ters the subject-matter ranges through enough physical optics, radiation theory, including electrical oscillations and waves, black body radiation, spectroscopy, x-rays, radioactivity, nuclear physics, to give the student a very good idea of the principal avenues of recent progress. The treatment is largely non-mathematical and can be followed easily by any one who has had a first course in college physics. An abundance of carefully drawn and well-reproduced figures, discussion of many applications of contemporaneous interest, collections of problems, lists of references, are all features which will appeal to the teacher who would supplement his physics course with a systematic treatment of modern physics or who might well give a three-hour year course in modern physics itself. The student who has the mathematics will doubtless prefer a treatment which will more effectively cross the threshold of this fascinating subject.

No part of the physics course has been under closer scrutiny for many years than the laboratory experiments. Many factors contribute to the present-day history of this subject. Laboratory equipment has become continually and ever more rapidly expensive, mass production has robbed much of it of the refinements and precision of an earlier day. Some of the arguments for physics for physics' sake have dwindled in importance. The mere acquisition of laboratory skill is no longer put forth as a principal objective in college physics courses. Nevertheless, there has never been a time when the importance of laboratory points of view and enough familiarity with instruments to remove the first awkwardness with them have been more clearly recognized. In Kilby's "Laboratory Manual of Physics" will be found a typical list of experiments, together with brief notes concerning their theory and directions for performance. The experiments for the most part require inexpensive apparatus and are suitable for a first course.

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SPECIAL ARTICLES

A QUANTITATIVE ANALYSIS OF SULFONAMIDE BACTERIOSTASIS

WOODS'S[1] observations on the relationship of para aminobenzoic acid to the bacteriostatic action of sulfanilamide and sulfapyridine have been amply confirmed and extended by other investigators.[2,3,4] However, his hypothesis that PAB is an essential metabolite of bacteria, and that the inhibition of bacterial growth by the sulfonamides "is due to competition for an enzyme between the essential metabolite and the inhibitor," has not been adequately supported as yet.

We have been engaged for some time in studies concerning the bacteriostatic potency of various sulfonamide derivatives in relation to (1) the minimal effective concentration of the drugs, (2) the type of media employed, (3) the size of inocula and (4) the amounts of PAB required to prevent bacteriostasis. Some of the results obtained are of interest and may shed new light on the mode of action of these compounds.

The bacteriostatic effects of sulfanilamide, sulfaguanidine, sulfapyridine, sulfathiazole and sulfadiazine were observed in two synthetic, inhibitor-free media, one of which affords sub-optimal growth of the test organism, *E. coli,* whereas the other gives growth comparable to that obtained in nutrient broth. The minimal effective concentration (MEC) of each drug was determined as the lowest molar concentration which prevented visible growth over a period of four days with inocula ranging from 25 to 25,000 cells per cc. These concentrations proved to be the same in both media. With all inocula the absolute amount of PAB required to abolish bacteriostasis was found to be the same for the MEC of each drug, as illustrated in Table I. It will be noted, however, that the $\frac{\text{PAB}}{\text{Drug}}$ ratio is inversely proportional to the MEC, which shows that the bacteriostatic potency of a sulfonamide is directly related to the quantity of the drug required to produce bacteriostasis in the presence of a given amount of PAB. Furthermore, the antagonistic effects of PAB and the sulfonamides are apparently related to their concentrations and are independent of the number of bacteria.

TABLE I

THE RELATIONSHIP BETWEEN THE MINIMAL EFFECTIVE CONCENTRATIONS OF SULFONAMIDES AND PARA AMINOBENZOIC ACID

	Minimal effective drug concentration $M \times 10^{-6}$	Minimal amount PAB required to prevent bacteriostasis $M \times 10^{-7}$	$\frac{\text{PAB}}{\text{Drug}}$ Ratio
Sulfanilamide ...	2500	5	1–5000
Sulfaguanidine ..	500	5	1–1000
Sulfapyridine ...	20	5	1–40
Sulfathiazole	4	5	1–8
Sulfadiazine	4	5	1–8

[1] D. D. Woods, *Brit. Jour. Exp. Path.,* 21: 74, 1940.
[2] E. Strauss, F. C. Lowell and M. Finland, *Jour. Clin. Invest.,* 20: 189, 1941.
[3] W. W. Spink and J. Jermsta, *Proc. Soc. Exp. Biol. and Med.,* 47: 395, 1941.
[4] E. Strauss, J. H. Dingle and M. Finland, *Jour. Immunol.,* 42: 313, 1941.

It was observed that the MEC of all the drugs apparently restrained inocula up to 25,000 cells per cc, but that visible growth invariably occurred with larger inocula, even when much greater amounts of the drugs were added to the cultures. In view of these results it was considered possible that the bacteria might be capable of undergoing a *definite, limited number of cell divisions in the presence of any effective drug concentration, regardless of the inoculum employed.* This hypothesis was examined by inoculating decreasing numbers of *E. coli* into media containing a bacteriostatic concentration of sulfathiazole (5×10^{-4} M), counting the number of viable organisms which developed from each inoculum at 6, 12 and 24 hours, and computing the number of cell divisions from the following formula:

$$S = A \frac{(r^n - 1)}{r - 1}$$

where S = count on developing culture
A = number of cells in inoculum
R = factor of increase (2)
N = number of cell divisions.

The results are recorded in Table II, and show that all the inocula underwent almost exactly the same

TABLE II
THE UNIFORM RESTRICTION OF CELL DIVISION BY SULFATHIAZOLE WITH VARIOUS INOCULA OF E. COLI

Inoculum per cc	Count at 6 hours	Number of divisions	Count at 12 hours	Number of divisions	Count at 24 hours
11,800,000	152,000,000*	3.61	170,000,000	3.80	116,000,000
1,180,000	58,000,000*	5.60	64,000,000	5.70	15,000,000
118,000	13,500,000*	6.85	14,000,000	6.86	5,180,000
11,800	1,190,000	6.65	1,600,000	7.08	267,000
1,180	112,000	6.56	110,000	6.54	5,800
118	11,000	6.54	11,600	6.61	210
11.8	1,180	6.64	1,250	6.72	Sterile

* Visible growth.

number of cell divisions within the first 6 hours, with the exception of the largest inoculum, which actually divided fewer times. At 12 hours no further significant change had occurred; at 24 hours the number of organisms had diminished.

The conclusion seems warranted that, in the presence of a bacteriostatic concentration of a sulfonamide, bacteria possess the ability to undergo only a certain limited number of cell divisions, regardless of the size of the inoculum. This readily explains why no apparent bacteriostasis may be observed when large inocula are employed, since even a small number of cell divisions will bring such cultures into the range of visible turbidity (*circa* 10,000,000 cells per cc). For example, Table II shows that cultures inoculated with more than 50,000 *E. coli* per cc attained visible growth, whereas those which received smaller inocula remained clear. The number of cell divisions in each culture, however, was approximately the same. Furthermore, the data also offer a reasonable explanation for the well-known but previously obscure finding that organisms subjected to the action of the sulfonamides grow as rapidly as do controls for a few hours before bacteriostasis becomes manifest.

The reason for this phenomenon is as yet unknown, but it seems possible that the bacterial cell contains a substance necessary for reproduction which is synthesized under normal conditions of growth. In the presence of bacteriostatic concentrations of the sulfonamides the synthesis of this substance is prevented, and the organism is forced to distribute its original supply in diminishing amounts to its progeny. After a certain number of cell divisions the quantity of the substance in the individual organisms becomes insufficient to permit further multiplication. PAB may be concerned with this substance in some way. The observed facts indicate that the antagonism between PAB and the sulfonamides is independent of the number of bacteria, but instead is related principally to critical concentrations of these compounds.

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THE RELATIVE EFFICIENCY OF STRAINS OF RHIZOBIUM TRIFOLII AS INFLUENCED BY SOIL FERTILITY[1]

Arachis hypogaea (peanut) was recently tested in the greenhouse to determine how the response to phosphatic and potassic fertilizers is conditioned by the strains of Rhizobia with which the plants are inoculated. The results suggested that certain cultures were better adapted than others to fix nitrogen in poorly nourished plants, although the cultures differed only slightly in efficiency in well-nourished plants. Since the design of this preliminary experiment did not permit reliability to be placed on the small differences observed, a second, more comprehensive experiment was set up, using *Trifolium pratense* (mammoth red clover) and proper cultures of Rhizobia.

In the second experiment five cultures of *Rhizobium trifolii* were compared on clover grown in Plainfield sand receiving four fertilizer treatments. Cultures 209, 238 and 239 were obtained from the University of Wisconsin, and cultures H and D were isolations from old commercial cultures which had been in the laboratory for two years. The four fertilizer treatments were (1) no fertilizer, (2) P, 100 p.p.m., (3)

[1] Journal Paper No. 9 of the Purdue University Agricultural Experiment Station.