

# The Next Generation of Training for Arabidopsis Researchers: Bioinformatics and Quantitative Biology<sup>1</sup>

It has been more than 50 years since *Arabidopsis* (*Arabidopsis thaliana*) was first introduced as a model organism to understand basic processes in plant biology. A well-organized scientific community has used this small reference plant species to make numerous fundamental plant biology discoveries (Provart et al., 2016). Due to an extremely well-annotated genome and advances in high-throughput sequencing, our understanding of this organism and other plant species has become even more intricate and complex. Computational resources, including CyVerse,<sup>3</sup> Araport,<sup>4</sup> The Arabidopsis Information Resource (TAIR),<sup>5</sup> and BAR,<sup>6</sup> have further facilitated novel findings with just the click of a mouse. As we move toward understanding biological systems, Arabidopsis researchers will need to use more quantitative and computational approaches to extract novel biological findings from these data. Here, we discuss guidelines, skill sets, and core competencies that should be considered when developing curricula or training undergraduate or graduate students, postdoctoral researchers, and faculty. A selected case study provides more specificity as to the concrete issues plant biologists face and how best to address such challenges.

## TRANSFORMING EDUCATION AND TRAINING—FROM UNDERGRADUATES TO FACULTY

An overhaul in training is necessary for plant biologists to make use of massive data sets and enabling technologies. This is not a novel idea in the life sciences. In fact, Bialek and Botstein (2004) articulated a concept for an integrated introductory quantitative science curriculum, primarily for undergraduates, to address this specific issue. Their publication has been highly cited and used as a foundational resource. They noted that biologists have too little education and experience in quantitative thinking and computation relative to what is needed for full participation in this new era of genomics research. Both then and now, many upper-level undergraduates in the life sciences versus quantitative sciences already speak noticeably different languages. Bialek and Botstein (2004) proposed that

instead of prerequisite courses in mathematics, physics, chemistry, and computation, the fundamental ideas of each of these disciplines should be introduced at a high level of sophistication. Their point is that these ideas should be presented in context and with relevant biological problems for a seamless educational experience. This would also avoid the delivery of these quantitative science courses as a service for the life sciences students. In a service course, students often exhibit a lack of enthusiasm due to the fact that they are required to take these courses. An additional issue is that many of the quantitative concepts presented are devoid of a biological perspective. Training at the graduate level must also necessarily integrate foundational concepts from biological science, chemistry, mathematics, statistics, computer science, bioinformatics, and data science. We stress that this is more than simply an understanding of bioinformatics, that is, more than just using computation to extract knowledge from biological data. Instead, education in plant biology should be truly interdisciplinary, perhaps as exemplified by (1) theoretical biology whereby theoretical perspectives (often mathematical) are used to give insights into biological processes, (2) quantitative biology whereby quantitative approaches and technologies are used to analyze and integrate biological systems or to construct and model engineered life systems, or (3) computational biology whereby biological data are used to develop algorithms or models to understand relationships among various biological systems.

## Implementation of Quantitative Training in the Life Sciences

Significant administrative, content, and logistical challenges often exist to impede the creation of new academic programs. Despite this, a growing number of institutions are developing undergraduate and graduate curricula in bioinformatics and computational biology for the life sciences, many of which incorporate the vision of Bialek and Botstein.<sup>7</sup> Practical strategies to overcome many of these challenges have been described for an overhaul in the graduate training program at Harvard Medical School (Gutlerner and Van Vactor, 2013). Our primary recommendation is to include in life sciences curricula the teaching of the skills and competencies described above, with the aim to develop students and future scientists that are adept at using transdisciplinary approaches to solve challenges in biology, and thus well adapted to addressing current and future needs in modern plant biology research.

<sup>1</sup> This work was supported by the U.S. National Science Foundation (award nos. NSF-RCN 1518280 and NSF-RCN 1062348, funding the workshop that led to generation of this Commentary).

<sup>2</sup> Address correspondence to sbrady@ucdavis.edu.  
[www.plantphysiol.org/cgi/doi/10.1104/pp.17.01490](http://www.plantphysiol.org/cgi/doi/10.1104/pp.17.01490)

<sup>3</sup><http://www.cyverse.org/>

<sup>4</sup><https://www.araport.org/>

<sup>5</sup><http://www.arabidopsis.org/>

<sup>6</sup><http://bar.utoronto.ca>

<sup>7</sup>[http://www.bioinformatics.org/wiki/education\\_in\\_the\\_united\\_states](http://www.bioinformatics.org/wiki/education_in_the_united_states)

### Minimal Skill Sets and Core Competencies

Over the last 15-plus years, a variety of meetings and task forces have been convened to determine the nature, extent, content, and available delivery tools for degree and training programs utilizing bioinformatics or computational biology in life sciences programs. Tan et al. (2009) proposed a generalized minimum set of competencies that the next generation of biologists will need to effectively cope with ever-increasing amounts of information and data sets, and the growth of importance in informatics in this genomics era. The following competencies have increased in relevance since they were first published and thus could guide curricula development (or revisions of existing curricula):

1. Basic knowledge in the specific domains of computer science, statistics, and mathematics that intersect with modern biology.
2. Expertise in communicating and representing biological knowledge and processes in mathematical, statistical, and computing terms and concepts.
3. The ability to use or develop efficient bioinformatics and biocomputational tools and techniques for the acquisition, interpretation, analysis, prediction, modeling, simulation, and visualization of experimental and other biological data.
4. Proficiency in the search, retrieval, processing, curation, organization, classification, management, and dissemination of biological data and information in databases for deriving biological insights and knowledge discovery.
5. Critical thinking and problem-solving skills in quantitative aspects of biology.

As a community with expertise in quantitative and computational plant biology, and using these competencies as a guideline, we further propose a suite of minimal skill sets (adapted from Rubinstein and Chor [2014] and Welch et al. [2014]) that will enable a plant biologist to generate and utilize multidimensional and scaled plant biology data to answer central biological questions (Table I).

We suggest two possibilities to implement across diverse institutions this integrated paradigm for training in this suite of minimal skill sets and core competencies. So as not to reinvent the wheel, it may be fairly straightforward for a plant biology program to participate in an extant integrative biology/quantitative sciences program within their respective institution, if those programs fulfill this suite of core recommended competencies/skill sets, simply by augmenting existing programs with elective plant courses. Alternatively, a program could implement course curricula (both undergraduate and graduate) that have been described in the literature and for which resources are available. These include the Course Source Bioinformatics Learning framework, which has been developed and reviewed

by members of the Genomics Education Partnership, the Network for Integrating Bioinformatics into Life Science Education, the Genome Consortium for Active Teaching of Next Gen Sequencing, and the Howard Hughes Medical Institute-sponsored Bioinformatics Workshop for Student/Scientist Partnerships (Rosenwald et al., 2016). Other curricula include a basic bioinformatics curriculum offered at the Free University of Berlin that emphasizes fundamentals in biology, mathematics, and computer science (Koch and Fuellen, 2008), and a first-year graduate course in quantitative biology that emphasizes the integrated curriculum proposed by Bialek and Botstein (2004). The latter example uses breakthrough papers in diverse areas of biology, and that emphasize quantitative reasoning, theory, and experimentation, to convey the importance of quantitative knowledge to understand basic biological processes (Wingreen and Botstein, 2006). Similar curricula have been implemented in the United Kingdom and are considered requisite training for graduate students in plant biology.<sup>8</sup> A course titled Computational Approaches for Life Scientists<sup>9</sup> has also been described that focuses on enriching the curriculum of life science students with abstract, algorithmic, and logical thinking and exposes them to computational culture (Rubinstein and Chor, 2014). Such curricula should be followed by a more focused track in plant biology, again emphasizing the quantitative premises underlying plant biology. Finally, a capstone problem-solving course that integrates teamwork could provide practical examples of how to integrate these diverse and interdisciplinary subject materials to address unsolved questions in plant biology.

### Bridge Programs, Boot Camps, and Supportive Environments for Quantitative-Based Plant Biology Education

Even without creating new programs, supportive environments for students interested in both plant and computational biology could help lower the intimidation barrier. For example, this could involve creating quantitative biology interest groups. Additional vehicles to encourage peer-to-peer learning could include hackathons (events that bring people together in teams for collaborative computer programming efforts to creatively solve a problem) that would provide training while encouraging interactions between plant biology and computational students.

Recently, organizations such as Software Carpentry<sup>10</sup> and Data Carpentry<sup>11</sup> (which are merging into one organization) and Amelieff<sup>12</sup> have been created to fill in some of the gaps in education for programming and data science skills. Since 2015, these organizations have

<sup>8</sup><https://sysmic.ac.uk>

<sup>9</sup><http://ca4ls.wikidot.com>

<sup>10</sup><https://software-carpentry.org/>

<sup>11</sup><http://www.datacarpentry.org/>

<sup>12</sup><http://amelieff.jp/english/>

**Table 1.** Minimal skill sets recommended for plant biology students

| Category                           | Specific Skills  |
|------------------------------------|--|
| Unix/Linux                         | Comfort/familiarity with using command line  |
| Scripting language                 | Perl or Python, for advanced students; C++; CUDA   |
| Database creation and query        | Mongo or MySQL, data mining  |
| Software carpentry                 | Best practices, proper commenting, version control   |
| Computation                        | Machine learning, algorithm design and analysis, distributed and high-performance computing  |
| Statistical methods                | Descriptive and inferential statistics, hypothesis testing, parameter estimation, power analysis, data transformations, meta-analysis, hierarchical clustering |
| Mathematical                       | Probability theory, differential equations, graph theory; linear algebra, information theory   |
| Statistical programming            | R/Bioconductor (particularly for analysis of next-generation sequencing data)  |
| Biological databases and resources | NCBI, EBI, Araport, TAIR, MaizeGDB, Gene Ontology, etc.  |
| Network analysis                   | Cytoscape plugins  |
| Data visualization                 | Could include ggplot, visualization of genome-scale data in genome browsers, volcano plots, heat maps, etc.  |

held workshops at institutions across the world. Other short courses also exist globally that focus on training experimental biologists in bioinformatics, statistical genetics, and mathematical modeling, including the Summer Institute in Statistical Genetics (United States),<sup>13</sup> the Summer School for Statistical Genetics (Japan),<sup>14</sup> the Santa Barbara Advanced School of Quantitative Biology (United States),<sup>15</sup> the BioComp training series (Austria), the de.NBI training courses (Germany),<sup>16</sup> the Saclay Plant Sciences summer schools (France),<sup>17</sup> the Integrative Database training course (Japan),<sup>18</sup> the Large Biological Data Analysis Course (Japan),<sup>18</sup> and the Cold Spring Harbor Laboratory courses<sup>19</sup> (United States) in Frontiers and Techniques in Plant Science and Programming for Biology. However, access to these courses is limited, and the course fees and travel necessary to participate may present significant barriers. To enhance the flexibility and to minimize financial output, curricula could be complemented with short courses or with certificates from online Massive Open Online Courses. As a community, developing a portal that provides reviews and ratings of these programs would be a valuable resource (Searls, 2012). It should be noted, however, that a recent report assessing boot camp programs (from 2 d to 2 weeks in length) typically designed to expose graduate students to data analysis techniques (among others) found a null difference when assessing research skill development, despite a statistically significant increase in perceived skill advancement (Feldon et al., 2017).

<sup>13</sup><https://www.biostat.washington.edu/suminst/sisg>

<sup>14</sup>[http://www.sg.med.osaka-u.ac.jp/school\\_2017.html](http://www.sg.med.osaka-u.ac.jp/school_2017.html)

<sup>15</sup><https://www.kitp.ucsb.edu/qbio>

<sup>16</sup>[https://tess.elixir-europe.org/content\\_providers/de-nbi](https://tess.elixir-europe.org/content_providers/de-nbi)

<sup>17</sup>[https://www6.inra.fr/saclay-plant-sciences\\_eng/Teaching-and-training/Summer-schools/Summer-School-2016](https://www6.inra.fr/saclay-plant-sciences_eng/Teaching-and-training/Summer-schools/Summer-School-2016)

<sup>18</sup><https://biosciencedbc.jp/en/>

<sup>19</sup><http://meetings.cshl.edu/coursehome.aspx>

## Funding

While many academic institutions recognize the importance of these training efforts, they need funding to come into existence. The U.S. National Science Foundation (NSF) Research Traineeship Program<sup>20</sup> Traineeship Track specifically fosters interdisciplinary training. The German Research Foundation provides funding for International Research Training Groups dedicated to a focused study abroad research program and a structured training strategy. In France, local funding agencies named Labex (for Laboratoire d'Excellence) fund interdisciplinary interactions between local partners, an example being Numev,<sup>21</sup> that promote interactions between computer and mathematical scientists and biologists with strong support for plant scientists. The Centre National de la Recherche Scientifique regularly promotes biology and math interactions through specific grant calls led by its Office for Interdisciplinary Research. In many of these cases, however, proposals are granted only for specific areas deemed to be a high priority to each funding organization, which may lower the success of proposals that do not fit easily into the chosen scope.

## Additional Recommendations for Postdoctoral Scholars and Faculty

At the moment, there are no standardized modes of quantitative or interdisciplinary training for postdoctoral fellows in plant biology. Thus, postdoctoral scholars often need to identify their own opportunities for additional training, if they have not received such training during their undergraduate or graduate training. Many competitive postdoctoral scholar fellowships offer funds for additional training, including the NSF's Plant Genome Research Program Postdoctoral Research Fellowships in Biology,<sup>22</sup> the U.S. Department of Agriculture's AFRI

<sup>20</sup>[https://www.nsf.gov/funding/pgm\\_summ.jsp?pims\\_id=505015](https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505015)

<sup>21</sup><http://www.lirmm.fr/numev/>

<sup>22</sup>[https://www.nsf.gov/funding/pgm\\_summ.jsp?pims\\_id=503622](https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=503622)

Food, Agriculture, Natural Resources, and Human Sciences Education and Literacy Initiative Fellowship program,<sup>23</sup> and the National Institutes of Health K99 grant program.<sup>24</sup> The Human Frontiers Science Program offers postdoctoral fellowships for citizens of many countries with a special category for cross-disciplinary fellowships to support training those in quantitative sciences in experimental biology.<sup>25</sup> Moreover, the European Union's Marie Skłodowska-Curie Actions Individual Fellowships offer funds for additional training and for short 3- to 6-month visits. The Plant Biology section of the General Program and the Young Scientists Fund of the National Natural Science Foundation of China encourages interdisciplinary research that combine methods from plant biology and other areas, such as mathematics, physics, and computer sciences.<sup>26</sup>

However, these fellowships are quite competitive and can be restricted to postdoctoral scholars trained in certain disciplines. What if a postdoctoral scholar is unsuccessful at receiving such funds but still wishes to undergo interdisciplinary training? In Germany, there is a growing number of structured postdoctoral fellowship programs funded by individual research institutions that offer institutional support in identifying interdisciplinary training opportunities. The Postdoctoral Fellowship Program by the Helmholtz Zentrum Munich ensures that fellows are integrated into international and interdisciplinary research groups, while the University Foundation Fellowship Program by the Technical University of Munich assists with the identification of interdisciplinary and collaborative research programs. Additional institutional solutions could provide the resources for postdoctoral participation (and instruction) in short courses that provide training in a particular competency or could integrate postdoctoral scholars in existing courses provided for graduate students. At the mid- and senior-postdoctoral scholar levels, perhaps the best way is to provide opportunities for senior biologically oriented postdoctoral scholars to engage in dedicated training via short-term residencies (3 to 6 months) in a laboratory that specializes in quantitative, computational, or modeling analyses. Such longer-term dedicated learning programs would have the advantage of carrying out a distributed practice of learning, which has proven more beneficial in long-term retention of concepts, relative to the shorter mass boot-camp-type strategy. (Feldon et al., 2017).

Short-term or long-term sabbaticals in a computational lab are also a good solution for faculty members to acquire computational skills. The NSF's Mid-Career Investigator Awards in Integrative Organismal Biology<sup>27</sup> could be a source of funding for associated travel costs. The German

Academic Exchange Service and the French AGreskills federal programs, as well as the local Labex programs (mentioned previously), financially support sabbaticals for this purpose. Alternatively, it may be better for faculty to focus on how they can better assess and support research activities in their own labs and be able to better understand how to review papers or grants that contain research of an interdisciplinary nature. Short workshops could be developed to provide training to faculty on quantitative and computational methods and how to conduct high-quality computational/quantitative research.

### Computational Training for Industry

The key attributes for researchers in industry with respect to projects involving computational approaches are strong interpersonal skills in teamwork, collaboration, communication, and project management. Industry requires individuals who are expert in one specific area but have the breadth of understanding that allows them to appreciate and respect the input of other disciplines to the overall project. This includes familiarity with biological databases and quantitative biology approaches. In addition, employees in industry benefit from training programs that expose workers in academia and industry to each other's ways of working. The European funding model encourages partnerships between researchers and industry (e.g. the bread wheat initiative led by INRA<sup>28</sup>). Another model is to embed master's or doctoral students in industry placements for 3 to 6 months. Two United Kingdom-specific examples of this are the compulsory program of the U.K. Biotechnology and Biological Sciences Research Council, called PIPS (for Professional Internships for PhD Students<sup>29</sup>), and the Flexible Interchange Programme<sup>30</sup> that operates at the postdoctoral scholar and faculty level to promote training and exchange between industry and academic partners. An additional twist on this theme is provided by the Chilean scientific funding agency CONICYT that offers a postgraduate thesis in industry.<sup>31</sup> At the institutional level, research institutions dedicated to applied sciences and industrial cooperation, like the Fraunhofer Institutes in Germany, traditionally work in close cooperation with industry, including master's and doctoral students.

### Arabidopsis Training for Plant-Curious Data Scientists

A rapidly growing world population and a changing climate demand development of improved crop varieties that yield more with fewer inputs, as well as advances in renewable fuels and biomaterials. Moving

<sup>23</sup><https://nifa.usda.gov/program/afri-education-and-literacy-initiative>

<sup>24</sup><https://www.nhlbi.nih.gov/research/training/programs/postdoc/pathway-parent-k99-r00>

<sup>25</sup><http://www.hfsp.org/funding/postdoctoral-fellowships>

<sup>26</sup><http://www.nsf.gov.cn/publish/porta12/tab189/info51759.htm>

<sup>27</sup><https://www.nsf.gov/pubs/2017/nsf17508/nsf17508.htm>

<sup>28</sup><http://www.wheatinitiative.org>

<sup>29</sup><http://www.bbsrc.ac.uk/funding/filter/professional-internships/>

<sup>30</sup><http://www.bbsrc.ac.uk/funding/filter/flexible-interchange-programme/>

<sup>31</sup><http://www.conicyt.cl/wp-content/uploads/2012/07/Brochure-Institucional-2011-Inglés.pdf>

forward, a community-wide effort to promote the value of plant science research to data scientists is needed. Arabidopsis training for plant-curious data scientists should emphasize (1) how knowledge gained from Arabidopsis research is relevant to crop improvement, and (2) how to utilize Arabidopsis as a tool to rapidly test gene function and optimize emerging technologies prior to delivery to a crop system. The advent of gene-editing technologies, such as CRISPR/Cas9-based approaches to specifically target loci for site-directed mutagenesis or sequence replacement, introduces a new paradigm. While these technologies create opportunities for targeted mutagenesis directly in crop species, significant bottlenecks in the transformation process limit the extent to which these experiments can be performed in crops. Therefore, Arabidopsis can be used to more quickly and efficiently test functional hypotheses and prioritize experiments for the more labor-, cost-, and time-intensive studies in crops.

The outcome of an active community of Arabidopsis researchers is the detailed curation of genes and pathways in the Arabidopsis genome, perfect for mining by data scientists. These curated data have been leveraged for annotating orthologous genetic components in other species and thus are invaluable resources. It is likely that many fundamental biological processes are conserved across plant species (McGary et al., 2010; Oellrich et al., 2015). As an example, agricultural biotechnology industries make use of this information through large-scale text-mining algorithms combined with comparative genomics approaches to project annotations and associations onto crop models (Holtan et al., 2011; Preuss et al., 2012). The depth and breadth of these resources in Arabidopsis also position this organism at the forefront of predictive modeling in plants through systems biology approaches. Moving forward, there is an immediate need to make better use of existing data from Arabidopsis studies by developing new data integration paradigms aimed at predictive modeling and subsequent discovery. Using Arabidopsis as a framework for how to integrate diverse data sets should facilitate similar analyses in species with less-developed resources.

On the other hand, Arabidopsis may not be the most appropriate model to understand traits related to domestication, physiology such as  $C_4$  photosynthesis, or other aspects of plant biology such as secondary metabolism. To address such questions, alternative model systems are being established; these include *Setaria viridis* and *Brachypodium distachyon* as model grass species (Brutnell, 2015; Brutnell et al., 2015) and *Camelina sativa* for metabolic engineering of coproducts (Bansal and Durrett, 2016; Zhu et al., 2016). We recommend that the communities developing these new systems leverage best practices from the Arabidopsis community, particularly with reference to genome annotation and data curation for these species. Fostering such interactions between scientists could occur through cross-species conferences in plant science; for example, a Keystone Meeting focused on Translational

Plant Biology. Inclusion of data scientists in these forums will be critical to ensure maximal usefulness of these emerging model systems.

## COLLABORATIONS

Taking advantage of large-scale data sets and technologies to reveal novel biological conclusions will require groups of people with diverse expertise, skill sets, and at different career levels to work well together. Thus, to train the next generation of Arabidopsis biologists in quantitative and computational biology, we also need to train scientists on how to initiate, define, manage, and maintain effective collaborations.

### Identifying Collaborators

It is often difficult for biologists to develop their research questions to include tangible opportunities for quantitative experts or to effectively articulate their specific needs in a vocabulary that is accessible to experts in those fields. Face-to-face communication is particularly important, and thus we attribute the highest priority to the identification of regional collaborators. Inclusive, regular, cross-faculty and cross-institute interactions at all career levels, with the clear objective to also empower early career researchers to take active roles, are required to initiate local collaborations. To implement role models for such collaborative efforts, hiring or recruiting researchers who already work across biological science and statistical, computational, or mathematical departments can be beneficial due to their ability to expose biological problems to theoreticians who might not typically see such data as valuable to analyze. However, the infrastructure for promotion and merit within most academic institutions has generally not advanced sufficiently to effectively hire and maintain theoreticians at the tenure-track level in biology departments.

Collaborations between disciplinary experts can be accelerated through intensive trainings and activities that promote networking and knowledge sharing. In-depth, week-long immersion sessions have proven effective at providing both the biologist and the quantitative expert with the proper, shared vocabulary, resulting in productive collaborations. For example, the Mathematics in the Plant Sciences Study Group in the United Kingdom<sup>32</sup> has been successful in generating both new collaborations and funded grant applications in short time frames.

Cosupervision of graduate students by a biologist and theoretician is another effective strategy to develop a collaboration. Initiating cross-disciplinary cohorts of graduate students is another approach. Complementing collaborative interactions or, in the absence of local cross-disciplinary opportunities, making available high-quality online video material outlining advances

<sup>32</sup><https://www.cpi.ac.uk/outreach/mpssg/>

in current plant biology, for example, in a jargon-free format, would be useful for quantitative experts. In the long term, graduate students and postdoctoral scholars who have been trained in an interdisciplinary environment will likely generate the best collaborations. By working together from an early career stage, a deep appreciation of diverse abilities will be engendered and the ability to communicate freely will enable new research avenues to be pursued.

### Defining Collaborations

An effective multidisciplinary collaboration must go beyond the mere provision of a service by a collaborator. As such, before initiating a project, all partners should jointly articulate and agree on the scientifically interesting research questions and discuss experimental design and data analysis. A management plan should involve contributors at all career levels and consider the benefit for each contributing individual. It is important for collaborators to recognize differences in cost bases for biological versus theoretical research (e.g. experimental laboratory-associated costs are quite high, whereas in the theoretical sciences, experts command higher salaries than experimental biologists). A realistic assessment of project timelines and deliverables is critical. Furthermore, a plan to include periodic assessment of progress with respect to the defined timelines and deliverables should be implemented to allow for adaptation, with the understanding that things do not always proceed expectedly. Contingency plans are also ideal to establish at the start, as are plans for publications, since biological and theoretical fields have fundamentally differing authorship rules and norms, publication strategies, and career recognition criteria. It is important to discuss and specify the time frames that are likely for the publication of biological data and how the development of novel theory or analysis tools could be published prior to their use in biological data analysis. To ensure recognition, CRediT<sup>33</sup> (through ORCID) comprises structured vocabulary for assigning author credit. It is also critical to put in place an explicit plan for the possibility of managing disagreements that may arise as well as the conditions under which a collaborator might exit a project.

In practice, project meetings between collaborators should be held at more frequent intervals than may normally occur in within-discipline collaborations. This is especially true at the beginning of the project where the development of mutual understanding and the building of close working relationships among the researchers are essential. If the collaboration is between local groups, regular, e.g. monthly, joint meetings would be ideal. If the collaboration involves partners at a considerable geographic distance, then monthly Web-based meetings are necessary, and the collaboration would benefit from face-to-face meetings with all team

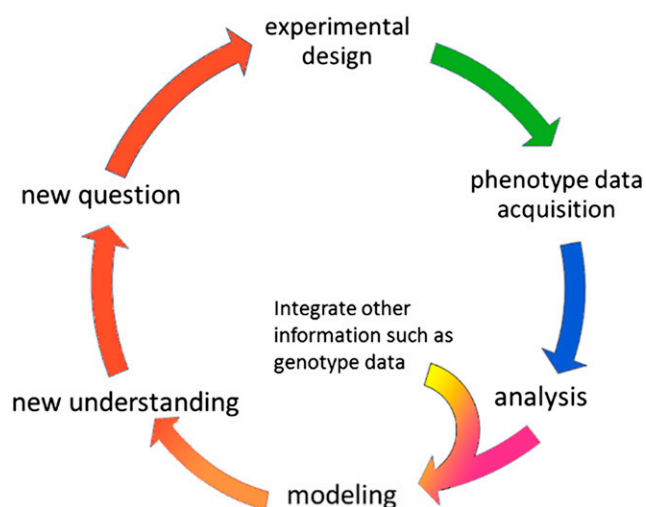
members, ideally once every 6 months at a minimum. Budgeting for necessary travel should be considered at the time of project design. Furthermore, the physical movement of postdoctoral scholars or graduate students between groups for reciprocal training or joint work contributes highly to the effective integration of projects. Appreciation of differences in language or culture should be conveyed, as should reciprocal trust and respect, interest in the mutual fields, and the willingness to learn from the expertise of a partner.

### CASE STUDY: TRAINING ARABIDOPSIS BIOLOGISTS FOR HIGH-THROUGHPUT PHENOTYPING

As a concrete example for how scientists can be trained and educated in an interdisciplinary, collaborative fashion using experimental biology and quantitative approaches, we consider phenomics as a case study. Phenomics is an emerging field at the intersection of plant biology, engineering, computer science, and mathematics that has led to a deeper understanding of mechanisms for acclimation to environmental variation (Miller et al., 2007; Slovak et al., 2014; Campbell et al., 2015; Fahlgren et al., 2015; Rellán-Álvarez et al., 2015). These studies evolved from the need to characterize phenotypic traits across large numbers of genotypes (Chen et al., 2014; Cruz et al., 2016; Ge et al., 2016).

A project using phenomics can be considered as a pipeline with three identifiable stages: data acquisition, data analysis, and data modeling (Fig. 1), all to answer a clear biological question. Generally, this question is: What genes or genetic regulation underlie a trait of interest? Generally, a consortium of scientists is needed to carry out a phenomic-scale project. Consortium members should have diverse skills, be able to interact collaboratively, and each researcher's role should be well defined. Prior to data acquisition, consortium members should collectively discuss and agree upon experimental design, biological replicates, statistical power, the type of data to be acquired, and appropriate models used for data analysis. The data acquisition stage includes the use of sensors such as cameras, fluorescent measurement devices, or any tool that can make a measurement when connected to a computer to measure a phenotype associated with a trait. This stage often leverages expertise in the engineering disciplines and may involve robotics. Input from biologists is needed to ensure that a physiologically relevant aspect of plant growth or response to the environment is being captured. The output of this stage is the generation of raw data files. The analysis stage includes the computer code needed to extract features from the raw data files—image analysis is a good example—to produce measurements. This stage also includes workflow software, which brings the raw data from the sensors to the analysis algorithms. The analysis phase passes processed data, or results, to the next stage.

<sup>33</sup><http://casrai.org/credit>



**Figure 1.** A computation-based phenotyping project requires a software continuum that takes raw data generated by acquisition activities, analyzes the raw data, integrates them with different data such as genotype or environmental information, and then produces new understanding through modeling activities such as statistical associations. The new understanding leads to new questions.

Again, input from an experimental biologist is needed to ensure that these data are within the expected range of values. The modeling stage involves synthesizing results for the purpose of generating new biological conclusions. A typical example would be integrating

phenotype results with genotype information to complete a statistical genetic analysis. However, the modeling stage can also be conceptually general enough to include any sort of analysis that converts phenotype measurements into a new biological understanding.

Phenomic projects using *Arabidopsis* are ideal for training students in collaborative, innovative, and interdisciplinary approaches. Outreach and training modules on plant phenotyping naturally bridge multiple disciplines, including plant biology, computer science, mathematics, and engineering, and provide alternative ways of attracting students to the plant sciences. Single-board computers like Raspberry Pi, Hummingboard, or Cubieboard are low-cost microcomputers originally built for educators, hobbyists, and researchers, and are currently being incorporated into plant phenotyping research and teaching modules. Online resources provide tutorials to set up imaging systems (Table II); however, next-generation resources should be designed in collaboration with educational experts.

**EXECUTIVE SUMMARY**

Historically, the *Arabidopsis* research community has been able to effectively combine efforts internationally and to provide a collective voice regarding our needs to facilitate fundamental biological discoveries. We propose that such synergism be employed, using the specific recommendations in this commentary as a guide, in training this next generation of plant biologists to be able to understand and implement, in

**Table II.** Online resources providing tutorials to set up imaging systems

| Resource                            | Description   | Website   | Reference  |
|-------------------------------------|---|---|--|
| scikit-image examples and tutorials | Comprehensive list of imaging tasks with example code. scikit-image is an imaging library for python.   | <a href="http://scikit-image.org/docs/dev/auto_examples/">http://scikit-image.org/docs/dev/auto_examples/</a>   | van der Walt et al. (2014)                         |
| OpenCV tutorials                    | A collection of tutorials for OpenCV in C++. OpenCV is a standard computer vision library available in C++, python, and other languages.  | <a href="http://docs.opencv.org/2.4/doc/tutorials/tutorials.html">http://docs.opencv.org/2.4/doc/tutorials/tutorials.html</a>   | Bradski and Kaehler (2008)                         |
| Mahotas documentation               | Mahotas is a python library written in C++. The documentation provides many examples for standard imaging tasks.  | <a href="http://mahotas.readthedocs.io/en/latest/">http://mahotas.readthedocs.io/en/latest/</a>   | Coelho (2013)                                      |
| DIRT tutorials and videos           | DIRT (for Digital Imaging of Root Traits) is an online root phenotyping platform that allows users to submit root images for phenotyping. The website contains tutorials and videos for nontechnical users as well as documentation for developers. It's source code is freely available. | Online interface:<br><a href="http://dirt.iplantcollaborative.org/get-started">http://dirt.iplantcollaborative.org/get-started</a><br>Source code:<br><a href="https://github.com/Computational-Plant-Science/DIRT">https://github.com/Computational-Plant-Science/DIRT</a> | Bucksch et al. (2014)<br>Das et al. (2015)         |
| Phenotiki                           | Hardware (Raspberry Pi) and software for analyzing growth chamber-collected phenotyping data.   | <a href="http://phenotiki.com/getting_started.html">http://phenotiki.com/getting_started.html</a>   | Minervini et al. (2014)<br>Giuffrida et al. (2015) |

a rigorous manner, quantitative approaches in their research.

Specifically, for undergraduate and graduate training, we recommend an overhaul in curriculum design for plant biology majors or plant biology graduate students that involves a seamless integration of concepts in math, physics, statistics, and computation within courses that illustrate biological processes. This could be done according to the recommendations of Bialek and Botstein (2004). We have adapted a set of core competencies and minimal skill sets, adapted from those of Tan et al. (2009), Rubinstein and Chor (2014), and Welch et al. (2014), and we strongly recommend that, when designing or revising curricula for this next generation of plant biologists, that these core competencies and skills are kept in mind. We have highlighted above a set of curricula based on these core competencies that are publicly available either within the United States or internationally; these may serve as a further resource. While there is no existing training standard for post-doctoral scholars in plant biology, we have identified a suite of fellowships for which postdocs may apply and that facilitate independent interdisciplinary training. We also advocate for programs that offer institutional support in identifying interdisciplinary and quantitative training for postdocs who wish to pursue such opportunities. Additional opportunities are outlined for faculty members who wish to undergo this training. Collaborations are often the cornerstone of successful quantitative projects, and we provide concrete recommendations to promote effective and meaningful collaborations that we hope will guide institutional and cross-institutional interdisciplinary efforts. We collectively advocate for the continued use of *Arabidopsis* as an ideal organism for use in quantitative training efforts. For cases in which other organisms are more appropriate, we recommend leveraging best practices from the *Arabidopsis* community (e.g. efforts in genome annotation and data curation). Our case study in high-throughput *Arabidopsis* phenotyping provides an example of effective interdisciplinary and quantitative training and of the merging of quantitative and biological science integral for plant breeding in the future.

**Joanna Friesner**  
**Agricultural Sustainability Institute and Department**  
**of Neurobiology, Physiology, and Behavior,**  
**University of California, Davis, California 95616**  
**ORCID ID: 0000-0002-6799-7808**

**Sarah M. Assmann**  
**Biology Department, Penn State University,**  
**University Park, Pennsylvania 16802**  
**ORCID ID: 0000-0003-4541-1594**

**Ruth Bastow**  
**GARNet, School of Biosciences, Cardiff University,**  
**Cardiff CF10 3AT, United Kingdom**

**Julia Bailey-Serres**  
**Center for Plant Cell Biology, Department of Botany**  
**and Plant Sciences, University of California, Riverside,**  
**California 92521**  
**ORCID ID: 0000-0002-8568-7125**

**Jim Beynon**  
**School of Life Sciences, University of Warwick,**  
**Coventry CV4 7AL, United Kingdom**  
**ORCID ID: 0000-0002-1855-3215**

**Volker Brendel**  
**Department of Biology and**  
**Department of Computer Science, Indiana**  
**University, Bloomington, Indiana 47405**  
**ORCID ID: 0000-0002-8055-7508**

**C. Robin Buell**  
**Department of Plant Biology, Michigan State**  
**University, East Lansing, Michigan 48824**  
**ORCID ID: 0000-0002-6727-4677**

**Alexander Bucksch**  
**Department of Plant Biology, Warnell School of**  
**Forestry and Natural Resources, and Institute of**  
**Bioinformatics, University of Georgia, Athens,**  
**Georgia 30602**  
**ORCID ID: 0000-0002-1071-5355**

**Wolfgang Busch**  
**Gregor Mendel Institute, Austrian Academy of**  
**Sciences, Vienna Biocenter, 1030 Vienna, Austria;**  
**Plant Molecular and Cellular Biology Laboratory,**  
**Salk Institute for Biological Studies, La Jolla,**  
**California 92037**  
**ORCID ID: 0000-0003-2042-7290**

**Taku Demura**  
**Graduate School of Biological Sciences,**  
**Nara Institute of Science and Technology,**  
**Ikoma, Nara 630-0192, Japan; RIKEN Center**  
**for Sustainable Resource Science, Yokohama,**  
**Kanagawa 230-0045, Japan**  
**ORCID ID: 0000-0002-2499-4738**

**Jose R. Dinneny**  
**Department of Plant Biology, Carnegie Institution**  
**for Science, Stanford, California 94305**  
**ORCID ID: 0000-0002-3998-724X**

**Colleen J. Doherty**  
**Department of Molecular and Structural**  
**Biochemistry, North Carolina State University,**  
**Raleigh, North Carolina 27695**  
**ORCID ID: 0000-0003-1126-5592**



Andrea L. Eveland  
Donald Danforth Plant Science Center, St. Louis,  
Missouri 63132

Pascal Falter-Braun  
Institute of Network Biology, Department of  
Environmental Science, Helmholtz Zentrum  
München, 85764 Neuherberg, Germany  
ORCID ID: 0000-0003-2012-6746

Malia A. Gehan  
Donald Danforth Plant Science Center, St. Louis,  
Missouri 63132  
ORCID ID: 0000-0002-3238-2627

Michael Gonzales  
Center for Applied Genetic Technologies,  
Athens, Georgia 30602

Erich Grotewold  
Department of Biochemistry and Molecular Biology,  
Michigan State University, East Lansing,  
Michigan 48824  
ORCID ID: 0000-0002-4720-7290

Rodrigo Gutierrez  
FONDAP Center for Genome Regulation,  
Millennium Nucleus Center for Plant  
Systems and Synthetic Biology, Departamento de  
Genética Molecular y Microbiología,  
Facultad de Ciencias Biológicas, Pontificia  
Universidad Católica de Chile, Santiago,  
Chile 8331150  
ORCID ID: 0000-0002-5961-5005

Ute Kramer  
Molecular Genetics and Physiology of Plants,  
Faculty of Biology and Biotechnology, Ruhr  
University Bochum, 44801 Bochum, Germany  
ORCID ID: 0000-0001-7870-4508

Gabriel Krouk  
Laboratoire de Biochimie et Physiologie Moléculaire  
des Plantes, CNRS, INRA, Montpellier SupAgro,  
Université Montpellier, Institut de Biologie  
Intégrative des Plantes "Claude Grignon," Place  
Viala, 34060 Montpellier cedex, France  
ORCID ID: 0000-0003-3693-6735

Shisong Ma  
School of Life Sciences, University of Science  
and Technology of China, Hefei, Anhui  
230027, China  
ORCID ID: 0000-0001-5563-448X

R.J. Cody Markelz  
Department of Plant Biology, University of  
California, Davis, California 95616  
ORCID ID: 0000-0003-4431-4258

Molly Megraw  
Department of Botany and Plant Pathology,  
Department of Computer Science, and  
Center for Genome Research and Biocomputing,  
Oregon State University, Corvallis,  
Oregon 97331  
ORCID ID: 0000-0001-6793-6151

Blake C. Meyers  
Donald Danforth Plant Science Center,  
St. Louis, Missouri 63132;  
Division of Plant Sciences, University of Missouri,  
Columbia, Missouri 65211  
ORCID ID: 0000-0003-3436-6097

James A.H. Murray  
School of Biosciences, Cardiff University, Cardiff  
CF10 3AX, Wales, United Kingdom  
ORCID ID: 0000-0002-2282-3839

Nicholas J. Provart  
Department of Cell and Systems Biology/Centre for  
the Analysis of Genome Evolution and Function,  
University of Toronto, Toronto,  
Ontario M5S 3B2, Canada  
ORCID ID: 0000-0001-5551-7232

Sue Rhee  
Department of Plant Biology, Carnegie Institution  
for Science, Stanford, California 94305  
ORCID ID: 0000-0002-7572-4762

Roger Smith  
Syngenta Crop Protection, Research Triangle Park,  
North Carolina 27709

Edgar P. Spalding  
Department of Botany, University of Wisconsin,  
Madison, Wisconsin 53706  
ORCID ID: 0000-0002-6890-4765

Crispin Taylor  
American Society of Plant Biologists, Rockville,  
Maryland 20855  
ORCID ID: 0000-0002-4669-3215

Tracy K. Teal  
Data Carpentry, Davis, California 95616  
ORCID ID: 0000-0002-9180-9598

**Keiko U. Torii**  
**Howard Hughes Medical Institute and Department**  
**of Biology, University of Washington, Seattle,**  
**Washington 98195**  
**ORCID ID: 0000-0002-6168-427X**

**Chris Town**  
**J. Craig Venter Institute, Rockville,**  
**Maryland 20850**

**Matthew Vaughn**  
**Life Sciences Computing, Texas Advanced**  
**Computing Center, Austin, Texas 78758**  
**ORCID ID: 0000-0002-1384-4283**

**Richard Vierstra**  
**Department of Biology, Washington University in**  
**St. Louis, St. Louis, Missouri 63130**  
**ORCID ID: 0000-0003-0210-3516**

**Doreen Ware**  
**Cold Spring Harbor Laboratory, Cold Spring**  
**Harbor, New York 11724;**  
**U.S. Department of Agriculture Agricultural**  
**Research Service, Ithaca, New York 14853**

**Olivia Wilkins**  
**Department of Plant Science, McGill University,**  
**Montreal, Quebec H9X 3V9, Canada**  
**ORCID ID: 0000-0001-9762-7069**

**Cranos Williams**  
**Department of Electrical and Computer**  
**Engineering, North Carolina State University,**  
**Raleigh, North Carolina 27695**

**Siobhan M. Brady<sup>2</sup>**  
**Department of Plant Biology, Genome Center,**  
**University of California, Davis,**  
**California 95616**  
**ORCID ID: 0000-0001-9424-8055**

Received October 23, 2017; accepted October 31, 2017; published December 4, 2017.

## LITERATURE CITED

- Bansal S, Durrett TP** (2016) Camelina sativa: an ideal platform for the metabolic engineering and field production of industrial lipids. *Biochimie* **120**: 9–16
- Bialek W, Botstein D** (2004) Introductory science and mathematics education for 21st-century biologists. *Science* **303**: 788–790
- Bradski G, Kaehler A** (2008) *Learning OpenCV*. O'Reilly, Sebastopol, CA
- Brutnell TP** (2015) Model grasses hold key to crop improvement. *Nat Plants* **1**: 15062
- Brutnell TP, Bennetzen JL, Vogel JP** (2015) Brachypodium distachyon and Setaria viridis: model genetic systems for the grasses. *Annu Rev Plant Biol* **66**: 465–485
- Bucksch A, Burridge J, York LM, Das A, Nord E, Weitz JS, Lynch JP** (2014) Image-based high-throughput field phenotyping of crop roots. *Plant Physiol* **166**: 470–486
- Campbell MT, Knecht AC, Berger B, Brien CJ, Wang D, Walia H** (2015) Integrating image-based phenomics and association analysis to dissect the genetic architecture of temporal salinity responses in rice. *Plant Physiol* **168**: 1476–1489
- Chen D, Neumann K, Friedel S, Kilian B, Chen M, Altmann T, Klukas C** (2014) Dissecting the phenotypic components of crop plant growth and drought responses based on high-throughput image analysis. *Plant Cell* **26**: 4636–4655
- Coelho LP** (2013) Mahotas: open source software for scriptable computer vision. *J Open Res Softw* **1**: e3
- Cruz JA, Savage LJ, Zegarac R, Hall CC, Satoh-Cruz M, Davis GA, Kovac WK, Chen J, Kramer DM** (2016) Dynamic environmental photosynthetic imaging reveals emergent phenotypes. *Cell Syst* **2**: 365–377
- Das A, Schneider H, Burridge J, Ascanio AKM, Wojciechowski T, Topp CN, Lynch JP, Weitz JS, Bucksch A** (2015) Digital imaging of root traits (DIRT): a high-throughput computing and collaboration platform for field-based root phenomics. *Plant Methods* **11**: 51
- Fahlgren N, Gehan MA, Baxter I** (2015) Lights, camera, action: high-throughput plant phenotyping is ready for a close-up. *Curr Opin Plant Biol* **24**: 93–99
- Feldon DF, Jeong S, Peugh J, Roksa J, Maahs-Fladung C, Shenoy A, Oliva M** (2017) Null effects of boot camps and short-format training for PhD students in life sciences. *Proc Natl Acad Sci USA* **114**: 9854–9858
- Ge Y, Bai G, Stoerger V, Schnable JC** (2016) Temporal dynamics of maize plant growth, water use, and leaf water content using automated high throughput RGB and hyperspectral imaging. *Comput Electron Agric* **127**: 625–632
- Giuffrida MV, Minervini M, Tsafaris S** (2015) Learning to Count Leaves in Rosette Plants. *British Machine Vision Association, Durham, UK*, pp 1.1–1.13
- Gutler JL, Van Vactor D** (2013) Catalyzing curriculum evolution in graduate science education. *Cell* **153**: 731–736
- Holtan HE, Bandong S, Marion CM, Adam L, Tiwari S, Shen Y, Maloof JN, Maszle DR, Ohto MA, Preuss S, et al** (2011) BBX32, an Arabidopsis B-box protein, functions in light signaling by suppressing HY5-regulated gene expression and interacting with STH2/BBX21. *Plant Physiol* **156**: 2109–2123
- Koch I, Fuellen G** (2008) A review of bioinformatics education in Germany. *Brief Bioinform* **3**: 232–242
- McGary KL, Park TJ, Woods JO, Cha HJ, Wallingford JB, Marcotte EM** (2010) Systematic discovery of nonobvious human disease models through orthologous phenotypes. *Proc Natl Acad Sci USA* **107**: 6544–6549
- Miller ND, Parks BM, Spalding EP** (2007) Computer-vision analysis of seedling responses to light and gravity. *Plant J* **52**: 374–381
- Minervini M, Abdelsamea MM, Tsafaris SA** (2014) Image-based plant phenotyping with incremental learning and active contours. *Ecol Inform* **23**: 35–48
- Oellrich A, Walls RL, Cannon EK, Cannon SB, Cooper L, Gardiner J, Gkoutos GV, Harper L, He M, Hoehndorf R, et al** (2015) An ontology approach to comparative phenomics in plants. *Plant Methods* **11**: 10
- Preuss SB, Meister R, Xu Q, Urwin CP, Tripodi FA, Screen SE, Anil VS, Zhu S, Morrell JA, Liu G, et al** (2012) Expression of the Arabidopsis thaliana BBX32 gene in soybean increases grain yield. *PLoS One* **7**: e30717
- Provart NJ, Alonso J, Assmann SM, Bergmann D, Brady SM, Brkljatic J, Browse J, Chapple C, Colot V, Cutler S, et al** (2016) 50 years of Arabidopsis research: highlights and future directions. *New Phytol* **209**: 921–944
- Rellán-Álvarez R, Lobet G, Lindner H, Pradier P-L, Sebastian J, Yee M-C, Geng Y, Trontin C, LaRue T, Schrager-Lavelle A, et al** (2015) GLO-Roots: an imaging platform enabling multidimensional characterization of soil-grown root systems. *eLife* **4**: e07597
- Rosenwald AG, Pauley MA, Welch L, Elgin SCR, Wright R, Blum J** (2016) The CourseSource bioinformatics learning framework. *CBE Life Sci Educ* **15**: le2
- Rubinstein A, Chor B** (2014) Computational thinking in life science education. *PLOS Comput Biol* **10**: e1003897
- Searls DB** (2012) An online bioinformatics curriculum. *PLOS Comput Biol* **8**: e1002632

- Slovak R, Göschl C, Su X, Shimotani K, Shiina T, Busch W** (2014) A scalable open-source pipeline for large-scale root phenotyping of *Arabidopsis*. *Plant Cell* **26**: 2390–2403
- Tan TW, Lim SJ, Khan AM, Ranganathan S** (2009) A proposed minimum skill set for university graduates to meet the informatics needs and challenges of the “-omics” era. *BMC Genomics (Suppl 3)* **10**: S36
- van der Walt S, Schönberger JL, Nunez-Iglesias J, Boulogne F, Warner JD, Yager N, Gouillart E, Yu T**; scikit-image contributors (2014) scikit-image: image processing in Python. *PeerJ* **2**: e453
- Welch L, Lewitter F, Schwartz R, Brooksbank C, Radivojac P, Gaeta B, Schneider MV** (2014) Bioinformatics curriculum guidelines: toward a definition of core competencies. *PLOS Comput Biol* **10**: e1003496
- Wingreen N, Botstein D** (2006) Back to the future: education for systems-level biologists. *Nat Rev Mol Cell Biol* **7**: 829–832
- Zhu L-H, Krens F, Smith MA, Li X, Qi W, van Loo EN, Iven T, Feussner I, Nazareus TJ, Huai D, et al** (2016) Dedicated industrial oilseed crops as metabolic engineering platforms for sustainable industrial feedstock production. *Sci Rep* **6**: 22181