# The Laboratory of the Living Organism.[1]

By DR. M. O. FORSTER, F.R.S.

MANY and various are the reasons which have been urged, at different periods of its history, for stimulating the study of chemistry. In recent years these have been either defensive or frankly utilitarian, in the latter feature recalling the less philosophic aspects of alchemy; moreover, it is to be feared that a substantial proportion of those who have lately hastened to prepare themselves for a chemical career have been actuated by this inducement. It is the duty, therefore, of those who speak with any degree of experience to declare that the only motive for pursuing chemistry which promises anything but profound disappointment is an affection for the subject sufficiently absorbing to displace the attraction of other pursuits. Even to the young chemist who embarks under this inspiration the prospect of success as recognised by the world is indeed slender, but, as his knowledge grows and the consequent appreciation of our ignorance widens, enthusiasm for the beauty and mystery of surrounding nature goes far in compensating for the disadvantages of his position. Not only do chemical principles underlie the operations of every industry, but every human being—indeed, every living plant and animal—is, during each moment of healthy life, a practical organic and physical chemist, conducting analytical and synthetical processes of the most complex order with imperturbable serenity. No other branch of knowledge can appeal for attention on comparable grounds; and without suggesting that we should all, individually, acquire sufficient chemical understanding fully to apprehend the changes which our bodies effect so punctually and so precisely—for this remains beyond the power of trained chemists—it may be claimed that an acquaintance with the general outlines of chemistry would add to the mental equipment of our people a source of abundant intellectual pleasure which is now unfairly denied them. In following the customary practice of surveying matters of interest which have risen from our recent studies, therefore, it is the purpose of this address to emphasise also those æsthetic aspects of chemistry which offer ample justification for the labour which its pursuit involves.

What is breakfast to the average man? A hurried compromise between hunger and the newspaper. How does the chemist regard it? As a daily miracle which gains, rather than loses, freshness as the years proceed. For just think what happens. Before we reach the table frizzled bacon, contemplated or smelt, has actuated a wonderful chemical process in our bodies. The work of Pavlov has shown that if the dog has been accustomed to feed from a familiar bowl the sight of that bowl, even empty, liberates from the appropriate glands a saliva having the same chemical composition as that produced by snuffing the food. This mouth-watering process, an early experience of childhood, is known to the polite physiologist as a "psychic reflex," and the various forms assumed by psychic reflex, responding to the various excitations which arise in the daily life of a human being, must be regarded by the chemical philosopher as a series of demonstrations akin to those which he makes in the laboratory, but hopelessly inimitable with his present mental and material resources. For, extending this principle to the other chemical substances poured successively into the digestive tract, we have to recognise that the minute cells of which our bodies are co-ordinated assemblages possess and exercise a power of synthetic achievement contrasted with which the classical syntheses, occasionally enticing the modern organic chemist to outbursts of pride, are little more than hesitating preliminaries. Such products of the laboratory, elegant as they appear to us, represent only the fringe of this vast and absorbing subject. Carbohydrates, alkaloids, glucosides, and purines, complex as they seem when viewed from the plane of their constituent elements, are but the molecular debris strewing the path of enzyme action and photochemical synthesis, whilst the enzymes produced in the cells, and applied by them in their ceaseless metamorphoses, are so far from having been synthesised by the chemist as to have not even yet been isolated in purified form, although their specific actions may be studied in the tissue-extracts containing them.

Reflect for a moment on the specific actions. The starch in our toast and porridge, the fat in our butter, the proteins in our bacon, all insoluble in water, by transformations otherwise unattainable in the laboratory are smoothly and rapidly rendered transmissible to the blood, which accepts the products of their disintegration with military precision. Even more amazing are the consequences. Remarkable as the foregoing analyses must appear, we can dimly follow their progress by comparison with those more violent disruptions of similar materials revealed to us by laboratory practice, enabling such masters of our craft as Emil Fischer to isolate the resultant individuals. Concurrently with such analyses, however, there proceed syntheses which we can scarcely visualise, much less imitate. The perpetual elaboration of fatty acids from carbohydrates, of proteins from amino-acids, of zymogens and hormones as practised by the living body are beyond the present comprehension of the biochemist; but their recognition is his delight, and the hope of ultimately realising such marvels provides the dazzling goal towards which his efforts are directed.

[1] Abridged from the presidential address delivered to Section B (Chemistry) of the British Association at Edinburgh on September 8.

*The Vegetable Alkaloids.*

It should not be impossible to bring the skeleton of these transformations within the mental horizon of those who take pleasure in study and reflection; and to those also the distinction between plants and animals should be at least intelligible. The wonderful power which plants exercise in building up their tissues from carbonic acid, water, and nitrogen, contrasted with the powerlessness of animals to utilise these building materials until they have been already assembled by plants, is a phenomenon too fundamental and illuminating to be withheld, as it now is, from all but the few. For by its operation the delicate green carpet, which we all delight in following through the annual process of covering the fields with golden corn, is accomplishing throughout the summer months a vast chemical synthesis of starch for our benefit. Through the tiny pores in those tender blades are circulating freely the gases of the atmosphere, and from those gases—light, intangible nothingness, as we are prone to regard them—this very tangible and important white solid compound is being elaborated. The chemist cannot do this. Plants accomplish it by their most conspicuous feature, greenness, which enables them to put solar energy into cold storage; they are accumulating fuel for subsequent development of bodily heat energy. Side by side with starch, however, these unadvertised silent chemical agencies elaborate molecules even more imposing, in which nitrogen is interwoven with the elements of starch, and thus are produced the vegetable alkaloids.

In this province the chemist has been more fortunate, and successive generations of students have been instructed in the synthesis of piperine, coniine, trigonelline, nicotine, and extensions from the artificial production of tropine; but until quite recently his methods have been hopelessly divergent from those of the plant. Enlightening insight into these, however, was given just four years ago by R. Robinson, who effected a remarkably simple synthesis of tropinone by the mere association of succindialdehyde, methylamine, and acetone in water, unassisted by a condensing agent or an increase of temperature. Based upon this experiment, R. Robinson (1917) has developed an attractive explanation of the phytochemical synthesis of alkaloids, in which the genesis of a pyrrolidine, piperidine, quinunuclidine, or *iso*-quinoline group is shown to be capable of proceeding from the association and interaction of an amino-acid, formaldehyde, acetonedicarboxylic acid and the intermediate products of these, taking place under the influence of oxidation, reduction, and condensation such as the plant is known to effect. Thus it may be claimed that Robinson's theory represents a notable advance in our conception of these vital changes, and that by means of the carbinolamine and aldol condensations involved fruitful inquiries into constitution and the mechanism of synthesis will follow.

*The Nucleic Acids.*

Owing to the venerable position occupied by alkaloids in the systematic development of chemical science, and to the success which has attended elucidation of their structure, many of us have become callous to the perpetual mystery of their elaboration. Those who seek fresh wonders, however, need only turn to the nucleic acids in order to satisfy their curiosity. For in the nucleic acid of yeast the chemist finds a definite entity forming a landmark in the path of metabolic procedure, a connecting link between the undefined molecules of living protein and the crystallisable products of katabolic disintegration. In the language of chemistry it is a combination of four nucleotides, linked with one another through the pentose molecule, *d*-ribose, which is common to each, and owing its acid character to phosphoric acid, also common to the component nucleotides. The latter differ from one another in respect of their nitrogenous factors, which are guanine (2-amino-6-oxypurine), adenine (6-aminopurine), uracil (2 : 6-dioxypyrimidine), and cytosine (2-oxy-6-aminopyrimidine), giving their names to the four nucleotides. The transformations undergone by nucleic acid in contact with tissue extracts have provided the subjects of numerous investigations extending over thirty years. In fact, the experimental material is of such voluminous complexity as to be unintelligible without the guidance of an expert, and in this capacity W. Jones has rendered valuable service by his recent lucid arrangement of the subject (1921). From this it is comparatively easy to follow the conversion of nucleic acid into uric acid through the agency of enzymes, and a review of these processes can serve only to increase our admiration for the precision and facility with which the chemical operations of the living body are conducted.

Considerable progress has been made also in localising the various enzymes among the organs of the body, particularly those of animals. Into the results of these inquiries it is not the purpose of this address to enter further than to indicate that they reveal a marvellous distribution, throughout the organism, of materials able to exert at the proper moment those chemical activities appropriate to the changes which they are required to effect. The contemplation of such a system continuously, and in health unerringly, completing a series of chemical changes so numerous and so diverse must produce in every thoughtful mind a sensation of humble amazement. The aspect of this miraculous organisation which requires most to be emphasised, however, is that an appreciation of its complex beauty can be gained only by those to whom at least the elements of a training in chemistry have been vouchsafed. Such training has potential value from an ethical standpoint, for chemistry is a drastic leveller; in the nucleic acids man discovers a kinship with yeast-cells, and in their common failure to transform uric acid into allantoin he finds a fresh bond of sympathy with apes. The overwhelming majority of people arrive at the grave, however, without having had the slightest conception of the delicate chemical machinery and the subtle physical changes which, throughout each moment of life, they have methodically and unwittingly operated.

*Chlorophyll and Haemoglobin.*

To those who delight in tracing unity among the bewildering intricacies of natural processes, and by patient comparison of superficially dissimilar materials triumphantly to reveal continuity in the discontinuous, there is encouragement to be found in the relationship between chlorophyll and hæmoglobin. Even the most detached and cynical observer of human failings must glow with a sense of worship when he perceives this relationship, and thus brings himself to acknowledge the commonest of green plants among his kindred. Because, just as every moment of his existence depends upon the successful performance of its chemical duties by the hæmoglobin of his blood corpuscles, so the life and growth of green plants hinge on the transformations of chlorophyll. The persevering elucidation of chlorophyll structure ranks high in the achievements of modern organic chemistry, and in its later stages is due principally to Willstätter and his collaborators, whose investigations culminated in 1913.

This is not an occasion to follow, otherwise than in the barest outline, the course of laboratory disintegration to which the chlorophyll molecules have been subjected by the controlled attack of alkalis and acids. The former agents reveal chlorophyll in the twofold character of a lactam and a dicarboxylic ester of methyl alcohol and phytol, an unsaturated primary alcohol, $C_{20}H_{39}.OH$, of which the constitution remains obscure in spite of detailed investigation of its derivatives; but the residual complex, representing two-thirds of the original molecule, has been carefully dissected. The various forms of this residual complex, when produced by the action of alkalis on chlorophyll, have been called "phyllins"; they are carboxylic acids of nitrogenous ring-systems, which retain magnesium in direct combination with nitrogen. The porphyrins are the corresponding products arising by the action of acids; they are carboxylic acids of the same nitrogenous ring-systems from which the magnesium has been removed. The phyllins and the porphyrins have alike been degraded to the crystalline base, ætioporphyrin, into the composition of which four variously substituted pyrrole rings enter. It is this assemblage of substituted pyrroles which, according to present knowledge, is the basic principle also of the blood-pigment, in which iron plays the part of magnesium in chlorophyll.

*Anthocyans, the Pigments of Blossoms and Fruits.*

Since the days of Eden, gardens have maintained and extended their silent appeal to the more gentle emotions of mankind. The subject possesses a literature, technical, philosophical, and romantic, at least as voluminous as that surrounding any other industrial art, and the ambition to cultivate a patch of soil has attracted untold millions of human beings. Amongst manual workers none maintains a standard of orderly procedure and patient industry higher than that of the gardener. Kew and La Mortola defy the power of word-painters to condense their soothing beauty into adequate language, whilst that wonderful triangle of cultivation which has its apex at Grasse almost might be described as industry with a halo.

Prior to 1913 the most fruitful attempt to isolate a colouring-matter from blossoms in quantity sufficient for detailed examination had been made by Grafe (1911), but the conclusions to which it led were inaccurate. In the year mentioned, however, Willstätter began to publish with numerous collaborators a series of investigations, extending over the next three years, which have brought the subject within the realm of systematic chemistry. For the purpose of distinguishing glucosidic and non-glucosidic anthocyans the names anthocyanin and anthocyanidin respectively were applied. The experimental separation of anthocyanins from anthocyanidins was effected by partition between amyl alcohol and dilute mineral acid, the latter retaining the diglucosidic anthocyanins in the form of oxonium salts and leaving the anthocyanidins quantitatively in the amyl alcohol, from which they are not removed by further agitation with dilute acid; the monoglucosidic anthocyanins were found in both media, but left the amyl alcohol when offered fresh portions of dilute acid.

The earliest of these papers, published in conjunction with A. E. Everest, dealt with cornflower pigments, and indicated that the distinct shades of colour presented by different parts of the flower are caused by various derivatives of one substance; thus the blue form is the potassium derivative of a violet compound which is convertible into the red form by oxonium salt-formation with a mineral or plant acid. Moreover, as found in blossoms, the chromogen was observed to be combined with two molecular proportions of glucose and was isolated as crystalline cyanin chloride; hydrolysis removed the sugar and gave cyanidin chloride, also crystalline. Applying these methods more generally, Willstätter and his other collaborators have examined the chromogens which decorate the petals of rose, larkspur, hollyhock, geranium, salvia, chrysanthemum, gladiolus, ribes, tulip, zinnia, pansy, petunia, poppy, and aster, whilst the fruit-skins of whortleberry, bilberry, cranberry and cherry, plum, grape, and sloe have also been made to yield the pigment to which their characteristic appearance is due.

*Micro-biochemistry.*

Amongst the many sources of pleasure to be found in contemplating the wonders of the universe, and denied to those untrained in scientific principles, is an appreciation of infra-minute quantities of matter. It may be urged by some that within the limits of vision imposed by telescope and microscope, ample material exists to satisfy the curiosity of all reasonable people, but the appetite of scientific inquiry is insatiable, and chemistry alone, organic, inorganic, and physical, offers an instrument by which the investigation of basal changes may be carried to regions beyond those encompassed by the astronomer and the microscopist.

It is not within the purpose of this address to survey that revolution which is now taking place in the conception of atomic structure. Fortunately for our mental balance the discoveries of the current century, whilst profoundly modifying the atomic imagery inherited from our predecessors, have not yet seriously disturbed the principles underlying systematic organic chemistry; but they emphasise in a forcible manner the intimate connection between different branches of science, because it is from the mathematical physicist that these new ideas have sprung. Their immediate value is to reaffirm the outstanding importance of borderline research and to stimulate interest in submicroscopic matter. This interest presents itself to the chemist very early in life and dominates his operations with such insistence as to become axiomatic. So much so that he regards the universe as a vast theatre in which atomic and molecular units assemble and interplay, the resulting patterns into which they fall depending on the physical conditions imposed by Nature. This enables him to regard micro-organisms as co-practitioners of his craft, and the chemical achievements of these humble agents have continued to excite his admiration since they were revealed by Pasteur.

Lamenting as we now do so bitterly the accompaniments and consequences of war, it is but natural to snatch at the slender compensations which it offers, and not the least among these must be recognised the stimulus which it gives to scientific inquiry. Pasteur's *Etudes sur la Bière* were inspired by the misfortunes which overtook his country in 1870–71, and the now well-known process of Connstein and Lüdecke for augmenting the production of glycerol from glucose was engendered by parallel circumstances. That acquaintance with the yeast-cell which was an outcome of the former event had, by the time of the latter discovery, ripened into a firm friendship, and those who slander the chemical activities of this genial fungus are defaming a potential benefactor. Equally culpable are those who ignore them. If children were encouraged to cherish the same intelligent sympathy with yeast-cells which they so willingly display towards domestic animals and silkworms, perhaps there would be fewer crazy dervishes to deny us the moderate use of honest malt-liquors and unsophisticated wines fewer pitiable maniacs to complicate our socia problems by habitual excess.

*Conclusion.*

In "The Salvaging of Civilisation," H. G. Wells has lately directed the attention of thoughtful people to the imperative need of reconstructing our outlook on life. Convinced that the state-motive which, throughout history, has intensified the self-motive must be replaced by a world-motive if the whole fabric of civilisation is not to crumble in ruins, he endeavours to substitute for a League of Nations the conception of a World State. In the judgment of many quite benevolent critics his essay in abstract thought lacks practical value because it underestimates the combative selfishness of individuals. Try to disguise it as one may, this quality is the one which has enabled man to emerge from savagery, to build up that most wonderful system of colonial organisation, the Roman Empire, and to shake off the barbaric lethargy which engulfed Europe in the centuries following the fall of Rome. The real problem is how to harness this combative selfishness. To eradicate it seems impossible, and it has never been difficult to find glaring examples of its insistence among the apostles of eradication. Why cry for the moon? Is it not wiser to recognise this quality as an inherent human characteristic, and whether we brand it as a vice or applaud it as a virtue endeavour to bend it to the elevation of mankind? For it could so be bent. Nature ignored or misunderstood is the enemy of man; Nature studied and controlled is his friend. If the attacking force of this combative selfishness could be directed, not towards the perpetuation of quarrels between different races of mankind, but against Nature, a limitless field of patience, industry, ingenuity, imagination, scholarship, aggressiveness, rivalry, and acquisitiveness would present itself; a field in which the disappointment of baffled effort would not need to seek revenge in the destruction of our fellow-creatures: a field in which the profit from successful enterprise would automatically spread through all the communities. Surely it is the Nature-motive, as distinct from the state-motive or the world-motive, which alone can salvage civilisation.

Before long, as history counts time, dire necessity will have impelled mankind to some such course. Already the straws are giving their proverbial indication. The demand for wheat by increasing populations, the rapidly diminishing supplies of timber, the wasteful ravages of insect pests, the less obvious, but more insidious depredations of our microscopic enemies, and the blood-curdling fact that a day must dawn when the last ton of coal and the last gallon of oil have been consumed, are all circumstances which, at present recognised by a small number of individuals comprising the scientific community, must inevitably thrust themselves upon mankind collectively. In the campaign which then will follow, chemistry must occupy a prominent place because it is this branch of science which deals with matter more intimately than any other, revealing its properties, its transformations, its application to existing needs, and its response to new demands. Yet the majority of our people are denied the elements of chemistry in their training, and thus grow to manhood without the slightest real understanding of their bodily processes and composition, of the wizardry by which living things contribute to their nourishment and to their æsthetic enjoyment of life.

It should not be impossible to bring into the general scheme of secondary education a sufficiency of chemical, physical, mechanical, and biological principles to render every boy and girl of sixteen possessing average intelligence at least accessible by an explanation of modern discoveries. One fallacy of the present system is to assume that relative proficiency in the inorganic branch must be attained before approaching organic chemistry. From the point of view of correlating scholastic knowledge with the common experiences and contacts of daily life this is quite illogical; from baby's milk to grandpapa's Glaxo the most important things are organic, excepting water. Food (meat, carbohydrate, fat), clothes (cotton, silk, linen, wool), and shelter (wood) are organic, and the symbols for carbon, hydrogen, oxygen, and nitrogen can be made the basis of skeleton representations of many fundamental things which happen to us in our daily lives without first explaining their position in the periodic table of all the elements. The curse of mankind is not labour, but waste; misdirection of time, of material, of opportunity, of humanity.

Realisation of such an ideal would people the ordered communities with a public alive to the verities, as distinct from irrelevancies of life, and apprehensive of the ultimate danger with which civilisation is threatened. It would inoculate that public with a germ of the Nature-motive, producing a condition which would reflect itself ultimately upon those entrusted with government. It would provide the mental and sympathetic background upon which the future truth-seeker must work, long before he is implored by a terrified and despairing people to provide them with food and energy. Finally, it would give an unsuspected meaning and an unimagined grace to a hundred commonplace experiences. The quivering glint of massed bluebells in broken sunshine, the joyous radiance of young beech-leaves against the stately cedar, the perfume of hawthorn in the twilight, the florid majesty of rhododendron, the fragrant simplicity of lilac, periodically gladden the most careless heart and the least reverent spirit; but to the chemist they breathe an added message, the assurance that a new season of refreshment has dawned upon the world, and that those delicate syntheses, into the mystery of which it is his happy privilege to penetrate, once again are working their inimitable miracles in the laboratory of the living organism.

## Metaphysics and Materialism.

By PROF. H. WILDON CARR.

"IF the illusion of the scholastic method is that from mere forms we can deduce essences, then the world-view which we call materialism is only a scholastic pastime." This is the concluding sentence of Hermann Weyl's "Raum, Zeit, Materie." Whatever may be the case with the physicists, the mathematicians are under no illusion with regard to the completeness of the scientific revolution. The principle of relativity has not merely complicated the concept of physical reality; it has re-formed it. Mathematics is, and has always been recognised as being, a constructive process of the human mind exercised on physical existence. The old mathematics took its matter from physics; the new mathematics gives matter to physics. The effect is that the world-view which had become for physical science in the nineteenth century practically unchallengeable, and the acceptance of which had come to be regarded as the indispensable condition and only passport for those who would enter the ranks of scientific investigators, has become suddenly incredible. It is true, indeed, that it still has its defenders, and that it is held as firmly as ever by many who continue to be in their special departments authoritative teachers; but this does not alter the fact that for us to-day the world-view is changed, and it is not even strange that many leaders in scientific research still cling fast to the old view when we remember that the great originator of the modern inductive method in the seventeenth century, Francis Bacon, to the end rejected the Copernican theory.

Materialism does not stand for any particular theory of the nature of matter, but for the general world-view that matter, something *de facto* objective the ultimate constitution of which we may not know, and even may not be able to know, but which is entirely independent of our reason and of any thoughts we may have about it, exists and constitutes the reality of the universe, including reason and will, which as qualities or properties of some of its forms give rise to knowledge of it. This materialism reached the zenith of its expression in the Darwinian theory of natural selection, not in that theory itself, the truth of which there is no intention in this connection to call in question, but in the implications which were generally accepted as contained in it, and especially in the application which was made of it to rationalise a world-view. It seemed to point a way by which it was possible to conceive, and to some extent to follow in its history, an evolution which had produced mind from an original matter.

It may not be obvious at once that the mere rejection of the Newtonian concept of absolute space and time and the substitution of Einstein's