Multi-Location Droplets for Digital Microfluidics

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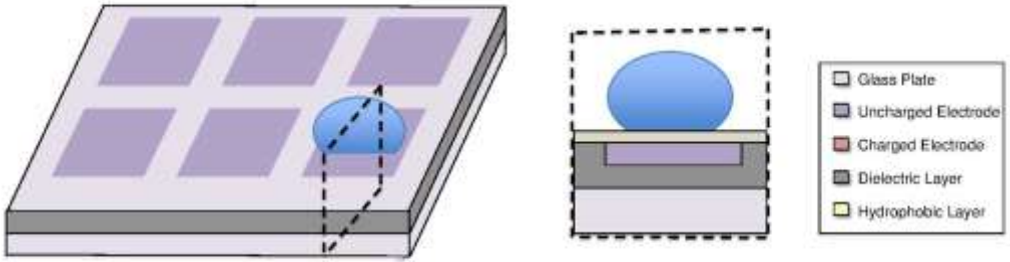
MISL

Dramatis Personae

- **Sarang Joshi:** 4th year student in UW CSE
- **UW Molecular Information Systems Lab:** esteemed lab at the UW exploring "the intersection of information technology and molecular-level manipulation"
- **Luis Ceze:** my faculty advisor
- **Max Willsey:** project leader and manager

Background: DMF

- **Digital Microfluidics**: controlling and manipulating droplets on a "micro" scale using insulated electrodes



- Three key principles at work:
  - **Electrowetting**: manipulation of wetting properties of a surface with electricity
  - **Dielectrophoresis**: phenomenon where a force is exerted on a dielectric particle when subjected to a non-uniform electric field
  - **Immiscible-fluid flows**: movement of fluids suspended in immiscible suspension

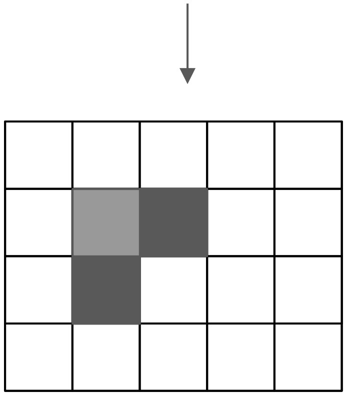
Background: DMF

- Applications:
  - DNA Storage: manipulating DNA as part of the encoding/decoding phase of storage, including PCR (polymerase chain reaction)
  - Chemical manipulation and analysis, mass spectrometry, synthetic biology, etc.
- UW MISL Architecture:
  - **Puddle**: DMF operating system that abstracts away the device-specific details for users
    - allows the system to perform optimizations, error corrections
    - goal is to allow mixing (no pun intended) of normal programs and DMF programs to seamlessly integrate the power of DMF experiments with computation
  - **PurpleDrop**: DMF device that provides the low-level software/hardware interface
    - Microcontroller on the board controls the electrode grid on the chip to actuate and manipulate droplets
    - Complements the Puddle software stack

Software: Multi-location Droplets

- Adding software support for droplets occupying more than one electrode
- Version 1: `location` + `shape`
  - shape is a set of *offsets* from the base location of the droplet
  - Flexible design, describing all possible multi-location droplets
- Version 2, simpler: `location` + `dimensions`
  - Most stable shape for a droplet is a square of electrodes (or square-like shapes)
  - Greatly simplifies implementation, allows for a proof-of-concept of multi-location droplets
- Python → Rust

```
{
  location: (1, 1)
  shape:
    {(0, 0), (1, 0), (0, 1)}
}
```



Software: Collision Checking

- Key aspect of Puddle architecture: place-and-route mechanism
  - Phase 1: **place** input droplets on the board
  - Phase 2: queue commands (such as "mix", "split") on droplets
  - Phase 3: Puddle system will compute the optimal sequence of operations to execute on the PurpleDrop board, and **route** them accordingly
- Routing uses the A* search algorithm, a heuristic-based pathfinding algorithm, by creating an `avoidance set` that ensures that no two droplets collide as part of executing the commands
- "Collision" also means droplets occupying adjacent cells
  - Prone to combining to form single larger droplet

Hardware

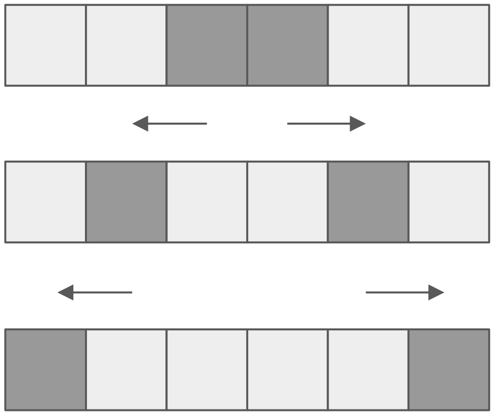
- With the basic software support in place, transitioned to implementing basic multi-location droplet support on the PurpleDrop cartridge
- **Move** and **mix** commands - similar to the single-location implementation
- **Split**, however, was a different story
  - Each shape can be split in a multitude of ways, i.e. "split patterns"
  - Dependence on physical variables that need to be abstracted away in the Puddle system
- Next, biggest step of the project: experimenting with the feasibility of splitting, and the effects of various variables on the process
- Focus on 2x1 droplet, with initial steps for 3x1 and 2x2 droplets

Approach and Methods

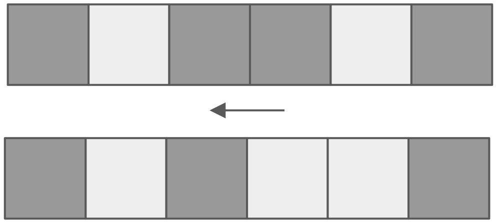
- Goal: evaluate splitting patterns for multi-location droplets on the PurpleDrop board
- Variables to test:
  - Split pattern, i.e. how the electrodes are actuated
  - Volume per electrode
  - Spacing between base plate and top layer
  - *Ratio of volume to spacing, i.e. droplet area*
  - Oil viscosity
- 10 trials per experimental combination of variables for statistical accuracy
- Results measured by:
  - Split ratio
  - Residue (explained later)
- Baseline experiment:
  - Pattern 1, 1.75 μL, 1-layer spacing, 196V top plate, 1.5 cSt viscosity

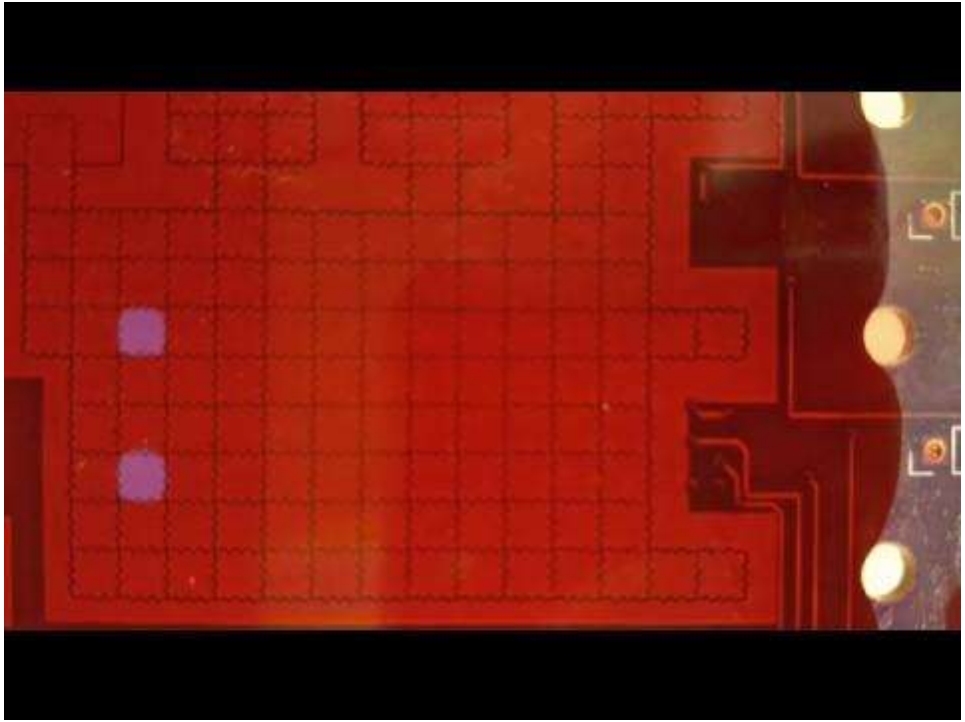
Experiments: Split Pattern

1. Basic Split:



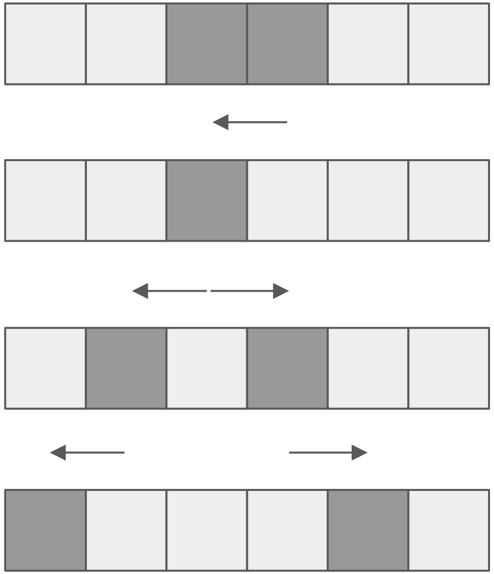
Residue collection:

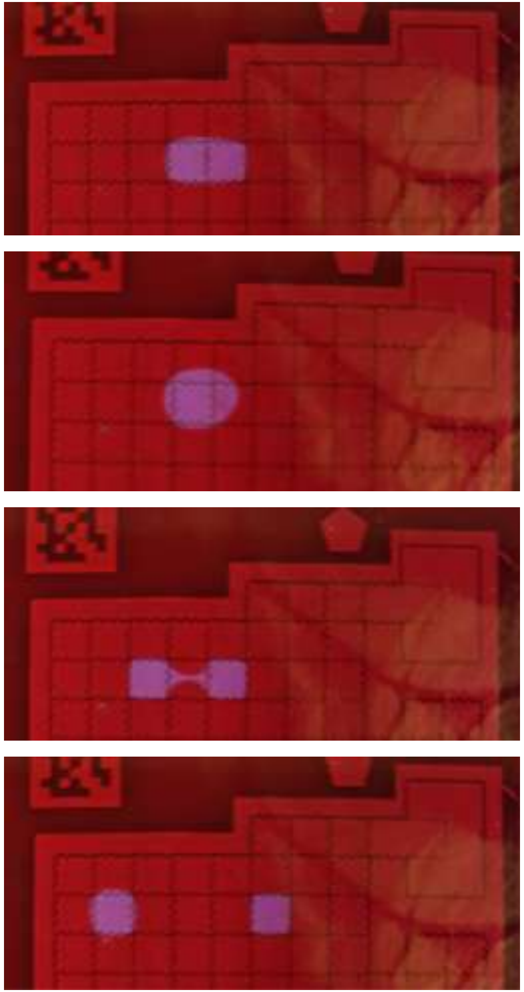




Experiments: Split Pattern

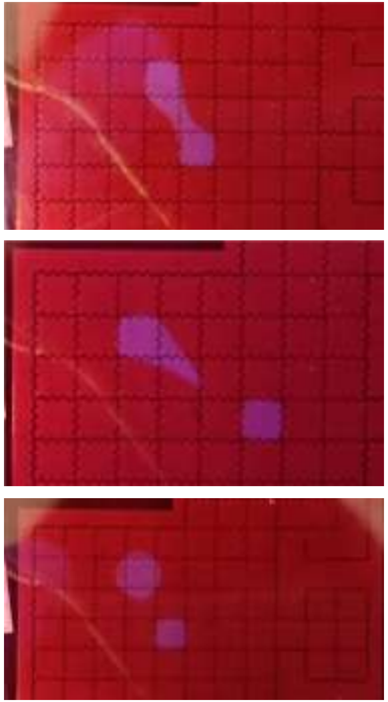
2. Combine into 1x1, and do normal split



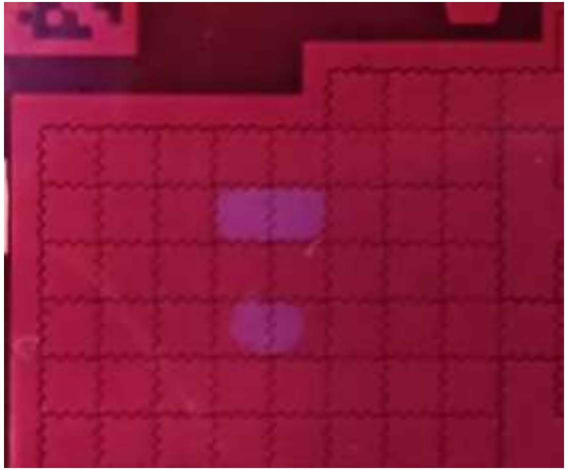


Experiments: Split Pattern

3. Up-Left, Down-Right

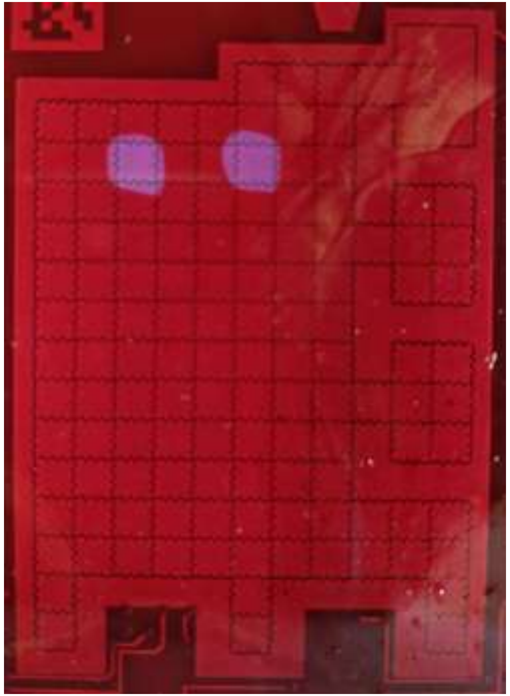


4. Lengthwise split as opposed to heightwise

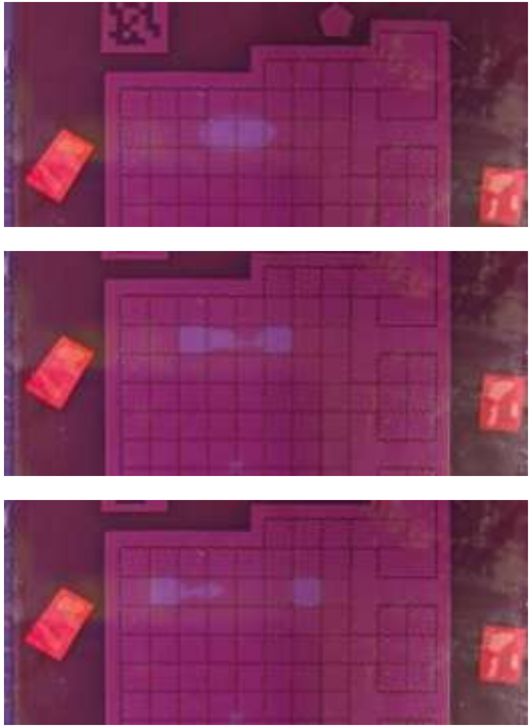


Experiments: Volume, Spacing, [V-S Ratio], Viscosity

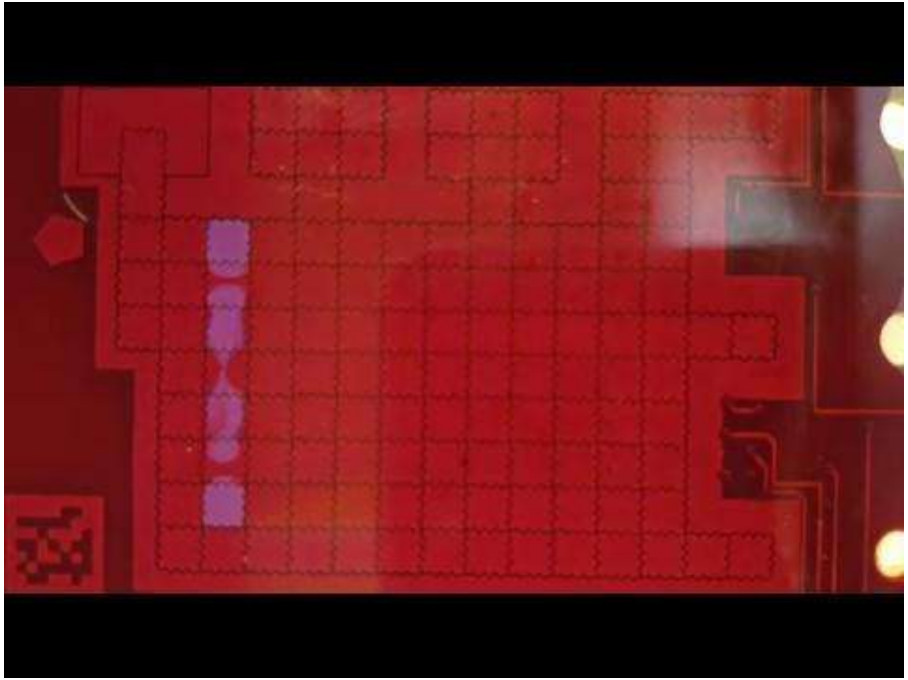
Larger volume/spacing ratio

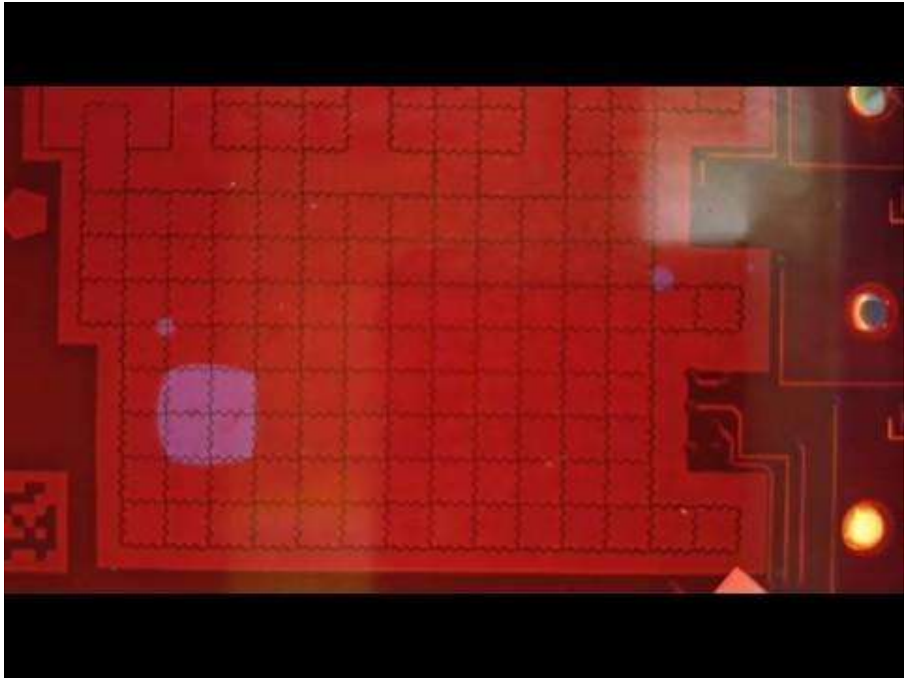


Higher oil viscosity



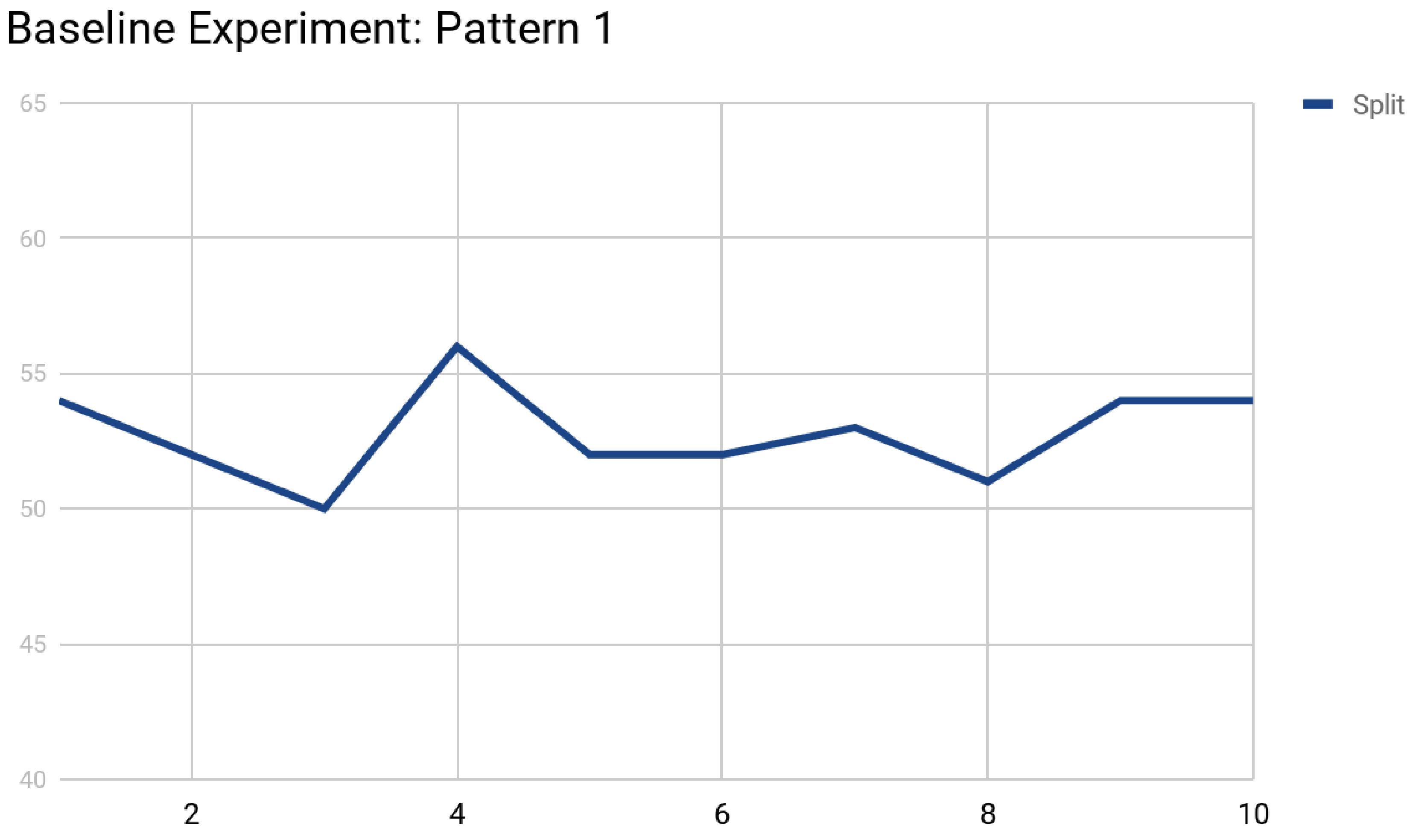
Other Shapes: 3x1, 2x2

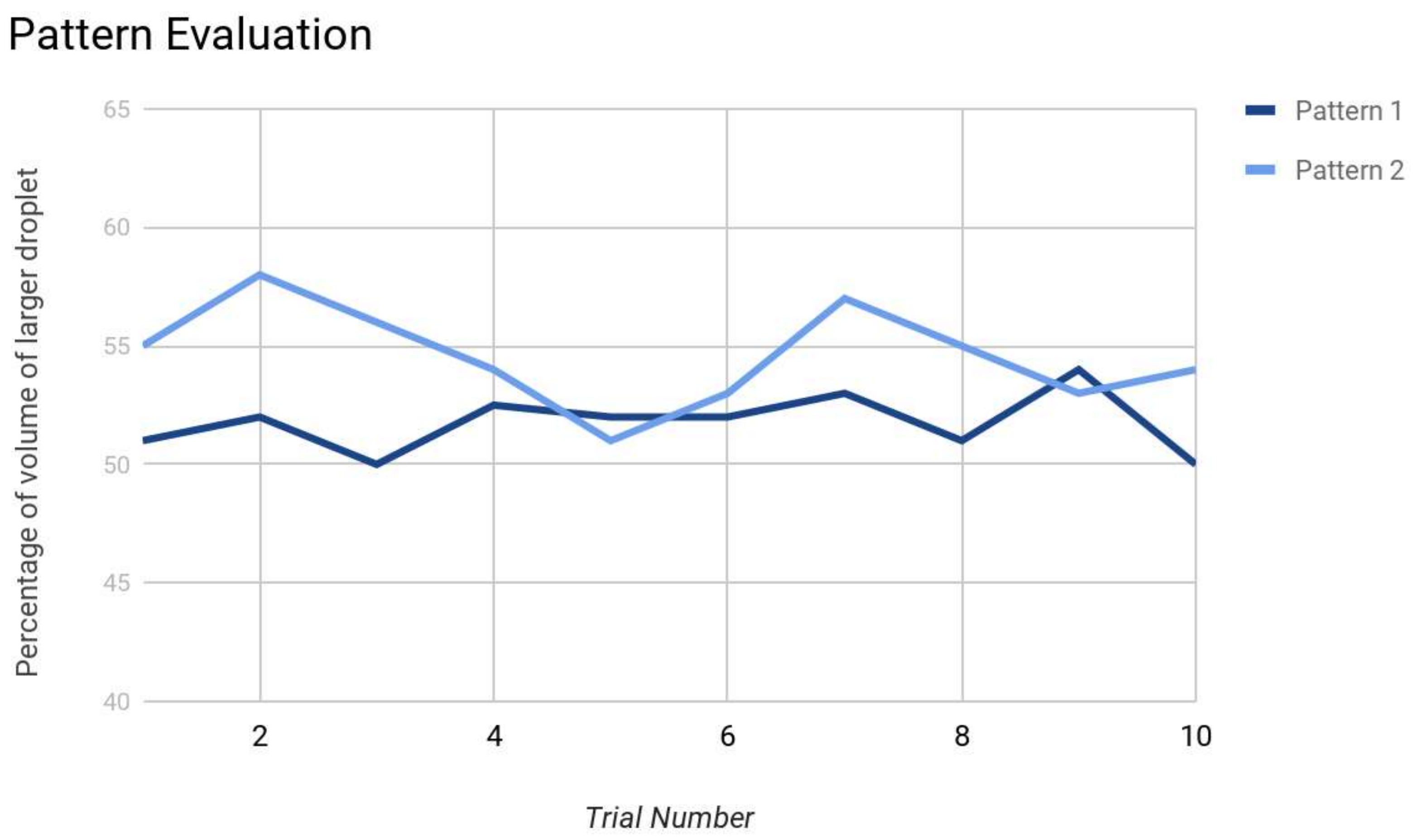


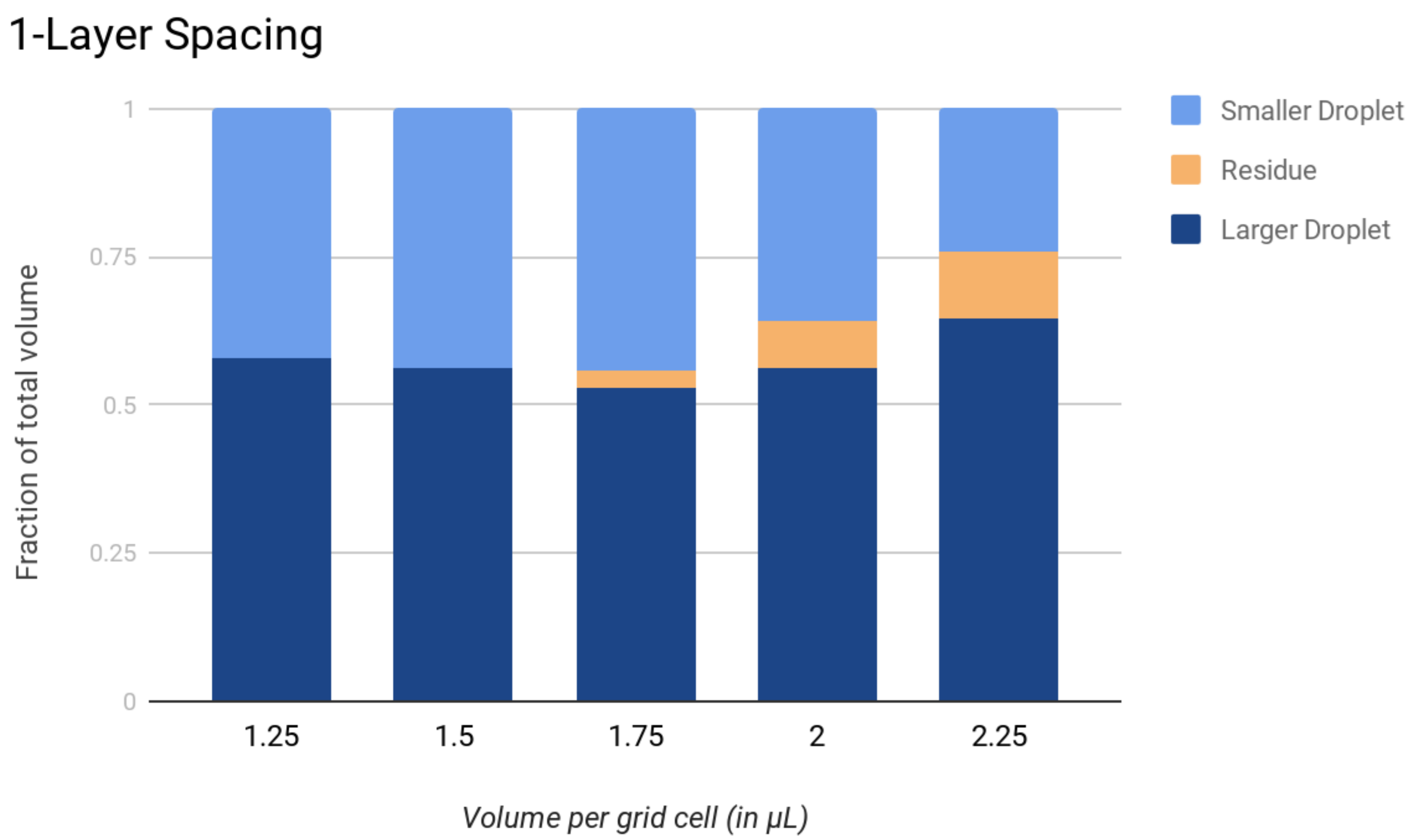


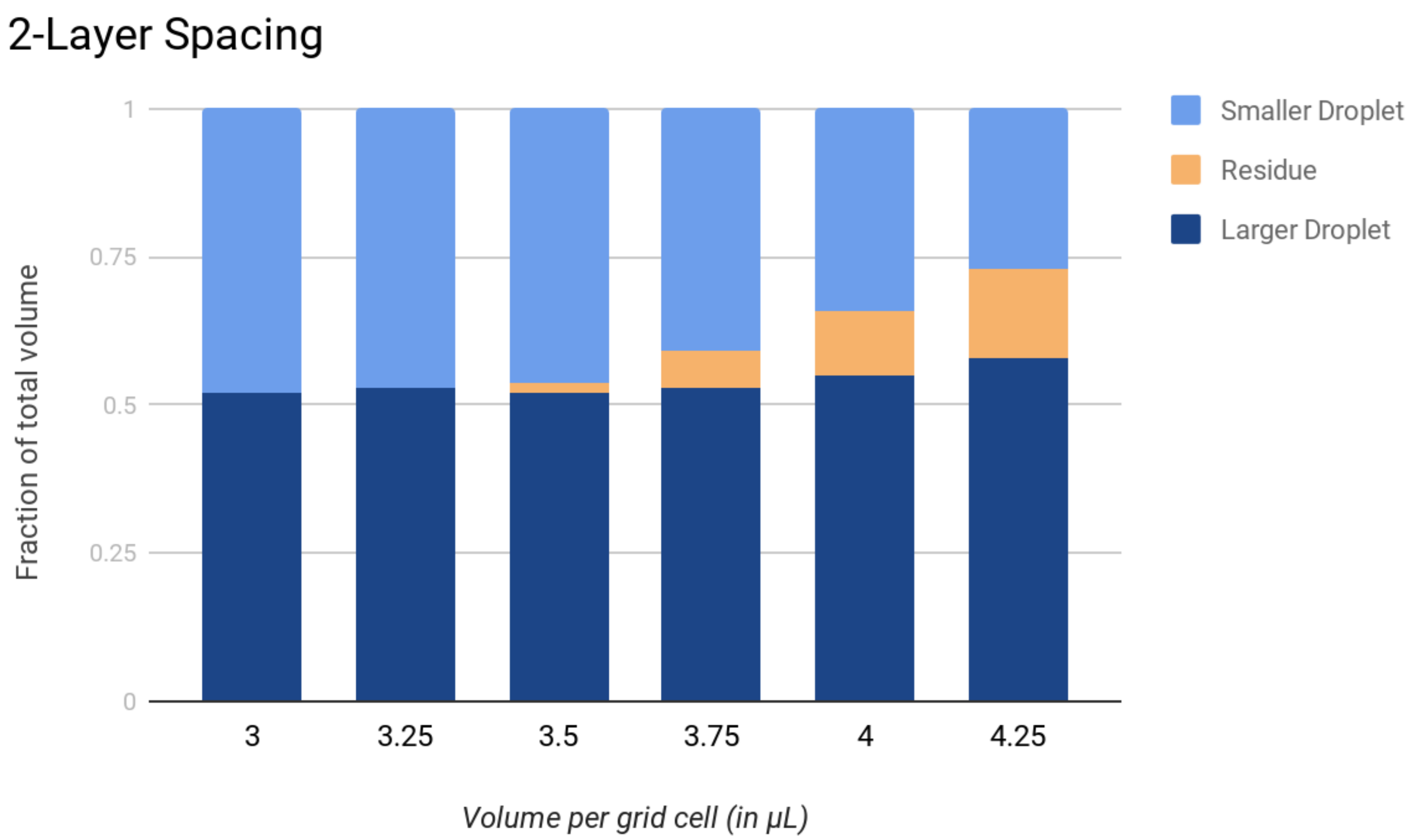
Results

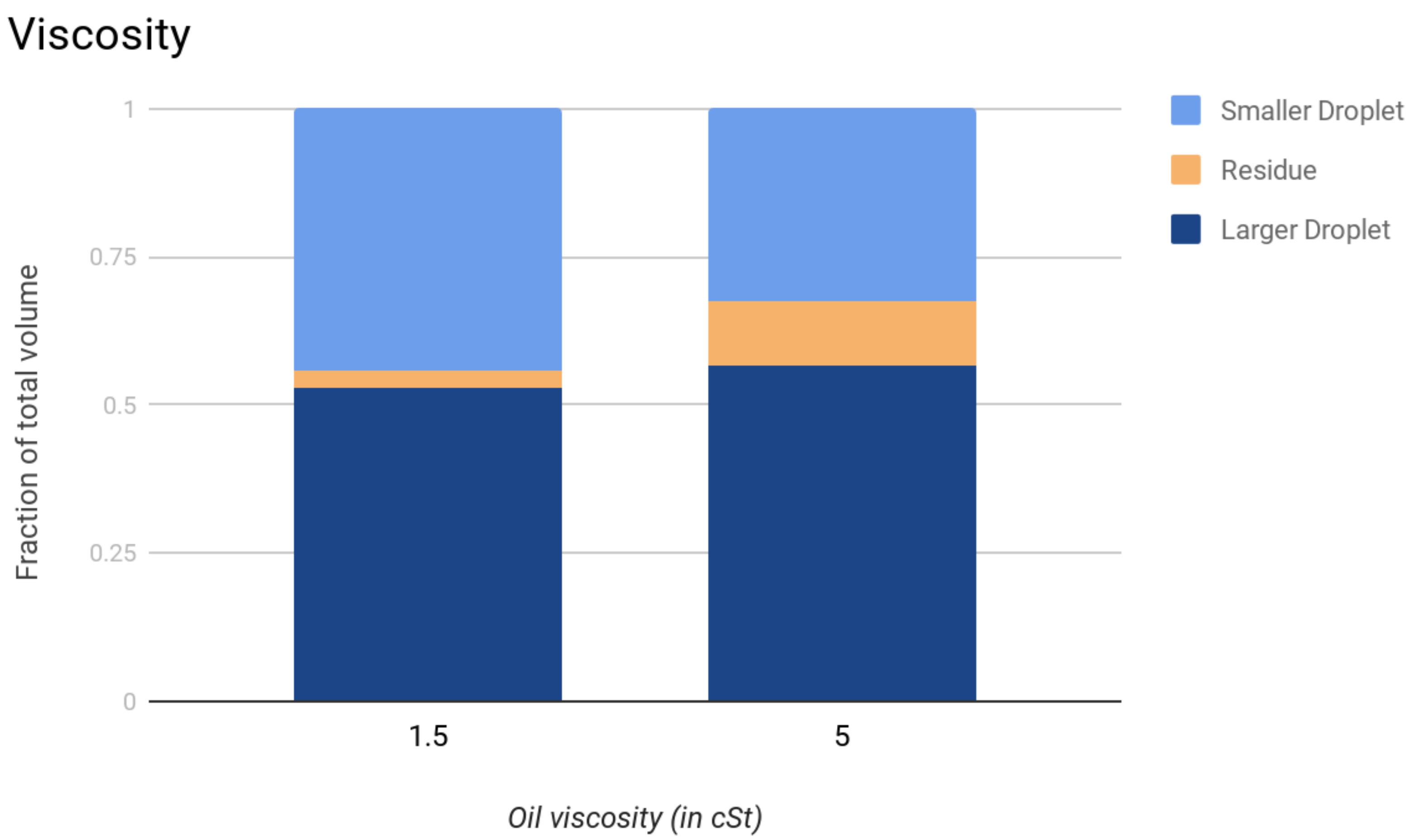
- Results were measured as the ratio of the split
- Approximately 20 total variable permutations, with 10+ experiments per permutation
- Ratio computation:
    - For each experiment, fixed camera was mounted facing the PurpleDrop board
    - Pictures taken of start and finish stages of the split
    - Using image analysis with the GIMP software, the sizes of the split droplets were identified and compared
- Residue
    - Occasionally because of the size of the droplets, the splitting experiments left behind residual fluid -- but this was clearly correlated to the variables being controlled in the experiment
    - This is also a clear indicator of the *possibility* of splitting, because residue indicates that the electrowetting force that should be pulling a droplet away is not strong enough to do so

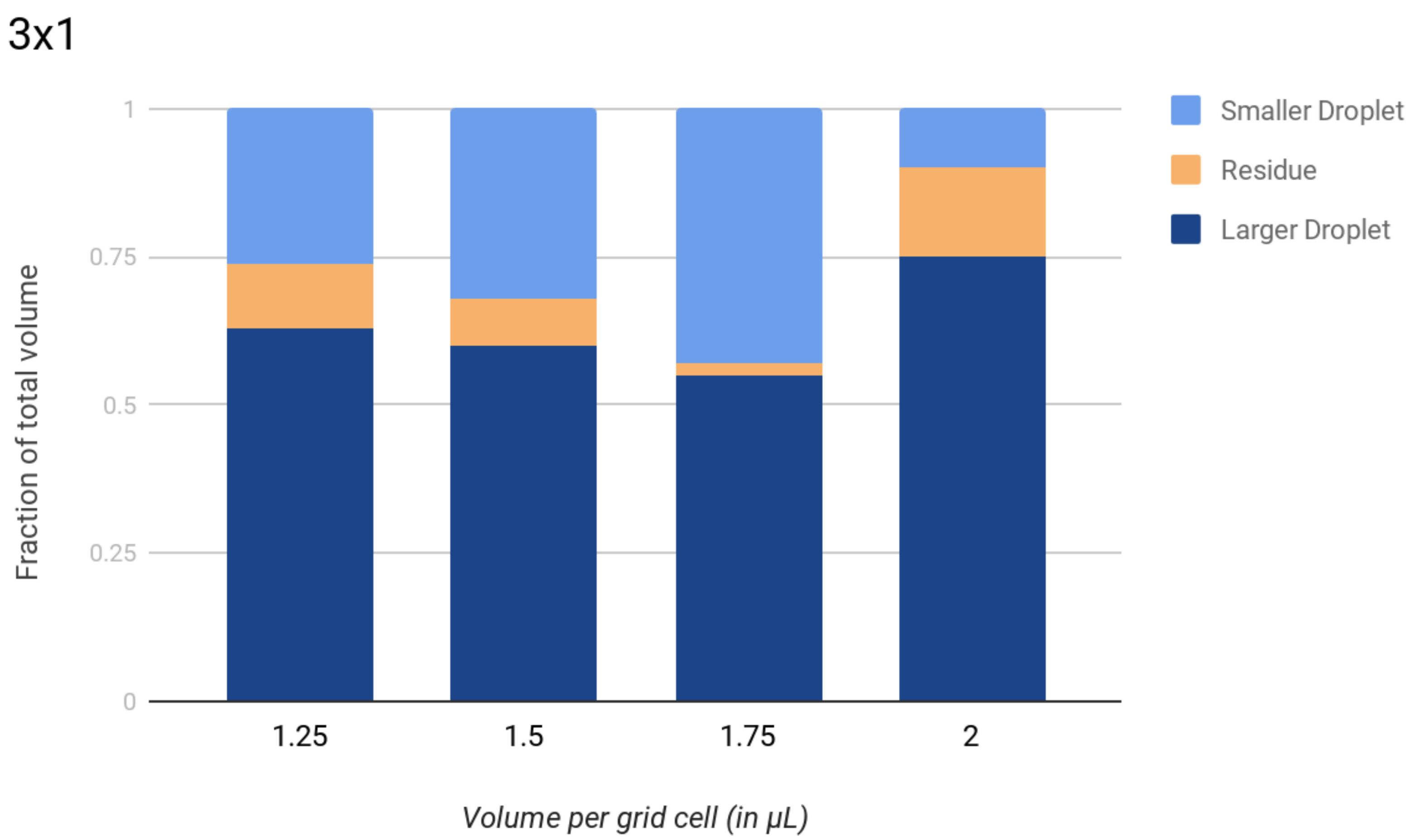

Baseline Experiment: Pattern 1
65
60
55
50
45
40
2
4
6
8
10
Split


Pattern Evaluation
Pattern 1
Pattern 2
Percentage of volume of larger droplet
65
60
55
50
45
40
2
4
6
8
10
Trial Number


1-Layer Spacing
Smaller Droplet
Residue
Larger Droplet
Fraction of total volume
1
0.75
0.5
0.25
0
1.25
1.5
1.75
2
2.25
Volume per grid cell (in μL)


2-Layer Spacing
Smaller Droplet
Residue
Larger Droplet
Fraction of total volume
1
0.75
0.5
0.25
0
3
3.25
3.5
3.75
4
4.25
Volume per grid cell (in μL)


Viscosity
Fraction of total volume
1
0.75
0.5
0.25
0
1.5
5
Oil viscosity (in cSt)
Smaller Droplet
Residue
Larger Droplet


3x1
Fraction of total volume
1
0.75
0.5
0.25
0
1.25
1.5
1.75
2
Volume per grid cell (in μL)
Smaller Droplet
Residue
Larger Droplet

Result Analysis

- Patterns:
  - Clearly the basic split (Pattern 1) is continuously the most accurate split
  - The second closest is Pattern 2, but the main drawback with this is that not all droplet sizes can be compressed from 2x1 to 1x1
- Volume
  - For a given spacing, there is a droplet volume that is closest to occupying an electrode's space almost perfectly, and thus resulting in the cleanest splits
  - For 1-layer spacing, this is 1.75 µL, and for 2-layer spacing this is between 3 and 3.5 µL
  - **Smaller droplet sizes** leads to inaccurate splits because the size of the to-be-split droplets are not large enough to be controlled by the electrowetting force
  - **Larger droplet sizes** also lead to inaccurate splits, but in this case the intermolecular force in the fluid is much greater than the electrowetting force
  - **Larger droplets** also resulted in greater frequency of causing residue buildup

Result Analysis

- Spacing
  - **1-layer spacing fared much better** and getting a cleaner split than 2-layer spacing, corroborating the theory
  - Less spacing affects the contact angle of the droplet on the hydrophobic surface (the base plate), thus resulting in a greater force by the electrowetting force compared the bonding force keeping the multi-location droplet together
- Oil Viscosity
  - **Lower viscosity** definitely resulted in more motile droplets, as they encountered less resistance
  - While the higher viscosity oil did not inhibit the electrowetting force entirely, the time it took for the droplets to reach their destination once the electrodes were activated resulted in larger scope for residue

Conclusion and Future Work

- All in all, the physical variables affecting multi-location droplets were accurately assessed, and provide a clean picture of the ideal setup for large droplet splits
- For future work, integration of these split patterns with the Puddle software stack would give more control to the user, including potentially adding support for customized patterns
- This work is also part of the bigger movement from silicon-only computer systems to combined silicon/biological systems, which I am excited to see grow in coming years!

Acknowledgements

- Luis Ceze -- for inspiring me to pursue the HW/SW interface in 351, and helping me find a research project I am passionate about
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- Friends and family -- for being there to support me through the yearlong journey