# Cartridge Concepts 1

Nemo

Sept 11, 2019

# Overview

- Issues
- State Tables
  - Lyse n Go/Archival 0
    - Existing state
  - Lyse n Go 1
    - 3-way uni-directional valve
  - Lyse n Go 2
    - 3-way uni-directional valve
    - no manifold check valves
    - fill from bottom
  - Lyse n Go 3
    - 3 way bi-directional valve
    - 1 manifold check valve
- Assembly Layout Concepts
  - Reduced part count
- Subassembly Concepts
- Next Steps/Questions

# Issues

# Issues

| Cartridge | Issue | Ideas |
|---|---|---|
| LnG | Due to low second cracking pressure duckbill valve cracks when lysate travels to Burkert valve, leaking unknown amounts of lysate into puck | Replace duckbill with ball check valve<br>Adjust valve states |
| LnG | Loss of contact between actuator and plunger of syringe 2 when recouping lysate due to either plunger stiction or check valve cracking pressure too high | Lower friction materials/finishes/lubricant<br>Looser fit<br>Use archive style check valve or other lighter alternative. |
| LnG | When recouping lysate in syringe 2, air pressure above filter reaches bubble point and breaks through | Reduce pressure needed to push lysate into syringe 2. |
| LnG | Loss of contact between actuator and plunger of syringe 4 when pumping air | Magnetic analysis to optimize, making sure actuator force > magnet force<br>Software error detect |
| Both | Too much user cleaning, assembly, and disassembly time and difficulty | Reduce part count, detail design for ease of cleaning, assembly, and disassembly |

# Issues

## Concerns

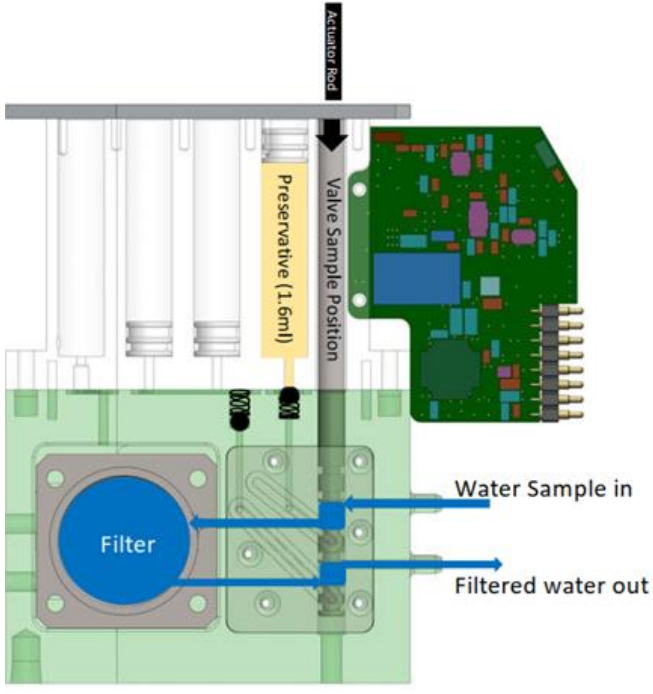
| Cartridge | Issue | Ideas |
|---|---|---|
| Both | Too much fabrication cost | Reduce part count, evaluate materials and prototype/production processes |
| Both | EPDM check valves swell or deform enough to get stuck resulting in a 3-4 month shelf life | Investigate alternative check valve materials/designs. |
| Archival | Preservative crystallizes when plunger isn't depressed past air vent | Add removable cap to ensure plunger is in correct location |
| Both | Improper assembly allows puck to leak | Reduce part count. Current post-assembly test seems to catch issues |
| LnG | As lysis buffer moves to puck, puck vents to syringe 4. Lysis buffer should not vent out syringe 4 | Continue as is.<br>Water/air filter, larger air volume above puck |
| Both | Salt crystals buildup from previous deployment in sample port | Adjust sample port cleaning process |

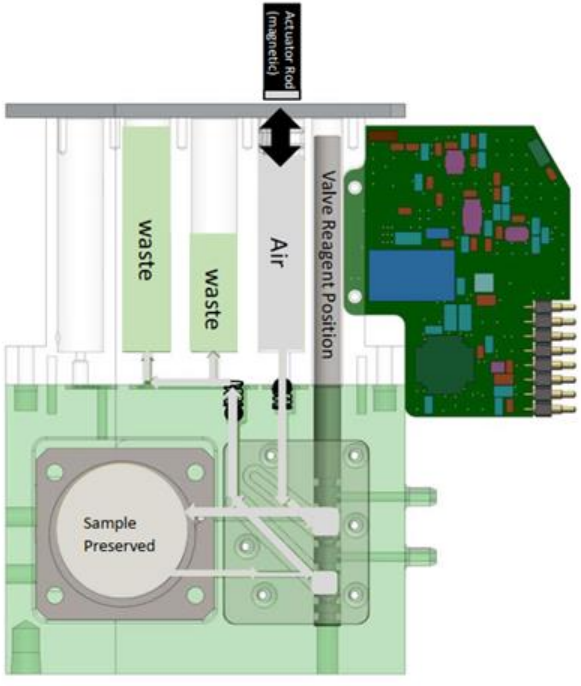
# State Tables

# State Tables

## Archival 0: Current

| | action | valve | | | syringe 1 | | | syringe 2 | syringe 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | preservative | | | waste | waste | | |
| | | | | | | | | manifold | | | |
| | | | | puck side | ▼ | | puck bottom | ▲ | | | |
| 1 | sample | sample | → | | | ← | | | | | Water in first to puck side, then water out for free flow |
| 2 | preserve | reagent | | ← | | | → | | | | Empty preservative from syringe 1. Incubate. Pump syringe 1 to push air and displace preservative, plungers not backed up |
| | | | water in | | | water out | | | | | |

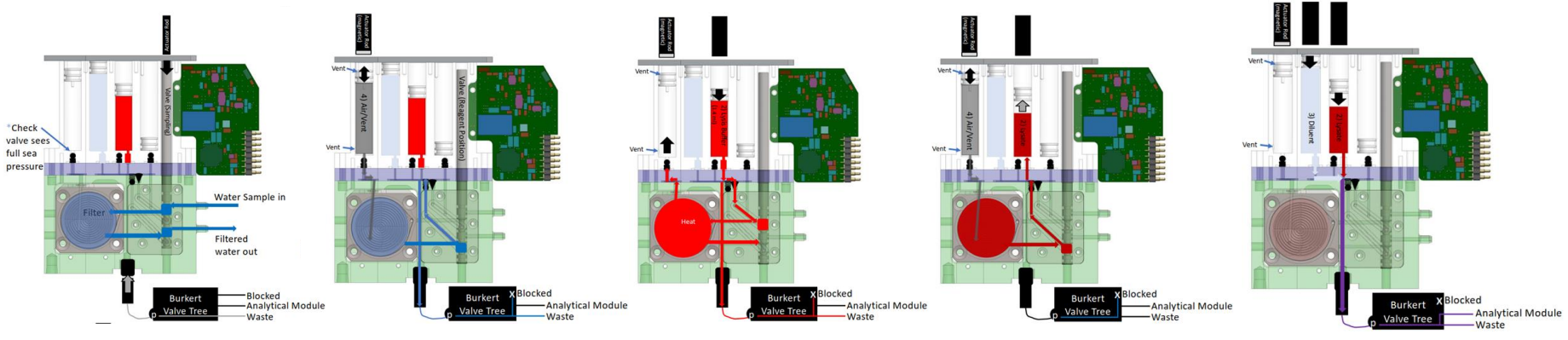


# State Tables

## Lyse n Go 0: Current

| | action | valve | syringe 4 | | | syringe 3 | syringe 2 | syringe 1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | air | | | diluent | lysis buffer | diluent 2 | | | |
| | | | ▼ | | | manifold | | | | | |
| | | | puck top | | puck side | duckbill▼ | | ▲ | puck bottom | | syringe 1 actuator used to lock cartridge in place |
| 1 | sample | sample | | → | | | | | → | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure |
| 2-4 | pressurize | reagent | ↓ | | | | X | | | | Pump syringe 4 air to exceed filter bubble point pressure, syringes 2&3 backed up |
| 5 | drain | reagent | | | | | ↓waste | ↑ | | | Open waste to drain water (30-60s), water remains between puck side and upper valve, air between upper valve and duckbill. Switch Bukert to check pressure and re-open drain as needed. Avoid leftover seawater that can lead to lysis buffer overflow into syringe 4 later |
| 6 | vent top | reagent | ↑ | | | | ↓waste | | | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | reagent | | | | | ↓waste | | | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml), duckbill should stay closed |
| 8 | fill puck | reagent | ↑ | | ↑ | ← | X | | | | Vent syringe 4, push syringe 2 to open duckbill and fill puck with puck side water, duckbill air, and lysis buffer. Air remains between puck bottom and checkvalve |
| 9 | pressurize | reagent | | | ↑ | ← | X | | | | Empty syringe 2, close syringe 4 checkvalve to set 20-60 psi pressure. Heat to 85°C, 14 minutes |
| 10a | pull bubble | | | | | | | ↑ | | | Pull syringe 2 0.2ml to extract puck bottom air |
| 10b | push bubble | | | | | ↓ | | | | | Push syringe 2 0.2ml to shunt air through duckbill and puck side |
| 10c | extract | reagent | ↓ | | | | X | ↑ | ← | | Pump syringe 4 to add pressure, servo retract syringe 2 to extract 0.9 ml lysate while sensing pressure. Need 15-16 psi to open small checkvalve (5 lb/in spring), but also <18 psi bubble point of filter |
| 11 | vent | reagent | ↑ | | | | ↓waste | ↑ | | | Relieve pressure from puck top and bottom |
| 12a | dump | reagent | | | | ← | ↓waste | | | | Push syringes 2 & 3 (lysate & diluent), dump initial mixture to waste, some leakage through duckbill. Want duckbill >4psi |
| 12b | analysis | reagent | | | | ← | ↓analysis | | | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, some leakage through duckbill. Some leakage may be OK (only with SPR |
| | | | | water in | | | Burkert | | | water out | |



# State Tables

## Lyse n Go 1: unidirectional 3-state valve

- Same as current process for steps 1-11
- 3rd position for sample/reagent valve - blocks manifold to puck channel forcing all lysate to exit through Burkert valve

| | action | valve | syringe 4 | | | syringe 2 | syringe 3 | syringe 1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | air | | | lysis buffer | diluent | diluent 2 | | | |
| | | | ▼ | | | manifold | | | | | |
| | | | puck top | | puck side | ▼ | | ▲ | puck bottom | | |
| 1 | sample | sample | | → | | | | | → | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure |
| 2-4 | pressurize | reagent | ↓ | | | | X | | | | Pump syringe 4 air to exceed filter bubble point pressure |
| 5 | drain | reagent | | | | | ↓waste | ↑ ← | | | Open waste to drain water, water remains between puck side and upper valve, air between upper valve and manifold |
| 6 | vent top | reagent | ↑ | | | | ↓waste | | | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | reagent | | | | | ↓waste | | | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml) |
| 8 | fill puck | reagent | ↑ | | | ↑ ← | X | | | | Vent syringe 4, push syringe 2 to fill puck with puck side water, manifold air, and lysis buffer. Air remains between puck bottom and checkvalve |
| 9 | pressurize | reagent | ↑ | | | ↑ ← | X | | | | Empty syringe 2, actuate syringe 4 checkvalve to set pressure. Heat to 85°C, 14 minutes |
| 10a | pull bubble | reagent | | | | | | ↑ | | | Pull syringe 2 0.2ml to extract puck bottom air |
| 10b | push bubble | reagent | | | | ↓ | | | | | Push syringe 2 0.2ml to shunt air through duckbill and puck side |
| 10c | extract | reagent | ↓ | | | | X | ↑ ← | | | Pump syringe 4 to add pressure, retract syringe 2 to extract puck bottom air then 0.9 ml lysate |
| 11 | vent | reagent | ↑ | | | | ↓waste | ↑ | | | Relieve pressure from puck top and bottom |
| 12a | dump | burkert | | | | | ↓waste | | | | Push syringes 2 & 3 (lysate & diluent), dump initial mixture to waste, burkert valve prevents leakage into puck |
| 12b | analysis | burkert | | | | | ↓analysis | | | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, check valve prevents leakage into puck |
| | | | | water in | | | Burkert | | | water out | |

# State Tables

## Lyse-n-Go 2: Uni-directional 3-state valve, fill from Puck Bottom

- 3 position valve similar to Lyse-n-Go 1 - blocks lysate from exiting via puck on step 12
- All manifold fluids enter puck from bottom eliminating manifold check valves. Flow can be adjusted or physical features can be added to prevent filter detachment

| | action | valve | syringe 4 | | | syringe 3 | syringe 2 | syringe 1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | air | | | diluent | lysis buffer | diluent 2 | | | |
| | | | ▼ | | | manifold | | | | | |
| | | | puck top | | puck side | | | | puck bottom | | |
| 1 | sample | sample | | → | | | | | → | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure |
| 2-4 | pressurize | reagent | ↓ | | | | X | | | | Pump syringe 4 air to exceed filter bubble point pressure |
| 5 | drain | reagent | | | | | ↓waste | | ↑ ← | | Open waste to drain water, water remains between puck top and upper valve, air between upper valve and manifold |
| 6 | vent top | reagent | ↑ | | | | ↓waste | | | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | reagent | | | | | ↓waste | | | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml) |
| 8 | fill puck | reagent | ↑ | | | | X | | → | | Vent syringe 4, push syringe 2 to fill puck with lysis buffer. |
| 9 | pressurize | reagent | ↑ | | | | X | | → | | Empty syringe 2, actuate syringe 4 checkvalve to set pressure. Heat to 85°C, 14 minutes |
| 10 | extract | reagent | ↓ | | | | X | | ↑ ← | | Pump syringe 4 to add pressure, retract syringe 2 to extract 0.9 ml lysate |
| 11 | vent | reagent | ↑ | | | | ↓waste | | ↑ | | Relieve pressure from puck top and bottom |
| 12a | dump | closed | | | | | ↓waste | | | | Push syringes 2 & 3 (lysate & diluent), dump initial mixture to waste, valve prevents leakage into puck |
| 12b | analysis | closed | | | | | ↓analysis | | | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, valve prevents leakage into puck |
| | | | | water in | | | Burkert | | | water out | |

# State Tables

## Lyse-n-Go 3: Bi-directional 3-state valve

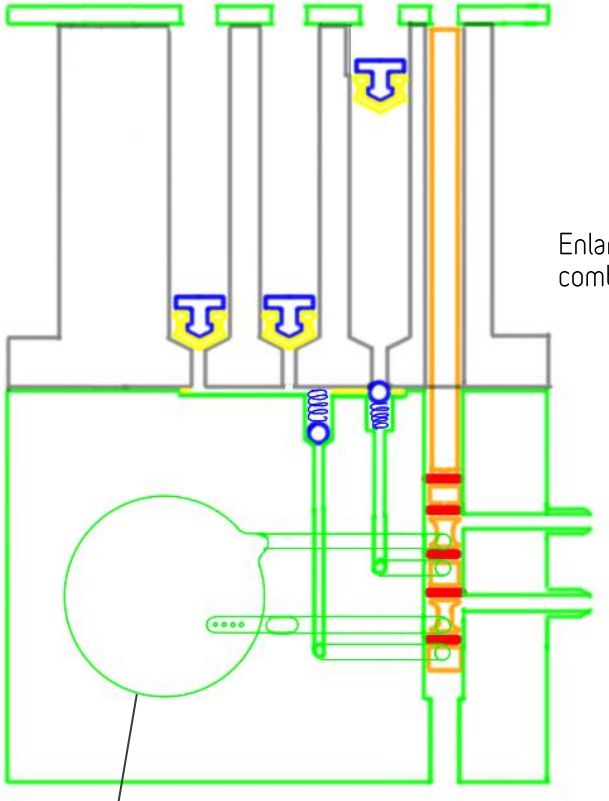
- 3 position valve connects sample to puck, manifold to puck side, and manifold to puck bottom
- Single manifold check valve still needed to prevent lysate from leaking into puck
- Valve is bi-directional and could use magnetic actuator. Alternatively, syringe 1 actuator can be repurposed for valve.
- Bi-directionality can be created with compression spring on bottom of valve

| | action | valve | syringe 4 | | | syringe 3 | syringe 2 | syringe 1 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | air | | | diluent | lysis buffer | diluent 2 | | | |
| | | | ▼ | | | manifold | | | | | |
| | | | puck top | | puck side | | | ▲ | puck bottom | | |
| 1 | sample | sample | | → | | | | | → | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure |
| 2-4 | pressurize | bottom | ↓ | | | | X | | | | Pump syringe 4 air to exceed filter bubble point pressure |
| 5 | drain | bottom | | | | | ↓waste | ↑ ← | | | Open waste to drain water, water remains between puck side and upper valve, air between upper valve and manifold |
| 6 | vent top | bottom | ↑ | | | | ↓waste | | | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | bottom | | | | | ↓waste | | | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml) |
| 8 | fill puck | side | ↑ | | ↑ ← | | X | | | | Vent syringe 4, push syringe 2 to fill puck with puck side water, manifold air, and lysis buffer. Air remains between puck bottom and checkvalve |
| 9 | pressurize | side | ↑ | | ↑ ← | | X | | | | Empty syringe 2, actuate syringe 4 checkvalve to set pressure. Heat to 85°C, 14 minutes |
| 10a | pull bubble | bottom | | | | | | ↑ | | | Pull syringe 2 0.2ml to extract puck bottom air |
| 10b | push bubble | side | | | | ↓ | | | | | Push syringe 2 0.2ml to shunt air to puck side |
| 10c | extract | bottom | ↓ | | | | X | ↑ ← | | | Pump syringe 4 to add pressure, retract syringe 2 to extract 0.9 ml lysate |
| 11 | vent | bottom | ↑ | | | | ↓waste | ↑ | | | Relieve pressure from puck top and bottom |
| 12a | dump | bottom | | | | | ↓waste | | | | Push syringes 2 & 3 (lysate & diluent), dump initial mixture to waste, check valve prevents leakage into puck |
| 12b | analysis | bottom | | | | | ↓analysis | | | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, check valve prevents leakage into puck |
| | | | | water in | | | Burkert | | | water out | |

# Assembly Layout Concepts

# Assembly Layout Concepts

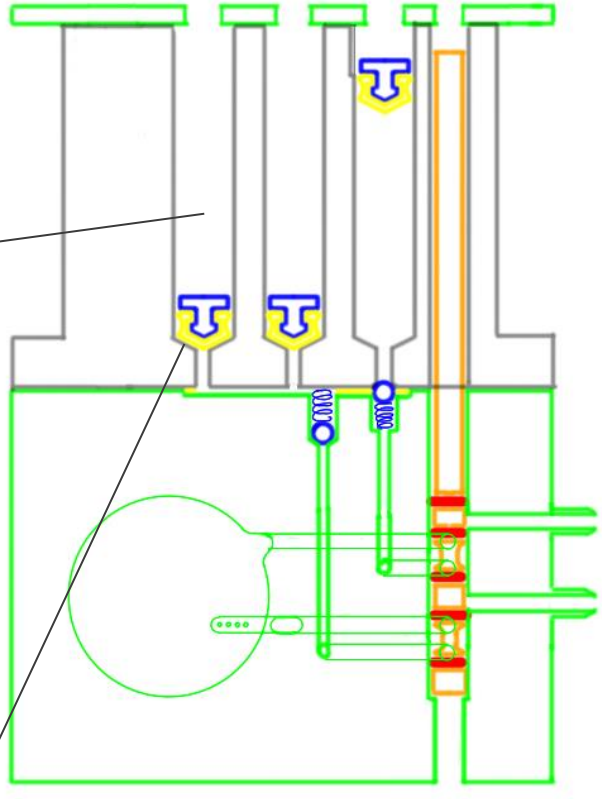
## Archival 0: Current



Sample

Combine Puck Bottom with Cartridge

Enlarged syringe 3 to combines 2 & 3

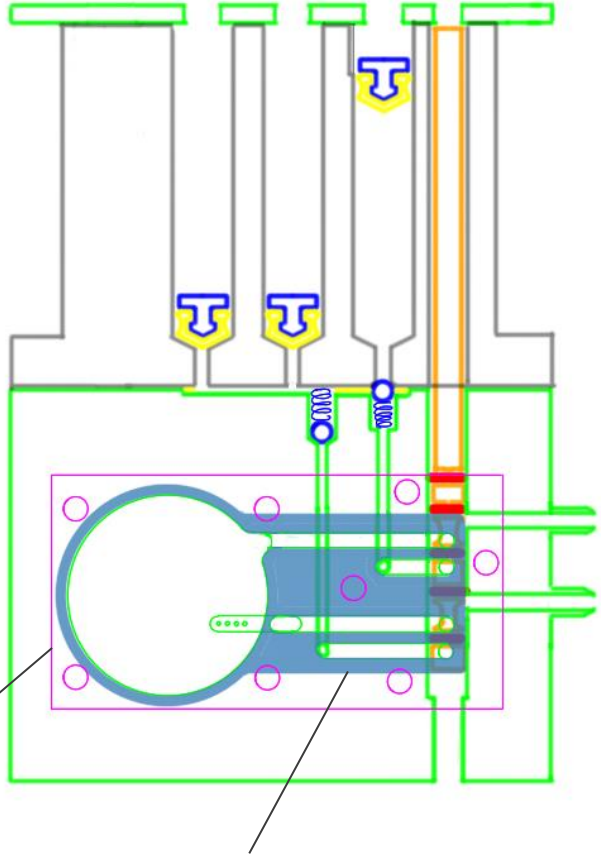


Reagent

Combine o-rings in syringe/cartridge interface plane into a single gasket

# Assembly Layout Concepts

Archival 0: Current

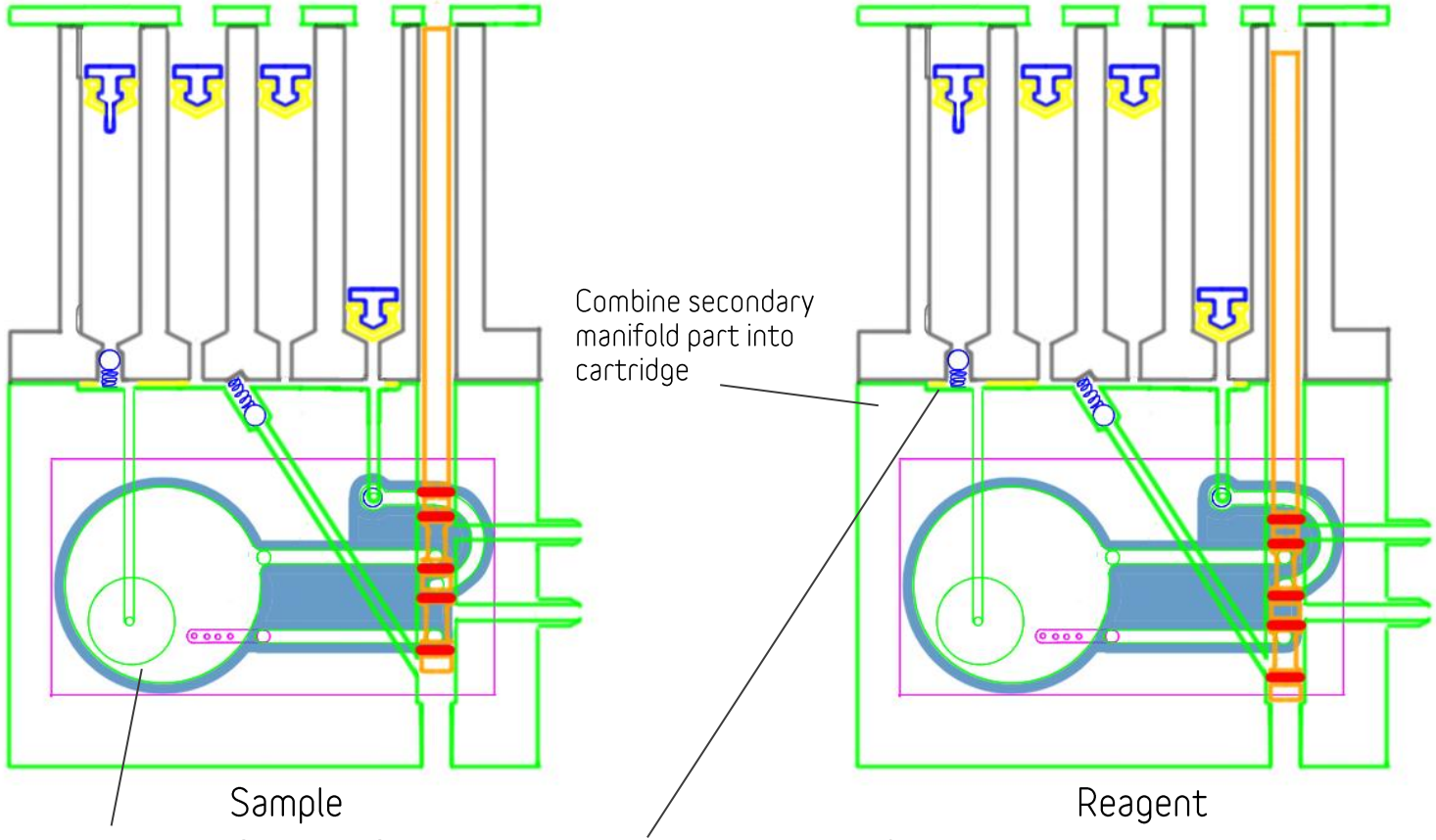


Combine Puck Top and Top Plate

Combine o-rings into planar gasket

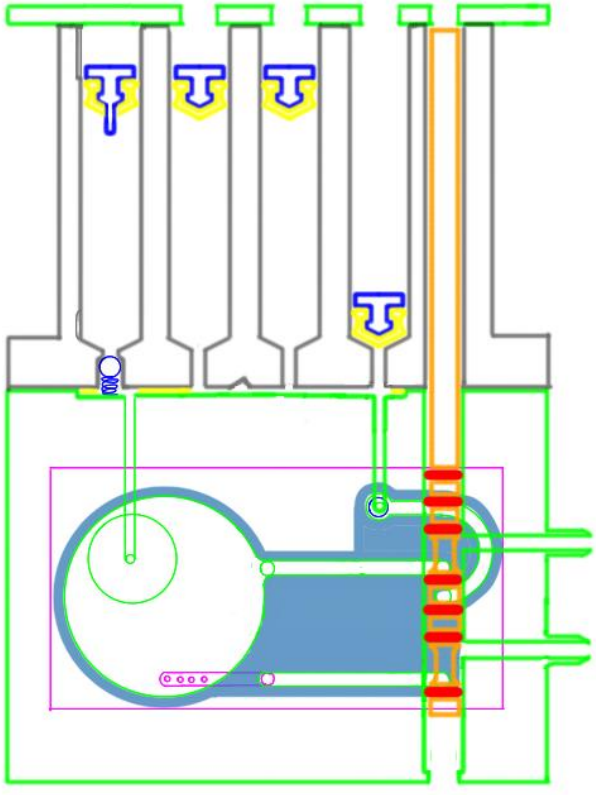
# Cartridge Concepts 1

Lyse-n-Go 0: Current

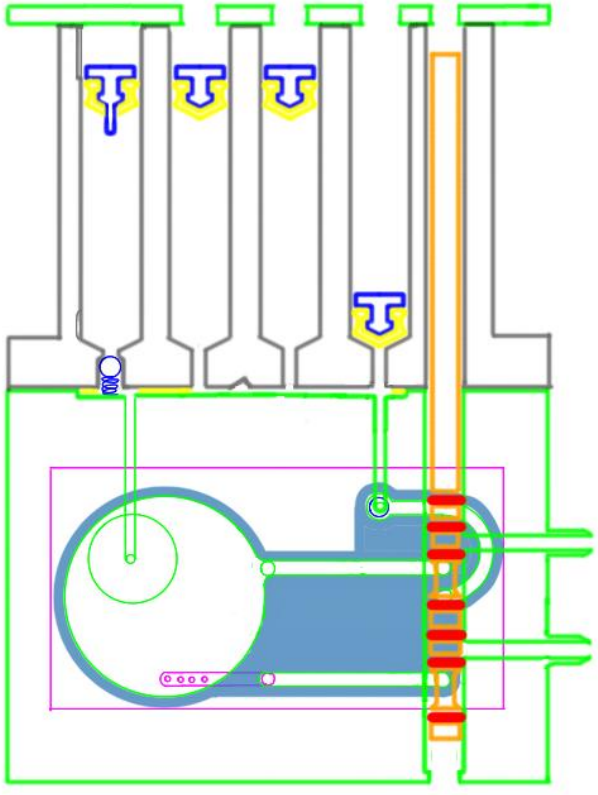


# Cartridge Concepts 1

Lyse-n-Go 2: Uni-directional 3-state valve, fill from Puck Bottom



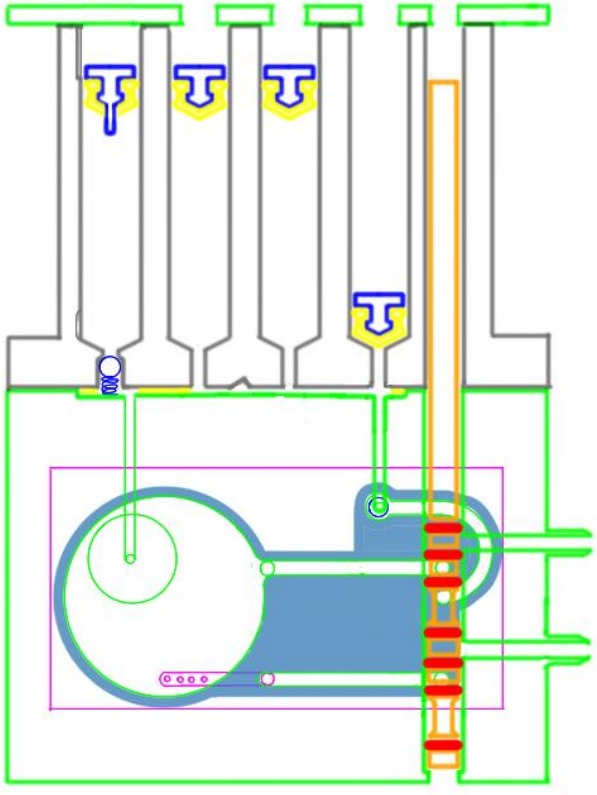
Sample



Reagent

# Cartridge Concepts 1

Lyse-n-Go 2: Uni-directional 3-state valve, fill from Puck Bottom



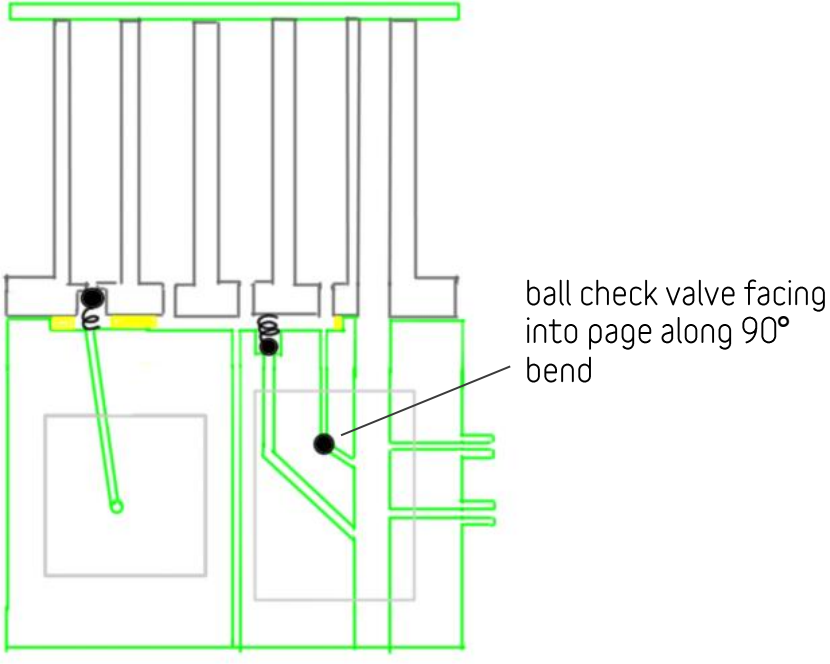
Closed

# Subassembly Concepts

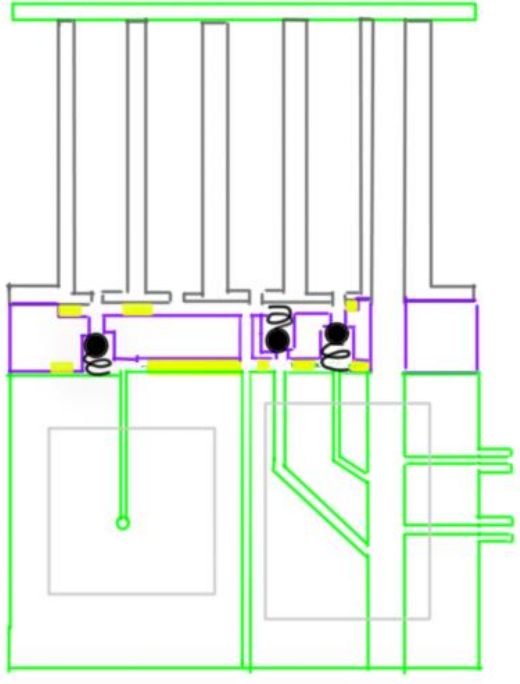
# Subassembly Concepts

## Check valves

- Reuse manifold spring and EPDM size balls from archival cartridge in Lyse n Go Cartridge




Example A



Example B

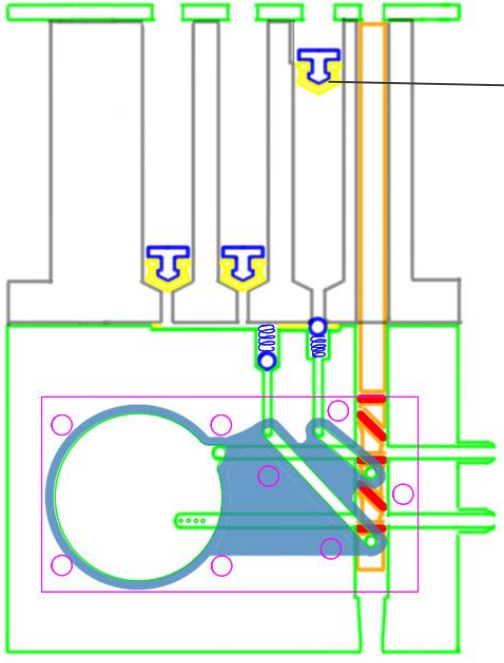
# Subassembly Concepts

## Check Valve Subassembly

- Make check valves subassemblies, similar to a ball detent.
- This might allow the use of a stiffer ball material (such as teflon or ceramic) to avoid sticking and moisture absorption.
- This would also allow quality checks outside of assembly.
- Subassembly or two matched parts

# Subassembly Concepts

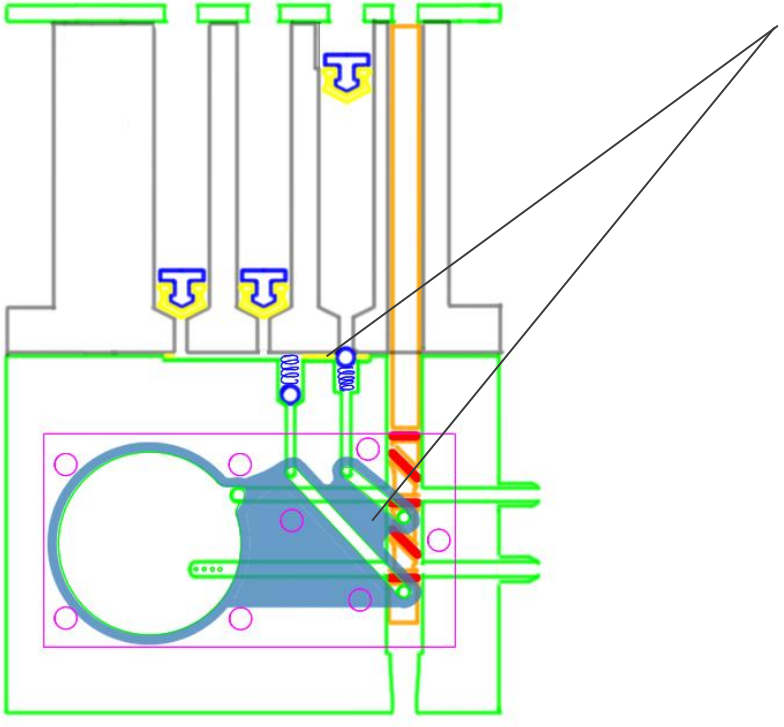
## Plungers



- Replace syringe o-rings with conical rubber plungers snapped over plated steel or plastic pistons.
- Moves plunger from 3-part to 2-part assembly
- Conical plunger/syringe is an independent feature to facilitate bubble removal when filling

# Subassembly Concepts

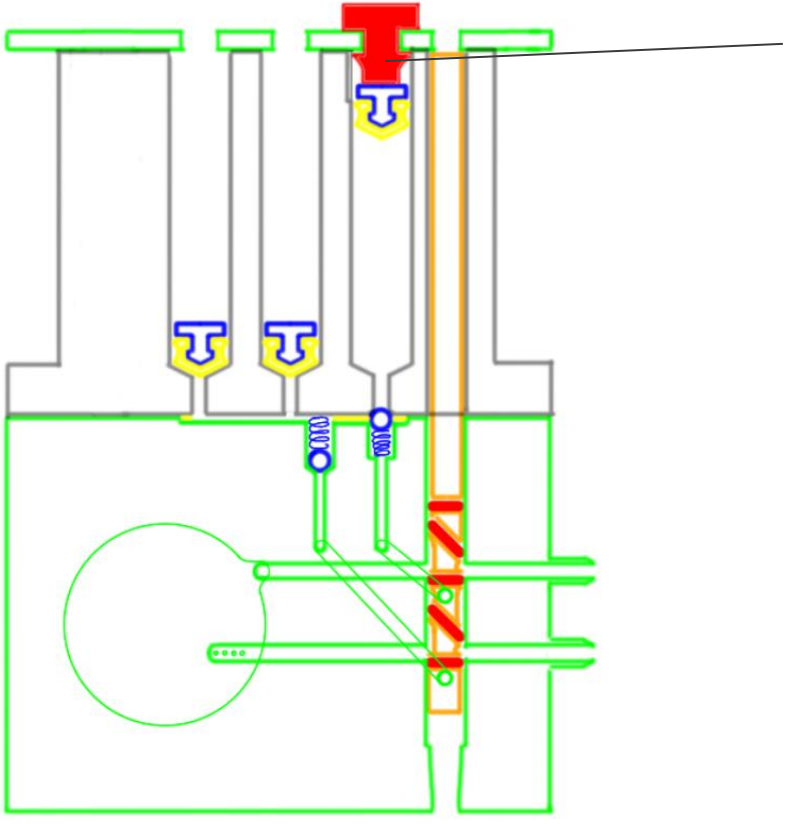
## Gaskets



- All gaskets on same plane to be combined into single cut or molded part
- Raised ridge could be drawn at seal location

# Subassembly Concepts

## Archival cap



- Snap on cap ensures preservative plunger is below vent
- Cap needs to be removed before installation into toroid

# Next Steps

Test pitch/roll corner cases (±20° pitch, ±?° roll)

Layout CAD for desired state/assembly arrangements

Additional Analysis:

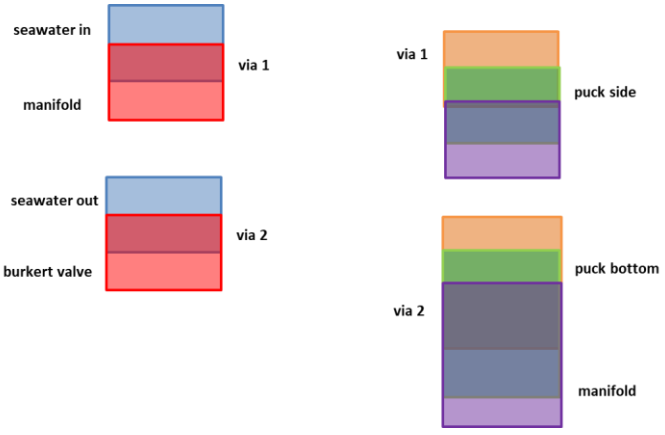
- valve study
- seal study (static & dynamic)
- magnet study
- material re-evaluation

# Appendix

# Appendix

## Lyse n Go 4: Dual Valves in Series

- Uses syringe 1 as a second valve
- Removes manifold check valves




| | action | valve | valve 2 (syringe 1) | syringe 4 | | | syringe 2 | syringe 3 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | air | | | lysis buffer | diluent | | | | | |
| | | | | ▼ | | | manifold | | | | | | |
| | | | | puck top | | puck side | | | | puck bottom | | | |
| 1 | sample | sample | puck side | | → | | | | | → | → | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure |
| 2-4 | pressurize | reagent/burkert | puck side | ↓ | | | | | | | X | | Pump syringe 4 air to exceed filter bubble point pressure |
| 5 | drain | reagent/burkert | puck side | | | | | | | | →↓waste | | Open waste to drain water |
| 6 | vent top | reagent/burkert | puck side | ↑ | | | | | | | ↓waste | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | reagent/burkert | puck side | | | | | | | | ↓waste | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml) |
| 8 | fill puck | reagent/burkert | puck side | ↑ | | ↑← | | | | | X | | Vent syringe 4, push syringe 2 to fill puck with puck side water, manifold air, and lysis buffer. Air remains betw checkvalve |
| 9 | pressurize | reagent/burkert | puck side | ↑ | | ↑← | | | | | X | | Empty syringe 2, actuate syringe 4 checkvalve to set pressure. Heat to 85°C, 14 minutes |
| 10 | extract | reagent/burkert | puck bottom | ↓ | | | | | ↑← | | X | | Pump syringe 4 to add pressure, retract syringe 2 to extract puck bottom air then 0.9 ml lysate |
| 11 | vent | reagent/burkert | puck bottom | ↑ | | | | | ↑ | | X | | Relieve pressure from puck top and bottom |
| 12a | dump | reagent/burkert | manifold | | | | | | | | ↓waste | | Push syringes 2 & 3 (lysate & diluent), dump initial mixture to waste, burkert valve prevents leakage into puck |
| 12b | analysis | reagent/burkert | manifold | | | | | | →← | | ↓analysis | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, check valve prevents leakage into puck |
| | | | | | water in | | | | | | Burkert | water out | |

# Appendix

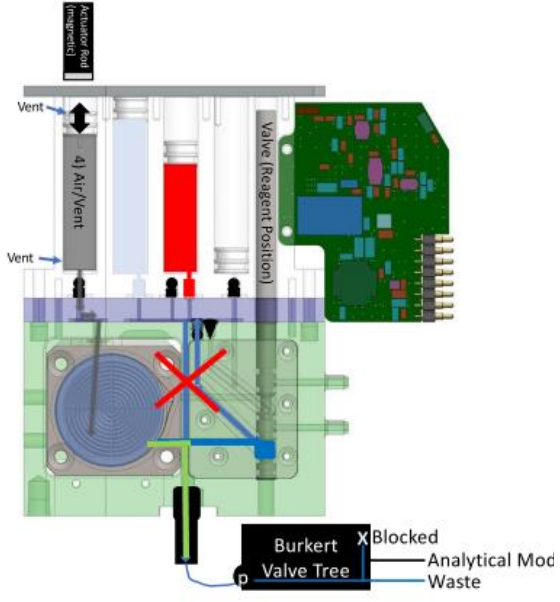
## Burkhert Valve from Puck

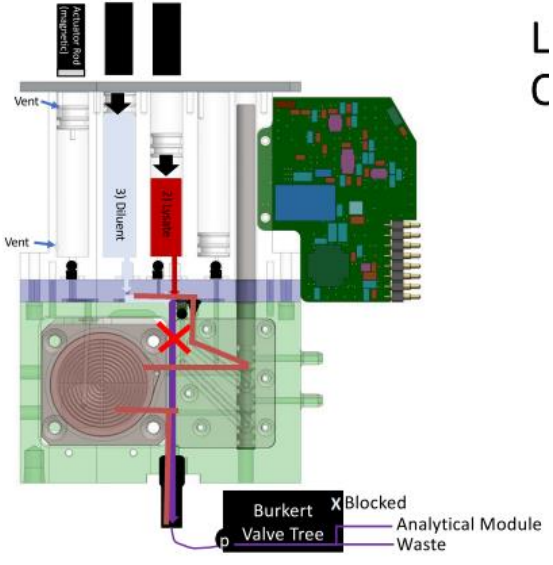
| | action | valve | syringe 4 | | | syringe 2 | syringe 3 | syringe 1 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | air | | | lysis buffer | diluent | diluent 2 | | | | |
| | | | ▼ | | | manifold | | | | | | |
| | | | puck top | | puck side | | | ▼ | puck bottom | | | |
| 1 | sample | sample | | → | | | | | → | X | | Water in first to puck side, then water out for free flow. Syringe 4 check valve sees full sea pressure. Burkert valve sees full sea pressure |
| 2-4 | pressurize | reagent | ↓ | | | | | | | X | | Pump syringe 4 air to exceed filter bubble point pressure |
| 5 | drain | reagent | | | | | | → | | ↓waste | | Open waste to drain water, water remains between puck side and upper valve, water remains between puck side and upper valve, air between upper valve and manifold |
| 6 | vent top | reagent | ↑ | | | | | | | ↓waste | | Vent syringe 4 to relieve puck top pressure |
| 7 | fill line | reagent | | | | | | | | ↓waste | | Push syringe 2 to displace Bukert line air with lysis buffer (0.3 ml) |
| 8 | fill puck | reagent | ↑ | | ↑ ← | | | | | X | | Vent syringe 4, push syringe 2 to fill puck with puck side water, manifold air, and lysis buffer. Air remains between puck bottom and checkvalve |
| 9 | pressurize | reagent | ↑ | | ↑ ← | | | | | X | | Empty syringe 2, actuate syringe 4 checkvalve to set pressure. Heat to 85°C, 14 minutes |
| 10 | extract | reagent | ↓ | | | | | ↑ ← | | X | | Pump syringe 4 to add pressure, retract syringe 2 to extract puck bottom air then 0.9 ml lysate |
| 11 | drain | reagent | ↓ | | | | | | | ↓waste | | Pump syring 4 to add pressure, open drain to waste to remove remaining lysate |
| 12 | vent | reagent | ↑ | | | | | ↑ | | ↓waste | | Relieve pressure from puck top and bottom, Push syringes 2 & 3 (lysate & diluent) into puck |
| 13a | analysis | reagent | | | | | | | | ↓analysis | | Continue to push syringes 2 & 3 (lysate & diluent) to analysis, |
| 13b | drain | reagent | ↓ | | | | | | | ↓analysis | | Push syringe 4 to displace lysate/diluent buffer to analysis |
| | | | | water in | | | | | | Burkert | water out | |

# Appendix

## Burkhert Valve from Puck

- Burkhert Valve moves from manifold to puck bottom
- Antibody and lysate mixing done through puck



# Appendix

## Moving Filter