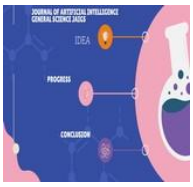
ISSN: 3006-4023 (Online), Vol. 2, Issue 1
Journal of Artificial Intelligence General Science (JAIGS)

Journal Homepage: **https://ojs.boulibrary.com/index.php/JAIGS**



Harnessing AI and Gut Microbiome Research for Precision Health

Ritcha Saxena[1]*, Vikas Sharma[2], Ananya Raj Saxena[3], Aakash Patel[4]

[1]*Department of Biomedical Sciences, University of Minnesota School of Medicine, Duluth, Minnesota, USA.

[2] Department of Computer Sciences, Delhi Technological University, New Delhi, India

[3] All Saints University School of Medicine, Dominica

[4] Department of Clinical Sciences, Medical University of the Americas, Nevis, West Indies

Abstract

The gut microbiome's impact on physiological processes, influenced by diet and lifestyle, is profound. Dysbiosis, an imbalance in microbiota composition, is associated with diseases like obesity. This review explores the gut microbiome's role in metabolism and calorie intake, alongside recent AI advancements impacting personalized nutrition. AI has revolutionized microbiome research, especially in multi-omics data analysis. AI-driven approaches enable the integration and interpretation of diverse omics datasets, including genomics, metabolomics, and proteomics, providing comprehensive insights into the gut microbiome's functional dynamics and its impact on host metabolism. These facilitate the identification of microbial biomarkers associated with disease states and dietary interventions, paving the way for personalized nutrition strategies tailored to individual gut microbiome profiles.

AI platforms can also offer tailored dietary recommendations based on microbiome composition and health objectives. Healthcare professionals leverage AI to optimize dietary interventions, promoting gut microbiome modulation and preventing chronic diseases. Challenges like data standardization and privacy persist, yet addressing them is vital for maximizing AI's benefits in health outcomes and precision medicine. Ongoing AI and microbiome research promise to revolutionize personalized nutrition and metabolic health worldwide.

Keywords: Gut microbiome, Calorie intake, Dysbiosis, Short-chain fatty acids, Obesity, Artificial intelligence in healthcare, Multi-omics, Personalized nutrition, Biomarkers

Article Information:
Received: 20/10/2023 *Revised:* 30/11/2024 *Accepted:* 10/01/2024 *Online:* 23/02/2024 *Published*: 23/02/2024

*** Corresponding author:** Ritcha Saxena
Department of Biomedical Sciences, University of Minnesota School of Medicine, 1035 University Dr, Duluth, MN 55812, United States. Email address: rsaxena@d.umn.edu

Background - Understanding the Human Gut Microbiota

The human microbiota is regarded as the assemblage of microorganisms, their genetic material, and their metabolic products that inhabit the human body from birth and are inherited vertically.[1,2] Although all bodily regions are colonized, the gut hosts the most significant microbial populations, a domain extensively researched.[3] The gut microbiome, a complex community of microorganisms residing in the gastrointestinal tract, plays a crucial role in human health. Notably, while survival without a colon is possible, it is impossible without a small intestine, which houses the largest mucosal surfaces in the human body. In the small intestine that houses the majority of gut receptors, nerve and immune cells, food undergoes further digestion and absorption.

The composition of the gut microbiota is dynamic and influenced by various factors, including diet, environment, drug intake, and mode of consumption. The microbiome influences how the host processes and metabolizes dietary nutrients, creating a reciprocal relationship between the gut microbiome and diet. Complex biological and chemical systems interact to modulate an individual's dietary responses, involving the interplay of diet, host, and microbiota.[4,5] The gut microbiome is involved in the metabolism of complex carbohydrates, synthesis of vitamins, and nutrient absorption. It also produces metabolites capable of affecting various physiological mechanisms within the host organism, such as inflammation, metabolism, and immune function. A healthy small intestine harbors a diverse array of microorganisms, predominantly represented by members of the Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria phyla, with Firmicutes and Proteobacteria being major phyla among obligate anaerobic bacteria, alongside Bacteroidetes, as noted in multiple metagenomic studies.[6-8] This microbial community reaches its peak in the distal gut, where communities containing up to 100 billion cells per gram can exist for several days, given that colonic transit is considerably longer than that in the small intestine. These microbes are excreted by the body as feces, constituting what is commonly referred to as the gut microbiome, which has been linked to a plethora of ailments and is profoundly influenced by diet and medications.

The gut microbiome is increasingly recognized as a pivotal contributor to regulating host health, encompassing functions such as nutrient provision, defense against pathogens, and fostering immune system maturation.[9] Indeed, the microbiota's role in human health and disease is substantial, sometimes likened to an overlooked organ.[10] Recent studies have broadened our comprehension of various microbiome aspects in humans, shedding light on its influence on diverse physiological processes such as metabolism and energy intake. Clear associations are emerging between the microbiome and its impact on host metabolic processes, with significant implications for human health, particularly in light of the escalating rates of obesity and metabolic syndrome in Western societies.[11] As our understanding of the gut microbiota's physiological role in metabolism advances, it elucidates the mechanisms by which alterations in its composition, both qualitatively and quantitatively, can precipitate metabolic disorders such as obesity.[12-14] This becomes particularly pertinent amidst a global surge in chronic diseases like obesity, which collectively contribute to substantial mortality and morbidity worldwide.[15-17] Indeed, a substantial body of evidence has accumulated, indicating that specific dietary factors and consumption patterns, such as excessive intake of refined carbohydrates coupled with low fiber intake, contribute significantly to the risk of obesity and related conditions, including cardiovascular disease and metabolic syndrome.[18]

Over the past decade, AI and precision medicine have exerted an equal, if not greater, impact on the trajectory of healthcare compared to artificial intelligence. Research in this field has progressed to comprehend how the characterization of health and disease states, along with treatment options for affected individuals, is precisely delineated by integrating multi-omic data with medical history, social/behavioral factors, and environmental insights.[19]

Considering the significant impact of the gut microbiome on metabolism and caloric intake, alongside the advancements in AI applications in medicine, it becomes evident that further exploration of the gut microbiota and the integration of AI could lead to the development of adjunctive treatments beneficially modulating various diseases, particularly those of metabolic nature. While some studies have initiated assessments in these areas, the characterization of the gut microbiota remains incompletely understood, resulting in discordant results in some instances. Here, we offer a comprehensive review of the physiology and composition of the human gut microbiota, with particular emphasis on critically evaluating the current understanding in this field. This review aims to underscore the crucial role of the gut microbiome in regulating calorie intake and metabolism while highlighting how AI is transforming our understanding of the gut microbiome and its impact on these processes. Ultimately, unraveling the complexity of gut microbes and harnessing AI in this domain will pave the way for novel therapies already in development.

Influence of Gut Microbiota on Calorie Intake and Metabolism

Calorie intake, representing the energy derived from food consumption, stands as a fundamental aspect of nutrition and weight management. Historically, it was believed that calorie intake was primarily influenced by the types and quantities of food ingested. Emerging evidence, however, suggests that the composition of the gut microbiome also significantly influences calorie intake and energy balance. Certain bacterial species within the gut microbiome possess metabolic

capabilities facilitating the extraction of calories from the diet. These bacteria can metabolize dietary components typically indigestible by the human host, thus increasing the overall energy yield from food. Also, certain microbial metabolites can influence appetite regulation and satiety signals, thereby affecting overall calorie intake. Alterations in the gut microbiome composition have been associated with increased fat deposition in adipose tissue and exacerbated hepatic inflammatory processes, both contributing to weight gain and metabolic dysfunction. The gut microbiota can also utilize dietary components to produce energy and nutrients for their own growth and proliferation, further influencing the host's energy balance.[20-21]

Studies have demonstrated that the gut microbiome can influence appetite and food preferences through its interaction with the brain-gut axis.[22-23] Certain species of gut bacteria produce signaling molecules that can affect appetite-regulating hormones, such as leptin and ghrelin, thereby influencing feelings of hunger and satiety.[24] The gut microbiome can also modulate taste receptors, influencing our perception of different foods and potentially affecting food choices and calorie intake.[25]

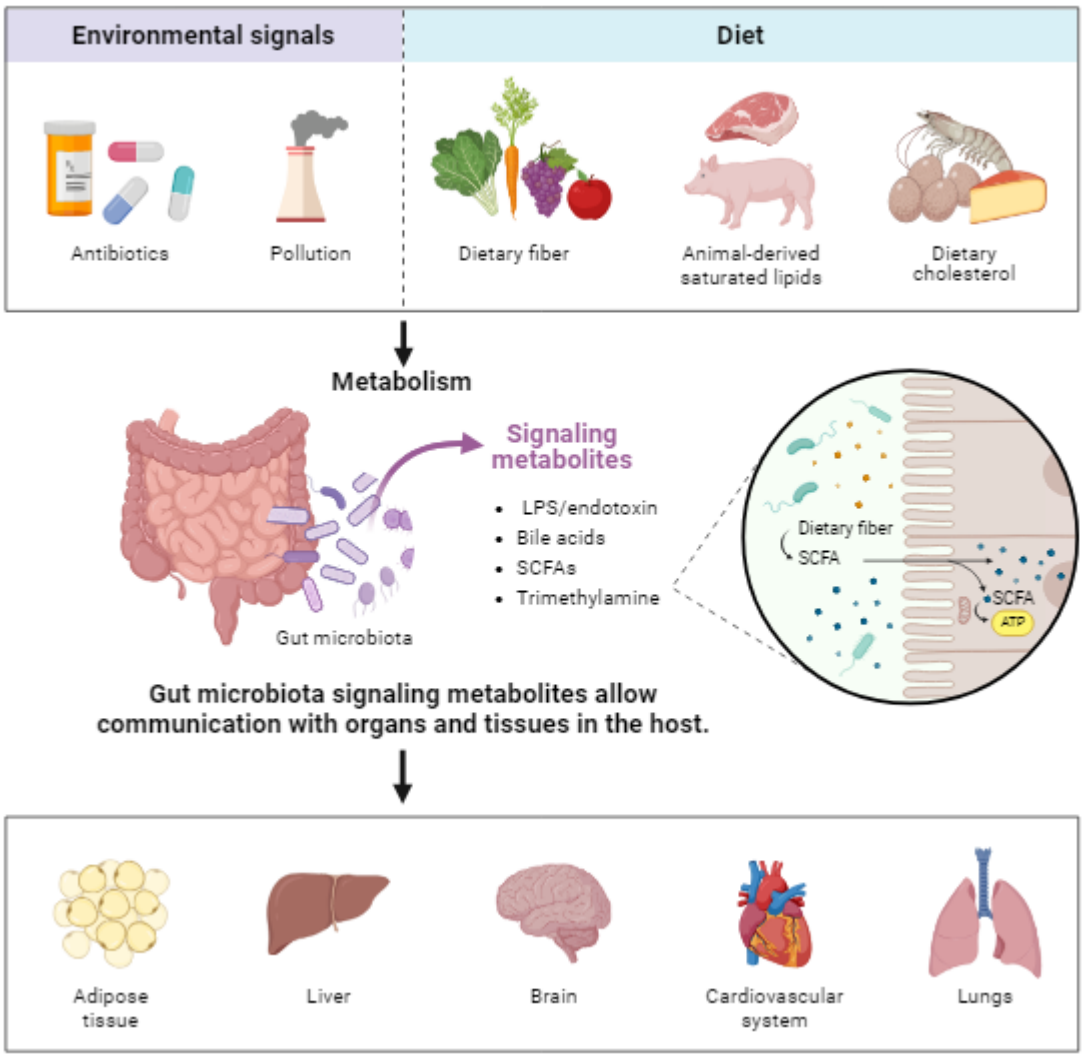


Figure 1: The gut microbiota convert environmental and dietary signals into signaling molecules, affecting host metabolism and inflammatory pathways. Various factors like diet can alter microbiota composition. Microbial metabolites, such as SCFAs and bile acids, signal to various organs, influencing host metabolic pathways and inflammatory responses. The gut microbiota then transforms these inputs into metabolites that signal to different organs and tissues within the host, as illustrated below. Disruptions in microbial balance may worsen the effects of risk factors like the Western diet on obesity and metabolic disorders. Figure adapted from Schroeder BO, Bäckhed F. Nat Med. 2016;22(10):1079-1089. Copyright (2016) by Springer Nature.[37]

The gut microbiota exerts its influence on health outcomes through the metabolization and alteration of various nutrients, giving rise to secondary metabolites with differing retention times, levels of bioactivity, and diverse effects. Examples of these metabolites include short-chain fatty acids (SCFAs), bile acids, hydrogen sulfite, trimethylamine and

lipopolysachharide endotoxins. Numerous metabolites produced by the gut microbiota have the ability to alter host metabolism and immune system pathways.[26-28] They can either promote health, such as SCFAs, or exacerbate disease, such as bile acids or hydrogen sulfite.[28,30] Further, the gut microbiota ferments complex sugars and dietary fibers that evade digestion by human enzymes.[31] Phyla such as Firmicutes and Bacteroidetes, which exhibit some tolerance to oxygen, encode a variety of enzymes necessary for breaking down complex carbohydrates, including fiber and resistant starch, which would otherwise remain indigestible.[32] This fermentation process yields SCFAs, including acetate, propionate, and butyrate, serving as an energy source for the host and influencing energy metabolism, glucose homeostasis and inflammation of tissues such as adipose.[33] In particular, SCFAs have been demonstrated to influence calorie consumption and storage by regulating hunger, raising energy expenditure, and promoting fat oxidation.[34,35] Several receptors, including free fatty acid receptor 3 (FFAR3 or GPR41) and niacin receptor 1 (GPR109A), have been identified for SCFAs, highlighting their diverse physiological roles in inflammation, atherosclerosis, and pancreatic β-cell growth and insulin secretion.[36]

Finally, the composition of the gut microbiome exhibits significant variability among patients, influenced by various factors including genetics, diet, lifestyle, and environmental exposures. Significant interindividual variations exist in the diversity, composition, and function of the microbiome.[38,39] Many observational and intervention studies have shown how host genetic, epigenetic, and lifestyle factors including nutrition shape and influence variance in the gut microbiota.[40-43]

Dysbiosis and Disease: The Impact of Gut Microbiota Composition on Metabolic Disorders

The composition, function, and diversity of the gut microbiome are closely associated with an individual's predisposition to a wide range of diseases, many of which are linked to diet. Dysbiosis, an imbalance in the gut microbiota, has been implicated in various diseases affecting different parts of the body.[44,45] It is now understood that alterations in the gut microbiome and microbial functions play a significant role in the pathogenesis of various diseases, including cancer and metabolic disorders. Such changes in the gut microbiota composition and function, when combined with traditional genetic predispositions and lifestyle factors, can contribute to the development and progression of these conditions.[46,47] On the other hand, reduced calorie consumption and better metabolic health are associated with a varied and balanced gut microbiome that is rich in beneficial bacteria. Studies have indicated that individuals with healthier metabolic profiles tend to have a more diverse microbiome composition, characterized by a greater abundance of beneficial bacterial species.[48] Studies also show that in the gut microbiomes of obese individuals, there tends to be a higher proportion of genes encoding membrane transport functions and those involved in butyrate synthesis. Conversely, genes linked to cofactor, vitamin, and nucleotide metabolism or transcription are more often depleted.[49,50] A study of human and mouse microbiota correlated obesity with differences in the relative abundance of two dominant bacterial divisions and showed that obese individuals have an increased capacity to harvest energy from the diet.[51] Relative abundance of certain bacterial phyla, particularly Bacteroidetes and Firmicutes, is altered in the gut microbiomes of obese individuals. Specifically, Bacteroidetes are often less common, while Firmicutes are more prevalent in obese individuals compared to lean individuals.[52] The development of gut microbe-targeted therapies by reversing dysbiosis of the microbiota, inhibiting microbial enzymes or genetically engineered probiotics, has been suggested to be feasible and efficacious.[53,54]

Comprehending the intricate connection between the intestinal microbiota and energy intake holds substantial ramifications for dietary patterns and well-being. Approaches directed towards fostering a robust intestinal microbiota, like ingesting a varied array of plant-derived foods abundant in fiber, probiotics, and prebiotics, might aid in bolstering optimal metabolic performance and managing energy consumption. a balanced diet that includes a sufficient amount of fiber promotes microbial fermentation of fiber into SCFAs, fosters microbial variability and stands as one mechanism by which high fiber consumption prevents weight gain, potentially outweighing inherited predispositions to obesity.[55-57] Hence, it is plausible that a broader dietary regimen supplemented with appropriate nourishment could rectify the intraluminal milieu in instances of dysbiosis.[58-60] Moreover, delving deeper into the mechanisms governing the influence of the gut microbiome on appetite control and metabolic activity could pave the way for tailored interventions targeting obesity and other metabolic conditions.

Therefore, the gut microbiome assumes a pivotal role in regulating energy balance and calorie intake by influencing appetite, metabolism, and food preferences. Encouraging a varied and well-balanced gut microbiome through dietary adjustments and lifestyle modifications could introduce innovative strategies for weight management and enhancing metabolic well-being. The effective fusion of dietary elements with the gut microbiome also holds considerable potential to transform disease management paradigms, offering personalized dietary suggestions, lifestyle alterations, or even the optimization of the gut microbiota tailored to individual needs and health objectives.[61,62]

Integration of AI into Bioinformatics

The rapid growth of computer hardware and software in the healthcare industry in recent years has facilitated the digitization of health data, opening up new avenues for the development of computational models and opportunities to utilize AI systems for deriving insights from data.[63]

In a recent paper, the authors underscored the "unprecedented opportunities" for boosting the expertise of professionals and the supportive function AI serves in alleviating human constraints like weariness and lack of focus, while also avoiding the dangers of mechanical fallibility. More significantly, the article stresses the importance of judicious implementation of these technological advancements while recognizing their significant potential.[64] The digitization of health-related data and the swift adoption of technology are driving transformation and advancement in the utilization of AI in healthcare.[65-67] Access to healthcare, environment, diet, and way of life all have a big impact on our personal health. The advent of wearable technology and other medical devices has enabled the monitoring and quantification of these behavioral, social, and external aspects. These variables collectively contribute to approximately 60% of our health determinants, encompassing physiological, psychological, behavioral, and socioeconomic data. In contrast, genetics constitute only 10% of these determinants, with medical history accounting for the remaining 30%.[68]

Integration of AI into bioinformatics has enabled the analysis of large datasets, a task often challenging with conventional statistical methodologies. AI is applied across various domains including medical diagnosis, support for therapeutic techniques, prediction of disease onset risks, and other related areas.[69] AI is even transforming our understanding of the gut microbiota and how it affects metabolism and calorie intake. A systems-wide mechanistic perspective that takes into account pre-disease, disease, and health states is necessary to gain a thorough knowledge of the dynamics within networks associated with nutrition and health benefits. This need emphasizes the need for cutting-edge techniques and procedures that can both quantify the effects of dietary changes in healthy persons and facilitate comparisons with patients who are diseased.[70] AI algorithms are finding increasing applications in personalized nutrition research, offering valuable insights and support for dietary activities, disease risk assessment related to food and nutrient patterns, and exploration of supplementation research.

AI Applications in Personalized Nutrition and Gut Microbiome Analysis

The primary aim of precision medicine is to tailor care to the specific needs of each patient.[71,72] The momentum behind precision nutrition is rapidly growing, underscoring its increasing significance as we come to acknowledge its breadth. de Toro-Martín and colleagues elaborate on precision nutrition methodologies, which extend far beyond genetics to encompass elements such as dietary patterns, eating habits, physical activity, the microbiome, and the metabolome.[73] Personalized nutrition stands on the cusp of a significant transformation with the advent of AI, which, through its capacity to analyze vast datasets, discern patterns, and make predictions, is opening up new avenues for personalized nutrition and precision medicine. Personalized nutrition is witnessing a surge, with advancements in AI and gut microbiome analysis revolutionizing our approach to diet and health. These personalized nutrition approaches have the potential to spearhead the development of information-processing representations of digestion, absorption, and metabolism.[74-76]

By harnessing advanced computational techniques, AI empowers researchers to uncover intricate patterns and relationships within large datasets that were previously difficult to discern. The escalating utilization of AI algorithms in this domain reflects scientific advancement and is increasingly becoming not just an asset, but a necessity in the quest for valuable outcomes. Through sophisticated AI systems, healthcare professionals can leverage data analysis capabilities to discern patterns and offer personalized diagnoses and treatment plans for various gastrointestinal conditions.

Numerous studies have highlighted that the underlying variability in the gut microbiome can be attributed to various factors, including diet, genetics, gender, age, lifestyle, environmental exposure, epigenetics, drugs, and geography. These intricacies may complicate the associations between the microbiota and human diseases.[77-80] Given these complexities, there is a pressing need to develop advanced computational methods capable of efficiently extracting key information from vast, heterogeneous, and complex multi-omics data. AI algorithms can leverage data from gut microbiome analysis, genetic makeup, and lifestyle to offer tailored dietary recommendations. This data-driven approach takes into consideration the interplay between the gut microbiome, diet, and environmental factors, ensuring individuals receive personalized nutrition guidance tailored to their specific requirements.[81,82]

In gut microbiome research, this is a primary application of AI involves analyzing microbiome composition and diversity. AI in biomedical sciences offers valuable tools and techniques for gathering, structuring, and scrutinizing vast biological datasets like nutritional, genomic, and related data.[83] AI systems are capable of analyzing high-throughput sequencing data to classify and determine the number of different microbial species in the gut. More research is now underway, including longitudinally individualized multi-omics profiling—which includes genomes, metabolomics, and proteomics—thanks to developments in high-throughput technology.[84] This method improves comprehension of the relationships between the gut microbiota and the host and provides a thorough grasp of human metabolism.[85-87] AI diagnostics employ advanced algorithms to scrutinize diverse data sources, including stool samples, blood analyses, and health records. This enables researchers to profile the microbiome of individuals and populations with unparalleled precision and detail.

Furthermore, AI algorithms can analyze the interactions between gut microbes and host physiology to elucidate the mechanisms underlying their effects on calorie intake and metabolism. The application of AI in biomedical nutrition research addresses the need for effective examination and understanding of the complex interactions between nutrition and human physiology, particularly in the context of the gut microbiome.[88-90] Important microbial metabolites, signaling pathways, and host-microbiome interactions that affect energy expenditure, calorie utilization, and appetite regulation can be identified using machine learning models. Utilizing a comprehensive approach facilitates the discovery of important markers that contribute to the development and progression of diseases such as colon cancer or irritable bowel syndrome (IBS). Timely detection and precise diagnoses are pivotal in ameliorating patient outcomes and enhancing treatment efficacy.

Predictive modeling driven by AI is also used to create individualized food plans based on each person's unique gut microbiota composition. The individuality of each person's gut microbiome is a critical facet of gut health. By examining the gut microbiome in conjunction with AI-powered diagnostics, researchers and healthcare professionals can better understand and address individual needs AI systems analyze a wide range of factors, including gut microbiota, lifestyle, and environmental factors, to provide deep insights and create customized treatment plans. These recommendations consider various reactions to specific nutrients obtained from food, resulting from the complex interplay between nutrients and biological processes.[91] These includes the correlation between external influences like food habits and physical activity, and internal factors like microbiota-metabolome interactions and genetics.[92] For instance, AI systems are able to provide personalized food recommendations based on an individual's genetic composition by combining genetic data with nutrition databases.[93] The variability in response to therapies and dietary advice among individuals is reflected in biomarker levels.[94] These anticipatory findings can be utilized to comprehend the complex regulatory mechanisms of dietary interventions at the convergence of immunity, metabolism, and gut flora. AI algorithms can forecast the potential impacts of various dietary strategies on an individual's gut microbiota and metabolic health by combining microbiome details with data on eating habits, lifestyle factors, and metabolic markers. This personalized approach enables precise dietary suggestions aimed at optimizing gut microbiota composition and regulating calorie intake.

AI can also be employed to explore dietary preferences and trends in relation to the gut microbiota's composition. AI systems can uncover correlations between specific food components and shifts in the gut microbiome's structure by analyzing extensive databases of microbiome profiles and dietary intake records. This information can guide the development of dietary advice and interventions aimed at nurturing a balanced gut microbiome and managing calorie consumption. In this direction, AI-driven personalized nutrition is poised for ongoing enhancements, potentially facilitating the creation of a global network capable of actively overseeing and enhancing each person's nutrient intake.[95]

AI's integration into gut microbiome research represents a groundbreaking frontier for advancing the understanding of the intricate interplays among the microbiome, calorie consumption, and metabolism. Through sophisticated computational analysis and data-driven methodologies, AI empowers scientists to navigate the complex mechanisms within the microbiome ecosystem. AI further enables the design of targeted interventions tailored to optimize metabolic well-being, paving the way for personalized nutrition.

Potential of AI in Advancing Gut Microbiome Research

In recent years, there have been several notable advancements in the field of AI and gut microbiome research, particularly concerning calorie intake and metabolism.

The field of microbiome-based therapeutics is rapidly expanding. A growing body of evidence suggests that modifying the gut microbiota through different therapeutic regimens such as dietary adjustments, fecal microbiota transplantation, or supplementation with probiotics and prebiotics holds promise for preventing or treating various illnesses.[96,97] AI is playing a crucial role in advancing the development of microbiome-based treatments for metabolic diseases like obesity. By identifying key microbial taxa and metabolites associated with metabolic health, researchers can tailor therapies such as microbial transplantation to optimize gut microbiome function and improve metabolic outcomes. Understanding the mechanisms underlying the functions of gut microbiota functions also opens up possibilities for developing highly effective probiotics with targeted benefits.[90,98]

AI algorithms focused on microbiome-host interactions are unraveling the complex connections between the gut microbiome and host physiology, shedding light on hunger regulation, energy metabolism, and gut-brain communication. AI has played a pivotal role in advancing our mechanistic understanding of the gut microbiome by identifying novel microbial genomes and proteins from uncultured species, leveraging vast amounts of gut metagenomic data. Additionally, machine learning techniques can predict protein structures based on unidentified protein sequences, aiding in enzyme design and drug development.[99] These breakthroughs enhance our understanding of how the gut microbiota influences calorie intake and metabolism, paving the way for innovative therapeutic strategies.

Using machine learning to find biomarkers connected to certain dietary treatments or health outcomes is greatly facilitated by advancements in bioinformatics and artificial intelligence. Researchers are increasingly leveraging machine learning techniques to uncover microbial biomarkers associated with metabolic health and disease. In earlier investigations of the microbiota, the interpretability of the models allowed for the simultaneous identification of biomarkers linked to disease, providing valuable biological insights into the data. This methodology enables the discovery of new insights into illnesses and facilitates the identification of viable treatment approaches.[100] For instance, Yu et al. (2017) employed the minimum redundancy–maximum relevance (mRMR) feature selection method to identify an optimal set of 20 microbial genes predictive of colorectal cancer, with four validated genes distinguishing patients from controls across different ethnic cohorts. These findings underscore the potential of machine learning in identifying microbial biomarkers for the early diagnosis of colorectal cancer.[101] Additionally, machine learning has been widely applied to the identification of microbial biomarkers for the purpose of evaluating the risk of disease and creating tailored treatments for gut microorganisms. Deep learning has shown great promise in a number of disciplines, such as AlphaGo and AlphaFold, which are applied to analyze large-scale microbiome datasets, offering new insights into microbial communities and their interactions with the host.[99,102] AI systems have the capability to identify microbial signatures indicative of an individual's risk for conditions like obesity, insulin resistance, and other metabolic disruptions by analyzing vast microbiome datasets. This facilitates early detection and the development of personalized treatment strategies.

Integrative methodologies in omics are essential for discerning the connections between the gut microbiota and human diseases. Single-omics analysis often provides only a partial view of the intricate biological systems. Recent research in gut microbiome highlights the vast potential of AI in integrating and analyzing diverse data sets.[103,104] AI algorithms enable the integration of various omics data types, including genomics, metabolomics, and microbiomics, leading to a deeper understanding of the gut microbiome and its role in metabolism. Despite challenges such as high dimensionality and limited sample sizes, deep learning has proven effective in handling and integrating multi-omics data.[105,106] By offering a comprehensive understanding of the molecular processes underlying both metabolic health and illness, these integrated approaches simplifying the identification of novel treatment objectives and strategies

The latest advancements in artificial intelligence and gut microbiome research are significantly enhancing our understanding of the complex interplay between the microbiota, caloric intake, and metabolism. Through the utilization of sophisticated computational techniques and data analytics platforms, there is the potential to revolutionize the development of health platforms, customize forthcoming dietary guidelines to optimize health outcomes, and expedite the integration of these guidelines into clinical practice. By leveraging AI-driven methodologies, researchers can glean novel insights into metabolic health and devise state-of-the-art strategies for personalized dietary and therapeutic interventions.

Challenges, opportunities, and practical implications of using AI in personalized nutrition

Several challenges must be overcome to effectively utilize AI in exploring the connection between the gut microbiota and calorie intake and to implement it in precision medicine for personalized therapy. Despite progress, this field still faces obstacles that hinder seamless integration into real-world healthcare. One major challenge is the establishment of gut microbiota biobanks using AI technology for scientific research, which looms as a significant hurdle on the horizon.[107] The incorporation of AI in healthcare introduces several challenges, including those related to multimodal data integration, federated learning, model performance, bias, and privacy concerns. Multimodal data integration entails merging information from diverse sources such as medical records, imaging studies, and genetic data, which can be intricate and demand advanced computational methods. Federated learning, which involves training machine learning models across multiple decentralized data sources, necessitates significant advancements in privacy-preserving techniques, large-scale machine learning, and distributed optimization to ensure data privacy and security while maintaining effective model performance.[108]

Ensuring consistent data quality and standardization across diverse sources is imperative. Discrepancies in data collection, sequencing methodologies, and preprocessing can introduce biases that affect the accuracy and reliability of AI predictions. Evaluating the credibility and reliability of test outcomes generated by AI techniques is a critical challenge.[109] The domain context and applications of AI in healthcare are closely intertwined with considerations of fairness and protected qualities. However, challenges arise due to limitations in the representativeness of training samples derived from patient data. Often, the sample sizes are insufficient to fully capture the diverse variations among patients and the complexity of their health conditions. The challenges are compounded by the curse of dimensionality, especially when dealing with gut microbiome data, where high dimensionality and limited sample sizes can hinder traditional AI methods.[110] This challenge is termed as bias, which remains one of the significant hurdles in the application of AI in healthcare. Data bias occurs when the training data used to develop AI models is not representative of the population it aims to serve. This can lead to inaccuracies or unfair outcomes, particularly for underrepresented groups, and can exacerbate existing health disparities.[111] Further research in the field of medical AI is essential to understand and address fairness and bias in AI models constructed using historical patient data. Collaboration between the biomedical and AI communities is crucial to tackle this challenge effectively. To mitigate bias and overfitting in AI models, it is imperative to validate algorithms derived from retrospective and single-center studies

and promote validation across multiple centers and in prospective studies. Standardizing data processing methods would not only streamline clinical data collection but also facilitate predictive analysis. This approach enhances the robustness and applicability of AI models, ensuring their effectiveness across diverse settings.[112] Standardizing data also promotes seamless communication among medical facilities, physicians, academic institutions, and data scientists involved in data evaluation. This facilitates quick and consistent identification of missing data for individual patients. Furthermore, ensuring data uniformity across healthcare organizations ensures the quality of patient care and facilitates monitoring of their records, thereby enabling evidence-based recommendations to be formulated.

The lack of clarity in complex AI algorithms, like deep learning, presents challenges in grasping underlying mechanisms. The demand for individuals adept at bridging computational and clinical fields has surged with the advent of new data-driven technologies. Ensuring model clarity is pivotal for effectively translating research findings into actionable insights. This highlights the necessity to train individuals with broad expertise in computer science, statistics, biology, nutrition, biomedicine, mathematics, and data science. Integrating concepts from statistics, machine learning, bioinformatics, mathematics, and computer science into training programs for students, trainees, and professionals in data science is imperative. Workshops and training events designed to unite researchers from diverse backgrounds can bolster response predictability.[113] The training of the new professionals should reflect the cutting-edge knowledge guided by the change in day to day informatics challenges.[114] Trainers stand to gain valuable insights from trainings and tutorials, obtaining up-to-date knowledge on the latest technology, data standards, and utilization procedures for infrastructure services.[115]

Robust AI models that accurately capture the dynamics of the gut microbiome across populations and dietary habits require large, diverse datasets for training. However, obtaining such databases can be costly and logistically challenging. Exploring alternative methods to facilitate the development of high-performing AI systems, such as generating synthetic data with realistic variations or leveraging simulated environments, is imperative. While early research shows promise, further investigation into AI is warranted.[116] Furthermore, despite AI's ability to identify relationships, distinguishing causation from correlation remains a challenge. Mere concatenation of raw data or model outputs from each perspective overlooks opportunities to explore potential connections and interactions among diverse multi-omic data. To establish causality and validate AI-driven predictions, longitudinal research and experimental interventions are essential.

Concerns regarding data ownership, consent, and privacy arise when AI utilizes gut microbiome data for personalized recommendations. The issue of trust in AI-based technologies, especially among the senior population, has not been fully addressed. Recent research has showcased the potential of new computational algorithms to identify individuals within public or commercial health databases.[117] A crucial consideration is that health data should not be used to discriminate against individuals in determining insurance costs or employment status.[95] The use of genetic data poses extra challenges since the drivers of prediction algorithms remain uncertain.[117] Unauthorized access to and misuse of electronic medical records present additional concerns. Improper access to medical records can lead to privacy breaches.[118] Establishing a secure and tightly regulated environment for data storage, management, and exchange is imperative. This necessitates the adoption of new technologies, collaborative efforts, and the development of new business models and legislation. Transparency, informed consent, and data security are essential for maintaining trust and protecting individuals' rights. One approach that AI system engineers can explore to address ongoing privacy concerns is the use of generative data. Generative models enable the creation of synthetic patient data that is realistic yet unrelated to actual individuals.[119,120] This makes machine learning possible without requiring the long-term use of actual patient data.

The cost of AI technology may render it inaccessible to certain individuals and healthcare facilities. Residents in rural or isolated areas, lacking adequate internet connectivity or technological infrastructure, may face limited access.[121] Thus, in order to improve access to social, economic, and educational opportunities, digital equity must be promoted. It is imperative to surmount financial obstacles and augment accessibility to guarantee universal availability of customized dietary plans and metabolic health treatments.

Collaboration across disciplines, rigorous study designs, transparent reporting, and adherence to ethical standards are effective strategies for addressing these challenges. Overcoming these challenges would allow AI to fulfill its potential in revolutionizing our understanding of how the gut microbiome regulates energy intake and metabolism. This enhanced understanding could lead to more effective approaches for improving metabolic health and preventing chronic diseases.

Conclusion

Recent studies have shed light on the multifaceted roles of the gut microbiota in human health, emphasizing microbial diversity as a principal indicator of overall well-being. However, substantial inter-individual variability exists, influenced by environmental factors and dietary quality.[122-126] Nutrition and diet are recognized as significant determinants of an individual's health, with a growing emphasis on understanding how dietary patterns and specific diets impact an individual’s health. This shift in research focus—from analyzing the effects of individual nutrients to examining the functional aspects

of dietary patterns—reflects a deeper understanding of the complex interactions between diet, gut microbiota, and human health.[127-129]

Due to the significant role that diet plays in influencing gut microbiota composition and host metabolism, our understanding of actions patients can take to enhance their systemic health is evolving.[130,131] The relationships observed in microbial diversity emphasize the significance of consuming a nourishing, diverse diet. They support the idea that dietary supplements containing particular nutrients should not be viewed as replacements for a balanced and healthy diet.[132,133] Nutrition and dietary habits exert a more substantial influence on the prognosis of chronic diseases such as diabetes, obesity, IBS and colorectal cancer compared to genetic and environmental factors. These elements impact metabolism and inflammation.[134-137]

Despite advancements, unanswered questions remain regarding the precise composition of an optimal health-promoting microbiome and strategies for cultivating such flora in individuals with initially diverse microbiotas. Standardized dietary approaches may not always yield desired outcomes. Discrepancies in the effectiveness of lifestyle interventions may be attributed to variations in gut flora among individuals.[77,137,138] It is noted that patients exhibit highly personalized reactions of their microbiomes to diverse meals, depending on their previous dietary experiences.[139] Consequently, owing to advancements in AI and gut microbiome research, personalized nutrition and healthcare are on the brink of a transformative shift. The use of AI in health research and initiatives has surged in recent years, facilitating the integration of various clinical data elements, establishing connections between biorepositories and clinical data, and bridging the gap between clinical data and pharmaceutical research and development.[140-143] AI-driven platforms have the potential to enhance metabolic health outcomes and prevent chronic diseases such as obesity by providing personalized food recommendations based on an individual's gut microbiome composition and metabolic profile. Future investigations should focus on elucidating the intricate functions of the gut microbiota in these processes. These findings may lead to the utilization of the gut microbiota and its metabolites in the treatment of metabolic disorders in the future. Probiotics and prebiotics exemplify customized interventions offered by microbiome-based therapies driven by AI, targeting specific microbial imbalances to provide more effective and personalized treatment options.

Moreover, AI algorithms can detect early signs of metabolic dysfunction through the analysis of microbial biomarkers. This enables timely intervention and the prevention of chronic disease. The advancement of medications designed to modulate the gut microbiota and the development of personalized treatment plans are facilitated by our expanding knowledge of how the gut microbiome influences drug metabolism. Early detection of metabolic abnormalities facilitated by AI-driven diagnostic technologies is another avenue through which patient outcomes can be enhanced and healthcare resources optimized.

Furthermore, in the realm of medical education, the incorporation of AI into personalized nutrition holds significant promise. For instance, the integration of digital pathology and AI, already in practice in several medical education settings, greatly enhances students' comprehension of pathophysiology concepts.[144] This integration can further offers insights into the complex relationship between cellular morphology and physiological processes, including those influenced by the gut microbiota. Through the use of AI-driven diagnostic tools, aspiring physicians can delve into the subtle connections between tissue pathology and systemic health, acquiring valuable insights to inform personalized nutrition strategies aimed at optimizing metabolic well-being for both themselves and their future patients.

Future research endeavors should aim to elucidate the roles of nonbacterial microorganisms in the human gut and the shifts in bacterial composition associated with different disease states. Future developments in AI and gut microbiome research have the potential to revolutionize precision medicine, public health initiatives, and healthcare efficiency. These advancements may offer unprecedented opportunities to enhance metabolic health and overall well-being on a global scale. Ultimately, leveraging AI across the field of gut microbiota research will facilitate advancements in precision nutrition, personalized medicine, and the development of next-generation probiotics tailored to individual patients.[77,27,145] While AI and precision medicine hold immense promise, efforts to test, validate, and refine treatment protocols require continued dedication. Overcoming challenges such as obtaining sufficient high-quality labeled data for algorithm training, navigating regulatory and privacy considerations, and adopting standardized data formats are crucial steps for researchers to address. This review highlights several key points for further consideration and investigation. Promising strides are being made in surmounting the obstacles faced by AI in healthcare, paving the way for continued growth and advancement in AI's role in both personal and population health.

References

1. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome [published correction appears in Nature. 2011 Jun 30;474(7353):666] [published correction appears in Nature. 2014 Feb 27;506(7489):516]. Nature. 2011;473(7346):174-180. doi:10.1038/nature09944

2. Korpela K, de Vos WM. Early life colonization of the human gut: microbes matter everywhere. Curr Opin Microbiol. 2018;44:70-78. doi:10.1016/j.mib.2018.06.003
3. Lloyd-Price J, Mahurkar A, Rahnavard G, et al. Strains, functions and dynamics in the expanded Human Microbiome Project [published correction appears in Nature. 2017 Oct 12;:]. Nature. 2017;550(7674):61-66. doi:10.1038/nature23889)
4. Kolodziejczyk AA, Zheng D, Elinav E. Diet-microbiota interactions and personalized nutrition. Nat Rev Microbiol. 2019;17(12):742-753. doi:10.1038/s41579-019-0256-8
5. Hughes RL, Kable ME, Marco M, Keim NL. The Role of the Gut Microbiome in Predicting Response to Diet and the Development of Precision Nutrition Models. Part II: Results. Adv Nutr. 2019;10(6):979-998. doi:10.1093/advances/nmz049
6. Seekatz AM, Schnizlein MK, Koenigsknecht MJ, et al. Spatial and Temporal Analysis of the Stomach and Small-Intestinal Microbiota in Fasted Healthy Humans. mSphere. 2019;4(2):e00126-19. Published 2019 Mar 13. doi:10.1128/mSphere.00126-19
7. Leite GGS, Weitsman S, Parodi G, et al. Mapping the Segmental Microbiomes in the Human Small Bowel in Comparison with Stool: A REIMAGINE Study. Dig Dis Sci. 2020;65(9):2595-2604. doi:10.1007/s10620-020-06173-x
8. Kaur K, Khatri I, Akhtar A, Subramanian S, Ramya TNC. Metagenomics analysis reveals features unique to Indian distal gut microbiota [published correction appears in PLoS One. 2020 Dec 1;15(12):e0243397]. PLoS One. 2020;15(4):e0231197. Published 2020 Apr 8. doi:10.1371/journal.pone.0231197
9. Gill SR, Pop M, Deboy RT, et al. Metagenomic analysis of the human distal gut microbiome. Science. 2006;312(5778):1355-1359. doi:10.1126/science.1124234
10. O'Hara AM, Shanahan F. The gut flora as a forgotten organ. EMBO Rep. 2006;7(7):688-693. doi:10.1038/sj.embor.7400731
11. Harakeh SM, Khan I, Kumosani T, et al. Gut Microbiota: A Contributing Factor to Obesity. Front Cell Infect Microbiol. 2016;6:95. Published 2016 Aug 30. doi:10.3389/fcimb.2016.00095
12. Jumpertz R, Le DS, Turnbaugh PJ, et al. Energy-balance studies reveal associations between gut microbes, caloric load, and nutrient absorption in humans. Am J Clin Nutr. 2011;94(1):58-65. doi:10.3945/ajcn.110.010132
13. Rowland I, Gibson G, Heinken A, et al. Gut microbiota functions: metabolism of nutrients and other food components. Eur J Nutr. 2018;57(1):1-24. doi:10.1007/s00394-017-1445-8
14. Gomes AC, Hoffmann C, Mota JF. The human gut microbiota: Metabolism and perspective in obesity. Gut Microbes. 2018;9(4):308-325. doi:10.1080/19490976.2018.1465157
15. Bauer UE, Briss PA, Goodman RA, Bowman BA. Prevention of chronic disease in the 21st century: elimination of the leading preventable causes of premature death and disability in the USA. Lancet. 2014;384(9937):45-52. doi:10.1016/S0140-6736(14)60648-6
16. van Dijk SJ, Tellam RL, Morrison JL, Muhlhausler BS, Molloy PL. Recent developments on the role of epigenetics in obesity and metabolic disease. Clin Epigenetics. 2015;7:66. Published 2015 Jul 11. doi:10.1186/s13148-015-0101-5
17. Heitmann BL, Westerterp KR, Loos RJ, et al. Obesity: lessons from evolution and the environment. Obes Rev. 2012;13(10):910-922. doi:10.1111/j.1467-789X.2012.01007.x
18. Liu S. Intake of refined carbohydrates and whole grain foods in relation to risk of type 2 diabetes mellitus and coronary heart disease. J Am Coll Nutr. 2002;21(4):298-306. doi:10.1080/07315724.2002.10719227
19. Ziegelstein RC. Personomics and Precision Medicine. Trans Am Clin Climatol Assoc. 2017;128:160-168.
20. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI. Host-bacterial mutualism in the human intestine. Science. 2005;307(5717):1915-1920. doi:10.1126/science.1104816
21. Neyrinck AM, Etxeberria U, Taminiau B, et al. Rhubarb extract prevents hepatic inflammation induced by acute alcohol intake, an effect related to the modulation of the gut microbiota. Mol Nutr Food Res. 2017;61(1):10.1002/mnfr.201500899. doi:10.1002/mnfr.201500899
22. Barrea L, Muscogiuri G, Annunziata G, et al. From gut microbiota dysfunction to obesity: could short-chain fatty acids stop this dangerous course?. Hormones (Athens). 2019;18(3):245-250. doi:10.1007/s42000-019-00100-0
23. van de Wouw M, Schellekens H, Dinan TG, Cryan JF. Microbiota-Gut-Brain Axis: Modulator of Host Metabolism and Appetite. J Nutr. 2017;147(5):727-745. doi:10.3945/jn.116.240481
24. Fetissov SO. Role of the gut microbiota in host appetite control: bacterial growth to animal feeding behaviour. Nat Rev Endocrinol. 2017;13(1):11-25. doi:10.1038/nrendo.2016.150
25. Turner A, Veysey M, Keely S, Scarlett C, Lucock M, Beckett EL. Interactions between Bitter Taste, Diet and Dysbiosis: Consequences for Appetite and Obesity. Nutrients. 2018;10(10):1336. Published 2018 Sep 20. doi:10.3390/nu10101336
26. Nicholson JK, Holmes E, Kinross J, et al. Host-gut microbiota metabolic interactions. Science. 2012;336(6086):1262-1267. doi:10.1126/science.1223813
27. Rooks MG, Garrett WS. Gut microbiota, metabolites and host immunity. Nat Rev Immunol. 2016;16(6):341-352. doi:10.1038/nri.2016.42

28. WJ, Hase K. Gut microbiota-generated metabolites in animal health and disease. Nat Chem Biol. 2014;10(6):416-424. doi:10.1038/nchembio.1535
29. Hughes RL, Marco ML, Hughes JP, Keim NL, Kable ME. The Role of the Gut Microbiome in Predicting Response to Diet and the Development of Precision Nutrition Models-Part I: Overview of Current Methods. Adv Nutr. 2019;10(6):953-978. doi:10.1093/advances/nmz022
30. Ni Y, Li J, Panagiotou G. A Molecular-Level Landscape of Diet-Gut Microbiome Interactions: Toward Dietary Interventions Targeting Bacterial Genes. mBio. 2015;6(6):e01263-15. Published 2015 Oct 27. doi:10.1128/mBio.01263-15
31. Lamichhane S, Sen P, Dickens AM, Orešič M, Bertram HC. Gut metabolome meets microbiome: A methodological perspective to understand the relationship between host and microbe. Methods. 2018;149:3-12. doi:10.1016/j.ymeth.2018.04.029
32. Sims IM, Ryan JL, Kim SH. In vitro fermentation of prebiotic oligosaccharides by Bifidobacterium lactis HN019 and Lactobacillus spp. Anaerobe. 2014;25:11-17. doi:10.1016/j.anaerobe.2013.11.001.
33. Janssen AW, Kersten S. Potential mediators linking gut bacteria to metabolic health: a critical view. J Physiol. 2017;595(2):477-487. doi:10.1113/JP272476
34. Murugesan S, Nirmalkar K, Hoyo-Vadillo C, García-Espitia M, Ramírez-Sánchez D, García-Mena J. Gut microbiome production of short-chain fatty acids and obesity in children. Eur J Clin Microbiol Infect Dis. 2018;37(4):621-625. doi:10.1007/s10096-017-3143-0
35. Liu JL, Segovia I, Yuan XL, Gao ZH. Controversial Roles of Gut Microbiota-Derived Short-Chain Fatty Acids (SCFAs) on Pancreatic β-Cell Growth and Insulin Secretion. Int J Mol Sci. 2020;21(3):910. Published 2020 Jan 30. doi:10.3390/ijms21030910
36. Ohira H, Tsutsui W, Fujioka Y. Are Short Chain Fatty Acids in Gut Microbiota Defensive Players for Inflammation and Atherosclerosis?. J Atheroscler Thromb. 2017;24(7):660-672. doi:10.5551/jat.RV17006
37. Schroeder BO, Bäckhed F. Signals from the gut microbiota to distant organs in physiology and disease. Nat Med. 2016;22(10):1079-1089. doi:10.1038/nm.4185
38. Koppel N, Balskus EP. Exploring and Understanding the Biochemical Diversity of the Human Microbiota. Cell Chem Biol. 2016;23(1):18-30. doi:10.1016/j.chembiol.2015.12.008
39. Yatsunenko T, Rey FE, Manary MJ, et al. Human gut microbiome viewed across age and geography. Nature. 2012;486(7402):222-227. Published 2012 May 9. doi:10.1038/nature11053
40. Bonder MJ, Kurilshikov A, Tigchelaar EF, et al. The effect of host genetics on the gut microbiome. Nat Genet. 2016;48(11):1407-1412. doi:10.1038/ng.3663
41. Benson AK, Kelly SA, Legge R, et al. Individuality in gut microbiota composition is a complex polygenic trait shaped by multiple environmental and host genetic factors. Proc Natl Acad Sci U S A. 2010;107(44):18933-18938. doi:10.1073/pnas.1007028107
42. David LA, Maurice CF, Carmody RN, et al. Diet rapidly and reproducibly alters the human gut microbiome. Nature. 2014;505(7484):559-563. doi:10.1038/nature12820
43. De Filippo C, Cavalieri D, Di Paola M, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proc Natl Acad Sci U S A. 2010;107(33):14691-14696. doi:10.1073/pnas.1005963107
44. Musso G, Gambino R, Cassader M. Interactions between gut microbiota and host metabolism predisposing to obesity and diabetes. Annu Rev Med. 2011;62:361-380. doi:10.1146/annurev-med-012510-175505
45. Zhang YJ, Li S, Gan RY, Zhou T, Xu DP, Li HB. Impacts of gut bacteria on human health and diseases. Int J Mol Sci. 2015;16(4):7493-7519. Published 2015 Apr 2. doi:10.3390/ijms16047493
46. Hope ME, Hold GL, Kain R, El-Omar EM. Sporadic colorectal cancer--role of the commensal microbiota. FEMS Microbiol Lett. 2005;244(1):1-7. doi:10.1016/j.femsle.2005.01.029
47. Vijay-Kumar M, Aitken JD, Carvalho FA, et al. Metabolic syndrome and altered gut microbiota in mice lacking Toll-like receptor 5. Science. 2010;328(5975):228-231. doi:10.1126/science.1179721
48. Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI. The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice. Sci Transl Med. 2009;1(6):6ra14. doi:10.1126/scitranslmed.3000322
49. Greenblum S, Turnbaugh PJ, Borenstein E. Metagenomic systems biology of the human gut microbiome reveals topological shifts associated with obesity and inflammatory bowel disease. Proc Natl Acad Sci U S A. 2012;109(2):594-599. doi:10.1073/pnas.1116053109
50. Ferrer M, Ruiz A, Lanza F, et al. Microbiota from the distal guts of lean and obese adolescents exhibit partial functional redundancy besides clear differences in community structure. Environ Microbiol. 2013;15(1):211-226. doi:10.1111/j.1462-2920.2012.02845.x
51. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006;444(7122):1027-1031. doi:10.1038/nature05414
52. Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. Nature. 2009;457(7228):480-484. doi:10.1038/nature07540

53. Yuvaraj S, Al-Lahham SH, Somasundaram R, Figaroa PA, Peppelenbosch MP, Bos NA. E. coli-produced BMP-2 as a chemopreventive strategy for colon cancer: a proof-of-concept study. Gastroenterol Res Pract. 2012;2012:895462. doi:10.1155/2012/895462
54. Chen K, Zhu Y, Zhang Y, et al. A probiotic yeast-based immunotherapy against Clostridioides difficile infection. Sci Transl Med. 2020;12(567):eaax4905. doi:10.1126/scitranslmed.aax4905
55. Chambers ES, Preston T, Frost G, Morrison DJ. Role of Gut Microbiota-Generated Short-Chain Fatty Acids in Metabolic and Cardiovascular Health. Curr Nutr Rep. 2018;7(4):198-206. doi:10.1007/s13668-018-0248-8
56. Fernandes J, Su W, Rahat-Rozenbloom S, Wolever TM, Comelli EM. Adiposity, gut microbiota and faecal short chain fatty acids are linked in adult humans. Nutr Diabetes. 2014;4(6):e121. Published 2014 Jun 30. doi:10.1038/nutd.2014.23
57. Menni C, Jackson MA, Pallister T, Steves CJ, Spector TD, Valdes AM. Gut microbiome diversity and high-fibre intake are related to lower long-term weight gain. Int J Obes (Lond). 2017;41(7):1099-1105. doi:10.1038/ijo.2017.66
58. Llewellyn SR, Britton GJ, Contijoch EJ, et al. Interactions Between Diet and the Intestinal Microbiota Alter Intestinal Permeability and Colitis Severity in Mice. Gastroenterology. 2018;154(4):1037-1046.e2. doi:10.1053/j.gastro.2017.11.030
59. Chiba M, Abe T, Tsuda H, et al. Lifestyle-related disease in Crohn's disease: relapse prevention by a semi-vegetarian diet. World J Gastroenterol. 2010;16(20):2484-2495. doi:10.3748/wjg.v16.i20.2484
60. Lewis JD, Abreu MT. Diet as a Trigger or Therapy for Inflammatory Bowel Diseases. Gastroenterology. 2017;152(2):398-414.e6. doi:10.1053/j.gastro.2016.10.019
61. Bashiardes S, Godneva A, Elinav E, Segal E. Towards utilization of the human genome and microbiome for personalized nutrition. Curr Opin Biotechnol. 2018;51:57-63. doi:10.1016/j.copbio.2017.11.013
62. Eetemadi A, Rai N, Pereira BMP, Kim M, Schmitz H, Tagkopoulos I. The Computational Diet: A Review of Computational Methods Across Diet, Microbiome, and Health. Front Microbiol. 2020;11:393. Published 2020 Apr 3. doi:10.3389/fmicb.2020.00393
63. Hinton G. Deep Learning-A Technology With the Potential to Transform Health Care. JAMA. 2018;320(11):1101-1102. doi:10.1001/jama.2018.11100
64. Matheny ME, Whicher D, Thadaney Israni S. Artificial Intelligence in Health Care: A Report From the National Academy of Medicine. JAMA. 2020;323(6):509-510. doi:10.1001/jama.2019.21579
65. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44-56. doi:10.1038/s41591-018-0300-7
66. Hashimoto DA, Rosman G, Rus D, Meireles OR. Artificial Intelligence in Surgery: Promises and Perils. Ann Surg. 2018;268(1):70-76. doi:10.1097/SLA.0000000000002693
67. Mayo RC, Leung J. Artificial intelligence and deep learning - Radiology's next frontier?. Clin Imaging. 2018;49:87-88. doi:10.1016/j.clinimag.2017.11.007
68. McGinnis JM, Williams-Russo P, Knickman JR. The case for more active policy attention to health promotion. Health Aff (Millwood). 2002;21(2):78-93. doi:10.1377/hlthaff.21.2.78
69. Kaput J. Lessons from application of data science strategies in nutritional research. Am J Clin Nutr. 2020;111(1):4-5. doi:10.1093/ajcn/nqz284
70. Verma M, Hontecillas R, Abedi V, et al. Modeling-Enabled Systems Nutritional Immunology. Front Nutr. 2016;3:5. Published 2016 Feb 16. doi:10.3389/fnut.2016.00005
71. Aronson SJ, Rehm HL. Building the foundation for genomics in precision medicine. Nature. 2015;526(7573):336-342. doi:10.1038/nature15816
72. Anderson JL, Horne BD, Stevens SM, et al. Randomized trial of genotype-guided versus standard warfarin dosing in patients initiating oral anticoagulation. Circulation. 2007;116(22):2563-2570. doi:10.1161/CIRCULATIONAHA.107.737312
73. de Toro-Martín J, Arsenault BJ, Després JP, Vohl MC. Precision Nutrition: A Review of Personalized Nutritional Approaches for the Prevention and Management of Metabolic Syndrome. Nutrients. 2017;9(8):913. Published 2017 Aug 22. doi:10.3390/nu90809130
74. Abrahams M, Matusheski NV. Personalised nutrition technologies: a new paradigm for dietetic practice and training in a digital transformation era. J Hum Nutr Diet. 2020;33(3):295-298. doi:10.1111/jhn.12746
75. Barrow M, Bell L, Bell C. Transforming personalized nutrition practice. Nutr Rev. 2020;78(12):1046-1051. doi:10.1093/nutrit/nuaa012
76. Adams SH, Anthony JC, Carvajal R, et al. Perspective: Guiding Principles for the Implementation of Personalized Nutrition Approaches That Benefit Health and Function. Adv Nutr. 2020;11(1):25-34. doi:10.1093/advances/nmz086
77. Sharma M, Li Y, Stoll ML, Tollefsbol TO. The Epigenetic Connection Between the Gut Microbiome in Obesity and Diabetes. Front Genet. 2020;10:1329. Published 2020 Jan 15. doi:10.3389/fgene.2019.01329
78. Deschasaux M, Bouter KE, Prodan A, et al. Depicting the composition of gut microbiota in a population with varied ethnic origins but shared geography. Nat Med. 2018;24(10):1526-1531. doi:10.1038/s41591-018-0160-1
79. Wu H, Esteve E, Tremaroli V, et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nat Med. 2017;23(7):850-858. doi:10.1038/nm.4345

80. He Y, Wu W, Zheng HM, et al. Regional variation limits applications of healthy gut microbiome reference ranges and disease models [published correction appears in Nat Med. 2018 Sep 24;:]. Nat Med. 2018;24(10):1532-1535. doi:10.1038/s41591-018-0164-x
81. Boland M, Alam F, Bronlund J. Modern Technologies for Personalized Nutrition. 2019; doi:10.1016/B978-0-12-816403-7.00006-4.
82. Forster H, Walsh MC, Gibney MJ, Brennan L, Gibney ER. Personalised nutrition: the role of new dietary assessment methods. Proc Nutr Soc. 2016;75(1):96-105. doi:10.1017/S0029665115002086
83. Lecroq T, Soualmia LF. Managing large-scale genomic datasets and translation into clinical practice. Yearb Med Inform. 2014;9(1):212-214. Published 2014 Aug 15. doi:10.15265/IY-2014-0039
84. Saxena R, Saxena RR, Saxena AR. Microbiomics in the Molecular Era: A Bird's Eye View into the Future of Personalized Medicine. Acta Scientific Microbiology. 2018;1(8):34-39.
85. Lloyd-Price J, Arze C, Ananthakrishnan AN, et al. Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases. Nature. 2019;569(7758):655-662. doi:10.1038/s41586-019-1237-9
86. Zhou W, Sailani MR, Contrepois K, et al. Longitudinal multi-omics of host-microbe dynamics in prediabetes. Nature. 2019;569(7758):663-671. doi:10.1038/s41586-019-1236-x
87. Integrative HMP (iHMP) Research Network Consortium. The Integrative Human Microbiome Project: dynamic analysis of microbiome-host omics profiles during periods of human health and disease. Cell Host Microbe. 2014;16(3):276-289. doi:10.1016/j.chom.2014.08.014.
88. Devika NT, Raman K. Deciphering the metabolic capabilities of Bifidobacteria using genome-scale metabolic models. Sci Rep. 2019;9(1):18222. Published 2019 Dec 3. doi:10.1038/s41598-019-54696-9
89. Shima H, Masuda S, Date Y, et al. Exploring the Impact of Food on the Gut Ecosystem Based on the Combination of Machine Learning and Network Visualization. Nutrients. 2017;9(12):1307. Published 2017 Dec 1. doi:10.3390/nu9121307
90. Mohammed A, Guda C. Application of a hierarchical enzyme classification method reveals the role of gut microbiome in human metabolism. BMC Genomics. 2015;16 Suppl 7(Suppl 7):S16. doi:10.1186/1471-2164-16-S7-S16
91. Celis-Morales C, Lara J, Mathers JC. Personalising nutritional guidance for more effective behaviour change. Proc Nutr Soc. 2015;74(2):130-138. doi:10.1017/S0029665114001633
92. Qi L. Personalized nutrition and obesity. Ann Med. 2014;46(5):247-252. doi:10.3109/07853890.2014.891802
93. Lee A, Mavaddat N, Wilcox AN, et al. BOADICEA: a comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors [published correction appears in Genet Med. 2019 Feb 21;:]. Genet Med. 2019;21(8):1708-1718. doi:10.1038/s41436-018-0406-9
94. van Ommen B, Keijer J, Kleemann R, et al. The challenges for molecular nutrition research 2: quantification of the nutritional phenotype. Genes Nutr. 2008;3(2):51-59. doi:10.1007/s12263-008-0084-3
95. Verma M, Hontecillas R, Tubau-Juni N, Abedi V, Bassaganya-Riera J. Challenges in Personalized Nutrition and Health. Front Nutr. 2018;5:117. Published 2018 Nov 29. doi:10.3389/fnut.2018.00117.
96. Jia W, Li H, Zhao L, Nicholson JK. Gut microbiota: a potential new territory for drug targeting. Nat Rev Drug Discov. 2008;7(2):123-129. doi:10.1038/nrd2505
97. Nagpal R, Mainali R, Ahmadi S, et al. Gut microbiome and aging: Physiological and mechanistic insights. Nutr Healthy Aging. 2018;4(4):267-285. Published 2018 Jun 15. doi:10.3233/NHA-170030
98. O'Toole PW, Marchesi JR, Hill C. Next-generation probiotics: the spectrum from probiotics to live biotherapeutics. Nat Microbiol. 2017;2:17057. Published 2017 Apr 25. doi:10.1038/nmicrobiol.2017.57
99. Senior AW, Evans R, Jumper J, et al. Improved protein structure prediction using potentials from deep learning. Nature. 2020;577(7792):706-710. doi:10.1038/s41586-019-1923-7
100. Wilmanski T, Rappaport N, Earls JC, et al. Blood metabolome predicts gut microbiome α-diversity in humans. Nat Biotechnol. 2019;37(10):1217-1228. doi:10.1038/s41587-019-0233-9
101. Yu J, Feng Q, Wong SH, et al. Metagenomic analysis of faecal microbiome as a tool towards targeted non-invasive biomarkers for colorectal cancer. Gut. 2017;66(1):70-78. doi:10.1136/gutjnl-2015-309800309800
102. Silver D, Huang A, Maddison CJ, et al. Mastering the game of Go with deep neural networks and tree search. Nature. 2016;529(7587):484-489. doi:10.1038/nature16961
103. Zeevi D, Korem T, Zmora N, et al. Personalized Nutrition by Prediction of Glycemic Responses. Cell. 2015;163(5):1079-1094. doi:10.1016/j.cell.2015.11.001
104. Singh A, Shannon CP, Gautier B, et al. DIABLO: an integrative approach for identifying key molecular drivers from multi-omics assays. Bioinformatics. 2019;35(17):3055-3062. doi:10.1093/bioinformatics/bty1054
105. Tsubaki M, Tomii K, Sese J. Compound-protein interaction prediction with end-to-end learning of neural networks for graphs and sequences. Bioinformatics. 2019;35(2):309-318. doi:10.1093/bioinformatics/bty535
106. Zhang L, Lv C, Jin Y, et al. Deep Learning-Based Multi-Omics Data Integration Reveals Two Prognostic Subtypes in High-Risk Neuroblastoma. Front Genet. 2018;9:477. Published 2018 Oct 18. doi:10.3389/fgene.2018.00477
107. Zhou T, Wang M, Ma H, Li X, Heianza Y, Qi L. Dietary Fiber, Genetic Variations of Gut Microbiota-derived Short-chain Fatty Acids, and Bone Health in UK Biobank. J Clin Endocrinol Metab. 2021;106(1):201-210.

doi:10.1210/clinem/dgaa740
108. Wang F, Preininger A. AI in Health: State of the Art, Challenges, and Future Directions. Yearb Med Inform. 2019;28(1):16-26. doi:10.1055/s-0039-1677908
109. Lu Y, Stathopoulou T, Vasiloglou MF, et al. An Artificial Intelligence-Based System for Nutrient Intake Assessment of Hospitalised Patients. Annu Int Conf IEEE Eng Med Biol Soc. 2019;2019:5696-5699. doi:10.1109/EMBC.2019.8856889
110. Clarke R, Ressom HW, Wang A, et al. The properties of high-dimensional data spaces: implications for exploring gene and protein expression data. Nat Rev Cancer. 2008;8(1):37-49. doi:10.1038/nrc2294
111. Parikh RB, Teeple S, Navathe AS. Addressing Bias in Artificial Intelligence in Health Care. JAMA. 2019;322(24):2377-2378. doi:10.1001/jama.2019.18058
112. Carter SM, Rogers W, Win KT, Frazer H, Richards B, Houssami N. The ethical, legal and social implications of using artificial intelligence systems in breast cancer care. Breast. 2020;49:25-32. doi:10.1016/j.breast.2019.10.001
113. Vodovotz Y, Xia A, Read EL, et al. Solving Immunology?. Trends Immunol. 2017;38(2):116-127. doi:10.1016/j.it.2016.11.006
114. Kannry J, Sengstack P, Thyvalikakath TP, et al. The Chief Clinical Informatics Officer (CCIO): AMIA Task Force Report on CCIO Knowledge, Education, and Skillset Requirements. Appl Clin Inform. 2016;7(1):143-176. Published 2016 Mar 16. doi:10.4338/ACI-2015-12-R-0174
115. Snoek HM, Eijssen LMT, Geurts M, Vors C, Brown KA, Zimmermann MJ, van't Veer PP. Advancing food, nutrition, and health research in Europe by connecting and building research infrastructures in a DISH-RI: Results of the EuroDISH project. Trends Food Sci Tech. 2018;73:58–66. doi:10.1016/j.tifs.2017.12.015
116. Ehteshami Bejnordi B, Veta M, Johannes van Diest P, et al. Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer. JAMA. 2017;318(22):2199-2210. doi:10.1001/jama.2017.14585
117. Na L, Yang C, Lo CC, Zhao F, Fukuoka Y, Aswani A. Feasibility of Reidentifying Individuals in Large National Physical Activity Data Sets From Which Protected Health Information Has Been Removed With Use of Machine Learning. JAMA Netw Open. 2018;1(8):e186040. Published 2018 Dec 7. doi:10.1001/jamanetworkopen.2018.6040
118. Mossotto E, Ashton JJ, O'Gorman L, et al. GenePy - a score for estimating gene pathogenicity in individuals using next-generation sequencing data. BMC Bioinformatics. 2019;20(1):254. Published 2019 May 16. doi:10.1186/s12859-019-2877-3
119. Yoon J, Drumright LN, van der Schaar M. Anonymization Through Data Synthesis Using Generative Adversarial Networks (ADS-GAN). IEEE J Biomed Health Inform. 2020;24(8):2378-2388. doi:10.1109/JBHI.2020.2980262
120. Baowaly MK, Lin CC, Liu CL, Chen KT. Synthesizing electronic health records using improved generative adversarial networks. J Am Med Inform Assoc. 2019;26(3):228-241. doi:10.1093/jamia/ocy142
121. Barker H. Global economic inequality and health. Med Confl Surviv. 2020;36(4):368-374. doi:10.1080/13623699.2020.1848577
122. Saxena R, Yakyomovych O. Gut Microbiome, A Link between Nutrition, Physiology, and Pathology: Insights into Current Status and Future Directions. Int J Collab Res Intern Med Public Health. 2023,15(3):1-5
123. Claesson MJ, Jeffery IB, Conde S, et al. Gut microbiota composition correlates with diet and health in the elderly. Nature. 2012;488(7410):178-184. doi:10.1038/nature11319
124. Pérez Martínez G, Bäuerl C, Collado MC. Understanding gut microbiota in elderly's health will enable intervention through probiotics. Benef Microbes. 2014;5(3):235-246. doi:10.3920/BM2013.0079.
125. Davenport ER, Mizrahi-Man O, Michelini K, Barreiro LB, Ober C, Gilad Y. Seasonal variation in human gut microbiome composition. PLoS One. 2014;9(3):e90731. Published 2014 Mar 11. doi:10.1371/journal.pone.0090731
126. O'Toole PW, Jeffery IB. Gut microbiota and aging. Science. 2015;350(6265):1214-1215. doi:10.1126/science.aac8469
127. Hills RD Jr, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut Microbiome: Profound Implications for Diet and Disease. Nutrients. 2019;11(7):1613. Published 2019 Jul 16. doi:10.3390/nu11071613
128. Jin Q, Black A, Kales SN, Vattem D, Ruiz-Canela M, Sotos-Prieto M. Metabolomics and Microbiomes as Potential Tools to Evaluate the Effects of the Mediterranean Diet. Nutrients. 2019;11(1):207. Published 2019 Jan 21. doi:10.3390/nu11010207
129. Lara KM, Levitan EB, Gutierrez OM, et al. Dietary Patterns and Incident Heart Failure in U.S. Adults Without Known Coronary Disease. J Am Coll Cardiol. 2019;73(16):2036-2045. doi:10.1016/j.jacc.2019.01.067
130. Gentile CL, Weir TL. The gut microbiota at the intersection of diet and human health. Science. 2018;362(6416):776-780. doi:10.1126/science.aau5812
131. Zmora N, Suez J, Elinav E. You are what you eat: diet, health and the gut microbiota. Nat Rev Gastroenterol Hepatol. 2019;16(1):35-56. doi:10.1038/s41575-018-0061-2
132. Zhernakova A, Kurilshikov A, Bonder MJ, et al. Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity. Science. 2016;352(6285):565-569. doi:10.1126/science.aad3369
133. Chen F, Du M, Blumberg JB, et al. Association Among Dietary Supplement Use, Nutrient Intake, and Mortality Among U.S. Adults: A Cohort Study. Ann Intern Med. 2019;170(9):604-613. doi:10.7326/M18-2478

134. Conlon MA, Bird AR. The impact of diet and lifestyle on gut microbiota and human health. Nutrients. 2014;7(1):17-44. Published 2014 Dec 24. doi:10.3390/nu7010017
135. Singh RK, Chang HW, Yan D, et al. Influence of diet on the gut microbiome and implications for human health. J Transl Med. 2017;15(1):73. Published 2017 Apr 8. doi:10.1186/s12967-017-1175-y
136. Thorburn AN, Macia L, Mackay CR. Diet, metabolites, and "western-lifestyle" inflammatory diseases. Immunity. 2014;40(6):833-842. doi:10.1016/j.immuni.2014.05.014
137. Sonnenburg JL, Bäckhed F. Diet-microbiota interactions as moderators of human metabolism. Nature. 2016;535(7610):56-64. doi:10.1038/nature18846
138. Baxter NT, Schmidt AW, Venkataraman A, Kim KS, Waldron C, Schmidt TM. Dynamics of Human Gut Microbiota and Short-Chain Fatty Acids in Response to Dietary Interventions with Three Fermentable Fibers. mBio. 2019;10(1):e02566-18. Published 2019 Jan 29. doi:10.1128/mBio.02566-18.
139. Johnson AJ, Vangay P, Al-Ghalith GA, et al. Daily Sampling Reveals Personalized Diet-Microbiome Associations in Humans. Cell Host Microbe. 2019;25(6):789-802.e5. doi:10.1016/j.chom.2019.05.005
140. Zhang P, Wang F, Hu J, Sorrentino R. Towards personalized medicine: leveraging patient similarity and drug similarity analytics. AMIA Jt Summits Transl Sci Proc. 2014;2014:132-136. Published 2014 Apr 7.
141. Zhang X, Chou J, Wang F. Integrative analysis of patient health records and neuroimages via memory-based graph convolutional network. In: Proceedings of the 2018 IEEE International Conference on Data Mining (ICDM), Singapore. 2018;767-770. doi:10.48550/arXiv.1809.06018
142. Gottesman O, Kuivaniemi H, Tromp G, et al. The Electronic Medical Records and Genomics (eMERGE) Network: past, present, and future. Genet Med. 2013;15(10):761-771. doi:10.1038/gim.2013.72
143. Li L, Cheng WY, Glicksberg BS, et al. Identification of type 2 diabetes subgroups through topological analysis of patient similarity. Sci Transl Med. 2015;7(311):311ra174. doi:10.1126/scitranslmed.aaa9364
144. Saxena R, Carnevale K, Sharma K. Digital Pathology and AI: A Paradigm Shift in Pathology Education. Journal of Population Therapeutics and Clinical Pharmacology, 2023;30(9):454-462. doi:10.53555/jptcp.v30i4.2672
145. Zhang N, Ju Z, Zuo T. Time for food: The impact of diet on gut microbiota and human health. Nutrition. 2018;51-52:80-85. doi:10.1016/j.nut.2017.12.005