wanted to avoid. It was possible to argue that the nutrition of animals occurred directly through the incorporation of essential principles which already existed in vegetable foods. This highly simplified account was in fact adopted by the leading chemists of the time. In so doing, they abandoned the organism and set up false barriers between animals and plants.

VITAL DUALISM

Besides albumen, which was known to exist in both organic kingdoms in the eighteenth century, the discovery of principles resembling milk or cheese in plants was another source of this simplification. Einhof, professor of chemistry at the agricultural institute at Möglin, announced the discovery of a white immediate principle, having the odour of cheese, in peas, lentils and other leguminous plants.[11] He said its similarity to the animal substance explained the nutritional value of these plants. It was called legumin by Braconnot who later said it was really no different from the casein of milk.[12] Braconnot even supposed lactose existed in plants. He applauded the anatomical comparison of cotyledons and mammals, and thought there was a development of milk in both.[13]

Attention also turned to milk of almonds,[14] which appeared to have an astonishing resemblance to cow's milk. On standing it turned sour, a white deposit formed on the surface and a cheese-like smell was given out. Certain fractions were compared to whey and butter.

The most striking example of all came in Humboldt's description of a tree, which he was amazed to find during his South American travels.[15] He had heard stories of a tree growing in the mountains of Venezuela, which the natives called the cow-tree on account of the milk it provided. Humboldt was sceptical, but soon found that the reports were true. He saw the thick, milky juice pour from the incisions in the trunk. It became sour on standing and formed a clot, which the natives called 'cheese'. Humboldt could not carry out chemical tests, since he said he was almost without

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[10] Ibid., pp. 84–85 and 90–91.

[11] H. Einhof, 'Chemische Analyse der Erbsen (Pisum sativum) und der reisen Saubohnen (Vicia faba)', *Neues allg. J. Chem.*, 1806, **6**, 115–40 and 'Chemische Analyse der Linsen (Ervum Lens) und der Schminkbohnen (Phaseolus vulgaris)', *Neues allg. J. Chem.*, 1806, **6**, 542–52.

[12] H. Braconnot, 'Mémoire sur un principe particulier aux graines de la famille des légumineuses, et analyses des pois et des haricots', *Ann. Chim. Phys.*, 1827, **34**, 68–69, and 'Mémoire sur le caséum et sur le lait; nouvelles ressources qu'ils peuvent offrir à la société', *Ann. Chim. Phys.*, 1830, **43**, 347.

[13] H. Braconnot, 'Analyse des glands, suivie des considérations sur la présence du sucre de lait dans les graines des végétaux', *Ann. Chim. Phys.*, 1849, **27**, 392–401.

[14] P. F. G. Boullay, 'Analyse des Amandes douces (Amygdalus communis)', *J. Pharm.*, 1817, **3**, 337–44; H. A. von Vogel, 'Recherches analytiques sur les amandes amères', *J. Pharm.*, 1817, **3**, 344–53. Comparative tests on milk and milk of almonds were tried by A. Payen and E. O. Henry, 'Note sur l'albumine et sur la matière caséeuse du lait et des amandes émulsives', *J. Chim. Méd.*, 1826, **2**, 156–62.

[15] A. von Humboldt, 'Sur le lait de l'arbre de la vache et le lait des végétaux en général', *Ann. Chim. Phys.*, 1817, **7**, 182–91. The juice of the tree is still used as a substitute for milk by the natives of Venezuela.

reagents, but he was convinced of the similarity with mammal's milk. He said he had drunk much of the vegetable milk without bad effects.

The opportunity of a detailed analysis came with the departure of Boussingault for the same region. Humboldt particularly asked him to study the juice. Boussingault reported that it was physically like cow's milk and had the same taste, but he thought it differed chemically in containing fibrine instead of casein.[16] Many years later he carried out a further analysis on the vegetable milk he had first mixed with his coffee in Venezuela. Some bottles of the milk had been sent by the Venezuelan government to the International Exhibition in Paris. This time Boussingault found casein, and he compared the juice of the cow-tree to cream.[17]

It was tempting to suppose that casein, albumen and other principles originated in plants and served as the sole source of the same principles in animals. Comparative analyses finally persuaded the chemists that this was how nutrition occurred. Mulder reported that there were identical percentages of carbon, hydrogen, oxygen and nitrogen in vegetable and animal albumen, fibrine of the blood, and the casein of animal milk. The differences in phosphorus and sulphur content were small and seemed unimportant. He believed these animal and vegetable principles consisted essentially of the same quaternary, nitrogenous compound, which he called 'protein'. He stated that protein originated in plants and then entered the animal kingdom through ingested food.[18]

In his laboratory at Giessen, Liebig supervised research along the same lines.[19] It was concluded that vegetable casein, vegetable albumen and vegetable fibrine (gluten) were isomeric, and individually identical with their animal counterparts.[20] Liebig wrote:

> How beautifully and admirably simple, with the aid of these discoveries, appears the process of nutrition in animals, the formation of their organs, in which vitality chiefly resides! Those vegetable principles, which in animals are used to form blood, contain the chief constituents of blood, fibrine and albumen, ready formed, as far as regards their composition. All plants, besides, contain a certain quantity of iron, which re-appears in the colouring matter of the blood. . . . Vegetables produce in their organism the blood of all animals, for the carnivora, in consuming the blood and flesh of the graminivora, consume, strictly speaking, only the vegetable principles which have served for the nutrition of the latter.[21]

The milk with which the mother fed her young also came from plants. It derived either from the casein in the peas and lentils she had eaten, or chiefly from the supposedly simple conversion to casein of the isomeric albumen and fibrine, the con-

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[16] J. B. Boussingault and M. de Rivero, 'Mémoire sur le lait de l'arbre de la vache (Palo de Vaca)', *Ann. Chim. Phys.*, 1823, **23**, 219–23.

[17] J. B. Boussingault, 'Sur la composition du lait de l'arbre de la vache', *Ann. Chim. Phys.*, 1878, **15**, 180–84.

[18] G. J. Mulder, 'Sur la composition de quelques substances animales', *Bull. Sci. phys. nat. Néerlande*, 1838, 104–19.

[19] J. Scherer, 'Chemisch-physiologische Untersuchungen', *Ann. Pharm.*, 1841, **40**, 1–64; H. Bence Jones, 'Zusammensetzung der stickstoffhaltigen Nahrungsmittel des Pflanzenreichs, des Albumins des Gehirns und des Eigelbs', *Ann. Pharm.*, 1841, **40**, 65–69.

[20] J. von Liebig, 'Sur les matières alimentaires azotées du règne végétal', *Ann. Chim. Phys.*, 1842, **4**, 190f.

[21] J. von Liebig, *Animal Chemistry, or Organic Chemistry in its Applications to Physiology and Pathology*, London, 1842, pp. 48–49. Vegetarianism was called 'unphilosophical and vain' because the diet was no different chemically from animal food: 'The chemistry of common life', *Edinb. Rev.*, 1855, **101**, 486.

stituents of her blood, which were of vegetable origin. In the young the ingested casein was converted back to blood.[22]

The constituents of the blood, which Liebig believed only plants could form, were the starting-point for animal syntheses, resulting in the production of their tissues, membranes, nerves and brains, materials which no vegetable could supply.[23] During the incubation of the chick's egg, albumen, in the presence of atmospheric oxygen, was somehow elaborated into membranes, veins, arteries, feathers and claws.[24]

Liebig therefore described the animal organism as 'a higher kind of vegetable'.[25] The syntheses initiated in the vegetable kingdom from simple starting materials (carbon dioxide, water and ammonia) and producing protein compounds, were continued in the animal kingdom, to form the complex substances of the nerves and brain, the seat of the distinctive animal functions of sensation and thought.

The separation of the two organic kingdoms, based on their ability to perform particular syntheses, was taken much further by Dumas. It was he who was most responsible for the false vital dualism which attributed different physiologies to animals and plants. He wrote: 'We have found, in fact, by results beyond the reach of question, that animals do not create any of the truly organic substances, that they consume or destroy them; that vegetables, on the contrary, habitually create these substances, and that they destroy but few. . . . It is in the vegetable kingdom therefore, that the great elaboratory of organic life is found.'[26]

Dumas argued that the inability of animals to synthesize protein was established by his analyses of foods and excreta. Through this technique, which he and Boussingault employed in collaboration, Dumas made the grave mistake of ignoring the changes taking place inside the organism. He compared the nitrogen content of vegetable foods with that of urea, the waste product of the animal's destructive action on proteins. The two quantities were about the same. He made a physiological deduction, in which his neglect of the organism was explicit: 'So, abstracting from all the phenomena occurring in the organs and only considering the balance of entry and exit, one finds that man converts nearly all the nitrogen he receives into urea.... Is it not easy to conclude that the nitrogenous material in our food produces this urea, and that the entire activity of the animal organism is confined to assimilate the nitrogenous material, when it needs to, or to convert it to urea?'[27]

Like the protein, all the fats and sugars in animals came from the plants, which alone could synthesize them. Their fate in the body was the same, either to be retained unchanged or to be destroyed. The process of destruction was revealed by the nature of the products eliminated in the excreta. Carbon dioxide and water, discharged from the lungs, and urea in the urine were all products of oxidation. Dumas concluded that oxidation was the characteristic feature of animal physiology. Employing the oxygen of respired air, the animals performed acts of combustion with the fuel

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[22] J. von Liebig (n. 21), pp. 51–52.

[23] Ibid., p. 49.

[24] Ibid., pp. 107–108.

[25] Ibid., p. 49, and (n. 20), p. 207.

[26] J. B. A. Dumas and J. B. Boussingault, *The Chemical and Physiological Balance of Organic Nature*, 3rd ed., London, 1844, p. 6.

[27] J. B. A. Dumas and A. Cahours, 'Mémoire sur les matières azotées neutres de l'organisation', *Ann. Chim. Phys.*, 1842, **6**, 391–92.

provided by the vegetable kingdom. In this way the animal restored the heat, which it was continually losing through radiation and other ways, and received the energy for locomotion.[28] Inevitably he was drawn into comparisons between the animal body and the steam-engine.

The approach, which Dumas had recommended as the best way in which chemistry could serve physiology, resulted in a drastic reduction of all animal functions to the chemical process of combustion. The extent to which he insisted on this as the criterion of animality was clear from his discussion of various phenomena exhibited by plants. Referring to the production of carbon dioxide by plants at night and by their flowers and ripening fruit during the day, and to the evolution of heat in plants, he remarked: 'In a word, in all circumstances in which the plant needs heat, and when it does not receive this from outside, it behaves like an animal . . . it becomes an apparatus of combustion, and one can say, without being metaphorical, that at this time the plant becomes animal and really forms a part of the animal kingdom, from the point of view of the general physics of the globe.'[29]

But he said the true nature of the vegetable kingdom was displayed in the other activities of plants, in which they behaved in the opposite way from animals. The simple oxides excreted by animals were absorbed by plants, which then synthesized them into the complicated proteins, sugars and fats, which animals consumed. Concerned with the eternal circle of this global exchange, and not with the individual organism, Dumas, assisted by Boussingault, summarized his conclusions in tabular form.[30] The table consisted of two contrasting columns which displayed the opposition of the two organic kingdoms. It rested on the false antithesis of plant synthesis and animal destruction.

This theory was first challenged by Liebig, who had denied only the animal synthesis of protein. He was convinced, from analyses of ingesta and excreta, that animals were able to synthesize fats from sugars and starch. He wrote: 'There is no butter in the cow's grass, nor goose-fat in potatoes or barley. They do contain substances like wax, but in such small quantities that I do not attribute the formation of fat to them.'[31]

Solubility in ether was the test employed for fat. Experiments at Giessen showed that only minute portions of potatoes and fodder behaved in this way, yet pigs fattened remarkably and cows yielded much butter. Liebig denied that the chlorophyll of ingested green vegetables was converted to fat, since the excreta of cattle was green. He found that the excreta contained the same small quantity of fat as the ingesta.[32] Liebig also asked how the origin of all the fish-oil and spermaceti could be

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[28] J. B. A. Dumas, *Traité de Chimie appliquée aux Arts*, Paris, 1828–1846, 8 vols., vol. 8, p. 417f.

[29] Ibid., vol. 8, pp. 450–51. Dumas also compared the mushrooms to animals, because they fed on organic matter. But he thought too little was known about them and confined his conception of vegetables to the green plants, ibid., vol. 8, pp. 439–40. For experiments on the respiration of mushrooms see F. Marcet, 'Recherches sur les modifications qu'éprouve l'atmosphere par le contact de certains végétaux dépourvus de parties vertes', *Ann. Chim. Phys.*, 1835, **58**, 407–27, and J. Schlossberger and O. Doepping, 'Chemische Beiträge zur Kenntniss der Schwämme', *Ann. Pharm.*, 1844, **52**, 106–20.

The comparison of plants in the dark to animals was further pressed by Boussingault, who said the former produced asparagine, an amide which he took to be the vegetable equivalent of urea. J. B. Boussingault, 'De la végétation dans l'obscurité', *Ann. Chim. Phys.*, 1868, **13**, 238.

[30] J. B. A. Dumas and J. B. Boussingault (n. 26), p. xiii.

[31] J. von Liebig, 'Sur la formation de la graisse dans le corps animal', *J. Pharm.*, 1843, **3**, 190.

[32] Ibid., p. 191f.

explained, since none was present in the marine plant food of cetacea and fish.[33] He could only assume what Dumas had denied: 'Can animals perform acts of the same nature as plants relative to the formation of their principles? One can scarcely doubt it.'[34] Dumas replied: 'The hay eaten by Liebig's cow was richer in fat than he thinks.'[35]

Dumas, Boussingault and Payen, who had worked on the problem together, still maintained that any fat in animals was due to an accumulation from vegetable sources.[36] Attention then turned to the production of beeswax, which Liebig had also referred to. This had continued to puzzle investigators, since the eighteenth century, and agreement had not yet been reached on whether bees synthesized wax or simply collected it from plants.[37] Dumas supposed the source was vegetable wax,[38] but decided to investigate the claim, based on Huber's experiments,[39] that bees fed on a diet of sugar could make wax.

Dumas and Milne Edwards[40] isolated a number of bees, and estimated the average quantity of fat already existing in their bodies, before feeding, to see if they held reserves taken from plants. The bees were then fed with honey, which was also examined for fat content, and left to construct a comb. The total quantity of wax which this contained was then determined, as was the average amount of wax left in the bees. The arithmetic, which involved minute quantities, seemed to show that there was not enough wax in the food or in the bees' reserves to explain the quantity produced. It was concluded that bees really made wax.

In the discussion of the results, the strength of the resistance to the idea of animal synthesis was apparent. Payen wondered if the fat content of honey had been understated, and speculated on other possible causes for the wax produced in the bees' prison: 'Perhaps the wood of the box, the mastic of the windowpanes, the paints, cements, or some cryptogamic plant developing in the humid conditions provided the elements of wax?'[41]

Payen added that even if the wax originated in the bees, this was a special act, unrelated to the formation of fat in the tissues of all other animals. He was far more impressed by the rapid fattening of cattle by fodder, and so retained his opinion of the vegetable source of animal fats.

Milne Edwards agreed that, in view of the peculiarity of bees' glands and of the wax produced, no general conclusions could be drawn from the experiments on the

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[33] J. von Liebig, 'Note sur la formation de la graisse chez les animaux', *C. r. hebd. Séanc. Acad. Sci., Paris*, 1843, **16**, 663.

[34] J. von Liebig (n. 31), p. 201. He supposed sugars were converted to fats by deoxidation processes. This reversed Dumas' theory that oxidations alone occurred in the body.

[35] J. von Liebig, 'Observations à l'occasion du mémoire de MM. Dumas, Boussingault et Payen', *C.r. hebd. Séanc. Acad. Sci., Paris*, 1843, **16**, 560. This source consists of a letter from Liebig and its discussion.

[36] J. B. A. Dumas, J. B. Boussingault and A. Payen, 'Recherches sur l'engraissement des bestiaux et la formation du lait', *Ann. Chim. Phys.*, 1843, **8**, 63–114. This account also confused fats and waxes, which had not yet been chemically distinguished. Fats are esters of glycerol; waxes are esters of other alcohols, such as cholesterol.

[37] For a typically indecisive statement on this problem see J. J. Berzelius, *Traité de Chimie*, trans. A. Jourdan and Esslinger, Paris, 1829–1833, 8 vols., vol. 5, p. 318.

[38] J. B. A. Dumas (n. 28), vol. 6, p. 699.

[39] F. Huber, 'Memoir on the origin of wax', *Nicholson's J.*, 1804, **9**, 182–92.

[40] J. B. A. Dumas and H. Milne Edwards, 'Note sur la production de la cire des abeilles', *C.r. hebd. Séanc. Acad. Sci., Paris*, 1843, **17**, 531–45.

[41] Ibid., p. 539.

origin of fats. But he preferred the simple explanation that animal fats resulted from an accumulated deposition from vegetable foods. He said the theory one adopted depended on what limits were placed on the animal's ability to modify foods. He approved of Dumas' restrictions on this. Edwards would allow animals to convert one protein to another, or to modify vegetable oil to animal fat, but he excluded what he regarded as greater transformations: the synthesis of fats from proteins, involving immediate principles of different families.[42]

Dumas commented that if animals made fat from sugars, as bees made wax, the process was to be regarded as one of fermentation, intermediate in nature between plant synthesis and animal destruction.[43]

Doubts remained on the production of beeswax, the formation of animal fat, and the possibilities of synthesis performed by animals. As Magendie said, the whole question of animal nutrition remained obscure. He warned that, while it was of interest to demonstrate the existence of analogous immediate principles in animals and plants, it was 'a great leap' to draw conclusions from this on the origin of substances in the animal body.[44] The inadequacy of the current methods of investigation was the chief obstacle, as Lehmann pointed out:

> We cannot, it is true, arrive at any conclusion regarding the working of the process itself by a mere juxtaposition and quantitative comparison of the ingesta and excreta of the animal organism. . . .
> It need scarcely be observed that science should not rest satisfied with a knowledge of the final results of chemical processes in the animal body. . . but should be made to enter more deeply into the course of the separate processes, and into the causal relations of phenomena. Here the statistical method cannot of course afford any satisfactory solution to our enquiries; for when we have ascertained by this experimental method that fat is formed in the animal body, we must learn from other methods the manner in which this substance is formed.[45]

A biological chemistry required far more attention to the living animal than Liebig, Boussingault and Dumas had shown. It was through the application of an improved experimental method that discoveries of fundamental physiological importance were made with the assistance of chemistry. This occurred, not in the context of fat or protein synthesis, but in the solution to the problem of the origin of carbohydrates in animals.[46]

ANIMAL CARBOHYDRATES

The related compounds of starch, cellulose and the sugars were regarded as the most characteristic products of the vegetable kingdom, because of their abundance there. They were ternary compounds of carbon, hydrogen and oxygen, created by green plants from water and the carbon dioxide exhaled by animals.

[42] Ibid., pp. 542–45.

[43] J. B. A. Dumas (n. 26), p. 119.

[44] F. Magendie (n. 35), p. 557.

[45] C. G. Lehmann, *Physiological Chemistry*, trans. George E. Day, London, 1851–1854, 3 vols., vol 1, pp. 14–15.

[46] The complicated details of the metabolism of fats, proteins and carbohydrates were not worked out until the twentieth century. This awaited the discovery of a technique which could for example distinguish an ingested fat from one that was already present in the body. A tracer in the form of a chlorinated fat was employed by Bernard and Berthelot: C. Bernard, *Leçons sur les Phénomènes de la Vie communs aux Animaux et aux Végétaux*, Paris, 1878–1879, 2 vols., vol. 2., pp. 31–32. But a satisfactory labelling method was not available until the recent application of radioactive isotopes.

The presence of sugars in animals was attributed to their vegetable diet, or to a pathological condition, diabetes. The existence of starch and cellulose in animals was hardly ever considered.[47] Indeed their supposed confinement to the plant world served as a basis for separating the two kingdoms, at a time when they had been brought together morphologically by the cell theory.

Payen maintained that the cells of plants were bounded by cellulose, while the exterior of animal cells consisted of a quaternary, nitrogenous principle. He drew up a table contrasting the chemical behaviour of these two types of cell.[48] Cellulose was generally resistant to the reagents which attacked animal cells. Above all it was detected by the blue colour which appeared when sulphuric acid, followed by iodine, were applied. Payen said this was never observed in animal cells. This test for cellulose resembled the important test for starch,[49] which gave a blue or red colour with iodine. But they differed in that cellulose had first to be swelled by sulphuric acid, before the iodine was introduced.

The same cellular distinction was made by Nägeli,[50] who saw in it the material cause for the functional differences of animals and plants. The nitrogenous boundary of the animal cell was the underlying cause of sensation and motion; plants, whose cell-walls were non-nitrogenous, lacked these faculties. He also believed that plant cells were peculiar in containing starch, which he said was never found in animal cells.

The presence of nitrogen, which the eighteenth century had proposed as a criterion for distinguishing animal and vegetable substances, had reappeared in this new version of qualitatively distinct cell-membranes. But this was soon invalidated by Schmidt's surprising discovery of cellulose in tunicates.[51] The chemically resistant covering of these animals was found by analysis to have the same composition as the cell-walls of plants. Schmidt remarked that tunicates lived within a plant-like exterior. He concluded that there was no chemical distinction between animals and plants, which could only be separated on psychological grounds.

Schmidt's results were checked, and reluctantly it had to be conceded that cellulose could no longer serve as a distinguishing sign of a vegetable nature.[52] The discovery

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[47] In 1821 Odier had reported the discovery of a resistant material, which he called chitin, in the elyptera of insects. He supposed it was identical with the structural material of plants. A. Odier, 'Mémoire sur la composition chimique des parties cornées des insectes', *Mém. Soc. Hist. nat., Paris,* 1823, **1**, 29–42. This was falsified by Lassaigne, who showed the compound to contain nitrogen. Nevertheless chitin is a derivative of cellulose, and the physiological function of both is to provide structural rigidity.

[48] A. Payen, 'Mémoire sur les développements des végétaux', *Mém. div. savants Acad. Roy.Sci.,* 1846, **9**, 1–42. See also his paper on 'Propriétés distinctives entre les membranes végétales et les enveloppes des insectes et des crustacés', *C.r. hebd. Séanc. Acad. Sci., Paris,* 1843, **17**, 227–31. The detection of cellulose in the *Corallina officinalis* was decisive in his judgment that it was a plant: A. Payen, 'Note relative aux caractères distinctifs qui séparent les végétaux des animaux, et aux sécrétions minérales dans les plantes', ibid., 16–19.

[49] Colin and H. Gaultier de Claubry, 'Mémoire sur les combinaisons de l'iode avec les substances végétales et animales', *J. Phys.,* 1814, **79**, 113.

[50] C. Nägeli, 'Ueber die gegenwärtige Aufgabe der Naturgeschichte, inbesondere der Botanik', *Z. wiss. Bot.,* 1845, part 2, 1–45. The existence of naked cells, without walls, created difficulties for this classification. F. Cohn, 'On the natural history of Protococcus Pluvialis', *Botanical and Physiological Memoirs,* ed. A. Henfrey, London, 1853, p. 540.

The same chemical differences appeared in the definitions of animals and plants proposed by Charles Robin, *Du Microscope et des Injections,* Paris, 1849, 2 parts, part 2, pp. 186–87.

[51] C. Schmidt, *Zur Vergleichenden Physiologie der wirbellosen Thiere,* Braunschweig, 1845, p. 61f. See Joseph Schiller, 'Controverses autour de certaines structures chez les Tuniciers au XIX^e^ siècle', *Bull. Inst. océanogr. Monaco,* No. spécial 2, 1968, pp. 387–96.

[52] C. Loewig and A. Kölliker, 'De la composition et de la structure des enveloppes des tuniciers',

also implied that animals were capable of synthesis. Loewig and Kölliker speculated on how this might occur. They ruled out a protein origin in animal food, since this seemed too unlike cellulose to be capable of conversion to it. But they remarked that tunicates also fed on vegetables, and the cellulose of these might be decomposed to sugar by their gastric juice. The sugar would then enter the blood, where it would somehow be converted to cellulose for circulation to the envelopes. They suggested an analysis of tunicate blood to study the process. They also looked to a chemical analysis of embryonic ascidia to explain the further difficulty of cellulose formation in the foetal stage.[53]

Amid the speculations, animal synthesis was finally demonstrated with Claude Bernard's momentous discovery of hepatic glycogenesis.[54] This destroyed the foundation of Dumas' vital dualism and provided the experimental method which all previous attempts had failed to find. The way in which Bernard combined chemistry with physiology constituted the beginnings of a true biochemistry.

His doctoral thesis on gastric digestion had convinced him of the primary importance of the organism itself in nutrition. Gelatine taken into the stomach reappeared in the urine, but glucose and cane sugar disappeared in the organism. It was clear to him that the organism was active in assimilating certain substances and eliminating others. He set out to trace the fate of ingested sugars, studying the interior of the organism.

Chemical techniques would be required, but chemistry alone could not solve problems relating to animal functions.[55] Nor could investigations be restricted, as the chemists had done, to the study of ingesta and excreta, since these were merely the beginning and end of a whole chain of events which constituted nutrition. In a remarkably clear and eloquent statement of the differences in the chemical and physiological approaches to the living organism, Bernard later wrote:

> We recognize the great importance of chemical statics, since it provides the preliminary data, which form the basis of the physiologist's study of the intimate phenomena of nutrition in our tissues. But experimental physiology teaches us that these intermediary problems of nutrition must then be investigated step by step with the aid of delicate experiments, instead of being deduced by hypothetical explanations based on the comparison of materials in entry and exit.
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> The phenomena of nutrition are too complicated to lend themselves to this type of investigation,

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Ann. Sci. Nat. Zool., 1846, **5**, 193–238. Nevertheless they argued that chemistry could still separate the two kingdoms quantitatively. If over three-quarters of some tunicates consisted of a cellulose exterior, their other animal parts inside the envelope consisted of cells with the usual nitrogenous membrane. They said that no animal was yet known in which every cell-membrane consisted of cellulose, as was the case in plants. Besides only animals had nitrogenous cell-membranes. The latter statement was invalidated with the discovery of chitin in fungi, towards the end of the nineteenth century.

[53] Ibid., p. 224f. Berthelot was not satisfied with an elementary analysis of the tunicate envelope. This merely showed it to be isomeric with cellulose. A more significant comparison required the demonstration of identical transformations, since this would imply the same physiological role. He showed that like cellulose, the tunicate envelope could be hydrolyzed to glucose, but with much greater difficulty. Another form of cellulose, he called it 'tunicine'. M. Berthelot, 'Recherches sur la transformation en sucre de divers principes immédiats contenus dans les tissus des animaux invertébrés, *C. r. Soc. Biol.*, 1857, **4**, 77–80, and 'Sur la transformation en sucre de la chitine et de la tunicine, principes immédiats contenus dans les tissus des animaux invertébrés', *Ann. Chim. Phys.*, 1859, **56**, 149–56.

[54] The most recent study of Claude Bernard is J. Schiller, *Claude Bernard et les Problèmes scientifiques de son Temps*, Paris, 1967. This is a profound study, which has been invaluable in the preparation of this paper.

[55] C. Bernard, 'De l'origine du sucre dans l'economie animale', *C. r. Soc. Biol.*, 1849, **1**, 132.

> which, we repeat, are only applicable to inorganic machines. We could cite many physiological errors which have resulted from this indirect mode of procedure, while, on the contrary, the experimental study of the phenomena of nutrition, conducted directly in the organs, tissues and even in the elements of tissues, have led to fruitful discoveries. The formation of sugar in the liver would never have been discovered if one had been restricted to the comparison of analyses of materials entering and leaving the organism. The physiologist must rely on these general chemical results, but he must not be content with them; he has to descend, with the aid of the direct experiment, into the intimacy of the organs, into the tissue, into the living cell whose function is identical in animals and plants. It is by this study alone that he will be able to grasp the mystery of intimate nutrition and succeed in mastering these phenomena of life, which is his supreme goal.[56]

Employing vivisection, Bernard tested various parts of the organism for sugars, using cupropotassium tartrate (reduced to red copper oxide) and yeast (alcohol and carbon dioxide were produced by fermentation). The experiments were conducted on dogs, fed on a sugar-free diet of meat, or starved. The tests showed an abundance of sugar in the blood leaving the liver by the ligatured hepatic veins; no sugar was found elsewhere. This indicated that sugar existed in the liver, and the tests confirmed it.

The control experiments had established that the sugar could not have come from ingested vegetable sources. The prolongation of the experiments excluded the possibility that the sugar had been merely deposited in the liver by an earlier vegetable diet. It was undeniable that sugar was produced in animals by a process that was independent of the diet. Bernard drew the important conclusion: 'Therefore the law that animals create no immediate principles, but only destroy those provided by plants must cease to be true, since, like plants, animals can create and destroy sugar physiologically.'[57]

This was the contradiction of Dumas' fundamental premise. This line of separation between the two organic kingdoms had been erased. Bernard proceeded to isolate the precursor of hepatic sugar, glycogen.[58] At first he had thought it was a protein, since cooking the liver inhibited the production of sugar. But it turned out to have the same properties as starch. It gave the characteristic reaction with iodine, and could be converted to dextrine and glucose by acid hydrolysis or fermentation. He called the new substance 'animal starch'.[59] Just as in plants, a starch formed in animals, and was subsequently converted to glucose. Bernard wondered if starch was synthesized in the same way in both. He said 'the most perfect parallelism' between the kingdoms was established by the conversion of the starch to sugar by ferments.[60]

THE FERMENTS

The ferments or enzymes (as they were later called by Bernard's pupil Kühne, from their presence in yeast) were unknown in a pure state, because of the technical difficulties which their isolation presented. Nevertheless enough was known of their properties to recognize their existence, and to establish their analogous functions in the digestive processes of animals and plants.

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[56] C. Bernard, *Leçons sur les Phénomènes de la Vie communs aux Animaux et aux Végétaux*, Paris, 1878–1879, 2 vols., vol. 1, pp. 153–55.

[57] C. Bernard (n. 55), p. 132.

[58] C. Bernard, 'Sur le mécanisme physiologique de la formation du sucre dans le foie', *C. r. hebd. Séanc. Acad. Sci., Paris*, 1857, **44**, 578–86.

[59] C. Bernard, 'Remarques sur la formation de la matière glycogène du foie', *C. r. hebd. Acad. Sci., Paris*, 1857, **44**, 1325.

[60] C. Bernard, 'Critique expérimentale sur le mécanisme de la formation du sucre dans le foie', *Ann. Chim. Phys.*, 1877, **12**, 404–5.

The first to be described was the agent in malt. This was called diastase,[61] from its ability to separate the contents of starch granules from their supposed teguments, converting the starch to dextrine and glucose. Payen and Persoz crushed germinated barley in cold water, added alcohol, and collected a nitrogenous, white precipitate. They were astonished by its powerful effects, since in a few minutes it could alter two thousand times its weight of starch. They also discovered that the activity of a solution of diastase was destroyed by boiling, a characteristic property of enzymes which was repeatedly observed. They found diastase in cereals and potatoes only after germination, and in those parts where starch was consumed. The physiological role of diastase in vegetation was already apparent.

A ferment with the same properties was then found in the human saliva by Mialhe,[62] who called it 'animal diastase'. He carried out comparative tests on vegetable diastase and the white substance which alcohol had separated from the saliva. It seemed that equal weights of the two decomposed the same quantities of starch. The two agents behaved identically, but he wondered if the substance in the saliva was simply vegetable diastase introduced with the food. He later denied that the origin was external, when he failed to detect the ferment in the saliva of herbivores.

A starch-digesting ferment was also discovered in the pancreas, though the investigators would not commit themselves to its identity with diastase, since they were unsure if they had studied the pure substance.[63] A clue to the existence of this type of ferment in the liver was given by the temperature dependence of the process of sugar production there. Bernard found that the process came to a halt when the liver was placed in boiling water.[64] He washed the liver to remove the sugar and glycogen, and then treated it with glycerol. The solution was precipitated by alcohol, the same technique, he said, for obtaining vegetable diastase. Like the latter, the liver ferment decomposed starch and glycogen to sugars. Bernard concluded that sugar was formed identically in animals and plants. In each case starch was created and converted to glucose by the same ferments. Wherever starch was digested, in the germinating potato, in the liver of animals, in their saliva and pancreas, the diastasic ferment was present. As Bernard explained, the complicated starch was decomposed to the simpler sugars which were soluble, and so could be circulated and assimilated.[65]

Bernard could draw similar parallels in the digestion of other foodstuffs. The growing beetroot consumed reserves of cane sugar and produced a mixture of laevulose and glucose. This was caused by a ferment which Bernard extracted. He found a similar substance in the intestines of dogs, rabbits and birds. In each case he followed its action in the inversion of cane sugar with a polarimeter.[66]

The digestion of fats involved the production of an emulsion, as Bernard had seen

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[61] A. Payen and J. F. Persoz, 'Mémoire sur la diastase, les principaux produits de ses réactions, et leurs applications aux arts industriels', *Ann. Chim. Phys.*, 1833, **53**, 73–92.

[62] L. Mialhe, 'De la digestion et de l'assimilation des matières sucrées et amilöides', *C. r. hebd. Acad. Sci., Paris*, 1845, **20**, 954–59 and 'Note sur le mode d'action qu'exerce la Diastase animale sur l'Amidon', ibid., 1485–88.

[63] A. Bouchardat and C. M. S. Sandras, 'Des fonctions du pancréas et de son influence dans la digestion des féculents', ibid., 1085–91.

[64] C. Bernard (n. 60), pp. 397–405.

[65] C. Bernard (n. 56), vol. 2, p. 331f.

[66] Ibid., vol. 2, pp. 340–45.

in his early experiments on dogs. He discovered that the pancreatic juice would emulsify fats, dividing them into minute globules, and also saponify them.[67] He said these changes were not due to the alkalinity of the pancreatic juice, but to the presence of ferments, since the action was suspended by boiling. He argued that the same ferment occurred in oleaginous grains. For example, crushed almonds also gave a milky emulsion, which was similarly precipitated by alcohol.[68]

Bernard said there must in addition be a protein-digesting ferment in plants similar to pepsin, which Schwann had found in the stomach of an ox. In this way germinating plants could convert their protein reserves to soluble peptones.[69] The prediction was confirmed in experiments on carnivorous plants. Lumps of meat placed on Drosera, Dionaea and Nepenthes were rapidly gelatinized and finally consumed, in a way that could only be compared to animal digestion. It was concluded that these plants produced a ferment like pepsin.[70]

The study of the ferments had led to profound physiological results. A remarkable organic unity was revealed in the acts of digestion of animals and plants. In both kingdoms, as Bernard said, the same reserves of carbohydrates, fats and proteins were decomposed by the same processes, and by identical, or at least similar ferments, to provide soluble substances for assimilation. He said the absence of a digestive apparatus in plants was unimportant, and had led to their false separation from animals. What really mattered was that the purely chemical processes of digestion were identical in both.[71]

In addition, the ferments clearly exhibited the peculiarity of the processes occurring in the organism. If digestion was entirely chemical, and if the reactions were of the same types as those occurring outside the body, the agents and the conditions were different.[72] In the laboratory the chemist had to employ mineral acids to hydrolyze starch to glucose, and caustic potash to saponify fats. The ferments produced by the organism allowed the same changes to occur in conditions of mild acidity or alkalinity, and at moderate temperatures. The drastic procedures of industrial chemistry, impossible in life, were avoided in the organism, but the results were the same.

THE UNITY OF RESPIRATION

It was through his general physiological approach, searching for the common phenomena of life, that Bernard was able to remove a further barrier between the kingdoms, which the chemical study of respiration had erected. The eighteenth-century contrast between the behaviour of green plants in sunlight, absorbing carbon

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[67] C. Bernard, *Mémoire sur le Pancréas et sur le Rôle du Suc pancréatique dans les Phénomènes digestifs, particulièrement dans la Digestion des Matières grasses neutres,* Paris, 1856, pp. 380–81 and p. 441f.

[68] C. Bernard (n.56), vol. 2, p. 351f. The existence of a ferment in milk of almonds had been deduced from its action on amygdalin: J. von Liebig and F. Wöhler, 'Sur la formation de l'huile d'amandes amères', *Ann. Chim. Phys.*, 1837, **64**, 185–209. They correctly interpreted the reaction as catalytic.

[69] C. Bernard (n. 56), vol. 2, pp. 358–59. For the discovery of pepsin see T. Schwann, 'Ueber das Wesen des Verdauungsprocesses', *Ann. Pharm.*, 1836, **20**, 28–33.

[70] Sir J. D. Hooker, 'The carnivorous habits of plants', *Nature, Lond.*, 1874, **10**, 366–72; E. von Gorup-Besanez and H. Will, 'Fortgesetzte Beobachtungen über peptonbildende Fermente im Pflanzenreiche', *Ber. dt. chem. Ges.*, 1876, pp. 673–678. Frankland assisted Darwin in the chemical study of the secretions of these plants. C. Darwin, *Insectivorous Plants,* London, 1875, p. 85f.

[71] C. Bernard (n. 56), vol. 2, p. 323.

[72] Ibid., vol. 1, p. 226.

dioxide and emitting oxygen, and the respiration of animals, had been continued by Dumas and others. Bernard would show that this too was a false contrast.

The green substance in plants had been characterized as a distinct immediate principle. Soluble in alcohol, non-nitrogenous, and bleached by chlorine, it had been called 'chlorophyll', from its presence in green leaves.[73] Nägeli had stated that it was exclusive to the plant kingdom, and therefore another basis for distinguishing animal and plant cells.[74] This was undermined by the discovery of its existence in infusoria, microscopic organisms of controversial status, although many were regarded as animals.

Ferdinand Cohn studied the green spherules in the euglena and stentor, and declared them to be chlorophyll, from their reaction with concentrated sulphuric acid, turning blue. He considered these infusoria to be green animals, breathing like plants.[75] Schultze referred to numerous green animals in ditches and ponds, such as the hydra viridis and volvox viridis. Their green substance behaved just like chlorophyll with acids and alkalis, and also faded in the dark. He kept the volvox viridis for a month in a dark room and found that the intense green had changed to a yellow.[76]

A spectroscopic examination of the green matter in the euglena was undertaken by Ångström. He found the spectrum to be similar to that given by chlorophyll in the leaf of a Trifolium plant, and identical with the spectral bands of chlorophyll in the conferva and other algae. He concluded that chlorophyll was not peculiar to plants, since it existed in the euglena, and that his experiments, far from supporting the separation of animals and plants, confirmed an old law: *natura non facit saltus.*[77]

It could be argued that the chlorophyll in infusoria had come from ingested vegetables, but this seemed unlikely from its presence within the parenchyma, instead of in the digestive system.[78] A different problem which had not yet been elucidated was whether the green colour in certain animals was due to symbiotic algae. This was certainly the case with the green planaria studied at Lacaze-Duthiers' marine zoological laboratory at Roscoff.[79] The green worms in the aquaria moved towards the light, and generated gas bubbles rapidly. These were collected in test-tubes and observed to rekindle a glowing match. There was no suspicion that the chlorophyll inside the worms actually belonged to smaller algae within them. The green colour of the freshwater sponge was misleading for the same reason.[80]

Claude Bernard said that a classification might be attempted of a kingdom of organisms with chorophyll and one without, but this would not correspond with the

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[73] J. Pelletier and J. B. Caventou, 'Sur la matière verte des feuilles', *J. Pharm.*, 1817, **3**, 486–91.

[74] C. Nägeli (n. 50), p. 21.

[75] F. Cohn, 'Beitrage zur Entwickelungsgeschichte der Infusorien', *Z. Wissen. Zool.*, 1851–1852, **3**, 264. Much earlier, Braconnot had discovered chlorophyll in the volvox, but his paper was not referred to. H. Braconnot, 'Expériences sur le Volvoce globuleux', *Ann. Chim. Phys.*, 1834, **57**, 439–42.

[76] M. Schultze, 'Note sur l'identité d'une matière colorante existant chez plusieurs animaux et identique avec la chlorophylle des végétaux', *C. r. hebd. Séanc. Acad. Sci., Paris*, 1852, **34**, 683–685.

[77] A. J. Ångström, 'Ueber die grüne Farbe der Pflanzen', *Ann. Phys. Chem.*, 1854, **93**, 475–80.

[78] J. E. Schlossberger, *Erster Versuch einer allgemeinen und vergleichenden Thier-Chemie*, Stuttgart, 1854–1856, 3 parts, part 3, p. 163.

[79] P. Geddes, 'Sur la fonction de la chlorophylle avec les planaires vertes', *C. r. hebd. Séanc. Acad. Sci., Paris*, 1878, **87**, 1095–96.

[80] J. Hogg, 'Further observations on the Spongilla fluviatilis', *Trans. Linn. Soc.*, 1841, **18**, 388. He classified the sponge as a plant, from the presence of chlorophyll.

division into animals and plants.[81] The euglena would have to be put with the plants on this view, and the whole class of mushrooms separated from the vegetables.

Bernard distinguished between plant and chlorophyll, which he said should not be confused. More important he distinguished the chlorophyll function of certain organisms from the respiration which was universal in life. Green plants absorbed oxygen and exhaled carbon dioxide, by the destructive act of respiration which they performed in common with animals. But this was obscured by the simultaneous evolution of oxygen, performed by the chlorophyll function. Bernard found that he could separate the two processes by the use of anaesthetics.[82] He placed two plants under bell-jars in sunlight, and near one he put a sponge with chloroform. The chlorophyllic function of this plant was suspended, and only carbon dioxide was emitted, like a breathing animal; the other plant exhaled oxygen as usual.

In another experiment he passed air, freed from carbon dioxide, into vessels containing a rat and a cabbage, and collected the gases which were given off. In both cases barytes was turned cloudy by carbon dioxide.[83] Far from establishing a system of separate physiologies for animals and plants, Bernard said the phenomena of respiration displayed a harmonious unity.

THE INFUSORIA

The decline of vital dualism can be traced in the classification of the infusoria. The study of these minute forms of life was facilitated by the nineteenth-century improvements in the microscope. Lamarck had declared them animals because of their irritability, a property which he said was caused by the distinctive chemical compounds which Nature had employed in the fabrication of animals.[84] But this chemical difference could not be found. Richard Owen later wrote that chemistry 'will not serve as a rigorous basis for definition in the lower forms where the aid of the chemist has been most wanted for that purpose.'[85]

The simultaneous presence of animal and vegetable characteristics in infusoria defied attempts to put them in either of the organic kingdoms. The enigmatic euglena moved like an animal and exhaled oxygen like a green plant. Ehrenberg[86] had taken its red spots to be eyes. He had observed its ingestion of indigo, and searched for an intestinal tube. Without hesitation he accepted the euglena as an animal. As for the evolution of oxygen, he simply said the euglena falsified the view that this faculty was restricted to plants. Similarly Ehrenberg classified other moving and feeding microscopic organisms as animals, and described imaginary anatomical analogies with the higher animals. He said these characters were 'more determinate' than chemistry in deciding which kingdom the infusoria belonged to.[87]

[81] C. Bernard (n. 56), vol. 1, p. 146 and p. 208f.

[82] Ibid., vol. 1, pp. 278–79.

[83] Ibid., vol. 1, p. 273.

[84] J. B. Lamarck, *Histoire naturelle des Animaux sans Vertèbres*, Paris, 1815–1822, 7 vols., vol. 1, p. 123 and p. 126.

[85] Richard Owen, *Lectures on the Comparative Anatomy and Physiology of the Invertebrate Animals*, 2nd ed., London, 1855, p. 5. He defined animals arbitrarily by a combination of chemical, physiological and anatomical criteria, ibid., pp. 7–8.

[86] C. F. Ehrenberg, 'Zusatz zu der vorstehenden Mittheilung', *Ann. Phys. Chem.*, 1842, **57**, 311–14.

[87] C. F. Ehrenberg, 'New observations on the blood-like phenomena observed in Egypt, Arabia and Siberia, with a view and critique of the early accounts of similar appearances', *Edinb. New phil. J.*, 1830–1831, **10**, 342.

Protests came from the botanists. They complained that Ehrenberg had taken some plants into the animal kingdom, particularly the desmids and diatoms, which he had classified as infusorial animals of the bacillaria family.[88] Ralfs said Ehrenberg had been led astray through the neglect of chemical evidence. At first he had also regarded the desmids as animals, from their forms:

> Their symmetrical division into two segments; the beautiful disciform, finely-cut and toothed Micrasterias, the lobed Euastrum, the Cosmarium glittering as if it were with gems, the Xanthidium armed with spines, the scimitar-shaped Closterium embellished with striae, the Desmidium resembling a tape-worm, and the strangely insect-like Staurastrum sometimes furnished with arms, as if for the purpose of seizing its prey, all these characters seem indeed to pertain more to the lower animals than to vegetables.[89]

But forms were misleading, and besides the desmids were of a herbaceous green colour. Above all they contained starch. Ralfs had tested the desmids with iodine solution, and observed the characteristic blue colour. He wrote: 'Of all the facts which indicate the vegetable nature of the Desmidieae, this is undoubtedly the most important, since it is the most easily subjected to the test of experiment.'[90]

He denied that the starch had come from ingested aquatic plants, deposited in the supposed stomachs of desmids. This would not explain the gradual increase of starch as the desmid seed formed, nor its absence in the earliest stages of development.[91] He appealed to impartial observers to repeat his tests for starch, which had been overlooked by Ehrenberg and his followers. He argued: 'Again, it has been seen that starch is abundantly produced in this family. Can a single example be referred to where it is an animal product? . . . Until these facts have been denied, or the arguments deduced from them refuted, I shall presume that the claim of the Desmidieae to be considered vegetables is firmly established'.[92]

The same arguments were used to reclaim the diatoms for botany.[93] They were rendered useless by Bernard's discovery of glycogen in the animal kingdom. In a treatment of the infusoria which appeared soon after, Claparède and Lachmann said chemistry was unable to guide their classification, since the claims based on the exclusive presence of starch, cellulose or chlorophyll in the vegetable kingdom had been disproved.[94] Similarly, referring to the significance of the discovery of cellulose in tunicates for the classification of unicellular organisms, von Siebold wrote: 'I must here remark that we can scarcely expect chemistry to decide what is animal and what plant, having several times been deceived in our hopes in this respect.'[95]

In a paper read to the British Association in 1860, John Hogg described the difficulties he had found in classifying ambiguous organisms. He said the discovery

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[88] C. F. Ehrenberg, 'On the distinctive characters between plants and animals', *Edinb. New phil. J.*, 1836–1837, **22**, 396–97.

[89] John Ralfs, *The British Desmidieae*, London, 1848, p. 18.

[90] Ibid., p. 34.

[91] Ibid., pp. 32–33. He was opposing the statement by J. W. Bailey, 'A sketch of the infusoriae, of the family bacillaria . . .', *Amer. J. Sci. Arts*, 1841, **41**, 301.

[92] Ralfs (n. 89), p. 36.

[93] C. Nägeli (n. 50), p. 44. See also G. Meneghini, 'On the animal nature of diatomeae, *Botanical and Physiological Memoirs*, ed. A. Henfrey, London, 1853, pp. 345–513.

[94] E. Claparède and J. Lachmann, *Études sur les Infusoires et les Rhizopodes*, Geneva, 1858–1861, 2 vols., vol. 2, pp. 61–62. They argued that the euglena was an animal because it possessed a contractile vacuole.

[95] C. T. von Siebold, 'On unicellular plants and animals', *Q. Jl microsc. Sci.*, 1853, **1**, 115.

of starch in animals had greatly weakened the determination of vegetability.[96] No more successful than other criteria, chemistry had failed to establish a sharp dividing-line. He therefore proposed that desmids, diatoms, infusoria and all other disputed creatures should be put into a fourth kingdom, which he called Regnum Primigenum. He said: 'Since, indeed, the vegetable and animal kingdoms have been well compared to two lofty pyramids, which diverge from each other as they ascend, but are placed on, or united in, a common base; this base, then, might fairly represent the *Primigenal* kingdom, which includes the lower creatures or organisms of both the former, but which are of a doubtful nature, and can in some instances only be considered as having become blended or mingled together.'[97]

Huxley[98] remarked that the failure of the chemical distinctions had caused fundamental changes in the naturalist's conception of animals and plants. The former clear divisions had gone. He despaired of finding a single character for the border territory between the kingdoms, which he called 'no-man's land'. He thought the last hope lay in protein synthesis, which perhaps only plants could achieve. The ambiguous bacteria multiplied in a solution of tartrates and phosphates, a process involving the synthesis of their proteins. Huxley therefore took them to be plants, but other infusoria left him in a state of indecision.

When Frankland, in a lecture to the Chemical Society, announced that all micro-organisms were animals, because of their destructive acts of oxidation, his firm tone shocked the biologists present.[99] Burdon-Sanderson commented that it was for the chemist to consult the biologist on this subject, and that in any case it was 'of little practical consequence' to decide whether the organisms were animals or plants. Foster added that the behaviour of the micro-organisms mattered far more than their classification.

These remarks were significant. The insistence on a classification into two organic kingdoms was receding, as the impossibility of this separation on any grounds became increasingly apparent. As one writer of the late nineteenth century put it: 'The entire fabric of living nature is, in truth, a great tree, the branches of which diverge most widely in their highest levels, but which in its lowest parts, unites and blends all diversities in a common and inseparable unity.'[100]

In looking to chemistry to divide this unity, he said the dilemma of the biologist becomes 'confusion worse confounded'.[101]

CONCLUSION

In this paper, and the previous one (*Med. Hist.*, 1971, **15**, 23–44), we have considered the relation between chemistry and physiology in the eighteenth and nineteenth

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[96] John Hogg, 'On the distinctions of a plant and an animal, and on a fourth kingdom of nature', *Edinb. New phil. J.*, 1860, **12**, 218.

[97] Ibid., p. 224. In an accompanying coloured diagram, the animal and vegetable kingdoms were represented as blue and yellow pyramids, merging to a common green base.

[98] T. H. Huxley, 'On the border territory between the animal and vegetable kingdoms', *Macmillan's Magazine*, 1876, **33**, 373–84.

[99] E. Frankland, 'On chemical changes in their relation to micro-organisms', *Trans. Chem. Soc.*, 1885, **47**, 159–83. The subsequent discussion at the meeting can be found in *Chemical News*, 1885, **51**, 78–80. Frankland was also criticized for trying to impose distinctions which did not exist in nature: Thos. P. Blunt, 'Plant versus animal', *Chemical News*, 1885, **51**, 106.

[100] A. Wilson, 'Can we separate animals from plants?', *Cornhill Magazine*, 1878, **37**, 350.

[101] Ibid., p. 346.

centuries. The problem of nutrition was approached by the analytical techniques which characterized organic chemistry up to the middle of the nineteenth century. In experiments which were conducted outside the living organism, vegetable foods and animal materials were analysed, and from the results, deductions were made on the action of the animal economy. In the eighteenth century, the process of animalization was attributed principally to nitrogenation, while in the next century, Dumas explained the entire animal economy by the single act of combustion. The neglect of the living organism had resulted in a reduction of physiology to chemistry.

This procedure left in obscurity the very facts which were being sought: the intimate events of creation and destruction occurring within the organism. It was through Bernard's insistence on the study of these, involving the detection of intermediates, such as glycogen, in living processes, that the way was opened to an understanding of nutrition. The acts of digestion were then shown to be purely chemical processes, but involving enzymes, a class of compounds peculiar to living organisms. Nutrition, previously assumed to occur directly, was found to be indirect. Food taken into the body was subject to destruction, synthesis and storage. The same processes were observed in animals and plants.

Bernard had shown how chemistry could be combined with physiology, so constructing a basis for biochemistry. Both sciences acquired benefits: physiology adopted chemical tests and received explanations for the phenomena of digestion; organic chemistry became synthetic, imitating, as Berthelot said, the synthesis of immediate principles and their metamorphoses in life.

We have also considered the part played by chemistry in classification. Its growing use in this way, since the eighteenth century, was apparent from the chemical analyses of ambiguous organisms, and from the chemical content of the definitions which were given to animal and plant by Dumas, Nägeli, and Charles Robin. But the chemical distinctions, on which the separation of the two organic kingdoms had increasingly relied, were found to be baseless. One by one, the chemical barriers between animals and plants fell. The claims for a monopoly in one kingdom of nitrogen, chlorophyll, sugar, cellulose and starch were all discredited by the middle of the nineteenth century. The fundamental antithesis of plant synthesis and animal destruction fell with them. Chemistry in the end provided strong arguments for the inseparability of the two kingdoms, from its demonstration of the identity of nutrition in both.