tency of natural stimuli has been observed already in the investigations of Sherrington and Graham Brown, when artificial stimuli were unable to call forth a reflex movement, but the natural stimuli arising in the spinal cord produced movements. In the case of our heart experiments the possibility appears of a fairly quantitative measurement.

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On the Ionization of Calcium Citrate.

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The hypothesis that citrate ions combine with calcium ions in some way and thus remove them from solution serves to explain a number of observations. Among these may be mentioned the following: non-precipitation of calcium phosphate in alkaline solutions when magnesium citrate is present; the failure of Shipley, Kramer and Howland[1] to obtain calcification *in vitro* even with a Ca x P product of 60 when the calcium is present as calcium citrate; the unpublished observations of Shelling and Maslow in this laboratory on the production, by intravenous injection of sodium citrate, of convulsions clinically similar to those of tetany, but with a normal total serum calcium and a greatly increased dialyzable calcium; and the results reported very recently in the important contributions of Hastings, Murray and Sendroy[2] on the solubility of calcium carbonate and calcium phosphate.

There are no studies, however, which bear directly on the ionization of calcium citrate. We are, therefore, reporting some experiments which give direct evidence in favor of the above hypothesis.

Conductivity titrations were performed using N/200 calcium chloride and N/200 sodium citrate solutions. The conductivity of each solution was measured, that of the citrate being found the greater. Measured volumes of the citrate solution were added to a measured volume of the calcium solution. The conductivity of the resulting mixture was measured after each addition. The first addition of the citrate produced a decrease in conductivity instead of an increase. Further additions of citrate caused further decreases. It was only after an equivalent quantity of citrate had been added that subsequent additions caused the conductivity to increase. The decrease in conductivity was marked; when an equivalent quantity of citrate was added, the resistance of the mixture was about 50 per cent higher than the value which would have been obtained had there been no ionic reaction.

Such decreases in conductivity are attributed to a decrease in the number of ions in the solution. To rule out any decrease in the number of hydrogen ions or hydroxyl ions, the pH of both solutions was first adjusted to 7.4 with N/10 sodium hydroxide or N/10 hydrochloric acid. The amount of sodium chloride formed in each case was quite small. The behavior of sodium chloride was, nevertheless, studied and was found to be normal, as was expected. Conductivity titration of N/800 sodium chloride with N/200 sodium acetate gave values which decreased steadily from that of the sodium chloride solution toward that of the acetate, as calculated on the assumption that no ionic reaction occurred.

The marked decrease in conductivity observed when a solution of sodium citrate is added to a solution of calcium chloride is, therefore, interpreted as being due to the removal from the solution of the calcium ions by the citrate ions. Un-ionized molecules of calcium citrate are probably formed although the formation of a complex ion of some sort is another possibility to be considered.

This is a preliminary report.

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[1] Shipley, P. G., Kramer, B., and Howland, J., *Biochem. J.*, 1926, xx, 379.

[2] Hastings, A. B., Murray, C. D., and Sendroy, J., Jr., *J. Biol Chem.*, 1927, lxxi, 723-846.