Estimating of Additive, Dominance, and Epistatic Genetic Variance in Eucalypt Hybrid Population

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Abstract

Additive, dominance and epistasis genetic variances were estimated from analysis of a clonally replicated full-sib progeny test grown in the Republic of Congo. Phenotypic variance components were estimated for ages 4 through 25 months for growth and at ages 8 and 18 months for ecophysiological traits. The estimation of genetics effects was derived from the individual mixed model. Genetic structure was incorporated into variances and covariance's effects based on markers information. The detected genetic effects of epistasis are significant in some traits. This study shows that epistasis variance can be non-zero and contribute significantly to the genetic variability of growth and ecophysiological traits. We conclude that the epistatic effect for quantitative traits may exist, but estimates may not be obtained, either because the models used are inappropriate or because the epistasis variance is too small relative to other components of the genetic variance to be estimated.

Keywords: *Eucalyptus, Genetic variance partitioning, Epistasis, SNP marker, Relationship matrix.*

Introduction

Study in quantitative genetics has been formulated in terms of trait variation (Falconer and Mackay 1996). The basic idea being the partition of this variation into components, each attributable to a different cause (Fisher 1918). The Genetic variance is partitioning into additive (A), dominance (D) and epistasis (I) components. These effects successively designate the intrinsic effects of the alleles, the intra-locus interactions, and the inter-loci interactions. The relative importance of the expected genetic gain by selecting population, family or clone varieties depends on the genetic variance components. In plant breeding, plant breeding, non-additive effects are generally neglected and in particular, the effects of interaction of the alleles between loci (Lynch and Walsh, 1998). The reason for this is due to the cumbersome and complex experimental designs needed for the decomposition of the genetic variance to the three components: additive, dominance and epistasis (Fisher, 1918). Ignoring non-additive genetic effects distorts the prediction of crossover values, as well as genetic variance components and the genetic merit of genotypes (Van der Werf and Boer, 1989; Shelbourne, 1991; Rosvall et al., 1998; Lu et al., 1999; Carlborg and Haley, 2004). Epistasis effects can also inflate additive and/or dominance variances (Goodnight, 1988; Cheverud and Routman, 1995; Lynch and Walsh, 1998). Epistatic interactions can occur between additive (A×A…), dominance (D×D…) and between additive and dominance effects (A×D…). The order of the interactions is higher as the number of loci involved increase. Some epistatic components are more important than others and especially the A×A component is of importance (Cheverud and Routman, 1996; Wade, 2002) and has been shown to be heritable (Goodnight, 1988) and thus much attention has been paid to studying A×A effects in response to selection and evolution (Goodnight, 2000; Jannink, 2003; Xu and Jia, 2007).

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Expression of additive and dominance (including epistatic effects without the possibility to distinguishing the two components separately) effects for *Eucalyptus urophylla* × *E. grandis* growth traits has previously been studied (Bouvet et al., 2009). However, those results were based on the classical quantitative genetics model (Gallais, 1990). Although this model allows for the evaluation of assessment genetic gain potential of many plants of interest. Thus, for a long time, genetic selection of quantitative traits in animals and plants focused solely on phenotypic performances of an individual and its relatives.

Quantitative genetic analyses based on the partition variances was initially proposed by Fisher (1918) and further developed by Cockerham (1954) and Kempthorne (1954) who derived methods that are used today.

Nevertheless, this variance partition does not dependent on the number of genes or the way they interact; the model is only tractable when the effects are orthogonal, which requires many assumptions. Thus, quantitative genetic analysis is something of a 'black box' (Hill, 2010). Today, the study of biological complexity and its applications is a new frontier that requires high-speed molecular technologies, high-performance computers with sufficient memory (Palucci et al., 2007), new approaches to analyze data (de los Campos et al., 2013), in short it requires the integration of interdisciplinary skills. With the availability of dense genome-wide molecular markers, genomic selection (GS) has now become practical in forestry breeding. One of the justifications for molecular genetic research in forestry species is the hope that DNA-level information will allow for more rapid genetic gain than what has been obtained from phenotypic data alone. The availability of marker genotypes for several thousand loci across the genome allows GS to predict genetic values more accurately than traditional breeding methods (Meuwissen et al., 2001; Bernardo and Yu, 2007; Jannink et al., 2010; Guo et al., 2012). Dense genome-wide markers allow to the incorporation of most variants using historical linkage disequilibrium in the population (Hill, 2010). Genomic selection is achieved by capitalizing on linkage disequilibrium between markers and QTLs but also on genetic relationships among individuals in the study population (Luan et al., 2012). In forest tree breeding, estimation of genetic variance components and prediction of breeding values are performed by applying the restricted maximum likelihood (REML) (Patterson and Thompson, 1971) and best linear unbiased prediction (BLUP) methods (Henderson, 1974). Today, more information is associated with the execution of these methodologies, such as the matrix of relationships related to additive, dominance and epistatic effects.

The use of this information increases the accuracy and precision of genetic selection by eliminating some of the inherent biases in collected data (Kerr et al., 2012). Relationship matrices can be constructed from pedigree information or genome-wide marker information (Habier et al., 2007; Heffner et al., 2009; Luan et al., 2012; Su et al., 2012). Pedigree information provides expected exact relationships whereas marker data provide realized estimated relationships. Relationship estimates based on markers are more accurate than pedigree-based estimates (Bouvet et al., 2016). Some mechanisms lead realized relationships to diverge from their expectations, such as random Mendelian segregation, segregation distortion, selection, and pedigree recording errors (Heffner et al., 2009). The matrix of realized relationship between individuals has as its elements the realized proportion of the genome that is identical by descent (IBD) between pairs of individuals (Lynch and Walsh, 1998; Luan et al., 2012; Garcia-Cortes et al., 2013). Revisiting additive and non-additive effects in *E. urophylla* × *E. grandis* are done by also considering epistatic variance, exploring variances in ecophysiological traits, and using information from genetic markers. Knowing that, when non-additive genetic effects have a substantial contribution to genetic variation, models including both additive and non-additive effects lead to predicting genetic merit with higher accuracies and with less bias (An et al., 2009; Su et al., 2012).

The aim of this paper was to determine the importance of the epistatic variation in the total genetic variation in hybrid *E. urophylla* × *E. grandis* from Congo regarding growth and some ecophysiological traits.

Materials and Methods

Location

The trial site is located at Kissoko north of Pointe-Noire (11°59' 21 " E 4°45' 51 " S). The average rainfall is 1200 mm/year. The soils are characterized by low water retention, very low organic matter (Epron et al., 2004; d'Annunzio et al., 2008) and low cation exchange capacity (Nzila et al., 2002).

Plant material and experimental design

An incomplete factorial mating design of 13 (female) x 11 (male) *E. urophylla* × *E. grandis* (Table 1) was used and generated 69 full-sib families by controlled pollination. A clonally replicated progeny test was planted with 1415 clones at a planting density of 833 trees ha^{-1}. A clonally replicated progeny test was planted with 1415 clones set up as a randomized block design at a planting density of 833 trees ha^{-1}. This progeny test was set up as a randomized block design. The experimental unit was 25 plants, composed of one representative of each of the 25 full-sib clones. Thus, each plot corresponds to a full-sib family. Thus, each plot corresponds to a full-sib family. Thus, each plot corresponds to a full-sib family. The total number of clones used in this study was reduced to 1415 because of natural mortality.

Phenotypic and marker data

Tree height (H) and Circumference at breast height (C) was measured between 4 and 25 months. In addition to these growth traits, three ecophysiological traits (leaf nitrogen content, specific leaf area and photosynthic activity of leaves) were considered at two ages, 8 and 18 months. Ten (10) leaves (5 from the upper crown and another 5 leaves from the lower crown) were harvested from all the individuals in the trial. Harvesting was done in all azimuths of the tree to account possible differences of sunlight. The leaves selected were mature

Table 1
Pedigree and number of clones per family for each cross

		Mâle (*Eucalyptus grandis*)											
		9-101	9-111	9-113	9-115	9-118	9-131	9-15	9-159	9-21	9-29	9-66	Total
Femelle (*Eucalyptus urophylla*)	14-109		25		25			25	25	25	24	25	174
	14-142				25			25		24	13	25	112
	14-144		25		24	13	10		10	25	25	14	146
	14-230		23		25			18	9	25	20	25	145
	14-233				9					14			23
	14-242		20		4					22	10	25	81
	14-289		25		24			5		25		25	104
	14-33									23	24	8	55
	14-63		24	4	25	10		25		15		26	129
	14-73	4	23							23		25	75
	14-74		25		25	24						28	102
	14-76		25			25		24	10	25	25	25	159
	14-82		25		10					25	25	25	110
	Total	4	240	4	196	72	10	122	54	271	166	276	1415

leaves, neither juvenile nor senescent, with completed limb expansion, free of any pathogen attack. Leaves were brought back to the laboratory where they were scanned, then oven dried at 65°C for at least 48h, after which the dry matter mass was determined. Leaf area and dry matter were used to calculate specific leaf area (SLA). Next, the leaves were powdered after grinding (< 0.1 mm). and the spectra were taken from each sample for the determination of predicted leaf nitrogen content (N) by near-infrared reflectance spectroscopy (NIRS). The N/SLA ratio was calculated to determine the leaf photosynthetic activity (LPA). LPA is the leaf nitrogen concentration per unit leaf area, which is a good indicator of photosynthetic potential.

SNP marker data were obtained from 3596 18-month-old trees that were genotyped using GBS technology implemented by Diversity Arrays Technology (DART). Of the 20,000 SNPs identified, 3,303 were selected based on repeatability (Bouvet et al., 2016).

SNP marker data were obtained from 3596 18-month-old trees that were genotyped using GBS technology implemented by Diversity Arrays Technology (DART). Among the 20,000 SNPs identified, 3,303 were selected based on repeatability (Bouvet et al., 2016), a minor allele frequency > 2.5 % and a rate of missing data per marker > 5 %. Haplotype phasing and missing-data inference were done with the localized haplotype clustering method developed in Beagle version 4.0 (Browning and Browning, 2007).

Data analysis

Three individual linear mixed model including all genetic effects were considered. In the individual model, the phenotype of each everyone is defined in terms of effects, and the genetic structure is incorporated into the variances and covariances of these effects (Hill, 2010). The model used is written as follow:

$$\mathbf{y} = \boldsymbol{\mu}\mathbf{1}_n + \mathbf{X}_{col} + \mathbf{Z}_{r(b)}^{r(b)} + \mathbf{Z}_{plot}^{plot} + \mathbf{Z}_a^a + \mathbf{Z}_d^d + \mathbf{Z}_i^i + \mathbf{e}$$

where **y** is the vector of observations, **X** and **Z** are the design matrices of fixed and random effects, respectively, **col** is the vector of columns effects **col** ~ N(0; σ^2_{col} **Id**), **r(b)** is the vector of rows in block effects **r(b)** ~ N(0; $\sigma^2_{r(b)}$ **Id**), **plot** is the vector of plot effects **plot** ~ N(0; σ^2_{plot} **Id**), **a** is the vector of additive genetic effects **a** ~ N(0; **G**σ^2_a), **d** is the vector of dominance effects **d** ~ N(0; **D**σ^2_d), **i** is the vector of epistatic effects **i** ~N(0; $\mathbf{G}_{aa}\sigma^2_{aa}$), **e** is the vector of residual effects **e** ~ N(0, σ^2_e**Id**), $\boldsymbol{\sigma}^2_a$ is the additive variance, $\boldsymbol{\sigma}^2_d$ is the dominance variance, $\mathbf{G}_{aa}$ is the epistatic variance, $\boldsymbol{\sigma}^2_e$ is the residual variance, **Id** is an identity matrix, $\boldsymbol{\sigma}^2_a$, $\boldsymbol{\sigma}^2_d$ and $\mathbf{G}_{aa}$ are the additive, dominance and epistatic genetic relationship matrices, respectively.

The additive genomic relationship matrix was constructed using SNP marker information, the matrix G is equal to this ratio:

$$: G = \frac{MM'}{\sum 2pq},$$

where *M* is a n×m matrix (n = number of individuals an, m = number of marker), *M'* is the inverse of *M*, p and q are the frequencies of allele 1 and 2 at a locus respectively.

The epistatic genomic relationship matrix was derived from additive genomic relationship matrix while performing the Hadamard product operation: $G_{aa} \approx G\#G$. The genomic dominance relationship matrix was calculated as follows

$D = \frac{HH'}{\sum 2pq(1-2pq)}$ $D = \frac{HH'}{\sum 2pq(1-2pq)}$, where H is

the n×m matrix of heterozygosity coefficients ($H = \frac{d}{u}$ $H = \frac{d}{u}$, d = n-dimensional vector of dominance effects and u = dominance value at single locus). The genomic dominance relationship matrix was calculated as follows,

$$D = \frac{HH'}{\sum 2pq(1-2pq)}$$

where H is the n×m matrix of heterozygosity coefficients ($H = \frac{d}{u}$, d = n-dimensional vector of dominance effects and u = dominance value at single locus). *H'* is the inverse of *H*.

The proportions of the following variances were calculated: proportions of additive ($\mathbf{A^2 = \sigma^2_A/\sigma^2_G}$), dominance ($\mathbf{D^2 = \sigma^2_D/\sigma^2_G}$) and epistasis ($\mathbf{I^2 = \sigma^2_I/\sigma^2_G}$) components in genetic variance.

Results

Variance components and ratios in growth traits

The variances components of the spatial effects (σ^2_{col} and $\sigma^2_{x(b)}$) were close to zero, except the column into blocks variance for circumference. The plot variance (σ^2_{plot}) increases with age. The residual component of the phenotypic variance was largest compared to the other sources of variation in the model (Table 2). Figure 1 shows the increase in genetic variance components observed for tree height and circumference. At 25 months we observe that the dominance genetic variance is larger than the additive and epistatic variances. The general trend is an increase in the ratio σ^2_D/σ^2_G with age, while a sawtooth evolution is observed in the ratio σ^2_A/σ^2_G and σ^2_I/σ^2_G for height. Concerning the circumference, the ratio σ^2_A/σ^2_G increases from 0.28 to 0.34 while the ratio σ^2_I/σ^2_G ratio decreases from 0.404 to 0.25, this according to the ages from 18 months to 25 months (Table 2), respectively. All ratios are close until 18 months; they are markedly different at 25 months. At this age, the σ^2_D/σ^2_G ratio (0.41-0.42) is higher than the σ^2_A/σ^2_G ratio (0.33-0.34) and epistasis (0.25-0.40), respectively.

Variance components and ratios in ecophysiological

The row and column into blocks variances are close to zero for all traits, except the column into blocks variance for SLA and LPA. For these two traits, the plot variance is higher than zero. As with the growth traits, residual variance explains most of the observed phenotypic variation.

Residual variance decreases with age (Table 2). All causal components of genetic variance decrease with age. A preponderance of additive variance is observed for SLA while the three components are nearly equivalent for N and LPA. Table 3 also shows that the ratio σ^2_A/σ^2_G is higher compared to the other two ratios (σ^2_D/σ^2_G and σ^2_I/σ^2_G) for SLA. We observed that σ^2_A/σ^2_G and σ^2_I/σ^2_G were equal for N and LPA. The general trend observed for all traits was an increase in the ratio σ^2_A/σ^2_G ratio then a decrease in σ^2_D/σ^2_G with age. However, the ratio σ^2_I/σ^2_G remained constant with age.

Discussion

Additive and non-additive components of genetic variance

For growth traits, the results showed a preponderance of dominance variance over additive and epistatic variances. Bouvet et al. (2009) explain this superiority by the effect of overdominance observed in hybrid population, especially when they are planted in marginal zones.

The epistatic effect of the genes was significant for some traits. This result brings us back to the heart of the problem of detecting epistasis. Paul et al. (1997) found similar results in two clonally replicated *Pinus teada* progeny tests, where they detected epistatic variance in only one of them at 1 and 3 years, while the study was conducted up to 5 years. On the other hand, Stonecypher and McCullough (1986) on *Pseudotsuga menziesii* found that dominance and epistatic variances are twice as large as additive variance in tree height. The preponderance of dominance variance was also reported by Tan et al. (2018) for growth in hybrid eucalyptus. The additive variance is in most cases larger than the dominance and epistasis variances for ecophysiological traits. Additive gene effects are therefore the main source of variability for these traits.

In general, pleiotropy is an important prerequisite for the existence of epistasis (de Visser et al., 2011). Functional redundancy can also cause epistasis in the sense that two or more genes perform a common molecular function (Lehner, 2011). Jasnos and Korona (2007) suggest that epistasis results from the buffering effects related to physiological homeostasis.

The consensus in quantitative genetics is that the epistatic action of genes is weak and transient in response to selection (Crow, 2008; Crow, 2010; Hill et al., 2008; Hansen, 2013). Interloci interactions are weak and difficult to estimate (Phillips, 2008) while Templeton (2000) suggests that epistasis is commonly determined when investigations are properly conducted. Considering these claims, what is the most appropriate method for estimating epistasis? The answer to this question is generally complex, but the research requirements are well known. First, an adequate experimental design is needed, and then one or more adequate statistical methods should be employed. In terms of experimental design, the clonally replicated progeny test used in this study allows for the partitioning of genetic variance into the three causal components (Isik et al., 2003; Costa e Silva et al., 2004). However, a clonally replicated progeny test is not enough, a good balance between the number of parents, progeny per family and clones within families is also needed. Pichot and du Cros (1989) find that the number of offspring per family can be reduced to 15 without affecting the parameter estimates.

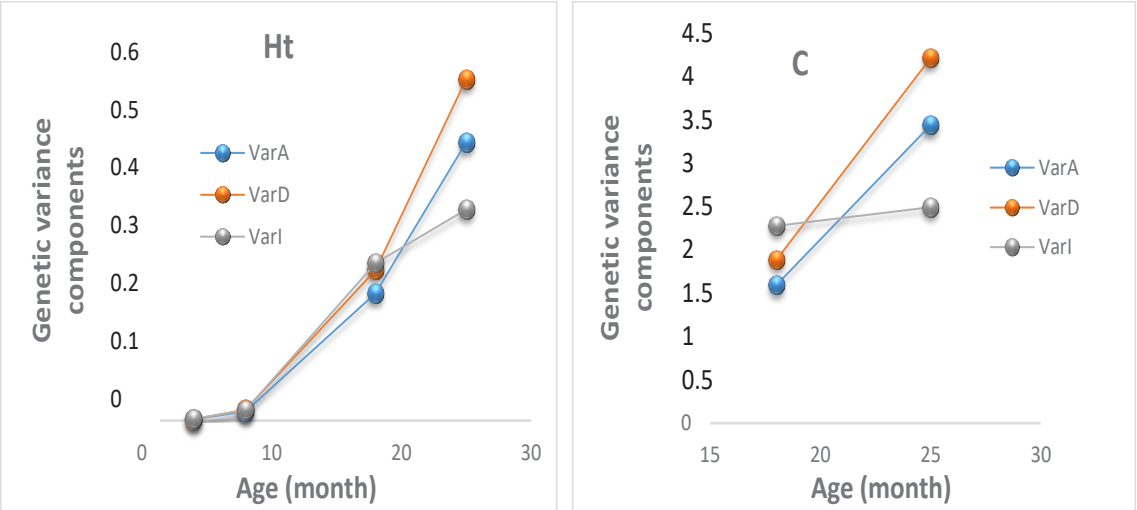
However, the genetic parameters are poorly estimated with the reduced number of parents and the low level of filling of the mating design.

Nevertheless, the number of offspring per family has a negligible or at least much smaller influence on the estimation of the genetic parameters. Our design has about ten parents, and for most families, the number of offspring is equal to 25 and the filling rate is about 50 %. The experimental conditions

Table 2
Phenotypic variance components (VC) and genetic variance ratios of growth and ecophysiological traits

VC	Ht4	Ht8	Ht18	Ht25	C18	C25	SLA8	SLA18	N8	N18	LPA8	LPA18
σ^2col	0.0	0.0	0.001	0.001	0.005	0.011	0.002	0.001	0.0	00	0.001	0.001
σ^2r(b)	0.004	0.044	0.257	0.583	2.762	3.997	0.694	0.378	0.023	0.016	0.49	0.334
σ^2plot	0.009	0.083	0.824	1.796	4.952	8.396	0.965	1.122	0.022	0.015	1.08	0.719
σ^2A	0.002	0.014	0.200	0.437	1.587	3.425	0.543	0.468	0.01	0.006	0.334	0.185
σ^2D	0.002	0.017	0.237	0.536	1.878	4.198	0.319	0.211	0.011	0.004	0.389	0.178
σ^2I	0.003	0.017	0.247	0.332	2.269	2.484	0.361	0.289	0.009	0.005	0.349	0.183
σ^2e	0.043	0.34	2.576	5.619	26.58	55.509	7.639	5.548	0.172	0.122	6.795	4.785
σ^2G	0.007	0.048	0.684	1.305	5.734	10.11	1.22	0.97	0.03	0.015	1.07	0.55
σ^2A/σ^2G	0.29	0.29	0.29	0.33	0.28	0.34	0.44	0.48	0.34	0.40	0.31	0.34
σ^2D/σ^2G	0.33	0.35	0.35	0.41	0.33	0.42	0.26	0.22	0.37	0.27	0.36	0.33
σ^2I/σ^2G	0.37	0.35	0.36	0.25	0.4	0.25	0.3	0.3	0.29	0.33	0.33	0.34

Ht: height, C: circumference, σ^2col: column variance, σ^2r(b): rows into block variance, σ^2plot: plot variance, σ^2A: additive variance, σ^2D: dominance variance, σ^2I: epistasis variance, σ^2e: residual variance, σ^2G: genetic variance, σ^2A/σ^2G (additive), σ^2D/σ^2G (dominance), and σ^2I/σ^2G (epistasis) proportion in genetic variance.



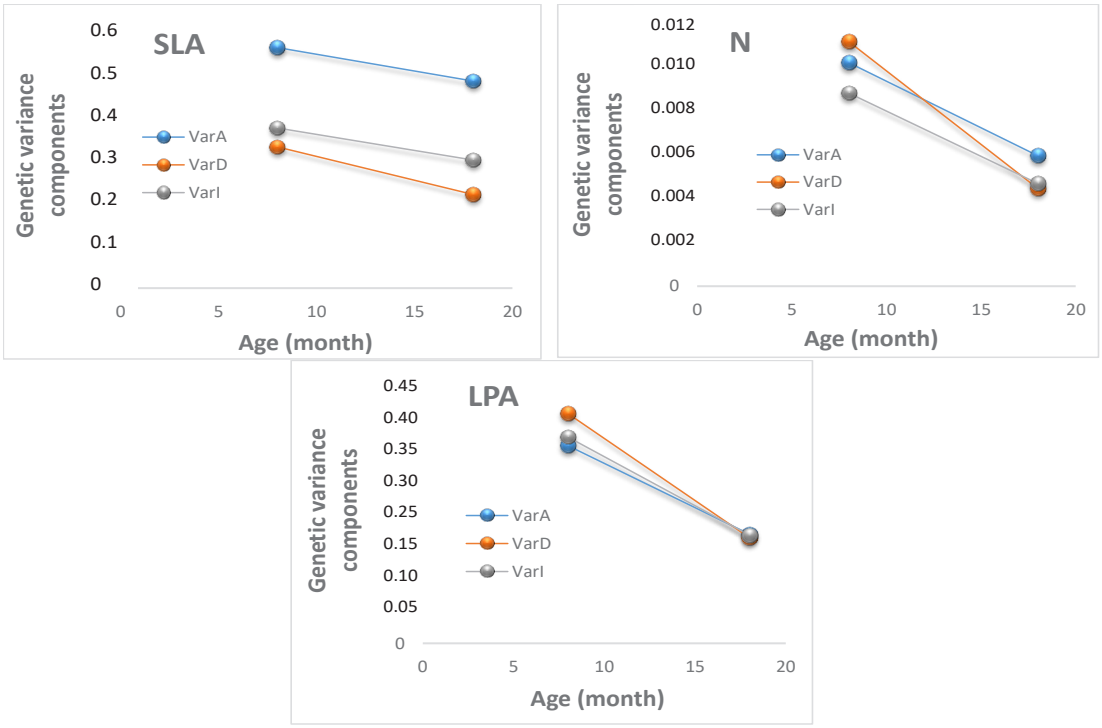
Ht: height, C: circumference, VarA: additive variance, VarD: dominance variance and VarI: epistatic variance.

Figure 1
Trend with age of genetic variance components for tree growth

are therefore theoretically promising for obtaining reliable estimates of genetic parameters. The populations studied do not always satisfy the hypotheses of an absence of cytoplasmic effects, of normal diploid behavior, absence of C effect (physiological or morphological characteristics unique to the ortet because of its specific environment), absence of linkage disequilibrium between different genes controlling the same trait and interacting with each other. Failure to satisfy these assumptions can lead to inconsistent estimates of epistasis. Fisher's infinitesimal model separates variances from orthogonal components (Falconer and Mackay, 1996; Lynch and Walsh, 1998), which is not true in most cases (Bernardo, 2020).

With molecular markers, the effects of a gene on a specific chromosome are well estimated (Hill, 2010; Grattapaglia et al., 2018). This provides a great improvement over other classical methods of quantitative genetics. This is because statistical epistasis is a population phenomenon that depends on the allele frequencies present in the population, whereas physiological epistasis is a genotypic phenomenon that is independent of allele frequencies. Cordell (2002) and Moore and Williams (2005) agree that the absence of epistasis in the statistical sense does not mean that there are no significant interactions between genes in the narrower biological sense.

In summary, it can be concluded that the estimation of epistatic variance is an ambivalent issue, due to its generally small contribution to the variability of traits of interest (Barker, 1979; Crow, 1987) despite its large importance in speciation and adaptation (Wright, 1980). The quantitative effect of



Ht: height, C: circumference, VarA: additive variance, VarD: dominance variance and VarI: epistatic variance.

Figure 2
Trend with age of genetic variance components for ecophysiological traits

epistasis is difficult to discern because of the complexities in estimating epistasis properly (Falconer and Mackay, 1996). The contribution of epistasis as a component of genetic variance therefore remains somewhat obscure. Nevertheless, statistical epistasis still does not account for the reality of physiological epistasis. Gene-gene interactions can be strong and yet generate little statistical epistasis and large epistatic variance components (Mäki-Tanila and Hill, 2014). Hill et al. (2008) conclude that gene-level interactions do not necessarily generate variance-significant interaction. This means that we may find ourselves in situations where the statistical approach to estimating epistasis does not clearly elucidate the underlying biological causes of the interaction between genes (Cordell, 2002). Thus, in terms of interpretating the phenomena, it is difficult to establish the exact correspondence between the biological and statistical models of epistasis (Witte, 1998; Cordell, 2002).

Nowadays, biological complexity is studied using genome-wide genotyping, combined with high computational capacity (Palucci et al., 2007; Paixão and Barton, 2016) and new approaches to data analysis (de los Campos et al., 2013).

The lack of epistasis may have several reasons (Okada et al., 2012; Mäki-Tanila and Hill, 2014; Paixão and Barton, 2016; Barton, 2017; Bernardo, 2020). For instance, markers are in imperfect linkage disequilibrium with causal variants, the curse of dimensionality, small effect sizes (Paixão and Barton, 2016; Barton, 2017), integration in higher dimensional gene-gene interactions (epistasis appears as additive variance), integration in gene×environment interactions or population substructure (heterogeneous integration). Wan et al. (2013) demonstrated that detection of all epistasis is possible with genomic studies but generally requires hundreds or thousands of individuals that are genotyped with several million SNPs. Mackay (2014) suggests that a better determination of epistasis would involve determining the effects of gene pairs, the effects of the molecular interactions generated, and assessing their effect on the phenotype. In modeling genomic studies, incorporating epistasis allows for improved estimation of genetic parameters (Verhoeven et al., 2010; Su et al., 2012).

Variance's ratios

The superiority of the ratio σ^2_D/σ^2_G over the ratios σ^2_A/σ^2_G and σ^2_I/σ^2_G reflects the preponderance of dominance variance in the total genetic variance for growth traits (Bouvet et al., 2009). Similarly, the superiority of the ratio σ^2_A/σ^2_G over the ratios σ^2_D/σ^2_G ratios and σ^2_I/σ^2_G indicates the preponderance of additive variance in the total genetic variance for ecophysiological traits. These results highlight the importance of the dominance proportion for growth traits and the additivity proportion for the ecophysiological traits. The proportion of epistasis is low, reflecting a small but non-zero contribution of the epistatic effects in the variation of the studied traits. The decrease of the ratio σ^2_I/σ^2_A found in growth traits shows that epistatic effects decrease with age compared to additive effects, which increase.

Conclusion

In the eucalyptus-breeding program in Congo, the contribution of epistatic effects in the variation of traits of interest has so far been considered to negligible or non-existent. The present study has showed that epistatic variance may be non-zero and contribute significantly to the genetic variability of growth traits (25-40 %) and ecophysiological traits (29-34 %). Additive gene effects represent only a part of total genetic effects for growth (28-34 %) and slightly more for ecophysiological traits (31-48 %). The contribution of dominance effects to the genetic variance is predominant for growth traits (33-42 %) and much less for ecophysiological traits (22-37 %). When epistasis contributes significantly to the genetic variability of trait, failure to distinguish the epistatic effect from the dominance effect leads to upwardly biased estimates of additive and dominance variances. Given the complexity of understanding the effects of the underlying genes, the unknown effects of some loci, and their interactions, quantitative analysis may not help us understand quantitative traits. The level of understanding of quantitative traits is still inadequate. In sum, epistasis for complex traits may exist but estimates may not be obtained either because the models used are inadequate, or because epistatic variance is too small relative to other components of the genetic variance to be estimated.

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