Indian Journal of Weed Science **50**(3): 201–208, 2018

Print ISSN 0253-8040 Online ISSN 0974-8164

Intractable weed problems need innovative solutions using all available technologies

Jonathan Gressel*

Plant & Environmental Sciences, Weizmann Institute of Science, Rehovot, 76100 Israel

**Email: jonathan.gressel@weizmann.ac.il*

Article information

DOI: 10.5958/0974-8164.2018.00049.7

Type of article: Review article

Received: 29 September 2018
Revised : 03 October 2018
Accepted: 16 October 2018

Key words
Gene drives
Herbicide resistance
Herbicide safeners
Herbicide synergists
Innovation
Multisite herbicides
Transgenics

ABSTRACT

There is often strong public dissent to innovations, typically fanned by those who lose out economically, but the reasons they promulgate are not economic and are targeted to public emotions. Agriculture has some problems that have been intractable to present technologies and we have no choice but to utilize new technologies to overcome them. These include developing new herbicides that affect multiple targets, new selective synergists and safeners, transgenic herbicide resistant plants that will not have the transgenes expressed in related weeds, using transposons or gene drives to disseminate deleterious genes in weeds, sterile pollen, enhanced-virulence biocontrol agents with sustaining formulations. These might be workable for multiple resistant *Amaranthus* and *Echinochloa* species, parasitic weeds, *Phalaris* in wheat as well as weedy rice in rice. Per force, most of the innovations must originate in the public sector, by weed scientists who have a broad training in basic sciences, in collaboration with experts from other fields.

INTRODUCTION

Innovation and its enemies

There are a growing number of seemingly intractable weed problems that are globally prevalent on a large scale, as discussed in the following sections. The present solutions are often not realistic solutions, as they may include compromises such as lower yield, more costly or expensive herbicides, or more environmentally-degrading cultivations, growing alternative less effected but lower yielding varieties or other crop species that are less appropriate. Innovative solutions may be out there already, or can be conceived and tested but are not – because too many weed scientists feel uncomfortable when out of the box, lack the basic knowledge on which to base innovation and/or are reluctant to collaborate with colleagues in other areas who could assist, as well as the many that fear the wrath of detractors who view innovation as a threat.

A book that is required reading for anyone interested in being an innovator was written by the late Kenya native, Harvard University Professor of the Practice of International Development, Calestous Juma. In “Innovation and its Enemies: Why people resist new technologies” (Juma 2016), he describes the many types of detractors of new technologies. They are all typically vested interests that will be the economic or political losers if the technology is adopted. They never tell you that their reason is their pocket book; they make up lies such as it is unsafe, will cause cancer, impotence, is unnatural, scientists are playing God, *etc*., *etc*., all targeted to achieve a hysterical response in the media, and an emotional negative response in the public. He points out that the general public typically is more convinced by pseudoscience over science.

Juma describes how these detractors may come from very different ends of the spectrum. In our case dealing with innovations in weed control they include:

- So-called environmental activists who need a target around which to garner financial contributions by generating hysteria – whether about herbicides or transgenics.

- It includes those who have anti-globalization politics and are against multinational corporations.

- It includes NGOs that want to keep the poor impoverished so that they can stay in business.

- It includes organic growers and their lobbyists who do not like seeing conventional growers using more cost-effective systems.

- Last but not least in this unholy alliance are the chemical companies who make far less profits from seeds, or herbicides with synergists and protectants, than high rate herbicides.

- The detractors are supported by an eminent (but misogynist) economist who claimed that the use of glyphosate resistant maize in Africa is a bad idea because it will take jobs (hand weeding) away from women.

Still – innovations do get adopted, as Juma points out – there is always someone wise enough to accept them. A local case in point is Bt brinjal, developed in India that replaces huge levels of insecticide. It is being grown in Bangladesh but banned in India.

This author is old enough to remember all those who were against the innovative green revolution in rice and wheat. There are still detractors claiming that it was a failure, but how many millions or billions of lives were saved by from starvation this counterintuitive innovation?

There has never been an agricultural innovation that has been sustainable forever. They all have and will have problems because weeds evolve. Let us remember that the green revolution was predicated on having adequate methods of selective weed control. If not for these chemicals, breeders would still be breeding taller and taller wheat and rice, ignoring that the weeds co-evolve to be taller and taller.

Detractors often lobby regulators that they should demand absolute proof of safety from new innovations, knowing full well that this is impossible. Safety assessments should be relative – is the innovation as safe or safer than currently used technologies used for the same purpose? If it meets those standards, farmers should be given the option of choice. In summary, we should not be afraid of being innovative – just be cognizant of the impediments that have little to do with our science. We must also conceive strategies that better explain the value and safety of our innovations that will preempt the detractors. The intractable weed problems, if not dealt with – threaten world food security. It is an existential matter of life or death.

Examples of major weed problems

We now have four species that supply 80% of the calories for humans and their livestock: rice, wheat, maize and soy. They had the genetic diversity to become global crops. Some weed species also have the genetic diversity to be camp followers and have evolved to cover most of the same agro-ecosystems as the crops they follow. Unfortunately, this same genetic diversity has allowed some of these weeds to evolve resistance to all our efforts, whether breeding, cultivation technologies, or herbicides. Herbicides are the last major innovation to be developed in this continual evolutionary race, and no new major mode of action has been released in decades, and the weeds have caught up, including to the mutational and transgenic development of new herbicide selectivities. Examples are discussed below.

Echinochloa species

Echinochloa species are especially prevalent in rice and maize where they had been effectively controlled for half a century by herbicides. They have evolved either metabolic or target-site resistance to herbicides having ten modes of action, especially in rice (Heap 2018).

Amaranthus spp

Amaranthus spp, which cross among themselves have evolved resistances to almost all the herbicides that had previously controlled them (Heap 2018). Farmers are having to perform more erosion causing tillage and other costly programs with only partial success. A major part of the problem was injudicious over and repeated use of the same herbicide until resistance evolved, then another was used, and then another, as each fell by the wayside to the inevitable forces of evolution. There are many workable strategies that could have delayed this evolution, but farmers were not willing to adopt them, often following the advice of salespeople who assured the farmers that should resistance evolve, industry would develop new compounds.

Root-attaching parasitic weeds

Striga species are widely spread throughout sub-Sahara Africa, especially on maize, the millets, sorghum, and recently in wheat. *Orobanche/Phelipanche* species are prevalent on all solonaceous, legume and umbelliferous crops as well as sunflowers in northern Africa, the Middle East, southern and eastern Europe and to a lesser extent in India. They were never selectively controlled by herbicides while still underground. The parasites inflict sufficient crop damage that it is uneconomical to control them after they emerge. Farmers could not afford to do so to prevent seed set and spread, exacerbating the situation. Most of the claimed successes with breeding have been transient; the parasites evolve too quickly. These weeds are the subject of a recent book that discusses all aspects about them and their control (Joel *et al.* 2013).

Phalaris in wheat

Phalaris species have evolved metabolic and target-site resistances to many herbicides globally in the semi-arid regions where wheat is grown (Heap 2018). The situation is especially acute in India with *Phalaris minor* (Chhokar and Sharma 2008), due to a special agro-ecosystem that exacerbates the problem. Contrary to what some scientists claim, *Phalaris* was not recently introduced to India on foreign grain – it has been in India since it was inadvertently brought by the Moghuls centuries ago when they introduced wheat. It became a major problem where summer rice/winter wheat is grown. The flooding of the paddies killed other winter-germinating weeds providing a niche where *Phalaris* had little competition, including from high-yielding dwarfed wheat. The use of a single herbicide, too often where at least part of a field had a low, near sub-lethal dose allowed for the evolution of a non-target site resistance that already pre-conferrs a modicum of resistance to herbicides that followed, and one by one the herbicides succumbed to the powers of evolution. More labour intensive cultural practices as well as alternative rotational crops have somewhat alleviated the problems thanks to the short seedbank longevity of *Phalaris* (this too could evolve). Most farmers would far prefer to return to a single treatment with an inexpensive herbicide, especially as labour costs become dearer thanks to industrialization that provides higher wages outside of agriculture.

Weedy rice in rice

Most of the domestication traits of rice are homozygous recessive, including non-shattering, uniform germination, lack of seed pigmentation, as well as suppressed height. Constantly occurring dominant back mutations to the feral weedy form had been culled when choosing good seed for the rice nurseries. Transplanting into flooded paddies gave the true rice a long head start on the weedy forms, limiting damage.

Direct seeding was implemented in every rice-growing area when industrial incomes precluded costly hand transplanting, allowing weedy rice to prosper (Ziska *et al.* 2015). Too often bulk seed contaminated with weedy rice was planted, and together with the weedy rice in the seedbank, the effects were devastating. As rice and weedy rice are the same species and have the same metabolic pathways, there could be no selective herbicides that control weedy rice. When mutant imidazolinone-resistant rice was introduced to control weedy rice, the trait was rapidly rendered worthless for weedy rice control because it crossed into weedy rice. The same will happen when transgenic herbicide resistance is introduced (Zhang *et al.* 2018), unless innovative measures are taken to mitigate transgene flow to weedy rice. The imidazolinone-resistant rice was effective for *Echinochloa* spp control for a longer period, but this weed too mutated to resistance. In parts of the world where they have considerable amounts of available land, crop rotation together with using certified rice seed became the control method for weedy rice. Those are not places where rice is a major part of the diet. The best that can be done in other areas is delayed planting followed by a general herbicide or cultivation before plant to kill emerged weedy rice with certified seed, and other expensive alternatives, but with lower potential yield.

Some possible innovative solutions

It is clear that we cannot revert back to back-breaking labour-intensive solutions to deal with these problems. If those who propose returning to manual cultivation were made to perform such labour, their attitudes would quickly change. Thus, for food security the above problems (and many others) require innovative and not retrogressive solutions.

Some of the solutions suggested below have been on the books for decades but were not implemented because companies, scientists, and politicians were cowed by detractors and the hysteria they generate. Advanced scientific knowledge has opened more windows showing that in theory other solutions should work. Some proposed solutions are still in the realm of science fiction and others will be conceived and developed by the most innovative among the readers.

Echinochloa, spp.

Transgenic glyphosate herbicide resistant maize has been highly effective in controlling *Echinochloa*. The same genes would be effective in rice and similar strains could possibly be obtained by gene editing (e.g. CRISPR Cas9, and the like). Gene edited plants are not considered transgenic (GMOs) by regulators in the USA, Japan, Israel, but are in technologically backward Europe. Most other jurisdictions have yet to decide. From a scientific point of view this is moot, as there is no credible evidence of danger from either transgenic or gene-edited technologies.

In at least one case, it was shown that adding a synergist that blocked resistant *Echinochloa* from catabolizing the herbicide allowed adequate control without affecting the crop (Leah *et al.* 1997). This and the following approach have not been followed up by the chemical industry.

Safeners (sometimes called protectants) are chemicals that activate a herbicide degradation pathway in the crop rendering the crop resistant to the herbicide. In sorghum, such compounds have allowed protection against members of the chloroacetamide group of herbicides. They are applied to the seed before planting and thus, the weed shattercane, which is a con-specific, feral form of sorghum, can be controlled. If there were such seed-applied safeners were marketed for rice, both *Echinochloa* spp., and weedy rice could be controlled.

With the introduction of inexpensive glyphosate, industry cut back on herbicide discovery and even more so on synergist and safener development. The US and European agrichemical and biotechnology companies pay less attention to rice, where *Echinochloa* is a major issue. It is unfortunate that the giant pesticide manufacturers in India and China do not seem to have had discovery programs that have led to new chemical control options for *Echinochloa* in rice. They should understand the local market need better than others.

Amaranthus, spp

These have evolved resistance somewhere to all the major herbicides, often in different locations using different modes of resistance for the same herbicide. This is especially evident with glyphosate due to the clearly unsustainable use of glyphosate as the sole herbicide multiple times per season, year after year on glyphosate-resistant maize and soy. The use of glyphosate mixtures with other herbicides might have delayed the evolution of resistance, had they been chosen based on criteria of similar biological half-lives, different control mechanisms, *etc.* (Wrubel and Gressel 1994). This is because the likelihood of a weed having mutations of resistance to two herbicides is like the mutation frequency of resistance to one herbicide multiplied by the mutation frequency to the second herbicide. The unbased and untenable view of the manufacturer was that it was nigh impossible for weeds to solve resistance to glyphosate (Bradshaw *et al.* 1997), a view that was contradicted before the Pollyanna view was published (Gressel 1996).

None of the resistances to glyphosate seem to be metabolic in nature, so classical synergists that prevent catabolism are out of the question. A new class of synergists, chemically synthesized double stranded interference RNA (RNAi) with a specific sequence that binds and prevents the messenger RNA expression that confers resistance, was trumpeted a few years ago (Arnason 2014), but little has been heard since, and there is no published evidence that it got further than a greenhouse. It would require a different synthetic RNAi for each mode of resistance as well as knowing what resistance occurs in each field.

A theoretical approach first suggested for insect control (Grigliatti *et al.* 2001) and later (theoretically) adapted for weeds. The suggestion for *Amaranthus* was to release transgenic *Amaranthus* seeds that contain multi-copy transposons that are either engineered to have deleterious genes that must be induced by a chemical treatment, or contain an RNAi that targets the mRNA that confers resistance (Gressel and Levy 2014). The advantage of using multicopy transposons to carry deleterious genes vs. engineering the same genes into the nucleus is that there is no genetic segregation with multi-copy transposons. The multicopy transposons appear in all subsequent progeny. To the best of my knowledge, no one has yet to try to convert this concept from science fiction to reality.

A possibly easier to regulate system for dealing with intractable weeds that are obligatory out-crossers or even predominantly out-crossers; the use of gene drive systems, was recently proposed (Neve 2018). Gene drive systems introduce deleterious genes or mutations into a population using gene-editing systems such as CRISPR-Cas9, but with a twist. The constructs are made in such a way that the Cas9, which cuts the genes targeted by CRISPR cannot be bred out. Thus a CRISPR that suppresses a gene, whether by directly rendering the weed unfit, or rendering it susceptible to a herbicide, will spread throughout the population of weeds bearing the construct after being planted in the field. The system has worked well mosquitoes, but is not infallible, and thus a weed such as an *Amaranthus*, will not go extinct but will eventually be reduced to a low frequency.

One start-up company is testing another concept – this one has proven highly successful in insects – the use of sterile males. In their case they collect pollen from *Amaranthus*, sterilize it and disseminate sterile pollen on patches of just flowering *Amaranthus* (Weedout 2018). They have shown that the sterile pollen successfully competes with fertile pollen and the resulting seeds have but vestiges of shrunken embryos. Their idea is to integrate their technology as a last resort with other technologies, and use it late in the season on remaining *Amaranthus* patches that were not otherwise controlled. Their first field trials are being evaluated. If successful, this technology could be used against other weeds that are obligate out-crossers.

Instead of long-ago using mixtures when they might have helped delay resistance, mixtures are now being developed especially for low canopy soy, which gets towered over by *Amaranthus* species. Most *Amaranthus* biotypes have yet to evolve resistances to auxin type herbicides, so the approach was to make transgenic soy resistant to these herbicides (Montgomery *et al.* 2018). The mixtures are not true mixtures against the resistant amaranths, as they are already resistant to one component. The soy transformations were successful, but the dicamba, which was formulated in such a way that the chemical companies were sure would not drift caused extensive damage in neighboring fields – drifting quite a distance damaging non-transgenic soy as well as other dicamba susceptible crops (WSSA 2018).

Root-attaching parasitic weeds

Over two decades ago it was demonstrated that transgenic crops, engineered to have target site resistance to systemic herbicides would allow control of these parasitic weeds (Joel *et al.* 1995). The systemic herbicides glyphosate, chlorsulfuron, and asulam were translocated undegraded from leaf to root, in such transgenic herbicide resistant crops where they killed the parasite. The costs of regulatory approval and the fear of the wrath of technology detractors prevented adoption. A modification of this technology was adapted for *Striga* control in eastern Africa; the use of mutant imidazolinone-resistant maize developed in the USA. The gene was backcrossed into African maize hybrids in the homozygous form and instead of expensively spraying the herbicide, tenfold less herbicide per hectare was applied as a seed treatment, and remained highly concentrated beneath the seed (Ransom *et al.* 2012). The concentration throughout the season of their 12-14 week to harvest maize is such that *Striga* would require having a simultaneous mutation to resistance on both alleles to become resistant to this local concentration. Despite widespread use of the technology, resistance has yet to evolve. It probably will evolve when adapted to western Africa 20-22 week maize, unless far more herbicide and/or slow release formulated herbicide is used. At the currently used herbicide level, by mid-season enough herbicide will probably be degraded to allow heterozygous resistant individuals to thrive in these long season varieties. Some of their progeny will have homozygous resistance, ending the utility of the technology.

Nucleic acids travel at least short distances between host and parasite. Host plants were engineered to produce an RNAi that targets a gene specific to the parasite. This resulted in a statistically significant but agronomically insignificant suppression of the parasite (Aly *et al.* 2009), and the concept was dropped nearly a decade ago. We now know more about how RNAi works, and it has given total suppression of some pathogen genes when multiple sites are targeted by having different RNAi producing segments in a construct (Gressel and Polturak 2018). These RNAi encoding segments are very short, so such constructs with many RNAi generating segments are easy to engineer. It was proposed to retry the process using this technique, while targeting genes that are heavily expressed at the time of parasite attachment to the crops (Gressel 2018).

There is a plethora of reports of finding specific pathogens against parasitic weeds, but except for one, all have been failures in the field. This is to be expected; if a weed-specific pathogen provided the high level of weed control desired by a farmer, the pathogen and the weed would have become extinct. Still, a hypervirulent pathogen can be produced and be continuously cultivated in the lab and continuously be disseminated in the field. This is still not sufficient; the biocontrol agent needs sustenance until it encounters the weed in the soil and can attack it. The one recently successful case had nearly double than average crop yield in 500 trials in *Striga* infested farmers' fields over two seasons (Nzioki *et al.* 2016). Their solutions were to mutagenize their fungal pathogen to overproduce and excrete amino acids that are lethal to the parasite and without effect on maize, affording the needed hypervirulence. The second issue was solved by having the farmers inoculate freshly boiled rice with pure strains of the pathogen supplied on toothpicks in sealed plastic drinking straws. When the pathogen had actively infected the rice, grains with pathogen were placed with maize seeds in the planting holes. The rice provides nutrition for the *Striga*-pathogenic mycelia to penetrate far afield in the soil profile near the germinated crop until it reaches a *Striga* seedling.

Phalaris in wheat

Transgenic, or possibly gene editing, derived wheat with target site or metabolic resistance to glyphosate as well as to other herbicides that control *Phalaris* would clearly be effective. It might last quite a long time if some of the lessons learnt with *Phalaris* and isoproturon (as well as glyphosate with other herbicides) are remembered and adopted. Under-dosing must be avoided (Gressel 2017), whether the under-dosing is due to adulterated herbicide, attempts to save by using lower doses, non-uniform application and/or late treatments where the dose is insufficient at that growth stage. The ability to have more than one wheat variety with resistances to different herbicides and have them used in rotation would clearly delay the evolution of resistance.

Industry has developed a safener/herbicide mixture pinoxaden, which selectively allows wheat to degrade the selective herbicide, allowing control of *Phalaris*. Alas, *Phalaris* has evolved resistance to this as well (Das *et al.* 2014). A better approach might be to develop a synergist that selectively prevents *Phalaris* degrading a herbicide, without affecting wheat. That would be a useful innovation. Modern computational predictive technologies for new chemical structures that affect specific enzymes have become highly advanced and should be used to innovate new synergists and safeners. The problem is that the multinational chemical companies are not that interested in problems outside their multi-storey headquarters in Europe, Japan, or the USA, far from most fields with intractable weed problems. Despite having large chemical companies in India and China, these produce generic products and buy their innovations elsewhere, which is unfortunate, as they best understand their home markets. Still, there is a spate of start-up companies using these tools that could possibly result in novel chemical synergists and safeners.

Weedy rice in rice

There is a recent report of a seed-applied safener that protected rice while controlling weedy rice (Shen *et al.* 2017). To the best of my knowledge, this is not yet commercial.

Generating genetically herbicide resistant rice is a tricky issue, because rice and weedy rice are the same species and there is gene flow between them. The rate of gene flow is quite low as rice is cleistogamous and most ovules are pollinated before the flowers open. The extreme selection pressure of herbicides makes up for the very low rate of gene flow. Once a resistance gene is in the weed, the herbicide further selects it and the spread is rapid. Thus, if one were to generate transgenic herbicide resistant rice, the gene flow to weedy rice would be as rapid as it was for the mutant imidazolinone resistant rice. Still, there is a way to use transgenic herbicide resistant rice while mitigating the problem of gene flow that cannot be done with the mutant or gene editing derived herbicide resistance. This is to tandemly attach a gene to the herbicide resistance gene that is neutral or positive for the rice but deleterious to weedy rice. The initially proposed "transgenic mitigator" genes were genes that induced dwarfing, non-shattering of seeds, anti-seed pigmentation, establishment of secondary dormancy (Gressel 1999), all of which would have no effect on the rice crop (or could increase yield) but would render weedy rice into a non-competitive weed. Because the mitigator gene is in tandem with the herbicide resistance gene, inheritance is linked, and there is no segregation of the traits. All further progeny are mitigated.

The technology was proven to be effective in model species such as tobacco and oilseed rape (Rose *et al.* 2009), and then in rice, but in rice with a new twist (Lin *et al.* 2008). Instead of using any of the mitigator genes described above, their mitigator was an anti-sense gene that suppresses the production of the enzyme that naturally degrades the herbicide bentazon (Lin *et al.* 2008). Thus, if rice that does not contain this gene construct is grown the following season, and bentazon is used for weed control, escapes and hybrids from the previous season will be killed. This was taken conceptually forward by suggesting that a series of different transgenic herbicide resistance rice varieties could be generated, each with a different mitigator, allowing suppression of any weedy rice x rice hybrids or their progeny in a system that should remain sustainable for a very long duration (Gressel and Valverde 2009). Such a system would also control *Echinochloa* spp and delay the evolution of resistance in that weed as well.

The chemical industry needs to change its herbicide discovery paradigm

The emphasis of industry discovery programs has been for many years on finding new target sites for herbicides and finding herbicides that control weeds by inhibiting a single target. Thus, there has been an emphasis on genomics for finding targets for potential herbicides. There is also the feeling that registration of single target herbicides is simpler as one can state that its mode of action is known. Conversely, if one looks at resistance with an epidemiological view to see which herbicides have been the most recalcitrant to evolutionary forces, it is those that have multiple targets of actions: the thiocarbamates, the long-chain fatty acid biosynthesis inhibitors and cell division inhibitors that affect more than one target, *etc*.

Metabolic or other non-target site resistances can evolve to multisite inhibitors, but these resistances can typically be overcome by structural modification of the herbicide. Industry has looked at weed-toxic natural products as herbicide leads, but abandoned those where they can find no single target of action. Perhaps nature has been more intelligent than discovery chemists and evolved natural products that are multi-site inhibitors and that is why the natural products have been active for millennia? Perhaps industry should be learning from nature by developing chemicals that inhibit more than one target? Such multisite inhibitors will usually be superior to herbicide mixtures, as they are more likely to meet the criteria for delaying resistance (Wrubel and Gressel 1994).

Training of weed scientists must be modified to meet the needs

Lets face the facts, most of today's weed scientists are under trained to meet the needs and provide the necessary innovations. Most weed science curricula are a sub-curriculum of agronomy. The other areas of plant protection that deal with insects and pathogens in agronomic crops are not sub-curricula of agronomy but are part of mycology and entomology curricula (respectively). Their students are much more broadly trained to understand and deal with their target pests. The innovative weed scientists of the future will come from the plant sciences, broadly trained in plant physiology, ecology, chemistry, molecular biology and genetics. One must have a deep understanding of the enemy in order to develop winning strategies. Spray and pray are not the answer. When this new generation have an innovative idea, they will know with whom to collaborate to bring it to fruition. The few innovations described in the above sections did not come from traditionally trained weed scientists.

An innovative concept always begins with a hypothesis to be tested. Roger Cousens (pers. comm.), a top Australian weed ecologist, analyzed the posters at a weed meeting and found that very few began with a hypothesis, most repeated what was already known. If research is not novel hypothesis driven, it cannot be innovative. This clearly demonstrates a lacuna in the education provided weed science students.

CONCLUSIONS

Despite the ag-chemical and ag-biotech's profits coming from products that control weeds, most of their research interest targets pathogens and insects. They are interested in but a few crops and most of their R & D is about problems they perceive to be tractable, ignoring the intractable. Of the problems described above, industry is dealing mainly with *Amaranthus* spp., and not too successfully. This means that it is up to innovative weed scientists in the public sector and start-ups to conceptualize innovations, collaborate with specialists in other areas, whether chemists, breeders, molecular biologists, agricultural engineers, specialists in remote sensing and analysis, as well as other *in silico* technologies (Smalley 2018), depending on the proposed innovation. Only the biological/chemical innovations were discussed above, but genetic engineering is not the only type of engineering where innovations are being made. Agricultural engineering is also coming up with innovative tools, including robots that distinguish between crops and weeds, and either physically remove the weeds or spot treat them (Fennimore *et al.* 2016). The weed scientist will discover that these people often have insufficient understanding of the weed problems, such that the collaboration with weed scientists will be synergistic. Only together will intractable problems be solved. Weed scientists should not fear new technologies. They should find ways to use them to the utmost to solve the intractable.

REFERENCES

Aly R, Cholakh H, Joel D, Leibman D, Steinitz B, Zelcer A, Naglis A, Yarden O, Gal-On A. 2009. Gene silencing of mannose 6-phosphate reductase in the parasitic weed *Orobanche aegyptiaca* through the production of homologous dsRNA sequences in the host plant. *Plant Biotechnology Journal* **7**: 487–498.

Arnason R. 2014. RNAi may hold key to glyphosate resistance. *https://wwwproducercom/daily/rnai-may-hold-key-to-glyphosate-resistance/ (accessed 27 Sept 2018).*

Bradshaw LD, Padgette SR, Kimball SL, Wells BH. 1997. Perspectives on glyphosate resistance. *Weed Technology* **11**: 189–198.

Chhokar RS, Sharma RK. 2008. Multiple herbicide resistance in littleseed canarygrass (*Phalaris minor*): A threat to wheat production in India. *Weed Biology and Management* **8**: 112–123.

Das TK, Ahlawat IPS, Yaduraju NT. 2014. Littleseed canarygrass (*Phalaris minor*) resistance to clodinafop-propargyl in wheat fields in north-western India: Appraisal and management. *Weed Biology and Management* **14**: 11–20.

Fennimore SA, Slaughter DC, Siemens MC, Leon RG, Saber MN. 2016. Technology for automation of weed control in specialty crops. *Weed Technology* **30**: 823–837.

Gressel J. 1996. Fewer constraints than proclaimed to the evolution of glyphosate-resistant weeds. *Resistant Pest Management* **8**: 2–5.

Gressel J. 1999. Tandem constructs: preventing the rise of superweeds. *Trends Biotechnol* **17**: 361–366.

Gressel J. 2017. Catch 22: All doses select for resistance. When will this happen and how to slow evolution?, pp 61–72 In: *Pesticide Dose: Effects on the Environment and Target and Non-Target Organisms*, Duke SO, Kudsk P, Solomon K (Eds) American Chemical Society, Washington DC.

Gressel J. 2018. Hit parasitic weeds hard with HIGS: They possibly can be transgenically controlled. *Haustorium* **73**: 4–7.

Gressel J, Levy AA. 2014. Use of multicopy transposons bearing unfitness genes in weed control: four example scenarios. *Plant Physiology* **166**: 1221–1231.

Gressel J, Polturak G. 2018. Suppressing aflatoxin biosynthesis is not a breakthrough if not useful. *Pest Management Science* **74**: 17–21.

Gressel J, Valverde BE. 2009. A strategy to provide long-term control of weedy rice while mitigating herbicide resistance transgene flow, and its potential use for other crops with related weeds. *Pest Management Science* **65**: 723–731.

Grigliatti TA, Pfeifer TA, Meister GA. 2001. TAC-TICS: Transposon-based insect control systems, pp 201–216 In: *Enhancing Biocontrol agents and Handling Risks*, Vurro M, Gressel J, Butt T et al. (Eds) IOS Press, Amsterdam.

Heap IM. 2018. International survey of herbicide-resistant weeds. *http://wwwweedscienceorg*: (accessed 27 Sept. 2018).

Joel DM, Gressel J, and Musselman L (eds). 2013. *Root Parasitic Orobanchaceae: Parasitic Mechanisms and Control Strategies*. Springer, Berlin.

Joel DM, Kleifeld Y, Losner-Goshen D, Herzlinger G, Gressel J. 1995. Transgenic crops against parasites. *Nature* **374**: 220–221.

Juma C. 2016. *Innovation and Its Enemies: Why People Resist New Technologies* Oxford University Press, Oxford UK.

Leah JM, Caseley JC, Riches CR, Valverde BE. 1997. Effect of mono-oxygenase inhibitors on uptake, metabolism and phytotoxicity of propanil in resistant biotypes of jungle-rice, *Echinochloa colona*. *Pesticide Science* **49**: 141–147.

Lin C, Jun F, Xu X, Te Z, Cheng J, Tu J, Ye G, Shen Z. 2008. A built-in strategy for containment of transgenic plants: creation of selectively terminable transgenic rice. *PLoS ONE* **3(3)**: e1818.

Montgomery GB, McClure AT, Hayes RM, Walker FR, Senseman SA, Steckel LE. 2018. Dicamba-tolerant soybean combined cover crop to control palmer amaranth. *Weed Technology* **32**: 109–115.

Neve, P. 2018. Gene drive systems: do they have a place in agricultural weed management? Pest Management Science (In press) available online. DOI 10.1002/ps.5137

Nzioki HS, Oyosi F, Morris CE, Kaya E, Pilgeram AL, Baker CS, Sands DC. 2016. *Striga* biocontrol on a toothpick: a readily deployable and inexpensive method for smallholder farmers. *Frontiers in Plant Science* **7**: Article 1121.

Ransom J, Kanampiu F, Gressel J, De Groote H, Burnet M, Odhiambo G. 2012. Herbicide applied to imidazolinone resistant-maize seed as a control option for small-scale African farmers. *Weed Science* **60**: 283–289.

Rose CW, Millwood RJ, Moon HS, Rao MR, Halfhill MD, Raymer PL, Warwick SI, Al-Ahmad H, Gressel J, Stewart CN. 2009. Genetic load and transgenic mitigating genes in transgenic *Brassica rapa* (field mustard) x *Brassica napus* (oilseed rape) hybrid populations. *BMC Biotechnology* **9**: Article 93.

Shen CC, Tang WW, Zeng DQ, Xu HL, Su WC, Wu RH. 2017. Isoxadifen-ethyl derivatives protect rice from fenoxaprop-P-ethyl-associated injury during the control of weedy rice. *Weed Science* **65**: 579–587.

Smalley E. 2018. *In silico* farming drives the next wave in agriculture. *Nature Biotechnology* **36**: 783–784.

Weedout. 2018. https://www.weedout-ibs.com/ (accessed 27 Sept. 2018).

Wrubel RP, Gressel J. 1994. Are herbicide mixtures useful for delaying the rapid evolution of resistance? A case study. *Weed Technology* **8**: 635–648.

WSSA. 2018. WSSA Research Workshop for Managing Dicamba Off Target Movement: Final Report *http://wssanet/wp-content/uploads/Dicamba-Report_6_30_2018pdf (accessed Sept 27, 2018).*

Zhang JX, Kang Y, Valverde BE, Dai WM, Song XL, Qiang S. 2018. Feral rice from introgression of weedy rice genes into transgenic herbicide-resistant hybrid-rice progeny. *Journal of Experimental Botany* **69**: 3855–3865.

Ziska LH, Gealy DR, Burgos N, Caicedo AL, Gressel J, Lawton-Rauh AL, Avila LA, Theisen G, Norsworthy J, Ferrero A, Vidotto F, Johnson DE, Ferreira FG, Marchesan E, Menezes V, Cohn MA, Linscombe S, Carmona L, Tang R, Merotto A. 2015. Weedy (red) rice: An emerging constraint to global rice production. *Advances in Agronomy,* **129**: 181–228.