Technology is driving the re-integration of plant and animal breeding to their mutual benefit

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Introduction

The world population is predicted to reach 9 billion within the next 35 years, requiring a 70-100% increase in food production relative to current levels (Thomson, 2003; Godfray Et al., 2010a; Nelson Et al., 2010; Godfray Et al., 2010b). Breeding of livestock and crops is one of the key routes through which this increased production, efficiency and sustainability can be delivered.

Although plant and animal breeding have similar objectives and have similar routes the two fields and their respective concepts and technology have diverged over the past 100 or so years. Although exceptions exist (e.g., trees, sugar cane), many plant breeders view selection as a process of accumulating favourable genes within a single individual and use a Mendelian approach to identify and incorporate favourable major genes. In contrast, animal breeders have viewed response to selection as a slow increase in the frequency of favourable alleles in a population, predictable from the 'breeders' equation'. Perhaps because of this focus and because of the different biological possibilities (e.g., inbred individuals and clonal propagation in crops versus outbred non-cloned individuals in livestock) quantitative genetics methods and the emphasis on physiology in plant and animal breeding have developed largely in parallel with different focuses.

The quantitative genetics methods in animal breeding have focussed on the statistical partitioning of phenotypic variation in a population into genetic and environmental components and on optimising the breeder's equation to drive gain for multiple traits simultaneously in an economically efficient way. The quantitative genetics methods in plant breeding have focused on the outcome of crosses between two inbred lines with emphasis on identifying "transgressive segregants" with merit exceeding that of the best parent.

Plant breeders have been much more explicit in their use of systematic experimental design, complex statistical models to analyse these designed experiments, and very deliberate efforts to understand and exploit physiology than animal breeders. This is perhaps because in crops it is possible to have inbred lines and clonal reproduction but also because, since the 1980's, plant breeders have been able to utilize various biotechnologies such as transgenics to a much greater degree. On the other hand, perhaps animal breeders have been more systematic in incorporating economics in the definition of their breeding goals than plant breeders ("breeder's art" is still a term often used in plant breeding).

All of this has meant that the fields of plant and animal breeding have diverged somewhat over the decades, leading to inefficiencies, delays in the adoption of technology and many missed opportunities. The advent of genomic selection, genome editing, surrogate sire technology, and a whole host of other technology is driving the re-integration of plant and animal breeding methods and driving new synergies, more gain, and biological discovery.

Within any given species there is a wide variety of different ways to implement a breeding program. This possible variety is greater across species within the plant or animal kingdoms and even greater when spanning both the plant and animal kingdom. However,

regardless of species, whatever the kingdom, all breeding programs have the same basic design (Figure 1a). They involve a recurrent selection process in which individuals are evaluated, selected and crossed repeatedly, as quickly and as accurately as possible with care taken to ensure sufficient genetic variance is maintained. Periodically, a product is extracted from this population, multiplied in some way, often further evaluated, and then delivered to commercial producers.

A simplified blueprint for an animal breeding program

Many of the features of animal breeding programs can be represented by a simplified breeding program that produces terminal sires for a meat producing species in which artificial insemination with frozen semen is not commonly used (Figure 1b). Such a breeding program is structured in a pyramid. At the top of the pyramid is a nucleus population. Genomic selection is used to turn the generations of the nucleus population over as quickly and as accurately as possible with optimal selection intensity and maintenance of genetic variation. At each generation males from the nucleus are passed to a multiplier layer. In the multiplier layer the genetic improvement is multiplied and then males from it are passed to the commercial layer.

A simplified blueprint for a plant breeding program

Many of the features of plant breeding programs can be represented by a simplified breeding program that produces a single inbred line, or handful of inbred lines, that are grown on a wide area (Figure 1c). Such a breeding program begins with a crossing block in which a number of inbred lines from previous generations are crossed to produce huge numbers (e.g., millions) of F_1 individuals. Over a number of years selfing and multi-stage selection are used to whittle this large number of outbred individuals down to a handful of inbred individuals (e.g., F_{10}). As these years of selfing and selection are traversed the number of individuals advanced is reduced and the accuracy with which they are evaluated is increased. Genomic selection is increasingly being used to increase the accuracy of selection at each of the stages. Finally, one or two inbred lines or their hybrids are released to growers.

Comparing and contrasting animal and plant breeding programs

Plant and animal breeding programs both aim to increase the mean of the population (population improvement) and to identify and test products for release to commercial producers (product development). However, the emphasis that they place on each of these is arguably different (Hickey Et al., 2017). Animal breeding emphasises population improvement while plant breeding emphasises product development. Arguably the reasons for this are due to differences in biological possibilities and the economic parameters that emerge from that.

Commercial plant producers grow a single inbred (or hybrid) cloned genotype on large areas. The value of this genotype is huge and should previously unidentified weaknesses emerge after it is released the consequences would be great. For these reasons plant breeders emphasise product development which is the identification and testing of specific genotypes from the huge number of candidate genotypes. Population improvement is arguably only a secondary consideration, perhaps because the product development component absorbs so many resources.

In contrast animal producers do not grow clones, instead every animal has its own unique genotype. Thus, rather than investing huge resources in testing each individual animal breeders emphasise the improvement of the population. A partial exception to this is the dairy

industry where artificial insemination with frozen semen enables individual bulls to have large footprints and prior to the adoption of genomic selection necessitated their intense testing.

Surrogate sire technology

Surrogate sire technology allows the creation of males that lack their own germline cells, but have transplanted spermatogonial stem cells from other "elite donor" males (Park Et al., 2017). With this technology, a single male could effectively produce huge numbers of progeny, potentially as much as all the production level animals in a particular time period. The footprint of such a donor would be much greater than even the most widely used dairy sires has been in the past. Using a single male to generate all production animals offers many advantages. Firstly, it would reduce the genetic lag between the elite nucleus animals and the production animals. Secondly, it would increase the uniformity of production animals, which would aid management and enable specific management plans to be supplied alongside the genetics. Thirdly, it could enable elite donors to be selected for combining ability.

A unified blueprint for plant and animal breeding programs

Recently we have performed two sets of simulations for the development of new breeding strategies, one for a plant breeding application and the other for animal breeding. The plant breeding set of simulations describe and test the potential of what we call a two-part strategy for using genomic selection to develop inbred lines in crops (Gaynor Et al., 2017). The two-part strategy involves explicitly splitting the breeding program into a population improvement part and a product development part (Figure 2). Within this framework, genomic selection can be used to identify promising lines sooner, thereby reducing cycle time and increasing genetic gain per year (Heffner et al., 2009). The animal breeding set of simulations describe and test the potential of a strategy to exploit surrogate sire technology (Gottardo Et al., 2017). While these studies may appear at some level to be different we believe that at a very basic level they are identical. Both strategies explicitly partition a breeding program into a part that seeks to improve the population using rapid recurrent selection based on genomic breeding values alone, referred to as population improvement, and a part that uses a multi-stage testing to identity and test a product, referred to as product development.

Compared to a classical plant breeding program the two-part plant breeding program generated as much as 2.5 times more gain per unit time and per unit cost (Figure 2) with prospects for even more if breeding cycle time in the population improvement component was more aggressively shortened and optimal contribution selection was used. Compared to a conventional animal breeding program that used a conventional multiplication pyramid to disseminate genetic improvement the breeding program design that exploited surrogate sire technology delivered sires whose genetic merit was up to 9.2 years' worth of genetic gain higher than a conventional scheme (Table 1), with prospects for even greater benefit through the exploitation of combining ability and tailored management programs. The breeding program design to exploit surrogate sire technology was very similar to the two-part plant breeding program design. It involved a population improvement component based on recurrent selection using genomic breeding values and a product development component to identify a single individual who would be used as a donor of spermatogonial stem cells or surrogate sires. Of the different identification strategies tested in the product development component the best performing involved three-stages, the first of which uses genomic selection while the subsequent stages use progeny testing, was the most effective strategy of

all of those tested. This type of multi-stage selection is very similar to what is been used in many plant breeding programs.

Further exploitation of data generated for genomic selection

Genome editing has a great potential for increasing the rate of genetic gain in plant and animal breeding programs. In cases where variants of large effect exist genome editing could be used to introduce them to elite individuals (e.g., CD163) (Whitworth Et al., 2015). It could be used to correct several variants that contribute to genetic load in populations, to generate surrogate sires or for improving quantitative traits using strategies such as promotion of alleles by genome editing (PAGE) (Jenko Et al., 2015).

Large amounts of phenotype and genomic data are being generated by breeding programs for the purposes of genomic selection. These data could also serve as 'test beds' for testing biological hypotheses as well as platforms for the discovery of targets for genome editing via "Allele Testing" (Hickey Et al., 2016). Perhaps the following cascade of technologies could be used in such testing schemes:

- all genomic variants could be initially assigned an equal probability of being causal
- genome wide association studies using large data sets could be used to increase the probability of a much smaller subset of the variants being causal
- functional annotation information and expression data could be used to further increase the probability of an even smaller subset
- there may be opportunity to study subsets using genome editing in cell lines to further increase the probability of an even smaller subset
- the resulting subset could then be edited into sires within the breeding program and have the effects analysed in the descendants as part of rolling breeding activities
- variants shown to have positive effects could be edited in all sires, those with negative effects could be reversed using editing, and those that are neutral could be ignored.

Conclusions

Plant and animal breeding program designs have the same basic aims. They have diverged somewhat over the years. Genomic selection and surrogate sire technology could lead to generic breeding program designs that are very similar across these two sectors. We have recently developed such strategies and used simulation to show that they would deliver significantly higher rates of genetic merit to commercial producers.

Table 1. Best performing strategies[1] for identifying elite donors for 3 different levels of genomic selection accuracy.

Accuracy GEBV	Sires tested S1	Sires tested S2	Sires selected*	Resources**	$\bar{X}_{YGG}$***
0.5	100	20	1	6000S1/8000S2	9.20
0.7	200	20	1	6000S1/8000S2	7.20
0.9	200	20	1	6000S1/8000S2	5.00

[1]*These strategies are a subset of those tested by Gottardo Et al., 2017*
GEBV = genomic estimated breeding value
S1 = first progeny test
S2 = second progeny test

**Number of sires selected to become elite donors*
***Total number of progeny allocated in the first progeny test (S1) and in the second progeny test (S2) respectively*
****Average Years' worth of genetic gain (YGG) calculated across 20 generations of future breeding*

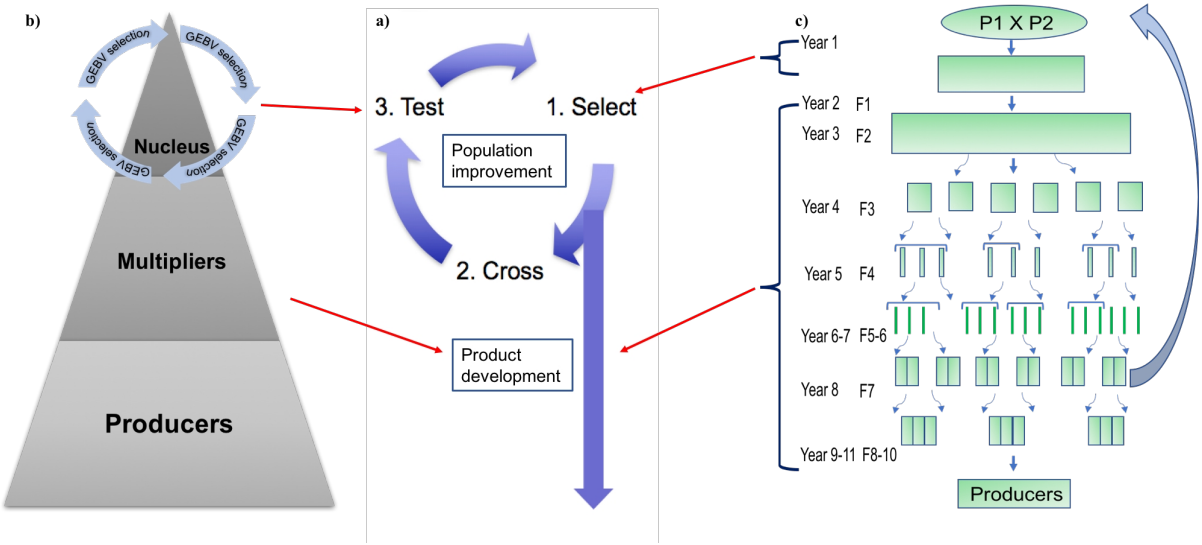

Figure 1. (a) A generalized schematic of breeding programs, (b) a generalized schematic of an animal breeding program; (c) a gneralised schematic of a plant breeding program

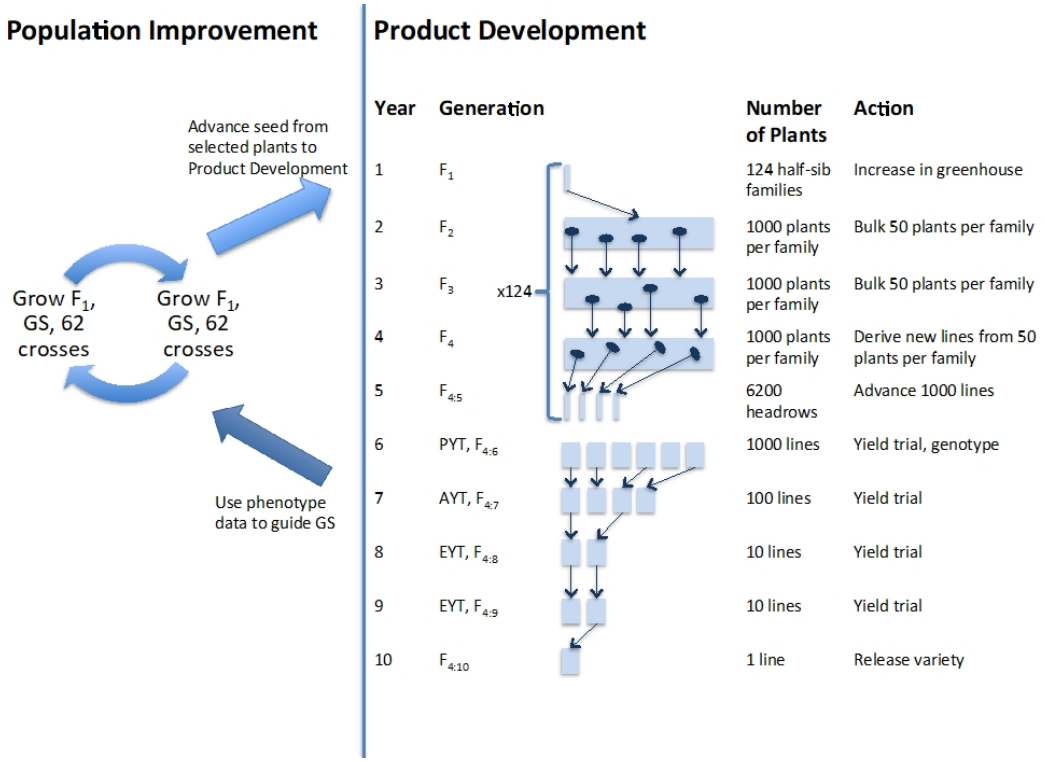

Figure 2. A schematic of a two-part plant breeding program design

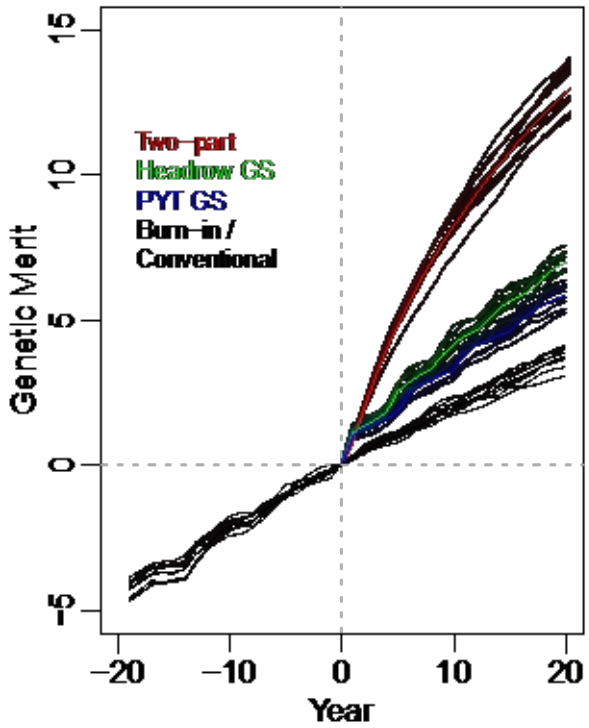

Figure 3. Genetic gain achieved by the two-part plant breeding scheme and alternative plant breeding schemes following Gaynor Et al., 2017

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