Response to Birchler: Heterosis is partly a sub-problem of quantitative genetics, but its solution may depend on understanding the mysterious genetics of quantity

Michael Freeling

Department of Plant and Microbial Biology, UC-Berkeley, Berkeley, CA 94720 USA
E-mail: freeling@berkeley.edu

Jim Birchler, in his thoughtful and cautionary commentary on heterosis, deduces from the literature that we can be reasonably sure that heterosis is a positive quantitative trait, and not the complementation of weakly deleterious alleles. Indeed, the reason this conclusion “might seem to be a small step forward” is not only that it is, but that the term “quantitative genetics” implies that heterosis (and its opposite phenomenon, inbreeding depression) is an emergent property of many, many genes, genes expected to follow the rules of polygenic inheritance. This implication is not necessarily true because the “genes” might well be rapidly changeable pairs of epialleles, these falling under no known theory.

There have been reports that smallRNA levels are not within the range of parental values in wide plant hybrids (Barber et al, 2012; Groszmann et al, 2011; Kenan-Eichler et al, 2011; Shen et al, 2012). Inbreeding depression may disappear in RMR1 knockouts along with many 24 nt smRNAs (Hale et al, 2009). On grand average, 24 nt RNAs are often depleted in the hybrid. Small RNAs of this sort are usually associated with directing methylation and generally suppressing expression—totally or partially-- so the soma of the hybrid would be expected, on grand average, to be temporarily over-expressing some transposons and perhaps some genes. A particularly important pair of papers by Hollister and Gaut (Hollister and Gaut, 2009; Hollister et al, 2011)(Brandon Gaut lab) compare gene expression between Arabidopsis thaliana and the comparatively transposon-rich Arabidopsis lyrata; they found an association between methylated transposons near genes and down-regulation of those genes, as if there were a whole genome trade-off between transposon silencing and steady state RNA levels. This “trade-off hypothesis” employs small RNAs to initiate and reinforce methylation. Do changes in smRNAs in the somas of wide hybrids really cause a cascade of gene regulation that ends with a one-time-only heterotic growth burst, or are they only associated with diverged parents and their hybrids? Birchler cautions us that confusing correlation for cause is not only ignorant and fallacious, but may be disrespectful of the long history of geneticists not solving heterosis. Respect is good, but discovering something new is better, and a bit of disrespect might sweeten the quest. Just because an idea has not been proved to explain heterosis does not mean that it is not true. It is or it isn’t. If the new idea or association helps you imagine, it’s beautiful to you.

My beautiful ideas about inbreeding depression and hybrid vigor are those that address heterosis as a transient, emergent property of two genomes simultaneously come together in the same nucleus by chance, genomes that evolved for some considerable period within their parental genomes, periods with different DNA/DNA-modification birth/death histories. I’m astounded by the diversity among maize inbreds for the quantitative levels of gene expression (in FPKM in normalized RNAseq experiments) acquired by genes after just a few or several thousand generations (Hansey et al, 2012). We don’t know how genes are quantitatively modulated explaining adequately balanced gene expression over the entire transcriptome of an organ or organ system, but this diversity must be acquired/lost very quickly, and transposon blooms and position effects are particularly fast. This evolutionary speed aspect is what makes Hollister and Gaut’s trade-off model of transposon silencing versus gene expression particularly useful (beautiful, but not proved). Research on genome dominance, where two parental genomes going into a wide-cross tetraploidy end expressed to different average mRNA levels (Flagel and Wendel, 2010; Schnable et al, 2011), also implicates fast whole-genome gene expression modulation. The clue: whole genomes can quickly alter overall levels of many individual gene expressions. My lab’s conceptual solution to the heterosis problem (extrapolated from Hollister and Gaut’s trade-off model to explain our own data) involves the genetics of mRNA quantity, is testable, and is presented as a cartoon to amuse our critics (Freeling et al, 2012). Our model hypothesizes that inbreeding expression = genome dominance.

It is always the time for academic rigor. But, now is the time to put the old ideas of quantitative inheri-
tance out of the way, try to do something about our ignorance of the genetics of mRNA quantity and follow the other enigmatic but beautiful new clues toward solving the heterosis / inbreeding depression problem.

Acknowledgements
Funded by NSF Plant Genome Research Program
Professor of Genetics

References