CONFIGURATIONAL DEPENDENCE OF MOLECULAR SHAPE

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Abstract

Some of the topological techniques developed for the description of molecular shape are studied, formulated as a problem of embedding nuclei within electronic clouds.

1. Introduction. The shape-configuration relation as an embedding problem

Chemists often think of chemical species at two levels: in terms of their energetic stability and in terms of their three-dimensional shape. It is well understood that the relative energetic stability of some families of nuclear configurations with respect to nuclear rearrangements is the ultimate reason for the existence of chemical species. The three-dimensional nature of molecules is often modeled by fixed or vibrating nuclear configurations where nuclei are treated as formal points in space, and by electron distributions represented as formal molecular bodies (almost classical entities) with well-defined shape.

Strictly speaking, the above view is not compatible with quantum mechanics. Nuclear positions have an uncertainty, though much smaller than that for the electrons, which cannot be neglected. As a consequence of this uncertainty, and the finite size of nuclei, it is not rigorous to represent or define chemical species in terms of point-like nuclear configurations [1,2]. Similarly, formal molecular bodies with sharp boundaries as formal molecular surfaces are only approximations of reality, since electron distributions of molecules have a fuzzy, quantum mechanical character. Once again, we find a conflict with rigorous quantum mechanics, since real molecules have no boundary. If the total electronic density is considered to model the molecular shape, one could talk of a molecular surface, at best, as a fuzzy object. The reasons for choosing a formal molecular surface or a set of molecular surfaces as representatives of molecular shape are often somewhat subjective.

Nonetheless, there are valid empirical reasons for depicting molecules as semiclassical objects with defined shape and size. Empirical parameters representing formal molecular volumes and areas can be measured [3–11]. The interpretation and prediction of these parameters is difficult without the notion of molecular surface [9,11,12], and some classical models provide remarkably good descriptions of the relevant molecular properties.
To a good approximation, one may regard a molecule as a family of nuclei embedded in an electronic cloud. If, following the commonly used terminology, molecular configuration is interpreted as the nuclear configuration, and if the shape of the molecule is regarded as the shape of the electron distribution, then the configurational dependence of molecular shape, the subject of this report, can also be described as a special embedding relation of nuclei immersed in electronic clouds.

This approach is facilitated if one considers the shape of electron distributions as the starting point and uses the concept of three-dimensional molecular shape to define chemical species. The implementation of this approach is perhaps the simplest if the shape characterization is based on formal molecular surfaces, and if some of the geometrical notions are replaced by topological models.

The semiclassical views of molecules can be reconciled with quantum mechanics if the geometrical notion of chemical species as fixed configurations is replaced by a topological one. In this latter approach, species are represented by open sets in configuration space, i.e., by a continuum of configurations. The construction of these continua from the properties of the potential energy surface has been discussed in the literature [13]. On the other hand, the identification of chemical species in terms of shape is a current development. This topic concerns various areas of applied science, such as pharmacology and biochemistry. Synthesis planning and computer-assisted drug design are among the fields where interrelations between energy, shape, and conformational changes are of relevance. The objective of this review is to provide an account of the present status of the study of conformational dependence of molecular shape, and to point out future lines of research.

The organization of this work is as follows. In section 2, we review some concepts relevant to the geometrical and topological treatments of configurational space. In section 3, some current methods for characterizing molecular shape are presented. These methods provide shape codes to identify conformations which are shapewise equivalent. Section 4 presents some results on the interplay between conformational changes and molecular shape. Applications to problems of assessing molecular similarity during a chemical reaction (e.g., the Hammond postulate) are also included in this section. Section 5 is devoted to the comparison between the partitionings of configuration space in terms of the curvature properties of the potential energy surface and in terms of the shape of molecular surfaces. In section 6, we present an extension of previous ideas to the analysis of the interplay between molecular shape and folding in large macromolecular structures. Conclusions and further comments on the development of this field are found in section 7.

2. Geometry and topology of configurational space

The topological model provides a description of molecules radically different from the conventional, geometrical description. Within the geometrical model, the concept of molecular structure is associated with nuclear geometries. By contrast,