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Review Article

How Metabolomics Drive agriculture innovation

Marcel Bahizire Rhushenge[1], Dieudonné Nyamaifofe[2]

[1]Department of Pharmacy, Faculty of Pharmaceutical Sciences and Public Health, Official University of Bukavu, Bukavu, 570, D.R Congo

[2]Department of Biotechnology, Faculty of Sciences, Official University of Bukavu, Bukavu, 570, D.R Congo

Corresponding author: rhushenge@uob.ac.cd

Abstract

Metabolomics, the comprehensive study of small-molecule metabolites, has emerged as a transformative driver of agricultural innovation by linking genotype, environment, and phenotype. As the closest molecular reflection of plant performance, metabolites integrate gene expression, protein activity, and environmental influences, providing real-time insights into stress responses, yield, nutritional quality, flavor, and overall crop performance. Advanced analytical platforms, including LC–MS, GC–MS, CE–MS, and NMR, enable both targeted and untargeted profiling across diverse sample types such as leaves, roots, seeds, fruits, soil, and phloem sap. Integration with bioinformatics, artificial intelligence, and multi-omics approaches allows high-dimensional data interpretation, metabolite-based biomarker discovery, and predictive modeling, accelerating selection in breeding programs and guiding the development of climate-resilient, high-quality cultivars. Furthermore, metabolomics enhances food safety, quality control, and sustainable intensification by elucidating metabolic signatures associated with plant–microbe interactions, nutrient cycling, and environmental adaptation. Emerging trends such as single-cell and spatial metabolomics, real-time field analysis, AI-driven metabolite discovery, and metabolomics-informed gene editing position the discipline as a cornerstone of predictive, systems-driven, and sustainable agriculture in the face of climate change and global food security challenges.

Keywords: Metabolomics, sustainable, agriculture, transcripts, breeding

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1.Introduction

Metabolomics as a transformative tool in agriculture

Metabolomics is the comprehensive study of the metabolome, defined as the complete set of small-molecule metabolites produced by cells and tissues that directly participate in metabolic processes within an organism (Lee & Banerjee, 2020). As an emerging and rapidly advancing discipline, metabolomics constitutes a key component of the broader *omics* technologies, which encompass large-scale analytical approaches designed to systematically characterize biological molecules and to provide integrated insights into the structure, function, and dynamic regulation of living systems. These *omics* platforms are primarily aimed at the global, non-targeted, and unbiased detection and analysis of genes (genomics), messenger RNA transcripts (transcriptomics), proteins (proteomics), and metabolites (metabolomics) within a given biological sample (Horgan & Kenny, 2011).

The genomics is the study of the genome. The genome is the complete sequence of DNA in a cell or organism. This genetic material may be found in the cell nucleus or in other organelles, such as mitochondria. With the exception of mutations and chromosomal rearrangements, the genome of an organism remains essentially constant over time. Complete or partial DNA sequence can be assayed using various experimental platforms, including single nucleotide polymorphism (SNP) chips and DNA sequencing technology. SNP chips are arrays of thousands of oligonucleotide probes that hybridize (or bind) to specific DNA sequences in which nucleotide variants are known to occur. Only known sequence variants can be assayed using SNP chips, and in practice only common variants are assayed in this way. Genomic analysis also can detect insertions and deletions and copy number variation, referring to loss of or amplification of the expected two copies of each gene (one from the mother and one from the father at each gene locus). Personal genome sequencing is a more recent and powerful

technology, which allows for direct and complete sequencing of genomes and transcriptomes (see below). DNA also can be modified by methylation of cytosines (see Epigenomics, below). There is also an emerging interest in using genomics technologies to study the impact of an individual's microbiome (the aggregate of microorganisms that reside within the human body) in health and disease (Micheel et al., 2012).

The transcriptome is the complete set of RNA transcripts from DNA in a cell or tissue. The transcriptome includes ribosomal RNA (rRNA), messenger RNA (mRNA), transfer RNA (tRNA), micro RNA (miRNA), and other non-coding RNA (ncRNA). In humans, only 1.5 to 2 percent of the genome is represented in the transcriptome as protein-coding genes. The two dominant classes of measurement technologies for the transcriptome are microarrays and RNA sequencing (RNAseq). Microarrays are based on oligonucleotide probes that hybridize to specific RNA transcripts. RNAseq is a much more recent approach, which allows for direct sequencing of RNAs without the need for probes. Onco*type* DX, MammaPrint, Tissue of Origin, AlloMap, CorusCAD, and the Duke case studies described in Appendix A and B all involve transcriptomics-based tests(Micheel et al., 2012).

The proteome is the complete set of proteins expressed by a cell, tissue, or organism. The proteome is inherently quite complex because proteins can undergo posttranslational modifications (glycosylation, phosphorylation, acetylation, ubiquitylation, and many other modifications to the amino acids comprising proteins), have different spatial configurations and intracellular localizations, and interact with other proteins as well as other molecules. This complexity can lead to challenges in proteomics-based test development. The proteome can be assayed using mass spectrometry and protein microarrays. Unlike RNA transcripts, proteins do not have obvious complementary binding partners, so the identification and characterization of capture agents is critical to the success of protein arrays(Micheel et al., 2012).

The epigenome consists of reversible chemical modifications to the DNA, or to the histones that bind DNA, and produce changes in the expression of genes without altering their base sequence. Epigenomic modifications can occur in a tissue-specific manner, in response to environmental factors, or in the development of disease states, and can persist across generations.

The epigenome can vary substantially among different cell types within the same organism. Biochemically, epigenetic changes that are measured at high-throughput belong to two categories: methylation of DNA cytosine residues (at CpG) and multiple kinds of modifications of specific histone proteins in the chromosomes (histone marks). RNA editing is another mechanism for epigenetic changes in gene expression, measured primarily by transcriptomic methods (Micheel et al., 2012).

The metabolome is the complete set of small molecule metabolites found within a biological sample (including metabolic intermediates in carbohydrate, lipid, amino acid, nucleic acid, and other biochemical pathways, along with hormones and other signaling molecules, as well as exogenous substances such as drugs and their metabolites). The metabolome is dynamic and can vary within a single organism and among organisms of the same species because of many factors such as changes in diet, stress, physical activity, pharmacological effects, and disease. The components of the metabolome can be measured with mass spectrometry as well as by nuclear magnetic resonance spectroscopy. This method also can be used to study the lipidome, which is the complete set of lipids in a biological sample (Micheel et al., 2012).

Metabolites as closest link to phenotype and agronomic performance

Metabolites are widely regarded as the molecular entities most closely linked to phenotype and agronomic performance because they represent the integrated outcome of gene expression, protein activity, enzymatic regulation, and environmental influences(van der Knaap & Verrijzer, 2016). Unlike genes or transcripts, which primarily reflect biological potential, metabolite levels capture the *real-time physiological and biochemical state* of an organism (Joshua et al., 2014). As highlighted by Arbona et al., metabolite abundances integrate multiple upstream regulatory layers—including transcriptional control, post-translational enzyme regulation, and metabolic fluxes—making them more directly associated with macroscopic phenotypes than genomic or transcriptomic markers alone (Arbona et al., 2013). For this reason, metabolites are frequently used as predictive biomarkers in biomedical research, although their application in crop improvement has historically been underutilized (Steinfath et al., 2010).

The strong relationship between metabolites and phenotype becomes

particularly evident under environmental stress conditions, which are major determinants of crop productivity. Certain stress factors such as heat, drought, salinity, tropospheric ozone, and excess UV radiation might become even more prevalent having impact on crop yields, their effects on crop quality by induces numerous physiological stress reactions in plants that can alter the chemical composition of crops and thus the quality of the harvested products. (Y. Wang & Frei, 2011). These compounds play direct functional roles in maintaining cellular homeostasis, protecting macromolecules, and sustaining plant growth under adverse conditions(Seki et al., 2007). Given that drought-induced biochemical changes strongly influence yield stability, metabolic profiling provides a powerful approach to elucidate stress tolerance mechanisms and to identify metabolic markers closely associated with agronomic performance (Arbona et al., 2013).

Secondary metabolites further reinforce the intimate link between the metabolome and phenotype. These compounds are often species- or genotype-specific and are directly responsible for key phenotypic characteristics such as color, taste, aroma, and texture. In addition to defining quality traits, secondary metabolites play essential roles in signaling, enzyme activation, catalytic regulation, plant–environment interactions, and defense against pathogens and herbivores. Environmental stresses—responsible for approximately 30% of global pre- and post-harvest yield losses—frequently perturb plant metabolic networks, leading to measurable metabolite changes that precede visible phenotypic decline(Djande et al., 2020). The exceptional diversity and chemical complexity of the plant metabolome enable it to capture a broad spectrum of phenotypic variation that cannot be fully explained by genomic information alone.

At a systems level, the plant metabolome is increasingly recognized as the functional bridge between the genome and the phenome, with metabolites effectively defining phenotype in its broadest sense (Yang et al., 2017). The integration of metabolomics with quantitative genetics—through approaches such as metabolic quantitative trait locus (mQTL) mapping and metabolome-wide association studies—has substantially improved the ability to link metabolic variation with phenotypic diversity and agronomic traits(Shi et al., 2020). Large-scale studies combining high-resolution metabolite profiling with dense SNP maps have demonstrated that metabolite traits are heritable, genetically tractable, and predictive of complex agronomic

outcomes, including yield and stress resilience.

Collectively, these findings establish metabolites as the most proximal molecular determinants of phenotype and agronomic performance. By capturing the integrated effects of genetic variation, environmental conditions, and management practices, metabolomics provides a functional and predictive readout of plant performance. This positions metabolite-based biomarkers as powerful tools for accelerating crop breeding, improving stress tolerance, and driving innovation in modern agriculture.

a. Limitations of Traditional Breeding and the Value of Metabolomics

Conventional plant breeding and agronomic practices have traditionally relied on phenotype-based selection, focusing on observable traits such as yield, growth rate, or disease symptoms. While effective for simple traits, this approach is inherently limited when addressing complex, quantitative traits such as drought tolerance, nutrient-use efficiency, and yield stability, which are governed by multiple genes, interconnected metabolic pathways, and strong environmental interactions(Liu et al., 2023). Phenotypic selection often overlooks the biochemical mechanisms underlying plant performance, leading to long breeding cycles, slow genetic gains, and limited predictability across diverse and changing environments. Despite advances in genomics-assisted breeding and genome editing, substantial yield gaps persist in major crops, particularly under abiotic stress conditions intensified by climate change(Fernandez et al., 2021b; Fiehn, 2002)Metabolomics overcomes these limitations by capturing the downstream molecular layer that most directly determines phenotype. As metabolites integrate gene expression, enzyme activity, and environmental influences, the metabolome provides a real-time snapshot of plant functional status and acts as a bridge between genotype and phenotype(Luo, 2015). By revealing stress-induced metabolic reprogramming and identifying metabolite biomarkers associated with yield, stress tolerance, and nutritional quality, metabolomics enables early, accurate prediction of complex agronomic traits and accelerates breeding decisions (Steinfath et al., 2010). When integrated with quantitative genetics and other omics approaches, metabolomics supports rapid, cost-effective selection for climate resilience, productivity, and crop quality, positioning it as a critical innovation for next-generation agriculture.

b. Role of metabolomics in addressing global challenges:

Food security

Metabolomics has emerged as a powerful driver of agricultural and food-system innovation by addressing critical global challenges related to food security, safety, quality, authenticity, and sustainability. Because food metabolites are strongly influenced by genotype, environment, cultivation practices, processing, and storage, metabolomic profiling provides a sensitive and holistic approach for monitoring compositional changes across the entire food value chain(Yunindanova & Putri, 2024). Advanced metabolomics techniques enable rapid detection of food adulteration and fraud, such as mislabeling of fruit juices, substitution of premium grains, adulteration of dairy products and oils, and misrepresentation of meat freshness and origin, thereby protecting consumers and supporting regulatory compliance(Johanningsmeier, S.D. et al., 2016). In food safety, metabolomics allows simultaneous detection of pesticide residues, veterinary drugs, processing-induced toxins, and microbial contamination with higher throughput and sensitivity than traditional analytical methods (Shi et al., 2020). Moreover, metabolomics supports food quality control and traceability by discriminating cultivars, geographical origin, and production systems, and by optimizing processing methods to enhance nutritional value, shelf life, and sensory attributes (Liang et al., 2025). When integrated with genomics, transcriptomics, and proteomics, metabolomics further strengthens predictive breeding, crop yield improvement, and sustainable food production strategies, contributing directly to reduced food loss, improved nutrition, and the achievement of Sustainable Development Goals related to zero hunger, health, and responsible consumption (Yunindanova & Putri, 2024).

Climate change

Climate change poses a major threat to global agriculture through increased temperatures, drought, salinity, flooding, and elevated atmospheric CO_2, all of which profoundly disrupt plant metabolism and crop productivity. Metabolomics has emerged as a critical tool for decoding plant metabolic reprogramming under these stresses, revealing how primary and secondary metabolites—including sugars, amino acids, organic acids, polyamines, flavonoids, and phytohormones—mediate stress tolerance and adaptive plasticity(Bulut et al., 2025). Beyond plant intrinsic responses, metabolomics has transformed our understanding of climate resilience by elucidating the chemical

dialogue between plants and beneficial microbes in the rhizosphere. Stress-induced root exudates act as signals that recruit and shape beneficial microbial communities, enhancing nutrient acquisition, hormone regulation, antioxidant defenses, and resistance to drought, heat, and salinity (Olanrewaju et al., 2024). Metabolomics-guided microbiome engineering enables the identification of key metabolites and signaling pathways that underpin plant–microbe mutualism, facilitating the development of eco-friendly, microbe-assisted strategies for climate adaptation. When integrated with genomics and systems biology, metabolomics provides a predictive framework for engineering climate-resilient crops, reducing reliance on chemical inputs, improving yield stability, and supporting sustainable food production under rapidly changing environmental conditions (Bulut et al., 2025; Olanrewaju et al., 2024)

Sustainable intensification

Metabolomics plays a pivotal role in addressing global challenges related to sustainable agricultural intensification by enabling the development of climate-resilient, resource-efficient crops under increasing drought and water scarcity. By providing a systems-level view of plant metabolic reprogramming under drought stress, metabolomics identifies key metabolites—such as amino acids, sugars, organic acids, phenolamines, and secondary metabolites—that regulate osmotic adjustment, redox balance, and cellular protection, thereby underpinning stress tolerance and yield stability. As demonstrated by Raza et al. (2025), metabolomics serves as a predictive tool for linking metabolic phenotypes with plant performance, allowing the rapid discovery of metabolic biomarkers and their genetic determinants through integrative approaches such as mQTL and mGWAS. This metabolomics-driven molecular breeding framework accelerates the development of drought-smart cultivars capable of maintaining productivity with reduced water and input requirements, minimizing environmental impact while safeguarding food security. Consequently, metabolomics supports sustainable intensification by enabling crops to produce higher and more stable yields under climate stress, directly contributing to global goals of climate resilience and zero hunger (Raza et al., 2025)

Crop quality and safety

Metabolomics plays a critical role in addressing global challenges related to crop quality and safety by enabling comprehensive characterization of plant biochemical composition and its

modulation by genetics, environment, and agronomic practices(Głuchowska et al., 2025). Through high-resolution profiling of primary and secondary metabolites, metabolomics allows the detection of quality-defining compounds such as sugars, amino acids, lipids, vitamins, and flavor- and aroma-related metabolites, thereby supporting the improvement of sensory attributes, nutritional value(Bhalavey et al., 2026), and processing quality of crops. Importantly, metabolomics also enhances food safety by identifying and quantifying harmful metabolites, including mycotoxins, pesticide residues, and naturally occurring antinutritional or toxic compounds, and by revealing metabolic signatures associated with contamination, spoilage, or adulteration(Wu et al., 2022). Consequently, metabolomics provides a powerful, predictive framework for improving crop quality and ensuring food safety, thereby contributing to healthier diets, consumer protection, and sustainable agri-food systems worldwide.

Metabolomics technologies and methodologies relevant to agriculture

Metabolomics technologies and methodologies provide a powerful framework for advancing agricultural research by enabling comprehensive characterization of plant metabolic states and their responses to genetic, environmental, and management factors. In agriculture, both targeted and untargeted metabolomics approaches are applied using advanced analytical platforms such as gas chromatography–mass spectrometry (GC–MS), liquid chromatography–mass spectrometry (LC–MS), nuclear magnetic resonance (NMR), capillary electrophoresis–MS, and high-resolution hyphenated techniques, each offering distinct advantages in sensitivity, metabolite coverage, and structural elucidation(Ibarra-Estrada et al., 2016).

a.Analytical platforms

Studies of the plant metabolome include the analysis of a wide range of chemical species with very diverse physico-chemical properties, and therefore powerful analytical tools are required for the separation, characterization and quantification of this vast compound diversity present in plant matrices.

Metabolomics relies primarily on mass spectrometry (MS)–based techniques and nuclear magnetic resonance (NMR) spectroscopy, which together provide complementary coverage of the metabolome.

- **LC-MS:** is a chemistry technique that combines the physical separation

capabilities of liquid chromatography (or HPLC) with the mass analysis capabilities of MS. LC-MS is a powerful technique used for many applications, which has very high sensitivity and selectivity. Generally its application is oriented toward the general detection and potential identification of chemicals in the presence of other chemicals (in a complex mixture). A preparative LC-MS system can be used for fast and mass-directed purification of natural-product extracts and new molecular entities important to food, pharmaceutical, agrochemical, and other industries. LC-MS is the key analytical technique on which the emerging "-omics" technologies of proteomics, metabolomics, and lipidomics are based. It provides both structural and quantitative data and can be used in a global or targeted manner, allowing on the one hand the identification of thousands of proteins from a tissue, or on the other the detection of biologically active metabolites at levels of a few parts-per-billion (Tilvi et al., 2014)

- **GC-MS:** Gas chromatography coupled with mass spectrometry (GC–MS) has emerged as a vital tool in metabolomics, enabling the analysis of both volatile and nonvolatile compounds through derivatization methods. GC–MS is particularly effective in identifying and quantifying small molecular metabolite classes, including organic acids, sugars, amino acids, fatty acids, and toxins, often enhancing volatility through chemical derivatization. It typically utilizes extensive metabolite libraries, such as the National Institute of Standards and Technology library, which contains mass spectra for 399,267 unique compounds, while other techniques may offer more limited libraries. Various mass spectrometry techniques can be customized to meet specific analytical needs, such as the nature of the sample, sensitivity requirements, and the need for structural information(Jha et al., 2026).
- **CE-MS:** Capillary electrophoresis-mass spectrometry (CE-MS) is now a mature analytical technique in metabolomics, notably for the efficient profiling of polar and charged metabolites. Metabolites in volume-restricted samples, and in strategies that further enhance the metabolic coverage(Zhang & Ramautar, 2020).
- **NMR spectroscopy:** Nuclear Magnetic Resonance (NMR) spectroscopy is a major analytical method used in the growing field of metabolomics. NMR is relatively less sensitive relative to mass spectrometry, the other major analytical

platform in the metabolomics field. However, numerous characteristics of NMR including its high reproducibility and quantitative abilities, its non-selective and non-invasive nature, and the ability to identify unknown metabolites in complex mixtures and trace the downstream products of isotope labeled substrates *ex vivo, in vivo or in vitro* offer numerous benefits to the metabolomics field(Gowda & Raftery, 2021)

a.Targeted vs. untargeted metabolomics approaches

Targeted and untargeted metabolomics are the two principal analytical strategies used to profile metabolites, differing primarily in scope, purpose, and data output. In targeted metabolomics, a predefined set of well-characterized metabolites is measured with high specificity and sensitivity, often using internal standards to achieve absolute quantification, optimized sample preparation, and streamlined data analysis for hypothesis-driven research such as pathway validation or biomarker verification. In contrast, untargeted metabolomics aims to survey *all detectable metabolites* in a sample, capturing thousands of features (including unknown compounds) to provide a comprehensive, unbiased metabolic fingerprint for discovery, biomarker identification, and systems-level insight. Untargeted workflows are inherently more complex due to the need for extensive data preprocessing, multivariate statistics, and metabolite annotation, and typically yield relative rather than absolute quantification. While targeted approaches excel in precision and quantitative accuracy, they are limited by prior knowledge of targets and the availability of reference standards, whereas untargeted methods provide broader coverage but require greater computational effort and face challenges in identifying unknowns. Hybrid strategies that combine both approache (or "semi-targeted" analysis with larger but defined compound sets) are increasingly used to balance discovery with quantitative rigor, enhancing metabolomic investigations across biomedical, agricultural, and food science applications(Couacault et al., 2024; J. Singh et al., 2025)

a.Sample types in agriculture

In agricultural metabolomics, a wide range of **sample types** is analyzed to capture spatially and functionally distinct metabolic processes that underpin plant growth, stress responses, yield, and quality. **Leaves** are commonly sampled to study photosynthesis, primary metabolism, and responses to abiotic stresses such as

drought, heat, and salinity, while **roots** provide insights into nutrient uptake, root–microbe interactions, and below-ground stress adaptation. **Seeds** are key targets for assessing storage metabolites (starch, lipids, proteins), nutritional quality, and traits linked to germination and yield stability. **Fruits** are extensively profiled to understand metabolites governing flavor, aroma, color, ripening, and post-harvest quality, which are critical for consumer acceptance and food safety. Beyond plant tissues, **soil** and the **rhizosphere** (the soil region influenced by root exudates) are increasingly analyzed to characterize plant–microbe–soil metabolic interactions that regulate nutrient cycling, disease suppression, and sustainable productivity. Finally, **phloem sap** represents a highly informative but technically challenging sample type, reflecting long-distance transport of sugars, amino acids, hormones, and signaling metabolites that directly link source tissues to sink organs and agronomic performance. Together, these diverse sample matrices enable a systems-level understanding of crop metabolism across plant organs and their environment, strengthening the application of metabolomics in crop improvement and sustainable agriculture (Fernie & Tohge, 2017; Raza et al., 2025; Sardans et al., 2011)

a.Data processing and annotation challenges

Data processing and metabolite annotation represent critical bottlenecks in metabolomics because high-resolution LC–MS, GC–MS, and NMR platforms generate large, complex datasets that require multiple preprocessing steps, including peak detection, deconvolution, alignment, normalization, and quality control, each of which can substantially influence downstream biological interpretation(Hooft & Hanhineva, 2021). A major challenge arises at the metabolite identification stage**,** where only a small fraction of detected spectral features can be confidently assigned chemical identities due to the chemical diversity of metabolites, limited availability of authentic standards, and incomplete spectral libraries, particularly for plant secondary metabolites(Sumner et al., 2007). Database-driven annotation further constrains confidence levels: KEGG is widely used for pathway mapping but offers limited experimental MS/MS spectra(Kanehisa et al., 2023); HMDB provides extensive chemical and spectral data but is largely human-centric and less representative of plant and crop metabolites(Wishart et al., 2022); METLIN contains one of the largest MS/MS libraries yet still lacks

comprehensive coverage of plant-specific compounds(Guijas et al., 2018); and PlantCyc is highly relevant for plant metabolism and pathway reconstruction but remains incomplete in terms of experimentally validated metabolite spectra(Hawkins et al., 2025). As a result, most metabolites in agricultural metabolomics studies are reported as putatively annotated (MSI levels 2–3), limiting cross-study comparability, pathway integration, and translational applications in crop improvement and food systems(Fernie & Tohge, 2017).

a.Integration with bioinformatics and AI tools.

Integration of metabolomics with bioinformatics and artificial intelligence (AI) tools has become essential for extracting biological meaning from high-dimensional metabolomics data and for translating metabolic variation into actionable agricultural insights. Bioinformatics pipelines enable automated preprocessing, statistical analysis, pathway mapping, and multi-omics integration, allowing metabolites to be linked with genes, transcripts, proteins, and phenotypes(Pang et al., 2021). Machine learning (ML) and AI approaches—including random forests, support vector machines, deep learning, and neural networks—are increasingly used to handle nonlinear relationships in metabolomic datasets, improve biomarker discovery, classify stress responses, and predict complex agronomic traits such as yield, quality, and stress tolerance (Ghahramani, 2015). In agriculture, AI-driven metabolomics has enabled the prediction of drought and disease resistance, identification of metabolite-based selection markers, and acceleration of breeding pipelines by linking metabolic fingerprints directly to performance traits(van Dijk et al., 2022). Moreover, advances in network analysis and systems biology models allow reconstruction of metabolic networks and inference of regulatory mechanisms underlying genotype × environment interactions, positioning AI-enhanced metabolomics as a cornerstone of data-driven, precision agriculture and next-generation crop improvement strategies (Tong & Nikoloski, 2021).

Metabolomics in crop improvement and plant breeding

Metabolite-based phenotyping (metabotyping) uses comprehensive metabolite profiles as quantitative descriptors of plant phenotypes, providing a biochemical readout that is closer to the functional state of the organism than genomic or transcriptomic data. Because metabolites integrate genetic regulation and environmental influences,

metabotyping captures genotype × environment interactions more effectively than traditional phenotype-based selection. This approach has been successfully applied to predict complex agronomic traits such as biomass, yield, and stress tolerance, positioning metabolomics as a central component of next-generation phenotyping platforms in plant breeding (Fernandez et al., 2021a).

Identification of metabolic markers linked to yield, nutritional quality, flavor, and aroma. Metabolomics enables the identification of specific metabolites that serve as reliable markers for key crop traits, including yield components, nutritional composition, and sensory attributes such as flavor and aroma. Primary metabolites such as sugars, amino acids, and organic acids are often associated with yield and grain quality, while secondary metabolites, including phenolics, terpenoids, and alkaloids, contribute to nutritional value, taste, aroma, and consumer preference. The use of such metabolic markers allows early and accurate selection of superior genotypes, moving breeding objectives beyond yield alone toward quality-oriented and consumer-driven traits(K. S. Singh et al., 2022).

Metabolite quantitative trait loci (mQTL) mapping: It integrates metabolite profiling with genetic linkage analysis to identify genomic regions controlling metabolite abundance. By treating metabolites as quantitative traits, mQTL analysis provides mechanistic insight into the genetic regulation of metabolic pathways and helps bridge the gap between genotype and phenotype. Numerous studies have demonstrated that mQTLs often co-localize with QTLs for agronomic traits, highlighting metabolites as intermediate phenotypes that can clarify the biological basis of complex trait variation(Fernie & Tohge, 2017).

Genome–metabolome associations (mGWAS): Metabolome-wide genome-wide association studies (mGWAS) extend traditional GWAS by associating natural genetic variation with metabolite levels across diverse populations. This approach has proven particularly powerful for dissecting complex metabolic traits, identifying candidate genes, and uncovering novel regulatory loci involved in primary and secondary metabolism. In major crops such as maize, rice, and wheat, mGWAS has revealed extensive genetic control of metabolic diversity and established direct links between allelic variation, metabolic pathways, and agronomic performance(Matsuda et al., 2015; Wen et al., 2014).

Accelerating selection in breeding programs: By using metabolites as predictive indicators of complex traits, metabolomics significantly accelerates selection in breeding programs. Metabolic profiles can be measured at early developmental stages and under controlled conditions, reducing the need for long and costly multi-environment field trials. When integrated with genomic selection and phenomics, metabolomics improves prediction accuracy for yield, quality, and stress tolerance, thereby enhancing breeding efficiency and supporting the development of climate-resilient and nutritionally improved crops(Fernandez et al., 2021b)

Stress biology and climate-resilient agriculture

Metabolic reprogramming under abiotic stresses: Under drought, plants commonly accumulate osmoprotective metabolites such as proline, trehalose, raffinose, and sucrose, which stabilize proteins and membranes and maintain cellular turgor (Obata & Fernie, 2012). Salinity stress induces shifts in ion-balancing metabolites (e.g., organic acids such as malate and citrate) and nitrogen metabolism, particularly amino acids like glutamate and asparagine (Kosová et al., 2011). Heat and cold stresses strongly affect lipid metabolism, leading to changes in fatty acid unsaturation, galactolipids, and membrane-associated sterols, while heavy metal stress promotes synthesis of chelators such as organic acids and sulfur-containing metabolites (glutathione, phytochelatins) to detoxify metals (Sun et al., 2023).

Stress biomarkers: osmolytes, antioxidants, and phytohormones: Metabolomics has identified reliable stress biomarkers across crops, including proline, glycine betaine, and mannitol as osmolytes under drought and salinity; ascorbate, glutathione, and tocopherols as antioxidants mitigating oxidative damage; and phytohormones such as abscisic acid (ABA), jasmonic acid (JA), and salicylic acid (SA) as key signaling molecules in stress perception and response (Khan et al., 2025; Kosová et al., 2011).

Early stress detection using metabolic signatures: Metabolic changes often precede visible stress symptoms, enabling early diagnosis. For example, drought-stressed wheat exhibits rapid increases in proline, branched-chain amino acids, and sugar alcohols before reductions in biomass are detectable(Michaletti et al., 2018; Roy et al., 2024). In maize, heat stress induces early perturbations in TCA-cycle intermediates and lipid-derived metabolites, which predict yield losses at later developmental stages (Sustek-

Sánchez et al., 2022). These findings highlight metabolomics as a sensitive early-warning system for crop stress monitoring under field and controlled conditions.

Crop-specific case studies in climate resilience: In rice, metabolomics has linked drought tolerance to enhanced accumulation of raffinose family oligosaccharides, polyamines, and ABA-related metabolites, distinguishing tolerant landraces from susceptible varieties(Casartelli et al., 2018). In maize, salt-tolerant genotypes show elevated levels of organic acids, proline, and phenylpropanoids, supporting osmotic adjustment and antioxidant defense (Głuchowska et al., 2025). Soybean metabolomic studies revealed that increased isoflavones and amino acid remodeling are associated with heat and drought tolerance, while in barley and wheat, maltose and sucrose accumulation correlates with cold acclimation capacity (Fang et al., 2025; Głuchowska et al., 2025)

Metabolomics-guided development of stress-tolerant cultivars: By integrating metabolomics with genomics, breeders can associate stress-responsive metabolites with genetic loci (mQTLs and mGWAS), enabling faster selection of resilient genotypes. For example, rice mGWAS studies identified loci controlling ABA, flavonoids, and amino acid metabolism that contribute to drought tolerance, while wheat mQTL mapping linked osmolyte accumulation to grain yield stability under water limitation. Such metabolite-guided strategies reduce breeding cycles and improve precision in climate-resilient crop development.

Integration with multi-omics and systems agriculture

Integrated multi-omics approaches that combine metabolomics with genomics, transcriptomics, and proteomics enable a systems-level understanding of crop performance by linking genetic variation and regulatory processes to biochemical phenotypes and agronomic traits. Because metabolites represent the functional endpoint of biological regulation and environmental interaction, metabolomics plays a central role in translating multi-omics data into predictive models of yield, stress tolerance, and quality(Fernie & Tohge, 2017). Systems biology frameworks, including metabolic network reconstruction and flux modeling, have been successfully applied to describe carbon and nitrogen allocation, stress-induced trade-offs, and genotype–environment interactions in major crops. When coupled with digital agriculture platforms and high-throughput phenotyping, metabolomics-driven models

support predictive analytics for precision breeding and crop management. The application of machine learning and artificial intelligence is increasingly essential for handling high-dimensional metabolomics and multi-omics datasets, enabling biomarker discovery, genotype classification, and phenotype prediction with high accuracy(Fan et al., 2025). Collectively, the integration of metabolomics, multi-omics data, and AI transforms agriculture from a descriptive discipline into a predictive, systems-driven science capable of addressing productivity, resilience, and sustainability challenges under climate change conditions.

Challenges, limitations, and ethical considerations

Despite its transformative potential, the widespread adoption of metabolomics in agriculture faces several technical, economic, and ethical challenges. High costs associated with advanced analytical platforms (LC–MS, GC–MS, NMR), skilled personnel, and computational infrastructure limit accessibility, particularly in low- and middle-income regions. The lack of standardization of the data production methods, together with the expression of results in a semi-quantitative manner, are frequently highlighted as factors preventing the sharing and reuse of metabolomics data, and their integration into multi-omics models(Castelli et al., 2022).

Moreover, metabolite annotation remains a major bottleneck in plant sciences due to the vast chemical diversity of plant metabolites and incomplete reference databases, resulting in a large proportion of unidentified or ambiguously annotated features(Ivanisevic & Want, 2019). Translating metabolomics insights from controlled laboratory or greenhouse conditions to heterogeneous field environments also remains challenging because of strong genotype – environment – management interactions (Alexandersson et al., 2014). Beyond technical barriers, ethical and socio-economic concerns related to data ownership, access, and benefit sharing—especially when metabolomics data are integrated with genomic and agronomic datasets—raise questions about equity, intellectual property, and the concentration of innovation within large agribusinesses(Amentae et al., 2024). Addressing these challenges through standardized workflows, open-access databases, cost-reduction strategies, and inclusive data governance frameworks is essential for ensuring that metabolomics contributes equitably and effectively to sustainable agricultural innovation

Future perspectives

The field of metabolomics is poised to enter a new era driven by technological innovation, computational advances, and deeper integration with plant biology and agriculture. One frontier is single-cell and spatial metabolomics, which seeks to resolve metabolite distributions at cellular and tissue scales, thereby revealing cell-type–specific metabolic states during development, stress responses, and plant–microbe interactions(Artyomov & Van den Bossche, 2020). Emerging mass spectrometry imaging (MSI) techniques and advances in spatially resolved sampling are enabling unprecedented insight into metabolic heterogeneity within organs such as roots, leaves, and seeds, opening the door to more targeted breeding and functional studies(X. Wang et al., 2023). Complementing this, real-time and in-field metabolomics—leveraging portable MS/NMR sensors and ambient ionization methods—will allow dynamic monitoring of crop metabolic states under actual growing conditions, facilitating responsive management and early stress detection directly in the field(Gautam et al., 2025).

As metabolomics datasets grow in size and complexity, artificial intelligence (AI)–driven metabolite discovery and annotation are rapidly transforming how data are interpreted. Deep learning models can predict chemical structures from spectral data, accelerate feature annotation, and uncover latent patterns linking metabolites to phenotypes(Coler et al., 2024). These AI tools will become integral to metabolomic pipelines, enabling rapid discovery of biomarkers for yield, quality, and resilience. At the interface of biology and engineering, metabolomics-guided gene editing and synthetic biology provide transformative opportunities to reshape crop metabolic pathways with precision. By identifying rate-limiting enzymes and regulatory nodes, metabolomics can inform CRISPR/Cas-based editing strategies and synthetic circuit designs that enhance stress tolerance, nutrient content, and resource use efficiency(Guo et al., 2025).

Finally, metabolomics is increasingly recognized as a cornerstone of sustainable and regenerative agriculture**.** By elucidating metabolite signatures associated with soil health, nutrient cycling, and plant–microbe interactions, metabolomics can guide the design of crop rotations, cover cropping systems, and microbial amendments that support ecosystem function. Metabolomic profiles of rhizosphere exudates will help tailor biological inputs to promote beneficial microbiomes that enhance carbon sequestration and reduce dependence on chemical fertilizers(Yusuf et al., 2025).

Together, these emerging trends position metabolomics as a catalyst for next-generation agriculture—one that is predictive, adaptive, and aligned with sustainability goals in the face of climate change.

Conclusion

Metabolomics has emerged as a transformative force driving agricultural innovation by providing the most direct and functional molecular link between genotype, environment, and phenotype. Throughout this chapter, it is evident that metabolites capture the integrated outcomes of genetic regulation, enzymatic activity, and environmental interactions, positioning metabolomics as a uniquely powerful tool for understanding and predicting agronomic performance. Unlike traditional breeding approaches that rely on visible traits or upstream molecular markers alone, metabolomics offers a real-time biochemical snapshot of plant function, enabling early, precise, and mechanistic insight into complex traits such as yield stability, stress tolerance, nutritional quality, and food safety.

Advances in analytical technologies, data processing, and AI-enabled bioinformatics have greatly expanded the scope and resolution of agricultural metabolomics, allowing comprehensive profiling across diverse tissues, developmental stages, and environmental conditions. When integrated with genomics, transcriptomics, proteomics, and quantitative genetics, metabolomics strengthens systems-level models of crop performance and accelerates breeding pipelines through metabolite-based phenotyping, mQTL mapping, and metabolome-wide association studies. These integrative approaches are reshaping crop improvement into a predictive, data-driven discipline capable of addressing pressing global challenges, including food security, climate change, sustainable intensification, and crop quality and safety.

At the same time, significant challenges remain, including high costs, data complexity, metabolite annotation gaps, and the translational divide between controlled experiments and field conditions, alongside ethical concerns related to data ownership and equitable access. Addressing these barriers through standardization, open data infrastructures, cost reduction, and inclusive governance will be essential to fully realize the potential of metabolomics. Looking ahead, emerging trends such as single-cell and spatial metabolomics, real-time field applications, AI-driven discovery, and metabolomics-guided gene editing promise to further deepen our understanding of

plant systems and to enable more resilient, sustainable, and productive agricultural systems. Collectively, metabolomics stands not merely as a complementary omics technology, but as a central pillar of next-generation agriculture, driving innovation toward a more predictive, adaptive, and sustainable global food system.

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