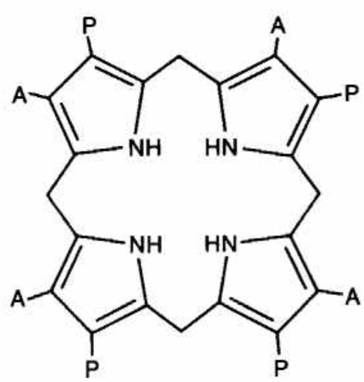
Marginalia

Creation and Discovery

Roald Hoffmann

In describing what they do, scientists have by and large bought the metaphor of discovery, and artists that of creation. The cliché "uncovering the secrets of nature" has set, like good cement, in our minds. But I think that the metaphor of discovery is effective in describing only part of the activity of scientists, and a smaller piece still of the work of chemists. The historical, psychological, and sociological reasons for the ready acceptance of the metaphor deserve a closer look.

First, the rise of modern science in Europe coincided with the age of geographical exploration. Men set foot on distant shores, explored *terra incognita*. Even in our century, a man I was named after first sailed the Northwest Passage and reached the South Pole. Voyages of discovery, maps filled in—these are powerful images indeed. So is penetration into a royal tomb full of glistening gold vessels. It's no surprise that these metaphors were and are accepted by scientists as appropriate descriptors of their generally laboratory-bound activity. Is there some vicarious sharing of imagined adventures at work here?



$A = CH_2COOH$
$P = CH_2CH_2COOH$

Second, the French rationalist tradition of philosophy, and the systematization of astronomy and physics before the other sciences, have left science with a reductionist core. There is supposed to exist a logical hierarchy of the sciences, and understanding is to be defined solely in vertical terms as reduction to the more basic science. The more mathematical, the better. So biological phenomena are to be explained by chemistry, chemistry by physics, etc. The logic of a reductionist philosophy fits the metaphor of discovery: one digs deeper and discovers the truth.

But reductionism is only one face of understanding. We have been endowed with the ability not only to disassemble, disconnect, and analyze, but also to build. There is no more stringent test of passive understanding than active creation. Perhaps "test" is not the right word here, for building or creation differs inherently from reductionist analysis. I want to claim a greater role in science for the forward, constructive mode *(1)*.

As for the sociology behind the metaphor: those philosophers of science who started out as practicing scientists have generally, I believe, come from physics and mathematics. The education of professional philosophers is likely to favor the same fields; there is a special role, quite understandably, for logic in philosophy. No wonder that the prevailing ideology of reasoning in the underlying scientific areas of expertise of philosophers of science has been extended by them—unrealistically, I believe—to all science.

What is strange is that chemists should accept the metaphor of discovery. Chemistry is the science of molecules (up to a hundred years ago one would have said "substances" or "compounds") and their transformations. Some of the molecules are indeed *there*, just waiting to be known by us. We come to "know" them in their static properties—what atoms are in them, how these are connected up, the shapes of molecules, their splendid colors. And in their dynamic characteristics—their internal motions, their reactivity. The molecules are those of the earth, for instance simple water and complex malachite. Or of life—pretty simple cholesterol, more complicated hemoglobin. The paradigm of discovery certainly applies to the study of these molecules.

But so many more molecules of chemistry are made by us, in the laboratory. We're tremendously prolific; a registry of known, well-characterized compounds now numbers near ten million. These were not on the earth before. It is true that their constitution follows underlying rules, and if chemist A had not made such-and-such a molecule on a certain day, then it is likely to have been synthesized a few days or decades later by chemist B. But it is a human being, a chemist, who chooses the molecule to be made and a distinct way to make it *(2)*. This work is not so different from that of the artist, who, constrained by the physics of pigment and canvas, and shaped by his or her training, nevertheless creates the new.

Even when one is operating clearly in the discovery mode in chemistry, elucidating the structure or dynamics of a known, naturally occurring molecule, one usually has to intervene with created molecules. I recently heard a beautiful lecture by Alan Battersby, an outstanding British organic chemist, on the biosynthesis of uroporphyrinogen-III. (Even in the trade, the name of this molecule is abbreviated as uro'gen-III.) It's not a glamorous molecule, but it should be. For from this precursor plants make chlorophyll, the basis of all photosynthetic activity. All cells use another derivative of uro'gen-III in cytochromes for electron transport. And the crucial iron-containing, oxygen-carrying piece of hemoglobin derives, too, from this small, disk-shaped molecule.

Uro'gen-III, pictured at left, is made from four rings, called pyrroles, themselves tied into a larger ring. Note the markers A and P in each ring. They're in the same order as one goes around the ring (from about 10 o'clock)—except for the last set, which are "reversed." So the markers read A, P, A, P, A, P, P, A.

How this natural molecule is assembled within us is clearly a question that is in the mode of discovery. In fact, the four pyrrole rings are connected with the aid of an enzyme into a chain, then cyclized. But the last ring is first put in "incorrectly"—that is, with the same order of labels as in the other rings, to give A, P, A, P, A, P, A, P. Then, in a fantastic separate reaction, just that last ring, with its attached labels, is flipped into position.

Roald Hoffmann is professor of chemistry at Cornell University.

This incredible but true story was deduced by Battersby and his co-workers using a sequence of synthetic molecules, which were made slightly different from the natural ones *(3)*. Each was designed to test some critical part of the natural process in the living system. Each was then treated under the physiological conditions to allow the sequence of the natural events to be traced out. Using molecules we've made, we learn how nature builds a molecule that makes life possible.

The synthesis of molecules puts chemistry very close to the arts. We create the objects that we or others then study or appreciate *(4)*. That's exactly what writers, composers, visual artists, all working within their areas—working perhaps closer to the soul—do. I believe that, in fact, this creative capacity is exceptionally strong in chemistry. Mathematicians also study the objects of their own creation, but those objects, not to take anything away from their uniqueness, are mental concepts rather than real structures. Some branches of engineering are actually close to chemistry in this matter of synthesis. Perhaps this is a factor in the kinship the chemist-narrator of *The Monkey's Wrench* feels for the builder Faussone, who is the main character in Primo Levi's recently translated novel *(5)*.

In the building of theories and hypotheses, even more than in synthesis, the act is a creative one. One has to imagine, to conjure up a model that fits often irregular observations *(6)*. There are rules; the model should be consistent with previously received reliable knowledge. There are hints of what to do; one sees what was done in related problems. But what one seeks is an explanation that was not there before, a connection between two worlds. Often, actually, it's a metaphor that serves as the clue: "Two interacting systems, hmm . . . let's model them with a resonating pair of harmonic oscillators, or . . . a barrier penetration problem" *(7)*. The world out there is moderately chaotic—frighteningly so, in the parts we do not understand. We want to see a pattern in it. We're clever, we "connoisseurs of chaos," so we find/create one. Had more philosophers of science been trained in chemistry, I'm sure we would have a very different paradigm of science before us.

Is art all creation? I don't think so. In substantial measure it is discovery—of the deep truths of what is also around us, often overlapping, but more often reaching outside the set of problems that science has set for itself to try to understand. Art aspires to discover, explore, unravel—whatever metaphor you please—the nonunique, chanced, irreducible world within us.

References

1. For a relevant debate on reductionism see S. Weinberg, 1987, *Nature* 330:433, and 1988, *Nature* 331:475; E. Mayr, 1988, *Nature* 331:475; E. Mayr, 1982, *The Growth of Biological Thought* (Harvard Univ. Press), pp. 59–63.
2. In this context, see G. Stent, 1972, *Sci. Am.* Dec., p. 84; 1985, *Eng. and Sci.* (Cal Inst. Technol.) Sept., p. 9; 1989, in *Progress in Science and its Social Condition*, ed. T. Ganelius, Nobel Symposium no. 58, Oxford: Pergamon Press.
3. For leading references to the beautiful chemistry discussed so cursorily here, see A. R. Battersby and E. McDonald, 1979, *Accounts Chem. Res.* 12:14; A. R. Battersby, 1989, *Pure Appl. Chem.* 61:337; A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, and E. McDonald, 1980, *Nature* 285:17.
4. Often quoted here is M. Berthelot, 1988, *Chimie Organique Fondée sur la Synthèse*, tome 2, Paris: Mallet-Bachelier, 1860. See also J.-P. Malrieu, 1987, *L'Actualité Chimique*, no. 3, p. ix; A. F. Bochkov and V. A. Smit, 1987, *Organicheskii Sintez*, Moscow: Nauka.
5. Primo Levi. 1986. *The Monkey's Wrench*. Simon & Schuster.
6. Baruch S. Blumberg has stressed the role of fantasy in model building, in an interesting recent article: 1989, *Med. J. Writers Assoc.* 4:2.
7. For a discussion of metaphor in science see various articles, especially that by R. R. Hoffmann, 1985, in *The Ubiquity of Metaphor*, ed. R. Dirvan and W. Paprotte, Amsterdam: John Benjamin.