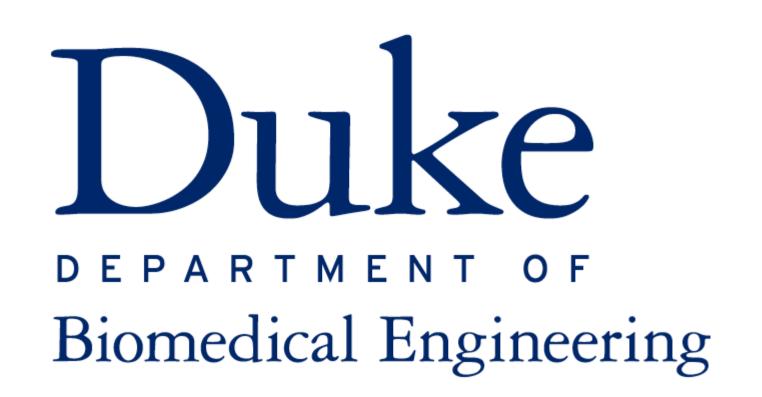
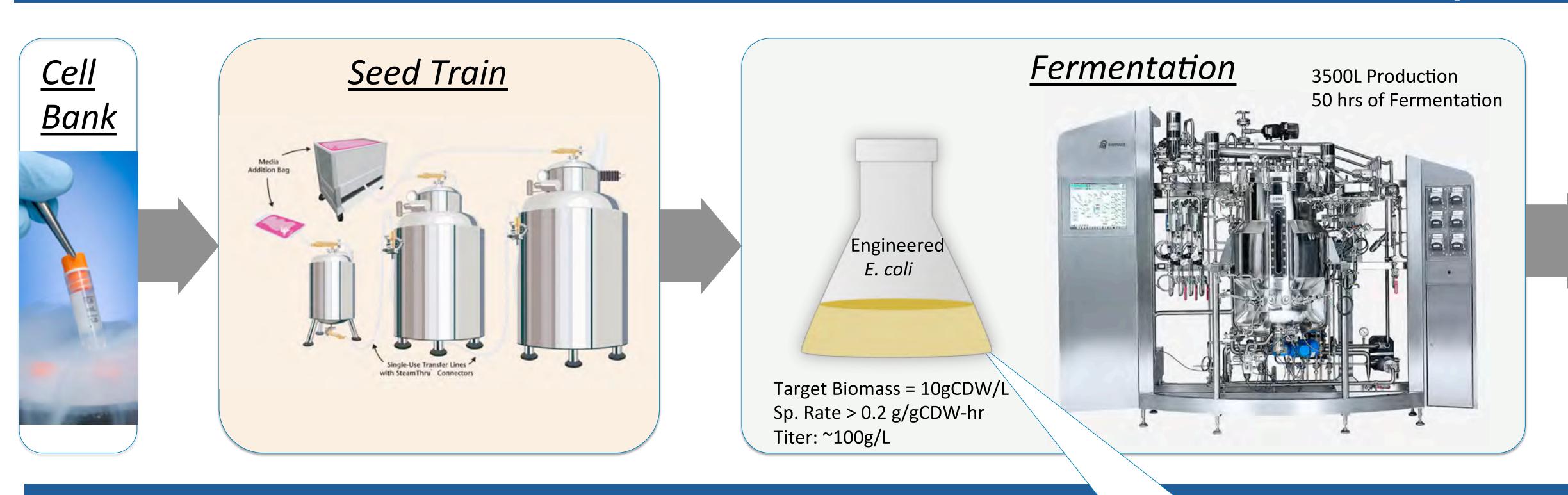


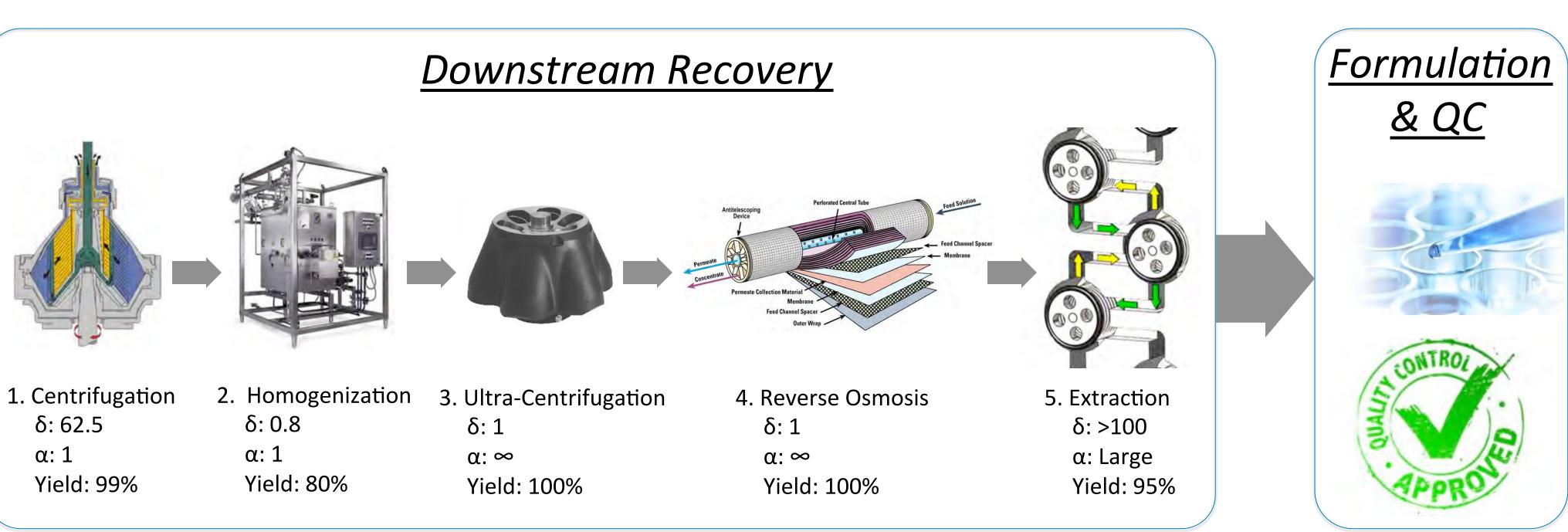
# A Bioprocess Design for Microbial Production of Taxol

Banskota, S., Ciesla T.J., Moreb, E. BME 590-02 Fall 2015



## Taxol Bioprocess Design



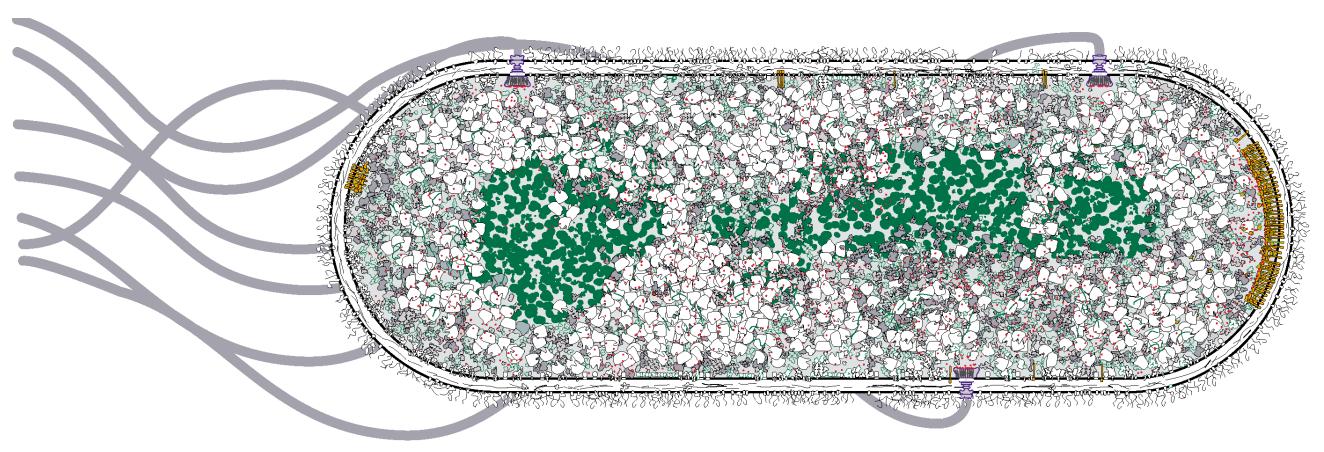


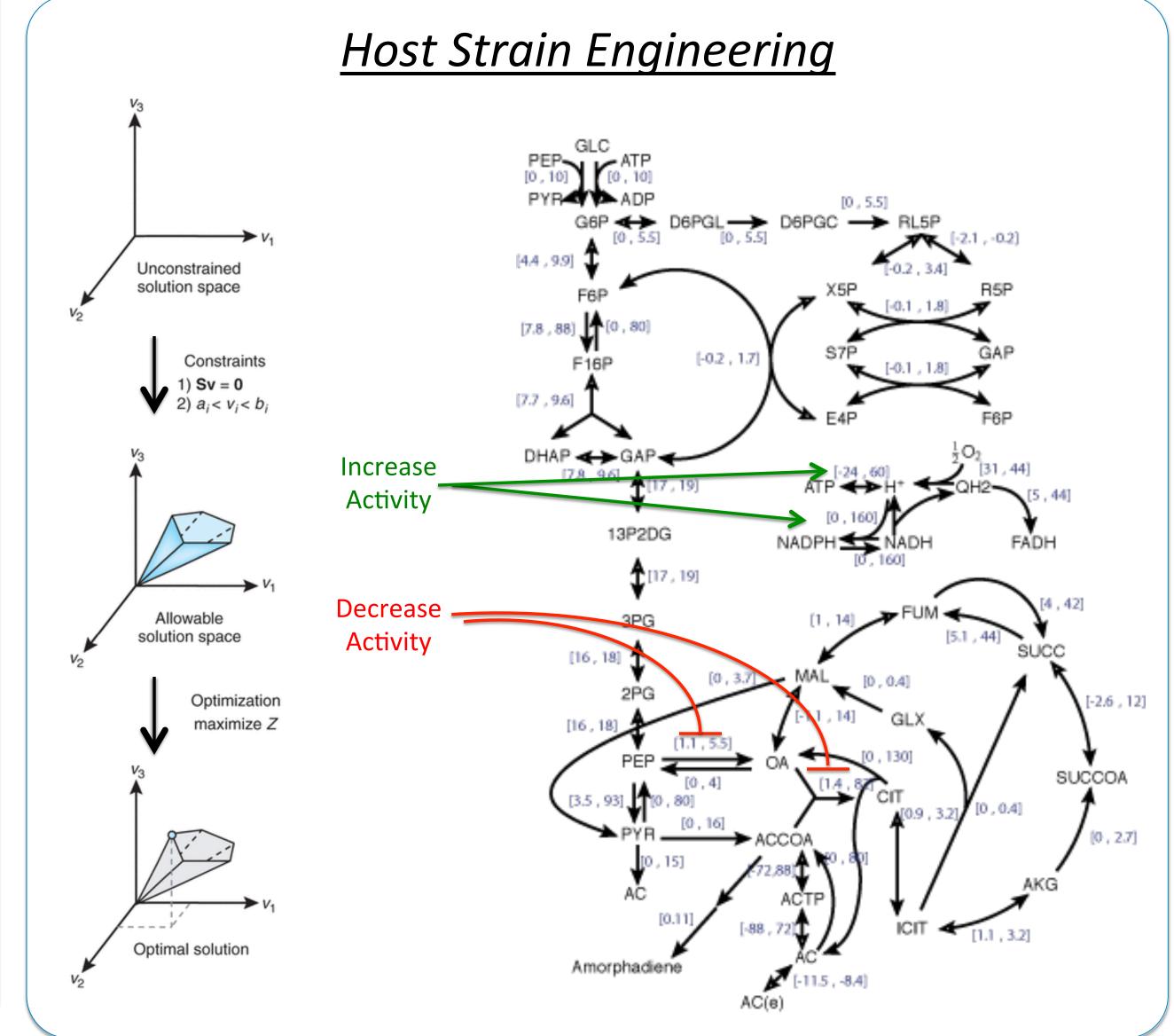


# Strain Design

# Metabolic Pathway Engineering

Enzyme	EC	Required Specific Activity [µmol/mi r/mg]	Gene	Organism	Vmax Units	Km (m M)	Max ratio to previous	Min. Needed express ion (%)	Uniprot
geranylgeranyl pyrophosphate synthase	2.5.1.29	0.78	hbgg	Hevea brasiliensis	0.123	0.0067 8	1463.49 9028	6.34	Q94ID7
taxadiene synthase	4.2.3.17	0.78	TDC1	Taxus canadensis	0.000	0.0026	1.57E+7 3	2602	Q9FT37
taxadiene 5α- hydroxylase	1.14.99.3 7	0.78	T5alph a-H	Taxus cuspidata	120	0.006	0.00127 2727	0.0065	Q6WG3
taxadien-5-α-ol O- acetyltransferase	2.3.1.162	0.78	TAT	Taxus canadensis	3.33E +06	4.20E- 03	1.53E+0 2	2.34E- 07	Unknow
taxane 10β-hydroxylase (Tc)	1.14.13.7 6	0.78	CYP72 5A1	Taxus cuspidata,	5.964 9	Unkno wn	8.09E+5 3	0.00130 8823	Q9AXM 6
Sponataneous	spontane ous	spontane ous			super fast	n/a	n/a	n/a	n/a
taxane 2α-O- benzoyltransferase	2.3.1.166	0.78	твт	Taxus cuspidata,	unkno wn	0.64	1.3104E -10	unknow n	unknow n
10-deacety lbaccatin III-10-O- acety ltransferase'	2.3.1.167	0.78	DBAT	Taxus cuspidata,	0.696	0.01	3.64135 E+11	112*	Q9M6E 2
Phenylpropanoyltransfe rase	2.3.1.B16	0.78	BAPT	Taxus Cuspidata	1.78	0.0049	14.2743 4235	0.00438 5955	Q8H2B 5
β-phenylalanoyl baccatin III-2'- hydroxylase*	1.14.13	0.78	Unkno wn		unko wn	unkno wn	2.90678 E-05	unknow n	unknow n
3'-N-debenzoyl-2'- deoxytaxol N- benzoyltransferase"	2.3.1	0,78	TAX10	Taxus canadensis	unkno wn	0.42	9.13E+1 9	unknow n (x1000)	unknow
phenylalanine aminomutase	5.4.3.10	0.78		Taxus canadensis	0.000			11.1528 5714	Q6GZ0 4
Benzoate-CoA ligase	6,2,1.25	0.78		PSeudomon as Sp	73	0.03	10107.6	0.00058	Q25C1 6





# Techoeconomic Analysis

### **Problem:**

Paclitaxel (Taxol) is a small molecule drug belonging to the taxane family. It is one of the most commonly used chemotherapeutics, used for treatment of many cancers, as a monotherapy or in combination with other drugs to treat breast, lung and ovarian cancer as well as Kaposi's sarcoma. Taxol is on the World Health Organization's (WHO) List of Essential Medicines, a list that includes most the important medications for basic health. The worldwide demand for paclitaxel is exceeding the current supply. In addition the current cost of paclitaxel limits use in many parts of the developing world. Lower cost sources of paclitaxel can have an immediate impact to human health world-wide. Currently taxol is approved in the U.S. as first line of treatment for breast, ovarian and non-small cell lung cancer. The annual new cases of these cancers are ~ 540,000 in the United States.

Market Size: US Market: 1100 kg per year.

### **Process Design included:**

Genetically Engineered *E. coli* Strain

- Heterologous Taxol Production Pathway
- Engineered Host Strain

**GMP Fermentation Process** 

5 Step Downstream Recovery Process

### **Results:**

Our conceptual design results in cost competitive production

- \$0.43/mg including a 25% Return
- ~\$ 5M in Capital investment
- Current Pricing is ~ \$0.50/mg

