QPix FLEX-Enabled Workflow: Accelerating Microbial Screening and Hit Selection Through Automated Plating, Streaking, Colony Picking and Liquid Handling

Sushmita Sudarshan, Krishna Macha, Carina Gao, Oksana Sirenko, Sheela Muley | Molecular Devices, LLC
Dehua Wang | Unisons Ningbo

Introduction

Microbial strains are central to advancements in biotechnology, healthcare, and environmental science, with applications in protein therapeutics, metabolic engineering, and synthetic biology. Manual workflows remain a limiting factor, introducing variability, contamination risks, and throughput bottlenecks. Manual or siloed steps like colony plating, picking, and liquid transfers fragment workflows and complicate data management, slowing innovation in biotech, healthcare, and environmental science. This study presents a microbial processing workflow driven by the QPix® FLEX™ Microbial Colony Picker, an integrated work cell designed to automate plating and streaking, colony selection, liquid transfer, and data management within a sterile framework. The QPix FLEX is designed to overcome these bottlenecks, eliminating manual variability and contamination risks while significantly boosting throughput and reproducibility.

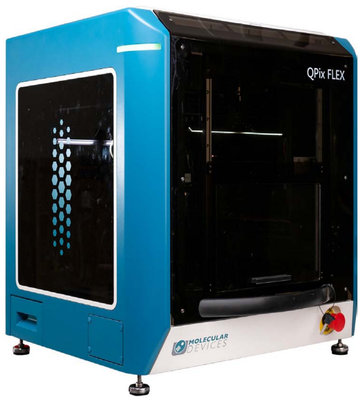
Microbial cultures (*Escherichia coli*, *Klebsiella aerogenes*, *Candida albicans* and *Saccharomyces cerevisiae*) were plated or streaked for single colonies using automated sample dispensing and spreading under sterile conditions and incubated (16 hours for bacteria and 24-36 hours for yeast). Colonies were selected using colorimetric screening — blue/white and blue/pink for bacterial colonies; green/purple for yeast — combined with morphology-based criteria. Targeted selection focused on colonies ranging from 0.5–3 mm. Picked colonies were transferred into 96-well plates with 95% picking efficiency, 99% accuracy, and zero contamination, verified via OD600 readings. The work cell's hit-picking module enabled strategic colony consolidation for downstream functional studies, while integrated data tracking software ensured full traceability and reproducibility, eliminating manual errors, fragmented records, and excessive hands-on time.

The QPix FLEX system's workflow was also applied to a microbiome study involving gut sample processing. Traditionally, these workflows are slow, labor-intensive, and require extensive anaerobic chamber handling. The QPix FLEX system's automation of plating, colony picking into liquid media, and onboard liquid handling and hit-picking reduced protocol complexity and cut turnaround time by up to three days. Enhanced recovery of isolated colonies, reduced operator fatigue, and standardized output make this integrated work cell a scalable solution for microbiome research and engineered microbial platforms.

In conclusion, these automated processes resolve key challenges in microbial workflows, enabling precise, contamination-free colony isolation and cultivation that support downstream applications such as gene expression studies, protein production, probiotic discovery and metabolic analysis.

QPix FLEX features and advantages

Microbiology laboratories rely on precision, reproducibility, and efficiency to ensure reliable microbial culture analysis. Plating and 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

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. This enables more efficient colony picking and microbial analysis without sacrificing environmental control, increasing throughput.

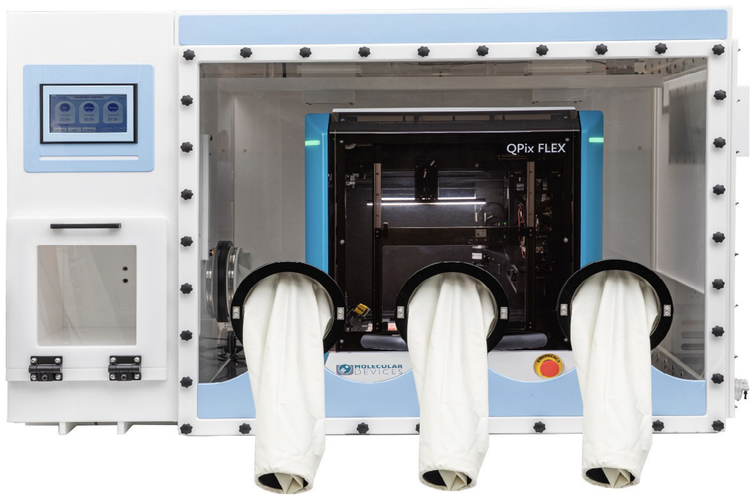


Figure 1. The QPix FLEX system placed within an anaerobic chamber.

Workflow processes

Media handling and inoculation

QPix FLEX supports a broad range of SBS-format labware, including 6- to 384-well plates, 1- and 12-well reservoirs, and 1.5 mL microcentrifuge tubes in a 24-position holder. It accommodates 1 mL, 200 µL, and 50 µL tips for flexible media prep and colony transfers. Tunable parameters like aspiration and dispense speeds ensure accurate, reproducible liquid handling, consistently achieving CVs below 5%, far outperforming manual methods in bacterial and yeast workflows.

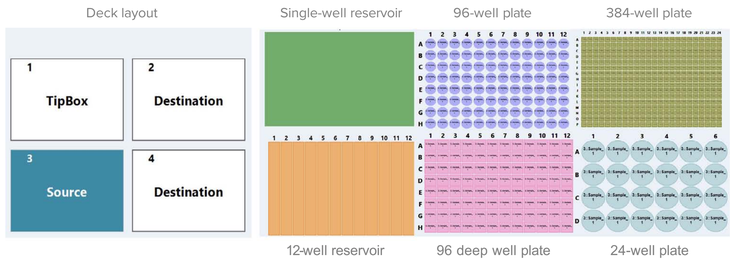


Figure 2. Deck placements for media or culture preparation with the compatible individual plate maps.

Plating and Streaking

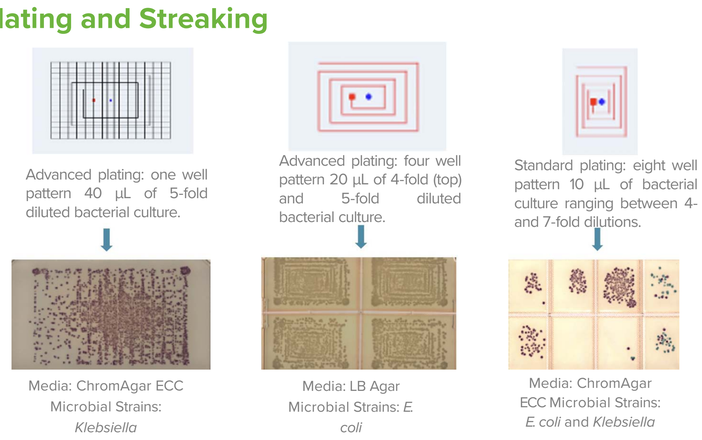


Figure 3. **Plating:** Various concentrations of the bacteria *E. coli* (blue, white) and *Klebsiella* (pink) were plated on the agar surfaces. Lowering the volumes with advanced plating or decreasing concentrations yields single colonies to pick from.

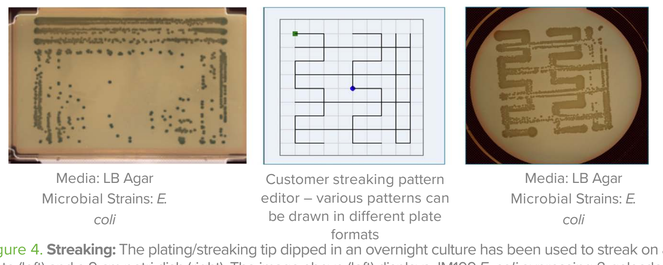


Figure 4. **Streaking:** The plating/streaking tip dipped in an overnight culture has been used to streak on an Omni-plate (left) and a 9 cm petri dish (right). The image above (left) displays JM109 *E. coli* expressing β-galacdosidase, streaked on LB agar containing 100 µg/mL ampicillin.

Colony picking

The QPix FLEX work cell enables high-precision color-based colony selection using RGB gradient analysis and morphological grouping. *Candida albicans* (green), *Saccharomyces cerevisiae* (purple), *Klebsiella aerogenes* (pink), and *E. coli* (blue) were differentiated on CHROMagar™ selective media, while blue-white screening identified recombinant *E. coli* on LB agar with ampicillin. Colonies were picked by color, shape, and region (e.g., 4- or 8-well omnitray), then transferred into liquid media across various plate formats. Each colony was assigned a unique ID for traceability, and high-resolution imaging allowed for retrospective analysis. Flexible source-destination mapping and sterile handling achieved >95% picking efficiency with >99% accuracy and zero cross-contamination.

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, enabling streamlined downstream processes such as plasmid preparation, sequencing, or phenotype validation.

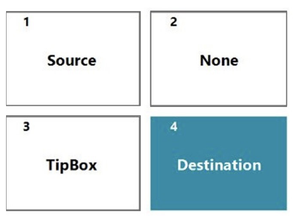


Figure 5. Deck layout

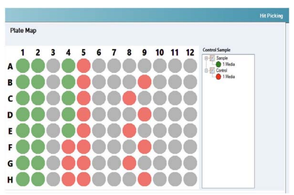


Figure 6. Source wells in the hit pick list.

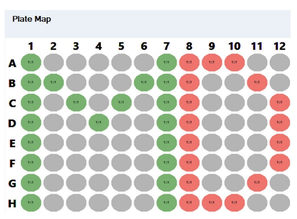


Figure 7. Destination wells in the hit pick list.

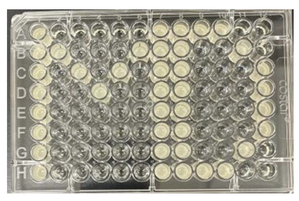


Figure 8. The destination plate hit picked wells – E. coli in LB broth.

Anaerobic Workflow (Unisons Ningbo)

In this study, we implemented an automated anaerobic microbiome workflow using the QPix FLEX system to isolate natural bacterial strains from human gut samples, with a focus on lactic acid bacteria (LAB) for downstream metabolic profiling. Traditional anaerobic culturomics involves manual plating, colony selection, and subculturing under hypoxic conditions, followed by MALDI-TOF identification and separate preparation for sequencing or metabolite analysis. These workflows typically span six to eight days and are limited to ~60 colonies per day, with high material consumption and prolonged operator time inside anaerobic chambers. To overcome these limitations, we integrated the QPix FLEX work cell into the workflow to enable high-resolution colony imaging and automated picking as early as day two post-plating. Colonies were selected based on morphology and size (≥0.2 mm) and transferred directly into 96-well deep well plates containing liquid media, bypassing manual streaking. MALDI-TOF identification was performed directly from liquid cultures, and confirmed LAB strains were automatically re-arrayed for archiving. This streamlined approach reduced the workflow duration to three to five days, increased throughput to over 120 colonies per day, and minimized agar plate usage. Barcode-based sample tracking ensured full traceability, while reduced operator time in anaerobic environments improved ergonomics and reproducibility. The automated system enabled efficient isolation of LAB strains for probiotic discovery and targeted analysis of metabolic products with enhanced precision and speed.

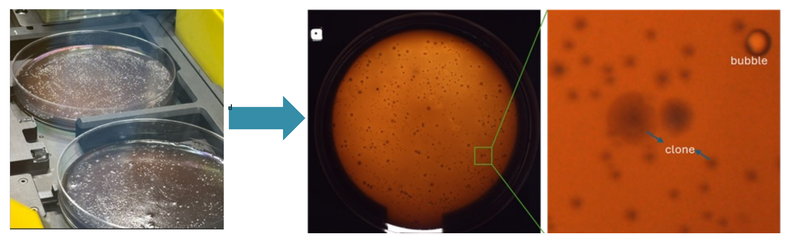


Figure 9 . Bacterial colony growth on blood agar after overnight anaerobic incubation (left). By day two, discrete clones began to emerge that could be detected by the software to be picked (right), but manual identification was hindered by low contrast and surface artifacts like bubbles. By days three through four, colony morphology improved, enabling manual picking, though visual inspection introduced delays and variability.

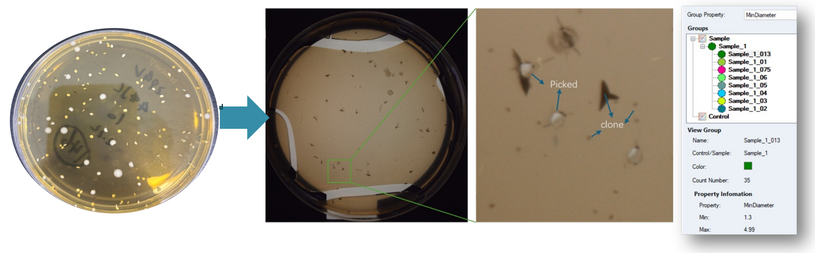


Figure 10. Colonies cultured on modified MRS media were stratified into eight groups based on diameter metrics derived from QPix FLEX imaging. Each group represented a distinct size range, enabling targeted selection of morphologically diverse clones. From each group, 12 colonies were picked, ensuring consistent representation across the diameter spectrum. Following overnight incubation under identical anaerobic conditions, a second cycle of colony picking was performed. The same imaging and classification settings were applied to identify newly emerged colonies. This iterative approach facilitated the selection of additional clones with distinct morphologies, expanding the diversity of the colony pool.

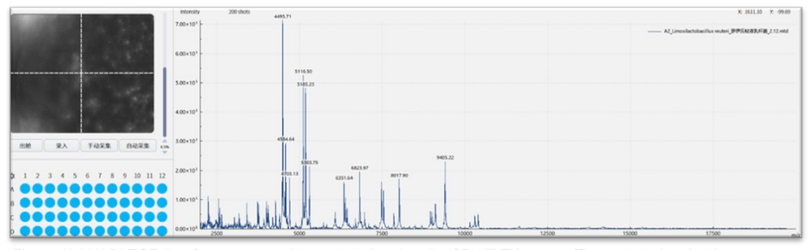


Figure 11. MALDI-TOF data from an anaerobic strain isolated on the QPix FLEX system. The strain isolated with the QPix FLEX system in anaerobic conditions displays the expected MALDI-TOF profile.

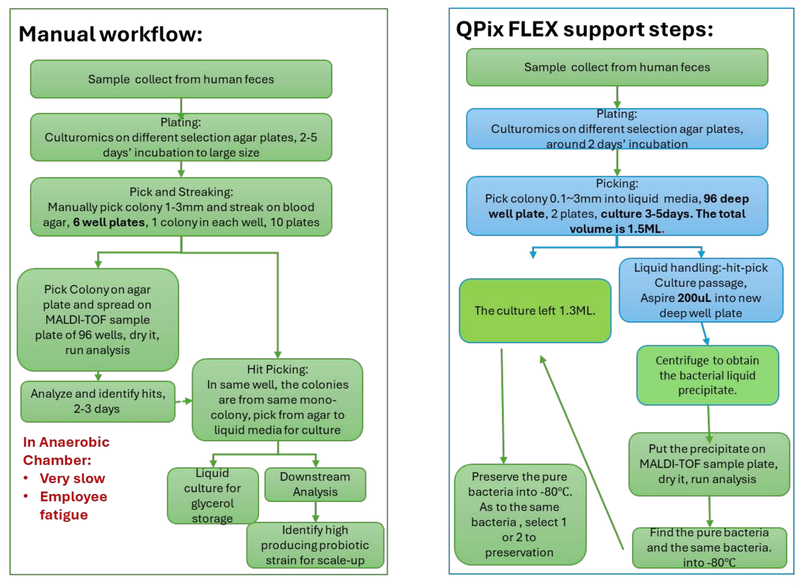


Figure 12. Comparative Anaerobic Workflows for Culturing Fecal-Derived Bacteria: Manual vs. QPix® FLEX™-Integrated Approach

Conclusion

- **Automation of Microbial Workflows:** The study demonstrates the microbial colony picker's ability to enhance accuracy (99%) and efficiency (95%) in processing bacteria and yeast, eliminating contamination (0%).
- **Colony Selection and Isolation:** Single colonies (0.5–2 mm for bacteria, 1–3 mm for yeast) were isolated using automated plating, UV-sterilized instruments, and blue-white screening. The QPix FLEX system enabled reliable identification of micro colonies (0.2 mm) using high-resolution imaging and detection algorithms, reducing reliance on manual visual inspection and accelerating time.
- **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 integration of the QPix FLEX system into anaerobic culturing workflows enabled early, automated, and morphology-based colony selection with high reproducibility. Stratifying colonies by diameter and applying iterative picking cycles expanded the diversity of recovered strains while minimizing manual intervention. Combined with MALDI-TOF validation, this approach streamlined the isolation of viable, phenotypically distinct clones, accelerating downstream microbiome analysis and strain development.

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