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EDITORIAL

Biophilia and Chemiphilia

Modern biology has produced a genuinely new way of looking at the world that is incidentally congenial to the inner direction of biophilia. In other words, instinct is in this rare instance aligned with reason. The conclusion I draw is optimistic: to the degree that we come to understand other organisms, we will place a greater value on them, and on ourselves.

Biophilia, E. O. Wilson
Harvard University Press
Cambridge, Massachusetts 1984, p. 2.

It may not going too far to suggest that the appeal of the abstract logic of organic chemistry, closely akin to that of Euclidean geometry, combined with the intriguing aromas of volatile compounds and the visual beauty of various crystals, inspires a sense of chemiphilia in many chemists, analogous in some ways to E. O. Wilson's biophilia.

J. Meinwald
Proc. Natl. Acad. Sci. USA, 2003, **100**, 14514.

E. O. Wilson, biologist and naturalist *par excellence*, defines biophilia 'as the innate tendency to focus on life and lifelike processes'. In a remarkable essay entitled 'Bernhardsdrop', in his book *Biophilia*, Wilson reflects on a naturalist's quest, at the end of a long day observing and collecting ant species in the South American rainforest. In Wilson's words: 'Mundane events acquired the raiment of symbolism, and this is what I concluded from them: That the naturalist's journey has only begun and for all intents and purposes will go on forever. That it is possible to spend a lifetime in a magellanic voyage around the trunk of a single tree. That as the exploration is pressed, it will engage more of the things close to the human heart and spirit. And if this much is true, it seems possible that the naturalist's vision is only a specialized product of a biophilic instinct shared by all, that it can be elaborated to benefit more and more people. Humanity is exalted not because we are so far above other living creatures, but because knowing them well elevates the very concept of life.' (*Biophilia*, p. 22).

My attention was drawn to the word 'biophilia', by an article entitled 'Understanding the chemistry of chemical communication: Are we there yet?', which appeared a few weeks ago (J. Meinwald, *Proc. Natl. Acad. Sci. USA*, 2003, **100**, 14514). Meinwald, while introducing a collection of papers from a symposium entitled 'Chemical communication in a post-genomic world', emphasizes the central role of organic chemistry in probing the molecular mechanisms of biological signalling and introduces the term 'chemiphilia'. Organisms communicate with one another and often control their environment by secreting specific chemicals, which home in on target receptors, with amazing economy and efficiency. 'Natural products chemistry', a branch of organic chemistry, is a discipline as old as 200 years. Meinwald quotes from a famous letter written by Jons Jakob Berzelius to Friedrich Wohler, in 1835: 'Organic chemistry just now is enough to drive one mad. It gives me an impression of a primeval tropical forest, full of the most remarkable things, a monstrous and boundless thicket, with no way to escape, into which one may well dread to enter.' In the century and a half that has passed since Berzelius' letter, natural products chemists have isolated and catalogued the structures of thousands of organic compounds from nature, focussing on 'secondary metabolites', which at first glance seem to have no real use in the organisms which produce them. Natural products researchers have been seduced by the complexity of nature's chemicals, turning into 'chemiphiles', who can, to borrow Wilson's phrase, 'spend a lifetime in a magellanic voyage', characterizing all the metabolites in the extract of a single plant.

The borders between primary and 'secondary' metabolism were drawn early in the development of biochemistry, which found a home within the broad disciplinary framework of biology. Organic chemistry developed by erecting barriers, excluding those who transgressed artificial boundaries. The divide between biochemists, who transformed themselves into molecular biologists, and natural products chemists was highlighted by Arthur Kornberg in 1987: 'By 1950, organic chemistry had been enriched by more than a century of impressive achievements. . . . They belonged to a proud and venerable science. . . . The problem was that organic chemists placed arbitrary boundaries on their science. Although in their pursuit of natural products, they might still eagerly seek the challenge of an Amazonian butterfly pigment, they would not accept nucleic acids, proteins, and enzymes as proper natural products. I recall in an organic chemistry textbook of 1960, a reference to the importance of proteins "as a source of amino acids for living cells". 'This is like saying the importance of the automobile is as a source of its parts.' Kornberg went on to chastise molecular biologists: 'In its rapid and turbulent growth, molecular biology has washed away much of the bridge to chemistry. . . . Molecular biology falters when it ignores the chemistry of the products of the DNA blueprint – the enzymes and proteins and their products – the integrated machinery and framework of the cell. Molecular biology appears to have broken into the bank of cellular chemistry, but for lack of chemical tools and training, it is still fumbling to unlock the major vaults.' (A. Kornberg, *Biochemistry*, 1987, **26**, 6888).

In the years following Kornberg's lament, a greater integration of chemistry and biology seems to have occurred with many departments of chemistry adding the term 'chemical biology' to their names. Analytical methods which have their roots in chemistry and physics are now the common tools of biology. The genomics and proteomics revolutions will be spearheaded by techniques which cut their teeth on chemical problems, X-ray crystallography, nuclear magnetic resonance (NMR) and mass spectrometry among them. Lasers are at the heart of the most powerful microscopic imaging methods which have transformed cell biology. But even as chemistry has moved to embrace biological problems, classical natural products chemists have become an endangered species. For the last few decades organic chemistry has been dominated by the practitioners of chemical synthesis and developers of methodology. The study of 'natural products' has been unfashionable. This is ironic because in the aftermath of genomics, it is now clear that 'secondary metabolites' are anything but secondary. Microorganisms and plants orchestrate the synthesis of these complex organic substances, using sequential enzymatic reactions, with modular multienzyme complexes produced by 'turning on' the expression of genes, lined up as a cluster, controlled by a single regulating element. The profusion and structural diversity of microbial metabolites is best illustrated by *Streptomyces*, which ushered in the 'golden age of antibiotics'. In his Nobel lecture of 1952, Selman Waksman (who many believe was wrongly credited as the discoverer of streptomycin, which for a while was the front-line drug against tuberculosis) quotes from the *Ecclesiastius* (XXXVII, 4): 'The Lord hath created medicines out of the earth; and he that is wise will not abhor them.' The reference here is to the abundance of soil microorganisms, which hold immense promise for the discovery of the next generation of antibiotics. The growing interest in 'secondary metabolites', the 'natural products' of classical chemistry is fuelled by the increasing importance of pharmaceutical leads based on plant extracts, that have been used in traditional, indigenous medicine. Microbial metabolites and marine natural products hold an enormous promise for the discovery of new molecules. This resurgence of interest in the molecules of nature comes at a time when the tools of purification and structural analysis have reached an extraordinary level of sensitivity and sophistication. Sadly, the chemists with interest and insight into natural products chemistry have long been sidelined. In India, few major institutions can boast of credible 'natural products' programs, although they all pay lip service to the importance of developing pharmaceutical leads.

The new and developing area of chemical ecology will also require considerable expertise in the chemistry of natural products. Thomas Eisner, one of the founders of the field, notes: 'New disciplines arise by a convergence of interest. Chemical ecology is the product of a partnership between biologists and natural products chemists united by a shared vision and empowered by complementary skills. The vision stems from the realization that all organisms emit chemical signals and that all, in their respective ways respond to the chemical emissions of others.' Eisner states emphatically: 'Chemical ecology is now embarking on the most ambitious and inventive phase of its existence. To stand by and allow natural products chemistry to vanish or even to be weakened, is to deny chemical ecology its future.' (*Proc. Natl. Acad. Sci. USA*, 2003, **100**, 14517).

In his book *Biophilia*, Wilson considers a 'superorganism', an ant colony and a symbiotic fungal mat. He calls the ant–fungus combination, 'one of evolution's master clockworks, tireless, repetitive, and precise, more complicated than any human invention and unimaginably old'. (p. 37). Nature is full of examples where chemistry, shared and complementary, controls the dynamics of ecology. The meeting of minds of 'biophiles' and 'chemiphiles' is necessary to restore natural products research to its rightful place at the advancing borders of chemistry and biology.

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