This Week's Citation Classic®

Williams D E. Nonbonded potential parameters derived from crystalline hydrocarbons. *J. Chem. Phys.* 47:4680-4, 1967.
[Institute for Atomic Research and Department of Chemistry, Iowa State University, Ames, IA]

Systematic computerized multivariable least-squares fitting was used to address the question: Why do hydrocarbon molecules pack together in a certain way in the crystal? The resulting (exp-6) nonbonded potential energy functions were a significant improvement over simple hard-sphere van der Waals radii. [The *SCI*® indicates that this paper has been cited in over 410 publications.]

Molecular Packing Analysis in Organic Crystallography

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After a number of delays, I took my PhD in physical chemistry (crystallography) from Iowa State University in 1964 under the supervision of Robert Rundle. I was Rundle's last PhD student before his untimely death. Like any new PhD, I needed to look for permanent employment, and without assistance from my mentor. I continued temporarily at Iowa State as a research associate.

It was only natural that after doing three crystal structure investigations for my dissertation I would continue in X-ray diffraction, choosing to determine the crystal structure of dibenzoylmethane (DBM). In 1964 DBM was considered a fairly difficult structure. However, at about this time the new and powerful "direct methods" of crystal structure determination were beginning to spread. Perhaps it was fate that I did not learn of these methods in time for DBM, which did not have the heavy atom usually needed for crystal structure determination in those days.

Instead, I thought that since the molecular structure of DBM in its enol form could be estimated, why not just find the location of the molecules in the unit cell by molecular packing analysis (MPA)? The crystallographer's familiarity with multivariable least squares to minimize the R factor for diffraction data led me to devise a packing factor for molecules that could be minimized. In a short time, the crystal structure of DBM was solved and published.[1]

I thought that MPA would become an important tool to solve the diffraction phase problem.[2] Perhaps success in MPA could lead to a good job with a university! The sharpening of that tool required better energy functions for intermolecular interaction. While browsing through the library, I came across A.I. Kitaigorodskii's book,[3] which greatly influenced my professional development. Kitaigorodskii advocated the use of (exp-6) atom-atom potentials.

Again, least squares to the rescue! The question was: What nonbonded energy must exist in known crystal structures? My answer was given in a paper[4] that appeared prior to the *Citation Classic* and dealt with aromatic hydrocarbon crystals. The classic paper was a follow-up that additionally treats nonaromatic hydrocarbons. It is probably cited more because it extended the results of the previous paper. The 18 crystal structures and 108 observational equations kept the computers humming back in those days. I would work into the wee morning hours.

Subsequently it turned out that multiple minima produced by MPA were its Achilles' heel, and direct methods took over the crystallography of small- to medium-sized organic molecules. However, there was considerable interest in nonbonded potential energy functions in the molecular mechanics community[5] and also in connection with protein folding and enzyme-substrate complexation. For a number of years the National Institutes of Health supported my research to further develop nonbonded potential energy functions and to study interaction between net atomic charges.[6]

1. **Williams D E.** Crystal structure of dibenzoylmethane. *Acta Crystallogr.* 21:340-9, 1966. (Cited 95 times.)
2. ------------. Computer calculation of molecular crystal structures. *Science* 159:645-6, 1968. (Cited 15 times.)
3. **Kitaigorodskii A I.** *Organic chemical crystallography.* New York: Consultants Bureau, 1961. 541 p. (Cited 500 times.)
4. **Williams D E.** Nonbonded potential parameters derived from crystalline aromatic hydrocarbons. *J. Chem. Phys.* 45:3770-8, 1966. (Cited 325 times.)
5. **Burkert U & Allinger N L.** *Molecular mechanics.* Washington, DC: American Chemical Society, 1982. 339 p. (Cited 355 times.)
6. **Williams D E & Yan J-M.** Point-charge models for molecules derived from least-squares fitting of the electric potential. *Advan. Atom. Mol. Phys.* 23:87-130, 1988.

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