Practicing biochemistry without a licence?

Steven Rose

Among the many revealing sidelights cast on the culture of molecular biology in Craig Venter's book *A Life Decoded,* there was one that particularly struck me. He describes his first encounter with Jim Watson, who was interested in some of the research Venter had presented. "That explains everything," Watson said. "You are a biochemist." Venter took this as a compliment, only later realizing that Watson meant it as anything but.

The turf wars between biochemistry and molecular biology go back a long way. In the aftermath of the Watson–Crick DNA paper, Erwin Chargaff—who had shown the constancy of the A:T and G:C ratios in DNA—described these young outsiders as "practising biochemistry without a licence". One could imagine that in his offhand comment to Venter, Watson was repaying in kind a long-standing insult.

Trained as a biochemist myself, I saw this hostility when, as a young post-doc working in the newly established biochemistry department at Imperial College in London in the 1960s, my boss, Nobel prize winner Ernst Chain, refused to appoint any molecular biologists to staff, and on his retirement fought a long and ultimately doomed battle to prevent his successor from being one.

Of course, when Chargaff made his remark, biochemistry was the more-established discipline. It represented a new and radical approach to understanding living processes, which had painfully fought itself free from the older disciplines of physiology and biological chemistry; it did not enjoy being overtaken on the left, as it were, by this new upstart.

'On the left' is slightly more than a metaphor—there was often a political radicalism among biochemists in the middle of the last century, as I discovered when applying for my first US visa, as I was hauled in for questioning by the London-based consular officials. When I asked them why, they replied that they saw from my passport that I was a biochemist and they knew that "you biochemists" were a left-wing lot. The geneticist John Maynard Smith said it was all to do with the reputation of J.B.S. Haldane.

You could readily dismiss this biochemistry–molecular biology fracas as nothing more than a fight over territory, journal space or grants, but it was and is, I think, more than this. Molecular biology is, after all, just what it says on the tin: a study of molecules, just as biological chemistry—with all due deference to the *Journal of Biological Chemistry*, whose contents transcend its title—is about the chemistry of those molecules. Neither say anything about the dynamics and interactions of the molecules, and it is these dynamics that biochemistry is about. The key lies in a classic definition given by that charismatic figure, who is so central to the history of biochemistry, Sir Frederick Gowland Hopkins, Nobel prize winner for the discovery of vitamins and professor of biochemistry at Cambridge during the 1920s and 1930s. "Life," he said, "is a dynamic equilibrium in a polyphasic system." My only problem with that definition is that it does not capture the fact that the equilibrium point is constantly shifting over time, which is why I prefer the term homeodynamics to homeostasis. Stasis is death.

This year sees the centenary of the Biochemical Society in Britain, and I am a bit startled to reflect that I have been a member for almost exactly half of its lifetime. For almost all of that time, molecular biologists have been convinced that their ways of understanding life are the royal road to success. Their culminating glory should have come at the millennium with the publication of the first draft of the human genome. For decades, they had been claiming that all human life would be able to be read off from that 3-billion nucleotide sequence. However, then came the cold shock of discovering that the human genome contains only 23,000 genes, around the same number as the fruitfly. You could not read off the life of a fly, let alone that of a human, just from the sequence.

As developmental biologists could have told them—if only genetics and developmental biology had not become divorced early last century—if life did not lie in the gene, then it must be in the way the gene is read during ontogeny. Hence the rediscovery of Waddington's epigenetics, along with another proclaimed new science, 'evo-devo', or evolutionary developmental biology. "I thought that's what we'd been doing all along," Waddington's student, and the first woman to become Foreign Secretary of the Royal Society, Ann McLaren, once remarked. But there are fashions in terminology. That is probably why, along with a genome, it turns out that we have an epigenome as well. Indeed, we have an entire wardrobe of 'omes.' There are transcriptomes, proteomes, signalosomes, even enviromes. The trouble for a biochemist is that all of these 'omes' seem to be essentially static compilations; a list of all available molecules or systems that can be shoe-horned into a fashionable portmanteau term. What is needed to bring them to life is an understanding of their dynamic interactions—their metabolism. True to form, we have a new word for it: the metabolome. However, as Hopkins would have pointed out, is that not what biochemists have been studying all along? If molecular biologists now start studying metabolism, perhaps they need to reflect on Chargaff's comment, and be sure that they have a licence for it.

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