Separations Consortium

Counter Current Chromatography

March 11, 2021

Technology Area Session: Performance-Advantaged Bioproducts, Bioprocessing Separations, and Plastics

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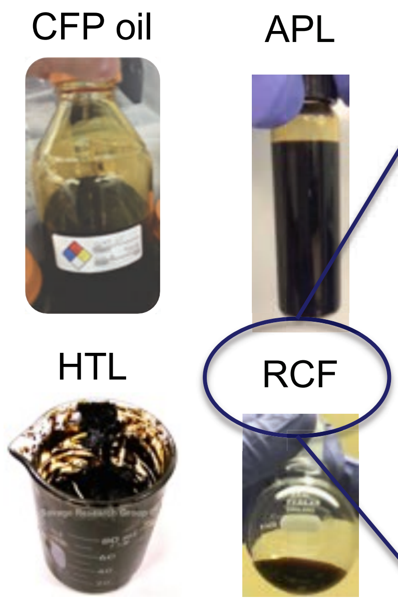
NREL, PNNL

Background



Chemical structure	wt.%	Application	$/kg value
Dimers (Calculated)	33.00%	HTF	$11 - 20
Sugars derived compounds	20.00%	unknown	unknown
Trimers (Calculated)	14.00%	HTF	$11 - 20
4-propylsyringol (PS)	11.73%	Adhesives	~$10
HMW lignin (calculated)	9.00%	Low grade Adhesives	~$5
4-propylguaiacol (PG)	7.47%	Adhesives	~$10
isoeugenol (IEG)	1.61%	Fragrance / cosmetics	~$55
4-propanolsyringol (P(OH)S)	0.96%	unknown	unknown
4-propanolguaiacol (P(OH)G)	0.95%	unknown	unknown
phenol (PhOH)	0.76%	Drop in	~$1.11
4-ethylsyringol (ES)	0.21%	Adhesives	~$10
4-(3-methoxy)propylsyringol (P(Ome)S)	0.14%	Adhesives	~$10
4-(3-methoxy)propylguaiacol (P(Ome)G)	0.11%	Adhesives	~$10

Deriving valuable compounds from renewable streams

- Complex mixtures are common in biorefining (CFP oil, HTL oil, lignin) but require extensive multistep filtration before traditional Simulated Moving Bed (SMB) chromatography can be applied Filtration steps lower yields (sometimes > 50%)
- There is a need to separate valuable LMW compounds for use in fuel, and commodity chemical applications as value added coproducts.

Project Overview

- ***Context:*** ***Counter Current Chromatography (CCC) is an emerging scalable technology that has potential for isolating co-products from biorefining streams to offset the MFSP.***
- ***Project Goals:*** *Develop methods, TEA, modeling tools, and demonstrate methods to isolate purified co-products from biorefining streams. Compare CCC to traditional SMB technology.*
- ***Heilmeier Catechism:***
  - ***What are you trying to do?*** *Isolate purified co-products from biorefining streams using CCC*
  - ***How is it done today and what are the limits?*** *Using SMB which requires extensive filtration to protect the stationary phase resulting in yield losses > 50%.*
  - ***Why is it important?*** *Co-products from biorefining waste streams can offset the MFSP up to 3$/GGE*
  - ***What are the risks?*** *CCC is an emerging technology and comparisons in terms of solvent demand, energy consumption, and TEA are lacking compared to SMB.*

Management

1. CCC methods for lignin streams and CFP oil

NREL

2. CCC methods for HTL and CFP oil

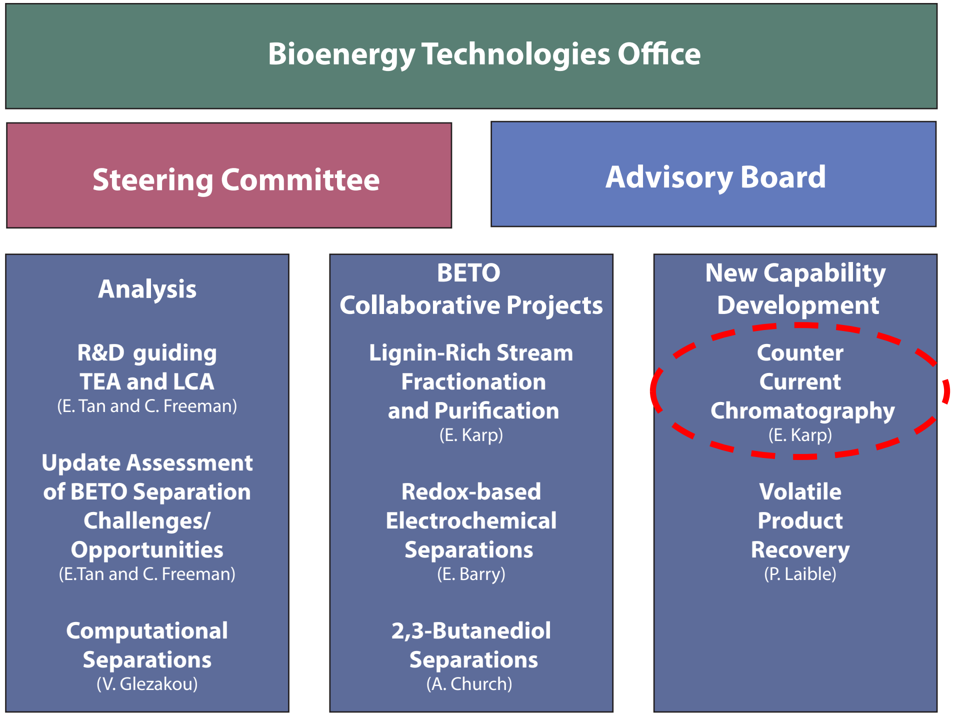
Pacific Northwest National Laboratory

3. System model development

NREL, Pacific Northwest National Laboratory

4. TEA & LCA

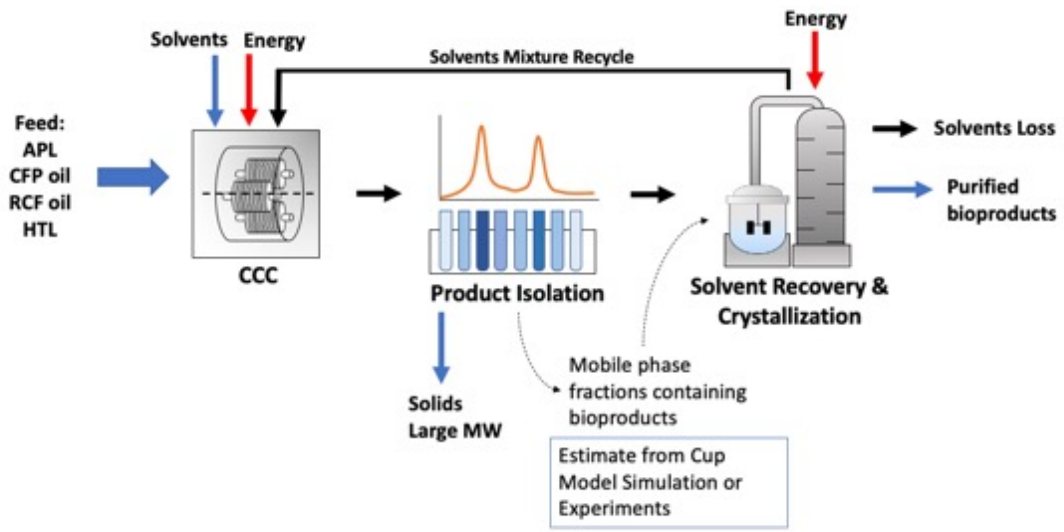
NREL, Pacific Northwest National Laboratory



- ***Smartsheet tool*** **–** used to coordinate milestones and joint work between labs. Manages risks in real time
- ***Progress tracking with monthly consortium meetings***
- ***Dedicated weekly analysis meetings***
- ***Monthly inter-lab meetings***
- ***Publish findings and IP for new concepts***

Approach

- **Identify co-products in streams with Sherwood plot analysis (slide 9)**
- **Risk Mitigation – mathematical models, TEA, and go/no-go decision points, benchmarked to SMB**
- **Challenges**
  - *Identifying robust Solvent System (S.S.'s) for each stream*
  - *Modeling advanced chromatography modes*
- **Go /No-go (slide 16)**
  - Energy footprint < 30% of the Higher Heating Value (HHV) of product
  - Product purity > 90%
  - 20% reduction in solvent load relative to SMB
  - 20% reduction in stationary phase relative to SMB
- **TEA targets**
  - *Relative to SMB in terms of throughput, yield, purity and energy footprint.*




Commercial CCC skid

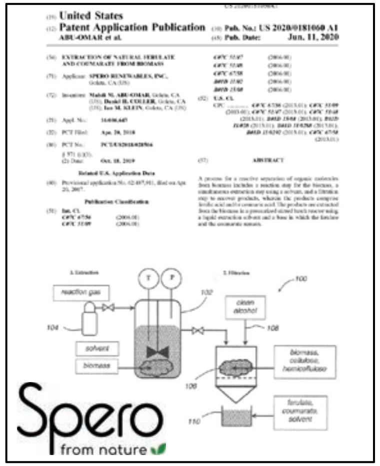
Impact

- **SMB is the conventional technology for direct production isolation**
- ***Removing S/L separation*** **increase yield by up to 50%.**
- **Co-product recovery can positively affect biorefinery economics**
  - ***Lignin co-products can add up to $3/GGE in revenue***
  - ***CFP co-products also improve thermochemical economics***
  - ***Tackifers, monomers, fuel additives, plasticizers, etc.***
- **Disseminating results with**
  - ***Patents (see slide 18)***
  - ***Peer reviewed papers (see slide 18)***
  - ***Consortium reports[1]***
  - ***Consortium website***
  - ***Biannual IAB meetings***

Lignolix

Spero from nature

blue california FLAVORS & FRAGRANCES [1]



United States Patent Application Publication ABU-OMAR et al.

Pub. No.: US 2020/0181060 A1

Pub. Date: Jun. 11, 2020

EXTRACTION OF NATURAL FERULATE AND COUMARATE FROM BIOMASS

News | July 12, 2017

Blue California Increases Commercial Production Of Ferulic Acid From Rice Bran

Rancho Santa Margarita, CA /PRNewswire/ - Blue California, a manufacturer of purified natural ingredients and flavor compounds for use in food products announced today that it is increasing their production capacity of Ferulic acid (FA) to an estimated 500 metric tons by 2018.

Ferulic acid (4-Hydroxy-3-methoxycinnamic acid, FA) is a ubiquitous phytochemical present in cell walls and found in foods such as rice, wheat, oats, seeds, beans, nuts, corn, etc. FA is an antioxidant that can be used in dietary supplements to combat free radicals and oxidative stress, in cosmetics and topical creams for UV protection, in food products as a potential natural preservative and in other commercial uses that include pharmaceutical products.

Cecilia McCollum, Blue California's executive vice president stated, "Our production capacity was no longer sufficient for the growing demand for natural ferulic acid so this increase will create new commercial opportunities for our business partners and will benefit consumers as well". Availability of natural ferulic acid is limited while demand for this antioxidant is growing. "We are doing our part in helping our customers deliver the natural products consumers want." Added McCollum. The global demand for natural ingredients is the new standard and manufacturers like Blue California are meeting the challenge.

Blue California is a recognized industry leader in innovation and manufacture of high purity natural compounds and botanical extracts for the food, beverage, cosmetics and flavor industries. Blue California's manufacturing facilities maintain GMP and BRC certifications to ensure the purity and consistent value and quality of its products.

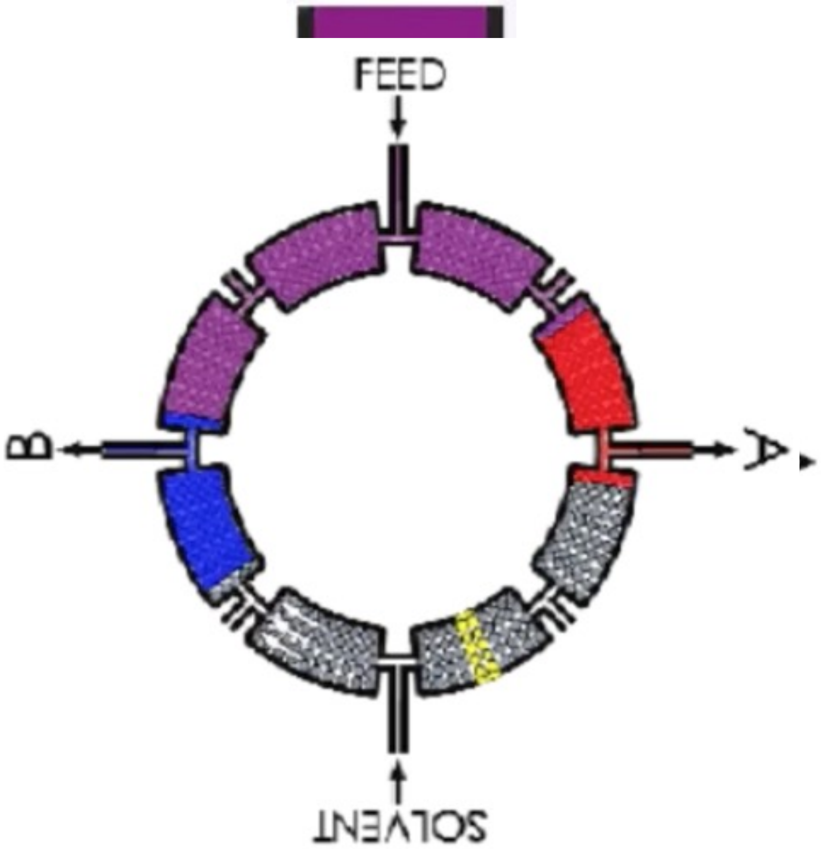
Source: Blue California

1. Extraction of natural ferulate and coumarate from biomass ,2018, US20200181060A1

Progress and Outcomes (Baseline)

Simulated Moving Bed (SMB) is the baseline for single product isolation[1]

- Generally only A/B separation
- Typically 8-10 kg mobile phase per kg crude sample
- Stationary phase is expensive
- Lifetime of resin is key OPEX driver
- ASPEN modeling tools well developed
- Solvent recycling is facile in normal phase but energy intensive in reverse phase



1. Rodrigues, A. E.; et. al. In *Simulated Moving Bed Technology*,. Butterworth-Heinemann: Oxford, 2015; p xi.

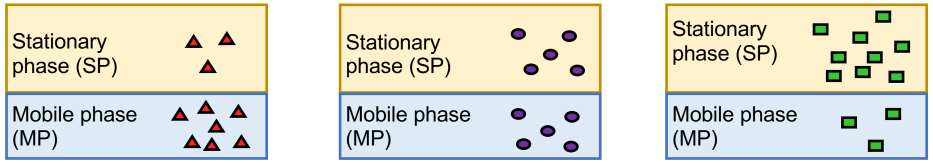
Principle of Operation

CCC principle of operation

- Liquid-liquid chromatography uses two immiscible liquids as the stationary and mobile phases

- Separation based on partition coefficient to upper and lower phase

$K_D < 1$ $\quad$ $K_D = 1$ $\quad$ $K_D > 1$



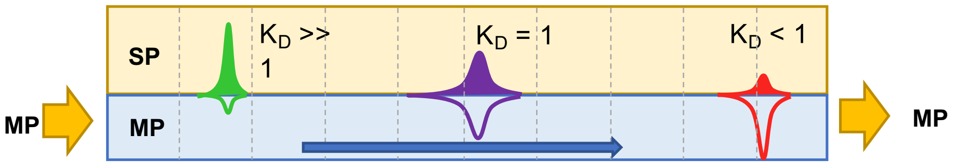
Partitioning Coefficient (K_D)

in LLE

$$K_D = \frac{[C]_{Heavy\ phase}}{[C]_{Light\ phase}}$$

in Chromatography

$$K_D = \frac{[C]_{Staionary\ Phase}}{[C]_{Mobile\ Phase}}$$



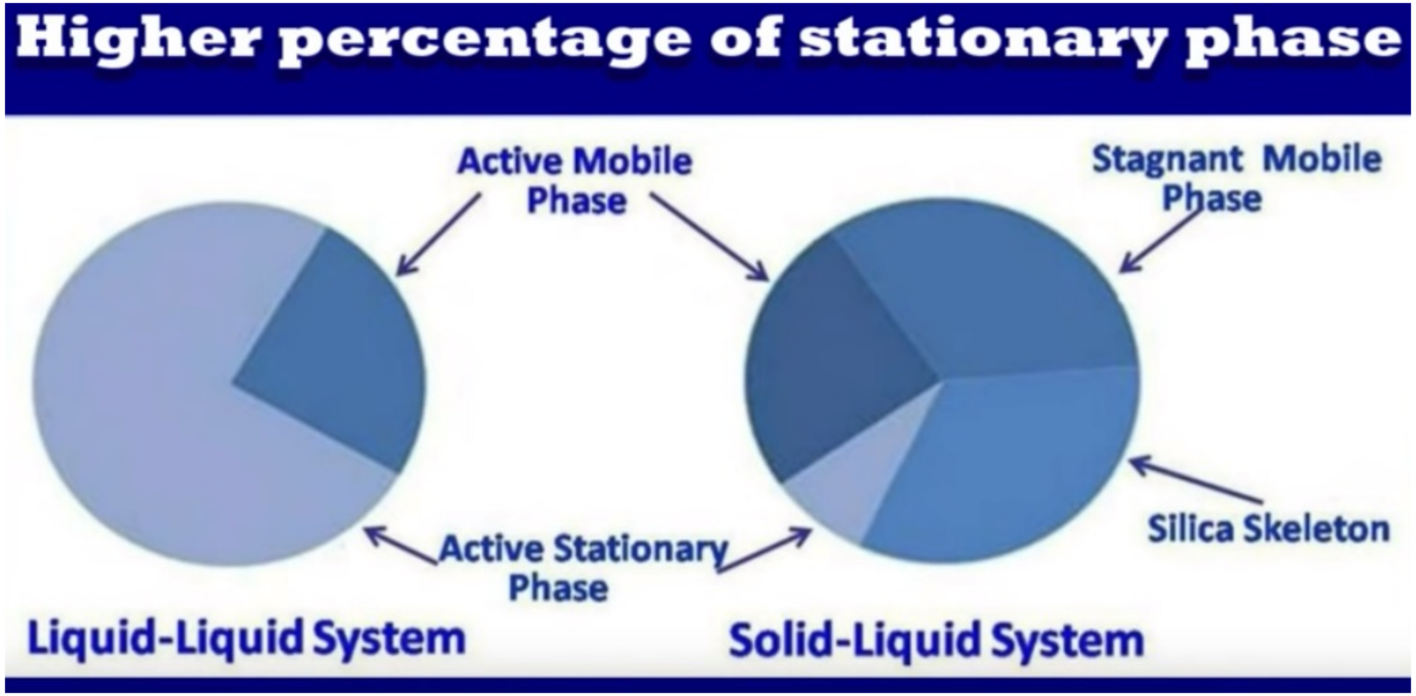
Solute having Low K_D elutes faster than others having high K_D

Commercial CCC skid

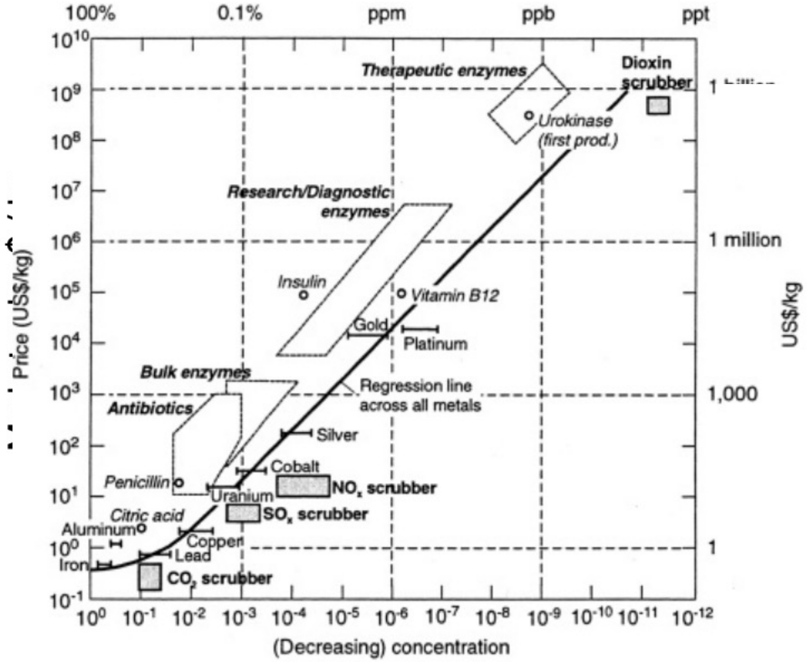
Advantages over SMB

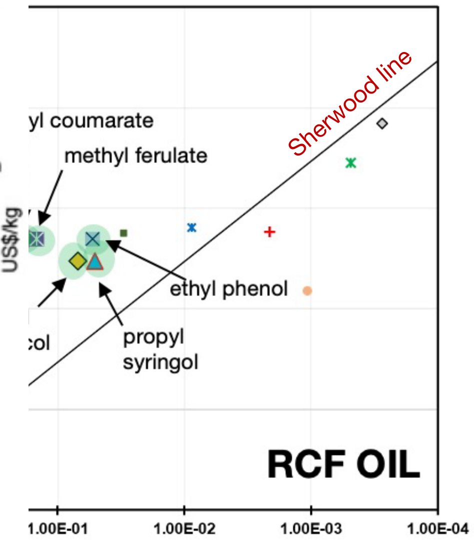
Why CCC could be cost and performance advantaged over SMB

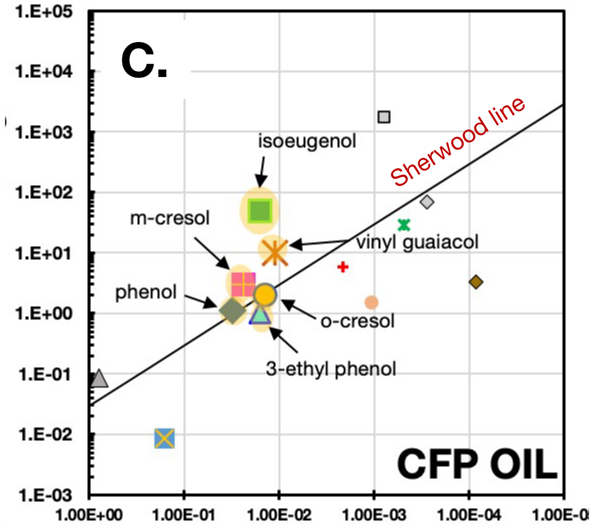
- Stationary and mobile phase are both liquids; ~60% less cost in stationary phase
- Can collect entire chromatogram at 1 ton / day scale → much faster throughput than SMB
- Can be run continuously in A/B separation if desired
- ***<u>Can handle solids in the feed!</u>***
- Relatively emerging technology

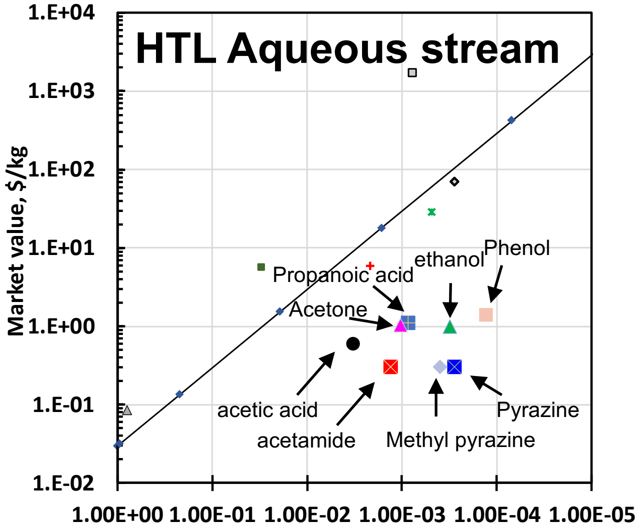


Sherwood Plot Analysis





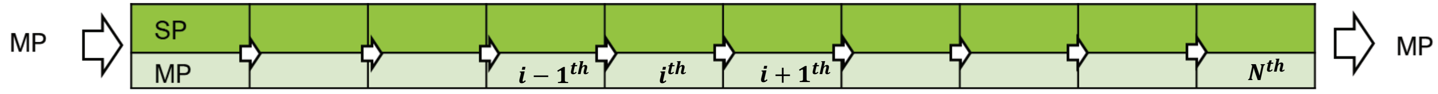




Step 1 identify compounds from streams worth recovering

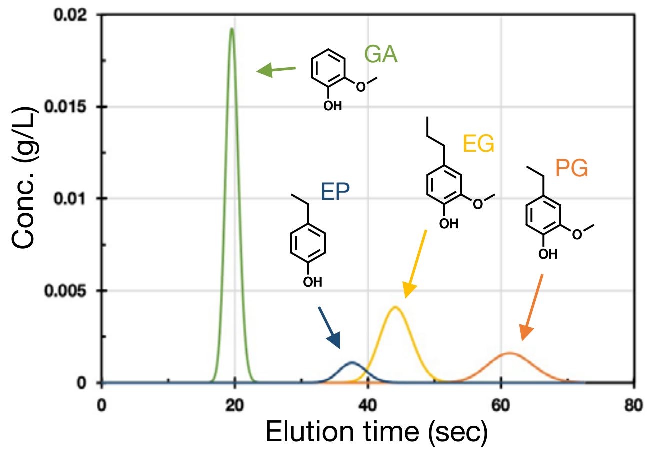
- Sherwood plot analysis
- Identifies high value co-products from these chemically complex streams that are at recoverable concentrations
- Recovery large classes of compounds from HTL aqueous not individual components

Modeling

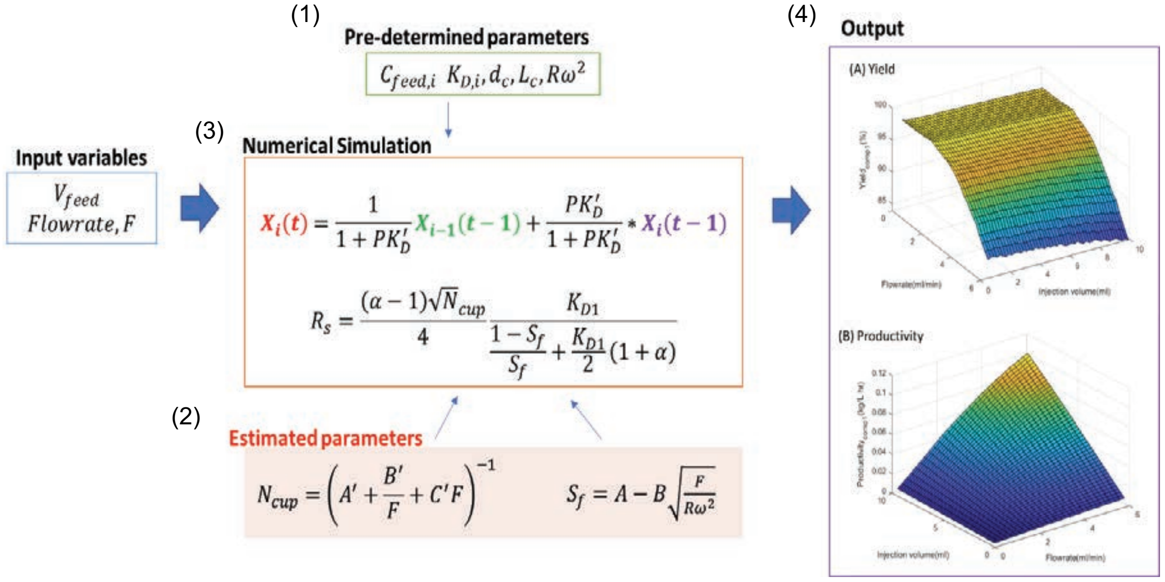


- Solving MB equations for N cells continuously

$$X_i(t_j) = \frac{1}{1+PK_D} X_{i-1}(t_{j-1}) + \frac{PK_D}{1+PK_D} * X_i(t_{j-1})$$



Optimization Overview

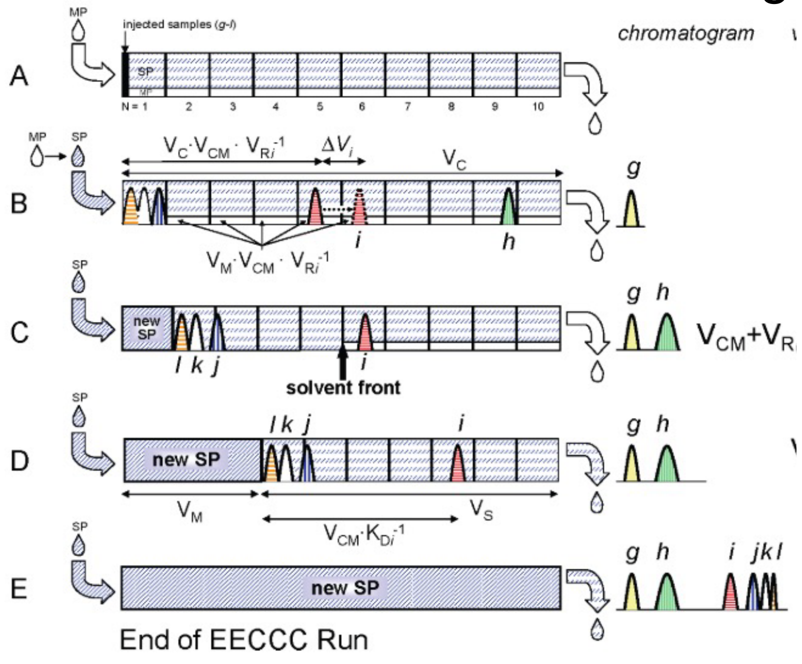


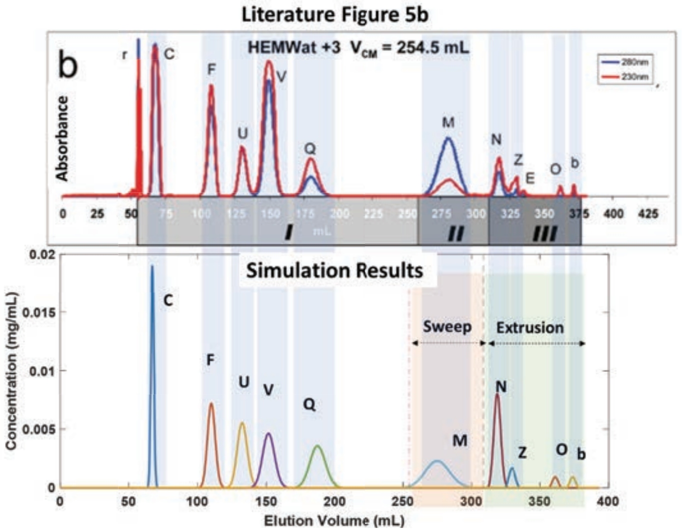
Step 2 Model the CCC separation and calculate needed K values

- Mathematical model developed collaboratively with NREL and PNNL
- ***Predicts elution times, and peak FWHM***
- ***Optimizes injection volumes and elution flowrates***
- ***Optimizes needed K values for S.S.'s***

Robust Chromatographic Models

Elution extrusion chromatography (ECC)





Dual Mode

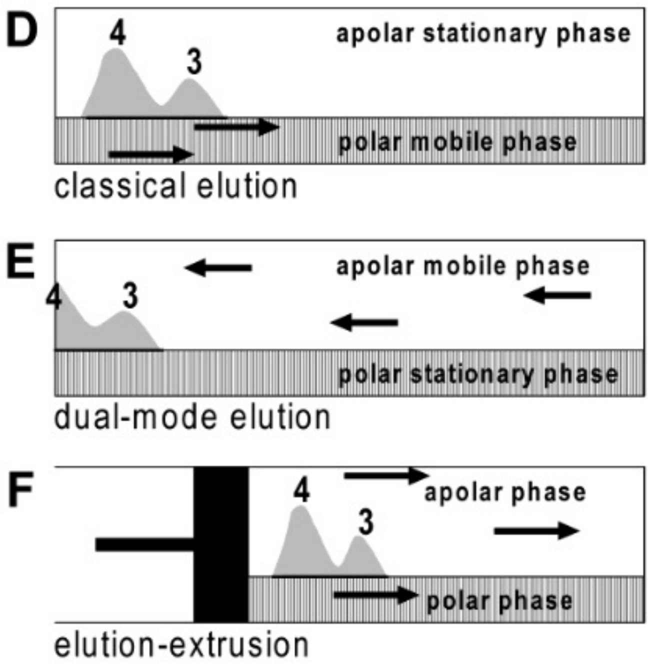


Figure 4. Different elution modes in CCC. (D) Classical mode following Figure 3 illustrations; (E) dual-mode method; the phase roles are reversed; (D) elution−extrusion method; the whole content of the column is extruded out of the column.

Step 2 Model is robust with alternative chromatography modes

- Elution extrusion chromatography (EEC)
- Dual Mode chromatography
- Models validated with experimental data
- ***Allows identification of most efficient chromatographic mode (e.g. ECC for coumaric acid)***

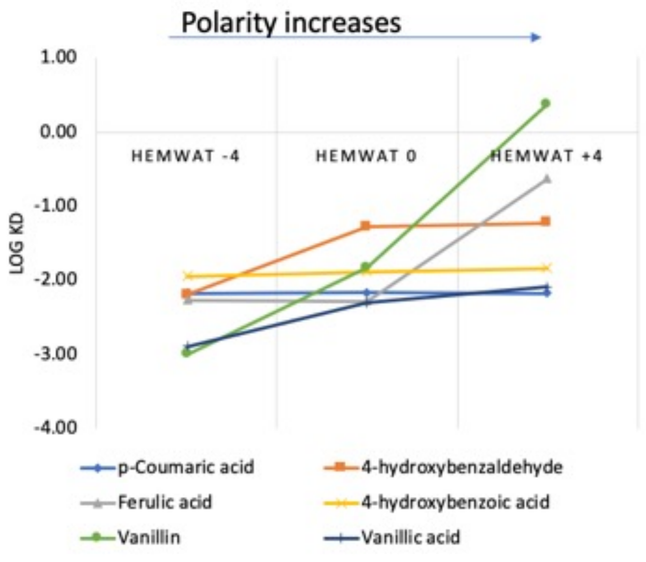
Berthod et al., Analytical Chemistry, Vol. 79, No. 9, May 1, 2007

Berthod et al., Analytical Chemistry, Vol. 75, No. 21, November 1, 2003

Solvent System Screening

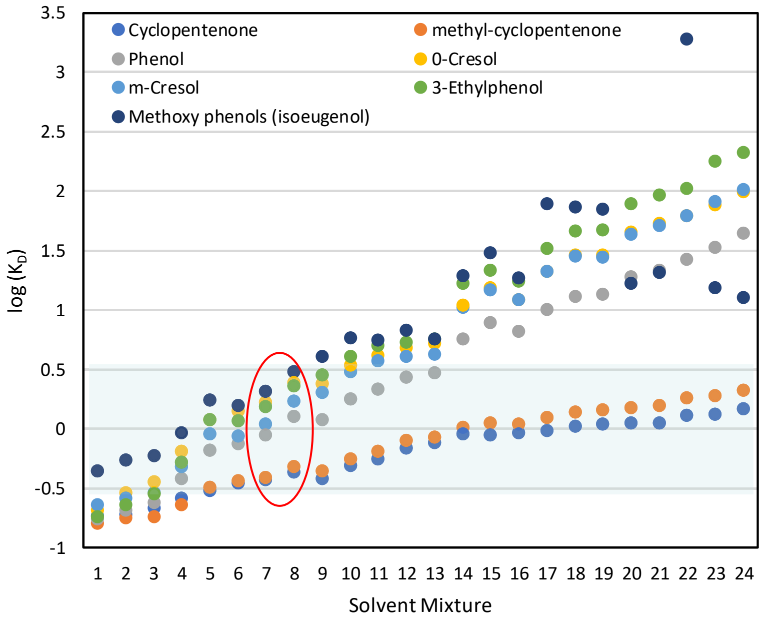
Partition coefficients

APL example

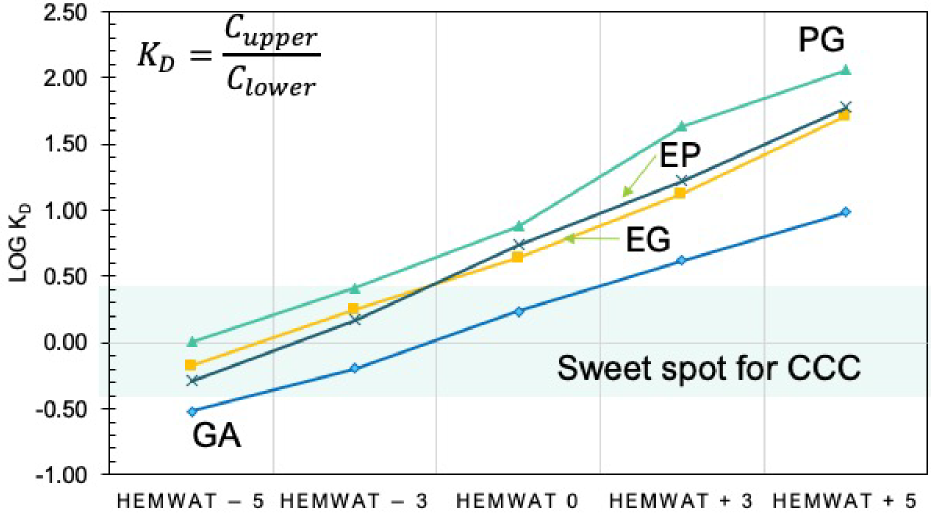


Prepared Sample pH 10

CFP oil



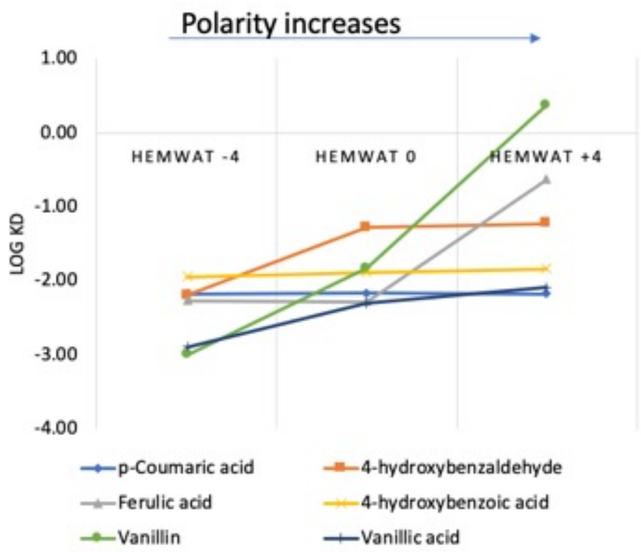
RCF oil



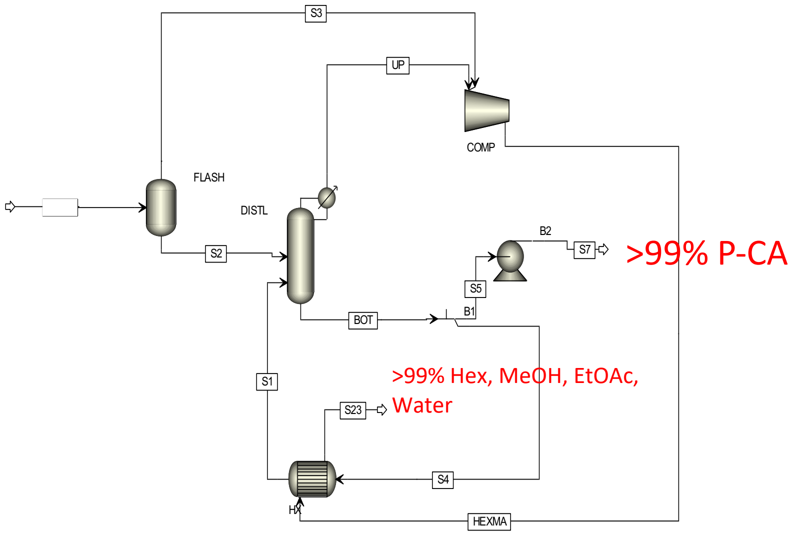
Step 3 Screen Solvent Systems (S.S.'s) for ideal K values

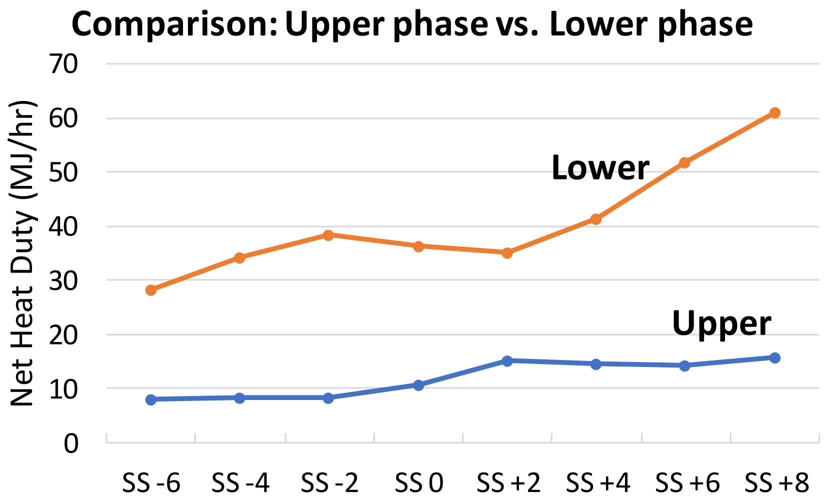
- HEMWAT (Hexane , ethyl acetate, methanol, water) Solvent System
- TerAcWat (Terbutylether, acetonitrile, water)
- Polarity is varied by changing the ratio of S.S. components

Energy Footprint Analysis



Prepared Sample pH 10

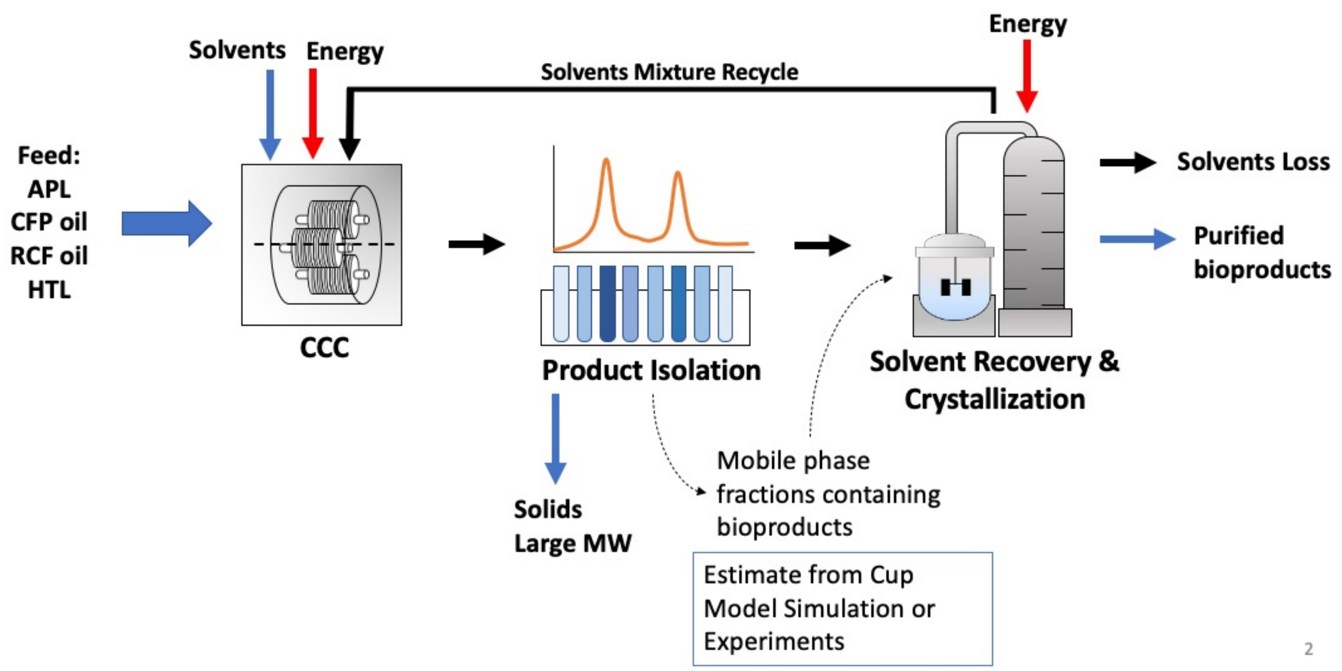


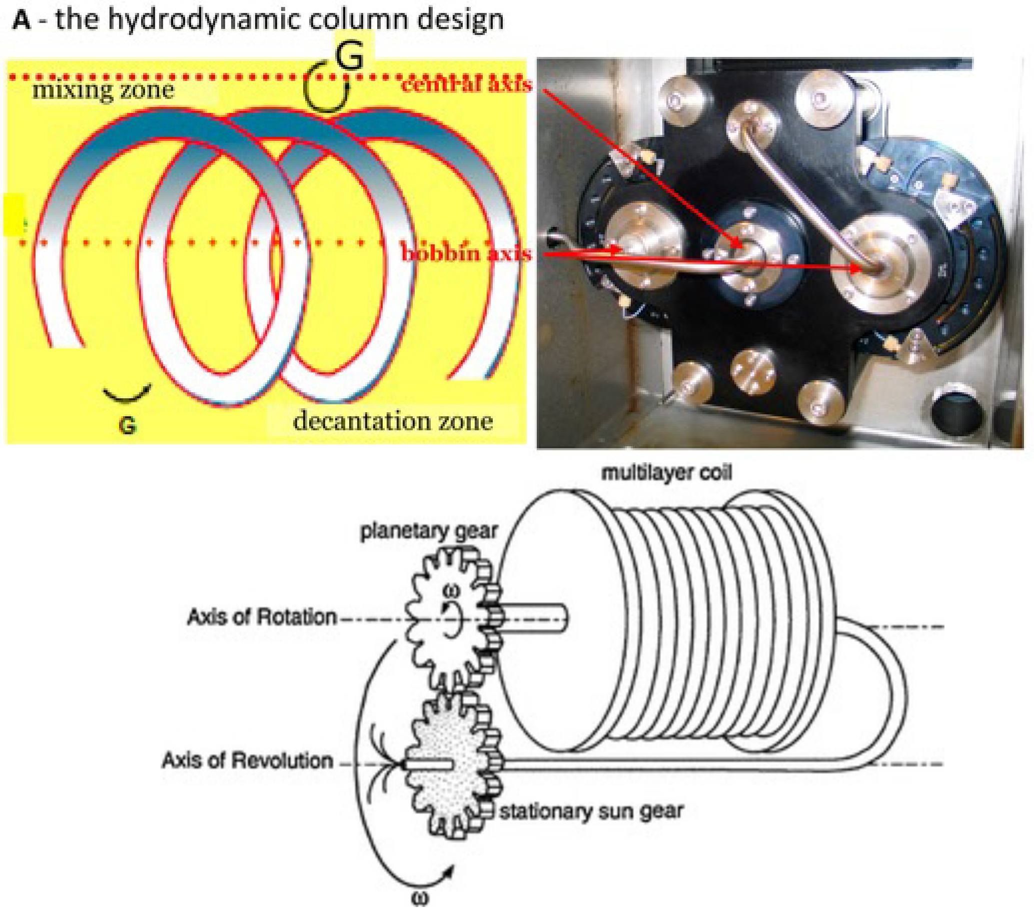


Step 4 Process modeling and energy footprint analysis

- K values and CCC process model predicting Solvent loads and stationary phase requirements
- Use modelling to focus process development on streams which make sense for CCC
- ASPEN model built for solvent recovery and recycling
- Various chromatography modes examined to determine lowest energy demand configuration

Demonstration of Integrated Process

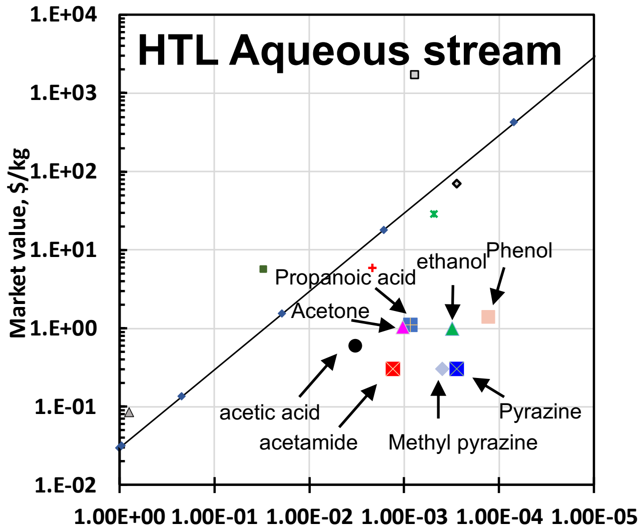




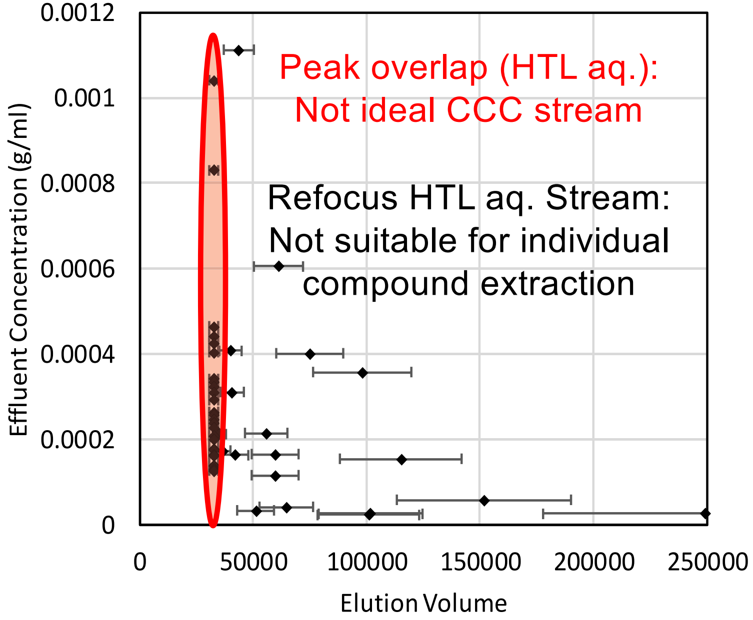
Step 5 Demonstrate process on CCC instrument

- End FY21 Isolate > 50 g of purified material for Performance Advantaged BioProducts (PABP) team
- Any isolated unknowns sent to analytical team (e.g. dimers & trimers)

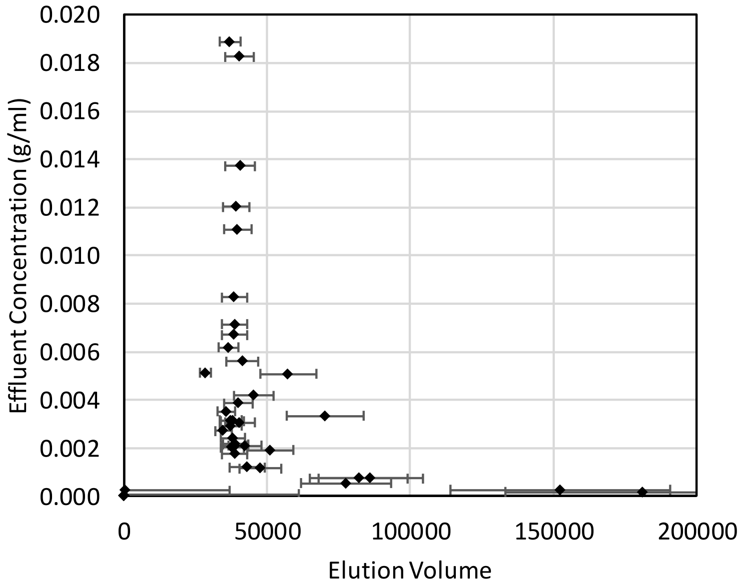
Special Cases of HTL and CFP Oil



HTL CCC simulation

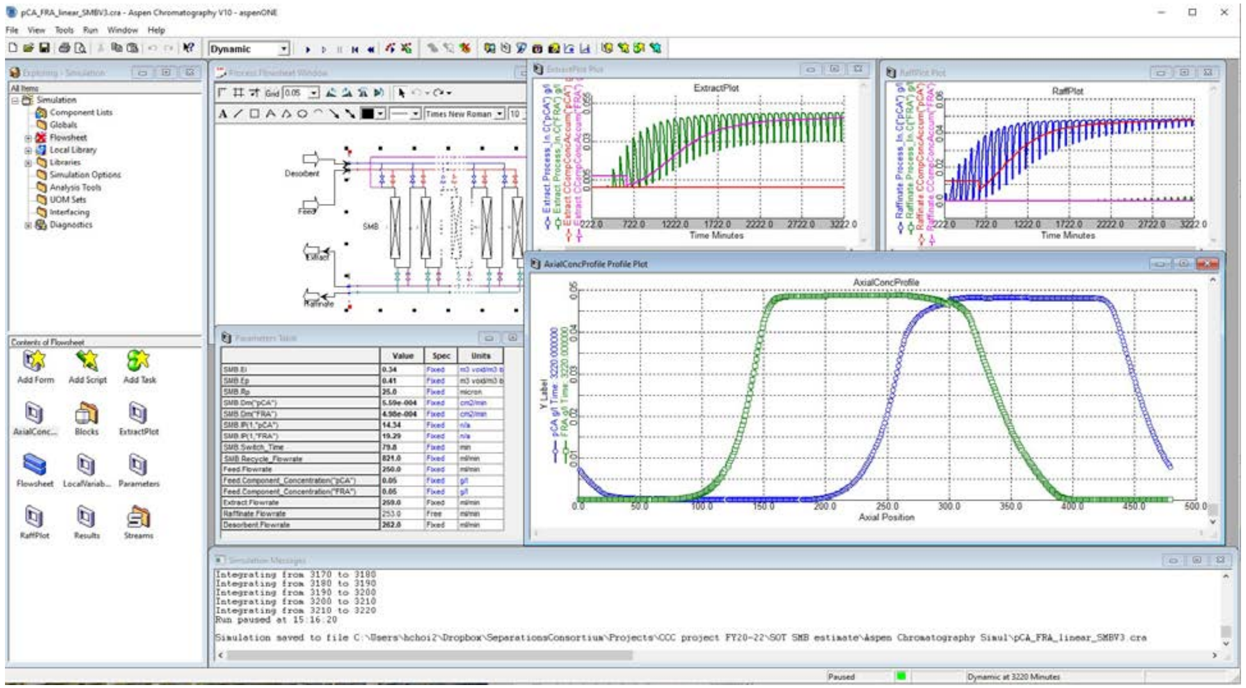


CFP oil CCC simulation



Raw material received from

- Identify if 2nd stage purification will be necessary or more attractive (e.g. pair with Liquid Liquid Extraction)
- CFP oil also need separation technology pairing, investigating upfront head distillation
  - Too many LMW compounds overlapping
- Collaborating with Brunel University on CCC process development



Direct comparison to the SOT

- Used PS/PG recovery from RCF oil
- Built model for SMB separation
- Built model for Flash chromatographic separation
- Built model for CCC chromatographic separation
- In progress of building continuous CCC model
- TEA forthcoming

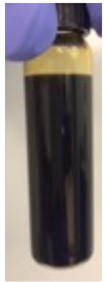
- **Reduced solvent loads with CCC imply lower energy consumption**

	Flash (Batch)	CCC (Batch)	SMB (Continuous)	CCC (Continuous)
	162	35.7	45.8	In progress
	2.8	1.0	1.4	In progress
	Q2 TEA Go/No-Go			
	Q2 TEA Go/No-Go			
	Q2 TEA Go/No-Go			

Collaborations

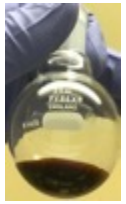
CFP oil

APL



HTL

RCF



Raw material received from

- CFP oil WBS # 2.3.1.314
- APL & RCF oil Lig. First WBS # 2.2.3.106
- Catalytic oxidation oil Lignin Utilization WBS # 2.3.4.100
- Bench Scale HTL WBS # 2.2.2.302

Purified material sent to the following tasks / companies

- RCF monomers (Guaiacol, 4-ethylguaiacol, 4, propylguaiacol, etc.) to PABP WBS2.3.4.501
- P-Coumaric and ferulic to BLV WBS 2.3.2.100
- CFP targets to Bioinsecticides from thermochemical biomass conversion WBS# 2.3.1.705
- Collaborating with Brunel University on CCC development
- Working with outside company Lignolix for RCF oil for scale up designs & MVPs

Lignolix

Publications

Publications C.1

1. Coproduct recovery from APL via CCC – NREL + PNNL (March 2021)
2. Coproduct recovery from RCF oil via CCC – NREL + PNNL (August 2021)
3. Energy footprint of common solvent systems in CCC – NREL + PNNL (December 2022)
4. Relevance and economics of CCC in commodity biorefining – NREL + PNNL (end of project)

Patents

1. CCC methods for isolation of Coumaric and Ferulic acid from lignin (ROI submitted Patent app drafted)

Quad Chart Overview - Analysis

Timeline
- 10/1/2020
- 9/30/2023

	FY20	Active Project
DOE Funding	(10/01/2019 – 9/30/2022)	*$1,650,000* *NREL: $1,200,000* *PNNL: $450,000*

Project Partners*
- NREL
- PNNL

Barriers addressed
Ot-B: Cost of production

Ct-O: Selective separations of organic species

Ct-D: Advanced bioprocess development

Project Goal
To develop CCC methods and mathematical tools for optimizing the purification of target from RCF oil, APL, and HTL streams. The mathematical tools will be made publicly available on github and are meant to be broad enough for optimizing any separation using CCC. Provide unique purified monomers from lignin valorization projects in the BETO portfolio using both membrane fractionation and CCC.

End of Project Milestone
Develop ASPEN model for solvent recovery that demonstrates an energy footprint <30% of the heating value of the targeted product and purity level >90% of the recovered products. Demonstrate stationary phase reduction of at least 20%, or eluent load reduction of at least 20% compared to traditional SMB as a benchmark. If CCC is not viable, suggest alternatives or quantify measurable targets that the feed stream needs to meet for coproducts to be recovered (e.g. concentrations). Deliver > 20g of purified monomers from APL and RCF to downstream valorization tasks.

Funding Mechanism
Merit reviewed AOP-based consortium

Summary

Key points

- CCC allows direct separation of coproducts from biorefining streams that SMB cannot recover
- Lower solvent consumption compared to SMB
- Lower energy consumption to SMB
- Could enable direct co-product recovery. TEA forthcoming
- Feed material received from several tasks
- Purified products sent to collaborating tasks
- CCC technology baselined to SMB
- Collaboration with outside companies and universities


Commercial CCC skid

Future work

1. p-coumaric and ferulic acid isolation at > 50g scale
2. RCF monomer isolation at > 50g scale
3. Complete energy analysis
4. Complete TEA & LCA
5. Catalytic oxidation oil

Lignolix Brunel University London

Questions

Additional Slides

Acknowledgements

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Steering Committee - **Jennifer Dunn, Taraka Dale, Gregg Beckham**

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- Matt Agboola
- Ting Wu
- Tim Theiss
- Zhenglong Li
- et al

Los Alamos National Laboratory EST. 1943
- Bill Kubic

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- Russell Meyer
- Alex Rosenthal inCTRL Solutions

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- Jipeng Yan
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- Eric Tan
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- Nancy Dowe
- Min Zhang

Pacific Northwest National Laboratory
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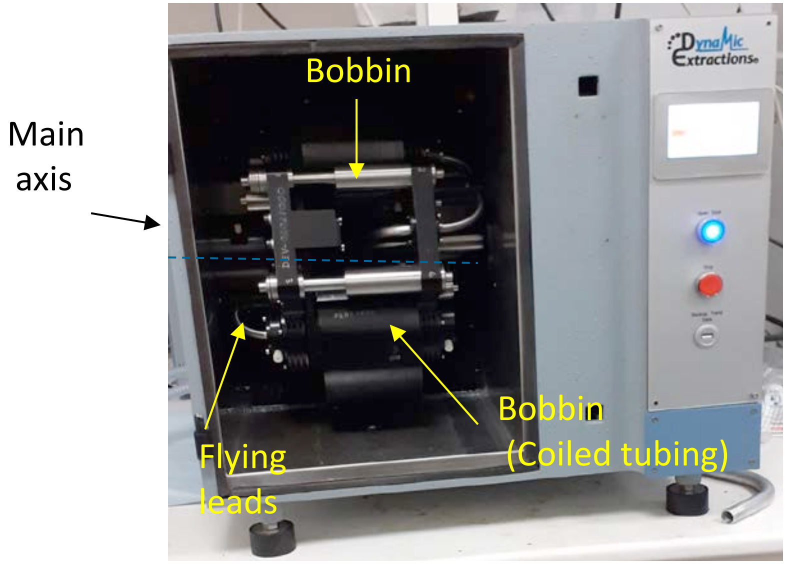
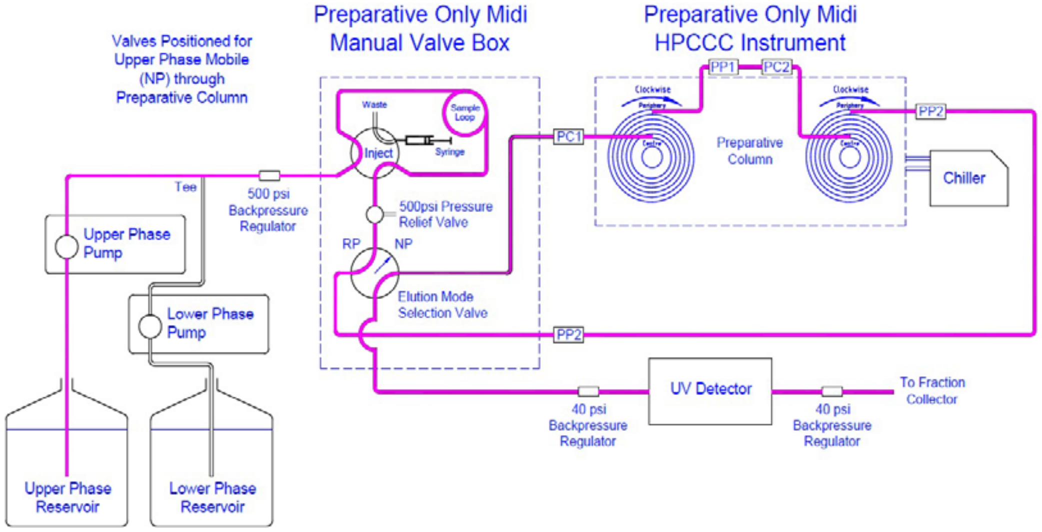
- Vanda Glezakou
- Charlie Freeman
- Jian Liu
- Pradeep Gurunathan
- Difan Zhang

Abbreviations

1. APL – Alkaline Pretreatment Liquor
2. CCC – Counter Current Chromatography
3. CFP – Catalytic Fast Pyrolysis
4. CPC – Centrifugal Partitioning Chromatography
5. LMW – Low Molecular Weight
6. MVP – Minimum Viable Product
7. P-CA – p-coumaric acid
8. RCF – Reductive Catalytic Fractionation
9. SMB – Simulated Moving Bed

CCC instrument





Basic information of Spectrum Series 1000

- Two rotors for column
- Fraction collector
- Recirculatory for temperature control
- Operation temperature range: 0~45 ^{o}C
- Pressure limit 500 psi (pressure regulator)
- Max rotation 1,400 rpm (240g)
- Beta (= r/R) range: 0.52 ~ 0.86
- Column ends – AP(periphery)/AC(center):
  Normal phase – AP→AC; reverse phase – AC→AP

Column	Analytical (Scout column)	Semi-preparative	Preparative
Coil volume (2ea Bobbin)	27.5 mL	159 mL	995 mL
Bobbin size (1ea)	0.8 mm ID X ~21.9 m Lc	1.6 mm ID X ~34.8 m Lc	4 mm ID x ~37.4 m Lc
Flow rate	0.5 ~ 2 ml/min	5 ~ 10 ml/min	10 ~ 100 ml/min
Beta (=r/R)	0.64 ~ 0.86	0.52 ~ 0.86	0.52 ~ 0.86