CBiRC
NSF Engineering Research Center for Biorenewable Chemicals

Biobased Chemicals through Integrated Chemistry and Biology

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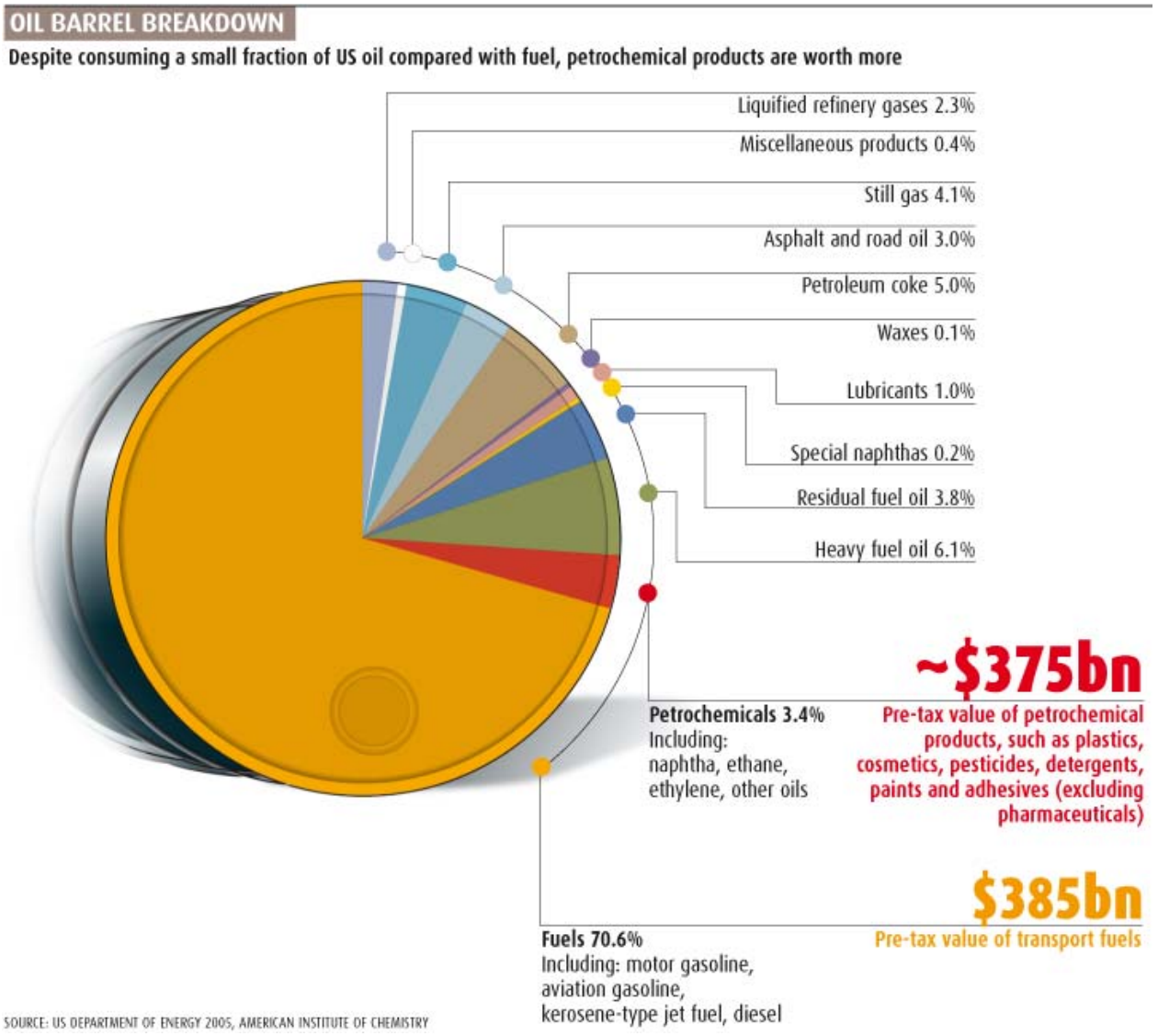
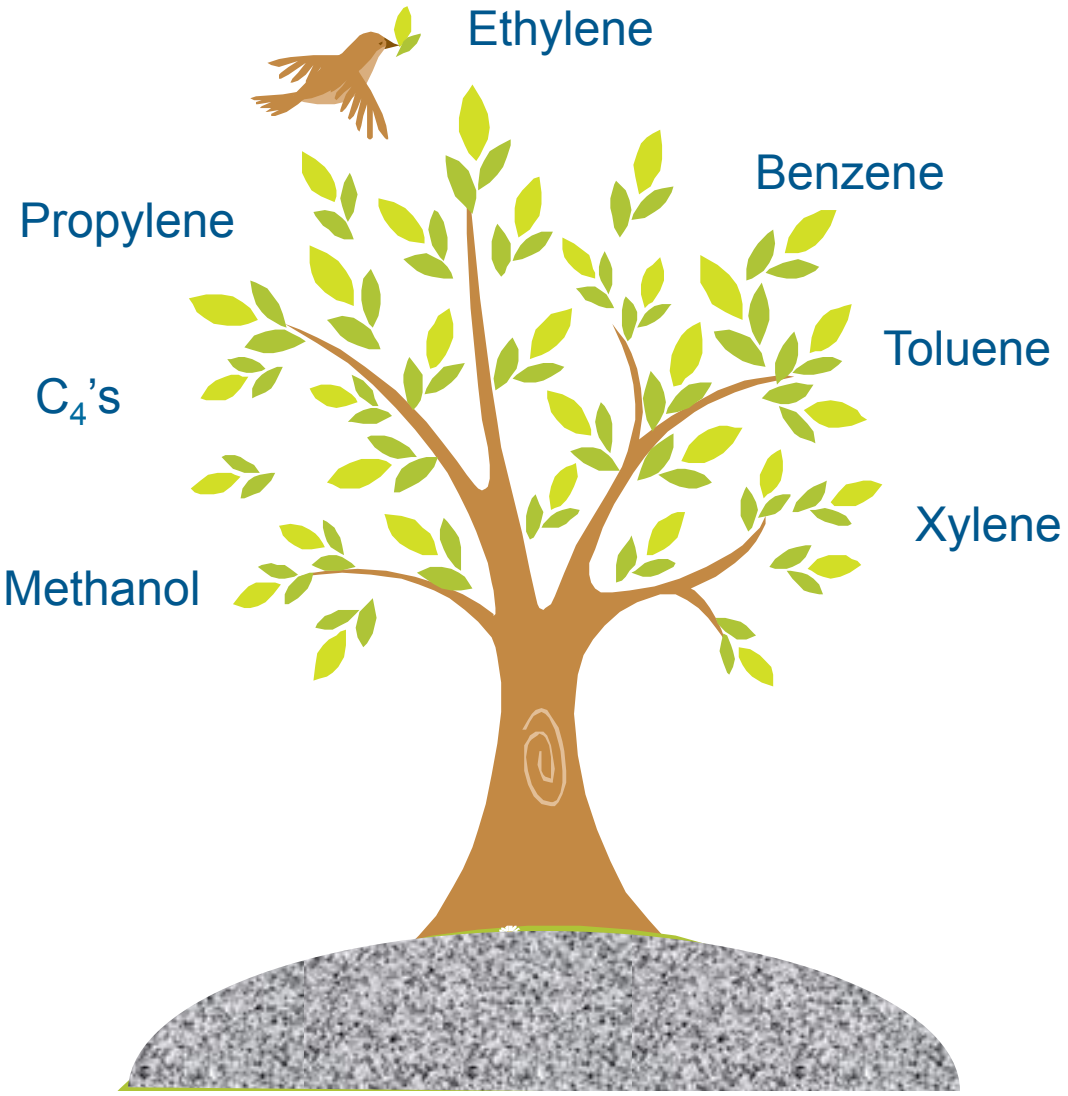
Director, CBiRC

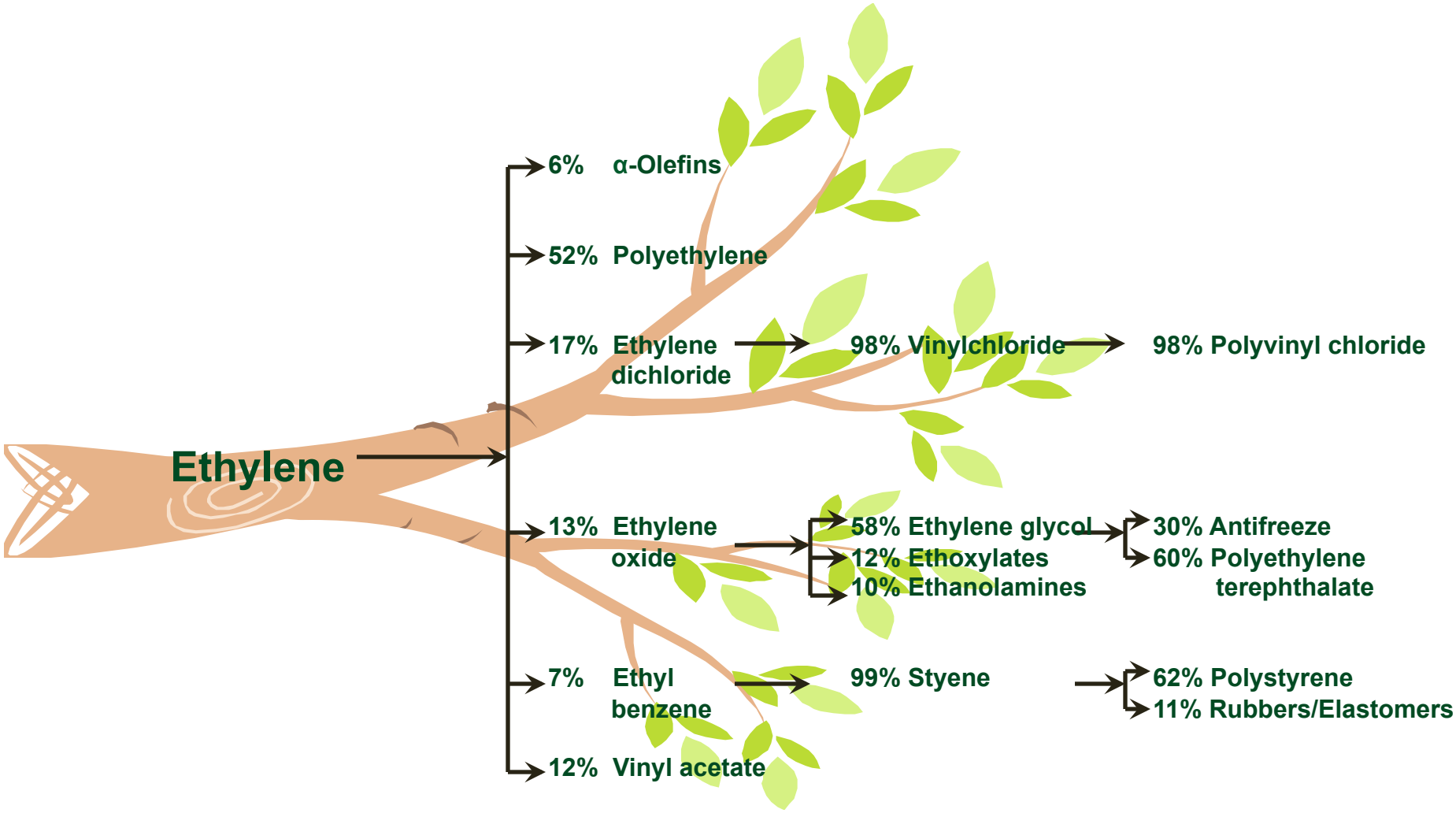
Chemicals


OIL BARREL BREAKDOWN
Despite consuming a small fraction of US oil compared with fuel, petrochemical products are worth more
Liquified refinery gases 2.3%
Miscellaneous products 0.4%
Still gas 4.1%
Asphalt and road oil 3.0%
Petroleum coke 5.0%
Waxes 0.1%
Lubricants 1.0%
Special naphthas 0.2%
Residual fuel oil 3.8%
Heavy fuel oil 6.1%
~$375bn
Petrochemicals 3.4%
Including:
naphtha, ethane,
ethylene, other oils
Pre-tax value of petrochemical products, such as plastics, cosmetics, pesticides, detergents, paints and adhesives (excluding pharmaceuticals)
$385bn
Fuels 70.6%
Including: motor gasoline,
aviation gasoline,
kerosene-type jet fuel, diesel
Pre-tax value of transport fuels
SOURCE: US DEPARTMENT OF ENERGY 2005, AMERICAN INSTITUTE OF CHEMISTRY

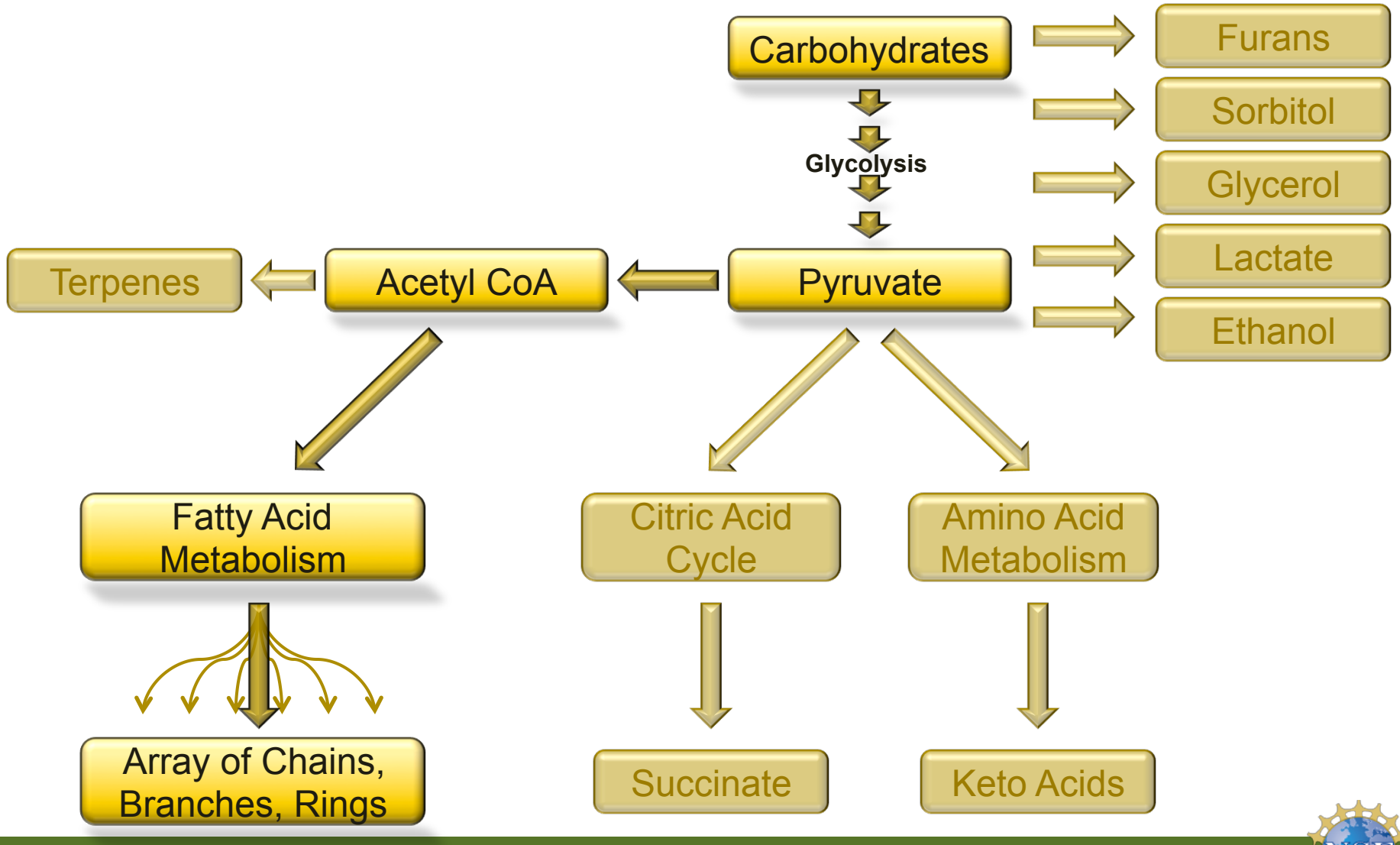
Petrochemicals



Ethylene and Derivatives



Pathways to Biorenewables



Vision

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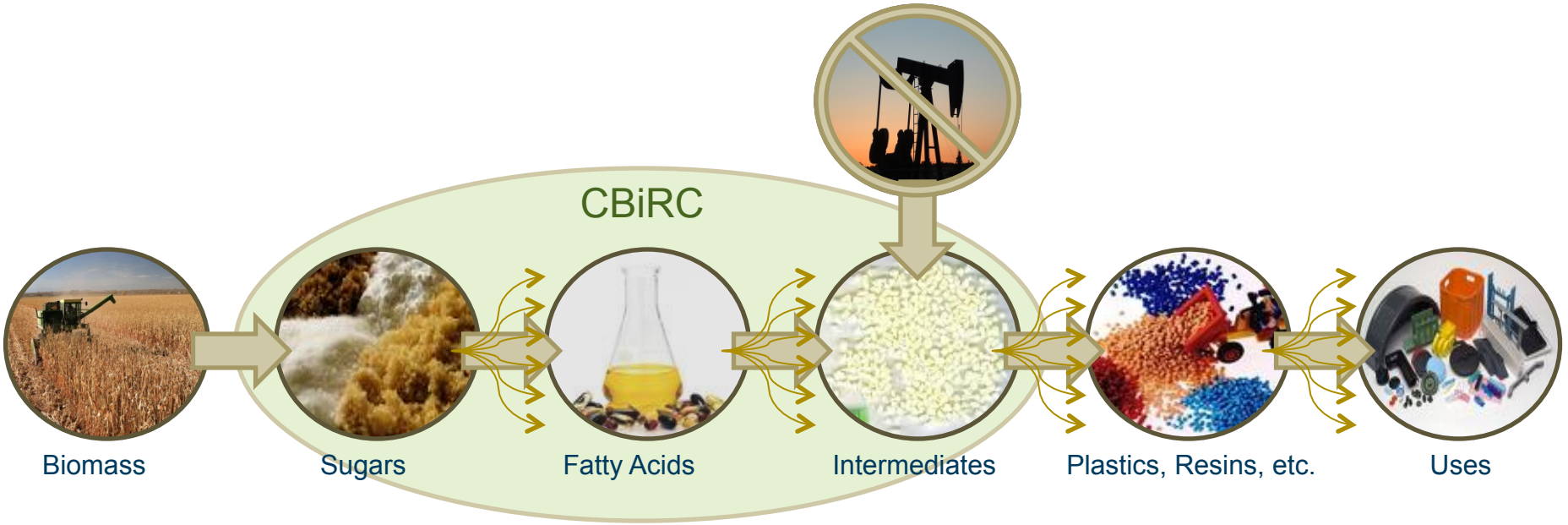
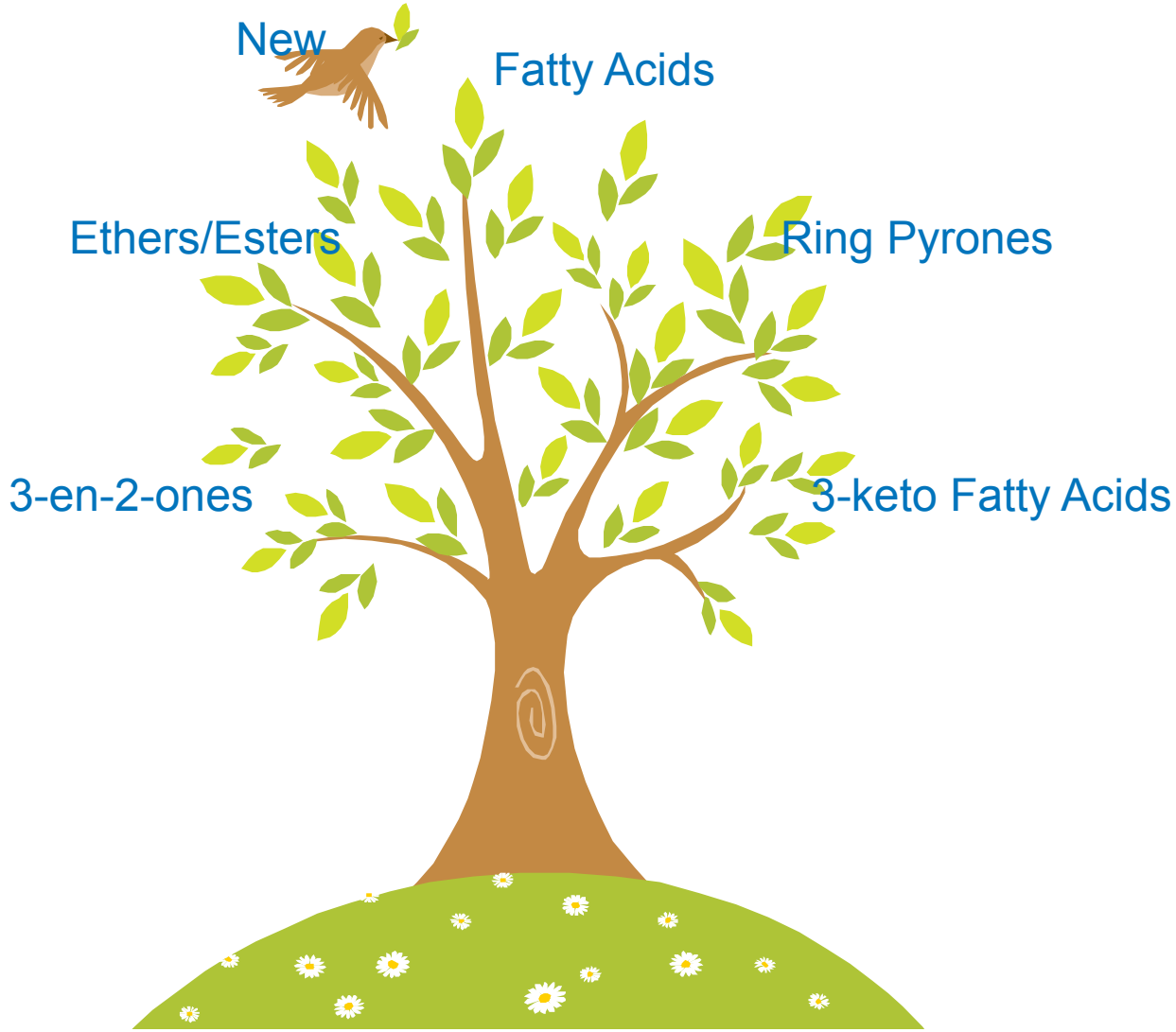


Biobased Chemicals



Array of Opportunities

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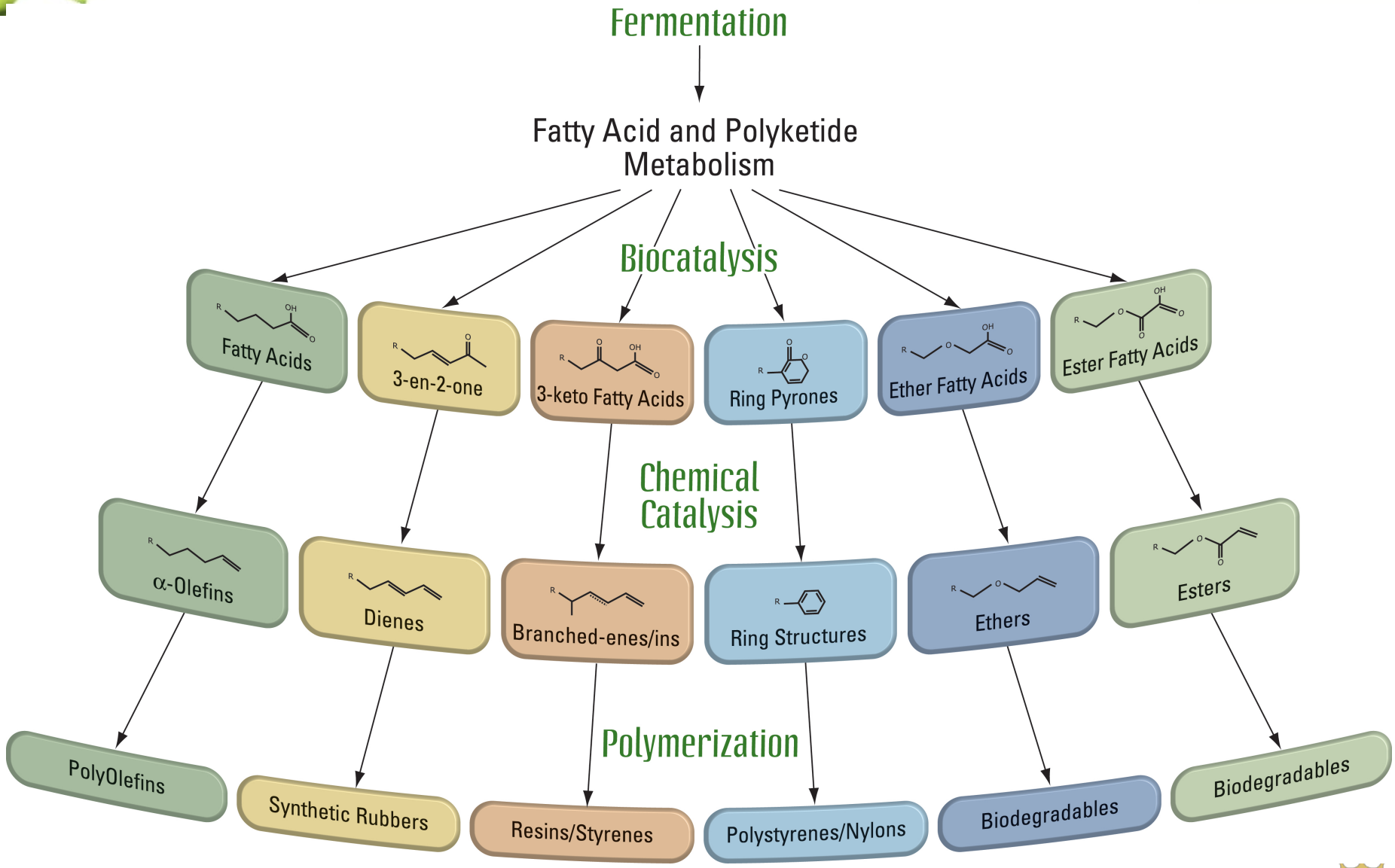

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Research Overview

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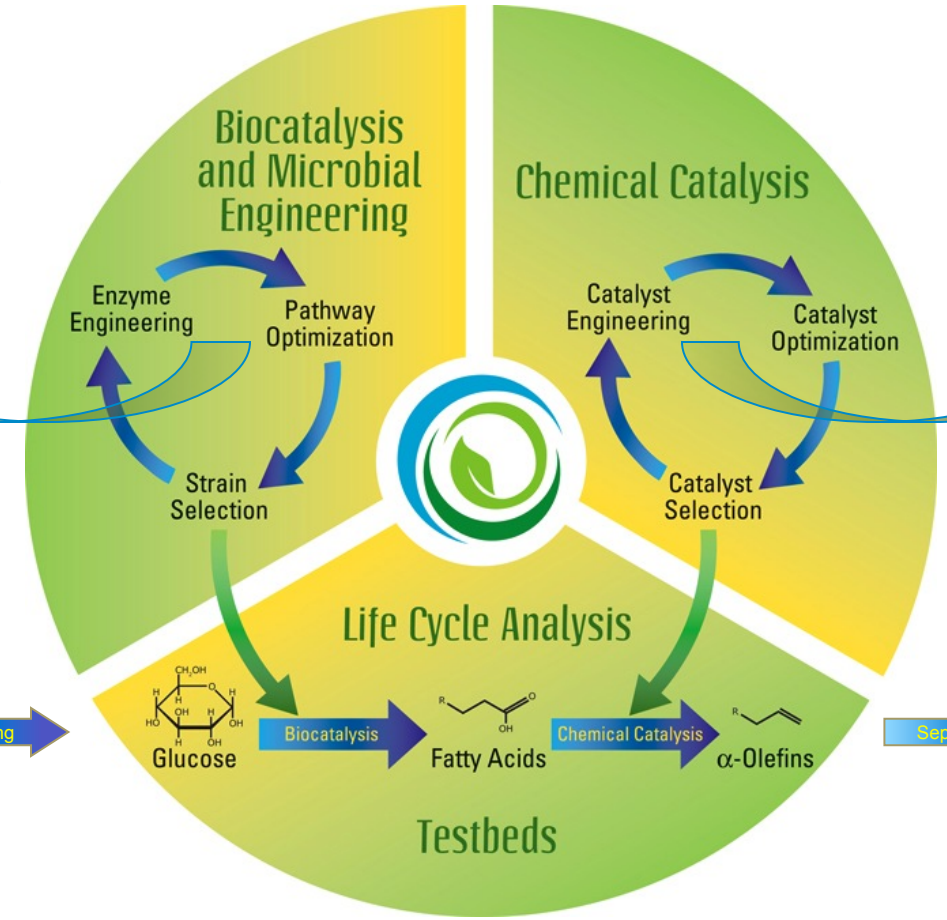
Innovation & Know How in Enzyme and Pathway Engineering

Innovation & Know How in Catalyst and Catalysis Engineering



Biomass Opportunity → Processing → Glucose → Biocatalysis → Fatty Acids → Chemical Catalysis → α-Olefins → Separation → ***Biorenewable Chemicals***

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Research Areas and Faculty

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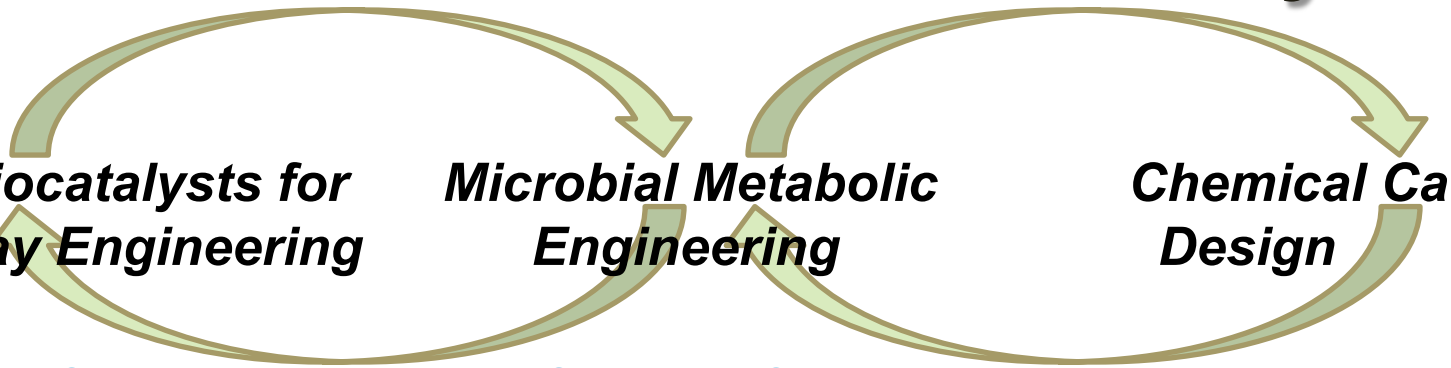

New Biocatalysts for Pathway Engineering

Joe Noel *(Salk) - Lead*
Basil Nikolau *(ISU)*
Eran Pichersky *(UMich.)*
Tom Bobik *(ISU)*
Eve Wurtele *(ISU)*
Adam Barb (*ISU*)
Peter Reilly (ISU)
David Oliver (ISU)

Microbial Metabolic Engineering

Jackie Shanks *(ISU) - Lead*
Nancy Da Silva *(UCIrv.)*
Julie Dickerson *(ISU)*
Ramon Gonzalez *(Rice)*
Laura Jarboe *(ISU)*
Costas Maranas *(PSU)*
Ka-Yiu San *(Rice)*
Suzanne Sandmeyer *(UCIrv)*
Zengyi Shao (*ISU*)

Chemical Catalyst Design

Robert Davis *(UVa) - Lead*
Brent Shanks *(ISU)*
Jim Dumesic *(UWisc)*
Abhaya Datye *(UNM)*
Matt Neurock *(UVa)*
George Kraus *(ISU)*
Klaus Schmidt-Rohr *(ISU)*
Jean-Philippe Tessonnier (*ISU*)
Keith Woo (ISU)
Richard Larock (ISU)

Technoeconomic and Life Cycle Analysis

Rob Anex (UWisc) - Lead
Raj Raman *(ISU)*

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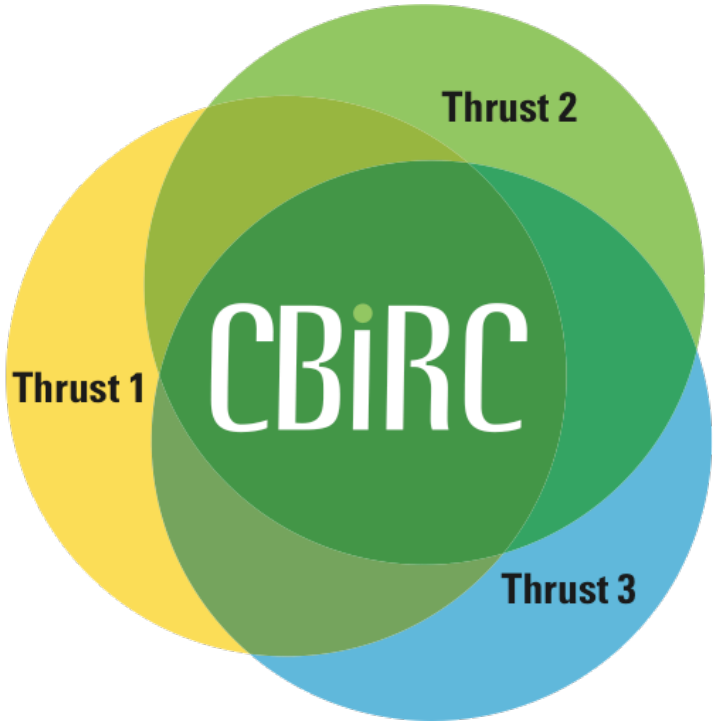
Defining Thrust Questions



Thrust 1: New Biocatalysts for Pathway Engineering

Can the biocatalytic machinery of the fatty acid/polyketide synthesis pathway be systematically harnessed? - *diversification*

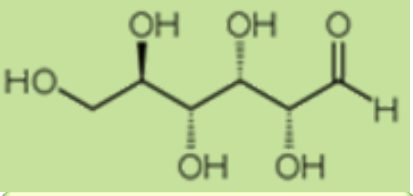
Thrust 2: Microbial Metabolic Engineering

Can microbial systems be designed for the efficient production of reduced carbon chemical species? – *flux control*

Thrust 3: Chemical Catalyst Design

Can catalysts be designed for the selective conversion of multifunctionalized substrates? – *design rules*

T1 Enzymes

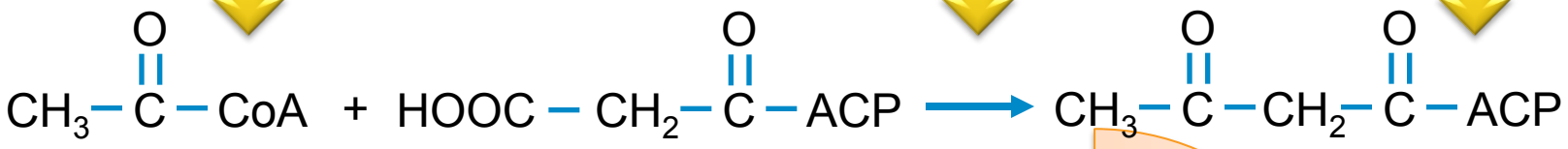


Carbohydrates

Acetyl-CoA Synthetase

3-Ketoacyl-ACP Synthase

Methylketone Synthase



starter

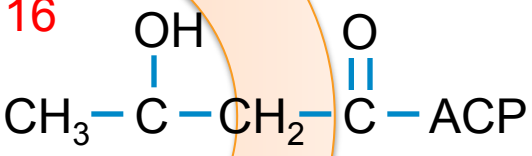
extender

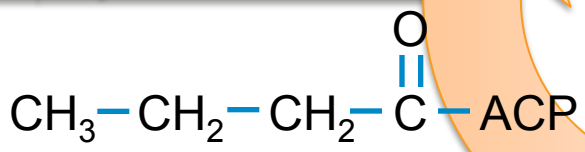
reduction

Acyl-CoA Carboxylase

CoASH Synthase/Reductase

4, 6, 8,,,,16





dehydration

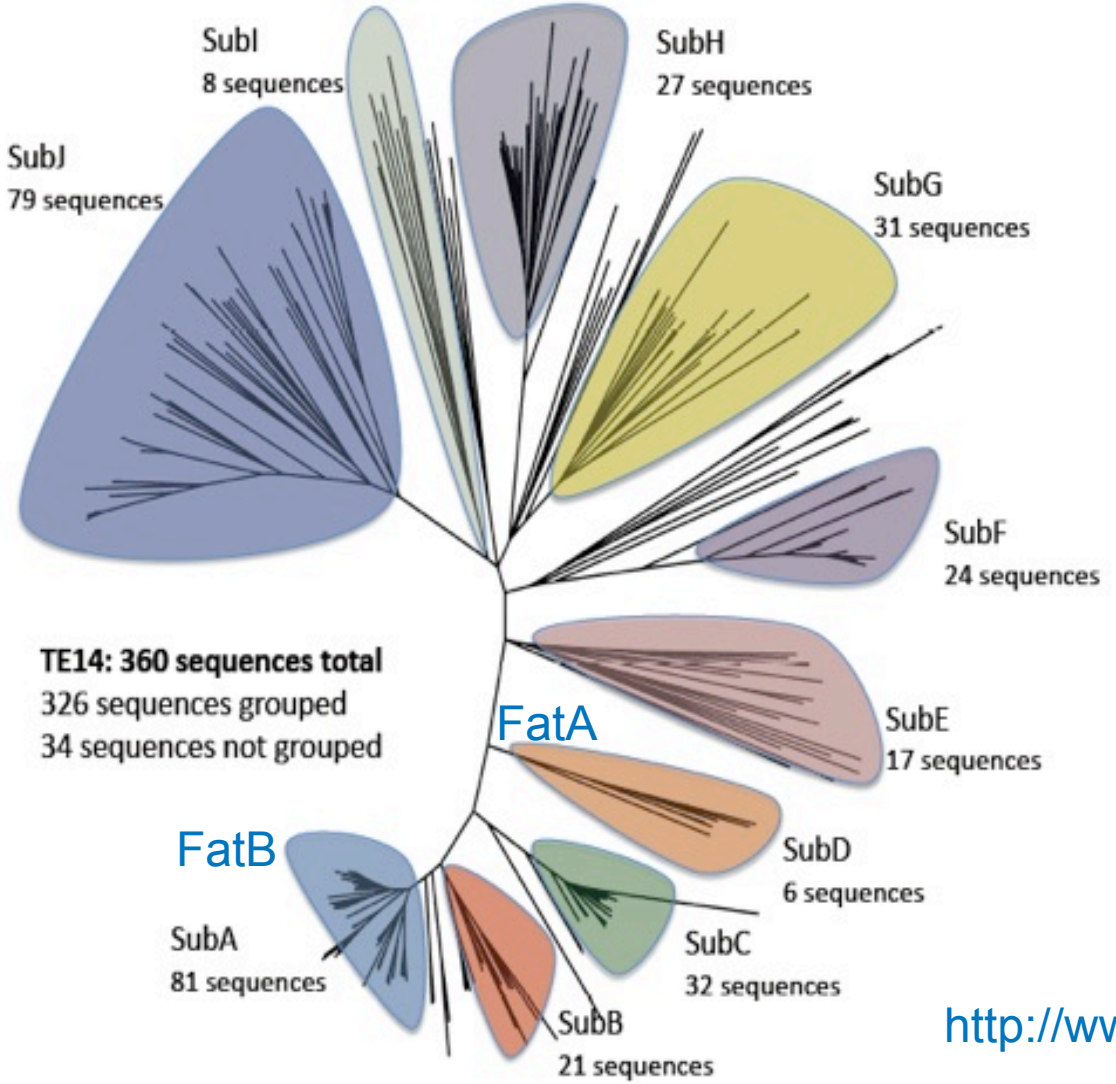
reduction

Thioesterase

Opportunities

1. Shorter & Longer Chains
2. Even and Odd numbered
3. Straight & Branched chains
4. Diversified Chemistry

ThYme Enzyme Database



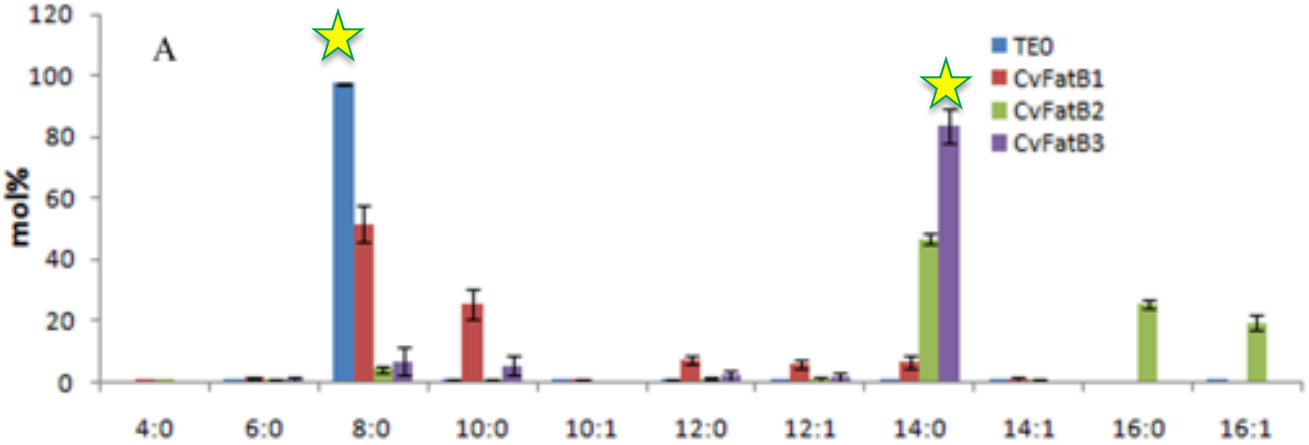
~ 1000 sequences
90% sequences are not characterized

http://www.enzyme.cbirc.iastate.edu/

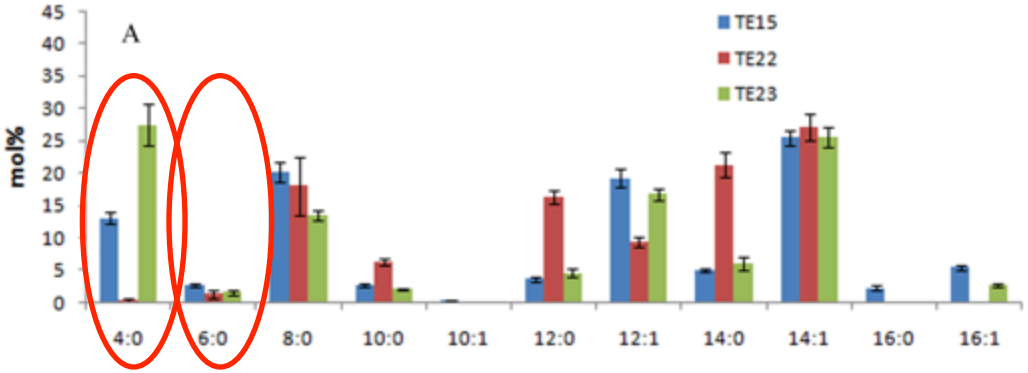
Cantu et al., *Nucleic Acids Res.*, **39**, D342 (2011).

Diverse Activities

- Monospecificity

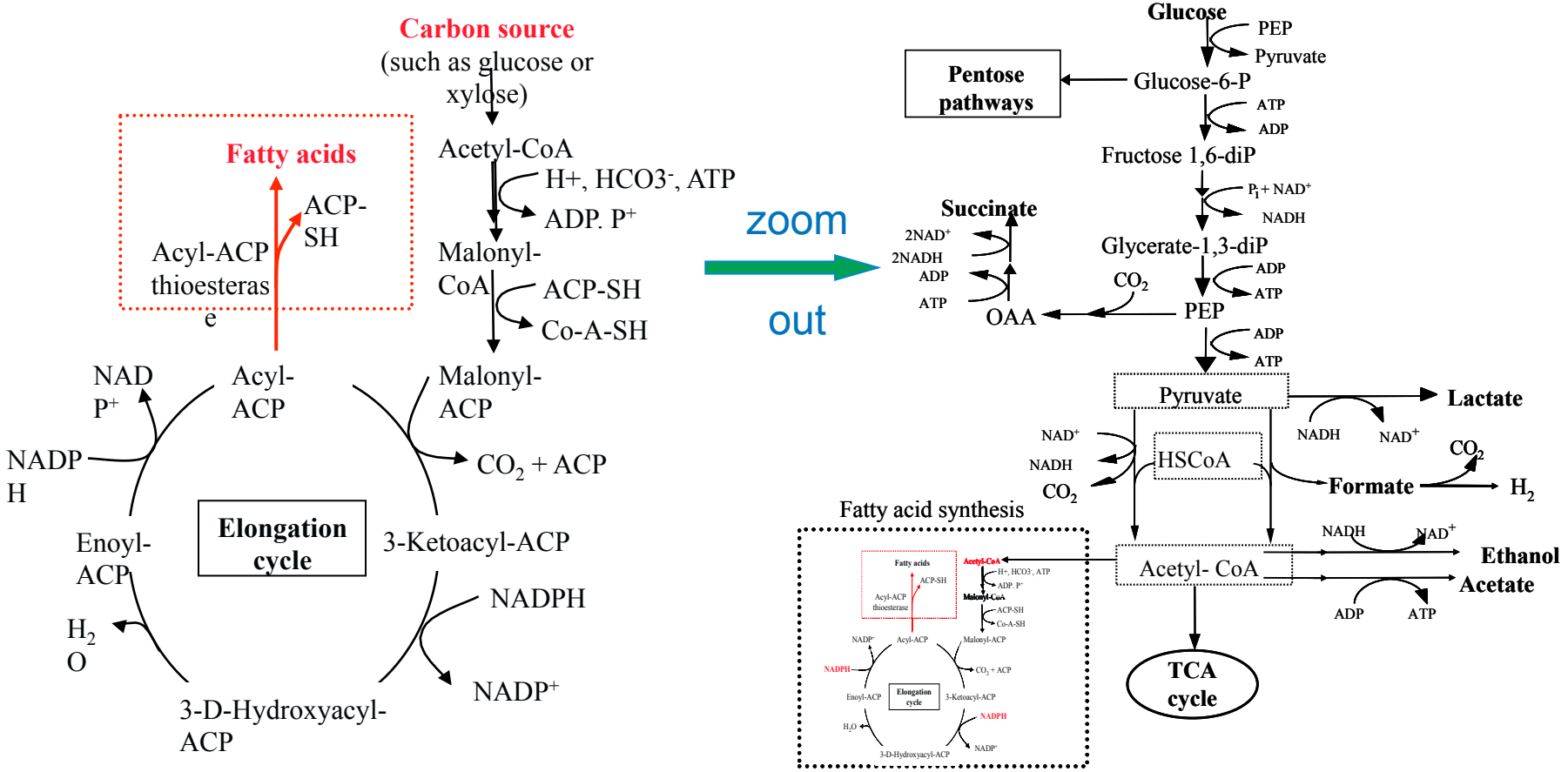


- Short chains



Jing et al., *BMC Biochem.*, **12**, 44 (2011).

T2 Microbial Engineering



T2 Metabolic Engineering

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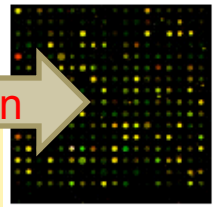
Strain Selection and Evolution

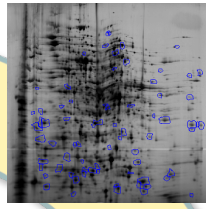
Omics and Flux Analysis

Metabolic Evolution

Characterization

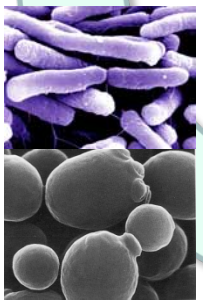


Transcriptomics

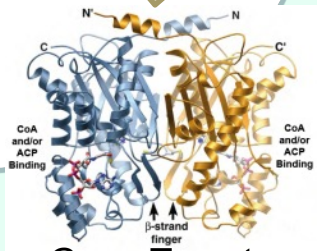


Proteomics

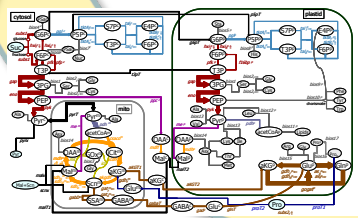
Information



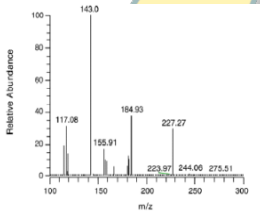
Strain Selection and Transformation



Gene Targets (from Thrust 1)



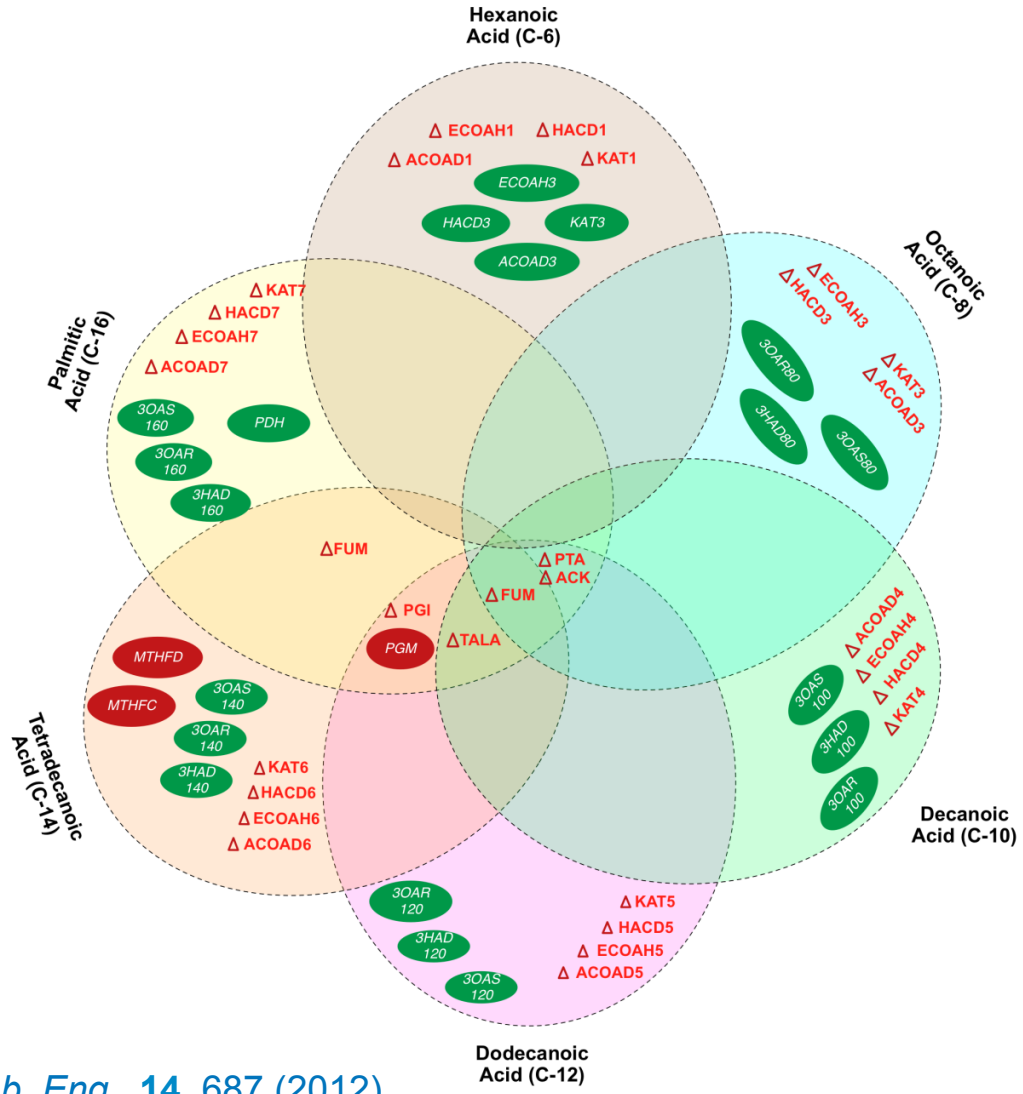
Flux Analysis



Metabolomics

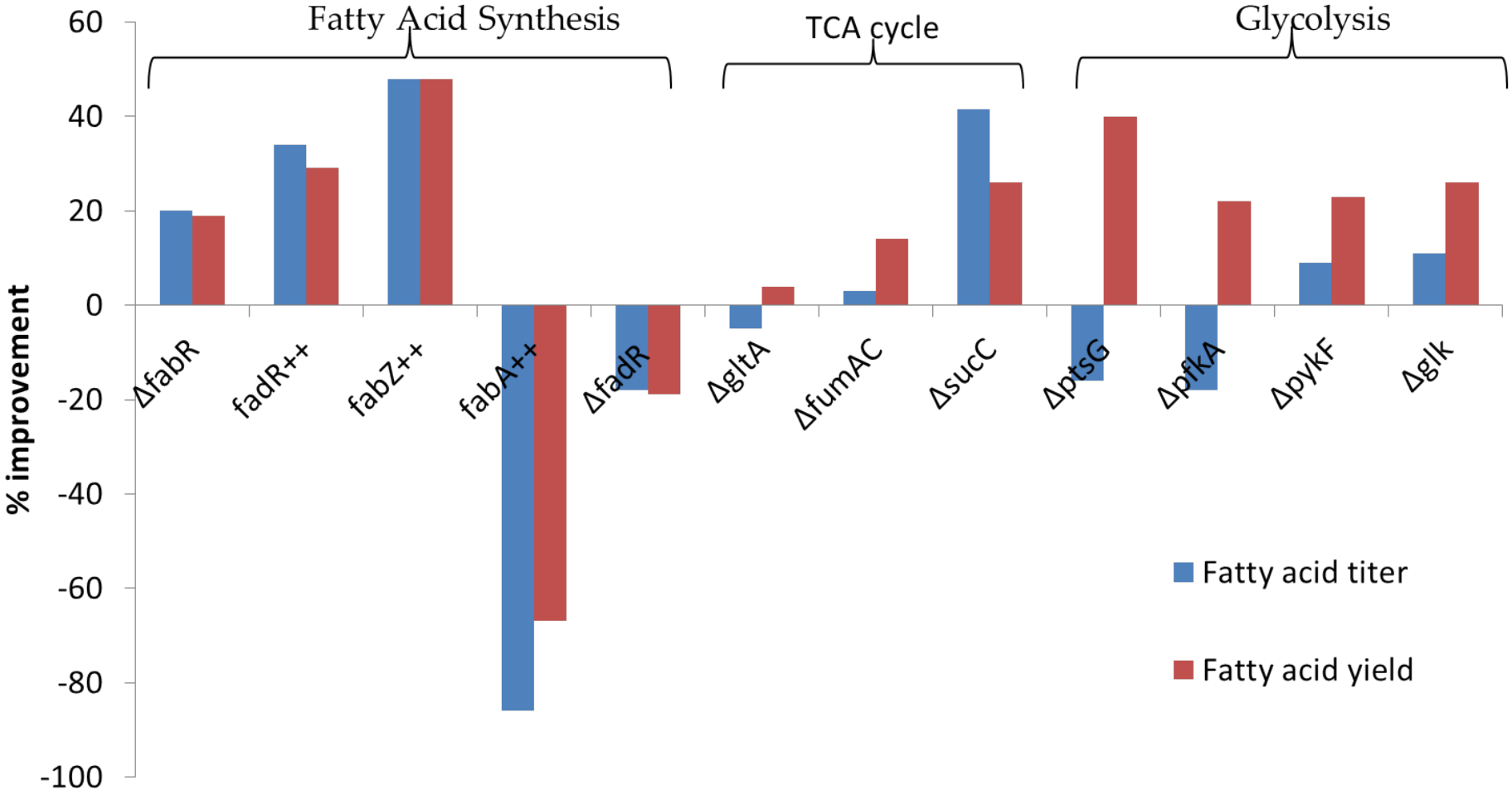
NSF

OptForce Gene Targets



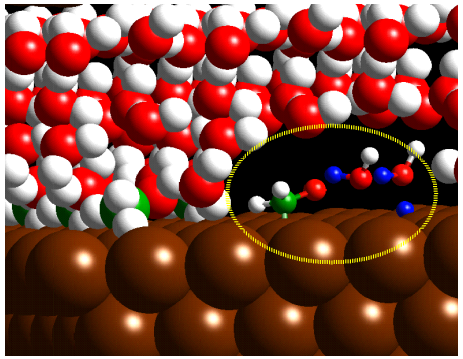
Ranganathan et al., *Metab. Eng.*, **14**, 687 (2012).

Experimental Results



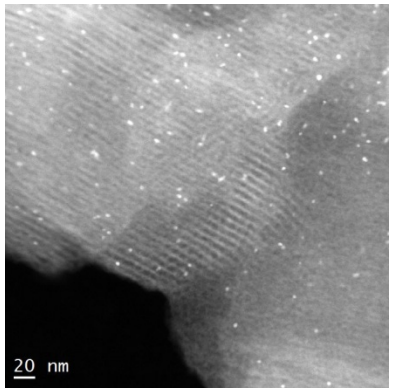
Ranganathan et al., *Metab. Eng.*, **14**, 687 (2012).

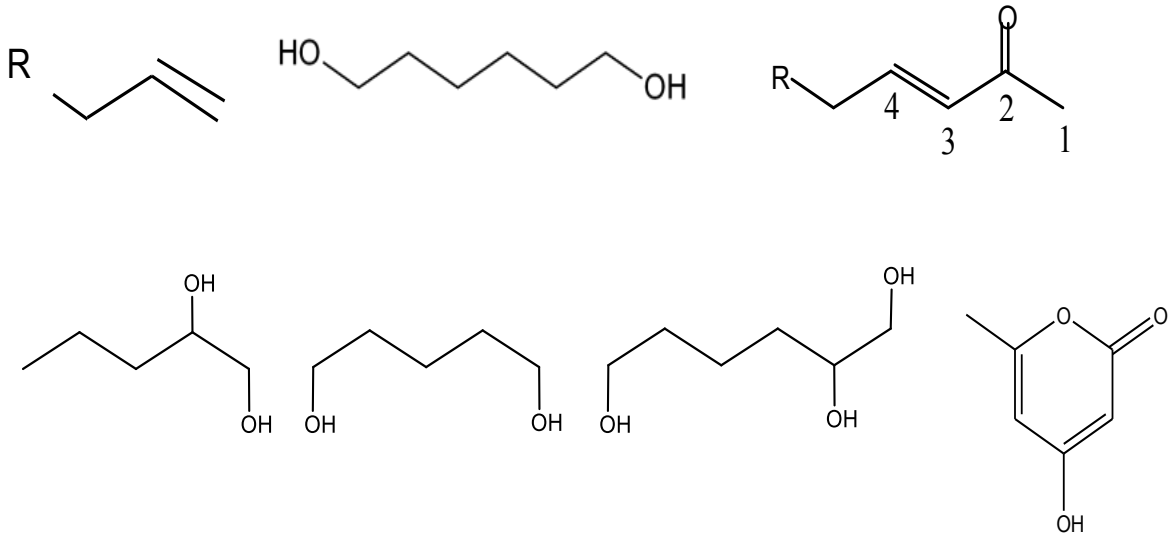
T3 Catalytic Toolbox



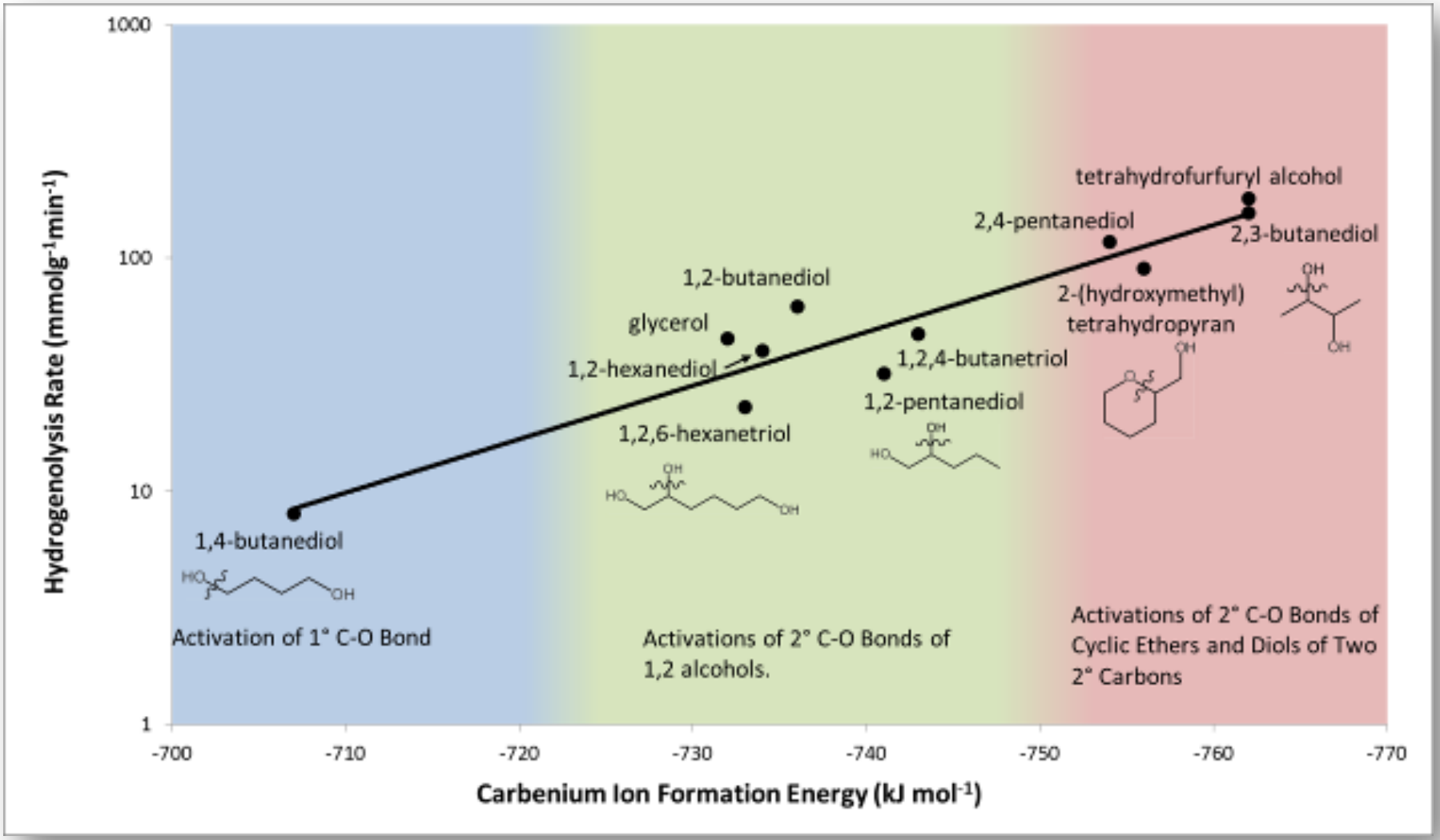
Selective Chemical Catalysis

1. Decarboxylation
2. Hydrogenation
3. Ring opening
4. Dehydration
5. Hydrogenolysis
6. Condensation
7. *Stable catalysts*



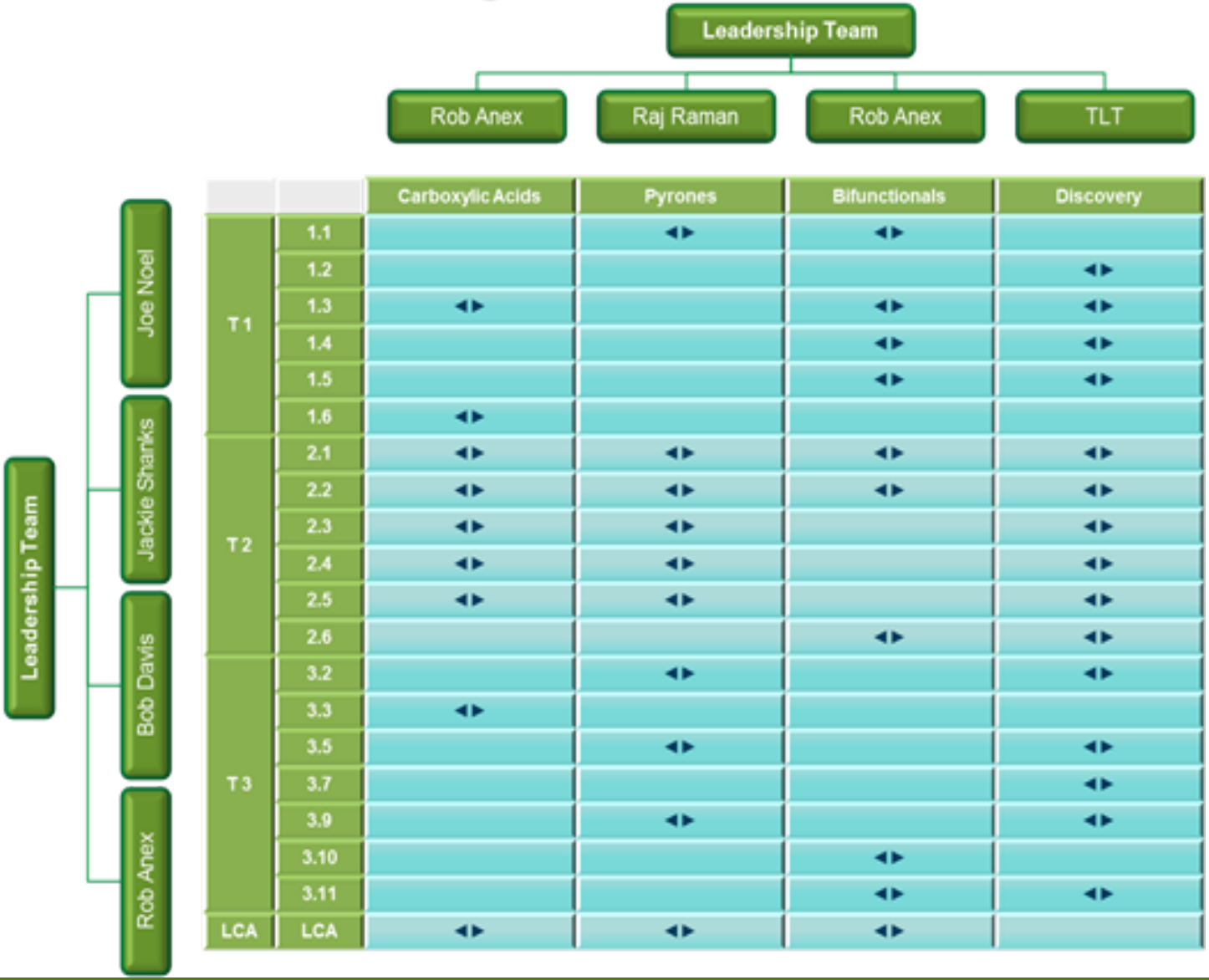


Hydrogenolysis with PtRe



Chia et al., *J. Amer. Chem. Soc.*, **133**, 12675 (2011).

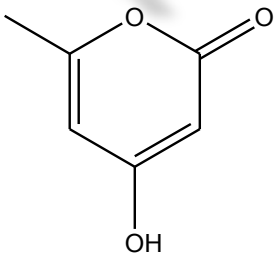
Center Projects



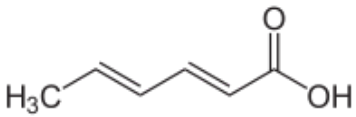
Pyrone (TAL) Test Bed

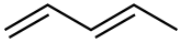
Sugars

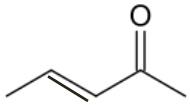
Biological Conversion

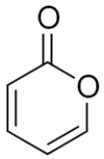


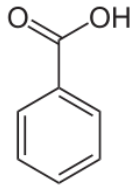
Catalytic Diversification





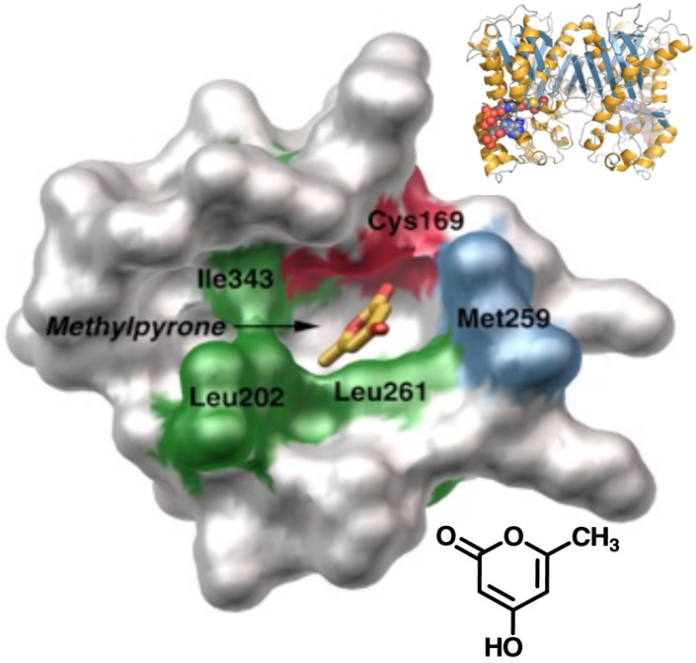






Sorbic Acid Pentadiene 3-Penten2one 2-Pyrone Benzoic Acid

Test Bed Integration



Thrust 1

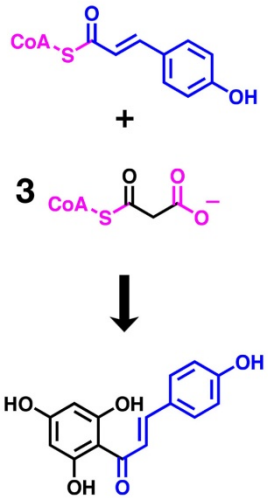
Thrust 2

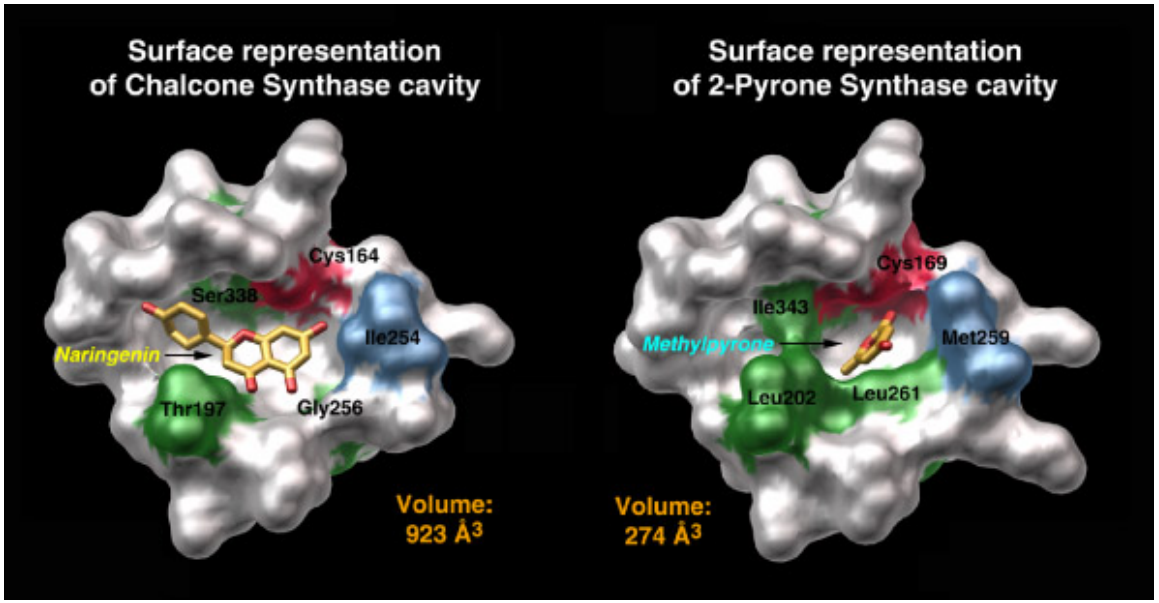
Thrust 3

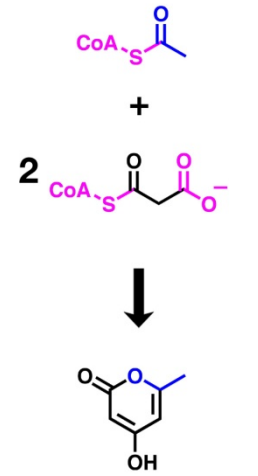
Enzymes:
- 2-PS
- CHS3X
- 2PS-1
- 2PS-2
- 2PS-3
- 2PS-4
- 2PS-5
- 2PS-6

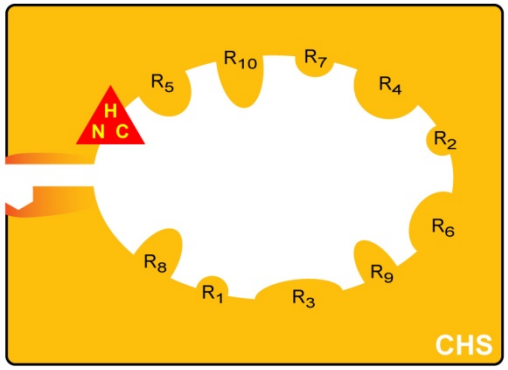
Nutrient Media Components

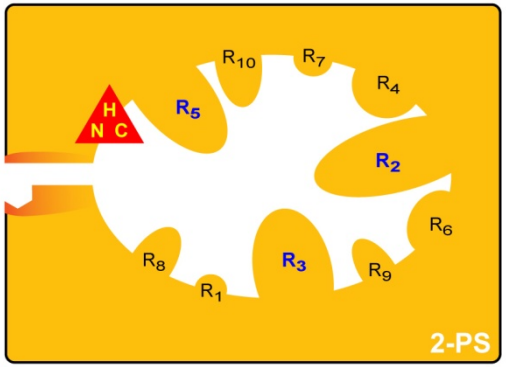
Pyrone Synthase





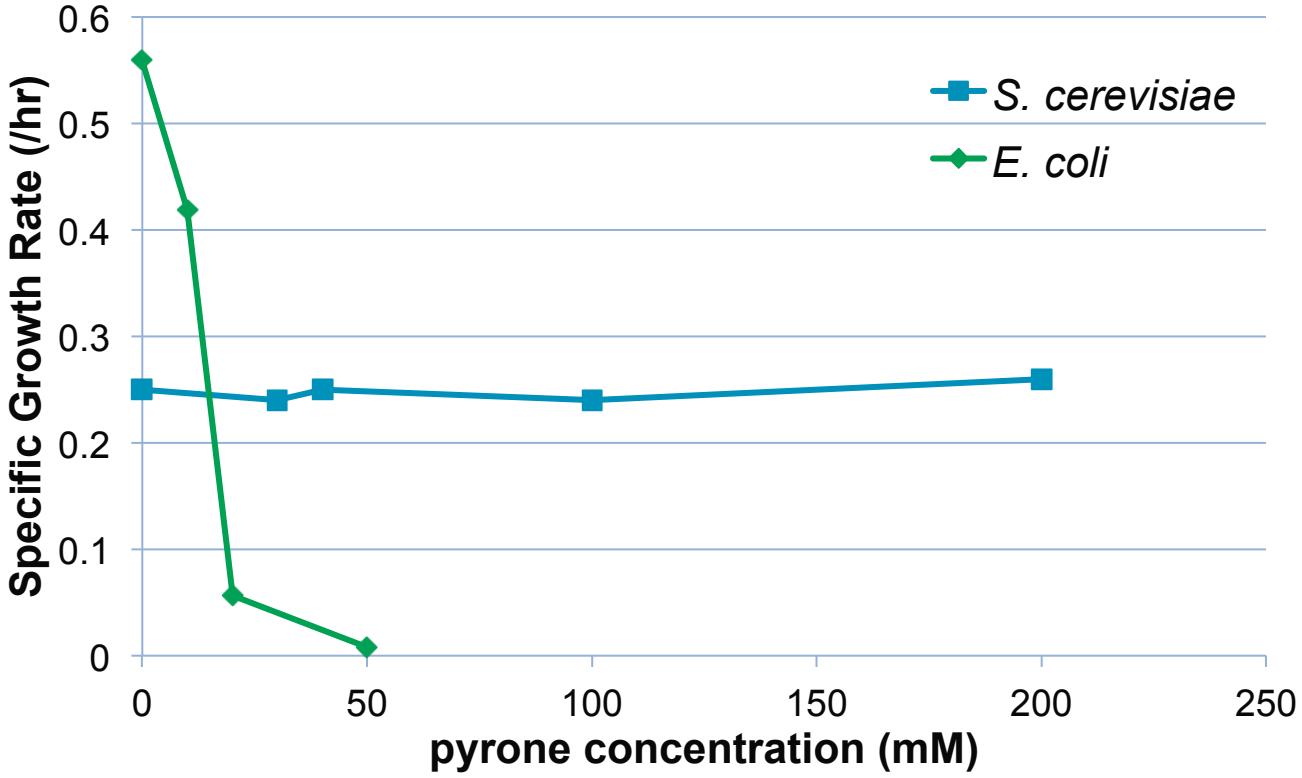






Noel et al.

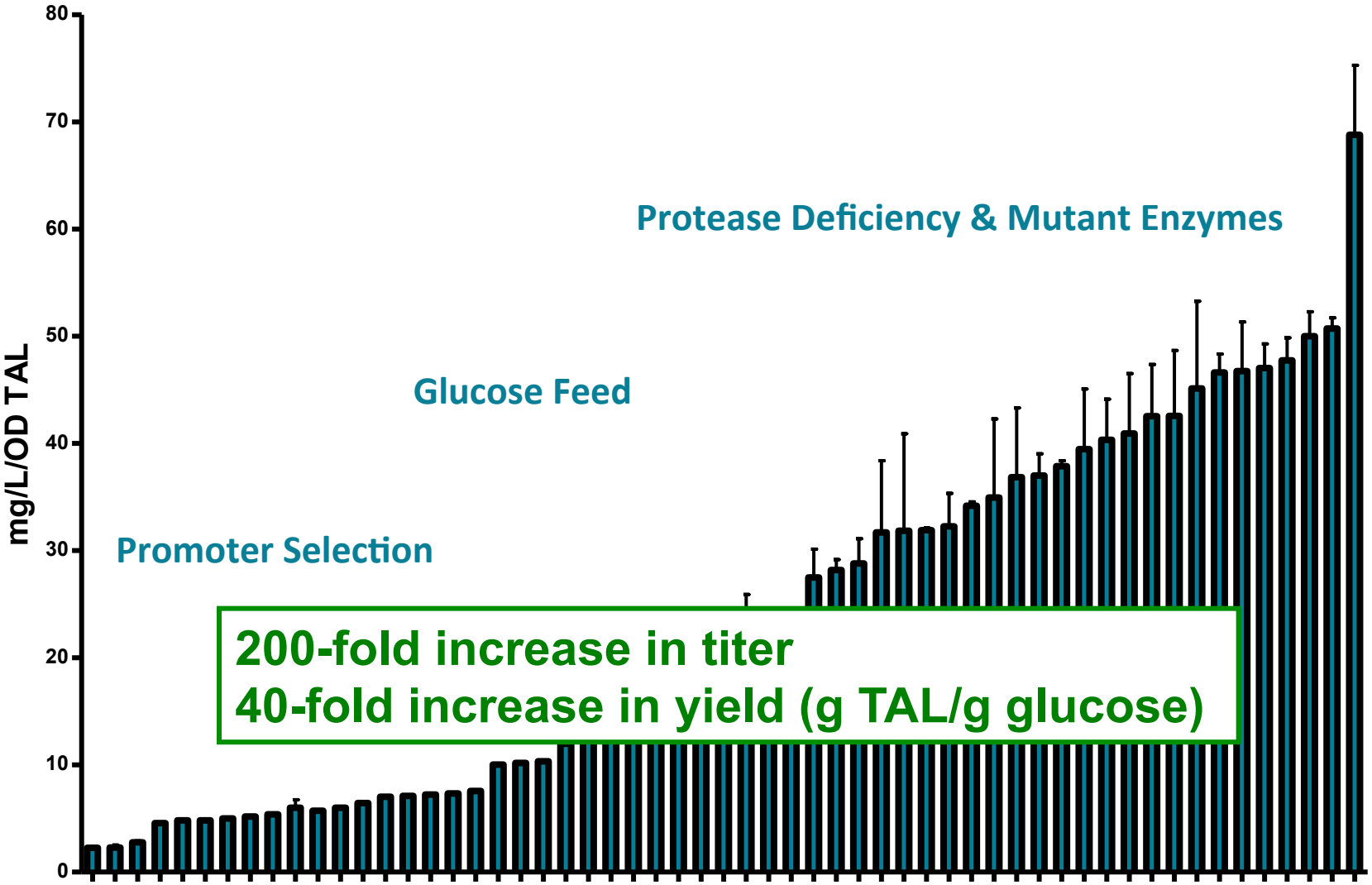
TAL Toxicity



- 25 g/L TAL does not inhibit *S. cerevisiae* growth
- < 2.5 g/L TAL significantly inhibits *E. coli* growth

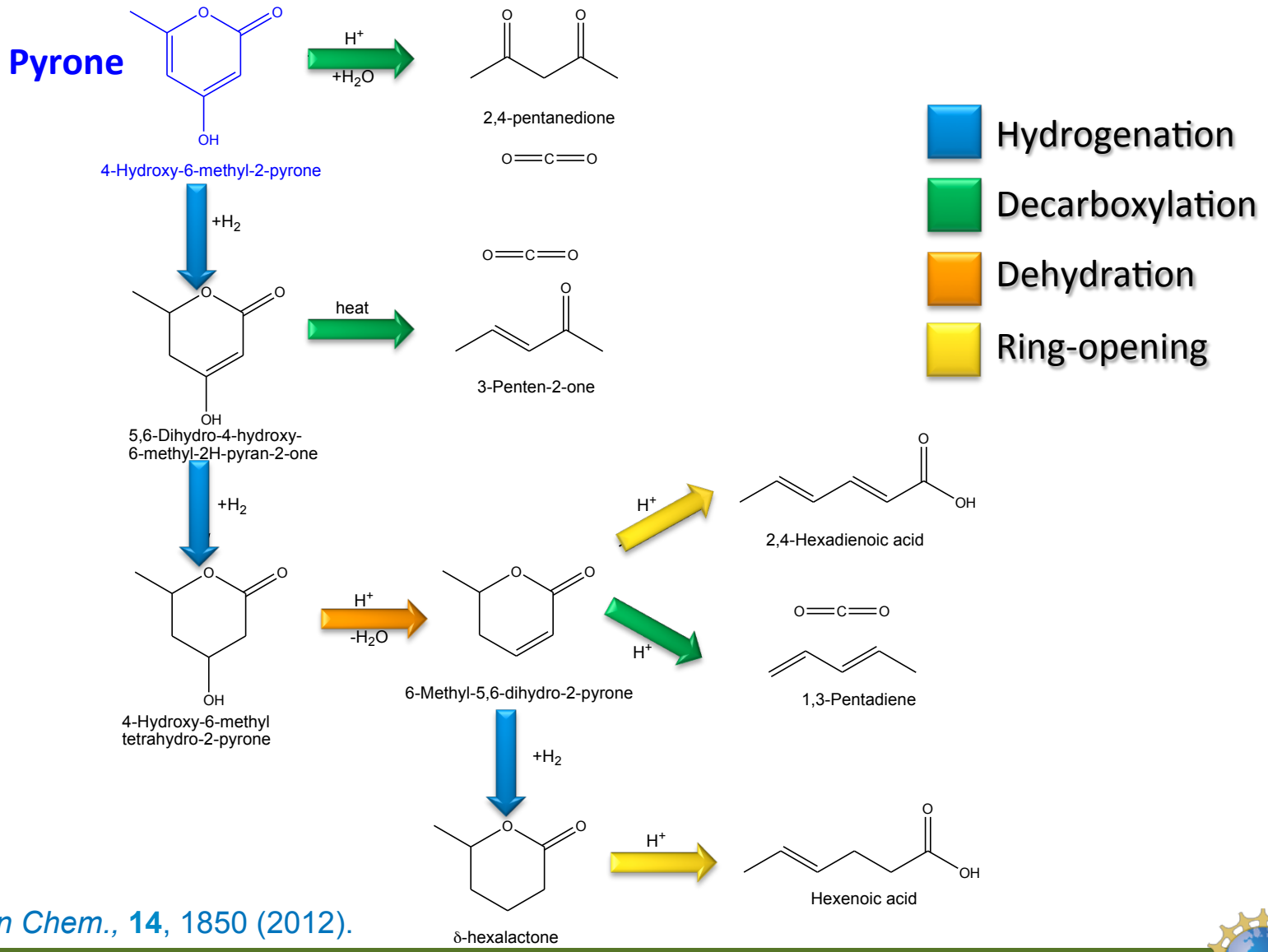
Jarboe et al.

TAL Levels – *S. cerevisiae* Series



Da Silva, Noel et al.

Reaction Scheme

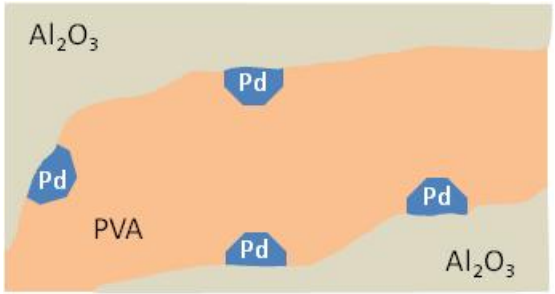


Chia et al., *Green Chem.*, **14**, 1850 (2012).

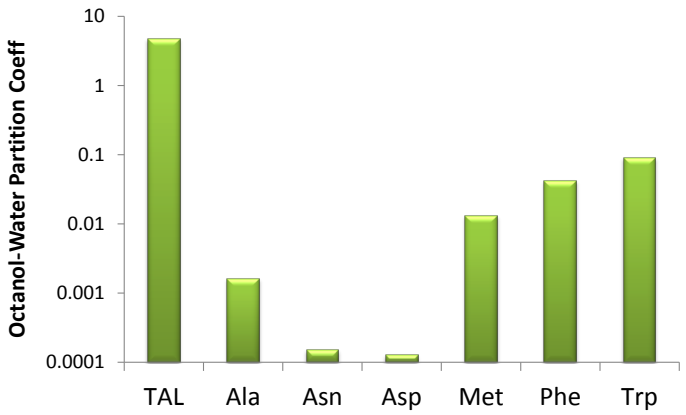
Designing Catalyst Tolerance

- **Inhibit adsorption of amino acids by creating a local chemical environment that favors less-polar species**

Creating a local chemical environment: Inside the catalyst pores, polymerize a solid solvent that favors TAL over amino acids – take advantage of solvent effects to make amino acid adsorption energetically unfavorable



	TAL Solubility (%w/w)
Water	0.86
THF	2
n-pentane	~0
n-butanol	4.9
n-hexanol	4
n-octanol	3.6

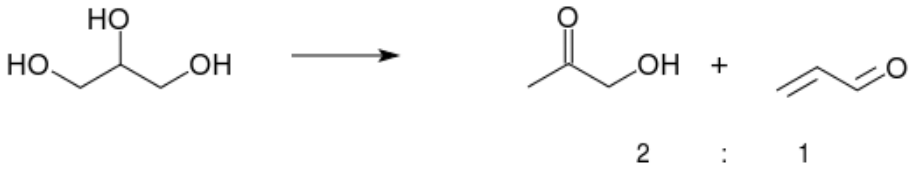


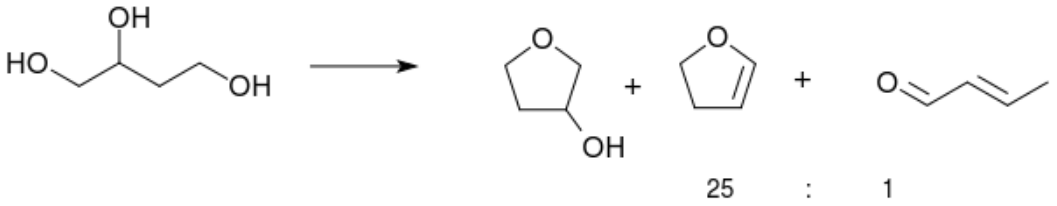
Dumesic et al.

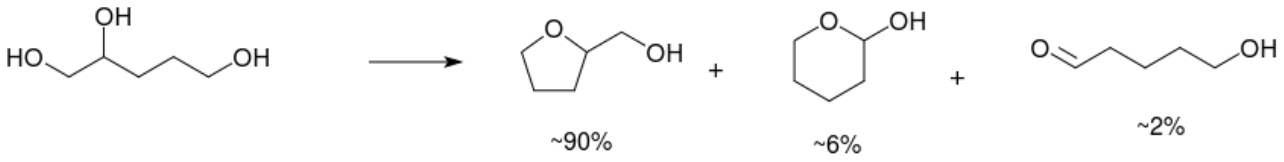
K_{OW} data from Chalcraft, et. al. *Anal. Chem.* 81, 2506-2515, 2009.

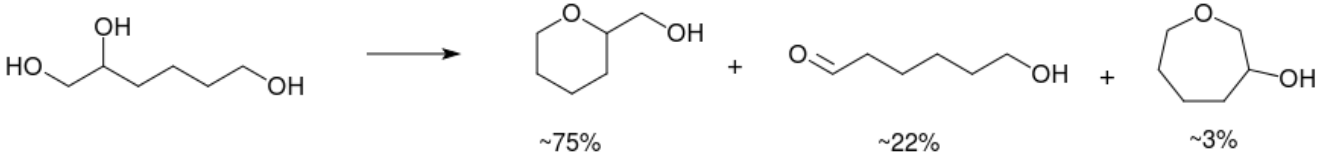
Dehydration Studies

- **Chain length effect for 1,2,ω triols**









Overall, most trends follow expected acid dehydration pattern

Glycerol unique as it is fully hydroxylated and too short to form rings

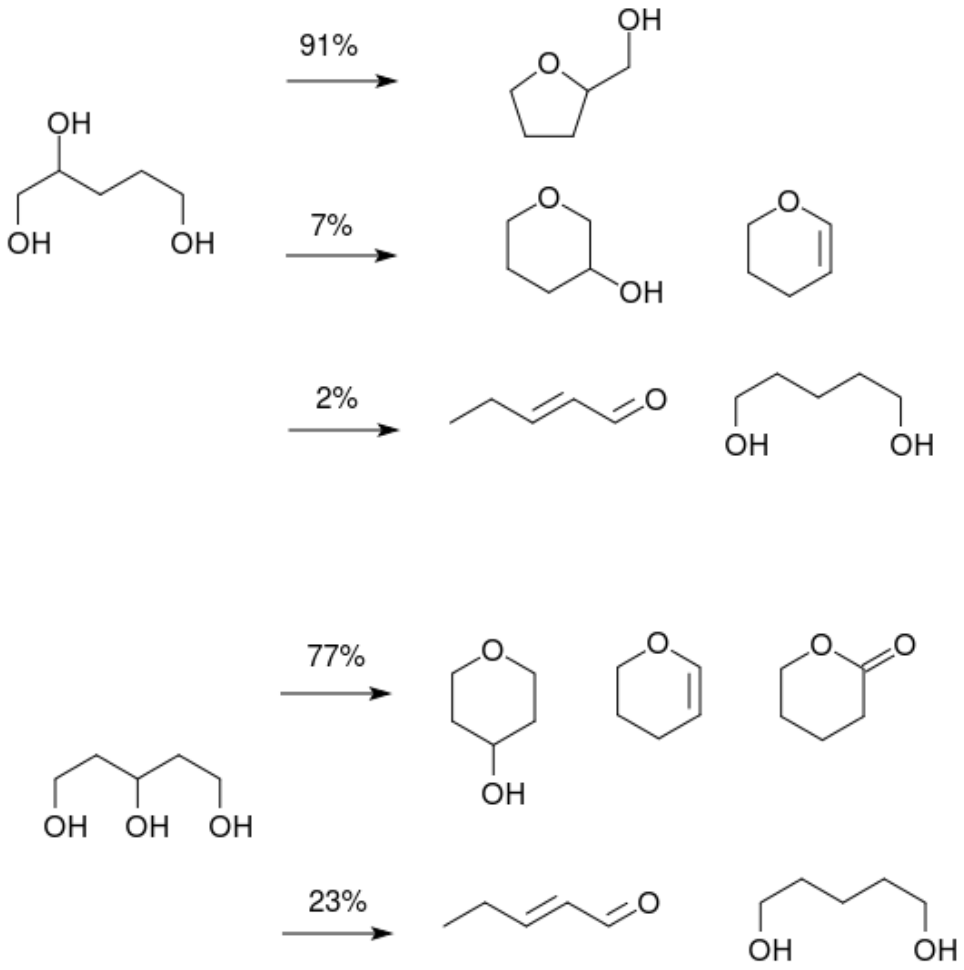
Ring formation more favored route than linear elimination

Linear products favored with longer chains

1,2 interaction may be favored over 2,ω interaction for long chains

Polyol Dehydration Products

- **Hydroxyl interactions – 1,2,ω versus 1,3,ω triols**



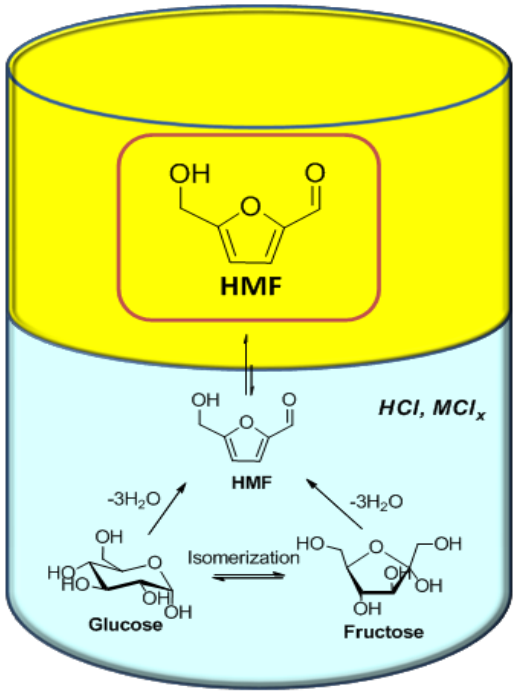
Tenfold linear selectivity increase when switch from 1,2,5- to 1,3,5-pentanetriol

Proposed Mechanism:

1) Protonation of the secondary hydroxyl, followed by either interaction with α hydroxyl or ω hydroxyl

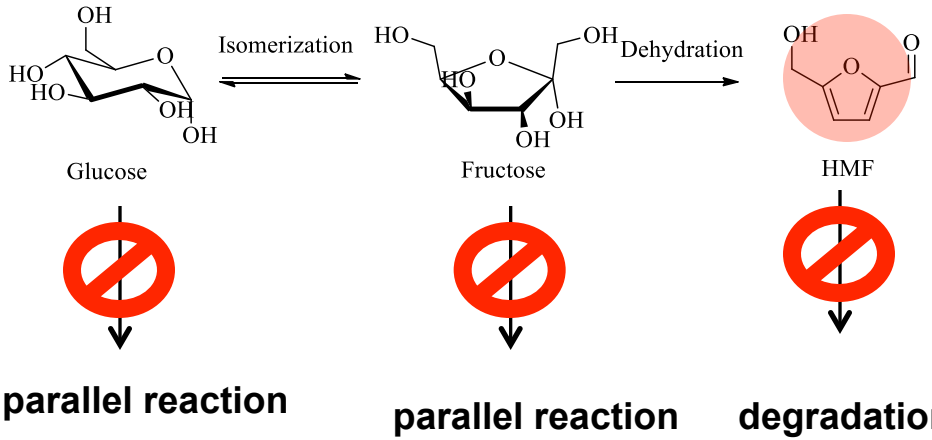
2) Elimination more likely with highly strained interactions

HMF from Glucose



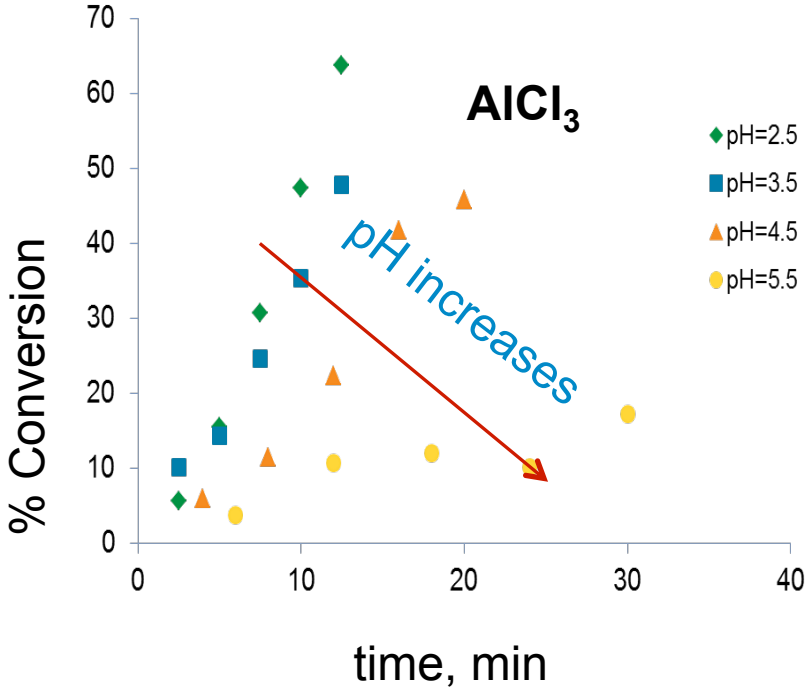
Organic layer:
Sec-butyl phenol

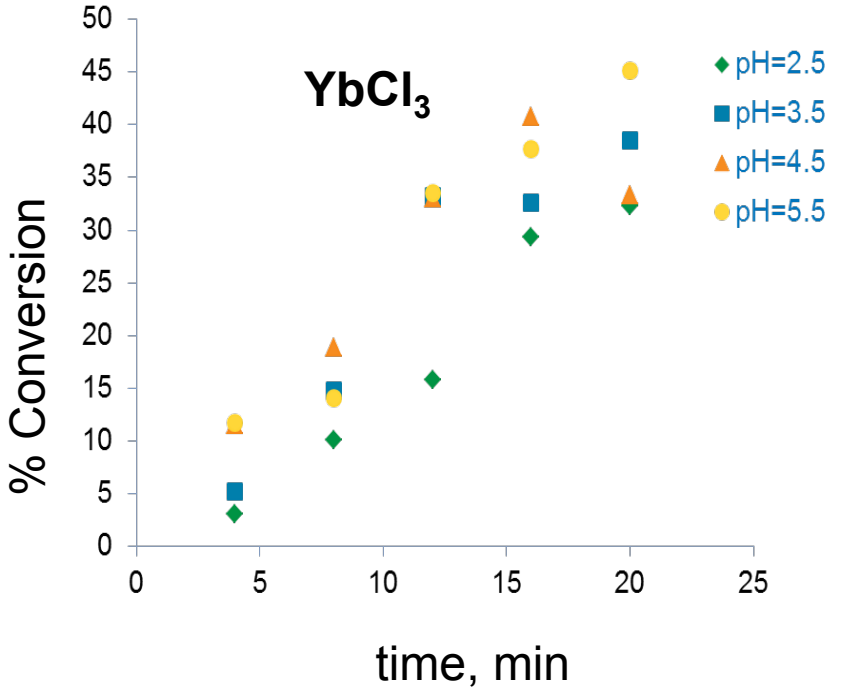
Aqueous layer:
Water
Glucose
MCl_3
HCl (pH adjusted to 2.5)
NaCl



Pagan-Torres et al., *ACS Catal.*, **2,** 930-934, 2012.

Glucose Dehydration: Effect of pH on the Lewis acid activity





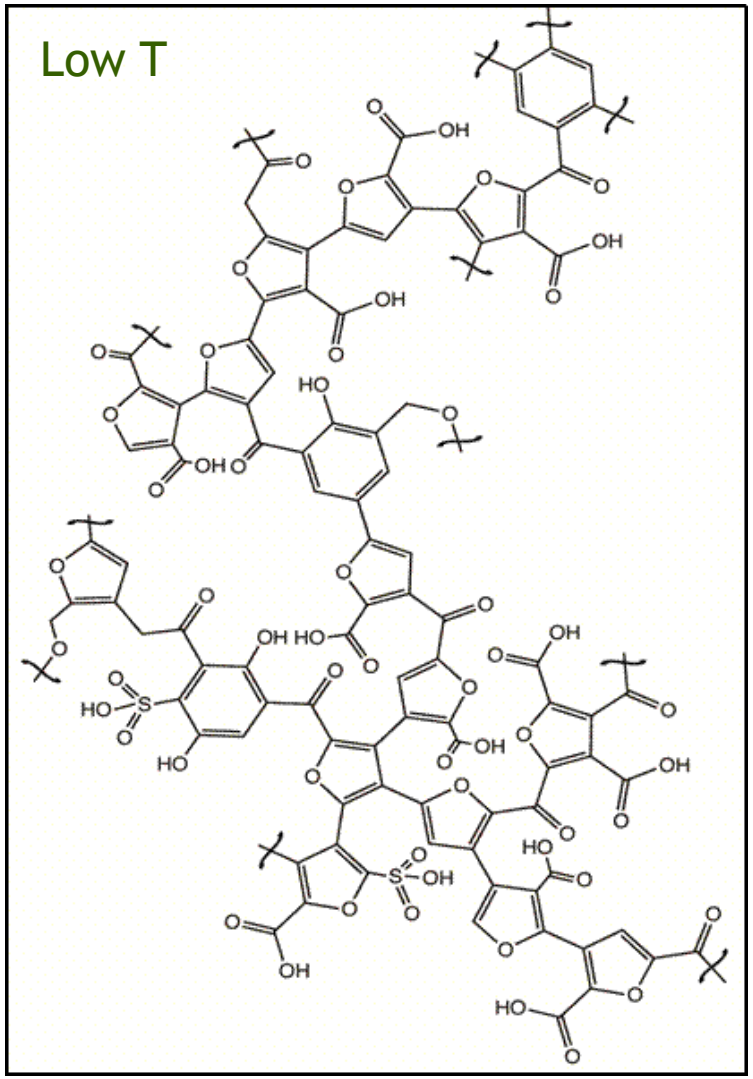
More active species

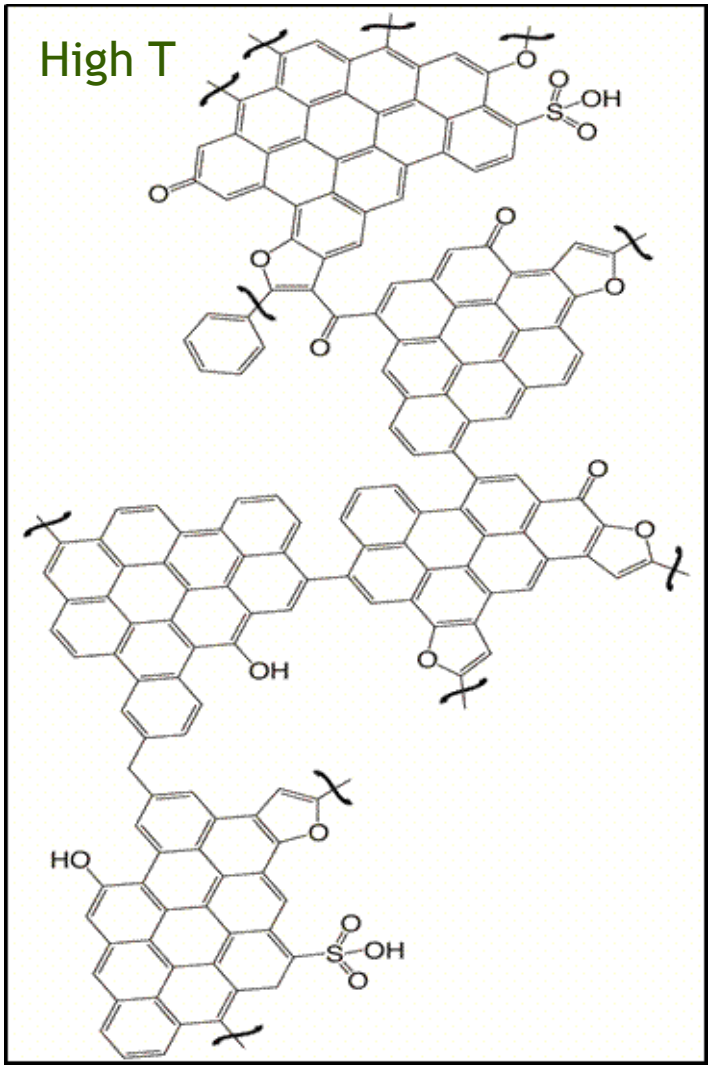
$$xM^{z+} + yH_2O \rightleftharpoons M_x(OH)_y^{(xz-y)+} + yH^+$$

$AlCl_3$ or $YbCl_3$, 5 wt% glucose in water saturated with NaCl, reaction temperature of 443 K, organic to aqueous mass ratio of 2, pH adjusted

Solid Acid Materials

CBiRC
NSF Engineering Research Center for Biorenewable Chemicals





None of the sulfonated carbons were stable!!

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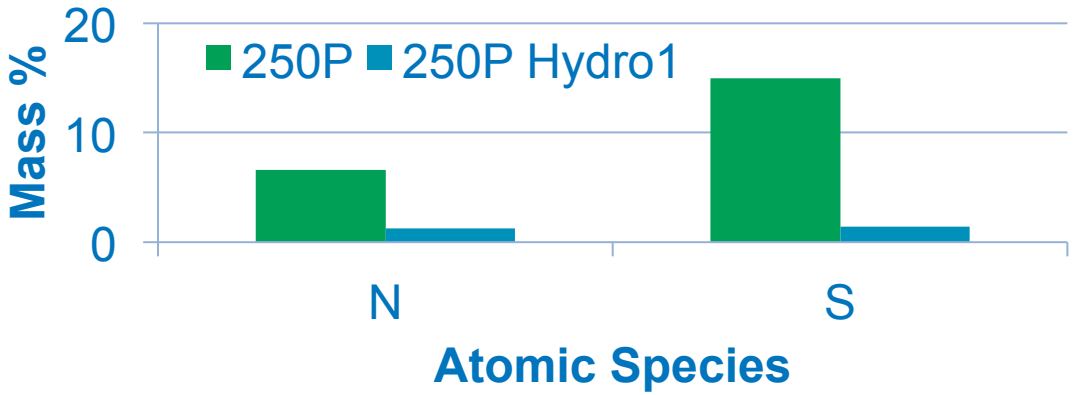
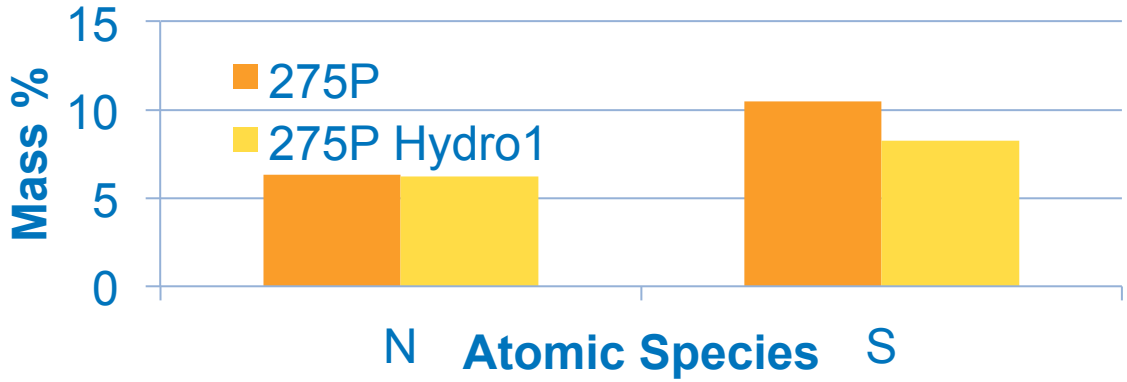
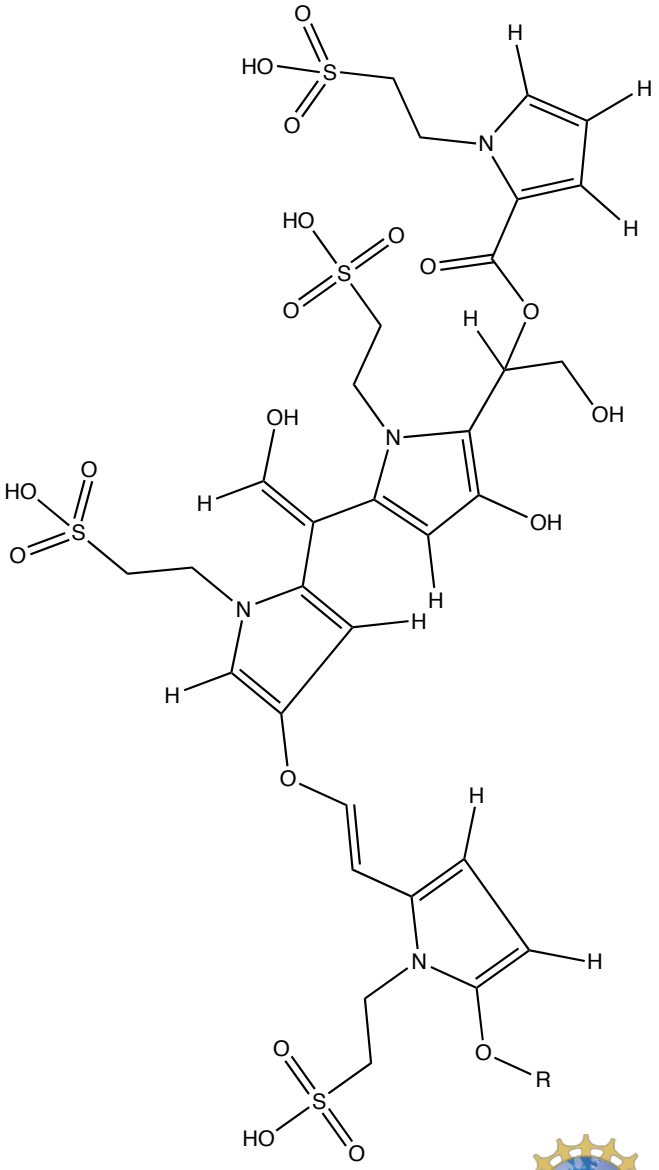
Synthesis Improvement

First Synthesis Approach



Improved Synthesis Approach





The carbon-sulfur bond is no longer the weakest link.

Industry Members

CBiRC
NSF Engineering Research Center for Biorenewable Chemicals

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Technology Transfer

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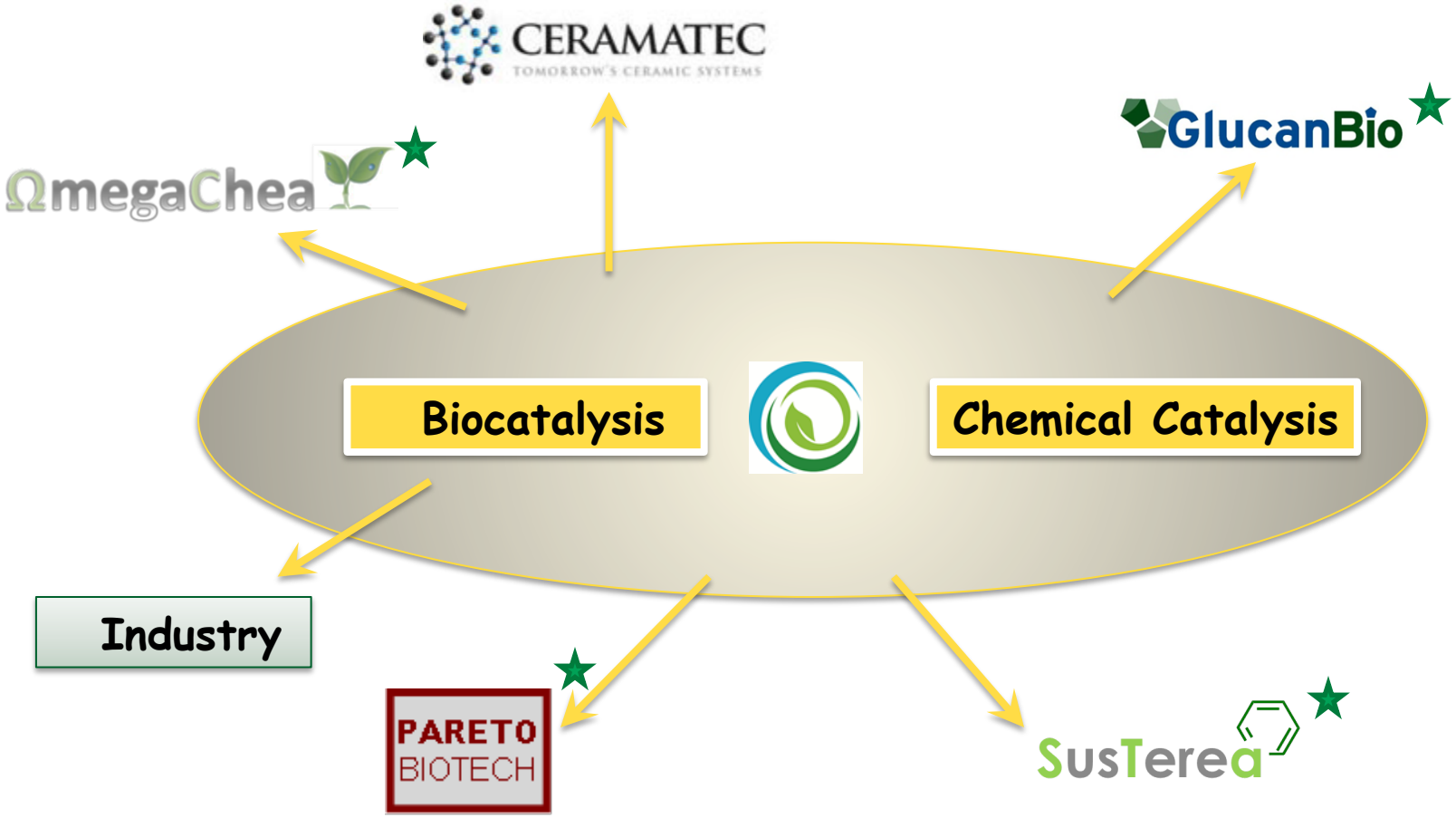
NSF Engineering Research Center for Biorenewable Chemicals



★ *CBiRC Startup Companies*

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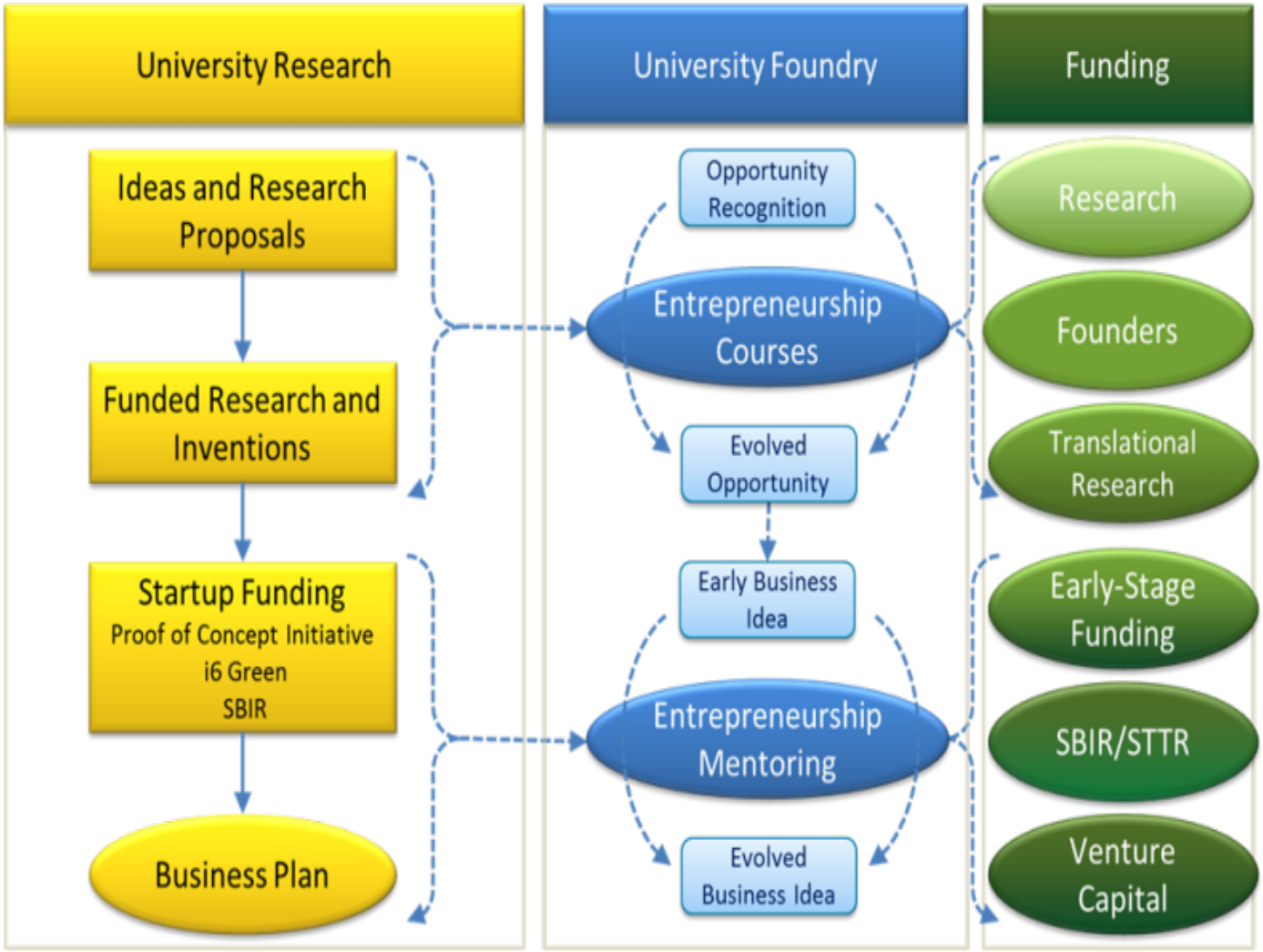
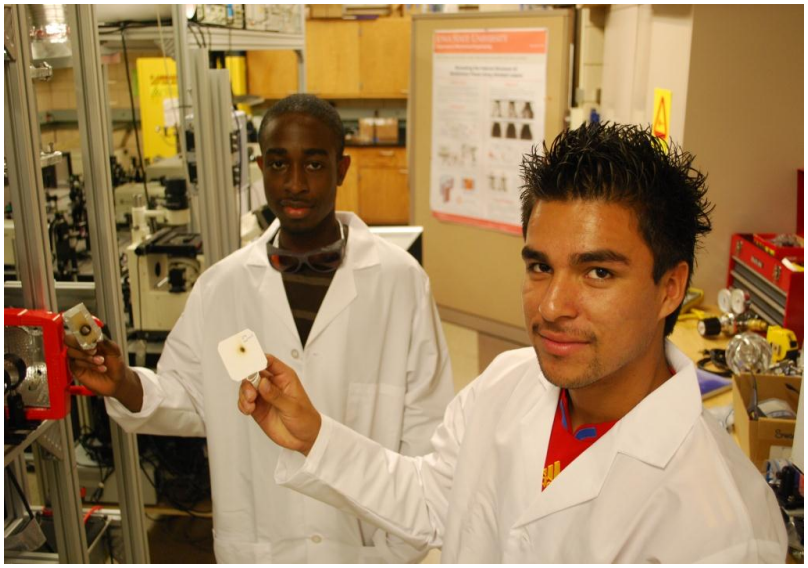
Entrepreneurial Education



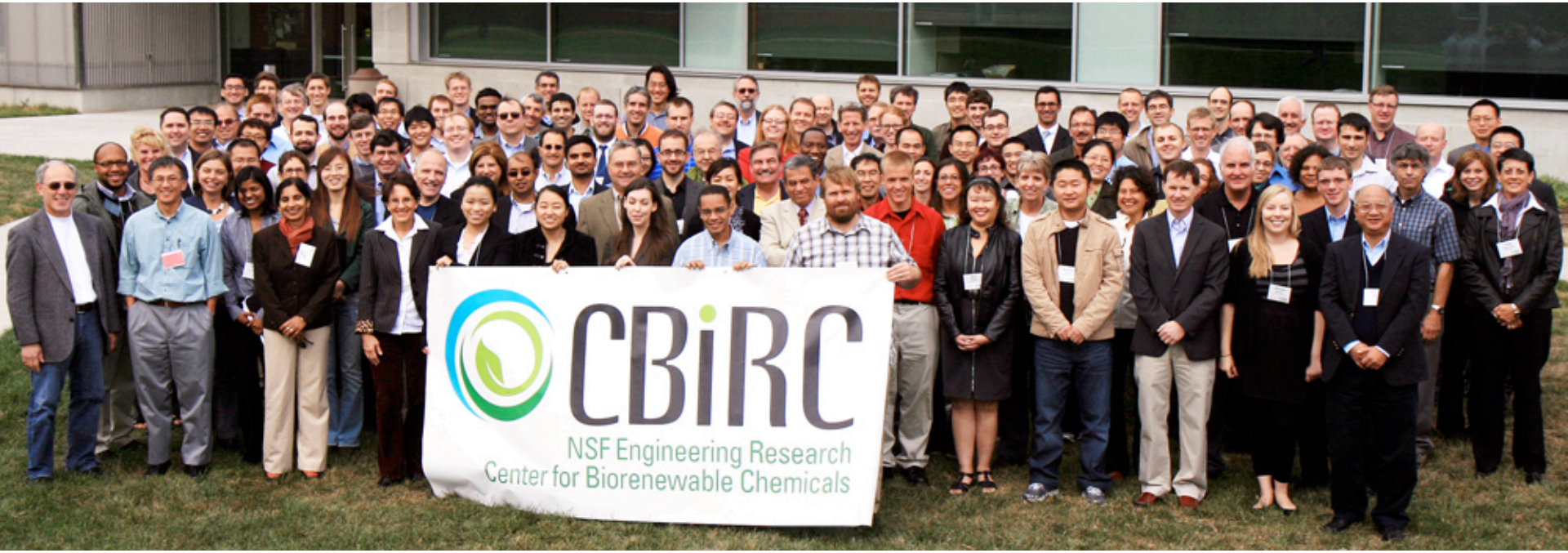
Pre-College Education

Des Moines Public School District Partnership

- Programs developed in collaboration
  - Professional Learning Community
  - STEM Academy (Hoover HS)



- ***>75 DMPSD teachers*** participated in *CBiRC* associated programs
- *Nearly* ***10,000 students/yr*** touched by *CBiRC* teachers
- ***>75%*** *CBiRC* YES alums in STEM fields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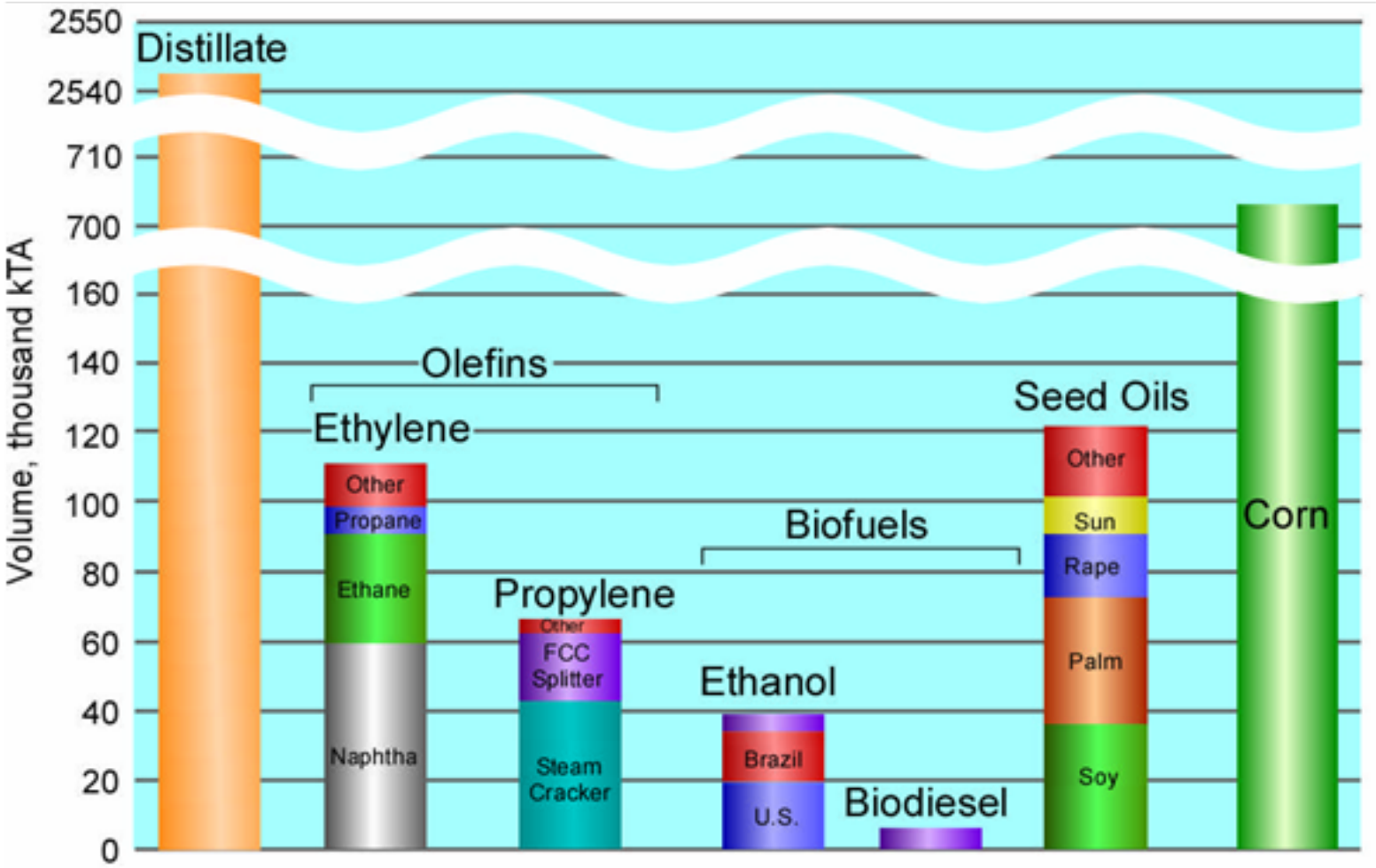
Center for Biorenewable Chemicals

Thank you

Some Context



Dow, Mark Jones (2011)