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Towards superior plant-based foods using metabolomics

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Metabolomics is proving a useful approach for many of the main future goals in agronomy and food production such as sustainability/crop resilience, food quality, safety, storage, and nutrition. Targeted and/or untargeted small-molecule analysis, coupled to chemometric analysis, has already unveiled a great deal of the complexity of plant-based foods, but there is still 'dark matter' to be discovered. Moreover, state-of-the-art food metabolomics offers insights into the molecular mechanisms underlying sensorial and nutritional characteristics of foods and thus enables higher precision and speed. This review describes recent applications of food metabolomics from fork to farm and focuses on the opportunities these bring to continue food innovation and support the shift to plant-based foods.

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Introduction

The food industry faces enormous challenges to continue to deliver tasty, healthy and sustainable foods in the future. Climate change, resource shortage, production efficiency, environmental consciousness, health awareness and sensorial quality requirements are some factors that need to be seriously taken into account when producing foods that live up to the demands of consumers while protecting the planet.

The basis of food innovation is having a thorough understanding of molecular mechanisms underlying their observable characteristics. Most foods, however, are complex, comprising multiple ingredients and/or are based on natural sources, and thus require thorough molecular analysis in order to start exploring and steering structure-function relationships. The depth of our knowledge of food ingredients and functions is still remarkably limited, and the (in)direct impact of food ingredients on our physiology may also be grossly underestimated as was recently referred to as 'The Dark Matter of Nutrition' [1••]. Metabolomics is a large-scale analytical approach for small molecules allowing for a comprehensive overview of biological systems or other complex materials. Since 2000 it has successfully found its way into many aspects of life [2] and also food [3] sciences.

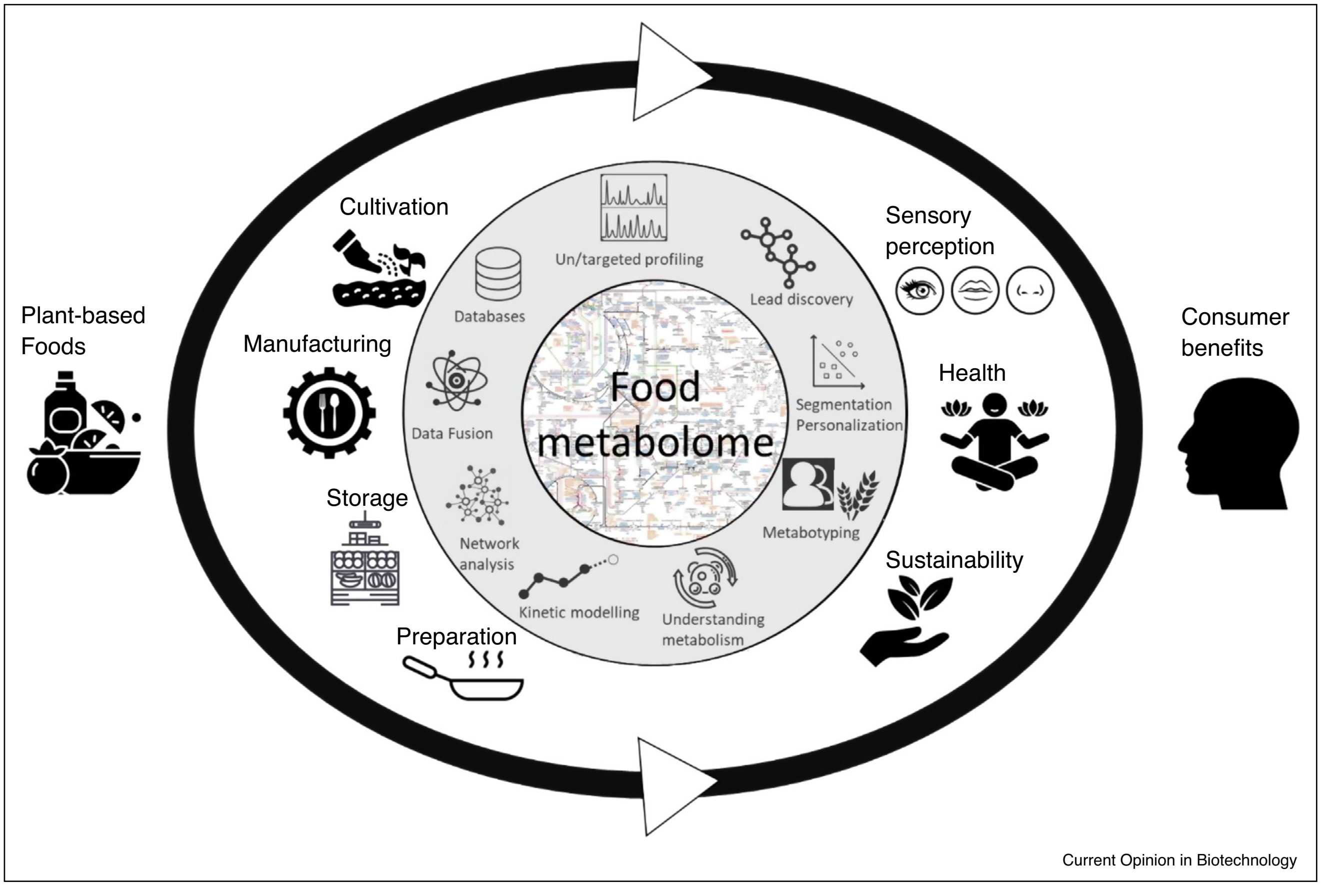
The advantage of metabolomics, as opposed to genomics and proteomics, is its close link to the phenotype or food characteristics. However, the huge diversity of chemical structures and the large differences in abundance are major challenges and there is no single technology capable of covering the entire metabolome. Depending on the question(s) to be addressed, untargeted and/or targeted profiling methods based on nuclear magnetic resonance spectroscopy, liquid chromatography-mass spectrometry or gas-chromatography-mass spectrometry are typically applied and coupled to multivariate statistics and pathway analysis to extract the relevant information.

There are manifold applications for metabolomics in food systems. Recently, Kim *et al.* reviewed them 'from farm to human' including food resource production, industrial food processing and food intake [4••]. Here, we will specifically focus on plant-based foods considering their growing future demand and report recent advances across the food chain aimed at enhancing the nutritional and sensorial quality of foods (Figure 1).

Crop selection and cultivation

A role for metabolomics was quickly found in the field of crop science where there is a strong desire to first understand better the basic chemical composition of plant-based foods — be they fresh or processed [1••] — and then correlate phenotype (flavour, appearance, nutritional value etc.) with chemotype [5]. But ultimately, from a crop improvement perspective we also need to link these findings to genotypic differences in order to facilitate the breeding process in delivering improved varieties as well as guiding food processors towards more sustainable and healthier consumer products. Certain crops emerged early to become model crops for the broad application of (metabol)-omics such as tomato [6•] and rice [7]. However, more recently, interest and application have become much broader to include many other major and minor crops such as grains [8] and lettuce [9]. Metabolomics is

Figure 1



Sketch illustrating how metabolomics can contribute to enhance the nutritional, sensorial and climate smart food production through cultivation, processing, preparation and storage.

proving a very useful approach for many of the main future agronomic goals such as sustainability/crop resilience [10], food quality [11••], food safety [12], food fortification [13] and the shelf life of fresh food materials [14]. It is here where untargeted approaches are especially valuable as our basic knowledge of the chemical background of the targets concerned (disease resistance, drought tolerance, flavour, etc.) is still limited (Box 1).

Food processing

The food industry aims to manufacture safe and sustainable foods with a desired balance between nutritional and sensorial quality. Metabolomics has aided our metabolic and functional understanding of the microbial communities and their impact on food products during fermentation of, for example, beer [15]. Considering the growing demand for plant-based foods, production and processing of non-animal proteins becomes an important target. Here, our understanding of the role of small molecules, peptides and proteins in taste and texture is still incomplete [16•]. Many studies have also unveiled chemical changes upon different heat treatments (e.g. coffee [17], pea protein beverage [18]) and drying technologies (e.g. tomato powder [19]). Thermal treatment or even changing the order of thermal and mechanical processing steps can alter the phytonutrient profiles and thus their bioaccessibility [20]. Moreover, heat can induce Maillard reactions between amino acids and reducing sugars that may lead to the formation of carcinogenic compounds and off-flavours, but also to desired savoury notes [21••]. For example, the evidence of advanced glycation end-products (AGEs) in processed foods is conflicting, except for a few cases (acrylamide, heterocyclic amines and 5-hydroxymethylfurfural) which potentially are toxic or carcinogenic [22]. Controlling the flavour formation, in particular Maillard reactions, is still challenging mainly due to the complexity of the reactions (Figure 2). It remains to be investigated to what extent novel approaches such as Reverse Pathway Engineering (RPE) where aroma molecules are linked to their possible metabolic precursors via plausible chemical and/or enzymatic reactions using bioinformatic analysis can direct flavour formation [23]. In addition, the time-dependent volatile release from complex food matrices [16•] is typically not considered but is

Box 1 Metabolomics in a nutshell

Metabolomics is dedicated to the analysis of the small molecules present in all living organisms. These small molecules determine many of the important features of crop plants and their derived food products. Included here are nutritional value, taste, fragrance, colour, disease resistance, abiotic stress tolerance, appearance, spoilage off-flavours and many more. The chemicals concerned cover the most important nutritional food ingredients such as sugars, amino acids, fatty acids, and so on, but also a myriad of 'minor' components including phenolics, terpenoids, alkaloids, and so on, which determine food quality and influence consumer perception and preference. Metabolomics approaches are centered around the use of state-of-the-art extraction, separation and detection technologies for both volatile and non-volatile components to generate rich datasets covering usually 1000's of metabolites which are then subjected to dedicated data processing and univariate or multivariate statistical software packages in order to mine the data for chemotype-relevant information.

important for the overall flavour of a food. Here, real-time techniques such as selected ion flow tube mass spectrometry (SIFT-MS) [24] or near infrared sensors [25] can play a prominent role in monitoring critical flavour-active molecules from manufacturing facility to the eventual release of flavours.

Food preparation

Knowing the nutritional and sensorial changes occurring in foods, from preparation to the table, are essential for consumers to make decisions about how to prepare healthy and tasty foods at home. Metabolomics has expanded our current knowledge to a broader range of molecules beyond vitamins, macronutrients and minerals. For example, different brewing methods of coffee [26] alter phytochemical composition which may further promote health benefits or risks. Furthermore, cooking plants rich in slowly digestible starch can have a profound impact on the gut microbiome and its function, and modulate host energy status [27]. Moreover, cooking can modulate the flavour profile. For example, pleasant aromas were identified from aromatic rice during cooking which may enable breeding programs to target markets with greater accuracy [28].

Ripening and storage of fresh and processed foods

Pre-harvest and post-harvest treatments of fresh foods and food ingredients are hugely influential to both quality and shelf-life attributes and ultimately, overall crop and product sustainability. Metabolomics is now regularly employed to investigate key aspects of fruit ripening physiology in, for example, strawberry [29] and tomato [30]; to determine the optimal time of harvest for tea [31] and to identify conditional determinants of overall quality depreciation during storage of a wide range of foodstuffs [32,33]. For fresh fruits and (leafy) vegetables in particular, shelf-life determines the value both to the supermarket and the consumer. Too short shelf lives are a major cause of commercial and domestic food waste which heavily impacts sustainability [34]. All food products, including dry ingredients and processed foods, deteriorate in time as a result of, for example, lipid oxidation, non-enzymatic reactions, autolysis, and so on. Here, also metabolomics is being used to help optimize storage conditions to reduce or delay off-flavour formation, discolouration and nutritional losses as in, for example, pea protein flavour [35], green coffee beans ([36] and food flavourings [21••]. Increased chemical knowledge through metabolomics analyses is already greatly contributing to improving food chain sustainability before and after products enter the factory and supermarket. For example, the ripeSense® concept (http://www.ripesense.co.nz/) is an excellent early proof-of-concept of what can be done by exploiting biochemical knowledge on fruit ripening with smart sensor technology to empower the consumer to make the right product choice in the supermarket.

Food consumption

Sensory quality

The sensory perception of a food product is still one of the most dominant quality criteria for consumer acceptance. However, products can only be optimized to their desired color, flavour and texture characteristics when their molecular drivers are known. The holistic approach of metabolomics helps considerably towards a better understanding by differentiating products with varying flavour qualities (e.g. soy sauce [37]), by identifying relevant and/or novel markers (review on fresh plant-based products [11••]), by improving flavour retention [16•] or by providing insights into the biosynthesis of sensory-relevant constituents (e.g. tea [38]).

Multiple analytical techniques including both volatile and non-volatile analyses have been more frequently utilized for a wider coverage of the sensory and molecular space (e.g. rice [7]). A few studies have also included consumer liking data to elucidate consumer preferences already at an early stage (e.g. mandarins [39]).

The relationships between flavour molecules and sensory attributes are complex, and chemometric models are indispensable to extract the relevant information. However, statistical relationships are not necessarily causal and require validation, for example, using chemosensory re-engineering experiments. In fact, the Sensomics concept comprises a whole workflow geared towards the discovery of sensory-active molecules [40]. It has been successfully applied to various foods in characterizing off-flavour (e.g. olive oil [41]), but also in food development (e.g. chocolate [42]). For instance, sensory-guided fractionation of thermally treated yeast extracts has provided insights into the conditions enhancing synthesis of bitter

Figure 2

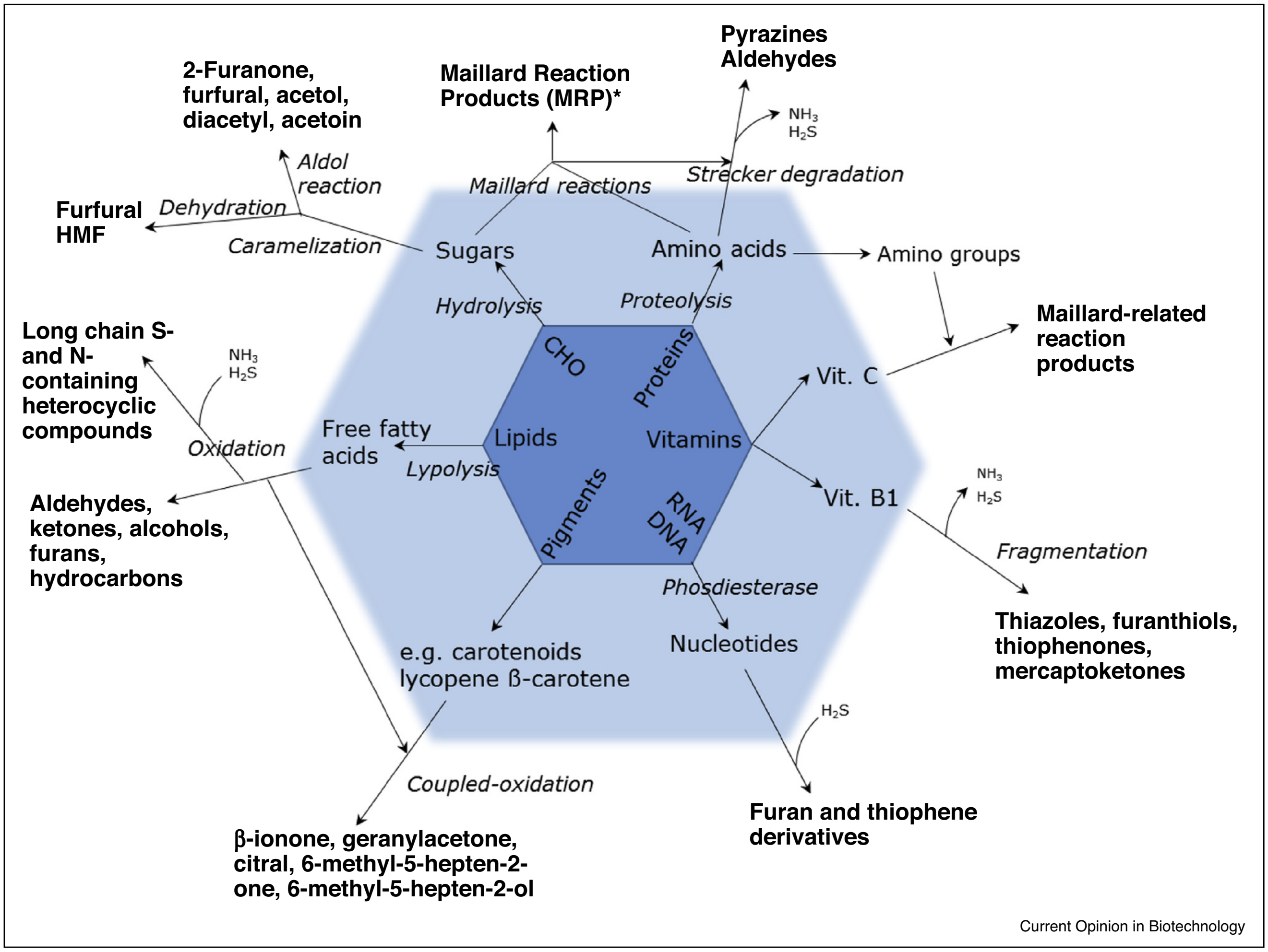


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Figure illustrating the complexity of the biochemistry behind food composition which arises during the processing of plant-based starting materials containing the basic set of typical nutrient classes (centre) through a variety of enzymic, chemical and thermo-induced reactions (middle) to produce sensory-relevant food bioactives (outside) comprising a wide variety of structural and chemical properties. In this case the illustration refers solely to volatile molecules which are of particular relevance to food aroma. (This figure has been reproduced from Diez-Simon *et al.* [24] with kind permission of the publisher Springer Nature. The figure has not been modified and is licensed under the Creative Commons license (http://creativecommons.org/licenses/by/4.0/)).

peptides maximizing umami flavour while maintaining bitterness in an acceptable range [43].

Nutritional value

Metabolomics has become an integral part of nutrition research pursuing two main objectives, (i) to quantify food intake [44••] and (ii) to determine the endogenous effects of dietary constituents on the host metabolism after a period of consumption (review in Ref. [45]).

Many potential biomarkers have been related to the intake of various foods such as coffee, tea, wine, nuts, vegetables, legumes, fruits and sugar-sweetened beverages [44••]. Among them, proline/betaine and tartaric acid are already well-established markers for citrus and grape intake, respectively. Most are curated in databases, such as Food Component Database (www.foodb.ca), Phenol-Explorer (www.phenol-explorer.eu), Human Metabolome Database (www.hmbd.ca), and PhytoHub (www.phytohub.eu).

Quantifying food intake facilitates more accurate and personalized dietary recommendations as a result of (i) more objective biomarker measurements — as opposed to questionnaires — and (ii) taking into account the inter-individual variation in digestion, absorption, metabolism and excretion (ADME) of food constituents. Knowing how food components are metabolized by the human host or gut microbiome helps to establish better relationships with health outcomes. A review on the healthy benefits of food intake markers is beyond the scope of this review. However, there is a growing body of evidence that many plant-based bioactives including macronutrients and micronutrients, dietary fibers, and phytochemicals such as (poly)phenols, carotenoids, glucosinolates, alkaloids, terpenes, peptides, and so on. likely play key roles in the prevention of cardiometabolic diseases [46]. Others, such as mycotoxins, pose serious risks in humans and animals.

Conclusion and outlook

Over the past few years metabolomics has produced an enormous amount of information allowing manufacturers to develop foods with superior nutritional and sensorial quality from fork to farm. The sustainability aspect is rather new, but runs like a thread through the entire food chain starting from investigations of plants under stress conditions [47•], to comparing net-house and open-field farming [48], to greener extraction of bioactives from natural sources [49], to waste optimization [50], to name but a few novel applications.

Metabolomics certainly has already unraveled a great deal of the complexity of plant-based foods, but there is more to do. On the one hand, there is still ‘dark matter’ to be discovered where the identification of unknowns is a major bottleneck. On the other hand, more effort is needed to turn the mostly descriptive changes into applicable knowledge. Open-source databases, absolute quantification, validation of markers, robust prediction models and comprehensive pathway analysis are key to further distill the wealth of information and ultimately to give us control over cultivation, processing, storage and intake conditions. Furthermore, metabolomics also needs to continue enhancing precision and speed to keep pace with food innovations nowadays finding their way to the consumer faster and faster. Here, real-time monitoring techniques together with computational tools have much to offer to control quality, predict dynamics and accelerate food production processes. Last but not least, the concepts of plant phenotyping and metabotyping in nutrition hold great potential to reduce the variability between plants and better understand individual consumer responses and thus target-specific subgroups.

Conflict of interest statement

Doris M. Jacobs and Marco A. van den Berg are employed by companies that manufacture and market food products.

CRediT authorship contribution statement

Doris M Jacobs: Writing - review & editing. **Marco A van den Berg:** Writing - review & editing. **Robert D Hall:** Writing - review & editing.

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