

Modular SFC: Value Proposition of CFC and Centrifan Technologies

04 December 2009

Herbert J. Hedberg

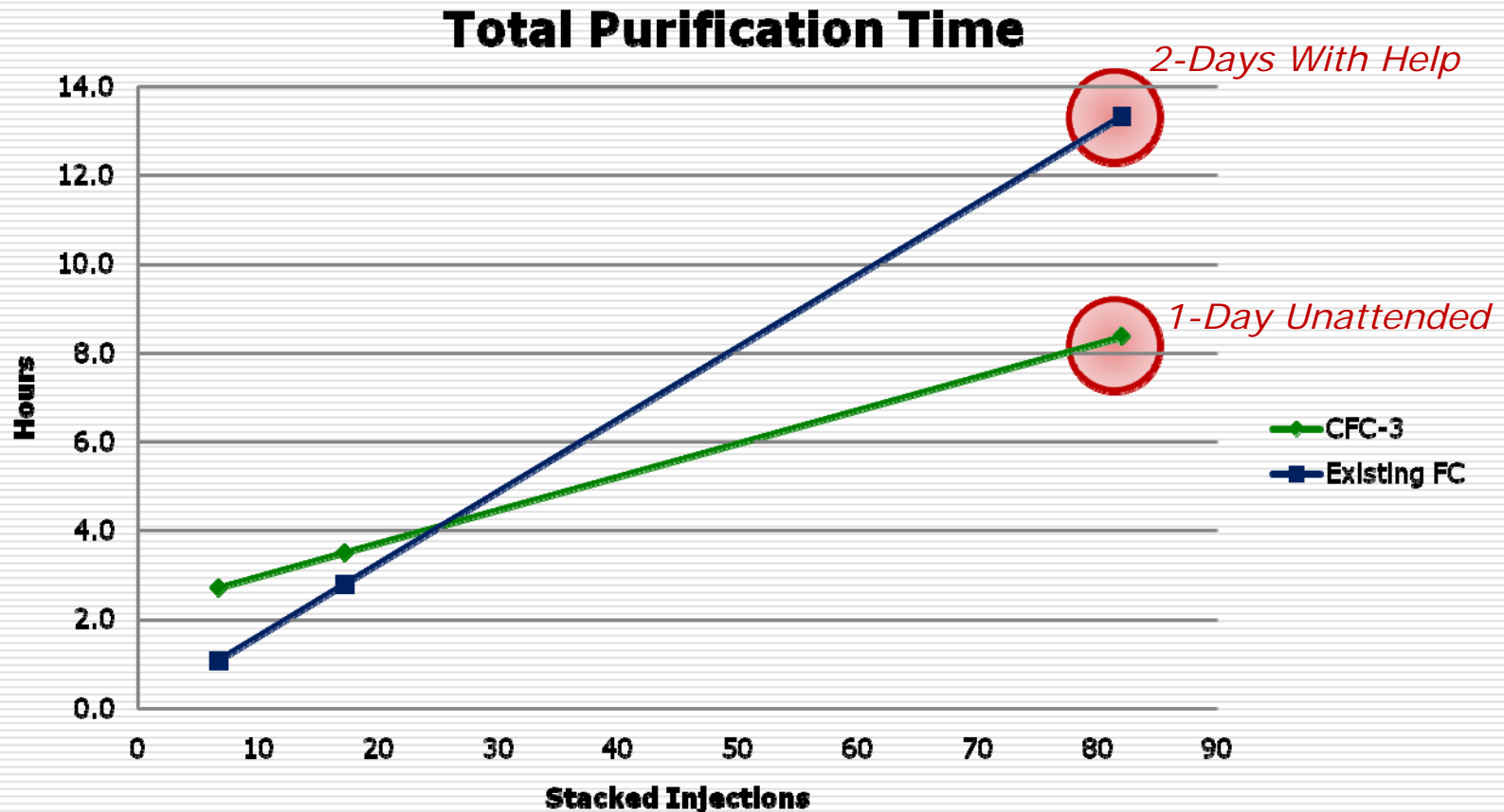


Simultaneous Evaporation

- Reduces stacked injection tasks*
 - **From:** two days with researcher help
 - **To:** one day unattended

*Reference: SFC Fraction Collection: Value of Simultaneous Evaporation, EAS 2009, Herbert J. Hedberg

Simultaneous Evaporation Reduces Purification Time



Value Increases with Scale

- Centrifugal fraction collector (CFC-3) technology is scalable
 - At higher flow rates, higher sample weights, return on instrument investment occurs much more quickly
 - Goal of 3 to 4 liters each for 2 fractions with simultaneous evaporation could be achievable goal of future instrument
 - Current prep rotor configurations:
 - 2 x 1L fractions
 - 3 x .66L fractions

Small Amounts of Difficult HPLC Compounds

- SFC Purification of hydrophobic peptides*
 - Sample quantity small
 - Recovery needs to have high purity
- Hydrophobic peptide impurities
 - Quantification
 - Isolation
- CFC-3 with 24-tube rotor
 - Yield and purity of HPLC fraction collection
 - Hi productivity from simultaneous concentration

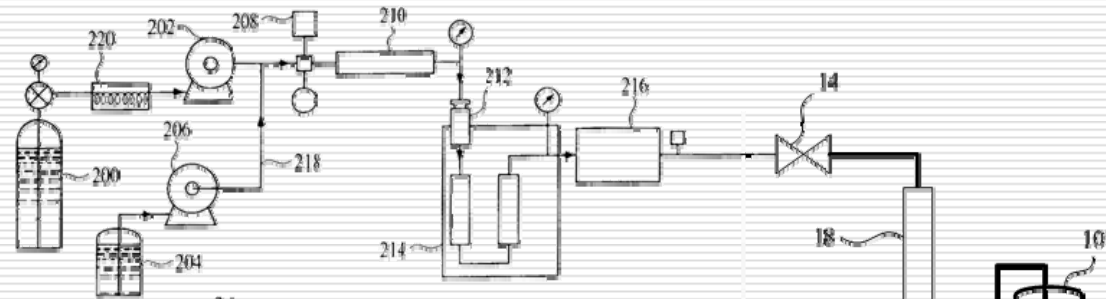
*Reference: Supercritical Fluid Chromatography of Peptides, Larry Taylor, Amer. Pharm. Review, Jul/Aug'09

Radiochemistry

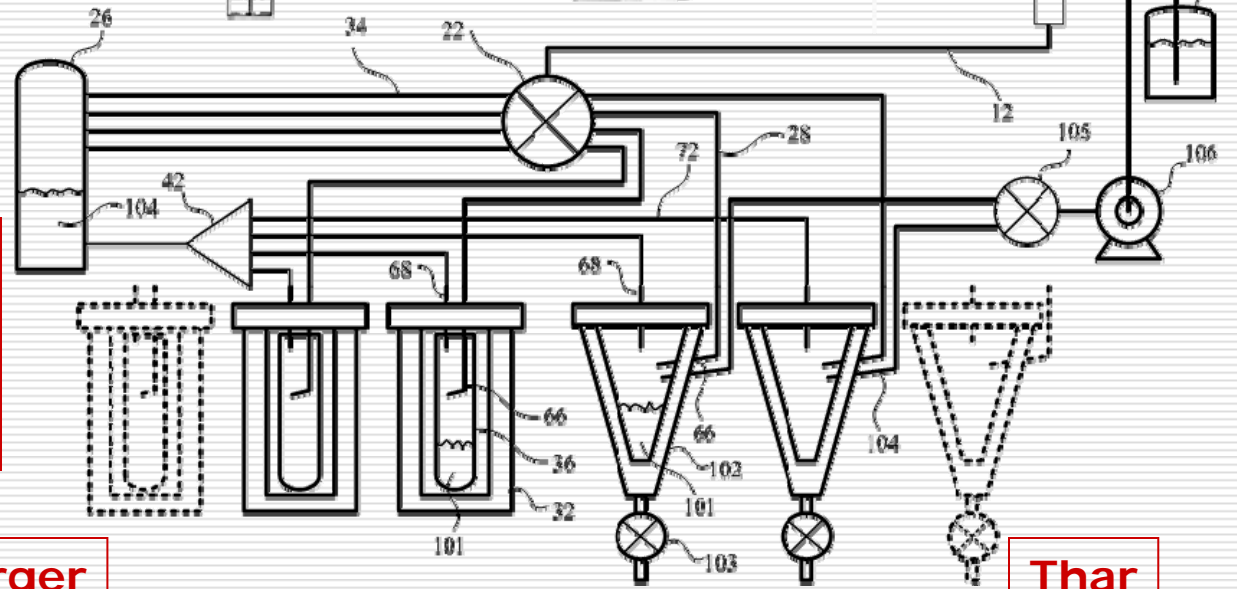
- Analysis of especially toxic compounds recommended only where eluant flow disposition can be assured
 - Less than 100% recovery has traditionally eliminated SFC from separations involving radioactive and other highly active and/or toxic compounds.
- CFC-3 Proof statement with radio-labeled compounds available 1Q10

System Cleaning Requires 3-Hours After Every Run

**Schematic
of Generic
SFC System**



**Typical
Fraction
Collector
Flow Path**

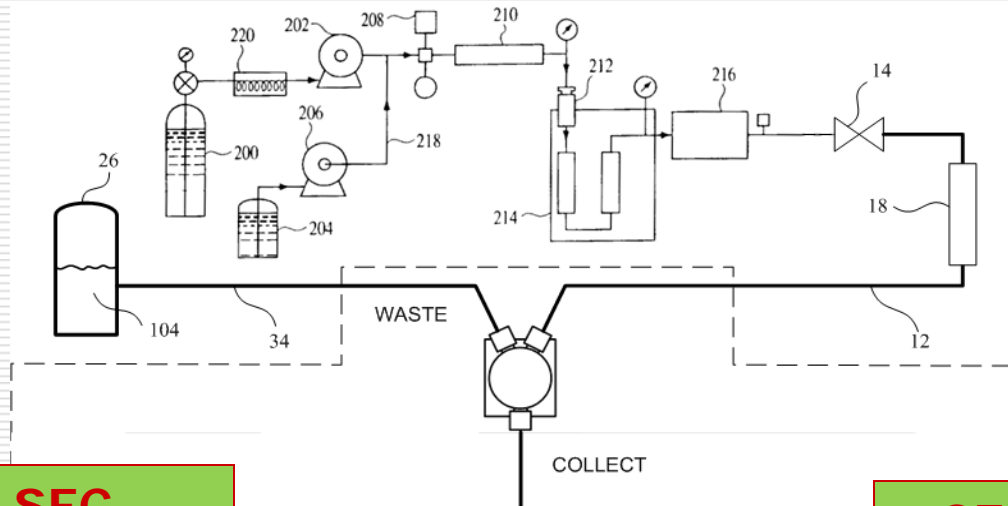


Berger

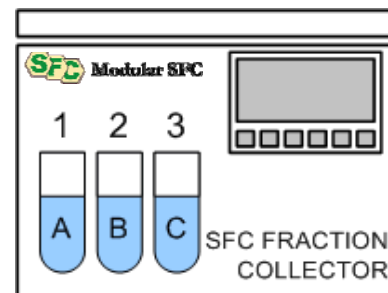
Thar

No Cleaning Downtime Between Runs with CFC-3

**Generic
SFC
System**



**Modular SFC
Fraction Collector
has single
continuously
flushed flow path
into replaceable
glassware**



**CFC-3 enables
multiple runs per
day instead of
single run plus
clean-up process**

Summary

- ❑ CFC-3 brings HPLC fraction collector performance and convenience to SFC
- ❑ Typical SFC instrument throughput increases because of single flow path
- ❑ Simultaneous evaporation reduces processing time for all purification jobs
 - SFC (organic modifiers)
 - HPLC (normal and reverse phase solvents)
 - Flash LC (normal phase solvents)

Contact Information

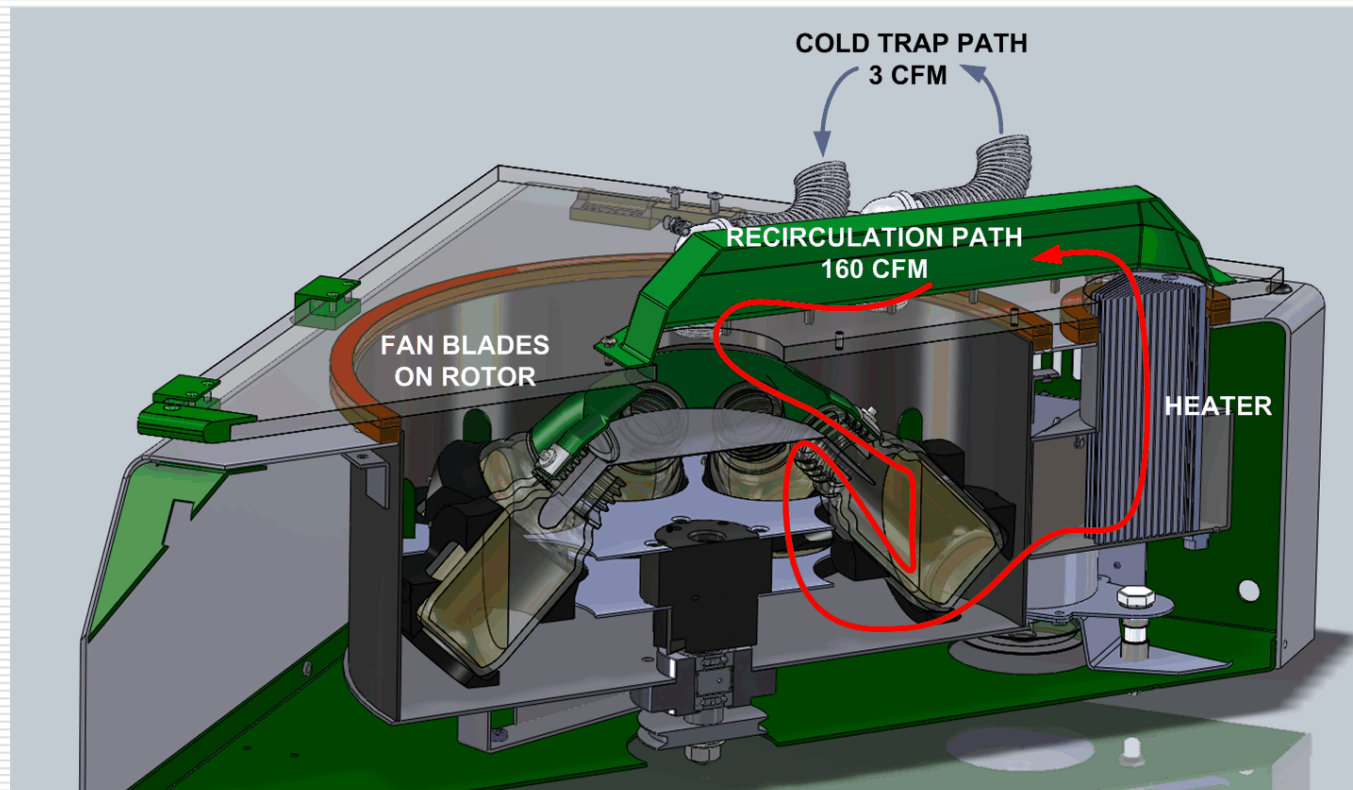
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Presentation



Backup Support Documents

Centrifan RE & AF



No vacuum... Recirculating Evaporation... Like nitrogen blowdown except centrifugal force preserves sample mass/integrity



Centrifan™ RE with Cold Trap

Shows optional connection for inert gas bleed and vent

C: Inert gas excess vents to hood (recommended)



C:

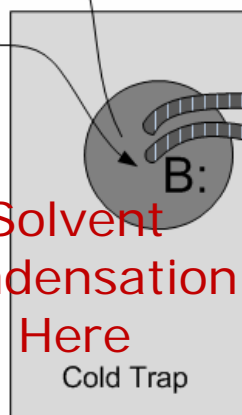
B: Inert gas and volatile solvent vapors circulate in closed loop through cold trap and back to Centrifan RE (3-5 cfm)

A: Inert gas and volatile solvent vapors circulate in closed loop through rotor containers and settable heater (ambient to 60°C) (100 - 200 cfm)

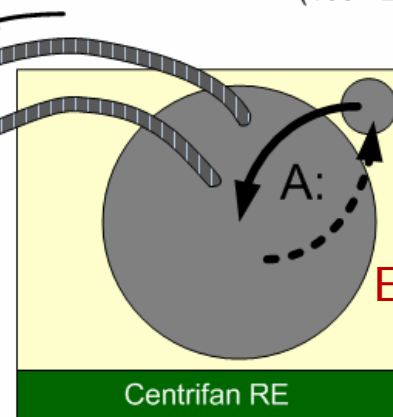
C: Inert gas bleeds into closed system to displace any volatile compound which could cause degradation (optional) (1 liter/hour typical)



Solvent Condensation Here



B: Volatile solvent vapors condense in cold trap



Solvent Evaporation Here

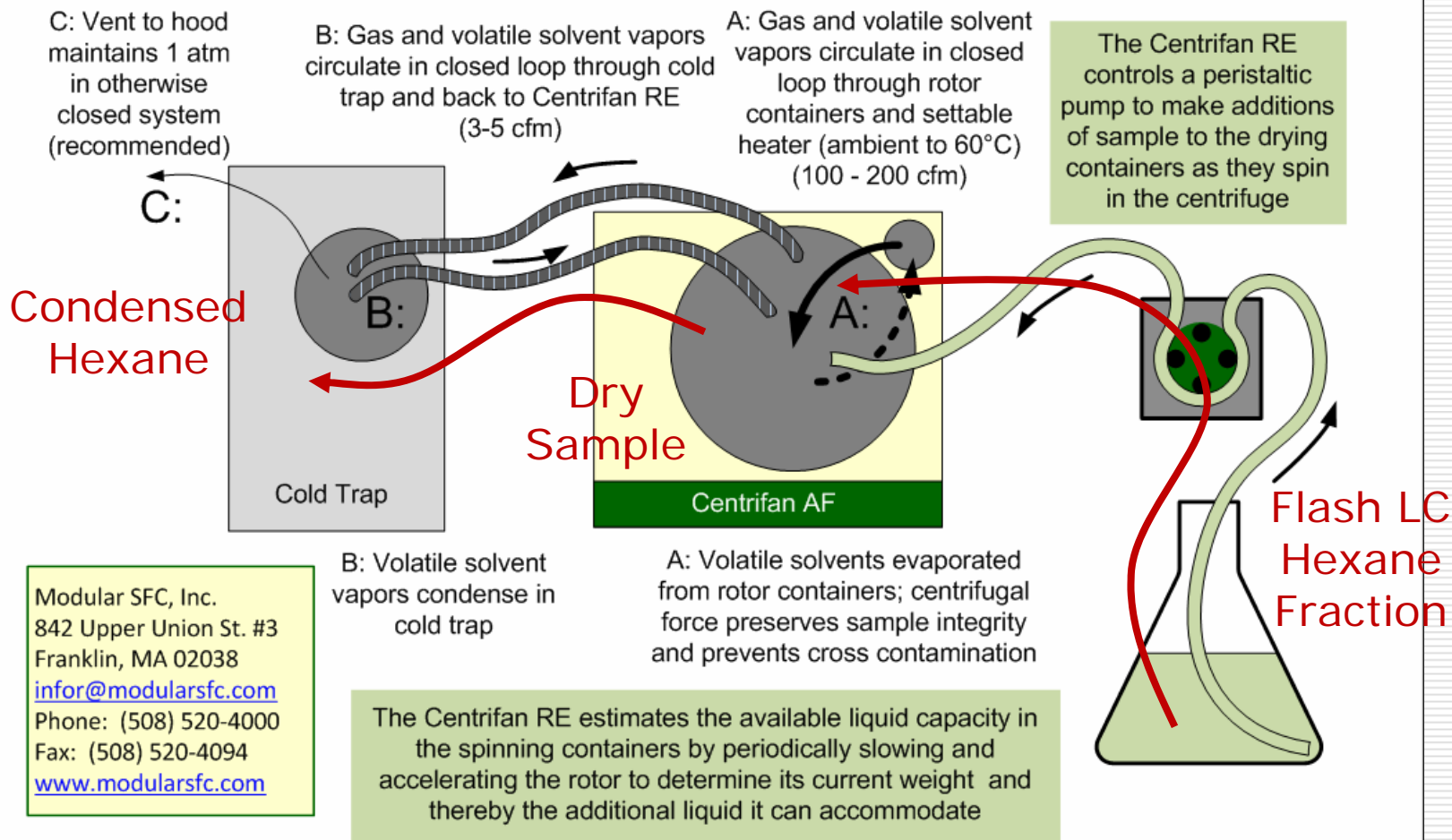
A: Volatile solvents evaporated from rotor containers; centrifugal force preserves sample integrity and prevents cross contamination

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Centrifan™ AF with Cold Trap

Shows optional connections for **Auto-Fill** feature



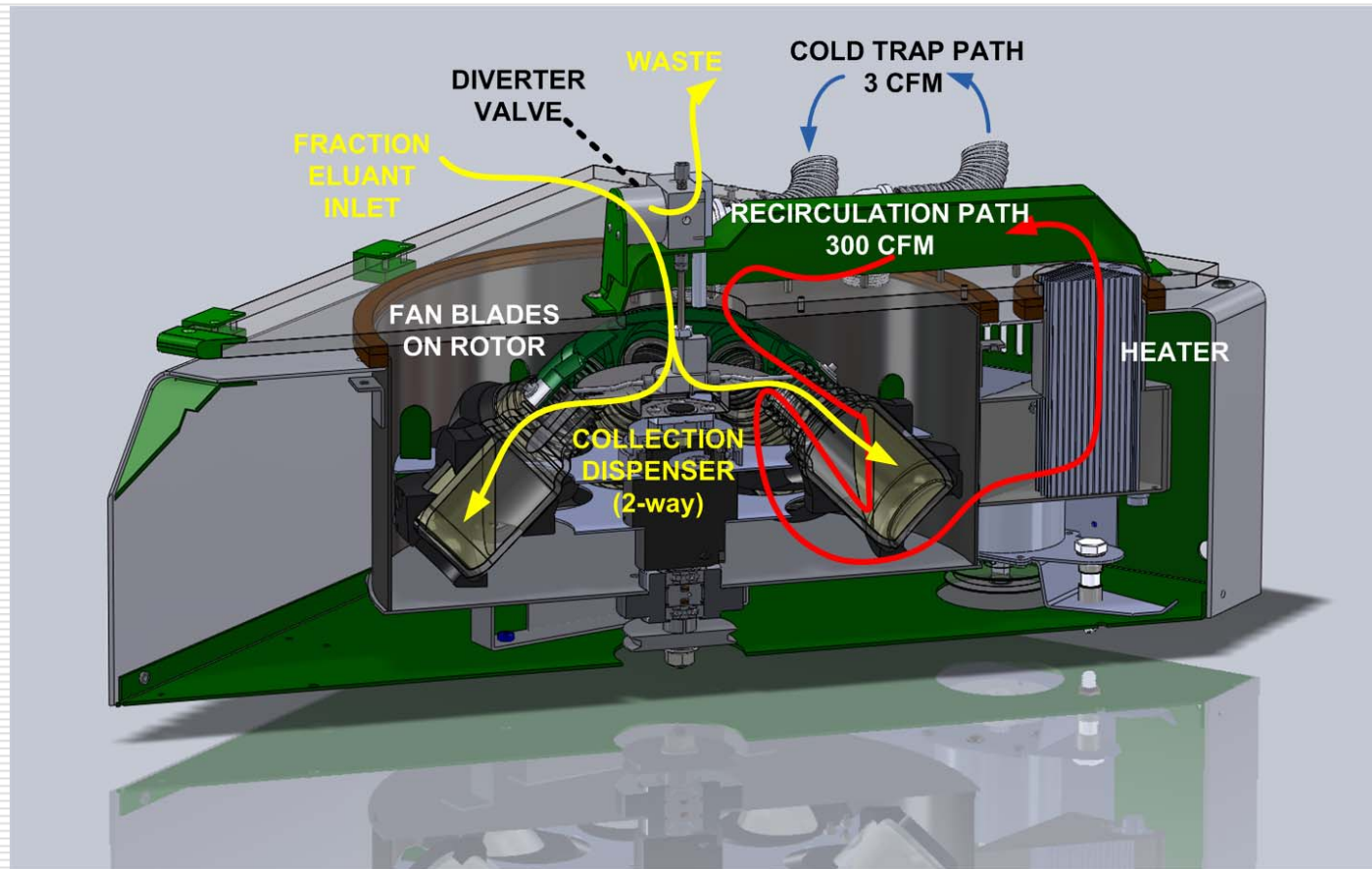
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Centrifan RE @ 40°C

- 250mL Bottle (rate is per bottle)
 - MeCl 1.5 mL/min; 90 mL/hr (720 mL/hr rotor)
 - Water .15 mL/min; 9 mL/hr (72 mL/hr rotor)
 - MeOH 1.5 mL/min; 90 mL/hr (720 mL/hr rotor)

- 96-well plate (2.2mL/well)
 - Water .13 mL/min; 7.8 mL/hr (31.2 mL/hr rotor)

CFC-3: Fraction Collection & Recirculating Evaporation



Multi-Dispensing Increases Capacity



	<i>Single Dispenser</i>	<i>Dual Dispenser</i>	<i>Quad Dispenser</i>
Evap rate per bottle (mL/min)	1.5		
Evap rate per fraction (mL/min)	1.5	3.0	6.0
Chiral 1 net gain (mL/min)	3.9	2.4	dry
Chiral 2 net gain (mL/min)	6.7	5.2	2.2
Run time to Chiral 1 = full (min)	51	164	dry
Run time to Chiral 2 = full (min)	30	77	369
Number of injections	7	17	82
Rotor capacity, processed sample (g)	1.3	3.4	16.4

*Suggests significant
unattended operation*

Process Time Savings with 2, 4 Dispensing



Number of injections	7	17	82
Rotor capacity, processed sample (g)	1.3	3.4	16.4
CFC-3			
Volume remaining to evaporate (mL)	200	400	800
Evap. rate (mL/min/container)	1.5		
Containers	1	2	4
Time to finish evaporation (hr)	2.2	2.2	2.2
Time to run stacks (hr)	0.5	1.3	6.2
Total purification time (hr)	2.7	3.5	8.4
Existing FC			
Chiral 1 volume - no evap (mL)	163	422	2010
Chiral 2 volume- no evap (mL)	245	632	3015
Rotorvap time at .7L/hr. (hr)	0.6	1.5	7.2
Time to run stacks (hr)	0.5	1.3	6.2
Total purification time (hr)	1.1	2.8	13.3
Rotorvap oper. at \$30/hr.	\$33	\$60	\$230

1-Day Unattended

2-Days With Help