committees will be organized for dealing with further sections. Professor Lehmer's Report on Section F-Theory of Numbers is now in the press and will probably occupy about 175 pages.

I should be especially glad to receive information from any one with reference to mathematical manuscript tables, of value for our survey, which may be in public or private hands.

I have stated that the chief aim of the committee was to prepare for publication by the National Research Council a series of reports such as are described above. But another aim of almost equal importance is to publish a series of new mathematical tables which

the committee has reason for believing to be of importance for different fields of research. In order to make such publications possible the Rockefeller Foundation, last May, appropriated \$15,000 to the National Research Council to be used for the establishment in the Division of Physical Sciences of the Council of a revolving fund "for the publication of mathematical tables and aids to computation and bibliography of such tables," under the direction of the Committee on Mathematical Tables and Aids to Computation.

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BROWN UNIVERSITY, JUNE 26, 1940

## SPECIAL ARTICLES

## RADIO-IRON IN PLASMA DOES NOT EXCHANGE WITH HEMOGLOBIN **IRON IN RED CELLS<sup>1, 2</sup>**

RADIO-IRON gives the investigator a relatively simple and accurate method of tracing the course of iron absorption and transfer within the body. When iron is absorbed in the anemic dog it heaps up rapidly in the blood plasma,<sup>3</sup> reaches a peak and falls close to the base line in 6 to 12 hours. Within 4 hours after feeding, radio-iron is found in significant amounts in the hemoglobin of red cells of the anemic dog.<sup>4</sup> When values shift with this rapidity, obviously we must be certain that the iron within the hemoglobin of these circulating cells does not exchange with the plasma radio-iron in the dog under investigation. The following experiments bear on this important point and give evidence that the iron bound in hemoglobin is fixed and incapable of exchange with plasma radio-iron or artificial solutions of radio-iron.

The following experimental procedure was employed. Iron containing the radioactive isotope was fed to a fasting anemic dog. One and a half hours later, 90 ml of blood was withdrawn into 20 ml of isotonic oxalate. Red cells were removed by centrifugalization. One aliquot of 10 ml of plasma was ashed for radioactive iron determination. Six other aliquots were added to washed red blood cells obtained from 10 ml of blood of animals whose blood levels ranged from severe anemia to normal. The suspensions were kept at 37° C. for 24 hours with

<sup>1</sup> From the Departments of Pathology and Radiology, the University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

<sup>2</sup> We are deeply indebted to Professor E. O. Lawrence and members of the Radiation Laboratory of the University of California for the radioactive iron used in these experiments, and in particular to Dr. M. D. Kamen, who was directly responsible for preparing the isotope.

<sup>3</sup> P. F. Hahn, W. F. Bale, E. O. Lawrence and G. H. Whipple, *Jour. Exp. Med.*, 69: 739, 1939. <sup>4</sup> L. L. Miller and P. F. Hahn, *Jour. Biol. Chem.*, 134:

585, 1940.

frequent agitation. The cells were removed in the centrifuge and washed three times with saline. Cells were laked and stroma precipitated by re-establishing isotonicity followed by centrifugalization. The supernatant solution of hemoglobin was ashed for radioactive iron determination.

Activity determinations were made using the Geiger-Müller counter as described in previous publications.<sup>3</sup>

The control plasma aliquot had an activity of 5.3 counts per minute above the background of 3.7 counts per minute on our scale-of-four counter.

In each case measurement of activity of the iron separated from the hemoglobin after the exchange experiment showed close to background rate of counting, indicating that no exchange within the accuracy of measurement had occurred.

From statistical considerations it is considered that in these individual experiments exchange could have been as high as 15 per cent. without having been detected, although in the average of six experiments it is certainly much less than this.

TABLE 1 LACK OF EXCHANGE BETWEEN THE IRON OF HEMOGLOBIN IN RED CELLS AND PHYSIOLOGICALLY BOUND PLASMA RADIO-IRON

Dog	Hemato- crit		Activity found		
		globin level	Hemo- globin	Plasma	– Remarks
39-196 39-53 39-144 37-227 39-80 39-169	$\% \\ 51.7 \\ 28.9 \\ 32.2 \\ 18.4 \\ 17.3 \\ 32.5 \\ \end{cases}$	$\begin{array}{c} {\rm gm} \ \% \\ {\rm 18.0} \\ {\rm 8.0} \\ {\rm 10.5} \\ \\ {\rm 5.4} \\ {\rm 4.8} \\ {\rm 10.9} \end{array}$	$0.2 \\ 0.0 \\ 0.0 \\ 0.0 \\ 0.0 \\ 0.4$	$\begin{array}{c} 4.4 \\ 4.8 \\ 5.5 \\ 4.8 \\ 5.9 \\ 6.1 \end{array}$	Normal adult Anemic, protein de- pleted Anemic, bile fistula Anemic, bile fistula

Control plasma shows an activity of 5.3 counts per minute.

An experiment was carried out to determine whether there was any exchange between hemoglobin in solution and inorganic iron in solution. Ninety ml of min.

blood from dog 38-112, an anemic animal with no circulating radioactive iron, was centrifugalized. Plasma was discarded. The cells were laked in distilled water and the stroma precipitated partially by the addition of 18 per cent. sodium chloride. The supernatant solution, largely hemoglobin, was separated and 2 ml of iron labelled with the radioactive isotope in the form of ferric ammonium citrate were added. After standing in the refrigerator for 24 hours the mixture was poured into aluminum cream to precipitate remaining stroma and any other protein material other than hemoglobin. Perhaps 15 per cent. of the original hemoglobin was lost in this step. The filtrate was poured into an equal volume of 10 per cent. trichloroacetic acid to precipitate hemoglobin and this precipitate was washed and ashed for determination of radioactivity.

## EXPERIMENTAL DATA

Iron content of hemoglobin from 90	
ml of blood	22 mg
Labelled iron added as ferric am-	
monium citrate	0.34 mg
Activity of radioactive iron added	66 counts per min.
Net activity of radioactive iron in	_
hemoglobin	0.1 counts per m

The amount of labelled iron found in the hemoglobin is within the experimental error. It is estimated that radioactive iron equal in activity to 0.4 counts per minute might have been present and escaped detection. This sets an upper limit of 1 per cent. on the amount of exchange which might have taken place and escaped detection under the conditions of the experiment.

These findings are supported by other experiments in which solutions of hemoglobin were tested with artificial solutions of radio-iron in plasma. There was no evidence of any exchange between the hemoglobin iron and the radio-iron in solution. These experiments were done before the final tests recorded in Table 1.

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## VISCOSITY AND THE SHAPE OF PROTEIN MOLECULES

IN some recent publications,<sup>1, 2, 3, 4</sup> attempts have been made to interpret protein viscosity data in terms of the asymmetry of the molecules. This has been

1 A. Polson; Koll. Zeits., 88: 51, 1939.

<sup>2</sup> Mark and Simha, Nature, 145: 571, 1940.

<sup>3</sup> V. L. Frampton and H. Neurath, SCIENCE, 87: 468, 1938

4 M. A. Lauffer, SCIENCE, 87: 469, 1938.

done by applying equations developed by Burgers<sup>5</sup> and Eisenschitz,<sup>6</sup> or by Kuhn,<sup>7</sup> on the assumption that there is no orientation of the molecules. The discrepancies between these values for the asymmetry and the values obtained by applying the equations of Perrin<sup>8</sup> to sedimentation velocity and diffusion data are considerable. It has been suggested that the differences arise from the failure to consider the effects of hydration. Recently the hydrodynamic behavior of ellipsoids has been reconsidered by Simha.<sup>9</sup> The results obtained seem to yield better agreement for the asymmetries of various proteins than previous equations without any assumption of hydration.

In the expression for the specific viscosity at infinite dilution.

n

$$/\eta_o - 1 = vc \tag{1}$$

(where c is the volume fraction of the solute), v is a function of the axial ratio,  $\rho$ , of an ellipsoid of revolution. Table I gives the numerical values of the factor

TABLE I

1/ρ	v		1/p	v		
orp	elongated	flattened	or p	elongated	flattened	
1.0	2.50	2.50	20.0	38.6	14.80	
$\frac{1.5}{2.0}$	$2.63 \\ 2.91$	$2.62 \\ 2.85$	$25.0 \\ 30.0$	$\frac{55.2}{74.5}$	$\begin{array}{c} 18.19 \\ 21.6 \end{array}$	
3.0	3.68	3.43	40.0	120.8	28.3	
$\frac{4.0}{5.0}$	$4.66 \\ 5.81$	$4.06 \\ 4.71$	$\begin{array}{c} 50.0\\ 60.0\end{array}$	$176.5 \\ 242.0$	$35.0 \\ 41.7$	
6.0	7.10	$5.36 \\ 6.70$	80.0	400.0	$55.1 \\ 68.6$	
10.0	13.63	8.04	150.0	1222.0	102.3	
$12.0 \\ 15.0$	$\tfrac{17.76}{24.8}$	$9.39 \\ 11.42$	$200.0 \\ 300.0$	$2051.0 \\ 4278.0$	$136.2 \\ 204.1$	

v for values of  $1/\rho$  and  $\rho$  from 1 to 300. These values have been applied to the same viscosity data as those used by Polson<sup>1</sup> and by Mark and Simha.<sup>2</sup> In Table II the axial ratios are compared with those from sedi-

TABLE II

· .	f/fo	∿ —	$1/\rho$ , elongated		$\rho$ , flattened	
Protein			Dif- fusion	Vis- cosity	Dif- fusion	Vis- cosity
Egg albumin Serum albumin Hemoglobin Octopus hemo- cyanin Homarus hemo- cyanin Helix pom. hemo- cyanin Helix pom. hemo- cyanin Serum globulin Lactoglobulin Pepsin	$\begin{array}{c} 1.17\\ 1.25\\ 1.16\\ 1.28\\ 1.38\\ 1.60\\ 1.27\\ 1.24\\ 1.41\\ 1.43\\ 1.26\\ 1.08\\ \end{array}$	5.7 6.5 5.3 7.0 9.0 14.6 6.4 9.0 9.9 9.0 9.2 .2 .2 .2 .2 .2 .2 .2 .2 .2	$\begin{array}{r} 3.8\\ 5.0\\ 3.7\\ 5.4\\ 7.2\\ 10.9\\ 5.2\\ 4.8\\ 7.6\\ 7.8\\ 5.2\\ 2.5\end{array}$	$5.0 \\ 5.6 \\ 4.6 \\ 6.0 \\ 7.3 \\ 10.5 \\ 5.5 \\ 5.5 \\ 7.3 \\ 7.9 \\ 5.1 \\ 4.5 \\ $	$\begin{array}{r} 4.0\\ 5.4\\ 3.9\\ 6.0\\ 8.2\\ 13.6\\ 5.8\\ 5.2\\ 8.9\\ 9.2\\ 5.7\\ 2.6\end{array}$	$\begin{array}{c} 6.7\\ 7.7\\ 6.0\\ 8.5\\ 11.4\\ 21\\ 7.5\\ 7.5\\ 11.4\\ 12.7\\ 6.9\\ 5.8\end{array}$
Helix hemocyanin pH 8.6	1.89	18.0	16.6	12.0	23.9	<b>26</b>

<sup>5</sup> J. M. Burgers, "Second Report on Viscosity and Plasticity," Amsterdam, 1938.

<sup>6</sup>Ř. Eisenschitz, Źeits. physik. Chem., A163: 133, 1933.

<sup>7</sup> W. Kuhn, Zeits. physik. Chem., A161: 1, 1932.

<sup>8</sup> F. Perrin, Jour. Phys. et Rad., 7: 1, 1936.
<sup>9</sup> R. Simha, Jour. Phys. Chem., 44: 25, 1940.