Thirty years of (bio)molecular simulation: How far have we come ?

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Computation based on molecular models is playing an increasingly important role in biology, biological chemistry, and biophysics. Since only a very limited number of properties of biomolecular systems is actually accessible to measurement by experimental means, computer simulation can complement experiment by providing not only averages, but also distributions and time series of any definable – observable or non-observable – quantity, for example conformational distributions or interactions between parts of molecular systems. Present day biomolecular modelling is limited in its application by four main problems: 1) the force-field problem, 2) the search (sampling) problem, 3) the ensemble (sampling) problem, and 4) the experimental problem. These four problems will be discussed and illustrated by practical examples. Progress over the past thirty years will be briefly reviewed. Perspectives will be outlined for pushing forward the limitations of molecular modelling.

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