The phase behavior of protein solutions is exploited in numerous applications, such as precipitation and crystallization in protein separations, crystallization in structural biology and gelation in food processing. However, the relation of these operations to the phase diagram is not always clearly defined, and detailed phase diagrams have been measured only sparingly, so the phase diagram per se has found only limited use in seeking optimal process conditions. Probably the closest explicit link between a direct property measurement and selection of process conditions for proteins is a correlation, developed by George and Wilson, of the osmotic second virial coefficient with solution conditions conducive to crystallization. This presentation will discuss efforts to build on the empirical correlation, including more efficient measurement of protein interactions by self-interaction chromatography, making possible a much more extensive exploration of protein interaction trends as a function of solution conditions than has previously been possible. Molecular mechanics simulations are used to explore the mechanistic basis for sometimes counterintuitive trends in virial coefficient measurements. Such measurements will also be related to protein phase behavior measurements, which are organized within the framework of the theoretical phase diagram for short-ranged colloidal interactions. However, a key feature remains the distinctive and complex nature of protein interactions, which give rise to rich and complex physicochemical phenomena and make life possible.