other elemental things, such as quantum interactions, are described in terms of conceptual experiments, and from simple properties deduce more complicated properties in much the fashion of Euclid. In fact, the resemblance between this ideal and Euclid is a rather close one, for that part of the analysis of Euclid which consists in moving figures about and comparing them by superposition amounts to nothing more than conceptual experiments with geometrical figures. A systematic development of the conceptual experiment would be found by many, I believe, to give a more illuminating insight than a painful acquisition of the details of the present mathematical picture.

As suggestive of what may be done here, I append a list of questions which are to be answered in terms of conceptual experiments allowed by the new point of view.

(1) Are experiments on single "naked" electrons possible? How may one be sure that he has a single electron in his apparatus? Are there any methods of detecting the presence of an electron that do not demand that the electron be traveling with fairly high velocity? Can a stationary electron be detected?

(2) How may the charge of a single electron be measured? Is there any theoretical limit to the accuracy with which a single measurement of charge may be made? Or is an accurate value of e obtainable only from statistical measurement?

(3) What is the evidence that an electron has independent existence in empty space? May one electron stream receive a deflection on impinging on another?

(4) Is the equivalence of the charge on electrons and protons a statistical or an individual effect? How accurately may the charge of an individual electron and proton be proved equal?

(5) How may the magnetic moment of a single electron be found?

(6) What properties may an electron have simultaneously? We know that it can not simultaneously have position and velocity. May the charge, the mass, the momentum and the energy be simultaneously determined?

(7) Is a single electron subject to a gravitational field?

(8) To what extent does an electron have identity? May it be observed continuously, or is there a minimum time between successive observations?

(9) How do the measurable properties of an electron in those places where, according to the wave mechanics, the kinetic energy is negative differ from those of a classical electron?

(10) How may the frequency of a single photon be measured?

(11) May the frequency of a single photon be measured without at the same time compelling it to have some direction, that is, are frequency and direction independent properties?

(12) May the energy of a single photon be measured independently of its frequency?

(13) Does a single photon have a plane of polarization, that is, may the plane of polarization of a single photon be measured? (I have been able to discover no method of doing this.)

(14) Can the velocity of a single photon be measured? All experimental determinations of the velocity of light have been essentially measurements on a steady state.

(15) What experimental method is there of detecting the motion of a single photon?

(16) How many properties does an individual photon have simultaneously? For example, may the velocity, the frequency, the direction, the momentum and the energy be measured simultaneously?

(17) Does a photon have independent existence in empty space? Can two crossed streams of photons be made to disturb each other?

(18) To what extent does a photon have identity?

(19) Is there any method by which the emission of a photon from an atom may be detected which does not involve receiving the emitted photon?

(20) What sort of a constant is h? May it be determined from a single quantum process, or is it essentially statistical? The six methods for determining h listed by Birge are all essentially statistical.

(21) Is there any evidence that two quantum processes ever interfere with each other, or that one begins before the other has ended?

It will very probably be found that the answers to some of these questions can not at present be given without a rather intimate acquaintance with mathematical theory, but I believe that this is merely a temporary phase and that ultimately we shall be able to demand that our theories be so formulated that we can answer these and other questions intuitively without recourse to formal mathematics. In the meantime, I believe that any one who attempts to devise the conceptual experiments by which these questions may be answered is not only increasing his own understanding of fundamentals but is also making an important contribution to physical progress.

THE MUTUAL INFLUENCE OF ORGANIC COMPOUNDS IN THE ANIMAL BODY

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SEVERAL papers read at the Thirteenth International Physiological Congress in Boston impressed the writer as showing that the ideas of the reciprocal influences between organic substances in the sense of an exchange of energy between each other are not sufficiently known. It seems to me to be important that the simple basis of this kind of consideration should become better appreciated by biologists, and I should like to try to collect into a generally comprehensible form what it was impossible to say in the short time allowed for discussion during the meetings.

Many processes of reduction occur in the animal body for which energy requirements can not, as in plants, be covered by the direct transformation of the rays of the sun. This energy may be supplied by the heat liberated by any process of combustion, as exemplified by fat-production following feeding carbohydrates exclusively. If the organism reduces a ketone to an alcohol, it needs H_2, which is not directly at its disposal. Therefore, another organic compound, undergoing oxidation, gives H_2 not to oxygen, but to the reducible substance and transfers with it part of its heat of combustion. The simplest example of this kind is the disproportion of 2 mol. of aldehyde into 1 mol. of alcohol and 1 mol. of acid (Canizzaro). The heats of combustion in this case are for acetaldehyde:

$$\underset{\text{2 mol. Aldehyde}}{(2 \times 282 =)564 \text{ Cal.}} = \underset{\text{Alcohol}}{340 \text{ Cal.}} + \underset{\text{Acid}}{209 \text{ Cal.}} + 15 \text{ free Cal.}$$

One molecule of alcohol gains 58 calories from the acid, which contains 75 calories less than the aldehyde. The 15 remaining calories are liberated as heat, thus indicating why the process may take place spontaneously according to general physical laws and can well be accelerated by catalysts. Parnas in Hofmeister's Institute has shown that there are ferments in the animal body which catalyze this reaction with numerous aldehydes.

Wieland has shown in his theory of dehydrogenation that for many oxidative processes the primary and essential reaction is not the entrance of oxygen, but the removal of hydrogen. This H_2 is mostly bound by O_2 when the oxidation takes place in a high O_2 concentration. And since Wieland could demonstrate that $H_2 + O_2$ form H_2O_2, so he proved definitely the value of his idea and, incidentally, the purpose of katalase. Wieland has shown that other substances than oxygen can bind this hydrogen in experiments which agree with those of Thunberg, Schardinger and others. Methylene-blue quinones and analogous substances act here principally as in Canizzaro's reaction —the aldehyde which takes up hydrogen is converted into alcohol. One substance is hydrogenated by another one: the first takes up energy which is provided by the second. The mutual relations of these two substances are believed to be analogous to those existing between many compounds *in vivo* and to typify the energy exchanges of many biological reactions.

The living organism is able to facilitate such oxido-reductions between substances of widely differing kind. It has been known for a long time that aldehydes can be converted into alcohols. The H_2 can only be supplied by other organic bodies. For the hydrogenation of unsaturated linkages and for the transformation even of carbonyl to methylene groups exact chemical proofs can be found in our first paper on β-oxidation. Benzallaevulinic acid is transformed by the dog into phenyl-α-oxybutyric acid, a change requiring both oxidation and hydrogenation of double bonds and carbonyl groups:

$$C_6H_5 \cdot CH = CH \cdot CO \cdot CH_2 \cdot CH_2 \cdot COOH \rightleftarrows$$
$$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CHOH \cdot COOH [+ C_2 \cdot {}^2]$$ [1]

Such a transference of hydrogen from one compound to another can also be effected by a third substance. It will always remain as a memorable contribution by Hopkins that he found in glutathione a substance illustrating this function. The SH-group of glutathione is able to furnish this hydrogen or to accept it, and so can reduce or oxidize other substances. Glutathione now is made responsible for all kinds of reductions, even where evidence is lacking. But there is no reason to believe that glutathione is a unique substance of this kind: certainly such processes are facilitated in the body by many compounds of different composition. We have long known that iron in its two stages of oxidation can perform the same function. Organic substances can doubtless act similarly.

Most oxy- and ketonic acids are mutually interconvertible; acetoacetic acid, for example, oxidizes another substance if it robs it of hydrogen and is converted into oxybutyric acid; on the other hand, acetoacetic acid reduces it, if the added hydrogen is transferred to other bodies. The foregoing example can not perhaps be regarded as proved in all details, but other analogous reactions are known. An interesting example is offered by the amino acids, which have thus a new and important function.

Neubauer has shown that the first phase of the decomposition of amino acids in the animal body is an oxidative transformation to a ketonic acid and ammonia. And we have been able to analyze the reaction further after we found the reaction to be reversible.[2] It can for the present be ignored whether an amino-, oxyamino- or an α-β unsaturated acid is first formed—the important fact is that the process of oxidation involving loss of hydrogen can be made retrogressive and the amino acids can be reformed.

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[1] *Hoppe Seyler's Ztschr. für physiolog. Chemie*, 89: 141, 1914.

[2] *Idem*, 67: 489, 1914; 71: 252, 1911.

When this was demonstrated, an old principle was abandoned according to which the chemistry of plants and animals could be fundamentally differentiated by the assumption that the plants can assimilate inorganic nitrogen, but that animals can not do so. This new discovery produced at first only a great deal of discussion concerning its quantitative value, which may be small. But the principle involved in this reaction was ignored. Therefore we have examined more closely the ease with which reduction occurs in this reaction. We have found the surprising result that the reaction takes place very easily. It is well known that a ketonic acid is easily reduced to an oxy acid and that the body can do the same thing. But in the presence of only a small amount of ammonia, and the theoretical quantity of hydrogen at room temperature, an α-ketonic acid yields α-amino acids, and little or no oxy acid—which was quite a new result. This synthesis of an amino acid needs less energy than the synthesis of the oxy acid, and this is probably the reason why the latter are usually formed in small amounts. Extended experiments with other ketonic acids and with secondary and tertiary amine bases clearly indicate the general form of the synthesis of the amino acids in nature, which certainly does not follow the same lines that chemists have found in their laboratories. The reaction can be accelerated by catalysts so that 75 per cent. yields of pure amino acids can be obtained at room temperature in a few minutes.[3]

Even if the reaction proceeds only to a limited extent, the system ketonic acid plus ammonia must be able to take up hydrogen from other substances and to oxidize them with regeneration of the original amino acid. The constant combustion of protein in the body provides continually for the new formation of this system, and we have concluded that this reversibility[4] of the first oxidative phase of the degradation of amino acids entitles them to the rôle first of hydrogen-donators and secondly of hydrogen-acceptors. They act after all in principle like Hopkins glutathione.[5] We have further found that this same system can oxidize cystein to cystin with simultaneous formation of the original amino acid.[6] And Bergmann and Enslin[7] have now confirmed the truth of our conclusions. They have demonstrated that the small differences in the redoxpotentials (Michaelis) of individual amino acids suffice to enable one amino acid undergoing the first phase of decomposition to oxidize a second one, with re-formation of the original amino acid. This relationship has been demonstrated between phenylalanin (as phenylpyruvic acid plus ammonia) and aspartic acid. . . .[7]

We must therefore attribute to a great number of organic compounds the capacity to transfer energy from other substances or to furnish it—to oxidize or reduce them. One may be allowed to generalize from these ideas and say that probably every organic substance in the body has in relation to every other one a certain redoxpotential, which will vary according to the conditions, for example, of the pH, of temperature, of O_2 concentration, of the catalysts present, etc. And since the animal can vary these external conditions to a considerable extent, we believe that in the living organism the processes of synthesis and decomposition are regulated by a continuous conflict of all kinds of substances with each other. The extraordinary fineness of the chemical adjustments of the animal body must be referred to this multiplicity of reciprocal actions between all the products of intermediary metabolism. It may be noted that according to this view chemical regulation of the organism's activity may be regarded for the moment to some extent independent of the essential supply of oxygen. We have for long urged that more attention be given to the reciprocal influences of organic substances on one another. In this way we shall acquire a greater knowledge of the chemical abilities of the living cell. I hope that the physical-chemical kind of treatment which Michaelis gives in his new book on redoxpotentials will give us great help. Certainly it emphasizes from a new side the importance of these questions to chemists and physiologists. Reactions such as those referred to are of great general biological interest; for example, the capacity to transform the groups of the main foodstuffs into one another.[8] Thus, the synthesis of fat from protein or sugar, the amino acids of proteins from carbohydrates, etc., gives to animals a wide independence as to the kind of food which is essential.[9] Without these chemical capabilities a much greater amount of animal life would die continually, and especially for the chemist of the anoxybiotics these abilities are of the greatest importance. The animal body can perform all these transformations only because it is enabled to bring in reaction all types of organic substances in a manner which can be here discussed only in general outlines.

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[3] *Idem,* 148: 294, 1925.

[4] The word reversible is used only in the sense of "biologically reversible" and not in the strict physicochemical sense.

[5] *Hoppe Seyler's Ztschr. für physiolog. Chemie,* 148: 302, 1925.

[6] *Idem,* 170: 186, 1927.

[7] *Idem,* 174: 76, 1928.

[8] *Klin. Wochenschrift,* 2: 60, 1923.

[9] *Münch. med. Wochenschrift,* 73: 2151, 1926.