and its substrate, preliminary to the particular chemical change brought about by the enzyme in question.

Adsorption between enzyme and substrate as affected by the presence of neutral salts is investigated and found to follow the laws of "electrical" adsorption.

The relation between the concentration of an enzyme and its activity is shown to be expressed by an exponential formula, the value of the exponent varying considerably according to circumstances. In certain conditions it may be unity and in others the square root, but is usually between the two.

Accordingly, the view that the rate of an enzyme action at any given moment is a function of the amount of the adsorption compound of enzyme and substrate in existence at that time is to be regarded as fairly well established.

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On the Distribution and Action of Soluble Substances in Frogs Deprived of their Circulatory Apparatus.

By S. J. Meltzer, New York.

(Communicated by Prof. A. R. Cushny, F.R.S. Received April 11,—Read May 18, 1911.)

(From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.)

In view of the great distributory efficiency of the cardio-vascular apparatus, no serious consideration has been given to the possibility of the existence of other modes of distribution of material in the animal body. In the following, results of experiments will be briefly presented which give unmistakable evidence of an efficient distribution of substances in cardiectomised frogs.

In these experiments the heart was exposed, ligated, and removed, and the incision closed again. Such a removal of the heart eliminates also the activity of the lymph vessels and the lymph hearts which empty their contents into veins. Injections were given into the various lymph sacs of the body and into the abdominal cavity. The results to be reported were

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derived from experiments made with three alkaloids presenting different types: adrenaline, strychnine, and morphine.

Adrenaline.—The dilating effect upon the pupil was the leading reaction. An injection of 1 c.c. of adrenaline causes in cardiectomised frogs sooner or later a dilatation of the pupil. It may appear in less than an hour (dorsal and lateral lymph sacs), or after two hours (abdominal cavity or in one leg). When injected into both legs the dilatation appears much sooner. Cutting both sciatic plexuses does not interfere with the appearance of the dilatation. The dilatation sets in even if the animal is suspended by the head. When injected into a lateral lymph sac the pupil of the corresponding side dilates first, to be followed 20 or 30 minutes later by a dilatation of the pupil of the other side.

When the frogs are kept moist and at a low temperature the pupils dilate after an injection of adrenaline even three or four days after cardiectomy, provided the eyes are not dried out. In the latter case the presence of adrenaline in the orbit is easily demonstrated by placing a fresh bulbus from a normal frog with the corneal surface inside. In this manner the pupils of several normal bulbi may become dilated by being placed in the orbit consecutively one after another.

These experiments demonstrate that adrenaline may become distributed through the entire body of a frog in the absence of the circulatory apparatus. In the case of the migration from a lateral lymph sac to the eye of the opposite side, the adrenaline has to pass through fairly solid membranes and voluminous masses. Diffusion alone will probably not accomplish it; osmosis will have to assist in the process. Gravity is not an essential factor. Movements of the animal, or "vital" activities of cells, are not parts of this peripheral mechanism of distribution.

Strychnine.—Frogs survive cardiectomy an hour or two, or even longer, according to the temperature at which they are kept; spontaneous and reflex movements disappear gradually. Strychnine exerts a definite influence upon the course of life after cardiectomy. When about 10 mgrm. of strychnine are injected, after a temporary insignificant depression, the animal develops in 30 or 40 minutes a definite tetanus. These animals invariably survive the controls, kept under the same condition, by an hour and longer. When a somewhat larger dose is administered, the first effect is a definite depression which may be accompanied by a semi-paretic state. Suddenly the animal asserts itself, becomes hyperæsthetic, and develops a tetanus. When a still larger dose of strychnine is injected, the essential effect is an early onset and development of an unmistakable paralysis; the latter can no longer be overcome by the hyper-excitability which ineffectively manifests itself later.

Animals in which strychnine produced an early definite depression and a paretic state are survived by the controls.

Strychnine, then, is readily distributed in the cardiectomised animals and produces there vital phenomena similar to those seen in normal frogs, that is, tetanus and paralysis. The paralysis in the cardiectomised frogs is central and is not due to fatigue. The occurrence of a violent tetanus in these animals refutes conclusively the theory of Verworn, that the paralysing action of strychnine is due to its paralysing effect upon the heart.

Morphine.—When about 10 or 15 mgrm. of morphine have been injected into a normal frog, no effects will be noticed until a few days later, when it may develop a tetanus. A cardiectomised frog, however, reacts to morphine in an entirely different manner. A small dose of morphine, 6 or 8 mgrm. for a medium-sized frog, will bring out a tetanus in 40 or 50 minutes. After a larger dose, the tetanus is preceded by depression and weakness. After a still larger dose, the effect is paralysis with very little evidence of hyper-excitation. In short, in cardiectomised frogs morphine affects the central nervous system very rapidly, the effects being nearly like those of strychnine, that is, tetanus with smaller doses, and paralysis with larger doses. The most plausible explanation of the surprising fact is, perhaps, this:—The central circulation receives secretions from all organs and tissues, and conveys them rapidly to all parts of the body; the action of each secretion, therefore, and of all substances taken up into the circulation, is modified by the neutralising effects of various secretions. In the absence of the circulation there are no such modifying effects to interfere with the specific action of some substances.

The experiments demonstrate that in the absence of the central circulation substances may be distributed through the body by a mechanism which in some instances may act even more promptly than the cardiac mechanism. In contradistinction to the central apparatus we may designate the distributing agent in question as a peripheral mechanism. The path of distribution employed by this mechanism can be nothing else than the tissue spaces. About 15 years ago we* insisted that these are more or less efficiently connected throughout the body, and present a unity, a system of their own. A similar peripheral mechanism, working through a similar path, is probably active in the distribution of mesolymph in animals still without a cardio-vascular apparatus. In animals possessing such an apparatus the peripheral mechanism may perhaps have the significance of a phylogenetic phenomenon.

* Adler and Meltzer, 'Jour. of Exper. Med.,' 1, 512, 1896.

The presence of an acting peripheral mechanism in cardiectomised animals suggests the following possibilities:—

1. That the peripheral mechanism is active to some small degree in all parts of the normal body; it is, perhaps, this mechanism which favours local action of substances. 2. That this mechanism may take an active share in the process of distribution in organs which are normally deficient in circulation. The brain, for instance, has no lymphatics, and the exchange of fluid material with the blood capillaries is said to be there somewhat deficient. 3. That the peripheral mechanism gets into prominence in pathological conditions in which there is either a local or general deficiency of the cardio-vascular circulation.

The Mechanism of Carbon Assimilation: Part III.

By Francis L. Usher and J. H. Priestley.

(Communicated by Dr. M. W. Travers, F.R.S. Received April 13,—Read June 1, 1911.)

Some experiments and conclusions recorded in two papers* published in 1906 have been subjected to criticism by several investigators, and the present paper has been written with the object of presenting some new facts bearing on the problem of carbon assimilation, which incidentally support some of those conclusions. We also take this opportunity to restate the theory originally advanced, with such modifications as may be necessary, and to reply to a few of the more important objections to it which have been raised.

The observations recorded below are concerned only with the initial stages of the photosynthetic process, that is to say, with the formation of the primary photolytic products from carbon dioxide, and with the evolution of oxygen. In the papers referred to some evidence was given in support of the belief that aqueous carbon dioxide is decomposed by light under the conditions obtaining in a green leaf, the immediate products of this decomposition being hydrogen peroxide and formaldehyde; and it is easy to see that the production of these two substances would satisfactorily account both for the oxygen and the carbohydrate, which are the first visible results of the natural process. As the evidence put forward was to some extent indirect,

* 'Roy. Soc. Proc.,' B, vol. 77, p. 369; and vol. 78, p. 318.