Abstract

The present work is divided into four sections: initially we present a simple model of spherical protein with directional forces. We evaluated the model within the framework of Wertheim's perturbation theory and determined the influence of model parameters on thermodynamic properties of proteins in water solution. We described the coexistence curves for solutions of lysozyme and γIIIa cystallin. In addition, we proposed a measure of ion specificity for protein–protein interaction due to added salt.

In the second section we generalized the theory to describe globular proteins with nonspherical shape. For this purpose we allowed penetration of spheres to form simplified model for proteins with nonspherical shape. Stability of such model fluid increased with deviation from spherical shape. We evaluated theoretical assumptions using complementary Monte Carlo simulations. We found out quantitative agreement for osmotic pressure and semi–quantitative agreement for excess internal energy.

In the third section we considered a binary mixture of proteins, composed from spheres, fused in contact. We presented the phase equilibrium by coexistence surface. The latter showed nontrivial isotherms in regard to the symmetry of interactions among proteins. The equilibrium phases were different not only in density, but also in protein composition: larger degree of asymmetry led to enhanced difference, in the extreme case to three coexisting liquid phases. We used the model of binary mixture to analyse measurements of cloud temperatures on mixtures of β and γ crystallins. Due to difference in quadrupole moment of proteins, we used different number of active sites on proteins to describe their stability in solutions.

In the last section we defined the model of antibodies as a limiting case of nonspherical shape. We constructed antibody from seven hard spheres, decorated with three active sites to allow formation of aggregates. We used the model to describe interactions between FAB–FAB and FAB–FC regions as well as the antibodies with dual function (bivalent antibodies) showing asymmetric FAB regions. We obtained corresponding distribution of aggregates and phenomenologically evaluated their contributions to viscosity. We used the FAB–FAB model to describe viscosity measurements of IgG_1 antibodies in water for several additions of salt, temperature and pH. We observed for viscosity to be correlated with the second virial coefficient. We found out for solutions of bivalent antibodies to have lower viscosities, while the model with FAB–FC interactions showed higher solution viscosities on account of formation of branched aggregates.

Keywords: directional forces, phase equilibrium, globular proteins, aggregation