Customer Spotlight

A Hub of Newfound Discovery: Inside Lesaffre's Automated Biofoundry

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For over 170 years, Lesaffre—a global leader in fermentation—has been at the forefront of harnessing the power of microbes to advance food, health, and biotechnology. Driven by the mission to "better nourish and protect the planet," the company is organized into four key business units: Baking, Food Taste & Pleasure, Healthcare, and Industrial Biotechnology.

Recognizing the need for speed and scale in modern biomanufacturing, Lesaffre opened the doors of its biofoundry in Lille, France in 2022. This highly automated facility represents a significant leap forward. "This is not just a new lab, but more like a different working method and a new way of integrating all our bioengineering stages," says Massimo Merighi, Chief Bioengineering Officer at Lesaffre's biofoundry and General Manager of Recombia Biosciences.

At the heart of the biofoundry's success is the Design-Build-Test-Learn (DBTL) cycle, a framework for rapid strain development powered by advanced automation technologies.

The DBTL Cycle: Precision and Throughput at Scale

Finding the ideal microbial strain for industrial applications is often a game of numbers and precision. As Merighi explains, "Finding the right strain for one industrial application is frequently a matter of probability. The higher the complexity, the higher the number of strains to be built and screened." This challenge necessitates a highly efficient, iterative process like DBTL.

DESIGN: Defining the Ideal Strain

Combining bioengineering principles with deep expertise in microbiology and bioprocess engineering, Lesaffre designs strain characteristics in silico, tailoring them to specific customer application needs and production constraints. Leveraging computational models helps identify optimal genetic targets for construction.

"We combine bioengineering principles with our in-house understanding of biology to design the characteristics that good strains should have," explains François Bertaux, Head of Synthetic and Systems Biology at Lesaffre's biofoundry.

BUILD: Engineering Diversity

To explore the vast potential of microbial genetics, they employ two main strategies:

- Rational design generates hundreds to thousands of strains via synthetic assembly.
- Directed evolution or mutagenesis creates millions to maximize genetic diversity.

Building such vast and varied strain libraries demands incredibly precise handling to ensure the integrity and accuracy of each construct. Effectively managing this high level of genetic diversity across the populations they create requires adapting workflows to ensure precise handling.

TEST: High-Throughput Screening & Validation

Evaluating the performance of thousands or millions of newly engineered strains demands unparalleled speed and precision. Lesaffre overcomes this challenge with a multi-stage process leveraging advanced robotics, microfluidics, and precision analytics.

Initial high-throughput screening rapidly processes large populations, efficiently eliminating strains that do not meet key cellular specifications such as viability or stress sensitivity. As Alicia Da Silva, R & D Microbiology Engineer, highlights, this initial step allows for the "fast and efficient elimination of all the strains which are not matching the expected cellular specifications … and allows the transition from a bulk population to a microtiter plate format compatible with liquid handling."

Following this, subsequent automated assays perform up to 20,000 tests per day in high-density plates to monitor strain growth and activity profiles.

The most promising candidates identified through high-throughput screening then undergo rigorous, scaled-down validation studies designed to mimic industrial fermentation conditions. This critical validation step confirms performance before the top-performing strains are selected for in-depth characterization in larger bioreactors.

LEARN: Data-Driven Optimization

The massive datasets generated from genomic, transcriptomic, proteomic, and metabolomic experiments are analyzed using advanced AI and machine learning algorithms. This deep analysis uncovers hidden patterns, correlations, and genetic variations linked to desired traits (e.g., stress tolerance, enzyme activity, yield). This knowledge refines design algorithms, feeding directly back into the next iteration of the DBTL cycle, accelerating the discovery process.

"We find new mechanisms, patterns, correlations, and hidden but useful relationships in the data. For example, we can discover which genetic variations are leading to desired traits or outcomes in biological systems," says Bertaux.

The DBTL Cycle: Precision and Throughput at Scale

Supporting the high speed, precision, and throughput of the biofoundry is a comprehensive suite of advanced laboratory systems and integrated instruments that have been key to their transformation from manually processing thousands of samples to seamlessly handling thousands daily.

The BioLector XT Microbioreactor and Biomek i5 Automated Workstation integration enables real-time measurement of biomass, pH, dissolved oxygen, and fluorescence—and use these signals to trigger well-specific liquid handling.

- **Biomek Automated Workstations:** These serve as central automation hubs, handling complex liquid transfers, preparing assays, and integrating with a variety of peripheral instruments throughout the DBTL cycle.
- **Echo Acoustic Liquid Handler:** This system is essential for the precise nanoliter volume transfers required for high-density plate formats and efficient, accurate strain construction during the BUILD phase.
- **Automated Primary Screening (including Cell Sorting technology):** Leveraging technologies like cell sorting, Lesaffre can quickly and efficiently screen bulk populations, eliminating strains that don't meet desired cellular requirements and transitioning promising candidates to plate formats for further analysis.
- **BioLector XT Microbioreactor & Biomek i5 Automated Workstation Integration:** This automated platform is specifically used for tertiary validation. It uniquely combines high-throughput cultivation, online monitoring, and precise liquid handling to mimic fed-batch fermentation and confirm strain performance in scaled-down models with multi-parameter measurements.
- **60+ Integrated Devices:** A vast network of over 60 integrated instruments creates seamless, end-to-end workflows for diverse tasks, including nucleic acid extraction, NGS library preparation, and sophisticated data management.

Carlos Alosilla, Head of Automation and Software Engineering at Lesaffre's biofoundry, underscores the significance of automation: "The integration of automation into our DBTL cycle has catalyzed a profound transformation in terms of robustness, repeatability, and accuracy."

Nourishing the Future

Lesaffre is at the forefront of biomanufacturing biological engineering, fostering a culture of continuous learning and pushing the boundaries of what's possible in the realms of synthetic biology and biotechnology.

Leveraging their advanced facility and collaboration with Beckman Coulter Life Sciences and others, Lesaffre is not just making strains—they are building a sustainable future by pushing the boundaries of biomanufacturing and synthetic biology.

Learn more about Lesaffre's biofoundry at lesaffre.com and about our biomanufacturing solutions at beckman.com/resources/industries/biomanufacturing.

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2025-GBL-EN-108309-v1

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