The earliest probability considerations in crystal structure analysis were introduced by Wilson (Nature (1942) 150, 1S2) who showed that intensity data could be corrected for vibrational effects and placed on an absolute scale by use of a statistical relationship between the intensities and the atomic scattering factors. This relationship is employed for the preparation of experimental data for direct phase determining procedures. Wilson pointed out that the expected values for absolute intensities is given by

\[ I_{h} = I_{\text{obs}} = \sum_{i=1}^{N} \Gamma_{i} f_{i}^{2} \]

where \( f_{i} \) is the atomic scattering factor for the \( i \)th atom in a unit cell containing \( N \) atoms. He also noted that the observed intensities \( I_{\text{obs}} \) differ from the \( I_{\text{calc}} \) by a scale factor, \( k \) independent of \( h \), and a temperature factor. By use of the above relation the observed data can be rescaled and corrected for positional disorder. Wilson (Acta Cryst. (1948) 2, 315) also found to a very good approximation, probability distributions for the intensities in non-centrosymmetric and centrosymmetric crystals that could be used to determine the presence or absence of a center of symmetry. A number of studies followed in the attempt to take account of the presence of heavy atoms, special positions, and the regularities that occur in crystal structures. One such study involved the use of the joint probability distribution (Hauptman and Karle, Acta Cryst. (1955) 8, 136). It had an additional purpose, namely, to develop a facility in deriving joint probability distributions to be associated with phase determining relations.

The basic phase determining relations, used in procedures for phase determination have had their origins in inequality theory (Karle and Kasper, Acta Cryst. (1948) 1, 76; Karle and Hauptman, Acta Cryst. (1950) 3, 151). Inequality theory per se, is only applicable to simple structures. However, it was apparent that the inequality relationships could be extended as probabilistic formulas in order to have formulas applicable to complex structures. For example, it was observed by Gillis (Acta Cryst. (1948) 1, 174) that inequalities of Karle and Kasper still gave correct phase indications even when the appropriate phase factor magnitudes were of too small a magnitude to satisfy the conditions of application of the inequalities. The appropriate mathematical tool for developing the probabilistic aspects of the inequality theory was the joint probability distribution. The first series of investigations concerned centrosymmetric crystals (Hauptman and Karle (1957) Proc. 3rd American Crystallographic Association, Polyomolecular Book Service; Western Springs). Further application of probability theory continued over the years, thus establishing the mathematical foundations of direct methods. The development involves the non-negativity of the electron density distribution, atomicity and the overdetermination of the experimental data. The foundation mathematics which is comprised of the phase determining formulas from inequality theory and their probabilistic implications takes proper account of the presence of atoms of unequal atomic number in crystals.