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Dynamic Life Cycle Assessment in Continuous Biomanufacturing

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ABSTRACT

This work introduces a *Python*-based interface that couples cradle-to-gate Life Cycle Assessment (LCA) with advanced process simulations in continuous biomanufacturing, resulting in dynamic process inventories and thus to dynamic LCA (dLCA). The open-source *Brightway2.5* framework is used to dynamically track environmental inventories of the foreground process and LCA indicators (e.g. damage to ecosystems according to ReCiPE 2016) from the v3.10 cut-off *ecoinvent* database. The framework is applied to KTB1, a dynamic *MATLAB–Simulink* benchmark model of continuous Lovastatin production. 580 data points are computed across four different 24-hour scenarios. The difference between the hourly and the averaged foreground scenario is between 20-30%; a more pronounced deviation is observed when both background and foreground are averaged. The dLCA framework precisely identifies optimal periods for cleaner electricity usage, enabling future work on direct environmental feedback into process control and optimization for greener high-quality biomanufacturing.

Keywords: Dynamic Life Cycle Assessment, Continuous Biomanufacturing, Python-Based Process Optimization, Life Cycle Assessment.

INTRODUCTION

Increasing sustainability targets have shift the paradigm in Process Systems Engineering (PSE), now requiring process simulation and optimization to incorporate broader sustainability metrics alongside economic and operational considerations. In the biopharmaceutical sector, continuous manufacturing is still in its early stages, offering potential advantages such as stable operation, enhanced product consistency, and improved operational control compared to traditional batch approaches. While continuous processes offer new opportunities, sustainability assessments of such systems typically rely on the E-factor as an environmental indicator[1]. This approximation neglects the transient behaviour and time-dependent changes in input-output flows. Dynamic LCA (dLCA) seeks to address this gap by integrating temporal resolution into life cycle inventories. Recent examples include real-time IoT-based LCAs for wind turbines[2].The importance of this temporal dimension is amplified when considering fluctuating energy inputs and operational strategies designed to meet product quality and environmental objectives simultaneously[3].

This study applies Brightway2.5, an open-source LCA framework[4], to the KTB1 MATLAB–Simulink biomanufacturing benchmark[5]. KTB1's hourly energy usage can be paired with v3.10 cut-off *ecoinvent* database under Danish electricity mixes[6]. The integration of dLCA with process control enables real-time environmental impact feedback, facilitating operational adjustments aligned with cleaner electricity periods.

This analysis opens the door to real-time or near real-time operational adjustments incorporating "environmental signals", establishing a foundation for further exploration into how time-resolved inventories can improve the accuracy of dLCA's , not only by diagnosing environmental impacts but also optimizing them on the fly, taking advantage of electricity mix fluctuations and process flexibility, underscoring the value of aligning operating strategies, such as maintenance scheduling and process restarts, with greener electricity profiles, thus guiding more sustainable continuous production.

METHODOLOGY

System Description & Functional Unit

The selected application is the production of the biopharmaceutical product, lovastatin, in a continuous process flow (the KTB1 model)[5]. KTB1 model provides a comprehensive dynamic representation of the entire biomanufacturing chain, including upstream (fermentation or bioreaction) and downstream (purification and finishing) stages. The functional unit is defined as the production of 40 mg of pure API Lovastatin, a representative maintenance dose commonly encountered in pharmaceutical formulations.

Table 1: Process Units and Corresponding Models of KTB1

Unit	Name	Model
Mixer	M-101	Dynamic mass balance
Fermenter	R-101*	Dynamic mass balance & Monod kinetics
Hydrocyclone	HC-101*	Mass balance fractionation, and separation factor
Centrifugue	C-101-102*	biomass removal with separation factor
Pump	VSP-101*	Pressure-driven flow
Nano-filtration	NF-101	pressure-driven nanofiltration, lactose rejection factor
HPLC	LC-101-106	Langmuir isotherm & film transfer

* Units explicitly considered in the dLCA

Figure 1 shows the boundaries of the system. **Table 1 briefly** concisely summarises the included process units and their respective models. For this dLCA, we specifically capture hourly electricity usage in the core upstream and downstream equipment's marked with an asterisk (*) in Table 1 as the dominant resource consumption relevant to time-varying impacts. Other flows (e.g., chemicals, water) can be treated as minor or average inputs and are not dynamically tracked in this study. Further methodological details are available in[5].

Dynamic Process Modeling & Scenario Design

The KTB1 simulation model captures the nonlinear behavior of continuous biomanufacturing, accounting for upstream and downstream interactions under changing operating conditions. We track hourly electricity consumption over a 24-hour horizon to capture a typical full operational day and reflect that the system stabilizes after a few hours, making longer observation periods less informative for this particular case study. The framework, however, allows flexibility to choose any time frame as long as the process consumption data and the electricity mix data are temporally synchronized at identical sampling intervals (e.g., a consumption measurement at 14:00 aligns with the 14:00 grid share of the same day). The study combines two operational modifications with two Danish electricity profiles:

- Case 1: Reactor working volume reduced from 5000 L to 4900 L at hour 0.
- Case 2: Feed carbon lowered from 20 g/L to 16 g/L at hour 0.
- Winter: Electricity mix on 2025-01-14.
- Summer: Electricity mix on 2024-08-08.

This results in the following scenarios: Scenario 1 (S1): case 1 + winter; scenario 2 (S2): case 1 + summer; scenario 3 (S3): case 2 + winter; scenario 4 (S4): case 2

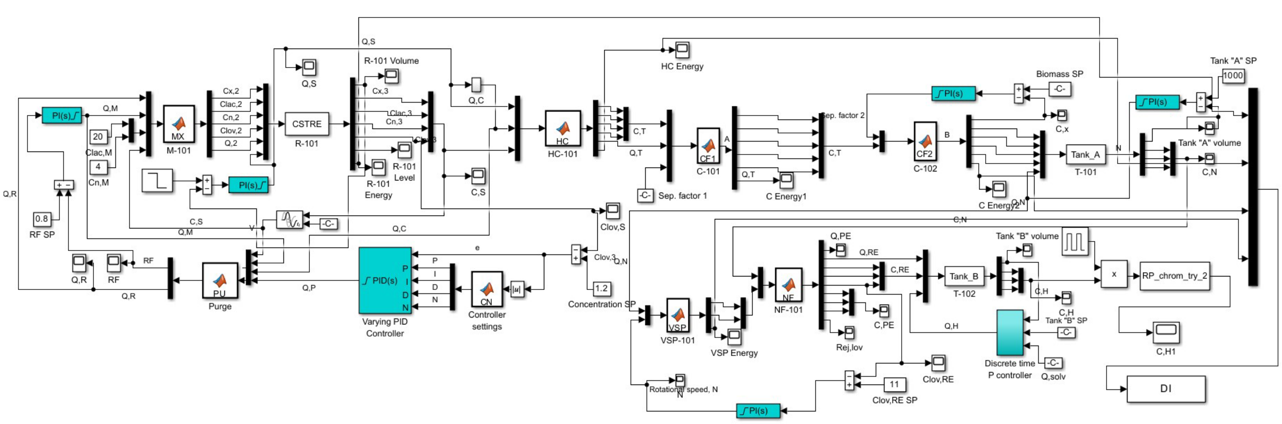

Figure 1: Visual representation of the process flow diagram for the production of the Active Pharmaceutical Ingredient (API) lovastatin.

+ summer]. **Figure 2** shows the graph obtained when representing the variation of electricity demand in case 1. For each hour, the model records energy usage in Watt for these critical units*. By tracking how these two operational adjustments shift consumption profiles, we construct time-resolved inventories for dynamic LCA (electricity demand databases available in supplementary material).

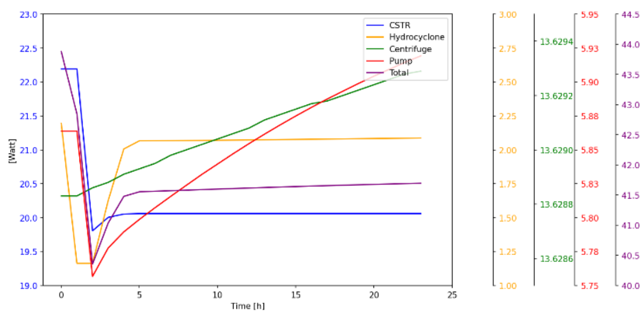

Figure 2. Foreground dynamism: CSTR, feed Pumps, Hydrocyclone, Centrifuge and Total hourly electricity consumption profile in Watt for the KTB1 model over a 24-hour horizon, illustrating how the reduction of the reactor working volume leads to varying power demands.

Thus, the dLCA framework can operate in real-time or near-real-time conditions (e.g., hourly electricity consumption data can also be captured by the sensors in CSV files). This can enable adjustments to improve operational conditions during the process based on a richer "signal" that contains environmental impact information, while of course meeting the production specifications (e.g., productivity, and product quality). This adaptive approach highlights the framework's potential to optimize decision-making during continuous operation rather than relying solely on retrospective analysis.

Electricity Mix Variation

Denmark's electricity supply fluctuates hourly, as it draws on a diverse range of sources: Wind Onshore, Wind Offshore, Solar, Waste, Fossil Oil, Hydro (Run-of-River and Poundage), Biomass, Fossil Hard Coal, Fossil Gas, and Other Renewables (see **Figure 3**). Each source carries distinct environmental intensities, and their proportional contributions vary significantly across the day. In this study, ENTSO-E data is used for 2025-01-14 (winter) and 2024-08-08 (summer) to obtain each hour's share of these generation types (electricity share databases available in supplementary material)[7]. The hourly share fraction of each electricity source type is determined from ENTSO-E database, and proportionally allocated to the Life Cycle Inventory (LCI) for that hour, reflecting the evolving grid mix in real time. Two representative days (winter and summer) were chosen. More extensive periods or alternative dates could equally be modeled if longer-term or season-specific trends were of interest. This background data can also be captured in CSV files and integrated hourly in real time or near-real time.

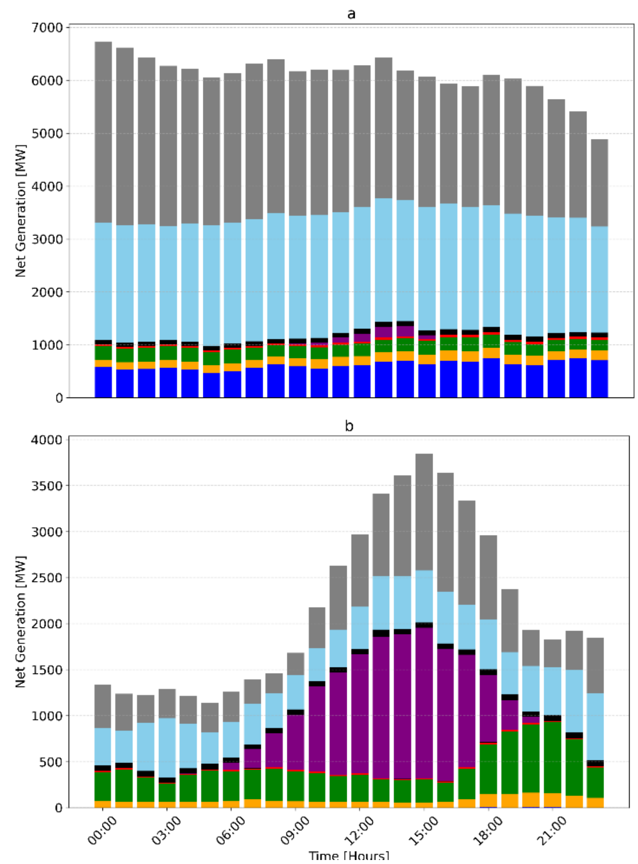

Figure 3. Background dynamism: Hourly net electricity generation in MW by technology for a 24-hour Danish grid profile. The stacked bars illustrate the contribution of different energy sources: Biomass (blue), Fossil Gas (orange), Fossil Hard Coal (green), Fossil Oil (red), Solar (purple), Waste (black), Wind Offshore (sky blue), and Wind Onshore (gray). (a) represents the winter electricity mix on 2025-01-14, while (b) illustrates the summer electricity mix on 2024-08-08.

Dynamic Life Cycle Inventory & Impact Assessment

A dynamic LCI is constructed by mapping each hour in KTB1 (demand in the foreground) to the corresponding electricity flows from Denmark's grid mix (background). Because the grid composition (wind, solar, fossil gas, waste, etc.) varies hourly, each equipment–hour node is matched to the relevant *ecoinvent* v3.10 activities. For instance, at hour 5 in the winter scenario, the grid shows 1.37 % waste incineration and 36.0 % wind offshore for the winter scenario; partial consumption is allocated to "electricity, from municipal waste incineration" and "electricity production, wind, 1–3 MW turbine, offshore."

Technically, each hour × equipment pair is treated as a distinct demand entry in Brightway25, forming a demand matrix that scales the appropriate *ecoinvent* processes by the hour's measured consumption in Watt. To perform the integral of energy use over each one-hour interval, we apply the following approximation given the relatively small variation:

$$\int_{t_i}^{t_i} \mathrm{X(t)dt} \approx \left[\mathrm{X(ti)} + \frac{X_{(t_{i+1})} - X_{(t_i)}}{2}\right] \times (t_{i+1} - t_i) \tag{1}$$

X(t) represents the time-varying energy-demand function, while $X_{(t_i)}$ and $X_{(t_{i+1})}$ denote its values at the start and end of the *i*-th hour, respectively.

A Python interface performs these conversions and compiles the time-resolved inventory, using *Temporalis*, a *Brightway25* extension, to run LCIA with the method *ReCiPe 2016 v1.03 endpoint (E), total: ecosystem quality*. Although only electricity is dynamically tracked here, the methodology readily supports adding other utilities or flows. By automatically updating the foreground model's consumption nodes each hour and linking them to background activities in *ecoinvent*, the approach captures temporal variations in environmental impacts. Consequently, it can continuously calculate any chosen LCIA indicators, given dynamic inventory data for any region or timescale.

Calculation strategy for dynamic and average scenarios

To systematically capture how variations in both the foreground (X(t)) and background (Y(t)) affect the results, we analyze four scenarios (S1–S4) as follows:

We perform a fully dynamic pairing of hourly equipment demands (foreground) with the hour-by-hour Danish electricity mix (background), yielding 24 points per scenario for five process units (CSTR, Hydrocyclone, Centrifuge, Pump, and "Total"). That is 480 points total across the four scenarios. These results are integrated and multiplied:

$$\int_{t_i}^{t_i} \mathrm{X(t)Y(t)dt} \tag{2}$$

We then create a "dynamic-background, average-foreground" variant by combining each scenario's average demand with the same hourly grid mix, producing 96 points in total:

$$\overline{\mathrm{X(t)}} * \int_{t_i}^{t_i} \mathrm{Y(t)dt} \tag{3}$$

Lastly, we use a single "average demand" and the *ecoInvent* average electricity mix, giving 4 points total:

$$\overline{\mathrm{X(t)}}\ \overline{\mathrm{Y(t)}} \tag{4}$$

RESULTS

Dynamic Life Cycle Assessment Profiles

In **Figure 4**, each sub-figure (4.a–4.d) shows the hourly ReCiPe endpoint (ecosystem quality) scores for one of the four scenarios (S1–S4). In Case 1, the reactor volume reduction (5000 L to 4900 L at hour 0) transiently changes each unit's power demands. **Figures 4.a** and **4.b** show the hour-by-hour impact of the CSTR, hydrocyclone, centrifuge, and pumping tasks, plus a "Total" curve, under winter and summer Danish grid compositions, respectively. This operational shift slightly lowers the equipments' electricity demand in the first few hours (see **Figure 2**). However, whether that translates to a larger or smaller overall score at each hour also depends on the background mix (e.g., higher fossil fractions or more renewable sources, see **Figure 5**). Comparing the purple curves (total impact calculated with hourly foreground × hourly background (2)) with the total black curves (total impact calculated with average foreground × hourly background (3)) shows that both the foreground and background influence the results. If the effect of hourly foreground changes were negligible, these lines would follow an identical pattern.

Figure 4.b and **Figure 4.d** illustrate two different foreground operational adjustments while sharing the same seasonal background profile (see **Figure 3.b**). Around hour 15, all impact score curves show a slight dip, coinciding with hours that have higher proportions of lower-impact technologies (e.g., solar and wind onshore). The strong fluctuation in the electricity mix seems to have significant relevance in the impact score around this hour.

Winter vs. Summer reveals how hour-to-hour variations in technology shares combine with the equipment's consumption changes. In some winter hours, a heavy fossil fraction (e.g., fossil hard coal) markedly increases the score for that time step, while summer hours with higher solar or wind can lower it. Comparing the LCA factor for each technology explains these patterns: one MWh from fossil oil may yield ~5 × 10^(-5) in ecosystem quality, whereas one MWh from solar might be near 1 × 10^(-5) (see **Figure 5**). Hence, an hour with 40 % fossil oil has a more pronounced impact than an hour with 40 % wind offshore (tables with numerical values available in supplementary material). Because these variations are applied each hour to whichever process unit is consuming energy at that time, the resulting ReCiPe scores (blue, orange, green, red lines in **Figure 4.a.** and **4.b**) do not simply mirror the consumption shape from **Figure 2**, but also reflect the changing background. Taken together, these results show that operational changes at hour 0 (Case 1 or Case 2) intersect with dynamic technology shares to yield unique hourly ReCiPe scores.

Comparative Analysis between Dynamic vs. Single-Average LCA

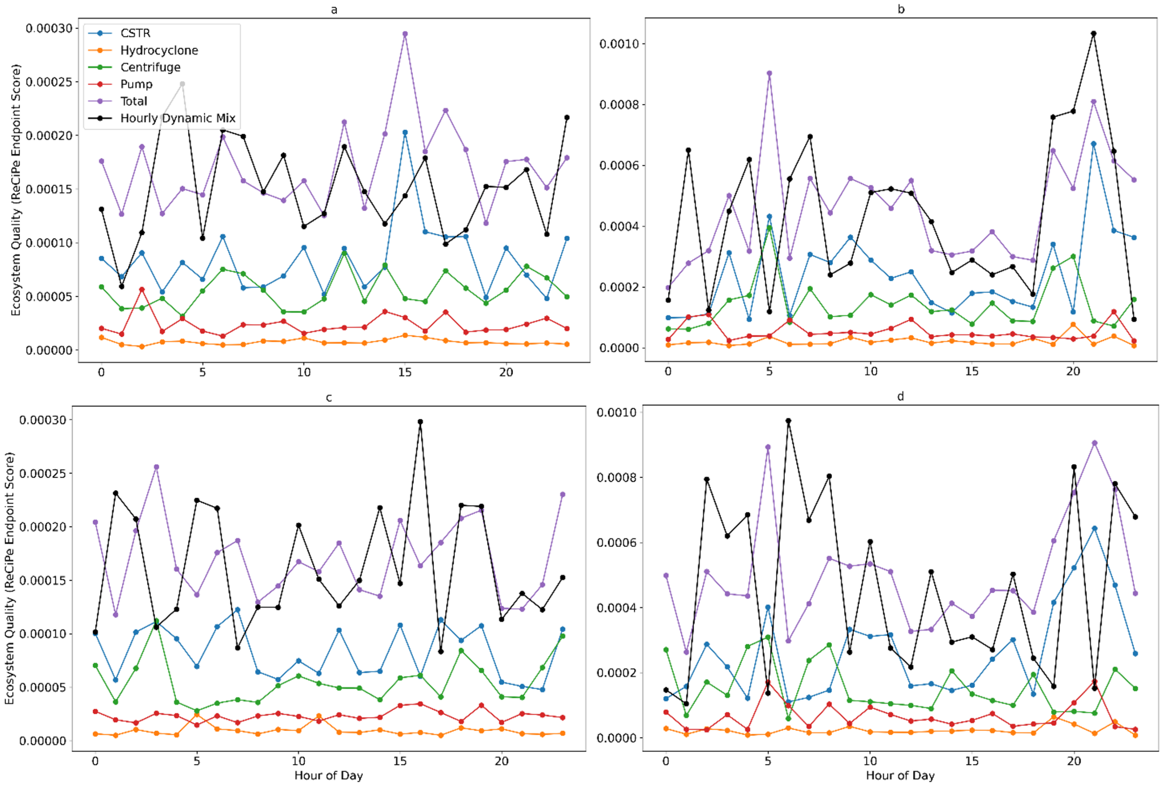

Figure 4: Hourly ReCiPe Endpoint (ecosystem quality) scores for the four scenarios, showing each KTB1 unit. Colored lines depict the foreground demand contributions of each critical unit calculated with (2): CSTR (blue), Hydrocyclone (orange), Centrifuge (green), Pump (red), while purple shows the hour-by-hour total. The black curve ("Hourly Dynamic Mix") represents a background-only dynamic approach where the average demand is allocated to the hourly electricity grid mix, calculated with (3). 4.a: S1; 4.b: S2; 4.c: S3; 4.d: S4.

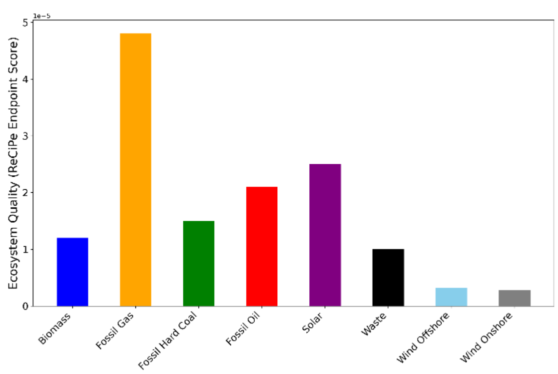

Figure 5. LCA Score *ReCiPe 2016 v1.03 endpoint (E), total: ecosystem quality* for 1 MWh Electricity by Technology from *ecoinvent*.

Table 2 reports the ReCiPe 2016 (ecosystem quality) results for four scenarios (S1–S4), each evaluated under three approaches: (2) fully dynamic (hourly foreground × hourly background), (3) dynamic background, average foreground, and (4) single-average (both foreground and background). For instance, S1 (Case 1, winter), dynamic calculation yields 4.08×10^{-3}, approach (3) gives 5.08×10^{-3}, and approach (4) is 2.73×10^{-2}.

Table 2: Comparison of Single-Average vs. Hourly-Summed LCA Scores

Scenario	(2)	(3)	(4)
S1	4.08E-03	5.08E-03	2.73E-02
S2	1.10E-02	1.56E-02	
S3	4.09E-03	5.83E-03	2.87E-02
S4	1.21E-02	1.65E-02	

Moving to S2, the single-average approach (4) remains constant (2.73 × 10^(-2)) irrespective of winter or summer, because the same average activity and identical average demand are used in both seasons to perform the calculation. The comparisons between (2) and (3) in the four scenarios underscore how hourly fluctuations in the foreground (electricity demand) can shift the LCA score by 19.75%, 29.52%, 29.77%, and 26.93% for S1-S4. The order of magnitude difference with respect to (4) is influenced by the way the average of the electricity mix is calculated in the *ecoinvent* inventory. By collapsing the dynamic variability into one blend, single-average LCA may underestimate or overestimate real burdens. Although the absolute scale of electricity demand in a typical biopharmaceutical process might appear smaller compared to large-scale chemical production, the energy consumed per kilogram of final product could have a cumulative energy demand (CED) 20 times higher, and a global warming potential (GWP) 25 times higher than typical large-scale basic chemical production[8] . In our KTB1 case, we measured an average electricity usage of 135 MJ kg^{-1} of product. Thus, even if the total energy consumption appears moderate in an absolute sense, the environmental burden per kilogram of pharmaceutical product remains substantial. This observation highlights why this application is a pertinent demonstration of the relevance of time-resolved LCA. With these hour-by-hour signals, a multi-objective scheduling algorithm could, for instance, delay a high-power centrifugation step by two hours until the fossil fraction drops, reducing its endpoint score by more than 25%. Similarly, model predictive control can exploit forecasted grid mix data to adjust flow rates, turn down certain pumps temporarily, or time process restarts so that the bulk of the energy draw coincides with greener electricity. In contrast, relying on a single, static grid-mix average overlooks these opportunities for optimization, potentially overestimating or underestimating true impacts and missing out on practical ways to cut emissions.

DISCUSSION & CONCLUSIONS

This work presents a dynamic LCA framework integrated with a continuous biomanufacturing model (KTB1). By linking a *Python*-based interface with the *Temporalis* (*Brightway2.5*), and utilizing the *ecoinvent* 3.11 database and ReCiPe characterization methods, we capture time-resolved environmental impacts that account for hourly fluctuations in the Danish electricity mix.

A total of 580 LCA points and 4640 nodes (580 × 8 activities) were computed in only 24 hours of operation considering electricity demand of a few equipments.

From an LCA perspective, two key conclusions emerge. Collapsing hourly variability into one mix can over- or underestimate actual burdens, especially in high-energy or fossil-heavy hours. A dynamic approach ensures that each operational load is mapped to the correct background technology, giving a more faithful representation of life-cycle impacts. The fine-grained LCA signals from hour-to-hour identify ideal windows presents a potential in continuous biomanufacturing to schedule energy-intensive operations (e.g., re-starts following contamination, maintenance).

Beyond these findings, the underlying framework and interface are generalizable. Any LCIA method may be substituted here, provided the user has time-resolved foreground consumption and background data. The approach scales to longer production cycles, larger databases (e.g., multiple regions, multiple seasons), or additional scenarios (e.g., different feed compositions, varied capacity expansions). In particular, other fields that could strongly benefit from dLCA are, for instance, batch processes due to its substantial variability in the foreground. Similarly, high-energy consuming operations can exploit background fluctuations for scheduling or control interventions. Regarding the background control, dLCA is particularly relevant in energy system optimization.

Future work will focus on extending programs to run longer cycles (e.g., multiple days or weeks), implementing advanced scheduling, and evaluating the economic–environmental trade-offs through *multi-objective optimization*. This logic extends to advanced *multi-objective model predictive control*, where real-time data on electricity sources could guide setpoints to concurrently optimize throughput, product quality, and environmental performance.

DIGITAL SUPPLEMENTARY MATERIAL

Digital supplementary materials for this study, including electricity demand datasets for cases 1 and 2, electricity share databases for Denmark, and numerical tables with results, are available at the following GitHub repository: https://github.com/AdaRobinsonMedici/ES-CAPE-35

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