RoboCulture: A General-Purpose Robotics Platform for Automated Biological Experimentation

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Acceleration Consortium

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Self Driving Labs for Biology

- Biological experiments are tedious and time-consuming; cell culture can take weeks of repetitive labour *[1]*
- Precision and consistency is important in biology
- Automation minimizes human contact; less risk of contamination
- Labour cost savings; more work hours directed toward research

Existing Approaches to Liquid Handling

Commercial Liquid Handling Devices

✓ Precise positioning with XYZ gantry
✓ High throughput

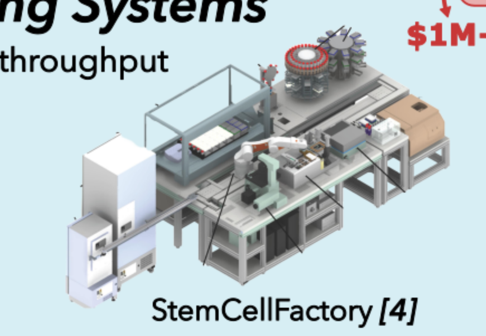
! Not fully automated
Still requires human in the loop

$10k - $60k
! Large initial cost
$1M+

Large Liquid Handling Systems

✓ Ultra-high parallelization and throughput
✓ End-to-end automated

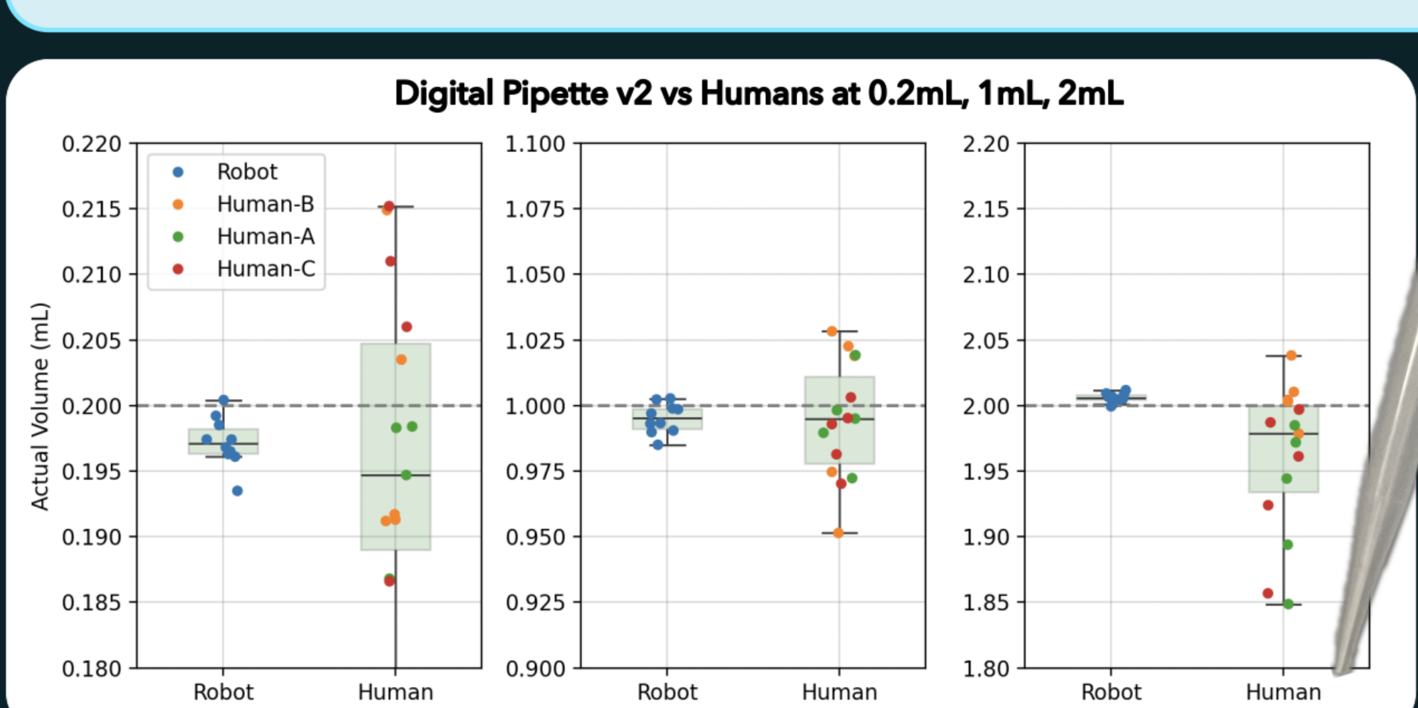
! Highly Specialized
Does not generalize to other tasks



We propose a generalizable approach to SDLs for biology - a robotics platform striving toward end-to-end autonomy of biomedical experimentation

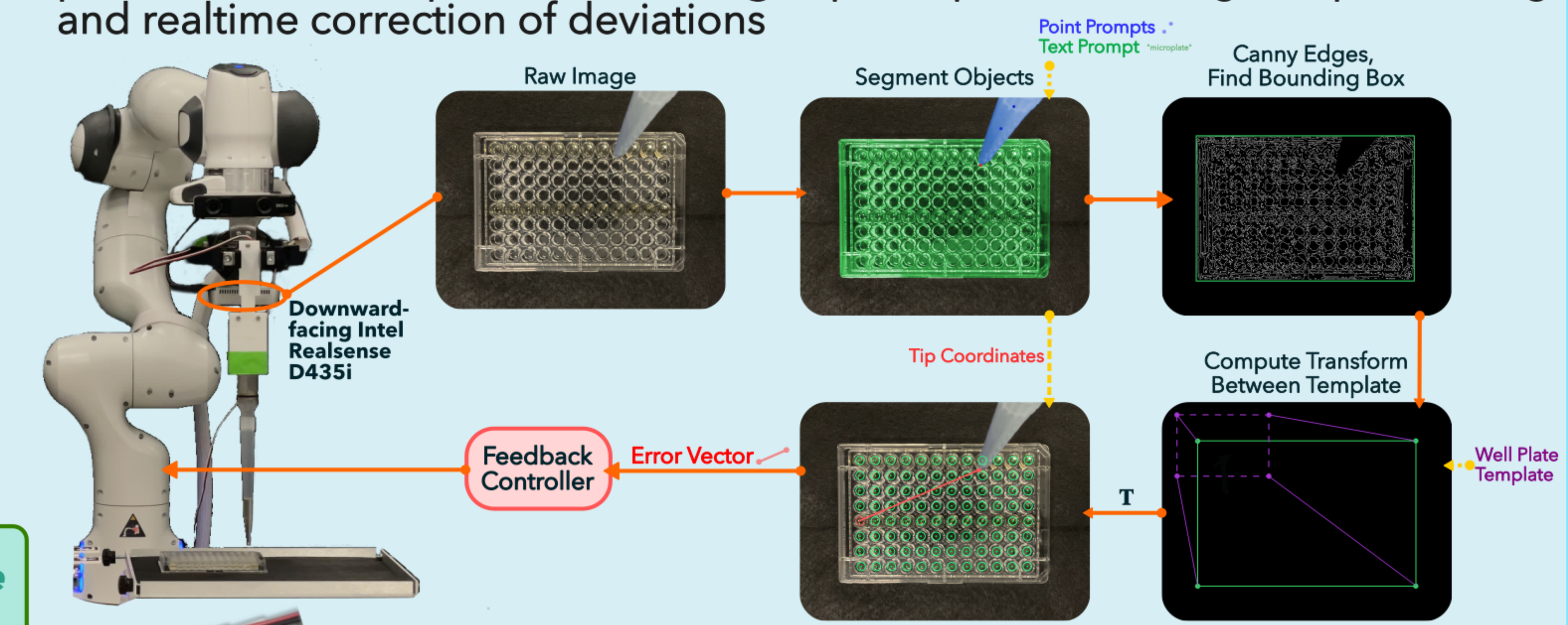
Digital Pipette v2

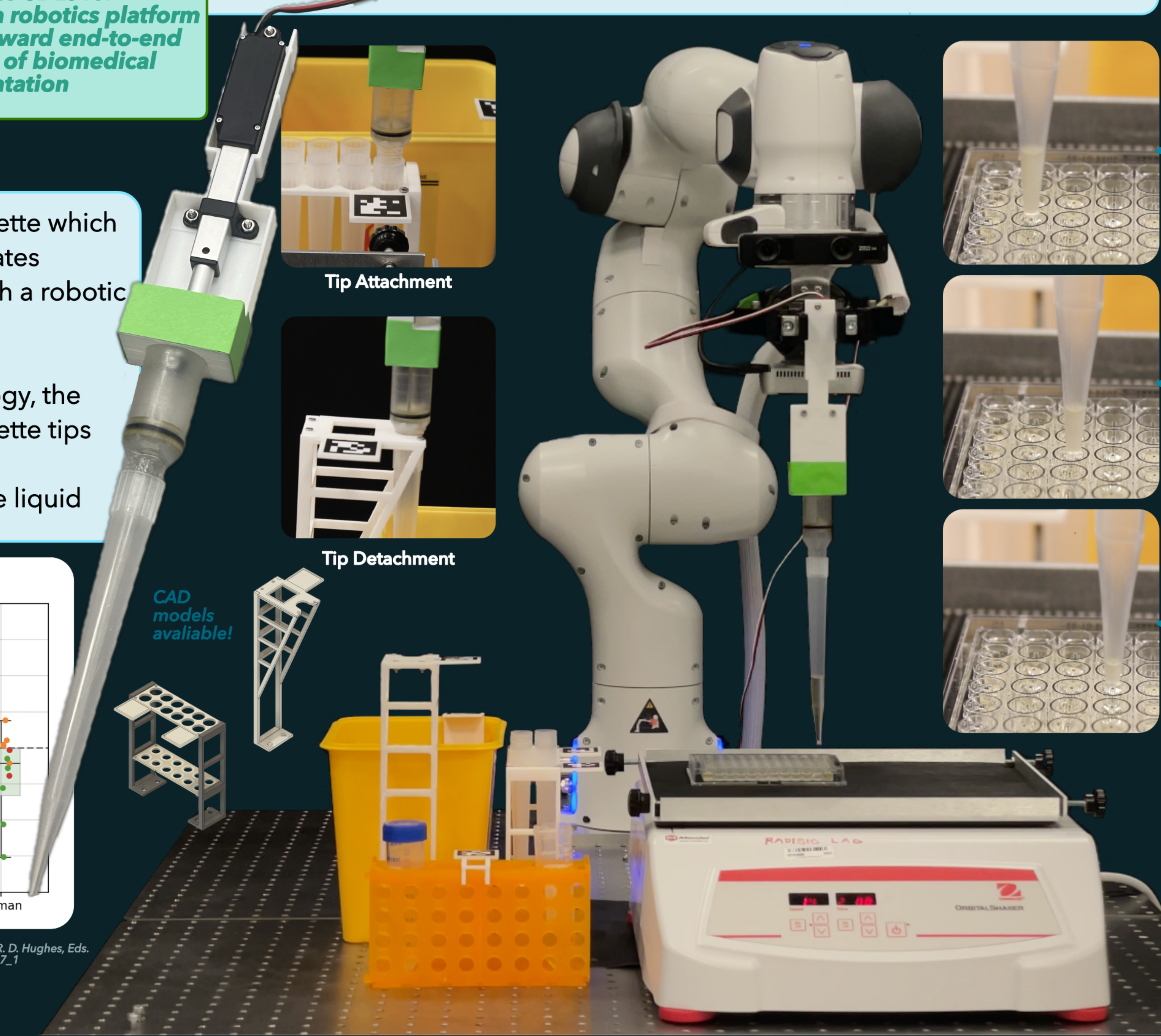
- The ***Digital Pipette*** *[5]* is a 3D printed, open source pipette which manipulates liquid via a linear actuator, and communicates directly with a computer to facilitate interoperability with a robotic manipulator
- Motivated by sterilization requirements present in biology, the updated ***Digital Pipette v2*** features interchangable pipette tips
- A 5cm actuator pulls on a gasket to inhale and dispense liquid



Visual Servoing Enabling Liquid Handling

- High precision is required for pipetting into a 96 well plate
- Naïve methods of perception are limited by camera calibration errors, open loop robot control yields poor alignment
- Fiducial markers are restrictive for objects interacting with other hardware
- The location of the pipette tip is not known in the world frame
- Instead, use visual feedback via a camera mounted on the end effector to perform closed loop **visual servoing** in pixel space, enabling fine positioning and realtime correction of deviations





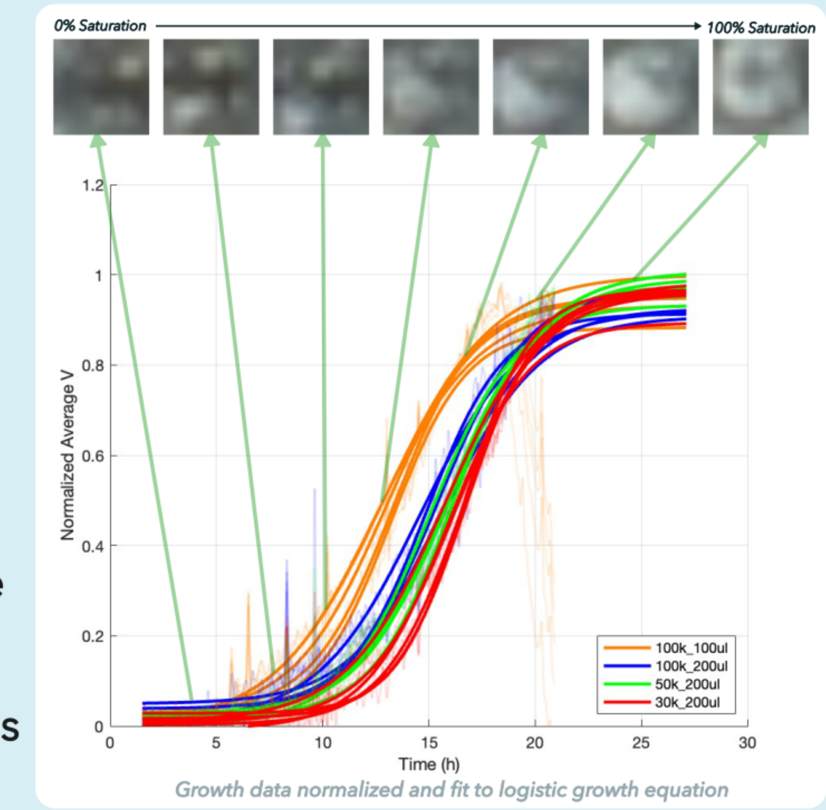
Yeast Experiment

- A yeast culturing experiment is performed to demonstrate the effectivness of the robotics system
- Start with a 96 well plate partially filled with yeast at varying concentrations, and autonomously perform a 3x dilution once the yeast reaches 100% confluency

Note: *Yeast is used as a safe alternative to other types of bacteria and a progression toward mammilian cells. It is assumed this robotics setup would be used in conjunction with a Bio Saftey Cabinet (BSC), so some sterilization requirements are omitted for this experiment.*

1) Monitoring

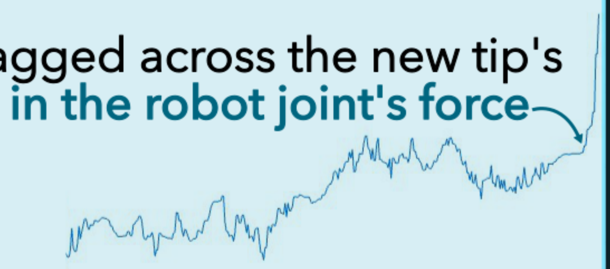
- Images of each well are captured and analyzed at regular intervals
- The result is a **growth curve**, resembling the curve obtained with a plate reader, though without additional hardware
- The growth curve dictates the execution of the experiment, i.e. determining when a well becomes confluent and needs to be split



Growth data normalized and fit to logistic growth equation

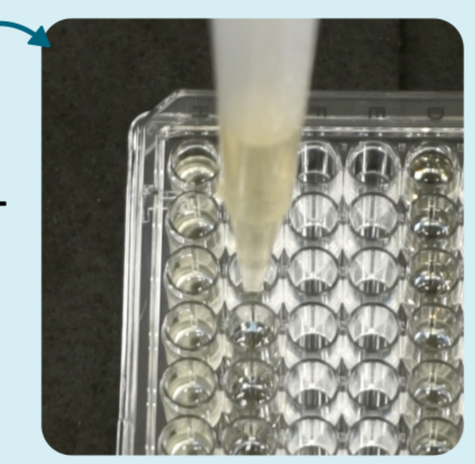
2) Pipette Tip Exchange

- The position of the pipette end is not known in space, and perception is more difficult for tight insertions
- **Spiral search** is used; the pipette is dragged across the new tip's opening in a spiral pattern until a jump in the robot joint's force indicates the insertion was successful



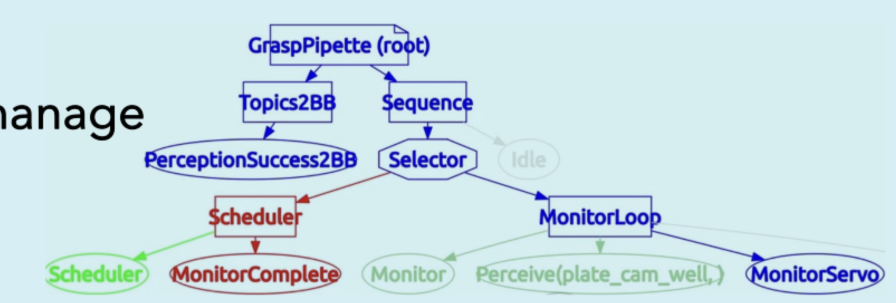
3) Liquid Handling

- a) Fill pipette with YPD media and deliver 0.15mL to empty wells
- **b)** Inhale saturated yeast and deliver 0.05mL each to three wells with media
- c) Replace pipette tip
- d) Repeat b-c until no more saturated wells remain



4) Behaviour Trees

- Use behaviour trees to manage high level actions of the experiment with reactive decision making



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[3] Hamilton Company, "Microlab STAR: Automated Liquid Handling Platform," Hamilton Company, 2024. [Online]. Available: https://www.hamiltoncompany.com/automated-liquid-handling/platforms/microlab-star-v.

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[5] N. Yoshikawa, K. Darvish, M. G. Vakili, A. Garg, and A. Aspuru-Guzik, "Digital pipette: open hardware for liquid transfer in self-driving laboratories," Digital Discovery, vol. 2, no. 6, pp. 1745-1751, 2023. [Online]. Available: http://dx.doi.org/10.1039/D3DD00115F. doi: 10.1039/D3DD00115F.