High-throughput data management and analysis in systems biology

Filippo Geuna Università degli Studi di Milano



From -omics to phenotyping for crop improvement Tuesday 26th-Thursday 28th, June 2018 - Aula Maggiore - Via Celoria, 2 (MI)



The complex and fascinating world of *-omics* analysis

Plant phenotyping has emerged as a comprehensive field of research as the result of significant advancements in the application of imaging sensors for high-throughput data collection. The flip side is the risk of drowning in the massive amounts of data generated by automated phenotyping systems.

Currently, the major challenge lies in data management, on the level of data annotation and proper metadata collection, and in progressing towards synergism across data collection and analyses. Progress in data analyses includes efforts towards the integration of phenotypic and -omics data resources for bridging the phenotype–genotype gap and obtaining in-depth insights into fundamental plant processes.

Imaging methodologies used in plant phenotyping generate huge amounts of complex data.

The major challenge is **data management**: metadata collection and data annotation.

Implementation of **standard ontologies** is key to integrate data efficiently. Data-driven approaches are promising to **generate new scientific insights**.

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The astonishing numbers of biological data Encyclopedia Genomica: UK Scientists Print the Book of Life in 130 Volumes



University of Leicester staff with the human genome (hard copy). Cas Kramer and Ed Hollox, back row (right).

http://www.bio-itworld.com/2012/12/28/encyclopediagenomica-UK-scientists-print-book-of-life-in-130volumes.html

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Nowadays it is cheaper to sequence the human genome than to print out a full hard copy. We know this because Cas Kramer and a group of scientists at the University of Leicester decided to print out a complete version of the human genome.

The genome print out spans **130** volumes, with each page printed on **both** sides in 4-point font, with precisely **43,000** characters per page. The X chromosome is made up of seven volumes, while the Y chromosome occupies one. The exercise costs a little less than 4,000 pounds (about \$6,000).

















High-throughput phenotyping facilities

IPK Institute Gatersleben - Macrophenomics Facility and Microphenomics Facility

Currently, the plant phenotyping infrastructure at the IPK is being expanded by the new Plant Cultivation Hall. On an almost 500 m² area, plants will be cultivated under field-like precisely adjustable environmental conditions, without undesigned external influences. This will allow to repeat experiments under highly reproducible conditions. In addition to a container system, a so-called rhizotron-system will be installed in the Plant Cultivation Hall which will allow both phenotyping of shoot and root features.

https://www.youtube.com/watch?v=psYu--xECDU

With the Macrophenomics facility leaf damages caused by pathogens and visible to the naked eye, can automatically and precisely be quantified. A camera creating RGB images and takeing pictures in four different wavelength ranges is applied to study the number and extent of fungal colonies per leaf area and the response of their host. Equipped with a multispectral 2D imaging station Macrobot (developed in cooperation with Fraunhofer IFF Magdeburg), up to 500 genotypes can be analyzed in a high-throughput process in 3-4 weeks.

https://www.youtube.com/watch?v=8Xp0f2B7mRM

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The 'Ontology' concept - *BioPAX*

_computational

PERSPECTIVE

The BioPAX community standard for pathway data sharing

Emek Demir et al.

NATURE BIOTECHNOLOGY VOLUME 28 NUMBER 9 SEPTEMBER 2010

Biological Pathway Exchange (BioPAX) is a standard language to represent biological pathways at the molecular and cellular level and to facilitate the exchange of pathway data. The rapid growth of the volume of pathway data has spurred the development of databases and computational tools to aid interpretation; however, use of these data is hampered by the current fragmentation of pathway information across many databases with incompatible formats. BioPAX, which was created through a community process, solves this problem by making pathway data substantially easier to collect, index, interpret and share. BioPAX can represent metabolic and signaling pathways, molecular and genetic interactions and gene regulation networks. Using BioPAX, millions of interactions, organized into thousands of pathways, from many organisms are available from a growing number of databases. This large amount of pathway data in a computable form will support visualization, analysis and biological discovery.

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The 'Ontology' concept - *BioPAX*

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NATURE BIOTECHNOLOGY VOLUME 28 NUMBER 9 SEPTEMBER 2010

What is an ontology?

An ontology is a formal system for representing knowledge. Such representation is required for computer software to make use of information. Example ontologies include organism taxonomies and the Gene Ontology. A formal representation allows consistent communication of knowledge among individuals or computer systems and helps manage complexity in information processing as knowledge is broken down into clear concepts that can be considered independently.

Ontologies also enable integration of knowledge between independent resources linked on the World Wide Web. Such linked, structured data form the basis of the semantic web, an extension of the web that promises improved information management and search capability.

Representing and sharing knowledge using ontologies is simplified by availability of the standard web ontology language (OWL; http://www.30.org/TR/owl-features/). Tools to edit OWL, such as Protégé, have been developed by the semantic web community and adopted in the life sciences. Implementing BioPAX using OWL enables both the ontology and the individuals and values to be stored in the same XML-based format, which makes data transmission easier. An ontology is composed of classes, properties (representing relations) and restrictions and is used to de ne individuals (instances of classes, also known as objects) and values for their properties. Classes (also known as concepts or types) are often arranged into a hierarchy (or taxonomy) where child classes are more speci c than, and inherit the properties (or parent classes.

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From -omics to phenotyping for crop improvement https://www.nature.com/articles/nbt.1666/figures/5 Tuesday 26th-Thursday 28th, June 2018 - Aula Maggiore - Via Celoria, 2 (Mi)



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Gene Regulatory	If you know of a pathway resource that is not listed here, or have other questions or comments, please send us an e-mail.	We now have information about					
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Protein Sequence	Protein-Protein Interactions						
Focused	Database Name (Order: alphabetically by web popularity e)	Full Record	Availability	Standard			
Other	2P2ldb - The Protein Protein Interaction Inhibition Database	Details	Free				
Search))	3D-Interologs - 3D-Interologs	Details	Free				
All	3DID - 3D interacting domains	Details	Free				
Availability	ACSN - Atlas of Cancer Signalling Network	Details	Free	BioPAX			
All	ADAN - Prediction of protein-protein interaction of modular domains	Details	X				
Standards	AHD2.0 - Arabidopsis Hormone Database 2.0	Details	Free				
All	AllFuse - Functional Associations of Proteins in Complete Genomes	Details	x				
	aMAZE - Protein Function and Biochemical Pathways Project	Details	X				
Reset Search	ANAP - Arabidopsis Network Analysis Pipeline	Details	Free				
Analysis	ANIA - ANnotation and Integrated Analysis of the 14-3-3 interactome	Details	Free				
Statistics	AnimalTFDB - Animal Transcription Factor Database	Details	Free				
Database Interactions	Anti-len - Anti-len a Kinetic, Thermodynamic and Cellular Database	Details	Free				



The Plant Ontology initiative

The Plant Ontology (PO; http://www.plantontology.org/) is a publicly available, collaborative effort to develop and maintain a controlled, structured vocabulary ('ontology') of terms to describe plant anatomy, morphology and the stages of plant development. The goals of the PO are to link (annotate) gene expression and phenotype data to plant structures and stages of plant development, using the data model adopted by the Gene Ontology.

From its original design covering only rice, maize and Arabidopsis, the scope of the PO has been expanded to include all green plants. The PO was the first multispecies anatomy ontology developed for the annotation of genes and phenotypes. Also, to our knowledge, it was one of the first biological ontologies that provides translations (via synonyms) in non-English languages such as Japanese and Spanish.

As of Release #18, there are about 2.2 million annotations linking PO terms to >110,000 unique data objects representing genes or gene models, proteins, RNAs, germplasm and quantitative trait loci (QTLs) from 22 plant species. The focus is on the plant anatomical entity branch of the PO, describing the organizing principles, resources available to users and examples of how the PO is integrated into other plant genomics databases and web portals.

Two examples of comparative analyses, demonstrate how the ontology structure and POannotated data can be used to discover the patterns of expression of the LEAFY (LFY) and terpene synthase (TPS) gene homologs.

Source: Cooper L, Walls RL. 2013. The Plant Ontology as a Tool for Comparative Plant Anatomy and Genomic Analyses. Plant & Cell Physiology. 54:1-23

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The Crop Ontology initiative

Given the Multi-disciplinary nature of the CGIAR Big Data For Agriculture, the Ontology Community of Practice (CoP) will span the knowledge domains of importance for the platform with the objective of establishing best practices, guidelines in the selection, use and application of semantics for data harmonization at the collect and storage levels, for data interoperability and data discovery following the FAIR principles. The CoP will contribute to make the best practices and recommended ontologies a long-term reference resource for the CGIAR Big Data in Agriculture in particular and for other platforms. The INSPIRE projects will offer opportunities to test the power of the ontologies and best practices for combining data sets to address a research question.











Table 2 OBO Foundry onto	logies (as of April 2007)		
Ontology	Scope	URL	Custodians
Mature ontologies undergoing inc	remental reform		
Cell Ontology (CL)	Cell types from prokaryotic to mammalian	http://obofoundry.org/cgi-bin/detail. cgi?cell	Michael Ashburner, Jonathan Bard Oliver Hofmann, Sue Rhee
Gene Ontology (GO)	Attributes of gene products in all organisms	http://www.geneontology.org	Gene Ontology Consortium
Foundational Model of Anatomy (FMA)	Structure of the mammalian and in particular the human body	http://fma.biostr.washington.edu	J.L.V. Mejino, Jr., Cornelius Rosse
Zebrafish Anatomical Ontology (ZAO)	Anatomical structures in Danio rerio	http://zfin.org/zf_info/anatomy/dict/sum. html	Melissa Haendel, Monte Westerfie
Mature ontologies still in need of	thorough review		
Chemical Entities of Biological Interest (ChEBI)	Molecular entities which are products of nature or synthetic products used to inter- vene in the processes of living organisms	http://www.ebi.ac.uk/chebi	Paula Dematos, Rafael Alcantara
Disease Ontology (DO)	Types of human disease	http://diseaseontology.sf.net	Rex Chisholm
Plant Ontology (PO)	Flowering plant structure, growth and development stages	http://plantontology.org	Plant Ontology Consortium
Sequence Ontology (SO)	Features and properties of nucleic acid sequences	http://www.sequenceontology.org	Karen Eilbeck
Ontologies for which early version	ns exist		
Ontology for Clinical Investigations (OCI)	Clinical trials and related clinical studies	http://www.bioontology.org/wiki/index. php/CTO:Main_Page	OCI Working Group
Common Anatomy Reference Ontology (CARO)	Anatomical structures in all organisms	http://obofoundry.org/cgi-bin/detail. cgi?caro	Fabian Neuhaus, Melissa Haendel David Sutherland
Environment Ontology	Habitats and associated spatial regions and sites	http://www.obofoundry.org/cgi-bin/detail. cgi?id=erwo	Norman Morrison, Dawn Field
Ontology for Biomedical Investigations (OBI)	Design, protocol, instrumentation and analysis applied in biomedical investigations	http://obi.sf.net	OBI Working Group
Phenotypic Quality Ontology (PATO)	Qualities of biomedical entities	http://www.phenotypeontology.org	Michael Ashburner, Suzanna Lewis Georgios Gkoutos
Protein Ontology (PRO)	Protein types and modifications classified on the basis of evolutionary relationships	http://pir.georgetown.edu/pro	Protein Ontology Consortium
Relation Ontology (RO)	Relations in biomedical ontologies	http://obofoundry.org/ro	Barry Smith, Chris Mungall
RNA Ontology (RnaO)	RNA three-dimensional structures, sequence alignments, and interactions	http://roc.bgsu.edu/	RNA Ontology Consortium





moment it is being generated.

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A world of databases and... a galaxy of data

The use of **advanced imaging** systems has **drastically increased the volume of data** from a couple of bytes, e.g. manually scored traits in a spreadsheet, to several megabytes (MB) or sometimes more than 100 MB, e.g. in the case of hyperspectral imaging or scene characterization by means of video capture.

Data are also stored in a myriad of formats on diverse types of media ranging from a researcher's hard drive to local server stations or in "the cloud". Proper annotation of data to ensure their continued relevance after acquisition is thus essential.

Furthermore, because the plant's phenotype is the result of a strong interaction between its genotype and the environment in which it grows (G × E), plant phenotyping efforts should **include the logging of environmental conditions**, which in turn requires the collection of metadata on the sensors in use.

Because of the tremendous amounts and diversity of data produced within the plant phenotyping research field, data management, storage and analysis are currently considered as the major challenges. On the other hand, large datasets may also create opportunities for data modeling and machine learning towards **"Big Data"** analyses.

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Open Science: the power of collaboration [...] Usually they imply the interactions between genotype (G), environment (E), and management **CellPress** (M), in short: the G E M interactions. Inevitably, the investigation of G x E x M interactions requires. in addition to genotypic variation, ranges of environmental factors or gradients, and variation Forum in agronomic management. In view of a growing The Future of Field world population, global climate change, and Trials in Europe: increasing strictness of environmental policies, we Establishing a can expect that the above-mentioned themes will gain importance in agricultural and plant research, Network Bevond and it is imperative to investigate whether we have Boundaries the appropriate infrastructure to meet these challenges ... Hartmut Stützel,^{1,*} [...] future research in plant and agro-ecological Nicolas Brüggemann,² and science will increasingly depend on large-scale and Dirk Inzé^{3,4} long-term data obtained from scientific experiments under real-world conditions. [...] Source: Trends in Plant Science, February 2016, Vol. 21, No. 2

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Open Science: the power of collaboration

ECOFE – A research network to meet the needs for 21st century crop science Support is sought for development and implementation of <u>harmonized</u> and <u>standardized</u> methodologies and to expand the infrastructure network in order to enhance the effectiveness and competitiveness of European crop science.



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