Algae and Environment
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Review

Bioinformatics and Multi-Omics-Driven Algal Systems Biology for Environmental and Biotechnological Applications

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How To Cite: Rehman, O.U.; Tayyab, M.; Liu, W.; et al. Bioinformatics and Multi-Omics-Driven Algal Systems Biology for Environmental and Biotechnological Applications. *Algae and Environment* **2025**, *1*(1), 7. https://doi.org/10.53941/algaeenviron.2025.100007

Received: 15 November 2025
Revised: 8 December 2025
Accepted: 18 December 2025
Published: 22 December 2025

Abstract: Significant improvement in bioinformatics and integrated multi-omics technologies that enable interrogation of biological complexity on the system level to advance algal research. Genomic analyses provide a foundational blueprint that enables the production of high-quality genomes and the identification of genes responsible for desirable characteristics, such as high lipid production and stress resilience. Transcriptomic profiling also describes the dynamics of gene expression, thereby explaining the regulatory networks that control key pathways, including photosynthesis and carbon partitioning. Proteomic analyses map the functional proteome and essential post-translational adaptations, whereas the study of endogenous small molecules by metabolomics can map metabolic flux and verify the rate-limiting step. This strong combination of heterogeneous data, facilitated by computational pipelines, enables the reconstruction of genome-scale metabolic models, which in turn facilitate the prediction of metabolic fluxes and the identification of strategic engineering leverage points. These efforts are complemented by machine-learning methods that identify subtle trends in large datasets to enhance gene annotation, predict gene behavior, and optimize cultivation in silico. Together, these bioinformatics-based procedures can provide an exceptional and widespread understanding of algal physiology. This systems-biology platform will expedite the rational design and development of engineered algal strains, thereby streamlining the use of algal strains for the generation of sustainable biofuels, high-value bioproducts, and industrial biotechnology.

Keywords: algal genetic engineering; multi-omics; bioinformatics; environment; metabolic pathway; industrialization

1. Introduction

Algae are a diverse and flexible group of photosynthetic organisms with high biodiversity. They have a lot of promise in a range of applications, including biofuels, bioremediation, pharmaceuticals, and food production [1,2]. Algal resources are not fully exploited, and yet their potential remains underutilized, leaving opportunities to address various global challenges. The versatility and performance of algal products and technologies drive the demand. Their ability to live in diverse water systems, such as freshwater and high-salinity habitats, coupled with high growth rates under favorable conditions, makes them central elements in biotechnological development in the future [3]. In addition, algae play a crucial role in carbon sequestration by absorbing large amounts of carbon dioxide and, therefore, contribute to mitigating the effects of climate change [4]. To achieve this potential, screening, monitoring, characterization, and mass-scale production are required.

Over the past few decades, algal technology has advanced significantly in response to global sustainability requirements, which include addressing climate change, meeting the need for renewable energy, and promoting environmental protection. The developments in science have transformed the image of algae from an ecological element into essential biotechnological tools. The intensive advancement of algal studies has been significantly promoted by the incorporation of advanced tools and technologies. For example, innovations in genome editing, particularly the CRISPR-Cas9 system, enable the creation of specific genetic changes that optimize growth performance, lipid production, and stress tolerance in algal strains [5]. In parallel, big-data analytics and computational biology have transformed high-throughput screening and strain characterization, delivering system-level insights into genetic, phenotypic, and metabolic traits and revealing actionable optimization levers (Figure 1). In its turn, the omics technologies provide a detailed systemic understanding of algal biology, which is the basis of new applications [6,7].

The above developments highlight the fact that algal technologies have a major challenge in their scalability. The automated imaging and computational modeling would be crucial to the accurate characterization, tracking, and scaling of production to bridge the gap between laboratory research and practical application. These innovations address scalability challenges and improve the viability of algae-based products. The development of innovative equipment and technologies also accentuates the revolutionizing nature of algal technology. The following sections outline cultivation and scale-up strategies. This mini-review paper aims to highlight the importance and relevance of algal technologies, demonstrate the development of algal technologies that has expanded their application, as well as underline the growing relevance of algal technologies in the current scientific, industrial and environmental realms.

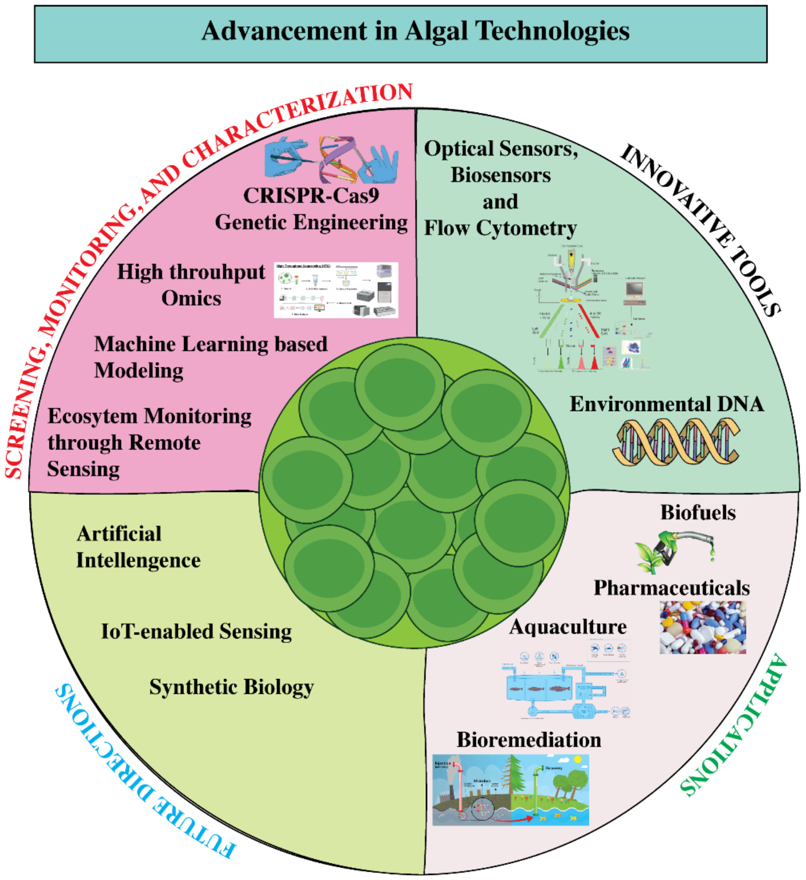

Figure 1. Integrative overview of key tools and applications in algal research, including screening and characterization, tools and methods, their applications, and future prospects. The most significant advancements include CRISPR-based engineering, high-throughput omics, machine learning, biosensing, and environmental DNA analysis. The use of such technologies in various industries, with special emphasis on biofuel production, aquaculture, pharmaceutical development, and bioremediation processes.

2. Decoding Algal Genome through Advanced Bioinformatics

Bioinformatics has developed new approaches for studying algae through computational-based analysis of algal data, enabling the combination and interrogation of large datasets in genomes, transcriptomes, and proteomes [8]. Algal genomes are assembled and annotated using advanced bioinformatics pipelines, thereby facilitating the identification of genes and pathways associated with desirable characteristics, such as high lipid content, high growth rates, and stress resistance [9]. Bioinformatics also plays a crucial role in establishing genetic clues of these desirable characteristics, which could be utilized in strain enhancement programs to boost breeding activities or serve as a base for genetic engineering (Figure 2). Moreover, computational comparative genomics assists in identifying evolutionarily close algal species and those with metabolically beneficial properties, thus providing genomic information that can be used to select strains for industrial or environmental use [10].

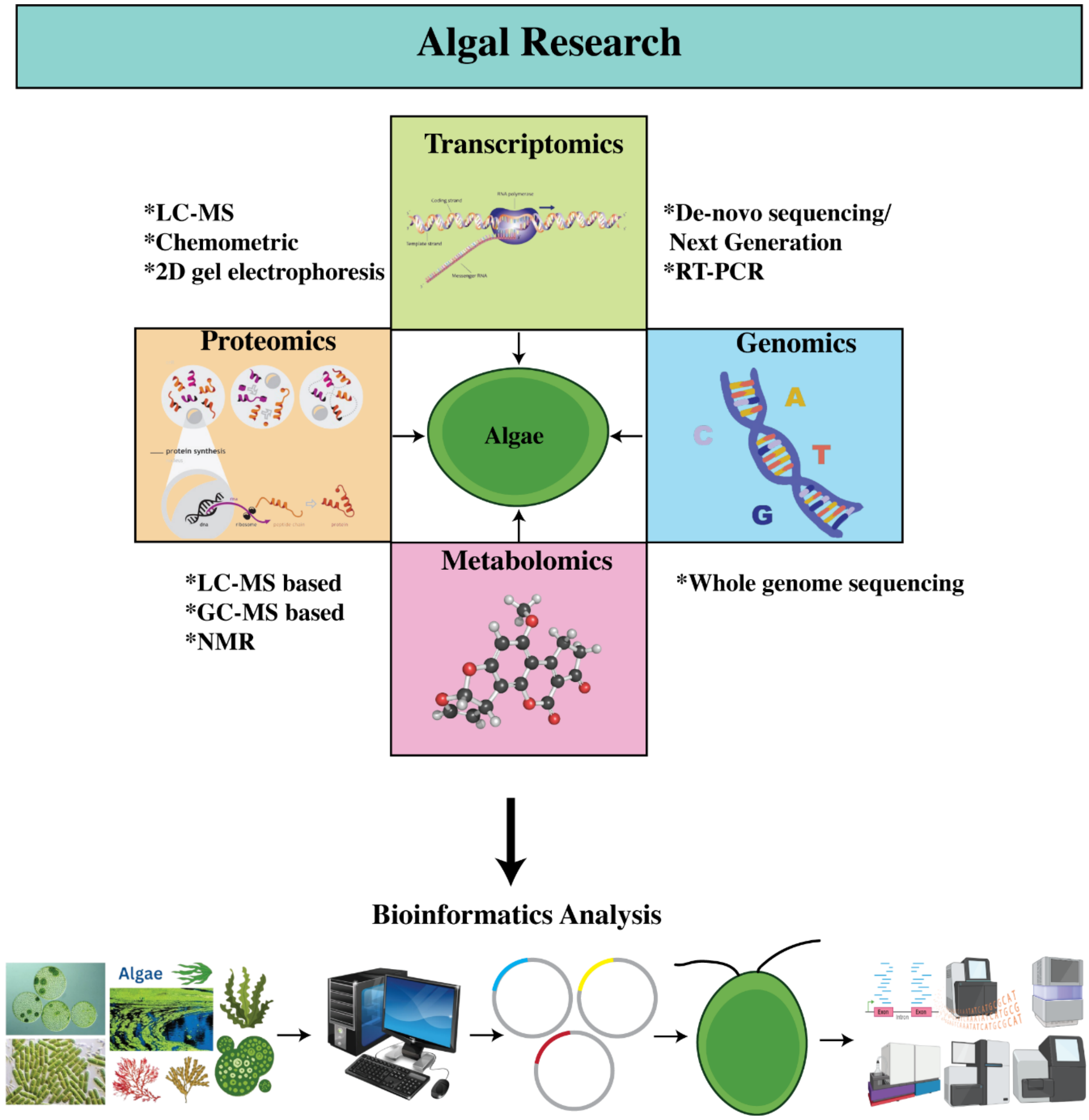

Figure 2. Multi-omics framework (genomics, transcriptomics, proteomics, metabolomics) linked to analytical platforms, and how these data inform metabolic modeling and engineering. Comprehensive integration of bioinformatics resources for the interpretation of algal functions, metabolic regulation, and biotechnological potentials. The multi-omics framework provides a description of the utilization of transcriptomics, genomics, proteomics, and metabolomics to study the algal systems. High-resolution characterization is enabled by sophisticated methods of analysis, such as next-generation sequencing, liquid chromatography-mass spectrometry, gas chromatography-mass spectrometry, nuclear magnetic resonance, and chemometric analysis.

Omics technologies such as genomics, transcriptomics, proteomics, and metabolomics are the tools that are able to give a complete picture of algal biology and allow the genetic, transcriptional, protein, and metabolic pathways to be analyzed in a comprehensive manner. High-throughput sequencing (HTS) systems enable a comprehensive study of the molecular mechanisms by which algal physiology, productivity, and adaptive responses to environmental changes are determined [11]. The arrival of omics data allows researchers to gain a deeper understanding of the complex interactions that control the various functions of algae, thus making it easier to make more specific strain improvements and optimized cultivation procedures (Table 1).

Table 1. Advanced bioinformatics-enabled approaches in algae research and biotechnology.

Research Area	Research Focus	Key Technology	Outcomes	Significance	References
Evolutionary genomics and adaptive evolution	Genome diversification consisting of hypermutation and wholesome phenotypic information of tolerance phenotyping by whole-genome and transcriptomic mapping	Whole-genome sequencing, RNA sequencing, variant calling, and evolutionary genomics	Cyanobacteria mutations that boost their tolerance to high light and high temperature were discovered	Such findings can be used to develop climate-adaptive microalgal cultures to be grown outside	[12]
Optogenetics and regulatory genomics	Mapping light-sensing and regulatory circuits of nonphotochemical quenching (NPQ) and photoprotection	CRISPR, functional genomics, photobiology, and regulatory motif mapping	An *AUREO1c* opto-switch that controls light acclimation in diatoms was discovered	offers adjustable light-control destination to maximize productivity	[13]
Genome-scale metabolism modeling (GEMs)	Resource-allocation modelling of the prediction of nutrient and carbon	GEM reconstruction, flux-balance analysis (FBA), as well as constraint-based modelling	Allowed minimized nutrient feeding tactics to be used in the cultivation of *chlorella* to lower the cost of cultivation, and biomass can still be formed	Enhances the efficiency of commercial production and reduces the media costs	[14]
Comparative and functional genomics	Expanding the genomic diversity of the algae and the discovery of industrially significant strains	General quality assembling of genomes, phylogenomic, and pan-genome	There was a new species of *Chlorella-purpolike* with isolated metabolic characteristics found in meromictic lakes	Increases the industrial strain library and improves the selection of selection accuracy of strains	[15]
Proteomics and cell biology	Metabolic partitioning and proteome organelle mapping	Confocal microscopy and subcellular protein localization with high-resolution proteomics	Discovery of a red-body organelle that coordinates lipid trafficking in *Nannochloropsis*	Identifies subcellular sites relevant to lipid trafficking and engineering	[16]
Machine-learning guided cultivation	Optimization of harvesting and production of biomass using data	Neural network, regression model, and optimization	Semi-continuous cultivation strategies enhanced by machine learning and avoided the high cost of harvesting	Helps in scaling up with real-time adaptive control	[17]

Table 1. *Cont.*

Research Area	Research Focus	Key Technology	Outcomes	Significance	References
Metabolomics/ toxin/pigment profiling	Unidentified metabolome mapping with the aim of determining biomarkers and high-value compounds	LC -MS / MS, GC -MS, NMR, high-dimensional metabolomics, and chemometrics	Toxin and pigmentation identification, and metabolism-related screening	Improves quality management and identification of bioproducts of high value	[18]
Synthetic engineering of bioenergy	Protein -fusion systems involving algal photosystems and hydrogenases	Design of biohybrid protein engineering, structural modelling, and PSI-hydrogenase protein engineering	Constant hydrogen production through PSI electron transfer	Takes microalgal hydrogen fuel production to realistic grounds	[19]
Bio-interfaces and bio-processing	Development of biomaterial systems of algal-hydrogel systems to be grown in a recovery manner	Polymer engineering, Material-computation	Development of scalable, retrievable microalgae-hydrogel networks for safe deployment	Decreases the leakage of culture and enhances the safety of the environment	[20]
Predicting the environment and forecasting bloom	The application of machine learning on environmental omics to forecast harmful algal blooms (HABs)	Remote sensing, environmental genomics, and machine learning	Prediction of *dinoflagellate* bloom initiation with high accuracy using multi-omics environmental signatures	Improves HAB early-warning measures	[21]
Engineering of high-value products strain	CRISPR-mediated pathway promotion of lipid, pigment, and metabolite	CRISPR-Cas9, target engineering, and targeted mutagenesis	Better lipid (2-3 times) and carotenoid (e.g., astaxanthin pathways) enrichment	Allows microalgal biorefinery of the next generation	[22]
Multi-omics at an ecosystem level	Algal-microbe interrelations, environmental metagenomics, and transcriptomics to comprehend the interaction	Meta-omics pipelines, network inference, and a model of microbial community	Determination of microbial partners to increase nutrient uptake in microalgal consortia	Directs bioculture engineering of wastewater treatment and bio-energy	[23]

One of the most important processes in bioinformatics is the reconstruction of the metabolic pathways, which provides a global metabolic map of the algal cell. These reconstructions provide a systems-level picture of algal metabolism, identifying potential bottlenecks and pinpointing metabolic engineering targets [24]. Bioinformatics enables the prediction of metabolic fluxes and the creation of custom metabolic pathways, which increase the yield of biofuel or bioproducts by integrating multi-omics datasets. The integration of multi-omics data with the genome-scale metabolic model, in turn, enables the prediction and optimization of metabolic pathways. Together, these studies define the rate-limiting stages and key enzymes that can be manipulated to enhance the yield of useful metabolites, which include itaconic acid in *Yarrowia lipolytica* and biofuels in microalgae [25]. This work broadens the application of density functional theory and bioinformatics by applying computational analysis with mathematical modelling, machine learning, and systems-biology methods and providing an integrative and predictive level. Numerical models are also used to simulate the algal culture growth, productivity and resource utilization under different conditions, thus becoming beneficial in optimization of cultivation and economic efficiency.

Machine-learning algorithms have the capability of discovering latent patterns and relationships in big data, especially those related to environmental disturbances like algal blooms. An example is that these algorithms are used to analyze information on dinoflagellates and biotoxin impacts in the water ecology [26]. These algorithms can be used to predict an algal bloom event or optimize the operating conditions of a photobioreactor when used on IoT-enabled sensors. Machine learning, when combined with bioinformatics, can enhance the accuracy of predicting gene function as well as help to determine new candidate targets of genetic engineering.

2.1. Unveiling Algal Blueprints via Genomics

Genomics forms the core basis of omics technologies, which provides a holistic understanding of an organism's genetic structure. The utility of high-throughput sequencing technologies, including next-generation sequencing (NGS) and third-generation long-read sequencing, has made the construction of high-quality algal genomes possible (Figure 2). These genomic resources can be used to discover genes that are linked to favorable phenotypes, such as increased lipid biosynthesis, stress tolerance, and increased growth kinetics. Comparative genomics studies have enhanced our knowledge of algae diversity by exposing evolutionary mechanisms and metabolism of the various taxa. The data obtained through the sequencing of algal strains of industrial interest, such as *Chlamydomonas reinhardtii*, have been used to help to explain metabolic pathways that are involved in the production of biofuels and bioproducts [27]. This information can therefore help to make genomic manipulation accurate with the use of CRISPR-Cas9 and optimized transformation procedures.

Recent studies have utilized the CRISPR-based platforms to introduce specific edits into the genomes of microalgae to examine how these edits can be used to optimize endogenous genetic processes to produce biofuels and additional uses. As an example, the creation of MIG and BC1 (Biobrick compatible) plasmid constructs in the Modular Cloning toolkit in the case of the green cell factory (that is, *Chlamydomonas reinhardtii*) can be seen as an example of such a strategy [28]; such constructs allow the synthesis of promoters and genetic elements, which can be rapidly and predictably manipulated, to facilitate the exploitation of microalgae as green cell factories. Making annotated genomes available will be valuable to genetic engineering and synthetic biology projects that seek to enhance productivity. The Algal Functional Annotation Tool, among other integrated systems, can be used to mine large volumes of genomic data to provide functional annotations of genes, which is a requirement to drive algal biotechnology forward. PhycoCosm, a database that provides genome sequences and annotations of more than one hundred algal genomes, is a valuable resource in bioenergy and environmental studies, offering both collaborative tools and access to other complementary databases [29].

2.2. Deciphering Algal Transcriptomic Dynamics

The analysis of gene expression dynamics reveals that the transcriptomics field primarily focuses on RNA molecules, providing a snapshot of gene expression under specific conditions at a given point in time (Figure 2). RNA sequencing (RNA-Seq) is a powerful methodological model, which can be used to measure the transcript abundance in a complex sample, which can be used to point to the identification of differentially expressed genes under certain environmental or experimental conditions. The method is especially effective when the metabolic responses of algae to a light, temperature, or nutrient are to be examined [30]. The transcriptomic studies have identified some important regulatory networks in the pathways such as photosynthesis, lipid biosynthesis and in stress responses. An example is the discovery of transcription factors that cause carbon distribution to storage lipids and not carbohydrates, which have been used to guide the approach in developing a high yield of biofuels [31].

Besides, combined analysis of transcriptomic samples by proteomic and metabolomic data allows building and evaluating predictive models of algal metabolic engineering. The biosynthesis of triacylglycerol and astaxanthin in response to salt stress in *Chromochloris zofingiensis* was coordinately regulated through a multi-omics strategy; this showed potential engineering prospects to produce more lipid [32]. Transcriptomic studies have found important genes and pathways involved in photosynthesis and lipid biosynthesis. Examples of up-regulated genes that were identified to be related to fatty acid biosynthesis and photosynthesis that were linked with increased lipid synthesis have been found in *Scenedesmus obliquus*, as were down-regulated genes that were related to starch metabolism [33]. Similarly, heat stress lipidomic and transcriptomic analyses of *Chlamydomonas reinhardtii* have revealed the direct conversion of membrane lipids to storage lipids, and several genes associated with the conversion, including phospholipase A2 and diacylglycerol acyltransferase, are central to this process [34]. The responses of algae to the stress conditions, such as salt and heat stress are regulated by complex regulatory networks. As an example, it was shown that high salinity and nitrogen deficiency induced gene modifications associated with photosynthesis and lipid metabolism (exemplified by the previously mentioned *Dunaliella tertiolecta*), transcriptomic analyses showed that particular genes were up-regulated significantly in response to the stressful conditions. On the same note, a clearer level of transcriptomic analysis in *Chlamydomonas reinhardtii* showed up-regulation of processing genes that are related to photosynthesis and signaling pathways in response to salt stress [35].

2.3. Algal Proteomics for Profiling Functional Proteins

Proteomics is a field of research that focuses on the detailed study of the proteome that is expressed by an organism and provides the much needed information about the functional components that are involved in the cell processes. Highly precise and sensitive detection and quantification of proteins can be done by the use of state-of-the-art mass spectrometric methodology such as the case of tandem mass spectrometry. Proteomic investigations into post-translational modification and protein-protein interactions are also invaluable in the explanation of regulatory process by which cell functions are regulated (Figure 2).

In the algal studies, proteomic analyses have given valuable information regarding the phototransduction processes and nutrient absorption in photosynthesis, which regulate its efficiency [36]. Indicatively, research work on protein structure of photosystems and light-harvesting complex has established how light absorption and energy transduction can be enhanced in algal cultures [37]. Moreover, environmental stress proteomics has enabled the design of algal strains that are resistant to environmental stressors including salinity, temperatures, and oxidative stress. Proteomic profiling can be used to determine these proteins, highlighting the adaptability of the organisms to changes in nutrient levels, salinity, and temperature. The mediation of such adaptability is through the modulation of the metabolic pathways and stress-tolerance mechanisms.

Proteomic studies in *Chlorella vulgaris* have confirmed that photosystem II is inhibited by environmental pollutants, such as cetyltrimethylammonium chloride, which suppresses the oxygen evolution process and the photosynthetic rate. This, in turn, suggests that the photosynthetic machinery can be easily compromised by extrinsic factors [36]. The analysis of proteins and transporters involved in nitrogen acquisition revealed that during growth under nitrogen-limiting conditions, proteins and transporters involved in nitrogen assimilation are upregulated, enabling the organism to effectively acquire nitrogen and maintain metabolic homeostasis. Proteomic profiling of *Polytomella* sp. during assimilation with butyrate revealed oxidative stress response pathways, and this may increase resilience in algae [38].

2.4. Exploring Algal Metabolomic Pathways

Metabolomics supports the comprehensive analysis of small-molecule metabolites therefore, providing direct information on cellular processes and metabolism. Considerable tools, such as nuclear magnetic resonance (NMR) spectroscopy and gas chromatography-mass spectrometry (GC-MS) are regularly used to recognize and quantify metabolites along biochemical pathways (Figure 2). This has been particularly useful in algal technologies where metabolomics has been widely implemented to determine bottlenecks and optimize the pathways in order to generate biofuels [39]. Metabolomic probes have shown the accumulation of lipid biosynthesis pathway intermediates, providing important information for instituting metabolic engineering interventions to increase lipid yield [40]. In addition, the prediction of the resultant metabolites of the stress has further complemented the understanding of how the algal acclimation occurs, and has thus enabled the optimization of the conditions in the algal cultivation process to maximize productivity. Metabolomics, as a part of systems biology, is a holistic analysis of the metabolism of algae through the combination of genomics, transcriptomics and proteomics. This integration is essential to uncover genes, metabolic pathways, and regulatory networks that are key to the development of strains and enhancement of biofuel production. The correlation between chemical quality properties and algal strain productivity makes it possible to further appreciate the potential of these properties in a wide range of applications.

The high-order analytical methods, including mass spectrometry (MS) and nuclear magnetic resonance (NMR), are essential for identifying the profile of the metabolites in algae as well as the identification of useful compounds, including lipids, proteins, and pigments [41]. These techniques have significantly improved the analysis of both microalgal lipids and metabolites with NMR technology, achieving extensive application in high-throughput metabolomics and lipidomics studies of microalgae. The technique provides both qualitative and quantitative data on endogenous metabolites and lipids, hence providing an extensive overview of the state of physiological conditions of the microalgae [42]. It is especially beneficial when it comes to breaking down the composition, structure, and activity of unusual metabolites, a task that is of utmost importance in the creation of sustainable biorefineries and the manufacture of value-added goods. The profiling of algal metabolites is widely used in conjunction with the application of mass spectrometry, including sophisticated approaches such as liquid chromatography-mass spectrometry (LC-MS). The methods provide the opportunity to profile exhaustively the types of metabolites/ lipids found in microalgae in a short time frame, thereby providing valuable data on the phytoplankton biodiversity and in the development of the biotechnological products. Indicatively, using LC-MS in screening and identifying metabolites like brevetoxins in dinoflagellate *Karenia brevis* improves the understanding of the ecological danger of harmful algal blooms [43]. The highly advanced method of PACyESI-MS also enables the rapid identification of single microalgal metabolites, which is a critical ability in metabolic engineering projects [44].

NMR- and MS-based algal metabolic profiling is a potent arsenal of methods for the integrated characterization of algal strains. Not only do these technologies help discover multifunctional compounds, but they also provide the basis of a large-scale sustainable application of biotechnology. Combined with bioinformatics tools, they make it possible to use microalgae in their entirety in numerous biotechnological applications within manufacturing and ecology sectors. The corresponding sophisticated data analysis methods play a crucial role in detecting and identifying high-value substances of interest in target microalgae, and the technique of their application has a wide range of biofuels, food, feed, medicine, and cosmetics [45]. The high-speed and accurate profiling of algal metabolites drives the design of high-performance microalgal strains, thus clarifying how they operate. With the emergence of omics technologies, even more opportunities to study algae have never been offered to researchers, and they have gained a profound understanding of the molecular processes underlying algal physiology and metabolism. By combining multi-omics datasets, scholars will be able to address not only the complex task of biofuel production but also the explanation of the ecosystem reaction to environmental alterations. These technologies are bound to be integrated into the Algae Toolbox as they keep innovating, thus helping in the development of solutions to the global problem of sustainable generation of food and energy.

3. Challenges and Future Prospectives

3.1. Challenges in Algal Research

Achieving a predictive, systems-level understanding of algal physiology remains challenging because multi-omics layers (transcripts, proteins, metabolites, fluxes) are only partly coupled in microalgae and can diverge under stress. For example, in *Chlamydomonas reinhardtii*, heat shock triggers rapid membrane-lipid remodeling and TAG accumulation that outpaces mRNA changes, reflecting strong post-transcriptional and post-translational control; similar stress-linked photosynthetic and proteomic shifts are reported in *Chlorella vulgaris* under pollutant exposure. These discordances complicate constraint-based modeling and the prioritization of engineering targets [46].

A persistent bottleneck in functional annotation is particularly prevalent in algae. Many genes in non-model taxa remain hypothetical, limiting rational pathway design for traits like high-light tolerance or lipid partitioning. Community resources such as PhycoCosm help, but large annotation gaps remain across diverse lineages [18]. Cell-wall architecture adds further complexity at scale. In *Nannochloropsis*, a newly described “red body” organelle traffics algaenan precursors, contributing to a recalcitrant cell wall that complicates extraction, imaging, and quantitative proteomics and influences downstream bioprocess choices [47].

Translating benchtop findings to industrial settings also exposes cross-scale performance gaps. Genome-scale models (GEMs) and machine-learning controllers are typically trained on small, well-mixed photobioreactors; their performance degrades outdoors where light fields, turbulence, temperature, and microbial consortia fluctuate at multiple time scales. Reviews and case studies document steep light gradients, intermittent mixing, and contamination pressure in open ponds and large PBRs that are rarely captured in laboratory datasets, causing “elite” lab phenotypes to underperform in the field [48]. Even where GEMs improve nutrient allocation or predict yields in defined regimes, their reuse across reactors and climates is limited without explicit coupling to hydrodynamics and measured light distributions. Complementary work shows that GEM-informed control can lower nutrient inputs while maintaining biomass, underscoring the need to fuse physiology with reactor physics [49].

Finally, ecosystem interactions, such as algal-bacterial exchanges that modulate growth, toxin risk, and nutrient cycling, remain incompletely resolved. Emerging environmental-omics studies link community composition and function to bloom dynamics and productivity, highlighting the importance of incorporating community signatures into design and control [50]. Closing these gaps will require (i) curated, algae-focused multi-omics resources with standardized metadata to improve annotation; (ii) cross-scale validation with in situ sensors and outdoor campaigns so that predictions hold within predefined error bounds across reactor types; and (iii) explicit integration of optics/hydrodynamics and community signatures into control strategies for robust productivity under real weather and contamination pressure.

3.2. Future Perspectives

The future of the algal biotechnology industry depends on the capability of moving away from divergent multi-omics analyses in favor of predictive integrated systems biology. One of the directions includes the formation of integrated data ecosystems and sealing the functional annotation gap. This will require the creation of centralized, curated repositories that follow the principles of FAIR data, and will not only contain genomes but also dynamically connected transcriptomic, proteomic datasets, as well as metabolomic datasets. At the same time, the use of high-throughput functional genomics technologies, such as genome-wide CRISPR knockout screens and single-cell RNA sequencing, will become necessary to assign biological functions to the many uncharacterized genes. The latter will shed light on the role of lineage-specific genes that could encode new enzymes to support bioproduction or specialists of stress response, and thus, the blueprints of genomes will be translated into practical results in synthetic biology (Figure 1).

Going even further into the future, the next wave is the ability to integrate the digital and physical world of algal cultivation with the power of bioprocess informatics and explainable artificial intelligence (AI). Data multi-omics models in combination with computational fluid dynamics (CFD) models will enable the creation of multi-scale digital twins capable of emulating the impact of large-scale reactor hydrodynamics and light regimes on cellular metabolism. Furthermore, the adoption of real-time device networks and edge computing will enable adaptive bioprocess management, where machine-learning algorithms informed by periodic in-line omics assays dynamically control nutrient feed and gas exchange to maximize productivity. The next step to get AI beyond the black-box approach will be an important shift to the paradigm of explainable AI models, which will enable one to build trust and generate testable hypotheses to ensure that the conclusions made are biologically explainable. Such a holistic, closed-loop solution of predictive design *in-silico* to self-optimizing cultivation *in-vivo* will eventually make microalgae programmable and robust as well as cost-effective cell factories towards a sustainable bioeconomy.

Building on recent advances in algal optogenetics, GEM-guided process control, ML-assisted cultivation, hydrogel bioprocessing, and stress-tolerance engineering, we outline a concise, testable roadmap. A multi-scale digital twin (GEM + reactor hydrodynamics/light) should predict biomass/lipid productivity within ±10% across three reactor types. An explainable AI controller should deliver ≥20% areal productivity gains versus PID in week-long outdoor trials. Optogenetic NPQ control should boost productivity ≥10% under fluctuating light; hydrogel immobilization should halve contamination (≥2× reduction) and raise volumetric productivity ≥15% in 30-day pilots. Directed evolution/hypermutation should improve survival ≥50% while retaining ≥80% baseline productivity over 14 days outdoors, and PSI–[FeFe] hydrogenase biohybrids should sustain O_2-tolerant H_2 output above a predefined flux for ≥6 h under solar-simulated light—together forming a reproducible basis for cross-lab benchmarking and scale-up.

4. Conclusions

The combination of multi-omics technologies and increased bioinformatics has essentially transformed the field of algal biotechnology, enabling systems-level understanding of algal physiology and offers in the rational strain engineering. Genomic blueprints, combined with the dynamism of the transcriptome, proteome, and metabolite fluxes, have enabled researchers to develop predictive and genome-scale models of essential metabolic bottlenecks and pathway optimization, enhancing the production of biofuels and bioproducts. However, a severe toughening of the field is the gap between the laboratory and industrial scales of predictions and cultivation. The further developments need to be focused on the creation of interconnected digital platforms that would combine data of multi-omics with the parameters of bioprocesses, thus, allowing optimization of cultivation systems in real-time. The effective application of these technologies has significant environmental implications, with microalgae serving as versatile cell factories in the production of biofuels, carbon sequestration, and bioremediation that is sustainable. Such a combined strategy is designed to accelerate the creation of a circular bioeconomy, thereby overcoming critical environmental issues and moving towards the attainment of climate change mitigation.

Author Contributions

O.U.R.: Conceptualization, Investigation, Visualization, Writing—original draft, Writing—review & editing. M.T.: Validation, Writing—review & editing. W.L.: Investigation, Writing—review. S.C.: Writing—review & editing. X.H.: Investigation, Writing—review & editing. M.U.: Writing—review & editing. F.Z.: Data curation, Visualization, Writing—review & editing. S.H.: Funding acquisition, Resources, Writing—review & editing, Supervision, Investigation, Project administration. All authors have read and agreed to the published version of the manuscript.

Funding

This research was supported by the National Natural Science Foundation of China (32361143786, 32370387, ZK20250158) and the Jiangsu Funding Program for Excellent Postdoctoral Talent (2024ZB884).

Data Availability Statement

No datasets were generated or analyzed during the current study.

Conflicts of Interest

The authors declare no competing interests. Given the role as Editor Board, Shuhao Huo had no involvement in the peer review of this paper and had no access to information regarding its peer review process. Full responsibility for the editorial process of this paper was delegated to another editor of the journal.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

References

1. Saravanakumar, K.; Sathyanarayanan, K.; Khan, M.; et al. Recent progress in biotechnological approaches for diverse applications of algae: An overview. *Int. J. Environ. Sci. Technol.* **2024**, *21*, 3453–3474.
2. Rehman, O.U.; Hu, X.; Cao, S.; et al. Unraveling the impact of Anabaena azotica and *Nostoc flagelliforme* on wheat performance under saline-alkali soil and combined abiotic stresses. *Algal Res.* **2025**, 104396.
3. Ma, M.; Hu, Q. Microalgae as feed sources and feed additives for sustainable aquaculture: Prospects and challenges. *Rev. Aquac.* **2024**, *16*, 818–835.
4. Gurau, S.; Imran, M.; Ray, R.L. Algae: A cutting-edge solution for enhancing soil health and accelerating carbon sequestration–A review. *Environ. Technol. Innov.* **2025**, *37*, 103980.
5. Dhokane, D.; Shaikh, A.; Yadav, A.; et al. CRISPR-based bioengineering in microalgae for production of industrially important biomolecules. *Front. Bioeng. Biotechnol.* **2023**, *11*, 1267826.
6. Chen, Y.; Pei, P.; Aslam, M.; et al. Microorganisms in Macroalgae Cultivation Ecosystems: A Systematic Review and Future Prospects Based on Bibliometric Analysis. *Microorganisms* **2025**, *13*, 1110.
7. Rehman, O.U.; Zhu, F.; Hu, X.; et al. Harnessing breeding and biotechnological innovations for global food security under climate change. *Funct. Integr. Genom.* **2025**, *25*, 1–27.
8. García-Moreno, P.J.; Yesiltas, B.; Echers, S.G.; et al. Recent advances in the production of emulsifying peptides with the aid of proteomics and bioinformatics. *Curr. Opin. Food Sci.* **2023**, *51*, 101039.
9. Hamzelou, S.; Belobrajdic, D.; Broadbent, J.A.; et al. Utilizing proteomics to identify and optimize microalgae strains for high-quality dietary protein: A review. *Crit. Rev. Biotechnol.* **2024**, *44*, 1280–1295.
10. Goold, H.D.; Moseley, J.L.; Lauersen, K.J. The synthetic future of algal genomes. *Cell Genom.* **2024**, *4*, 100505.
11. Zaytsev, P.A.; Rodin, V.A.; Zaytseva, A.A.; et al. Advances of high-throughput sequencing for unraveling biotechnological potential of microalgal-bacterial communities. *J. Appl. Phycol.* **2024**, *36*, 1901–1919.
12. Sun, H.; Luan, G.; Ma, Y.; et al. Engineered hypermutation adapts cyanobacterial photosynthesis to combined high light and high temperature stress. *Nat. Commun.* **2023**, *14*, 1238.
13. Zhang, H.; Xiong, X.; Guo, K.; et al. A rapid aureochrome opto-switch enables diatom acclimation to dynamic light. *Nat. Commun.* **2024**, *15*, 5578.
14. Li, C.-T.; Eng, R.; Zuniga, C.; et al. Optimization of nutrient utilization efficiency and productivity for algal cultures under light and dark cycles using genome-scale model process control. *NPJ Syst. Biol. Appl.* **2023**, *9*, 7.
15. Saini, J.S.; Manni, M.; Hassler, C.; et al. Genomic insights into the coupling of a *Chlorella*-like microeukaryote and sulfur bacteria in the chemocline of permanently stratified Lake Cadagno. *ISME J.* **2023**, *17*, 903–915.
16. Gee, C.W.; Andersen-Ranberg, J.; Boynton, E.; et al. Implicating the red body of *Nannochloropsis* in forming the recalcitrant cell wall polymer algaenan. *Nat. Commun.* **2024**, *15*, 5456.
17. Long, B.; Fischer, B.; Zeng, Y.; et al. Machine learning-informed and synthetic biology-enabled semi-continuous algal cultivation to unleash renewable fuel productivity. *Nat. Commun.* **2022**, *13*, 541.
18. Ghallab, D.S.; Shawky, E.; Ibrahim, R.S.; Mohyeldin, M.M. Comprehensive metabolomics unveil the discriminatory metabolites of some Mediterranean Sea marine algae in relation to their cytotoxic activities. *Sci. Rep.* **2022**, *12*, 8094.
19. Rumbaugh, T.D.; Gorka, M.J.; Baker, C.S.; et al. Light-induced H_2 generation in a photosystem I-O_2-tolerant [FeFe] hydrogenase nanoconstruct. *Proc. Natl. Acad. Sci. USA* **2024**, *121*, e2400267121.
20. Jiang, M.; Zheng, J.; Tang, Y.; et al. Retrievable hydrogel networks with confined microalgae for efficient antibiotic degradation and enhanced stress tolerance. *Nat. Commun.* **2025**, *16*, 3160.
21. Zhang, K.; Xi, M.; Wu, G.; et al. Environmental drivers and microbial interactions in harmful dinoflagellate blooms: Insights from metagenomics and machine learning. *Process Saf. Environ. Prot.* **2025**, *199*, 107205.
22. Ahmad, A.; Banat, F.; Alsafar, H.; Hasan, S.W. Recent breakthroughs in integrated biomolecular and biotechnological approaches for enhanced lipid and carotenoid production from microalgae. *Phytochem. Rev.* **2023**, *22*, 993–1013.
23. Nagarajan, D.; Lee, D.-J.; Varjani, S.; et al. Microalgae-based wastewater treatment–microalgae-bacteria consortia, multi-omics approaches and algal stress response. *Sci. Total Environ.* **2022**, *845*, 157110.

24. Ray, A.; Kundu, P.; Ghosh, A. Reconstruction of a genome-scale metabolic model of *Scenedesmus obliquus* and its application for lipid production under three trophic modes. *ACS Synth. Biol.* **2023**, *12*, 3463–3481.
25. Poorinmohammad, N.; Kerkhoven, E.J. Systems-level approaches for understanding and engineering of the oleaginous cell factory Yarrowia lipolytica. *Biotechnol. Bioeng.* **2021**, *118*, 3640–3654.
26. Cruz, R.C.; Reis Costa, P.; Vinga, S.; et al. A review of recent machine learning advances for forecasting harmful algal blooms and shellfish contamination. *J. Mar. Sci. Eng.* **2021**, *9*, 283.
27. Kuo, E.Y.; Yang, R.Y.; Chin, Y.Y.; et al. Multiomics approaches and genetic engineering of metabolism for improved biorefinery and wastewater treatment in microalgae. *Biotechnol. J.* **2022**, *17*, 2100603.
28. Melero-Cobo, X.; Gallemí, M.; Carnicer, M.; et al. MoCloro: an extension of the *Chlamydomonas reinhardtii* modular cloning toolkit for microalgal chloroplast engineering. *Physiol. Plant.* **2025**, *177*, e70088.
29. Grigoriev, I.V.; Hayes, R.D.; Calhoun, S.; et al. PhycoCosm, a comparative algal genomics resource. *Nucleic Acids Res.* **2021**, *49*, D1004–D1011.
30. Li, H.; Sun, X.; Li, W.; et al. Comparative transcriptomic insights into key genes for biomass production and lipid synthesis in *Chlorella sorokiniana* mutated by argon and air atmospheric and room temperature plasma at different culture stages: Common mechanisms and unique differences. *J. Clean. Prod.* **2024**, *474*, 143590.
31. Wang, M.; Ye, X.; Bi, H.; Shen, Z. Microalgae biofuels: illuminating the path to a sustainable future amidst challenges and opportunities. *Biotechnol. Biofuels Bioprod.* **2024**, *17*, 10.
32. Wang, H.; Zhang, X.; Gao, M.; et al. Multi-omics insights of biotin-enhanced astaxanthin and total fatty acid productivity in heterotrophic *Chromochloris zofingiensis* under stress conditions. *Algal Res.* **2025**, 104158.
33. Xi, Y.; Yin, L.; Chi, Z.Y.; Luo, G. Characterization and RNA-seq transcriptomic analysis of a *Scenedesmus obliqnus* mutant with enhanced photosynthesis efficiency and lipid productivity. *Sci. Rep.* **2021**, *11*, 11795.
34. Zhang, Y.; Gu, Z.; Ren, Y.; et al. Integrating transcriptomics and metabolomics to characterize metabolic regulation to elevated CO_2 in Chlamydomonas Reinhardtii. *Mar. Biotechnol.* **2021**, *23*, 255–275.
35. Ves-Urai, P.; Krobthong, S.; Thongsuk, K.; et al. Comparative secretome analysis between salinity-tolerant and control *Chlamydomonas reinhardtii* strains. *Planta* **2021**, *253*, 68.
36. Cecchin, M.; Simicevic, J.; Chaput, L.; et al. Acclimation strategies of the green alga *Chlorella vulgaris* to different light regimes revealed by physiological and comparative proteomic analyses. *J. Exp. Bot.* **2023**, *74*, 4540–4558.
37. Perin, G.; Morosinotto, T. Understanding regulation in complex environments: a route to enhance photosynthetic light-reactions in microalgae photobioreactors. *Front. Photobiol.* **2023**, *1*, 1274525.
38. Lacroux, J.; Atteia, A.; Brugière, S.; et al. Proteomics unveil a central role for peroxisomes in butyrate assimilation of the heterotrophic Chlorophyte alga *Polytomella* sp. *Front. Microbiol.* **2022**, *13*, 1029828.
39. Sreenikethanam, A.; Raj, S.; Rajesh Banu, J.; et al. Algal lipids for biofuel production: strategies, environmental impacts, downstream processing and commercialization. *Phytochem. Rev.* **2023**, *22*, 1127–1145.
40. Wang, J.; Tian, Q.; Zhou, H.; et al. Key metabolites and regulatory network mechanisms in co-culture of fungi and microalgae based on metabolomics analysis. *Bioresour. Technol.* **2023**, *388*, 129718.
41. Ghassemi, N.; Poulhazan, A.; Deligey, F.; et al. Solid-state NMR investigations of extracellular matrixes and cell walls of algae, bacteria, fungi, and plants. *Chem. Rev.* **2021**, *122*, 10036–10086.
42. Chen, H.; Wang, Q. Regulatory mechanisms of lipid biosynthesis in microalgae. *Biol. Rev.* **2021**, *96*, 2373–2391.
43. Shen, H.; Song, X.; Zhang, Y.; et al. Profiling of brevetoxin metabolites produced by *Karenia brevis* 165 based on liquid chromatography-mass spectrometry. *Toxins* **2021**, *13*, 354.
44. Yao, H.; Yang, J.; Wang, Z.; et al. High-throughput metabolite analysis of unicellular microalgae by orthogonal hybrid ionization label-free mass cytometry. *Anal. Chem.* **2024**, *96*, 11404–11411.
45. Eladl, S.N.; Elnabawy, A.M.; Eltanahy, E.G. Recent biotechnological applications of value-added bioactive compounds from microalgae and seaweeds. *Bot. Stud.* **2024**, *65*, 28.
46. Sun, Y.; Jing, H.; Li, Z.; et al. Integrated transcriptomic, metabolomic and lipidomic analyses uncover the crucial roles of lipid metabolism pathways in oat (*Avena sativa*) responses to heat stress. *BMC Genom.* **2025**, *26*, 780.
47. Liu, M.; Yu, L.; Zheng, J.; et al. Turning the industrially relevant marine alga *Nannochloropsis* red: one move for multifaceted benefits. *New Phytol.* **2024**, *244*, 1467–1481.
48. Razzak, S.A.; Bahar, K.; Islam, K.O.; et al. Microalgae cultivation in photobioreactors: Sustainable solutions for a greener future. *Green Chem. Eng.* **2024**, *5*, 418–439.
49. Li, C.-T.; Eng, R.; Zuniga, C.; et al. Optimization of nutrient utilization efficiency and productivity for algal cultures under light and dark cycles using genome-scale model process control. *NPJ Syst. Biol. Applications.* **2023**. *9*, 7.
50. Patidar, S.K. Metabolic interactions between microalgae and bacteria: Multifunctional ecological interplay and environmental applications. *Algal Res.* **2025**, 103904.