Biofuel Research Journal 45 (2025) 2319-2349

Biofuel Research Journal

Journal homepage: www.biofueljournal.com

Review Paper

Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production

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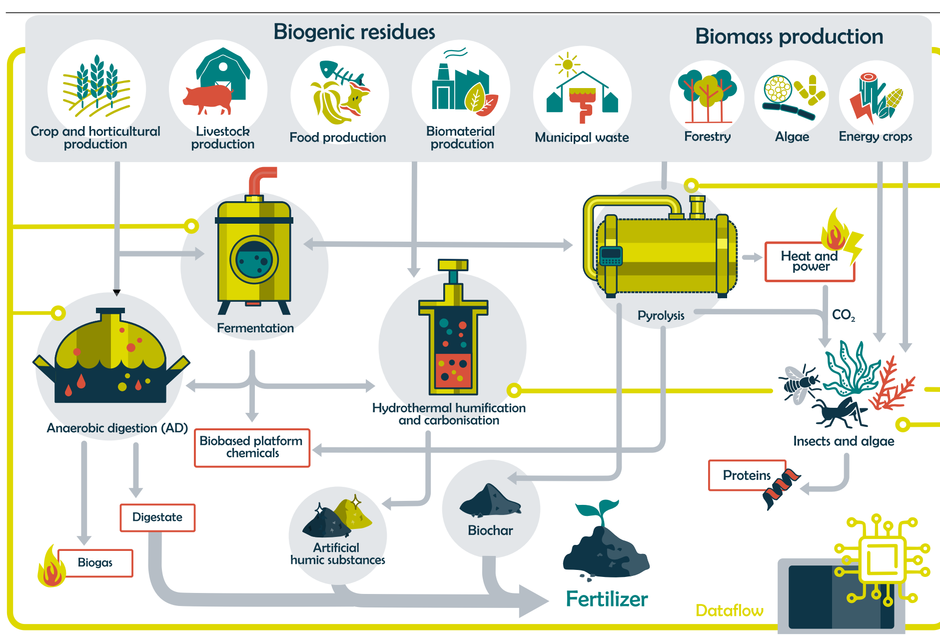
HIGHLIGHTS

- ➢Concept of sustainable and circular bioeconomy systems is introduced.
- ➢Smart integrated biorefineries reduce waste/emissions and boost energy self-sufficiency.
- ➢Machine learning optimizes smart integrated biorefineries for efficiency and profit.
- ➢Digital twins enhance control, efficiency, and optimization in smart biorefineries.
- ➢Cost-benefit analysis tackles economic challenges in smart integrated biorefineries.

GRAPHICAL ABSTRACT



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Please cite this article as: Marzban N., Psarianos M., Herrmann C., Schulz-Nielsen L., Olszewska-Widdrat A., Arefi A., Pecenka R., Grundmann P., Schlüter O.K., Hoffmann T., Rotter V.S., Nikoloski Z., Sturm B. Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production. Biofuel Research Journal 45 (2025) 2319-2349. DOI: 10.18331/BRJ2025.12.1.4.

ARTICLE INFO

Article history:
Received 6 January 2025
Received in revised form 19 February 2025
Accepted 19 February 2025
Published 1 March 2025

Keywords:
Smart integrated biorefineries
Sustainable circular bioeconomy systems
Zero-waste
Self-sufficient energy production
Artificial humic substances
Machine learning

ABSTRACT

Integrated biorefineries play a transformative role in sustainable development by converting biomass and biogenic residues into high-value products while minimizing waste, emissions, and resource inefficiencies. This review explores innovations in biorefinery processes, emphasizing the synergy between thermochemical, biochemical, and biological technologies such as pyrolysis, fermentation, anaerobic digestion, hydrothermal carbonization, and algae and insect systems. Recent advancements, including hydrothermal humification and fulvification, enhance nutrient recovery, carbon sequestration, and near-zero waste production by generating artificial humic substances. Smart integrated biorefineries and the sustainable and circular bioeconomy systems are introduced as frameworks that promote synergy, interconnectivity, and resource optimization. These concepts emphasize that biomass valorization should be maximized before its final use. Biochar plays a multifaceted role beyond carbon sequestration. Rather than premature burial, it can be derived from fermented residues for lactic acid production or used to enhance fermentation and methane yields in anaerobic digestion. Additionally, nutrient-loaded biochar serves as a slow-release fertilizer, mitigating runoff, and GHG emissions. Meanwhile, heat from biochar production can generate electricity, and CO_2 emissions can support algae cultivation. Bio-oil, another byproduct, can be upgraded into platform chemicals, forming a closed-loop system that optimizes biomass utilization and minimizes environmental impact. Conventional biomass treatment methods, such as incineration, combustion, and composting, waste valuable resources and contribute to environmental degradation. Instead, a closed-loop, self-optimizing approach ensures full biomass utilization while addressing planetary boundaries. By integrating machine learning, digital twins, and decision-support systems, smart integrated biorefineries enhance resource efficiency, adapt to market demands, and accelerate the transition to a low-carbon, resource-efficient future.

Contents

Abbreviations

AHSs	Artificial humic substances	GDP	Gross domestic product	OLR	Organic loading rates
A-HAs	Artificial humic acids	GHG	Greenhouse Gas	PLSR	Partial Least-Squares Regression
AD	Anaerobic Digestion	HRT	Hydraulic Retention Time	PSO	Particle Swarm Optimization
ANN	Artificial Neural Networks	HTC	Hydrothermal carbonization	RF	Random Forest
BMP	Biochemical methane potential	HTF	Hydrothermal fulvification	SCBS	Sustainable and circular bioeconomy systems
CBE	Circular Bioeconomy	HTH	Hydrothermal humification	SIBs	Smart Integrated Biorefineries
DOP	Dynamic orthogonal projection	IBs	Integrated biorefineries	SVM	Support Vector Machine
DTR	Decision tree regression	LCA	Life Cycle Assessment	TEA	Techno-economic analysis
FNN	Feedforward neural network	MIR	Mid-Infrared spectroscopy	TRL	Technology Readiness Level
GB	Gradient Boosting	ML	Machine Learning	VS	Volatile Solids
GBR	Gradient Boost Regression	NIR	Near-Infrared spectroscopy	XGBoost	Extreme Gradient Boosting

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1. Introduction

The global rise in population and consumption has escalated the demand for goods and energy, placing immense strain on natural resources and intensifying environmental degradation. Historically, economies have relied heavily on fossil fuels, leading to severe ecological consequences, including greenhouse gas (GHG) emissions and resource depletion (Hasan and Habiba, 2015; Ganivet, 2020; Maja and Ayano, 2021). Today, the agri-food sector faces a converging planetary crisis—encompassing climate change, pollution, and biodiversity loss—while key environmental thresholds are already being exceeded (Engström et al., 2020; Ayesha et al., 2023; Richardson et al., 2023). One of the most pressing challenges within this sector is food loss and waste, which accounts for nearly 30% of total global food production—an estimated 1.3 billion tonnes annually ("Food loss and waste," 2024). If left unaddressed, this inefficiency will continue to exacerbate environmental and socio-economic challenges, highlighting the urgent need for sustainable and circular solutions.

In response to these challenges, the bioeconomy has emerged as a transformative model that integrates biological resources, sustainable production, and circular economy principles to improve resource efficiency and environmental sustainability (D'Amato et al., 2017; Strategy, 2018). Agricultural residues, food waste, and other biomass can be converted into bio-based chemicals, fuels, and materials, offering a sustainable alternative to fossil-based industries. By enhancing waste valorization, reducing dependence on non-renewable resources, and closing material loops, biorefineries contribute to the reduction of GHG emissions, restoration of soil health, and management of the nutrient cycle, all of which support climate mitigation and biodiversity conservation. However, concerns related to competition for resources, land use conflicts, and the carbon neutrality of bio-based production persist, emphasizing the need for balanced bioeconomy strategies that optimize environmental and socio-economic benefits (Ramcilovic-Suominen and Pülzl, 2018; Starke et al., 2023). By integrating novel concepts of biorefineries as interconnected systems into the bioeconomy—which, by itself, is neither inherently circular nor sustainable—we create an opportunity to align them with principles of sustainability and decelerate the rate at which planetary boundaries are crossed. This practice provides humanity with more time to develop long-term sustainable solutions and restore environmental balance, ensuring a resilient and regenerative future. Thus, transitioning to green technologies and renewable resources is no longer an option but rather a necessity in order to ensure sustainable development and mitigate environmental impacts (Kavanagh et al., 2018; Nelles et al., 2018).

Biorefineries represent a critical component in this transition, offering a means to convert biomass and biogenic residues into biofuels, chemicals, and materials that align with the principles of a circular economy. By promoting resource efficiency and reducing waste, biorefineries support both environmental protection and economic growth (Brosowski et al., 2019; Velvizhi et al., 2022). Unlike traditional single-process systems, integrated biorefineries combine multiple processes, including, but not limited to, thermochemical processes such as pyrolysis and bioconversion processes, including fermentation and anaerobic digestion (AD), to enhance energy recovery and the creation of value (Maity, 2015; Velvizhi et al., 2022). These systems establish a foundation for achieving near-zero waste production while advancing sustainable energy goals (Vehlow et al., 2007; O'Callaghan, 2016).

Traditional biorefineries primarily focus on single-process approaches, limiting their ability to maximize resource efficiency and fully utilize biomass components. Standalone processes, while valuable, often fall short in efficiency and scalability. Pyrolysis, for instance, efficiently produces biochar and bio-oil (Ascher et al., 2022; Balsora et al., 2022) but underutilizes the heat it generates. Similarly, fermentation, while suitable for the production of ethanol and bio-based platform chemicals (Zhu et al., 2019; Khaleghi et al., 2021), is hindered by the need for costly pretreatments to mitigate inhibitors. Likewise, AD, used for the production of biomethane (Rutland et al., 2023; Yildirim and Ozkaya, 2023), struggles with methane leakage and the slow degradation of certain feedstocks. These limitations underscore the need for a more advanced, interconnected approach that optimizes resource utilization, energy recovery, and waste reduction.

Integrated biorefineries address these challenges by leveraging the synergies between different processes. For example, heat from pyrolysis can be used to fuel AD, while biochar can serve as an adsorbent in fermentation to enhance microbial efficiency (Cinar et al., 2022; Hosseinzadeh et al., 2022). Hydrothermal carbonization (HTC) processes can complement these systems by converting wet biomass into hydrochar while recovering valuable nutrients (Djandja et al., 2023; Leng et al., 2024). This integration not only maximizes resource utilization but also reduces environmental impacts through carbon sequestration and nutrient recovery (Zhu et al., 2023; Liu et al., 2024).

Finding the optimized interconnection between multiple systems, which includes a wide range of biomass and biogenic residues, in order to create integrated biorefineries—where the output of one system still holds potential for conversion and the addition of value—is a complex, time-intensive, and costly process, especially if the search relies solely on experimental approaches (Tay et al., 2011; Kokossis et al., 2015; Maity, 2015; Punnathanam and Shastri, 2020; Velvizhi et al., 2022). This challenge can be effectively addressed by leveraging advanced modeling tools to optimize operations (Djandja et al., 2021; Pandey et al., 2023). Techno-economic analyses and Life Cycle Assessments (LCA) are vital in identifying optimal configurations and predicting outputs, as well as determining the environmental footprint of products. These tools can be increasingly supported by machine learning (ML). For instance, ML models have demonstrated exceptional accuracy in predicting biogas production, optimizing fermentation conditions (Pandey et al., 2023), and simulating pyrolysis and hydrothermal process yields (Hough et al., 2017; W. Zhang et al., 2023), thereby supporting data-driven decision-making in biorefinery design. These tools enable researchers to explore scenarios that align with sustainability goals while enhancing system resilience and scalability (Tang et al., 2021; Adeleke et al., 2023).

Integrated biorefineries represent a transformative approach to sustainable resource utilization, addressing global challenges related to energy security, waste management, and environmental degradation. By integrating processes and adopting advanced optimization methodologies, these systems can revolutionize biomass utilization, advancing zero-waste and energy self-sufficiency goals (Tay et al., 2011; Maity, 2015). Future research is needed to overcome scalability barriers, enhance feedstock flexibility, and incorporate emerging technologies—such as artificial intelligence and the Internet of Things (IoT)—to refine and expand biorefineries' potential while minimizing waste production (Oruganti et al., 2023; Nawoya et al., 2024; Zhang et al., 2025). Consequently, transitioning from conventional integrated biorefineries to self-optimized systems requires adaptive, data-driven decision-making that optimizes dynamic multi-system interactions, enhancing process efficiency and sustainability.

This review provides a comprehensive perspective on the evolution of biorefineries and introduces smart integrated biorefineries (SIBs) as a framework for optimizing biomass valorization within a sustainable and circular bioeconomy. Unlike conventional biomass processing, these systems leverage multi-system interconnectivity to achieve near-zero waste, self-sustained energy generation, and minimal GHG emissions. The proposed framework integrates HTC and its modified versions—hydrothermal humification and fulvification—along with AD, pyrolysis, fermentation, and algae- and insect-based conversion technologies. Achieving such integration requires advanced modeling approaches, including ML, digital twins, and decision-support tools like LCA, exergy analysis, and techno-economic evaluations for real-time optimization and predictive analytics. This review advocates for a shift from isolated process optimization toward an interconnected, intelligent biorefinery system that enhances efficiency and sustainability. **Table 1** compares this approach with previous review papers, highlighting its advancements and key differentiating features.

2. The circular bioeconomy

2.1. The concept of the bioeconomy

The circular bioeconomy (CBE) is a visionary framework that aims to transform how societies utilize biological resources, focusing on sustainable development while addressing global challenges like climate change and resource scarcity. By integrating renewable resources, innovative biotechnologies, and zero-waste strategies, the bioeconomy minimizes reliance on finite fossil fuels and promotes environmental resilience and economic sustainability (Birner, 2018; Strategy, 2018; Schüch and Hennig,

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Table 1.
Comparison of key features across selected review studies on biorefineries, highlighting technological integration, sustainability assessments, and emerging innovations in a circular bioeconomy.

Hydrothermal Humfication and Fulvification	Integration of Thermochemical & Bioconversion and Biological Processes	Process Synergies and energy Efficiency	Zero-Waste and Self-Sufficient Energy Production	ML Process Modeling	ML Process Integration	Multi-Feedstock Integrated Biorefinery	Concept of Smart Integrated Biorefinery	Ref.
×	×	×	×	✓	×	✓	×	khan et al. (2023)
×	✓	✓	×	✓	×	✓	×	Velidandi et al. (2023)
×	✓	✓	×	×	×	✓	×	Maity (2015)
×	✓	✓	×	×	×	✓	×	Maity (2015)
×	✓	✓	×	×	×	✓	×	Kokossis et al. (2015)
×	✓	✓	×	×	×	✓	×	Kashif et al. (2025)
×	✓	✓	×	×	×	✓	×	Naik et al. (2025)
×	✓	✓	×	×	×	✓	×	Koubaa, (2024)
×	✓	✓	×	×	×	×	×	Kumar et al. (2024)
×	✓	✓	×	×	×	×	×	Narayanan (2024a)
×	✓	✓	×	×	×	✓	×	Mohammad et al. (2024)
×	✓	✓	✓	×	×	✓	×	Feng and Lin (2017)
✓	✓	✓	✓	✓	✓	✓	✓	**Present Review**

2022). A key aspect of the bioeconomy is its alignment with the principles of a circular economy, where biological resources are reused and recycled, thereby reducing GHG emissions and minimizing the generation of waste (Carrez et al., 2017; Strategy, 2018; Ponnusamy et al., 2019).

The European Union, and Germany in particular, have been at the forefront of implementing bioeconomy strategies by creating policies that integrate waste management systems with bioeconomic objectives, emphasizing renewable energy production and material recovery (Ponnusamy et al., 2019; Kristensen and Dubois, 2021). In 2022, both the United States and China implemented their own bioeconomy strategies (White House, 2022; Zhang et al., 2022). Both countries strongly emphasized the potential of biotechnology and its importance for domestic economic growth. This milestone marked significant progress in the promotion of bioeconomic principles.

Beyond environmental benefits, the bioeconomy fosters job creation, particularly in rural areas, and supports the transition to low-carbon economies. Advances in biotechnology, such as microbial engineering and process optimization, play a pivotal role in this transition, offering innovative solutions for producing bio-based fuels, chemicals, and materials from a variety of biogenic sources (Carrez et al., 2017; Birner, 2018; Kristensen and Dubois, 2021). Ultimately, the bioeconomy provides a comprehensive framework for achieving global sustainability goals by enhancing resource efficiency, economic resilience, and environmental protection (Budzianowski and Postawa, 2016; Kristensen and Dubois, 2021; Leong et al., 2021).

2.2. The concept of sustainable and circular bioeconomy systems

While the bioeconomy and CBE emphasize the efficient use of biological resources, challenges remain in ensuring that these systems operate within planetary boundaries. Expanding bio-based industries often requires using more land and increases competition for resources and GHG emissions, which raises concerns about the long-term sustainability of bioeconomic models (Starke et al., 2023). To address these challenges, it is essential to move beyond conventional CBE approaches and develop a more holistic, systemic perspective that aligns bioeconomic expansion with planetary boundaries, ensuring that resource use remains within safe environmental limits while fostering long-term resilience.

Building upon the concept of CBE and addressing its limitations, the Leibniz Institute for Agricultural Engineering and Bioeconomy (ATB) has developed a strategic framework known as the Sustainable and Circular Bioeconomy Systems (SCBS), which integrates primary agricultural production into both upstream and downstream industries. This framework emphasizes the principles of circularity by maximizing the use of resources, minimizing emissions, and fostering the recycling of biological materials. With a focus on systemic innovation, ATB combines advanced technologies, such as digital twins, with interdisciplinary approaches to evaluate and implement SCBS principles. These efforts support global sustainability goals by addressing resource efficiency, environmental protection, and economic resilience.

As illustrated in **Figure 1**, ATB's work is organized into five interconnected program areas that reflect critical components of the CBE. Diversified crop production develops tools for managing diverse and resilient cropping systems, while individualized livestock production integrates sustainable livestock practices into bioeconomic frameworks. Healthy foods focus on reducing food loss and advancing alternative protein sources (such as algae and insects), and multifunctional biomaterials target the development of innovative products from underutilized biomass and waste streams. Finally, integrated residue management optimizes the utilization of residue through advanced technologies and environmental assessments (**Fig. 2**), ensuring the identification, valorization, and full utilization of biomass and biogenic residues.

A key principle of integrated residue management is the sequential valorization of biomass and biogenic residues to maximize their utility before reaching their final stage of use. For instance, directly converting biomass to biochar through pyrolysis and burying it underground may overlook other high-value opportunities. Instead, biomass could first be processed through biorefinery systems to extract platform chemicals, biofuels, or bio-based materials, and only then could the residual biomass be converted into biochar. Furthermore, biochar itself can play a transformative role when integrated into AD process, enhancing biogas yield (Vayena et al., 2024) while acting as a nutrient-loaded slow-release fertilizer (Thiele-Bruhn and Ngigi, 2021). Ensuring that aged biochar, enriched with essential nutrients, does not compete with plants for nutrients but instead functions as a nutrient reservoir, improving soil health and crop productivity (Mia et al., 2017) while also promoting soil microbiome diversity, which can serve as a natural alternative to chemical pesticides (Tan et al., 2022). Additionally, integrating biochar into animal manure slurry management can potentially prevent the loss of nutrients through runoff, leaching, and GHG emissions, thereby reducing environmental pollution and enhancing nutrient cycling (Dougherty et al., 2017). These examples demonstrate how interconnecting multiple bioeconomic systems can create synergistic benefits, improving efficiency, sustainability, and resource recovery. Furthermore, such interconnections can contribute to bioheat and bioenergy production, ensuring that waste streams are utilized optimally, thereby strengthening the self-sufficiency of bioeconomic systems.

Within this novel concept of SCBS, each subsystem seeks synergy and interconnectivity with others, forming an integrated and scalable framework. This interconnectedness ensures that biological resources are

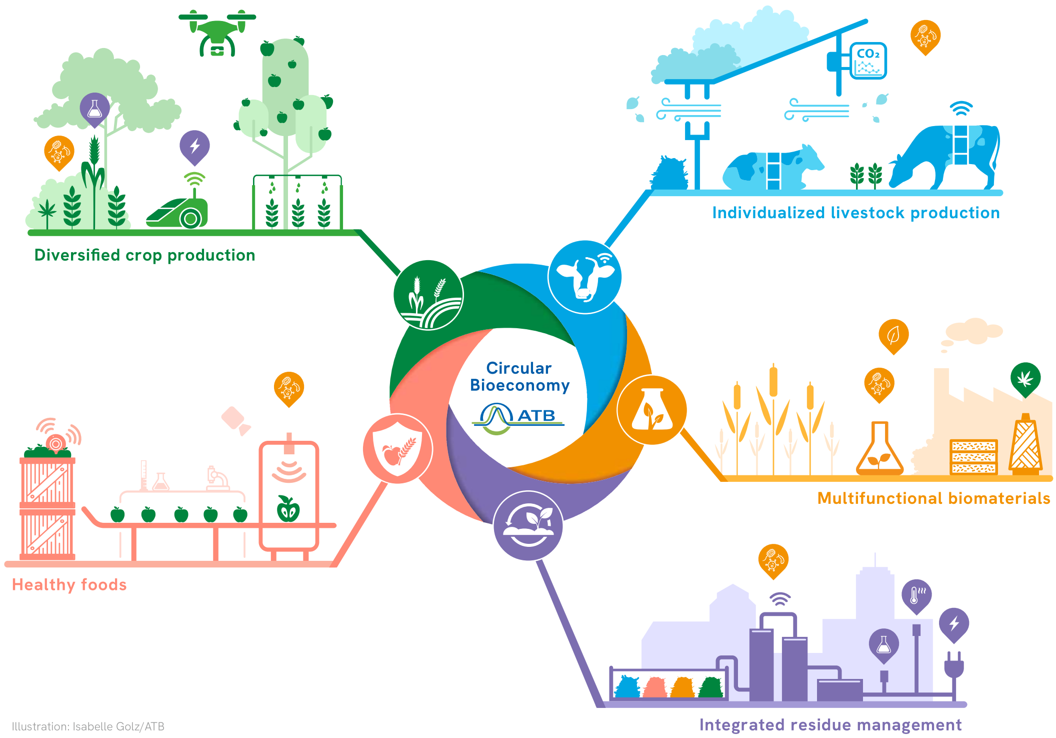

Fig. 1. The five program areas representing the five integral sub-domains of the sustainable and circular bioeconomy from the ATB Research Strategy 2024–2033. Copyright: Isabelle Golz/ATB.

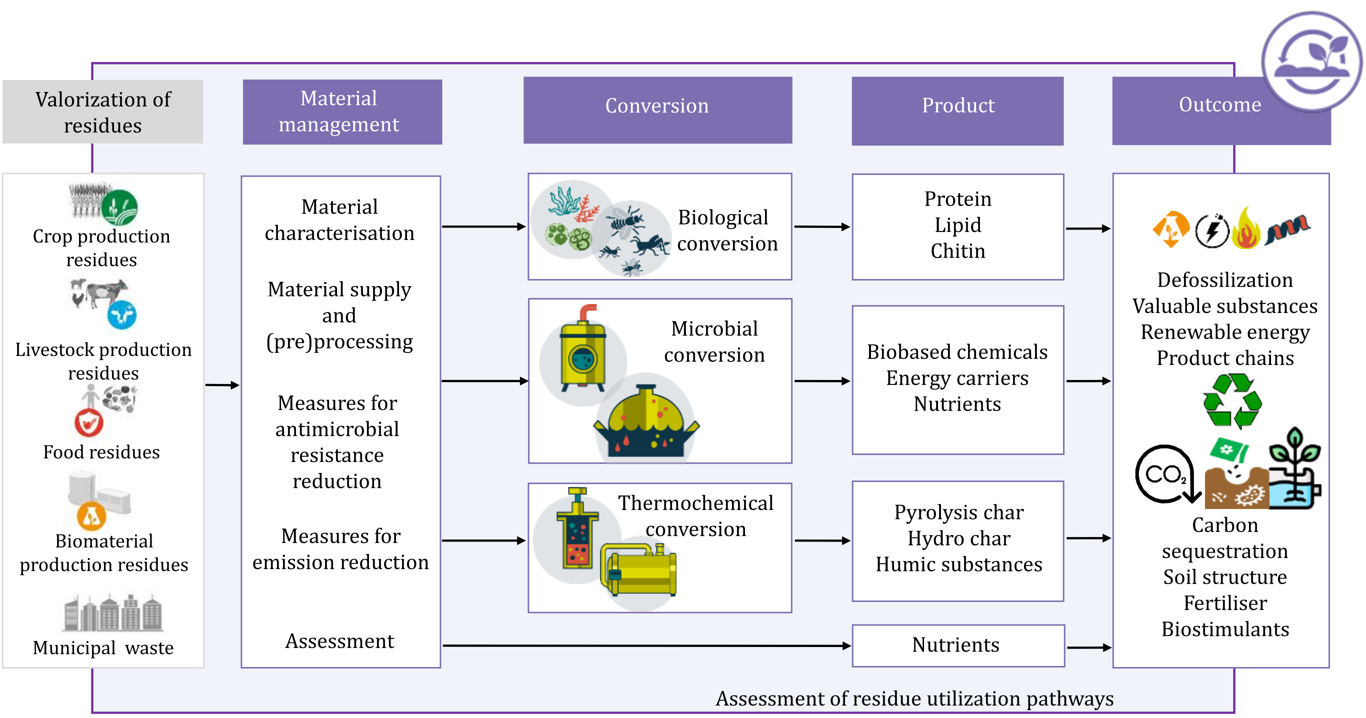

Fig. 2. Integrated residue management by the sustainable circular bioeconomy systems (SCBS) approach.

managed regeneratively and efficiently, progressing toward an optimal state where planetary boundaries are respected. Achieving this level of systemic integration requires cutting-edge tools in data science, enabling predictive modeling, resource optimization, and life-cycle assessments across the entire bioeconomy. Moreover, microbiome management plays a pivotal role in enhancing bioprocess efficiency, soil and gut health, and biological waste valorization, reinforcing sustainability across all areas of the program. Through this approach, existing gaps can be identified, allowing for new

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uses of available systems or the introduction of novel solutions to bridge these gaps effectively.

By harnessing the power of interdisciplinary research and technological innovation, ATB's approach ensures that SCBS can evolve dynamically, maintaining a balance between environmental sustainability, economic feasibility, and social equity. Through these efforts, the CBE can transition from a theoretical model into a practical and scalable reality, fostering a resilient, regenerative, and resource-efficient future.

2.3. Types, characteristics, and potentials of biomass and biogenic residues

Biomass and biogenic residues are critical components of the renewable energy landscape, serving as sustainable feedstocks for energy, fuels, chemicals, and materials. They originate from various sources, including energy crops, agricultural and forestry residues, industrial byproducts, municipal solid waste (MSW), and aquatic biomass. Their abundance, renewability, and diverse compositions make them pivotal to achieving sustainability goals within the CBE (Maity, 2015; Nelles et al., 2018).

Biomass and biogenic residues provide a diverse range of feedstocks for biorefineries, each offering unique opportunities for bioenergy and bioproduct production. Energy crops such as switchgrass and miscanthus are cultivated specifically for bioenergy. They are valuable for their high yields, adaptability to marginal lands, and low inputs while also minimizing GHG emissions (Forster-Carneiro et al., 2013; Maity, 2015). Agricultural residues such as straw, husks, and manure hold vast potential for bioenergy and material production but remain underutilized despite their availability and compatibility with biorefineries (Forster-Carneiro et al., 2013; Nelles et al., 2018). Forestry residues, including wood chips and sawdust, serve as lignocellulosic feedstocks widely used in thermochemical and biochemical processes for biofuels and biomaterials (Tay et al., 2011; Velvizhi et al., 2022).

Industrial and MSW, such as food waste and paper, contribute to AD and thermochemical conversions, providing waste-to-energy opportunities while reducing reliance on landfills (Vehlow et al., 2007; Demirbas, 2011). Aquatic biomass, including microalgae and macroalgae, stands out due to its rapid growth and nutrient uptake capabilities, making it ideal for producing biodiesel, bioethanol, and high-value bioproducts like nutraceuticals (Khoo et al., 2019; Catone et al., 2021; Salami et al., 2021).

The composition of biomass plays a crucial role in determining its potential applications. Lignocellulosic residues, which are rich in cellulose, hemicellulose, and lignin, are versatile but require pretreatment to address challenges related to enzymatic hydrolysis (Nelles et al., 2018; Velvizhi et al., 2022). High moisture and ash content in MSW and manure reduce energy efficiency, necessitating preprocessing (Vehlow et al., 2007; Forster-Carneiro et al., 2013). Lipid- and protein-rich residues, such as algae, are ideal for biodiesel and bioplastics production (Thomassen et al., 2017; Salami et al., 2021). Similarly, plant oils have emerged as promising feedstocks for industrial applications. Advancements in genetic and metabolic engineering have significantly enhanced oil yields and optimized fatty acid compositions to meet biofuel production demands (Hajinajaf et al., 2024). Efficient utilization of these resources requires tailored strategies to optimize feedstock properties and maximize sustainability.

Biomass and biogenic residues offer significant potential for advancing renewable energy systems and fostering sustainability. They are crucial for bioenergy production, where lignocellulosic biomass is converted into bioethanol via enzymatic hydrolysis, while lipid-rich algae contribute to biodiesel production through transesterification (Tay et al., 2011; Velvizhi et al., 2022). AD of MSW, agricultural residues, and manure generates methane-rich biogas, supporting heat and electricity generation (Tay et al., 2011; Nelles et al., 2018). Additionally, biomass serves as a source of high-value chemicals and materials, such as bioplastics derived from algae, agricultural byproducts, and platform chemicals like furans and alcohols, which are essential intermediates for various industries (Catone et al., 2021; Salami et al., 2021; Velvizhi et al., 2022). Furthermore, soil amendments like biochar, produced through pyrolysis, enhance soil fertility and carbon sequestration, while digestates from AD act as organic fertilizers, closing nutrient cycles in agriculture (Tay et al., 2011; Nelles et al., 2018; Velvizhi et al., 2022). By aligning with CBE principles, biomass utilization minimizes waste and maximizes resource reuse. Studies in Germany highlight this potential, revealing that out of 98.4 million tons of available dry mass, 30.9 million tonnes remain untapped, representing a substantial opportunity to meet renewable energy goals and support climate protection efforts (Brosowski et al., 2016 and 2019; Nelles et al., 2018).

Unlocking the full potential of biomass and biogenic residues depends on efficient and innovative conversion technologies, which will be explored in the next section. These technologies enable the transformation of diverse biomass feedstocks into valuable energy, fuels, and materials, paving the way for a more sustainable future.

3. Integrated biorefinery: A holistic approach

3.1. Biorefinery concepts

Biorefineries serve as sustainable systems for converting biomass and biogenic residues into a wide range of products, including fuels, chemicals, and energy. Modeled after traditional petroleum refineries, they aim to utilize renewable feedstocks to produce high-value outputs while minimizing environmental damage and waste generation. The primary goal of biorefineries is to cascade the use of resources, integrating multiple processes to exploit the potential of feedstocks fully. This approach supports the circular economy by creating closed-loop systems that minimize emissions, maximize value recovery, and promote the production of environmentally friendly alternatives to fossil-based products (Körner, 2015; Birner, 2018; Kristensen and Dubois, 2021).

Implementing the biorefinery concept is crucial for addressing global challenges such as climate change, energy shortages, and resource depletion. By utilizing biomass as a renewable raw material, biorefineries help reduce reliance on fossil fuels, mitigate GHG emissions, and support the transition to a bio-based economy. The success of biorefineries hinges on the integration of advanced technologies, process efficiency, and sustainable practices to create value-added products while ensuring economic viability (Carrez et al., 2017; Strategy, 2018; Brosowski et al., 2019).

3.2. Conversion within biorefineries vs. traditional methods

Biorefineries represent a significant advancement over traditional residue management methods, such as composting, landfilling, and combustion. These facilities function as controlled systems that optimize resource efficiency, recycle nutrients, sequester carbon, and produce value-added products like biofuels and bioplastics, all while reducing GHG emissions and environmental pollution (O'Callaghan, 2016). Although traditional methods are economically viable and scalable—especially for small-scale applications—they often fail to manage emissions effectively or recover nutrients optimally (Maity, 2015). As a result, they contribute to significant environmental issues, such as uncontrolled GHG emissions and leachate pollution. By addressing these limitations, biorefineries offer a transformative pathway toward a sustainable and CBE. However, challenges related to scalability and economic feasibility persist, particularly for large-scale implementation (Kokossis et al., 2015).

As summarized in **Table 2**, biorefineries provide clear advantages over traditional methods in several key areas. They excel in emission control, where advanced systems help reduce GHG emissions, and in nutrient recycling, efficiently supporting soil health and agricultural productivity (Demirbas, 2011; Nelles et al., 2018). Additionally, biorefineries enable the production of value-added products like biofuels and bioplastics while significantly minimizing waste through advanced conversion processes such as AD and pyrolysis (Forster-Carneiro et al., 2013; Velvizhi et al., 2022). In contrast, traditional methods like composting, landfilling, and combustion tend to be less efficient, often resulting in nutrient loss, limited energy recovery, and environmental degradation. Despite these advantages, biorefineries face challenges related to scalability and economic viability, as their complex systems require significant upfront investment (Tay et al., 2011; Forster-Carneiro et al., 2013).

3.3. Biomass and biogenic residue pretreatment technologies in biorefineries

Pretreatment is a critical step in processing biomass and biogenic residues, playing a pivotal role in most biorefinery applications. It facilitates

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Table 2.
Advantages and disadvantages of biorefineries compared to traditional biomass management methods.

Aspect	Biorefineries	Traditional Methods (Composting, Landfilling, Combustion/Incineration)
Emission control	Controlled systems reduce GHG emissions through carbon capture (Mahendrasinh Kosamia et al., 2022), biochar application, and sequestration strategies (Matovic, 2011)	Uncontrolled release of methane and other GHGs contributes to climate change.
Nutrient recycling	Efficient recovery and reuse of nutrients, supporting soil health and agricultural productivity (Velvizhi et al., 2022).	Nutrients are often lost or remain unused, reducing long-term agricultural benefits.
Value-added products	Produces renewable fuels, bioplastics, and platform chemicals, adding economic value (Velvizhi et al., 2022).	Limited to low-value products like compost, with no generation of renewable energy.
Waste minimization	Converts biomass into energy or valuable materials, significantly reducing landfill dependency (Demirbas, 2011).	Biomass waste accumulates in landfills, leading to environmental degradation.
Process efficiency	Optimized systems enhance energy yield and resource utilization (Demirbas, 2011).	Processes are inefficient and prone to losses of energy and material.
Carbon sequestration	Biochar production for soil application effectively sequester carbon in stable forms (Matovic, 2011), while CO_2 can be utilized for algae production	Carbon is either released into the atmosphere without sequestration or remains unstable in the final product.
Environmental impact	Controlled operations minimize pollution and environmental risks (Demirbas, 2011).	Potential leaching of pollutants into soil and water, leading to contamination.
Scalability	Complex biorefinery systems face significant scale-up challenges, requiring substantial initial capital investment and operating costs (Mahendrasinh Kosamia et al., 2022).	Simple and widely applicable with lower initial infrastructure requirements.
Economic viability	High upfront costs, but long-term profitability through value-added products (Tay et al., 2011).	Lower costs and immediate viability for small-scale operations or local use.
Energy recovery	High energy recovery from AD, pyrolysis, or gasification (Velvizhi et al., 2022).	Little to no energy recovery; energy is lost during decomposition.

the breakdown of complex structures like lignocellulose, enhancing enzymatic accessibility and improving the overall efficiency of conversion processes (Alam et al., 2019; Rezania et al., 2020). This process reduces particle size, lowers cellulose crystallinity, removes lignin, and increases the bioavailability of polysaccharides for downstream conversion techniques such as fermentation or AD (Chen and Fu, 2016; Narayanan, 2024b). Pretreatment methods vary depending on the type of biomass used and the desired products.

Physical methods, such as milling, extrusion, and irradiation, reduce particle size and disrupt structural complexity, improving enzymatic digestibility. However, these methods often require significant energy inputs (Rezania et al., 2020; Bhushan et al., 2023). Physicochemical approaches, including steam explosion and liquid hot water treatments, effectively disrupt lignocellulosic structures and increase surface area for enzymatic action. Nonetheless, they can produce byproducts like inhibitors and require high-pressure batch processing systems (Kawaguchi et al., 2016; Hellsmark and Söderholm, 2017). Chemical pretreatments, such as acid hydrolysis and ionic liquids, offer high sugar recovery and efficient lignin removal but face challenges, including high costs and the formation of toxic byproducts (Gatt et al., 2018; Narayanan, 2024b). Biological pretreatments using microbial or enzymatic methods are eco-friendly, requiring lower energy and fewer chemicals, although their slow rate and scalability remain limiting factors (Alam et al., 2019; Sanoja-López et al., 2024). Additionally, combined methods, such as integrating physical and chemical approaches, leverage synergistic effects to enhance efficiency but often come with increased complexity and higher costs (Osman et al., 2021). The choice of pretreatment method depends on biomass characteristics, energy requirements, and the intended conversion pathway (Rezania et al., 2020).

3.4. Conversion processes in biorefinery

Biorefineries encompass a wide range of processes designed to convert biomass and biogenic residues into diverse value-added products, including biofuels, biochemicals, and energy. Key processes include thermochemical conversions such as pyrolysis, gasification, and hydrothermal processes (e.g., carbonization), alongside biochemical pathways like fermentation, AD, and enzymatic hydrolysis (Tay et al., 2011; Velvizhi et al., 2022; Cavali et al., 2023). Emerging technologies, such as hydrothermal humification and fulvification, offer additional pathways for valorizing biomass (Tkachenko et al., 2023; Marzban, 2024; Marzban et al., 2024b). Biological systems, including algal bioreactors and insect-based processing, play a pivotal role in resource recovery and carbon utilization (Uggetti et al., 2014; Catone et al., 2021; Cláudia da Costa Rocha et al., 2021). While conventional methods like combustion, composting, and landfilling are effective for waste management, they are less favorable due to high emissions and limited product recovery (O'Callaghan, 2016). Advanced systems integrate multiple processes to maximize resource efficiency, such as using byproducts from one process (e.g., biochar) to enhance another (e.g., biogas production) (Demirbas, 2011; Tay et al., 2011). This discussion highlights potentially applicable processes for integrated biorefineries, illustrating their roles, potential, and limitations in standalone applications.

3.4.1. Thermochemical processes

Thermochemical conversion processes produce stable byproducts compared to raw biomass and biogenic residues (Harvey et al., 2012; Luo et al., 2023), achieving this in significantly shorter timeframes than bioconversion or biological processes. This efficiency enhances their applicability across a wide range of fields, including agricultural soil amendments, environmental remediation, and biofuel production (Libra et al., 2011). This section focuses on two thermochemical processes: pyrolysis for biochar production and hydrothermal methods, such as HTC, for the production of artificial coal (hydrochar). Emerging technologies like hydrothermal humification (HTH) and fulvification (HTF), which produce artificial humic substances (AHSs), show promise for enhancing soil health and supporting environmental remediation. The potential integration of these technologies into biorefinery systems will also be discussed.

3.4.1.1. Pyrolysis

Pyrolysis effectively converts biomass in an oxygen-limited environment into biochar, syngas, and bio-oil (Chopra et al., 2022). Biochar, produced at temperatures ranging from 300 to 800°C (Xu et al., 2021), is a highly porous material with a functionalized surface, making it valuable for diverse applications such as soil enhancement (Brassard et al., 2019), carbon sequestration, GHG mitigation (Gupta et al., 2020), and pollutant removal from soil and water (H. Chen et al., 2022) (**Fig. 3**). Activated biochar further enhances its utility as a catalyst in biohydrogen production and transesterification reactions, playing a crucial role in sustainable energy systems (Chi et al., 2021). Due to its high surface area and stability, biochar is also employed in energy storage applications, including hydrogen and

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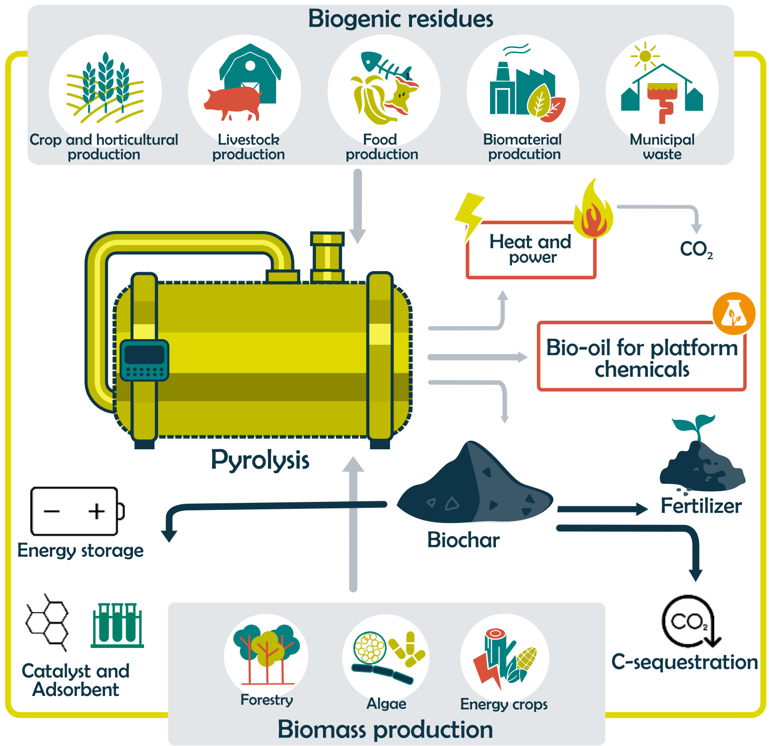

Fig. 3. Pyrolysis-based valorization of biogenic residues and biomass into biochar, bio-oil, and energy—an example of a sustainable and circular bioeconomy system (SCBS).

methane storage, microbial fuel cells, and supercapacitors, where it improves charge transfer and efficiency (Chandrasekaran et al., 2024).

Additionally, its catalytic properties support biomass conversion and biofuel synthesis, contributing to cleaner energy production with minimal environmental impact (Velusamy et al., 2021).

The Stability of biochar increases with higher pyrolysis temperatures, producing carbon with a recalcitrance index (R50) higher than that of raw biomass (Harvey et al., 2012). However, higher temperatures reduce biochar yield, with optimal carbon sequestration efficiency achieved in biochars produced at 500–550°C, retaining 41.4% of the initial carbon in soil over 100 years (Rodrigues et al., 2023). Biochars are classified by stability: Class A (R50 ≥ 0.70) offers exceptional durability and is suitable for long-term sequestration, while Class B (R50 0.50–0.70) and Class C (R50 < 0.50) degrade more readily (Harvey et al., 2012). Despite its benefits, pyrolysis requires pretreatment to lower the moisture content of biomass below 40 wt%, which increases costs, particularly for high-moisture feedstocks (Akhtar and Amin, 2011). Nonetheless, the heat generated during the process can offset drying costs and be utilized to generate electricity. At the same time, CO_2 emissions from the combustion of gaseous products or bio-oil can be captured for use in greenhouse or algal cultivation, further enhancing sustainability. Additionally, biochar can be integrated into AD or fermentation processes prior to applying it to the soil, enhancing biogas (Vayena et al., 2024), or fermentation product yields (L. Zhang et al., 2023), while enriching the biochar with nutrients; this enables it to function as a slow-release fertilizer (Thiele-Bruhn and Ngigi, 2021). By employing these optimized strategies, pyrolysis significantly contributes to carbon storage, climate change mitigation, and achieving CBE goals.

3.4.1.2. Hydrothermal carbonization

Hydrothermal carbonization (HTC) efficiently processes wet biomass and biogenic residues without the need for drying by operating at moderate temperatures (180–250°C) and pressures, converting biomass into hydrochar in the presence of water (Libra et al., 2011). Hydrochar finds applications as a fuel, a soil amendment, and in environmental remediation (Libra et al., 2011; Marzban et al., 2024b), with its energy yield and content—when applied as fuel—being influenced by process parameters such as time, temperature, and the biomass-to-water ratio (Marzban et al., 2022). Compared to pyrolysis, HTC generates fewer gaseous byproducts; however, hydrochar has lower carbon content, porosity, and surface area (Libra et al., 2011; Marzban et al., 2022). Nonetheless, hydrochar's hierarchical pore structure and oxygen-rich surface make it a promising material for electrocatalysis, particularly in oxygen reduction reactions, where it enhances reaction efficiency (Lu et al., 2017; Nicolae et al., 2020). Hydrochar-based carbon materials have also demonstrated excellent performance as anode materials in lithium-ion and sodium-ion batteries, offering high capacity and stability, which makes them attractive for next-generation energy storage systems (Imtiaz et al., 2017).

The application of hydrochar as an efficient material for hydrogen and methane storage (Sevilla et al., 2016; Cruz et al., 2018), as well as for energy, supercapacitors, and ion batteries (Nicolae et al., 2020), presents a valuable opportunity to integrate renewable energy sources such as solar and wind power. The stored energy can then be effectively utilized in biorefineries, enhancing sustainability and energy efficiency in bio-based industrial processes. However, when hydrochar is used for applications other than direct energy production, such as soil amendment or pollutant removal, its production requires additional energy input. This energy demand must be met through renewable sources to maintain environmental sustainability. One potential approach is integrating HTC with pyrolysis to utilize excess heat, reducing the need for external energy input. Alternatively, heat can be supplied via renewable technologies, such as solar energy (Ischia et al., 2020). A promising solution involves coupling an HTC reactor with a solar concentrator. A parabolic dish concentrator equipped with a nanostructured copper oxide coating enhances light absorption, achieving up to 95.6% absorptance and enabling a zero-energy HTC process (Ischia et al., 2020).

The solid yield from HTC typically surpasses that of pyrolysis, and the liquid fraction produced, rich in aromatic compounds and organic acids, has been utilized in AD to enhance biogas production (Wirth et al., 2015; Ipiales et al., 2021; Marzban et al., 2023). However, the application of this liquid

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in soil and seed germination remains limited due to potential phytotoxicity (Bargmann et al., 2013).

Recent research has highlighted the antibacterial properties of hydrothermal process liquid (Mohammadi et al., 2024), making it one of the most promising potential applications of HTC liquid to be explored in the future. Furthermore, the migration of inorganics and nutrients from the solid to the liquid phase during the HTC process (Reza et al., 2013) significantly enhances its potential for nutrient recovery (Alhnidi et al., 2020). However, the nutrient content of the process liquid depends on various process parameters, and additional steps are necessary to efficiently extract these nutrients from the liquid phase after the HTC process to fully realize its potential (Aragón-Briceño et al., 2021). These findings suggest that, in contrast to the predominant focus on hydrochar as a solid product, the liquid product from the HTC process requires significant further research (Dang et al., 2024).

Hydrochar, also known as artificial coal, offers a high energy density, making it suitable for biofuel applications (Marzban et al., 2022). However, its aromatic compound content and lower stability limit its use in soil and environmental applications unless pre-treated to remove toxic elements (Fornes and Belda, 2017; Marzban et al., 2024b). To address these challenges, alternative hydrothermal processes, such as HTF and HTH, within the time and temperature constraints of the HTC process have recently been developed (Ischia et al., 2024). Additionally, with the HTC process advancing toward industrial-scale readiness (Farru et al., 2024), it presents significant potential for integration with existing biorefinery and waste treatment systems, offering key advantages in processing wet feedstocks, reducing waste, and enhancing nutrient and carbon recovery.

3.4.1.3. Hydrothermal humification and fulvification: Emerging technologies for biorefinery

Recent advancements in hydrothermal technologies have addressed key limitations in the conversion of biogenic residues. The HTH process, recognized by IUPAC in 2021 as one of the top ten emerging technologies, facilitates the comprehensive conversion of lignin, fibers, and proteins without generating gaseous byproducts (F. Yang et al., 2019; Yang and Antonietti, 2020; Marzban et al., 2024b). Building on this, hydrothermal HTF, introduced by Marzban in 2024 (Marzban, 2024), further enhances HTC by producing humic substances such as humin, humic acids, and fulvic acids (Kohzadi et al., 2023; Tkachenko et al., 2023; Marzban et al., 2024b). The transition from hydrochar production in HTC to AHSs involves maintaining an alkaline environment, typically using agents like KOH. During this process, furanic and phenolic compounds are converted into humic substances, with higher KOH concentrations shifting the reaction from HTH to HTF, resulting in smaller macromolecular structures. The initial alkalinity, determined by the carbohydrate content of the feedstock, is expressed as the molar ratio of KOH to carbohydrates. These values define process thresholds: HTC < 1, $1 \leq$ HTH ≤ 2, and $2 \leq$ HTF (Tkachenko et al., 2023; Marzban, 2024; Marzban et al., 2024b).

The HTH and HTF processes offer substantial agricultural and environmental benefits by significantly reducing harmful phenolic and furanic compounds (Tkachenko et al., 2023; Marzban et al., 2024b), which can otherwise impair soil and plant health (Ghaslani et al., 2024; Volikov et al., 2024). Similar to natural humic substances (Vallini et al., 1997; Pukalchik et al., 2019), AHSs function as soil conditioners and biostimulants. They enhance water retention, buffer soil pH, mobilize nutrients, and foster beneficial microbial interactions. Research has shown that A-humic acids (A-HAs) improve nitrogen use efficiency (Jin et al., 2023), phosphorus uptake (Yuan et al., 2022; Ghaslani et al., 2024), seed germination rates (Ghaslani et al., 2024), and plant resilience to saline toxicity, as evidenced by improved maize growth under alkaline stress (Yang et al., 2023). These properties make A-HAs valuable for enhancing soil health, supporting carbon sequestration (Tang et al., 2022), and mitigating the effects of climate change.

The integration of HTH and HTF technologies within biorefineries offers a transformative approach to sustainable waste management. These processes convert both upstream and downstream biogenic residues into artificial humic acids (A-HAs), establishing a closed-loop system that minimizes waste and maximizes resource efficiency. For instance, HTH has demonstrated a 158.6% increase in biomethane yields by converting digestate into A-HAs and enriching process liquids with soluble organic carbon (Marzban et al., 2024b). Furthermore, A-HAs improve soil health, as shown by their ability to stabilize bacterial diversity in sandy soils under drought conditions and enrich beneficial microbial taxa (Hoefle et al., 2024). Additionally, HTH and HTF produce fewer carcinogenic polycyclic aromatic hydrocarbons (PAHs) than pyrolysis, making them safer for environmental applications (Jeon et al., 2024). These technologies are quickly becoming essential components of a SCBS, advancing soil resilience, nutrient recycling, and environmental restoration while simultaneously reducing GHG emissions and the reliance on environmentally harmful materials like peat (Hoefle et al., 2024; Marzban, 2024).

3.4.2. Bioconversion processes

3.4.2.1. Fermentation

Microbial fermentation is a cornerstone technology for producing a wide range of bio-based products. Although fermentation is one of the oldest techniques, it has evolved from a method for food preservation into a foundational element of modern biotechnology. This evolution, known as the “biotech revolution,” combines microbiology, process engineering, and data analysis, giving rise to precision fermentation (Banovic and Grunert, 2023). Precision fermentation optimizes large-scale fermentation by integrating advanced technologies, resource efficiency, and sustainable practices. Bio-based products, particularly chemical building blocks such as carboxylic acids, play a critical role in developing sustainable alternatives to petrochemical routes (Alexandri and Venus, 2017). For example, the production of lactic acid (LA) and the potential use of process side-products could pave the way for a waste-free process that leads to sustainable bioplastics (Alves de Oliveira et al., 2020). Expanding the range of substrates, particularly through waste utilization, presents opportunities for reducing production costs, as feedstock accounts for up to 90% of total costs. Utilizing waste substrates also mitigates the challenges of using food crops, while advanced modeling and bioinformatics enable a holistic optimization of the fermentation process (Olszewska-Widdrat et al., 2023; Marzo-Gago et al., 2024). Fermentation also provides a sustainable solution for producing high-value proteins, including functional animal proteins, in an animal-free manner through submerged fermentation with biotechnologically optimized hosts (Aita et al., 2019). Moreover, advanced bioprocessing techniques, such as continuous and high-performance fermentation with in situ product recovery, enhance efficiency by maintaining optimal growth conditions and product formation over extended periods (Rübenach et al., 2019).

The production of carboxylic acids is most cost-effectively achieved under low pH and high-temperature conditions. However, few microbial strains are capable of withstanding both high temperatures and acidic environments, which is essential for attaining high titers of organic acids near the pKa value of the product (Liu et al., 2008; Soghomonyan et al., 2011; Abdel-Rahman et al., 2021). Furthermore, efficient utilization of low-cost, complex substrates, such as industrial waste hydrolysates and byproduct streams, requires the development of tailored enzyme systems that are compatible with both acidic pH and high-temperature conditions (Meng and Ragauskas, 2014; Siepmann et al., 2018; Marzo-Gago et al., 2022).

Simultaneous fermentation of pentoses and hexoses further boosts product yield per tonne of substrate, making it a critical factor in maximizing bioconversion efficiency (Tarraran and Mazzoli, 2018; Peinemann et al., 2020). The production of pure isomers, such as D(-)-lactic acid (LA) and L(+)-LA with high optical purity (>99%), is essential for chemical and polymer synthesis, as the steric orientation significantly impacts the stability and biodegradability of stereocomplexes. For poly-lactic acid (PLA) production, both isomers are necessary to ensure stability. However, the production of D-LA remains a challenging task (Cubas-Cano et al., 2018; Alexandri et al., 2019a; Talebi et al., 2021).

Optimizing process parameters such as time, temperature, pH, and biomass composition is crucial for scaling up production and improving downstream processing (DSP). This optimization also involves evaluating the best conditions for preculture preparation, including sugar source and inoculum size (Klotz et al., 2017; Olszewska-Widdrat et al., 2023 and 2024).

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Downstream processing typically involves separating and purifying the product from the fermentation broth, often using bipolar electrodialysis membranes (Alexandri et al., 2019b; Alvarado-Morales et al., 2021; Chuang Chen et al., 2022). The choice of process type—batch, fed-batch, or continuous—has a significant impact on fermentation efficiency and product yields (Olszewska-Widdrat et al., 2019 and 2020; de Oliveira et al., 2021).

Advancements in on-line monitoring technologies have also improved process control, leading to enhanced purification efficiency and optimized resource utilization (Joglekar et al., 2006; Bekatorou et al., 2016; Dai et al., 2020). Since fermentation is a water-based process, water removal during DSP substantially increases purification costs. To reduce these costs, it is critical to implement a sustainable feedstock strategy and optimize DSP processes in alignment with bioeconomy goals (Kumar et al., 2019; López-Gómez et al., 2020; Lithourgidis et al., 2023). Thus, developing a strategy for the sustainable production of such molecules is essential for minimizing costs and supporting long-term viability (Abdel-Rahman and Sonomoto, 2016; Ioannidou et al., 2023).

Fermentation plays a key role in integrated biorefineries, facilitating the efficient conversion of biomass and residues into valuable products. Both solid and liquid residues can be sanitized and transformed into high-value outputs through processes like AD, HTC, HTH, and pyrolysis. Additionally, fermentation residues can be repurposed as insect feed, while the CO_2 generated during fermentation can be captured and utilized in algae-based systems. Advanced technologies such as Digital Twin simulations and ML-driven modeling further enhance process control, resource optimization, and sustainability, driving the development of a resilient and CBE.

3.4.2.2. Anaerobic digestion

AD is a complex biochemical process that breaks down a wide range of organic biomass compounds, converting them into gaseous products, primarily methane and carbon dioxide, in the absence of oxygen. The process consists of a series of degradation steps and biochemical reactions carried out by diverse microbial consortia, primarily bacteria and archaea (Verstraete et al., 1996). Due to its versatility in feedstock requirements, along with its ability to efficiently recover energy, recycle nutrients, and reduce pathogens, AD is considered a cornerstone of organic waste and residue management (Fröschle et al., 2015). As a result, AD is highly suitable for integration into biorefineries or various bioeconomic production systems (Theuerl et al., 2019). Moreover, ongoing developments in pretreatment and process-integrated treatment steps are expanding the range of feedstocks that can be utilized, including nitrogen-rich substrates and lignocellulose-based material flows (Cai et al., 2021; Kumar Prasad et al., 2024).

Biogas, the main product of AD, typically comprises 50–70% methane and 25–50% carbon dioxide, along with trace gases such as hydrogen sulfide, ammonia, and water vapor (Ahmed et al., 2021). Its high methane content makes biogas a valuable energy carrier that can be converted into electricity and heat or, after further upgrading, used as transport fuel or as a replacement for natural gas in the gas grid (Ahmed et al., 2021). Upgraded bio-CO_2 further valorizes biogas by mitigating GHG emissions and enabling its use in chemical synthesis, food preservation, algae production, and industrial processes, thus providing high-quality bio-products (Ahmed et al., 2024).

In addition to biogas, digestate is another product of the AD process. It is a nutrient-rich slurry commonly applied as fertilizer or soil amendment (Kunatsa and Xia, 2022). When used as fertilizer on arable land, digestate returns organic carbon to the soil replaces mineral fertilizers (N, P, K), and helps close nutrient cycles (Theuerl et al., 2019). However, digestate's lower C/N ratio and readily accessible organic carbon fractions make it prone to carbon degradation (Tambone et al., 2009; Möller, 2015). To address this, integrating AD with processes like HTH, HTF, and pyrolysis can significantly enhance digestate's stability and value. For example, converting digestate into AHSs improves its environmental benefits and overall efficiency (Marzban et al., 2024b). Moreover, incorporating biochar into AD stabilizes nitrogen, prevents NH_3 and N_2O emissions, reduces mineral nitrogen release, and increases stable carbon for long-term storage (Viaene et al., 2024).

Several factors influence product formation, quality, and the overall performance of AD. One of the most critical factors is the chemical composition of the feedstock, as proper macro- and micronutrient levels are necessary to ensure stable biogas production. However, an excess of certain elements, such as nitrogen, can reduce efficiency or inhibit the process by generating inhibitory metabolites like ammonia (Chen et al., 2008). Smart co-digestion can help balance nutrient composition and prevent such process inhibition. The degradability of feedstock is another key factor, with lignin content playing a significant role. Lignin is not anaerobically degradable and can form recalcitrant compounds that hinder the breakdown of hemicellulose, cellulose, and proteins (Herrmann et al., 2016; Wang et al., 2023). Additionally, physical feedstock characteristics, such as particle size, are important for both degradability and degradation kinetics (Herrmann et al., 2012).

Among the operating parameters, temperature, organic loading rates (OLR), and retention time are among the most influential. Process temperatures within the mesophilic (35-42°C) or thermophilic (45-60°C) range are generally considered optimal for AD (Weiland, 2010). While higher temperatures can increase microbial growth rates, they can also inhibit the process if they exceed optimal levels (Angelidaki and Ahring, 1994). Organic overload is one of the most frequent causes of instability or failure in AD systems (Wu et al., 2019), so OLR is typically kept in a lower range of 1 to 4 kg VS/(m³ d) to avoid disturbances in full-scale AD plants (Wu et al., 2019). OLR is closely related to the hydraulic retention time (HRT) in common continuously stirred tank reactors (CSTR). A sufficiently long HRT is required to allow for adequate feedstock degradation based on feedstock-specific degradation kinetics and to prevent the wash-out of slowly growing methanogens (Herrmann et al., 2018; Cremonez et al., 2021).

Methanogenic archaea are known for their slow growth rates, with duplication times that can span several days. As a result, complete feedstock degradation requires relatively long AD durations. Retention times typically range from 30 to 60 days and can exceed 100 days in CSTRs particularly when lignocellulosic feedstocks are used (Herrmann et al., 2018; Cremonez et al., 2021). While lower organic loading rates (OLR) and longer HRT help reduce the risk of process instability, they necessitate large reactor sizes and lead to slower gas production rates. These factors contribute to high operational costs, limiting the economic feasibility of the process (Wu et al., 2019). However, some of these challenges can be mitigated through adaptations in reactor design and process configurations (Herrmann et al., 2018).

Despite the need for process optimization, AD offers the ability to utilize a remarkably wide range of feedstocks under low temperature and pressure conditions, making it an ideal process for integration into multi-faceted production systems for food, feed, bioenergy, and biomaterials. As a result, AD has become a crucial component of smart biorefineries. When coupled with other thermo- or biochemical conversion systems, such as lactic acid fermentation, AD provides several benefits, including reduced waste formation, extended product utilization, GHG emission mitigation, and improved economic viability (Herrmann et al., 2024).

3.4.3. Biological conversion processes

Biological conversion processes, such as algae cultivation and insect-based systems, harness natural systems to produce biofuels, biomaterials, and protein-rich products, all while recycling nutrients and reducing waste. These processes play a key role in advancing sustainable bioeconomy goals by integrating waste valorization with innovative biorefinery applications.

3.4.3.1. Algae cultivation

Micro- and macroalgae are pivotal feedstocks in biorefineries, valued for their rapid growth rates, nutrient recovery potential, and carbon dioxide sequestration capabilities. These attributes align well with bioeconomy and circular sustainability objectives. Algae-based systems are key in producing biofuels, biomaterials, and high-value products, all while minimizing environmental impacts, making them integral to advanced biorefinery configurations (Chew et al., 2017; Otálora et al., 2021; Syed et al., 2024). A significant application of both micro- and macroalgae is in food and feed, with particular focus on their role in aquaculture feed (Packer et al., 2016;

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Ahmad et al., 2022; Bakky et al., 2022). Macroalgae, rich in lipids, proteins, minerals, and bioactive compounds (such as phenolics, carotenoids, and pigments) (Garcia-Vaquero and Hayes, 2016; Afonso et al., 2019), are used for nutrient extraction and recovery. Additionally, macroalgae have a long history of consumption as food in East Asia, particularly in Japan (Nisizawa et al., 1987; Young et al., 2022). Beyond direct consumption, macroalgae are also utilized as food ingredients to improve nutritional profiles, texture, color, appearance, and flavor. They can even serve as edible wrappings, such as in the case of nori seaweed, replacing traditional cutlery (Blikra et al., 2021). Similarly, microalgae offer substantial potential for use as food due to their high protein and oil content, as well as their rich profile in amino acids, fatty acids, and bioactive compounds (Torres-Tiji et al., 2020). Microalgae can also enhance the physicochemical and sensory qualities of conventional food products when incorporated as ingredients (Draaisma et al., 2013).

Microalgae are highly valued for their lipid-rich biomass, which plays a crucial role in biodiesel production. In contrast, macroalgae, which are carbohydrate-rich, are primarily used in bioethanol and biogas production. Algae-derived products, including pigments, bioactive compounds, nutraceuticals, and feed additives, contribute to the economic diversification of biorefineries (Khoo et al., 2019; Otálora et al., 2021; Salami et al., 2021). Algal cultivation depends on sunlight, CO_2, water, and essential nutrients like nitrogen and phosphorus. Microalgae are grown in photobioreactors or ponds at temperatures between 20–30°C and a pH range of 7–9, while macroalgae thrive in marine environments. Lipid extraction from microalgae is essential for biodiesel production, while macroalgae undergo saccharification to produce bioethanol. The residual biomass of both types of algae can be repurposed as fertilizer or biochar (Uggetti et al., 2014; Catone et al., 2021; Syed et al., 2024).

Optimizing cultivation parameters enhances algal yields. For microalgae, nitrogen starvation increases lipid accumulation, while acid hydrolysis enhances carbohydrate availability in macroalgae. However, challenges remain, including the color and flavor impact of microalgae, the need for drying after harvest, high energy requirements in photobioreactors, and low productivity rates (Raha et al., 2018; Cheng Chen et al., 2022). Innovative food processing techniques, such as pulsed electric fields, have been proposed to address these challenges. These methods can improve productivity by stressing microalgae under mild processing conditions while enhancing the efficiency of drying and extraction under more intensive processing conditions (Buchmann et al., 2018).

Fermentation processes optimized for bioethanol production operate at temperatures of 30–40°C with specialized microbial strains to maximize yields. CO_2 supplementation and light-intensity management during cultivation also play key roles in boosting growth rates and improving lipid or carbohydrate productivity (Chew et al., 2017; Eppink et al., 2019; Otálora et al., 2021). Microalgae generally require 7 to 14 days to cultivate, while macroalgae farming can take several weeks to months, depending on the species and environmental conditions. Despite their potential, algae-based systems face economic and technical hurdles. Photobioreactors are costly to scale, and microalgae harvesting demands significant energy inputs. For macroalgae, challenges include spatial limitations and ecological concerns, such as nutrient overloading and habitat disruption, which can hinder large-scale production (Catone et al., 2021; Otálora et al., 2021; Syed et al., 2024).

3.4.3.2. Insect-based systems

Edible insects have gained attention for their role in closing the loop in the CBE through their application in the biochemical conversion of organic wastes (Ojha et al., 2020). Organic waste can serve as a feeding substrate for insects, which grow on these wastes and can later be harvested for various uses (Rossi et al., 2024; Rajendran et al., 2018). A similar waste valorization strategy has been demonstrated in the cassava starch industry, where optimized biorefinery pathways transform waste streams into high-value products, such as animal feed, fish feed, and fungal protein, offering both economic and environmental benefits (Ravichandran et al., 2024). Post-harvest, insects can be reintroduced into the agri-food chain in a process known as insect-based biorefinery (Baumberger, 2024). These biorefineries generate a wide array of products (Cláudia da Costa Rocha et al., 2021), with the primary uses being food for human consumption and animal feed (Kee et al., 2023). Insects are valued for their high nutritional content, including proteins that can make up to 70% of their dry weight, depending on the species (Rumpold and Schlüter, 2013). They also contain both essential and non-essential amino acids (Queiroz et al., 2023), as well as beneficial fatty acids (Perez-Santaescolastica et al., 2023). Additionally, insects are a source of chitin and chitosan (Mohan et al., 2020; Rehman et al., 2023), along with bioactive compounds such as phenolics (Nino et al., 2021) and bioactive peptides (Teixeira et al., 2023), which have potential medicinal applications (Ratcliffe et al., 2014). Beyond direct consumption, insects can also be utilized to isolate biopolymers like chitin, which has applications in food, medicine, and wastewater treatment as an adsorbent (Simionato et al., 2006). Furthermore, insect fat can be recovered and used as a feedstock for biodiesel production (Nguyen et al., 2019).

When organic wastes are used as feed for insects, they can be provided either directly (Shumo et al., 2019) or incorporated into more complex diets (Kuo and Fisher, 2022). The primary objective is to ensure that the diet meets the nutritional requirements of each insect species, enabling their successful growth (Leni et al., 2021). Moreover, the selection of organic waste for insect feed can be strategically made to manipulate the insect's composition, potentially increasing the content of targeted compounds, such as vitamins (Kotsou et al., 2023). Successful insect growth also depends on providing conditions that are specific to each species, including appropriate temperature, population density, and humidity (Kinyuru and Kipkoech, 2018), while protecting the insects from diseases, biological hazards, and predators (Orinda et al., 2021). Common organic wastes considered for use in insect-based biorefineries include food waste (Skrivervik, 2020) and manure from other farmed animals (Cammack et al., 2021). The overall duration of the rearing process varies depending on the insect species, the rearing system, and the growth stage at which the insects are harvested. Economic challenges in insect-based biorefineries include low consumer acceptance of insects as food (de Castro et al., 2018). Technical challenges encompass inefficiencies in waste utilization for meeting nutritional requirements, legal barriers to using certain substrates like manure, and the need to optimize rearing conditions and diets. Environmental constraints include high energy consumption for temperature control, although insects generally have a lower environmental impact than conventional livestock (Oonincx and De Boer, 2012). Another issue is that some organic wastes cannot be fully utilized by insects and must be mixed with conventional feedstuffs (Rossi et al., 2023).

The production of edible insects generates its own waste, primarily insect frass, which refers to the solid excreta of insects (Poveda, 2021). Another waste product is the exuviae of holometabolous insects, which is the shed exoskeleton (Wantulla et al., 2023). Both frass and exuviae hold significant potential for use in the bioeconomy, particularly in promoting plant growth (Barragán-Fonseca et al., 2022). Exuviae, rich in chitin, can be utilized as a valuable source of chitin (Hahn et al., 2022). Insect frass is also considered a lignocellulosic biomass with a high protein content, making it a suitable feedstock for biogas production (Dal Magro et al., 2024) and bioethanol (Psarianos et al., 2024). The conversion of frass into biogas has been successfully demonstrated with various insect species, indicating its potential for broader application (Bulak et al., 2023; Wedwitschka et al., 2023). Additionally, frass can be converted into biochar, which has been shown to serve as an effective adsorbent for wastewater treatment, including the removal of ionic dyes and heavy metals (S.S. Yang et al., 2019a and b).

3.5. Environmental impact assessment of stand-alone conversion methods

Biomass conversion methods vary in their environmental impacts, depending on the specific process used. Traditional methods like combustion and composting, while effective for waste management, contribute significantly to GHG emissions and nutrient losses. Combustion and incineration release carbon as carbon dioxide and generate other GHGs, as noted by Gómez-Sanabria et al. (2022). Composting, commonly used for municipal organic waste and biowaste, produces methane and nitrous oxide emissions, further exacerbating climate change and can lead to nutrient leaching into groundwater (Demirbas, 2011; Hasan and Habiba, 2015). The stability of carbon in the compost product remains a topic of debate (Jiao et al., 2025). In contrast, AD offers a dual benefit: it captures methane in a controlled manner for biogas production and reduces emissions compared to traditional methods (Demirbas, 2011; Ma et al., 2024). However, one of the major trade-offs is the occurrence of diffuse emissions during operation, such as substrate handling, gas and product storage, and challenges with the separation of solid and liquid phases. Methane leakage during this process is estimated to be as high as 5% (Mahdi et al., 2024).

Thermochemical methods like pyrolysis and gasification offer environmental advantages by producing value-added products such as biochar and syngas, which can reduce some of the risks associated with biomass conversion. However, uncontrolled processes can still result in moderate emissions (Shahbeig and Nosrati, 2020; Ascher et al., 2022). When syngas is fully combusted, it can provide CO_2 for algae cultivation and generate moderate heat for greenhouse operations. However, standalone thermochemical processes face several challenges. For instance, biochar may need aging or post-treatment before soil application to prevent nutrient competition with plants. This issue can be addressed by integrating biochar with AD processes or digestate, which enhances conversion efficiency and ensures nutrient retention, functioning as a slow-release agent for carbon sequestration in soil (Viaene et al., 2024). Moreover, the heat generated during pyrolysis is often underutilized in standalone setups, yet it holds potential for biopower generation or for supporting processes like AD or fermentation.

Emerging technologies such as HTC and HTH play a key role in mitigating emissions while enabling nutrient recycling and carbon sequestration, providing a sustainable pathway for biomass valorization (Kokossis et al., 2015; Shahbeik et al., 2022; Zhu et al., 2023). However, these processes require moderate temperature and pressure conditions, meaning external energy sources are needed if the goal is to focus on soil and environmental applications rather than biofuel production. This energy demand can be met by leveraging heat and electricity from other processes. Advanced systems, such as algae-based biorefineries and insect farming, integrate nutrient recovery and carbon utilization into sustainable conversion pathways. Algae biorefineries are particularly effective at carbon sequestration but face challenges like energy-intensive harvesting and processing (Coşgun et al., 2023; Oruganti et al., 2023). Insect-based systems efficiently convert organic waste into feedstock for AD or composting, reducing emissions in the process (Ites et al., 2020; Nawoya et al., 2024). These innovative technologies highlight the importance of overcoming the limitations of traditional biomass management systems while enhancing resource efficiency and minimizing environmental impact (**Table 3**).

3.6. Integrated biorefineries: needs and benefits

Integrated biorefineries combine a variety of processes and technologies into a single system, maximizing biomass utilization and minimizing waste. By creating synergies, where outputs from one process serve as inputs for another, these systems enhance resource efficiency, reduce costs, and mitigate environmental impacts. The synergies between these processes are summarized in **Table 4**, which compares the limitations of standalone technologies and the benefits of integrating processes like pyrolysis, HTC, fermentation, algae cultivation, and insect farming. For example, biochar produced through pyrolysis enhances biogas yields in AD, reduces emissions, and contributes to carbon sequestration (Viaene et al., 2024). This strategy overcomes potential challenges with biochar application to soil, such as nutrient competition with plants, by boosting agricultural productivity through improved nutrient retention and acting as a carbon sink, similar to biochar aging (Mia et al., 2017). Moreover, biochar-supported catalysts have proven effective in converting biomass-derived feedstocks like glucose into valuable chemicals under mild conditions, showcasing their role in sustainable catalytic pathways within integrated biorefineries (Hao et al., 2024). Biochar can also remove inhibitors from fermentation processes, facilitating smoother conversions. Additionally, CO_2, a byproduct of fermentation, can be used to support algae cultivation, promoting closed-loop systems in line with CBE principles (Tay et al., 2011; Coşgun et al., 2021; Velvizhi et al., 2022). The cultivated algae can be employed for protein extraction (Eppink et al., 2019), biofuel production (Tomar et al., 2023), or as feedstock for pyrolysis (de Morais et al., 2023), further enhancing resource efficiency. Additionally, the bio-oil derived from pyrolyzed algae can be upgraded into higher-value biofuels through advanced catalyst optimization. For instance, increasing the acidity of beta zeolite has proven effective for upgrading oleic acid, and optimizing this process can significantly increase biofuel yields, boosting the overall efficiency of the biorefinery system (AlAreeqi et al., 2024).

Fermentation solids can be repurposed for insect production, such as rearing black soldier fly larvae (Norgren et al., 2023), which can then be used to extract valuable compounds like protein and chitin (Smets et al., 2020). Meanwhile, the remaining waste can be further processed within the biorefinery using integrated systems, maximizing resource recovery and efficiency. Solid wet residues from fermentation (Lombardi et al., 2024), downstream liquid waste, and residues from algae systems (Kozyatnyk et al., 2023) can all undergo HTC to convert them into valuable, stable

Table 3.
Environmental impact assessment of biomass conversion methods: comparative analysis of emissions, energy recovery, and sustainability potential.

Method	Environmental Impact	Energy Perspective
Fermentation	Low direct emissions but the potential for wastewater generation; requires pretreatment energy.	High-energy demand for feedstock pretreatment; potential to use residues for biogas production.
Anaerobic Digestion (AD)	Potential emission due to leakages during the process, mitigates organic waste pollution and uncontrolled methane emissions; digestate can be used as a biofertilizer.	Self-sufficient energy production from biogas, which can provide heat and electricity for other processes.
Algae-based Biorefineries	Carbon sequestration through photosynthesis; wastewater reuse minimizes nutrient runoff; water-intensive.	High energy demand for harvesting and lipid extraction; co-products like biofuels can offset energy use.
Insect Farming	Organic waste conversion with minimal emissions; localized ammonia emissions possible.	Energy required for climate-controlled farming systems; residual biomass usable as feedstock for AD, HTC, pyrolysis
Pyrolysis	Moderate emissions without control systems; biochar can offset soil degradation and sequester carbon.	Bio-oil and syngas can provide process heat and electricity; external energy is required for heating in the initial stages. In general, it can provide heat and electricity for other systems as well.
HTC	Low emissions; hydrochar aids carbon sequestration; aqueous by-products require management.	No energy is needed for the dewatering of feedstock, the potential to generate self-sufficient energy by fuel application of hydrochar, and the potential to produce biogas in AD
HTH/HTF	Carbon sequestration in soils through humic and fulvic acids; minimal emissions.	No energy is needed for the dewatering of feedstock and products, potential for self-sustaining energy if combined with AD processes.
Incineration/Combustion	Emission control is possible through advanced flue gas cleaning. Potentially sink for pollutants	Only applicable for dry biomass, self-sufficient process possible
Composting	Uncontrolled methane and nitrous oxide emissions; nutrient leaching into groundwater possible.	Low energy demand; limited potential for energy recovery.
Landfilling	High methane and CO_2 emissions from anaerobic degradation; significant leachate pollution.	Limited energy recovery through landfill gas capture; inefficient compared to other methods.

Table 4.
Integration synergies and benefits of biorefineries.

Process	Standalone Limitations	Integration Synergies and Benefits
HTC, HTH, and HTF	High energy requirement, scalability challenges, water management issues	Integrated with AD: digestate converted to hydrochar and artificial humic substances, improving methane production, nutrient recycling and reducing emissions. Integrated with fermentation: converting the fermentation solid residues and liquid by-products
Pyrolysis	Feedstock sensitivity; byproducts require additional treatment (e.g., bio-oil upgrading)	Integrated with AD: heat generated dries digestate; biochar enhances AD yield and serves as a catalyst. Integrated with fermentation: biochar removes inhibitors from fermentation feedstocks, improving yield and acting as a catalyst. Integrated with algae cultivation: co_2 from pyrolysis syngas supports algae growth.
AD	Sensitive to feedstock variability, long residence times, and methane leakage	Integrated with HTC: digestate converted to hydrochar or HTH products for enhanced carbon sequestration. Integrated with pyrolysis: biogas powers pyrolysis equipment; digestate improves feedstock quality for pyrolysis. Integrated with biochar: biochar removes impurities and serves as a catalyst, enhancing digestion efficiency.
Fermentation	Inhibition by feedstock impurities (e.g., inhibitors, antibiotics) requires pre-treatment	Integrated with algae cultivation: co_2 from fermentation supports algae growth for biodiesel and bioactive compound production. Integrated with insect farming: residues provide feedstock for insect farming, enhancing circular waste utilization. Integrated with biochar: biochar removes fermentation inhibitors, enhancing yield and acting as a catalyst.
Algae cultivation	High energy for harvesting and dewatering; requires CO_2 supply	Integrated with HTC: residual biomass converted into hydrochar. Integrated with liquefaction: residual biomass processed into biocrude. Integrated with fermentation: co_2 from fermentation supports algae growth, reducing emissions and enhancing productivity.
Insect farming	Limited feedstock types (organic waste)	Integrated with fermentation: fermentation by-products provide feedstock for insect farming, completing the waste utilization loop.

products. This process ensures that the outputs are sanitized and free of microbes, with temperatures exceeding 150°C effectively eliminating microbially derived DNA (Ducey et al., 2017). The hydrothermal products can then be integrated into AD processes, enhancing biogas production (Wirth and Mumme, 2014; Wirth et al., 2015). Nitrogen-rich substrates, in particular, are highly beneficial, as they significantly increase biogas yields.

Advanced techniques, such as methanotroph-based biotransformation platforms, provide innovative strategies for nutrient recovery within integrated biorefineries. By utilizing biogas as a carbon source and wastewater as a nitrogen source, these systems enhance nutrient circularity, improving the environmental sustainability of biogas production (Zheng et al., 2024). Additionally, both hydrothermal processing and AD do not require pre-drying of the inputs (Wood et al., 2013), offering a more energy-efficient solution. However, a key challenge lies in the high cost of post-solid/liquid separation of digestate. HTC can be employed after AD to address this issue by producing hydrophobic solids that are easily filtered from the liquid, enabling efficient separation (Ferrentino et al., 2023). The nutrient-rich solid and liquid products from these processes can be stored and utilized in a wide range of applications, such as recycling into AD for further biogas production, carbon sequestration, nutrient recovery, biofuel production, and enhancing artificial humic acid content in soil (Marzban et al., 2023 and 2024a). This integration of processes optimizes resource recovery and supports the production of value-added outputs.

Hydrothermal humification (HTH) exemplifies the integration of thermochemical and biochemical processes to maximize resource efficiency (Marzban, 2024). This method converts digestate, a common byproduct of AD into A-HAs in both solid and liquid phases while recycling the process liquid back into the biorefinery system. Recycling the liquid significantly boosts biomethane yields—up to 158.6%—compared to untreated digestate (**Fig. 4**). By preventing the further decomposition of carbohydrates into GHG, HTH transforms them into humic-rich products that replicate natural humic substances, which typically take years to form in nature but can be synthesized in hours in controlled systems. Additionally, HTH reduces inhibitory compounds such as phenolics and furanics by over 70% in solids and 90% in liquids, resulting in a nutrient-rich effluent that promotes plant growth (Marzban et al., 2024b). The integration of HTH and hydrothermal liquefaction (HTL) into biorefineries presents a promising route to convert solid and liquid residues into value-added products, thereby enhancing both system efficiency and sustainability (Marzban, 2024).

Emerging technologies further underscore the advantages of integration. For example, temperature-phased anaerobic digestion has shown promise in improving the circularity of nutrients like nitrogen, phosphorus, and carbon in agricultural residues such as rice straw. This approach helps reduce open burning while recovering valuable resources for local use (Fritze and Rotter, 2024). Likewise, the co-digestion of rice straw with cow manure in innovative AD systems has resulted in higher methane yields and enhanced digestion efficiency, further supporting renewable energy production and nutrient recycling (Muhayodin et al., 2021). Several case studies illustrate the benefits of integrated systems. A rapeseed straw biorefinery, for example, combined hydrothermal pretreatment, ethanol fermentation, and AD to produce biofuels, biogas, and mycoprotein, improving enzymatic accessibility and energy recovery (Abbasi-Riyakhuni et al., 2025). Similarly, furfural residues were upcycled into bioethanol and pyrolytic oil, achieving energy conversion efficiencies as high as 51.3% (M. Elsayed et al., 2024). In another example, a sunflower-based biorefinery used seed oil for biodiesel production and lignocellulosic residues for biomethane generation, delivering high energy outputs with minimal waste (Ebrahimian et al., 2022).

LCA studies further emphasize the environmental benefits of integrated systems. A biphasic pinewood biorefinery, for instance, achieved a 13.05% reduction in its environmental burden by reducing electricity consumption and boosting bioethanol yields (Khounani et al., 2024). Similarly, a safflower-based system reduced its environmental impact by 64% by substituting fossil fuels with biofuels and biogas. An exergy analysis highlighted wastewater treatment as a critical area for improvement (Khounani et al., 2021; Hosseinzadeh-Bandbafha et al., 2022). Innovative strategies, such as a three-stage wastewater biorefinery, have demonstrated a 56.8% reduction in chemical oxygen demand while simultaneously producing high-quality mycoprotein and biomethane (Hashemi et al., 2023).

Integrated biorefineries are crucial in achieving sustainability goals by facilitating efficient resource recovery, minimizing environmental risks, and promoting a CBE. Given the diversity of processes, the variety of available biomasses and biogenic residues, and the broader goals of sustainability and circularity, the potential for integration is vast, with thousands of possible scenarios. Advanced techniques, such as ML modeling, are essential for accurately predicting these scenarios, ensuring the full utilization of biomass and biogenic residues while optimizing resource efficiency.

Please cite this article as: Marzban N., Psarianos M., Herrmann C., Schulz-Nielsen L., Olszewska-Widdrat A., Arefi A., Pecenka R., Grundmann P., Schlüter O.K., Hoffmann T., Rotter V.S., Nikoloski Z., Sturm B. Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production. Biofuel Research Journal 45 (2025) 2319-2349. DOI: 10.18331/BRJ2025.12.1.4.

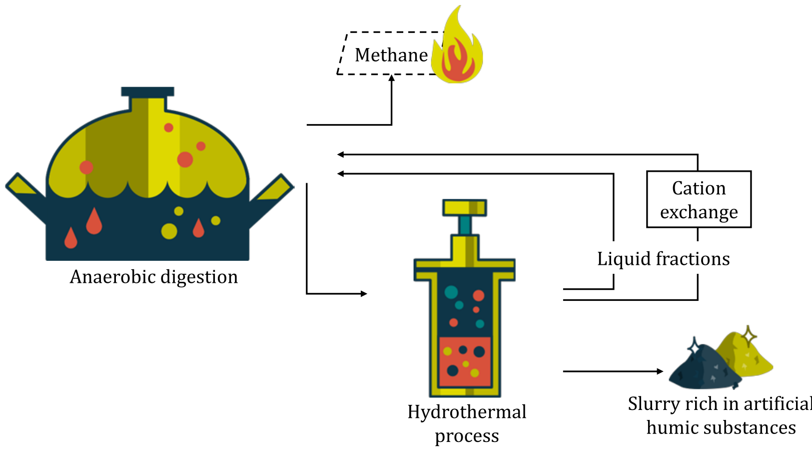

Fig. 4. Integration of hydrothermal carbonization and with adopted from (Marzban et al., 2024b). Licensed under CC BY 4.0.

4. Smart integration of processes to create smart biorefineries

4.1. Smart integrated biorefinery concept

Integrated biorefineries represent a transformative approach to sustainable biomass utilization by combining diverse conversion technologies to maximize the value of biomass and biogenic residues. These advanced systems produce high-value products, such as biofuels, biochemicals, biomaterials, and energy, while striving for carbon neutrality and zero waste (Hough et al., 2017; Djandja et al., 2023). By interlinking processes, integrated biorefineries effectively address environmental challenges, such as GHG emissions and waste generation, aligning with the principles of a CBE (Forster-Carneiro et al., 2013; Velvizhi et al., 2022).

The concept of a smart integrated biorefinery (SIB) focuses on identifying optimized standalone and integrated scenarios for processing a wide range of biomass and biogenic residues. These systems incorporate various technologies aimed at achieving SCBS goals. The integration of processes, where the output of one system serves as input for another, is determined through a network of optimized models. This approach ensures a zero-waste system by converting all waste into value-added products, boosting profitability, reducing emissions, and optimizing energy production and distribution within the biorefinery. Such advancements decrease reliance on external energy sources, further enhancing both sustainability and efficiency.

Flexibility is a key feature of integrated biorefineries. These systems can dynamically adjust their product outputs—whether fuels, chemicals, or energy—based on market demands, enhancing their economic viability (Forster-Carneiro et al., 2013; W. Zhang et al., 2023). However, their implementation faces significant challenges, including feedstock variability, process integration, emission control, and cost optimization. Addressing these challenges requires the use of advanced tools such as ML and LCA to optimize performance (Wei et al., 2022; Gupta et al., 2023; W. Zhang et al., 2023).

4.2. Challenges in integration and overcoming them

The integration of processes in biorefineries encounters multiple challenges, ranging from feedstock variability to technological and economic constraints. Below is the structured **Table 5** summarizing these challenges and potential solutions.

4.3. Digitalization in biorefinery processes

Efforts to optimize biorefinery processes have been enhanced by Digital Twin technology, which enables real-time, bidirectional communication between physical processes and digital replicas, thereby improving efficiency (Wu et al., 2021). Although its application in biorefineries is still emerging, sensor-based process monitoring has made significant strides, with spectroscopic techniques now recognized as non-destructive, rapid, and versatile tools (Wu et al., 2019). Ultraviolet-visible (UV-Vis) spectroscopy (190–450 nm), in combination with ML models such as Partial Least-Squares Regression (PLSR), can accurately quantify concentrations of lignin, acetic acid, and furfural (Beisl et al., 2018; Haque et al., 2021). UV-Vis and Support Vector Machine (SVM) models have been shown to predict organic acid levels in biogas plants with an accuracy of 87%. Specific spectral ranges, such as 250–280 nm for lignin, provide insights into organic transformations during AD (Zbytniewski and Buszewski, 2005; Wolf et al., 2010; Liu et al., 2019; Fernández-Domínguez et al., 2022).

Near-Infrared (NIR) spectroscopy (700–2500 nm) extends the monitoring capabilities of biorefineries to a wide range of substrates, including municipal waste (Lesteur et al., 2011), macroalgae (Doublet et al., 2013), and plant biomass (Triolo et al., 2014). Prediction accuracies, measured by the coefficient of determination (R^2), range from 0.76 to 0.98, with PLSR being the most commonly used prediction model (Mortreuil et al., 2018; G. Yang et al., 2021; Liu et al., 2021). NIR has been successfully applied to predict the biochemical methane potential (BMP) of various organic wastes, including tomato pomace (Almeida et al., 2021), grape residues (Almeida et al., 2021), and banana waste (Rodrigues et al., 2019). It has also proven effective in predicting BMP for MSW (Lesteur et al., 2011) and urban organic waste (Fitamo et al., 2017). Furthermore, NIR has shown efficiency in monitoring co-digestion substrates, such as straw and manure, achieving high accuracy in predicting volatile solids (VS) and fatty acids (G. Yang et al., 2021; Liu et al., 2021). Classical PLSR models have been used for real-time monitoring of VS (Raju et al., 2012), fatty acids (Holm-Nielsen et al., 2008), and ammonia nitrogen (Krapf et al., 2012), with excellent predictive performance ($R^2 > 0.9$).

Furthermore, NIR spectroscopy has proven highly effective in monitoring glucose fermentation. It accurately estimated lactic acid concentrations ($R^2 = 0.98$) and glucose concentrations ($R^2 = 0.95$) (Vaccari et al., 1994; C. Yang et al., 2021). In-situ NIR process monitoring of glucose fermentation showed high accuracy for VS, ammonia nitrogen, and other critical parameters, with R^2 values reaching up to 0.98 (Krapf et al., 2012; C. Yang et al., 2021). Inline monitoring of biomass, glucose, lactic acid, and acetic acid using NIR (700–1800 nm) demonstrated promising results, with significant improvements in accuracy (Tosi et al., 2003). NIR-based learning algorithms have also been effective in monitoring glucose fermentation processes, though reduced accuracy was observed when applied to biowaste substrates (Arefi et al., 2024). Real-time monitoring of volatile fatty acids and total inorganic carbon in AD processes achieved high accuracy ($R^2 = 0.94$ and 0.97, respectively) using NIR spectroscopy (Stockl and Lichti, 2018). What remains to be explored is how transferable these trained models are to other real-world scenarios and whether their performance can be further enhanced by utilizing advanced non-linear ML models as alternatives.

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Table 5.
Challenges and solutions for process integration in biorefineries: addressing technological, economic, and environmental barriers.

Challenge	Description	Proposed Solutions
Feedstock variability	Biomass heterogeneity in moisture, calorific value, and chemical properties affect process efficiency.	Standardized classification based on elemental analysis, higher heating value measurement, and nutrient profiling; use of advanced modeling tools like ML.
Technology compatibility	Synchronizing diverse processes like pyrolysis, fermentation, and AD requires aligned operating conditions.	Advanced simulation tools for process modeling; utilization of outputs (e.g., biochar) as inputs in other processes to enhance synergy.
Emission control	Processes emit GHGs (e.g., CO_2) and produce waste streams.	Carbon capture and utilization (e.g., CO_2 of pyrolysis for algal cultivation), recycling of by-products, and integration of renewable energy systems.
Economic viability	High capital and operational costs of biorefineries.	Diversification of product streams (e.g., biofuels, biochemicals), TEA for cost assessment, and focus on high-value products like bioplastics.
Market uncertainty	Fluctuating demand for bio-based products impacts profitability.	Flexible designs for switching outputs; adaptability to feedstock variability and market demands to ensure resilience.
Life cycle and economic analysis	Difficulty in evaluating sustainability and economic feasibility of integrated systems.	Use of LCA and TEA to assess environmental impacts, energy efficiency, and profitability; incorporation of exergy analysis for targeted optimization.

Mid-Infrared (MIR) spectroscopy provides functional group-specific data and outperforms NIR in estimating ammonia and lactic acid concentrations, achieving R^2 values above 0.9 (Falk et al., 2015; Li et al., 2022; Zeaiter et al., 2022). This high accuracy is achieved using various models, including PLSR (Eccleston et al., 2016; Li et al., 2022; Zeaiter et al., 2022), Support Vector Regression (Eccleston et al., 2016), and Dynamic Orthogonal Projection (DOP) combined with PLSR (Zeaiter et al., 2022). Classical PLSR models based on MIR data have been successfully used to predict volatile fatty acids and ammonium concentrations with superior precision and reduced errors (Eccleston et al., 2016; Păucean et al., 2017; Li et al., 2022). Additionally, preprocessing MIR spectra with DOP has significantly improved ammonia prediction in AD systems (Zeaiter et al., 2022). MIR also demonstrates enhanced capabilities in monitoring bacterial glucose fermentation and biowaste compared to other methods (Sivakesava et al., 2001; Arefi et al., 2024). Complementing MIR, Nuclear Magnetic Resonance (NMR) spectroscopy provides detailed molecular insights, further advancing our understanding of biorefinery processes (Fayolle et al., 1997; Fernández-Domínguez et al., 2022). Together, ML models trained on data from UV-Vis, NIR, MIR, and NMR spectroscopies offer scalable, non-destructive solutions for optimizing biorefineries, enhancing both efficiency and sustainability (**Table 6**).

4.4. Applications of ML in biorefineries

Biorefineries can be seen as input-output systems that operate under chemical-physical constraints. The functions of biorefineries over time and space can be described using: (1) kinetic models, which capture the chemical reactions taking place (Takkellapati et al., 2018; Shahbeig and Nosrati, 2020), (2) process models, which simplify the description of underlying chemistry (Khan et al., 2023), and (3) hybrid models, which combine both approaches, often with assumptions about time-scale separation. Regardless of the modeling type, the underlying equations are typically non-linear and involve numerous parameters whose values depend on the applied conditions. Consequently, simulations of these models require detailed knowledge, which is not always readily available for all reactions and process combinations.

In contrast, ML offers a 'black-box' approach to describing input-output systems. Instead of providing detailed mathematical descriptions of how inputs are transformed into outputs through various intermediates, ML uses a mathematical function to predict outputs based on a given set of inputs. These inputs can describe not only the characteristics of the biomass entering the biorefinery but also include aspects of the process conditions, which can enhance the accuracy and performance of predictions.

The mathematical or computational framework underlying a ML model can serve two purposes: it can predict quantitative values for one or more outputs, resulting in a regression model, or it can predict qualitative values or categories for one or more outputs, leading to a classification model. The choice between these two model types depends on the modeling goal and the level of detail required in the predictions. The objective of ML is to learn the parameters of the model that minimize a loss function, which measures the difference between the predicted and actual outputs, using a set of data with known inputs and outputs. This process is typically carried out in a cross-validation setting, where the data is split into disjoint subsets for model training, validation, and independent testing. Cross-validation helps to prevent overfitting and improves the model's ability to generalize to unseen scenarios (Hastie et al., 2009).

Given the availability of input-output data pairs, along with data on process conditions, it is not surprising that a wide variety of ML models have been trained and applied to various processes in biorefineries, demonstrating the versatility and power of this approach. These models include random forest (RF) (J. Li et al., 2020; Cheng and Luo, 2022; Katongtung et al., 2022), SVM (J. Li et al., 2020; Zhao et al., 2021), and various types of neural networks, such as artificial neural networks (ANN) (Zhao et al., 2021; Jiang et al., 2022; Sun et al., 2022). For example, in pyrolysis, ML models have been used to predict biochar properties, enabling optimization for specific applications, such as soil amendments or feedstock for further processing. These models improve efficiency by tailoring biochar production to meet targeted end-use requirements, thereby maximizing resource utilization (Tang et al., 2021; Ma et al., 2024).

Beyond pyrolysis, ML has been successfully applied to optimize HTC and AD processes by predicting process yields and optimizing operating conditions. In HTC, ML-based models such as Decision Tree Regression (DTR) and Feedforward Neural Networks (FNNs) have enhanced hydrochar quality by optimizing key process parameters, including reaction temperature, residence time, and feedstock composition (Djandja et al., 2021; Shafizadeh et al., 2023). These predictive models account for feedstock variability and operating conditions, helping to maximize hydrochar yields and adapt to diverse feedstock inputs (W. Zhang et al., 2023; Liu et al., 2024). Similarly, in AD systems, RF and Extreme Gradient Boosting (XGBoost) models have improved methane yield predictions by analyzing critical parameters like carbon-to-nitrogen ratios and HRT (Sonwai et al., 2023; Fard and Koupaie, 2024). ML techniques optimize methane production and nutrient recovery by fine-tuning variables such as carbon-to-nitrogen ratios and operating temperatures. This capability allows for precise adjustments to operating conditions, enhancing overall performance and increasing process efficiency (Shahbeig and Nosrati, 2020; Ma et al., 2024). These data-driven approaches enable biorefineries to adjust operational parameters in a real-time manner, improving energy recovery and resource efficiency.

ML has also been integrated into fermentation, algae, and insect-based biorefinery systems, highlighting its broad applicability. For example, in fermentation, ANN and Gradient Boosting (GB) models have been used to optimize ethanol and hydrogen production by fine-tuning process variables such as substrate concentration and retention time, resulting in improved biofuel yields (Pandey et al., 2023; Vinitha et al., 2023). ML techniques enhance ethanol production by optimizing fermentation conditions and minimizing by-product formation, which reduces operational inefficiencies and increases product yields. As a result, fermentation processes become

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Table 6.
Comparative overview of spectroscopic techniques to be used in smart biorefineries.

Technique	Applications	Accuracy (R^2)	Advantages	Ref.
UV-Vis	Lignin, acetic acid, furfural quantification	Up to 0.87	Non-destructive, rapid data acquisition	Haque et al. (2021)
	Organic acids estimation in biogas plants	0.87	High accuracy with ML models	Beisl et al. (2018)
	AD process monitoring	-	0.87	Wolf et al., 2010)
NIR	Glycerol-boosted AD monitoring	0.96–0.98	High accuracy for glycerol, volatile fatty acids, acetic acid	Holm-Nielsen et al. (2008)
	Real-time monitoring of volatile fatty acids and inorganic carbon	0.94–0.97	Effective process monitoring	Stockl and Lichti (2018)
	VS, ammonia nitrogen, and process parameters	Up to 0.98	Accurate estimation of key fermentation parameters	Krapf et al. (2012)
	In-situ process monitoring of glucose fermentation	0.95–0.98	Real-time tracking of glucose and lactic acid	Qu et al. (2022)
MIR	Acetic acid, propionic acid, volatile fatty acids in AD	>0.9	Functional group-specific, high precision	Falk et al. (2015)
	Total volatile fatty acids and ammonium estimation	>0.9	Improved accuracy with advanced models	Eccleston et al. (2016)
	Preprocessing with DOP for ammonia prediction	-	Significant reduction in prediction errors	Li et al. (2022)
NMR	Molecular insights, structural analysis	-	Detailed molecular-level information	Fayolle et al. (1997); Fernández-Domínguez et al. (2022)

more cost-effective and sustainable (Oruganti et al., 2023; Vinitha et al., 2023).

In algae-based systems, Bayesian regularization-based artificial neural networks (ANN) models have enhanced biomass productivity and lipid content by precisely controlling nutrient supply and CO_2 utilization (Zhang et al., 2021; Gruber et al., 2022). By efficiently utilizing CO_2 emissions and managing nutrient supply, these predictive models boost biomass growth and lipid content, supporting the production of biofuels and other bio-based products (Coşgun et al., 2023; Syed et al., 2024). Similarly, in insect-based biorefineries, ML-driven image analysis and ANN models have been employed to monitor larvae growth, substrate reduction, and lifecycle prediction, ensuring optimized production processes and resource recovery (Proietti et al., 2022; Arshad et al., 2023). By maximizing nutrient recovery and optimizing production, ML contributes to the development of sustainable and efficient insect biorefinery systems (Hansen et al., 2022; Nawoya et al., 2024). These examples underscore the growing impact of ML in making biorefinery operations more efficient, scalable, and adaptable to various feedstocks and processing conditions.

Through these diverse applications, ML demonstrates its ability to optimize processes, enhance resource utilization, and drive the development of smart, integrated biorefineries that align with sustainability and economic goals. A comprehensive summary of these applications, along with their respective ML models, parameters, and outcomes for thermochemical, biochemical, and biological conversion systems, is presented in **Table 7**. The table highlights the broad applicability of ML across pyrolysis, HTC, AD, fermentation, and insect-based systems. Unlike Khan et al. (2023), which focuses solely on thermochemical conversion processes such as pyrolysis and gasification, and Velidandi et al. (2023), which emphasizes biomass characterization and pre-treatment stages, this review provides a unique integrated perspective. It bridges ML applications across thermochemical, biochemical, and hybrid systems, highlighting their synergistic potential to achieve sustainable and economically viable biorefineries, thereby advancing the field toward holistic biorefinery development.

Despite recent advances in applying ML models to biorefinery scenarios, several pressing challenges and opportunities remain. Since ML models are often considered 'black boxes,' they do not inherently incorporate the constraints that biorefinery processes must adhere to. As a result, predictions may not respect the conservation of mass or align with energy transfer principles. These constraints can be integrated into the optimization of a hybrid loss function that jointly considers both the data and the underlying processes, as demonstrated by physics-constrained learning using neural networks (Liu and Wang, 2019). Additionally, the generalizability of developed ML models to accurately predict input scenarios and process conditions that differ significantly from those used in training remains underexplored, which limits the potential benefits of these computational advancements. Finally, many recently developed ML frameworks, particularly those based on deep learning, require large amounts of data. We foresee that the data demand could be reduced by enriching ML models with physicochemical principles and constraints, opening up new directions for the application of ML in biorefineries.

4.5. Scenario evaluation, optimization, and model networking

MLenables the simulation and evaluation of thousands of potential system configurations, optimizing key metrics such as energy efficiency, carbon sequestration, and economic profitability. For example, residual heat from pyrolysis can be redirected to support fermentation or hydrothermal treatments, while syngas can power energy-intensive processes or generate electricity for internal use (Velvizhi et al., 2022; Ma et al., 2024). By identifying interconnections and synergies between processes, ML helps design biorefineries that achieve maximum resource efficiency.

Emission and carbon management also benefit from ML-driven optimization. For instance, models can propose strategies to incorporate CO_2 emissions into algal cultivation systems, reducing the overall carbon footprint while generating additional biomass (Oruganti et al., 2023; Ma et al., 2024). Similarly, nutrient recovery from processes like AD supports algae or insect production, creating a circular resource flow within the biorefinery (Hansen et al., 2022; Ma et al., 2024). Energy optimization is another key focus; ML ensures processes like pyrolysis achieve positive energy balances by redistributing surplus energy to power-demanding operations or converting it into electricity for external use (Tang et al., 2021; Velvizhi et al., 2022).

4.6. Zero waste, reduced emissions, and self-sufficient energy biorefineries

SIBs aim to achieve zero waste by converting residual streams into valuable by-products. For example, digestate from AD can be processed into fertilizers, while fermentation effluents support algal cultivation. These approaches minimize waste generation and enhance system profitability (Oruganti et al., 2023; Ma et al., 2024). Carbon capture and sequestration through the application of biochar not only offsets emissions but also improves soil health, providing dual environmental benefits (Tang et al., 2021; Zhang et al., 2023). Integrating algal cultivation systems further reduces emissions by utilizing CO_2 and generating additional biomass for bio-based products (Coşgun et al., 2023; Oruganti et al., 2023). Thermochemical processes like pyrolysis and gasification produce syngas and bio-oil, which can be converted into electricity or heat for internal use. The redistribution of residual heat across processes ensures optimal energy utilization, reducing external dependencies and enabling self-sufficient energy production (Shahbeig and Nosrati, 2020; Tang et al., 2021; Ma et al., 2024).

As illustrated in **Figure 5**, ML plays a pivotal role in advancing these improvements by optimizing process integration and resource efficiency. By identifying synergies across systems, ML enables more efficient utilization of residual heat, CO_2, and other by-products, facilitating the

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Table 7.
Machine Learning Applications in Biorefineries: Feedstock-Specific Models and Key Parameters for Pyrolysis, HTC, Fermentation, AD, and Insect-Based Systems.

Process	Feedstock	Specific Model	Input Parameters	Predicted Parameters	Prediction Performance	Parameter Importance	Ref.
Pyrolysis	Agricultural residues	XGBoost	Temperature, residence time, particle size	Char yield, bio-oil quality	$R^2 = 0.91$	Temperature, residence time	Tang et al. (2021)
	Municipal Solid Waste (MSW)	Gradient BoostingGB	Ash content, temperature	Syngas quality, carbon recovery	RMSE = 0.15	Temperature, ash content	Ascher et al. (2022)
	Biomass-coal blend	Gradient Boost Regression (GBR)	Blending ratio, operating temperature, heating rate	Product distribution, pyrolysis oil yield	$R^2 > 0.96$, RMSE < 3.01	Operating temperature, blending ratio, heating rate	Shafizadeh et al. (2024)
	Mixed biomass	RF, SVM	Feedstock type, pyrolysis temperature	Bio-oil yield, energy efficiency	$R^2 = 0.88$	Feedstock type, temperature	Shahbeig and Nosrati, (2020)
	Biomass-polymer waste	Gaussian Process Regression + Particle Swarm Optimization	Biomass-to-polymer ratio, temperature, residence time, heating rate	Pyrolysis oil yield, syngas yield	$R^2 > 0.90$, RMSE < 0.06	Biomass-to-polymer ratio, temperature, heating rate	Shahbeik et al. (2023)
	Sludge	Random Forest Regression (RFR)	Ash content, fixed carbon, volatile matter	Bio-oil yield, syngas yield	$R^2 > 0.81$, RMSE < 12.51	Ash content, fixed carbon	Shahbeik et al. (2022)
HTC	Variable	DTR	Biomass ash/carbon content, operating temperature, reaction time	Hydrochar yield, physicochemical properties	$R^2 > 0.88$	Temperature, biomass carbon/ash content	Shafizadeh et al. (2023)
	Sewage sludge	FNN	Reaction temperature, carbon/nitrogen content, volatiles	Hydrochar nitrogen content	$R^2 > 87.5\%$	Feedstock nitrogen content	Djandja et al. (2021)
	Mixed biomass	RF	Temperature, reaction time	Hydrochar yield, carbon content	$R^2 = 0.92$	Temperature, reaction time	Liu et al. (2024)
	Organic wastes	RF	Carbon content, solids concentration, reaction time	Hydrochar yield, recoverable energy	$R^2 > 0.85$	Feedstock carbon content, solids concentration	L. Li et al. (2020)
Fermentation	Bioethanol from biomass	ANN	Biomass type, enzymatic hydrolysis conditions	Bioethanol yield, process efficiency	$R^2 = 0.92$	Substrate concentration, temperature	Vinitha et al. (2023)
	Hydrogen from dark fermentation	GB	Organic loading rate, retention time, substrate concentration	Hydrogen yield	$R^2 = 0.89$	Organic loading rate, substrate concentration	Pandey et al. 2023)
	Industrial fermentation	Image processing with ML	Real-time image data, microbial density	Fermentation endpoint, microbial activity	RMSE = 0.12	Microbial density, reactor conditions	Khaleghi et al. (2021)
AD	Hydrothermally pretreated waste-activated sludge	RF, XGBoost, ANN, SVM, K-Nearest Neighbors	Feedstock characteristics, pretreatment parameters (Temp., HRT, MY)	Methane yield, sludge solubilization	$R^2 > 0.87$ (solubilization), $R^2 > 0.70$ (methane yield)	Pretreatment parameters dominate: temperature, heating time, and holding time	Fard and Koupaie (2024)
	Lignocellulosic Biomass and Cow Manure	RF, XGBoost, Kernel Ridge Regression	C, N, C/N ratio, cellulose, hemicellulose, lignin, operating conditions: biomass-manure ratio, OLR, particle size, reactor volume, HRT, Temp., VS, pH	Methane yield, biomass-to-manure optimization	Highest accuracy for RF: $R^2 = 0.85$	Most influential: cellulose, lignin content	Sonwai et al. (2023)
	Co-digestion of manure & residues	RF	Feedstock properties, operational parameters	Biogas yield, methane yield	$R^2 = 0.82–0.99$	Pretreatment time, feedstock lignin	Kovačić et al. (2024)
	Wood waste	SVM, ANN, RF	Wood type, inoculum type, digestion time	Methane yield	$R^2 = 0.96$	Digestion time, particle size	Gao et al. (2024)
	Organic waste	Elastic Net, XGBoost	Input waste composition	Methane production	$R^2 \leq 0.88$	Biowaste input interaction effects	De Clercq et al. (2020)
Insect systems	Kitchen waste	ANN	Larval quantity, waste composition, aeration frequency	Insect growth, substrate reduction	Accuracy = 99.5%	Substrate reduction, larval density	Arshad et al. (2023)
	Mixture of organic waste	Image Analysis	Real-time monitoring	Lifecycle prediction	Accuracy = 61–68%	Waste composition, lifecycle stage	Proietti et al. (2022)
Algae	Algal biomass (42 types of microalgae)	GBR and RF	Operating conditions of hydrothermal liquefaction	Bio-oil yield, O and N	train $R^2 > 0.90$, test $R^2 > 0.85$	Product recovery	Zhang et al. (2021)
	Algal biomass (*Chlorella vulgaris)*	Bayesian regularization (BR)-ANN algorithm	Ratio of feedstock to suspension, combined severity factor from operational parameters such as temperature, time, and pH	Solid, liquid, and gaseous products	R^2 between 0.989 and 0.999	Hydrogen production from HTC, catalyzed by formic acid	Gruber et al. (2022)

transition of biorefineries into sustainable, zero-waste, and energy self-sufficient systems that align with SCBS goals.

4.7. Scalability of technologies within smart integrated biorefineries

The readiness level of bio-based products varies significantly, with some technologies nearing commercial viability while others remain in the early stages of development. HTC has reached a Technology Readiness Level (TRL) of 7–8 (Farru et al., 2024), while its alkaline-modified variants, HTH and HTF (Ischia et al., 2024), are still at TRL 5–6 and require further pilot demonstrations. Similarly, pyrolysis has reached TRL 7–8, but catalytic upgrading remains at TRL 5–6, limiting its scalability (Beims et al., 2019). AD technologies exhibit variability, with micro-aeration AD and anaerobic membrane bioreactors (AnMBR) at TRL 7, while microbial electrolysis

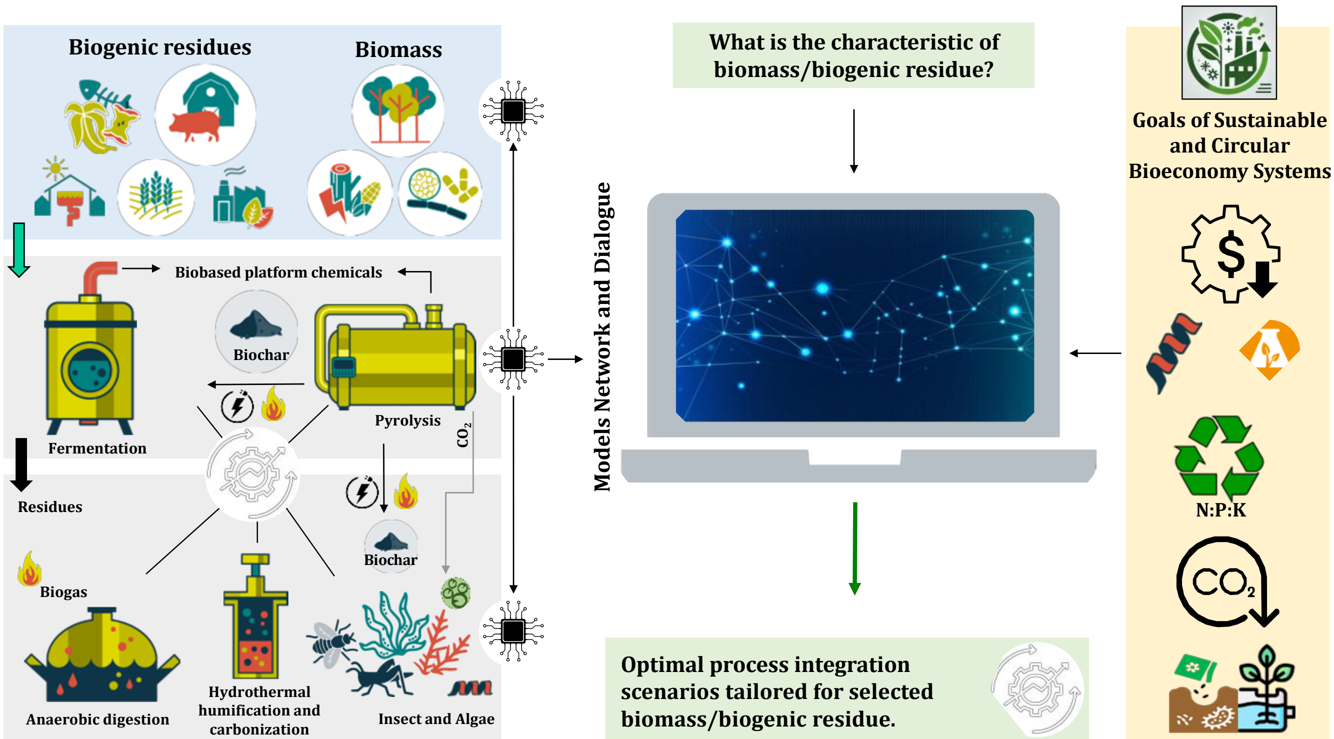

Fig. 5. ML-enabled optimization of biorefineries, showcasing process integration for zero-waste strategies, carbon reduction, and energy self-sufficiency in line with the goals of sustainable and circular bioeconomy systems (SCBS).

cell-AD (MEC-AD) and hydrogen-enhanced processes remain at TRL 5, requiring additional validation (A. Elsayed et al., 2024). Despite their commercial availability, biomethane and syngas production still face scalability challenges when compared to large-scale fossil fuel alternatives (Lanjekar and Panwar, 2024).

Lignocellulosic bio-based chemicals largely remain below TRL 8, requiring further process optimization, cost reduction, and market alignment for broader adoption (Rosales-Calderon and Arantes, 2019). Similarly, the European Commission's report *From the Sugar Platform to Biofuels and Biochemicals (2015)* highlights that many bio-based products are still below TRL 5, requiring advancements in efficiency and cost reduction. Microalgal biorefineries currently operate at TRL 5–6, with projects progressing toward commercial feasibility, but they remain constrained by policy and investment limitations (Behera et al., 2022). Insect bioconversion technologies generally range from TRL 5 to 6, where insect farming, distribution, processing, and the production of food and feed have been demonstrated and piloted (Veldkamp et al., 2022). However, different insect-based processes show varying TRLs due to the diversity and complexity of the technologies involved (Smetana et al., 2016). For example, conventional protein extraction from insects has reached TRL 8–9, but challenges remain with the incorporation and functionalization of proteins, while the implementation of emerging food processing technologies could lower the TRL of the resulting protein ingredients (Corona-Mariscal et al., 2024).

Digitalization plays a crucial role in overcoming scalability barriers by integrating AI-driven process optimization, predictive analytics, and IoT-based monitoring systems, thereby reducing costs and energy consumption during industrial scale-up. AI, ML, and automation facilitate process optimization from the lab to industrial applications, while techniques such as retrosynthetic approaches, text mining, and active learning enhance discovery and process simulation. Automated multiscale computation improves efficiency by generating data without human intervention (Batchu et al., 2022), and real-time monitoring through spectroscopy and IoT connectivity ensures adaptive optimization for scalable, sustainable biorefineries. Scaling biorefinery processes from laboratory to commercial applications remains complex and resource-intensive, particularly in lignocellulosic biomass conversion. Traditionally, researchers relied on experimental design methodologies to optimize catalysts, solvents, and adsorbents, which is both time-consuming and costly (Loy et al., 2023). However, AI, ML, and metaverse-based modeling accelerate this transition by improving process optimization and increasing Technology Readiness Levels (TRLs). The integration of big data analysis for literature screening and high-throughput experimental validation speeds up the shift from bench-scale research to industrial implementation, reducing energy and cost barriers while improving scalability (Loy et al., 2023).

One of the primary goals of SIBs is to provide scalable and economically viable technologies that integrate multiple bio-based conversion processes. By leveraging automation, process integration, and AI-driven decision-making, SIBs have the potential to enhance industrial scalability and accelerate commercialization. Additional key criteria supporting scalability, including techno-economic assessments and sustainability considerations, will be discussed in *Section 4.8*.

4.8. Meeting economic, policy, and environmental requirements for biorefineries

4.8.1. Smart biorefineries: reducing costs and emissions

SIBs supported by advancements in digitalization, artificial intelligence (AI), and ML, hold the potential to significantly enhance the economic viability and environmental sustainability of biorefinery systems. Advanced process optimization, including predictive modeling and real-time data analysis, enables more efficient resource use, reduced emissions, and the optimized diversification of high-value products such as biofuels, biochemicals, and bioplastics (Arias et al., 2023; Culaba et al., 2023). This approach can also contribute to waste reduction and add higher value within value chains and networks (Allee, 2008). By focusing on waste and residues as feedstocks, SIBs ensure that biorefineries do not compete with food and

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feed markets, thus contributing to global sustainability goals (Subhadra and Grinson-George, 2011; Venkata Mohan et al., 2019). For example, integrating biochar from pyrolysis into AD has demonstrated improvements in biogas yields, while CO_2 produced during fermentation processes is increasingly being utilized for algae cultivation, creating efficient resource cycles (Dragone et al., 2020; Chávez et al., 2024). However, economic challenges, including high capital costs and slow returns on investment, require targeted governmental support to bridge the gap between innovation and profitability (Martins et al., 2022; Schaper et al., 2025).

4.8.2. The economic rationale for biorefinery investments

The economic risks associated with climate change far exceed the mitigation costs required to combat its effects. By 2048, global GDP is projected to decline by approximately 19% due to climate-related damages, with losses exacerbated in regions already facing income inequality (Kotz et al., 2024). Moreover, the increasing scarcity and potential depletion of fossil and biogenic raw materials are becoming more likely—and, in some cases, already evident—while pressure on natural resources continues to rise, sometimes exceeding sustainable limits (Rockström et al., 2024). Investing in biorefineries presents a strategic solution to mitigate these losses, as these systems not only reduce dependency on fossil-based products but also have the potential to sequester carbon, generate renewable energy, and enhance waste valorization (Venkata Mohan et al., 2019; Culaba et al., 2023). Financial support for biorefinery innovations, such as the development of carbon-neutral processes and CBE frameworks, offers long-term savings by preventing catastrophic environmental and economic outcomes (Subhadra and Grinson-George, 2011; Dragone et al., 2020). These efforts align with global policies aimed at meeting net-zero emissions targets and ensuring a sustainable economic future.

A comparative cost-benefit analysis further illustrates the economic viability of SIBs over traditional non-integrated systems. The case of lactic acid production exemplifies how process optimization, waste valorization, and carbon integration significantly enhance efficiency and financial returns. Lactic acid production from lignocellulosic residues has been extensively explored, with reported values covering a wide range of biomass types (Patel et al., 2025). Shifting to waste biomass, rather than relying on dedicated feedstocks, increases the production of value-added products, thereby enhancing economic resilience. This flexibility is a key advantage of SIBs, as they can efficiently adapt to a wide range of input materials, maximizing resource utilization and sustainability. While SIBs typically have higher initial costs than traditional single-process systems, long-term operational savings and environmental benefits justify the investment. Automation and predictive modeling help lower costs by optimizing processes and reducing the need for extensive feasibility testing. For example, in lactic acid production, integrating pyrolysis, AD, HTH, and CO_2 capture not only reduces costs but also creates multiple revenue streams, making smart biorefineries financially viable.

The economic impact of SIBs is evident in increased revenue from waste valorization, higher profitability, and improved financial stability compared to traditional systems. Multiple waste utilization strategies significantly reduce operational costs while generating revenue. Biochar enhances fermentation efficiency, reducing enzyme and chemical costs, while CO_2 from pyrolysis supports algae-based biofuel and nutraceutical production. Solid fermentation residues are repurposed for insect-based protein, lowering feed costs. The remaining wet residues undergo AD and HTH, producing biogas for energy and biofertilizers while also sequestering carbon. These processes lower net production costs and increase financial returns. Although SIBs require higher initial investment, their return on investment (ROI) is accelerated by reduced operational expenses, diversified revenue streams, and lower environmental compliance costs, ensuring long-term profitability and sustainability in lactic acid production. **Table 8** presents a comparative cost-benefit analysis of traditional systems (Patel et al., 2025) and SIBs for lactic acid production.

The economic future of SIBs hinge on their ability to efficiently convert biomass and biogenic residues into high-value products while maintaining high adaptability to regional, seasonal, and feedstock variability. This flexibility promotes a circular economy and minimizes environmental impact. Advancements in multi-process integration, including thermochemical, biochemical, and microbial conversion methods, enhance resource efficiency, reduce costs, and improve product yields (Velvizhi et al., 2022). The valorization of waste through integrated biorefineries offers significant economic opportunities, enabling the recovery of biofuels, platform chemicals, and biomaterials while addressing the challenges of waste disposal (Kumar et al., 2024). However, the large-scale deployment of integrated biorefineries requires overcoming key economic bottlenecks, such as ensuring a consistent biomass supply, developing cost-effective conversion technologies, and integrating new processing infrastructures into existing industrial frameworks (Maity, 2015).

By adopting SCBS principles and optimizing system efficiency, smart integrated biorefineries can enhance profitability, reduce dependence on fossil fuels, and contribute to the long-term economic sustainability of the bioeconomy sector. Furthermore, their high adaptability to regional demand variations, economic constraints, and policy frameworks ensures that biorefineries can dynamically adjust feedstock sourcing, production outputs, and market strategies to remain financially viable and environmentally responsible. This flexibility positions smart integrated biorefineries as a key driver in the transition toward a resilient, low-carbon economy, aligning with global efforts to promote resource efficiency and energy independence.

Table 8.
Comparative cost-benefit analysis of traditional vs. smart SIBs for lactic acid production.

Parameter	**Traditional (Decentralized) Biorefineries** (Patel et al., 2025)	**Smart Integrated Biorefineries (SIBs)**
Capital expenditure	USD93.1M - USD186M	Increase (higher initial costs due to multi-process optimization, but lower long-term expenses through energy and resource efficiency)
Operational expenditure	USD6.84M -USD27.6M/year	Decrease (significantly lower due to waste valorization, energy self-sufficiency, and process automation)
Product yield efficiency	50-75%	Increase (higher efficiency due to optimized processes and multi-feedstock utilization)
Electricity & heat demand	High	Decrease (substantially reduced by integrating pyrolysis, biochar application, and self-sustaining energy systems)
CO_2 emissions (kg CO_2/tonne)	800-1400 kg CO_2/tonne	Decrease (much lower due to CO_2 capture for algae cultivation and circular carbon integration)
Flexibility & market adaptability	Limited	Increase (high adaptability through multi-product streams and resource optimization)
Economic return period	7.6 - 15 years	Decrease (much faster due to diversified revenue streams and operational cost reductions)
Waste generation	High (30-40% of biomass lost as waste)	Decrease (near-zero waste through full valorization, including biochar use, HTH, AD, and insect protein production)
Return on investment (ROI)	13.1% (based on literature for standalone lactic acid production)	Increase (significantly higher due to lower operational costs, diversified revenue streams, and faster payback periods)

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4.8.3. Policy and government support

Governmental policies and subsidies are essential to accelerating the development and deployment of smart biorefineries. For example, implementing CO_2-equivalent taxes on emission-intensive goods has proven effective in reducing GHG emissions while generating revenue for reinvestment in renewable technologies (Schaper et al., 2025). Such taxes can support the development of infrastructure for biorefineries, enabling their scalability and financial viability. Policies that prioritize carbon sequestration initiatives, incentivize public-private partnerships, and establish regulations for sustainable waste management are crucial for achieving a CBE. Public investment in capacity development, training, and education is also key to supporting biorefinery business development (Ding and Grundmann, 2022). These measures not only address environmental and economic challenges but also foster innovation and market competitiveness in the biorefinery sector (Martins et al., 2022; Culaba et al., 2023). By leveraging optimized and smart biorefineries, policymakers can strategically identify and invest in areas based on biogenic and biomass types and content, thereby fostering job creation and supporting regional economic development.

5. Conclusions

The concept of smart integrated biorefineries, introduced in this review, presents a promising approach powered by ML, digital twins, and decision-support systems to optimize biomass conversion while minimizing waste, emissions, and inefficiencies. This review emphasizes the integration of thermochemical, biochemical, and biological technologies—such as pyrolysis, fermentation, anaerobic digestion, and hydrothermal carbonization—within a sustainable and circular bioeconomy framework. Additionally, HTH and HTF show significant potential in enhancing nutrient recycling and carbon sequestration, further advancing near-zero waste strategies and integrating effectively within biorefinery systems. Biochar plays a multifunctional role by enhancing fermentation, stabilizing anaerobic digestion, and acting as a slow-release fertilizer. Although pyrolysis technology has limitations, it remains central to integrated biorefinery systems and requires further evaluation. The integration of renewable energy sources, such as solar power, and AI-driven optimization will enhance the adaptability of smart integrated biorefineries, supporting the transition to a zero-waste, low-emission, and energy-autonomous bioeconomy while aligning with and adapting to the dynamic needs and goals of planetary boundaries.

Future research should focus on optimizing biorefineries for diverse biogenic residues and biomass types while developing interconnected models to simulate conversion processes, identify synergies, and improve scalability. Additionally, comparing biorefinery systems from both economic and environmental perspectives—whether in conventional, standalone, or smart integrated setups—should be a key research priority. Addressing challenges such as varying technology readiness levels and data limitations will strengthen the sustainability, circularity, and feasibility of the bioeconomy, providing a scalable model for future bioprocessing advancements.

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Please cite this article as: Marzban N., Psarianos M., Herrmann C., Schulz-Nielsen L., Olszewska-Widdrat A., Arefi A., Pecenka R., Grundmann P., Schlüter O.K., Hoffmann T., Rotter V.S., Nikoloski Z., Sturm B. Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production. Biofuel Research Journal 45 (2025) 2319-2349. DOI: 10.18331/BRJ2025.12.1.4.

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Please cite this article as: Marzban N., Psarianos M., Herrmann C., Schulz-Nielsen L., Olszewska-Widdrat A., Arefi A., Pecenka R., Grundmann P., Schlüter O.K., Hoffmann T., Rotter V.S., Nikoloski Z., Sturm B. Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production. Biofuel Research Journal 45 (2025) 2319-2349. DOI: 10.18331/BRJ2025.12.1.4.

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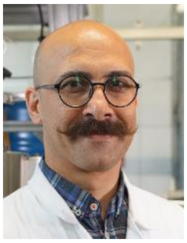

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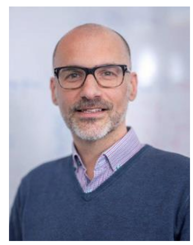

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Please cite this article as: Marzban N., Psarianos M., Herrmann C., Schulz-Nielsen L., Olszewska-Widdrat A., Arefi A., Pecenka R., Grundmann P., Schlüter O.K., Hoffmann T., Rotter V.S., Nikoloski Z., Sturm B. Smart integrated biorefineries in bioeconomy: A concept toward zero-waste, emission reduction, and self-sufficient energy production. Biofuel Research Journal 45 (2025) 2319-2349. DOI: 10.18331/BRJ2025.12.1.4.