

MOLECULAR HARMONY

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Publications:

Náray-Szabó, G. (1988) The harmony of molecules, In: Maruani, J., ed., *Molecules in Physics, Chemistry, and Biology*, Vol. 1, Dordrecht: Kluwer, 205-231.

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Náray-Szabó, G. (1994) Analysis of molecular recognition: Steric, electrostatic and hydrophobic complementarity, *Journal of Molecular Recognition*, 6, 205-210.

Abstract: According to the Oxford Dictionary the meaning of the word "harmony" is "agreement", "congruity", "combination or arrangement of parts and orderly whole". Furthermore, "harmonise" is equivalent to "be agreeable in artistic effect". These everyday concepts are also very important in the world of molecules though they are described in other terms. In this paper we try to show that various meanings are related in the scientific sense, too, and even harmonise to a certain extent. Following various aspects of harmony we will discuss molecular similarity and host-guest complementarity, which concepts offer important tools in the understanding of the phenomenon of molecular recognition. Since molecules are part of Nature, like other macroscopic objects as landscapes, plants, animals or humans, they may also have a certain intrinsic beauty. An aspect of molecular beauty is symmetry. We will illustrate the above concepts by various models represented by molecular graphics.

1 INTRODUCTION

The meaning of the word “harmony” is “agreement”, “congruity”, “combination or arrangement of parts to form consistent and orderly whole”. Furthermore, “harmonize” is equivalent to be “agreeable in artistic effect” (Coulson et al., 1982). These everyday concepts are also very important in the world of molecules though they are described by other words. In the following we try to show that the various meanings are related in the scientific sense, too.

Analysis of molecular harmony may lead to simple and general rules that are qualitative but help very much in understanding important aspects of non-covalent bonding in molecular associations. Present-day science has achieved enormous advancement in quantifying the description of natural phenomena, however, we need qualitative descriptions because mathematical formulation alone is not sufficient for the complete understanding of a natural phenomenon (Heisenberg, 1971). Qualitative rules may become an integral part of the scientist’s knowledge, and have an impact on the formulation of working hypotheses. What we need at the very end, is to bring exact thinking and emotions, two complementary ways leading to truth, closer to each other.

In the world of molecules agreement or congruity means *similarity*, while arrangement of parts to form an orderly whole corresponds to *molecular recognition*, with a specific aspect, the phenomenon of *induced fit*, which we can associate with tolerance. Scientists cannot disregard the esthetic impact, variety and wealth of computer models of simple and complex molecules, so we can speak about *beauty* in the world of molecules. Let us discuss these aspects in some more detail.

2 SIMILARITY

Maybe the most important aspect of molecular similarity is related to biological activity and it is supposed that similar molecules have similar biological action. If we restrict ourselves to biopolymer-ligand binding, an event triggering a certain biological response, the meaning of similarity may be understood in terms of the lock-and-key model of *Emil Fischer* (1894). In this model enzymes are represented by the lock, and various keys (the bound ligands) fit to this lock. Similar, though not identical, keys may fit into the same lock leading to a similar biological response. Molecular similarity has three aspects: steric, electrostatic and hydrophobic (Náray-Szabó, 1989). On Fig. 1 we present an example for steric similarity of two molecules having about the same antihypertensive activity. It is seen that at one end, where they fit into the crevice of the target biopolymer, the molecules are quite easily superimposable, while the other ends are dissimilar.

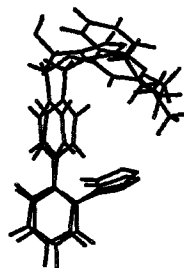


Figure 1. Steric similarity of two angiotensin II antagonist molecules.

3 MOLECULAR RECOGNITION

Larger molecules with a hollow crevice specifically recognise certain smaller ones, the ligands. This means that only certain structures will fit into this crevice to trigger the biological response, others not. Molecular recognition originates in lock-and-key complementarity, which, like similarity, has three main aspects: shape, electrostatic and hydrophobic (Náray-Szabó, 1989). Steric and hydrophobic complementarity is illustrated on Fig. 2, where the hydrophobic, i.e. water repellent, arylalkylamine ligand fits nicely into the macromolecular cavity, which is surrounded by hydrophobic amino-acid residues. This is a representation of the *similis simili gaudet* principle (Náray-Szabó, 1989): host-guest (biopolymer-ligand) binding prefers hydrophilic/hydrophilic and hydrophobic/hydrophobic associations.

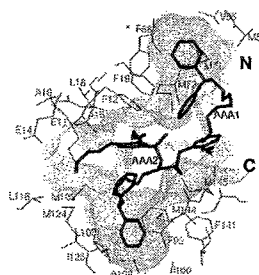


Figure 2. Complementarity between calmodulin and its arylalkylamine ligand (Harmat et al., 2000).

4 BEAUTY

Molecules are parts of Nature, therefore, like other macroscopic objects as landscapes, plants, animals or humans, they may have a certain intrinsic beauty. An aspect of beauty is symmetry, which is nicely illustrated in a cathedral window, as well as in a cross section of the molecular model of deoxyribonucleic acid (cf. Fig.3). Tenfold symmetry is

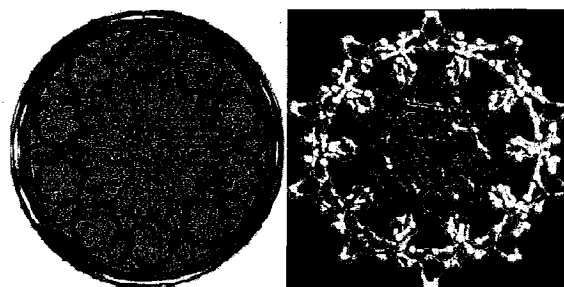


Figure 3. Tenfold symmetry in the Washington National Cathedral „creation” window designed by Rowan LeCompte (left), and in the cross-section representation of the DNA double helix. (Right, graphics after Paul Thiessen, <http://www.chemicalgraphics.com/paul/DNA.html>) quite rare among cathedral windows, 6-, 8-, 12- and 16-fold symmetries are most common. The coincidence between a window paying tribute to creation and the molecular basis of life, deoxyribonucleic acid, is striking.

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