power of intimidation and "bluff" which can not be generated by a single individual or family group. Perhaps groupings of this sort, with some faint instrumental inclinations of a dim "eolithic" nature, may successfully have pursued small game and the young of larger mammals. Cliff and cave refuges may have contributed to their survival.

Their odd continuance into times late enough to have brought them in contact with more advanced and truly human forms is by no means their least interesting feature. What curious reactions must have been observable if either group ever encountered the other —the savage first men and these living fossil ancestors of the Pliocene, still apes but more human than any now alive. Was it man himself who swept them out of existence? Probably we shall never know.

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"DORMANT" VERSUS "ADVENTITIOUS" BUDS

A RECENT note by Diehl[1] on the sprouting of a staghorn sumac (*Rhus typhina* L.) log begins thus: "Sprouting of adventitious buds in logs or twigs of woody species freshly cut . . ." With no other comment concerning the origin of the sprouts in sumac, the implication is that they, too, are *adventitious*. As the species grows in New York State, however, most and perhaps all of the sprouts found on older stems have arisen from dormant buds.

It would seem profitable to restrict use of the term *dormant* or *latent* to buds formed in the axils of leaves (including scales) on the young annual shoots. These buds then persist in a dormant condition for an indefinite time with only sufficient elongation of their steles to keep the buds outside of the enveloping xylem. *Adventitious* buds, by contrast, arise outside of the normal phyllotaxy. It is recognized that adventitious buds, once formed, may also remain dormant, as is true of the root initials in the bark of willow stems. Where the origin is in doubt, or an inclusive term is desired, *epicormic* is advantageous and non-committal.

A considerable amount of unnecessary confusion has arisen from the loose or mistaken usage of the term "adventitious," particularly when the origin of the buds or sprouts in question has not been known. Foresters frequently have been at fault in this respect, but they are not alone. A popular botany text[2] makes the statement "They [adventitious buds] also give rise to the common water sprouts of apple trees and other species," although, as a matter of fact, water sprouts in apple are clearly from dormant buds.[3] Similarly, the stem sprouts of oak[4] and probably most hardwoods of the northeast,[5] as well as pitch pine[6] (*Pinus rigida* Mill.), arise in general from previously existing dormant buds, rather than adventively. In the trunk and branches of apple true adventitious buds do occur rarely in the bark but their usual origin in hardwood stems is from callus masses. A familiar example is the abundance of adventitious shoots from the callus on a cut stump of beech (*Fagus grandifolia* Ehrh.).

This question of terminology is not wholly academic. A large proportion of the northeastern hardwood forest is of sprout origin, and sprouting following thinning or pruning is of concern to both foresters and horticulturists. Reliance on literature requires that terms be specific.

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ACIDITY AND ACTIVITY OF SULFONAMIDES

RECENT work[1] has shown that a definite correlation exists between the bacteriostatic effectiveness and acid ionization constants of sulfonamides. The functional form of this relationship indicates that the drug activity is the resultant of two opposing tendencies, one of which increases effectiveness as the pK increases and the other of which decreases effectiveness. In view of the current opinion that sulfonamide activity is due to the blocking of an enzyme system,[2] it was considered advisable to examine the available data from the point of view of the general concepts of acidity[3] and the law of mass action. Interestingly enough, this fundamentally simple approach leads to qualitative and quantitative predictions which are in good accord with the available facts.

Qualitatively speaking, one would expect the compound of intermediate pK in a group of sulfonamides of widely varying pK to be most effective in producing bacteriostasis, from the following considerations. If the sulfonamide, HD, is a weak acid, then the anion, D^-, may be treated as a base. Similarly, the enzyme, or protein, P, can combine with OH^- and hence may be considered an acid. If P is an acid and D^- is a base, compounds of the type PD^- may be formed. If we assume that the activity of the drug depends on

1 W. W. Diehl, SCIENCE, 96: 2498, 448–9, November 14, 1942.

2 J. Hill, L. Overholts and H. Popp, "Botany," p. 138. New York, 1936.

3 V. T. Stoutemeyer, *Iowa Research Bull.*, 220: 308–52, September, 1937.

4 E. R. Roth and B. Sleeth, *U. S. D. A. Tech. Bull.* No. 684: 4, October, 1939.

5 M. Büsgen and E. Münch, "The Structure and Life of Forest Trees," pp. 73–74. New York, 1931.

6 E. L. Stone, Jr., and M. H. Stone, *Am. Jour. Bot.*, 30: No. 4, 1943.

1 Bell and Roblin, *Jour. Am. Chem. Soc.*, 64: 2905, 1942.

2 Woods, *Brit. Jour. Exptl. Path.*, 21: 74, 1940; Fildes, *Lancet*, 238: I, 955, 1940.

3 Lewis, *Jour. Franklin Inst.*, 226: 293, 1938.

the amount of PD^- that is formed, and recent work[4] indicates that sulfonamide potency is a direct function of its protein-combining capacity, then in a series of drugs of various pK's acting in a solution at pH near 7, for example, those of intermediate pK should be most effective. For if the drug is a very weak acid, the number of D^- ions is very small, even though most of them may combine with the acid P to form PD^-. On the other hand, if the drug is a very strong acid, the number of D^- ions would be quite large in a solution of pH 7, but since D^- is weakly basic, little PD^- would be formed. The maximum PD^- concentration, for equal additions of sulfonamide, would be formed by a drug with some intermediate value of pK.

The same considerations apply when one considers a basic sulfonamide such as sulfaguanidine, except that in this case the neutral molecule D can combine directly with the acid P to form PD. For basic sulfonamides the same correlation should exist between pK and potency, except that pK now refers to the equilibrium $HD^+ = H^+ + D$.

This qualitative description is supported fully by a detailed, quantitative consideration of the equilibria involved. Complete details of this treatment will be given in a forthcoming publication. For the present it will be sufficient to point out that the equations finally reduce to the following condition relating the pK of the sulfonamide of maximum activity to the pH of the solution:

$$pK_{HD} = pH - \log \frac{1-f}{f} \qquad (1)$$

where

$$f = \frac{d \ln K_{PD}}{d \ln K_{HD}}, \qquad (2)$$

K_{PD} being the dissociation constant of the enzyme-sulfonamide complex. When f is determined for a given bacterial system, pK_{HD} can be predicted immediately.

Unfortunately we can not make a direct test of this prediction at present, because data for the direct evaluation of f for bacteria are unavailable. Nevertheless, we can evaluate f indirectly for *E. coli* and compare the value so obtained with that derivable from work[4] on the combination of serum albumin with sulfonamides.

Bell and Roblin[1] have found that in a solution of pH 7, maximum bacteriostasis of *E. coli* was obtained with a sulfonamide with a pK of about 6.7. Substituting the appropriate values in (1) we find f is 0.3. Such a value of f is apparently very reasonable if we may compare it with the approximate value derived for serum albumin. From the work of Davis and Wood[4] one can calculate relative values of K_{PD}, for sulfonamides of various K_{HD}'s. A plot of log K_{PD} vs. log (K_{HD}) fits a straight line fairly well and the slope of this line is f. For serum albumin f turns out to be 0.5.

The inhibition of sulfa action by p-aminobenzoic acid is also amenable to the type of treatment described above. In this case we assume that when the ratio of PA^- (the p.a.b.-enzyme combination) to PD^- reaches some fixed value, inhibition sets in. The mass law treatment then predicts that the ratio of the total amount of p-aminobenzoic acid necessary to cause inhibition, to the total amount of sulfonamide present, will be a maximum for the sulfa compound of greatest potency. This is in agreement with the data of Rose and Fox.[5]

Thus, the law of mass action, as applied to a system consisting of a sulfonamide and an enzyme in a buffer solution, predicts the existence and acid dissociation constant of a drug of maximum potency, correlates the effectiveness of basic as well as acid sulfa compounds with their acid ionization constants, and accounts quantitatively for the inhibitory effect of p-aminobenzoic acid.

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CORRECTION

IN a revision of the proof a serious omission was made in the inadvertent dropping of "and 1 ml. of 0.1% $CuSO_4 \cdot 5H_2O$ solution" after "Aliquots of 2.0 ml are mixed with 6 ml of clear 12.5 per cent Na_2CO_3 solution" on p. 405. Addition of copper is essential in enhancing the sensitivity of the Folin reagent, as already noted by others.

MICHAEL HEIDELBERGER
CATHERINE F. C. MACPHERSON

SCIENTIFIC BOOKS

PHYSIOLOGICAL CHEMISTRY

The Dynamic State of Body Constituents. By R. SCHOENHEIMER. Harvard University Monograph in Medicine and Public Health No. 3. 79 pp. Harvard University Press. 1942. $1.75.

THE nineteenth century, which ended about 1914, was the callow age of the physiological chemist. Rudolph Schoenheimer's "The Dynamic State of Body Constituents" marks the transition to a humbler, more realistic and more mature state of mind.

Until recently, the physiological chemist described

[4] Davis, SCIENCE, 95: 78, 1942; Davis and Wood, *Proc. Soc. Exptl. Biol. Med.*, 51: 283, 1942.

[5] Rose and Fox, SCIENCE, 95: 412, 1942.