Quantitative genetics and the design of breeding programs

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INTRODUCTION

Barring major catastrophies the human population of the world appears destined, at minimum, to double before it stops growing. Moreover, this doubling must be anticipated within the next 35-40 years. Possibly population growth will never stop before food is limiting but unless and until that is established there will be compelling reasons for keeping food production abreast with population. And in view of problems posed by transportation and by trade balances among nations, the geographic distribution of food production should, to the extent possible, parallel that of population.

Genetic improvement is by no means the only avenue through which increases in food production can be achieved but, assuming its potential contribution to be substantial, it will be my point of departure that we must now become very serious concerning maximum exploitation of the allele resources of our economic species in minimum time. By maximum exploitation of the allele resource of a species, I mean synthesis of ideal genotypes,

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genotypes that possess the most useful allele (or alleles, in the case of overdominance) of each gene that has any bearing on value of the genotype. Obviously, in view of genotype-environment interaction, the allele composition of ideal genotypes will vary depending on the population of environments in which the genotypes are to be used.

Optimum procedure for synthesis of such ideal genotypes is not obvious in all details. However, because phenotypic value in agricultural species depends on various traits of which most are multifactorial and incompletely heritable, it appears certain that recurrent selection (defined to embrace all cyclic systems in which the selections of any one cycle are employed as the parents or gene source for the first generation of the following cycle) will be required. It is worth noting and emphasizing that the theory and a substantial portion of the empirical evidence that justify this conclusion are contributions from quantitative genetics.

Assuming that recurrent selection will be necessary, I shall discuss the present state of quantitative genetics, as it relates to breeding, in terms of its contributions to the breeders bases for making the prime decisions required in the design of adequate recurrent selection programs. What has quantitative genetics accomplished and what has it failed to accomplish that is relevant to those decisions? In view of present urgency I will focus on programs aimed at close approach to ideal genotypes without any outcrossing (allele introduction) after the initial foundation population has been put together.

Before going further, let me say that what follows is presented with functionally diploid species in mind. You are all aware that quantitative genetics has given little attention to other species.

CONDITIONS FOR SUCCESS VIA RECURRENT SELECTION

In the preceding remarks "success" has been identified as the

development of a genotype having the best possible allele at each locus. The required conditions are:

(1) that locus by locus the rank order values of alleles are not conditioned by allele frequencies at other loci,

(2) that the selection criterion is such that the most useful allele of every segregating gene is favored, and

(3) that effective population size is sufficient to trivialize the ultimate consequence of genetic drift.

The first of these has to do with epistasis. It reflects the important fact that simple epistasis (rank order values of alleles not conditioned by background genotype) does not interfere with success via recurrent selection. In contrast, given multiple peak epistasis, the allele frequency changes fostered by recurrent selection may be such that the limit approached is associated with a lesser peak (a genotype that is not ideal); i.e., the end result will be conditioned by the matrix of allele frequencies in the initial foundation population.

Condition (2) poses the following pair of questions:

(a) Given a specific definition of the ideal phenotype, how should the selection criterion be constructed?

(b) Can the phenotype that will be ideal in the future (e.g., 30 or 40 years from now) be foreseen with sufficient accuracy?

The first of these is a genetic issue that will be discussed later. The second is a nongenetic issue but critical in relation to the genetic consequences of recurrent selection. Given the wrong goal, the selection criterion will doubtless be wrong with the result that alleles other than the most useful will be increased in frequency, perhaps fixed, before the proper goal correction is made. The possibility that phenotypic need will not be correctly perceived 10 or more years in advance poses a flaw in the concept of synthesizing ideal genotypes by recurrent selection. However, there seems no way out of the dilemma other than continuing realistic review of phenotypic goals in the light of whatever socioeconomic logic, facts, or trends are relevant.

MAJOR DECISIONS IN THE DESIGN OF A RECURRENT SELECTION PROGRAM

In my judgment these are the decisions relative to the issues in the following list.

(1) The goal of the program
   (a) Phenotypic goal
   (b) Target population of environments
(2) Foundation population(s)
(3) Selection system
(4) Selection criterion
(5) Effective population size

Most of what follows will be devoted to these issues with specific attention to the underlying genetic issues and to whether those in the realm of quantitative genetics have or have not been resolved.

Phenotypic Value

The phenotypic goal of a program is conveyed by statements concerning the measurement of phenotypic value. While this in itself is not a genetic issue, it is important in relation to much that is genetic that we remind ourselves that, in the real world of the breeder, the value of a breed, variety, or cultivar always depends on a number of traits. If any of us is ever inclined to minimize that fact, we have only to reflect briefly on such a list of variables as yield, quality of product, production efficiency, aspects of reproduction, disease resistances, and adaptations to environment.

Before leaving this subject, I feel bound to warn that unjustified convictions concerning what is genetically feasible can have unfortunate effects on goal identification. As an example consider "litter size" in beef cattle. Many have believed, and probably still do, that the allele resource of the bovine species is too limited to support the development of cattle with an average "litter size" closer to two than to one. But this has not been proven beyond doubt and such an increase would bring a major reduction in the production cost of beef. It appears

axiomatic that if a close approach to the full genetic potential of a species is to be realized, all changes that would have substantial value should be attempted. In support is one of the major contributions of quantitative genetics, the experimental demonstration that a very great variety of quantitative traits, including ones strongly canalized, responds to selection in well-conceived programs.

Target Population of Environments and Number of Programs

Environment varies in many ways; some highly predictable, others less so with predictability ranging downward from moderate to perhaps zero. Because the rank order values of genotypes are not constant over the vast array of environments in which a species may have utility, decisions are required relative to the populations of environments for which high genotypic value will be sought in a single variety, cultivar, or breed. For example, corn breeders might identify such a target population of environments (TPE) with a geographical region (consisting perhaps of two or more disconnected portions) and within that region with particular soil types, plant densities, levels of fertilization, etc.

It is readily apparent that the subdivision of the totality of environments into TPE's has conflicting dimensions. Homogeneity within populations with respect to predictable aspects of environment can be increased by finer subdivision. But because the number of recurrent selection programs must be at least equal to the number of TPE's the total cost for programs of adequate size is thereby increased. The TPE's of an optimum set would be structured to minimize the joint costs of (a) the recurrent selection programs required and (b) the rank order changes in genotype value associated with intrapopulation variation in predictable aspects of environment.

This problem area has received minimal attention from quantitative genetics. Procedure for estimation of genotype-environment interaction variances has been outlined and numerous

estimates have actually been obtained and reported. In general, however, these have been interpreted with reference to genotype-environment interaction as a source of nongenetic variance among selection units of one kind or another.

In contrast, quantitative genetics has not shown how such estimates can logically be employed in decisions concerning TPE's. For example, I do not know how large a component of genotype-environment interaction variance can be, as a fraction or multiple of genetic variance, when there is no variation among environments in the rank order values of genotypes (or family groups of genotypes) nor am I aware that this has been discussed in the literature. Perhaps the situation is best summarized by asserting that quantitative genetics might reasonably be expected to develop a description of the kind of data and analysis that would provide an objective basis for delineation of TPE's but that to date this has not been done.

Selection System

This is the decision area in which quantitative genetics has made its greatest contribution.

The major question is whether the ideal genotype sought can be synthesized by recurrent selection in a one population program or whether a two (or more) population program with selection for combining ability is required. The underlying genetic issue is overdominance and the question stated above can be restated as follows. Can the ideal genotype be homozygous (for the best allele) at nearly all loci or is it one that must be heterozygous at a substantial number of loci?

The overdominance issue is not completely resolved but important evidence, mostly from two types of work, has been produced. Studies of genetic variance components indicate that overdominance is not a major feature in the genetics of single quantitative traits, not excepting such highly heterotic ones as grain yield of maize. The second major source of evidence has

been long-term recurrent selection for single traits in pilot species. Correlated responses (normally negative in the case of reproduction), residual genetic variance at plateaus, and the changes in levels of the selected trait and reproduction following relaxation or reversal of selection have provided strong evidence for a substantial amount of pleiotropy. More specifically to the point, the totality of this evidence indicates that alleles favorable relative to one trait are often unfavorable relative to another. The obvious corollary, considering the multi-trait nature of total phenotypic value in economic species, is that overdominance can be (probably is) important at the level of total value without being important in the genetics of single traits. In saying this, I think I am echoing ideas expressed by Dr. Falconer on Monday.

The elements of a theoretical base for comparing recurrent selection systems within either of the major classes of systems implied at the beginning of this section are the following.

(1) Expressions that approximate $E(\Delta\bar{Y})$, the expectation of change in the mean value of genotype per cycle of selection. In their usual form, these are premised on a no-epistasis genetic model and have been or can be obtained for every selection system that I have thought about. These always involve a genetic variance or covariance. Bases for estimating these parameters have been or can be provided but often are not required because in many systems comparisons the parameter is the same for both systems and therefore cancels out.

(2) The probability of fixation of an allele has been shown to increase as the product, Ns, increases. Here N = effective population size, or more precisely, the number such that variance of allele frequency during one selection program cycle is $q(1 - q)/2N$ and $\underline{s}$ = the "selective value" of the allele in question.

(3) A general procedure for approximating $\underline{s}$ as a function of $\underline{k}$, u/σ_x, and $\underline{f}$. Here $\underline{k}$ = the selection differential as a

multiple of σ_x, σ_x = the standard deviation of the selection criterion (x), u = one-half the effect on x of substituting, at the locus in question, the best homozygous genotype for the other homozygous genotype, and f, when it is not zero, is a coefficient of inbreeding common to all selection units (or the parents of those units). As implied by the definition of u, this procedure assumes only two alleles per gene. It probably could be generalized but probably then would have no greater value relative to selection system comparisons.

Selection systems have ordinarily been compared in terms of (1) $E(\Delta\bar{Y})$ per unit of time and (2) their costs for operation, given that number of selections is sufficient to make inbreeding per generation quite small; e.g., ≤ 0.03. In the present context; i.e., recurrent selection aimed at achieving ideal genotypes, I propose that the bases for comparison should be

(1) $E(\Delta\bar{Y})$ per unit of time,

(2) operation costs, and

(3) the product, Ns. While the quantity, u, in s cannot ordinarily be evaluated, it is invariant relative to selection systems and hence cancels from comparisons.

Because effective empirical comparisons of recurrent selection systems are ruled out by considerations of time and costs, the theoretical base for comparisons provided by quantitative genetics (and sketched above) must be viewed as a contribution of very special value despite the degree of approximation introduced by the enabling assumptions involved.

Selection Criterion

The multi-trait composition of phenotypic value in economic species poses the problem of how variations in the contributing traits should be reflected in the selection criterion employed in a recurrent selection program. As a base for thinking about this problem, we should recall that if the s-value for an allele is zero, the probability of fixation of the allele in the final

product of recurrent selection will be equal to the original frequency of the allele. The probability will be higher or lower than that depending on whether the s-value is positive or negative. It follows that the selection criterion in recurrent selection programs from which the breeder hopes to obtain ideal genotypes should make $s > 0$ for each useful allele.

The best known solution to the trait-weighting problem is the one embodied in the criterion usually denoted as the selection index which I will refer to as the Smith-Hazel (S-H) index. It must be viewed as a major contribution of quantitative genetics. At the same time, we need to keep in mind that it is designed to maximize the effect of selection on total phenotypic value in the cycle immediately ahead, not the total change in phenotypic value that can be achieved by recurrent selection. Stated differently and more specifically, the procedure for construction of the S-H index does not insure $s > 0$ for all useful alleles. On the contrary, even if all traits contributing to phenotypic value were included in an S-H index and the parameter estimates employed were all accurate, some of the consequent s-values could be negative.

The problem appears to deserve renewed attention. One way to confer positive s-values on all useful alleles is by use of the system of weights inherent in the specification of total phenotypic value; i.e., by using total phenotypic value as the selection criterion. I suspect that this may be the only way. It would require measurement of all traits contributing to phenotypic value and would shift comparative values of selection systems toward those in which there is high genetic variance among selection units (to minimize measurement costs per unit of response) and in which the selection units are families of sufficient potential size to allow optimizing measurement heritabilities.

Clearly there is more work for quantitative genetics in this area.

Effective Population Size

Among conditions, listed early in this paper, for success via recurrent selection was effective population size (N) sufficient to trivialize the ultimate consequence of genetic drift. The theory developed relative to probability of fixation is a major contribution of quantitative genetics (broadly defined) that provides very useful insights to required values of N. Consider the expression

$$P = \frac{1 - e^{-2Nsq}}{1 - e^{-2Ns}} \qquad (1)$$

that has become more and more familiar to us over the past two decades. Here P = the probability of fixation of an allele, q = the initial frequency of the allele, e is the base of the natural system of logarithms, and s has meaning specified earlier. We have learned that equation (1) is an excellent approximation when N and s are constant through time and the gene in question segregates independently from all others with effects on the selection criterion. Thus, assuming knowledge of s and q and ignoring possible linkage effects, this expression, used iteratively, gives us the value of N required to achieve any chosen value of P. Our problem is to supply appropriate values of s and q.

It was noted earlier that an expression giving s as a function of k, u/σ_x, and f can be obtained for any selection system. The most familiar example is $s = 2ku/\sigma_x$ for the case of selection among individuals on the basis of their own phenotype. Unfortunately, we have almost no direct information concerning u-values when x is total phenotypic value or whatever other selection criterion that is appropriate in the kinds of recurrent selection program being discussed. In this circumstance I find it useful to note that

$$\frac{u}{\sigma_x} = \frac{u}{\bar{R}} \frac{\bar{R}}{\sigma_x}$$

where $\bar{R}$ = mean phenotypic value. Once the selection criterion (x) has been decided and a selection program is underway, data providing good estimates of $\bar{R}$ and σ_x should soon be available. Then, using equation (1), one can answer questions of the following nature: "What N is required to make P = 0.98 if $u/\bar{R}$ = 0.01 and q = 0.10?" Out of this, useful insights to guide decisions concerning effective population size can be obtained. Crucial, of course, are the lowest values of $u/\bar{R}$ and q that should be considered and the possible magnitudes of linkage effects.

Present information concerning linkage effects can be summarized in a rough way as follows. In general, linkage decreases fixation probabilities so the value of N must be increased to compensate. This unfavorable effect will be greatest when there is linkage disequilibrium of the type that must be anticipated when the foundation population is structured with the objective of aggregating useful alleles from diverse sources; e.g., when attempting to develop ideal genotypes (as the latter have been defined for the purposes of this paper). Insights concerning increases in N required to compensate for linkage effects have been provided by computer simulation studies but conclusions, even rather loose conclusions, depend on the assumptions made about linkage intensities.

We are also in serious need of better information concerning values of $u/\bar{R}$. Specifically, our need is for answers to questions such as these. How much of the potential for genetic improvement is associated with alleles for which $0.01 \leq u/\bar{R} < 0.02$, how much with alleles for which $0.005\ u/\bar{R} < 0.01$, etc.? I cannot suggest good or obvious ways for obtaining such information but it is obvious that information on numbers of genes that affect value of the organism is relevant. The greater the number of these, the less the average value of $u/\bar{R}$ must be. It should be added that information on gene number contributes as well to our base for reasonable assumptions concerning linkage intensities.

The most important thing to be said about frequencies of

favorable alleles (q-values) is that our information is inadequate. Another point worth making is the obvious one, that if any "strain" is used as the source of a fraction, p, of the original genes of a foundation population in the belief that useful alleles absent from all other components of the foundation may be contributed by that "strain," then q-values as low as p should be assumed when the decision concerning N is made.

To summarize, the now available theory relating probability of fixation to effective population size has special value despite our need for more complete information concerning allele frequencies, u-values, and linkage effects. Applications of that theory, using assumptions concerning q, s, and linkage that are clearly too favorable, demonstrate that effective population size required in recurrent selection programs aimed at synthesis of ideal genotypes is a lot greater than many of us had realized.

Foundation Population(s)

Ideal genotypes cannot be synthesized by recurrent selection unless all the required alleles are present ($q > 0$) in the foundation material or arise at some point by mutation. However, it can be shown that the expectation of generation time required to obtain a favorable allele in homozygous state if it must arise in the population by mutation is much greater than required if the allele is present originally in a frequency even as low as 0.05 or 0.1. Therefore, in the context of attempts to produce ideal genotypes in 100 generations or less, mutations can be ignored as a source of useful alleles.

How can the probability of $q > 0$ for each useful allele be maximized in a foundation population? It appears that this would be accomplished by a stratified sampling of the entire species so that all subpopulations would contribute genes to the foundation population. The major counterargument is that the frequencies of alleles superior relative to a specific TPE would then be lower on average than if the foundation population were constructed from

the sources reasonably adapted to the TPE. Thus the achievement of high genotypic value will take longer when the broad sample approach is employed but the final level achieved may (not certainly will) be higher if effective population size has been adequate.

The genetic issue is the distribution of alleles and allele frequencies within species. Opinion among quantitative and agricultural geneticists ranges from the view that each subpopulation (race, strain, local population of pure lines, etc.) probably possesses one or more useful alleles that is absent in all or almost all of the rest to the view that all or almost all useful alleles are present ($q > 0$) in every subpopulation. The latter view is predicated on sufficient effective population size of subpopulations and the migration among them.

Instead of attempting further discussion, let me re-emphasize the existing divergence of opinions and summarize by saying that we need either (1) more information concerning allele distributions within species or (2) better synthesis and exposition of what is already known.

SUMMARY

The preceding discussion has been centered around the problems of synthesizing ideal genotypes for all of the environment populations in which an agricultural species has utility and doing it in minimum time. Quantitative genetics has made major contributions to the bases for the major design decisions involved in the performance of that task. At the same time there are significant issues in the realm of quantitative genetics that have not been resolved. Some of these appear tractable, others relatively intractable.

Finally, it is obvious that a complete set of ideal genotypes represents a goal that can be approached but not fully achieved because for that infinite investment would be required. It follows that optimum utilization of resources actually available

will pose various problems. What, for example, is the optimum balance in worldwide maize breeding among number of recurrent selection programs (closely related to number of target populations of environment to be delineated), effective population size in single programs, and breadth of genetic base in foundation populations?

It appears from the perspective of the breeder that quantitative genetics still has a challenging future.