

THE DUBLIN JOURNAL

OF

MEDICAL SCIENCE.

JANUARY 1, 1907.

PART I.

ORIGINAL COMMUNICATIONS.

ART. I.—*Catalysis and Some of its Applications to the Arts and Medicine.*^a By WALTER G. SMITH, M.D., F.R.C.P.I.; King's Professor of Materia Medica, School of Physic; Physician to Sir Patrick Dun's Hospital.

CATALYSIS.

Chemical Affinity.—Of all the great old-standing problems of chemistry that of chemical affinity has been least developed. Chemical affinity is the name given to that property of bodies in virtue of which when brought into contact they react with each other, forming new bodies. It is the driving power of a chemical reaction. There is always a change of energy, and, in fact, transformation of energy is at the root of every chemical or physical process. The term affinity (*affinitas*—i.e., relationship) reaches back to Greek philosophy. The Grecian philosophers considered it as somewhat similar to human qualities—e.g., sympathy and antipathy. The meaning now attaching to it in chemistry is exactly the converse

^a Read before the Dublin Biological Club, February 13, 1906; and before the D. U. Exper. Assoc., February 20, 1906.

of the ancient notion: not "likes" but "unlikes" attract each other. The conception, however, of affinity as an attractive force is of little or no use in explaining chemical phenomena. What the intimate nature of chemical affinity really is we know no more to-day than did the chemists of old.

No satisfactory hypothesis has yet found acceptance among scientific men, and I will not spend time in discussing the different hypotheses which have been advanced.

Light is, however, beginning to dawn upon the darkness, and it comes from four quarters:—

(a) The introduction of mechanical ideas into chemistry. For this we have to thank Galileo. Chemical statics and dynamics are now securely established, and have yielded fruitful and stimulating results in the hands of van 't Hoff, Arrhenius, and many others.

(b) The introduction of quantitative determinations of the rate and amount of chemical change, as distinguished from vague data, such as the older tables of affinity and the like. One of the main objects of scientific chemistry is to measure the intensity of chemical affinity in different cases.

(c) The bringing of chemical problems under the controlling sway of mathematical calculation. The higher walks of theoretical chemistry and of physiology are becoming difficult or impossible to follow without some mathematical training.

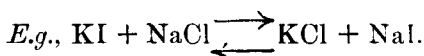
The modern chemist may almost say with Descartes:—"I will accept nothing as true but what is declared (from the first principle that matter can be divided, figured, and moved in all sorts of ways) by direct evidence which can take rank of a mathematical demonstration."

(d) The growth and extraordinarily rapid development of physical chemistry.

The three forms of energy which normally undergo alteration in value when a chemical reaction occurs in solution are the chemical energy, the heat energy, and

the osmotic energy (B. Moore). The algebraic sum of the three alterations must be zero.

We have gradually got accustomed to the mode of thought involved by saying that chemical equilibrium is dynamical rather than statical. Chemical equilibrium between two substances in solution really results only when the velocities of the opposing reactions balance each other.



In this department Guldberg and Waage's investigations (1867) mark an epoch. A fundamental idea to grasp is that of chemical velocity.

This term must not be confounded with the meaning attached to the term in physics. In mechanics velocity is defined as the rate of motion of a point.

$$v = \frac{s}{t} \text{ e.g., } \frac{100 \text{ ft.}}{10 \text{ sec.}} = v. \text{ of 10 feet per second.}$$

In chemistry we mean by velocity the *rate of material transformation* of a substance. Chemical velocity is the ratio of the amount of substance transformed (in a given process) to the time required for its transformation.

$v = \frac{x}{t}$ or $-\frac{dx}{dt} = kc$ (c = concentration, i.e., quantity of substance in unit volume).

E.g., inversion of cane sugar—(Law of Mass Action, Wilhelmy, 1850).

(a) In water only. This takes place with extreme slowness.

(b) By acids. Lessen the resistance—i.e., increase the velocity. For chemical conductivity is the reciprocal of the resistances.

(c) By Pt.-black.

The actual mechanism of inversion is still unknown.

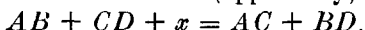
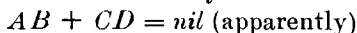
Now, many circumstances and conditions, such as pressure, temperature, &c., are able to influence the velocity of a reaction. For example, take phosphorus. Phosphorus matches, when kept in their boxes, are really

undergoing slow combustion—so slowly that no perceptible change is apparent even after a long time. But if we raise the temperature slightly by friction active combustion at once sets in. On the other hand, reduction of temperature notably retards chemical reactions, and many interesting observations have been recently made upon the effects of very low temperatures upon chemical change. Oxygen, at elevated temperatures, a highly reactive element, is strikingly inert at ordinary temperatures, not because its affinity but because its reactivity is small (Nernst). Metallic sodium has no action on dilute alcohol at -80°C . (Pictet).

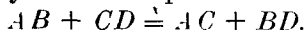
In this connection we bethink ourselves of febrile phenomena, and are led to reflect how far pyrexia may alter the velocity of chemical reactions that go on in our own bodies.

The chief topic to which I wish to direct your attention in this paper is that known as catalysis (Berzelius, 1835), or, contact action (Mitscherlich).

An immense number of chemical reactions are known in which two substances, which, by themselves, appear to undergo little or no change, are rapidly altered under the influence of a third body.



Dr. H. Armstrong (*Encyclop. Brit.*, xxvi., p. 734) considers there can be little doubt that the evidence is sufficient to justify the conclusion that chemical interactions are not generally of the simple form:—



Their occurrence is, as a rule, dependent on the introduction of some “third component” into the system. It is even probable that this is a rule absolute.

Perhaps this means, in accordance with Faraday’s doctrine of the unity of chemical and electrolytic change, that a circuit of change must comprise three distinct terms or components, one of which must be an electrolyte.

Hence, for example, the remarkable effects, in many

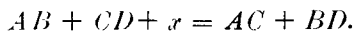
cases, of the introduction of a minute trace of moisture in determining a chemical reaction. A *completely dry* mixture of CO and O cannot be made to explode by means of the electric spark.

When we reflect that the whole group of enzyme or ferment actions comes under the head of catalysis it is needless to enlarge upon the significance of catalytic phenomena in medical science, and in the problems of organic life.

Doubtless, also, some of the events concerned in photography belong to this class.

I hope presently to show some illustrative experiments, but let us first seek for a working definition of catalysis. Taking the most common case of chemical interaction—*i.e.*, in homogeneous liquid solutions—I will accept Ostwald's definition.

A catalyst, or catalyser, is any substance which alters the velocity of a chemical reaction without itself appearing in the final product. A catalyser oils the wheels of a chemical reaction, and, like the lubricating oil of an engine, is not itself used up. The essential point is the acceleration.



The alteration may consist either in hastening or in slowing the reaction. In a large number of cases the numerical value of the acceleration or retardation of the reaction has been experimentally determined. Bredig has made 850 measurements of reaction velocities.

There seems to be no kind of chemical reaction which cannot be catalytically influenced, and no chemical substances, whether elements or compounds, which cannot act catalytically.

E.g., Hydrogen ions, the essential radical of all acids, accelerate most chemical reactions. On the other hand, some enzymes act selectively, and exert their accelerating action only upon certain specific substances. The beautiful and wonderful investigations of E. Fischer have shown that the very slight physical differences, known as

stereo-chemical, can bring about alteration in the action of a given enzyme.

ENZYMES (SOLUBLE FERMENTS).

The catalytic action of ferments has only within the last few years been carefully studied from the standpoint of dynamical chemistry (Cohen). Yet the process is one known to the ancients, although not baptised with its modern name. "Catalysis is as old as drunkenness, for alcohol is produced by fermentation, and ferments are catalysts" (Duncan).

An enzyme may be looked upon as a catalyst which arises in the organs during the life of the cell, and by whose action it discharges the greater part of its duties.

Digestion and assimilation are from beginning to end regulated by enzymes, and without their aid the maintenance of life would be impossible. Physiological chemistry is largely catalytic chemistry. In plants, chlorophyll is the master catalyst, or energy transformer. Chlorophyll possesses the very specific power of converting light energy into chemical energy.

Seventy years ago Berzelius, with acute insight, had perceived the decisive importance that attaches to enzymes in the economy of the living being. What is the physico-chemical criterion of the phenomena of life? Shall we not answer—"An automatically regulated production and use of chemical energy, for the animation, maintenance, and increase of the living thing" (Ostwald)?

There are three principal means of influencing the velocity of chemical reaction—viz., temperature, concentration, and catalysis, and, for living beings, the greatest of these is catalysis.

The difficulties of investigating enzyme actions quantitatively are enormous, and little progress has yet been made. A *finite* amount of enzyme can convert an *infinite* amount of material. Pepsin can dissolve in seven hours 500,000 times its weight of fibrin (Schäfer).

In ferment action, the chemical energy of the resulting

products is always less than that of the substances from which they were formed (as shown by heats of combustion). This is but a special case of the important generalisation that all reactions advance only in the sense of a diminution of free energy.

Of great interest are the analogies recently discovered by Bredig and Müller von Berneck, between the action of enzymes and the action of a number of colloidal solutions (termed *sols*) of very finely divided metals, especially platinum.

This colloidal (*i.e.*, indiffusible) Pt is much more active than spongy Pt, or, "platinum black." It will "invert" cane sugar, blue guaiacum, &c. The platinsol is readily prepared by passing a current of high potential between two platinum electrodes under distilled water (Bredig).

Strongest solution obtainable = 1 gm. atom in 1300 L. Quantitative measurements are now possible for first time. Cf. Bredig and R. Müller v. Berneck, *Ztsch. f. physikal. Chem.* 31, 258 (1899). Bredig and Ikeda, *do.*, *do.*, 37, 1 (1901). Brode, *do.*, *do.*, 37, 257 (1901).

$\frac{1}{500000}$ mgm. of Pt. in 1 cc. of solution catalyses peroxide of hydrogen. (Experiment shown.) Schönbein was of opinion that dissociation of H_2O_2 by Pt was the prototype of organic fermentations.

These "inorganic ferments," as they are somewhat fancifully called, can be "paralysed," or, at any rate, inhibited, by various poisons—*e.g.*, H_2S :HCN.

1 grm. molecule (27 grm.) of HCN in 20 million liters (0.0014 mgrm. of HCN per liter) suffices to decrease the velocity of catalysis of O_2H_2 by Pt by one-half.

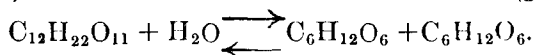
It is a remarkable fact that the hæmic and respiratory poisons, HCN and H_2S , should be the very ones to act as paralysing agents. A point of difference should be noted. The reactions that are catalysed by organic ferments are incomplete—*i.e.*, there is a *limit*. The catalysis of H_2O_2 by platinsol is complete. Hæmoglobin has two stages of oxidation—oxyhæmoglobin and met-hæmoglobin—and the investigations of Schützenberger and

others show that in oxyhæmoglobin half the oxygen is more easily split off than the other half. The first half is to be regarded as peroxide oxygen, of the type of H_2O_2 , the second half as oxide oxygen (Nernst). This bears upon the comprehension of the guaiacum test for blood, and must have a deep physiological meaning.

Organic ferments are probably dual bodies. Pancreatic juice contains no trypsin, but trypsinogen. When it meets *succus entericus* trypsin is liberated. The discovery of entero-kinase (a "ferment of ferments") has led to the discovery of other kinases, and a whole field of exploration of mutual action of ferments has been opened up. There are also anti-ferments—*e.g.*, anti-rennet, anti-pepsin, &c.

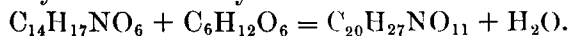
The old difficulty of why the alimentary canal does not digest itself is thus capable of a rational explanation. Similarly, anti-trypsin is said to exist ready formed under normal conditions in the cells of intestinal worms.

There are also now known what may be called *reversing* ferments. Croft Hill has proved that, *in very concentrated solutions*, maltase, the ferment of malt, can cause the condensation of two molecules of hexoses into a di-saccharide (revertose). In *dilute solution*, as has been long known, the ferment hydrolyses the di-saccharide (maltose) into two molecules of mono-saccharide (glucose).



So, thus, ferment actions come under the head of reversible reactions, and enzymes are not devoid of synthetic powers.

Still more notable is Emmerling's discovery. He has shown that amygdalin, which is decomposed by emulsin into glucose, benzaldehyde, and HCN, can be reconstructed from the glucoside of mandelic nitrile and glucose by means of the yeast maltase.



Lactase (a ferment from *Kefir*) can, under suitable conditions, condition the formation of iso-lactose from a solu-

tion containing a mixture in equal concentration of its constituent hexoses—viz., glucose and galactose.

Theoretically, in fact, all reactions are reversible.

INDUSTRIAL APPLICATIONS OF CATALYSIS.

These are innumerable, but time will not allow of reference to more than one or two examples. Some of them have revolutionised important chemical industries.

(a) *Sulphuric Acid*.—The uses of sulphuric acid are countless. In 1904 its total consumption exceeded eight billion pounds weight. All the sulphuric acid is made from three cheap things—viz., SO_2 , air, water. The difficulty is to marry the SO_2 and the oxygen. In the old leaden-chamber process the transfer of atmospheric oxygen to the SO_2 was catalytically effected by the aid of oxides of N. It has been long known (Phillips, 1831) that SO_2 and air easily interact in presence of Pt. After many trials, and at much cost, the Badische Anilin und Soda-Fabrik (Ludwigshafen) have triumphantly utilised this principle. The hot SO_2 gas and air are dried, cooled, and passed over platinised asbestos. Sulphuric acid is readily produced, and 200,000 tons were manufactured by this "contact-process" in 1904. At Mannheim Fe_2O_3 is employed as the catalyser.

(b) *Indigo*.—The commercial synthesis of indigo has reversed the economic relations of States. A few years ago £5,000,000 worth of natural indigo were exported annually from India. The distinguished German chemist, Baeyer, spent thirty-five years' labour on the chemical study of indigo. Indigo is now made from naphthalene, a cheap and abundant hydrocarbon, C_{10}H_8 .

By a lucky accident it was discovered (1897) that the presence of a trace of Hg (or Hg and Cu) renders easy the conversion of naphthalene into phthalic acid by H_2SO_4 , and from this body indigo is derived.

In 1903 the German export of artificial indigo was worth over £1,000,000.

In 1904 the export of natural indigo from India had

fallen to less than 30 per cent. of what it had been. Now, artificial indigo is actually imported *into* India. The artificial indigo is purer and cheaper.

The "Badische Fabrik" now uses annually 10,000 tons of naphthalene, 10,000,000 pounds of NaCl, and 50,000 tons of H_2SO_4 in the process. The amount of indigo which this represents would require more than a quarter of a million acres of land for its cultivation. The indigo planter's occupation is gone.

(c) *Catatype Photographs*.—These are produced without sunlight (Ostwald and Gros). The face of a photographic negative is quickly rubbed with cotton dipped in H_2O_2 and ether. This is allowed to remain for an instant. Wherever metallic Ag has been deposited, the H_2O_2 is catalysed into H_2O . Where there is no reduced Ag, then H_2O_2 is left unaltered. The negative is now placed on gelatinised paper in a "printing frame," and immediately transferred to an alkaline solution of Mn SO_4 . The picture develops in brown tones. With an alkaline silver solution the print will be black.

APPENDIX.

The following experiments were demonstrated, most of them by lantern:—

1. Decomposition of chromic chloride by a minute trace of chromous chloride.
2. Solution of pure tin in HCl, effected by a trace of PtCl_4 .
3. Action of Pt-black on H_2O .
4. Paralysing action of HCN on (3).
5. Action of platinsol on H_2O_2 .
6. Paralysing action of HCN on (5).
7. Reaction of guaiacum + blood + H_2O_2 .
8. Reaction of guaiacum and Pt-black.
9. Action of emulsin on amygdalin and on salicin.
10. Colour-reaction of guaiacum with potatoes (raw, boiled), and on turnip.