Dreamers and dilettantes

Some scientists spend their entire career doggedly pursuing one single idea, problem, or object of study. Others flit from topic to topic with no apparent focus. The former are often judged to be ‘successful’, at least within a certain intellectual territory. The latter often have great difficulty obtaining grants, attracting students, or getting stuff published.

I suppose I lie somewhere in between, probably leaning towards the fuzzy-focus end of the spectrum, except that I have been lucky enough to have escaped most of those negative consequences. But, having darted about from RNA metabolism to evolutionary genomics, respiratory bioenergetics, the mechanics of DNA replication, pathophysiology, biogerontology, gene therapy, and finally skirting the issue of intracellular temperature, I find myself invited to review manuscripts and funding applications in fields where I have limited knowledge, or where my expertise is 10 or 20 years out of date. Even worse is when I am approached by journalists, believing me to be a reliable source on some topic I have merely brushed up against many years ago, and long since abandoned. The only thread linking everything is ‘mitochondria’.

One obvious downside is that a career such as this leaves many loose ends: issues that I would love to return to and tease out further if I had the time, energy, or funding. Unfinished business in science is often ignored or dismissed as an artefact or a statistical freak. Conversely, sometimes it is elevated to the status of a standalone result worthy of being quoted or cited, even though, in the absence of follow-up experiments, the evidence is weak. But, if a curious result is not followed up, the field usually just moves on. Getting the next steps funded many years later is even harder, unless a powerful new technique comes along just at the right moment.

The literature is full of such loose-end findings. In many instances, the necessary tools to make further progress were simply not available at the time. Or the investigator ran out of money. Nowadays we are even encouraged by funders to seek new directions in research. The current funding system places a premium on novelty and relevance to wider societal issues, while ‘incremental research’ that just proceeds logically to the next step is often frowned upon. So, it’s doubtful that many overhanging results will ever be actively followed up, at least until someone else stumbles into the issue much later by chance.

When trying to locate some long-lost relatives online, I recently came across a pertinent example of all this, in the person of a distant cousin, Allen S. Fox, who conducted research in various midwestern universities in the US from the late 1940s until his untimely death in 1977. When I looked at his papers, I realized that he had made important discoveries in *Drosophila* and fungal genetics, but never really followed them up because the methods to do this were only developed decades later. Perhaps if he had lived another 30 years, he would have been able to capitalize on his findings. Or maybe he would have just got diverted onto something else.

Fox’s work began in an era when the relationship of genes, proteins and antigens was unclear, when the co-linearity of chromosome segments and genetic determinants remained unresolved, and when the nature of the genetic code was still debated. In his early work he made important contributions towards addressing these fundamental issues.

In parallel, he found time to make the first steps towards establishing *Drosophila* cell culture (Horikawa & Fox, 1964; Horikawa *et al*, 1966), a tool that has become a standard complement to whole-organism studies. His lab was also the first to develop protocols for cell-free protein synthesis

from a genetically tractable ‘higher’ eukaryote (Fox *et al*, 1965). Subsequently he pioneered early attempts at DNA transformation of flies (Fox *et al*, 1966, 1970a, 1970b, 1971). Although only somatic transformation was achieved, this laid the groundwork for others to develop the techniques of germline genetic manipulation that have today become routine. Along the way, he discovered sex peptide, a male accessory gland protein that plays a crucial role in modulating female reproductive behaviour following insemination (Fox *et al*, 1959). And he even published an early piece of evidence for developmentally regulated alternative splicing, although he didn’t see it in those terms at the time (Wallis & Fox, 1968).

None of his studies came fully to fruition and today he is largely forgotten. But his story is far from unique: in fact, we might wonder whether some of today’s most original scientific thinkers languish in similar obscurity, their ideas decades ahead of any technical advances that might test them, and therefore dismissed as dreamers and dilettantes?

Howy Jacobs

References

Fox AS, Kan J, Kang SH, Wallis B (1965) Protein synthesis in cell-free preparations from *Drosophila melanogaster*. *J Biol Chem* 240, 2059–2065.

Fox AS, Mead CG, Munyon IL (1959) Sex peptide of *Drosophila melanogaster*. *Science* 129: 1489–1490. doi: 10.1126/science.129.3361.1489.

Fox AS, Duggleby WF, Gelbart WM, Yoon S (1970) DNA-induced transformation in *Drosophila*: evidence for transmission without integration. *Proc Natl Acad Sci USA* 67: 1834–1838. doi: 10.1073/pnas.67.4.1834.

Fox AS, Yoon SB (1966) Specific genetic effects of DNA in *Drosophila melanogaster*. *Genetics* 53: 897–911. doi: 10.1093/genetics/53.5.897.

Fox AS, Yoon SB (1970) DNA-induced transformation in *Drosophila*: locus-specificity and the establishment of transformed stocks. *Proc Natl Acad Sci USA.* 67: 1608–1615. doi: 10.1073/pnas.67.3.1608

Fox AS, Yoon SB, Gelbart WM (1971) DNA-induced transformation in *Drosophila*: genetic analysis of transformed stocks. *Proc Natl Acad Sci USA* 68: 342–346. doi: 10.1073/pnas.68.2.342.

Horikawa M, Fox AS (1964) Culture of embryonic cells of *Drosophila melanogaster in vitro*. *Science* 145: 1437–1439. doi: 10.1126/science.145.3639.1437

Horikawa M, Ling LN, Fox AS (1966) Long-term culture of embryonic cells of *Drosophila melanogaster*. *Nature* 210: 183–185. doi: 10.1038/210183a0

Wallis BB, Fox AS (1968) Genetic and developmental relationships between two alkaline phosphatases in *Drosophila melanogaster*. *Biochem Genet* 2: 141–158. https://doi.org/10.1007/BF01458713