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Ions from the Hofmeister Series: Effects on Proteins in Solution and in the Crystallization Process. Kim Collins, Biochemistry & Molecular Biology, Univ. of Maryland Medical School, 108 N. Greene St., Baltimore, MD 21201-1503 USA.

Sephadex G-10 gel sieving chromatography, Jones-Dole viscosity B coefficients, and solution neutron and x-ray diffraction are used to show that small ions of high charge density (*e.g.*, sulfate, phosphate, the carboxylate, sodium and fluoride) are strongly hydrated (kosmotropes) whereas large monovalent ions of low charge density (*e.g.*, ammonium, chloride, potassium and the positively charged amino acid side chains) are weakly hydrated (chaotropes). The heats of solution of the crystalline alkali halides are then used to show that only oppositely charged ions of equal water affinity spontaneously form inner sphere ion pairs, and that this controls ion binding to proteins. The net charge on a protein is a major determinant of its solubility. Finally, the surface potential difference and surface tension at an air/salt solution interface are used to generate a simple model for how ions affect protein stability and solubility through indirect interactions at the protein/solution interface.