and how far, these deductions are verified experimentally. This is being done repeatedly with the chemical theory of the dynamics and statics of the hæmoglobin reactions. If only those who believe in the adsorption theory would make some precise deductions from their theory, it would be easy to test that also. At present it evades any quantitative trial.

Attempts have been made to apply the Phase Rule, and to attribute the properties of large-scale matter to the single ultimate unit of hæmoglobin as it exists in solution. Presumably this ultimate unit has a diameter about 10 times that of the oxygen molecule; it is presumably in violent, oscillatory (thermal) movement; there is no good evidence that it has ever been observed with the ultramicroscope. To regard it therefore as a separate phase is to disregard the statistical basis of the Second Law from which the Phase Rule is deduced. *If* the hæmoglobin unit be indeed a separate phase, then admittedly the known number of degrees of freedom of the hæmoglobin-oxygen system prohibits the possibility of regarding oxy- and reduced hæmoglobin as separate chemical compounds. No evidence, however, can be given for the existence of hæmoglobin, in solution in water, as a phase separate from the water, except that it can be precipitated by various violent means—which surely is not evidence; the separate phase is a pure hypothesis and must be judged by its fruits, which at present are difficult to discern.

Sir William Bayliss's attitude of continual and friendly scepticism, on this particular subject, has had one important and valuable effect, the effect which he set out to achieve, which, however, his modesty prevents him acknowledging, or possibly even from appreciating. It has urged a number of workers to produce, what was badly needed, a body of sound quantitative experimental evidence on one of the most fascinating problems in the borderland between biology and chemistry. The evidence is not complete and we cannot convince him yet; but if he will only maintain his scepticism, in an equally friendly way, for a few years more, he will really force us to produce all the testimony which he requires. A. V. HILL.

The University, Manchester,
May 31.

In the recent correspondence touching the nature of the combination of hæmoglobin with oxygen, references have been made to Wo. Ostwald's adsorption theory. It may clarify the issue if I remind readers of NATURE what that theory was. Wo. Ostwald argued that the equilibrium between oxygen and hæmoglobin could be expressed by a curve based on the following equation, $X = KC^m$, where X is the amount of oxygen combined with the hæmoglobin, C the concentration of oxygen in solution, K a quantity proportional to the total mass of hæmoglobin present, and m a constant. The graphic expression of this equation must necessarily be a simple curve which is at all points concave to the abscissa. No published curve representing the equilibrium between hæmoglobin and oxygen, which has been determined experimentally, is of this character, all being more or less S-shaped, though in some cases the convex inflection is very slight.

It may seem strange that a theory should have been put forward which is at variance with the facts in so fundamental a respect. In justice to Wo. Ostwald it must be pointed out that he wrote before the experimental technique now in use had been elaborated. The most recent curves at his disposal were those of Bohr, Hasselbalch, and Krogh (for the oxygen hæmoglobin equilibrium at various CO_2 pressures). These are S-shaped in character, but at the time commanded less confidence than they deserved; I think because they were determined not as individual curves but as a surface in three dimensions, the published curves being contours. All modern work has confirmed the essential character of the curves of Bohr, Hasselbalch, and Krogh.

Finally, may I pay a tribute to the helpful nature of Sir William Bayliss's criticism (NATURE, May 19, p. 666), and suggest an extension of that help in the direction of his modifying Ostwald's theory, expanding it into an equation which would fit the facts sufficiently exactly to stimulate further research on the subject. J. BARCROFT.

Physiological Laboratory, Cambridge,
June 6.

In his letter published in NATURE of May 19, Sir William Bayliss suggests that two cases of adsorption do not come within the definition of adsorption to which I directed attention in NATURE of April 14. These are the cases when two or more substances are adsorbed upon a surface, and when a substance is adsorbed to a thickness of several molecules. Both these cases were intended by me to be included, and I think reasonably so, with the definition that it is a case of adsorption, if the substance is taken up uniformly over the whole surface; uniformly, that is, when the scale of measurement is large compared with individual molecules. This sense of uniformity is well understood in the theory of gases, where a mixture of gases or a single gas may be said to fill space uniformly, with equal correctness. I had no intention of limiting the definition to layers only one molecule thick; indeed perhaps I may be permitted, as it is suggested that I accept Langmuir's views, to point out that the theory employed by Langmuir does not seem to me necessarily to postulate that adsorbed layers are always one molecule thick. Such a proposition could only be established by estimating the amount adsorbed on unit area and calculating the thickness of the layer in terms of known data as to the size of the molecules in every case of adsorption; it does seem to be established by the beautiful experimental work of Langmuir in many cases, but is not, I think, claimed by him to be an invariable law governing adsorption.

Sir William Bayliss says in his first paragraph that no serious attempt has been made to consider surface phenomena in the combination of oxygen and hæmoglobin, since Wo. Ostwald showed that the data of the taking up of oxygen by hæmoglobin could be expressed by the adsorption formula; but he seems to have overlooked that the *sole* argument put forward in my letter of April 14, to prove that the attraction of hæmoglobin for oxygen is a highly localised property of the hæmoglobin particle, was that the hæmoglobin is so much larger than the oxygen with which it combines that the oxygen must be attached to only a very small portion of the surface. If there were general attraction of the surface of the hæmoglobin particle for oxygen, then combination would not stop when only a small fraction was covered, but hæmoglobin would take up much more oxygen than it actually does. Surely this is a very definite attempt to consider the surfaces of the particles. It is a mistake to confuse the argument used in my letter with those based on the well-known mass-action formulæ of Barcroft and Hill; it is entirely independent of them, and essentially treats the hæmoglobin in solution as a hetero-