Crucial factors for the feasibility of commercial hybrid breeding in food crops

Nature Plants

Steeg, Emily M.S.; Struik, Paul C.; Visser, Richard G.F.; Lindhout, Pim

https://doi.org/10.1038/s41477-022-01142-w nature plants

PERSPECTIVE

https://doi.org/10.1038/s41477-022-01142-w

Crucial factors for the feasibility of commercial hybrid breeding in food crops

Emily M. S. ter Steeg [1]✉, Paul C. Struik [2], Richard G. F. Visser [3] and Pim Lindhout [4]✉

There is an ongoing societal debate about plant breeding systems and their impact on stakeholders in food systems. Hybrid breeding and hybrid seed have become controversial topics as they are believed to mostly serve high-tech agricultural systems. This article focuses on the perspective of commercial plant breeders when developing new cultivars of food crops. Arguably, hybrid breeding is the most effective breeding system for genetic improvement of crops, enhancing yields, improving product quality and increasing resistance against (a)biotic stresses. Nonetheless, hybrid breeding is not commercially applied in all crops. We analyse how biological and economic factors determine whether a commercial plant breeder opts for the hybrid system or not. We show that the commercial feasibility of hybrid breeding depends on the crop and business case. In conclusion, the commercial application of hybrid breeding in crops seems to be hampered mostly by high costs of seed production. Case studies regarding the hybrid transitions in maize, wheat and potato are included to illustrate these findings.

Hybrid breeding represents a technology with the potential to strengthen global food and nutrition security[1,2]. The concept of hybrid breeding and hybrid cultivars (also referred to as F_1 hybrids) is based on crossing two parent lines that usually are fixed for the most important traits and reside in two different gene pools[2]. There is an ongoing societal debate regarding the desirability of promoting this technology. The debate is shaped by conflicting narratives on global food security[3–5]. While proponents associate hybrid breeding with scientific and genetic advancement, opponents associate hybrid breeding with unsustainable cropping systems, reduced biodiversity and market consolidation by multinational breeding companies[5–7]. This paper aims to contribute to the discussion by explaining the perspective of commercial plant breeders. To serve a diverse readership, we attempted to avoid technical jargon and details without compromising the content.

Plant breeding entails the art and science of changing the genetic composition of plants to improve their economic utility to humans[8]. Four classic plant breeding systems can be distinguished: vegetative, open-pollinated, self-pollinated and hybrid. In this paper, we follow the principles outlined by Brown and Caligari, while excluding exceptions such as the development of synthetic and composite varieties, whereby mixtures of breeding systems are applied[9]. This classification is based on the reproduction processes of crop species. Breeders make crosses between individual plants and produce seeds or clonal propagules. The first three systems are based on the natural reproductive systems of plants. These systems have been used since the domestication of wild species and the onset of agriculture. Hybrid breeding was introduced only at the beginning of the twentieth century[1]. The hybrid system is based on human intervention in the natural reproductive systems of crop species.

The hybrid breeding system is arguably the most advanced of the four classic breeding systems, because it allows breeders to efficiently estimate and exploit genetic components of individual traits[2]. It remains challenging to distinguish between the impact of genetics and that of the environment or crop management on traits. Still, hybrid varieties are generally considered to enhance productivity and plant uniformity[10,11]. Apart from yield, numerous other traits (such as resistance to biotic stresses, tolerances to abiotic stresses and product quality) are important drivers of breeding programmes. Such traits can be introduced much faster and can be efficiently combined in one variety thanks to hybrid breeding[11,12]. Moreover, breeding companies prefer to combine the best traits in hybrid varieties because these have 'natural' intellectual property protection based on the genetic segregation of harvested selfed seeds of hybrid plants[1,2].

Close to 400,000 plant species exist today, of which 6,000 are being cultivated and less than 200 are of substantial importance for global food production[13,14]. Only six crops account for 60% of global food production: sugar cane, maize, rice, wheat, potato and soybean[15]. In this paper, we emphasize food crops. The hybrid breeding system has been applied to fewer than 50 food crops. The aim of this article is to identify prerequisites for the development of a hybrid cultivar from the perspective of the commercial plant breeder. The question arises: why has hybrid breeding been used for the improvement of some crops but not for others? First, we discuss the biological and legal frameworks of plant breeding. It is important to build an understanding of the structures within which a commercial plant breeder is operating, imposing limits and providing opportunities. Second, we introduce the four plant breeding systems, describing features with regard to the process of making crosses and seed multiplication. Third, we discuss biological and economic characteristics that influence decision-making in the hybrid breeding process. Finally, we categorize existing hybrid crops where breeding systems are used, to identify determinants for commercial plant breeding programmes.

Basics of commercial plant breeding

In nature, plants evolve under natural conditions by mutations and natural selection[8,16]. Plant breeders change the genetic composition of plants to meet human preferences and match farming conditions. Domestication entails the process during which a plant is deliberately transitioned from a wild species, growing in a natural vegetation with many competing species, into a crop adapted

[1]Development Economics, Wageningen University & Research, Wageningen, the Netherlands. [2]Centre for Crop Systems Analysis, Wageningen University & Research, Wageningen, the Netherlands. [3]Plant Breeding, Wageningen University & Research, Wageningen, the Netherlands. [4]Solynta, Wageningen, the Netherlands. ✉e-mail: emily.tersteeg@wur.nl; pim.lindhout@solynta.com

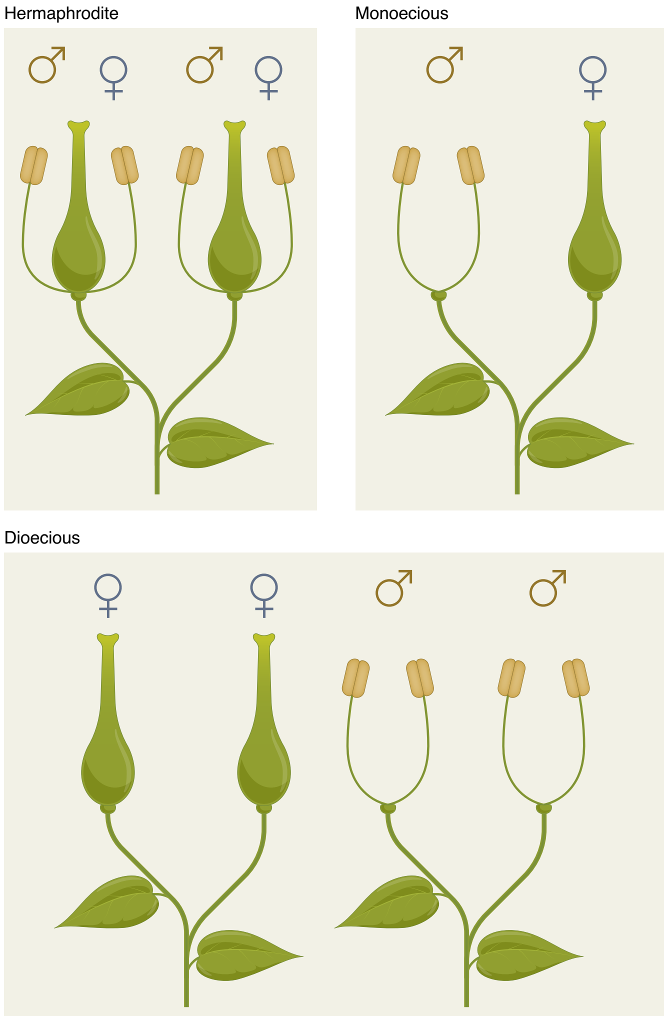

Fig. 1 | Variation in the occurrence of sexual organs in plants. Species have different mating systems defined by the sexual organs of flowers on plants. Hermaphrodite plants have flowers with both female and male sexual organs. In monoecious species, separate female and male flowers are found on the same plant. In dioecious species, female and male flowers are present on different plants.

to farming conditions in an artificial, species-poor environment and for human needs. Farmers started the process of domestication through the selection of individual plants of wild species from natural vegetation and turning these into manageable crops to feed themselves and their domesticated animals. This selective domestication process took thousands of years for the crops widely grown today[14]. Directed selection by farmers may be considered the first act of plant breeding.

In the past 200 years, the process of directed selection developed into a process of genetic recombination, during which crosses are made between the most promising plants to 'combine' their genetic compositions. Plant breeding is a repetitive process during which breeders recombine genes by making deliberate crosses and select the best plants from the offspring. Genetic recombination by crossing is a random process. Until today, the breeder is bound to trial and error to generate superior cultivars. This process has been confounded by genotype-by-environment interactions. The genetic potential of a new cultivar can be reliably assessed only by repeated trials under the specific and variable conditions for cultivation. This process usually requires one or several rounds of crossing, repeated trialling and selecting the best plants. New cultivars are thoroughly tested by the breeder, often in collaboration with farmers.

Upon the commercialization of cultivars, starting materials for cultivation by farmers are produced on a large scale. This is realized generatively or vegetatively: generative multiplication is done via seed, while vegetative multiplication is done via plant parts such as roots, cuttings, tubers, bulbs, rhizomes, shoots or tissue culture. Starting materials are sold to farmers for agricultural production. Alternatively, companies specializing in young plant raising may buy seed and grow seedlings, which are then sold to the farmers. This is common practice in many vegetable crops. Commercial plant breeders obtain returns on their investments through seed sales and/or royalties by licensing others to sell seed. Costs entail research and development, seed production and processing, and commercialization (marketing and sales).

A successful cultivar has added value for the entire food chain. Upstream, farmers seek marketable crops that can be produced efficiently. Important characteristics are high yields, uniformity, resistance to biotic stresses, tolerances to abiotic stresses and minimal input requirements in terms of water, fertilizers and crop protectants. Downstream, processors, retailers and consumers prefer uniform crop products, good storability, high nutritional value, consistent quality and low prices. Plant breeders must therefore focus on a wide variety of traits. An additional requirement for breeders is efficient multiplication of starting materials, enabling seed to be produced and sold at a competitive price.

Biological framework

Plant breeding systems are based on natural processes. Opportunities for and limitations of plant improvement are therefore determined by the biological traits of a species. It is necessary to understand the biology underlying and defining breeding programmes before one can explain commercial feasibility. An explanation of the biological framework is provided below.

Genotype and phenotype. 'Genotype' refers to the complete genetic composition of a plant; 'phenotype' refers to the entire set of observable traits. The same genotype can result in different phenotypes across environments, and, vice versa, different genotypes can show a similar phenotype. Generally, plant species have over 30,000 genes that are responsible for their traits[17]. Some genes can be directly linked to specific traits such as colour, while other 'polygenic' traits, such as quality or yield, are more complex and depend on many genes, which also show interactions[2,18]. A breeder identifies preferred plant traits and designs experiments to assess the occurrence and inheritance of these traits[19]. Subsequently, the breeder combines traits into one genotype through crossing. Selection is still mostly done on the basis of phenotypes. For qualitative traits, the number of genes is very high, and single genes have only a small impact on the phenotype[19]. As the functions of most of the genes remain unknown and the phenotypic expression of genes may differ over locations, seasons and years, many trials are required to select the best cultivars. Molecular markers may facilitate and speed up breeding, being a diagnostic tool for genes that influence crop traits[20]. This process is designated 'marker-assisted selection'[14].

Cultivars. There are two types of cultivated varieties or 'cultivars'. Plant breeders aim to develop 'commercial' or 'modern' cultivars with a distinct, well-defined and stable genotype[13]. Modern cultivars are often preferred by farmers, as these reduce the risk of harvest failure thanks to their stable performance. Modern commercial cultivars tend to be legally protected because of their high economic value. By contrast, farmers' cultivars, also known as landraces or traditional cultivars, may be less uniform and contain high(er) levels of genetic diversity[13,14]. Farmers' cultivars may be well adapted to local dietary preferences and environmental circumstances.

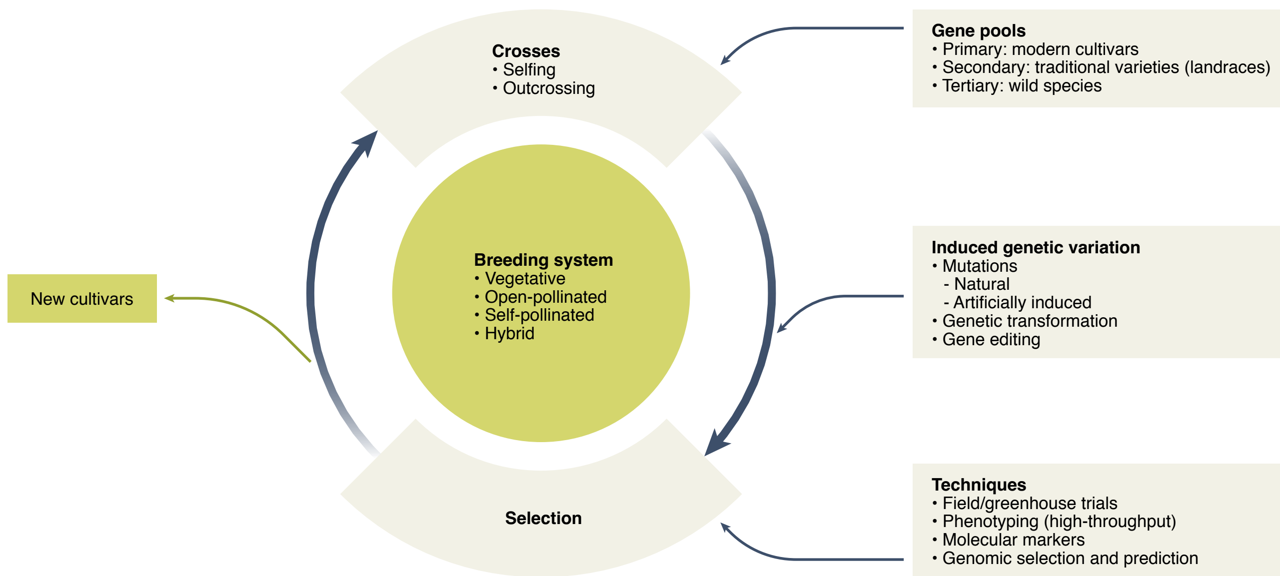

Fig. 2 | Plant breeding cycle for the development of new cultivars. The continuous cycle of plant breeding results in the development of new cultivars based on crosses and selections among plants of a crop species, whereby the breeder applies one of the breeding systems supported by biological techniques. Existing genotypes for breeding are derived from the gene pools, and new genotypes are created using tools to induce genetic variation.

Mating system. The mating system of a plant is defined by the sexual organs of its flowers[21,22]. A plant may have hermaphrodite flowers with both female and male sexual organs. A plant can also have male flowers or female flowers on the same or different plants (Fig. 1). The female organs of plants are the pistils, comprising an ovary with the ovules. The male organs of plants are the anthers, which release pollen. When a pollen grain lands on the female stigma, it grows through the style to the bottom of the pistil, where the ovules with egg cells are located; the egg cells are then fertilized. This results in an embryo that grows into a seed of the next generation: the progeny.

In plant species, a distinction is made between self-pollinators and cross-pollinators[21]. In self-pollinators, seeds are the result of self-fertilization: a pollen grain fertilizes the egg cell of its own flower or of another flower on the same plant, generating 'selfed progeny'. By contrast, seeds may be generated via outcrossing, whereby a pollen grain fertilizes the egg cell of another plant with a different genotype, resulting in outcrossing and 'hybrid progeny'. Self-fertilization may be prohibited by a natural system, designated 'self-incompatibility', whereby the pollen growth is arrested[22]. The division between self-pollinators and cross-pollinators is a gross generalization: species show a continuum in mating types[23]. Some self-pollinators are very strict, whereas others can occasionally outcross; some cross-pollinating species may also produce viable seed after selfing.

Homozygosity and heterozygosity. Zygosity refers to the degree of similarity of alleles of a particular gene. If the alleles for a gene on a chromosome pair are the same, a gene is fixed[24]. In homozygotes, all the alleles of each gene are identical. This means that a line is genetically pure and all genes are fixed. In heterozygotes, alleles are different. There are dominant alleles, which show activity, and recessive alleles, which show activity only in the absence of dominant alleles. Homozygosity is the result of repeated self-fertilization, which leads to inbreeding and reduced genetic variation[24,25]. Strict self-pollinators are natural inbreds, while non-strict self-pollinators and cross-pollinators vary in their level of inbreeding[24]. Reduced genetic variation often results in weak plants, a phenomenon called 'inbreeding depression'[26]. Some outcrossing species might not tolerate inbreeding at all, as the progeny plants obtained after selfing are too weak, non-flowering and/or sterile[26].

Gene pools. Plant breeders use three types of gene pools for breeding[27,28]. The primary gene pool consists of the genotypes of a breeding programme, including modern cultivars ('active breeding germplasm'). The breeder uses these genotypes to generate new cultivars. The market constantly demands new traits, and these may not be present in existing marketed cultivars. Genetic variation is increased by making crosses with genotypes beyond the primary gene pool. The secondary gene pool includes older farmers' cultivars (landraces) and closely related species. The tertiary gene pool consists of other related species and wild relatives that are genetically more distinct. Important genetic improvements and traits are often derived from secondary and tertiary gene pools. These pools contain higher genetic variation; hence, more innovative and rare traits can be exploited. Still, breeders prefer to use germplasm from the primary gene pool, as this is the most adapted to the market needs. Moreover, using germplasm from the secondary or tertiary pool is challenging. The introduction of desired traits goes hand in hand with the introduction of numerous undesired traits, which must be removed through a lengthy process of repeated backcrossing[29].

Induced genetic variation. Additional technologies exist to improve plant genetics and induce genetic variation, such as artificially induced mutations, genetic transformation and gene editing[14]. These tools should be separated from breeding systems, as they are not based on the recombination of natural genes that are present in the breeders' germplasm. Mutations are 'random' changes in DNA, which have been of crucial importance for evolution[9]. They can result in an altered plant, a mutant—for example, with a different flower colour or chemical composition of the seed. In nature, spontaneous mutations result in genetic variation and occur frequently. Mutations are induced by agents such as UV light, chemicals or random errors in DNA replication[30]. Plant breeders can artificially trigger mutations using the same agents. In the past 70 years, over 2,000 mutant cultivars have been released, mainly in ornamental species, for which an altered flower colour can result in a new cultivar[30,31]. Furthermore, technologies allow for the introduction of

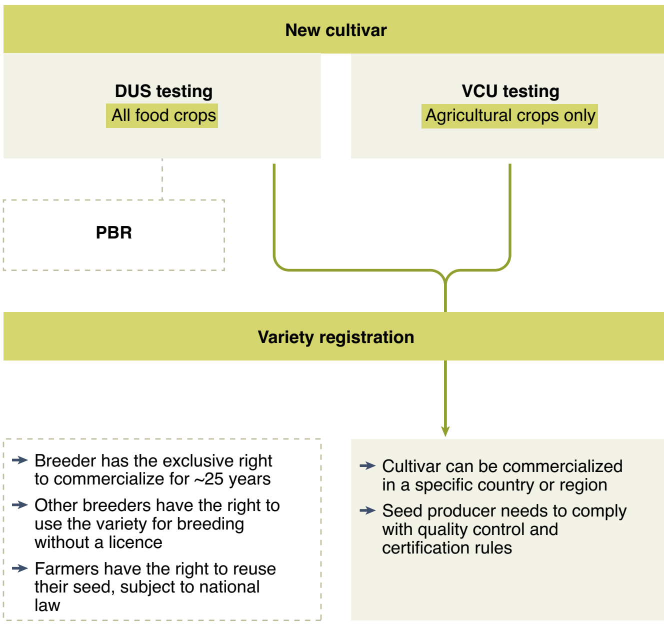

Fig. 3 | Formal legal framework guiding commercial plant breeding. In most seed regulatory systems, new cultivars of food crops are submitted to DUS and VCU tests for variety registration and release to the seed market. DUS means distinct, uniform and stable. VCU testing requires values similar to or better than existing varieties. DUS and VCU are required for variety registration of agricultural crops. Only DUS data are required for the registration of other food crops. Additionally, DUS data are used to apply for PBR, providing breeders with the exclusive right to commercialize the cultivar, commonly for 25 years. Application for PBR is voluntary.

specific (trans)genes, resulting in the creation of genetically modified organisms. Innovations (such as CRISPR–Cas9) can induce site-specific mutations, designated 'gene editing'. This article does not further discuss these tools but focuses on the four classic plant breeding systems (Fig. 2).

Legal framework

The business of commercial plant breeding is based on a legal framework, through which a breeder can become the owner of new cultivars[32,33]. It is possible for a plant breeder to obtain plant breeder's rights (PBR) for newly developed cultivars, which meet the so-called DUS criteria: distinct from existing cultivars; uniform, meaning that individual plants look similar; and stable, meaning that the cultivar remains true to its description through generations and multiplications. PBR give a breeder the exclusive right for a fixed period (generally 25 years) to commercialize the cultivar by producing and selling propagation material—seeds, tubers and plants[33]. In Europe, the seeds of vegetable and field crop cultivars can be commercialized only if they have passed the DUS test. PBR application is voluntary, but plant breeders will usually obtain PBR to protect their varieties before commercialization.

There are two exceptions to the PBR rule. The first exception is farmers' privilege (also known as farm-saved seed)[32,34]. It safeguards the right of farmers to save seeds from the plants they grow. Farmers have the right to use these seeds by themselves during the next season, but they are not allowed to sell them. In some countries, farmers need to pay a fee to the owner of PBR when saving seeds. The farm-saved seed exemption applies to field crops to support food security. It does not apply to vegetables or ornamentals, because these are considered to have a more commercial character. The second exception is the breeders' exemption, which allows for the use of protected varieties without authorization for further crossing, breeding and selection.

In most countries, there is an additional requirement to pass the test for Value for Cultivation and Use (VCU) for agricultural crops (Fig. 3)[33]. VCU concentrates on the agronomic characteristics and economics of a new cultivar, assessing features such as yield, disease resistance and (processing) quality[33]. Only cultivars that outperform existing cultivars already available in the country are placed on the 'National List'. This National List determines which cultivars are recommended to farmers in a country. In a few countries, VCU is not required, and plant breeders can sell their DUS varieties—it is up to breeders and farmers to do performance trials and decide which varieties to sell or grow[33].

Plant breeding systems

Plant breeding systems are defined by processes of genetic recombination and reproduction. Four classic breeding systems can be distinguished: vegetative, open-pollinated, self-pollinated and hybrid (Table 1)[16]. All breeding systems start with the generation of new genetic combinations based on crosses between favourable genotypes and subsequent selection of the best plants in the consecutive progenies. They represent a continuous process of improvement through crossing, testing, selecting and fixing of genotypes. The four systems differ in terms of the breeding process, the type of starting material generated, the multiplication of the starting material and the speed of genetic improvement.

Vegetative breeding system. The vegetative breeding system is the most basic and empirical breeding system. Crosses are made to produce new genetic combinations, and the best plant is selected after repeated trials. It is the dominant system in genetically complex species (see below, 'Ploidy level'). Cultivars are reproduced vegetatively: clones are made from selected plants. In this way, breeders ensure that the genetic composition of the plant remains constant. Examples are root and tuber crops, ornamental crops and fruit crops.

Open-pollinated breeding system. The open-pollinated system is based on population management. The breeding process is less controlled than in other breeding systems. Most crosses occur without the involvement of a breeder as plants within a selected population spontaneously outcross. Plant species often have a natural (self-incompatibility) system that prevents them from self-fertilization, and plants are randomly pollinated and fertilized by neighbour plants[22]. Seeds of a new (open-pollinated) cultivar are produced in the same way by open pollinations. Genetic variation in open-pollinated cultivars remains relatively high. Each plant represents a unique genotype, meaning that it has a unique genetic composition. Open-pollinated cultivars are not very uniform and may not be stable due to genetic drift during the multiplication process. The DUS criteria are less strict when seeking to obtain PBR for open-pollinated crops. Demand for highly uniform crops has resulted in a shift from the open-pollinated system to the hybrid system in many crops. Examples of crops in which a transition from the open-pollinated system to the hybrid system has occurred are maize, cabbage, carrot, leek, onion and sunflower. For major crops such as maize, hybrid cultivars are preferred by commercial farmers, although some open-pollinated cultivars are still being used, mainly by smallholder farmers[35].

Self-pollinated breeding system. Self-pollinators reproduce via a natural system whereby their own pollen fertilizes flowers of the same plant. As explained previously, repeated selfing results in offspring in which all chromosome pairs are eventually identical. This phenomenon is called 'homozygosity'. Genetic variation within a self-pollinated population gradually decreases. In this system, the breeder starts by making manual crosses of parent plants with desired characteristics, and the progenies are selfed for

Table 1 | Overview of four plant breeding systems

Breeding system	Breeding process	Generation of new starting material	Starting material for cultivation	Speed of genetic improvement
Vegetative	Crosses and selection in consecutive vegetatively propagated progenies	Vegetative propagation	Clones	Slow[a]
Open-pollinated	Mass selection in open-pollinated populations	Mass pollination	Seeds of the population	Medium
Self-pollinated	Crosses, backcrosses and repeated selfings	Selfings	Selfed seeds	Fast
Hybrid	Crosses, backcrosses and repeated selfings to generate inbred parents and crosses between parents to generate the hybrid	Crosses between (homozygous) parent lines	Hybrid seeds	Fast[b]

[a]Vegetative breeding moves slowly for polygenic traits such as yield and drought resistance. It can be a fast way to introduce genetically simple traits such as flower colour in ornamental crops. [b]It may take a long time to develop inbred lines; once these exist, hybrid breeding is the fastest system to realize genetic improvement.

many generations, whereby the best plants are selected. This results in a homozygous cultivar that can easily be reproduced by harvesting the selfed seeds.

Hybrid breeding system. Hybrid breeding is based on human interventions in natural reproductive systems. The system is based on the development of inbred lines and subsequent crossing of two selected inbred lines to generate the hybrid cultivar (Fig. 4). Upon selfing, the offspring of homozygous genotypes remain homozygous, while the offspring of heterozygous genotypes segregate into homozygous and heterozygous genotypes. The eventual deliberate crossing of two homozygous parent lines results in heterozygous offspring, which usually leads to enhanced uniformity, stronger and more resilient plant growth and higher yields. This phenomenon whereby the progeny of crosses among parent inbred lines outperforms its parents is designated 'heterosis' or 'hybrid vigour'[36].

The main advantage of hybrid breeding is the improved predictability of the outcomes of crosses. The homozygous character of inbred parent lines results in improved control over genetics. Furthermore, inbred lines enable the breeder to use (marker-assisted) backcrossing to add new traits to existing cultivars while maintaining other traits. This process is called 'trait stacking' and is impossible in the vegetative and open-pollinated breeding systems. Another reason why commercial breeders prefer hybrid cultivars is the natural protection of intellectual property. Seeds harvested from a hybrid plant are genetically diverse and hence differ from the original hybrid. Plants raised from these saved seeds are inferior to the plants grown from the hybrid seeds. Farmers need to buy new hybrid seeds every season to maintain crop performance.

The multiplication of starting materials for hybrid cultivars is a resource-intensive and expensive process. It requires more resources than for the other three breeding systems because each hybrid seed is the product of a deliberate cross between two specific parent plants. Also, due to inbreeding depression, inbred lines tend to produce fewer seeds; thus, many plants are required to produce the desired amounts of seeds. Male parent lines produce no hybrid seeds at all and occupy a varying part of the field (5–40%), depending on the crop species[37]. The production of hybrid seeds can be done manually, or by wind or insects when male-sterile female plants are used. As a result of the development of parent lines and the labour required for seed production, the costs of hybrid seeds are usually higher than the seed production costs of open-pollinated or cross-pollinated crops.

Biological and economic characteristics of crops

Breeding programmes are shaped by economic and biological feasibility. Below, we discuss biological and economic characteristics of crops that influence the commercial feasibility of a hybrid breeding programme. Certain characteristics are identified as determinants from the perspective of the plant breeder.

Mating system: inbred lines and heterosis. The preferred breeding system is largely determined by the mating system of a crop[8]. Mostly, it is directly linked to the feasibility of generating inbred lines. The hybrid breeding system was easily applied to (strict) self-pollinators such as tomato, pepper and eggplant. A natural inbreeding process had already been completed, resulting in the selection of alleles with an evolutionary advantage. The mating system of (strict) self-pollinators is optimal because all genetic combinations can be made: selfings and (back)crosses. The mating system of cross-pollinators often prevents self-fertilization, and crosses are made between different genotypes. This results in genetically diverse and highly heterozygous crops, in which alleles with a negative effect on plant performance can remain hidden, especially in polyploid crops[38]. Upon selfings, deleterious alleles may pop up in homozygous loci. This is the main reason for inbreeding depression observed in such crops. The development of inbred lines poses a great challenge, especially in cross-pollinators. Parent lines are generally weak and, in particular, too weak to support commercial seed production. This is why the degree of inbreeding for parent lines of hybrid cultivars may differ. When seed yields of pure inbreds are too low, breeders prefer 'impure' parent lines. A lower degree of uniformity is then accepted. Once viable inbred parent lines have been developed, applying the hybrid breeding system is straightforward: the inbred parents are improved through intercrosses and backcrosses[38].

Furthermore, the mating system may also determine the level of heterosis. Some breeders link the magnitude of heterosis to genetic diversity: combining more genetically distinct parent plants leads to a greater manifestation of heterosis[9]. Among selfers, a degree of heterosis can be found, but it is generally more erratic[39]. Maize, an outcrossing species, shows an enormous degree of heterosis, incentivizing breeders to pursue hybrid breeding[40]. However, it must be stressed that the cause of heterosis is still disputed[36]. At this point, plant breeders simply benefit from the manifestation of heterosis without knowing the scientific cause underlying the phenomenon. Breeders can develop heterotic pools of contrasting parents to maximize the heterosis effect. Such pools have been very important for some cross-pollinators such as maize and pearl millet[40]. For self-pollinating vegetables such as tomato, breeders use inbred lines with high general combining ability rather than heterotic pools.

Ploidy level. In nature, plants may have two, four or more copies of all chromosomes. This is referred to as a plant being 'diploid' (two copies), 'tetraploid' (four copies) and so on. A wide variation in ploidy level occurs in plants. In polyploid species, a high number of disadvantageous alleles accounting for a particular gene can be tolerated thanks to alternative advantageous alleles on the sister

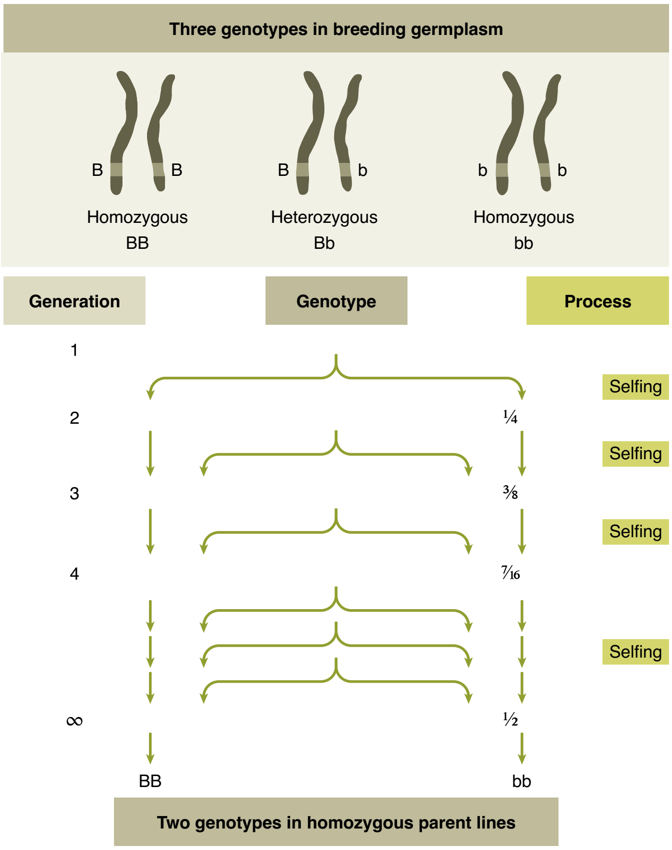

Fig. 4 | Development of homozygous inbred lines. The diploid breeding germplasm consists of three genotypes, 'BB', 'Bb' and 'bb', with B and b representing two different alleles of one locus. In the end, there are two homozygous parent genotypes left: BB and bb. A cross is made between two individual homozygous parents with different alleles to create a hybrid that is heterozygous (Bb).

chromosomes. Simply put, good sister alleles compensate for the deleterious effects of bad sister alleles[41]. The unfavourable alleles become a problem only during the development of inbred lines, which is a prerequisite for hybrid breeding. This explains why the great majority of hybrid crops are diploids. Polyploid crops can be converted into diploids, but this is a lengthy process that requires a lot of resources[12].

Plant generation time. Plant generation time refers to the duration of the life cycle of a plant, which is the cycle from seed to seed. It is possible to distinguish among annual, biennial and perennial crops. Annual crops have a life cycle of one year in which they germinate, flower, set seed and die. The world's main staple foods—wheat, rice, maize, potato and beans—are all annual crops. Biennial plants take two years to complete their life cycle. Perennial species, such as trees, grow and flower for many years and have a long generation time. Plant generation time influences the speed of the breeding programme. From a plant breeders' perspective, shorter generation times are preferred because the breeding programme can move faster in developing inbred lines and selecting offspring. Breeders may attempt to reduce the generation time through the use of artificial environments, which speed up plant development.

Seed production and male sterility. Seed production costs of hybrid cultivars depend on crossing efficiency and labour costs. The crossing efficiency of a crop refers to the number of seeds produced per pollination of a single flower or per crossing. If the crossing efficiency is low, many crosses are required to produce a certain number of seeds, resulting in higher costs. Large differences exist between the crossing efficiencies of plant species. For some crops, such as lettuce, cereals and beans, a few seeds are produced per cross. For other crops, such as tomato, potato and pepper, one cross can result in over 100 seeds. Seed production costs are an important reason why hybrid cultivars have not been developed for certain crops, such as wheat[42].

A prerequisite for commercial feasibility is the capability of the plant breeder to manipulate the plant in such a way that it efficiently produces hybrid seed, reducing labour costs. Costs depend on the ability to pollinate via wind or insects instead of manual pollination. Male and female plants can then be placed in specific designs in isolated fields to maximize the success of natural crosses via wind or insects. Plants can also be placed in isolated cages in greenhouses where insects pollinate the flowers. In case of wind or insect pollination, crossing efficiency is less critical because labour costs are low. By contrast, manual hybrid crosses are economically feasible only if the crossing efficiency and the commercial value of the harvested hybrid seeds are also high[43].

Moreover, breeders can use male sterility to reduce the costs of seed production. Male-sterile plants do not produce fertile pollen; hence, the seeds produced are by definition obtained by outcrossing. Male sterility exists in nature and is frequently used in hybrid breeding programmes. Labour costs are significantly reduced when manual emasculation (the removal of the male sexual organs of a plant) is no longer needed. Alternatively, male flowers can be mechanically removed from monoecious plants, as is done in maize. A challenge in the usage of male sterility is the maintenance and reproduction of the female lines that are male sterile. Genetic systems for the restoration of male fertility are being used to reproduce male-sterile female lines through selfings. This further complicates the breeding and seed production of hybrid crops[44].

Value of the harvested product per plant. The output of a breeding programme is commercial seeds (or plants), which are used by farmers to cultivate a crop. The commercial output of farmers is the harvested product per plant, such as staple foods, fruits and vegetables. The price of commercial seed is connected to the market value of the harvested product per plant. A high market value per plant means that the price of commercial seed can be higher: farmers are willing and able to invest in expensive seed when expecting returns on the investment. A hybrid cultivar should enable a farmer to obtain sufficient added value in terms of quantity and quality (such as shelf life and uniformity).

A greenhouse tomato is an example of a crop with an extremely high value of harvested product per plant. A tomato seed may produce a plant that grows year-round in a greenhouse with a production value per plant of dozens of euros[45]. This means that the price of commercial tomato seed may exceed one euro. By contrast, a field-grown industry tomato plant may have a production value of only five to ten eurocents. Commercial seed of an industry tomato cultivar must therefore be at least 10 to 20 times cheaper than the seed of a greenhouse tomato cultivar. In summary, industry tomatoes are a low-margin, high-volume product, whereas greenhouse tomatoes are a high-margin, low-volume product.

Market size. Investments in breeding programmes are linked to the size of the local, regional or global market. The market for hybrid seeds needs to be sufficiently large to cover the investments in breeding, production and commercialization. The effect is twofold. First, plant breeders will invest more money in global crops with a large global market (such as maize). Second, breeders will seek to develop cultivars suited for diverse climatological conditions, maximizing their potential market per cultivar. It is less

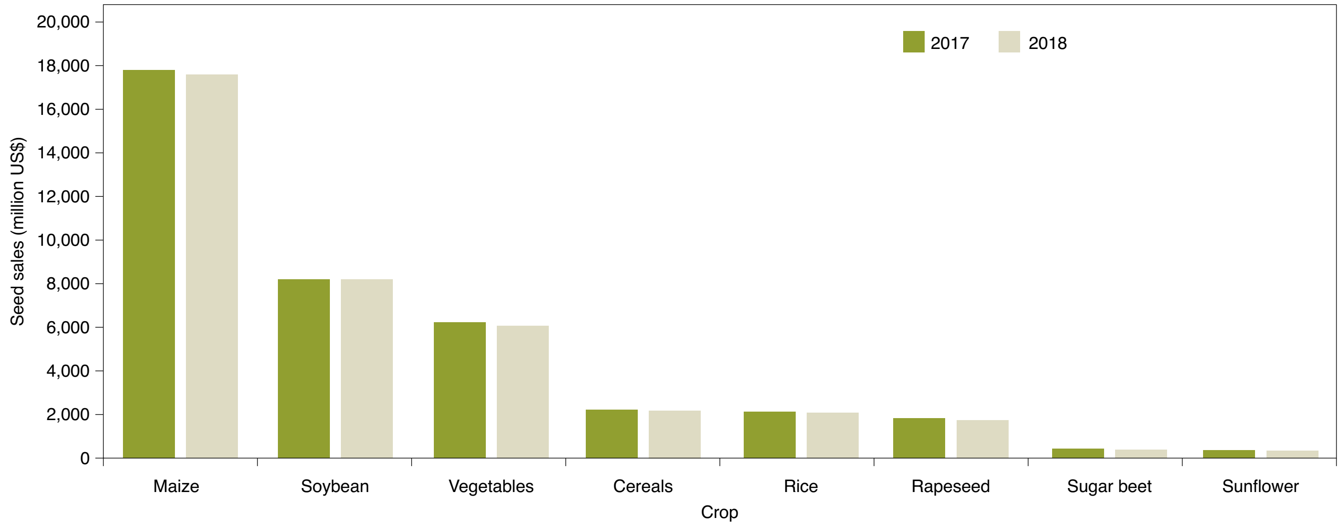

Fig. 5 | Global seed markets. Formal global seed market by food crop, excluding informal sales and farm-saved seed. Figure adapted with permission from ref. [68], IHS Markit.

attractive for commercial plant breeders to focus on niche markets, meaning local crops, specific consumer preferences and climatological conditions, because the costs of such breeding programmes are not easily returned by the limited seed sales. Figure 5 shows the major global seed markets for some food crops.

Case studies

Below, three examples are outlined: maize, wheat and potato. Maize is a cross-pollinator and is the first crop for which a hybrid breeding programme was launched, over 100 years ago. Nowadays, most modern maize cultivars are hybrids, and these are also bred and grown in developing countries[46]. Wheat is a self-pollinator for which the self-pollinated system is still being used. Breeding companies have shifted between investing and divesting in hybrid wheat[42]. Hybrid breeding has only recently been applied to potato, for which a shift from the tetraploid potato to a diploid potato was required[12]. These cases illustrate the impacts of the different biological and economic factors, which are described above.

Hybrid maize. The hybrid breeding system was developed and implemented for maize at the beginning of the twentieth century[47]. Maize is a diploid cross-pollinator but also has limited self-fertilization, allowing for the development of inbred lines[48]. It took several decades to overcome inbreeding depression and develop well-performing inbred parent lines and hybrids. The first commercial hybrid cultivars were released in 1930. Initially, maize hybrids were generated through 'double crossing', whereby commercial seed was produced by crossing two pure F_1 hybrids. This was required because the seed production costs of true hybrids were too high. Later on, three-way crosses were made. 'True' hybrid maize was commercialized only from 1960 onwards, meaning crosses were made between highly homozygous parent lines.

Maize is a monoecious species with separate female and male inflorescences (Fig. 1). This has been highlighted as one of the main reasons why maize became the first hybrid cultivar[49]. Plants only containing viable female reproductive organs can be generated (manually or mechanically) by the removal of male inflorescences or tassels before flowering. Hybrid seeds can then easily be collected from female plants, which are naturally pollinated by the male plants, that are placed in between female plants. This is still the main way in which hybrid maize seed is produced—it results in relatively low seed production costs.

Maize is now the crop with the highest economic value in the world. Maize became the major global crop only after the development and application of hybrid breeding, which resulted in a wide variety of hybrid cultivars that were well adapted to lower temperatures and suitable for the production of biofuels[41]. Since the first hybrid varieties were introduced, yields in commercial maize production have increased by a factor six, of which approximately half is thanks to genetic improvement and the other half to improved cultivation techniques (Fig. 6)[48,50].

Hybrid wheat. Like maize and potato, wheat is one of the most important food crops in the world. Wheat is an allohexaploid or amphidiploid self-pollinator, which means that the lines are highly homozygous, and it is not difficult to develop inbred lines. There have already been two waves of interest in hybrid wheat breeding, in the 1960s and 1990s[42]. However, the success of hybrid breeding programmes has been limited, and hybrid wheat has not been commercialized on a large scale. The key obstacle blocking a hybrid transition for wheat is that the low added value of hybrid varieties is insufficient to cover the high costs of seed production[42,51]. Also, the market for wheat is segmented, with strong quality preferences for bread making.

Reported performance differences between pure line and hybrid wheat cultivars vary and remain small[20,51,52]. The heterosis effect has been small, as wheat is a selfer with limited genetic variation. Hybrid wheat offers a yield increase of about 10%[42,51]. Pure line cultivars produced via the self-pollinated system also improve each year[53]. As line cultivars enter the market two years earlier, hybrids may be outdated upon variety release. Most importantly, seed production costs for hybrid wheat are too high. Wheat produces only one seed per crossed flower, and its pollen is heavy, which limits the success of natural pollination by wind[54]. Hence, manual pollination is far too expensive, and wind pollination may be less effective. Moreover, it has been difficult to introduce male sterility.

At this point, a hybrid wheat transition remains uncertain due to the remaining biological and economic challenges linked to seed production, heterosis and a fragmented market. The transition will require a significant reduction in seed production costs and identification of heterotic pools to obtain strong heterosis effects[55]. The development of heterotic pools is a costly, lengthy process, which can now be accelerated using modern breeding tools such as big data

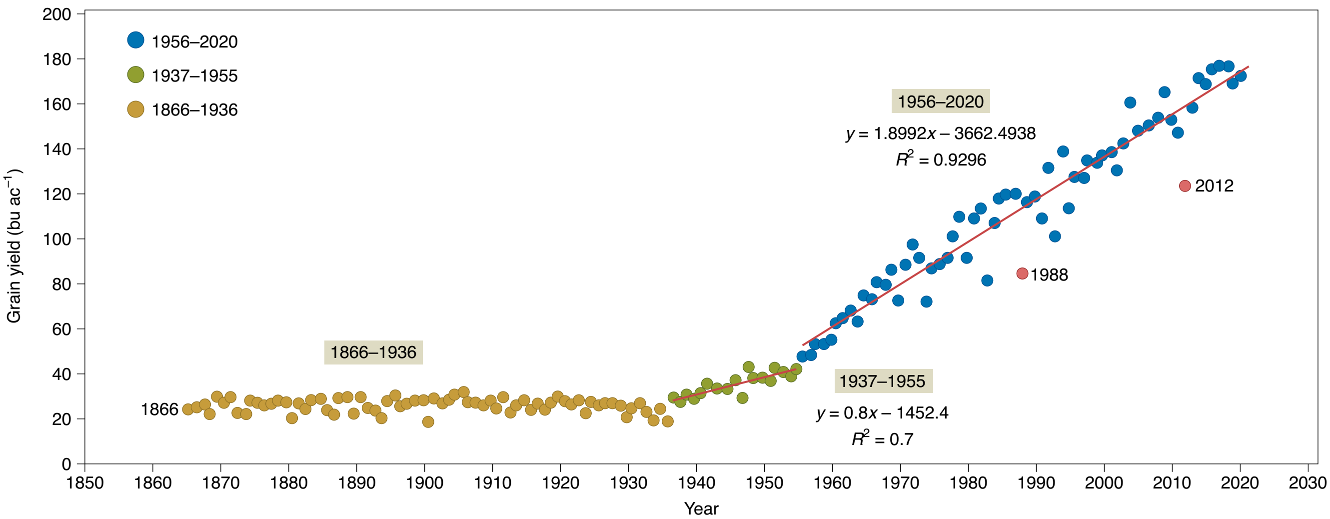

Fig. 6 | Maize yield increases in the United States since 1866. Since the introduction of hybrid cultivars, maize yields have increased more than five times thanks to breeding progress and improved cultural practices. Note that 100 bushels per acre is equivalent to 6.73 t ha^{-1}. Three phases can be distinguished. From 1866 to 1936, the use of open-pollinated varieties resulted in stagnant yields of about 26 bushels per acre (1.75 t ha^{-1}). From 1937 to 1955, the adoption of double-cross hybrid maize resulted in grain yield improvement of about 0.8 bushels per acre per year (0.05 t ha^{-1}). From 1956 to 2020, single-cross hybrids combined with the adoption of nitrogen fertilizer, higher plant densities, pesticides and mechanization resulted in grain yield improvement of 1.9 bushels per acre per year (0.13 t ha^{-1}). Figure adapted with permission from ref. [69], Purdue University.

and markers to improve prediction abilities[20]. Attempts to realize male sterility genetically or chemically have not yet resulted in commercial usage of wheat hybrids over large acreages[42].

Hybrid potato. Traditionally, potato breeding is 'empiric' due to the complex genetic structure of the potato[56,57]. The cultivated potato is tetraploid: it has four sets of chromosomes. In the past century, the vegetative breeding system has been the dominant system, and yield increases were based on improved cultivation practices rather than real genetic improvement[56]. While maize cultivars are usually replaced after five to ten years, two of the most prominent potato cultivars, Bintje and Russet Burbank, which were introduced over 100 years ago, are still grown on large acreages in Europe and the United States[57,58].

There was a long-standing conviction that it is impossible to apply the hybrid breeding system in potato[12]. A reduction in ploidy level from tetraploid to diploid made it possible to produce inbred lines more efficiently than when using tetraploids[38]. However, the diploid potato is a strict cross-pollinator, and it seemed unfeasible to create inbred lines due to potato's self-incompatibility and strong inbreeding depression. After these challenges were overcome, it became possible to systematically combine genes and exploit heterosis, introducing desirable traits such as disease resistance[59]. Moreover, diploid potato can be grown from hybrid true seed, through either direct sowing or transplanting seedlings. Tetraploid potatoes are multiplied via the vegetative system with a multiplication rate of a factor of ten[12,57]. By contrast, one diploid potato plant may produce thousands of seeds per season.

The potential of diploid potato has now been generally recognized, and hybrid breeding programmes have been launched by the public and private sectors in Europe, the United States and China[12,57,58]. After ten years, yield trials have demonstrated that the potential of the diploid hybrid potato is similar to that of the traditional tetraploid potato[60,61]. The question is now when hybrid potatoes will start outperforming tetraploid varieties. This timeline reflects the large initial investment required for a hybrid breeding programme for a new crop.

Synthesis

The decision of commercial plant breeders to launch a hybrid breeding programme depends on the biological and economic characteristics of a crop. The hybrid breeding system is the preferred system for commercial plant breeders. First, it enables breeders to most effectively and efficiently develop and produce new cultivars tailored to human needs and preferences. Second, it offers breeders natural protection of intellectual property and the opportunity to obtain return on investments. History has shown that once hybrid breeding is successfully applied in a crop, it becomes the dominant breeding system for commercial plant breeders[14].

Representative crop species are listed in Table 2 with qualifications for relevant characteristics. What are the economic and biological determinants to breed or not to breed? Table 2 highlights several determinants, among which seed production costs are the most crucial. These costs can be high for hybrid cultivars due to the required labour and land. The value of the harvested product and the seed market size are other important economic factors defining potential returns on investment. It should be stressed that profitability for the farmer is always a prerequisite for a breeding programme: farmers will invest in expensive seeds only if they can obtain a return on this investment.

Scientific breakthroughs in breeding show how biological limitations imposed by the mating system and ploidy level of a crop can be overcome. The limits of biological feasibility are constantly shifting—for example, potato used to be considered one of the least suitable crops for hybrid breeding, but hybrid breeding is now being applied in potato. The question arises whether hybrid breeding programmes should be launched for crops with commercially disadvantageous or discouraging characteristics. Breeding has been limited for indigenous leafy vegetables and fruit trees, but these crops are very important for global food security[62]. The same applies to cassava, sweet potato and quinoa.

How can stakeholders work together to improve the performance of these crops? In the absence of an immediate business case, public–private partnerships may offer a way to organize the required resources to achieve shared goals. Collaboration is necessary

Table 2 | Biological and commercial characteristics of examples of crop species and their dominant breeding systems

	Mating system used by breeder	Ploidy level	Plant generation time	Efficiency of hybrid seed production		Market value per plant for crop cultivation	Current value of the global seed market	Breeding system			
				Number of seeds per manual crossing	Male sterility applied			Vegetative	Self-pollinated	Open-pollinated	Hybrid
				Low, <10 Medium, 10–60 High, >60 (seeds per crossing)		Low, <0.05 Medium, 0.05–1 High, >1 (euros)	Low, <50 Medium, 50–500 High, >500 (million euros)	1, dominant system 2, secondary system			
Field crops											
Barley, oat, rice, rye, wheat[a]	Selfer	2*n*	Annual	Low	Yes[a]	Low	High		1		2
Cassava, sweet potato, yam	Outcrosser	2*n*	Annual	Low		Low	Low	1			
Maize	Outcrosser	2*n*	Annual	High	Yes	Low	High			2	1
Millet, sorghum	Selfer	2*n*	Annual	Low	Yes	Low	High			1	2
Mustard, rapeseed	Outcrosser	2*n*	Annual	Low	Yes	Low	High			2	1
Potato	Outcrosser	2*n*, 4*n*	Annual	Medium	No	Medium	High	1			2
Sesame	Outcrosser	2*n*	Annual	High		Medium	Low			1	
Sugar beet[b]	Outcrosser	2*n*	Biennial	Low	Yes	Medium	Medium			2	1
Sunflower	Outcrosser	2*n*	Annual	Low	Yes	Low	Medium			2	1
Legumes											
Bean, pea, peanut	Selfer	2*n*	Annual	Low		Low	Medium		1		
Soybean	Selfer	2*n*	Annual	Low		Low	High		1		
Vegetables											
Asparagus[c]	Outcrosser	2*n*	Perennial	Low	Dioecy[c]	High	Low		2		1
Brassicaceae (broccoli, Brussels sprout, cabbage, cauliflower)	Outcrosser	2*n*	Biennial	Low	Yes	Medium	High			2	1
Carrot	Outcrosser	2*n*	Biennial	Medium	Yes	Low	Medium			2	1
Onion, leek	Outcrosser	2*n*, 4*n*	Annual/biennial	Medium	Yes	Low-Medium	Medium			2	1
Cucurbitaceae (cucumber, gourd, melon, watermelon, squash)[d]	Selfer	2*n*	Annual	High	Monoecy[d]	High	High		2		1
Eggplant	Selfer	2*n*	Annual	High	No	High	Medium		2		1
Lettuce	Selfer	2*n*	Annual	Low	No	Medium	Medium		1		2
Okra	Selfer	2*n*	Annual	High	Yes	Medium	Low			2	1
Spinacia (spinach)[e]	Outcrosser	2*n*	Annual	Low	Dioecy[c]	Low[e]	Medium			2	1
Tomato, sweet/hot pepper[f]	Selfer	2*n*	Annual	High	Yes[f]	High	High		2		1
Other											
Fruits, berries, banana, palm	Outcrosser	2*n*–8*n*	Perennial	Low		Medium	Medium	1			
Coffee, tea, cacao	Outcrosser	2*n*	Perennial	Low		Medium	Low	1		2	

The economic data included in this table are based on the experience of the authors and senior experts from the commercial plant breeding industry and the *Access to Seeds Index*[63]. The names of the senior experts are mentioned in the Acknowledgements. 'Selfer' and 'outcrosser' refer to self-pollinators and cross-pollinators, respectively. [a]Traditionally, rice cultivars are self-pollinated. Male sterility has been introduced, reducing the costs of hybrid seeds[22]. Commercial production of hybrid rice started in China in 1976[22,64,65]. Barley and rye are more successful hybrid crops thanks to the application of male sterility. No hybrid system has been developed for oats. Successful rye hybrids have been developed on the basis of male sterility and self-incompatibility[66]. [b]Hybrid sugar beet varieties were introduced in the 1950s. Initially, hybrid sugar beet varieties were tetraploid. Triploid varieties were used from the 1970s onwards, and from the 2000s onwards, diploid varieties were introduced[67]. Ever since, yields have increased by 60%, and the lifetime of cultivars has been reduced to two to three years. [c]Asparagus and spinach are dioecious species, allowing separation into female and male plants for hybrid seed production (see also Fig. 1). [d]Most cucurbitaceous crops are monoecious, with separate female and male flowers on the same plant. Male flowers of the male parent line are used to pollinate the female flowers of the female parent line. [e]The value of a spinach plant from one seed is low. Still, hybrids are used because the production costs of hybrid seeds are equally low. [f]In pepper and tomato, male sterility is available, but it is not yet of crucial economic importance because of the high number of seeds per cross and the high market value per plant. Nonetheless, male sterility in hot pepper is of increasing importance to avoid the difficult and time-consuming practice of emasculation of its small flowers.

to mobilize funding and technologies. Food systems around the world are under unprecedented pressure due to population growth and climate change. Through collaboration, we can ensure that the potential impact of plant breeding, and hybrid breeding in particular, will materialize. The common objective should be to breed robust, resilient and constantly high-yielding cultivars to contribute to food and nutrient security for the future world population.

Received: 23 October 2021; Accepted: 22 March 2022;
Published online: 5 May 2022

References

1. Labroo, M. R., Studer, A. J. & Rutkoski, J. E. Heterosis and hybrid crop breeding: a multidisciplinary review. *Front. Genet.* **12**, 643761 (2021).
2. Mackay, I. J., Cockram, J., Howell, P. & Powell, W. Understanding the classics: the unifying concepts of transgressive segregation, inbreeding depression and heterosis and their central relevance for crop breeding. *Plant Biotechnol. J.* **19**, 26–34 (2021).
3. Béné, C. et al. Understanding food systems drivers: a critical review of the literature. *Glob. Food Sec.* **23**, 149–159 (2019).
4. Clapp, J. *Food* 3rd edn (Polity, 2020).
5. Lammerts van Bueren, E. T., Struik, P. C., van Eekeren, N. & Nuijten, E. Towards resilience through systems-based plant breeding: a review. *Agron. Sustain. Dev.* **38**, 42 (2018).
6. Kantar, M. B. et al. The many-faced Janus of plant breeding. *Plants People Planet* **1**, 306–309 (2019).
7. Lammerts van Bueren, E. T. et al. The need to breed crop varieties suitable for organic farming, using wheat, tomato and broccoli as examples: a review. *NJAS* **58**, 193–205 (2011).
8. Chahal, G. S. & Gosal, S. S. *Principles and Procedures of Plant Breeding: Biotechnological and Conventional Approaches* (Alpha Science International, 2002).
9. Brown, J. & Caligari, P. D. S. *An Introduction to Plant Breeding* (Blackwell, 2008).
10. Rijk, B., van Ittersum, M. & Withagen, J. Genetic progress in Dutch crop yields. *Field Crops Res.* **149**, 262–268 (2013).
11. Rudolf-Pilih, K. et al. Proposal of a new hybrid breeding method based on genotyping, inter-pollination, phenotyping and paternity testing of selected elite F_1 hybrids. *Front. Plant Sci.* **10**, 1111 (2019).
12. Lindhout, P. et al. Towards F_1 hybrid seed potato breeding. *Potato Res.* **54**, 301–312 (2011).
13. Bélanger, J. & Pilling, D. *The State of the World's Biodiversity for Food and Agriculture* (FAO, 2019).
14. Priyadarshan, P. M. *Plant Breeding: Classical to Modern* (Springer, 2019).
15. *World Food and Agriculture Statistical Pocketbook 2019* (FAO, 2019).
16. Acquaah, G. *Principles of Plant Genetics and Breeding* 3rd edn (Wiley, 2020).
17. Sterck, L., Rombauts, S., Vandepoele, K., Rouze, P. & Vandepeer, Y. How many genes are there in plants (…and why are they there)? *Curr. Opin. Plant Biol.* **10**, 199–203 (2007).
18. Crouch, D. J. M. & Bodmer, W. F. Polygenic inheritance, GWAS, polygenic risk scores, and the search for functional variants. *Proc. Natl Acad. Sci. USA* **117**, 18924–18933 (2020).
19. Bernardo, R. Reinventing quantitative genetics for plant breeding: something old, something new, something borrowed, something BLUE. *Heredity* **125**, 375–385 (2020).
20. Zhao, Y. et al. Unlocking big data doubled the accuracy in predicting the grain yield in hybrid wheat. *Sci. Adv.* **7**, eabf9106 (2021).
21. Barrett, S. C. H. Mating strategies in flowering plants: the outcrossing–selfing paradigm and beyond. *Phil. Trans. R. Soc. Lond. B* **358**, 991–1004 (2003).
22. Charlesworth, D., Vekemans, X., Castric, V. & Glémin, S. Plant self-incompatibility systems: a molecular evolutionary perspective. *N. Phytol.* **168**, 61–69 (2005).
23. Whitehead, M. R., Lanfear, R., Mitchell, R. J. & Karron, J. D. Plant mating systems often vary widely among populations. *Front. Ecol. Evol.* **6**, 38 (2018).
24. Lande, R. & Schemske, D. W. The evolution of self-fertilization and inbreeding depression in plants. I. Genetic models. *Evolution* **39**, 24–40 (1985).
25. Porcher, E. & Lande, R. The evolution of self-fertilization and inbreeding depression under pollen discounting and pollen limitation: pollination biology and evolution of selfing. *J. Evol. Biol.* **18**, 497–508 (2005).
26. Husband, B. C. & Schemske, D. W. Evolution of the magnitude and timing of inbreeding depression in plants. *Evolution* **50**, 54–70 (1996).
27. Harlan, J. R. & Wet, J. M. J. Toward a rational classification of cultivated plants. *TAXON* **20**, 509–517 (1971).
28. Palmer, R. G. & Hymowitz, T. in *Reference Module in Food Science* B9780081005965002146 (Elsevier, 2016).
29. Tourrette, E., Falque, M. & Martin, O. C. Enhancing backcross programs through increased recombination. *Genet. Sel. Evol.* **53**, 25 (2021).
30. Brock, R. D. The role of induced mutations in plant improvement. *Radiat. Bot.* **11**, 181–196 (1971).
31. Ahloowalia, B. S., Maluszynski, M. & Nichterlein, K. Global impact of mutation-derived varieties. *Euphytica* **135**, 187–204 (2004).
32. Louwaars, N. *Seeds of Confusion: The Impact of Policies on Seed Systems* (Wageningen University and Research, 2007).
33. Jamali, S. H., Cockram, J. & Hickey, L. T. Is plant variety registration keeping pace with speed breeding techniques? *Euphytica* **216**, 131 (2020).
34. De Jonge, B., Salazar, R. & Visser, B. How regulatory issues surrounding new breeding technologies can impact smallholder farmer breeding: a case study from the Philippines. *Plants People Planet* **4**, 96–105 (2022).
35. Almekinders, C. J. M., Hebinck, P., Marinus, W., Kiaka, R. D. & Waswa, W. W. Why farmers use so many different maize varieties in West Kenya. *Outlook Agric.* **50**, 406–417 (2021).
36. Kaeppler, S. Heterosis: many genes, many mechanisms—end the search for an undiscovered unifying theory. *ISRN Bot.* **2012**, 682824 (2012).
37. Virmani, S. S., Sun, Z. X., Mou, T. M., Ali, A. J. & Mao, C. X. *Two-Line Hybrid Rice Breeding Manual* (International Rice Research Institute, 2003).
38. Lindhout, P. et al. in *Burleigh Dodds Series in Agricultural Science: Achieving Sustainable Cultivation of Potatoes* (ed. Wang-Pruski, G.) 99–122 (Burleigh Dodds Science, 2018).
39. Nienhuis, J. & Sills, G. in *Reproductive Biology and Plant Breeding* (eds Dattée, Y. et al.) 387–396 (Springer Berlin Heidelberg, 1992).
40. Singh, S. & Gupta, S. K. Formation of heterotic pools and understanding relationship between molecular divergence and heterosis in pearl millet [*Pennisetum glaucum* (L.) R. Br.]. *PLoS ONE* **14**, e0207463 (2019).
41. Allard, R. W. History of plant population genetics. *Annu. Rev. Genet.* **33**, 1–27 (1999).
42. Gupta, P. K. et al. Hybrid wheat: past, present and future. *Theor. Appl. Genet.* **132**, 2463–2483 (2019).
43. Xiao, Z. et al. Overcoming cabbage crossing incompatibility by the development and application of self-compatibility-QTL-specific markers and genome-wide background analysis. *Front. Plant Sci.* **10**, 189 (2019).
44. Chen, L. & Liu, Y.-G. Male sterility and fertility restoration in crops. *Annu. Rev. Plant Biol.* **65**, 579–606 (2014).
45. Peet, M. M. & Welles, G. in *Tomatoes* (ed. Heuvelink, E.) 257–304 (CABI, 2005).
46. Erenstein, O. & Kassie, G. T. Seeding eastern Africa's maize revolution in the post-structural adjustment era: a review and comparative analysis of the formal maize seed sector. *Int. Food Agribus. Manage. Rev.* **21**, 39–52 (2018).
47. Crow, J. Anecdotal, historical and critical commentaries on genetics. *Genetics* **148**, 923–928 (1998).
48. Duvick, D. N. The contribution of breeding to yield advances in maize (*Zea mays* L.). *Adv. Agron.* **86**, 83–145 (2005).
49. Andorf, C. et al. Technological advances in maize breeding: past, present and future. *Theor. Appl. Genet.* **132**, 817–849 (2019).
50. Troyer, A. F. Adaptedness and heterosis in corn and mule hybrids. *Crop Sci.* **46**, 528–543 (2006).
51. Longin, C. F. H., Reif, J. C. & Würschum, T. Long-term perspective of hybrid versus line breeding in wheat based on quantitative genetic theory. *Theor. Appl. Genet.* **127**, 1635–1641 (2014).
52. Jiang, Y., Schmidt, R. H., Zhao, Y. & Reif, J. C. A quantitative genetic framework highlights the role of epistatic effects for grain-yield heterosis in bread wheat. *Nat. Genet.* **49**, 1741–1746 (2017).
53. Voss-Fels, K. P. et al. Breeding improves wheat productivity under contrasting agrochemical input levels. *Nat. Plants* **5**, 706–714 (2019).
54. Boeven, P. H. G., Würschum, T., Rudloff, J., Ebmeyer, E. & Longin, C. F. H. Hybrid seed set in wheat is a complex trait but can be improved indirectly by selection for male floral traits. *Euphytica* **214**, 110 (2018).
55. Boeven, P. H. G., Longin, C. F. H. & Würschum, T. A unified framework for hybrid breeding and the establishment of heterotic groups in wheat. *Theor. Appl. Genet.* **129**, 1231–1245 (2016).
56. Douches, D. S., Maas, D., Jastrzebski, K. & Chase, R. W. Assessment of potato breeding progress in the USA over the last century. *Crop Sci.* **36**, 1544–1552 (1996).
57. Jansky, S. H. et al. Reinventing potato as a diploid inbred line-based crop. *Crop Sci.* **56**, 1412–1422 (2016).
58. Zhang, C. et al. Genome design of hybrid potato. *Cell* **184**, 3873–3883. e3812 (2021).
59. Su, Y. et al. Introgression of genes for resistance against *Phytophthora infestans* in diploid potato. *Am. J. Potato Res.* **97**, 33–42 (2020).
60. Hutten, R. C. B. *Basic Aspects of Potato Breeding via the Diploid Level* (Wageningen University and Research, 1994).
61. Stockem, J., de Vries, M., van Nieuwenhuizen, E., Lindhout, P. & Struik, P. C. Contribution and stability of yield components of diploid hybrid potato. *Potato Res.* https://doi.org/10.1007/s11540-019-09444-x (2020).

62. Steenhuijsen Piters, B. D. et al. *Global Scoping Study on Fruits and Vegetables: Results from Literature and Data Analysis* (Wageningen Economic Research, 2021).
63. *Access to Seeds Index* (Access to Seeds Foundation, 2019); https://www.accesstoseeds.org/
64. Yuan, L. P. Hybrid rice in China. *Chin. J. Rice Sci.* **1**, 8–18 (1986).
65. Cheng, S. H., Zhuang, J. Y., Fan, Y. Y., Du, J. H. & Cao, L. Y. Progress in research and development on hybrid rice: a super-domesticate in China. *Ann. Bot.* **100**, 959–966 (2007).
66. Miedaner, T. & Laidig, F. in *Advances in Plant Breeding Strategies: Cereals* (eds Al-Khayri, J. M. et al.) 343–372 (Springer International, 2019).
67. McGrath, J. M. & Panella, L. in *Plant Breeding Reviews* (ed. Goldman, I.) 167–218 (Wiley, 2018).
68. Oliver, E. & Shoham, J. *Analysis of Sales and Profitability within the Seed Sector* (IHS Markit, 2019); https://cdn.ihsmarkit.com/www/pdf/0320/202001-Seedsectorsale-Analysis-LD-Unknown-Version001-pdf.pdf
69. Nielsen, R. L. *Historical Corn Grain Yields in the U.S.* (Purdue Univ., 2021); https://www.agry.purdue.edu/ext/corn/news/timeless/yieldtrends.html

Acknowledgements

N. Louwaars, O. de Ponti, K. Reinink, T. Schotte and J. Trouw are acknowledged for reviewing the manuscript and providing input for Table 2. H. Buerstmayr and V. Korzun are acknowledged for providing input for the wheat case study. C. Bachem and E. Jacobsen are acknowledged for reviewing the manuscript.

Author contributions

E.M.S.t.S. and P.L. were the lead authors working on the analysis, drafting and revision of the manuscript. P.C.S. and R.G.F.V. helped improve the analysis and took on an editorial role in revising the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence should be addressed to Emily M. S. ter Steeg or Pim Lindhout.

Peer review information *Nature Plants* thanks Ryan Whitford, Xiang-Yuan Wan and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.