NEWS & VIEWS

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ON THE NATURE OF THINGS: ESSAYS

New Ideas and Directions in Botany

Systems genetics of plant adaptation to environmental stresses[1]

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> *"But that by turning the fertile clods with the share,*
> *and subduing the soil of the earth*
> *we summon them to birth,*
> *of their own accord the crops could not spring up into the liquid air;*
> *and even now sometimes, when won by great toil*
> *things grow leafy throughout the land, and are all*
> *in flower, either the sun in heaven burns them with too much heat,*
> *or sudden rains destroy them*
> *and chill frosts, and the blasts of the winds*
> *harry them with headstrong hurricane."*
> —from Titus Lucretius Carus, *On the Nature of Things*, *Book V*
> (trans. C. Bailey, 1910)

This excerpt from Lucretius' *On the Nature of Things* beautifully illustrates how plants are confronted with abiotic stresses in natural and agricultural field environments. To add insult to injury, plants can also be attacked by pests and pathogens and have to compete with neighboring plants. Plants are thus faced with multiple, complex, and fluctuating environmental conditions with different levels of predictability. The frequency and severity of environmental stress occurrences are exacerbated in many areas through climate change, making it all the more important that we understand plant stress responses.

Plant biologists have long tried to characterize the genetic architecture of plant adaptive responses to these complex stresses and have been hampered by the fact that these traits are quantitative and multigenic in nature. Especially after the establishment of *Arabidopsis thaliana* as the main model plant, a large proportion of these efforts have become more reductionist in scope. Many experiments are focused on the role of single genes in response to single stresses in carefully controlled environments. This reductionist approach has proved enormously fruitful, especially in characterizing gene function at the molecular and cellular levels. However, it has also contributed to a disconnect between research in field and laboratory environments (Plessis et al., 2015). This disconnect is illustrated by recent findings that the genetic architecture, gene expression profiles, and physiology of plant responses to combined stresses cannot be inferred from data on plant responses to single stresses alone (Suzuki et al., 2014; Davila Olivas et al., 2016; Gray et al., 2016). It is therefore difficult to place laboratory-obtained data in the context of organismal fitness in the field environment.

Alongside the rise of reductionism, a countervailing approach has developed over the last two decades in the form of systems biology. Benefitting from ever-increasing computational power, high-throughput genetic technologies, and the growing wealth of genomic data, systems biology uses genome-scale measurements and mathematical modeling to gain novel insights into the mechanisms through which phenotypes are shaped by different genotypes and environmental factors (Loewe, 2016). Originally developed in single-celled organisms, systems biology is increasingly used to infer plant metabolic and gene regulatory interaction networks and their behavior in response to genetic or environmental perturbations (e.g., Gulati et al., 2013; Lakshmanan et al., 2015; Wilkins et al., 2016). Although this more holistic perspective has now been brought to bear on plant stress responses in field environments (Lovell et al., 2016; Plessis et al., 2015; Richards et al., 2012; Wilkins et al., 2016), it is as yet unknown how natural genetic variation influences network architecture and behavior and the adaptive consequences of network properties (Joly-Lopez et al., 2016).

HARNESSING GENETIC DIVERSITY

In the excerpt from *On the Nature of Things*, Lucretius makes the poignant observation that without the careful nurturing by farmers, crops typically do not fare well in the face of environmental adversity. Since selection on crop varieties in managed conditions goes back to Lucretius' time and beyond (Ellis et al., 2013), it is likely that genetic variants that confer effective responses to environmental stress have been lost through genetic drift, while deleterious variants may have been selected inadvertently through linkage to loci of agronomic importance (Kono et al., 2016).

Over the centuries, agricultural practices have intensified and the area of land under cultivation has grown, which has been to the

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detriment of the genetic diversity of crop landraces, their wild relatives, and many other wild species (e.g., Dwivedi et al., 2016). However, efforts to reverse this trend and to preserve and characterize plant genetic diversity are underway (Matasci et al., 2014; The 3,000 Rice Genomes Project, 2014; Lasky et al., 2015). Wild plants and crop landraces have experienced more natural rather than artificial selection pressures and contain genetic variants that confer fitness benefits under adverse environmental conditions (e.g., Dwivedi et al., 2016). This genetic diversity can be harnessed in multiple ways to study the genomic basis of as well as the gene networks that underlie plant adaptation to stressful field environments.

One approach is through genome–environment association studies. Pioneered in the wild model plant species *A. thaliana* (e.g., Fournier-Level et al., 2011), these studies use georeferenced, genomically characterized accessions from a diversity of environments to associate single-nucleotide polymorphisms (SNPs) with soil and climatic conditions in plants' native environments. This method has since been applied to landraces of sorghum (Lasky et al., 2015) and to pine and spruce trees (Yeaman et al., 2016). Environment-associated SNPs linked to candidate loci that could underlie adaptive responses to abiotic stresses such as cold and drought, and predicted genotype-by-environment (G × E) interactions in field experiments. This approach has also been used to study plant adaptation to selection pressures from biotic stresses such as insect herbivores in *A. thaliana* (Brachi et al., 2015), but has yet to be applied to other species in this context.

Another approach uses real-time changes in environmental factors to study the genome-wide genetic changes in plant populations during adaptation to a novel set of environmental conditions. This approach identified many genetic changes in populations of *Brassica rapa* in response to long-term drought (Franks et al., 2016). Also this method has been used with plant adaptation to biotic stresses (e.g., Agrawal et al., 2012; Züst et al., 2012), although not yet on a genome-wide scale.

The fitness consequences of genetic variants could be explored in even more detail through the integration of field-collected "phenomic" data: the totality of molecular, physiological, morphological, and fitness phenotypes. First attempts at this approach have already been made with *A. thaliana*, in which laboratory-collected data on genome-wide gene expression and DNA methylation have been integrated with data from genome-environment association studies (Kawakatsu et al., 2016; Lasky et al., 2014). The results of such detailed studies in crops and their wild relatives might suggest breeding targets using genomic selection.

CHARACTERIZING THE PHENOME IN THE FIELD

Methods for automated monitoring of plant growth and other morphological and physiological traits are becoming ever more sophisticated and are increasingly deployed in the field (e.g., Gray et al., 2016; see Pauli et al. [2016] for an overview). Although this will go some way to deepen our understanding of the link between genotype and phenotype, the application of molecular "omic" techniques on field-grown plants will be necessary to further illuminate this link. High-throughput molecular techniques such as RNA sequencing and mass spectrometry have already been used on field-grown crop plants such as rice and on wild species (e.g., *A. thaliana*, *Nicotiana attenuata*, *Panicum hallii*, *Shorea beccariana*) for some years (Nagano et al., 2012; Richards et al., 2012; Kobayashi et al., 2013; Kallenbach et al., 2014; Plessis et al., 2015; Lovell et al., 2016). However, the use of these "omic" technologies has yet to be adopted throughout large-scale field experiments with many genotypes grown in more than one environment.

Detailed comparisons of the phenome across many genotypes and multiple environments will uncover more details of the regulatory architecture of a plant's response to complex combinations of environmental factors through mapping quantitative trait loci that regulate gene expression, protein activity, and metabolite levels, morphological and physiological traits and, ultimately, fitness.

Thus far, comparisons of time-series expression of transcriptomes across several environments have already revealed some important findings. In Asian rice, different environmental factors such as water availability and wind had additive effects on transcriptional patterns. Although patterns were largely constant across seasons in the tropics, effects seemed to be dampened in a temperate climate (Nagano et al., 2012; Plessis et al., 2015). The next step will be to expand such studies to more genotypes and to place data in the context of organismal fitness.

APPLYING AN EVOLUTIONARY SYSTEMS GENETICS APPROACH

Systems biological methods have recently started to be applied in plants, allowing us to infer metabolic and gene regulatory influence networks that reveal the transcriptional control of cellular metabolism. Models of plant metabolism rely on time-series of "omic" data and can be used to predict the balance of fluxes through a network of metabolic pathways in response to environmental signals (Gulati et al., 2013; Lakshmanan et al., 2015). Although metabolic flux balance models have been used to predict how single-celled organisms evolve in response to environmental perturbations (Loewe, 2016), this has yet to be done for field-grown plants.

A final example of an evolutionary systems genetics approach is the creation of environmental gene regulatory influence networks (EGRINs) in rice (Wilkins et al., 2016), which define a plant's response to environmental signals. Using EGRINs as a framework to compare the transcriptional responses and fitness of many genotypes in different field environments will allow the study of adaptive divergence and local adaptation of genotypes.

The rediscovery during the Renaissance of Lucretius' views on the universe as a system of atoms subsequently fuelled the Enlightenment and scientific progress. Likewise, we propose that, by applying a systems genetics view, we can enrich our understanding of plant adaptation to stresses in the field and speed up the utilization of basic research findings in meaningful applications.

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