What is the Shape of a Molecule?

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*Molecular visualization* has become an indispensable part of molecular analysis and represents one of the particularly successful branches of data visualization. Various graphical representations of molecules have been invented and serve different needs in molecular sciences.

Are these representations suited, if one is aiming at *visual analysis, i.e.* if one wants to draw physically correct conclusions from molecular depictions? Important biophysical phenomena, like the transport of molecules through a biological membrane, often depend on fine details. It turns out that commonly used types of molecular depictions sometimes do not allow us to draw correct conclusions.

When trying to depict molecular details more accurately, a key question is: What is the shape of a molecule? In contrast to macroscopic objects, this cannot be determined with geometrical optics. An operational procedure to determine the shape is via repulsive forces that prevent interpenetration of bodies. However, also in contrast to the macroscopic domain, no fine tip is available for “scanning” the molecule. Instead, only similarly sized objects, namely other atoms or molecules (which carry own force fields) can be used. The resulting shape therefore depends on the ‘probe’. Nevertheless, using this kind of procedure, one gets exactly the information that is required when mutual accessibility of molecules is analyzed.

Two recent developments will be sketched that are based on this operational definition of molecular shape: (a) data-driven determination of effective atomic radii and (b) computation of molecular surfaces that characterize approachability by other molecules. The methods will be illustrated using analysis examples from biophysics, structural biology and drug design.