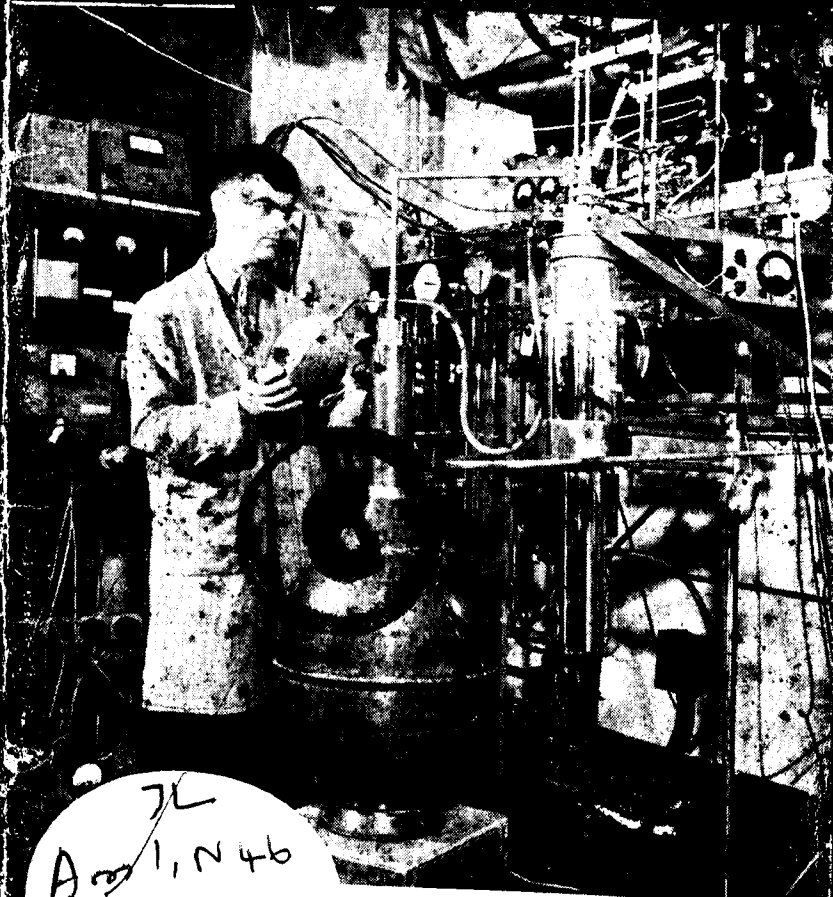




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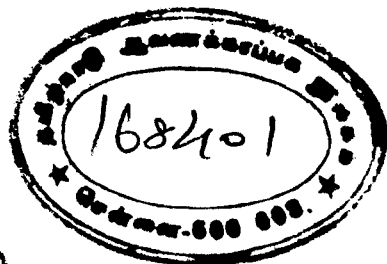
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VOYAGES OF H.M.S. BEAGLE

D. B. CARLISLE

AT daybreak on Tuesday, 27 December 1831, His Majesty's Surveying Ship *Beagle*, after twice being delayed by storms, slipped her moorings on a fine windless morning, and, as soon as the tide would allow, warped out of Plymouth Sound. The barometer stood high, smoke from the chimneys of Plymouth rose straight into the air, the sky was blue and streaked with mare's tails, and distant land loomed close – all signs of a coming easterly wind. Part way across the Sound a cat's paw rippled the water; the *Beagle* made all sail; the breeze increased and by noon the little barque was outside the breakwater with a fresh easterly wind. She did not see England again until Sunday, 1 October 1836, when she made Falmouth after circumnavigating the globe. Her commander was a young man of twenty-six, Captain Robert Fitzroy, R.N., and she carried as supernumerary a would-be clergyman of twenty-two, Charles Darwin, who had left his studies at Cambridge to accompany the expedition. There can be few with any interest in science who have not at least heard of Darwin's *Naturalist's journal of a voyage round the World*, but few people realize that it was first published as the third volume, little more than an extended appendix, to the *Narrative of the surveying voyages of H.M.S. Adventure and Beagle*, written by the commanders of the two ships. To most scientists nowadays the voyage lives only because of Darwin's *Journal*. Yet the surveying voyages of these two ships rank as among the first great geophysical expeditions, while the navigational charts of great parts of South America in current use today are, with only minor revisions, based on the surveys made by them. A ship rounding Cape Horn or passing through the Straits of Magellan navigates by Fitzroy's chart.

THE SURVEY OF 1826

With the departure of the *Beagle* from Plymouth in 1831 we have started half-way through the story, which really begins in 1795 when the Hydrographic Office of the Admiralty was established to collect data and to prepare the secret charts by which the warships of Britain were to navigate. At first the charts so printed were compilations from British and foreign sources, with additions and corrections supplied by the commanders of warships. A little later ships began to be commissioned for specific cruises to survey selected regions, at first at home, then overseas. By this time any intention of keeping the charts secret had been abandoned and by 1823 the charts were published for the use of British mariners. The *Adventure* and the *Beagle* (the second ship to carry the name) were among the first vessels to be specifically commissioned and equipped for survey work.

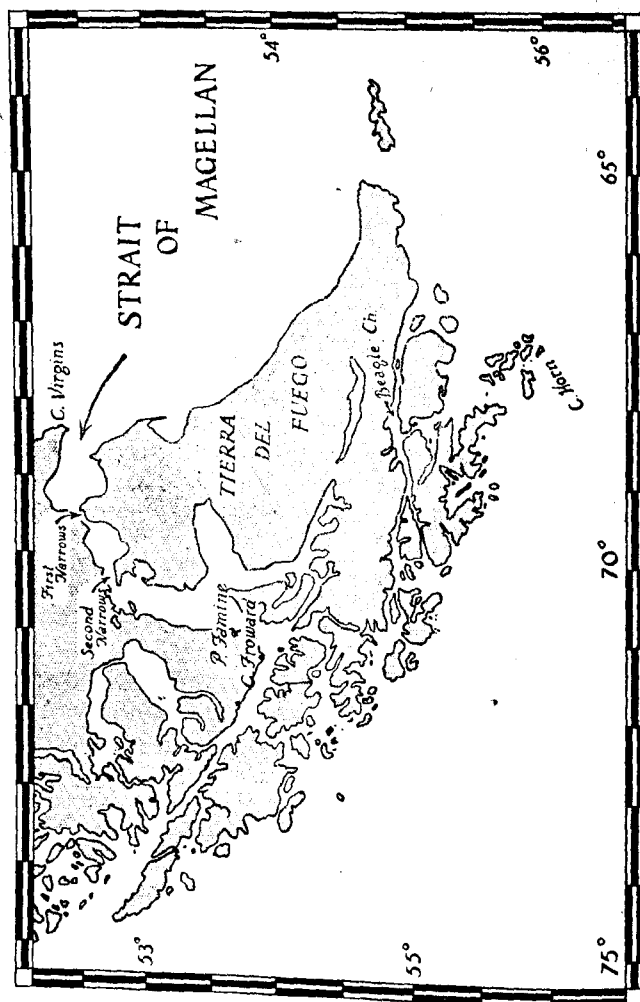
In 1825, then, the Lords Commissioners of the Admiralty directed two ships to be prepared for the survey of the southern coasts of South America. The *Adventure* and the *Beagle* were therefore fitted out at Woolwich and in May of the following year they were commissioned at Plymouth for the first expedition. The *Adventure* was a roomy ship of 330 tons, manned by 18 officers, petty officers, and midshipmen, 15 marines, and 40 seamen. The *Beagle* was a smaller sloop of 235 tons, at first rigged as a brig but later as a barque, and carrying 12 officers, 10 marines, and 38 seamen. She was one of the *Cherokee* class, later nicknamed the *Coffin* class because of their liability to go down in severe weather! The presence of marines on surveying vessels may seem strange, but they were invaluable in protecting land parties in uncivilized regions. The commander of the expedition was Captain Phillip Parker King, R.N., F.R.S., who had previously surveyed the coasts of New Holland (Northern Australia and adjacent islands). Captain Pringle Stokes, R.N., was commander and surveyor of the *Beagle*.

The prime motive of the survey was plainly navigational, but the Hydrographic Office also intended that the ships should carry out geophysical surveys. Indeed in many respects navi-

gational and geophysical surveys must merge into one another, for an exact knowledge of magnetic phenomena, especially of magnetic variation, is essential to navigation, while currents, tides, salinity, and meteorology are subjects for study jointly shared between geophysics and seamanship. The orders transmitted by the Admiralty to Captain King also directed that they should 'take every opportunity of collecting and preserving specimens of such objects of natural history as may be new, rare, or interesting'. The messing list of H.M.S. *Adventure* accordingly includes 'J. Anderson, Botanical Collector'.

On May 22nd, 1826, the *Adventure* and *Beagle* sailed from Plymouth for Rio de Janeiro before proceeding to the River Plate, where the survey was to begin. They dropped anchor there on October 13th and spent a month taking on stores and water. On November 19th they set sail for the Straits of Magellan, where King had decided to begin his survey. They arrived off Cape Virgins, near the entrance to the Straits, shortly before Midsummer's Day, but the 7-knot current and 50-foot tide of the First Narrows prevented their entering the Straits proper until 11 days had passed. Once through the narrows they made for Port Famine, where they were to be based for some months. Here it was that in 1584 Sarmiento established a colony of 300 men. After his departure from the colony in 1585 he tried repeatedly to return with supplies but was driven back time and again by gales, frostbite, snow, and finally by the loss of his ship. Two years later when an English ship under the command of Cavendish, anchored off the Port the only survivor on board a single survivor, and Cavendish named the place Port Famine. Port Famine was the headquarters of the *Adventure* and *Beagle* surveying expedition until August, 1828, a period of some eighteen months. During this period the ships separated and, working from the Port in different directions, surveyed the greater part of the Straits of Magellan.

Much of the survey was carried out from open boats. In a region of high rainfall, where the wind more often than not blew with gale force and often reached hurricane force, where the midsummer temperature was about 48° F, and where icebergs



littered the channels, and where Sarmiento's colony had starved to death because of the weather, in such a region the men camped each night on shore in temporary tents constructed from the sails of the whaleboats in which they had been working all day, often drenched to the skin. They wore outer garments of painted canvas – seemingly the best weather-proofing then known. Conditions were bad enough in 1827, but by the beginning of 1828, despite a certain amount of fresh food, scurvy was beginning to make itself felt. On board the *Beagle* in particular was it rife. The two ships made rendezvous in Port Famine on July 28th that year, the *Beagle* arriving with not a bite of food left on board. On August 1st, Captain Stokes, in a fit of despondency, shot himself. His colleagues blamed his death on 'the severe hardships of the cruise, the dreadful weather experienced, and the dangerous situations in which they were constantly exposed'. They clearly did not regard his death as suicide, but as brought about by external conditions, for his body was buried with all ceremony in the private burial ground which the expedition had established at Port Famine. The ceremony would certainly have been omitted in the burial of a plain suicide. On August 16th the two ships left the Straits bound towards the River Plate. The sick-list was such that of the 24 officers of the two ships only Lieut Skyring (now promoted to temporary command of the *Beagle*) and Captain King were able to keep the deck. Once arrived at the River Plate they found that a war was in progress and Montevideo was blockaded. Fresh provisions were almost unobtainable, except for Seville oranges. The free use of these, however, cured the scurvy and within a week every man was at his duty. From the River Plate the *Adventure* sailed to Rio de Janeiro to refit, leaving the *Beagle* behind at Montevideo. At Rio, Sir Robert Otway, Admiral of the South American Station, despite Captain King's representations that Skyring be appointed to command the *Beagle*, nevertheless promoted his own Flag Lieutenant, Lieut Robert Fitzroy, to the vacant post. Events proved him right. Skyring, although an able surveyor and officer, had not the forceful personality and leadership of Fitzroy, nor had he his intense scientific curiosity, to which we

owe Darwin's participation in the second Expedition, and indirectly one of the great classics of science.

In October the ships sailed to complete the survey of the channels that connect with the Straits of Magellan at its easterly end, to make a running survey of the Pacific coast as far north as Chiloe (about 1,000 miles north of Cape Horn), and to chart roughly the southern region of Tierra del Fuego. In this work they were occupied until June 1830, when they turned for home, to anchor in Plymouth Sound on October 14th.

With them they brought back to England four Fuegians, three men and a girl. Shortly before the end of the survey of Tierra del Fuego one of the whaleboats of the *Beagle* had been stolen by the natives. Fitzroy had thereupon set about recovering the boat and punishing the tribe responsible. First he landed his carpenter with a few men to build a new boat (they had to start by cutting down the trees). Then, with eleven men in an open boat and two weeks' provisions, he set off in pursuit. During the next 18 days they sailed and rowed more than 1,000 miles, surveyed thoroughly the inlets and islands of the thievish tribe (the chart of this region is littered with such names as Thieves' Sound and Whaleboat Sound) and found some traces of the boat's gear, but not the boat itself. Fitzroy drove his men and himself to exhaustion, and as for the weather he writes: 'The men's clothes were seldom dry, either by day or night. Frequently they were soaked by rain during the greater part of the day, and at night were in no better condition; for although a large fire (when made) might dry one side the other as quickly became wet. . . We were more than once awakened out of a sound sleep by finding that we were lying partly in the water, the night-tide having risen very much more than that of the preceding day.' They took prisoner the families of the men who had stolen the boat, but all except three escaped. A few weeks later a fourth native was enticed on board the *Beagle* and all four were taken back to England. Fitzroy made one attempt to land them in Tierra del Fuego, but they made him understand that they were now on the coasts of a different tribe who would certainly kill them. So back to England they were brought. Fitzroy believed that if

he could teach them English and learn their native language from them, if he could teach them the rudiments of agricultural methods, and convert them to Christianity, then on their return to their native land they would lead their people from savagery into the ways of civilization and Christianity. For he fully believed that a second expedition to complete the survey of South America would be sent out within a couple of years after the return of this first one.

Survey Methods

At the time of the commissioning of this expedition the general methods of survey that are in use today had been evolved almost in their entirety. The basis of the survey was, as on land, a geodetic triangulation. Nowadays it is frequently possible to use the framework of the land survey for this purpose, but in 1827 in South America such a survey did not exist. A modern base-line for triangulation is measured, where possible with a steel tape, under constant tension, with corrections for temperature. Fitzroy, to whom we owe the best description of contemporary surveying methods in rough country, did not like the use of the tape, even where the ground was flat enough – a rare occurrence in Tierra del Fuego. He obtained his base-lines by a combination of astronomical fixes and chronometric measurements. Wherever possible he set up his portable astronomical observatory on land and obtained observations for latitude and longitude, and for the true bearing of all prominent objects in sight. Though he placed great reliance on his chronometers (of which he carried 24 on the second expedition) for obtaining measurements of longitude, he nevertheless, whenever opportunity arose, determined it by absolute methods from observations of lunar distances of moon-culminating stars. This method is now completely obsolete, because radio transmissions of time signals make chronometric determinations of far greater reliability. Before the development of radio communications, however, purely astronomical methods of checking longitude were useful, though laborious.

The triangulation itself was carried out by the methods that

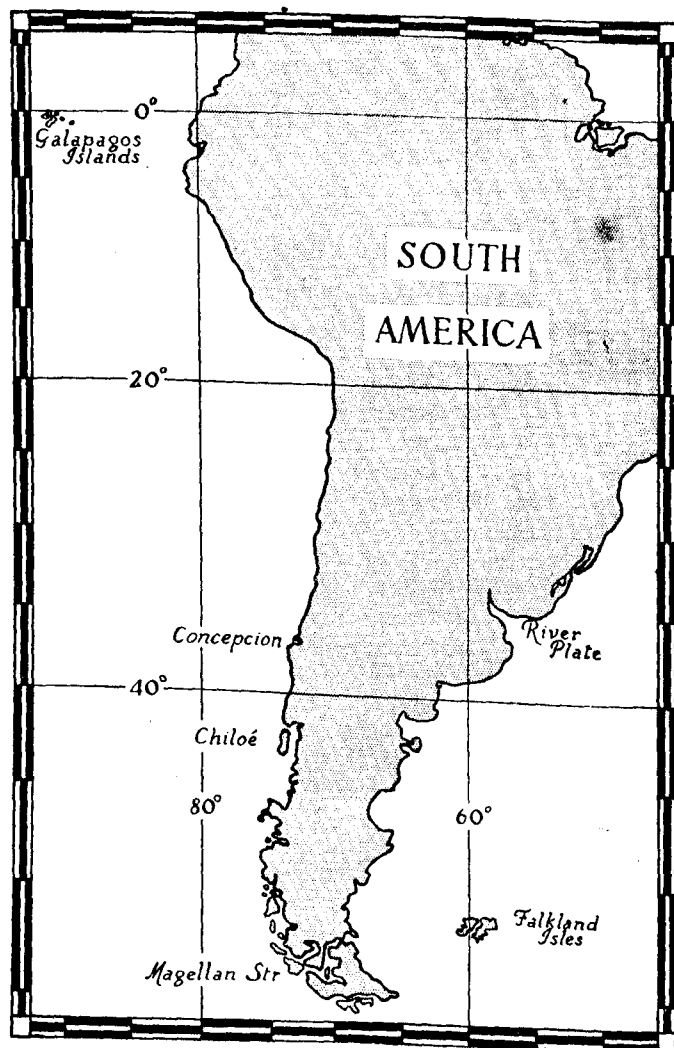
are orthodox today, by the use of theodolites. The nature of the terrain that he was surveying made it both feasible and imperative to conduct all theodolite observations from mountain tops. This had the added advantage that from each observation post it was possible to make a sketch plan of the coast line that could be seen, and the plotting rays for his chart could be 60-80 miles long in some cases.

Though logically the first part of a survey, the triangulation is in fact carried out alongside other activities, but it must of course be computed and plotted before the remainder of the survey is transferred to paper. The second stage of the survey is to delineate the coast and major topographical features. Then, as now, this was mainly performed, in a large-scale survey, by traversing the whole region on foot, with theodolites as the main instruments. Where the coast was too intractable, or where no useful purpose could be served by detailed charting, the coast was delineated from boats, by means of simultaneous sextant angles. So far as possible every inlet was followed to its head, a tremendous undertaking in a region so dissected as Tierra del Fuego. Wherever possible tide gauges were set up to determine the rise and fall of the tide and the time of low and high water at various phases of the moon. Tidal currents, tide rips, and eddies were noted, and then began the work of sounding as completely as possible the area to the seaward of high water mark. All the soundings must of course be reduced to the same datum, the zero level of the chart, usually coincident with low water mark of spring tides. Fitzroy's lines of soundings are not enough to satisfy any modern surveyor, for they give soundings too widely spaced, but he was aided in his attempt to locate shoals and rocks by the giant kelp, so that he missed no major obstacle to navigation, despite this sparseness of soundings. The kelp grows attached to any shoal less than about 20 fathoms deep and the fronds of the larger plants may stream for as much as 100 fathoms along the surface, thus forming a most noticeable feature of the seascape. Whenever such areas of kelp were noticed (or indeed any other indication of shoal water, such as breakers, ripples, or discoloration) much more numerous sound-

ings were taken to determine the depth and position of the 'least depth' of the shoal. Sounding leads armed with tallow provided information about the nature of the bottom.

Interspersed with these purely navigational observations, were others with a more scientific import. Wherever possible the geomagnetic intensity, variation, and dip were recorded both on land and afloat. From time to time pendulum observations were made to determine the local gravitational constant. And all the time, astronomical observations were made with the purpose, among others, of helping to determine the shape and the degree of oblateness of the spheroid. Eclipses of Jupiter's moons and movements of comets were among other astronomical observations made on the expeditions. The observations on tides made a considerable contribution to the theory of tides and to knowledge of the tidal wave. The second expedition of the *Beagle* was one of the earliest in which regular daily measurements of the sea temperature were made, and much knowledge of currents was obtained by this means. Fitzroy seems to have appreciated that cold water in low latitudes implies that the current has risen from the deeps, and he states that 'there may be a circulation of water in a vertical direction'. He noted the sharp edges that major currents often preserve, and remarked on the Chilean current. 'The Chile current, after coasting Peru, preserves a temperature of about 60° up to the Galapagos, and there it meets a warm stream out of the Gulf of Panama, at a temperature of about 80°, the two unite together and turn westward along the equatorial zone.' This is the current which carried the Kon-Tiki across the Pacific.

One notable innovation made on the *Beagle's* second cruise was the keeping of a detailed meteorological journal. Fitzroy had suggested that this should be done and the new Hydrographer, Captain Beaufort, agreed with him. Beaufort drew up for this purpose a table of wind forces and of other weather conditions and pointers. This scale is still in use today, though we should not now define 'force-7', a moderate gale, as 'a wind in which a well-conditioned man-of-war could just carry in chase, full and by, treble-reefed top-sails, top-gallant-sails and jibs'.



The *Beagle's* meteorological journal is a model of clarity and conveys a clear picture of the weather in the regions she visited.

THE SECOND EXPEDITION

Because King and Fitzroy surveyed so well the Lords of the Admiralty at first felt that the completion of the survey could not justify another expedition and the *Beagle* very nearly did not make a second cruise to South America. When Fitzroy received this information he began to charter a ship at his own expense to return the three surviving Fuegians to their native land (one had died of smallpox). Beaufort, however, cherished other ideas than the simple hydrographic survey of South America. Longitudes of many important places had been very imperfectly determined. There was for instance disagreement up to 2° (about 100 miles) between the various determinations of the longitude of Rio de Janeiro. And the whole survey of South America took this town as the reference point to which all other longitudes were referred. It is therefore fair to say that in 1830 no one knew for certain to within a hundred miles just where South America was. This applied even more strongly to much of the survey of the Pacific Ocean. Beaufort therefore suggested that an expedition to complete the charting of the South American shores, from the River Plate, round Cape Horn and north to the Equator, taking in the Falkland Islands and the Galapagos Islands, could also carry out the determination of the longitude of the various reference points by as exact methods as available. The Lords of the Admiralty agreed with Beaufort's suggestion, the *Beagle* was considered suitable for the purpose, and her commander had proved himself both an able surveyor and more particularly a master in the use of chronometers to determine longitude. In July 1831, then, the *Beagle* was commissioned at Plymouth for this work and immediately went into dock to be refitted. In order to have as good a check as possible upon the chronometric measurements it was necessary for the ship to circumnavigate the globe and spend some prolonged period in tropical waters. For protection against *Teredo* she was sheathed with two-inch fir planks covered outside by copper sheeting. Her

decks were raised by a foot or so and the newly invented lightning conductors affixed to her masts. Seven boats were built for the *Beagle* and so fixed that they could be carried in any weather. In November she was ready for sea.

In the meantime Beaufort and Fitzroy saw to the manning of the ship. They selected the officers and midshipmen in person. The judgement of one of them at least must have been good, for included were five future admirals. Two-thirds of the ratings who had served on the first expedition volunteered for the second, which speaks much for Fitzroy's powers of leadership, for these men knew the appalling conditions they were likely to meet. With them travelled the three Fuegians, a missionary who intended to spend some years in Tierra del Fuego, a draughtsman and an instrument maker engaged at the Captain's own expense, and finally - Charles Darwin. Fitzroy writes: 'Anxious that no opportunity of collecting useful information, during the voyage, should be lost; I proposed to the Hydrographer that some well-educated and scientific person should be sought for who would willingly share such accommodation as I had to offer, in order to profit by the opportunity of visiting distant countries little known . . . Professor Henslow . . . named Mr Charles Darwin, grandson of Dr Darwin the poet, as a young man of promising ability, extremely fond of geology, and indeed all branches of natural history.' The last seems a fair description of Darwin, the dilettante of this period. Henslow had in fact first suggested Leonard Jenyns, but Jenyns was recently married; Darwin was only second choice. He first refused on the advice of his father, who thought it would prejudice his ecclesiastical preferment, but Josiah Wedgwood persuaded his brother-in-law that the reverse was true. Charles Darwin and Fitzroy met, liked each other, discussed the cruise and Darwin was made the offer that was to change his life.

Darwin found his accommodation aboard the *Beagle* to his liking; his cabin was 'a capital one, certainly next best to the Captain's and remarkably light'. He shared it with an officer, and room was so cramped that the top drawer of a chest had to be removed when his hammock was slung, for otherwise there

was not sufficient length. His only place for working and dressing was the narrow space left clear at the end of the chart table, which occupied the centre of the cabin, and over this his hammock was slung at night. Certainly this was comfort indeed compared with what he was to experience in Tierra del Fuego: 'The greatest luxury here is to find a beach of pebbles, for they are both dry and yield to the body. The peaty soil is damp; rock is uneven and hard; sand gets into one's meat, when cooked and eaten boat-fashion; but when lying in our blanket bags, on a good bed of smooth pebbles, we passed most comfortable nights.'

To Darwin's great disappointment quarantine arrangements prevented the *Beagle* from putting in at Tenerife, a place he had longed for years to visit. Their first landfall in South America was Bahia, where they rated the chronometers and watered ship before sailing south to Rio and thence to the River Plate, where their presence quelled a revolution. Here Darwin left the ship to make excursions into the surrounding countryside, a procedure he followed at each point where the ship made a prolonged stay. When the *Beagle* had completed her survey of the immediate surroundings he rejoined her as she made her way south surveying the Patagonian coast. To assist in this, Fitzroy chartered at his own expense two decked boats with local pilots. These he placed under the command of his assistant surveyors. The *Beagle* made a running survey of the coastline, while the boats charted the bays, inlets, and anchorages. Once the running survey was complete the *Beagle* sailed for Tierra del Fuego to land the missionary and the Fuegians. They set up huts for them and planted out vegetable gardens, then left for a surveying trip up a nearby inlet. On their return they found the gardens trampled down and the missionary in terror of his life. He came on board (to be settled a couple of years later in New Zealand, where his brother was a missionary), and would never set foot on Tierra del Fuego again. The three educated Fuegians, when they were next seen, a year later, had relapsed to the condition of their fellow tribesmen. This was one experiment of the voyage that was not a success.

The year's interval between landing the natives and seeing

them again was spent in the main in the survey of the Falkland Islands, and the region of Cape Horn. Once the charting of the south-eastern part of Tierra del Fuego was completed the ship returned to Montevideo for overhaul and revictualling. Sailing south once more the *Beagle* grounded on a rock and sprang a leak. Fitzroy beached her in the estuary of the Santa Cruz river at high tide. By half tide she was on hard and the carpenter could reach and repair the damage to the fore-foot where part of the false keel had been ripped off and the copper plating torn away. Since the *Beagle* was now heading for tropical waters it was most important that this should be replaced to protect the timbers against shipworm. The next day a party set out to explore the Santa Cruz river. This was one of the expeditions that helped to convince Darwin of the vast extent of geological time, and of the vertical movements of land masses. Not that he needed convincing intellectually of these, for Lyell's works had done this, but these vast basaltic plains, cliffs, and erosion channels engaged his imagination, and strongly fortified the dry bones of book studies.

From the Santa Cruz they made for Port Famine, almost a homecoming for Fitzroy, but Darwin wrote, 'I never saw a more cheerless prospect; the dusky woods piebald with snow, could be only indistinctly seen through a drizzling hazy atmosphere.' From here they passed into the Pacific by the Magdalen and Cockburn Channels, surveying as they went this route which had not been used before by ships. The next thirteen months were devoted to a running survey of the Chilean and Peruvian coasts as far north as the Equator. For this work, carried out without a triangulation, the open shore line was charted from the ship. Every anchorage and cove was entered and charted more completely by conventional methods and the longitude relative to some convenient point determined. Wherever possible Fitzroy landed and set up his portable astronomical observatory (constructed in ninety pieces so that it could be transported in boats) and made the necessary observations on moon-culminating stars and other celestial phenomena to determine the geographical co-ordinates.

While at sea near the port of Concepción on this coast they experienced one of the great earthquakes of the nineteenth century which wiped out the town of Concepción (the capital of Chile at that time) and caused unequal elevation of the land around. Fitzroy gives a most graphic account of the event, mostly from data collected second-hand, because it was all over before the ship reached land. But even at sea they had felt and heard the tremors: 'Sometimes I thought that the anchor had been accidentally let go, and the chain was running out; and while at anchor, I often fancied the ship was driving, till I saw that there was neither swell, current, nor wind sufficient to move her from her anchorage.' Interpreting these signs as the workings of an earthquake, Fitzroy made all sail for Concepción to offer what assistance he could. They found the city in ruins. Much of the damage at the nearby town of Talcahuano had been caused by three great tidal waves which rose to a level of thirty feet above high water mark and swamped the whole town. A large stretch of the coast in the vicinity was raised during the earthquake. The southern end of the island of Santa Maria was raised eight feet while the northern end was elevated by ten feet – the stench of the dead animals exposed and killed by this upraising can be imagined. This alteration to the level of the land and the associated volcanic activity made an impression on Darwin which, once more, reinforced Lyell's teaching of the elevation of mountains and the raising of rocks (and fossils) from the sea to great heights in the mountains.

The Circumnavigation

From the South American coast they steered direct for the Galapagos Islands, where they remained for two months surveying. There is no need to emphasize here the influence that the biology of this archipelago had upon Darwin's thinking. Darwin had further opportunities to study the biology of islands at the next port of call – Tahiti (Otahite) and the Society and Tuamotu Islands. All Cook's surveys of the South Seas had Tahiti as the reference point for the determination of longitude, so that it was important to fix its longitude as exactly as possible. It was

in this archipelago that Darwin first saw any large number of coral islands, but it was not until the *Beagle* reached the Keeling Islands that he was able to make a really thorough study of an atoll. Meanwhile the ship called at New Zealand, Hobart, and Sydney to obtain observations for longitude. From the Keeling Islands they steered for Mauritius, Madagascar, Ascension Island and then over once more to Bahia in Brazil, before making home for Falmouth, where they arrived on Sunday, 1 October 1836.

So ended Darwin's voyaging: he never left England again. Nor did Fitzroy ever command in sail again. Shortly after the affairs of the expedition had been wound up he was appointed the first governor and commander-in-chief of the new British colony of New Zealand. Later he became the first head of the Meteorological Office and instituted the system of gale warnings which is in use today, and was elected a fellow of the Royal Society. He devoted his last years to work in improving lifeboats and methods of saving life at sea, until in 1865, shortly after he had attained the rank of vice-admiral, 'in a fit of mental aberration', as one biographer puts it, 'he put an end to his existence', thus following the example set by his predecessor in the command of the *Beagle*.

As for the work of the expedition, the results in natural history are too well known to need repeating. The excellence of the survey carried out may be judged by the Hydrographer's report to the House of Commons in 1848: 'From the Equator to Cape Horn, and from thence round to the River Plate on the eastern side of South America, all that is immediately wanted has already been achieved by the splendid survey of Captain Robert Fitzroy'. Many of his charts are still in use, and although the British *Sailing Directions for South America* no longer quote *literatim* from Fitzroy's first edition of this work, the sailing directions published by the Chilean and Argentine authorities consist even now (except for the directions for the newer ports) of word for word translations from Fitzroy. The positions of Rio de Janeiro, Port Famine, and other important points of reference on the South American coast were fixed within two

seconds of arc – less than 100 yards in those latitudes. In the five-year circumnavigation of the globe they made the circumference of the earth to be 24 h. 0 m. 33 sec., an error of only 33 seconds in five years. This represents an accumulated error in longitude at the latitude of England or of Tierra del Fuego, of only four or five miles. Since the links in the chain of chronometric measurement that were most liable to error were those across the Pacific, longitudes measured east or west from Greenwich towards the Pacific are only out by fractions of a mile, or a mere few seconds of arc. This is a most remarkable achievement for the period before radio communications.

The *Beagle* was used on one more surveying commission, before being placed ordinary. This was carried out under the leadership first of Commander Wickham and later of Commander Stokes, both of whom had served with Darwin under Fitzroy. This commission was to survey Australia. The ship left England early in 1837 and sailed via the Cape of Good Hope to Perth, taking five months over the voyage. For three years under Wickham's command she surveyed the western and north-western coasts. Quite early on Wickham was taken ill with dysentery and in 1840 he handed over his command to Stokes. On his last trip before resigning his command, the ship sailed eastabout from Sydney, where she had been refitting, to survey Van Diemens Gulf (not to be confused with Van Diemens Land) in north Australia. Here he discovered and surveyed a 'deep bay to the N.E. of Paterson Bay, [which] was found to be very extensive and to branch off from a spacious port in three different directions. . . . This place has been named Port Darwin.' It is now the capital of the Northern Territories of Australia.

After completion of this commission, the *Beagle* was paid off at Woolwich in October, 1843, and placed ordinary with the fleet at Sheerness. Two years later she was transferred to the Commissioners of Customs for service as a Watch Vessel at Southend. In 1870 she was sold by public auction and ended her official career. Five ships have borne the name *Beagle* since; the last was a destroyer, built on Clydebank in 1930, which served through the war. She, the last to bear the name, was scrapped in

1946, and the name, for the present at least, is not borne by any craft of the Royal Navy.

* * *

I should like to acknowledge with grateful thanks the assistance afforded to me by the Hydrographic Department of the Admiralty, and in particular by the Assistant Superintendent of Sailing Directions, Lt-Cdr E. E. Croome, by the Curator, Mr C. W. Watts, and by the Assistant Curator, Mr F. J. Cochrane.

BOOKS ARISING DIRECTLY OUT OF THE VOYAGES OF H.M.S. Beagle

- Darwin, C. (1842): *The Structure and Distribution of Coral Reefs*.
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CYCLOTRON RESONANCE

A. C. ROSE-INNES

SOLIDS which are conductors of electricity contain electrons that are free to move through the solid, and it is the flow of these electrons that constitutes the electric current. Such electrons are called *conduction electrons*. There have recently been many developments in devices, such as transistors, whose action depends on the passage of electricity through solid materials, and it is important, therefore, to try and discover exactly how electrons pass through these solids. Cyclotron resonance is one of the latest experimental techniques used in this type of investigation. Cyclotron resonance measures the properties of conduction electrons in solids, particularly a quantity called their 'effective mass', which is rather difficult to determine by normal electrical measurements.

Before we describe the cyclotron resonance experiment, we shall examine briefly some of the properties of electrical conductors so that we can understand the information obtainable from the measurement, and some of the experimental difficulties that have to be overcome.

Those substances, such as metals, that are good electrical conductors contain a large number of conduction electrons, about 10^{23} in a cubic centimetre. On the other hand, electrical insulators, like rocksalt or glass, contain hardly any such electrons. A third class of solids is that of the *semiconductors*. These have electrical conductivities lying between metals and insulators and may contain between 10^{12} and 10^{19} conduction electrons per cubic centimetre. Semiconductors, of which germanium and silicon are typical examples, are of increasing technical importance, and are the substances from which transistors and similar devices are made.

PROPERTIES OF SEMICONDUCTORS

Electrons

We need only consider the simplest kind of semiconductor, called the 'covalent' semiconductor, and we can take silicon as a typical example. On the outside of the silicon atom there are four electrons, and it is these 'valency' electrons that form the bonds that hold the atoms together in a crystal. Each valency electron pairs off with a valency electron from another silicon atom so that every atom is surrounded by four other atoms in the form of a tetrahedron. A model of such a crystal is shown in Inset 14 and is illustrated diagrammatically in Figure 1. Dia-

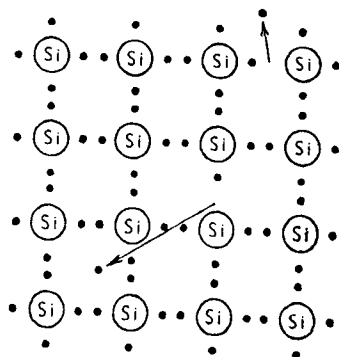


Fig. 1. Two-dimensional diagram of a silicon crystal, showing each atom bound to four others by two-electron bonds. A few of these bonds are shown broken by the thermal vibrations of the atoms.

mond, germanium, and grey tin also crystallize in this form which is known as a 'diamond-type' structure. Another kind of valency crystal is that formed by the 'intermetallic' compounds, of which indium antimonide is an example. These form structures similar to the diamond-type except that the two different kinds of atom occupy alternate positions in the lattice (Inset 15).

The two-electron bonds holding the atoms together are very strong, but the atoms vibrate about their mean positions and this

motion is sufficient to break a number of the bonds. The higher the temperature the more vigorously do the atoms vibrate, and the more bonds that will be broken. At room temperature about one bond in 10^8 is broken. The electrons that formed the bonds broken by the thermal motion are then free to move through the crystal: these are the conduction electrons (Figure 1). Semiconductors whose conduction electrons come from broken bonds are called 'intrinsic semiconductors'. (There is another kind of semiconductor whose conduction electrons come from impurities in the crystal rather than from broken bonds, but we need not consider these 'impurity semiconductors' here.) At low temperatures the vibrational energy of the atoms will be small so practically none of the bonds will be broken, and there will be very few conduction electrons.

The properties of conduction electrons inside a solid may be surprisingly different from their properties when these are measured in free space. For example, the mass of a conduction electron in a conductor may appear to be quite different from the usual electron mass. In germanium, for instance, it may be only about one four-hundredth of the normal electron mass. This mass, which the electron appears to have when it is in a conductor, is called the *effective mass*. Of course the properties of the electrons themselves do not depend on whether they are in a crystal or not. What we observe is the effect of the crystal atoms on the motion of the electrons passing between them.

Consider an electron in free space with energy E and momentum p . These are given by

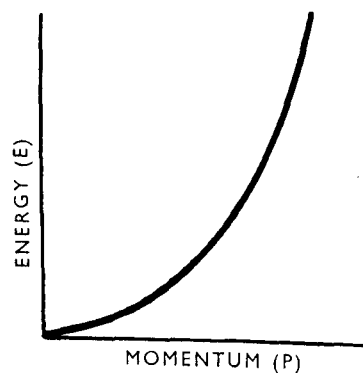
$$E = \frac{1}{2}mv^2 \text{ and } p = mv$$

where m is the mass of the electron and v its velocity. We see that energy and momentum are connected by the formula

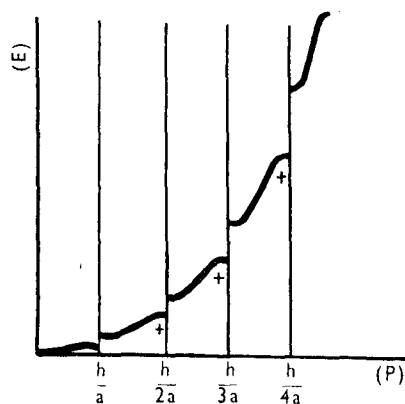
$$E = \frac{1}{m} \cdot \frac{p^2}{2} \quad (1)$$

We may regard the mass m as a constant which connects the energy and momentum in formula (1). If we plot energy against momentum for this electron in free space we obtain the parabola shown in Figure 2(a).

Now, we know that a particle, such as an electron, has a wave associated with it, whose wavelength is inversely proportional to its momentum. In fact, if λ is the wavelength then $\lambda = h/p$ where h is Planck's constant. It turns out that, for the momenta that conduction electrons have in crystals, the wavelength is of



(a) IN FREE SPACE



(b) IN A CRYSTAL

Fig. 2. Energy-momentum diagrams for electrons.

the same order as the spacing between the atoms. In this case the wave interacts strongly with the atoms of the crystal, affecting the motion of the electron through the crystal. In particular, if the momentum is such that the wavelength equals an exact number of atomic spacings, as shown in Figure 3, it will be completely reflected by the atoms of the crystal, and electrons of the corresponding momentum will not be able to pass through the crystal. In Figure 3 we see two such electron waves, with wavelengths

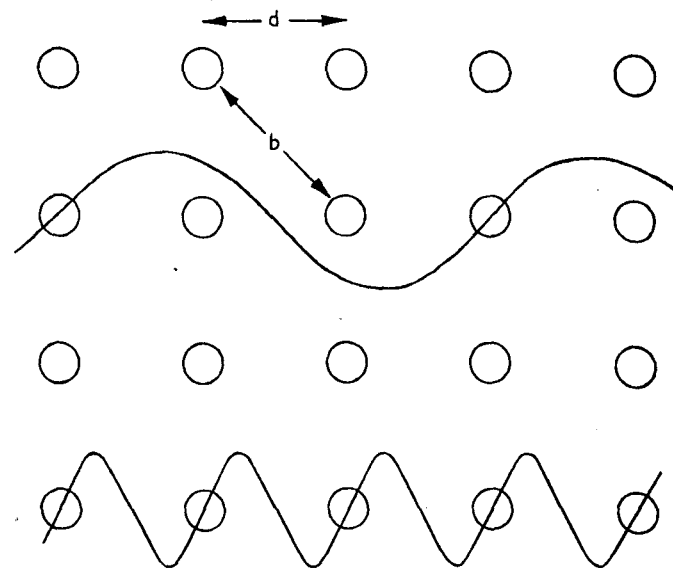


Fig. 3. Electron-waves corresponding to forbidden momenta in a crystal.

two and four times the atomic spacing, neither of which will be able to pass through the crystal. The electrons have, therefore, a set of 'forbidden momenta' corresponding to those wavelengths that equal a whole number of atomic spacings. If d is the distance between the atoms, waves with momenta $p = h/nd$ are forbidden, when n is a whole number. If we draw the energy-

momentum diagram for electrons in a crystal, we obtain, not the simple parabola that we had for electrons in free space, but the curve shown in Figure 2(b). It can be seen that the shape of this graph is similar to the parabola of the electron in free space except near the forbidden momenta where there are discontinuities. Now the simple parabola was the energy-momentum curve for a particle of fixed mass, m : hence where the curve for the electrons in a crystal departs from this parabola the mass must differ from a free space electron mass, m . Thus electrons with momenta near the forbidden values have an effective mass m^* , which differs from the mass of an electron measured in free space. In particular, at the points just below the forbidden momenta, marked '+' in Figure 2(b), the curvature is in the opposite direction to that of the parabola. This means that in these regions the effective mass of the electron is negative. This rather surprising result implies that such electrons move in a direction opposite to a force acting on them. This is not, however, so strange as it may seem; the electrons are, so to speak, being reflected by the crystal lattice.

The effective mass of the electron may not only be different from the usual electron mass but may vary with the direction of motion of the electron through the crystal. Thus in Figure 3 the distance b differs from the distance d and so an electron travelling in the direction of b will have different forbidden momenta and, therefore, its energy-momentum diagram will be somewhat different from Figure 2(b). This means that effective masses will differ for electrons travelling in this direction.

Cyclotron resonance is a direct method of measuring the effective masses of electrons in solids and, by making the measurements on electrons travelling in different directions, we are able to determine both the value of the effective mass and the way it depends on the direction of the motion of electrons through the crystal.

Holes

When we measure the electrical properties of conductors we sometimes find that the electric current appears to consist of the

motion of positively charged particles in addition to the negatively charged electrons. For reasons that we shall see, these positive components of the electric current are called 'holes'.

Let us go back to Figure 1. When an electron bond is broken and the electron moves away through the crystal it leaves a vacancy behind it. This is called a 'hole'. Now an electron from another bond may move into this space and in doing so leave a hole at the place where it came from. Hence the hole seems to have moved to this other place. This may happen over and over again so that the hole appears to move about the crystal. It will be understood that the holes travel in the direction opposite to the electrons and so, if we apply an electric field to the crystal which makes the negatively charged electrons move to the left, holes will move to the right. It therefore appears as though one part of the current is due to particles that move in the direction opposite to the electrons, i.e., to particles which have a positive charge. Like electrons, these holes have an effective mass that we may measure by cyclotron resonance, and which varies with their direction of movement through the crystal. It will be seen that holes do not exist until some bonds have been broken making a space and so, when we create a number of conduction electrons by breaking bonds, an equal number of holes are created at the same time. (In the 'impurity' semiconductors, which are mentioned above, either holes or electrons can, however, exist without the other.)

We have now sufficiently discussed the properties of electrons in semiconductors to be able to examine the experiment of cyclotron resonance in detail.

CYCLOTRON RESONANCE EXPERIMENTS

The conduction electrons in a conductor behave rather like the molecules of a gas, dashing through the material with various velocities and in various directions. If we apply a magnetic field to the substance, the electrons, instead of travelling in straight lines, travel in helices about the direction of the magnetic field as shown in Figure 4. We may think of this motion as made up of a circular rotation in a plane perpendicular to the direction

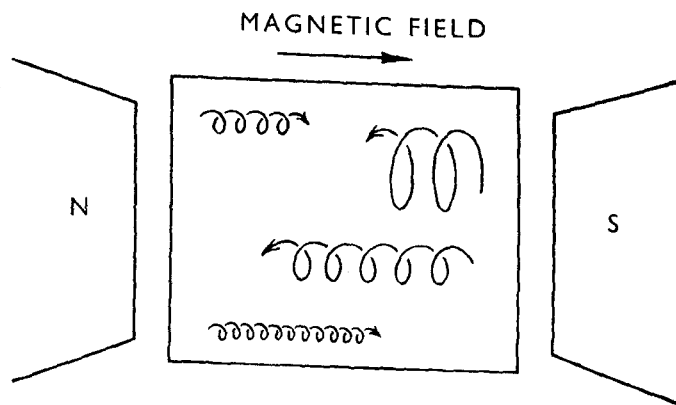


Fig. 4. Paths of conduction electrons in a magnetic field.

of the magnetic field (i.e., coming out of the paper in Figure 4) added to which is a simple straight motion parallel to the direction of the magnetic field. The stronger the magnetic field the more tightly will the electron paths be coiled, and the more quickly will they revolve. In fact the number of revolutions per second is given by

$$\nu_c = \frac{eH}{2\pi m^*} \quad (ii)$$

where e is the electrical charge of one electron, H is the strength of the magnetic field which we are applying, and m^* is the effective mass of the electron. ν_c is called the 'cyclotron resonance frequency'. It will be seen that ν_c only depends on the effective mass and the electronic charge, and not on the velocity of the electron. Hence, if we can measure ν_c , we can calculate the effective mass directly. Cyclotron resonance is a way of determining the effective mass of electrons by measuring their frequency of rotation in a magnetic field.

To perform the experiment we apply an alternating electric field of frequency ν to the substance and a steady magnetic field perpendicular to it. The magnetic field makes the electrons re-

volve in the plane of the electric field. We then increase the magnetic field strength so that the electrons revolve faster, and when we reach a certain strength their frequency of rotation, ν_c , will be the same as the frequency ν of the alternating electric field. When this occurs the electrons will be accelerated in a similar manner to particles in a cyclotron and will travel in spiral paths of increasing radius, picking up energy from the electric field. We say that 'resonance' has occurred. At this point, therefore, the energy of the electric field will be absorbed by the electrons in the substance. If we measure the amount of absorption of the alternating electric field and plot this against the magnetic field strength we obtain an absorption peak like Figure 5(a). We know the frequency of the alternating electric field, ν , and so, if we put the value of H for which the peak occurs into formula (ii), we obtain the effective mass of the electrons, m^* .

There is, however, a snag in this apparently simple experiment. Every semiconductor, no matter how carefully we prepare it, contains a small number of impurities. Thus a crystal of germanium will contain a few atoms of copper, boron, and other elements. As the electrons move through the crystal they sometimes bump into these foreign atoms and are scattered by them, and, if the electrons were in a helical orbit, this is destroyed and they have to start again. When there are a lot of impurity atoms, the electrons bump into them before they have time to perform even one revolution in the magnetic field and they never get into proper orbits at all, so it is not possible to carry out the cyclotron resonance measurement. The effect of the impurities is to broaden the absorption peak of the alternating electric field, and too many impurities cause so much broadening that the peak disappears. This is illustrated in Figure 5(b): curves 1, 2, and 3 show the effect of increasing impurity. Curve 3 shows the result of so many collisions with impurities that the peak has disappeared altogether. We can, however, help the electrons to miss the impurities. The stronger the magnetic field we apply, the more tightly coiled are the electron orbits and the less the distance they will sweep out in the crystal per revolution. Hence in a strong field they are less likely to bump into an impurity atom.

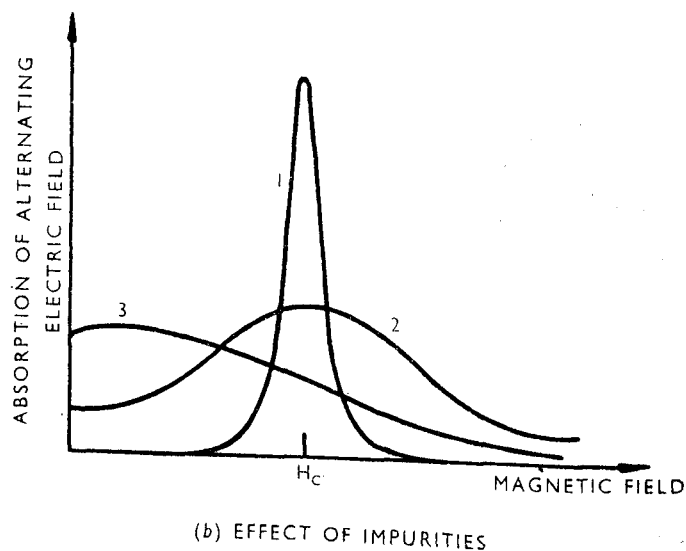
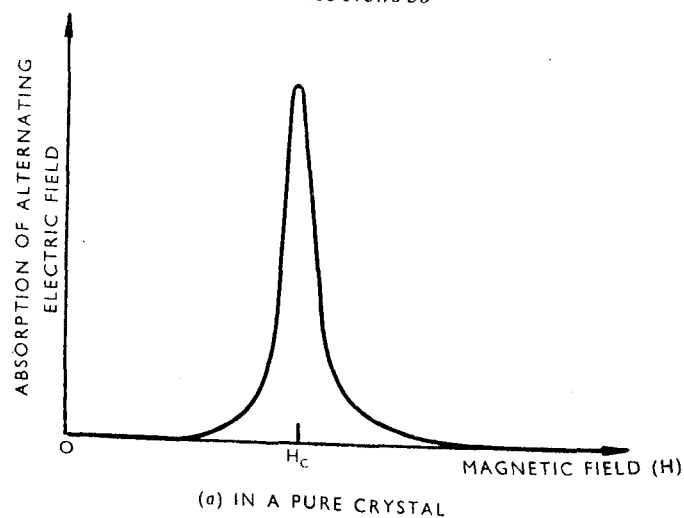


Fig. 5. Cyclotron resonance absorption.

Germanium and silicon crystals can be prepared very pure indeed, with less than one impurity atom for every 10^8 crystal atoms. For such crystals we find that we need a magnetic field of about 1000 gauss in order to coil the electron paths so that they do not have too many collisions. Now the stronger the magnetic field the more quickly will the electrons revolve and the higher will the frequency of the alternating electric field have to be. For fields of about 1000 gauss the frequency turns out to be about 10^{10} cycles per second. This frequency corresponds to that of the 'microwaves'. These very high frequency radio waves, which were first developed for radar, have the property that they will travel along the inside of metal tubes, rather like sound along a voice-pipe. Such metal tubes are called 'waveguides'.

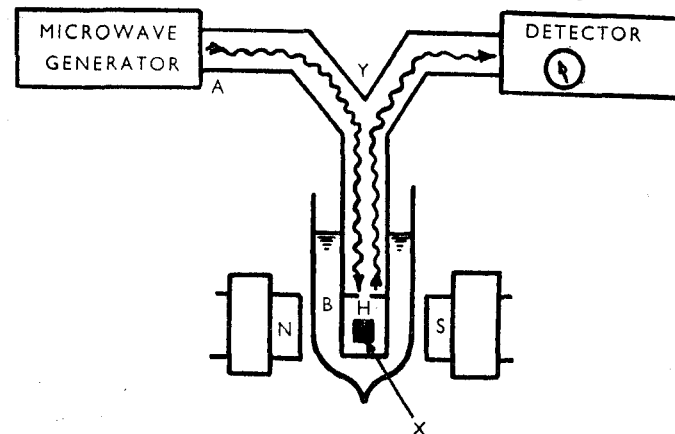


Fig. 6. Arrangement for a cyclotron resonance experiment.

Figure 6 shows an arrangement for a cyclotron resonance experiment. The specimen, X , is in a copper box, B , placed between the poles of an electromagnet, NS (the box is inside a Dewar vessel for reasons that will be explained later). Microwaves from a generator are fed to the box along the waveguide AB , and they pass into the box through a hole, H . Absorption by cyclotron resonance of energy from the alternating electric

field of the microwaves is very small and, if the waves only passed the crystal once, the loss by absorption would be too small to measure. However, the box *B* is exactly half a wavelength long, and in this case the waves are reflected to and fro between its ends, passing through the specimen many times before escaping out again through the hole *H*. Such a box is called a resonant cavity. The outgoing wave travels up the waveguide to a device, shown diagrammatically in Figure 6 as a 'Y', which sorts the outgoing wave from the incoming one. The outgoing wave then travels to a detector which measures its intensity. This intensity is measured while the strength of the magnetic field applied to the specimen is increased from zero, and a graph like Figure 5(a) is plotted. The effective mass m^* can then be calculated from formula (ii). If the measurement is repeated for various orientations of the crystal relative to the magnetic field, we can find how the effective mass changes with the direction of motion of the electron through the crystal.

It is now necessary to explain why the box containing the crystal in Figure 6 is inside a Dewar vessel. In a crystal at a finite temperature all the atoms are vibrating and, at room temperature, this vibration is fairly strong. The vibrating atoms collide with the conduction electrons and scatter them. As a result the peaks are broadened in a manner similar to the broadening by collision with impurities. At room temperature this broadening is so great that the cyclotron resonance peaks are not visible at all. However at low temperatures the vibration of the atoms is small and there will be little broadening of the peaks. In order to see the peaks in germanium and silicon it is necessary to cool the samples to within a few degrees of absolute zero and this is done by filling the Dewar vessel with liquid helium (see Inset 16). Figure 7 shows cyclotron resonance peaks obtained from germanium and silicon at this temperature, 4° K.

If the cyclotron resonance peaks are to be sharp enough to observe, the electrons must not collide with impurities more than once per revolution. If τ is the time between collisions, the time of revolution must be less than τ . The purest semiconductors that can be made at present contain about 10^{13} impurities

per cubic centimetre. For these materials τ is about 10^{-9} seconds and it is necessary to use frequencies of 10,000 Mc/s and magnetic fields of several hundred gauss to observe the resonance. The use of higher frequencies and magnetic fields would make the peaks sharper and enable cyclotron resonance to be observed in more impure materials. However, it becomes inconvenient to use frequencies higher than about 50,000 Mc/s and to generate magnetic fields greater than about 12,000 gauss. So far, cyclotron resonance using microwaves has been carried out at frequencies of 10,000, 30,000, and 50,000 Mc/s, which are frequencies that have been developed for radar. These frequencies are high enough for cyclotron resonance to be observed in germanium and silicon, but are too low for other semiconductors that have yet to be prepared in such a pure form.

There is another difficulty that must be overcome. We have seen that, in order to reduce the vibration of the atoms, the experiment must be performed at very low temperatures. At these low temperatures, however, very few of the bonds are broken, and so there will be hardly any conduction electrons and holes. We must therefore arrange to break some of these bonds when the substance is cold. This is done by shining light on to the specimen. The energy of the light breaks some of the bonds, creating conduction electrons and holes. The light from an ordinary small electric lamp is quite suitable, but this cannot be placed near the sample, because the heat would boil away the liquid helium and raise the temperature. The lamp must therefore be placed outside the Dewar vessel and the light allowed to fall on the specimen through transparent windows in the Dewar vessel and resonant cavity.

CYCLOTRON RESONANCE IN SEMICONDUCTORS

Cyclotron resonance has been very successful in the study of the two important semiconductors germanium and silicon. Most of this work has been carried out by Dresselhaus, Kip, and Kittel at the University of California, and by Lax, Dexter, and Zeigler at the Massachusetts Institute of Technology. Figure 7 shows cyclotron resonance curves derived from crystals of germanium

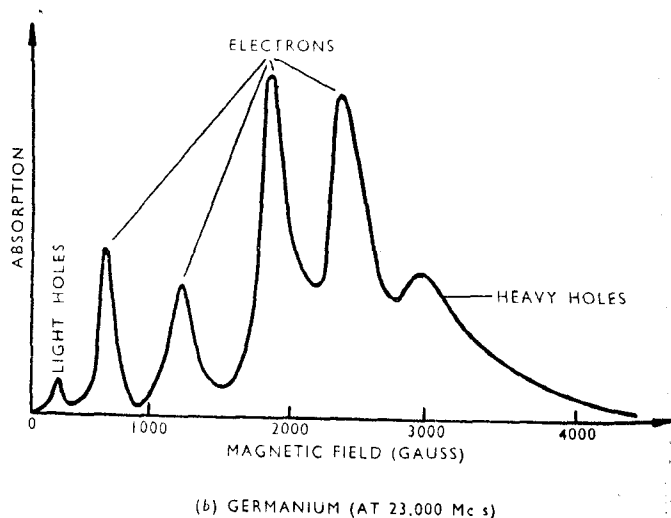
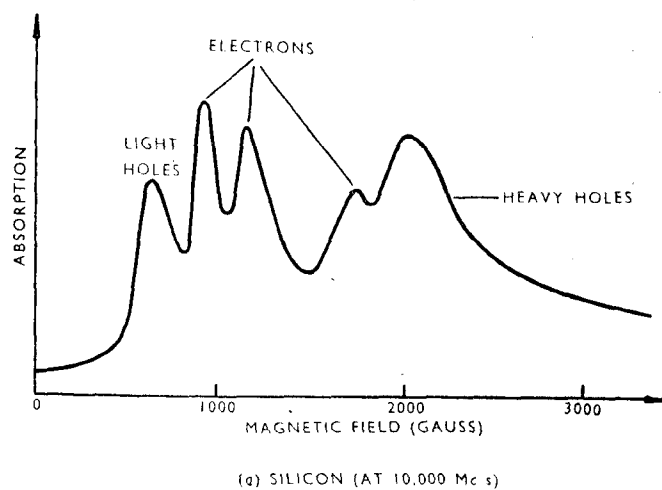


Fig. 7. Cyclotron resonance peaks from silicon and germanium at 4° K.

and silicon. The spectra are complicated, with several peaks both for electrons and holes. This implies that there are several kinds of electrons and holes in the semiconductors, each with a different effective mass. Measurements with the magnetic fields pointing in different directions relative to the crystal axes have shown how the effective masses of the electrons vary with their direction of motion through the crystal. This variation can be illustrated by means of an effective mass diagram such as Figure 8. Suppose that an electron travelling in a certain direction has an effective mass m^* ; we can represent this by an arrow in this direction with length proportional to the value of m^* . There will be an arrow for every possible direction of motion of the electron and the tips of all these arrows will lie on a three dimensional surface. If there is more than one value of the effective mass there will be more than one surface. In silicon there are two kinds of holes. There are 'heavy' holes whose effective mass is about one half that of the electron mass but which varies slightly with direction. This gives the effective mass diagram of Figure 8(b), a cube with rounded corners and dimples in the centres of the faces. There are also 'light' holes whose effective mass does not vary with direction and which are only a tenth of the normal electron mass. In Figure 8 the peak of the light holes is smaller than that of the heavy holes and this means that there are fewer of the former. Nevertheless these light holes make quite a large contribution to the electric current because their small mass enables them to travel very rapidly through the material.

In Figure 7 there are three peaks from electrons, showing that there are three kinds of electron in silicon. Cyclotron resonance has shown that their effective masses vary strongly with direction (Figure 8(b)). Each of the three kinds of electron has an effective mass whose directional variation is like a flat disc-shaped surface. The three kinds are similar, except that the three surfaces point in the three different directions at right angles. The effective masses for germanium are rather like those of silicon. There are 'light' and 'heavy' holes, but there are four electron surfaces instead of three. These lie along the directions

of the body diagonals of a cube. The effective masses of electrons and holes in germanium are rather less than those in silicon.

Cyclotron resonance has also been performed on indium antimonide, but this semiconductor has not yet been prepared sufficiently pure to obtain detailed results. It appears that the electrons have a very light effective mass, which is only a hundredth of the normal electron mass, and which does not vary with direction. Cyclotron resonance at microwave frequencies has not been observed in other semiconductors because they have

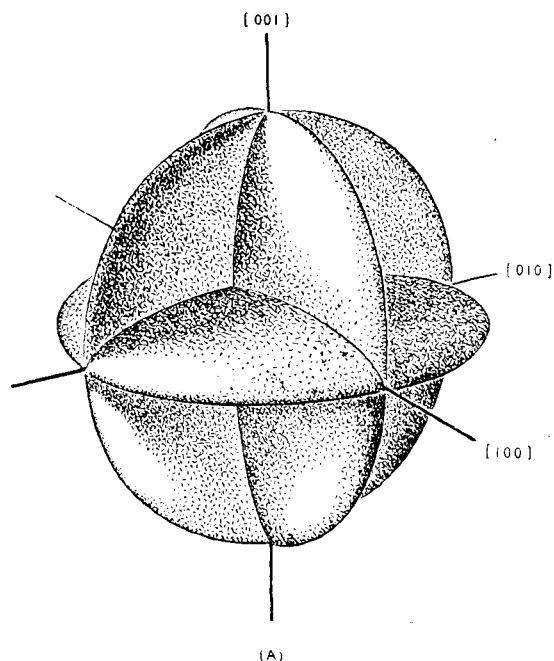
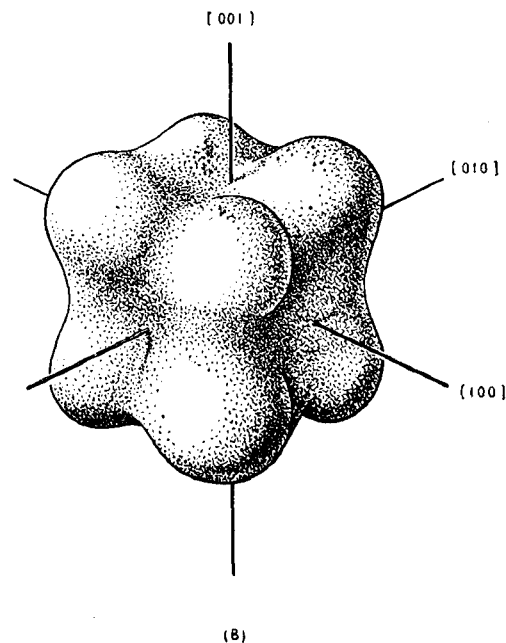


Fig. 8. Effective mass diagram for silicon. The distance from the centre of the solid to a point on the surface is proportional to the effective mass of an electron or hole travelling in that direction: (a) electrons, (b) heavy holes.

not yet been prepared sufficiently pure. We saw that the resonance in less pure materials could be observed if we could use a higher frequency. Some experiments have been carried out using infra-red waves instead of microwaves. These are electromagnetic waves with frequencies about 3,000 times those of the microwaves. But, because of the high frequency, very strong magnetic fields must be used. Recently special magnets have been made which can produce fields of up to several hundred thousand gauss, and cyclotron resonance has been observed at room temperature in indium antimonide and gallium arsenide.

Although this article is primarily about semiconductors, some mention should be made of metals, because these are, after all, the most important electrical conductors. Metals might seem to be good materials on which to perform cyclotron resonance, since they can be prepared in a high state of purity, and they



contain a large number of conduction electrons. It turns out in practice, however, that they have *too many* electrons. Because of this high concentration the motion of each electron influences the motion of the others, and the electrons do not move independently but all together in a cloud or 'plasma'. This collective motion can give rise to an absorption peak, but we cannot calculate the effective mass from this because the magnetic field at which the peak occurs depends both on the number of electrons and the shape of the specimen. In addition, the high conductivity produces a 'skin effect' which prevents the alternating electric field penetrating the metal. Recently, however, two Russians, Azbel and Kaner, have suggested a method for observing cyclotron resonance in metals. The magnetic field and the alternating electric field are applied perpendicular to each other but *parallel* to the surface of the specimen which is made to form part of the inner wall of the resonant cavity. Under these conditions cyclotron resonance has been observed at Berkeley, Ottawa, and Cambridge, in the metals tin and bismuth.

CONCLUSION

Cyclotron resonance is, of course, only one of many techniques used in the study of conduction electrons. X-ray and infra-red spectroscopy, magnetic and electrical measurements are widely used, but the special value of cyclotron resonance lies in its giving the detailed behaviour of the effective masses of electrons and holes in solids. Such data are very difficult to obtain by other methods. In particular the values and variation of the effective masses in the two important semiconductors germanium and silicon are now fairly fully understood as a result of cyclotron resonance experiments.

There is great interest in new kinds of semiconductors, such as the intermetallic compounds, which may have many practical uses, and cyclotron resonance measurements would be very valuable in trying to understand these materials. So far, only preliminary results have been obtained because of the difficulty of preparing them in a sufficiently pure state. Cyclotron resonance is, however, still a fairly new technique (the first experi-

ments were reported in 1953), and with improvements in the purifying of materials and advances in cyclotron resonance methods, such as the use of infra-red waves and very strong magnetic fields, it should be possible to investigate these substances in detail.

The new special technique for cyclotron resonance in metals looks very promising as an aid to understanding their electrical properties. In spite of the fact that metals are the most important conductors of electricity, very little is known about the effective masses of electrons in them, and any information we can obtain concerning this will be of very great scientific interest.

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A SCEPTICAL CHEMIST

CHARLES VERNON

IN the early days of organic chemistry there was a widespread belief in what was called the vital force – the force of life. The life of living things was thought to be sustained by this force. Furthermore, it was supposed that the chemicals made by living organisms – organic chemicals – were, in some way, different from the inorganic substances of the mineral world. In organic substances the known chemical forces were thought to be insufficient to explain all their properties. Over and above the usual chemical forces is superimposed the vital force and this modifies the properties of organic substances in unique and characteristic ways. For example, Berzelius invoked vital force to explain why oxalic acid – an organic substance – is a stronger acid than carbonic acid, and many similar explanations were in vogue at that time.

Now to modern ears the vital force theories of early organic chemists sound slightly ridiculous, but we have to remember that theories are put forward to explain facts. It is better, therefore, if we try to understand why the early chemists found it necessary to draw such a distinction between organic and inorganic substances. The essential point is that living organisms are obviously quite different from minerals. They are organized: they show purposeful activity: they resist and adapt to changes in their external environment. We must remember that at the beginning of the nineteenth century chemistry was such a primitive science that there seemed no possibility that the complicated patterns of biology could ever be 'explained' in chemical terms. Vitalism, as used by the early organic chemists, was really an announcement that living and non-living matter are clearly different. It seemed reasonable to suppose that some of this difference would persist even in the substances isolated from

living organisms. Vitalism expressed the fact that scientists found it incredible that chemical and physical laws alone can account for the properties of living matter.

It is often supposed that the vital force theory dropped out of organic chemistry after 1828 – the year in which Wohler made urea, to quote his own words, 'without kidneys or any animal tissue at all'. But in fact vitalism survived well into the middle of the century. In 1842, for example, Liebig wrote: 'the chemical forces of cohesion and affinity in food substances are overcome by the force of life which causes them to fall apart and to recombine in a new order of arrangement'. Eventually, however, vitalism dropped out of fashion. There were two reasons for this. First, it could get nowhere. It had no predictive power. It produced no new experiments. Its explanations were only pseudo-explanations, encompassing only the facts available to it and predicting no new ones. Secondly, classical organic chemistry, based on a few simple postulates, seemed to show that there was no end to the synthetic possibilities open to it and that, at least in outline, the properties of organic molecules could be quite well understood without recourse to vitalism. Kekulé, writing in 1859, defined organic chemistry simply as the chemistry of carbon, and could see no distinction between organic and inorganic chemistry.

Analysis of Vitalism

An analysis of vitalism is of interest because the difficulties that led to vitalism in early chemistry are very similar to difficulties that exist at present on the boundaries of organic chemistry and biochemistry. Historically, vitalism is concerned with whether it is possible to develop a set of concepts that would be equally applicable to organic and inorganic chemistry. The vitalist view was that this is not possible; the properties of organic compounds need some concept over and above the purely chemical ones that emerge from the study of inorganic compounds. Vitalism dropped out of fashion not because a real unity of the various branches of chemistry was actually achieved – this did not happen until the twentieth century – but because

it seemed more reasonable that the chemical properties of substances were governed by laws applicable to all substances, whether organic or inorganic.

Now most scientists think of science as a kind of hierarchy. Physics, the most fundamental science, is at the base of the hierarchy. Above come chemistry, biochemistry, and biology in that order. In common language we talk of 'explaining' biology in terms of chemistry, or of 'explaining' chemistry in terms of physics – but we do not talk of 'explaining' physics in terms of biology. In rather more precise terms what this means is that we seek to explain the concepts used in one science in terms of concepts used at a lower level of the hierarchy. An example will make this clearer. In chemistry the idea of bonding between atoms is fundamental. Two atoms of hydrogen, for example, join together to form a hydrogen molecule. The two atoms behave as though they were linked together or held together by some strong force. This force was usually called, during the last century, chemical affinity, but its nature was unknown. It could not be immediately related to the forces known to physics. It was a chemical force, separate and distinct. As a concept it was necessary to chemistry, but it could not be 'reduced' to the concepts of physics. It was autonomous and belonged to its own level in the hierarchy. With the advent of quantum mechanics, however, it became possible to show, given the properties of protons and electrons and the validity of the Schrodinger equation, that a hydrogen molecule is a more stable arrangement than two hydrogen atoms. Hence to make two hydrogen atoms from a hydrogen molecule will cost energy. The calculated energy cost was found to be in close agreement with the experimentally determined value. In other words, the chemical binding or chemical force existing between the atoms of a hydrogen molecule has been shown to be a natural consequence of the properties of the fundamental particles. In principle this can be done for any bond or set of bonds in any molecule. In practice it cannot yet be done because the mathematics is far too difficult. However, since there is no reason to suppose that the bond in the hydrogen molecule is fundamentally different from the

bonds of other molecules, it may be said that, in principle, a statement about chemical bonds can always be translated into an equivalent statement about the properties of nuclei and electrons.

Physics and chemistry form a unity then, in the sense that there are no forces known to chemistry that are not known to physics and therefore any concept used in chemistry can, in principle, be ultimately reduced to concepts used in physics. This is not to say, however, that chemistry is nothing but physics – chemistry uses and always will use its own distinctive concepts. However, these can always be 'translated out'.

Now what about sciences higher up in the hierarchy? Can biology and biochemistry, for example, be reduced to chemistry and physics in the same way that chemistry can be reduced to physics? Most people would want to say that at some point in the hierarchy the kind of reduction of concepts that we have been considering becomes impossible. Obviously mental events present a difficulty. It is not easy to see what is meant, or could be meant, by a reduction to physical principles of the concepts used in connexion with mental events. Between chemistry and biochemistry, however, the problem is simpler. Biochemistry is the chemistry of living organisms. As such it is to be expected that its concepts should be reducible to chemical ones. If they are not, and if the residue relates to the fact that living processes are concerned, then they will properly be called vitalist. They will be vitalist in the sense that chemical laws are not enough; over and above these, some other concept will have been added.

Distinctness of Biochemistry

Now just as chemistry is not simply physics, so biochemistry is not simply chemistry. Complexities exist in biochemistry that are not found in simpler chemical systems. For example, chemical reactions in living organisms are highly organized. There are complicated sequences and cycles of reactions, feed-back devices, and the whole is so organized that it maintains itself and can, at the same time, react and adapt to external changes. Furthermore, the molecules that control the functioning of the

whole, the proteins and nucleic acids, are far more complex than those encountered in pure chemistry. This complexity is such that certain concepts, such as those of purity and structure, cannot be simply carried over from the chemistry of small molecules to the chemistry of proteins and nucleic acids. It is worth pointing out that, although the commonly accepted death-blow of vitalism was the synthesis of a substance previously known only in living things, the most important constituents of living tissue cannot, at present, be synthesized, and this is likely to be the case for some time to come.

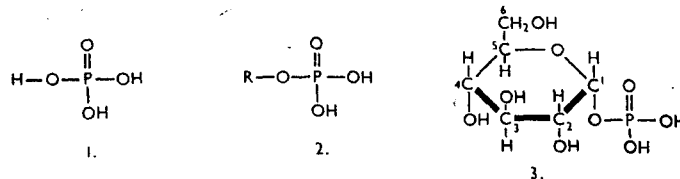
Biochemistry, then, obviously needs concepts peculiar to itself. What is important, as we saw above, is that these concepts shall be ultimately reducible to chemical ones. Are there, at present, any theories or concepts in biochemistry that are vitalist in the sense given? In my view, the so-called 'high-energy phosphate bond' theory is of this kind, and an analysis of this theory will now be given.

PHOSPHATE ESTERS IN BIOCHEMISTRY

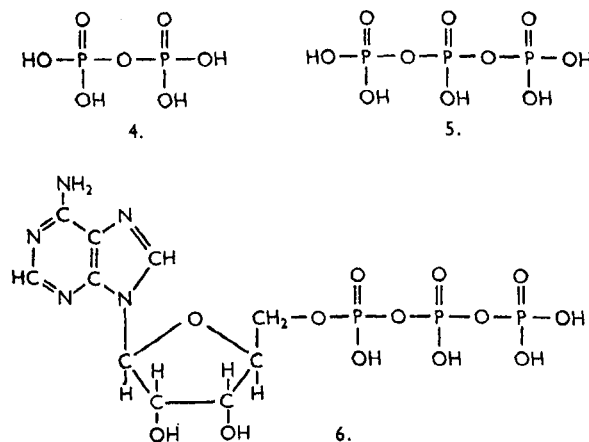
Scientists have always been fascinated by the energetics of biological processes. Animals perform mechanical work: the energy that enables them to do this somehow comes from the breakdown of foodstuffs. However, animals are different in certain important respects from the machines with which we are familiar. The steam-engine, for example, works between a temperature difference: animals work at approximately constant temperature. Nevertheless, the analogy is there and is expressed, for example, in the use of the word 'fuel' to describe assimilable foodstuffs. The problem is this: how does the splitting up and degradation of glucose – which is, in the main, the ultimate carbohydrate foodstuff of animals – occur and what are the mechanisms by which this process is linked to synthetic activities, and to the performance of mechanical work? Only in the last two or three decades has any progress been made with these problems. It has been discovered that the degradation of glucose always takes place in a large number of distinct chemical steps and that many of these steps involve phosphate esters. These

substances are so important in biochemistry that we must digress slightly and say something about them.

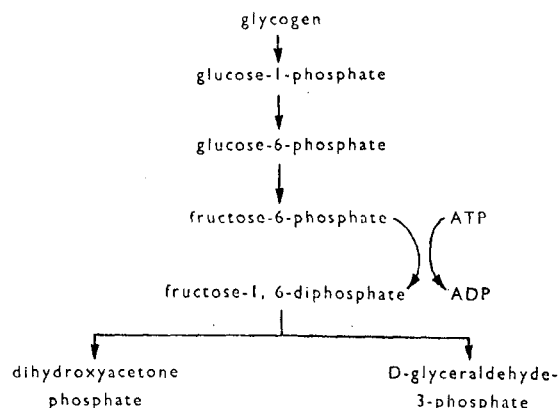
Formula 1 shows the structure of phosphoric acid; formula 2 represents an *ester* of phosphoric acid, the symbol R standing for any organic radical. Formula 3 shows the structure of the important ester, α -(D)-glucose-1-phosphate. The complicated ring arrangement of carbon, oxygen, and hydrogen atoms is the glucose structure (the numbers are used to identify the different possible positions of the phosphate group).



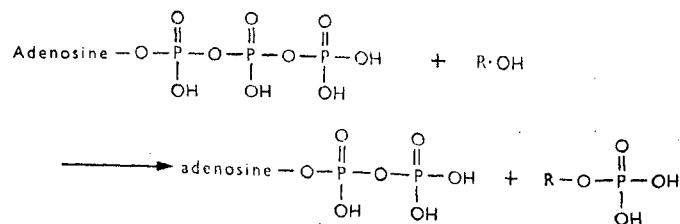
Other important phosphorus-containing acids are pyrophosphoric (or diphosphoric) and triphosphoric acids (4 and 5). The most important esters of these are adenosine diphosphate (ADP) and adenosine triphosphate (ATP). The structure of this latter compound, one of the most important substances in biochemistry, is shown in formula 6.



In Figure 1 are shown the first few steps of the breakdown of glycogen (animal starch) as it occurs in muscle. Two interesting things should be noticed about this sequence of reactions: one, all the compounds involved are phosphates; two, a second phosphate group is introduced between fructose-6-phosphate and fructose-1, 6-diphosphate. This is achieved by the intervention of ATP which loses one of the phosphate groups from its chain and so becomes ADP.



ATP frequently acts like this, i.e., as a phosphorylating agent. The general reaction may be represented by the equation,

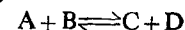


where R.OH is the acceptor molecule. Now the whole sequence (of which only the first part is shown in Figure 1) contains points at which phosphate groups are transferred from ATP or to ADP. The net effect is to produce 30-40 units of ATP for each

unit of glucose degraded. The degradation of glucose, then, results in the formation of ATP and this substance is known to be required for many of the synthetic activities of organisms and to be involved in muscular contraction. It is, in a sense, the linking substance between the oxidation of glucose and many essential chemical and physical activities. There is a temptation to say that the energy derived from the oxidation of glucose is made available to the organism through the mediation of ATP. Before we discuss this we must first understand some thermodynamic concepts which are used in the treatment of energy transfers.

Free Energy

A chemical reaction,



can, in principle, proceed in either direction. That is, starting from A and B some C and D will be produced and vice versa. If we start from either side and wait until no further change occurs the final mixture is called the equilibrium mixture and the whole system is said to be at equilibrium. Now there is a rather simple relationship between the concentrations of the four components present at equilibrium. The relationship is that

$$\frac{C_E \times D_E}{A_E \times B_E} \text{ is a constant}$$

where the symbols stand for the equilibrium concentrations of the four components. This constant is called the equilibrium constant (*K*) and is characteristic of a particular reaction at a particular temperature.

Now suppose we want the chemical reaction to do electrical or mechanical work. It is found that the amount of work that the reaction will do depends on the conditions, but the maximum amount is given by the change in a quantity called the *Gibbs function*, and is usually written ΔG . It is often called the *free energy change* although, for various reasons, this name can be misleading. Now ΔG , which is not, except under special circumstances, equal to the amount of heat which the reaction will produce, is related to the equilibrium constant *K*. The appropriate equation is

$$\Delta G = -RT \log K + RT \log \frac{C \cdot D}{A \cdot B}$$

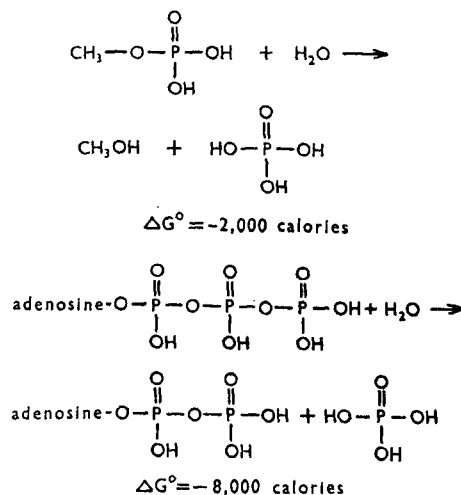
where A, B, C, and D refer to the actual concentrations of reactants and products. If these are all set to unity, then the equation very simply reduces to

$$\Delta G = -RT \log K.$$

Under these circumstances ΔG is usually written ΔG° and called the *standard free energy change*. It is another way of considering equilibrium constants and refers to the maximum work (electrical or mechanical) which a reaction can do under highly artificial conditions, i.e., conditions of unit concentrations in products and reactants.*

High-Energy Phosphate Bonds

It was Lipmann¹ who first pointed out that the standard free energies for the hydrolysis of simple phosphates and of ATP were very different, i.e.,



*More strictly we should talk of *activities* instead of concentrations, but no new principle would be introduced by this complication.

This means that the equilibrium for the second reaction lies rather more to the right than for the first. In simple, although misleading, language the ATP wants to get rid of its terminal phosphate group rather more than does the simple phosphate. On the basis of these figures and the fact that ATP is involved in many synthetic reactions, Lipmann put forward a new point of view which has become known as the high-energy phosphate bond theory. The theory can be summarized as follows:

- (a) The free energy derived from the oxidation of glucose is 'stored' in the terminal phosphate bonds of the ATP produced.
- (b) When the terminal phosphate group is removed, as in hydrolysis or in phosphate transfer, this free energy is released and may be used to drive recalcitrant synthetic reactions or for the production of mechanical work.

A special symbol has been invented to denote a high-energy bond and discussions of metabolic processes are often given in terms of the handing on of free energy from one reaction to another. There has been discussion on whether free energy escapes in stages or all at once and the function of intermediates is sometimes considered to be understood if it is said that they possess a high-energy bond. Later we shall consider a specific example of how the theory is used.²

Now the peculiarity of this view is that it cannot be reduced to, nor is it consistent with, orthodox chemical concepts. Bond energy means something quite different to a chemist: one cannot get energy out of breaking a bond — this is a process that consumes energy and does not release it. Furthermore, standard free energy changes, which provide the experimental basis for the theory, are not actual free energy changes but only hypothetical quantities relating to changes which would be observed under hypothetical conditions. Standard free energy is a mathematical parameter: it cannot be handed from reaction to reaction; it is not that kind of entity. If it were called the standard change in the Gibbs function the absurdity would, perhaps, be more apparent. Some biochemists will reply that the phosphate bond theory is only a shorthand way of dealing with equilibrium constants — no inconsistency with chemistry is really present: it

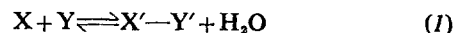
is merely convenient to call everything by different names. My view is that this defence will not stand – the biochemists really do want something to be handed on from reaction to reaction, and this something is a vital force. Under the respectable guise of thermodynamics biochemistry has slipped into vitalism.

Now this criticism is, of course, essentially destructive. It is important to inquire whether it is possible to use thermodynamic data in a way which avoids vitalism and at the same time does not ignore the uniqueness of living processes.

PSEUDOMERIC REACTIONS

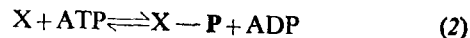
As we have indicated, the most important feature of biochemical processes is that they are highly organized. Reactions are coupled together under the influence of specific catalysts – called *enzymes* – in such a way as to produce desired substances. One of the best accounts of the present state of knowledge on this subject has been given by Dixon.³ It is proposed here to discuss one of the multi-enzyme systems described by him.

There is a whole series of reactions of the general form,



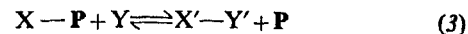
X and Y can be hexose sugars as in the case of the synthesis of sucrose and other disaccharides, or a ribose and a purine as in the synthesis of nucleosides and so on. Now most of these reactions have rather unfavourable equilibrium constants ($\Delta G^\circ = c. +2000$ cal.) from the point of view of the synthesis of $X' - Y'$. The organism cannot, therefore, synthesize $X' - Y'$ by elaborating enzymes catalysing the reactions as they are written above. Such enzymes occur, but their function is presumably to catalyse the hydrolysis of $X' - Y'$.

Now these reactions are often brought about indirectly. Firstly, one of the molecules, say X, is phosphorylated by ATP. We may represent this by

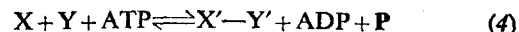


where P stands for the phosphate group. This type of reaction is catalysed by enzymes called *phosphokinases*. The next step is

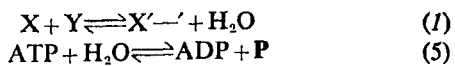
the reaction between $X - P$ and the molecule Y with elimination of the phosphate group,



and these reactions are catalysed by enzymes called *phosphorylases*. Now the net reaction is



in the sense that X and Y disappear and form $X' - Y'$ and ATP disappears forming ADP and phosphate. Now we saw that the equilibrium constant for reaction (1) was unfavourable for the synthesis of $X' - Y'$. What about the new reaction (4)? It happens that thermodynamics permits the calculation of unknown equilibrium constants from known ones if the latter are *algebraically* equivalent to the former. Reaction (4) is algebraically equivalent to the two reactions (1) and (5).



in the sense that if the chemical symbols are manipulated as if they were algebraic symbols then the addition of (1) and (5) gives (4). Now ΔG° for reaction (1) is, as we saw, usually about +2000 cal. (i.e., unfavourable). That for (5), the hydrolysis of ATP is, as Lipmann pointed out, about -8000 cal. (i.e., very favourable). Hence (4) has an equilibrium constant which is favourable ($\Delta G^\circ c. -6000$ cal.) and $X' - Y'$ has been synthesized from X and Y.

The high-energy phosphate bond theory would interpret this by saying that the free energy released in the hydrolysis of ATP (reaction (5)) is utilized to drive reaction (1). Furthermore, -6000 cal. are left over after the arithmetic is done and this free energy is 'wasted', appearing as unproductive heat. This view is not only vitalist but is also wrong. It is vitalist because it is supposed that something (vital force) is handed from reaction (5) to reaction (1) and wrong because reactions (5) and (1) are precisely the ones that *do not* occur. The only reactions which actually happen are (2) and (3). If there were catalysts appropriate to (1) and present at the same time and in the same place, then $X' - Y'$ having been formed by the phosphokinase-

phosphorylase reactions would hydrolyse back to X and Y and the organism would be back where it started. Similarly, if an enzyme hydrolysing ATP were present, it would compete with the phosphokinase and X—P would not be formed. Reactions (1) and (5) are, therefore, only computational devices — they are used in the algebra, but for the purpose of the synthesis of X'—Y' they must not occur. I call reactions of this kind *pseudomers* — false components. For any given reaction there is an infinite set of pseudomers. In this particular case the pseudomeric reactions (1) and (5) are important simply because we have the free energy data for them.

The above discussion shows the real peculiarity of such processes. The organism has overcome the difficulty of an unfavourable equilibrium constant by an indirect route — in this case by the use of two specific enzymes. It is in this way that the organization present in all living tissue is revealed at the chemical level.

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THE MASER

J. R. SINGER AND W. B. BRIDGES

THE term Maser is an acronym coined by Professor Townes of Columbia University to shorten the phrase 'microwave amplification by stimulated emission of radiation'. He, with Gordon and Zieger, developed the first maser, an ammonia gas amplifier which could serve as an ultra-stable source of microwaves (wavelengths of a few centimetres or less) or as a non-tunable narrow band amplifier. Before discussing this particular amplifier, it is appropriate to discuss the need for such devices and their general principles.

Previous to the maser, all very high frequency amplifiers depended upon the interaction of fast-moving electron beams with electromagnetic waves, but electron beams superimpose considerable noise upon the signals to be amplified. For most purposes such noise is not a serious problem, because strong signals may still be detected easily. However, long range radar and radio astronomy signals are of very small amplitude, and are easily masked by noise generated internally in the receiving apparatus. Radio astronomy particularly demands very low noise levels in amplifiers because the signals are small and travel phenomenal distances. Maser devices give promise of being able to assist in the probing of space because they generate little internal noise.

General Principles

Quantum theory determines the pattern of energy relationships among particles. For example the bound electron in a hydrogen atom can change its energy level, or 'quantum level', by jumping from one energy level to another. When it does so, it takes on, or gives off a photon of energy equal to the energy difference between the two states. The formula

$$E_1 - E_2 = h\nu$$

expresses this relationship succinctly. E_1 and E_2 designate the two levels of energy, h is Planck's constant, and ν is the frequency of the radiated photon. In maser systems the frequency ν is usually in the microwave range.

Masers are devices which stimulate the radiation of energies in the microwave region in order to amplify an electro-magnetic field. At the present time the two most common ways of doing this are to use the energy structure of ammonia molecules, or the paramagnetic spins of certain metallic salts. These physical systems can provide energy levels of the desired magnitude. Suppose that we consider a single quantum system (molecule, atom, etc.) which has energy levels differing by some microwave frequency. To simplify the picture, consider a system that has only two possible states, E_1 and E_2 as indicated in Figure 1. Each

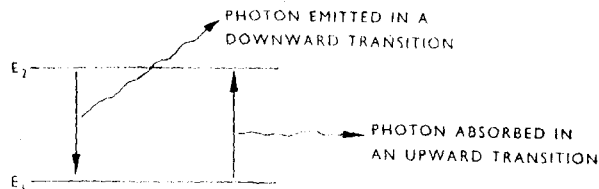


Fig. 1. Energy levels in a single two-level quantum system.

transition from upper state to lower state requires the emission of one photon. If many such transitions can be triggered off at a rate proportional to the strength of an electromagnetic wave, amplification is achieved. This implies that more energy leaves the device than enters — an impossible situation. The conservation law is satisfied, however, because energy is expended when the molecules initially change to the upper state.

Consider a molecule with only two energy states. Somehow one puts it in the upper energy state. Now let an electromagnetic field interact with this molecule. The electric or magnetic field may be intensified by a resonant circuit (a coil and condenser, or a resonant microwave cavity). The molecule is compelled by the field to return to the lower state, without absorbing energy from the field. In making the transition a photon emerges which

adds to the strength of the field. Note that an energy balance is maintained. The energy needed to drive the molecule to the higher energy condition is returned when the molecule emits a photon due to stimulation of the electro-magnetic field.

The Ammonia Maser

The ammonia molecule (NH_3) belongs to a class known as 'symmetric top' molecules, because of its physical structure (Figure 2). In ammonia, the nitrogen atom and the three hydrogen atoms form the vertices of a tetrahedron. The three hydrogens are located symmetrically about the nitrogen and form a plane. The axis of symmetry of this 'top' molecule passes through the nitrogen and is perpendicular to the plane.

At any temperature greater than absolute zero the molecule will have energy in the form of internal vibrations of the chemical bonds, and rotations about the axis of symmetry. The motion of interest to us here is the vibration of the nitrogen atom with respect to the plane of the hydrogens. Figure 2 shows the potential energy that the nitrogen atom would have if displaced from its equilibrium position; also shown are the actual allowable energy levels. The magnitude of the splitting of the two levels corresponds to frequencies in the microwave region, approximately 20,000 megacycles. Transitions between these levels give rise to the so-called microwave inversion spectrum of ammonia. The photons most often emitted are those that have energy corresponding to 23,870,110 megacycles and this is the frequency commonly used for the ammonia maser. This frequency is due to the vibration of the nitrogen atom which spends only half its time on each side of the plane of the hydrogens. The resultant potential of this system is shown in Figure 2. Note that the quantum levels are split, owing to the coupling between the two potential wells. Split lines at other frequencies could be used but with less power output for a given amount of ammonia.

A selection of molecules in the higher energy state is accomplished by use of electric fields. A schematic diagram of an ammonia maser is shown in Figure 3. The operation of the maser may be described as follows. Ammonia gas enters at the

top at very low pressure and passes through a bundle of many small tubes, each about 0.005 inches in diameter and 0.25 inches long, usually called an effuser, which aims the molecules into the vacuum. The stream of molecules, which are in thermal equilibrium at room temperature, next passes through the focuser, which consists of four cylindrical electrodes shown in end view in Figure 3b. The ammonia atoms are deflected by the non-uniformity of a strong electric field which is maintained in the focuser. The direction of deflection depends upon the energy state of the ammonia molecules. Those in the higher of the two energy states are deflected toward the axis of the focuser while molecules in the lower energy state are deflected away from the axis. Because the molecules have random velocities, the focuser cannot completely eliminate the molecules in the lower state, but it does increase the relative number of molecules in the upper state over its normal value. The selected stream of molecules then passes through a resonant cavity where they give up energy which augments the electro-magnetic field strength. This increased field is then taken into further stages of the system for further amplification. The molecules, now returned to their normal energy state, pass on through the cavity and are discarded by being pumped out of the system.

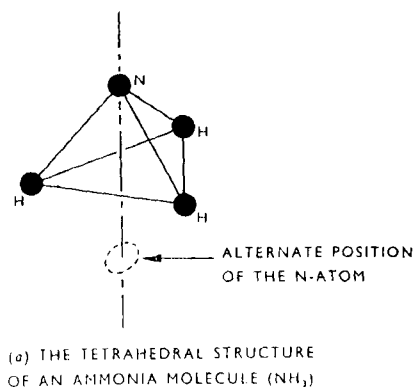
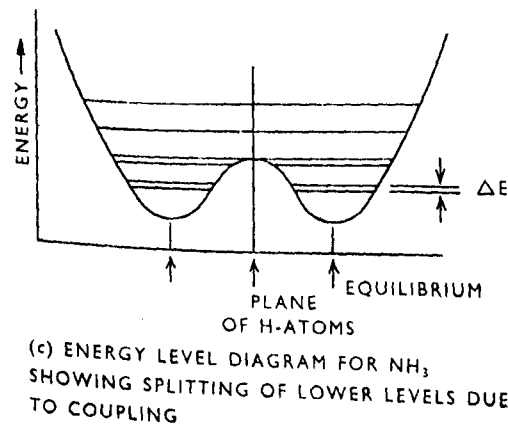
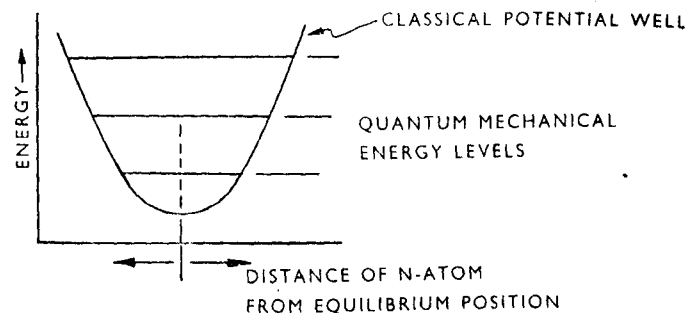


Fig. 2. The ammonia molecule and (opposite) its energy levels.

The amplification of the ammonia molecule system is limited by the fact that the gas must be at a low pressure in order that there shall not be many collisions. Such collisions would affect the energy levels. Since the amplification depends directly upon the number of atoms available to emit photons, this severely limits the amplification of the system. The power output of the system is, in general, less than one thousand millionth of a watt.



Probably the chief use of the ammonia maser is as a frequency standard. The frequency of the emitted photons is determined entirely by the nature of the ammonia molecule, which is practically a natural constant.

MASER USING SOLIDS

The use of solids in the form of paramagnetic materials has two important advantages over the use of gases. The number of

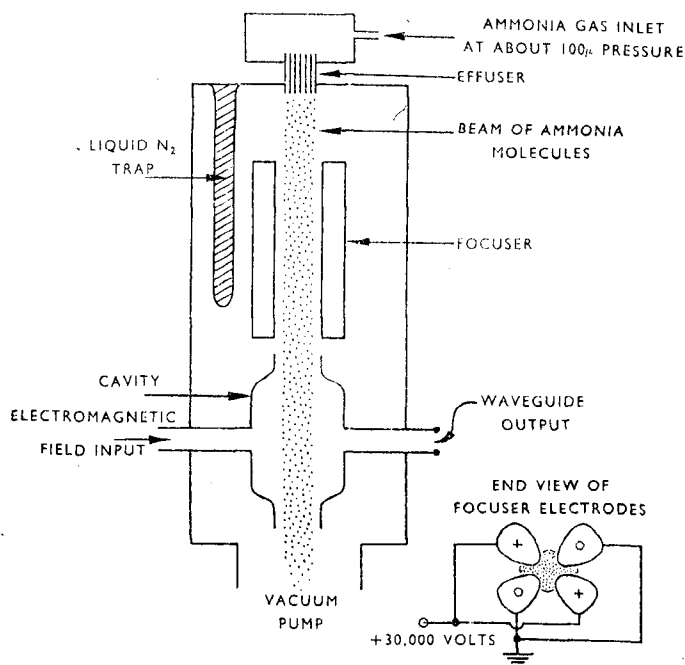


Fig. 3. A schematic drawing of an ammonia maser.

atoms one can pack into a given volume is greater, and the amplification is proportionally increased. Secondly, the problem of tuning to a given frequency is simplified. The reason for this ease of tuning is that the Zeeman effect in a magnetic field

is utilized, and the energy of Zeeman splitting is proportional to the magnetic field, and a field is easily changed.

On the other hand numerous experimental difficulties have appeared. The problem of actually obtaining a useful amplifier and building it into a radar or radio astronomy receiver has not been accomplished so far. The difficulties, however, are being attacked vigorously and it appears quite likely that a successful system will emerge within a year or two.*

Electrons in a Magnetic Field

The Zeeman splitting of atomic energy levels is most easily described by considering an electron isolated in space. The electron possesses spin and a magnetic moment. One may consider

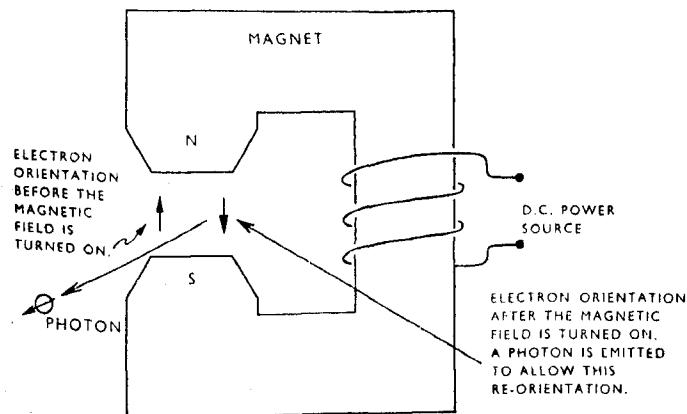


Fig. 4. The isolated electron 'sees' all directions as equivalent before the magnetic field is turned on. When the field suddenly appears, the directional 'degeneracy' is removed and one direction is energetically lower than another. A photon is emitted when the electron flips.

* Since the above was written, Professor Townes has directed the construction of a maser in the U.S. Naval Research Laboratory Radio Telescope. The new installation has been operated successfully.

it to be a small spinning bar magnet. Now turn on a magnetic field. A torque is exerted upon the electron – but not a force – and the torque tends to align the electron along the field direction (see Figure 4). In order to line up with the field, the electron must rotate and change energy. Two basic laws of physics are the conservation of angular momentum and energy. Hence, the change in electron orientation can only occur when another particle carries off the angular momentum and energy. For the isolated electron the other particle is a photon.

Suppose we use a magnetic field of 3000 gauss – an easily obtainable field from a large permanent magnet or a laboratory electro-magnet. Initially we presume that the electron has its north pole up. The magnet has its north pole above the electron. If the magnetic field suddenly becomes 3000 gauss, what is the frequency of the photon emitted when the electron flips over? This is an easy calculation. The change in energy of the electron is

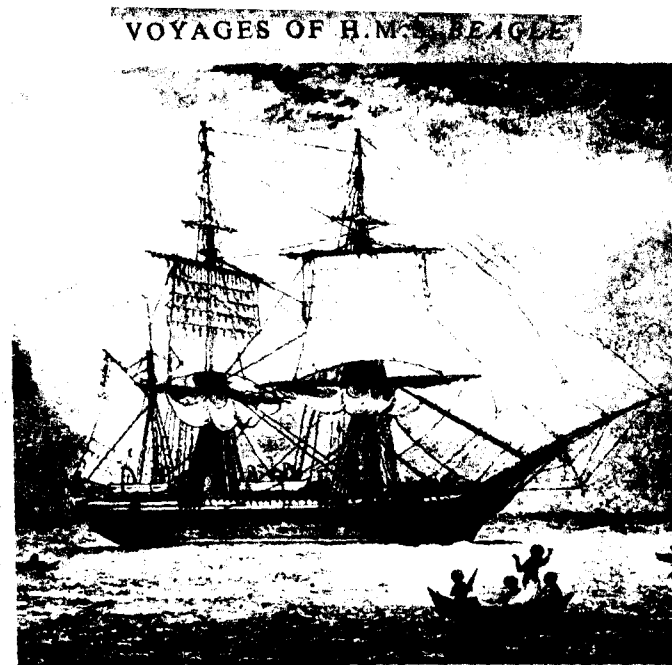
$$2mH = E$$

where m is the magnetic moment of an electron (approximately 10^{-20} ergs per gauss) and H is our field of 3000 gauss. Hence E is just 6×10^{-17} ergs. We know also that the energy of a photon is

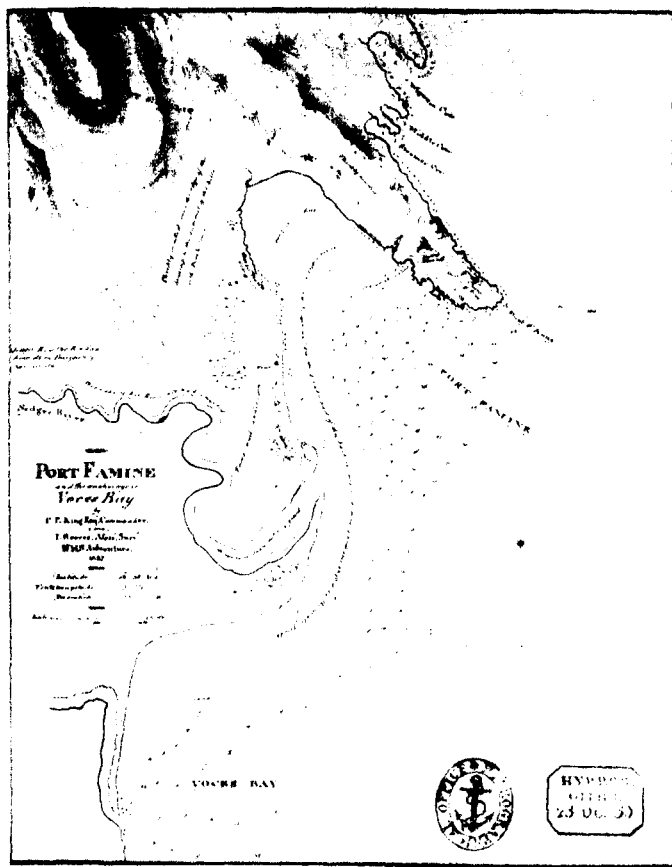
$$E = h\nu$$

which simply states that the energy is proportional to the frequency ν , and h , Planck's constant, is the factor of proportionality. Since h is approximately 6×10^{-27} , we find that for the energy to be equal, ν is exactly ten thousand million cycles per second. It is no coincidence that this frequency is in an important radar band. The 3000 gauss magnetic field was selected with this frequency in mind. If one wishes to work at other frequencies, one simply changes the magnetic field.

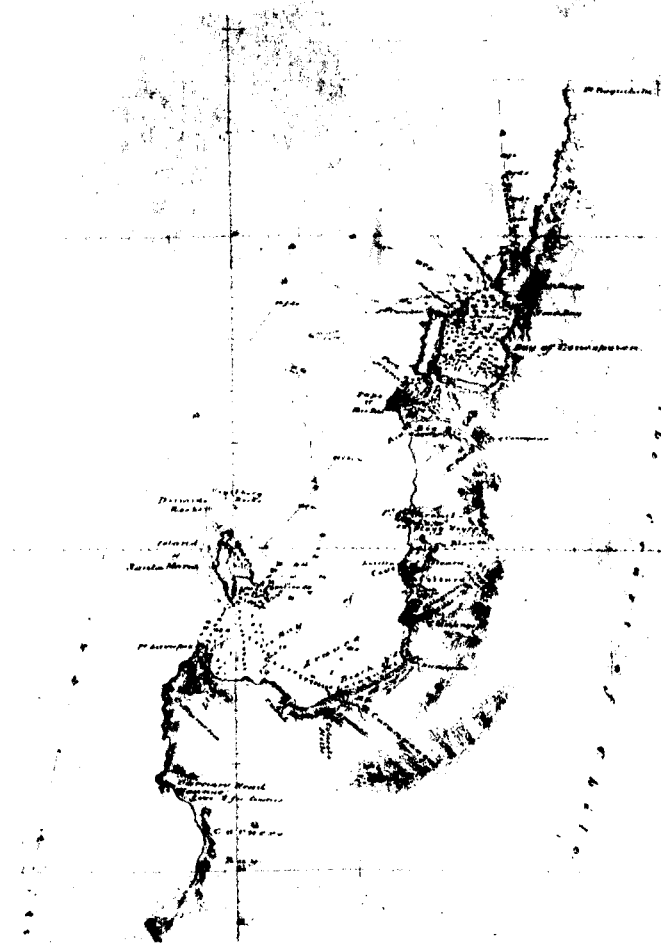
If free electrons are placed in a strong magnetic field with the north poles of the magnet and the electrons pointing toward each other, it will take a relatively long time for the electrons to flip over and spontaneously radiate a photon. The process is called spontaneous emission (Einstein) and has a low probability per second. Instead of waiting for the spontaneous process to occur, it is possible to stimulate or induce the photon emitting



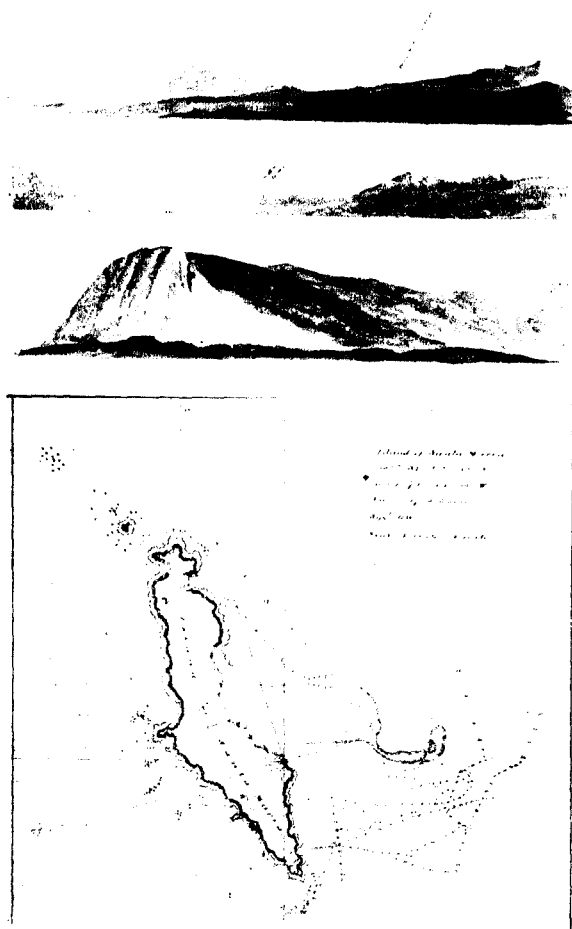
1. H.M.S. *Beagle* from a woodcut after R. T. Pritchett. (Courtesy of the National Maritime Museum, Greenwich.)



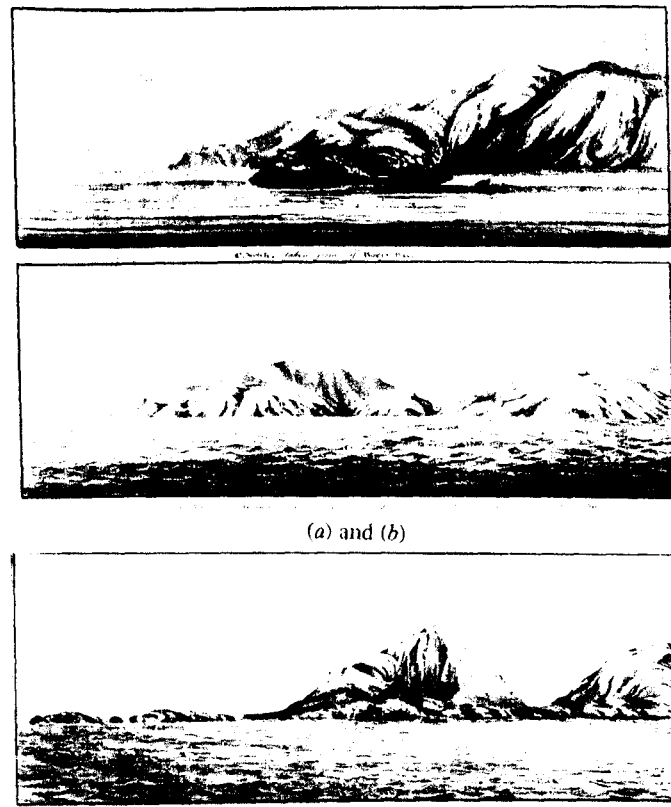
2. Port Famine, the base camp of *Adventure* and *Beagle*, as surveyed by Captain King and Lieutenant Graves during the expedition. The use of colour wash to denote slope of ground is characteristic of King's surveys, and was not used by Fitzroy (see Inset 6), who preferred a clean pen line. (Courtesy of the Hydrographic Department of the Admiralty.)



3. The rough draft of the chart of Concepción, capital of Chile, surveyed by Fitzroy and the officers of *Beagle* in 1835. *Beagle* was lying nearby when the town of Concepción was overwhelmed by an earthquake. The disaster seems to have made a strong impression on Darwin. (Courtesy of the Hydrographic Department of the Admiralty.)



4. (top) A view of the Beagle Channel, Tierra del Fuego, made on board *Beagle* in 1834, probably by the draughtsman, 'Mr Martins,' who was engaged at Montevideo at Fitzroy's own expense for this kind of work. (Courtesy of the Hydrographic Department of the Admiralty.) (bottom) Santa Maria Island, Chile: a manuscript survey by the officers of *Beagle*, 1835. The island was upraised 8-10 feet by the earthquake that destroyed Concepción. Note the position where Fitzroy erected his portable astronomical observatory to fix the accuracy of the geographical co-ordinates. (Courtesy of the Hydrographic Department of the Admiralty.)



(a) and (b)

(c)

5. (a) and (b) Cape Notch and Cape Tamar and Island in the Straits of Magellan, viewed from *Adventure* sometime on the first cruise. This sepia wash is probably by Captain King, rather than his assistant surveyor, who, however, later surveyed much of the Mediterranean and painted views there in much the same style as this. (c) P. Hocico de Caiman in Concepcion Strait viewed from *Adventure*. Like the above views, this is probably by Captain King. (Courtesy of the Hydrographic Department of the Admiralty.)



6. Manuscript survey of Cape Horn by Commander Fitzroy, plotted on H.M.S. *Beagle* in 1829. This was from the first commission of *Beagle*, and the longitudes are given as east of Port Famine and not west of Greenwich, because at this time the longitude of no part of South America was sufficiently determined. The charts of Cape Horn and Tierra del Fuego in use today are those prepared by Fitzroy during the second commission of *Beagle*. (Courtesy of the Hydrographic Department of the Admiralty.)



7. A view of the Straits of Magellan taken from the manuscript journal of Commander Pringle Stokes, Captain of *Beagle*, 1826-8. This view is signed Lt Scholl, and is taken from a height overlooking the Straits. The ship in the foreground is rigged as a barque and appears to conform to the lines of the *Cherokee* class. Since the class as a whole were rigged as brigs, this vessel seems almost certain to be *Beagle*. (Courtesy of the Hydrographic Department of the Admiralty.)

INDUCTIVE METHODS IN
PALAEONTOLOGY



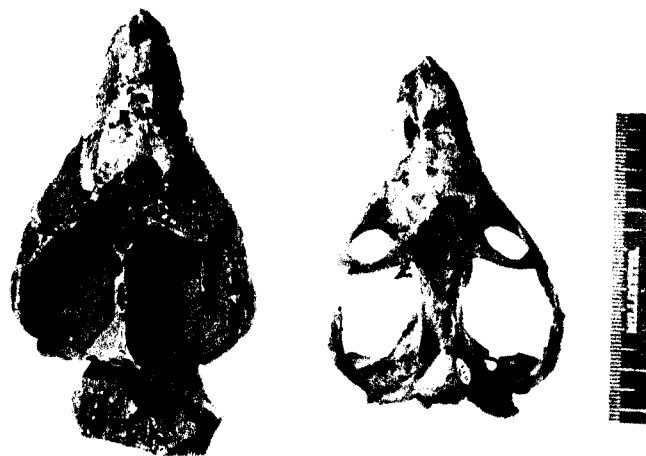
8. Skeleton of a race-horse, showing the cantilever vertebral column.



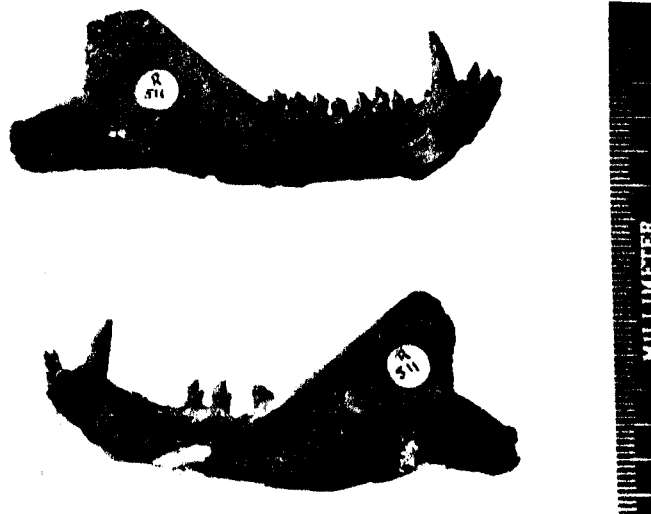
9 (*top*). The tail of the duck-billed dinosaur, *Edmontosaurus*, showing tuberculated skin pattern and scalloped upper edge. (*bottom*) Nest of dinosaur eggs from the Lower Cretaceous of the Gobi Desert.



10. Reconstruction of baby Protoceratops emerging from nest. (Model by courtesy of the American Museum of Natural History.)



11. (a). The skull of a Therapsid reptile. Thrinaxolon: (left) before acetic acid treatment, (right) after treatment.



11 (b) Lower jaws after development.

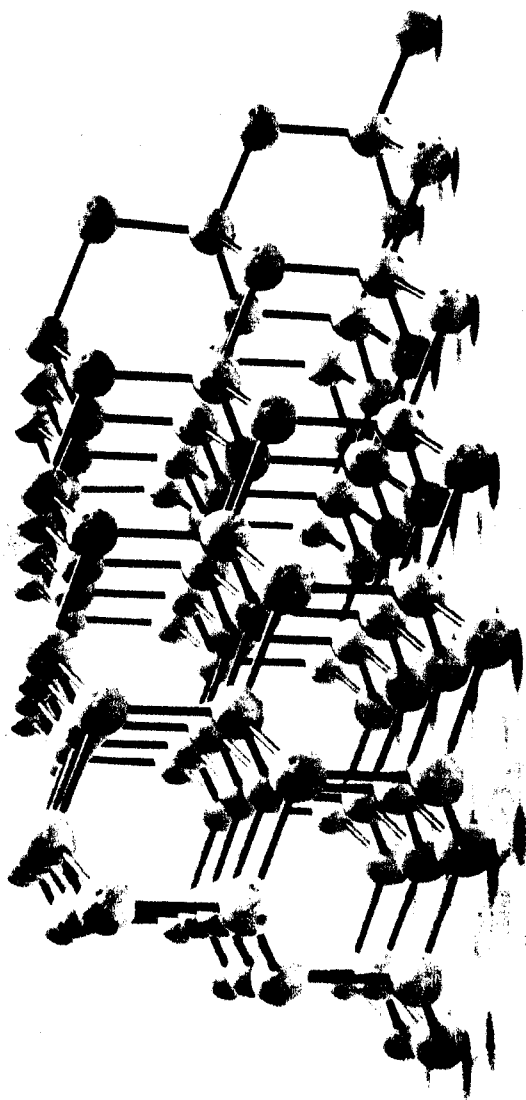


12. *Archaeopteryx lithographica*. The specimen in the British Museum (Natural History), London.



13. The same specimen but seen in ultra-violet light. (Courtesy of the Director of the British Museum [Natural History].)

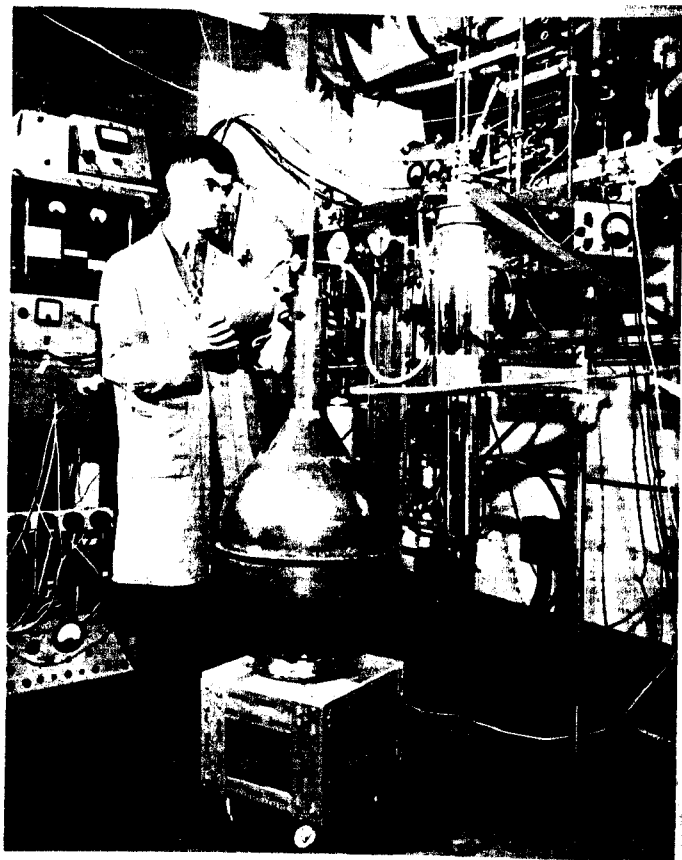
CYCLOTRON RESONANCE



14. Model of part of a diamond-type crystal showing how each atom is bound to four others. The substance is silicon



15. The same as opposite but part of the lattice of an intermetallic compound.



16. Filling a cyclotron resonance apparatus with liquid helium. The helium is being transferred from the large metal storage vessel to the glass Dewar vessel of the apparatus. For this operation the electromagnet has been rolled away. (*Crown copyright reserved.*)

transition by providing a properly oriented radiation field; that is, by sending photons of energy E into the field of the electrons, the electrons are induced to make the transition to the lower energy state. In making the transition, the number of photons present is increased. Thus amplification of the radiation occurs by a stimulated (induced) emission process.

The assumption that it is possible to obtain free electrons oriented parallel to a strong magnetic field needs closer examination. It is necessary to work with electrons in matter; these are not at all the same thing as free electrons. However, an examination of the properties of electrons in crystals reveals some of the potentialities for their approximating to the conditions for free isolated electrons.

Suppose we look at some of the paramagnetic resonance experiments performed at the Clarendon Laboratory, Oxford. A vast number of investigations by Bleaney, Bowers, Bagguley, Owens, Griffiths, and others, indicate that with most common salts (e.g., the alums such as chrome ammonium alum), the orbital motion of electrons is 'quenched', i.e., locked into the crystal lattice and not affected by an external magnetic field. The electron spins, however, are not strongly affected by the lattice, and act almost as if they were free. The electrons of interest here are those in an inner shell of a transition metal ion – iron, chromium, nickel, etc.

One complication resulting from the use of solids immediately appears. The electrons affect the freedom of each other. Since they are all small magnets they perturb their neighbours' motions through the interaction of magnetic fields. This is called spin-spin broadening. It can be partially avoided by growing diluted crystals, that is, by putting only relatively few magnetic atoms in a crystal. The missing magnetic ions may be replaced by diamagnetic ions in growing suitable crystals. If it appears that obtaining a collection of isolated electron spins is easy, this is an illusion.

The electrons in a solid do not necessarily have to emit photons when changing orientation in a magnetic field. Vibrations of the crystal lattice also can carry off angular momentum

and energy. The lattice vibrations (or phonons) are not useful in maser operation at all. It is much more probable that an electron will lose energy via lattice vibrations than by photon emission. Hence additional experimental ingenuity is needed to avoid loss of energy via the heat of lattice vibrations.

In order to obtain a useful maser, two major requirements must be met. First, the 'almost free' electrons must be oriented in a high energy position in the magnetic field. Secondly, before they can relax spontaneously with the resultant emission of phonons or a photon, they must be induced to make the transition by incoming radiation. Since phonon relaxation is much more probable than spontaneous photon emission, major consideration must be with phonons, or heating of the lattice.

NEGATIVE TEMPERATURES

The orientation of electron spins in a magnetic field is either parallel or anti-parallel. If the number of anti-parallel spins are denoted by N and those parallel by n , one obtains the relative statistical population due to thermal vibrations,

$$n = N e^{-W/KT}$$

where e is 2.718 . . . , w is the energy difference between the upper and lower energy position, k is 1.4×10^{-16} ergs per degree (the Boltzmann constant), and T is the Kelvin temperature. That is, the number in the lower energy state is larger by the exponential factor than those in the higher energy position. If one defines the spin temperature as Ramsey does, one obtains,

$$T = - \frac{W}{K \log n/N}$$

by algebraic manipulation of the previous equation.

The value of T is negative whenever n is greater than N since then the logarithm (base epsilon) is positive. Physically the significance of negative temperatures is that the populations of energy levels are inverted from their normal values. For the specific case of electrons in a magnetic field, negative temperatures occur when more electrons are parallel than anti-parallel.

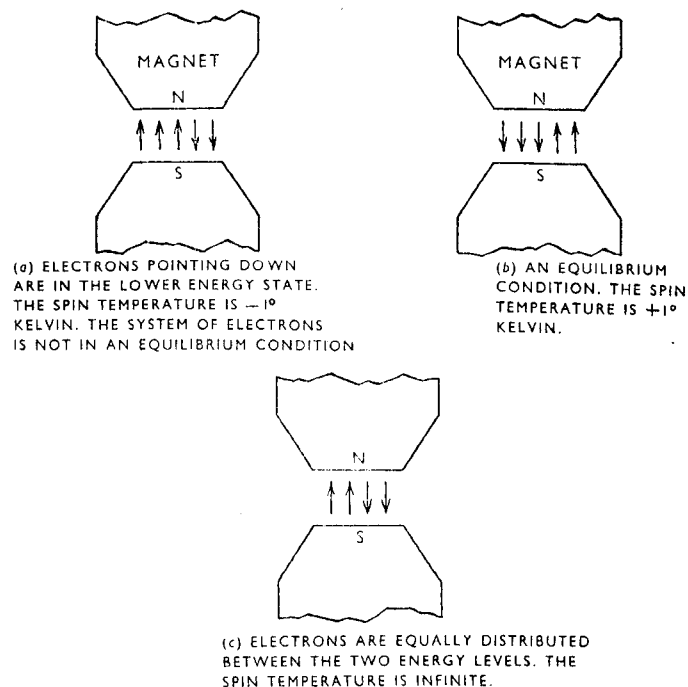


Fig. 5. Electrons in a magnetic field of 3000 gauss and the corresponding 'temperature'. The arrows represent electron magnetic moments with the arrowhead as the north magnetic pole.

Figure 5 shows some negative temperatures corresponding to various configurations of electrons in a magnetic field.

Negative spin temperatures and an infinite spin temperature (see Figure 5) are conveniences for purposes of discussing the relative energy level populations, but are not completely satisfactory thermodynamically without modifying the formalism. Consequently much opposition to the concept of negative temperatures has arisen. It appears likely that an alternative approach – use of the chemical potential function – may some

day replace the spin temperature concept. However, spin temperatures are a useful means of description for population levels.

Use of Negative Temperatures in the Maser

We have introduced negative temperatures in order to describe an interesting experiment by Pound, Purcell, and Ramsey. They worked with the nuclei of a lithium fluoride crystal rather than electron spins, but the principles are the same. With nuclei one has the observational advantage of relatively more isolated spins, but the disadvantage of smaller magnetic moments than obtained with electrons (by about 1,800 times).

The experiment consists of placing a crystal of LiF in a strong magnetic field of about 6000 gauss. After the time needed to reach equilibrium, the nuclear level population may be described as being at room temperature, about 300° K. The magnetic field was then rapidly inverted through zero field. The nuclear spins could not follow this rapid change and so the energy state populations were inverted. The spin temperature was then -300° K.

A negative temperature is not an equilibrium state. Spins in a negative temperature condition will spontaneously return to equilibrium by radiating photons or exchanging energy with the crystal lattice. This negative temperature is important because we may choose a radio frequency ν satisfying the equation,

$$2\pi\nu = mH/s$$

where m is the nuclear magnetic moment, s is the nuclear spin, and H is the static magnetic field which will stimulate the spins to return to a positive temperature with the emission of photons. Purcell and Pound found that this occurred in their experiment. In essence, then, the nuclear spins provide a system which, once put into a negative temperature condition, will act as an amplifier for a radio frequency determined by the equation above. This was the first amplifier that could be used at very low temperatures. The efficiencies possible are, however, extremely small. Consequently, the major effort in solid state maser amplifiers has utilized electron spins rather than nuclear spins. Both the magnetic fields required, and magnetic moments of electrons, are suited to very high frequencies (microwaves).

One successful scheme involves changing the magnetic field or the frequency of a microwave oscillator relatively slowly compared to all electron motions – this is called adiabatic fast passage. It is not particularly complicated in principle, but difficult to achieve. The main factor needed for success is to obtain a material with very isolated electrons. So far, only George Feher and the Bell Laboratory group has found a suitable material and performed a successful experiment. The material used was silicon with phosphorus impurities added to provide the electrons. The silicon was 99.88 per cent pure silicon-28. In nature, silicon-28 (28 protons and neutrons) is mixed with silicon-29. The removal of the silicon-29 reduces the electron interaction with the nuclei, since silicon-29 has a much larger nuclear magnetic moment than silicon-28. However, this isotopic purification costs about a thousand dollars per gram, consequently other materials are being investigated.

Another scheme for obtaining negative temperatures is to find a material with three or more allowed electron orientations in a magnetic field. The Clarendon Laboratory group, Bleaney, Bowers, *et al.*, have investigated many such materials in their basic research programme. A description of the process for securing a negative temperature with these materials follows.

If the spin population for two levels of such salts can be equalized, then a third level between them may turn out to have a spin population greater than the lowest of the three levels. This provides a negative spin temperature. Consider the case of a solid with atoms that have several electrons free to orient themselves in a magnetic field. The equations of quantum mechanics permit the net magnetic moment to take the orientations shown in Figure 6. The higher energy orientations are, of course, those positions that have north poles aligned. Negative temperatures may sometimes be achieved by providing much radio-frequency energy of the proper frequency to cause transitions between orientations 1 and 4. This is called saturation of levels 1 and 4 by 'pumping'. Once levels 1 and 4 are equalized by absorption and induced emission due to 'pumping', it would appear that level 3 has a higher population than level 1. This is

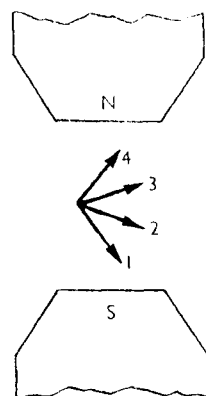


Fig. 6. The allowed spatial orientations of atomic spins in a magnetic field when the total electron spin of each atom is $S = 3/2$. The four positions possible come from the $2S + 1$ possible states. Assuming the arrowhead is the north pole of atomic magnets, the orientations are numbered relative to the lowest energy state as unity.

a negative temperature condition between levels 1 and 3 since the electrons in level 3 are denser and in a higher energy condition than level 1.

Amplification of energy appearing with a frequency ν given by

$$W = h\nu$$

can now be achieved. W is the difference in energy between levels 1 and 3, and h is Planck's constant.

Several such 3-level maser devices have been successfully operated. Bloembergen at Harvard was the first to suggest such a system, and McWhorter and Meyer at Lincoln Laboratories, of the Massachusetts Institute of Technology were the first to observe usable amplification from such a system. Present experimental difficulties are caused by a lack of understanding of solid materials. The Oxford University group has contributed much to our present knowledge of paramagnetism in crystals. Further work needs to be done toward achieving an understanding of the interactions between phonons and spins. Pioneering

efforts in this direction by Waller, Kramers, Van Vleck, and others will be pushed further both because of the increased interest in maser materials and because of the discovery that some of the theory is not borne out by experimental data. Recently Charles Townes and the Columbia University group have raised a whole series of important basic questions primarily as a result of experimental difficulties in trying to operate a maser. The tie between basic theoretical and experimental investigations and technological application seems complete. The maser came from fundamental research and now it both tests and stimulates further basic research.

SUGGESTED FURTHER READING

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- Giordmaine, J. A., Alsop, L. E., Nash, F. R., and Townes, C. H.: 'Paramagnetic Relaxation at Very Low Temperatures', *Physical Review*, 1958 **109** 302.
- Wittke, J. P.: 'Molecular Amplification and Generation of Microwaves', *Proceedings of the Institute of Radio Engineers*, 1957 **45** 291.
- Townes, C. H., and Schawlow, A. L.: *Microwave Spectroscopy* (New York, McGraw-Hill, 1955).

INDUCTIVE METHODS IN PALAEOLOGY

W. E. SWINTON

PALAEOLOGY is the science of ancient life; its materials are fossils. Fossils are, by definition, things 'dug up', whether by the continuation of geological processes or by man is immaterial, though they will, of course, have been buried in the first instance by geological agents. It follows from this that a considerable element of chance must operate in the formation, preservation, and discovery of these animal or plant remains. Under observable conditions at the present time, animals that die upon land or in woods soon disintegrate if left alone, but are usually devoured by scavengers. By their very nature plants and trees are usually growing in conditions that would appear to preclude fossilization. On the other hand, remains, whether whole or partly in decay, stand a much greater chance of permanent preservation if they are deposited soon after death in water, especially in streams or deltaic areas where rapid accumulations of mud and sand are likely to cover up the specimen. If this deposition continues, a considerable thickness of deposit may ensue. This will include a sample of the original animal or plant population surrounded by enough sedimentary material to ensure the preservation of the fossil until such time as a reversal of the geological conditions, or the operations of man, may again disclose it.

It follows that some specimens, because of their inherent nature, will withstand geological processes better than others, that fossilization has many hazards, and that rediscovery of the specimen is one of the greatest problems. It also follows that nothing like completeness can be expected in the case of an ancient and complex structure. As far as terrestrial organisms

or flying animals are concerned, fossil populations are not statistical samples.

Bearing all these things in mind the non-geologist may well ask how far the study of palaeontology is scientifically rewarding, and whether the reconstructions of the palaeontologist have in their make-up as much fact as fancy. The following account shows how much has been deduced in recent years from a number of converging lines of investigation. Though it contains much that is commonplace to the student of fossils, it will give some information to the non-geologist who is interested in the past, about the evidence that has been collected in the century that has elapsed since Charles Darwin drew attention to the historical and scientific possibilities of the record of the rocks.

FOSSILS

The earliest fossils are found in rocks of Cambrian age. These already include representatives of many groups of invertebrate animals, among them impressions of such fragile creatures as jelly-fish. On the whole, however, animals with shells of calcium carbonate, or of chitin, or having a bony skeleton, are the commonest survivors. It is from them that our knowledge of fossils has largely been derived.

There is, however, also less positive evidence such as the trails of snails, tracks of reptiles and birds, and footprints. Some of these can be related to particular species and they help us to form the general ecological picture.

Fossils are remnants of once living things; they are, in fact, usually the remnants of the larger or more complete structures in which life has been contained, and are, therefore, the abandoned vehicles of that life. It is consequently possible to evolve a descriptive palaeontology, in which these fossil structures are described in detail, and compared with their counterparts of similar or of more recent age, and even with related living forms should any such exist today. It might be argued that the technique is akin to that of the postage stamp expert, but it is of value to both geology and zoology. The more detailed the knowledge of a structure, the clearer become the interrelationships of the

animal or plant represented. This helps to give a clarity of conception to the individual form concerned, and it provides a firm foundation for nomenclature and classification, because there can be no lasting value in deductions made from materials whose systematic position is not clearly established. The stratigraphical position of the specimen must equally be well defined. After that the value of taxonomy becomes manifest, and studies of populations, growth stages, and age differences can be postulated, and the materials themselves become valuable as indicators in stratigraphy, with wide scientific and sometimes even commercial evidence. This, however, is the geological use of palaeontological evidence, rather than the advance of palaeontology itself.

The Basis of Palaeontology

It is true that other important results can follow from such general studies – the determination of past geographical and climatic conditions, and the resultant effects on animal and plant distribution.

Obviously, too, the detailed investigation of fossil remains, as such, will occasionally have results of biological value in suggesting sexual differences, and in denoting the circumstances of population assemblage and dispersal. But the basis of real palaeontological work is through comparative anatomy and physiology: the study of fossil evidences against a background of a knowledge of the bodily structure and the physiological consequences of that structure as seen in animals today. Obviously the vertebrate groups – fish, amphibians, reptiles, birds, and mammals – afford the most rewarding fields for this study.

Vertebrate palaeontology is best approached by way of zoological or anatomical knowledge because it is unwise, for example, to apply characters to bone that do not exist, and the palaeontologist may be apt to do this unless, as osteologist, he is aware of the variability of bone under pressure or strain, and of the erosive effect of wear. The remarkable bridge-like structure of the skeleton of a horse, especially a race horse, demonstrates some of these points (Inset 8): the more or less straight

line of the backbone, the posterior inclination of the anterior dorsal neural spines and the anterior inclination of the lumbar neural spines show the effects of the muscular pull at the extremities of the bridge, which is an exact parallel of suspension bridge construction. The strength and inclination of these processes have been used by Brazier Howell,¹ Slijper,² and others to estimate the speeds of animals. The wear of the later dorsal spines under the saddle shows the effect of constant pressure. Age variations in horses are easily observable and the relative rugosities and erosions on shoulder blades and limb bones are instructive as to the moulding process that goes on.

Another example is the South American ground sloth, *Mylo-don*, in which some of the thoracic vertebrae are frequently eroded through pressure of the aorta that becomes applied to them. Pathological variations in fossil vertebrates are frequent, and are usually the result of age or trauma, rather than disease.

Histology

Sections of bones, even of great antiquity, still bear witness to the characteristic Haversian systems of their modern counterparts and on occasion show bone tumours. However, attempts to use such sections even for group identification have so far been ineffective.

Much can be deduced by comparison of past and present osteological remains and it can be assumed that the muscles based upon the bones can be similarly compared. No muscles of ancient vertebrates have been petrified, though evidence of muscle blocks is occasionally seen; but naturally ossified tendons are not unusual, especially on the tails of bipedal dinosaurs. In many fossils some of the muscular arrangements can still be deduced through the presence of scars and rugosities. At any rate, there have been many contributions to Palaeomyology. Skin is not known in any fossil of antiquity, apart from that of the ground sloths of South America. The skin of *Grypotherium*, for example, with dense coarse hair on its outer side and with a layer of mail consisting of small bony nodules underneath, is well known. These giant ground sloths may have been semi-

domesticated by man and are thus not very ancient. Hair and some integument of mammoths are also known.

Dinosaurs have yielded frequent impressions of skin. There are even several 'dinosaur mummies' in American museums, specimens which must have dried quickly after death – perhaps on a sandbank where, at an opportune moment, floods brought down sufficient material to cover up the shrunken skin and retain its imprint when solidification took place. Subsequently the skin decayed, but left impressions that can be studied in much detail.

Dinosaur skin thus often leaves its pattern and evidence of its thickness. Melanin granules in the skin of *Ichthyosaurus* have been examined recently in detail by Dr Mary Whitear³ who comes to the conclusion, on the evidence of fossil melanocytes, that the colour of an *Ichthyosaurus latifrons*, which died approximately 150 million years ago, was dark brown. The scalloped and otherwise sculptured tails of dinosaurs also yield interesting information as to their former appearance (Inset 9a). Perhaps the most important evidence of this kind comes from the fine-grained lithographic limestone of Solnhofen, Germany, which yielded the remains of *Archaeopteryx lithographica*, the oldest bird known. At some time many millions of years ago, the bird lay on soft oozy mud, its feathers very gently rocked in the tidal stream or current, and made a deep enough impression to be retained in the mud and ultimately hardened into limestone. As now preserved and exhibited in the Natural History Museum in London, the imprint is clear enough for the arrangement of the feathers to be elucidated, as has indeed been done by several investigators.

None of the smaller body feathers has been discovered, though it is worth recalling that the first evidence of fossil birds in this deposit was not the more or less complete specimen discovered in 1862 and now in London, but the part (now in Munich) and counterpart (in Berlin) of a single feather found in 1861.

Extraneous materials that have yielded important sidelights upon vertebrate palaeontology are eggs. Many reptilian eggs

have been found in England, France, the United States, and Mongolia. The 1922–5 Expedition of the American Museum of Natural History made outstanding discoveries of fossilized eggs and nests of eggs of a small armoured dinosaur, *Protoceratops*, of Lower Cretaceous age in the Gobi Desert of Mongolia. Many of these eggs contained the remains of embryo skeletons; some had embryos emerging from the egg and interesting reconstructions of these have been made. (Inset 9b and 10.) The shells of the eggs were intensively studied by Professor V. van Straelen of Brussels⁴, who concluded that the shell was unlike that of modern reptiles, and had a prismatic layer closely akin in constitution to that of birds' eggs. Nests of eggs have also been found that indicate methods of laying not unlike those of modern crocodiles and turtles. Some of these nests in Mongolia contained eggs in various states of development; some eggs being broken and the young obviously hatched, while others contained the remains of embryos. Soviet expeditions have very recently discovered many further specimens.⁵

From some of these, and other skeletons of baby dinosaurs, it has been possible to work out the developmental stages of certain important features, among them the method of ossification of bony plates on the back. These, in turn, throw light on the homologies of the armour structures.

A certain amount can be deduced from persistent structures, but there are still other avenues of approach. In many cases it is possible, and in some it is easy, to make plaster, or plastic, casts of the brain cavity. Frequently these are referred to as 'brain casts'. It should, however, be remembered that in very few cases, except among the highest vertebrates, does the brain occupy the whole of the cavity. In some cases the brain tissue is surrounded by almost a cocoon of connective tissue that may occupy varying amounts of the endocranial space in different animals; in others, the non-brain space may be occupied by liquid. Despite the amount of vertebrate dissection that has been done, it is still difficult to obtain satisfactory figures for the relative occupancy of the endocranium. For example, in both the living crocodile and the Tuatara the brain takes up half the space and this may

well have been the proportion in many of the reptiles of the past, though it is difficult to believe that some of the dinosaurs could have operated on half of their already very small endocranial capacity.

None the less, it is reasonable to suppose that even in a cast of the brain cavity that may be flattering, the relative proportions occupied by the different parts of the brain may be significant. Many brain casts can thus be used to give the relative efficiencies of the senses of smell, sight, and hearing. More than this, the relative importance of the pituitary gland can be assessed.

One of the recent advances in vertebrate palaeontology has been the investigation of growth and overgrowth. Once again, dinosaurs provide a splendid field for study. In one group great increase in bodily size is associated with a relatively prominent pituitary gland; in another there is a suggestive overgrowth of bone in certain regions of the skull. In several instances this overgrowth is clearly related to an unusually large pituitary fossa. One knows, of course, that other structures, such as arteries and optic muscles, may be included in the fossa. There are modern counterparts to this pituitary action, and hyperplasia has been studied especially in Pacific salmon, in which the accompanying pituitary degeneration has led quickly to the death of the fish. Pituitary hyperfunction has been held by the writer, among others, to be a factor in the extinction of some, though certainly by no means all, dinosaurs.

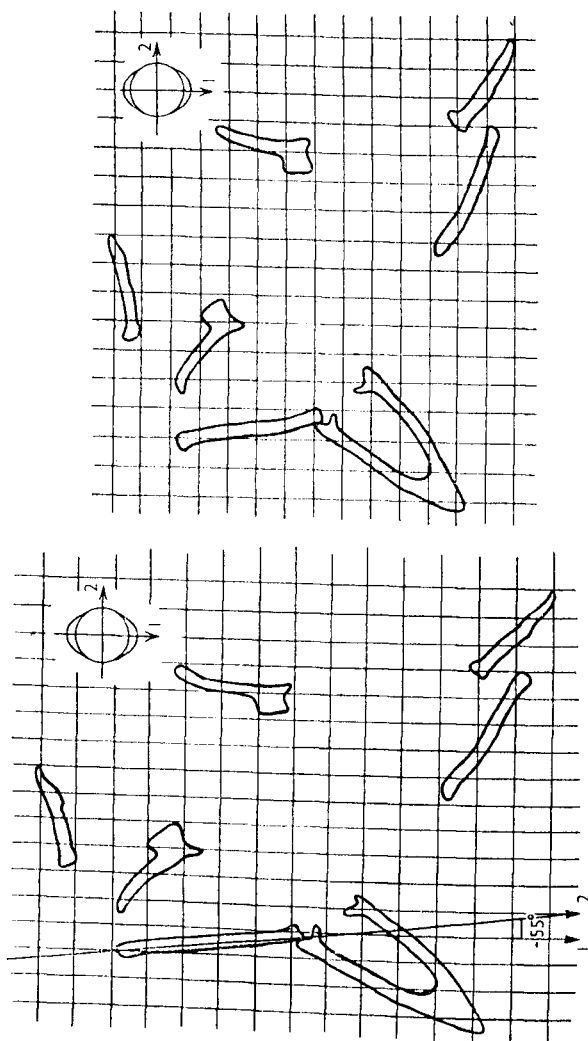
Other nervous structures of widespread interest are the large nervous masses in the sacral cavities of Sauropod dinosaurs, especially in *Diplodocus*, and in the armoured dinosaur *Stegosaurus*. It is unfortunate that these have been described as 'second brains', because they are not brains at all, and to call them so confuses an otherwise straightforward neurological picture. These enlarged ganglionic centres are the meeting places of the nerve trunks from the hind limbs and the spinal cord. In the dinosaurs that have long and stout legs as propulsive agents for their heavy bodies, they are of great size and are thus 'boost centres' for the motor control of the hind legs. Similar enlarge-

ments, on a proportionately smaller scale, are found among Chelonians, and to an even smaller but still noticeable extent in Man. There is absolutely no evidence that these nervous centres have any intellectual significance in any extinct or living form. Chromatographic investigations have been carried out on these brain and sacral cavities, but so far without any positive indications.

The ordinary nerve channels are often to be seen, and their location and function follow those for the comparable parts of the skeleton of living creatures, and most of the structures mentioned speak for themselves; but there are other methods of investigation that are possible for their elucidation. For example, the first fossil bird ever discovered was a partial skeleton of a Passerine of unknown affinities. The specimen came from the Oligocene fish-shales of Matt in Switzerland and is now in the Zoological Museum of the University of Zürich. The fish beds from which it came have been subjected to a considerable amount of deformation, with the result that this historic specimen shows paired bones of different length and thickness, even the two halves of the lower jaw being unequal (see Figure 1).

These features were drawn to the attention of Professor F. Stüssi⁶, who has applied the mathematical formula for engineering deformation to the evidence, with the result that undeformed dimensions have been obtained, making comparison with other Passerine skeletons more profitable systematically.

A similar technique was recently applied in University College, Dublin, and in the National Museum of Ireland, on fossil Coelacanths from the Carboniferous of south-western Eire. Already some four species of *Rhabdoderma* had been established – or were suspected of being represented – in the deposits, the standard component for comparison being the operculum. The fossils of the beds concerned are markedly deformed by tectonic processes, but, using an equation derived from a study of the fairly constant degree and direction of deformation, Dr J. S. Jackson of the National Museum has re-examined and figured the specimens with much more conservative systematic results.

Fig. 1. *Protornis glaronensis*.

It is obvious that a very great deal of mathematical treatment remains to be done, not only so that deformed and undistorted specimens may be compared, but also so that different elements in an apparently normal skull or skeleton may be analysed for signs of independent or abnormal growth. Already this latter quest has produced interesting results in the skulls of the large, herbivorous horned dinosaurs known as the Ceratopsia.

Here it has been found practicable to take what appears to be a normal skull out of a series of closely similar skulls or those of the same species and, by placing the prominent 'land marks' of the skull on a grid, to compare the outline of these other skulls and their individual bones *vis-à-vis* their fellows on the norm, putting the results on a grid also. The deformation on these secondary grids⁷ gives at once an interesting picture of specific, age, and perhaps sexual growth differences, and certainly draws immediate attention to allometric growth. (Figs. 2 and 3.)

NEW METHODS OF DEVELOPMENT

Side by side with these interpretative methods there are new methods of developing fossils: materials once thought to be locked for ever, wholly or in part, in their stony prisons may now be released for study. New techniques of acid development, particularly acetic acid, have been developed in the Palaeontology Department of the British Museum (Natural History) by H. A. Toombs and A. Rixon. With care and patience it is now possible to extract fossil materials from certain kinds of matrix in a condition that compares very favourably with that of

Fig. 1. *Protornis glaronensis*. The figure on the left shows how a small degree of distortion produces inequalities that lead to obvious difficulties in comparing the bones with those of other forms. The lower jaw (bottom left) makes this clear. As a result of calculations based on the standard degree of deformation in the rock containing the specimen, it was possible to redraw the bones, as shown on the right, without distortion. (After Stüssi.)

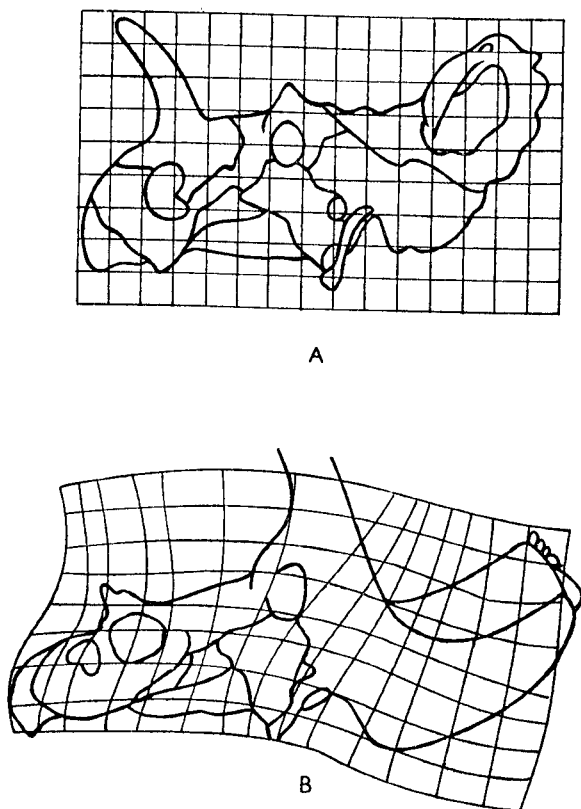


Fig. 2. Sir D'Arcy Thompson, in *On Growth and Form*, suggested that a system of co-ordinate lines undergoing deformation could be used to show the relationship between homologous parts of the bodies of related animals. In his book he treated the phylogeny of the horse in this way. The horned dinosaurs or Ceratopsia also appear to provide excellent skull material for this treatment, and it might even be possible to predict intermediate stages, as yet unknown, from such a series. The upper figure (a) shows the basic system used on the skull of the single-horned genus, *Monoclonius*, as compared with (b) in which the system has been deformed to fit a species of the three-horned genus, *Triceratops*.

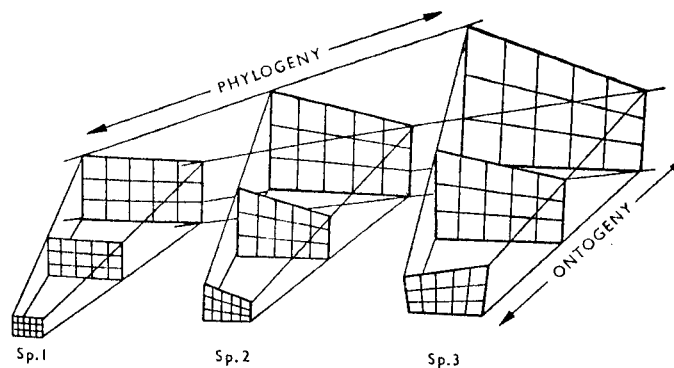


Fig. 3. The D'Arcy Thompson system of co-ordinates can be used to obtain generalized information. In this figure several ages of three species of horned dinosaurs have been used. The youngest in individual age are at the bottom of the diagram, the adults at the top. The series from bottom to top thus yields an ontogenetic range, the adults providing the phylogenetic series. The geologically oldest adult is on the left and the youngest on the right. Conversely the diagram could be used to help determine age stages, and paedomorphosis has thus been demonstrated in dinosaurs. (After Lull & Gray.)

macrated recent specimens. Even so, there are several matrixes upon which these chemical methods are as yet unavailing, but on these the new supersonic dental drills are effective. With this physical method of development, even greater anatomical knowledge and skill in handling must be exercised, for the slightest slip or inattention may easily ruin the whole specimen in an instant. (Insets 11a and 11b.)

X-rays are being used increasingly to reveal materials buried in matrix, and to investigate the nature of bones themselves. Ultra-violet light, which shows up bone very clearly compared with the material in which the fossil is embedded, has become a valuable aid in the palaeontological laboratory in the resolution of doubtful structures and also as the background for photography. *Archaeopteryx lithographica* by Sir Gavin de Beer⁸ contains

several photographic plates taken in ultra-violet light which reveal this advantage. Insets 12 and 13.)

Given these preliminary lines of approach and using at least some of these aids, what are the palaeontological deductions that have recently been made? And how far do they supplement previously held ideas of the evolutionary lines and the living habits of, for example, the vertebrate groups?

It is only within the last twenty years that the main steps in the evolution of class to class have been discovered and described.

We know now, thanks to the work of T. S. Westoll and others, the steps that link the Rhipidistian fishes and the Ichthyostegalian amphibians; and almost all the main stages in the consequent skull reductions, in limb development, and in skeletal adjustments are available. Then, too, in considering the evolution of reptiles from amphibians, the discovery of the skull and skeleton of an almost transitional form, *Seymouria*, in the Lower Permian red beds of Texas, has yielded important evidence of the line along which the change must have been accomplished. It is true that *Seymouria* itself, by reason of its age, is debarred from this ancestry, but its evidence is none the less admissible. The first full description of this interesting fossil was made by Dr T. E. White⁹ in 1939 and the implications of its mosaic of amphibian and reptilian characters have been evaluated mainly by D. M. S. Watson in England, and by A. S. Romer in the United States.

The reptiles gave rise indubitably to the birds and to the mammals, and both portentous occasions are well authenticated. As has been said, the stratigraphically oldest bird is *Archaeopteryx lithographica* found in the Upper Jurassic of Germany in 1862.

In the near-century that has since passed, there have been many attempts to assess its palaeontological significance, some of which exaggerate its importance. It has been suggested that the London specimen is the ancestor of the ratites; the Berlin specimen, found some years later in a different locality, being in this argument the ancestor of the carinates. Both specimens belong, in fact, to the same species (*A. lithographica*) and are

together in the ancestral line of all the birds, both flying and flightless. That it was itself not a fully functional flying bird is proved by its solid bones and its long reptilian tail, even though the latter had a pair of feathers for each vertebra. The comparatively long jaws, with reptilian kinds of teeth in both upper and lower, express strong probabilities as to the anatomical position this bird must occupy in any logical series of reptile-bird transition. The small, keel-less sternum, on the other hand, speaks, as does the long tail, of a flight that was unstable and imperfect but which was almost certainly on the way to modern bird flight. Recent studies have established the fact that transitional forms show not half-way stages, as so long demanded by the 'missing-link' enthusiasts, but a mosaic of characters, some reminiscent, others anticipatory. Such characters are, of course, demonstrable only on the bones, but physiological characters in keeping with the evidence can be inferred. Both these facts are amply borne out by recent work – indeed, some of it is current – in the interesting field of the mammal-like reptiles.

The existence of reptiles of mammalian similarities, or quasi-mammals, has long been known – the date 1824 could be placed on the first description of mammalian or alleged mammalian teeth by Dean Buckland of Oxford. This was the beginning of a controversy that was to continue for over a century and that has just attained its settlement. It is true that some of the materials discussed were mammals but others were reptiles, and a true understanding of the evolutionary route to the one from the other had to await better materials, wider knowledge of the diagnostic criteria, and much more accurate and definitive palaeontological methods. All three avenues of approach have coincided only in the last ten years.

MAMMAL-LIKE REPTILES

Advances of science are, however, often coincidental. And it was coincidence alone that connected the discovery of a new quasi-mammal, named *Bienotherium*, in the Trias of China in 1939, with work that was going on in England on the analysis and determination of hundreds of tiny bone fragments extracted

from infillings of Liassic age in older rocks of the West Country.

The teeth of both these animals had very close affinities with those of a skull, from South Africa, named *Tritylodon* in 1884 by Richard Owen. The name expresses the three-cusped nature of the upper teeth, where the cusps are arranged in three longitudinal rows with grooves between the rows. The movement of lower teeth (which had two rows of cusps) on upper teeth was confined by these grooves into an anterior-posterior propalinal movement. The teeth show that the animals were vegetarian. The many fractured bones studied in London were broken up by a carnivore's teeth, though not one fragment of that carnivore itself has been preserved. This English material has been identified as *Oligokyphus* and has formed the subject of a monograph published by the Natural History Museum¹⁰. But the discovery of several complete skeletons of a Tritylodont in the United States has given a new unification to this primitive scene, with the result that we realize that all these quasi-mammals are indeed reptiles, but reptiles with a mammalian physiology. The nature of the vertebrae shows that this reptile could turn to lick fur; and fur may be presumed, for the structure and articulation of the ribs suggests a rhythmic and diaphragmatic respiration, which in turn would demand the insulation of fur.

These advances in palaeontology are based upon facts and logical deduction. They are important in that they stress that anatomical and physiological evolution are not necessarily co-incident or contemporaneous; that in fact the significant stages in these class-to-class connexions are of a mosaic type. It is well that this should be stressed in the year that celebrates the centenary of the Darwin-Wallace pronouncement. Darwin in his *Origin of Species*, published in 1859, gave a new impetus to the study of fossils, and revealed the probable wealth of material that might come from the reservoir of the life of the past. With more than usual bravery he even suggested a range of geological time which so startled contemporary thought that subsequent editions of his work omitted it. But Darwin appreciated the vastness of geological time and in celebrating his prescience it is well to remember how many of his other forecasts were right.

It has been alleged that comparative anatomy fell into disrepute in Edwardian times because of the museum influence; of the divorcement of structure from function in taxonomic studies. It is pleasant to think that present-day work, often in museums, in descriptive and inductive palaeontology, has established the fact that it is not only the characters that have evolved but also the organism. It is this comprehensive, even ecological view, that is so important.

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THE METABOLISM OF DRUGS AND OTHER FOREIGN ORGANIC COMPOUNDS

R. H. NIMMO-SMITH

DURING the last quarter of the nineteenth century a great expansion in organic chemistry gave impetus to a young biochemistry. As new compounds were synthesized they would be fed to animals and a search made in the urine for further compounds formed from them in the animal body. During this period were discovered many of the general ways in which foreign organic molecules can be transformed biologically. Although this in turn stimulated organic chemistry, and although it provided an invaluable basis for our knowledge of such biochemical reactions, the manner of their discovery gave rise to false concepts that are only now being dispelled.

The belief grew that the biological reactions revealed in this way were peculiar to foreign compounds, and that the reactions were developed by the animal to protect itself from noxious compounds. Not until recently were techniques available for looking to see whether these same reactions might not be (as at least some of them in fact are) features of normal metabolism as well. Thus grew the concept of 'detoxication mechanisms'. The term has still a limited usefulness, but it is too narrow to include all the mechanisms of interest to the present-day investigator in this field. Many of them are not 'detoxications', in the sense that the parent compound need neither be toxic, nor even give rise to toxic metabolites during the process. The chief objection to the term is the implication it continues to carry that foreign compounds are metabolized by systems that are necessarily distinct from those that metabolize normal compounds of similar structure.

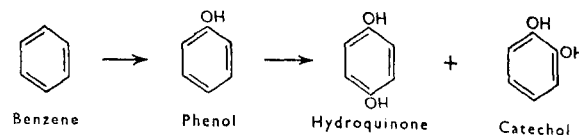
Before examining this concept at greater length it would be profitable to consider the major known metabolic reactions involving foreign organic molecules.

METABOLIC MECHANISMS

Oxidation

An ability to oxidize molecules, and to use part of the resulting energy, is a universal attribute of living cells. From what is known of the wide chemical potentialities of cells, it is not surprising to find that compounds which the organism has never 'seen' before can be oxidatively modified. Biologically, oxidation is limited to the removal of hydrogen (or electrons) from a molecule. Direct addition of oxygen, as seen in chemical combustion, does not occur. When the oxygen content of a molecule is increased biochemically it is as the result of a two-step process; in the first step water is added, and in the second hydrogen is removed.

One very general mechanism is ring hydroxylation - the oxidation of aromatic compounds to phenolic substances. Benzene, for instance, is partly oxidized to phenol, which is further hydroxylated to give small amounts of hydroquinone and catechol.



This provides an example, also, of the general finding that substituted aromatic rings are much more likely to be hydroxylated at the positions *ortho* and *para* to an existing substituent rather than at the *meta* position.

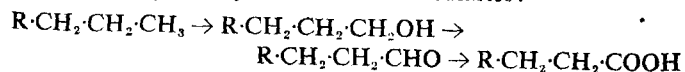
Not very much is known yet about the precise mechanisms of this biological ring hydroxylation. In some very interesting experiments Brodie and his colleagues in Bethesda have shown that a 'model system' consisting simply of ascorbic acid (vitamin C), ferric ions, and oxygen can bring about oxidation of a variety of aromatic drugs. The products formed are identical

with those formed *in vivo* from the same drugs. Ascorbic acid is an essential component of the system; that it may be involved in hydroxylation *in vivo* is suggested from the results of further experiments by the same workers.

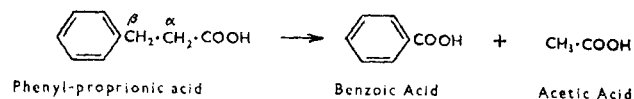
Like man, the guinea pig cannot synthesize its own ascorbic acid, and is entirely dependent on its food for a supply of this essential metabolite. In their experiments Brodie *et al.* fed guinea pigs on a diet free from ascorbic acid. In the first experimental period the diet was supplemented with ascorbic acid and the ability of the animals to hydroxylate a number of drugs was measured. Ascorbic acid was then withdrawn, whereupon the rate of hydroxylation of the test drugs was markedly reduced. A return to the original ascorbic acid supplement was followed by a regain of the animal's original rate of hydroxylation.

These results strongly suggest that ascorbic acid plays some part in ring hydroxylation; but how directly it is concerned with the process, and whether its *in vivo* action is in any way comparable with its function in the model system, have yet to be determined.

It has been known for long that the terminal methyl group of alkyl side-chains of aromatic compounds can be oxidized (ω -oxidation) to a carboxyl group. The corresponding alcohol and aldehyde are probably formed as intermediaries:



Further oxidation of the carboxylic acid so formed can now take place, with the production of a new carboxylic acid two carbon atoms shorter than the original, and of a 'two-carbon fragment' conveniently thought of as acetic acid.

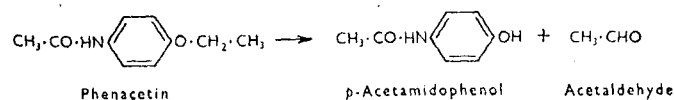


Indeed, it was the classic work of Knoop and of Dakin on the oxidation of such foreign compounds as these that led to the modern view of fatty-acid oxidation, a very important source of

energy in the animal body. It is believed that by this process of β -oxidation two-carbon fragments are sequentially chopped off the end of the fatty acid molecule and are then completely oxidized. Here is a good example of the way in which study of the metabolism of foreign molecules can lead to a better understanding of normal metabolism.

A 'new' mechanism of alkyl side-chain oxidation was revealed in a study of the fate of barbiturates. Besides the expected ω -oxidation, sometimes followed by β -oxidation, it is now known that the penultimate $-\text{CH}_2-$ group can be oxidized to an alcohol or a ketone. The significance of this type of oxidation in normal metabolism has yet to be explored.

Another oxidative reaction of some importance in the metabolism of drugs is that in which an aromatic ether is split to give a phenol and an aldehyde. Such diverse drugs as phenacetin, codeine, and mescaline, all of which contain an aromatic ether grouping, are to some extent involved in what is known as *ether cleavage*. From codeine, morphine is released; in the case of phenacetin (*p*-ethoxyacetanilide), *p*-acetamidophenol and acetaldehyde are produced.



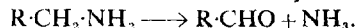
Alkyl (especially methyl and ethyl) groups attached to the nitrogen atoms of an aromatic amine (i.e., in secondary and tertiary amines) can be oxidatively removed. In this way secondary amines can be produced from tertiary, and primary amines from secondary. As in ether cleavage the alkyl fragment is apparently released as an aldehyde,



and thus qualifies for classification as an oxidative process. Recent work with isolated biochemical systems has shown, moreover, that oxygen is essential for the reaction to go on.

Enzymes which can catalyse the oxidative deamination of

aliphatic amines are very widely distributed in nature. The primary products of the reaction are an aldehyde and ammonia,



The aldehyde can be further oxidized to a carboxylic acid; and in mammals the ammonia is largely incorporated into urea and excreted in that form.

Many foreign amines are treated in the same way, and removal of the amino group is usually followed by a dramatic change in biological activity. The animal body is constantly exposed to amines (some of them rather poisonous) produced *in*, but not *by*, the body. This apparent paradox is explained by the fact that in the digestive tract of all species there are to be found very large numbers of micro-organisms, mainly bacteria. Although these microbes of many species and comprising the *intestinal flora* represent a very small fraction of the weight of their host, they have a very high rate and wide diversity of metabolic activity. Together with the products of the animal's own digestion, the products of bacterial action are absorbed into the circulation. Among such products are amines derived from amino acids, and these are rapidly deaminated in the animal's tissues. In general, aldehydes are much less poisonous than the amines from which they are derived, so this may be regarded as a true type of 'detoxication', with the reservation that the enzymes responsible are probably the very ones that are concerned with the amines produced by the animal's own metabolism.

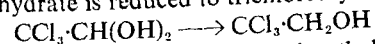
To sum up, the potentialities of living organisms to oxidize organic molecules are enormous. The few examples given above serve to indicate the main *types* of reaction to which a foreign compound may be subject. From what is now known it is often possible to predict with some success whether, and in what fashion, a new drug is likely to be oxidized.

Reduction

Each biological oxidation is inevitably accompanied by a reduction, yet the range of compounds that can be reduced is very small compared with the wide variety that can be oxidized. This is reflected in the limited number of instances in which

reduction is known to play a part in the metabolism of foreign organic compounds.

Nevertheless there are several instances in which reduction is important in modifying the structure (and thus the biological activity) of a drug molecule. A simple example is provided by chloral hydrate, a most effective hypnotic which nowadays seems to be losing the position it deserves to have in the physician's armoury. It has been known for some time that in the body chloral hydrate is reduced to trichlorethyl alcohol:



More recently it has been shown that trichlorethyl alcohol is just as efficient in inducing sleep as is chloral hydrate. Thus it seems quite likely that chloral hydrate is not a hypnotic *per se*, but acts as one by virtue of the product to which it gives rise.

Incidentally, the alcoholic nature of the metabolite may give a basis for explaining an interesting effect. When chloral hydrate and ethyl alcohol are given together the hypnotic result achieved is much greater than the sum of the effects produced by the same dose of either separately – a situation known to pharmacologists as *synergism*. Unscrupulous persons have sometimes exploited this action to put a victim to sleep. The mixture of chloral hydrate and strong alcoholic drink, apparently not so popular nowadays, was known familiarly as a Micky Finn.

Azo compounds can also be modified by reduction, with the formation of two molecules of aromatic amine. A possible mechanism is:



The importance of the discovery of this reaction in relation to the sulphonamide drugs will be referred to later.

Conjugation

The metabolic reactions considered so far result in relatively small changes in the chemistry of the parent compounds, although the associated changes in biological activity may be enormous. They are frequently followed by more far-reaching modifications in which the size of the molecule is increased by one or more *synthetic* reactions, whereby another molecule is

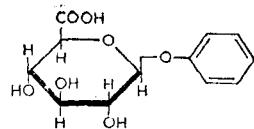
condensed or *conjugated* through a reactive group of the original drug, or of its metabolites. So far as is known at present, the number of compounds used by the body for conjugation is strictly limited, and nearly all contain acidic groups.

Again it should be pointed out that conjugation is a process going on all the time. Not only are some of the substances produced by microbial action in the intestine excreted in a conjugated form, but many of the end-products of the animal's own metabolism as well.

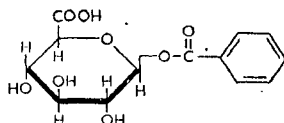
Conjugation with glucuronic and sulphuric acids

Glucuronic acid is a hexose in which the terminal alcoholic group has been oxidized to a carboxyl group – a hexuronic acid. It is an essential component of many important natural compounds and is found, for instance, in the mucopolysaccharides (See Barker and Stacey, *Science News*, 45 81).

Through the aldehyde group on carbon atom 1, and with the elimination of water, glucuronic acid is condensed with a grouping on the metabolite molecule to give *glucuronide* or *glucosiduronic acid*. The groupings most commonly involved in this conjugation are (a) phenolic and alcoholic hydroxyls and (b) carboxylic:



(a) 'ether' glucuronide



(b) 'ester' glucuronide

Glucuronides of type *a* (derived, e.g., from phenol) are often referred to as 'ether' glucuronides and those of type *b* (derived, e.g., from benzoic acid) as 'ester' glucuronides.

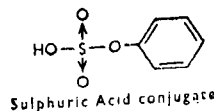
It was from the urine of cows fed on mango leaves that in 1855 the first glucuronide was isolated. Since then a very large number of organic compounds have been found to give rise to the excretion of conjugates of glucuronic acid. As a result, conjugation came to be associated with the metabolism of foreign compounds, many of them toxic. In 1936, however, it was shown

that conjugation could involve compounds quite normal to the animal organism, when the glucuronic acid conjugates of two oestrogenic steroids (oestriol and pregnanediol) were isolated. Yet the current teleological concept was little shaken by this finding: it was simply modified to include the possibility that oestrogenic activity could be terminated through 'detoxication' by conjugation. It is only during the last decade, with the realization of the biochemical ubiquity (and presumably, therefore, the physiological importance) of compounds containing glucuronic acid, that conjugation has been envisaged as a mechanism of much more general significance.

Evidence is growing to suggest that groups other than those containing oxygen can be conjugated in a similar fashion. It seems likely, for instance, that a variety of primary aromatic amines (including the simplest, aniline) are excreted partly as N-glucuronides. Chemically they are much more labile than the commoner O-glucuronides and are readily degraded to free aromatic amine and glucuronic acid. Only with the more delicate methods of analysis which have been recently introduced can their existence be detected. Another 'new' type is the S-glucuronide, derived from certain thiol (—SH) groups.

In most tissues and body fluids enzymes, called *glucuronidases*, are to be found. These can catalyse the hydrolysis of glucuronides into the parent compound and glucuronic acid. They are quite distinct from the systems that synthesize glucuronides, but in spite of very extensive work their function remains a mystery.

Sulphuric acid is also used by the body for conjugation, but so far as is known the types of compound so conjugated are fewer than those that enter into glucuronic acid conjugation. Until 1957 it was thought to be confined to phenolic hydroxyl groups, to yield acid derivatives in many ways comparable with

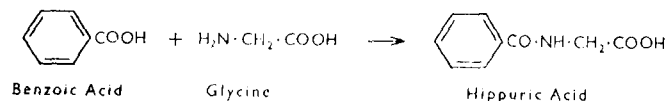


Sulphuric Acid conjugate

glucuronides of type *a*. It has just been discovered that aromatic amino groups can also be conjugated with sulphuric acid to yield sulphamic acids. Like the related N-glucuronides they are rather delicate compounds, readily mistaken for free aromatic amines, and in both cases characterization of the N-conjugates was a considerable achievement.

Conjugation with amino acids

It is over a hundred years since the conjugation of benzoic acid with the amino acid glycine was clearly demonstrated. Liebig had even earlier found an unidentified derivative of benzoic acid to be excreted by the horse and had accordingly named it *hippuric acid*.



Conjugation with glycine seems to be restricted to carboxyl groups attached to a ring system either directly or through a short chain. By a very similar mechanism other α -amino acids are used for conjugation and in this connexion there are some interesting species differences to be noted. Birds are unable to use glycine in this way, and excrete benzoic acid in conjugation with ornithine. This is a diamino acid, and each amino group is conjugated with a benzoic acid molecule to give *ornithuric acid* (N:N'-dibenzoylornithine).

Another interesting difference is found in the conjugation of phenylacetic acid. Whereas birds conjugate it with ornithine, and most mammals with glycine, humans and chimpanzees excrete it in conjugation with glutamine. This conjugation appears to be rather specific for phenylacetic acid and becomes even more interesting when we remember that it is not (as in birds) due to an inability to use glycine, because man excretes many end-products (including some of normal metabolism such as bile acids) in conjugation with glycine. This is only one of the many curious species differences recorded; and certainly there are very many more yet to be revealed. It is quite possible, too,

that more amino acids enter into conjugate formation than are at present known to. Serine has very recently been added to the list.

Cysteine, one of the sulphur-containing amino acids, is involved in rather a different sort of conjugation. It is restricted to certain aromatic compounds, and in it the sulphur atom of cysteine is linked to a carbon atom (usually a nuclear carbon) of the aromatic system to give a *mercapturic acid*. At some stage in the process the amino group of cysteine is acetylated. So far the sequence of events in mercapturic acid synthesis has not been elucidated in detail, but it seems likely that acetylation takes place after the carbon-sulphur linkage has been forged.

Conjugation with acetic acid

Amino groups of (a) amino acids and (b) aromatic amines can be biologically acetylated. We have already seen an example of (a) in the acetylation of cysteine in mercapturic acid formation; it is probably a relatively unimportant feature of the metabolism of natural amino acids. Acetylation of aromatic amines, on the other hand, is an important aspect of their metabolism. All aromatic amines are at least to some extent acetylated in vertebrates – with one known exception. Curiously, the dog cannot perform this particular metabolic trick, although it can acetylate amino acids. Together with other observations this suggests that different systems are concerned in the two types of N-acetylation.

Acetylation of the sulphonamides provides a good example of how the study of the metabolism of foreign compounds can widen our knowledge of normal metabolism. In this case it led to a much closer understanding of one of the most important energy-yielding systems of cells in which acetylation (though not of an amine) is an essential step.

Summation of effects

So far it has been convenient to consider, separately from each other, the various major changes to which a foreign compound may be subjected. But the reader will probably have realized that even a fairly simple compound can undergo, in

parallel or in series, a variety of changes. This in fact happens. Ring hydroxylation, for instance, can be followed by conjugation with both sulphuric and glucuronic acid; ring hydroxylation, moreover, can occur at different positions in the same molecule, as we have already seen in the simple case of benzene.

Let us consider for a moment the case of an aromatic system containing two reactive groups, a phenolic and an amino. Each can be conjugated in different ways: the phenolic group may be converted to a sulphate and a glucuronide; the amino group to a N-acetyl, a N-glucuronide, and a sulphamic acid. Conjugation need not be complete, so we must add the possibility of compounds being excreted with one or both groups unconjugated. So in this example at least eleven different metabolites might be produced. We have to say 'at least' because we have not included the possibility of, e.g., further ring hydroxylation, and because almost certainly yet other reactions remain to be discovered.

From the quantitative point of view there are great differences in the way in which a particular compound may be excreted by a particular species. A major metabolite may appear in the urine at a thousand times or more the concentration of a minor one; and the pattern may vary greatly from one species to another. From such quantitative disparity and from the rather large number of metabolites to which one compound can give rise, the difficulties of obtaining a comprehensive picture of even the metabolism of one drug can be appreciated. A further difficulty is introduced by the fact that some metabolites (e.g., the conjugates of aromatic amines mentioned above) are readily decomposed and therefore not easy to detect. As a consequence it is perhaps not going too far to suggest that in only a very few cases (if any) have we a complete picture of the overall metabolism of any one drug in any one species.

Nevertheless it is possible to attempt some generalizations on the net effect of their metabolic adventures upon foreign molecules. The parent compounds are usually weakly acidic or basic compounds more soluble in fat than in water, and as such are excreted by the kidney very inefficiently. Their biological activity depends upon the integrity of reactive groups in the molecule.

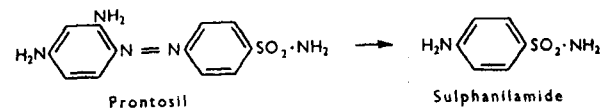
Now it is very striking that often the very groups in a molecule that endow a compound with its own physico-chemical characteristics (acid strength, fat solubility, etc.) are at the same time partly responsible for its biological activity. In most cases examined the effect of conjugation is simultaneously to increase acid strength, increase water solubility, lower fat solubility and, by 'masking' active groups, to decrease or abolish biological activity. At one fell swoop conjugation tends to produce a readily excreted molecule of low biological activity from one with very different characteristics.

Conjugation can be regarded, therefore, as offering considerable advantages to the organism. Before pursuing this point further and attempting to assess its significance, it might be interesting to look at some more specific effects of metabolism.

METABOLIC ACTIVATION

Activation of drugs

Sometimes, perhaps more often than we imagine, an intermediary metabolic change is accompanied by a gain, rather than a loss, of biological activity; we have already considered this in relation to chloral hydrate. One of the best examples of such a change is to be found in the story of the sulphonamides. The first compound of this series to be used successfully in the treatment of bacterial infections was a coloured azo-derivative. A study of its metabolism undertaken by workers in the Pasteur Institute in Paris and in England showed that in the body the azo linkage of 'prontosil rubrum' is reductively cleaved with the liberation of sulphanilamide.



From this observation, coupled with the fact that sulphanilamide is a powerful inhibitor of bacterial growth *in vitro*, whereas prontosil is quite inactive, it was rapidly realized that the dye was only effective *in vivo* because it acted as a source of sulphanilamide. The logical step was to use sulphanilamide

itself, the active metabolite of prontosil. Since sulphanilamide is released rather slowly from prontosil, and since much prontosil is excreted unchanged, this is a much more efficient method of treatment. From such work as this has grown the wide range of sulphonamide drugs now available.

Acetanilide and phenacetin are used extensively in the symptomatic treatment of mild pain and fever, and have an effect similar to that of aspirin. Both can be toxic, acetanilide (which was introduced into medicine as the result of a dispensing error in 1886) rather more so than phenacetin. Both are converted largely to *p*-acetamidophenol in the human body; acetanilide by hydroxylation, and phenacetin, as we have already seen, by ether cleavage. Extensive comparisons with its two precursors further suggest that *p*-acetamidophenol is (a) at least as good an analgesic, and (b) considerably less toxic than either. At the moment it therefore looks as though the replacement of acetanilide and phenacetin by their common metabolite has considerable advantages.

It seems more than likely that future work will greatly increase the number of known instances in which biological activation of drugs occurs and will have an important part to play in the development of new therapeutic agents.

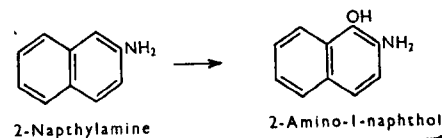
Activation of carcinogenic compounds

Great interest attaches to the possibility that some cancer-producing substances exert their effect through the formation of metabolites. A long time ago it was established that prolonged exposure of the human body to coal tar and soot produces cancer of the skin, and the relationship prompted a wealth of work on the nature of the active constituents. Many of the polycyclic hydrocarbons originally isolated from such sources are known now to be potent carcinogens. Yet they are fairly inert and unreactive compounds, and the belief is growing that it is not the hydrocarbons themselves that initiate the extremely complex series of events leading to a recognizable cancer, but that it is certain metabolites, probably hydroxylated, that act as the primary chemical agents in the process.

Attacks on the problem of that 'anarchy of the cell' – cancer – must come from many sides at once. It is an everyday experience that we are at an enormous disadvantage in putting something right that has gone wrong unless we have a good idea of what it is that has gone wrong – and that depends in turn upon having some knowledge of how it works normally. Living cells are no exception in this respect; to be in a position to break with confidence the chain of changes leading to a cancer or, better still, to prevent it from starting, requires more knowledge than is at present available. But this knowledge – of the biochemistry and physiology of normal cells and precisely how it has gone wrong – will certainly be built up on the broad foundations already laid.

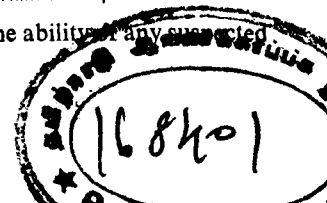
Carcinogenic agents, naturally occurring and synthetic, are powerful weapons in the attack. From the present point of view it is in studies on the metabolism of amino derivatives of the hydrocarbons that we can find points of special interest.

2-Naphthylamine is a compound used in the manufacture of dyes. People who are in contact with it for a long time tend to develop cancer, but it is a cancer of the urinary bladder and not of the skin that is induced. Although it is with the skin (and probably with the mucous membranes of the respiratory and digestive tracts) that the compound most persistently comes in contact, the cancer develops at a site remote from these and which it could only reach after passage through the body. It therefore seemed possible to investigators of this problem that it is not the parent amine, but one or more of its metabolites, that is the active carcinogen. Naphthylamine, as might be imagined, is metabolized to a large number of derivatives in the animal body. One of these is 2-amino-1-naphthol, formed by ring hydroxylation.



There is a very neat way of testing the ability of any suspected

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compounds to induce bladder cancer in experimental animals. It was introduced by two French workers in 1924 and consists essentially of making a pellet of the test compound in a biologically inert carrier such as paraffin wax. The pellet is implanted in the bladder wall, which can thus be exposed to the suspected substance over a long period.

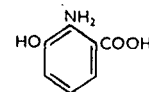
When naphthylamine itself is tested in this way it is quite without effect. Several of its metabolites have also been tested and shown to be inactive, with the single exception of 2-amino-1-naphthol. So it looks as though the carcinogenicity of naphthylamine depends upon the oxidation of some of it to the *ortho*-phenol. At this point it might well be asked: is not the aminonaphthol excreted in the form of O-conjugates, in a form in which the postulated active group is masked? This is certainly true; but the curious fact has emerged that the urine of man and laboratory animals contains a glucuronidase enzyme which can free phenols from their glucuronides.

From the available facts this is probably what happens: after absorption into the circulation naphthylamine is carried to the liver, metabolized there, and the metabolites then excreted by the kidney. Most of them are harmless, but in the bladder the carcinogenic aminonaphthol is set free from its O-glucuronide. If an individual is exposed to the parent amine for long enough a bladder cancer is likely to develop.

Conjugation of the amino group of 2-amino-1-naphthol, even when the phenolic group is free, results in a loss of carcinogenicity. So a free amino and a free phenolic group are both necessary for initiating the process. Moreover it seems likely that the two groups must be *ortho* to each other, for 2-amino-6-naphthol does not produce cancers.

There are indications that other aromatic amines which are carcinogenic become so after conversion to *o*-aminophenols. On the basis of their own extensive investigations and those of other workers, Boyland and his associates at the Royal Cancer Hospital, London, considered the possibility that *o*-aminophenols produced as normal metabolites might be involved in cancers of the bladder arising in people not known to have been exposed

to carcinogens from without. One possibility was 3-hydroxy-anthranilic acid,



3-hydroxy-anthranilic acid

which was recently found to be a metabolite of the amino acid tryptophan, and to be excreted in the urine of normal people. They proceeded to test it in mice by the technique mentioned above and were able to show convincingly that this compound can, indeed, induce cancer of the bladder.

Discoveries of this calibre have far-reaching implications and lend support to the hypothesis that some types of cancer are precipitated by the presence of normal metabolites in abnormally high concentrations, or by an increased sensitivity of tissues to normal concentrations.

METABOLIC INACTIVATION

Biochemical conversion to derivatives with little or no activity is the fate of most drugs. Even when an intermediary step produces an active agent from an inactive precursor, subsequent steps, particularly conjugations, remove activity. Metabolism of a drug is, therefore, an important factor in determining the duration of its effect.

An example is to be found in the barbiturates, a group of drugs of great value as hypnotics and anaesthetics. Alkyl side-chains are essential parts of their molecules; they are prone to oxidation, which is followed by inactivation. Individual barbiturates have markedly different durations of activity, and to some extent this can be correlated with the length of the side-chain. A short side-chain is less rapidly oxidized than a longer one; barbiturates with short side-chains tend to have a prolonged action. The shorter-acting members of the group have longer, more vulnerable, side-chains.

Clearly, if enough is known about the ways in which a drug is inactivated, we are in a better position so to modify the

groups involved as to alter the rate of inactivation in the desired direction. Mostly it is a longer action that is wanted.

BIOLOGICAL SIGNIFICANCE

In 1935 Ambrose and Sherwin were able to conclude that it 'has been necessary for the body to call to its aid a chemical defence mechanism to guard against the poisons absorbed from the gastro-intestinal tract. After many generations this chemical defence mechanism has been so perfected in its battle against putrefaction products absorbed from the intestine that it is now quite able to cope with many of the foreign organic compounds.' Since the time when the 'chemical defence' hypothesis began to take shape it has been gradually realized that normal body constituents can undergo precisely the same types of metabolic changes as foreign compounds.

The attitude adopted by such workers as R. T. Williams in England and by Fishman and by Teague in America seems to be a much more logical one. Williams reminds us that when 'a foreign compound is introduced into the body it comes in contact with certain biochemical systems, mainly enzymic, which carry out the oxidations, reductions, hydrolyses, syntheses, etc., of the body in its normal state'. It is interesting to extend this simple but highly important statement of fact. From what is known of the biochemical systems referred to, their specificity is such that a foreign compound with the right sort of architecture might readily be caught up in their workings and transformed in the same way as are the normal constituents with which the systems are normally associated. They are locks, to adapt Ehrlich's classic analogy, into which a variety of keys can be fitted; so long as the foreign compound (a key) possesses the necessary chemical groups (the wards) in the right spatial relationship, it may be able to turn the lock, albeit with greater difficulty, than the 'proper' key.

A working hypothesis based on the simple possibility that the relevant biological systems cannot distinguish between native and foreign molecules seems now to be greatly preferable to one that envisages a set of similar systems specially developed to

deal with foreign compounds. The biochemical systems we are concerned with have as their natural substrates the naturally occurring amines, phenols, carboxylic acids, alcohols, etc., perhaps as represented especially by the hormones. Teague has referred to this hypothesis as 'biological antagonism', a term already used to describe other well-established situations in which foreign compounds compete, as the result of a chemical similarity, with natural substrates. It is also more helpful in elucidating the problems of drug *action* than the 'chemical defence' hypothesis. In certain cases it is now accepted that a drug (e.g., ephedrine) can exert at least part of its action by competing with natural substrates for the attention of an enzyme system.

Nevertheless the 'chemical defence' hypothesis has recently been revived in a slightly different form. When a piece of tissue such as liver is disintegrated under the right conditions, the presence of different types of subcellular particles, still retaining a high degree of organization, can be demonstrated. On the basis of size, the particles can be separated into groups by differential centrifuging. Brodie, Axelrod, and their colleagues have shown in a series of extremely interesting experiments that the ability of liver cells to bring about many of the oxidative reactions of foreign compounds mentioned above is localized in the smallest type of subcellular particle, the *microsome*. A comparative survey has shown that the liver microsomes of land-dwelling animals (mammals, marsupials, birds, reptiles) can all oxidize a profusion of foreign substances, but that the microsomes of fish and amphibia are much less versatile in this respect. Microsomal oxidation of a number of possible natural substrates could not be demonstrated in any species.

From such observations Brodie has argued the possibility that 'the primary function of the microsomal hydroxylating system is to "detoxify" nonpolar aromatic compounds'. The need for such mechanisms, it is further argued, arose during evolution from an aquatic to a terrestrial habitat; aquatic animals can readily excrete nonpolar substances unchanged through the lipoidal membranes of the skin and gills. A successful evolution to land-

dwelling would depend on the development of other mechanisms for excreting them.

At this point it might be instructive to consider briefly how different vertebrates excrete ammonia, a normal metabolite derived mainly from the deamination of amino acids. Ammonia is extremely toxic; for instance a concentration in the circulation of only 50 parts in a million is lethal to rabbits. From the way in which they excrete ammonia animals can be divided into two very broad groups: (a) those that excrete it unchanged and (b) those that synthesize it first into urea or uric acid, both of which are very much less toxic than ammonia. Further, there is a close correlation between the availability of water and the way in which ammonia is excreted. Most aquatic animals excrete it directly; all vertebrates that live out of water incorporate it largely into urea or uric acid. It seems that in the presence of an unlimited water supply ammonia is kept below the toxic level by simple diffusion into the surrounding medium. To live in conditions of limited water supply required the development of the systems that transform ammonia into a non-toxic derivative. In the evolutionary process individuals that showed signs of developing these mechanisms would be at a selective advantage.

It seems not unreasonable to postulate that at the same time there would be a need for the development of more efficient mechanisms for the excretion of other normal metabolites, including the conversion, by oxidation and conjugation, of non-polar substances to compounds of higher solubility in water. Unfortunately there are as yet few facts to guide the speculator in this field, and he must do more experiments. The findings of Brodie's school and their evolutionary implications are of great value; but they are just as consistent with the 'biological antagonism' as with the 'chemical defence' hypothesis. Failure so far to detect the natural substrates of the microsomal hydroxylating systems is not sufficient ground for supposing that there are none. It should be pointed out that liver microsomes contain many other enzymic systems including one or more that catalyse the synthesis of glucuronides.

It will be clear by now that huge areas of this biochemical

region have yet to be explored, that the region is really part of biochemistry as a whole and that there are no natural barriers between it and the terrain explored by pharmacologists, physiologists, and pathologists. A broadening of the basis of our general knowledge of biological transformations of foreign compounds is still essential. At the same time the need is now fully appreciated of obtaining a precise biochemical definition of the *interaction* of drugs with cellular systems, not only from the aspect of drug metabolism, but to reach a better understanding of drug action, carcinogenesis, and biochemical evolution.

FURTHER READING

- Boyland, E., and Watson, G.: *Nature*, 1956 **177** 837.
 Brodie, B. B., and Hogben, C. A. M.: *Journal of Pharmacy and Pharmacology*, 1957 **9** 345.
 Fishman, W. H.: *Annual Review of Biochemistry*, 1956 **25** 659.
 Teague, R. S.: *Advances in Carbohydrate Chemistry*, 1954 **9** 185.
 Williams, R. T.: *Detoxication Mechanisms* (London, Chapman and Hall, 1947).
 Williams, R. T.: *Annual Review of Biochemistry*, 1951 **20** 441.
 For more detailed studies, references in the above reviews can be followed up. There are also the reports of investigations from the laboratories of E. Boyland, of W. V. Thorpe, and of R. T. Williams to be found in the *Biochemical Journal*.

RESEARCH REPORT

A. W. HASLETT

EVOLUTION AND A CONGRESS

THE centenary of the publication by reading of the Darwin-Wallace theory of evolution by natural selection (on 1 July 1858) provided an inevitable background for the XVth International Congress of Zoology, held during the same month in London. Through an exhibition at the British Museum (Natural History), addresses by Sir Gavin de Beer and Sir Julian Huxley, and many articles, we were reminded – in the end a bit repetitively – how well in essentials the theory has been justified, in spite of all (not really so much) that has been learnt since about mutations. One result, which it may be useful to mention, has been the republication in book form of Darwin's *Sketch* of 1842 and *Essay* of 1844, together with the 1858 papers. Without throwing stones at identifiable targets, it was noticeable as the centenary approached how many authors have referred in the past to the unorthodox assembly of papers, which formed the 1858 publication, without apparently having read them.

Another result has been the provision of a platform by the Congress for efforts to establish a biological station on the Galápagos Islands for the combined purposes of research and the enforcement of protection. A recent expedition, undertaken in cooperation with the International Union for the Conservation of Nature and the Ecuador Government, reported 'continuing destruction of the unique forms of Galápagos plants and animals – tree composites, marine iguanas, giant tortoises, penquins, flightless cormorants, finches, fur seals, to mention only a few – by local inhabitants and visiting yachtsmen', and that further destruction by colonists and tourists appeared imminent. This is not merely sentiment; on purely scientific grounds,

the case for such a station is much stronger than, for example, for a British sputnik at a cost of some millions of pounds.

From the proceedings of the congress, only a few papers can be picked out. A contribution related directly to evolution, but also a little out of the ordinary, was one by Academician E. N. Pavlovsky, of the Zoological Institute of the Academy of Sciences of the U.S.S.R. His subject was the evolution of diseases caused by parasites, including micro-organisms, and especially those which show natural foci of infection. Since such discussion is necessarily speculative, it should be said that Academician Pavlovsky and his colleagues have done good and solid research in directions relevant to his argument, and that the synthesis which he attempted was notable for its breadth and marshalling of examples.

One starting point is the fact that more diseases transmitted by insect vectors are common to man and one or more species of animals than are exclusively human. Exclusively human diseases such as malaria are rare. Those in the first group make a long list; among them are plague, brucellosis, anthrax, scrub typhus, African sleeping sickness, tick-borne and mosquito-borne encephalitis, yellow fever, and probably kala-azar – one of the more important diseases in Asia. Most, if not all, of them have natural foci 'situated in wild nature, either in virgin territory or in surroundings modified by human activities'. An example is mosquito-borne (Japanese) encephalitis; its foci along the coasts of the Yellow Sea are represented by nests of birds, which may serve as carriers of the virus, while the mosquito-vector breeds in shallow pools along the rocky coast. Another, more often quoted, is the fact that the primary natural foci of yellow fever are in the Amazon jungles, where monkeys serve as carriers and mosquitoes as vectors.

A second starting point is the fact that infectious diseases almost certainly afflicted animals long before man had evolved. This is a question primarily for anatomists and was not discussed in detail by Dr Pavlovsky. Added to the first point, it leads to a strong presumption that most human infectious diseases originated in animals. In his own statement, 'when man

came on the scene, he began to intrude into the territory occupied by valent natural foci, where he was exposed to the attacks of infected vectors, attracted by a new source of a blood-meal. In this way the vectors transmitted the infection to susceptible human beings, who accidentally became either symptomless carriers or contracted the disease.'

Various other points come also into the pattern. One of them, on which Dr Pavlovsky and a colleague have done experiments, is the comparative ease with which animals may become inoculated against lethal infections, new to them, by acquiring an earlier sub-lethal dose. Others are concerned with the insect vectors and the parasites. One such is the fact that a female tick, infected with tick-borne encephalitis, may convey the infection directly through at least two generations of its own kind, so that they are already infective at their first blood-meal. The parasite – a virus – penetrates the stomach wall, ovaries and ova, yet does not appear in any way to interfere with its host. Another point again is that variation in the incubation time of a parasite in an insect vector may become fixed as an inherited character, so that a new race of the parasite emerges. An example is the finding that *Plasmodium vivax*, the parasite of benign tertian malaria, exists in two forms, one with the usual incubation period of 14 days, and the other with one of 8–12 months.

With so many factors involved, it becomes necessary in the end to fall back on generalization. The problem has as its component pieces in any one case a parasite, an insect vector, an animal reservoir which suffers little or not seriously from the disease, and a recipient host (animal or man) which does. Over long periods of time, there must be complications also from changing conditions. Dr Pavlovsky's formula is 'adaptive evolution involving all these organisms'. If this may seem to some to approach the category of meaningless noise, it is at the same time a generalization backed by observation and experiment at many more points than could before have been claimed for it.

A current attempt to assess the value of blood serum (precipitative) reactions in determining the degree of relationship between different genera or families of animals was described by Dr A.

Boyden of the Serological Museum, Rutgers University, the United States. His work has clearly some long way to go before he can hope to get beyond the stage reached by his predecessors – that of providing linear sequences of 'relationship', which cannot easily be given meaning. The argument is, however, difficult to resist that 'if the amounts of serological correspondence revealed are based on conservative hereditary characteristics of the serum proteins' – for which there is much evidence – 'then the serologist can contribute something of importance to systematics. What remains to be established is that the more complex patterns of relationship, which he hopes to obtain by using as indices antisera evoked by larger numbers of animals, can be related to the similarly complex patterns of relationship with which systematists deal. Because both are complicated, it does not follow that the two sets of complications can be readily induced to marry up – although it is obviously worth while to try.

As an example of a comparatively new line of work on which progress is rapid and encouraging, the most obvious choice is probably the study of form and function in the thread-like flagella and cilia of protozoa. Comparisons between such small contractile fibrils and muscle are of sufficient promise to bring the subject within the range of potential usefulness. At the same time, there is an attraction – no less real from being simple – in starting with an organism, for example *Stentor polymorphus*, which with the naked eye can be barely distinguished, and proceeding through optical micrographs, with magnifications of the order of 1000, to electron micrographs with a useful resolution at least a hundred times better – and in that way getting a view not only of the over-all design of the organism, but also of some of the fine detail and the relation of this to the whole. A couple of sessions on fine structure in protozoa were opened by Professor J. T. Randall, Wheatstone Professor of Physics at King's College, University of London, and honorary director of the Medical Research Council Biophysics Research Unit.

In *Stentor polymorphus* and in *S. coeruleus*, Professor Randall has tried to obtain an unequivocal answer to the nature of the contractile structure. The body cilia are linked by long

narrow fibrils lying roughly parallel to the long axis of the organism. These fibres are joined to each other laterally in groups of about twenty, and each group has therefore something of the appearance of a long narrow ribbon. The ribbons are almost certainly contractile; and, for each group of these structures, there is another, less well-defined, axial structure lying deeper in the cytoplasm. This, too, is thought to be associated with the contractile process. Comparisons have been made between these structures and the fibrils of other small organisms, both contractile and otherwise, and studies made of the root systems from which the contractile fibres emerge. There is obviously a long way to go, especially in the relation of structure and physiology, as well as patterns of movement which themselves are complex. But it would need a hardened cynic to dismiss curtly the attractiveness and promise of this research – and the attitude at the congress came close to enthusiasm.

Those interested in animal behaviour were pleased by an experimental study, undertaken by H. F. Harlow of the University of Wisconsin, on 'the development of affection in infant monkeys'. One suspects that he had an eye from the beginning on those psychologists who have considered lactation to be the one factor that mattered – or at least the most important. The point of Dr Harlow's experiments was to provide alternative substitute-mothers, and so to arrange matters that the effects of a comforting surface and of lactation could be studied separately. One substitute, described as the cloth mother, consisted of 'a block of wood, covered by sponge rubber, and sheathed in terry-cloth skin'. The other, the wire mother, 'was fashioned from hardware cloth, a substance entirely adequate to provide support and nursing capability, but to give little contact comfort'. Both mothers were maintained at a temperature slightly higher than that of their surroundings. For one group of newborn monkeys, it was arranged that one mother provided milk, while the other was merely available, and for a second group the arrangement was reversed. As well as straightforward comparisons of time spent and frequency of contact with the two mothers, there were other experiments in which the infant

monkeys were released in strange situations. If the cloth mother was present, the infant monkeys would rush to her and literally clutch her; then, using her as a centre of exploration, they would investigate the new world about them. In her absence, they would 'crouch, rock back and forth, and clutch their bodies, and then sometimes run rapidly round the room, screaming and crying'. These experiments were illustrated by film shots which those who saw them found convincing. Dr Harlow's conclusion is that, in the development of affection in young monkeys, access to a suitably textured surface is of overwhelming importance compared with lactation.

METEORITE CRATERS

Up to the 1939–45 war, the only known meteorite crater of more than a few hundred feet in diameter was the Barringer crater in Arizona – a little over three-quarters of a mile in diameter, and estimated to have been formed some 50,000 years ago. After the war, there followed in turn the discovery of the Wolf Creek crater in northwestern Australia – somewhat smaller than the Barringer crater – and that of the Chubb crater in northern Quebec, more than two miles in diameter. Of these, the origin of the Wolf Creek crater has been confirmed; the status of the Chubb crater, formed in granite, later much eroded by glaciers, might be described as plausible but unconfirmed.

Partly because of these discoveries, and partly because terrestrial meteorite craters are of interest in relation to craters on the moon, supposedly of similar origin, Dr C. S. Beals of the Dominion Observatory, Ottawa, arranged for a systematic search to be made on 400,000 air photographs covering roughly half the land surface of the Dominion. This has so far brought to light a dozen further circular features, which are regarded as 'possibles'. Three of these have been examined on the ground, and two of them placed definitely as meteorite craters; the third, like the Chubb crater, remains in the 'plausible' category.

The one most fully examined is on farm land near Holleford, Ontario. It is half a mile in diameter, and has been studied by

gravity surveys, magnetic surveys, and test borings. Cores from three drill-holes show the crater to be filled with Palaeozoic sediments to a depth of 800 ft. Below these, there lie several hundred feet of 'fractured, granulated and powdered rock, weakly cemented together'. Below this again, there is undisturbed Pre-Cambrian rock. The age of the crater is placed at about 500 million years. It could not be volcanic; and given that meteoritic iron could hardly be expected to have remained uncorroded during that period or anything like it, it is difficult to see in what way its origin could be better established.

A second and bigger crater near Brent, Ontario, has been as well examined as circumstances permit. It is in rough wooded country, with part of the circle filled up by small lakes. In air photographs the complete circumference is defined with about the same degree of precision as might be achieved by a housewife's pastry-cutter, enlarged to 2 miles diameter. Here, too, a test boring has been made. It showed the bottom of the crater to have been about 200 ft below present ground level; and, as in the Holleford crater, there is a deep layer of shattered rock.

The third example is both the biggest and the least definite. Unlike the others – which, at ground level, had not attracted attention – the Deep Bay crater in northern Manitoba is an obvious and spectacular feature of the landscape. There are Indian legends about it, and it has been noted by travellers; but partly because of its size, and still more perhaps because of its remoteness, it has never been considered as a meteorite crater. It is still a difficult place to get at and work in; and, to make matters worse, the crater is almost completely filled up with water, being joined by a narrow and rocky channel to Reindeer Lake. Mr J. S. Innes of the Dominion Observatory visited the crater by seaplane and boat in 1956. The evidence for its origin is partly geological, and partly from a gravity survey round the more accessible parts of the lake. The rock strata surrounding the crater break off sharply at the rim, which is fractured into large angular blocks. The measurements of gravity that were made are consistent with a deep hole filled with loosely packed rocks. A minimum age of 60 million years is given by fossils,

found in shale round the edge of the crater. Being less filled in than the other two, it may be supposed to be younger, so that the minimum age may be little short of the actual age. Since these results have been obtained from a still incomplete examination of air photographs covering half of one country, Canada, it can only be concluded that enterprise similar to that of Dr Beals could lead to many more meteorite craters being discovered.

Beals, C. S. *Scientific American*, July 1958, p. 33.

PHONS AND SONES

A new and more widely intelligible unit of noise is much to be welcomed. Known as the 'sone', it meets for the first time the simple condition that when the neighbour of someone of unimpaired hearing seems to him to be making twice as much noise as before, he will be making a noise of twice as many sones. The advantage in everyday use – including courts of law, where it is important that scientific evidence should be presented clearly – should justify the trouble of getting used to it.

The loudness of a noise is subjective by definition. It is subjective in two respects – one qualitative, and the other quantitative. It is determined, first, by the response of the human ear to different frequencies (the qualitative aspect); and, secondly, by the fact that judgement of relative loudness, even when comparing qualitatively similar sounds, is a question in the end of how one feels about it – not necessarily related in a direct way to energy measurements.

The decibel scale of sound intensity is a measure of the rate at which sound energy falls on a given area. To get from a scale of sound intensity to one of noise, it is necessary to use human subjects. The difference between the existing 'phon' scale of noise levels and the new one using 'sones' is in the way that the human subjects are used. The phon scale is essentially the decibel scale of sound intensity, modified to take account of the varying sensitivity of the human ear to pure tones of different frequencies. It takes care only of the qualitative aspect of sub-

jective loudness, not the quantitative. It is thus neither a physical nor a subjective scale, but something betwixt and between. Above all, it is logarithmic, which means that only those accustomed to it can appreciate quickly the effect of a given increase or decrease in noise level, expressed in the phon scale. The sone scale, on the other hand, is fully subjective – even if it is necessary, as clearly it is, to return to instruments for the making of measurements. It is the result of research by D. W. Robinson of the Acoustics Section, the National Physical Laboratory, and Professor S. S. Stevens of Harvard University. It is based on the averaged impressions of individuals of unimpaired hearing in identifying the loudness of different sounds such that they are two, three, four times as loud as a sound of one sone. For those familiar with the old units, one sone is equal to 40 phons. For those interested in sensory perception, it has been shown that, in the case of sound at least, the 'natural' scale of sensation follows something not greatly different from a simple power law.

CALDER HALL

While research directed to thermonuclear reactions has been claiming the limelight, it appears worth recording that the heat output of No 1 reactor at Calder Hall 'A' station – which is, after all, working – has been increased to 200 MW, and its electrical output to 42 MW. The increase has been achieved by introducing neutron-absorbing material in the central part of the reactor in such a way as to enable a more even release of energy to be obtained. In addition, it can be assumed that the neutron-absorbing material is such as to give some value from its presence in the reactor. Possible candidates – not necessarily exclusive, are the production of tritium (hydrogen-3) for military use and of cobalt-60 for use in hospitals.

THE BRITISH ASSOCIATION

The Study of Cell Movements

A new microscope has been developed for studying the way in which living cells are able to move about, with particular

reference to the activity of cancer cells. The microscope makes use of certain properties of light when reflected at the surface of a glass prism. When cells in contact with a surface are examined in this way, only those areas of the cell that are in close contact are visible. The microscope is able to detect these contacts at distances of a few hundred Ångströms, well below the resolving power of the ordinary microscope. This was reported on by Dr E. J. Ambrose of the Chester Beatty Research Institute, London.

Previous studies of normal and cancer cells have shown that the surface of the cancer cell differs from that of the normal cell from which it is derived. The membrane of the cancer cell shows reduced adhesive properties. The surface contact microscope has now shown that when tissue cells are actively migrating, the contacts between the cell and the surface on which they are moving appear to be in a constant state of flux, the adhesions between the cell and the surface being continuously broken and remade. For this reason, a change in the adhesive properties of the cancer cell will be expected to produce a marked increase in its ability to move actively over neighbouring cells and to invade neighbouring tissues.

The type of movement observed in the surface contact microscope and confirmed by interference microscopy, indicates that tissue cells move as a result of active undulations of their membranes and that streaming of the cytoplasm does not occur. In this respect the movement differs from the movement of amoebae. The surface contact microscope shows that simple organisms such as blue green algae, which do not show protoplasmic streaming, also move by wavelike movements of their membranes. This type of movement therefore appears to be established as a basic mechanism of movement in biological systems.

Diamonds in the Sky

Many people are astonished to learn that diamonds have been found in meteorites, but this is not really surprising, since chemical analyses show that meteorites generally consist either of nickel iron, similar to that which we suppose to form the core

of the earth, or of minerals not unlike our own igneous rocks, in which diamonds are sometimes found.

According to H. Judith Grenville-Wells, who spoke to the British Association at Glasgow at the end of August, the first diamonds to be discovered in meteorites (in 1888) were found in the small stony meteorite of Novo Urei, U.S.S.R. In these meteorites diamonds made up 1 per cent by weight of the sample analysed – a fabulously rich yield when compared with the diamond yield of even the richest terrestrial mines. Not all meteorites, however, contain diamonds, and a recent search by Professor H. C. Urey in stony meteorites revealed diamonds only in Goalpara. Diamond has, however, repeatedly been found in the meteoritic iron of Canyon Diablo in Arizona, of which large quantities exist and are available for further study.

Scientifically, a significant point is that most of the carbon found in meteorites is in the form of graphite, often impure and poorly crystallized. The question still to be answered is whether this graphite results from the heating of diamond, which may originally have been present in the meteorites, in the absence of oxygen. (Oxygen would, of course, combine with heated diamond to give CO or CO₂.) In the first place, X-ray studies made at University College London have shown that the graphite obtained from the Dayton, Ohio, meteorite is not quite the same as ordinary terrestrial graphite, either natural or synthetic, but it is like the graphite obtained by graphitization of diamond. On the other hand, that form of meteoritic graphite which is found as small cubes and is known as Cliftonite, also gives the same X-ray pattern, but it is unlikely to be a pseudomorph after diamond because its preferred orientation is not what would be expected by such a transformation.

One of the reasons for studying the occurrence of graphite and diamond in meteorites is that the presence of one or the other may tell us something of the temperatures and pressures that must have prevailed when they were formed. Urey considers that the presence of diamond in a meteorite implies that that particular meteorite was once part of a mass at least as large as the moon.

A second reason, more interesting to crystallographers, is the fact that a study of meteoritic diamonds may help to elucidate the question of the synthesis of diamond. Some early workers, notably Moissan, believed, from a study of meteoritic diamonds, that the presence of iron must be necessary to the formation of diamond. The workers at the General Electric Research Laboratories in the U.S.A. announced that a study of the diamonds from Arizona meteorites had helped them in their successful synthesis, which involved the use of nickel rather than iron. But nickel is not present in observable amounts in terrestrial diamonds and is therefore presumably not essential to their formation in nature.

Evolution in Gastropoda in Fresh Waters

According to W. D. Russell Hunter of the University of Glasgow, for the last eleven years the Zoology Department of the University has maintained a field laboratory at Rosdhu on Loch Lomond-side, which has been used as a centre for the training of students and for research work on the biology of animals living in and around the loch. An account of research on the freshwater snails living in Loch Lomond was given by Dr Hunter to the Association.

Many of these snails belong to a group in which gills are absent and an air-breathing 'lung' developed – the group being primarily terrestrial. Some populations of these snails have to migrate periodically to the water's surface to breathe. Other populations of the same species can live in deeper water and far offshore in Loch Lomond, and show a variety of conditions in their lungs. In some the lung is water-filled and the snails respire by different means, while in others it contains a gas-bubble, which may be used to obtain dissolved oxygen, or merely to give buoyancy. Similar variation between different populations within each species is found in their reproduction: the breeding periods, the numbers of eggs produced, and the survival of the young vary from one population to another. Adaptive plasticity in their methods of breathing, feeding, and reproducing is characteristic of fresh water molluscs as a whole.

The process of evolution in animals like snails living in fresh waters has been markedly different from evolution in the same groups of animals living in the sea or on land. Freshwater environments are characterized by the high degree of small-scale, short-term, isolation that can occur within them. In other words, most lakes are separated from each other, and lakes do not exist unchanged for more than a few thousand years (unlike conditions on land where a relatively constant environment may persist for a million years, or in the sea for many times this period). Thus, it seems likely that the variability found in several aspects of the physiology of freshwater snails results from the discontinuity in space and the impermanence in time of most fresh waters.

SOME BOOKS RECEIVED

A HISTORY OF TECHNOLOGY—Volume IV, The Industrial Revolution, c.1750 – c.1950, edited by Charles Singer, E. J. Holmyard, A. R. Hall, and Trevor I. Williams (Oxford, at the Clarendon Press, 1958), pp. 728, 168s.

It is a pleasure to record the appearance of yet another, and now the penultimate, volume of *A History of Technology*. To many, and particularly British, readers this, the fourth, volume will present a greater attraction than its predecessors because it covers that unique period of human endeavour, commonly called the Industrial Revolution, which changed the face of England and Scotland, and subsequently most of Europe and parts of North America.

The approximate dates of the period covered are 1750–1850. The former date just anticipates the coming of economic steam power and is almost coincident with the establishment of the first chemical enterprise worth the name of 'works', while the latter comes in that lull in technical innovation between the establishment of the factory system in textiles and the mass production of iron, and the rise of the synthetic (principally dyestuff) industry and the invention of the great steel processes associated with the names of Bessemer and Siemens.

This was the period of Britain's greatness, when she undisputably held the title of 'workshop of the world'. Since the end of the period covered by this volume the whole pattern of world technology has changed, and, regrettably, in few fields has Britain retained the lead that once was hers. Nevertheless, many of the developments, and indeed the names, that appear in these pages are still familiar to us: our coalmines are in process of modernization but the Davy lamp retains its value: Lancashire, despite its difficulties, remains an important venue of textile production: the industrial belt of Scotland retains its interest in heavy metallurgy: Wedgwood, still retailing patterns designed in the period under discussion, is a name synonymous with elegance and grace: even that smoked delicacy 'finnon haddock' receives a couple of lines.

To write a short review of this vast storehouse in a few hundred words is a sheer impossibility. One is ensnared by every second page and held to follow up in detail some fascinating line of thought. The production of the volume is of the standard we expect from the

Clarendon Press; the illustrations are remarkable for their charm and clarity, and the indexes have every appearance of being adequate for a volume of its size, though 'kippers' may have to be sought under 'fish, preserved, mild smoked'.

Apart from the chapters dealing with specific technologies such as glass, pottery, chemicals, and so on, the volume ends with an essay on 'The beginnings of the change from craft mystery to science as the basis for technology'. Such treatment helps to give perspective to masses of otherwise indigestible detail, and it is significant to note a remark in the editors' preface. They now announce that they have reserved 'all discussion of the profound economic and social changes that resulted from the tremendous technological process [the Industrial Revolution]' to the last volume. It is much to be hoped that they will reserve adequate space in what must obviously be the most crowded volume of all to treat this vitally important, and most neglected, aspect of the subject properly, because, if one were to level a criticism at an otherwise estimable team of editors, it is that so far they have displayed a blindspot for the social and economic consequences of the techniques they have otherwise so admirably presented.

EVOLUTION BY NATURAL SELECTION with a foreword by Sir Gavin de Beer (Cambridge, at the University Press, 1958, for the XV International Congress of Zoology and the Linnean Society of London), pp. 288, 25s.

A HANDBOOK OF EVOLUTION (London, British Museum (Natural History), 1958), pp. 110, 5s.

A CENTURY OF DARWIN edited by S. A. Barnett (London, Heinemann, 1958), pp. 376, 30s.

The twelve months from the beginning of July 1958, i.e., between the centenary of the communications to the Linnean Society of London of the papers on the origin of species by natural selection by Charles Darwin and Alfred Russel Wallace, and the centenary of the publication of Darwin's *Origin of Species*, is witnessing a great revival of interest in things Darwinian.

There can be few who are not familiar, at least in name, with Darwin's great production of 1849, but much less well known, though undeservedly, are the preliminaries to that great work. These trial canters, so to speak, have now been made available through the

volume from the Cambridge University Press published for the International Congress of Zoology and the Linnean Society.

The idea that species might be modified and the principle of natural selection whereby the changes might be produced occurred independently to Darwin and his younger contemporary Wallace. Darwin set down his ideas in a *Sketch* written in 1842, and amplified them into a more finished *Essay* in 1844. Neither received contemporary publication, however. The most that Darwin did was to arrange for his wife to have them published should he die prematurely, and as a result of the overwhelming success of the *Origin of Species* publication of the *Sketch* and *Essay* had to wait till 1909.

Wallace's ideas on the same subject crystallized fourteen years later than Darwin's, and it was the fact that Wallace sent Darwin a paper for criticism that stimulated the presentation to the world of the concept of natural selection. Now, the *Sketch*, *Essay*, and the papers presented to the Linnean Society by Darwin and Wallace have been published in one volume, with an introduction by Sir Gavin de Beer and the introduction to the *Sketch* and *Essay* written by Sir Francis Darwin when they were first published. Taken together these form a valuable and convenient contribution to the history of biology, and Sir Gavin claims for the *Essay* that 'it bears comparison with the *Origin* and, in some ways, may be preferred to it. It is [he says] fresher, shorter, simpler, more direct, and spends less space in countering possible objections which are now known to have been groundless. As Sir Ronald Fisher has pointed out, the *Essay* shows the reasons which led Darwin to his conclusions, whereas the *Origin* and later works only give the evidence on which they are based.' De Beer does not, however, stop at a critique of Darwin's writings. His twenty-page introduction constitutes a valuable outline of the history of evolution, covering not only Darwin's predecessors but evolutionary thought down to the present day, and the place it occupies in present-day thought.

To coincide with the visit of the International Congress to London, the British Museum (Natural History) has arranged a comprehensive new evolutionary exhibit, and has produced the second volume noticed above. The Handbook is intended to be a complement to the exhibits, part one being a brief introduction to evolution by natural selection, while the second part is devoted to a more detailed description of the various displays that can be seen in the Museum. There are a number of illustrations, not the least interesting of which is

the composition by the chimpanzee 'Congo'. As the International Congress was entertained with a Zoological Concert (The Wasps etc.) while in London, Congo's prowess with the brush suggests an extension to a 'salon des chimpanzés' at some future meeting.

Although the title of the third of the volumes, *A Century of Darwin*, which is competently edited by Dr S. A. Barnett of Glasgow, suggests a historical study, it is, in fact, considerably more. Fifteen authors, including many of the leading thinkers in the evolutionary field, contribute up-to-date reviews of the progress made in many of the topics touched by Darwin and impinged on by his work. C. H. Waddington deals with 'Theories of Evolution', Le Gros Clark with 'Man's Descent', J. Maynard Smith with 'Sexual Selection', and Daiches Raphael with 'Darwin and Ethics', to give but a few examples. As is obvious, a very wide stretch of human thinking is covered, and the volume can confidently be recommended to those, whether scientists or non-scientists, who are seeking an analysis of Darwin and his status in the contemporary scene.

NEW CHEMISTRY – A Scientific American Book (London, Bell, 1958), pp. 206, 13s 6d.

This is a further collection of articles reprinted from recent issues of *The Scientific American* which in small space gives a useful picture of current growing points in chemistry. The articles fall into four groups: new reactions, new methods, new elements, and new compounds.

Under new reactions, W. F. Libby, of radio-carbon dating fame, describes some ways in which radio atoms can be used to obtain new insight into chemical reactions; L. P. Lessing, flame reactions; F. Daniels, chemistry at 2,000° C; and P. D. Bartlett, the behaviour of free radicals. New methods include the ultramicrochemistry, brought into being by the development of nuclear energy; infra-red analysis; and the applications of chelation. New elements cover not only the man-made series beyond the naturally occurring uranium, but also the new significance that has been acquired by the once neglected rare earths.

Finally, four classes of new compounds are described; the silicones, the fluorine compounds of carbon that have opened up a new chapter in organic chemistry, synthetic rubber, and synthetic detergents. None of the chapters is long, but each gives a fully adequate review of developments in the field dealt with. There is no index, but

readers wishing to follow up the various topics will find a useful, and not wholly American, bibliography.

BIG MOLECULES – based on the Royal Institution Christmas Lectures by H. W. Melville (London, Bell, 1958), pp. 180, 15s.

At the Royal Institution over a hundred and twenty-five annual series of lectures have been given to children at Christmas. The latest in the series is covered by the present volume on the new and fascinating story of the chemical and physical investigation of molecules containing hundreds and even thousands of atoms.

For long such molecules defeated the ingenuity of chemists to take them apart, but the last twenty years have seen the development of techniques that enable chemists not only to get a knowledge of their structure but to design and build them so as to be suitable for specific purposes.

Many of these new molecules are of the greatest economic importance. They include all man-made fibres, electrically conducting rubber for aeroplane tyres and synthetic rubbers generally, ion-exchange resins for the purification of water, adhesives that will bond metal to metal, substitute blood plasma, soil conditioners, and so on.

While the Royal Institution Christmas Lectures are, to use the nineteenth century phrase, 'adapted to a juvenile auditory', the present series will appeal most to science sixth-formers, and to the many adults who were born before the present plastics age.

ABOUT OUR CONTRIBUTORS

W. B. BRIDGES was born in 1934 at Inglewood, California. He holds the B.S. and M.S. degrees of the University of California, where he is currently a doctoral candidate and teaching-research associate in the Electrical Engineering Department. His present research interest is noise in electron streams. He became acquainted with maser theory while with the research division of Varian Associates. He is a member of the Institute of Radio Engineers, American Institute of Electrical Engineers, American Radio Relay League, Eta Kappa Nu, Tau Beta Pi, Sigma Xi, and Phi Beta Kappa.

D. B. CARLISLE has been for the last eight years on the staff of the Marine Biological Laboratory at Plymouth where he holds the posts of endocrinologist and bursar. After graduating at Magdalen College, Oxford, he spent two years at the Naples Zoological Station. His interest in voyages of exploration in general dates from his childhood and seems to be almost a family failing. His brother engages in deep-sea exploration at the present day, while his wife wrote a thesis on the poet John Milton's use of the accounts of the old voyages of exploration in providing him with material for poetic imagery.

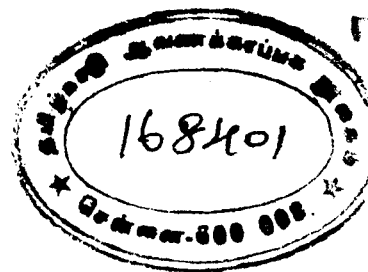
R. H. NIMMO-SMITH was born in Edinburgh in 1917, and educated at Fettes. He read in the Honours School of Animal Physiology at Oxford and completed his medical training in Edinburgh, where for three years he was a Lecturer in Physiology and worked on the mechanism of phosgene poisoning. In 1946 he returned to Oxford as a Demonstrator in Biochemistry, where he collaborated with D. D. Woods on inquiries arising out of the latter's discovery of the mode of action of sulphonamides and on other aspects of microbial metabolism. He obtained his D.Phil. in 1951 and four years later was appointed Biochemist in the Wellcome Laboratories of Tropical Medicine. All biochemical aspects of the host-drug-parasite 'triad' he finds intriguing. Broader interests include means of bridging the unnecessary gulf between scientists and non-scientists, and the part that science can play in reducing international tension. His non-scientific likings include trout-fishing, 'vintage' motor-cars, and exploring London.

A. C. ROSE-INNES began to study law at Merton College, Oxford, during the war, but after service in the Navy as a radar instructor changed to physics. Following graduation he remained at the

Clarendon Laboratory for three years in the low temperature department, studying organic free radicals by microwave methods, and obtained his D.Phil. in 1954. He is now at the Services Electronics Research Laboratory of the Admiralty where he has built a low temperature laboratory and is engaged in research on the conduction of electricity through solids. Married, with one son, he is interested in drawing and painting, but hates gardening.

J. R. SINGER. Since writing an earlier article, 'The Twilight of Parity Conservation', for *Science News* 46, Dr Singer, formerly Chief Staff Physicist of the National Scientific Laboratories, Inc., has joined the Electrical Engineering Department as an associate professor at the University of California, Berkeley, California. His interests are in magnetic materials, masers, and raising a family, though perhaps not in that order.

W. E. SWINTON is a Principal Scientific Officer of the Palaeontological Department of the British Museum (Natural History) where he is concerned with the fossil amphibians, reptiles, and birds. He has been especially interested in dinosaurs and has travelled extensively in both Europe and America visiting dinosaur localities and collections. He was educated at Trinity College, Glenalmond, and at Glasgow University. He is the author of *The Dinosaurs*; *The Corridor of Life*; *Geology in the Museum*; and the British Museum handbooks *Fossil Amphibians and Reptiles* and *Fossil Birds*. He is a Fellow of the Royal Society of Edinburgh, a member of Council of the British Association, and President of the Museums Association.



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