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Acetate: A New Feedstock for Biomanufacturing

The Emergence of Acetate as a Sustainable Carbon Source

The transition towards a sustainable, bio-based economy is fundamentally dependent on the availability of low-cost, renewable feedstocks that can replace fossil fuel-derived precursors. In this context, acetate has emerged as a particularly promising candidate for biomanufacturing applications [2]. Its appeal stems from its versatile and increasingly cost-effective production pathways, which position it as a key molecule at the nexus of waste valorization, renewable energy conversion, and advanced chemical synthesis. Industrial acetate is conventionally produced via methanol carbonylation, a well-established petrochemical process [41]. However, the global acetic acid market is not solely reliant on this route; it was 16.3 million tons in 2020 and is projected to grow to 19.6 million tons by 2027, driven by diverse downstream applications [41]. This existing industrial scale provides a robust foundation for its use as a commodity chemical. More importantly, novel and environmentally friendly production methods are expanding the supply chain. Acetogens—anaerobic bacteria such as Clostridium ljungdahlii, Clostridium autoethanogenum, and Acetobacterium woodii—can convert syngas (a mixture of carbon monoxide, CO_2, and H_2) into acetate with high efficiency, offering a pathway to valorize industrial off-gases and biomass-derived synthesis gas [5 16 31]. These organisms utilize the highly efficient Wood-Ljungdahl pathway (WLP) for CO_2 fixation, making them central players in gas fermentation technology [16]. Companies like LanzaTech and SEKAB are pioneering the commercial-scale deployment of these systems [41].

Beyond gas fermentation, acetate can be generated through microbial electrosynthesis, where microorganisms use electrical current to reduce CO_2 into organic acids, including acetate [4]. Furthermore, lignocellulosic biomass, a major component of agricultural and forestry waste, contains acetyl groups that are released as acetic acid during pretreatment processes [2 5]. This makes waste streams from the pulp and paper industry or cellulosic ethanol production potential sources of acetate. The convergence of these production routes—from both legacy petrochemical processes and emerging green technologies—creates a resilient and scalable supply chain for acetate. Economically, acetate is already competitive; its market price ranges from approximately USD 350 − 450 per ton, which is slightly cheaper than glucose, currently priced around USD 500 per ton [13]. This economic parity, combined with its liquid state which simplifies handling and feeding in bioreactors, gives acetate a distinct operational advantage over solid sugars.

However, the path to widespread adoption is not without challenges. The complexity of acetate's role in cellular metabolism presents a significant hurdle. For decades, acetate in microbial fermentations, particularly in Escherichia coli, was viewed primarily as an unwanted metabolic byproduct resulting from "overflow metabolism" when cells are grown on rapidly metabolized carbon sources like glucose under aerobic conditions [11 23]. This perspective has created a deeply ingrained bias against acetate in many industrial processes. Overcoming this requires a paradigm shift, recognizing acetate

not as a waste stream to be minimized but as a valuable co-substrate to be actively consumed. This necessitates a more nuanced understanding of its dual nature: while it can be toxic at high concentrations, it also serves as a potent source of acetyl-CoA and can enhance growth under specific physiological conditions [28 41]. Addressing the technical and biological bottlenecks associated with acetate assimilation, transport, and tolerance will be critical to unlocking its full potential as a dedicated feedstock for a new generation of bioprocesses. The successful integration of acetate into biomanufacturing workflows depends on moving beyond its historical stigma and capitalizing on the technological advancements that enable its efficient and controlled utilization.

Metabolic Pathways for Acetate Assimilation Across Microbial Platforms

The ability of a microorganism to utilize acetate as a sole carbon source is governed by a suite of conserved metabolic pathways, though their presence and organization vary significantly across different phylogenetic groups. Understanding these differences is fundamental to selecting and engineering appropriate host organisms for acetate-based bioproduction. The core challenge for any organism is to convert the two-carbon acetate into the three-carbon compound acetyl-CoA, which can then enter central metabolism. This conversion represents a critical metabolic checkpoint with profound implications for cellular energetics and regulation.

In the vast majority of bacteria and archaea, including the extensively studied model organism Escherichia coli, this conversion is catalyzed by one of two distinct enzymatic systems [4 13]. The first is a reversible pathway involving two enzymes: phosphotransacetylase (Pta), which transfers a phosphoryl group from acetyl phosphate (Ac∼P) to CoA, and acetate kinase (AckA), which generates ATP from ADP [11 19]. This Pta-AckA pathway is responsible for acetate excretion during overflow metabolism in rapidly growing cells and can be operated in reverse for scavenging acetate when other carbon sources are depleted [7 11]. The second system is an irreversible reaction catalyzed by acetyl-CoA synthetase (Acs), which activates acetate to acetyl-CoA at the expense of an ATP molecule [11 13]. The choice between these pathways is tightly regulated. In E. coli, Acs activity dominates at low extracellular acetate concentrations (below ~3.5 mM), whereas the Pta-AckA pathway becomes more prominent at higher concentrations [4 30]. This regulatory switch is a cornerstone of the "acetate switch," a phenomenon central to bacterial physiology [11].

For growth on acetate as the primary carbon source, however, a third, essential pathway is required: the glyoxylate shunt [4 13]. This bypasses two decarboxylation steps of the tricarboxylic acid (TCA) cycle, allowing the net assimilation of acetyl-CoA units to form gluconeogenic precursors like succinate and malate. The genes encoding the key shunt enzymes, isocitrate lyase (AceA) and malate synthase (GlcB), are organized in the aceBAK operon and are regulated by the transcriptional repressor IclR [4]. Consequently, strains lacking functional versions of AceA or IclR cannot grow on acetate as a sole carbon source. This dependency on the glyoxylate shunt is a common vulnerability exploited in metabolic engineering to create acetate auxotrophs for synthetic consortia [14].

In stark contrast to this diversity in heterotrophic bacteria, autotrophic acetogens utilize a single, highly evolved pathway for all aspects of their metabolism: the Wood-Ljungdahl pathway (WLP) [3 31]. The WLP is considered one of the most primitive and energetically efficient natural pathways for CO_2 fixation, converting CO_2 and CO into acetyl-CoA [3 24]. This same pathway allows acetogens to assimilate externally supplied acetate. The versatility of the WLP is remarkable, enabling organisms like Moorella thermoacetica and Acetobacterium woodii to grow on a wide range of substrates, including C1 gases (CO, CO_2, H_2), sugars, alcohols, and organic acids [16 31]. The pathway culminates in the formation of acetyl-CoA, which can then be used for biosynthesis or converted to acetate for export, a process coupled to the generation of a sodium or proton motive force for ATP synthesis [31]. This central role makes the WLP a prime target for engineering in acetogens to redirect carbon flux towards the production of value-added chemicals and fuels [16].

The evolutionary divergence in acetate assimilation strategies highlights the strategic importance of choosing the right microbial chassis. While engineered E. coli offers immense genetic tractability and a wealth of characterization tools, it must contend with complex regulatory networks and inherent toxicity [4 11]. Acetogens, conversely, have a streamlined metabolism optimized for acetate utilization, but historically suffer from poor genetic manipulation and oxygen sensitivity [16 40]. Recent breakthroughs in genome editing for acetogens are beginning to close this gap, potentially unlocking their full potential as robust, self-sufficient platforms for acetate valorization [5 16].

Feature	Escherichia coli (Heterotroph)	Acetogens (Clostridium, Acetobacterium)
Primary Acetate Activation	Two parallel pathways: reversible Pta-AckA and irreversible Acs [4 13]	Single pathway: Wood-Ljungdahl Pathway (WLP) [3 31]
Key Assimilation Pathway	Glyoxylate Shunt (via AceA/IclR regulation) [4]	Direct entry of acetyl-CoA from WLP into central metabolism [31]
Regulatory Complexity	High; involves cAMP-CRP, RpoS, OmpR, PhoB regulons; global protein acetylation [19 35 43]	Lower complexity; less characterized regulation, often linked to growth rate and redox state [40]
Energy Conservation Mechanism	Chemiosmotic gradient (H+ or Na+) via respiratory chains	Chemiosmotic gradient (Na+ or H+) generated directly by the WLP complex [31]
Feedstock Range	Primarily sugars and organic acids [4]	Broad range including C1 gases (CO, CO_2, H_2), sugars, alcohols, organic acids [16 31]

Physiological Effects and Toxicity of Acetate in Microbial Hosts

While acetate presents a compelling opportunity as a carbon feedstock, its utility is critically constrained by its inherent physiological effects and toxicity to microbial hosts. The mechanisms of this toxicity are multifaceted, stemming from its weak acid nature, its interference with central metabolism, and its role as a global regulator of cellular processes. A comprehensive understanding of these effects is paramount for designing robust bioprocesses and engineering tolerant strains. The most widely accepted primary mechanism of acetate-induced growth inhibition is cytoplasmic acidification and anion imbalance [35 41]. As a weak acid with a pKa of 4.75, acetate exists in equilibrium between its dissociated form (the inhibitory acetate anion, CH_3COO^-) and its undissociated form (acetic acid) [41]. The undissociated acid can readily diffuse across the lipid bilayer of the cell membrane down its concentration gradient. Once inside the relatively neutral cytoplasm (pH ~7.4-7.6), the acid dissociates, releasing a proton (H^+) and the acetate anion, leading to a localized drop in internal pH and a massive influx of negatively charged ions [11 41]. This disrupts delicate pH homeostasis, impairs enzyme function, and creates a significant osmotic and ionic stress that the cell must expend considerable energy to counteract.

In addition to this classical acidosis, acetate has been shown to act as a non-classical uncoupling agent, dissipating the electrochemical proton gradient across the membrane, which is essential for ATP synthesis via oxidative phosphorylation [7 11]. Studies in E. coli have quantified the contribution of the Pta-AckA pathway to this effect, finding that the accumulation of acetyl-phosphate (Ac~P), an intermediate of this pathway, accounts for approximately 20% of the total growth-inhibitory effect of acetate [7 35]. This suggests that Ac~P is not merely a metabolic intermediate but also a signaling molecule that contributes to toxicity. This toxicity is amplified by the fact that Ac~P is a potent acetyl donor, leading to the global hyper-acetylation of proteins, particularly lysine residues [27 35]. This post-translational modification can alter the function, stability, and localization of numerous proteins, including key enzymes in glycolysis and the TCA cycle, further disrupting metabolism [19 27].

The impact of acetate toxicity varies significantly among different microbial species and even between strains of the same species. For instance, E. coli typically experiences severe growth impairment above 5 g/L (approximately 85 mM) acetate [4 13]. Specific strain tolerances differ, with some engineered strains showing improved performance, such as E. coli W, which can tolerate up to 166.5 mM acetate with the help of yeast extract [4]. In contrast, Komagataella phaffii (formerly Pichia pastoris) is inhibited by acetate concentrations above just 40 mM [21]. Yeasts generally exhibit lower tolerance compared to bacteria. In Saccharomyces cerevisiae, programmed cell death (PCD) is triggered by acetic acid at concentrations between 20 and 120 mM, involving mitochondrial-dependent apoptosis [42]. Other yeasts show similar vulnerabilities; Rhodococcus sp. BH4 grows preferentially on sodium acetate, indicating a reliance on acetyl-CoA synthetase for uptake, while the microalga Chlorella sorokiniana demonstrates high tolerance up to 30 g/L [41].

Interestingly, recent research reveals a more complex and context-dependent relationship between acetate and cell growth. Under certain conditions, acetate can be beneficial rather than purely inhibitory. When glycolytic flux is low, such as during nutrient limitation, acetate can serve as a co-

substrate that enhances bacterial growth and buffers carbon uptake [28]. In these scenarios, the Pta-AckA pathway mediates a beneficial effect, boosting growth on various substrates. This duality underscores that acetate's effect is not absolute but is dictated by the cell's overall metabolic state. This insight opens up new avenues for bioprocess design, suggesting that carefully controlling the availability of primary carbon sources could allow for periods of acetate consumption that benefit productivity. The table below summarizes reported tolerance levels for various microbes, highlighting the significant variation and the need for tailored engineering solutions.

Microorganism	Maximum Tolerable Acetate Concentration	Notes	Citations
Escherichia coli	>5 g/L (~85 mM)	Growth severely impaired; strain-dependent tolerance varies.	4 13
E. coli W	~166.5 mM	Tolerance improved with yeast extract supplementation.	4
E. coli BL21(DE3)	~0.36 g/L	Strain-specific baseline toxicity.	4
Komagataella phaffii (Yeast)	<40 mM	Exhibits strong growth inhibition and programmed cell death.	21 42
Saccharomyces cerevisiae (Yeast)	Not explicitly stated, but sensitive	Programmed cell death occurs between 20-120 mM.	21 42
Rhodococcus sp. BH4	Preferential utilization of acetate	Relies on acetyl-CoA synthetase (acs) for uptake.	41
Chlorella sorokiniana (Microalgae)	Up to 30 g/L	Demonstrates high tolerance and potential for lipid production.	41
Clostridium sp. AWRP	~5-10 g/L	Adaptive laboratory evolution increased tolerance to 10 g/L.	20

Engineering Strategies for Enhanced Acetate Utilization and Productivity

The successful implementation of acetate as a routine feedstock in biomanufacturing hinges on sophisticated metabolic engineering strategies designed to overcome its inherent toxicity and redirect carbon flux towards desired products. These strategies span from targeted gene deletions and pathway overexpression to the application of advanced synthetic biology tools for precise, dynamic control of cellular functions. The overarching goal is to create microbial cell factories that can efficiently consume acetate while simultaneously channeling metabolic precursors into high-value product pathways.

One of the foundational approaches involves manipulating the acetate node itself—the set of enzymes responsible for activating acetate to acetyl-CoA. To minimize the negative feedback and toxicity associated with overflow metabolism, engineers have focused on eliminating or modulating

the Pta-AckA pathway. Deletion of the pta and ackA genes in E. coli effectively prevents the organism from excreting acetate, thereby avoiding the associated energetic costs and toxic effects of acetyl-phosphate accumulation [23,27]. This strategy has proven effective in reducing acetate titers in industrial producers of 2'-fucosyllactose and fumarate [23]. Another approach is to enhance the expression of acetyl-CoA synthetase (Acs), the irreversible pathway for acetate assimilation, ensuring that any incoming acetate is immediately funneled into central metabolism rather than being stored as acetyl-phosphate [4]. Beyond the acetate activation step, engineering the central carbon metabolism is crucial. For growth on acetate, the glyoxylate shunt is indispensable, so its enhancement via the deletion of its repressor, iclR, is a common tactic [23]. Similarly, for producing acetyl-CoA-derived products like mevalonate or polyhydroxyalkanoates (PHA), enhancing the flux of carbon from acetyl-CoA is key. This can be achieved by overexpressing citrate synthase (gltA) to increase TCA cycle flux or by deleting competing pathways, such as lactate dehydrogenase (ldhA) [10,23].

The advent of powerful synthetic biology tools has revolutionized the ability to fine-tune these metabolic pathways. CRISPR-based technologies, originally developed for genome editing, have been adapted for precise transcriptional regulation. CRISPR interference (CRISPRi) uses a catalytically dead Cas9 (dCas9) protein to block transcription by physically obstructing RNA polymerase, allowing for the downregulation of target genes without permanent DNA changes [8,9]. Conversely, CRISPR activation (CRISPRa) uses dCas9 fused to an activator domain to enhance gene expression [8]. These tools have been successfully applied in acetogens like Clostridium ljungdahlii to reprogram metabolic flux and improve production titers [16]. For example, CRISPRa has been shown to increase reporter gene expression 2.8-fold in E. coli, demonstrating its power for optimizing metabolic pathways [8]. These regulatory tools are not just for silencing or boosting single genes; they enable the construction of complex gene circuits, such as logic gates, allowing for sophisticated, multi-input control over entire metabolic networks [8].

These engineering principles are being applied across a diverse range of microbial hosts. In acetogens, the focus is on rewiring the Wood-Ljungdahl pathway and integrating heterologous pathways for producing longer-chain products like butanol [16]. In E. coli, the extensive toolbox of genetic parts and techniques is leveraged to balance acetate assimilation with product formation, as seen in the nitrogen-starvation process for isopropanol production [12]. Yeasts present unique challenges and opportunities. In the methylotrophic yeast Ogataea polymorpha, native promoters and terminators are being used for tunable expression of pathways for fatty acid and terpenoid production from acetate [17]. In Saccharomyces cerevisiae, engineered strains have demonstrated enhanced free fatty acid production by redirecting carbon flow toward acetyl-CoA generation [33]. In non-conventional yeasts like Issatchenkia orientalis (Candida krusei), which shows high tolerance to acetate, metabolic models have guided the production of succinic acid and ethanol from glucose and acetate co-substrates [15]. The development of genome-scale metabolic models (GEMs) for these organisms, such as iMK735 for S. cerevisiae and iIsor850 for I. orientalis, provides a rational framework for identifying metabolic bottlenecks and guiding engineering decisions [15]. The synergy between these modeling efforts and experimental validation using tools like proteomics and metabolomics is accelerating the pace of discovery and optimization in acetate-based biomanufacturing.

Comparative Analysis of Acetate-Based Bioproduction in Bacteria and Yeasts

The utilization of acetate as a feedstock for bioproduction spans a wide array of microbial hosts, each with distinct metabolic architectures, genetic toolkits, and physiological characteristics. A comparative analysis of acetate upgrading in bacteria, particularly Escherichia coli, and yeasts, including both conventional and non-conventional species, reveals fundamental trade-offs between genetic tractability, metabolic robustness, and final product portfolio. This comparison is crucial for selecting the optimal platform for a given bioprocess.

Escherichia coli stands as a paragon of genetic engineering, offering a vast arsenal of well-characterized tools, including the Keio collection of knockout strains, standardized promoter libraries, and refined CRISPR-based editing systems [8 9 19]. This deep level of characterization enables rational, multi-target metabolic engineering. For instance, researchers can systematically modify dozens of genes involved in central metabolism to optimize flux towards a desired product, as demonstrated in the five-fold increase in lycopene production through MAGE-mediated modifications of 24 genes [9]. This precision is invaluable for tackling the complex regulatory network surrounding acetate metabolism. However, this genetic sophistication comes with a physiological cost. E. coli is notoriously susceptible to acetate toxicity, which arises from its default "overflow metabolism" on preferred carbon sources like glucose [11 23]. Engineering strategies to mitigate this, such as deleting the pta and poxB genes to prevent acetate formation, must be balanced against the need to maintain sufficient metabolic flexibility and energy generation [23]. The table below showcases a selection of products synthesized from acetate in engineered E. coli strains, illustrating the breadth of possibilities.

Product	Strain/Platform	Titer	Yield	Citation
Isopropanol	E. coli W, N-starvation	13.3 g/L	0.262 mol/mol	12
Succinate	E. coli HB03	194 mM	0.50 mol/mol	13
Itaconic Acid	E. coli WY002	0.157 g/L	0.052 g/g	13
Mevalonate	E. coli XU143	1.06 g/L	0.30 g/g	13
β-caryophyllene	E. coli FP06	1.05 g/L	2.1% (conversion)	13
Acetone	E. coli ATCC 11303	~40 mM	~0.29 mol/mol	26
PHB	E. coli	0.25 g/g	-	4 30

In contrast, yeasts offer a different profile. Conventional yeasts like Saccharomyces cerevisiae are workhorses of industrial fermentation but face challenges with acetate utilization. They lack the endogenous glyoxylate shunt, requiring the introduction of foreign pathways for growth on acetate [10]. Non-conventional yeasts, however, are proving to be exceptionally promising platforms. Species like

the oleaginous yeast Yarrowia lipolytica and the extremophilic yeast Issatchenkia orientalis (Candida krusei) possess innate robustness and specialized metabolic traits. I. orientalis exhibits remarkable tolerance to acetate, capable of growth in the presence of 4 g/L acetic acid, and has been engineered to produce high titer succinic acid (109.5 g/L) and ethanol (41.4 g/L) [15]. Y. lipolytica has demonstrated exceptional performance, producing 209.7 g/L succinic acid from crude glycerol, showcasing its capacity for high-density cultivation and product formation [15]. The key advantage of these non-conventional yeasts lies in their ability to thrive in harsh environments, such as acidic conditions, which is ideal for processes involving acetate that can lower local pH. Their lipid-overproducing capabilities also open up avenues for producing value-added biochemicals from acetate. The table below compares products from acetate in selected yeast strains, highlighting their unique strengths.

Product	Strain/Platform	Titer	Yield	Citation
Ethanol	I. orientalis	41.4 g/L	-	[15]
Succinic Acid	I. orientalis	109.5 g/L	0.65 g/g	[15]
Resveratrol	Y. lipolytica	22.5 g/L	-	[15]
α-bisabolene	R. toruloides	2.6 g/L	-	[15]
Triacetic Acid Lactone (TAL)	S. cerevisiae	23.91 g/L	-	[15]
6-MSA	K. phaffii	83.2 mg/g DCW	+55% over control	[21]

The choice of platform is therefore a strategic decision based on the specific application. For processes demanding maximum genetic precision and the production of complex, multi-step molecules, engineered E. coli remains a top contender. For applications requiring robustness to acidic conditions, high cell density, and lipid or specialty chemical production, non-conventional yeasts represent a superior choice. The future likely lies in a hybrid approach, leveraging the best of both worlds. For instance, a synthetic consortium could use an acetogen to efficiently convert syngas into acetate, which is then consumed by a carefully engineered E. coli or yeast strain for final product synthesis, combining the robustness of acetogenesis with the synthetic biology prowess of a genetically tractable host [14,24].

Future Outlook: Synergistic Systems and the Next Decade of Acetate Biomanufacturing

The field of acetate-based biomanufacturing is poised for transformative growth over the next five to ten years, shifting from a niche area of research to a mainstream industrial practice. This trajectory is driven by a confluence of converging trends that promise to unlock new efficiencies, expand the product portfolio, and accelerate the commercialization of sustainable chemical production. The future landscape will be defined by the maturation of integrated, synergistic systems that combine

advanced feedstock generation with sophisticated downstream processing and intelligent process control.

A primary driver of this transformation will be the continued advancement and economic scaling of acetate production from renewable sources. Gas fermentation technology, pioneered by companies like LanzaTech, is becoming increasingly mature, offering a direct route to convert industrial waste gases into commodity acetate [41]. Simultaneously, innovations in microbial electrosynthesis and the development of consolidated bioprocessing for lignocellulosic biomass are expected to diversify and stabilize the supply of low-cost acetate [24]. As the cost and availability of acetate improve, its position as a competitive feedstock will become undeniable, prompting a broader adoption across industries. Process intensification will also play a critical role. Research indicates that operating acetogenic fermentations at thermophilic temperatures (e.g., 60° C) can dramatically increase gas-to-liquid mass transfer rates and volumetric productivities, overcoming long-standing bottlenecks in reactor performance [22]. Such improvements in process engineering will make acetate production from C1 gases more economically viable and scalable.

The second major trend is the emergence of highly integrated and synergistic bioprocesses. The concept of using acetate as a co-substrate in synthetic microbial consortia is gaining significant traction. Engineered consortia, where one strain produces acetate and another consumes it to make a value-added product, offer several advantages over monocultures. This division of labor can lead to higher overall productivity and resilience. For example, a consortium could feature a carboxydotrophic acetogen producing acetate from CO, which is then consumed by a genetically engineered E. coli strain to produce isopropanol or other chemicals [14]. This sequential culture system effectively decouples the energy-intensive CO_2 fixation step from the product synthesis step, allowing each organism to perform its function optimally [24]. Such modular systems are inherently more flexible and robust, paving the way for more complex, multi-step biomanufacturing pipelines.

Third, the field will see deeper integration of real-time monitoring and process control. The inherent toxicity and dynamic nature of acetate metabolism necessitate tight control over process parameters. Advanced analytical tools, combined with automated feedback loops, will enable dynamic adjustments to nutrient feeds, pH, and dissolved oxygen to maintain optimal conditions for both acetate consumption and product formation. The use of CRISPR-based regulatory tools, which can be induced by external signals, will be instrumental in creating responsive cell factories that can adapt to changing environmental conditions within the bioreactor [8 9]. This level of process intelligence will be critical for scaling up production and ensuring reproducibility in large-scale industrial settings.

Finally, the knowledge gaps identified in this review will be progressively addressed. Further research into the detailed molecular mechanisms of acetate toxicity, particularly the roles of acetylation and anion imbalance, will inform the design of even more robust and tolerant host strains. The development of more comprehensive genome-scale metabolic models for a wider range of acetate-utilizing organisms will provide more accurate predictive power for metabolic engineering. In conclusion, the next decade will likely witness a paradigm shift in how we view and utilize acetate. It will transition from a problematic byproduct to a purpose-built, high-value feedstock, integral to a circular economy. The combination of advanced feedstock generation, sophisticated synthetic biology, and intelligent process engineering will collectively drive the next wave of innovation in biotechnology, firmly establishing acetate as a cornerstone of sustainable chemical manufacturing.

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