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GM Crops, Organic Agriculture and Breeding for Sustainability

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Abstract: The ongoing debate about the use of genetically-modified (GM) crops in agriculture has largely focused on food safety and genetic contamination issues. Given that the majority of GM crops have been produced to respond to the problem of crop yield reductions caused by diseases, insects and weeds, the paper argues that in those cases, the currently used GM crops are an unstable solution to the problem, because they represent such a strong selection pressure, that pests rapidly evolve resistance. Organic agriculture practices provide a more sustainable way of producing healthy food; however, the lower yields often associated with those practices, making the resultant healthy food more expensive, open the criticism that such practices will not be able to feed human populations. Evolutionary plant breeding offers the possibility of using the evolutionary potential of crops to our advantage by producing a continuous flow of varieties better adapted to organic systems, to climate change and to the ever changing spectrum of pests, without depending on chemical control.

Keywords: genetic engineering; organic agriculture; evolutionary plant breeding; sustainability

1. Introduction

Foreign genes were successfully introduced into plants for the first time 30 years ago [1]. Ever since, genetically-modified (GM) crops have promised to deliver a second green revolution: a wealth of enhanced foods, fuels and fibers that would feed the starving, deliver profits to farmers and promote a greener environment [2].

For some, that revolution has arrived; their strongest argument is that crops engineered to carry useful traits now grow on 170 million hectares in at least 28 countries. Of those, 152 million hectares

are grown in five countries, namely the United States, Canada, Argentina, Brazil and India, with China being the sixth, with four million hectares [3].

Yet, to many others, GM crops have been a failure. The arguments used by those are the absence of or modest yield increases [4,5], the evolution of pest resistance (for example, the resistance to the herbicide Roundup by pig weed, *Amaranthus palmeri* or Palmer pigweed and *A. tuberculatus* or tall waterhemp, in a number of crops in the USA [6]), the evolution of resistance to Bt maize by western corn rootworm [7] and the increase in non-target insects (for example, the widespread infestation with mirid bug in China following the introduction of Bt cotton [8]).

The debate between the two groups has been very heated [9]. Those (mostly, but not only, activists) against GM crops, often referred to as genetically-modified organisms (GMOs), have focused the debate mainly on the safety of food derived from GM crops and on genetic contamination. Both are legitimate concerns, but weak arguments in the debate against GM crops.

The first is a weak argument, because: (1) it is not easy to demonstrate scientifically that GMO food is unsafe, as shown by the controversy spurred by Seralini's paper [10]; and (2) one wonders why the same argument is not used with the same passion and level of media coverage against food produced by crops treated with pesticides, which have been proven to be, beyond any reasonable doubt, among the most dangerous chemicals in circulation today [11].

The second is also a weak argument for the same reason as (1) above and because transgenic contamination is continuously occurring and its potential aspects have been discussed extensively by Ellstrand (2012) [12].

2. Biotechnologies

In the debate, GM technologies are often dealt with, particularly by activists, as part of biotechnologies at large, as if all gene manipulations were the same. The use of the term “biotechnology” or “biotechnologies” in a loose, or even worse, ideological sense ignores that genes do change naturally in a phenomenon known as spontaneous mutation and that spontaneous mutations have been one of the driving forces of evolution. If it were not for a mutation that occurred about 10,000–13,000 years ago and that changed shattering wild barley and wheat into non-shattering plants and for the Neolithic men and women who understood the value of that mutation, today, we would still collect wheat and barley from the ground. Another example of a major change during domestication is the large difference between cultivated maize and its ancestor, teosinte.

Therefore, when discussing GM crops, it is important to consider that they are the products of one specific type of biotechnology based on the introduction of foreign genes through vectors, in a process that will not occur naturally: in no way can this be considered as a technology similar to those biotechnologies that “read the DNA” without changing it (for example, marker-assisted selection, genomic selection, genome sequencing, *etc.*) or those that change the DNA within the same species (we have seen that this happens naturally with mutations). One exception is cisgenic plants that differ from transgenic plants, because the genes being transferred through vectors are not foreign genes [13].

We started using DNA changes with domestication, and we change DNA deliberately in conventional plant breeding every time we make crosses.

3. Unstable Solutions

The main undisputable weakness of GM crops, which is the same weakness of varieties produced by conventional methods and which carry a single-gene resistance to a specific pest (disease, insect or weed), is that they ignore one fundamental biological principle. To explain this principle, we need to remember two things. Firstly, that the fungi causing diseases, the insects eating our crops and the weeds competing with them, all are living organisms, and as such, they are variable, reproduce, mutate and evolve to adapt to current conditions. Secondly, to grow and reproduce, they need a host (this is true mostly for the fungi causing diseases and for the insects, but also for some weeds, the so-called parasitic weeds), the host being the plant (or the organism that they attack). If that organism is completely resistant, most of them will die. However, since they are variable, rare, spontaneous mutants capable of attacking the resistant host will always occur. In the absence of the resistant host, these individuals will not have any specific advantage; in fact, they are actually at some disadvantage [14]. However, if suddenly, as happens with the uniform varieties that are now predominantly grown in modern agriculture, a new, genetically-uniform and -resistant variety is planted, whether GM or conventional, these individuals will suddenly become the only one capable of reproducing, responding to a drastic change of the surrounding environment; because all of the plants of the host are genetically identical, they will spread very rapidly. The next generation will be mostly made up of the new types capable of attacking the host. If the host variety does not change, we will have an epidemic and extensive crop loss. This is what happened with the spreading of the pig weed species, quoted earlier, resistant to Roundup in cotton and soybean in some areas of the USA [6].

Incidentally, this happens in humans, as well, when bacteria develop resistance to antibiotics: each year in the United States, at least two million people become infected with bacteria that are resistant to antibiotics, and at least 23,000 people die each year as a direct result of these infections. Many more people die from other conditions that were complicated by an antibiotic-resistant infection [15]. Another example is the development of insecticides-resistant mosquitoes causing malaria, which has increased exponentially in the last decade [16].

In conventional plant breeding, this is very well known, and in fact, in plant breeding for disease resistance, there has been a long debate between the supporters of so-called “horizontal resistance” as opposed to “vertical resistance”, a distinction first made by Vanderplank [17,18]. He defined “vertical resistance” as the resistance of a qualitative type, *i.e.*, due to the action of single genes capable of providing complete protection, and “horizontal resistance” as the resistance due to the action of multiple genes and, hence, capable of providing every degree of protection from the minimum to the maximum [19].

Any protection mechanism against a crop pest, whether genetic or chemical, may be described as unstable or stable [19]. An unstable protection mechanism is within the capacity for the micro-evolutionary change of the pest. This means that the pest (fungus, insect or weed) is able to evolve and produce a new strain or race that is unaffected by that protection, which is then said to have “broken down” (strictly speaking, the protection is unaltered, and it is the pest that has changed [19]). Many synthetic insecticides, fungicides and herbicides provide unstable protection, and sooner or later, they “break down” in the face of new strains of the pest, a phenomenon known for many years [20–22]. Similarly, single-gene, vertical resistances are almost always unstable, and they too

break down as new races of the pest emerge. GM crops belong to the same category of unstable solutions to the problem of protection against pests, and this is why, in the best of the hypotheses, they only provide a temporary solution, which, in turn, as described above, creates a new problem (a resistant pest), which requires a different solution (a new GM variety). Thus, the introduction of GM crops in agriculture initiates a chain reaction that only benefits the company producing GM crops. This is often accompanied by a monopoly of the seed market, as in the case of GM corn and soybean in the USA [5], which leaves little or no choice to farmers about which seed to plant.

If, by the time the resistance of the GM crop breaks down, all of the previously available varieties, including landraces, have been displaced, farmers are left with no alternatives.

Horizontal resistances provide stable protection. That is, they are beyond the capacity for the micro-evolutionary change of the pest, which is consequently unable to produce a new strain that is unaffected by that resistance [20]. This is because they do not represent such a strong selection in favor of new strains as vertical resistances do. Horizontal resistance will assume even greater importance, as climate change will increase pathogen infection [23].

Biotechnology companies are currently promoting second-generation GM crops resistant to a combination of glyphosate (first-generation GM crops) with additional herbicides, namely the synthetic auxin class of herbicides, such as dicamba and 2,4-D, as a solution to glyphosate-resistant weed problems [6]. They argued that synthetic auxin-resistant weeds will not be a problem because: (1) currently, very few weed species globally have evolved synthetic auxin resistance, despite decades of use; (2) auxins play complex and essential roles in the regulation of plant development, which suggests that multiple independent mutations would be necessary to confer resistance; and (3) synthetic auxin herbicides will be used in combination or rotation with glyphosate, which will require weeds to evolve multiple resistance traits in order to survive [24,25]. The counter arguments have been that: (1) during the release of glyphosate-resistant crops, it was also indicated that the evolution of resistant weeds was a negligible possibility [26]; (2) it is not true that “very few species” have evolved synthetic auxin resistance, as globally, there are 28 species, with six resistant to dicamba, 16 to 2,4-D and at least two resistant to both active ingredients; in at least two cases, resistance is conferred by a single dominant allele, indicating that resistance could develop and spread quite rapidly [27]; and (3) the argument that multiple independent mutations would be necessary to confer resistance is contradicted by the evidence that weed species resistant to multiple herbicide modes of action are becoming more widespread and diverse: there are currently 108 biotypes in 38 weed species across 12 families possessing simultaneous resistance to two or more modes of action, with 44% of these having appeared since 2005 [28] (common waterhemp (*Amaranthus tuberculatus*) is simultaneously resistant to glyphosate, ALS and PPO herbicides and infests 0.5 million ha of corn and soybean in Missouri [28]; rigid ryegrass (*Lolium rigidum*) populations resistant to seven distinct modes of action infest large areas of southern Australia [28]). In the specific case of herbicide resistance, studies in Europe show a decrease of biodiversity over the period of increasing herbicide use (1950–1985), with broad spectrum herbicides playing a prevailing role in reducing biodiversity [29].

Therefore, the evidence shows that weeds can defy the probabilities and evolve resistance through a number of mechanisms [6], and this raises legitimate concerns that second generation GM crops will eventually face the same problems as first generation GM crops and may well be another unstable solution to the problem of resistance to pests

4. Organic Agriculture

It is now widely recognized that industrial agriculture is associated with several penalties, which have to be borne by society [30]: among those are the reduction in food diversity with negative consequences on human health [31], the leaching into the ground water of fertilizers residues, due to the overuse of fertilizers above the amount that plants can utilize [32], the water shortage, the emergence of pesticide resistance and the increase in the population of harmful insects.

Organic or biological farming has emerged in the second half of the last century as a more sustainable agricultural model to avoid/reduce the penalties described above. Organic farming agricultural practices include integrated biological pest management, cropping systems that minimize soil erosion and reduce water loss, the use of organic fertilizers and green manures and crop rotations to minimize the buildup of weeds, diseases and insect populations [33].

An advantage, not often recognized, of organic agriculture is its ability to mitigate the ecological damage caused by pest management practices based on the use of pesticides that alter the food web structure, so that communities becomes dominated by a few common species, which, together, contribute to pest outbreaks [34]. Organic farming methods promote evenness among natural enemies, and this avoids the selection of new, often more aggressive strains of fungi, insects or weeds. They continue to appear in nature as a consequence of mutations, but they will not have the advantages found in agricultural systems depending on the use of chemicals. The advantages of plant diversity, one of the expected beneficial effects of organic agriculture, on pest suppression, the increase of natural enemies and reduction of natural enemies have been shown to be large and significant, but not unequivocal [35].

Organic farming regulations ban, together with synthetic fertilizers, chemical pesticides and herbicides, and also GM crops; although, for some biotechnologists, organic farming and GM crops are friends [30,36]. Proposals have been made to produce new generations of GM plants, called organic plants, compatible with organic farming [37], and suggestions have been put forward that high technology farming can and should integrate organic/ecological methods. [38]

One of the main arguments used against organic or biological farming is that yields under organic systems are lower than in conventional agriculture; for example, in the case of cereals, 60%–70% of those under conventional management [30]. Although organic farming maintains fertility [39,40] and preserves part of the biodiversity of the cropped land [41], the idea of using 30%–40% more land to produce the same amount of crop biomass is unacceptable [30].

The issue of whether organic farming is compatible with human needs and population growth is, however, a controversial one and has been recently the subject of three meta-analyses [42–44]. The first [42] compiled and analyzed a meta-dataset of 362 published organic-conventional comparative crop yields and showed that organic yields of individual crops are on an average 80% of conventional yields, but variation is substantial (standard deviation, 21%). The second [43] compared yields of organic *versus* conventional or low-intensive food production for a global dataset of 293 examples and estimated the average yield ratio (organic: non-organic) of different food categories for the developed and the developing world. For most food categories, the average yield ratio was slightly <1.0 for studies in the developed world and >1.0 for studies in the developing world. The same paper modeled the global food supply that could be grown organically on the current agricultural land base and

concluded that organic methods could produce enough food on a global per capita basis to sustain the current human population and potentially an even larger population, without increasing the agricultural land base. The third [44] showed that, overall, organic yields are typically lower than conventional yields. However, these yield differences are highly contextual, depending on the system and site characteristics, and range from 5% lower organic yields (rain-fed legumes and perennials on weak acidic to weak-alkaline soils), 13% lower yields (when the best organic practices are used), to 34% lower yields (when the conventional and organic systems are most comparable). Under certain conditions—that is, with good management practices, particular crop types and growing conditions—organic systems can thus nearly match conventional yields, whereas under others, at present, they cannot [44].

On the other hand, a study examining sustainable agriculture initiatives in developing countries comprising the analysis of 286 projects covering 37 million hectares in 57 countries found that when sustainable agricultural practices were adopted, average crop yields increased by 79% [45] with significant increases of organic matter accumulation in the soil, carbon sequestration and reduced pesticides use. However, this study has spurred a controversy, as it has been criticized [46], because it offers, at most, weak evidence for what can be achieved by sustainable agriculture technologies. The authors of the original paper responded to the comments rejecting the objections raised [47]; this is only one example of the controversies that these topics raise.

A United Nations Conference on Trade and Development (UNCTAD) study reanalyzed the database on agricultural sustainability to produce a summary of the impact of organic and near-organic projects on agricultural productivity in Africa: the average crop yield increases were 116% for all African projects and 128% for the projects in East Africa [48]. Organic agriculture has the merit of representing a model of sustainable agriculture and the demerit of lower yields. GM crops are not the solution to the lower yields in organic systems, because: (1) they do not consistently increase yields, even in conventional agriculture [49], even though GM crops were not directly altered to increase yield; and, (2) as indicated earlier, they provide an unstable protection against pests, and therefore, when the protection fails, farmers have no other alternatives other than either using chemicals and losing the crop as “organic” or suffering yield losses. The solution to the problem of the lower yields in organic agriculture is to select varieties specifically adapted to organic systems by organizing breeding programs based on direct selection within organic systems [50–52]. This solution is, however, hampered by the limited number of public and private plant breeding programs addressing the specific needs of organic agriculture. This also suggests a flaw in those comparisons quoted earlier [42–44], because most of the varieties currently used by organic farmers were not actually bred for organic systems.

Climate change poses an additional challenge to organic agriculture, because of the expected increase in the damage due to pests [53,54] and the increased severity of diseases vectored by hosts and insects [55]. Because of the imprecision in the quantitative prediction of both temperature and rainfall [56], the climate change effect on both crop yield and quality through pests is difficult to predict; therefore, particularly in the case of organic agriculture, functional diversity, particularly in tolerance traits for both abiotic and biotic stress, and building spatial and temporal heterogeneity into the cropping systems will become one of the most effective targets for improved sustainability and resilience to both biotic and abiotic stresses [23].

What then is the future?

5. Evolutionary Plant Breeding

The future is to exploit to our advantage the evolutionary potential of living organisms that we described earlier, *i.e.*, the mechanism by which fungi, insects and weeds evolve and overcome the resistance of our crops, including GM crops, or the protection of pesticides. In fact, like the fungi, the insects and the weeds, also our crops have the ability to evolve and to adapt to changes. The advantages of exploiting this ability were first understood by Coit Suneson, an American agronomist, who, in 1956, proposed an evolutionary breeding method [57], even though the same idea is implicit in a more than 100 year-old publication by Herbert Webber [58].

The method consists in planting in farmers' field mixtures (evolutionary populations) of very many different genotypes of the same crop, preferably, but not necessarily, using early segregating generations [59]. These populations (one for each crop) will be planted and harvested year after year, and due to the natural crossing (higher in some crops and less in others, see below), the genetic composition of the population that is harvested is never the same as the genetic composition of the population that was planted as a result of differences in individual's fitness. In other words, and in the presence of directional selection, the population will evolve to become progressively better adapted to the environment (soil type, soil fertility, agronomic practices, including organic systems, rainfall, temperature, *etc.*) in which it is grown. As the climatic conditions vary from one year to the next, the genetic makeup of the population will fluctuate, but if the tendency is towards hotter and drier climatic conditions, as expected in view of climate change, the genotypes better adapted to those conditions will become progressively more frequent.

While the base population is evolving, breeders and/or farmers can practice artificial selection, with specific modalities depending on the crop and on the objective(s), thus deriving a flow of continuously better adapted improved varieties. Thus, evolutionary-participatory (when farmers do participate in the process) plant breeding (EPPB) reconciles agro-biodiversity (because a given base population will evolve differently in different locations, thus generating differently-adapted varieties), sustainable production increases (based on the amount of inputs farmers can afford) and adaptation to climate change (as a result of the evolutionary process) [59]. EPPB assumes that, while the population evolves, it maintains sufficient genetic diversity for evolution to proceed. However, it can accommodate the injection of novel genetic diversity any time it is required. It is also possible and indeed desirable for farmers to share the seed of the population with other farmers in other locations affected by different stresses or different combinations of stresses [60].

One of the issues is whether this methodology can work for self-pollinated crops, which include some of the most important food crops, such as wheat, rice, barley, some grain legumes and crops of greater potential interest in the future for their nutritional value, such as the millets. This issue has been addressed, indirectly, through an experiment conducted by Morran *et al.* [61], who used experimental evolution to test the hypothesis that outcrossing organisms are able to adapt more rapidly to environmental changes than self-fertilizing organisms. The experiment suggests that even low out-crossing rates (e.g., <0.05), comparable with those observed in self-pollinated crops, such as barley, wheat and rice, allow adaptation to stressful conditions. Most interestingly, the outcrossing rate increased in the course of the experiments, offering a partial solution to the problem of linkage drag discussed below.

Even though obtained on a nematode, this result is relevant for both self- and cross-pollinated crops and provides strong justification for evolutionary plant breeding.

The speed with which these populations evolve and adapt depends, among other factors, on the intensity of stress imposed [62]: in the case of a severe stress, selection may be so strong, that only rare mutants with extreme, perhaps innovative, phenotypes can survive the stress. The disadvantage of too strong a selection pressure is that it may reduce the diversity to the extent that the population will not be able to adapt to additional and different stress factors. To avoid this risk, it is recommended that farmers keep always, for example in a common refrigerator or in a cool dry place, a sample of the seed of the population sown the previous year. In the case of very strong selective pressures in any given year, the farmer could select the few surviving plants and sow again the seed sample stored in the refrigerator, thus avoiding a drastic reduction of genetic diversity. In the case of catastrophic events, which lead to a complete crop failure, using the seed stored in the refrigerator limits the loss to only one year of evolution.

When selection is less stringent, more genetic diversity can usually be sustained, which allows more adaptive opportunities for the population.

Linkage drag is a drawback in evolutionary breeding, particularly in self-pollinated species [63]. This can be overcome by increasing recombination through the use of male sterility when available [63], or cisgenesis [13], or by genetic manipulation of flower biology [64–67].

Evolutionary plant breeding has been put into practice recently, and hard data showing that it actually works are not available, with the possible exception of extrapolating to plants the results of Morran's experiment cited earlier [61]. However, similar concepts are used in population breeding and have been applied with success to the management of mixtures in relation to resistance to diseases and insects [68–70].

Evolutionary plant breeding is, therefore, much more dynamic than either conventional or GM varieties, in providing farmers with a continuous flow of novel varieties, and appears as the most dynamic and cheap way of adapting crops to a moving target, such as climate change and its collateral effects on pests. Evolutionary populations of different crops are currently grown by farmers in Jordan, France, Ethiopia, Iran and Italy on cereal crops (maize, barley, bread and durum wheat), grain legumes (common bean) and horticultural crops (tomato and summer squash). Research activities on evolutionary populations are ongoing in a number of European countries [63]. While it was anticipated that evolutionary populations will mostly represent a source material, in Iran, an evolutionary population of bread wheat has been actually used in two different provinces to produce bread, which has been highly appreciated by local markets. Farmers growing evolutionary populations in France and Italy confirmed that creating mixtures not only brings greater yield stability, but also greater aroma and quality to the bread [71].

Evolutionary plant breeding has the potential of making farmers independent of the seed market, which is now, globally, in the hands of large corporations (the world's top three corporations control 53% of the world's commercial seed market; the top 10 control 76% [72]), while small farmers overwhelmingly rely on seeds that they save from their own crops and which they donate, exchange or sell [73].

In several countries, seed laws state that, in order to be legally commercialized, varieties must meet the criteria of being new, distinct, uniform and stable. Uniformity and stability seem to be at odds with

the diversity needed to adapt crops to climate change. On the one hand, evolutionary populations could well be the source of varieties that meet those criteria, particularly if farmers can count on the collaboration of scientists; the advantage will be that, because the evolutionary populations will evolve differently in different areas, the varieties could maintain spatial agro-biodiversity and meet the requirement to be “legal varieties”; they can also satisfy the market if uniformity is required. On the other hand, if farmers decide to use the evolutionary population as their main crop (like in the case of Iran, Italy and France), the population will never meet the criteria to be “legal”, even though the European Commission has recently started discussing the possibility of “legally” cultivating mixtures [74]: it is precisely their diversity and dynamic evolution that are their main advantages. However, in either cases, farmers and farmers’ communities will re-acquire seed ownership, which is implicit in the recommendations of the report of the special rapporteur on the right to food [73] and is the essence of Article 9 of the International Treaty on Plant Genetic Resources for Food and Agriculture [75]. The evidence is mounting that the yield of the major crops, such as wheat, rice, maize and soybean, which together produce nearly 64% of agricultural calories, never improved and are stagnating or collapsing in more than a quarter (24%–39%) of the respective growing areas [76,77]. In a subsequent study [78], it was shown that global average rates of yield increase per year are 1.6% for maize, 1.0% for rice, 0.9% for wheat and 1.3% for soybean. These figures are lower than the 2.4% per year rate of yield gains (non-compounding) needed to double crop production by 2050. This raises major concerns that we may not be able to feed the nine billion people projected for 2050 if we assume that production *per se*, rather than availability and accessibility of food, is the key to eradicate hunger.

6. Conclusions

The industrial type of agriculture, of which GM crops are the most recent aspect, led to an extension of monocultures, to a significant loss of agro-biodiversity and to accelerated soil erosion; one of its most potentially devastating impacts is its contribution to increased greenhouse gas emissions, which amounts to 30%–32% of the total man-made greenhouse gas emissions attributable to food systems [73,79]. Under a business-as-usual scenario, we can anticipate an average of a two percent productivity decline over each of the coming decades, with yield changes in developing countries ranging from –27% to +9% for the key staple crops.[56]. In such a scenario of stagnating or declining crop yields, or of insufficient yield increases, depending on the estimates cited above, and of accelerated rates of climate change with the likelihood of not being able to remain below the 2 °C target of temperature increase [80], a new paradigm focused on agro-ecological modes of production, such as organic agriculture, on well-being, resilience and sustainability must be designed to replace the productivist paradigm and, thus, better support the full realization of the right to adequate food [72]: one of the recommendations of the report of the special rapporteur on the right to food [72] is “Fund breeding projects on a large diversity of crops, including orphan crops, as well as on varieties for complex agro-environments, such as dry regions, and encourage participatory plant breeding”. Evolutionary-participatory plant breeding, being a relatively inexpensive and highly dynamic strategy to adapt crops to a number of combinations of both abiotic and biotic stresses and to organic agriculture, is the most suitable method to generate, directly in farmers’ hands, the varieties that will feed the current and the future populations.

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Conflicts of Interest

The author declares no conflict of interest.

References

1. Herrera-Estrella, L.; Depicker, A.; van Montagu, M.; Schell, J. Expression of chimaeric genes transferred into plant cells using a Ti-plasmid-derived vector. *Nature* **1983**, *303*, 209–213.
2. Editorial. Tarnished Promise. *Nature* **2013**, *497*, 21.
3. Editorial. GM crops: A story in numbers. *Nature* **2013**, *497*, 22.
4. Gurian-Sherman, D. *Failure to Yield: Evaluating the Performance of Genetically Engineered Crops*; UCS Publications; Two Brattle Square: Cambridge, MA, USA, 2009; p. 44.
5. Xu, Z.; Hennessy, D.A.; Sardana, K.; Moschini, G. The Realized Yield Effect of Genetically Engineered Crops: U.S. Maize and Soybean. *Crop Sci.* **2013**, *53*, 735–745.
6. Mortensen, D.A.; Egan, J.F.; Maxwell, B.D.; Ryan, M.R.; Smith, R.G. Navigating a Critical Juncture for Sustainable Weed Management. *BioScience* **2012**, *62*, 75–84.
7. Gassmann, A.J.; Petzold-Maxwell, J.L.; Keweshan, R.S.; Dunbar, M.W. Field-Evolved Resistance to Bt Maize by Western Corn Rootworm. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 5141–5146.
8. Lu, Y.; Wu, K.; Jiang, Y.; Xia, B.; Li, P.; Feng, H.; Wyckhuys, K.A.G.; Guo, Y. Mirid Bug Outbreaks in Multiple Crops Correlated with Wide-Scale Adoption of Bt Cotton in China. *Science* **2013**, *328*, 1151–1154.
9. Buiatti, M.; Christou, P.; Pastore, G. The application of GMOs in agriculture and in food production for a better nutrition: two different scientific points of view. *Genes Nutr.* **2013**, *8*, 255–270.
10. Séralini, G-E.; Clair, E.; Mesnage, R.; Gress, S.; Defarge, N.; Malatesta, M.; Hennequin, D.; Spiroux de Vendômois, J. Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Food Chem. Toxicol.* **2012**, *50*, 4221–4231.
11. Enserink, M.; Hines, P.J.; Vignieri, S.N.; Wigginton, N.S.; Yeston, J.S. The Pesticide Paradox. *Science* **2013**, *341*, 728–729.
12. Ellstrand, N.C. Over a Decade of Crop Transgenes Out-of-Place. In *Regulation of Agricultural Biotechnology: The United States and Canada*; Wozniak, C.A., McHughen, A., Eds. Springer: Berlin, Germany, 2012; pp. 123–135.
13. Telem, R.S.; Wani, S.H.; Singh, N.B.; Nandini, R.; Sadhukhan, R.; Bhattacharya, S.; Mandal, N. Cisgenics—A sustainable approach for crop improvement. *Curr. Genomics* **2013**, *14*, 468–476.
14. Georgiou, G.P. The Evolution of Resistance to Pesticides. *Annu. Rev. Ecol. Syst.* **1972**, *3*, 133–168.

15. Frieden, T. *Antibiotic Resistance Threats in the United States*; Centers for Disease Control and Prevention: Atlanta, GA, USA, 2013; p. 114.
16. Coetzee, M.; Koekemoer, L.L. Molecular Systematics and Insecticide Resistance in the Major African Malaria Vector *Anopheles funestus*. *Annu. Rev. Entomol.* **2013**, *58*, 393–412.
17. Vanderplank, J.E. *Plant Diseases: Epidemics and Control*; Academic Press: New York, NY, USA; London, UK, 1963.
18. Vanderplank, J.E. *Disease Resistance in Plants*; Academic Press: New York, NY, USA; London, UK, 1968.
19. Robinson, R.A. Breeding for quantitative variables. Part 2: Breeding for durable resistance to crop pests and diseases. In *Plant Breeding and Farmer Participation*; Ceccarelli, S., Guimaraes, E.P., Weltzien, E., Eds.; FAO: Rome, Italy, 2009; pp. 367–390.
20. Melander, A.L. Can insects become resistant to sprays? *J. Econ. Entomol.* **1914**, *7*, 167–173.
21. Stern, V.M.; Reynolds, H.T. Resistance of the spotted alfalfa aphid to certain organo-phosphorus insecticides in Southern California. *J. Econ. Entomol.* **1958**, *51*, 312–316.
22. Teetes, G.L.; Schaefer, C.A.; Gipson, J.R.; McIntyre, R.C.; Latham, E.E. Greenbug Resistance to Organophosphorous Insecticides on the Texas High Plains. *J. Econ. Entomol.* **1975**, *68*, 214–216.
23. Newton, A.C.; Johnson, S.N.; Gregory, P.J. Implications of climate change for diseases, crop yields and food security. *Euphytica* **2011**, *179*, 3–18.
24. Behrens, M.R.; Mutlu, N.; Chakraborty, S.; Dumitru, R.; Jiang, W.Z.; LaVallee, B.J.; Herman, P.L.; Clemente, T.E.; Weeks, D.P. Dicamba resistance: Enlarging and preserving biotechnology-based weed management strategies. *Science* **2007**, *316*, 1185–1188.
25. Wright, T.R.; Shan, G.; Walsh, T.A.; Lira, J.M.; Cui, C.; Song, P.; Zhuang, M.; Arnold, N.L.; Lin, G.; Yau, K.; *et al.* Robust crop resistance to broadleaf and grass herbicides provided by aryloxyalkanoate dioxygenase transgenes. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 20240–20245.
26. Bradshaw, L.D.; Padgett, S.R.; Kimball, S.L.; Wells, B.H. Perspectives on glyphosate resistance. *Weed Technol.* **1997**, *11*, 189–198.
27. Jasieniuk, M.; Maxwell, B.D. Population genetics and the evolution of herbicide resistance in weeds. *Phytoprotection* **1994**, *75*, 25–35.
28. Heap, I. International Survey of Herbicide Resistant Weeds. Available online: <http://www.weedscience.org/summary/home.aspx> (accessed on 29 March 2014).
29. Schütte, G. Herbicide resistance: Promises and prospects of biodiversity for European agriculture. *Agric. Hum. Values* **2003**, *20*, 217–230.
30. De Oliveira, D.E.; van Montagu, M. GMOs and organic agriculture: Friends or foes for a sustainable agriculture? In Proceedings of the International Congress “*In the Wake of the Double Helix: From the Green Revolution to the Gene Revolution*”, Avenue media, Bologna, Italy, 27–31 May 2003; Tuberosa, R., Phillips, R.L., Gale, M., Eds.; pp. 689–698.
31. Von Hertzen, L.; Hanski, I.; Haahtela, T. Natural immunity: Biodiversity loss and inflammatory diseases are two global megatrends that might be related. *EMBO Reports* **2011**, *12*, 1089–1093.
32. Good, A.G.; Beatty, P.H. Fertilizing Nature: A Tragedy of Excess in the Commons. *PLoS Biol.* **2011**, *9*, e1001124.

33. Shaver, J.M. Toward a greener agriculture. In *Plant, Genes and Crop Biotechnology*; Chrispeels, M.J., Sadava, D.E., Eds.; Jones and Bartlett Publishers: Burlington, MA, USA, 2003; Chapter 18, pp. 473–499.
34. Crowder, D.W.; Northfield, T.D.; Strand, M.R.; Snyder, W.E. Organic agriculture promotes evenness and natural pest control. *Nature* **2010**, *466*, 109–113.
35. Letourneau, D.K.; Armbrrecht, I.; Rivera, B.S.; Lerma, J.M.; Carmona, E.J.; Daza, M.C.; Escobar, S.; Galindo, V.; Gutiérrez, C.; López, S.D.; *et al.* Does plant diversity benefit agroecosystems? A synthetic review. *Ecol. Appl.* **2011**, *21*, 9–21.
36. Ammann, K. Integrated farming: Why organic farmers should use transgenic crops. *Nat. Biotechnol.* **2008**, *25*, 101–107.
37. Ryffel, G.U. Organic plants: Gene-manipulated plants compatible with organic farming. *Biotechnol. J.* **2012**, *7*, 1328–1331.
38. Ammann, K. Why farming with high tech methods should integrate elements of organic agriculture. *Nat. Biotechnol.* **2009**, *25*, 378–388.
39. Bedini, S.; Avio, L.; Sbrana, C.; Turrini, A.; Migliorini, P.; Vazzana, C.; Giovannetti, M. Mycorrhizal activity and diversity in a long-term organic Mediterranean agro ecosystem. *Biol. Fert. Soils* **2013**, *49*, 781–779.
40. Migliorini, P.; Moschini, V.; Tittarelli, F.; Ciaccia, C.; Benedettelli, S.; Vazzana, C.; Canali, S. Agronomic performance, carbon storage and nitrogen utilization of long-term organic and conventional stockless arable systems in Mediterranean area. *Eur. J. Agron.* **2014**, *52*, 138–145.
41. Migliorini, P.; Vazzana, C. Biodiversity Indicators for Sustainability Evaluation of Conventional and Organic Agro-ecosystems. *Ital. J. Agron.* **2007**, *2*, 105–110.
42. De Ponti, T.; Rijk, B.; van Ittersum, M.K. The crop yield gap between organic and conventional agriculture. *Agric. Syst.* **2012**, *108*, 1–9.
43. Bennett, M.; Franzel, S. Can organic and resource-conserving agriculture improve livelihoods? A synthesis. *Int. J. Agric. Sustain.* **2013**, *11*, 193–215.
44. Seufert, V.; Ramankutty, N.; Foley, J.A. Comparing the yields of organic and conventional agriculture. *Nature* **2012**, *485*, 229–232.
45. Pretty, J.N.; Noble, A.D.; Bossio, D.; Dixon, J.; Hine, R.E.; Penning de Vries, F.W.; Morison, J.I.L. Resource-Conserving Agriculture Increases Yields in Developing Countries. *Environ. Sci. Technol.* **2006**, *40*, 1114–1119.
46. Phalan, B.; Rodrigues, A.S.; Balmford, A.; Green, R.E.; Ewers, R.M. Comment on “Resource-conserving agriculture increases yields in developing countries”. *Environ. Sci. Technol.* **2007**, *41*, 1054–1055.
47. Pretty, J.; Hine, R.E.; Morison, J.I.L.; Noble, A.D.; Bossio, D.; Dixon, J.; Penning de Vries, F.W.T. Response to Comment on “Resource-Conserving Agriculture Increases Yields in Developing Countries”. *Environ. Sci. Technol.* **2007**, *41*, 1056–1057.
48. UNCTAD-UNEP. Organic Agriculture and Food Security in Africa. Available online: http://unctad.org/en/docs/ditcted200715_en.pdf (accessed on 29 March 2014).

49. Fernandez-Cornejo, J.; Wechsler, S.J.; Livingston, M.; Mitchell, L. Genetically Engineered Crops in the United States. Economic Research Report No. (ERR-162) 60 pp, February 2014. Available online: <http://www.ers.usda.gov/publications/err-economic-research-report/err162.aspx> (accessed on 29 March 2014).
50. Murphy, K.M.; Campbell, A.K.G.; Lyon, S.R.; Jones, S.S. Evidence of varietal adaptation to organic farming systems. *Field Crops Res.* **2007**, *102*, 172–177.
51. Wolfe, M.S.; Baresel, J.P.; Desclaux, D.; Goldringer, I.; Hoad, S.; Kovacs, G.; Löschenberger, F.; Miedaner, T.; Østergård, H.; Lammerts van Bueren, E.T. Developments in breeding cereals for organic agriculture. *Euphytica* **2008**, *163*, 323–346.
52. Burger, H.; Schloen, M.; Schmidt, W.; Geiger, H.H. Quantitative genetic studies on breeding maize for adaptation to organic farming. *Euphytica* **2008**, *163*, 501–510.
53. Bebbber, D.P.; Ramotowski, M.A.T.; Gurr, S.J. Crop pests and pathogens move polewards in a warming world. *Nat. Clim. Change* **2013**, *3*, 985–988.
54. Keatinge, J.D.H.; Ledesma, D.R.; Keatinge, F.J.D.; Hughes, J.D'A. Projecting annual air temperature changes to 2025 and beyond: Implications for vegetable production worldwide. *J. Agric. Sci.* **2013**, *152*, 38–57.
55. Canto, T.; Aranda, M.A.; Fereres, A. Climate change effects on physiology and population processes of hosts and vectors that influence the spread of hemipteran-borne plant viruses. *Glob. Change Biol.* **2009**, *15*, 1884–1894.
56. Nelson, G.C.; Rosegrant, M.W.; Koo, J.; Robertson, R.; Sulser, T.; Zhu, T.; Ringler, C.; Msangi, S.; Palazzo, A.; Batka, M.; *et al.* *Climate Change: Impact on Agriculture and Costs of Adaptation*; IFPRI Report: 1–19; International Food Policy Research Institute: Washington, DC, USA, 2009.
57. Suneson, C.A. An Evolutionary Plant Breeding Method. *Agron. J.* **1956**, *48*, 188–191.
58. Webber, H.J. Plant-Breeding for Farmers. *Cornell Univ. Bull.* **1908**, *251*, 289–332.
59. Ceccarelli, S. Evolution, plant breeding and biodiversity. *J. Agric. Environ. Int. Dev.* **2009**, *103*, 131–145.
60. Ceccarelli, S.; Grando, S.; Maatougui, M.; Michael, M.; Slash, M.; Haghparast, R.; Rahmanian, M.; Taheri, A.; Al-Yassin, A.; Benbelkacem, A.; *et al.* Plant breeding and climate changes. *J. Agric. Sci.* **2010**, *148*, 627–637.
61. Morran, L.T.; Parmenter, M.D.; Phillips, P.C. Mutation load and rapid adaptation favour outcrossing over self-fertilization. *Nature* **2009**, *462*, 350–352.
62. Barrick, J.E.; Lenski, R.E. Genome dynamics during experimental evolution. *Nat. Rev. Genet.* **2013**, *14*, 827–839.
63. Döring, T.D.; Knapp, S.; Kovacs, G.; Murphy, K.; Wolfe, M.S. Evolutionary Plant Breeding in Cereals—Into a New Era. *Sustainability* **2011**, *3*, 1944–1971.
64. Ghani, A.H.; Parzies, H.K.; Ceccarelli, S.; Grando, S.; Geiger, H.H. Evaluation of floral characteristics of barley in the semi-arid climate of north Syria. *Plant Breeding* **2003**, *122*, 273–275.
65. Virmani, S.S.; Athwal, D.S. Genetic variability in floral characteristics influencing outcrossing in *Oriza sativa* L. *Crop Sci.* **1973**, *13*, 66–67.
66. Suso, M.J.; Harder, L.D.; Moreno, M.T.; Maalouf, F. New strategies for increasing heterozygosity in crops: *Vicia faba* mating system as a study case. *Euphytica* **2005**, *143*, 51–65.

67. Palmer, R.; Perez, P.; Ortiz-Perez, E.; Maalouf, F.; Suso, M. The role of crop-pollinator relationships in breeding for pollinator-friendly legumes: From a breeding perspective. *Euphytica* **2009**, *170*, 35–52.
68. Wolfe, M.S. Crop strength through diversity. *Nature* **2000**, *406*, 681–682.
69. Finckh, M.R. Integration of breeding and technology into diversification strategies for disease control in modern agriculture. *Eur. J. Plant Pathol.* **2008**, *121*, 399–409.
70. Tooker, J.F.; Frank, S.D. Genotypically diverse cultivar mixtures for insect pest management and increased crop yields. *J. Appl. Ecol.* **2012**, *49*, 974–985.
71. Rahmanian, M.; Salimi, M.; Razavi, K.; Haghparast, R.; Ceccarelli, S. Evolutionary populations: Living Gene Banks in Farmers Fields. Available online: <http://www.agriculturesnetwork.org/magazines/global/cultivating-diversity/plant-breeding> (accessed on 7 July 2014).
72. Fuglie, K.O.; Heisey, P.W.; King, J.L.; Pray, C.E.; Day-Rubenstein, K.; Schimmelpfennig, D.; Wang, S.L.; Karmarkar-Deshmukh, R. *Research Investments and Market Structure in the Food Processing, Agricultural Input, and Biofuel Industries Worldwide*; Economic Research Report No. 130; United States Department of Agriculture: Washington, DC, USA, 2011; pp. 1–147.
73. De Schutter, O. *Final Report: The Transformative Potential of the Right to Food*; Report of the Special Rapporteur on the Right to Food, A/HRC/25/57; United Nations General Assembly, UN Human Rights Council: New York, NY, USA, 2014; pp. 1–28.
74. Bocci, R. Seeds between freedom and rights. *Scienze del Territorio* **2014**, *2*, 115–122.
75. FAO (Food and Agriculture Organization). International treaty on plant genetic resources for food and agriculture. Available online: http://www.planttreaty.org/texts_en.htm (accessed on 30 June 2014).
76. Ray, D.K.; Ramankutty, N.; Mueller, N.D.; West, P.C.; Foley, J.A. Recent patterns of crop yield growth and stagnation. *Nat. Commun.* **2012**, *3*, 1–7.
77. Grassini, P.; Eskridge, K.M.; Cassman, K.G. Distinguishing between yield advances and yield plateaus in historical crop production trends. *Nat. Commun.* **2013**, *4*, 1–11.
78. Ray, D.K.; Mueller, N.D.; West, P.C.; Foley, J.A. Yield Trends Are Insufficient to Double Global Crop Production by 2050. *PLoS One* **2013**, *8*, e66428.
79. Vermeulen, S.; Campbell, B.; Ingram, J. Climate change and food systems. *Annu. Rev. Environ. Resour.* **2012**, *37*, 195–222.
80. Hansen, J.; Kharecha, P.; Sato, M.; Masson-Delmotte, V.; Beerling, D.J.; Hearty, P.J.; Hoegh-Guldberg, O.; Hsu, S.-L.; Ackerman, F.; Parmesan, C.; *et al.* Assessing “Dangerous Climate Change”: Required Reduction of Carbon Emissions to Protect Young People, Future Generations and Nature. *PLoS One* **2013**, *8*, e81648.