absolutely refractory periods to conduction rates the result is a similar hyperbolic curve. The refractory periods without exception are longer than the corresponding times to maximum. The data on action voltage, due to possible occasional failure to recognize deflections produced by 2 perfectly superimposed axon potentials, are not absolutely reliable. The individual curves of correlation with conduction rate seem to deviate around a straight line inclined steeply downwards from the quicker to the slower axons. Since the slower fibers have the smaller diameters and since a larger fraction of the intrinsic potentials of the former must be shunted by inactive tissue, this result may not be inconsistent with the assumption[5] that the intrinsic potentials all are alike in amplitude.

Comparison of these several properties is complicated by the fact that they have some, seemingly spontaneous, variability. The points in every case distribute themselves somewhat irregularly about the plotted curves but the curves seem to be free of discontinuities in the range of fibers conducting faster than 2 m.p.s.; beyond that there still is some uncertainty. The results, therefore, fail to support the view that there are fiber types distinguishable by time to maximum, conduction rate, irritability and refractory period. Nevertheless, in keeping with our observations on large nerves we find that the conducted axon potentials tend to sum to form some 3 elevations corresponding in general with A, B, and C of the action potential of large nerves, but the relative positions of these elevations in the different nerves, particularly in skin nerves, is quite variable. Since it is possible to recognize differences in the physiological responses of individual axons it is no longer incumbent upon physiologists to adhere to the doctrine of specific nerve energies.

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True Polyvalence of Pure Bacteriophages.*

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As found in their natural environment, bacteriophages often exhibit lytic activity against a variety of organisms sometimes

[5] Gasser, H. S., and Erlanger, J., *Am. J. Physiol.*, 1927, **80**, 522.

* This work was supported from a grant by the Rockefeller Foundation to Washington University for Research in Science.

quite unrelated to each other. This polyvalence is usually due to the presence of several independent phages which can be separated from each other by special procedures. Frequently, however, even such isolated single phages, satisfying all known criteria of purity, may exhibit activity against several more or less closely related species of bacteria. In such cases the characteristics of these bacteriophages usually remain immutable no matter which one of the organisms susceptible to their activity is used for their propagation.[1] Since the active principle in such instances is regenerated equally well on either one of the several susceptible organisms, it is perhaps possible to suppose that the active principle is represented by a very similar if not an identical substance in each case, and that the bacteria in turn have a common element in their composition ("receptor") rendering them susceptible to it. If this could be proven, the nature of this true polyvalence of pure phages would be satisfactorily explained. We have recently made some observations which bring supporting evidence for such a view.

One of the coli-phages in our collection, used in the various experiments in our laboratory for nearly 6 years and invariably found to be pure according to all accepted criteria, exhibits the same degree of lytic activity against our type strains of *B. coli, B. dysenteriae* "Shiga", and *B. dysenteriae* "Flexner", irrespective of whether it is propagated with one or another of these organisms. When this phage is subjected to heating, all 3 valencies disappear at the same time. However, if the speed of inactivation by heat is delayed by the addition of glycerin or of saccharose,[2] the Shiga and Flexner valencies disappear slightly in advance of that against *B. coli* (see protocol). It is thus that after the exposure to heat at 70°C. for 30 minutes it is possible to recover a weak phage (titer 10^{-3} cc.) active against *B. coli* only.

If this monovalent phage is now introduced into the broth cultures of each of the organisms separately it is regenerated only in the presence of *B. coli* and not in the presence of *B. dysenteriae* "Shiga" or *B. dysenteriae* "Flexner". However, the phage after a single passage on *B. coli* is found to have recovered its power to cause lysis of *B. dysenteriae* "Shiga" and *B. dysenteriae* "Flexner" (titer 10^{-1} and 10^{-3} cc. respectively) and after a third consecutive passage *with B. coli* its lytic activity for *B. dysenteriae* "Shiga" and *B. dysenteriae* "Flexner" has been quantitatively restored (titer 10^{-9} cc.).

[1] Bronfenbrenner, J., and Korb, C., *J. Exp. Med.*, 1925, **42**, 821.

[2] Bronfenbrenner, J., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 802.

	(Control) Unheated				Mixtures heated, submerged in sealed tubes at 70°C. and tested at 10 min.								20 min.								30 min.			
P. C. phage (coli)	cc. 1			cc. 1	cc. 1			cc. 1	cc. 1			cc. 1	cc. 1			cc. 1	cc. 1			cc. 1	cc. 1			cc. 1
Plain broth	2			—	2			—	2			—	2			—	2			—	2			—
Sat. solution of sucrose in plain broth	—			2	—			2	—			2	—			2	—			2	—			2
Organisms subjected to lysis	1*	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Extent of lysis observed (+ = lysis; — = no lysis) cc.																								
10^{-1}	+	+	+	—	+	+	+	—	+	+	+	—	+	+	+	—	—	—	—	—	+	+	+	—	—	—	—	—	+	—	—	—
10^{-2}	+	+	+	—	+	+	+	—	+	+	+	—	+	+	+	—	—	—	—	—	+	+	+	—	—	—	—	—	+	—	—	—
10^{-3}	+	+	+	—	+	+	+	—	+	+	+	—	+	+	+	—					+	+	+	—					+	—	—	—
10^{-4}	+	+	+	—	+	+	+	—	+	+	+	—	+	+	+	—					+	—	+	—					—	—	—	—
10^{-5}	+	+	+	—	+	+	+	—	+	+	+	—	+	+	+	—					—	—	—	—								
10^{-6}	+	+	+	—	+	+	+	—	+	—	—	—	+	+	+	—																
10^{-7}	+	+	+	—	+	+	+	—	—	—	—	—	+	+	+	—																
10^{-8}	+	+	+	—	+	+	+	—					+	+	+	—																
10^{-9}	+	+	+	—	+	+	+	—					—	—	—	—																
10^{-10}	—	—	—	—	—	—	—	—					—	—	—	—																

Bacteriophage after heating at 70°C. 30 minutes propagated on each of the organisms and the resulting filtrates tested for lytic activity against each of the organisms for 3 successive passages.

	Titer in cc.	(Control) 1	2	3	4	*B. coli* Tested for activity against 1	2	3	4	Propagated with *B. dys.* "Shiga" Tested for activity against 1	2	3	4	*B. dys.* "Flexner" Tested for activity against 1	2	3	4	*B. dys.* "Hiss" Tested for activity against 1	2	3	4
Heated (30 min.) Phage retested before propagation	10^{-1}	+	—	—	—																
	10^{-3}	+	—	—	—																
	10^{-6}	—	—	—	—																
	10^{-9}	—	—	—	—																
After first attempt at propagation	10^{-1}					+	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—
	10^{-3}					+	—	+	—												
	10^{-6}					+	—	—	—												
	10^{-9}					+	—	—	—												
After second attempt	10^{-1}					+	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—
	10^{-3}					+	+	+	—												
	10^{-6}					+	+	+	—												
	10^{-9}					+	—	—	—												
After third attempt	10^{-1}					+	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—
	10^{-3}					+	+	+	—												
	10^{-6}					+	+	+	—												
	10^{-9}					+	+	+	—												

* 1 = *B. coli.* 2 = *B. shiga.* 3 = *B. Flexner.* 4 = *B. Hiss.*

Entirely analogous results were obtained with a *B. typhosus* phage exhibiting a secondary valency for *B. dysenteriae* "Flexner" and with *Staphylococcus aureus* phage, exhibiting a secondary valency for *Staphylococcus albus*. On the other hand when a polyvalent phage was produced by deliberately mixing several independent and unrelated phages (such as anti-coli and anti-typhosus or anti-staphylococcus) and the mixture was subjected to heating, some of the valencies lost during the heating could not be regenerated by the passage of the residual phage with a susceptible organism.

These experiments show, therefore, that when true multiple valencies are present in pure phages they are determined by some sort of a specific relationship among the susceptible bacteria perhaps remotely analogous but not identical with the relationships determining serological group reactions.

Incidentally, these results offer additional evidence against the parasitic nature of phage—for if phage were a parasite capable of invading *B. coli*, *B. dysenteriae* "Shiga", and *B. dysenteriae* "Flexner", it is difficult to see how heat could destroy its power of invading the 2 latter organisms while leaving the invasive power for the first unimpaired.

Furthermore, the subsequent recovery of lytic power for *B. dysenteriae* "Shiga" and *B. dysenteriae* "Flexner" can not be explained on the basis of "adaptation" of the parasite, since in these experiments the development of additional valencies by the monovalent anti-coli-phage took place as a result of the passage with *B. coli* only, and did not take place when *B. dysenteriae* "Shiga" or *B. dysenteriae* "Flexner" were exposed to it.

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Stimulation of Bacterial Metabolism by Bacteriophage.*

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Examination of an automatic cinematographic record of the progress of lysis of *B. coli* in the presence of bacteriophage suggested that addition of phage to pure cultures of *B. coli* causes an increase

* This work was supported from a grant of the Rockefeller Foundation to Washington University for Research in Science.