Gas Phase Molecular Recognition Using Fourier Transform Mass Spectrometry

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The Dearden group's research centers on the development and use of state-of-the-art, extremely sensitive chemical analysis tools. The instrument we work with, a Fourier transform mass spectrometer (FTMS), weighs molecules with accuracies of about one part per million, and can distinguish between molecules with similar weights better than any other available technique. With this kind of accuracy, merely weighing a molecule is usually enough to unambiguously identify it, and this can be done with samples whose total mass is less than one billionth of a gram. Further, because the instrument "levitates" and traps molecules in a strong magnetic field, it serves as a sophisticated "test tube" in which we can carry out and study complex reactions with these tiny quantities of material.

We are using FTMS to do fundamental studies of molecules that react with each other selectively because one fits well inside the other, in much the same way as only the correct key will open a lock. This kind of chemistry, called "molecular recognition," is of general importance, especially for living things. For example, molecular recognition is what enables the body to distinguish between its own cells and those of foreign invaders, leaving the former alone and resulting in an immune response to the latter. Our experiments are designed to find out what features of a molecule cause it to be recognized by other molecules. By understanding the basis for molecular recognition, we lay a foundation upon which important applications can be built.

Three examples illustrate potential applications of our work:

- As a byproduct of weapon production during the cold war, huge amounts of radioactive waste were generated. This waste is currently stored in corroding tanks at various sites around the U.S. Further, modern society continues to generate wastes in conjunction with nuclear power production. The costs of cleanup have been estimated to be on the order of a trillion dollars. Molecular recognition has been identified as one of the most promising approaches to removing important radioactive metals, such as cesium and strontium, from this waste. Our work provides a basis for designing the right molecules to do that job most effectively and economically.

- Second, about half of all pharmaceutical molecules are "handed," so they differ from other very similar molecules in the same way that a person's right hand differs from the left. Using pharmaceuticals of the wrong "handedness" can have disastrous consequences, because rather than having a beneficial effect, the wrong "handed" drugs can be toxic. These pharmaceuticals present a very difficult analytical challenge, because right- and left-handed molecules are very difficult to distinguish. Our work in molecular recognition investigates molecules that have this "handedness" property, and is developing very sensitive analytical tools to tell them apart.

- Third, 21st century chemistry holds promise for developing a completely new technology based on molecule-sized machines that could perform medical diagnostics or treatment, for example.

Already, simple molecular machines such as wheels and levers have been demonstrated. We are using FTMS to study the properties of molecule-sized boxes that can hold other molecules of the proper size and be chemically opened to release their contents on demand. We envision that someday the things we are learning will be used to design containers that could enter the bloodstream, travel to a disease site, and release therapeutic drugs directly where they are needed. This work is funded through the Chemistry Division of the National Science Foundation.

Our gas phase experiments are ideal for complementary modeling studies using computational methods, which are increasingly becoming important parts of our research. Computational techniques are well suited for characterizing isolated molecules and supramolecular complexes in the gas phase. We use BYU's extensive supercomputing resources to solve the Schrödinger equation for the same systems we are studying experimentally, making it possible to obtain information about conformations, energetics, and spectroscopic properties that are very difficult to measure experimentally. At the same time, the experimental data provide benchmarks against which the computed results can be tested. We frequently work with complexes involving more than 100 non-hydrogen atoms, at chemically-accurate levels of theory.

In summary, our work probes the fundamental interactions that underlie molecular recognition and supramolecular self-assembly. This basic science is laying a foundation upon which exciting new applications in molecular nanotechnology will be based.