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ESSENTIAL GUIDE TO CELL CULTIVATION IN BIOREACTORS

Cell Cultivation in Bioreactors

Cell cultivation is fundamental to studying viruses, determining the role of genes in diseases, and the development of vaccines and other biopharmaceuticals.

Bioreactors provide precise control over cultivation processes. Equipped with new-generation sensors and software, these sophisticated vessels continuously monitor critical operating parameters such as temperature, pH, and oxygen levels in order to maintain optimal cell growth conditions.

Bioreactors such as the IKA HABITAT also facilitate the transition of optimized conditions from the laboratory to industrial scale, enabling commercial-scale production of cells and cell-derived products. These sophisticated support systems nurture cell cultures, enabling the scalable production of therapeutics, biofuels, and more. With their ability to maintain optimal growth conditions and enable scalability, bioreactors have become indispensable equipment in biomedical research and biotechnology.

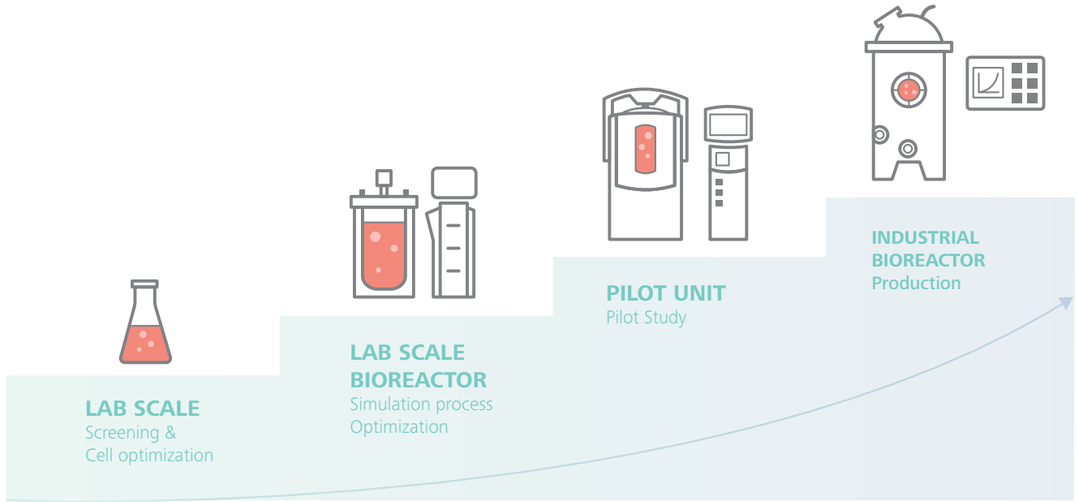


Figure legend: Upscaling process

Bioreactor Bioprocess Control

Effective bioprocess control within bioreactors is crucial for ensuring the vitality and productivity of cell cultures. Key parameters—including nutrient balance, waste management, and environmental conditions—must be meticulously managed to promote optimal cell growth and maintain culture longevity.

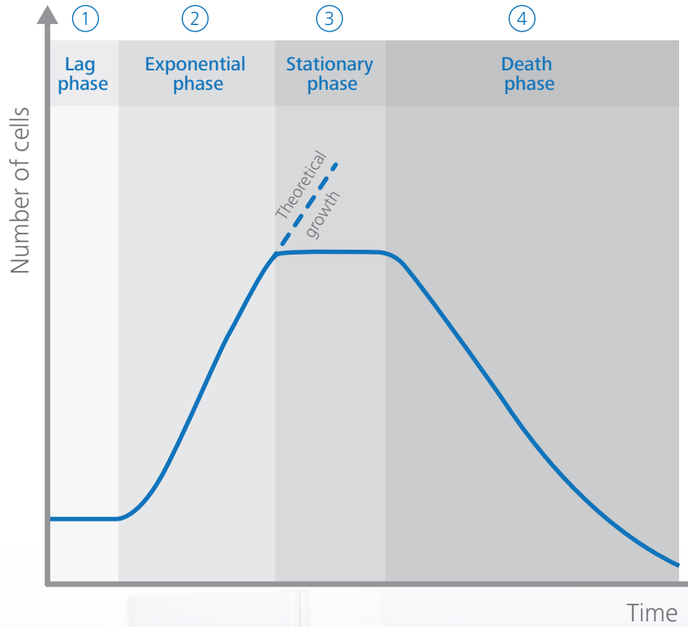
For example, adjusting nutrient concentrations and effectively managing waste products within a culture environment can significantly influence cell health and the duration of the bioprocess. These adjustments also have downstream effects on the final product's concentration and efficacy.

Precisely adjusting variables requires a deep understanding of the cells' biological requirements and metabolic responses. As the culture develops, these parameters require continuous recalibration to prevent nutrient depletion or toxic byproduct accumulation. A responsive control system of the bioreactor adapts to real-time feedback from the bioprocessing environment.

This nuanced control directly influences product consistency, downstream processing efficacy, and the economic viability of the production process. Adeptness of these elements ensures both maximal yield and high-quality production in biomanufacturing.

/// Cell Growth Phases in Bioreactor Cultures

Mastering the complexities of cellular development is a fundamental aspect of advanced bioprocessing. The following is a detailed examination of the cell growth phases within bioreactor cultures.



① Lag Phase

When cells are first introduced into a reactor (inoculation), they must adjust to their new environment and respond with a slowed growth (lag phase). Shortening the lag phase is achieved by starting a preculture in a small vessel within the bioreactor under the same conditions (medium, temperature) and, then, rapidly transferring the cells to the next sized vessel during their exponential growth phase.

② Exponential phase

After cells have adapted to the reactor, the rate of cell division reaches its maximum (exponential or log) phase. Cell numbers increase exponentially and biomass increases. Nutrients and O_2 are metabolized at the maximum rate and production of CO_2 increases. Many waste products (e.g. organic acids) are produced, affecting pH levels. At this phase, it is important to maintain conditions that best support cellular growth. During the log phase, some cells decompose (lyse), introducing free cellular proteins into the medium and increasing the risk of foam formation.

③ Stationary phase

During this phase of nutrient depletion, cell growth starts to slow. Cell division and the death of microorganisms or cell cultures still are balanced.

④ Death phase

In this phase, nutrients become depleted and conditions in the bioreactor become increasingly unfavorable for cells resulting in cell death.

/// IKA HABITAT's Cell Cultivation Advantages

Precise environmental control for cell cultivation

Mass flow controllers precisely regulate the input of air, nitrogen, and oxygen, optimizing cell growth. Dissolved oxygen (DO) levels are a critical parameter in this process.
A dedicated carbon dioxide supply system maintains optimal pH levels, while headspace gassing options facilitate efficient oxygen transfer with minimal cellular perturbation. This precise control over the cell culture environment promotes consistent and reproducible experimental results.

Advanced monitoring with next generation sensors

Advanced sensors for comprehensive bioprocess monitoring, including new-generation sensors for biomass, cell viability, and off-gas analysis, offer high selectivity, sensitivity, and long-term stability. These sensors enable contamination-free bioprocessing and improved operator efficiency by monitoring dissolved carbon dioxide, conductivity, turbidity, Redox, cell viability, off-gas, temperatures, and non-intrusive foam.
Soft-sensors can be used to calculate and display specific batch data, such as parameter setpoints, organism-specific rates (μ, qs, RQ, etc.), and extended batch values (culture broth weight, biomass).

Reducing shear stress

IKA HABITAT Bioreactors have a reactor geometry with a pitched blade and impeller design that ensures a gentle yet efficient mixing without the risk of damage from excessive shear forces. This approach optimizes the growth and maintenance of suspension and sensitive adherent cells. A new chaotic mixing mode that follows mathematical principles of chaotic-dynamic systems also provides for a more homogeneous mixture.

DESIGN AWARD 2023

/// IKA HABITAT's Operational Benefits

IKA Bioreactors are more than mere cultivation tools; they are integrated solutions designed to enhance operations with smoother, more efficient workflows tailored to the dynamic needs of our customers.

Award-Winning Design

Recognized by the iF DESIGN AWARD 2023, the IKA HABITAT Bioreactor integrates the capabilities of a bioreactor, photobioreactor, and fermenter, reducing the need for multiple setups and switching. Its ergonomic handling, intuitive operation, and user-friendly features, such as an open skid, unique lid stand, and lightweight components, reduce operator fatigue and improve portability. The compact design maximizes bench space. The bioreactor's intelligent support systems and controls make it accessible to both beginners and experts.

Consistent Quality

The IKA HABITAT Bioreactor sets the benchmark for consistent quality in bioprocessing by ensuring that each production cycle meets the high standards expected in the industry.
Its sophisticated control systems and precision engineering provide a dependable foundation for operations, guaranteeing uniform outputs that streamline the entire downstream process. Variable-speed, bi-directional peristaltic pumps and an optional fifth pump provide for diverse fluid management. This fidelity in performance facilitates the scalability of production and significantly reduces the occurrence of batch failures, mitigating downtime and waste.

Solutions that Scale

HABITAT Bioreactors excel from micro-scale research to industrial production. They feature a chaotic mixing option for faster mixing, an advantage especially beneficial at the beginning of an experiment. The bioreactor's design includes a range of vessel volumes from 0.5L to 10L, available in both single and double-wall configurations. Properly-sized motors for each volume—small for up to 2L, and larger for 5L to 10L—ensure efficient operation and customization in contrast to the standard one-size-fits-all motor approach. Advanced, integrated control systems guarantee consistent scale-up processes, enabling seamless capacity growth.

Cross-Platform Integration

OPC UA integration and extensive interface options including USB, Ethernet, and RS-232 to provide comprehensive data connectivity. The lid's additional ports enable customized modifications to accommodate a range of bioprocessing applications.

Worldwide Presence, Local Support

IKA's global presence provides comprehensive support, including technical service, spare parts, calibration, qualification, and commissioning, empowering customers to achieve their bioprocessing goals.

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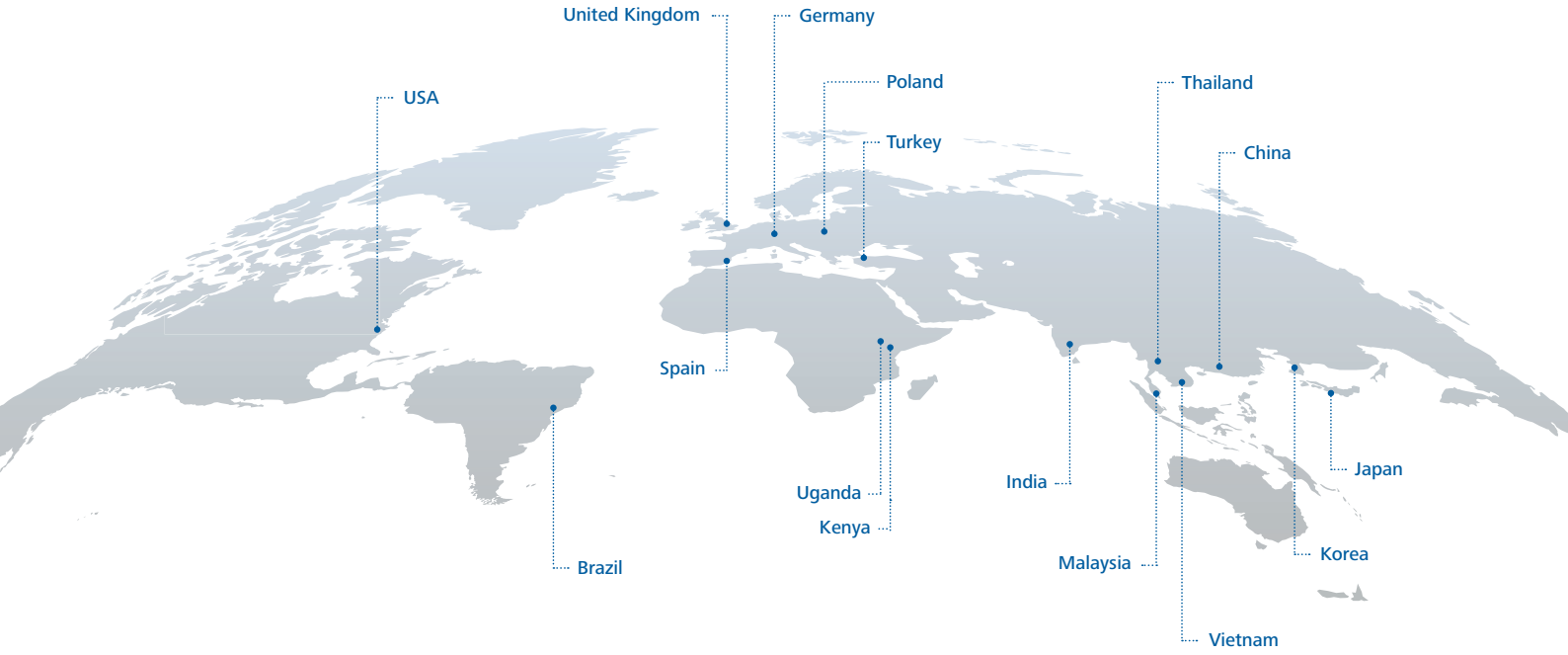

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