Opportunities in Eco-Innovation

Chemistry

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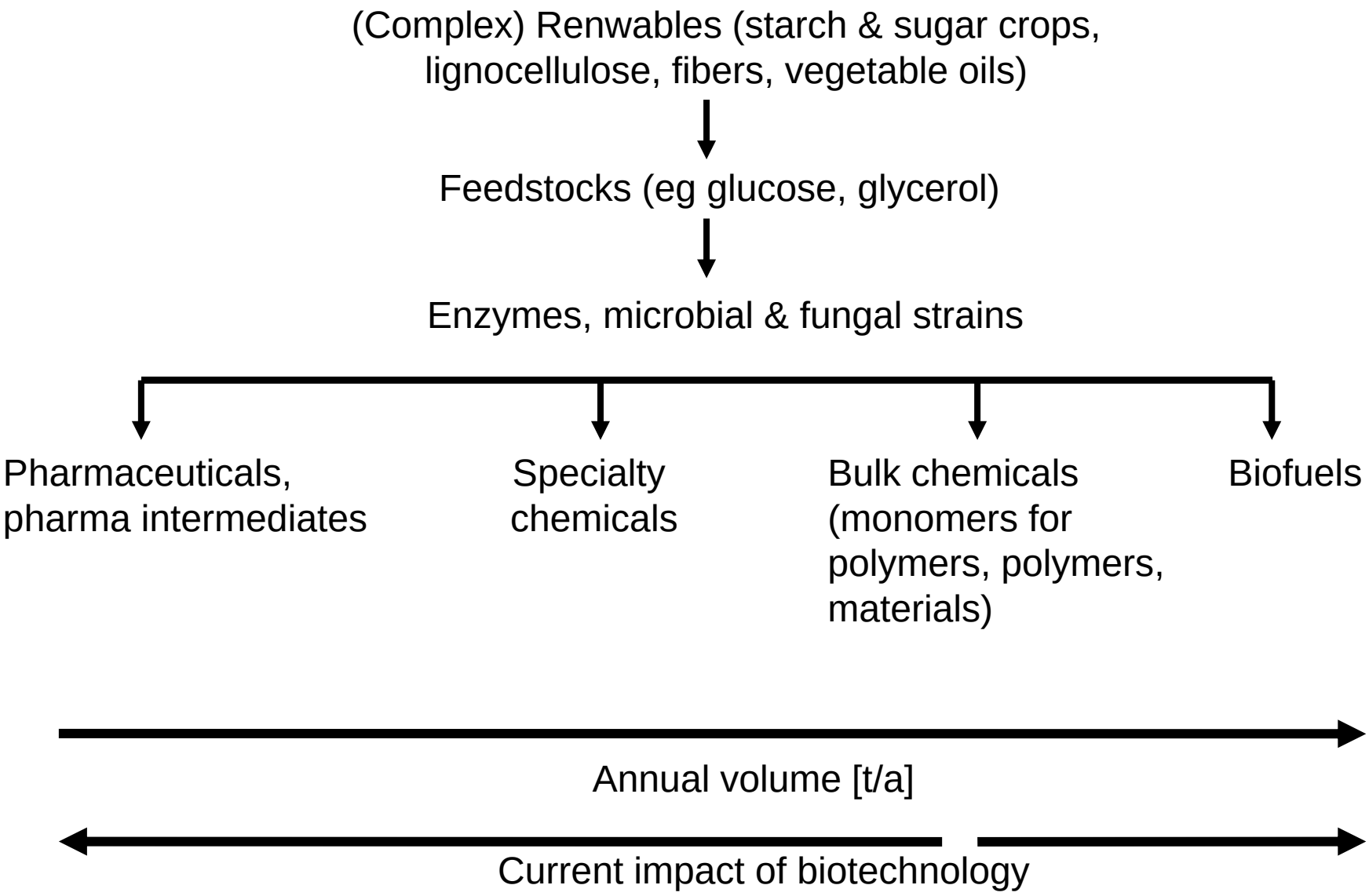
1. Synthetic biology is a set of technologies to do biotechnology much more efficiently than before

2. Biotechnology is crucial for a future sustainable chemical industry

3. Synthetic biology is the way to advance to accelerate this transition

Biotechnology and the chemical industry (w/o food)



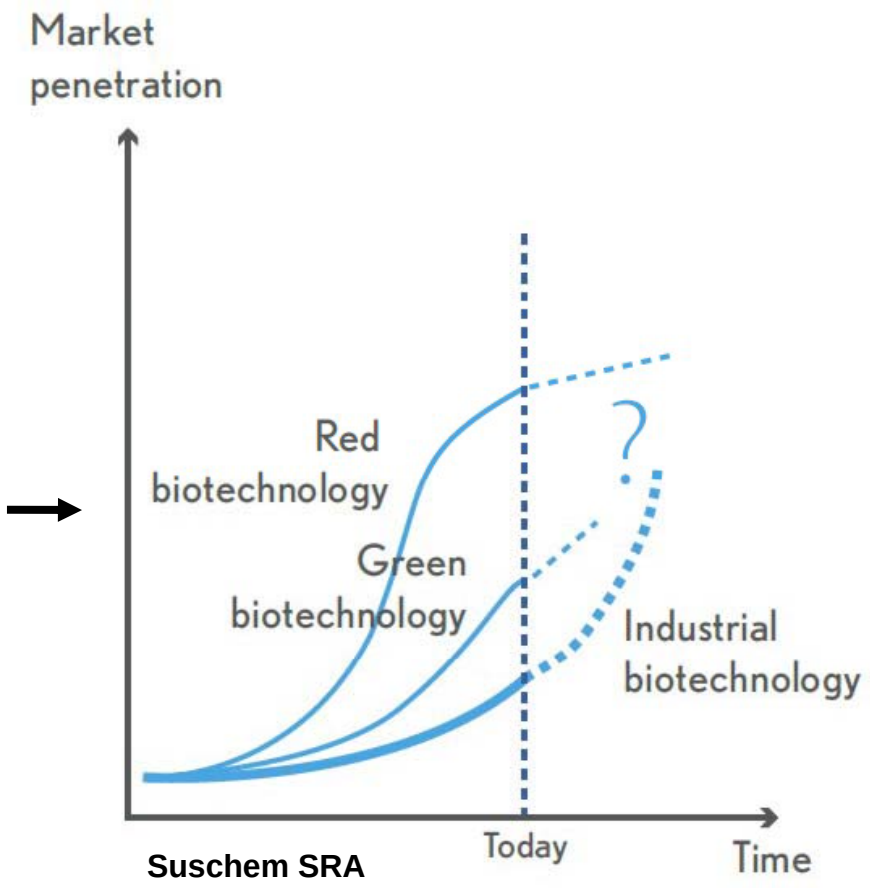
Biotechnology‘s role in the chemical industry is predicted to grow

Changing raw materials

Novel products

Environmentally sustainable production

Price/costs



Suschem SRA

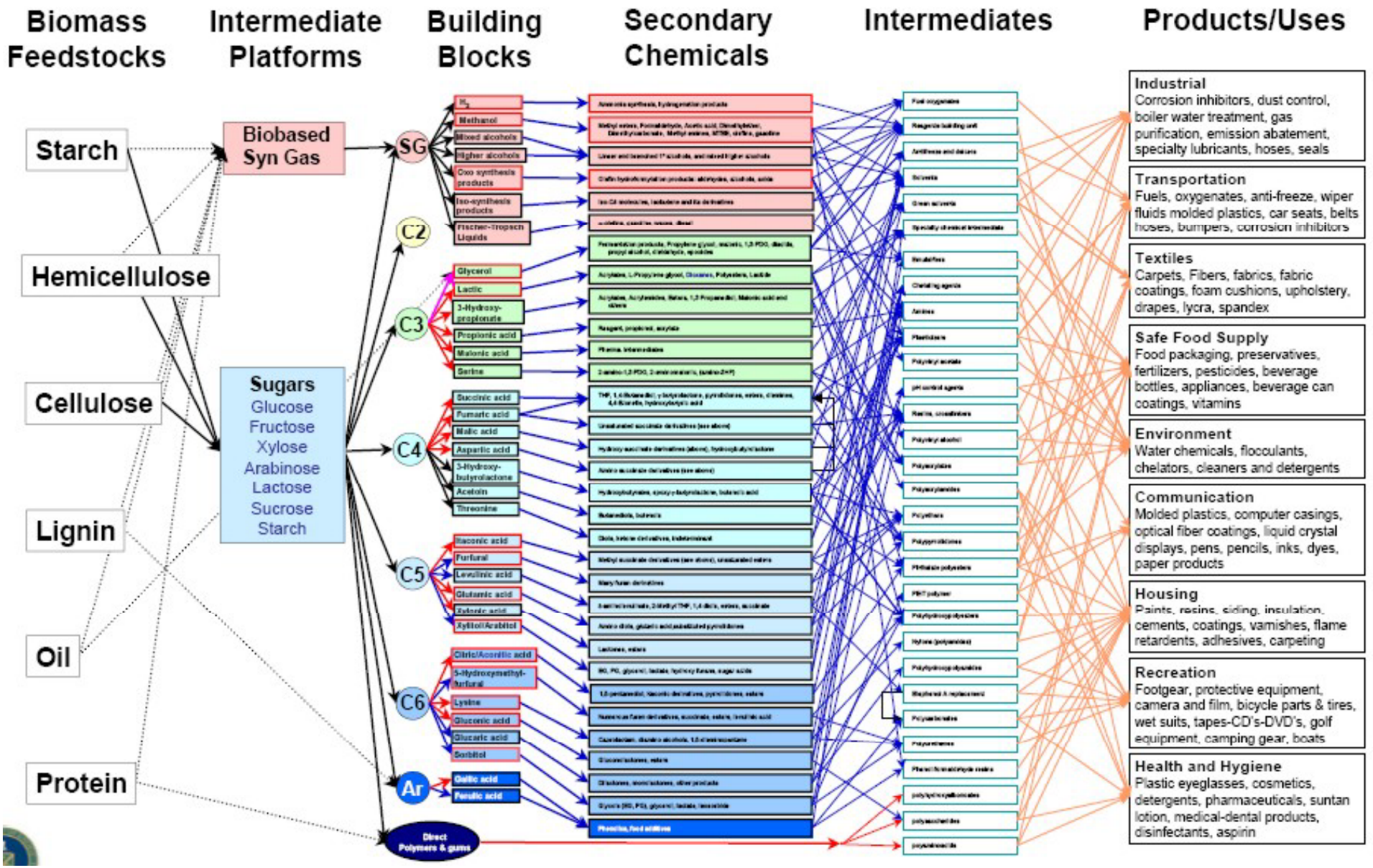
BCC Inc.,
Freedonia : 5%/a
fermentation products

McKinsey: 10% of all chemicals by 2010
Fine chemicals: up to 60% by 2010

Biofuel targets EU
2010: 5.75%
2020: 20%
Of both, diesel and fuel

The biotech-product tree

(2004 DOE Report)



The potential for sustainability

Energy	energy resource, amount, efficiency	(yes)
Raw materials	efficiency, environmental impact, availability	**yes**
Waste production	amount, type, biodegradability, recyclability, environmental impact	**yes**
Products, by-products	recyclability, stability, biodegradability, side effects	yes
Process	streamlining, number of steps, time reduction	**yes**
Safety	by-/product, waste, raw materials, human safety, environmental safety, process safety	**yes**

OECD, The application of biotechnology to indutrial sustainability, 2001

Is sustainability a driver?

21 industrial cases

Table 3. **Cost and environmental benefits from cases**

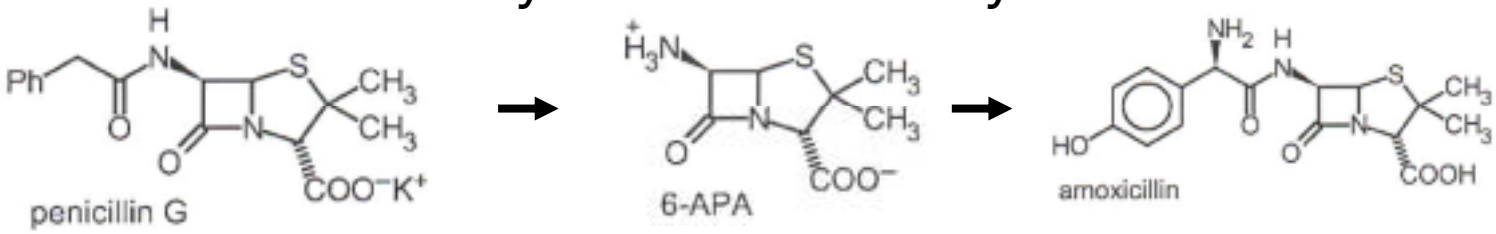
Case	Energy	Raw materials	Waste to air	Waste to water	Operating costs
1	Same	−75% (non-renewables)	−50%	−66%	−50%
2			−90%	−33%	−90% (environment related)
3	Electricity +; steam −		−80%	−80%	Considerable reduction
4	Same				−43%
6	−80%		Down	Down	Down
7		Down	Down	Down	−54% (raw materials)
8	Down		Down		Down
10	−70%			−80%	−40%
11		−50% (groundwater)			−30% (groundwater)
12	−15%	Down (water)		Down	−9%
13	−30-40%	Down		Down	
16		−35% (Cl_2), −65% (ClO_2)		Down	
17		Down (recycle)		Down	
18	Down		Down		Down
21				Down	Increased productivity

1: Vit B2; 2: 7-ACA; 3: Cephalexin; 4: amino acid acylase process; 5: S-Cl-propionic acid; 6: acrylamide; 7: acrylic acid; 8: polyesters; 9: polylactide polymers; 10: degumming; 11: water recycling; 12-16: cases from paper production; 17: biological Zn-removal; 18: copper bioleaching; 19: corn ethanol; 21: oil well completion

OECD, The application of biotechnology to indutrial sustainability, 2001

Yes,…

Pen-acylase Pen-acylase



Pen G **6-APA** **Amoxicillin**

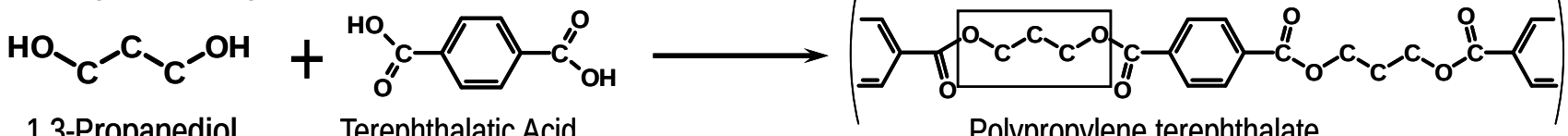
Comparison of chemical and biotechnology processes for producing cephalexin (Demain, 2000)

Production category	Process type		
	Conventional chemical	Enzyme biocatalysis	Direct fermentation
Waste (kg/kg cephalexin)	50 (1970) to 15 (1995)	10 (1995) to 5 (2000)	2–5
Inorganics (kg/kg)	0.5	0.5	
Organics (non-halogenated) (kg/kg)	1.0	0.2	
Solvents (non-halogenated) (kg/kg)	1.7	0.3	
Solvents (halogenated) (kg/kg)	0.9	0	
Electricity (%)	100	150	
Steam (%)	100	40	
Water (%)	100	300	
Liquid nitrogen (%)	100	0	

Gavrilescu et al., Biotechnology Advances 23 (2005): 471

…, but not always

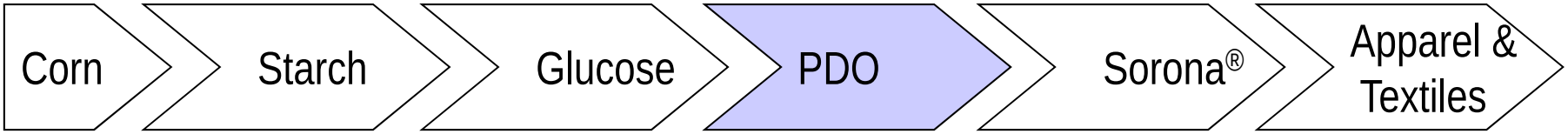
3GT (Sorona®)



1,3-Propanediol (3G)

Terephthalatic Acid

Polypropylene terephthalate (3GT)



Life cycle analysis (Data from R. Anex, Iowa State):

PDO production bio vs chem: energy/kg PDO down by 35%

3GT production: 3GT with bio-PDO vs chem PDO: energy/kg 3GT down by 9%

No significant profile with respect to CO2 and methane emissions

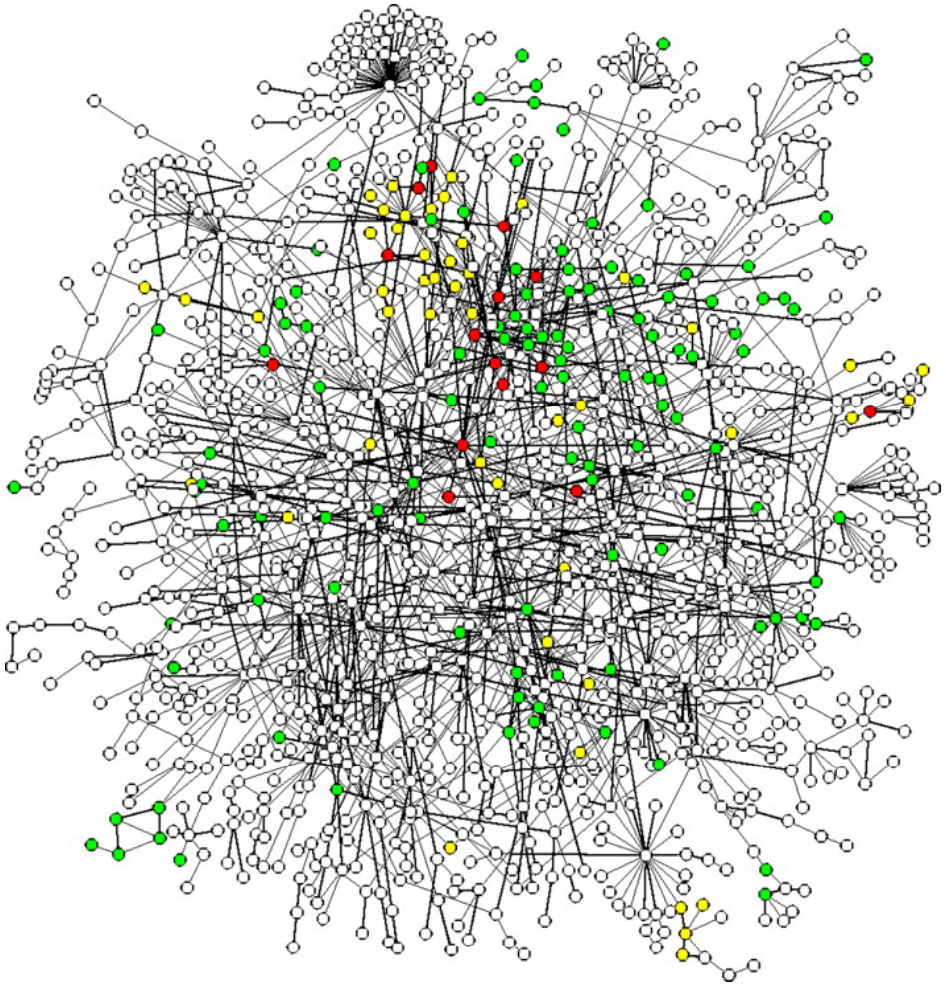
Summary - I

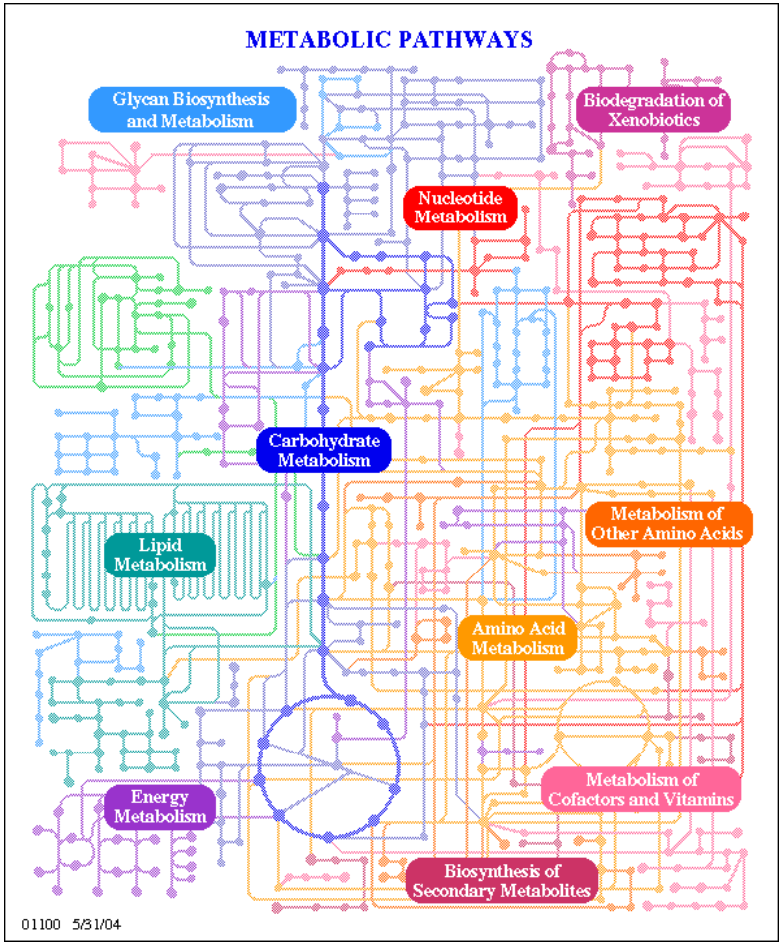
Yes, biotechnology will have a strong influence on

1) the structure
2) the products
3) the environmental foot print

of the chemical industry

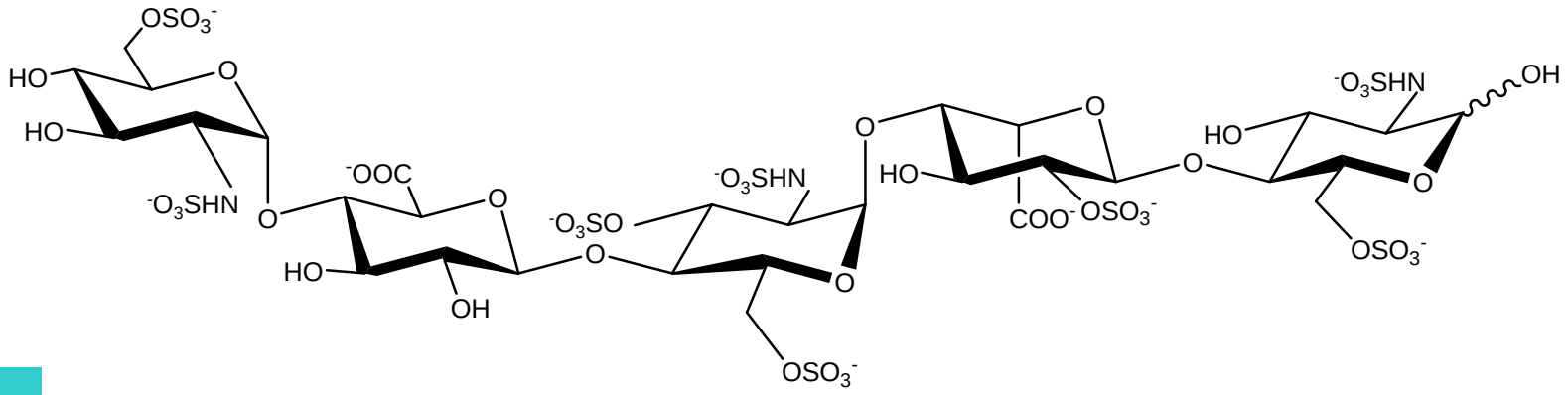
Problems in current metabolic engineering - complexity

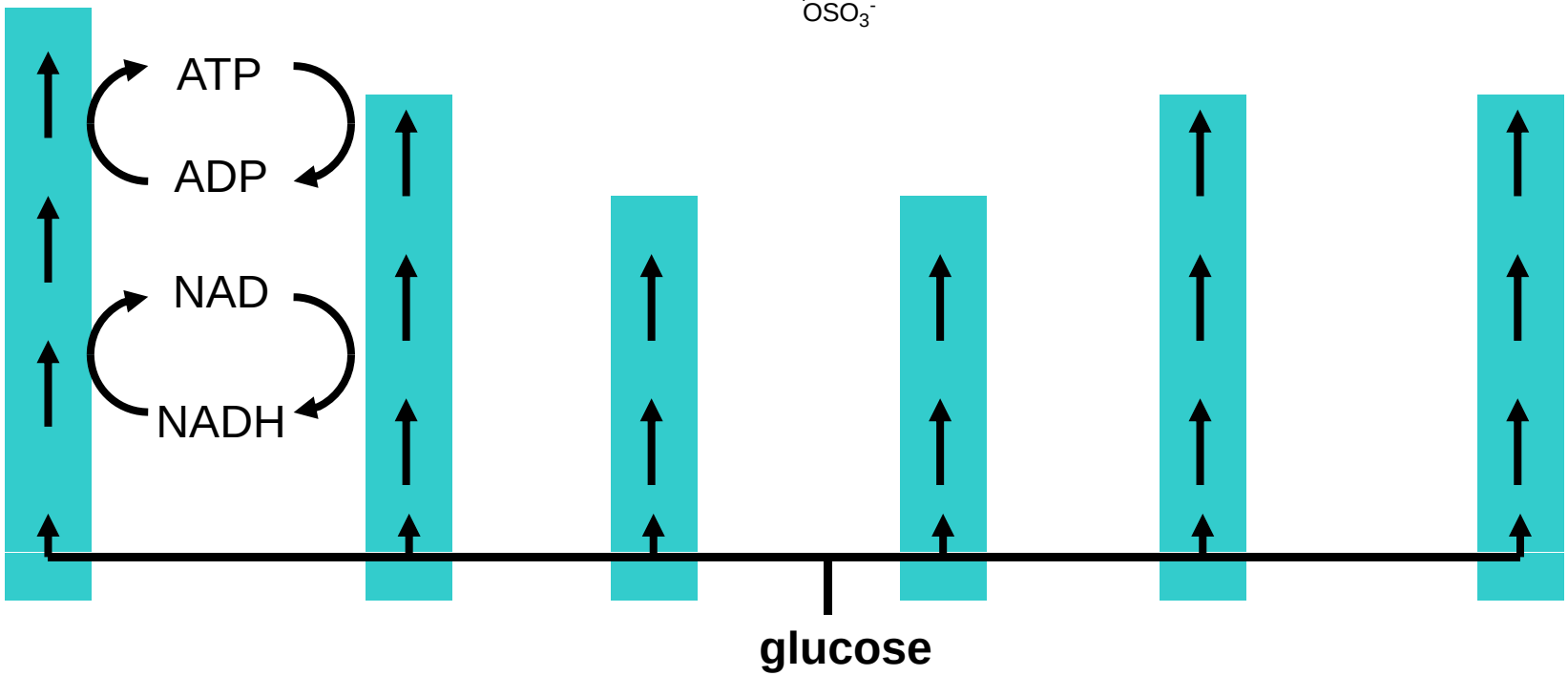




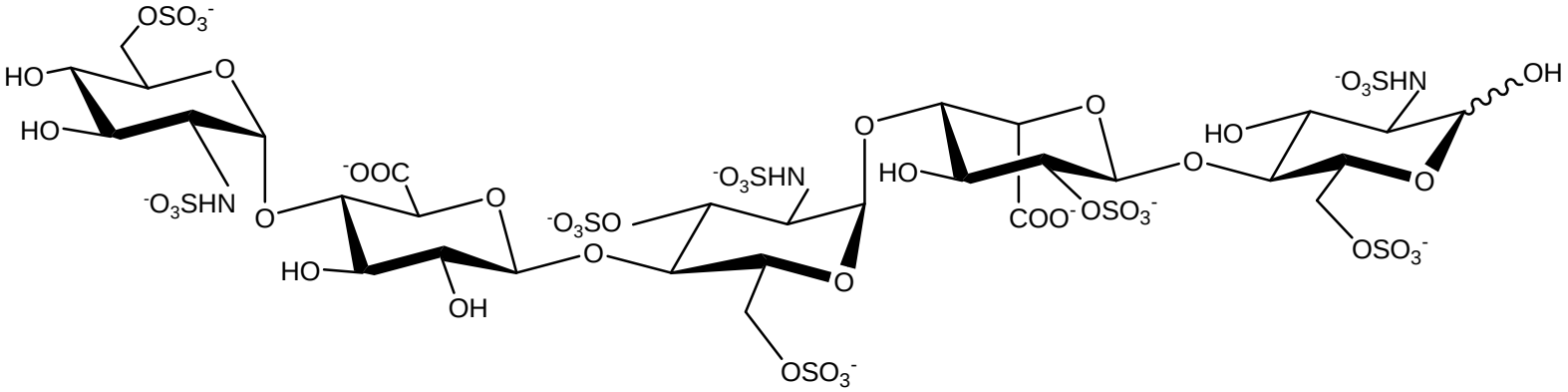
Forgacs et al., J. Cell Science 117: 2769

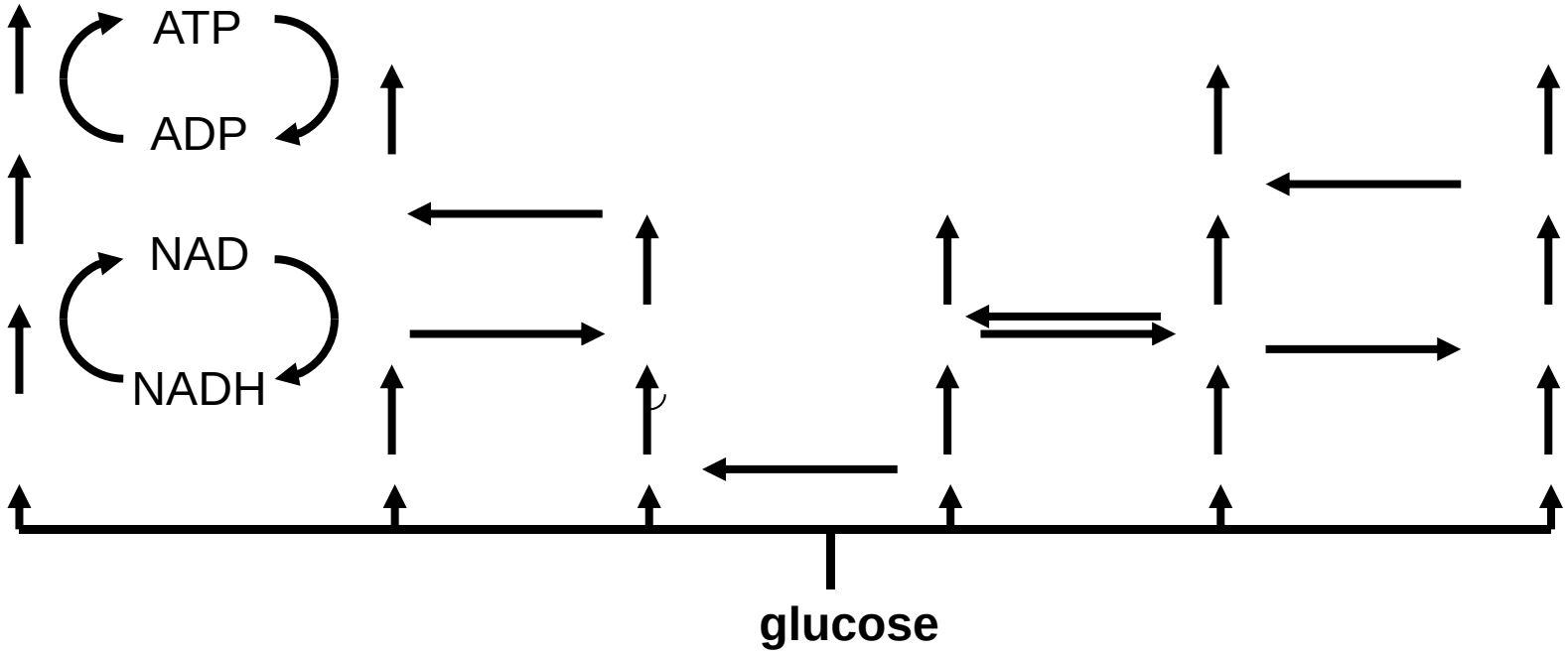
Wish…


OSO3-
HO
HO
O
-O3SHN
O
-OOC
O
HO
OH
O
-O3SO
O
-O3SHN
O
O
HO
O
COO-
OSO3-
O
HO
-O3SHN
OH
O
OSO3-
OSO3-

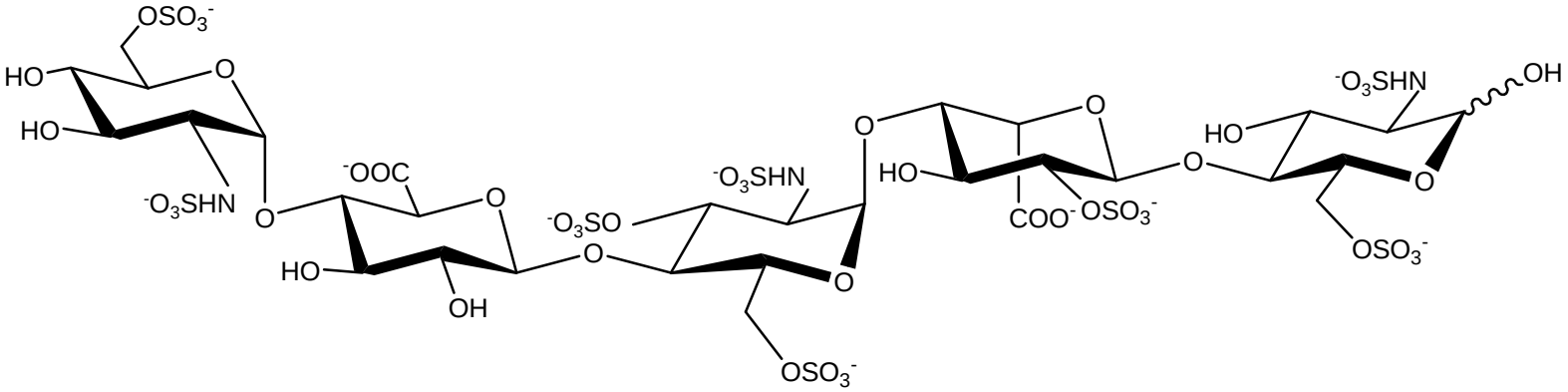

ATP
ADP
NAD
NADH
glucose

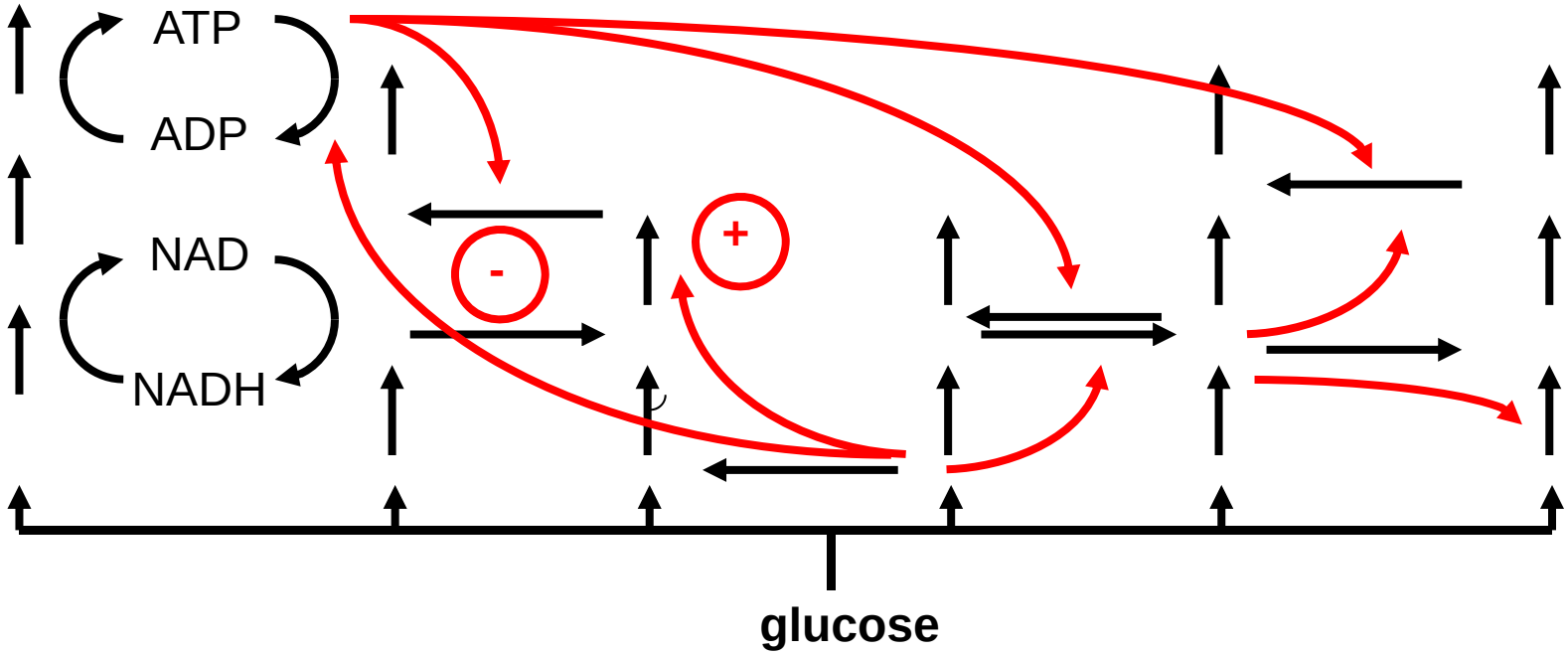
Wish…& reality I





Wish…& reality II





Problems in current metabolic engineering

- dealing with complexity (eg the complex interconnected metabolic network, stiff metabolic nodes)

- availability of system-wide tools for cell/pathway engineering

- availability of pathways/enzymes for quick pathway assembly in your favorite host

IN OTHER WORDS: Metabolic engineering is at ist heart still more of a discovery science than a true engineering discipline

These problems lead to…

- A disproportionally large number of failed projects (failure at any level, from catalyst design to process implementation)

- Reinforcement of the chemical mindset (chemistry is better, more reliable, quicker, cheaper, etc)

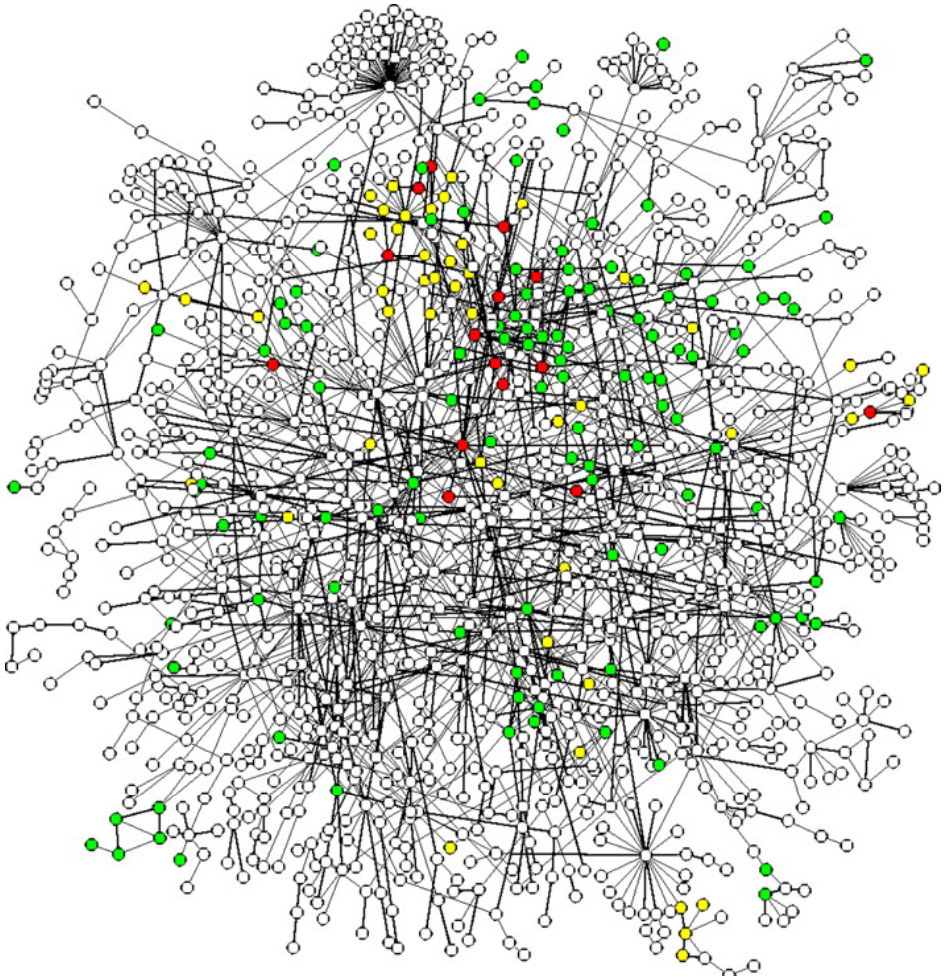
- A lack in chemical talent suitably trained in biochemical opportunities

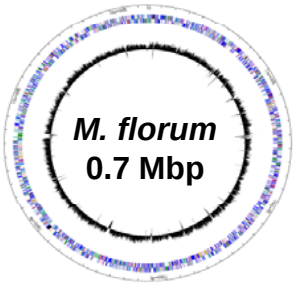
- A severe delay in delivering on the “Biotechnology Promise“ of a sustainable and competitive chemical industry

Problem		Synthetic Biology
- dealing with complexity (eg the complex interconnected metabolic network, stiff metabolic nodes)	←	Chassis strains - minimal strains - parallel metabolisms - alternative chemistries - …..
- availability of system-wide tools for cell/pathway engineering	←	- DNA synthesis/foundries - Large scale synthetic labs - CAD
- availability of pathways/enzymes for quick pathway assembly in your favorite host	←	- Registries - Circuits - CAD

Chassis strains

Reduced genomes – reduced networks





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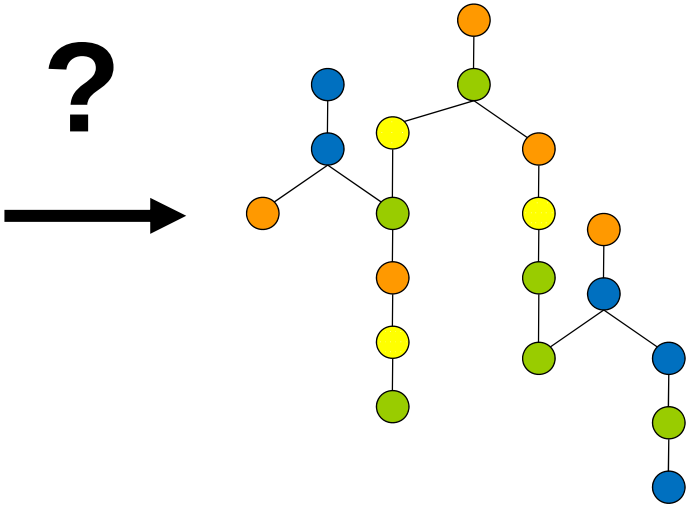
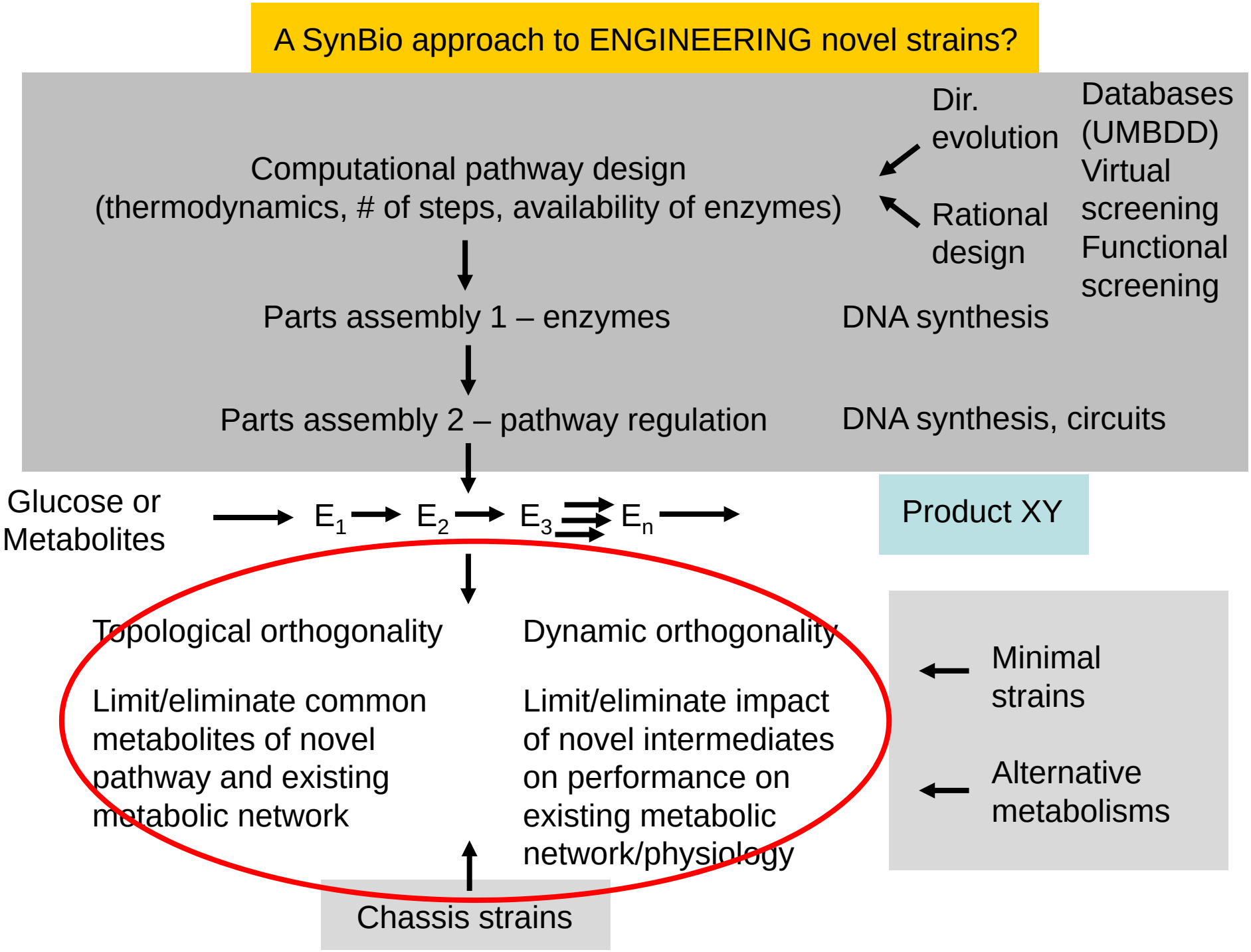
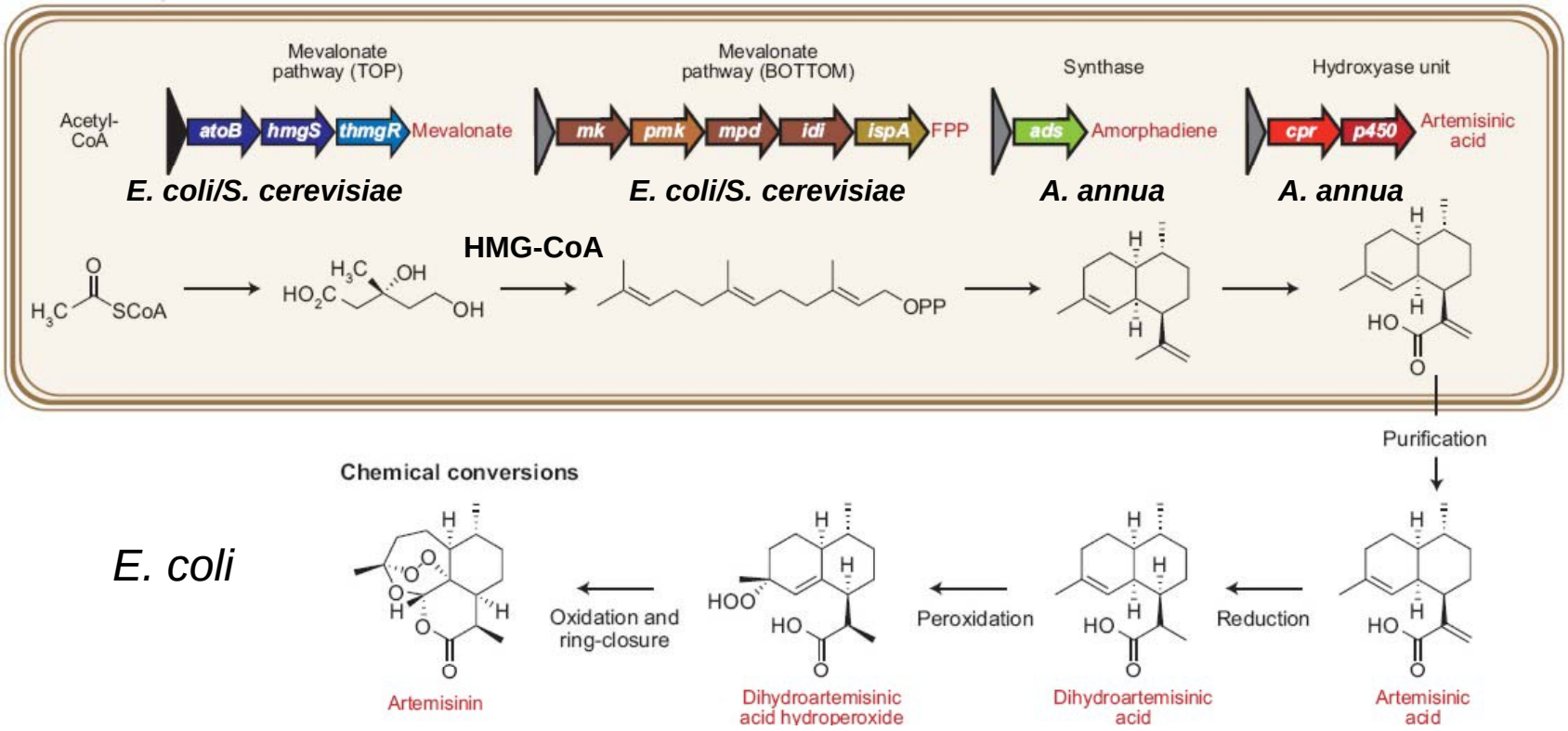
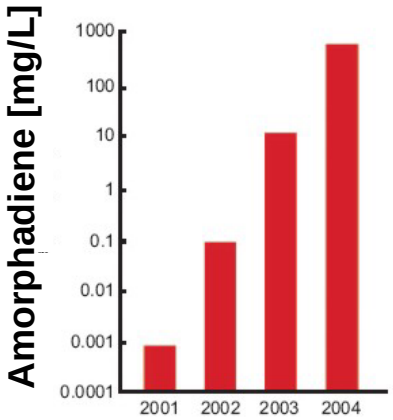



A SynBio approach to ENGINEERING novel strains?
Computational pathway design
(thermodynamics, # of steps, availability of enzymes)
Dir. evolution
Rational design
Databases (UMBDD)
Virtual screening
Functional screening
Parts assembly 1 – enzymes
DNA synthesis
Parts assembly 2 – pathway regulation
DNA synthesis, circuits
Glucose or Metabolites
E1
E2
E3
En
Product XY
Topological orthogonality
Limit/eliminate common metabolites of novel pathway and existing metabolic network
Dynamic orthogonality
Limit/eliminate impact of novel intermediates on performance on existing metabolic network/physiology
Minimal strains
Alternative metabolisms
Chassis strains

The version 1.0 example





Recombination of 11 genes from three different hosts in *E. coli* for the production of an antimalarial intermediate

J. Keasling – Labor, UC Berkeley

Version 2.0 ?

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Synthetic biology and the chemical industry

In chemistry, successfull implementation of synthetic biology would:

a) make developments more predicatble and faster – ROBUSTNESS OF DEVELOPMENT

b) allow more complex production pathways – NOVEL PRODUCTS (see artemisinin & polyketides)

c) offer a true option for metabolic ENGINEERING

d) be at the heart of a true paradigm shift in the chemical industry

Bottlenecks

- Research in chassis strains
- Compartmentalized IP structure
- High quality registries

Thank you for your attention!

Questions ?