

QPix FLEX: Automated microbial plating, picking, and liquid handling for streamlined screening and hit selection

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Introduction

Bacterial and yeast strains are essential in microbiology, driving innovations in healthcare, biotechnology, and environmental science, including therapeutic protein production, biofuels, and biodegradable materials. This study focuses on automating workflows using the QPix® FLEX™ Microbial Colony Picker, specifically for *E. coli* and yeast, to enhance accuracy and efficiency. Automating colony picking ensures contamination-free environments, improves workflow, and provides reliable data for applications like gene expression studies, protein production, and metabolic analysis.

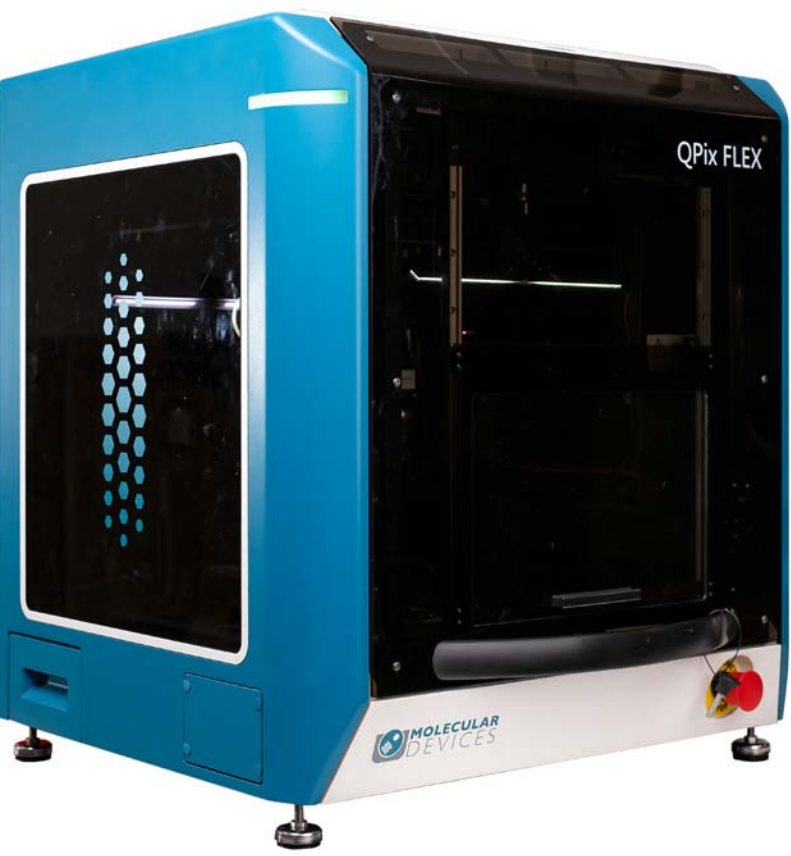
E. coli and yeast cultures were prepared in overnight growth media and adjusted to varying concentrations for automated processing. Using UV-sterilized instruments and wash troughs to maintain sterility, the cultures were plated on agar using an automated approach designed to ensure single colony isolation after 16 hours of incubation (*E. coli*) and 16–24 hours for yeast. Colony selection and screening were performed based on blue/white screening and colony morphology, such as shape and size, allowing for precise identification of desired clones. Selected colonies ranged from 0.5 to 2 mm for *E. coli* and 1–3 mm for yeast.

Post-picking, colonies were transferred into 96-well culture media plates for further growth, and the picking process achieved an efficiency of 95%, an accuracy of 99%, and a contamination rate of 0%. Optical density (OD600) readings confirmed successful cultivation, enabling downstream processes. The system also consolidated colonies through cherry-picking to prepare samples for downstream studies. Integrated data tracking further enhanced the reproducibility of microbial workflows while addressing bottlenecks associated with manual methods, such as picking errors, data tracking, long hours, and no reproducibility.

In conclusion, this picker enabled precise isolation and cultivation of bacterial and yeast colonies, achieving 95% picking efficiency, 99% accuracy, and zero contamination. Colony sizes ranged from 0.5–2 mm for *E. coli* and 1–3 mm for yeast, with successful growth confirmed by optical density measurements. The workflow provides a reliable foundation for facilitating microbial workflows and preparing samples for future downstream applications, such as functional studies or metabolic analysis.

QPix FLEX features and advantages

In a microbial lab, bacterial transformation involves introducing DNA into host cells, followed by plating on selective media. Streaking ensures colony isolation, and media preparation requires sterility and accuracy. Colonies are picked based on traits (e.g., color), and hit picking identifies positive clones for sequencing. Glycerol stocks are prepared for long-term storage. Challenges in these workflows include contamination, manual error, and low throughput. The QPix FLEX system automates plating, streaking, media prep, colony and color picking, hit selection, sequencing prep, and glycerol stock creation. Designed for precision and efficiency, it streamlines microbial workflows and supports scientists in conducting reproducible, trackable, and reliable experiments.



Multi-Functionality

- Liquid handling
- Plating and streaking
- Hit picking, colony picking (morphology and color)

Flexibility

- Seamlessly switch between sterilizable and disposable tips
- Deck layout adaptability
- Variety of labware

Accuracy

- Multipoint ultrasonic sensor
- High precision mechanical stepper

Compact Design

- Easily fits on a lab bench, in anaerobic chambers, and in constrained lab spaces

Sterility

- UV light, ultrasonic, 3-bath washing system, optional HEPA

Traceability

- 2D barcode reading

Integrability

- Automation

Workflow processes

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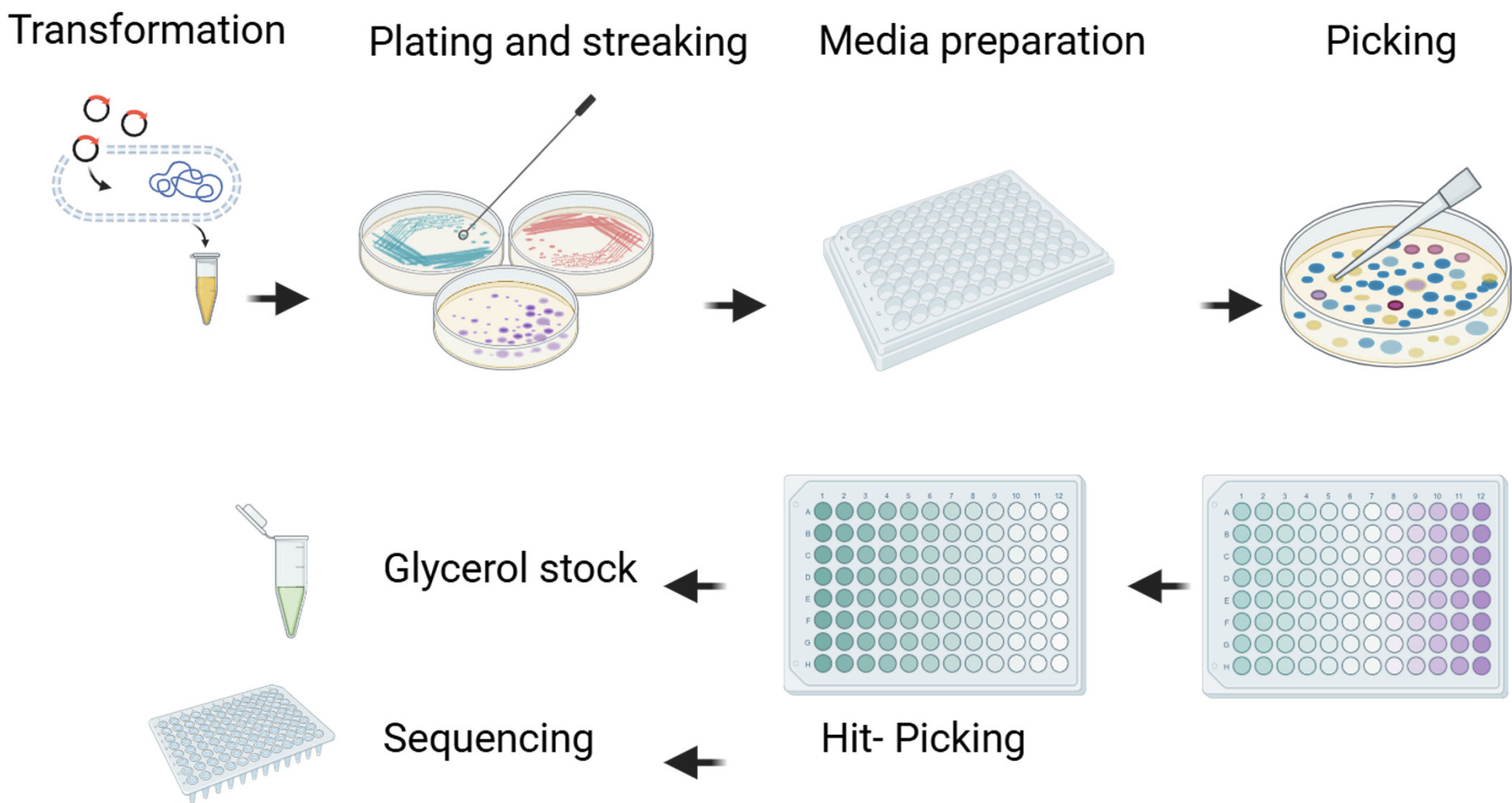


Figure 1. The microbial workflow involves multiple steps.

Workflow processes

Media handling and inoculation

Supports a wide range of labware and SBS format plates, including 384-, 96-, 48-, 24-, and 6-well plates, as well as single and 12-well reservoirs and microwell plates. It accommodates 1 mL, 200 µL, and 50 µL tips for flexible liquid handling and media preparation, making it ideal for bacterial and yeast workflows. Key parameters such as aspiration and dispense speeds, as well as other liquid handling settings, can be finely tuned to enable accurate fluid transfers. This ensures precise and reproducible experiments, often achieving a coefficient of variation (CV) of less than 5%, significantly lower than typical manual handling methods.

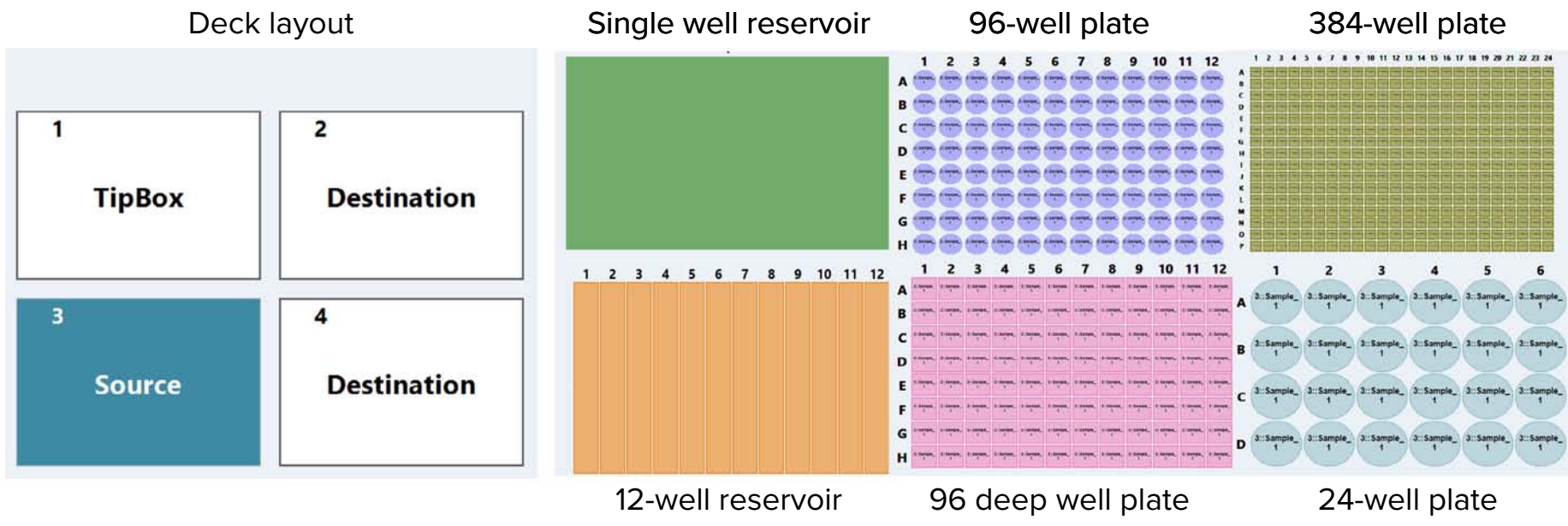


Figure 2. Deck placements for media or liquid culture preparation with the compatible individual plate maps.

Plating

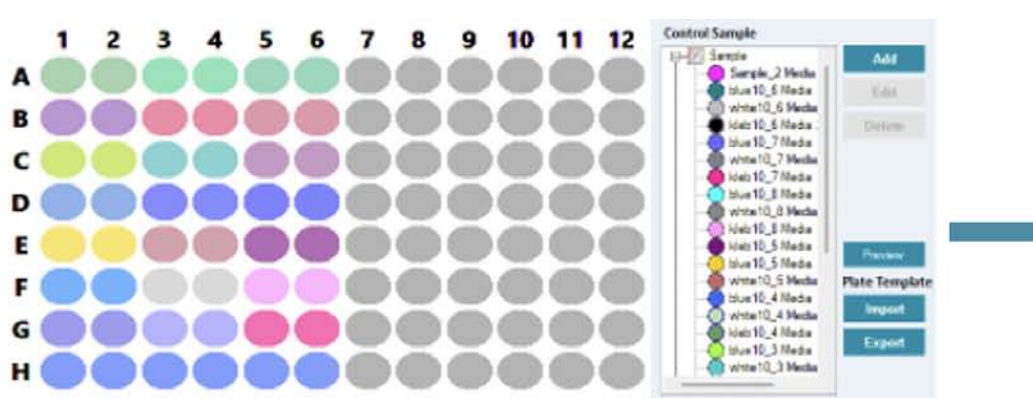


Figure 3. Source plate with user-defined bacteria and dilutions 96-well format (exportable and importable)

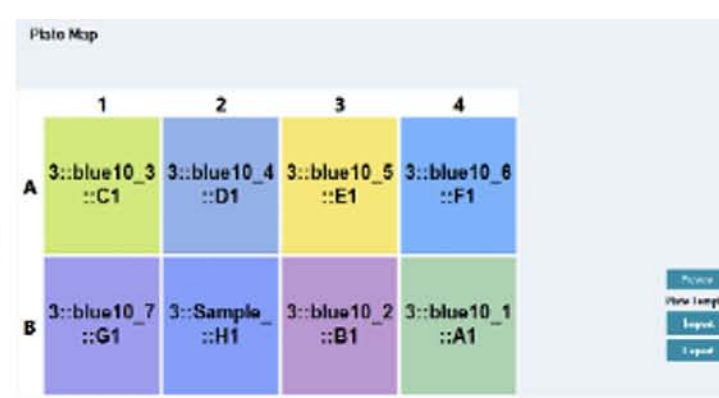


Figure 4. Destination plate with user-defined select bacteria and dilutions – 8-well divider plate (exportable and importable)

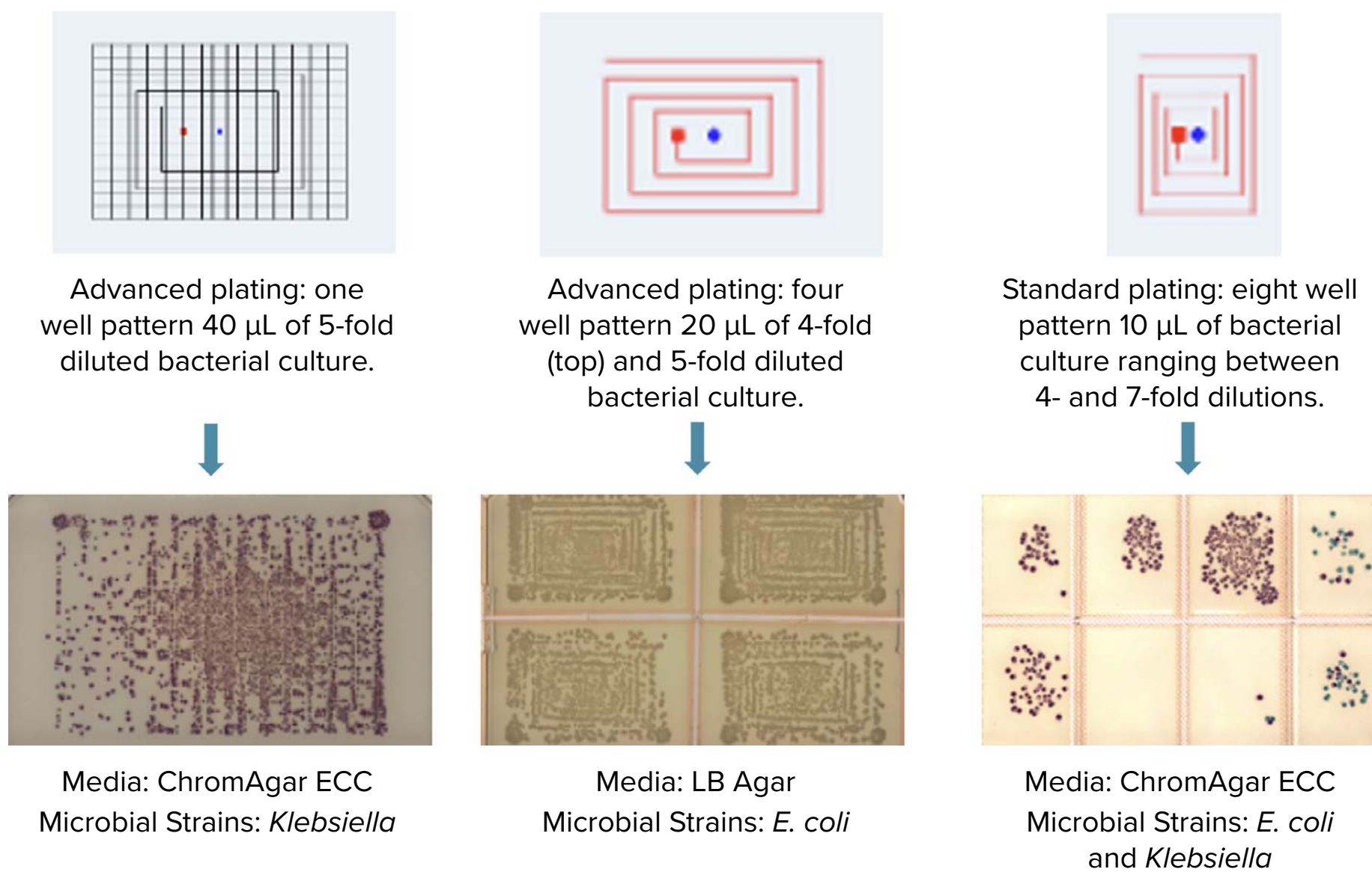
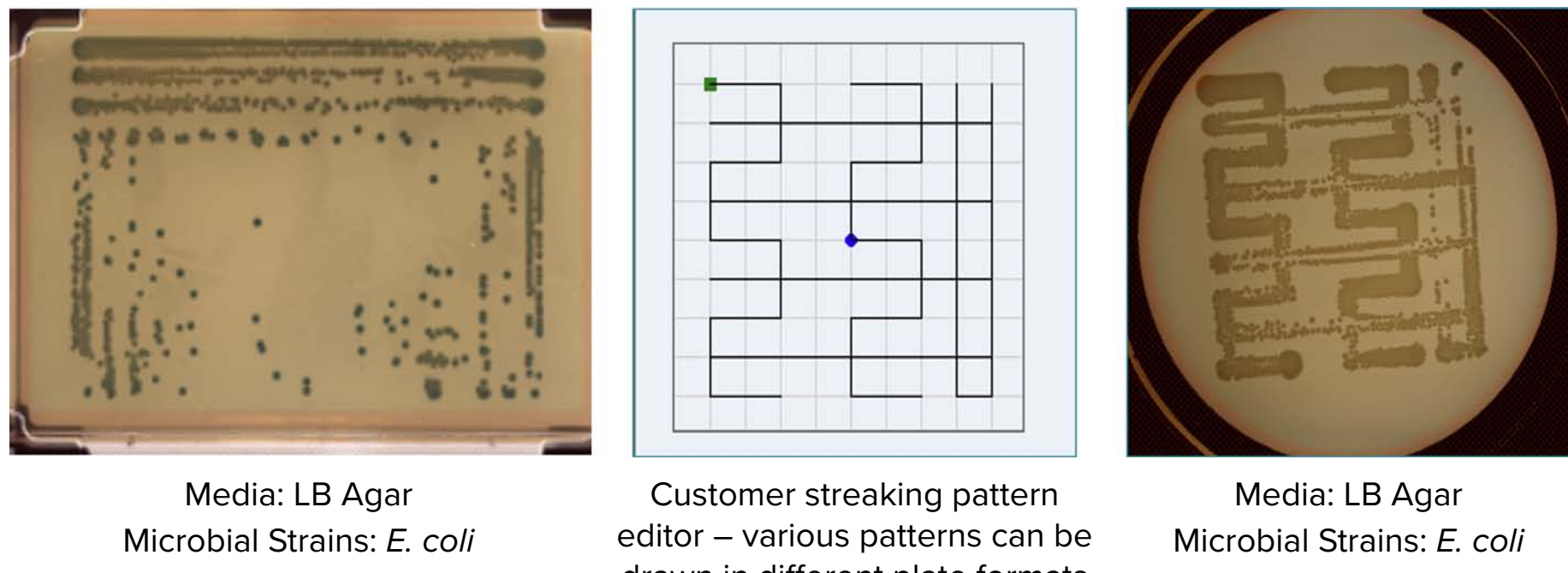


Figure 5. Various concentrations of the bacteria *E. coli* (blue, white) and *Klebsiella* (pink) were plated on the agar surfaces. Lowering the volumes with advanced plating or decreasing concentrations yields single colonies to pick from.

Streaking

The plating/streaking tip dipped in the overnight culture has been used to streak on an Omni-plate (left) and a 9 cm petri dish (right).

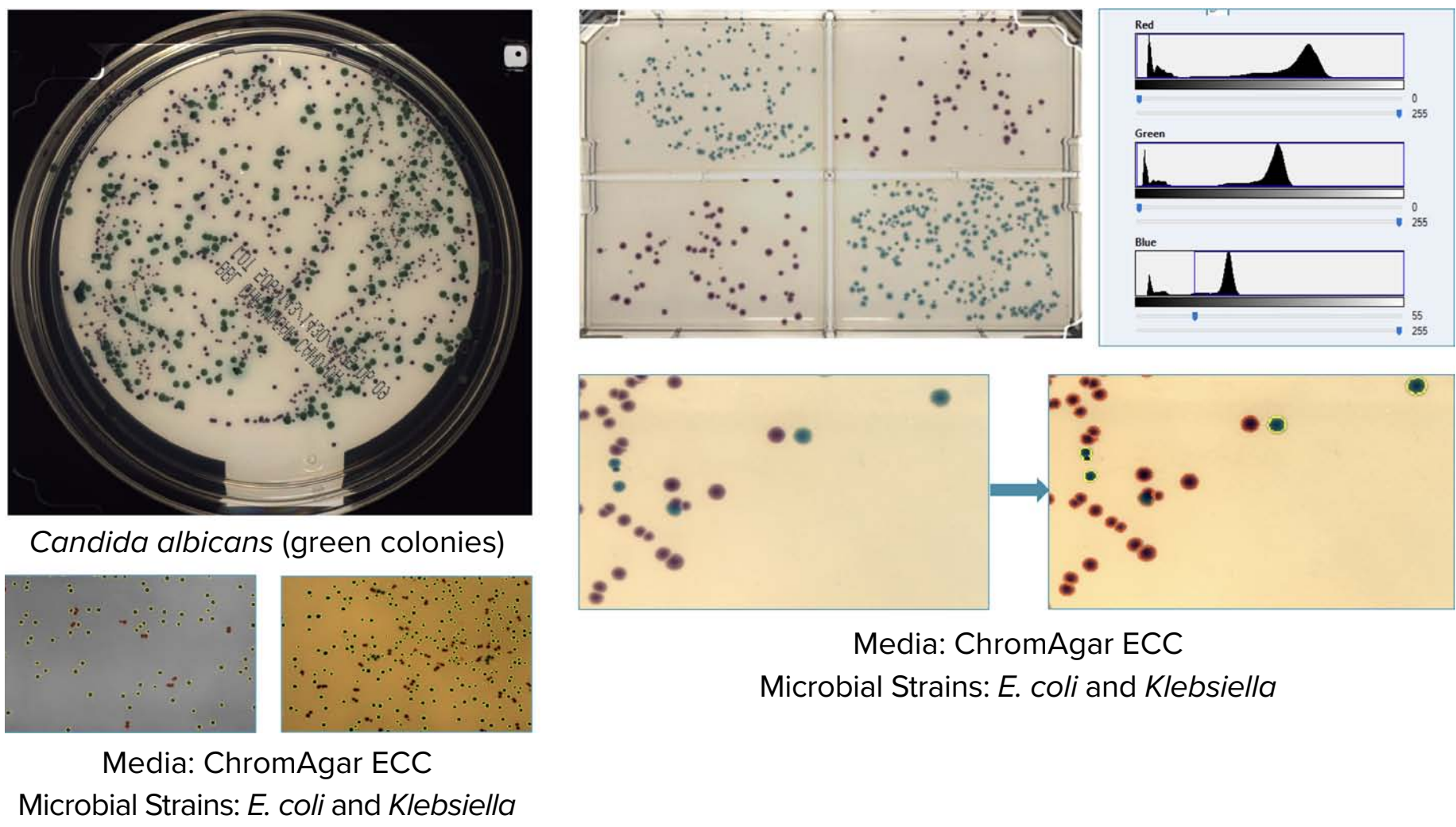


The image above (left) displays DH5α *E. coli* expressing β-galactosidase, streaked on LB agar containing 100 µg/mL ampicillin.

Advantage: Dip and streak without bacterial concentration dilutions.

Colony picking

Color colony picking was performed using RGB gradient analysis and morphological grouping to identify and select microbial colonies. *Candida* (green) was isolated from CHROMagar™ *Candida*, while *Klebsiella* (purple) and *E. coli* (blue) were differentiated on CHROMagar™ ECC. Blue-white screening on LB agar with ampicillin enabled the grouping of recombinant *E. coli*. Colonies were picked based on color, morphology, and region (e.g., 4- or 8-well divisions), and transferred into pre-prepared liquid media in various well plate formats. Each colony was assigned a well ID for full traceability. High-resolution plate images were captured for retrospective analysis. The system allowed flexible source-destination mapping during the picking cycle. Picking efficiency exceeded 95%, with 100% accuracy and no cross-contamination observed during testing.



Workflow processes

Hit picking

Hit picking is a targeted selection process used in microbial screening to isolate specific wells, typically those showing a desired phenotype or activity, such as bacterial growth or inhibition, for further analysis. The system allows researchers to generate a custom hit picking list as a CSV file, specifying source plate IDs, well positions, and corresponding destination wells. This file is then imported into automated software that guides robotic liquid handlers to accurately transfer selected bacterial colonies (e.g., *E. coli*) from source plates to pre-defined positions in destination plates. This automated, data-driven approach ensures efficient consolidation of target strains, minimizing manual error and enabling streamlined downstream processes such as plasmid preparation, sequencing, or phenotype validation. On the right, selected colonies have been picked from the source into the mapped destination plate based on the curated list, facilitating focused follow-up analysis.

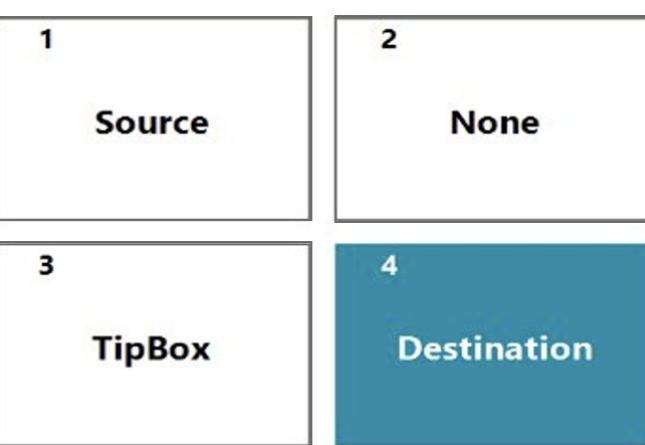


Figure 6. Deck layout

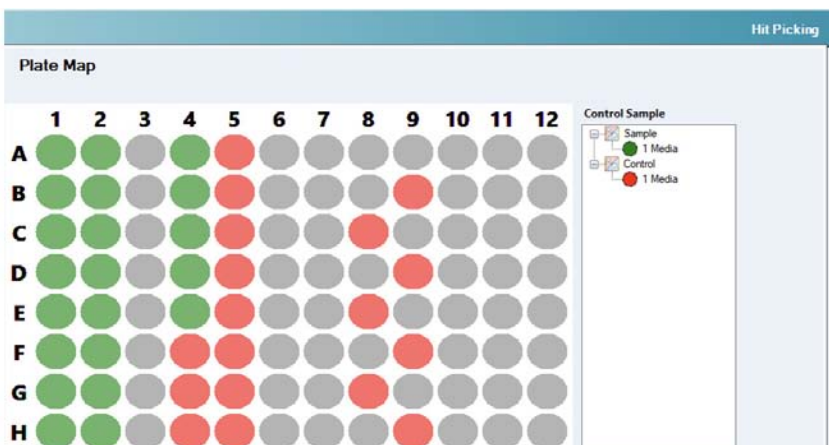


Figure 7. Source wells in the hit pick list.

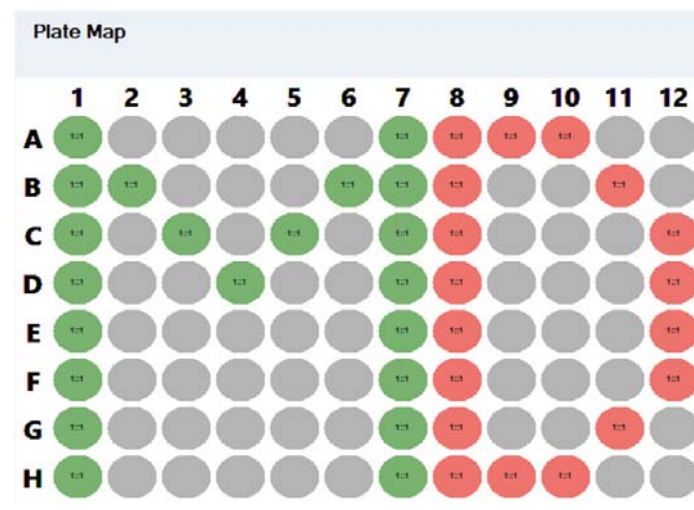


Figure 8. Destination wells in the hit pick list.

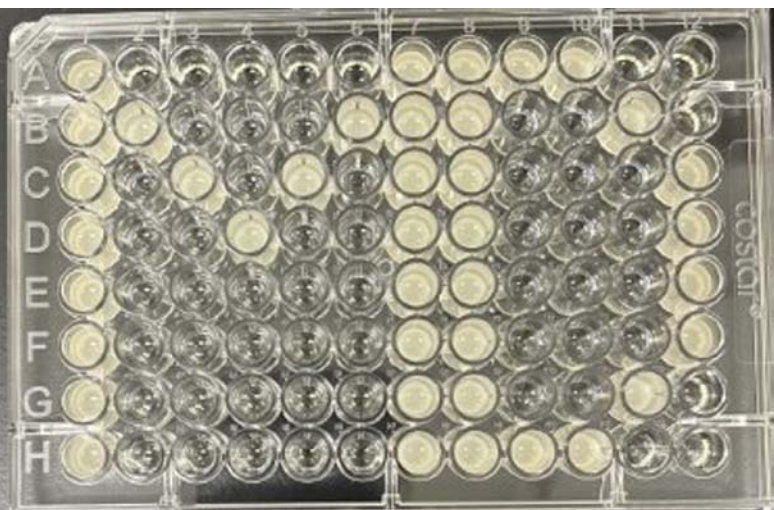


Figure 9. The destination plate hit picked wells – *E. coli* in LB broth

Downstream processes

Glycerol stocks are essential for long-term microbial strain preservation, ensuring genetic stability and reproducibility in downstream applications. Creating them manually is labor-intensive, requiring accurate pipetting and sterility. The QPix FLEX system streamlines this by enabling 24-tube racks, automating glycerol addition, and aliquoting. It also supports PCR plate preparation for sequencing. Downstream processing – post-picking and culturing – involves microbial sample collection, preservation, and DNA extraction, crucial for consistent genomics or metabolic profiling. Efficient downstream workflows reduce variability, improve data quality, and accelerate strain validation or synthetic biology workflows. Automation here minimizes errors and maximizes output, ensuring robust strain management pipelines.



Hypoxic chamber compatible and smaller footprint

Hypoxic chamber microbial work can be incredibly tedious, requiring careful handling of delicate microbial cultures in low-oxygen environments. Unfortunately, there were no colony pickers designed with a smaller footprint and compatibility for hypoxic conditions. However, for the first time, the QPix FLEX system offers a streamlined solution by providing a robust workflow that integrates seamlessly into hypoxic chamber environments, enabling more efficient colony picking and microbial analysis without sacrificing environmental control, increasing throughput.



Figure 10. Hypoxic chamber parameters were optimized, and the QPix FLEX system was used in the growth of bacteria.

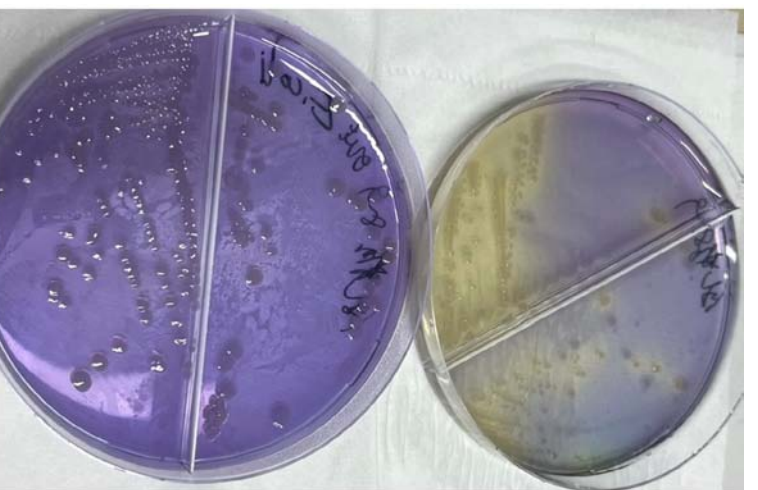


Figure 11. Lactose broth Agar with *E. coli* in ambient (left), in hypoxic chamber (right). Significant color changes due to pH change were observed in agar with *E. coli* grown in anaerobic conditions.

Conclusion

- **Automation of Microbial Workflows:** The study demonstrates the Microbial Colony Picker's ability to enhance accuracy (99%) and efficiency (95%) in processing *E. coli* and yeast, eliminating contamination (0%).
- **Colony Selection and Isolation:** Single colonies (0.5–2 mm for *E. coli*, 1–3 mm for yeast) were isolated using automated plating, UV-sterilized instruments, and blue-white screening.
- **Data Tracking and Workflow Reproducibility:** Integrated tracking improved efficiency in minimizing manual errors and enhancing reproducibility.
- **Hit Picking and Glycerol Stock Preparation:** Automated processes streamline targeted colony selection and long-term microbial preservation, reducing labor-intensive steps.
- **Flexible Liquid Handling:** The QPix FLEX system supports various plate formats and tip volumes, achieving precise experiments with a coefficient of variation (CV) below 5%, surpassing manual handling methods and errors.
- **Color Colony Picking and Morphological Analysis:** RGB gradient analysis enabled differentiation of species on selective media (e.g., CHROMagar™ *Candida*, CHROMagar™ ECC) with 100% accuracy.
- **Integration into Hypoxic Environments:** The QPix FLEX system uniquely accommodates low-oxygen chamber workflows, ensuring environmental control and increased throughput.