Chapter 5
Integrative Multi-Omics Through Bioinformatics

Hoe-Han Goh

Abstract This chapter introduces different aspects of bioinformatics with a brief discussion in the systems biology context. Example applications in network pharmacology of traditional Chinese medicine, systems metabolic engineering, and plant genome-scale modelling are described. Lastly, this chapter concludes on how bioinformatics helps to integrate omics data derived from various studies described in previous chapters for a holistic understanding of secondary metabolite production in *P. minus*.

Keywords Genome-scale model · Omics integration · Multi-omics · Network analysis · Systems metabolic engineering

5.1 Introduction

The overwhelming trend in omics studies relies heavily on bioinformatics to store, mine, process, analyse, interpret, and curate biological big data. Bioinformatics includes computer science, statistics, and mathematical methods, with computer programming for the analysis of various sequence data in molecular biology. The term bioinformatics was introduced in 1970 for the study of biosystems information processes, which has evolved into an interdisciplinary field largely dealing with computational methods for comparative genomic data analysis since the late 1980s [1]. In general, bioinformatics refers to biological studies aided by computer programming apart from data analysis pipelines, especially in the field of genomics such as that of illustrated in previous chapters.

H.-H. Goh (✉)
Institute of Systems Biology, Universiti Kebangsaan Malaysia (UKM), Bangi, Malaysia
e-mail: gohhh@ukm.edu.my

5.2   Different Aspects of Bioinformatics

Bioinformatics covers many aspects of fundamental and applied research, from hypothesis-driven to data-driven (Fig. 5.1). The hypothesis-driven bottom-up approach is largely knowledge based and depends strongly on modelling and computational simulation for understanding of biological processes. For example, mathematical modelling of enzyme kinetics in a reaction pathway or simulation of flux distribution in a genome-scale model can help identify rate-limiting enzyme/metabolite [2, 3].

On the other hand, data-driven bioinformatics evolved in the mid-1990s as demanded by the Human Genome Project, which led to the explosion of high-throughput omics data. The advancement in sequencing technology dominates the development of bioinformatics, for the acquisition, analysis, and management of tremendous volume of biological data. This is paralleled by the advancement of information technologies, algorithms, and computational and statistical methods. Computationally intensive techniques, such as data mining [4], machine learning, visualisation [5], and pattern recognition, are indispensable with continuous improvement of bioinformatics software and tools for efficient access, analysis, and curation of heterogeneous datasets. Bioinformatics even encompasses solving problems arising from database management. Common sequence analyses include sequence alignment, genome assembly, gene prediction, and functional annotation, as compared to gene and protein expression studies which are based on abundance analysis, in which the latter relies on mass spectrometry for protein fragment identification. Image analysis involves important automated techniques for the microscopic tracing of subcellular molecular movement, as well as phenotypic tracking of
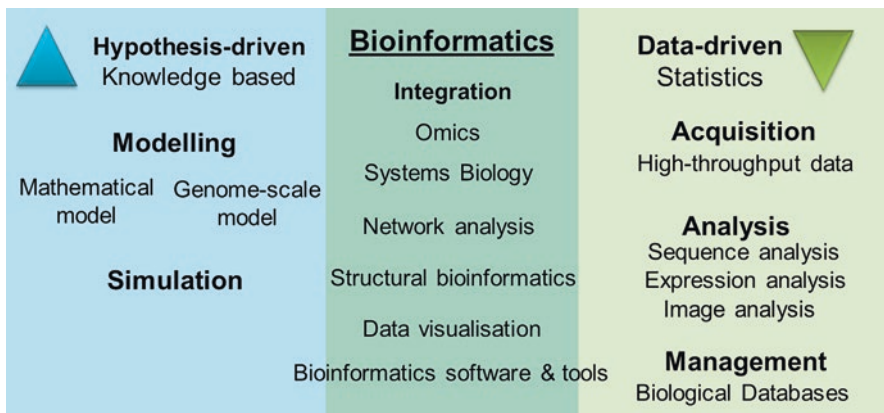
Fig. 5.1 An overview of different aspects of bioinformatics, from knowledge-based hypothesis-driven bottom-up approach to top-down statistics and data-driven

organ growth in real time. Protein structure prediction is a field of structural bioinformatics important for the inference of structure-function relationship to understand the molecular mechanism or protein-protein/metabolite interactions, which can be applied for drug design.

Nowadays, the field of bioinformatics is largely data-driven. Computational modelling and simulation in network analysis have become increasingly important for the integration of multi-omics in the context of systems biology. Table 5.1 summarises the different aspects of bioinformatics.

Table 5.1 Different aspects of bioinformatics with examples

Aspect	Example
Sequence analysis	DNA/RNA sequencing
	Sequence assembly
	Genome annotation
	Genetics of disease
	Cancer genomics (oncogenomics)
	Comparative genomics
	Genetics and population analysis
	Computational evolutionary biology
Expression analysis	Gene expression
	Protein expression
	Metabolite profiling
	Analysis of expression regulation
Structural bioinformatics	Genome modelling (3D chromatin)
	RNA secondary structure prediction
	Protein structure prediction
	Homology modelling
	Structure-based drug/chemical design
	Molecular docking
Image analysis	Microscopy image analysis
	Automated cell tracking
	Pattern recognition
	Bioimage annotation
	Visualisation
Data management	Database development
	Web services
	Curation
	Meta-analysis
	Workflow management system
Network and systems biology	Biological network analysis
	Gene co-expression analysis
	Genome-scale modelling
	Molecular interaction networks
Others	Ontology and data integration
	Literature/text mining
	Software/tool development

5.3 Bioinformatics for Systems Biology

Essentially, systems biology constitutes a crossover between knowledge-based modelling and omics data-driven approaches. Bioinformatics is a broad multidisciplinary field which is indispensable for systems biology that deals with omics data, mathematical modelling, and network analysis. This is because the dynamic behaviours of biological systems are beyond human intuitive grasp due to the sheer number of components (biomolecules, cells, drugs, and each other) which interact. System-level understanding is only possible through computational models and simulations. Metabolic, gene regulatory, and protein-protein interaction networks are the core of common systems studies, with many examples in *E. coli* [6, 7] and yeast [8–10]. Detailed descriptions and discussion are beyond the scope of this chapter. Readers can refer to recent literature [11–13] to understand further the bioinformatics tools available for systems biology.

5.4 Applications of Bioinformatics

In this section, examples of bioinformatics applications on integrative omics are described for molecular medicine, systems metabolic engineering, and plant genome-scale modelling.

5.4.1 Integrative Omics in Network Pharmacology

Network pharmacology is a new paradigm in postgenomic era of molecular medicine for drug design or discovery [14]. This is based on the realm that one drug often targets many proteins and one protein can be targeted by many drugs. Hence, a combination of different drugs could be beneficial synergistically in treating complex diseases. This also led to the current trend of drug repositioning/repurposing, whereby known drugs/compounds are applied for treatment of new diseases.

Network pharmacology relies on a multi-omics systems biology approach, which analyses various omics data together using bioinformatics tools [5, 15] to develop disease networks, drug-target networks, or drug-disease networks [16, 17]. One good example is the use of this approach to discover multicomponent drugs from traditional Chinese medicine (TCM) for multi-target therapy [18–20]. To achieve this, TCM pattern in a disease can be identified using molecular network biomarkers and integrate with pharmacological network of herbal formulas (Fig. 5.2).

The construction of disease-TCM pattern molecular network depends on multi-omics data analysis of categorised patients, according to TCM pattern based on expert consensus or literature analysis. Text mining of SinoMed database helps identify TCM herbal combinations for the treatment of disease with specific TCM

Fig. 5.2 A conceptual framework of network pharmacology for multiple compound drug discovery from TCM
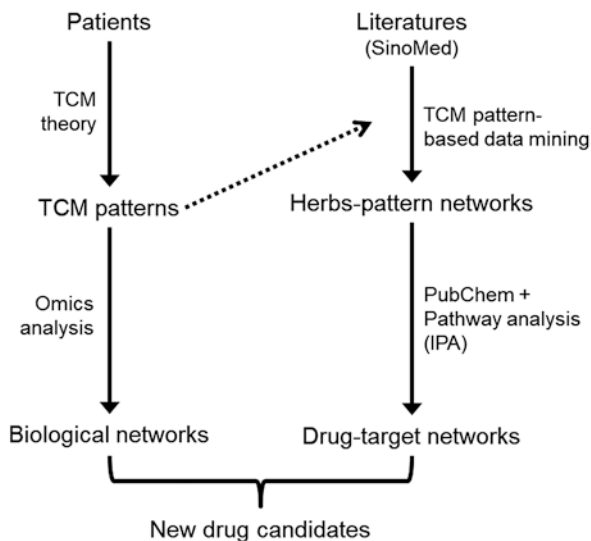
patterns. Targeted proteins by the active compounds in the TCM herbal formula obtained from PubChem are used to construct drug-target networks. Potential multiple-compound drug candidates can then be shortlisted from well-matched compound combinations between disease-TCM pattern molecular network and pharmacological network of herbal formulas. This is not possible through reductionist approach in the past without systems approach of network analysis which requires computing resources. A good example of TCM drug repositioning is reported recently on the use of systems pharmacology approach in the discovery of Liuweiwuling therapeutic use for liver failure [21].

5.4.2 Integrative Omics for Systems Metabolic Engineering

The emergence of ethnomedicine as alternatives of disease treatment has increase the demands for natural products and bioactive compounds as drugs [22], For example, an antimalarial drug artemisinin from a TCM *Artemisia annua* has driven engineered production of its precursor artemisinic acid in yeast [23].

There is a growing trend of employing synthetic biology approach for genetically engineering metabolic pathways in microbial system to produce natural and synthetic compounds. For this purpose, bioinformatics plays a key role in the selection, synthesis, assembly, and optimisation of the parts (enzymes and regulatory elements), devices (pathways), and systems [24]. Furthermore, systems metabolic engineering often employs genome-scale models for flux analysis of the metabolic reconstruction [25]. Hence, fluxomics play important role for optimising flux distribution towards target compound production. Genome-scale metabolic reconstructions allow the modelling on the effects of gene knockouts. However,

this is largely dominated by microbes such as *E. coli* and *S. cerevisiae*. Much of the curated/predicted metabolic reconstructions can be found at MetaCyc and BioCyc databases [26]; see http://systemsbiology.ucsd.edu/InSilicoOrganisms/OtherOrganisms for an updated list. This systems approach has accelerated the development of metabolic engineering, such as that of the use of *E. coli* for the production of terpenoids [27] and bioethanol [28].

Recently, multi-omics has become a common approach for comprehensive understanding of different microbial strains by compensating each omics' limitations as illustrated in Fig. 5.3. The ultimate aim is to improve titre, yield, and productivity of engineered microbial cell factories. For that purpose, multi-omics systems biology contributes in the understanding of cellular metabolic status, genome-wide identification of knockout or overexpression targets, pathway prediction, and even enzyme design through computational structural prediction. Further descriptions and discussion on systems metabolic engineering with the integration of systems and synthetic biology with evolutionary engineering can refer to the next chapter and a recent review [29] with references therein. Fondi and Liò (2015) provide a good review for tools used in integrating multi-omics for metabolic modelling pipelines [30].

5.4.3   Integrative Omics for Genome-Scale Modelling in Plants

As mentioned above, genome-scale metabolic model (GEM) is an in silico metabolic flux model constructed from genome annotation-derived metabolic networks with stoichiometry of all known metabolic reactions. GEM is often built by algorithms with constraint-based flux (reaction rate) analysis within defined system boundaries to bridge between modelled metabolic network structure and observed metabolic processes. Constraints are important to limit possible flux values (solution space) in the studied system, which include mass balancing, physico-thermochemical, and actual flux measurements [31]. Flux balance analysis (FBA) is the most popular mathematical method for the phenotypic solution space exploration through linear programming.

GEM allows the assessment of the essentiality of metabolic steps. This enables the prediction of gene targets for knockout or overexpression and is useful for flux optimisation and designing rational metabolic engineering strategies, especially for microbial systems. It is more challenging to construct GEM for higher organisms, especially plants due to complexity of plant cells with photosynthesis/photorespiration, compartmentation, tissue differentiation, diverse metabolic processes, and responses to endogenous (phytohormones) and environmental stimuli [31]. The first ever plant GEM was reported in 2009 for *Arabidopsis thaliana* cell suspension cultures [32]. Other selected examples and their significance are provided in Table 5.2. Previously neglected secondary metabolism is also gaining momentum with the latest advancement of omics approaches in filling in the gaps of metabolomics and proteomics data, especially in medicinal plants producing important bioactive compounds [33].
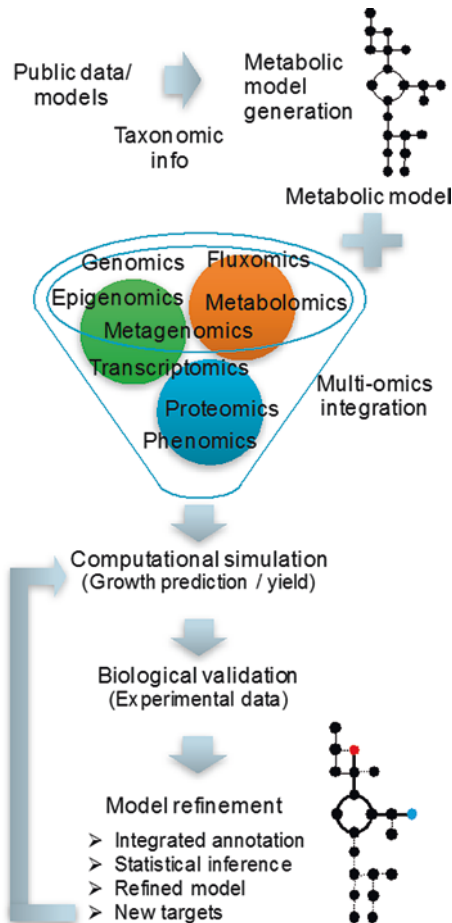
Fig. 5.3 Overall framework of a metabolic modelling/reconstruction pipeline with multi-omics integration, computational simulation, biological validation, and iterative model refinement. Pre-existing genome annotation in public repositories provides information on the presence/absence of metabolic pathways and overall metabolic capabilities of a microbe. For a novel microbe, a metabolic model can be generated from the closest related species with publicly available data based on taxonomic information or from de novo genome sequencing and assembly. Next, different layers of datasets resulting from the application of different omics technologies can be integrated for computational simulation of phenotype prediction. Multi-omics integration provides a more comprehensive perspective on the microbe under study, statistically grounded inferences, novel questions to be addressed, or new target genes to be manipulated, possibly through reiterating the pipeline based on experimental data for further refinement of model.

Despite that GEM is now possible in plants, challenges remain on filling in missing metabolic information with the integration of regulatory and signalling components in dynamic simulation. In this respect, multi-condition, single-platform omics studies such as transcriptomics will be useful for mapping gene expression

Table 5.2 Selected examples of plant GEMs

Species	GEM	Significance	Reference
Arabidopsis thaliana	Suspension cell culture	The first GEM of a heterotrophic plant cell derived from AraCyc with 855 mass-balanced reactions	Poolman et al. [32]
	AraGEM (*i*RS1597)	Compartmented C_3 mesophyll cell model of photosynthesis, photorespiration, and heterotrophic metabolism	Dal'Molin et al. [34]
Brassica napus	Developing embryo	Compartmented FBA model to predict the regulation of oil biosynthesis	Pilalis et al. [35]
	bna572 (oilseed)	Flux balance and variability analyses based on highly comprehensive and compartmentalised oilseed model with in silico mutant analysis in relation to carbon use efficiency	Hay and Schwender [36, 37]
Hordeum vulgare	Seed endosperm	Tissue-specific compartmented FBA model with 65 transporters for study of hypoxia and aerobic conditions	Grafahrend-Belau et al. [38], Rolletschek et al. [39]
Zea mays, Saccharum officinarum, Sorghum bicolor	C4GEM	Compartmented two-cell (mesophyll and bundle sheath cells) model representing C_4 plants with 112 transporters	Dal'Molin et al. [40]
Zea mays	*i*RS1563	Expanded C4GEM model with secondary metabolism validated using lignin biosynthetic mutants	Saha et al. [41]
Oryza sativa	General	First model in rice with 1736 reactions to study metabolism under varying light intensity	Poolman et al. [42]
	*i*OS2164	A fully compartmentalised model with multi-omics analysis	Lakshmanan et al. [43]
Solanum lycopersicum	*i*HY3410 leaf	Compartmentalised metabolic model of leaf with five organelles to describe metabolic response to drought, particularly photorespiratory metabolism	Yuan et al. [44]
Vitis vinifera	Suspension cell culture	Established cell energy, redox status, and α-ketoglutarate availability as metabolic drivers for anthocyanin accumulation under nitrogen limitation	Soubeyrand et al. [45]

data onto GEM to generate condition-specific models for more realistic depiction of actual metabolic states. Similarly, quantitative proteomics can also be applied for modelling system-level metabolic changes following experimental perturbations, assuming that gene expression or protein abundance correlates with metabolic fluxes. Incorporating multi-conditions transcriptomics and proteomics data will enable condition-based simulation with the elements of gene/protein regulation in switching a pathway on/off. Lastly, metabolomics profiling under different conditions allows the comprehensive identification of metabolite compositional changes

to narrow down target pathways for further fluxomics analysis (^{13}C-based) under different experimental conditions. With multi-omics, multi-conditions data, a more realistic dynamic GEM can be simulated to predict outcomes for various scenarios. In plants, GEMs of different tissues, such as root to shoot, can be integrated for whole-plant simulation [46]. With the integration of regulation into GEMs, we can gain important insights of plant metabolic plasticity for rational metabolic engineering to improve plant biomass production through higher tolerance and resistance to biotic and abiotic stresses.

5.5   Case Study: Integrating Multi-Omics in *Polygonum minus*

Over the past 10 years, extensive studies using different omics approaches have been performed on aromatic herb *Polygonum minus* as described in previous chapters. Much is learnt about *P. minus* on the transcriptomes [47–49] and metabolomes [50–52] from different tissues, as well as molecular responses towards elicitors [53–55]. The integration between transcriptomics and metabolomics studies [56] allows the reconstruction of secondary metabolite biosynthetic pathways. This also helps in the elucidation of global gene reprogramming which resulted in the compositional changes of volatile organic compounds (VOCs) in response to elicitation or other environmental factors. Furthermore, the established transcriptome sequences provide a reference for the identification of proteins in shotgun proteomics through proteomics informed by transcriptomics (PIT) approach [57].

General research framework of integrating multi-omics results in *P. minus* is shown in Fig. 5.4. This is applicable for other plants/organisms without a reference genome, particularly tropical medicinal plants, which have scarce sequence information and limited knowledge on the production of bioactive compounds. By eluci-
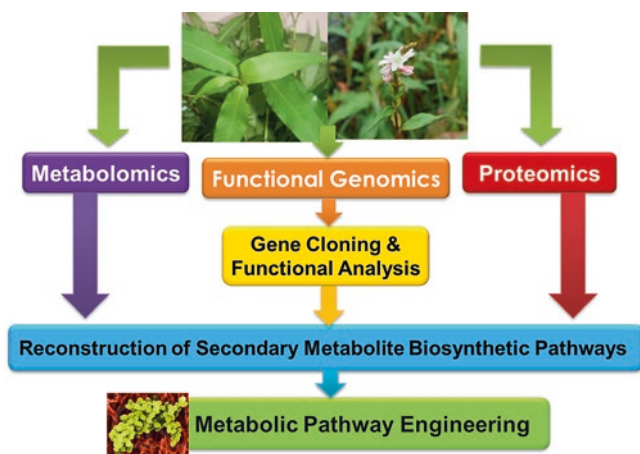

Fig. 5.4 Research framework for the integration of multi-omics studies in *P. minus*

dating the genes and enzymes involved in pathways of secondary metabolite biosynthesis, metabolic engineering in microbial system becomes possible through synthetic biology approach (described in the next chapter). Hence, integrative omics through systems biology approach provides a fundamental blueprint to enable applied large-scale production of targeted compounds through microbial bioengineering.

References

1. Hogeweg P (2011) The roots of bioinformatics in theoretical biology. PLOS Comput Biol 7:e1002021
2. Henry CS et al (2010) High-throughput generation, optimization and analysis of genome-scale metabolic models. Nat Biotechnol 28:977–982
3. Oberhardt MA, Palsson BØ, Papin JA (2009) Applications of genome-scale metabolic reconstructions. Mol Syst Biol 5:320
4. Prasad TV, Ahson SI (2007) Bioinformatics: applications in life and environmental sciences. Springer Netherlands Capital Publishing Company, New Delhi, India. pp 145–172
5. Tao Y, Liu Y, Friedman C, Lussier YA (2004) Information visualization techniques in bioinformatics during the postgenomic era. Drug Discov Today BIOSILICO 2:237–245
6. Shen-Orr SS, Milo R, Mangan S, Alon U (2002) Network motifs in the transcriptional regulation network of *Escherichia coli*. Nat Genet 31:64–68
7. Feist AM et al (2007) A genome-scale metabolic reconstruction for *Escherichia coli* K-12 MG1655 that accounts for 1260 ORFs and thermodynamic information. Mol Syst Biol 3:121
8. Duarte NC, Herrgård MJ, Palsson BØ (2004) Reconstruction and validation of *Saccharomyces cerevisiae* iND750, a fully compartmentalized genome-scale metabolic model. Genome Res 14:1298–1309
9. Lee TI et al (2002) Transcriptional regulatory networks in *Saccharomyces cerevisiae*. Science 298:799–804
10. Schwikowski B, Uetz P, Fields S (2000) A network of protein-protein interactions in yeast. Nat Biotechnol 18:1257–1261
11. Krawetz S (2009) Bioinformatics for systems biology. Humana Press, Totowa
12. Likić VA, McConville MJ, Lithgow T, Bacic A (2010) Systems biology: the next frontier for bioinformatics. Adv Bioinforma 2010:1
13. Tran QN, Arabnia HR (2016) Emerging trends in applications and infrastructures for computational biology, bioinformatics, and systems biology: systems and applications. Elsevier/Morgan Kaufmann, Amsterdam/Boston
14. Tang J, Aittokallio T (2014) Network pharmacology strategies toward multi-target anticancer therapies: from computational models to experimental design principles. Curr Pharm Des 20:23–36
15. Valencia A (2002) Bioinformatics and computational biology at the crossroads of postgenomic technology. Phytochem Rev 1:209–214
16. Ostrowski J (2008) Integrative genomics – a basic and essential tool for the development of molecular medicine. Acta Pol Pharm Drug Res 65:621–624
17. Yan Q (2013) Handbook of personalized medicine: advances in nanotechnology, drug delivery and therapy. Pan Stanford, New York, pp 191–220
18. Hao DC, Xiao PG (2014) Network pharmacology: A Rosetta stone for traditional Chinese medicine. Drug Dev Res 75:299–312
19. Li S, Zhang B (2013) Traditional Chinese medicine network pharmacology: theory, methodology and application. Chin J Nat Med 11:110–120

20. Tao WY, Wang LY, Huang GQ, Luo M (2013) *Applied mechanics and materials*, vol 411–414. Trans Tech Publications Ltd., Durnten-Zurich, pp 3141–3145
21. Wang J-B et al (2018) A systems pharmacology-oriented discovery of a new therapeutic use of the TCM formula Liuweiwuling for liver failure. Sci Rep 8:5645
22. Li JWH, Vederas JC (2009) Drug discovery and natural products: end of an era or an endless frontier? Science 325:161–165
23. Ro DK et al (2006) Production of the antimalarial drug precursor artemisinic acid in engineered yeast. Nature 440:940–943
24. Carbonell P et al (2016) Bioinformatics for the synthetic biology of natural products: integrating across the Design-Build-Test cycle. Nat Prod Rep 33:925–932
25. Blazeck J, Alper H (2010) Systems metabolic engineering: genome-scale models and beyond. Biotechnol J 5:647–659
26. Caspi R et al (2009) The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of pathway/genome databases. Nucleic Acids Res 38:D473–D479
27. Martin VJJ, Piteral DJ, Withers ST, Newman JD, Keasling JD (2003) Engineering a mevalonate pathway in *Escherichia coli* for production of terpenoids. Nat Biotechnol 21:796–802
28. Yim H et al (2011) Metabolic engineering of *Escherichia coli* for direct production of 1,4-butanediol. Nat Chem Biol 7:445–452
29. Chae TU, Choi SY, Kim JW, Ko Y-S, Lee SY (2017) Recent advances in systems metabolic engineering tools and strategies. Curr Opin Biotechnol 47:67–82
30. Fondi M, Liò P (2015) Multi -omics and metabolic modelling pipelines: challenges and tools for systems microbiology. Microbiol Res 171:52–64
31. Collakova E, Yen JY, Senger RS (2012) Are we ready for genome-scale modeling in plants? Plant Sci 191–192:53–70
32. Poolman MG, Miguet L, Sweetlove LJ, Fell DA (2009) A genome-scale metabolic model of Arabidopsis and some of its properties. Plant Physiol 151:1570–1581
33. Rai A, Saito K, Yamazaki M (2017) Integrated omics analysis of specialized metabolism in medicinal plants. Plant J 90:764–787
34. Dal'Molin CGO, Quek LE, Palfreyman RW, Brumbley SM, Nielsen LK (2010) AraGEM, a genome-scale reconstruction of the primary metabolic network in Arabidopsis. Plant Physiol 152:579–589
35. Pilalis E, Chatziioannou A, Thomasset B, Kolisis F (2011) An in silico compartmentalized metabolic model of *Brassica napus* enables the systemic study of regulatory aspects of plant central metabolism. Biotechnol Bioeng 108:1673–1682
36. Hay J, Schwender J (2011) Computational analysis of storage synthesis in developing *Brassica napus* L. (oilseed rape) embryos: flux variability analysis in relation to 13C metabolic flux analysis. Plant J 67:513–525
37. Hay J, Schwender J (2011) Metabolic network reconstruction and flux variability analysis of storage synthesis in developing oilseed rape (*Brassica napus* L.) embryos. Plant J 67:526–541
38. Grafahrend-Belau E, Schreiber F, Koschützki D, Junker BH (2009) Flux balance analysis of barley seeds: a computational approach to study systemic properties of central metabolism. Plant Physiol 149:585–598
39. Rolletschek H et al (2011) Combined noninvasive imaging and modeling approaches reveal metabolic compartmentation in the barley endosperm. Plant Cell 23:3041–3054
40. Dal'Molin CGO, Quek LE, Palfreyman RW, Brumbley SM, Nielsen LK (2010) C4GEM, a genome-scale metabolic model to study C4 plant metabolism. Plant Physiol 154:1871–1885
41. Saha R, Suthers PF, Maranas CD (2011) Zea mays irs1563: a comprehensive genome-scale metabolic reconstruction of maize metabolism. PLOS ONE 6:e21784
42. Poolman MG, Kundu S, Shaw R, Fell DA (2013) Responses to light intensity in a genome-scale model of rice metabolism. Plant Physiol 162:1060
43. Lakshmanan M et al (2015) Unraveling the light-specific metabolic and regulatory signatures of rice through combined in silico modeling and multiomics analysis. Plant Physiol 169:3002

44. Yuan H, Cheung CYM, Poolman Mark G, Hilbers Peter AJ, Riel Natal AW (2015) A genome-scale metabolic network reconstruction of tomato (*Solanum lycopersicum* L.) and its application to photorespiratory metabolism. Plant J 85:289–304
45. Soubeyrand E et al (2018) Constraint-based modeling highlights cell energy, redox status and α-ketoglutarate availability as metabolic drivers for anthocyanin accumulation in grape cells under nitrogen limitation. Front Plant Sci 9:421
46. Gomes de Oliveira Dal'Molin C, Quek L-E, Saa PA, Nielsen LK (2015) A multi-tissue genome-scale metabolic modeling framework for the analysis of whole plant systems. Front Plant Sci 6:4
47. Roslan ND et al (2012) Flavonoid biosynthesis genes putatively identified in the aromatic plant *Polygonum minus* via expressed sequences tag (EST) analysis. Int J Mol Sci 13:2692–2706
48. Loke K-K et al (2016) RNA-seq analysis for secondary metabolite pathway gene discovery in *Polygonum minus*. Genomics Data 7:12–13
49. Loke KK et al (2017) Transcriptome analysis of *Polygonum minus* reveals candidate genes involved in important secondary metabolic pathways of phenylpropanoids and flavonoids. Peer J 5:e2938
50. Ahmad R et al (2014) Volatile profiling of aromatic traditional medicinal plant, polygonum minus in different tissues and its biological activities. Molecules 19:19220–19242
51. Goh HH, Khairudin K, Sukiran NA, Normah MN, Baharum SN (2016) Metabolite profiling reveals temperature effects on the VOCs and flavonoids of different plant populations. Plant Biol 18:130–139
52. Hassim N et al (2015) Antioxidant and antibacterial assays on polygonum minus extracts: different extraction methods. Int J Chem Eng 2015:1–10
53. Ee SF et al (2013) Transcriptome profiling of genes induced by salicylic acid and methyl jasmonate in *Polygonum minus*. Mol Biol Rep 40:2231–2241
54. Rahnamaie-Tajadod R, Loke KK, Goh HH, Noor NM (2017) Differential gene expression analysis in *Polygonum minus* leaf upon 24h of methyl jasmonate elicitation. Front Plant Sci 8:109
55. Nazaruddin N et al (2017) Small RNA-seq analysis in response to methyl jasmonate and abscisic acid treatment in *Persicaria minor*. Genomics Data 12:157–158
56. Mehrotra B, Mendes P (2006) Biotechnology in agriculture and forestry, vol 57. Springer, Berlin/Heidelberg, pp 105–115
57. Aizat WM et al (2018) Extensive mass spectrometry proteomics data of *Persicaria minor* herb upon methyl jasmonate treatment. Data Brief 16:1091–1094