In the address on Pasteur, delivered before the British Association at Ipswich, Prof. Percy Frankland distinctly attributes this discovery to Héricourt and Richet. He said: "This astounding antitoxic property of the blood-serum of an artificially immunised animal was first discovered by Héricourt and Richet in respect of animals immunised against one of the common abscess-producing organisms." [1]

Now Dr. Welch goes out of his way in a foot-note reference to Babès and Lepp to mention that "Richet and Héricourt are sometimes quoted as the first experimenters to show that the blood of animals is capable of conferring protection upon susceptible animals, but their work *has no reference to modern serum-therapy, as their experiments were made with the blood of dogs which had not previously been vaccinated or treated in any way*."

If we refer to the *Comptes rendus* for 1888, we shall find a paper by Héricourt and Richet entitled "Sur un microbe pyogène et septique (*Staphylococcus pyosepticus*) et sur la vaccination contre ses effets." In this memoir the authors describe their experiments on procuring immunity in rabbits towards this organism by inoculating them with weakened cultures of it. They conclude by saying: "The methods which we have used to procure these vaccinations are those in general use by Pasteur and his pupils. But we have conceived of a new method (the peritoneal transfusion of a dog's blood into rabbits), a process which also produces vaccination; in a subsequent communication we shall describe in detail the results obtained by this method."

It is this subsequent paper which has been entirely overlooked by Welch and other investigators. Strange to say, also, there is absolutely no reference to it in the *Centralblatt für Bakteriologie*, although a very incomplete abstract of the earlier paper did appear in this journal. This second communication, to which, in the light of recent scientific investigations on the use of antitoxic serum, much interest and importance attaches, is entitled "De la transfusion péritonéale, et de l'immunité qu'elle confère" (*Comptes rendus*, 1888, p. 748).

The following passage, taken from this memoir, will perhaps most clearly convey some idea of what results were obtained by Héricourt and Richet in these first investigations in serum-therapy:—"On October 4, seven rabbits were inoculated with four drops of a culture of the *Staphylococcus pyosepticus*, six having received 48 hours previously some dog's blood in the peritoneum. The control animal [2] died in less than 20 hours after the inoculation. Of the six others, three died, one 50 hours, the other 70 hours, and the third 90 hours after the inoculation. The three others survived; they are still alive at the present time. To explain the apparent inconsistency of these results, it must be noted that the transfused blood was obtained from two different sources: first, from a dog which had never been experimented upon—the rabbits which received this blood did not survive the inoculation; secondly, from a dog which had survived inoculation made some months previously with the *Staphylococcus pyosepticus*: the three rabbits which received this blood survived the subsequent inoculation with the *Staphylococcus pyosepticus*." These results were confirmed by further investigations, proving, as the authors say, that it was not "un fait exceptionnel." In the course of their experiments Héricourt and Richet found that the blood of untreated dogs did endow rabbits with a certain degree of protection from subsequent inoculation with this micro-organism, inasmuch as the course pursued by the disease in the case of these rabbits was distinctly modified, being less virulent and less rapid, but they expressly state that they consider the assumption justified that the blood of dogs inoculated with this *Staphylococcus*, is capable of conferring immunity of a more complete nature than that obtained by using the blood from untreated dogs.

It is sufficiently apparent, therefore, that these experiments of Héricourt and Richet, far from having "no reference to modern serum-therapy," are the original investigations from which the antitoxic treatment of disease by means of blood-serum has directly followed.

The authors conclude this most interesting memoir by expressing the hope that the injection of the blood of an animal endowed with a natural power of resisting a particular disease may possibly be able to protect other animals, not so fortunately endowed, from attacks of this disease So far, however, this hope has not been realised. In an article entitled "Recent Studies on Diphtheria" (NATURE, August 22, 1895, p. 393), it was pointed out how the natural or race immunity of one animal to a particular disease was not capable of being transferred, by means of its blood-serum, to another animal susceptible to this disease. We read: "This remarkable circumstance has been once more very clearly demonstrated by Wassermann in the case of diphtheria, to which disease white rats are absolutely immune. In order to test the character of white-rat-serum as regards diphtheria infection, fatal doses of diphtheria toxin were administered to guinea-pigs along with such serum, but in no case did the latter survive, showing that this serum possessed no anti-diphtheritic properties whatever, and was incapable of protecting animals from diphtheria infection."

In connection with the wider application of anti-toxic serum in the treatment of disease, it is interesting to note that already in 1889 Messrs. Babès and Lepp experimented with it successfully in the treatment of rabies, obtaining the anti-toxic serum from a dog rendered artificially immune to hydrophobia. So far, but little advance has been made with it in this direction; since, however, scientific attention has been so attracted to this subject by the success which has attended the use of anti-toxic serum in diphtheria, we may certainly anticipate many fresh developments in its beneficent application.

[1] *Times* Report, September 17, 1895.
[2] Not previously inoculated with dog's blood.

THE MAJOR PREMISS IN PHYSICAL CHEMISTRY.[1]

CHEMISTRY is essentially an inductive science, mathematics is essentially deductive, while physics holds an intermediate position. Yet in our own science, generalisations are reached from time to time, which serve as major premises for syllogistic reasoning. For example, the proposition that each portion of matter has constant weight is at the basis of our knowledge of chemical equivalents as determined by the balance; the isolation of the metals of the alkalis and alkaline earths led to an insight into the nature of salts in general as metallic compounds; and the "periodic law," though not expressed in precise mathematical language, is a most fruitful generalisation of generalisations.

Physical chemistry, following the logical methods already so largely adopted in physics, is characterised by a readiness to use the major premiss. Instead of making a separate experiment to answer each question of fact, the conclusion may often be reached on theoretical grounds, in the same sense as an engineer may demonstrate the stability of the structure he has designed, or the movements of a newly invented machine. What, then, is the leading major premiss in modern chemistry? and what shall be the conditions of fruitfulness?

The doctrine of energy, as based upon thermo-dynamics, embraces the two laws of conservation and correlation; first, energy (while convertible from one form to another) is constant in amount; second, while work may be wholly converted into heat, only a definite fraction of heat can be converted into work. To specify more clearly, if a quantity of heat, H, is received at temperature T (from absolute zero), and if this is converted into work as far as possible by any ideal process until there remains the quantity H′ at temperature T′, then the simple theorem holds that the two quantities of heat are proportional to the two temperatures; and of course the difference between heat received and heat remaining (that is, the work) is proportional to the difference in temperature. Or in algebraic language,

$$H : H' :: T : T'$$
$$H : H-H' :: T : T-T'$$
$$\text{Work}, = H-H' = \frac{T-T'}{T} . H$$

This equation shows what *fraction* of the heat may be converted into work, under the most favourable conditions; namely, the fall in temperature divided by the absolute temperature at which the heat is supplied.

My present purpose is to present this topic in its bare outlines, and with the greatest simplicity possible. Those who wish to follow the deductive reasoning in detail must use the notation of the calculus, in accordance with the following steps. Combining the formula for the total work (as implied in the first law) with that for work derived from change of temperature (the second

[1] Abstract of a paper prepared by request, to introduce the topic of Physical Chemistry, for the American Association for the Advancement of Science. Read September 2, 1895. (Reprinted from *Science*.)

law), we deduce a differential equation for the work obtained or required in isothermal changes. The change under consideration may involve external work, as when a vapour or gas is generated against atmospheric pressure; or it may be internal work of different kinds, as when the molecules are endowed with increased kinetic energy in volatilising, or when a compound is decomposed into its constituents, with increased potential energy.

A somewhat difficult but important paper by J. Willard Gibbs[1] treats of the equilibrium of heterogeneous substances, giving deductions from the two laws of thermo-dynamics, which in turn become major premises for a host of further deductions; so broad, indeed, are the propositions of Gibbs, that the distinctions between chemistry and physics do not appear; there may be two "heterogeneous substances" of like chemical nature, as water and its vapour; there may be three chemical bodies, as limestone with the lime and the carbon dioxide obtained by ignition; or there may be several physical mixtures, as solution of water in ether, solution of ether in water, and the mixed vapour resting upon both liquids. Now, a little consideration will show the importance of knowing when equilibrium is established, for this is equivalent to saying that no further action can take place; the solution is saturated, no longer acting upon the salt; or the gas which has been generated under pressure is no longer evolved. When a change takes place spontaneously, as when I drop a stone, or mix sulphuric acid with water, heat is developed from some other form of energy. To reverse the process, work must be done. The conversion of heat into work is limited by natural law; when a given change implies the doing of work, and that work is forbidden by the terms of our major premise, the change is impossible, equilibrium prevails.

"Osmotic pressure" in dilute solutions is analogous to the pressure of gases; the Gay-Lussac-Marriotte law, with slight modification of terms, applies to molecules in the liquid state. If work is required to diminish the volume of a gas by means of pressure, work is likewise required to diminish the volume of a body in dilute solution, whether the solvent be removed by evaporation or by freezing. Boiling point and freezing point of the solvent are changed by the presence of the dissolved body. The agreement of observed facts with theoretical deductions has led to important methods of determining molecular weights, while the apparent discrepancies in the case of electrolytes have proved an important argument for the doctrine that these compounds are dissociated into their ions.

The mutual indebtedness of technology and pure science has already been pointed out. Manufacturing processes afford many examples of change which are not carried to completion; it is important to know how far the operation can be improved to afford a larger yield, a purer product or less waste. Combustible gases issue from the blast furnaces. There is still a great reducing power in this mixture of carbon monoxide with carbon dioxide. Can it be utilised by enlarging the furnace? Immense furnaces were built in order to secure a larger yield of iron, but the results were disappointing. The law of mass action shows that the equation

$$Fe_2O_3 + 3CO = 2Fe + 3CO_2$$

is limited by certain conditions of equilibrium, and that the ratio of the two oxides of carbon could not be greatly improved over that already secured in practice. The expense of a technological experiment might have been saved, had the indications of mathematical chemistry been heeded.

What hopeless confusion seems to prevail in our present knowledge of solubilities; yet how important in the separations required for chemical analysis. Here, again, we deal with questions of equilibrium. Will work be done at the expense of heat or not?

There are two special difficulties in the general application of thermo-dynamical principles: first, the minor premise is often wanting; and, second, the mathematical form of reasoning is often difficult for the best laboratory workers. Among the published data of thermo-chemistry, some have been determined directly, some indirectly; it is often difficult to find the data desired, or to judge of their accuracy. A critical compilation of all available thermal data, conveniently arranged for reference, with at least some indication of the probable errors, would be very desirable. Many such data might be computed indirectly from experimental determinations of equilibrium. Many empirical equations have been computed, showing solubility as a function of temperature. Who will trace the correlation among such, and thus add a large chapter to thermo-chemistry? What genius shall discover that form of mathematical function that shall substitute rational for empirical equations with a clear interpretation for each constant required? "But this work is mathematical rather than chemical," you will say. Yes, it is applied mathematics; and mathematicans (not being chemists) are not likely to undertake such a task for us, unless we ask their counsel and aid. Specialisation is inevitable; yet by too arbitrary a specialisation, we may inadvertently lose the very help we need. Again would I emphasise the fruitfulness which follows a "cross-fertilisation of the sciences" (*Journ. Amer. Chem. Soc.*, 15, 601 (1893). Judging from the advances recorded in late years, especially in the *Zeitschrift für physikalische Chemie*, it is safe to predict great developments for the rising generation. I heartily echo the sentiment that we need more data; yet great stores of observations upon record have not yet been coordinated and put to use. Ostwald, desiring to know the influence of free iodine upon a reduction process, made three series of determinations (twenty-four in all) from which he concludes that the influence is *not* proportional to the mass. It was no part of his purpose to discover what the law of retardation is; but others might well follow out this clue, using also the data supplied by Meyerhoffer, and supplementing these with further experiments if needed. A glance at the literature of solubilities, and the lack of rational formulæ to express broad generalisations, may convince us that a great mine, with abundant ore "in sight," is awaiting development; or, rather, that ore has been run through a stamp-mill to extract half the gold, while fully half still remains in the tailings, awaiting more perfect methods of treatment.

Much may be learned from the systematic habits of the astronomer, dividing his work among the several observatories in a spirit of helpful co-operation, and assigning the labour of computation to those who are fitted thus to follow the lead of others. What better service can we do for the University student than to set before him some of the problems in mathematical or physical chemistry that require patient toil, and give him the pleasure of assisting in their solution by the use of logarithms and squares? What is more practical than to utilise any service he can render?

In conclusion, I beg leave to suggest the appointment of a joint Committee (representing Sections A, B and C of the American Association) to consider the feasibility of striving towards the following ends:

(1) The compilation of all reliable data of physical chemistry in convenient form for reference, distinguishing those determined directly from those calculated indirectly.

(2) The calculation of empirical formulæ, to combine any series of data, when some better form of generalisation is not already at hand.

(3) The preparation and use of rational formulæ, wherever possible, to deduce the natural constants from series of observations, and to express the conditions that may be expected to hold between observations of different kinds.

(4) The organisation of a band of volunteer compilers and computers from among advanced students, who (with the counsel and aid of their instructors) may assist in the work of compiling data and computing formulæ.

While the time did not seem ripe for the appointment of such Committee at the late meeting of the A. A. A. S., the writer would be pleased to receive any further suggestions from those interested, regarding the points noted above.

ROBT. B. WARDER.

[1] *Trans.* Conn. Acad., 3, 108, 343 (1874-78). See also, *Amer. Jour. Sci.* [3] 16, 441 (1877); 18, 277 (1878).

UNIVERSITY AND EDUCATIONAL INTELLIGENCE.

OXFORD.—At the 160th meeting of the Junior Scientific Club, held on Wednesday, November 17, the following officers for next Term were elected:—President, E. C. Atkinson; permanent treasurer, D. H. Nagel; treasurer, N. V. Sidgwick; biological secretary, R. Warren; chemical secretary, H. P. Stevens; editor, A. W. Brown; committee, R. A. Baddicom, M. Hesketh, T. J. Garstang. It was announced that Prof. W. Ramsay had consented to deliver the fifth Robert Boyle Lecture in the Summer Term, 1896.

CAMBRIDGE.—The late Mr. James Carter has bequeathed his collection of fossil Crustacea, on which he was a recognised authority, to the Woodwardian Museum. A portrait of the late