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Insect resistance to *Bt* revisited

To the editor:
Two timely and thoughtful articles in *Nature Biotechnology*, a review by Estruch et al.[1] and a commentary by Roush and Shelton[2], provide information about insect resistance to insecticidal proteins produced by the common bacterium *Bacillus thuringiensis* (*Bt*). Transgenic crops that express *Bt* proteins could be a cornerstone of ecologically sound pest management, but if pests adapt quickly, the success of this approach will be short-lived. Because of the importance and urgency of this issue, some clarifications about points raised in the aforementioned articles are warranted.

First, both articles note that the diamondback moth has already evolved resistance in the field in response to repeated exposure to foliar sprays containing *Bt* proteins. Resistance to *Bt* in the diamondback moth is described by Estruch et al.[1] as restricted to "geographically isolated" populations and by Roush and Shelton[2] as occurring "in several tropical countries." In fact, diamondback moth resistance to *Bt* has been documented in field populations from the United States (Florida, Hawaii, and New York), Asia (China, Japan, Malaysia, Thailand, and the Philippines), and Central America (Costa Rica, Guatemala, Honduras, and Nicaragua)[3,4].

Second, Roush and Shelton[2] raise questions about the frequency of a *Bt* resistance allele in the susceptible LAB-P strain of the diamondback moth, which had been reared for >100 generations in the laboratory without exposure to *Bt*[5]. A series of single-pair crosses and bioassays conducted from 1992–1995 showed that a recessive allele conferring resistance to at least four *Bt* toxins occurred at a frequency of about 10% in 41 families from the LAB-P strain[5]. In the paper reporting these results[5], we suggested that intense selection and the surprisingly common presence of a multiple-toxin resistance gene might explain rapid evolution of resistance to *Bt* in the diamondback moth, but we also cautioned, "The frequencies of multiple-toxin resistance genes in other populations of diamondback moth and in other pests remain to be measured." We included this caveat because meaningful generalizations about resistance allele frequencies require additional direct empirical estimates.

Although the frequency of *Bt* resistance alleles in most diamondback moth populations may well have been substantially less than 10% before the widespread use of *Bt* foliar sprays, the indirect argument of Roush and Shelton for this contention is based largely on untested assumptions. In particular, the intensity of selection associated with foliar sprays of *Bt* may be lower in the field than in the glasshouse. For example, because of overlapping generations of diamondback moth and the brief persistence of *Bt* foliar sprays (unlike *Bt* proteins in transgenic plants), the percentage of a field population escaping exposure to *Bt* might greatly exceed the 20% escaping exposure in the unpublished glasshouse study mentioned by Roush and Shelton. We found that five foliar applications of *Bt* to a field population of diamondback moth in Hawaii caused no detectable increase in resistance in a moderately resistant population[6]. In contrast, five selections with *Bt*-treated foliage caused five to sevenfold increases in resistance in a replicated laboratory experiment in which few, if any, larvae escaped exposure[6].

In commenting on the empirical estimates of resistance frequency in *Heliothis virescens* reported by Gould et al.[7], Roush and Shelton note that the rate of evolution of resistance is much more sensitive to changes in selection than in the initial resistance allele frequency. Therefore, without precise knowledge about selection, the initial resistance allele frequency in field populations cannot be inferred reliably from rates of resistance development in the field. Nonetheless, Roush and Shelton apply this indirect approach to the diamondback moth in their commentary. The work by Gould et al.[7] on *Heliothis* represents a breakthrough because it provides a direct estimate of the initial frequency of resistance in field populations. Direct experimental field tests of resistance management tactics, including those currently being used in *Bt* cotton, are sorely needed.

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Paradigm lost?

To the editor:
I must commend *Nature Biotechnology* for maintaining a reasoned and highly relevant debate[1]. To summarize: Strohman questions whether an inordinate amount of the research effort should be going into molecular, rather than more complex, biology. He implies that delays in developing new drugs could be down to a failure of therapeutic reductionism. Bains[2] disagrees with this implication, repeatedly citing soaring stock prices as evidence of why genetic determinism should be of absolutely no concern to anybody, except perhaps an ivory tower epistemologist. One has to admire such open opportunism, but given recent events in Hong Kong and elsewhere, one must wonder whether his confidence in shares as a reliable scientific indicator remains unshaken.

What is interesting is that Strohman, Bains, Streelman and Karl[3], and Persson[4] all more of less agree that: (1) genetic determinism is flawed; (2) molecular genetics has emerged with the lion's share of research dollars (notwithstanding the fabled center at Santa Fe); and that (3) even so, molecular genetics has not completely replaced *a posteriori* rationalization with *a priori* reasoning in biological research.

What then is the real issue at the heart of this debate? Strohman, perhaps wisely, avoids addressing it directly. Bains treads closer when he points out that the ideas of genetic determinism fell on relatively deaf ears in the 1960s. Could it concern another very complex system, namely the wider historical context?

It was not until the late 70s and early 80s that the molecular genetic cause, in all its forms, really began to gather momentum and funding. Would it be surprising if the zenith of 'triumphant molecularism' turned out to coincide with a period in which an economic model based on competitive individualism was being vigorously promulgated? Or that in the relatively liberal late 90s, views such as Strohman's, that were once less popular, are more readily accepted?

Whether a molecular paradigm exists to be shifted in the sense that Kuhn intended remains unclear; but at least one of his ideas seems as true today as it did in 1962: like it or not, the path of scientific enquiry is intimately and inexorably linked to the wider concerns of the day[5].

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