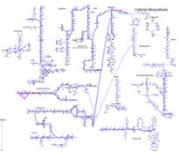


# *E.coli* Core Model: Metabolic Core



# LEARNING OBJECTIVES

Each student should be able to:

- Describe the glycolysis pathway in the core model.
- Describe the TCA cycle in the core model.
- Explain gluconeogenesis.
- Describe the pentose phosphate pathway in the core model.
- Describe the glyoxylate cycle and anapleurotic pathways in the core model.
- Describe the oxidative phosphorylation and electron transport chain pathways in the core model.
- Describe the fermentation pathways in the core model.
- Describe the nitrogen metabolism pathways in the core model.

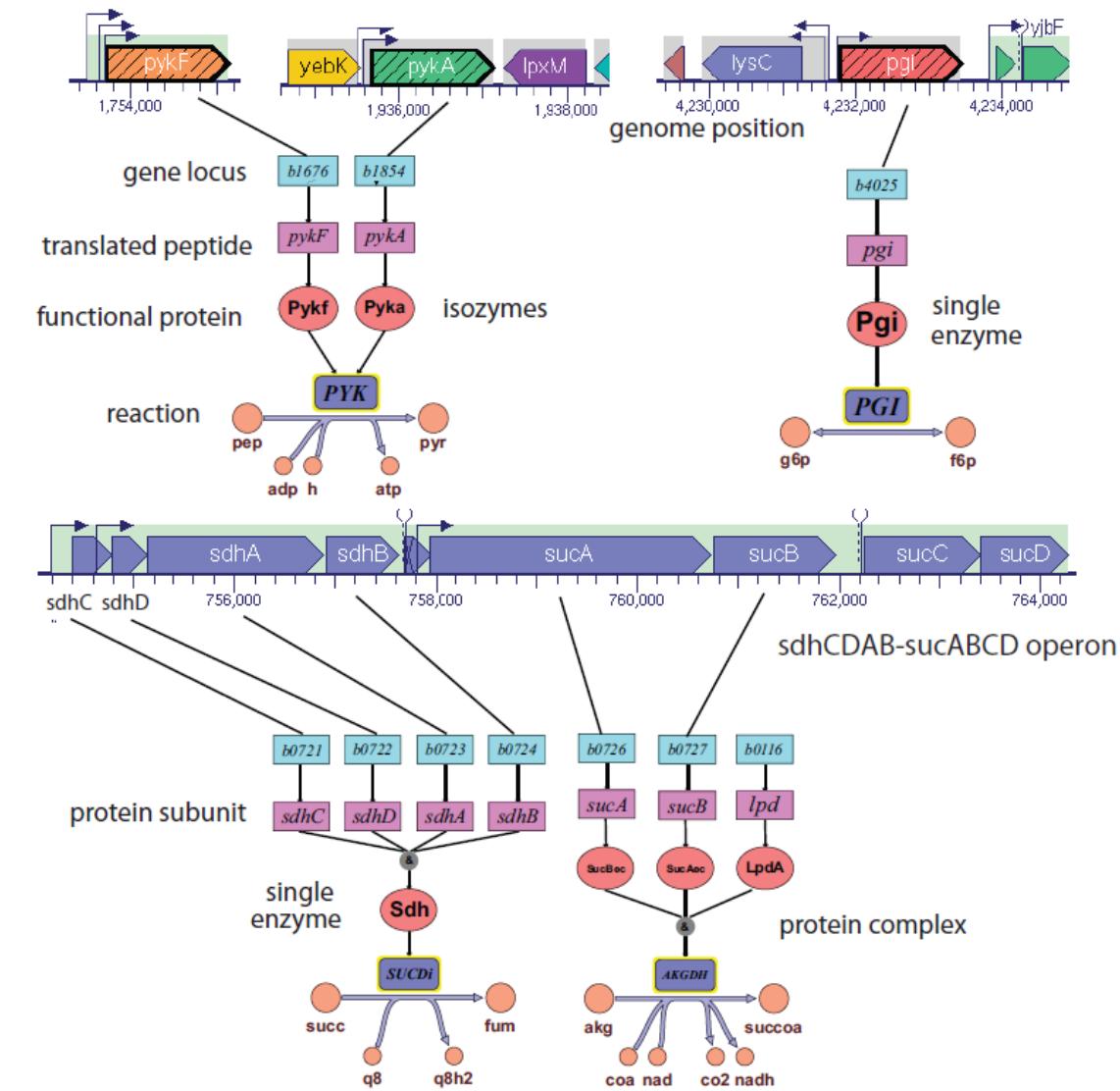


# *E.coli* Core Model

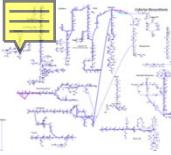
- Component Parts of the *E. coli* Core Model
- Glycolysis
- Pentose Phosphate Pathway (Shunt)
- Tricarboxylic Acid (TCA) Cycle
- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism



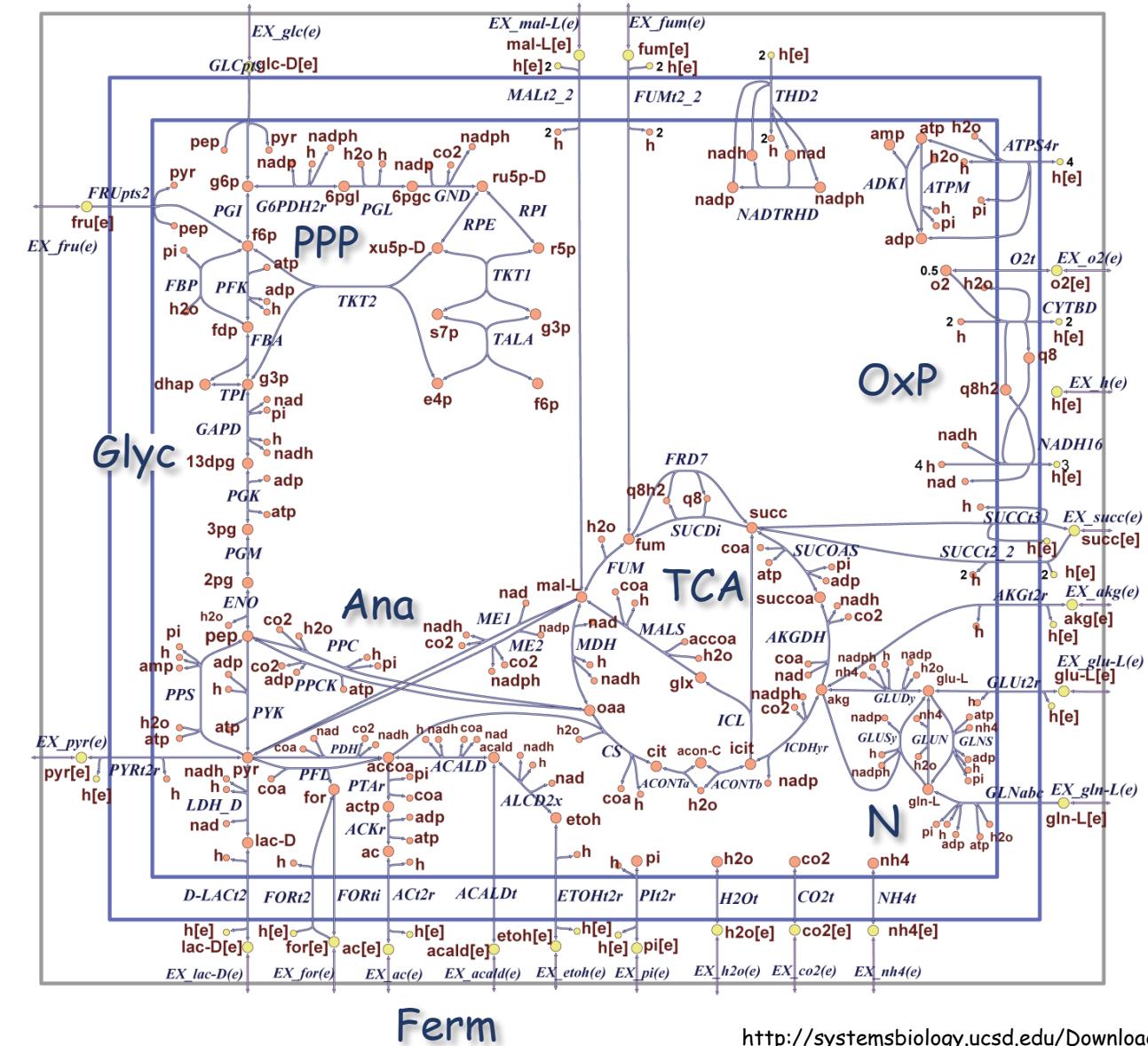
# Component Parts of the *E. coli* Core Model



Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)

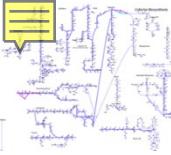


## E.coli Core Model

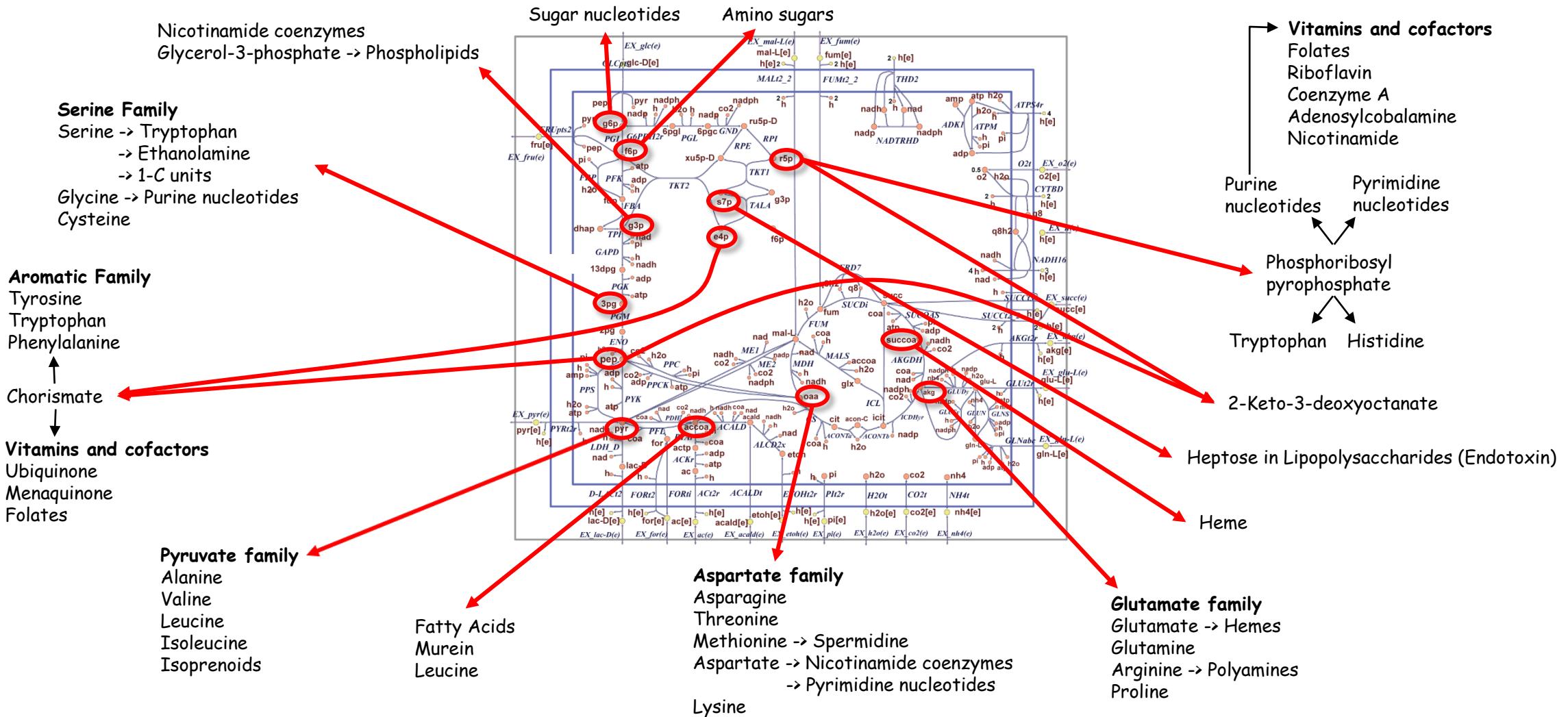


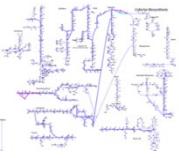
Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.

[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



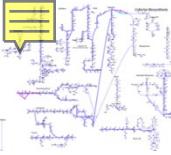
# E.coli Precursor Metabolites





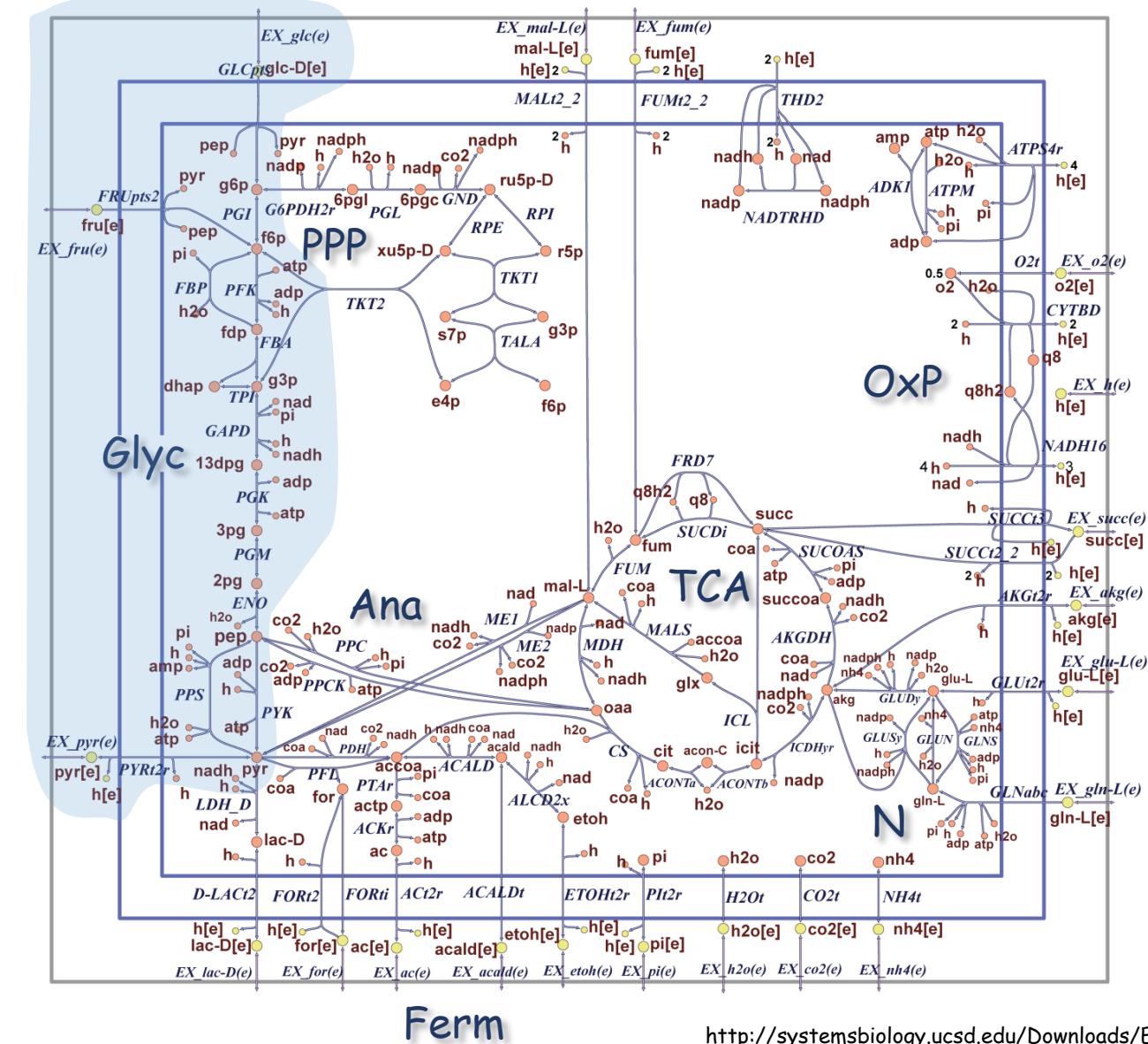
# *E.coli* Core Model

- Component Parts of the *E. coli* Core Model
- • Glycolysis
- Pentose Phosphate Pathway
- Tricarboxylic Acid (TCA) Cycle
- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism



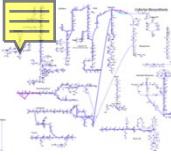
# Glycolysis

## *E.coli* Core Model



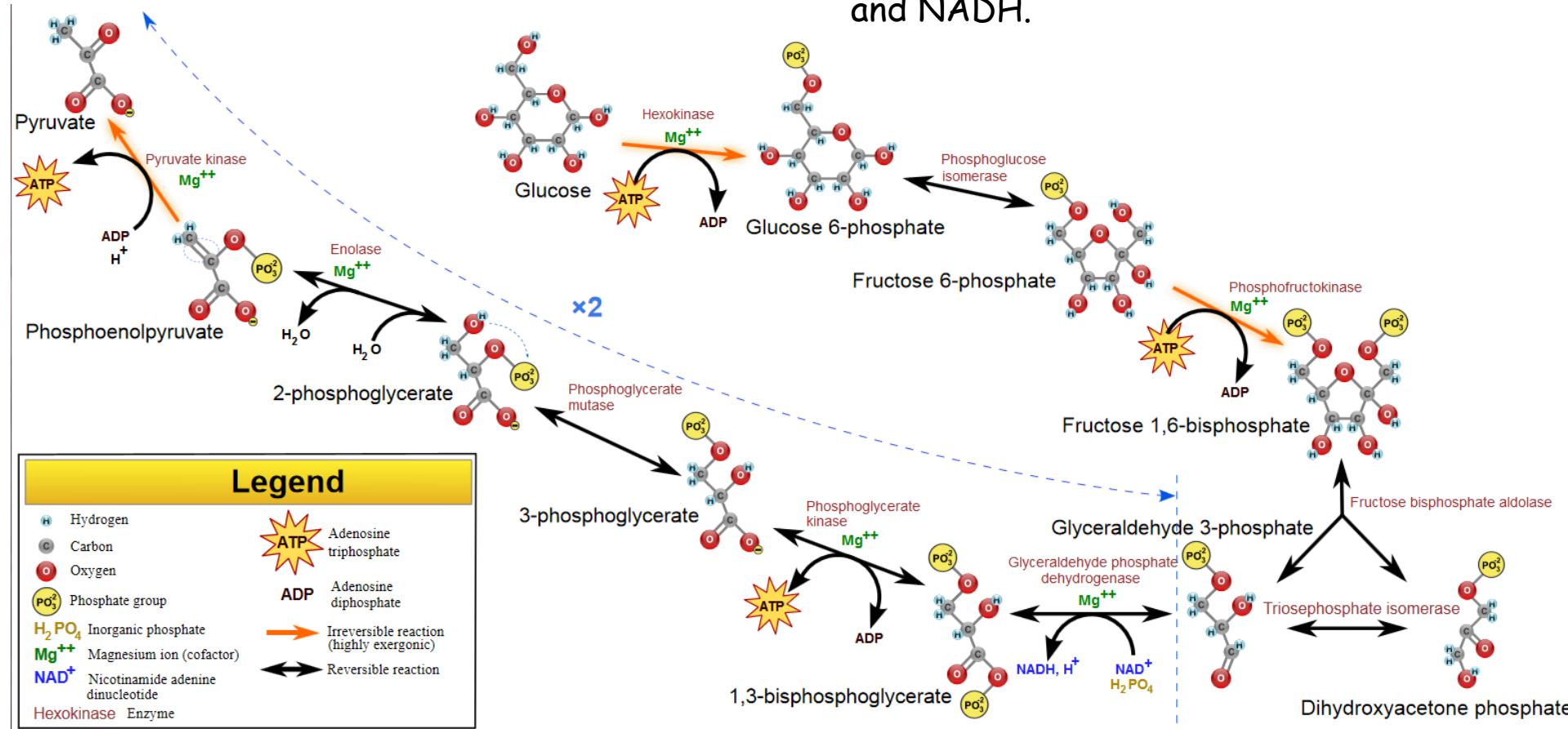
Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.

[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



# Glycolysis

Glycolysis is the metabolic pathway that converts glucose into pyruvate. The free energy released in this process is used to form the high-energy compounds of ATP and NADH.

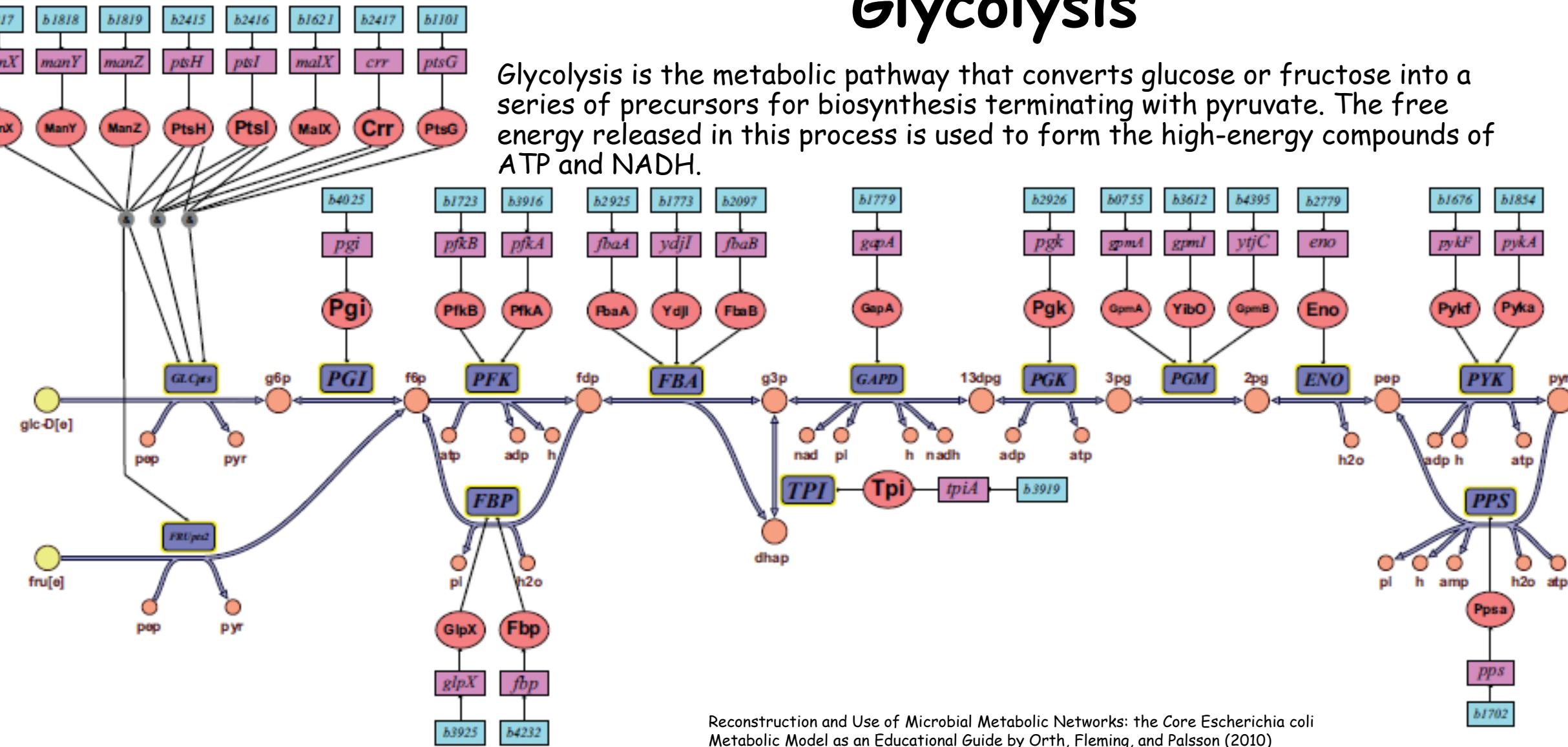


<http://en.wikipedia.org/wiki/Glycolysis>



# Glycolysis

Glycolysis is the metabolic pathway that converts glucose or fructose into a series of precursors for biosynthesis terminating with pyruvate. The free energy released in this process is used to form the high-energy compounds of ATP and NADH.

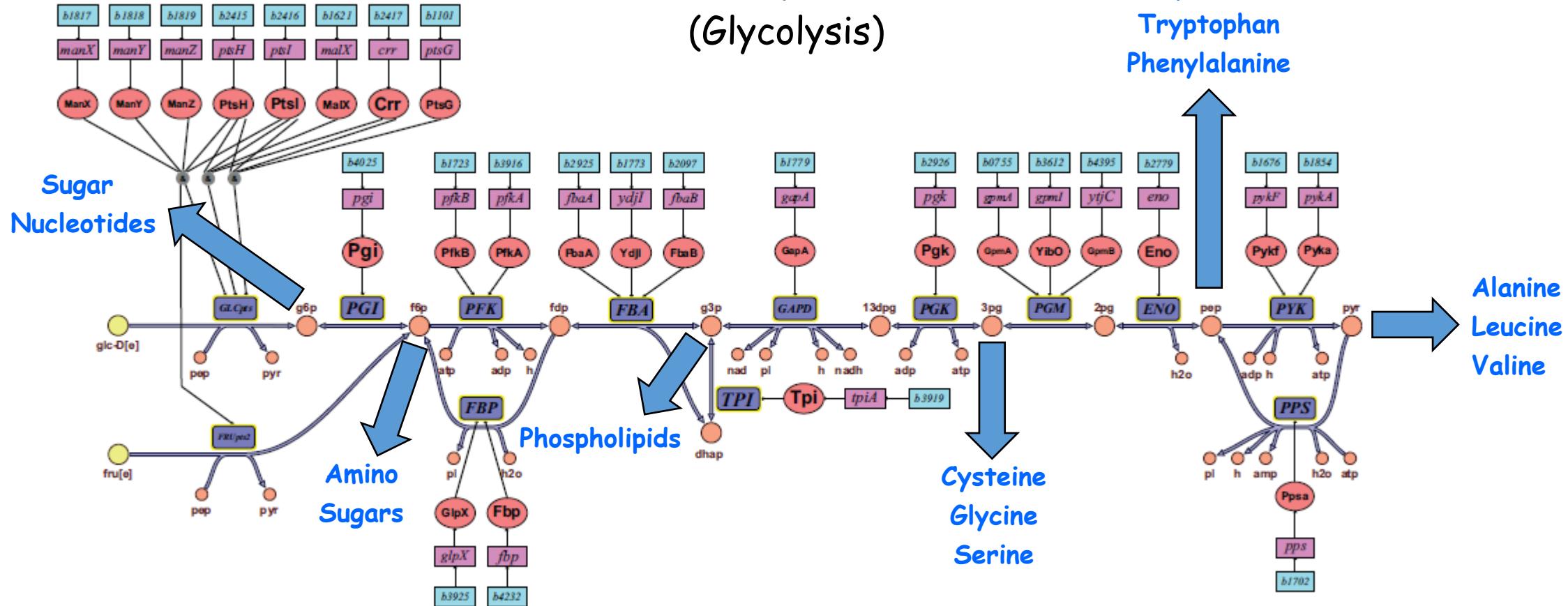


Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# Biosynthetic Precursors

## (Glycolysis)



Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# Metabolites & Reactions

## Glycolysis

Abbr.	Metabolite	Formula	Charge
glc-D	D-Glucose	C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>	0
g6p	D-Glucose-6-phosphate	C <sub>6</sub> H <sub>11</sub> O <sub>9</sub> P	-2
fru	D-Fructose	C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>	0
f6p	D-Fructose-6-phosphate	C <sub>6</sub> H <sub>11</sub> O <sub>9</sub> P	-2
fdp	D-Fructose-1,6-bisphosphate	C <sub>6</sub> H <sub>10</sub> O <sub>12</sub> P <sub>2</sub>	-4
dhap	Dihydroxyacetone-phosphate	C <sub>3</sub> H <sub>5</sub> O <sub>6</sub> P	-2
g3p	Glyceraldehyde-3-phosphate	C <sub>3</sub> H <sub>5</sub> O <sub>6</sub> P	-2
13dpg	3-Phospho-D-glyceroyl-phosphate	C <sub>3</sub> H <sub>4</sub> O <sub>10</sub> P <sub>2</sub>	-4
3pg	3-Phospho-D-glycerate	C <sub>3</sub> H <sub>4</sub> O <sub>7</sub> P	-3
2pg	D-Glycerate-2-phosphate	C <sub>3</sub> H <sub>4</sub> O <sub>7</sub> P	-3
pep	Phosphoenolpyruvate	C <sub>3</sub> H <sub>2</sub> O <sub>6</sub> P	-3
pyr	Pyruvate	C <sub>3</sub> H <sub>3</sub> O <sub>3</sub>	-1

Abbr.	Reaction	Equation
GLCpts	D-glucose transport via PEP:Pyr PTS	glc-D[e] + pep → g6p + pyr
PGI	glucose-6-phosphate isomerase	g6p ⇌ f6p
FRUpts2	Fructose transport via PEP:Pyr PTS (f6p generating)	fru[e] + pep → f6p + pyr
PFK	phosphofructokinase	atp + f6p → adp + fdp + h
FBP	fructose-bisphosphatase	fdp + h <sub>2</sub> o → f6p + pi
FBA	fructose-bisphosphate aldolase	fdp ⇌ dhap + g3p
TPI	triose-phosphate isomerase	dhap ⇌ g3p
GAPD	glyceraldehyde-3-phosphate dehydrogenase	g3p + nad + pi ⇌ 13dpg + h + nadh
PGK	phosphoglycerate kinase	3pg + atp ⇌ 13dpg + adp
PGM	phosphoglycerate mutase	2pg ⇌ 3pg
ENO	enolase	2pg ⇌ h <sub>2</sub> o + pep
PYK	pyruvate kinase	adp + h + pep → atp + pyr
PPS	phosphoenolpyruvate synthase	atp + h <sub>2</sub> o + pyr → amp + 2 h + pep + pi

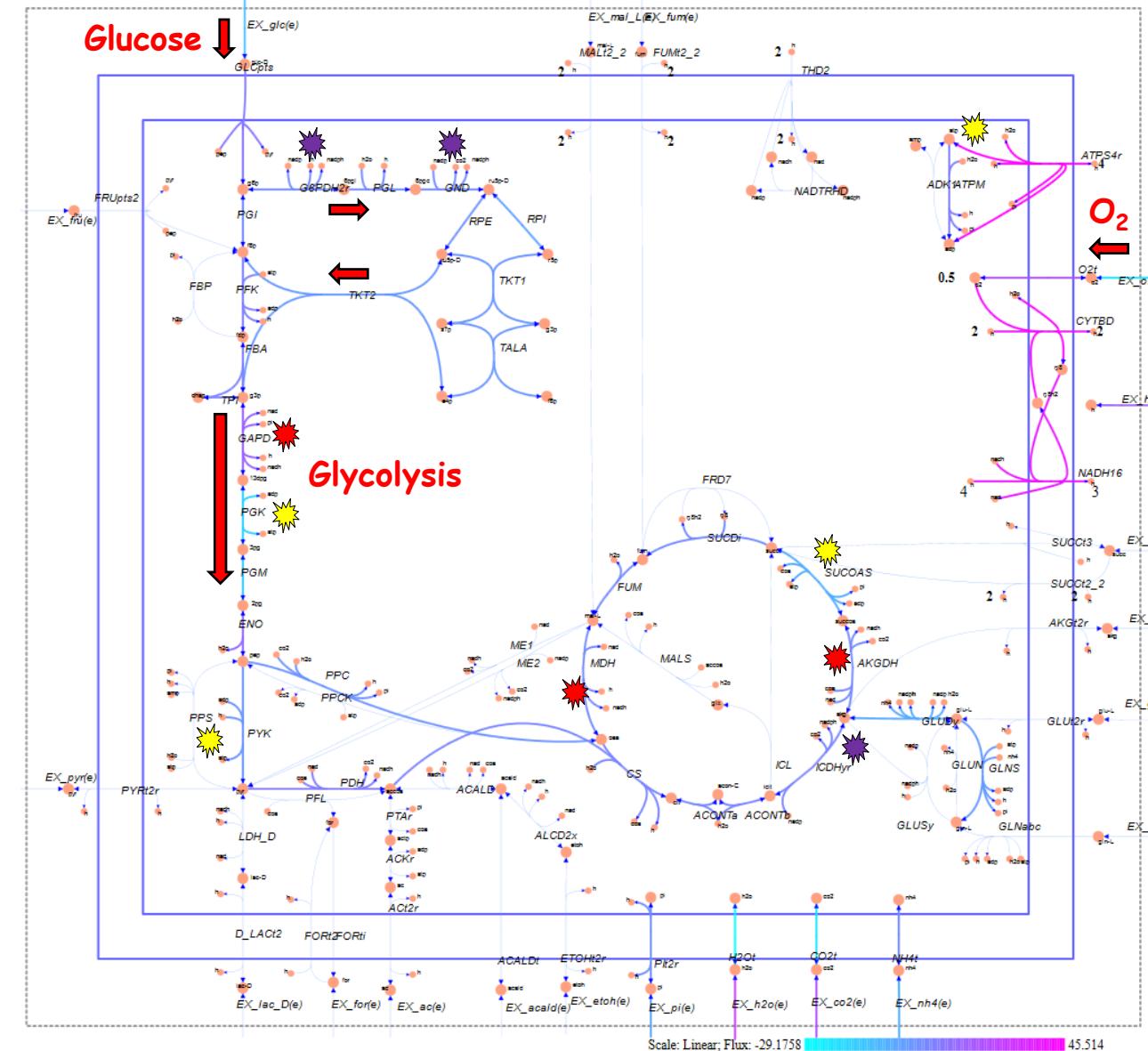
Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)

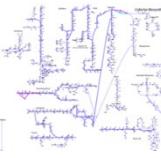


Aerobic Conditions  
Carbon Source: Glucose

ATP =   
NADPH =   
NADH =

AerobicGlucoseBioMass.m



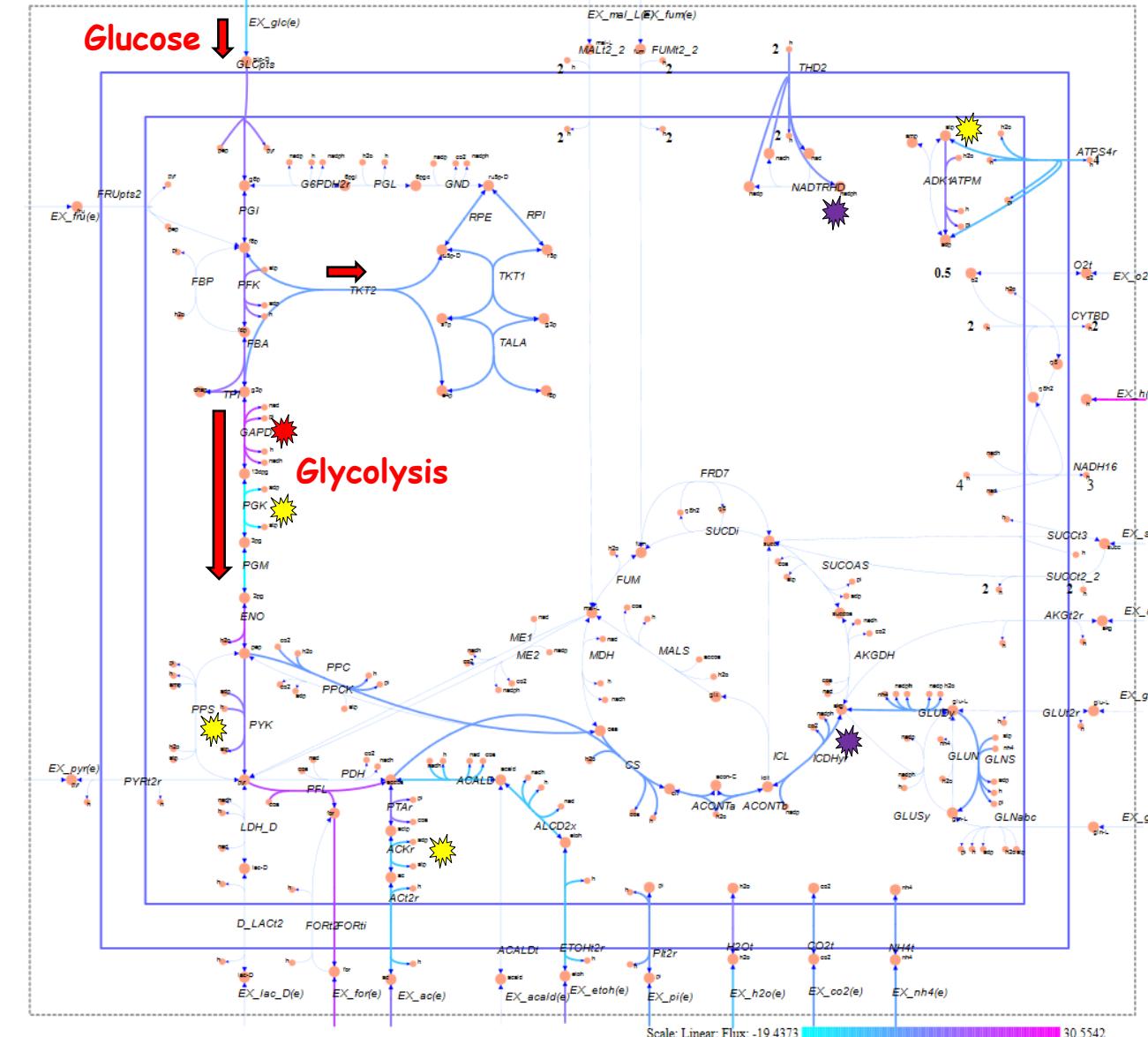


Anaerobic Conditions  
Carbon Source: Glucose

ATP =

NADPH =

NADH =



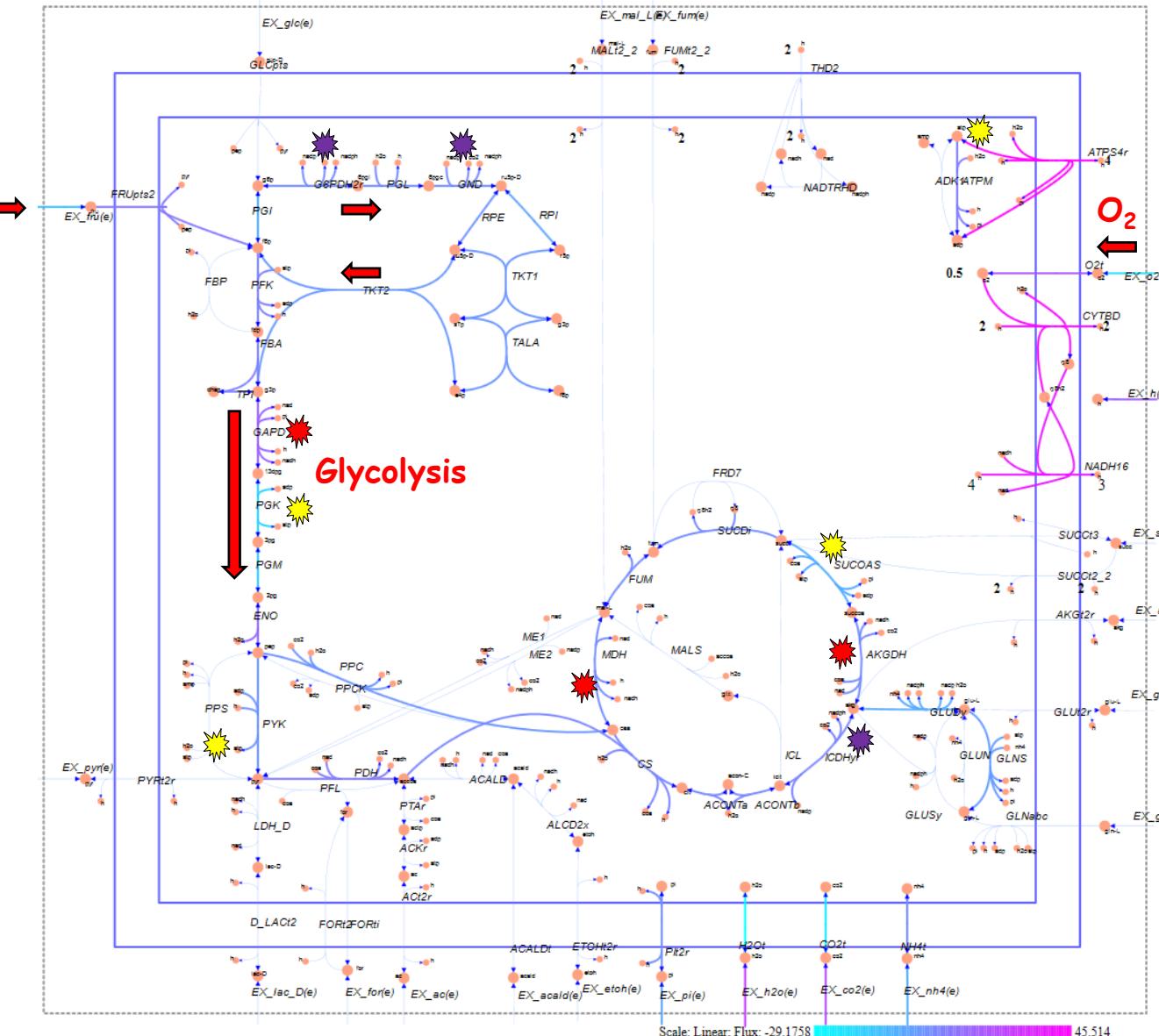
AnaerobicGlucoseBioMass.m

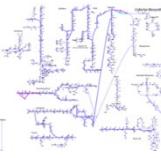


**Aerobic Conditions  
Carbon Source: Fructose**

Fructose →

ATP =   
NADPH =   
NADH =

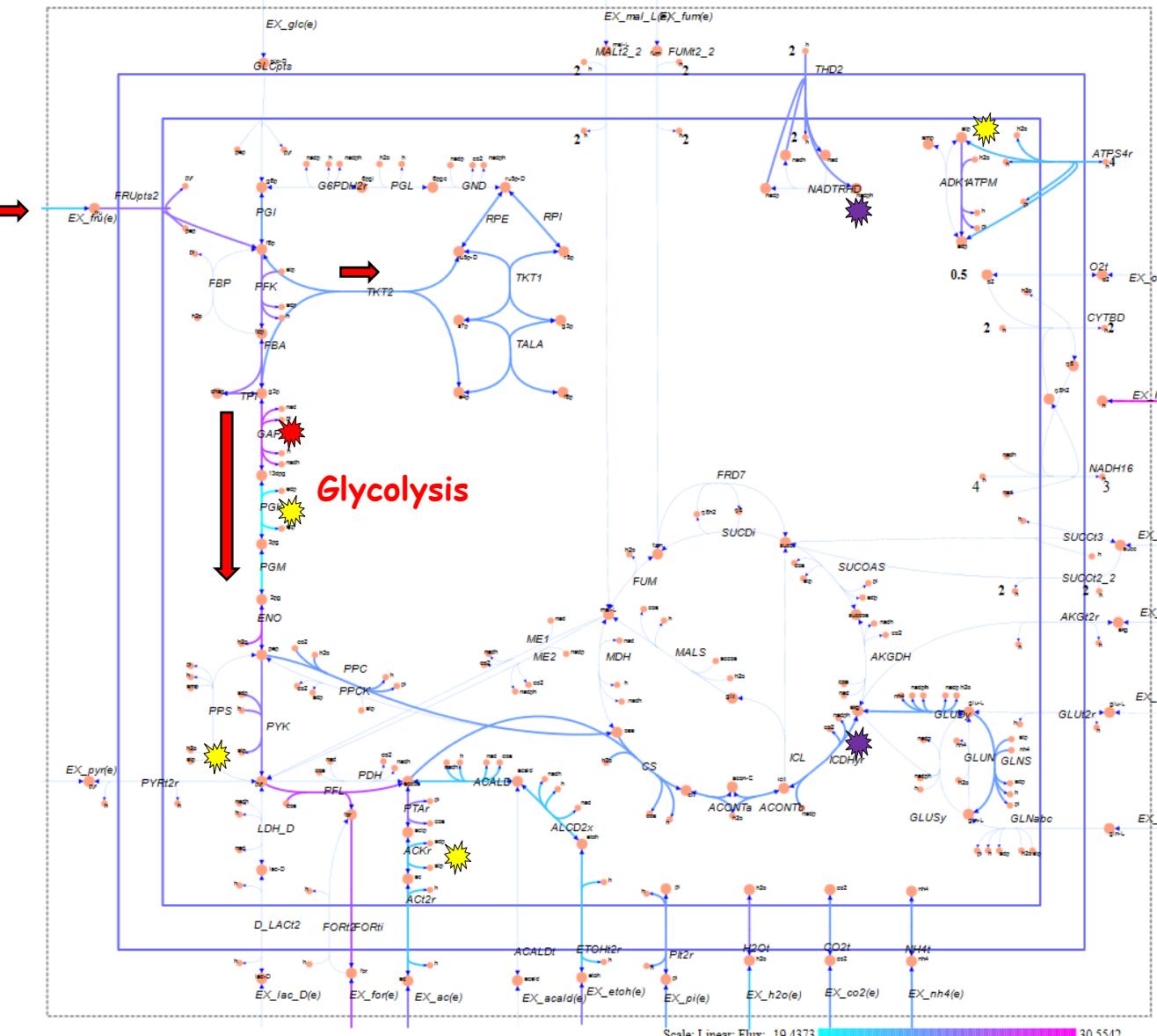




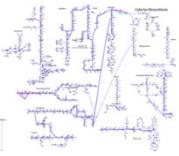
**Anaerobic Conditions  
Carbon Source: Fructose**

Fructose →

ATP = ☀  
NADPH = ⚡  
NADH = ⚡

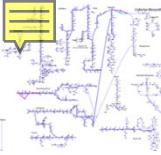


AnaerobicFructoseBioMass.m



# *E.coli* Core Model

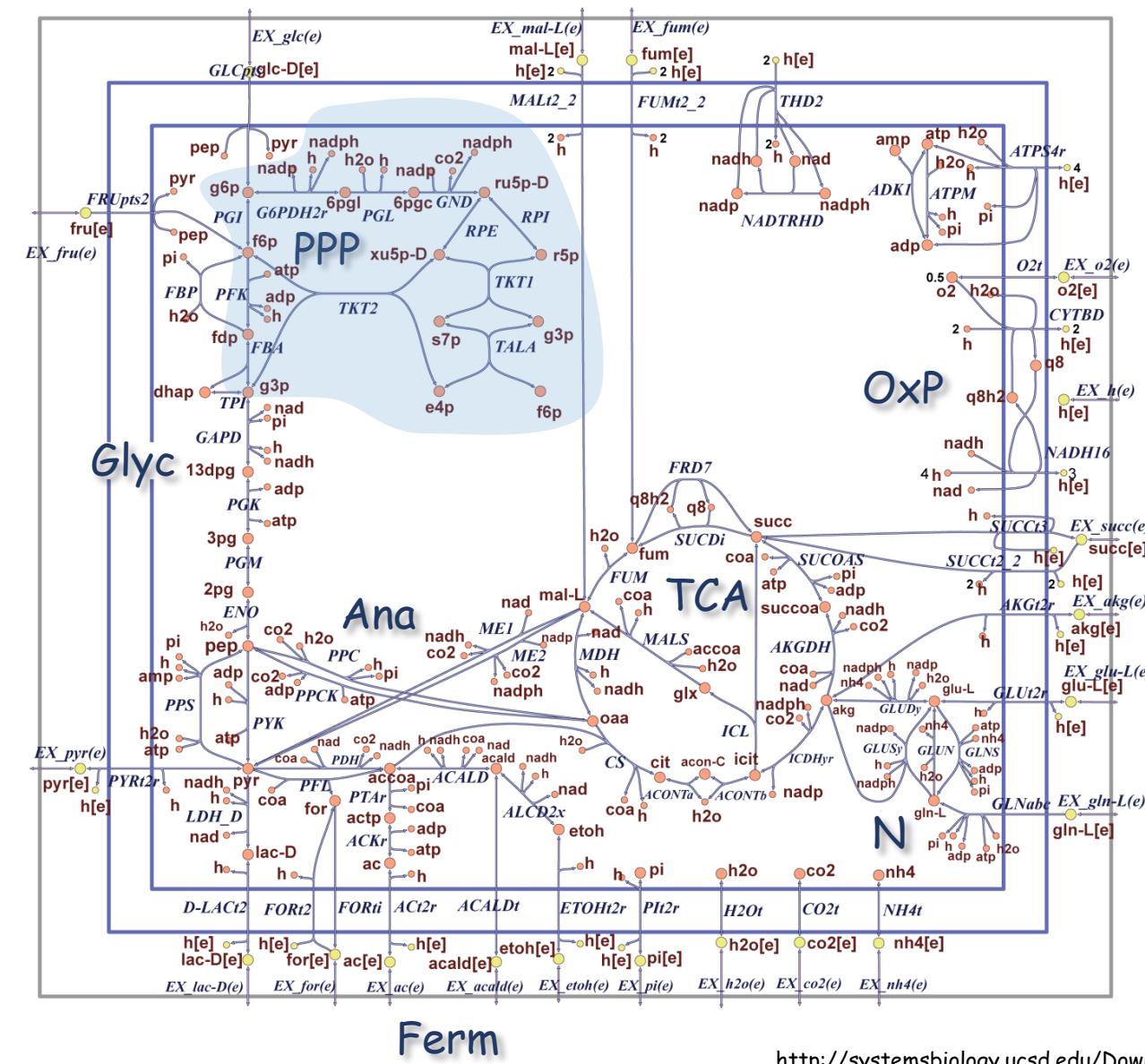
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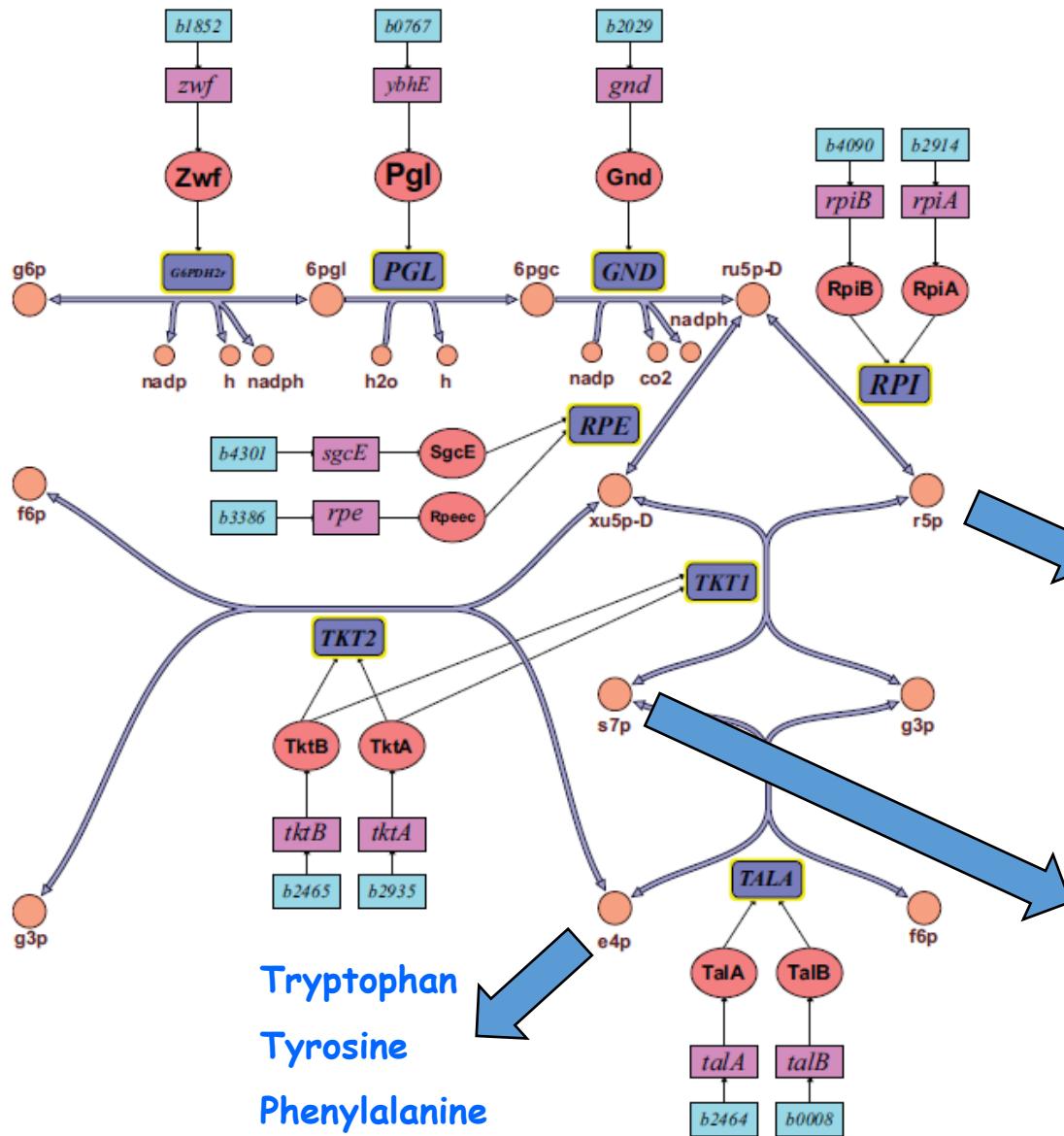


# Pentose Phosphate Pathway

## *E.coli* Core Model

Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.





## Biosynthetic Precursors (Pentose Phosphate Pathway)

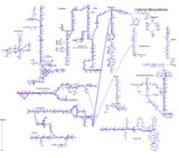
Histidine

Purines (ATP, GTP, dATP, dGTP)

Pyrimidines (UTP, CTP, dCTP, dTTP)

Heptose in Lipopolysaccharides (Endotoxin)

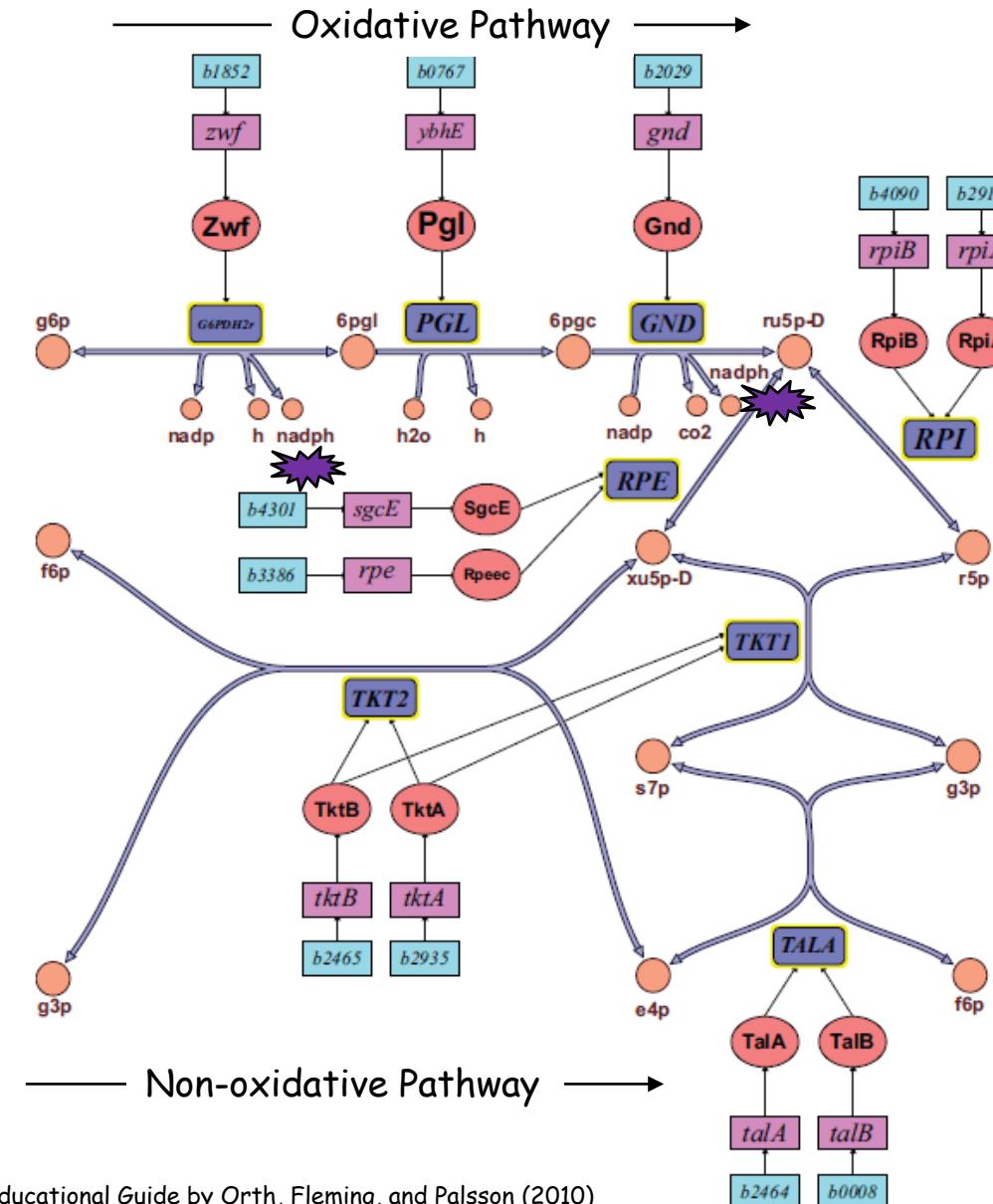
Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# Pentose Phosphate Shunt (Pentose Phosphate Pathway)

The pentose phosphate pathway generates NADPH and provides the 5-carbon (alpha-D-ribose-5-phosphate, "r5p"), 4-carbon biosynthetic precursors (D-erythrose-4-phosphate, "e4p"), and the 7-carbon, sedoheptulose-7-phosphate.

There are two distinct phases in the pathway. The first is the **oxidative phase**, in which NADPH is generated, and the second is the **non-oxidative** synthesis of 5-carbon and 4-carbon precursors.





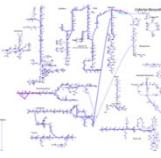
# Metabolites & Reactions

## Pentose Phosphate Pathway

Abbr.	Metabolite	Formula	Charge
g6p	D-Glucose-6-phosphate	C <sub>6</sub> H <sub>11</sub> O <sub>9</sub> P	-2
6pgl	6-phospho-D-glucono-1-5-lactone	C <sub>6</sub> H <sub>9</sub> O <sub>9</sub> P	-2
6pgc	6-Phospho-D-gluconate	C <sub>6</sub> H <sub>10</sub> O <sub>10</sub> P	-3
ru5p-D	D-Ribulose-5-phosphate	C <sub>5</sub> H <sub>9</sub> O <sub>8</sub> P	-2
r5p	alpha-D-Ribose-5-phosphate	C <sub>5</sub> H <sub>9</sub> O <sub>8</sub> P	-2
f6p	D-Fructose-6-phosphate	C <sub>6</sub> H <sub>11</sub> O <sub>9</sub> P	-2
g3p	Glyceraldehyde-3-phosphate	C <sub>3</sub> H <sub>5</sub> O <sub>6</sub> P	-2
xu5p-D	D-Xylulose-5-phosphate	C <sub>5</sub> H <sub>9</sub> O <sub>8</sub> P	-2
s7p	Sedoheptulose-7-phosphate	C <sub>7</sub> H <sub>13</sub> O <sub>10</sub> P	-2
e4p	D-Erythrose-4-phosphate	C <sub>4</sub> H <sub>7</sub> O <sub>7</sub> P	-2

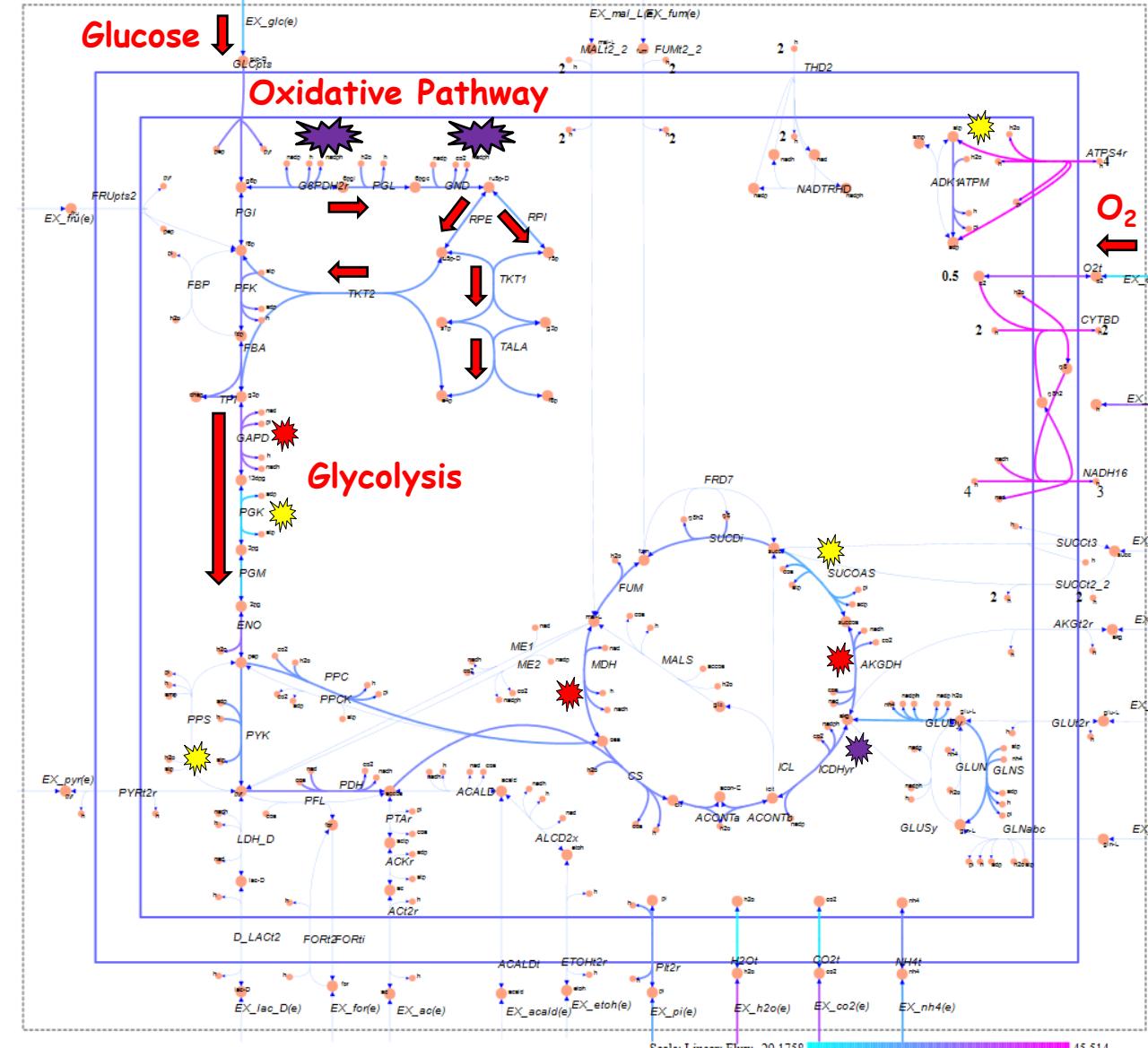
Abbr.	Reaction	Equation
G6PDH2r	glucose 6-phosphate dehydrogenase	g6p + nadp $\rightleftharpoons$ 6pgl + h + nadph
PGL	6-phosphogluconolactonase	6pgl + h <sub>2</sub> o $\rightarrow$ 6pgc + h
GND	phosphogluconate dehydrogenase	6pgc + nadp $\rightarrow$ co <sub>2</sub> + nadph + ru5p-D
RPI	ribose-5-phosphate isomerase	r5p $\rightleftharpoons$ ru5p-D
TKT2	transketolase	e4p + xu5p-D $\rightleftharpoons$ f6p + g3p
TALA	transaldolase	g3p + s7p $\rightleftharpoons$ e4p + f6p
TKT1	transketolase	r5p + xu5p-D $\rightleftharpoons$ g3p + s7p
RPE	ribulose 5-phosphate 3-epimerase	ru5p-D $\rightleftharpoons$ xu5p-D

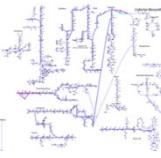
Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



## Aerobic Conditions Carbon Source: Glucose

ATP = ☀  
 NADPH = ⚡  
 NADH = ⚡



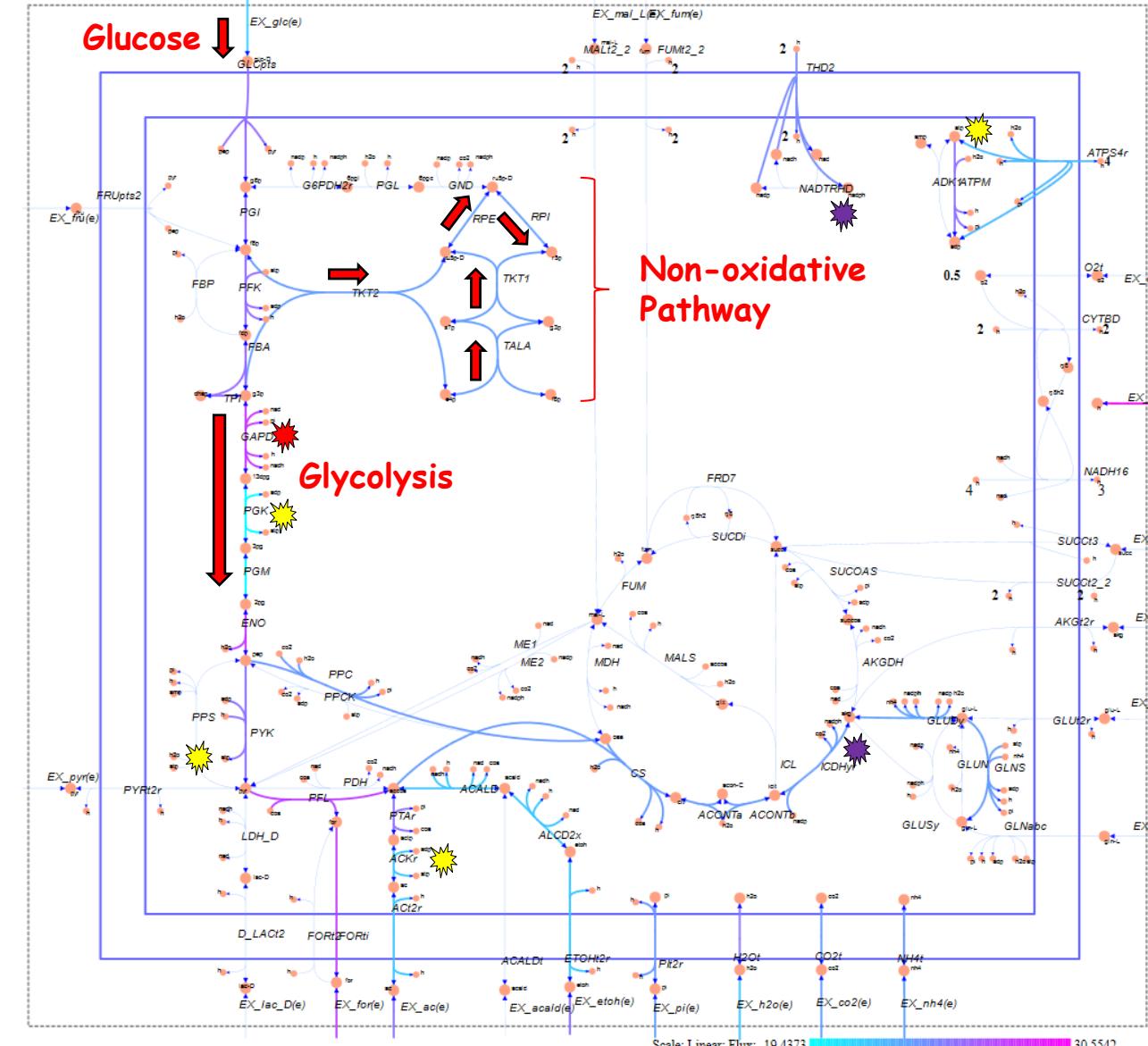


## Anaerobic Conditions Carbon Source: Glucose

ATP =

NADPH =

NADH =

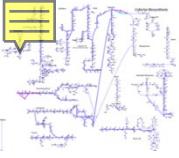


AnaerobicGlucoseBioMass.m



# *E.coli* Core Model

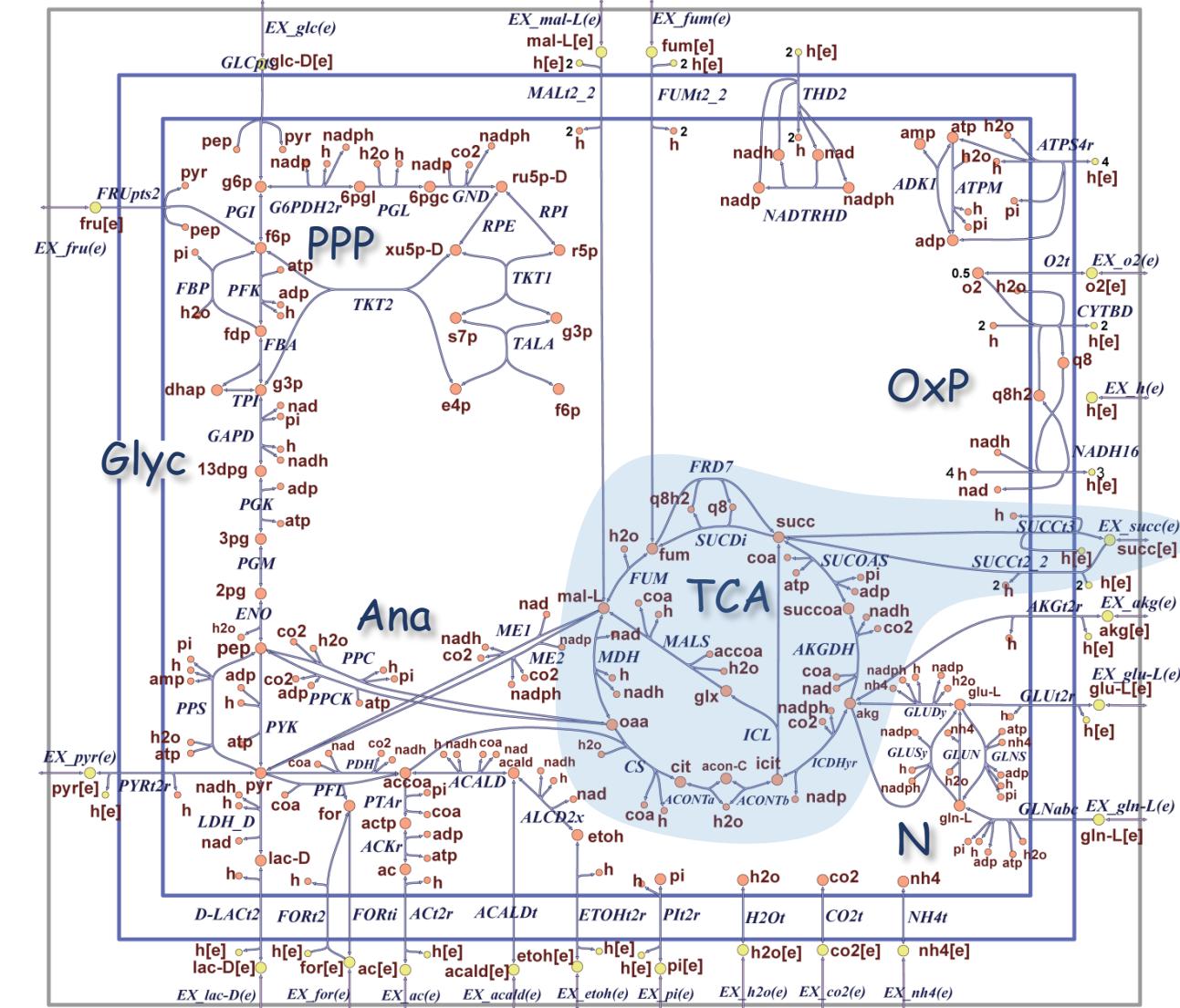
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- Fermentation
- Nitrogen Metabolism



# Tricarboxylic Acid Cycle (TCA)

*E.coli* Core Model

Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.



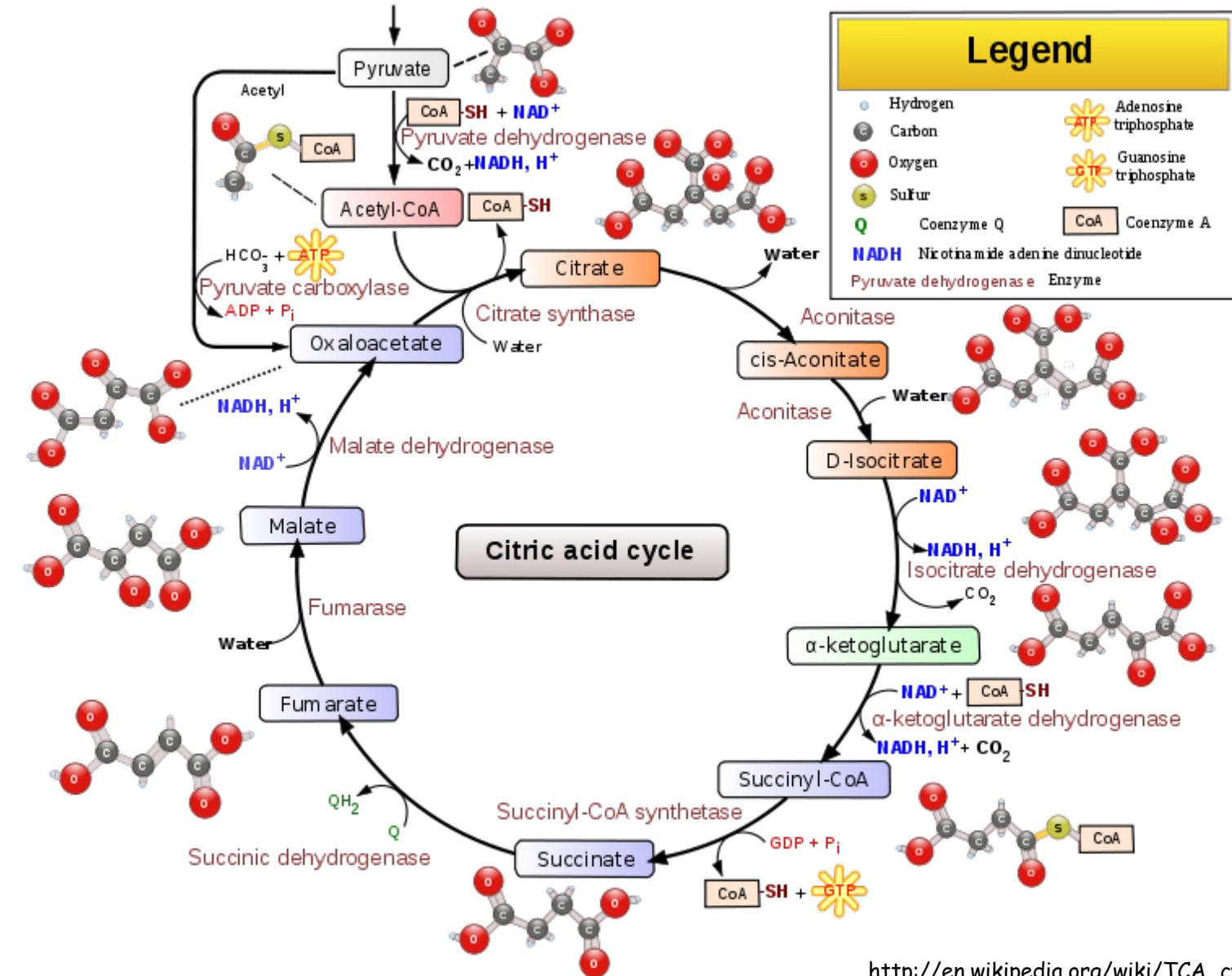
Ferm

[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



# TCA Cycle

The tricarboxylic acid cycle (TCA cycle), citric acid cycle – also known as the citric acid cycle, the Krebs cycle – is a series of chemical reactions used by all aerobic organisms to generate energy through the oxidation of acetate derived from carbohydrates, fats and proteins into carbon dioxide. In addition, the cycle provides precursors for certain amino acids as well as the reducing agent NADH.

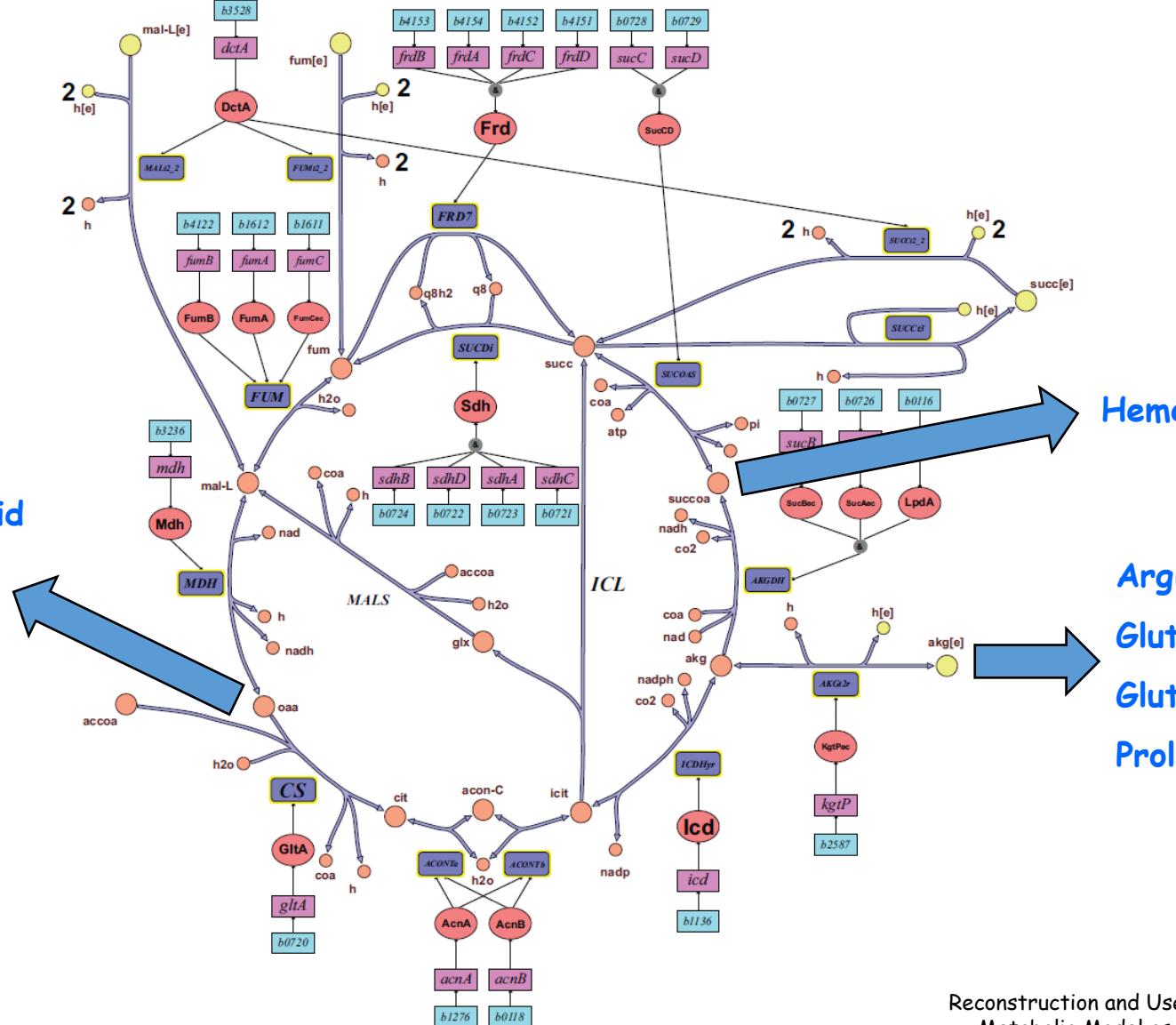


[http://en.wikipedia.org/wiki/TCA\\_cycle](http://en.wikipedia.org/wiki/TCA_cycle)



## Biosynthetic Precursors (TCA Cycle)

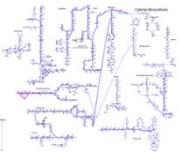
Asparagine  
Aspartic acid  
Isoleucine  
Lysine  
Methionine  
Threonine



Heme

Arginine  
Glutamine  
Glutamic acid  
Proline

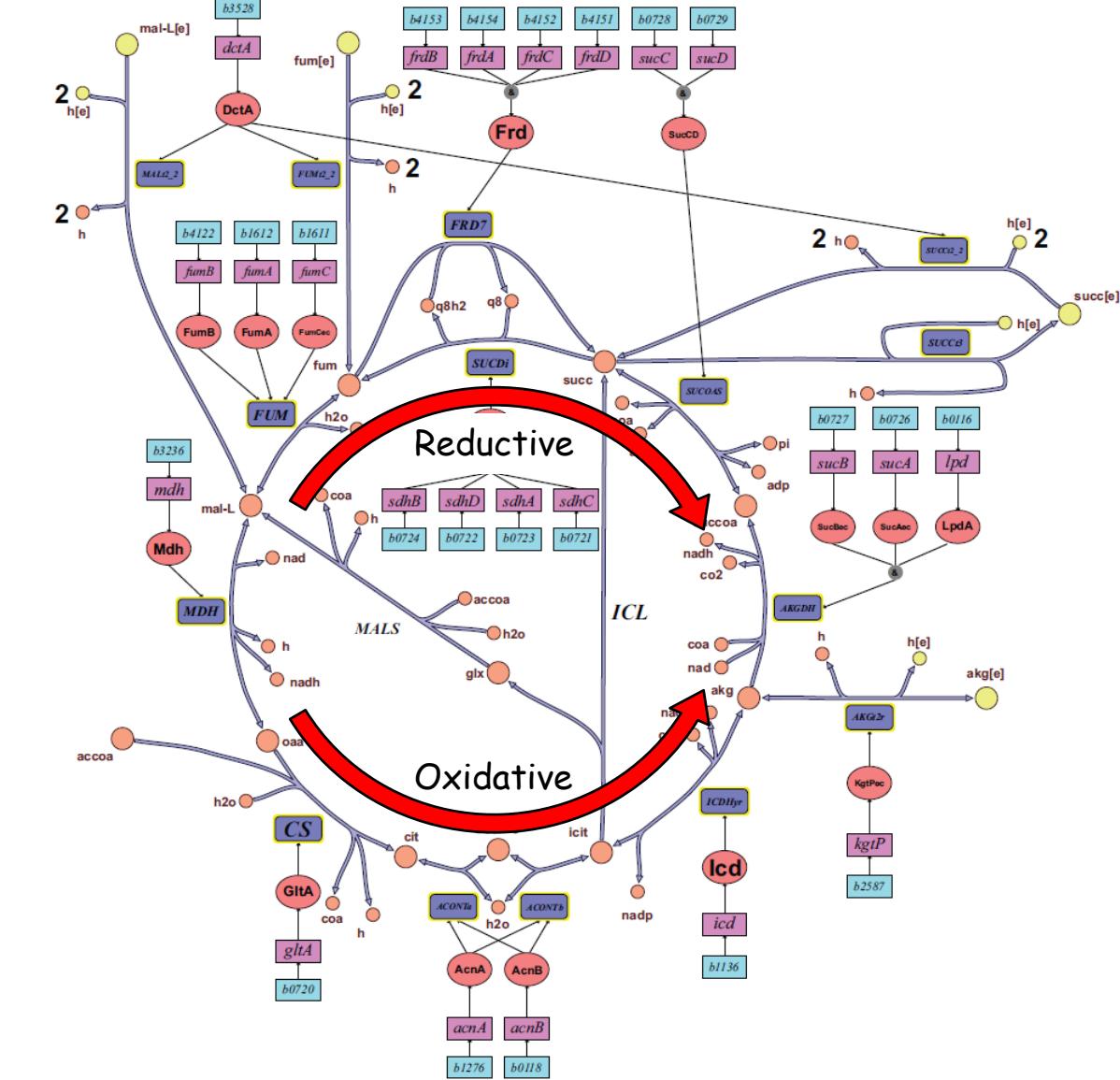
Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# TCA Cycle

The oxidative pathway of the TCA cycle runs counterclockwise in the lower part of the cycle, from oxaloacetate, oaa, through 2-oxoglutarate, akg. Continuing counterclockwise from 2-oxoglutarate, the full tricarboxylic acid cycle can totally oxidize acetyl-CoA, but is only functional during aerobic growth on acetate or fatty acids.

Under anaerobic conditions, the TCA cycle functions not as a cycle, but as two separate pathways. The **oxidative pathway**, the counterclockwise lower part of the cycle, still forms the precursor 2-oxoglutarate. The **reductive pathway**, the clockwise upper part of the cycle, forms the precursor succinyl-CoA.



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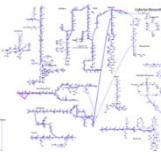
# Metabolites & Reactions

## TCA Cycle

Abbr.	Metabolite	Formula	Charge
accoa	Acetyl-CoA	C <sub>23</sub> H <sub>34</sub> N <sub>7</sub> O <sub>17</sub> P <sub>3</sub> S	-4
cit	Citrate	C <sub>6</sub> H <sub>5</sub> O <sub>7</sub>	-3
acon-C	cis-Aconitate	C <sub>6</sub> H <sub>3</sub> O <sub>6</sub>	-3
icit	Isocitrate	C <sub>6</sub> H <sub>5</sub> O <sub>7</sub>	-3
akg	2-Oxoglutarate	C <sub>5</sub> H <sub>4</sub> O <sub>5</sub>	-2
succoa	Succinyl-CoA	C <sub>25</sub> H <sub>35</sub> N <sub>7</sub> O <sub>19</sub> P <sub>3</sub> S	-5
fum	Fumarate	C <sub>4</sub> H <sub>2</sub> O <sub>4</sub>	-2
mal-L	L-Malate	C <sub>4</sub> H <sub>4</sub> O <sub>5</sub>	-2
oxa	Oxaloacetate	C <sub>4</sub> H <sub>2</sub> O <sub>5</sub>	-2

Abbr.	Reaction	Equation
CS	citrate synthase	accoa + h <sub>2</sub> o + oaa → cit + coa + h
ACONTa	aconitase (half-reaction A, Citrate hydro-lyase)	cit ⇌ acon-C + h <sub>2</sub> o
ACONTb	aconitase (half-reaction B, Isocitrate hydro-lyase)	acon-C + h <sub>2</sub> o ⇌ icit
ICDHyr	isocitrate dehydrogenase (NADP)	icit + nadp ⇌ akg + co <sub>2</sub> + nadph
AKGDH	2-Oxoglutarate dehydrogenase	akg + coa + nad → co <sub>2</sub> + nadh + succoa
SUCOAS	succinyl-CoA synthetase (ADP-forming)	atp + coa + succ → adp + pi + succoa
FRD7	fumarate reductase	fum + q <sub>8</sub> h <sub>2</sub> → q <sub>8</sub> + succ
SUCDi	succinate dehydrogenase (irreversible)	q <sub>8</sub> + succ → fum + q <sub>8</sub> h <sub>2</sub>
FUM	fumarase	fum + h <sub>2</sub> o ⇌ mal-L
MDH	malate dehydrogenase	mal-L + nad ⇌ h + nadh + oaa
AKGt2r	2-oxoglutarate reversible transport via symport	akg[e] + h[e] ⇌ akg + h
SUCCt3	succinate transport out via proton antiport	h[e] + succ → h + succ[e]
SUCCt2_2	succinate transport via proton symport (2 H)	2 h[e] + succ[e] → 2 h + succ
FUMt2_2	Fumarate transport via proton symport (2 H)	fum[e] + 2 h[e] → fum + 2 h
MALt2_2	Malate transport via proton symport (2 H)	2 h[e] + mal-L[e] → 2 h + mal-L

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)

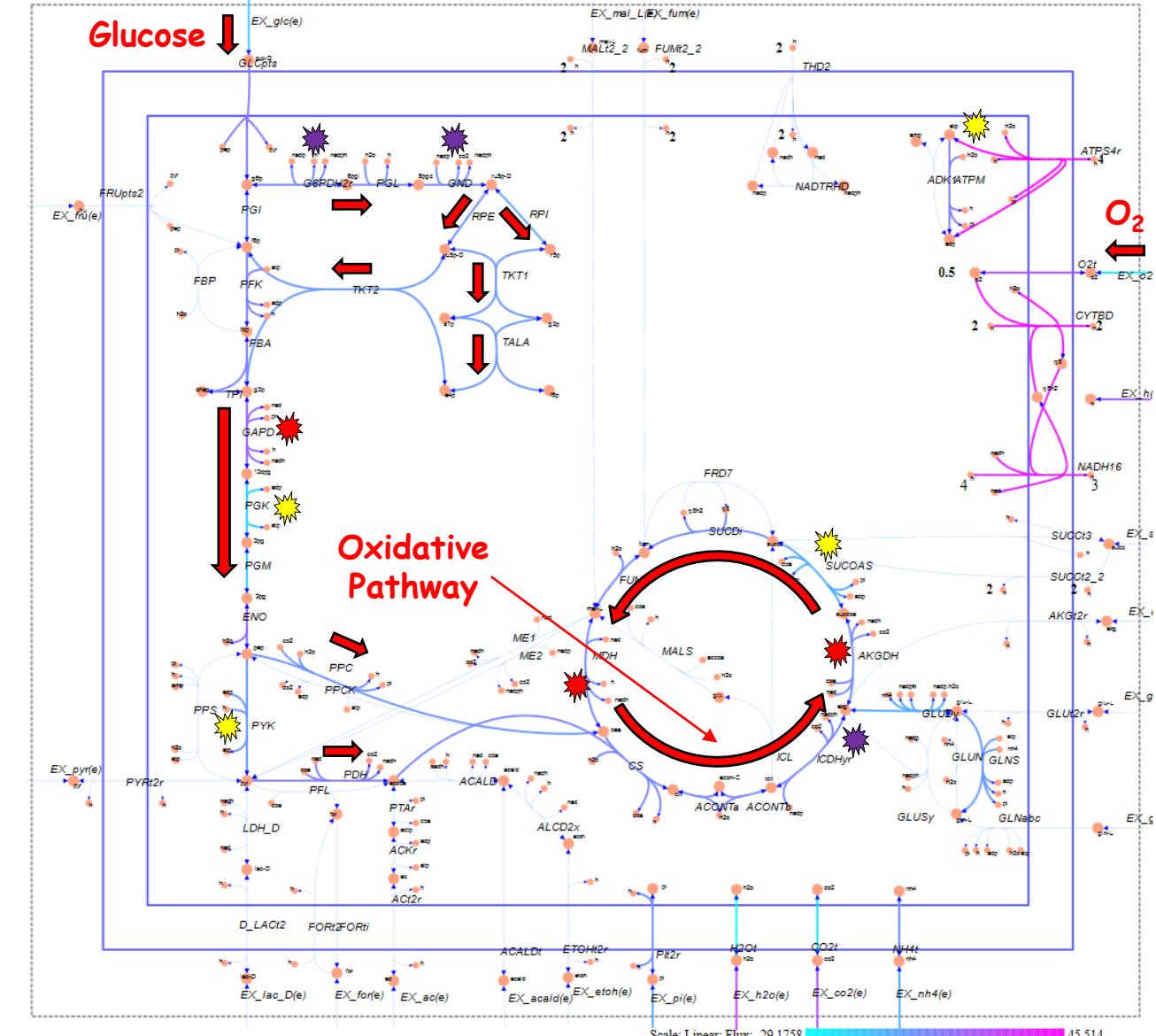


## Aerobic Conditions Carbon Source: Glucose

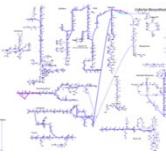
ATP =

NADPH =

NADH =



AerobicGlucoseBioMass.m



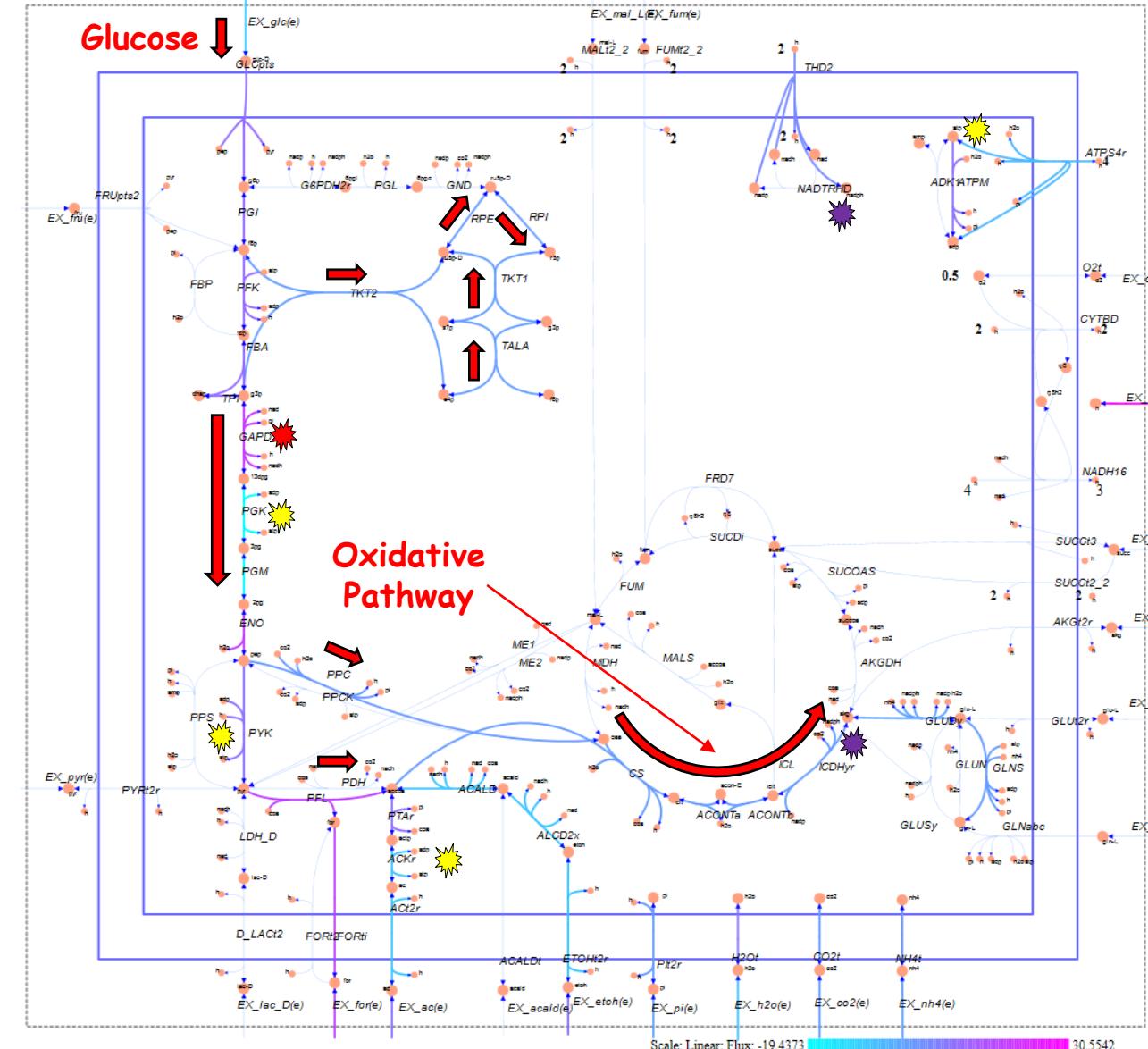
# Anaerobic Conditions

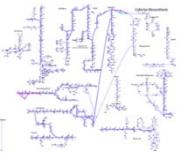
## Carbon Source: Glucose

ATP = 

NADPH = 

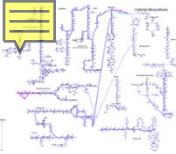
NADH = 





# *E.coli* Core Model

- Component Parts of the *E. coli* Core Model
- Glycolysis
- Pentose Phosphate Pathway
- Tricarboxylic Acid (TCA) Cycle
- • Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism



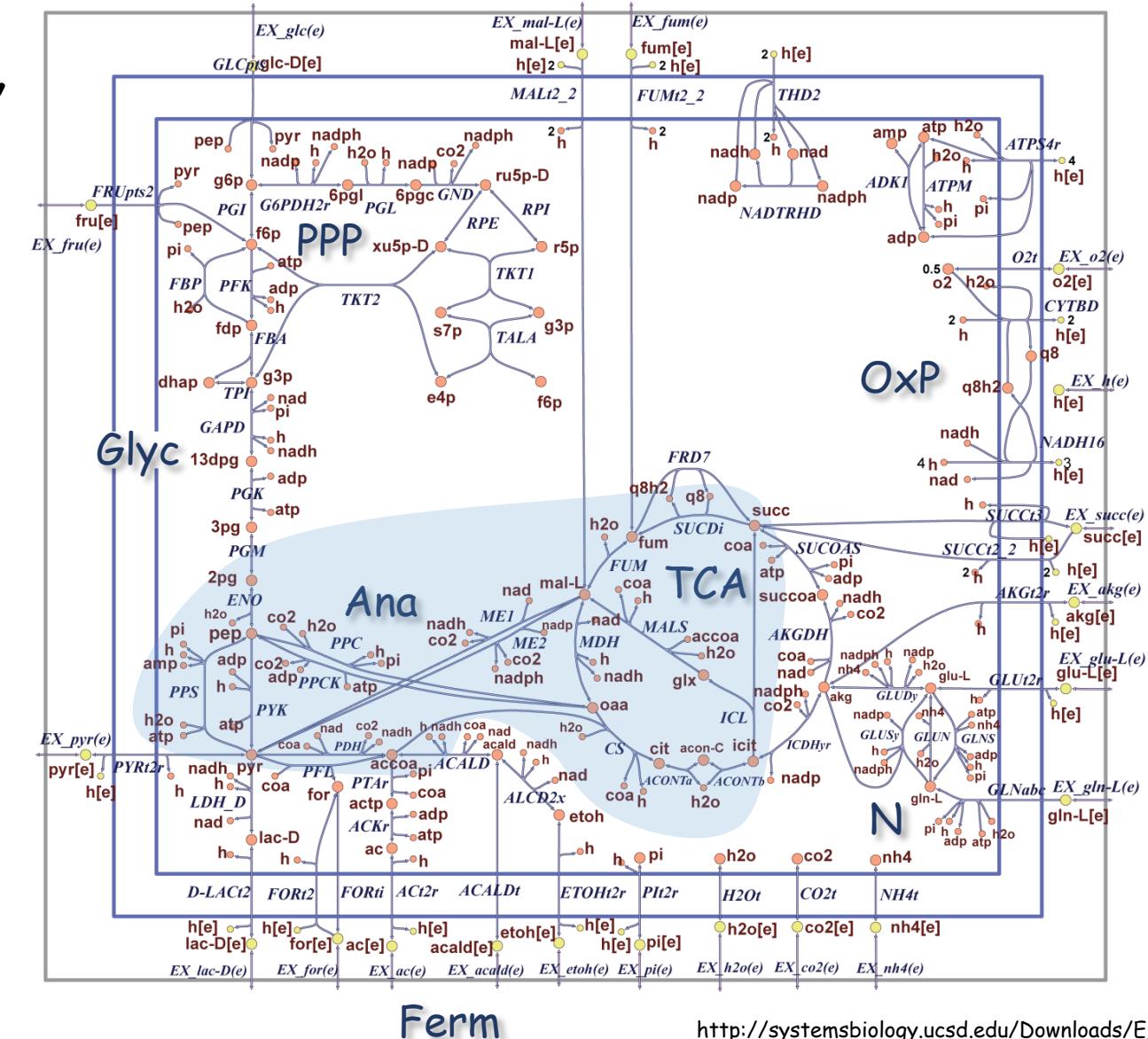
# Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

## *E. coli* Core Model

The glyoxylate cycle and gluconeogenic reactions allow *E. coli* to grow on 3-carbon (pyruvate) and 4-carbon compounds (malate, fumarate, succinate) by avoiding the loss of carbon to carbon dioxide from the TCA cycle, providing a pathway for generation of glycolytic intermediates from TCA intermediates, and reversing the carbon flux through glycolysis to produce essential precursors for biosynthesis.

Anapleurotic reactions replenish TCA intermediates drained of for biosynthesis

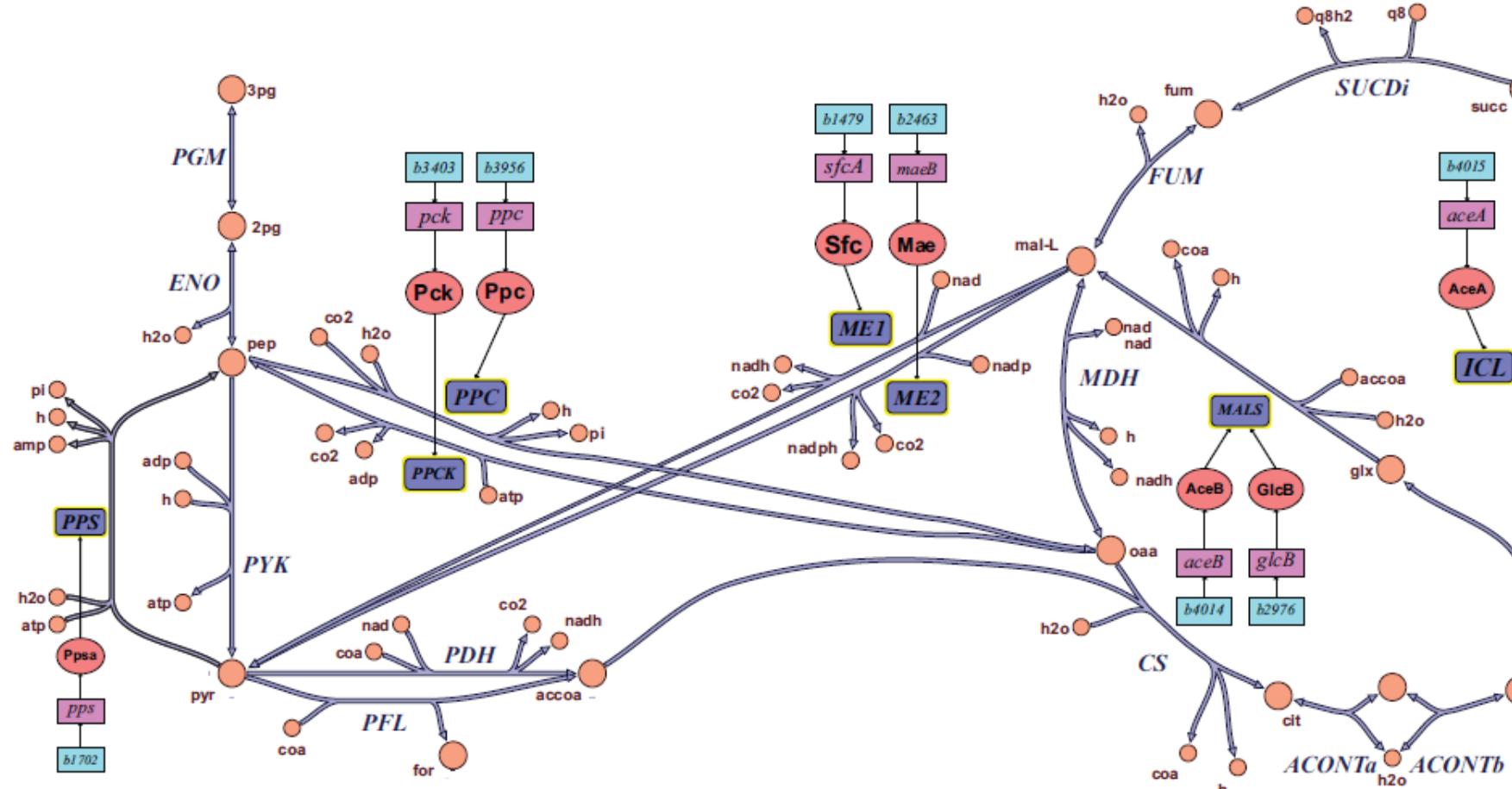
Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.



[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



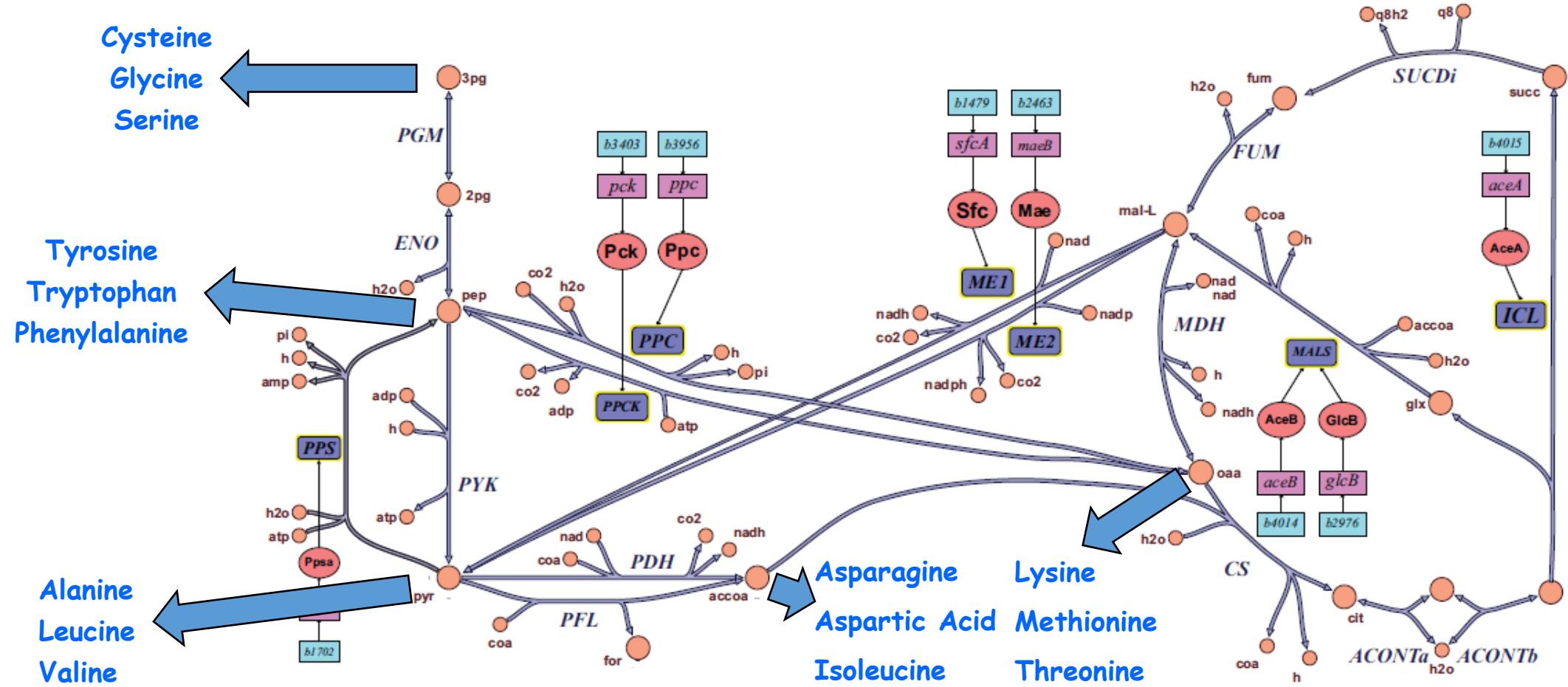
# Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions



Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# Biosynthetic Precursors for Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions



Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



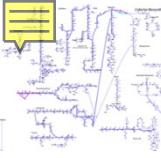
# Metabolites & Reactions

Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

Abbr.	Metabolite	Formula	Charge
glx	Glyoxylate	C <sub>2</sub> HO <sub>3</sub>	-1

Abbr.	Reaction	Equation
ICL	isocitrate lyase	icit → glx + succ
MALS	malate synthase	accoa + glx + h <sub>2</sub> o → coa + h + mal-L
ME1	malic enzyme (NAD)	mal-L + nad → co2 + nadh + pyr
ME2	malic enzyme (NADP)	mal-L + nadp → co2 + nadph + pyr
PPS	phosphoenolpyruvate synthase	atp + h <sub>2</sub> o + pyr → amp + 2 h + pep + pi
PPCK	phosphoenolpyruvate carboxykinase	atp + oaa → adp + co2 + pep
PPC	phosphoenolpyruvate carboxylase	co2 + h <sub>2</sub> o + pep → h + oaa + pi

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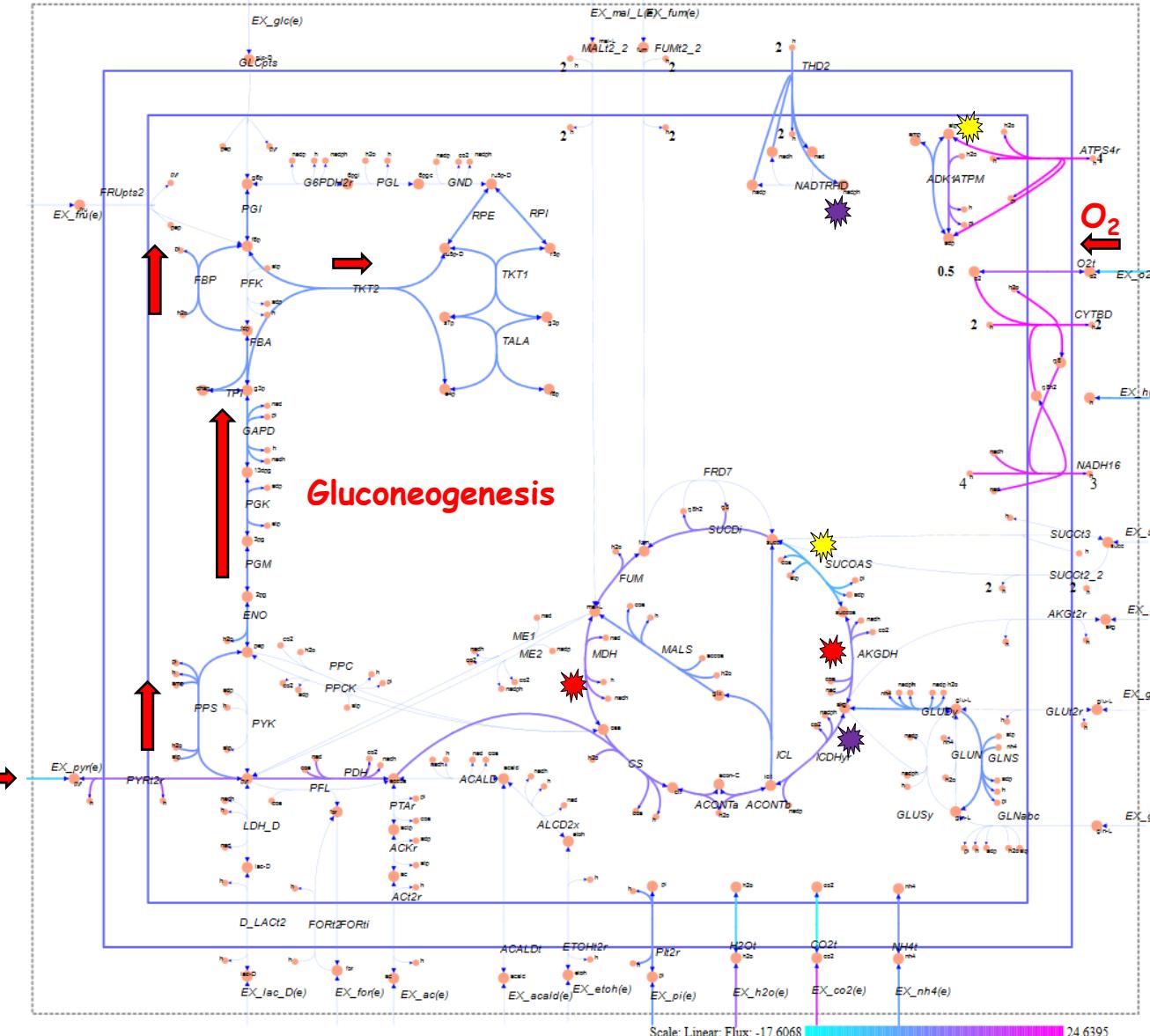
Aerobic Conditions  
Carbon Source: Pyruvate

Pyruvate →

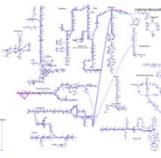
ATP = ☀

NADPH = ⚡

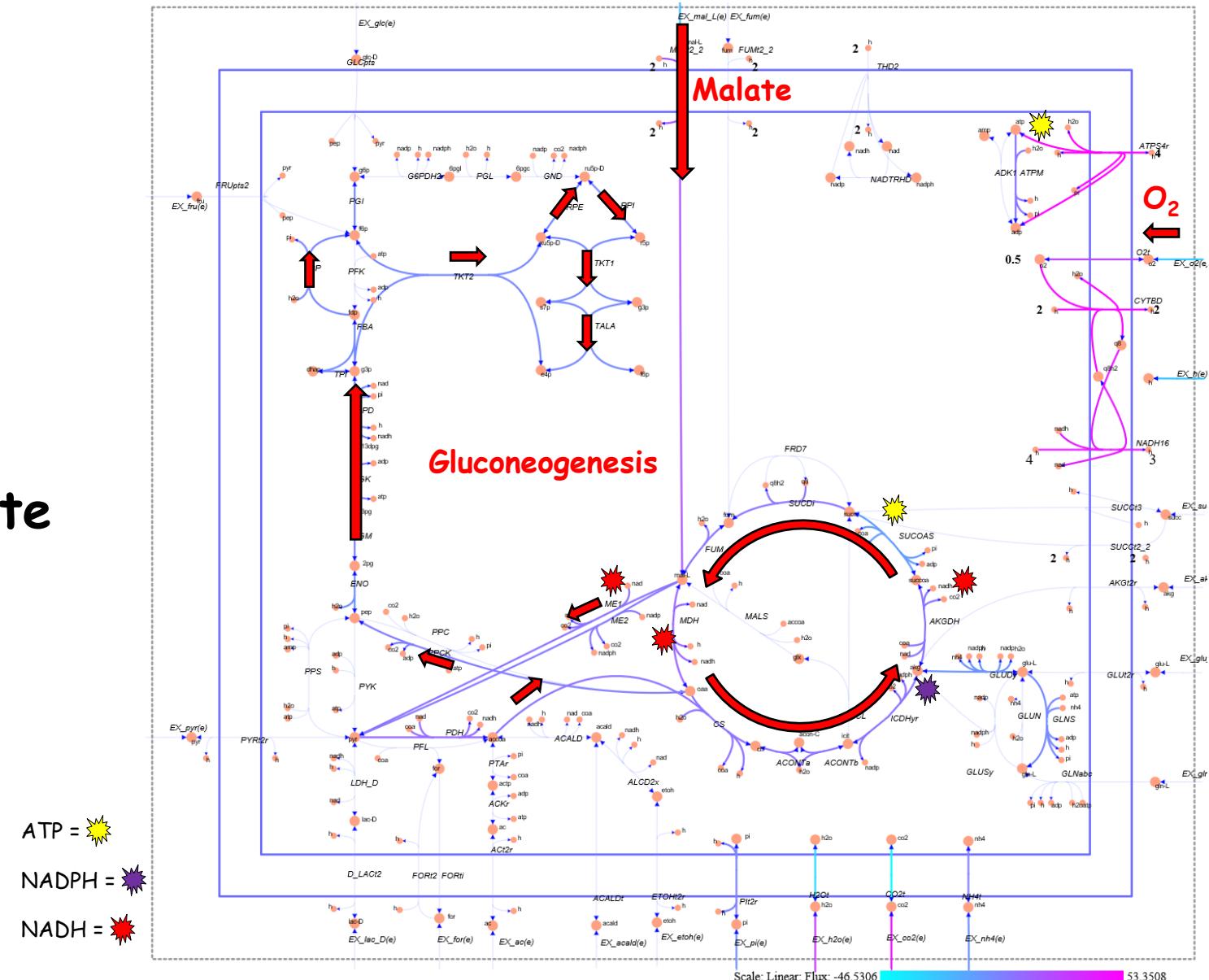
NADH = ⚡



AerobicGlucoseBioMass.m



## Aerobic Conditions Carbon Source: Malate



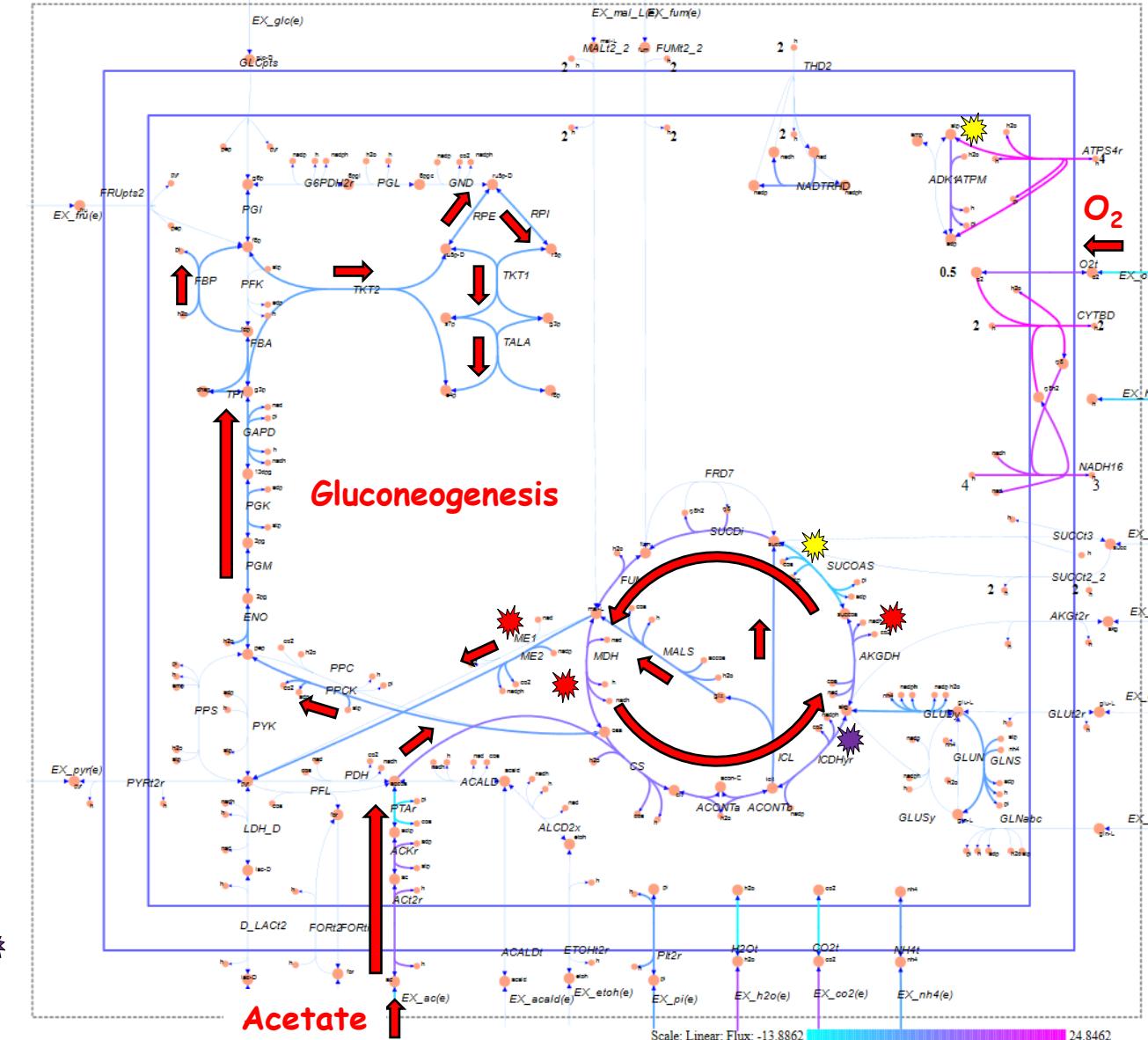


## Aerobic Conditions Carbon Source: Acetate

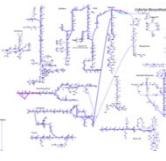
ATP =

NADPH =

NADH =



AerobicAcetateBioMass.m



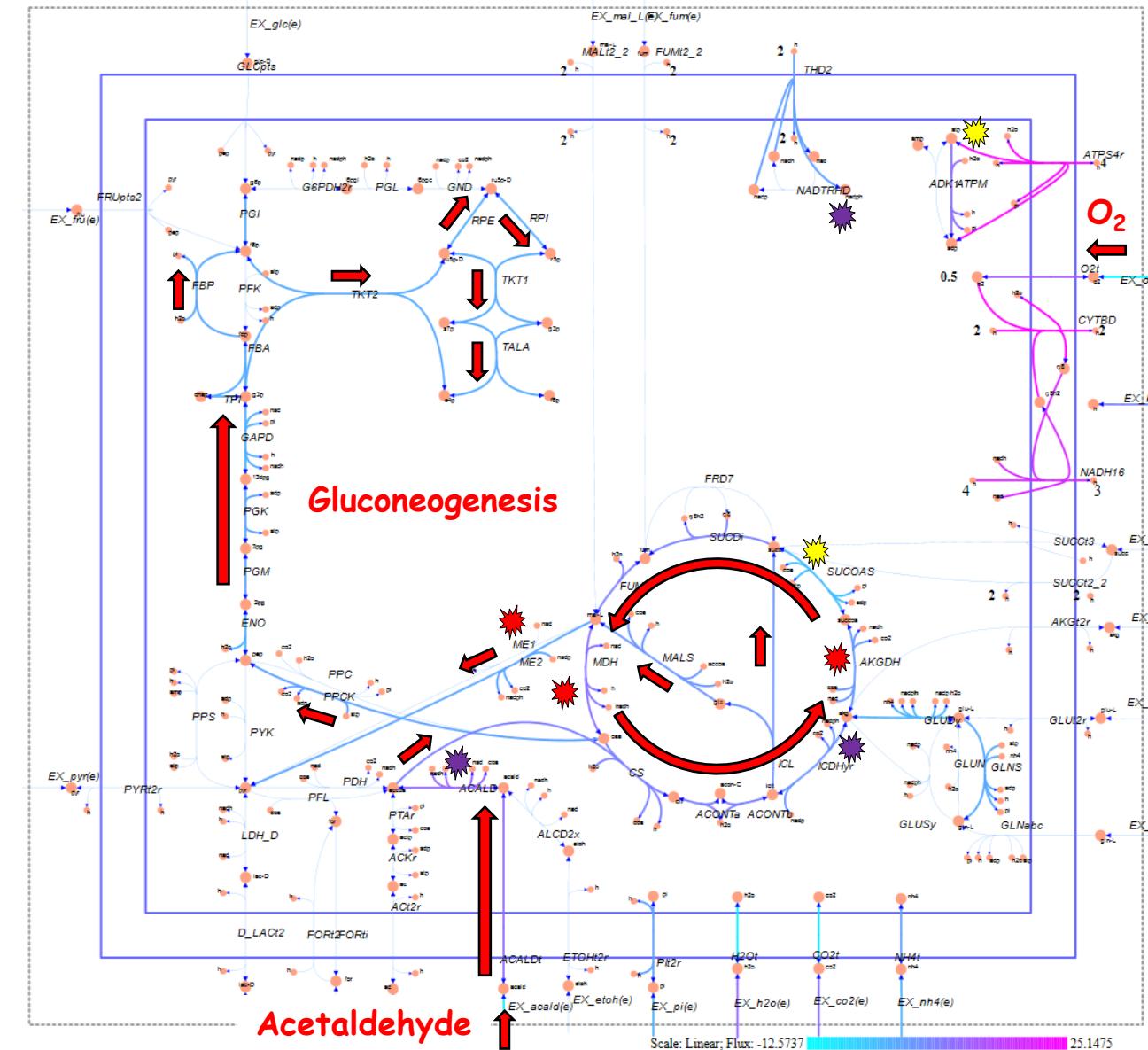
# Aerobic Conditions

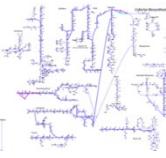
## Carbon Source: Acetaldehyde

ATP = 

NADPH = \*

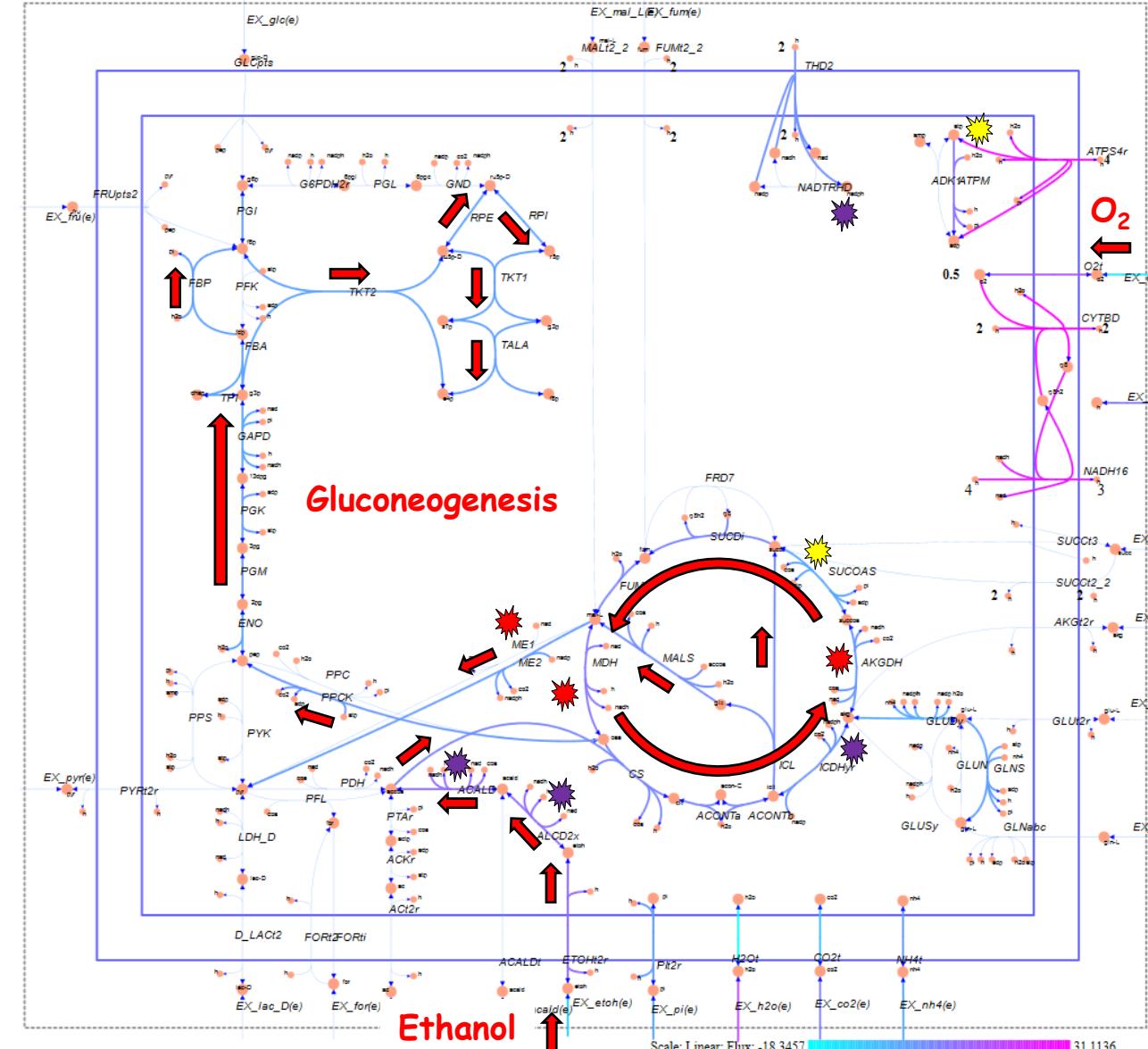
NADH = \*

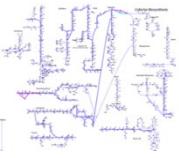




## Aerobic Conditions Carbon Source: Ethanol

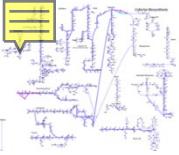
ATP =   
NADPH =   
NADH = 





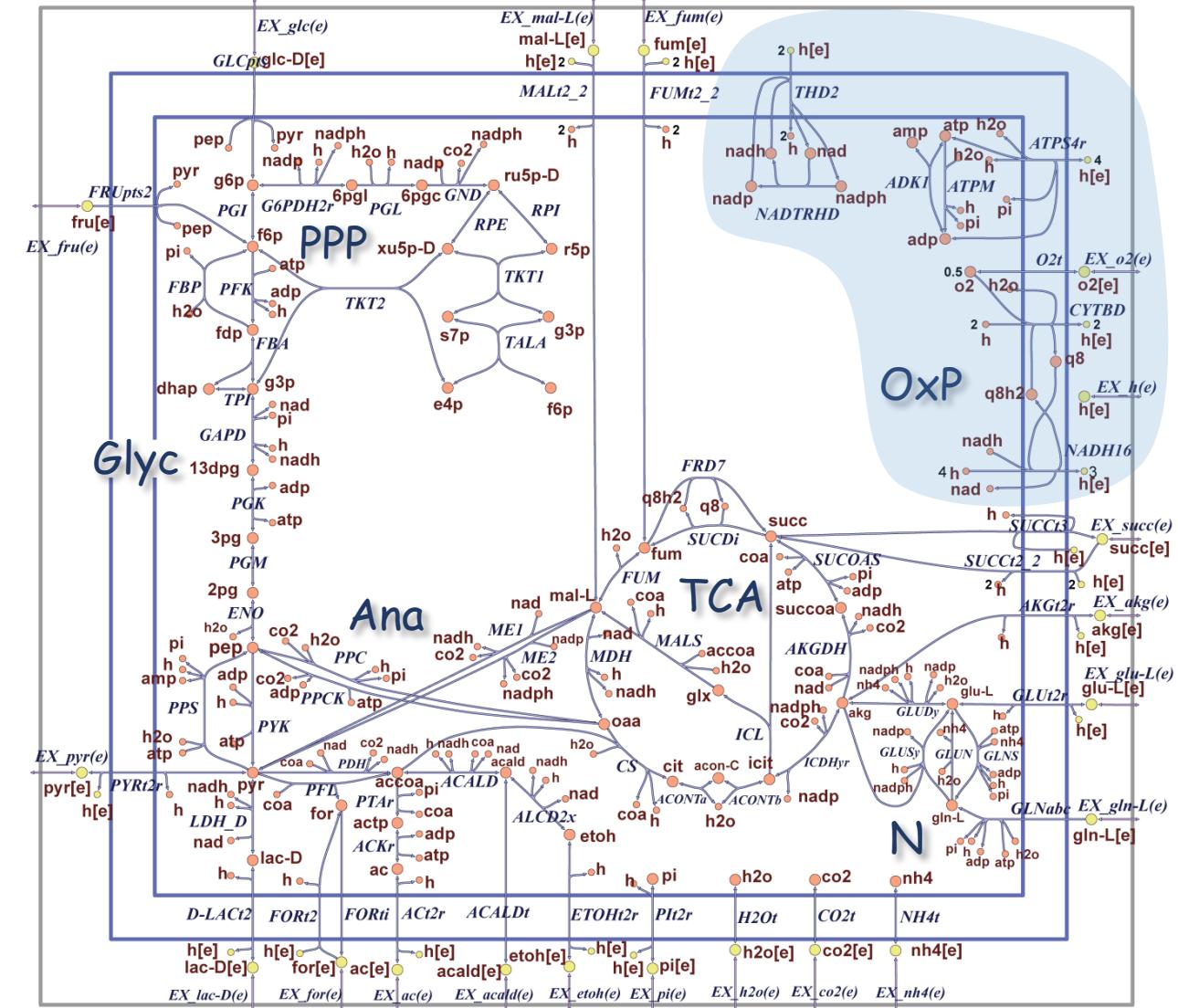
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- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism



# Oxidative Phosphorylation and Transfer of Reducing Equivalents

## E.coli Core Model



Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.

[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



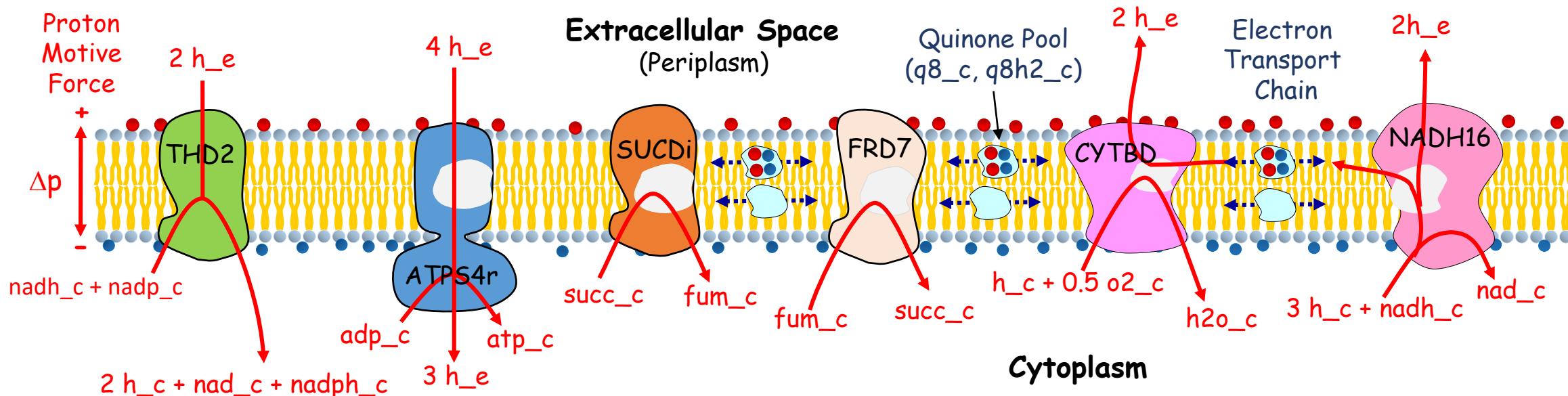
# Oxidative Phosphorylation and Transfer of Reducing Equivalents

- Energy is required to drive endergonic processes such as biosynthesis, polymerization, active transport of substrate into the cell against concentration gradients, maintaining internal pH, and motility. There are two main mechanisms for the production of energy, **substrate level phosphorylation**, and the **electron transport chain**.
- Substrate level phosphorylation is where ATP is formed by a reaction between ADP and a phosphorylated intermediate of a fueling pathway. Examples include: phosphoglycerate kinase, PGK, and pyruvate kinase, PYK, in glycolysis, and succinyl-CoA synthetase, SUCOAS, in the tricarboxylic acid cycle. Each molecule of glucose can potentially lead to the net generation of four molecules of ATP.
- The electron transport chain which produces the bulk of the cell's ATP under aerobic conditions. Mitchell's chemiosmotic theory describes the mechanism by which electron transport is coupled to the generation of ATP. The electron transport chain translocates protons,  $H^+$ , from the cytoplasm, across the cytoplasmic membrane into the periplasmic space. Since the cytoplasmic membrane is effectively impermeable to protons and hydroxyl ions,  $OH^-$ , this establishes a difference in concentration of protons, and a difference in electrical charge, across the cytoplasmic membrane. This thermodynamic potential difference gives rise to a **proton motive force** which can be utilized to drive a myriad of endergonic reactions, such as synthesis of high energy currency metabolites, such as ATP.

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



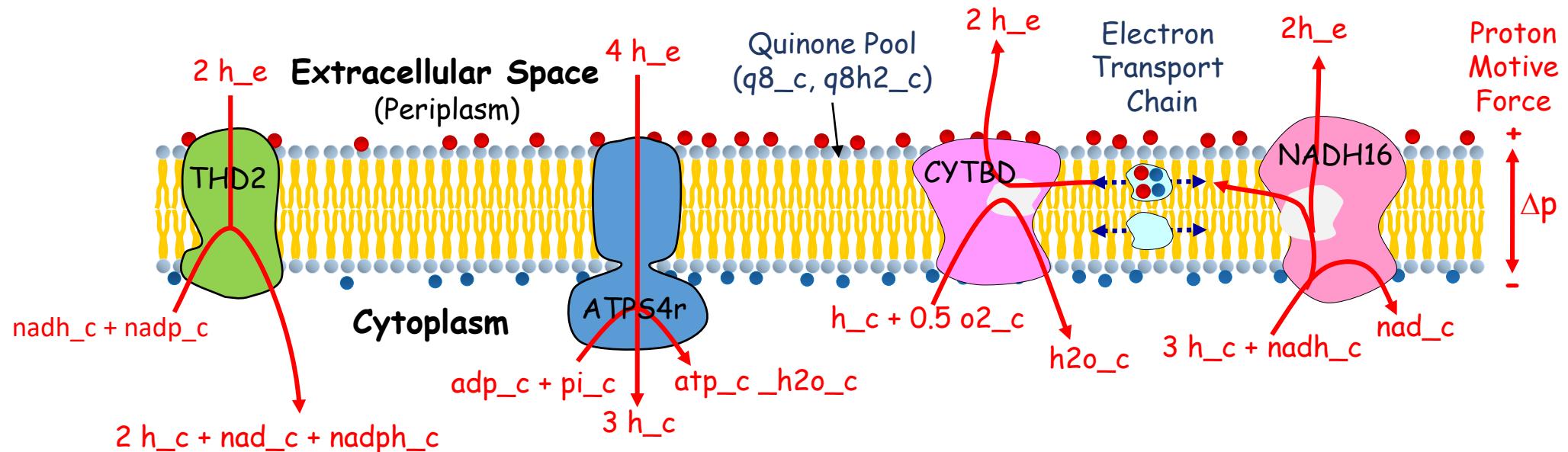
# Aerobic Respiration in Core Model



ADK1	Adenylate kinase	$\text{amp}_c + \text{atp}_c \leftrightarrow 2 \text{adp}_c$	ATP/ADP Balance
ATPM	ATP maintenance requirement	$\text{atp}_c + \text{h}_2\text{o}_c \rightarrow \text{adp}_c + \text{h}_c + \text{pi}_c$	ATP Maintenance
ATPS4r	ATP synthase (four protons for one ATP)	$\text{adp}_c + 4 \text{h}_e + \text{pi}_c \leftrightarrow \text{atp}_c + \text{h}_2\text{o}_c + 3 \text{h}_c$	ATP Production
CYTBD	Cytochrome oxidase bd (ubiquinol-8: 2 protons)	$2 \text{h}_c + 0.5 \text{o}_2_c + \text{q}_8\text{h}_2_c \rightarrow \text{h}_2\text{o}_c + 2 \text{h}_e + \text{q}_8_c$	Electron Transport Chain
FRD7	Fumarate reductase	$\text{fum}_c + \text{q}_8\text{h}_2_c \rightarrow \text{q}_8_c + \text{succ}_c$	TCA Cycle
NADH16	NADH dehydrogenase (ubiquinone-8 & 3 protons)	$4 \text{h}_c + \text{nadh}_c + \text{q}_8_c \rightarrow 3 \text{h}_e + \text{nad}_c + \text{q}_8\text{h}_2_c$	Electron Transport Chain
NADTRHD	NAD transhydrogenase	$\text{nad}_c + \text{nadph}_c \rightarrow \text{nadh}_c + \text{nadp}_c$	NADH/NADPH Balance
SUCDi	Succinate dehydrogenase (irreversible)	$\text{q}_8_c + \text{succ}_c \rightarrow \text{fum}_c + \text{q}_8\text{h}_2_c$	TCA Cycle
THD2	NAD(P) transhydrogenase	$2 \text{h}_e + \text{nadh}_c + \text{nadp}_c \rightarrow 2 \text{h}_c + \text{nad}_c + \text{nadph}_c$	NADH/NADPH Balance



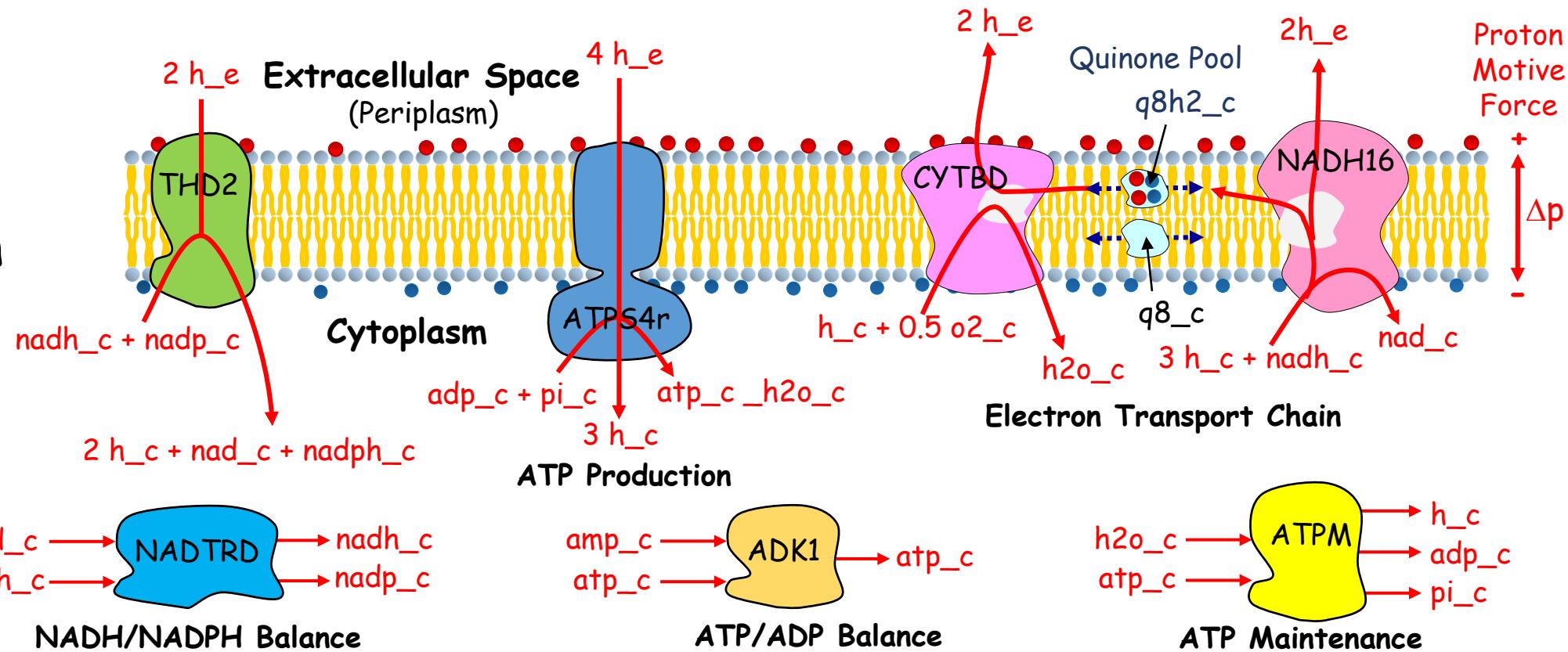
# Aerobic Respiration in Core Model



ADK1	Adenylate kinase	$amp_c + atp_c \leftrightarrow 2 adp_c$	ATP/ADP Balance
ATPM	ATP maintenance requirement	$atp_c + h2o_c \rightarrow adp_c + h_c + pi_c$	ATP Maintenance
ATPS4r	ATP synthase (four protons for one ATP)	$adp_c + 4 h_e + pi_c \leftrightarrow atp_c + h2o_c + 3 h_c$	ATP Production
CYTBD	Cytochrome oxidase bd (ubiquinol-8: 2 protons)	$2 h_c + 0.5 o2_c + q8h2_c \rightarrow h2o_c + 2 h_e + q8_c$	Electron Transport Chain
FRD7	Fumarate reductase	$fum_c + q8h2_c \rightarrow q8_c + succ_c$	TCA Cycle
NADH16	NADH dehydrogenase (ubiquinone-8 & 3 protons)	$4 h_c + nadh_c + q8_c \rightarrow 3 h_e + nad_c + q8h2_c$	Electron Transport Chain
NADTRHD	NAD transhydrogenase	$nad_c + nadph_c \rightarrow nadh_c + nadp_c$	NADH/NADPH Balance
SUCDi	Succinate dehydrogenase (irreversible)	$q8_c + succ_c \rightarrow fum_c + q8h2_c$	TCA Cycle
THD2	NAD(P) transhydrogenase	$2 h_e + nadh_c + nadp_c \rightarrow 2 h_c + nad_c + nadph_c$	NADH/NADPH Balance



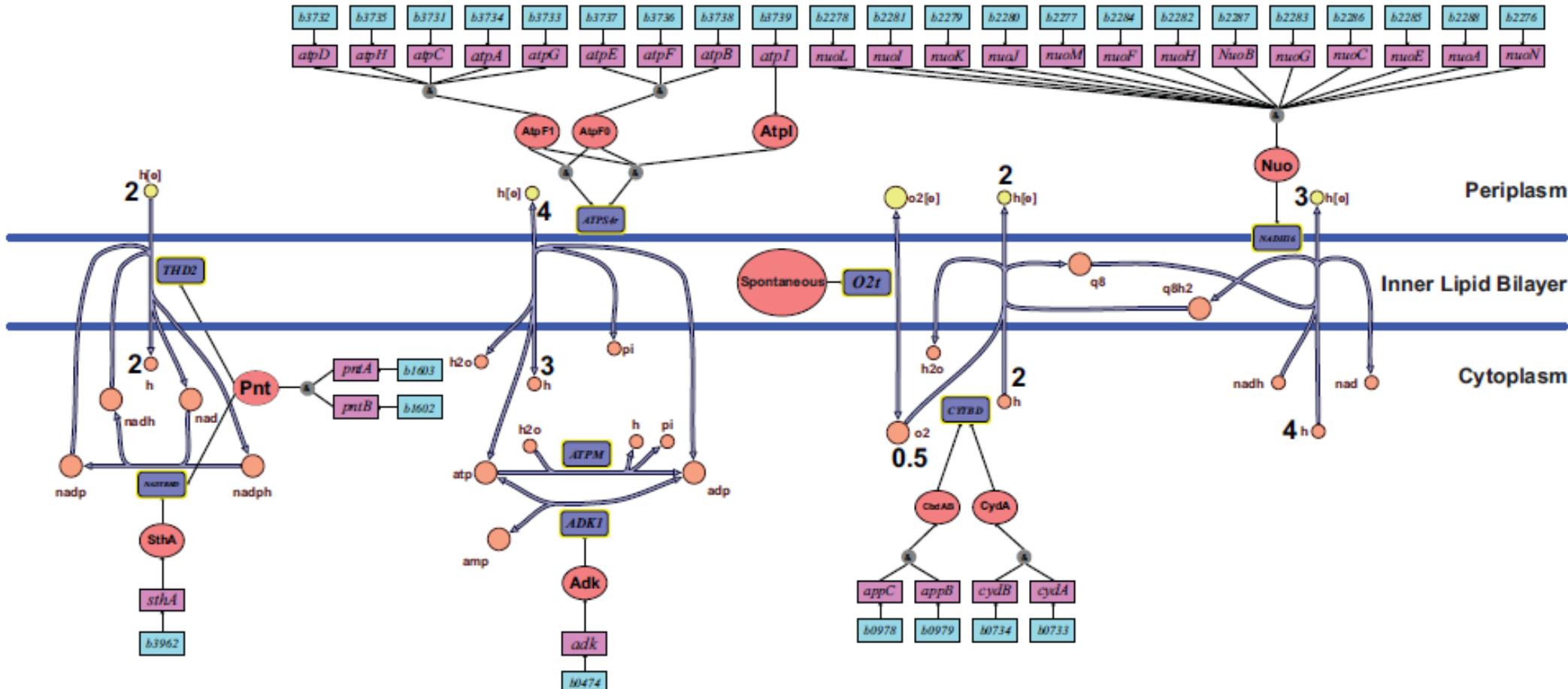
# Oxidative Phosphorylation and Transfer of Reducing Equivalents



ADK1	Adenylate kinase	$amp_c + atp_c \leftrightarrow 2 adp_c$	ATP/ADP Balance
ATPM	ATP maintenance requirement	$atp_c + h2o_c \rightarrow adp_c + h_c + pi_c$	ATP Maintenance
ATPS4r	ATP synthase (four protons for one ATP)	$adp_c + 4 h_e + pi_c \leftrightarrow atp_c + h2o_c + 3 h_c$	ATP Production
CYTBD	Cytochrome oxidase bd (ubiquinol-8: 2 protons)	$2 h_c + 0.5 o2_c + q8h2_c \rightarrow h2o_c + 2 h_e + q8_c$	Electron Transport Chain
NADH16	NADH dehydrogenase (ubiquinone-8 & 3 protons)	$4 h_c + nadh_c + q8_c \rightarrow 3 h_e + nad_c + q8h2_c$	Electron Transport Chain
NADTRHD	NAD transhydrogenase	$nad_c + nadph_c \rightarrow nadh_c + nadp_c$	NADH/NADPH Balance
THD2	NAD(P) transhydrogenase	$2 h_e + nadh_c + nadp_c \rightarrow 2 h_c + nad_c + nadph_c$	NADH/NADPH Balance



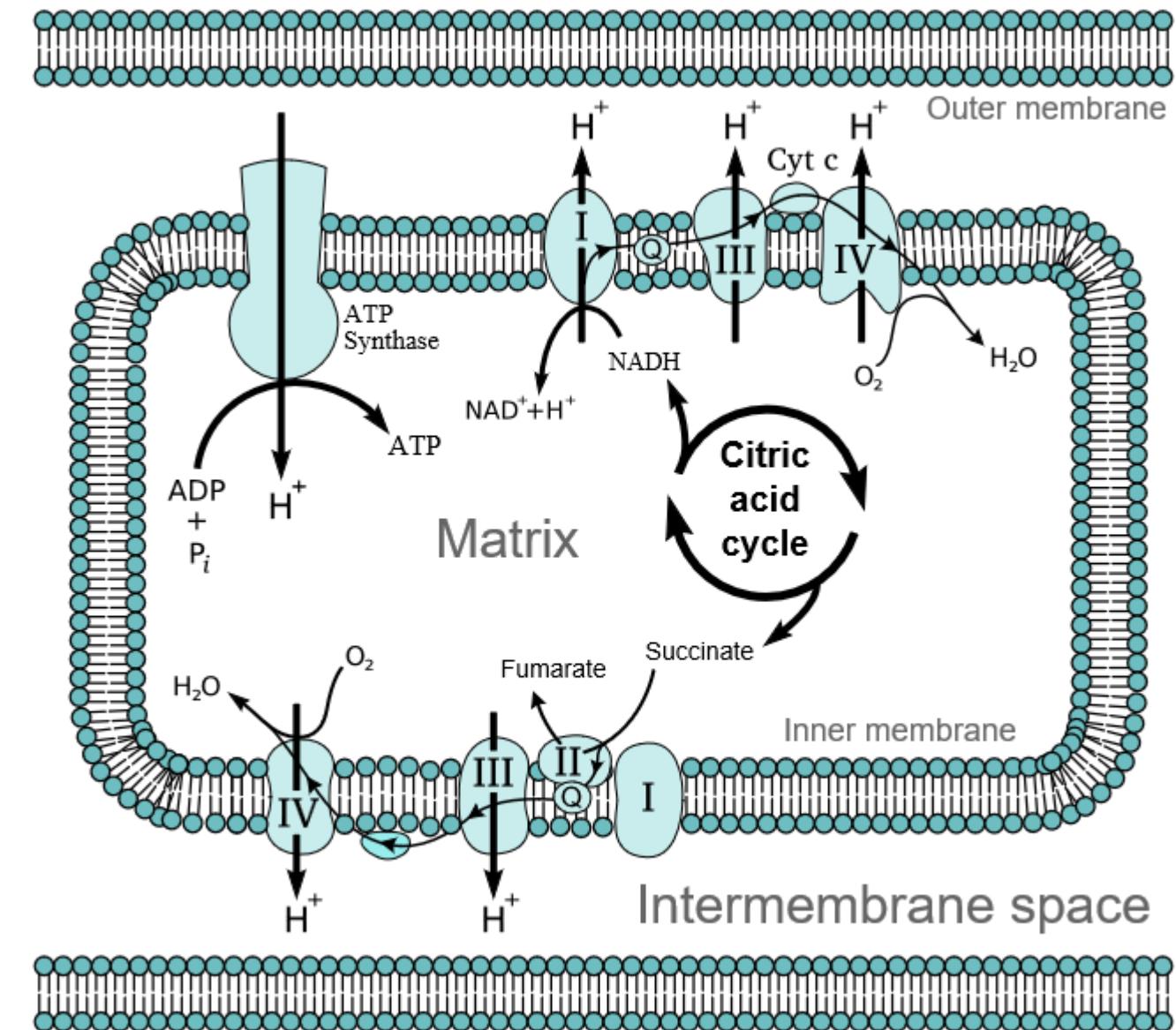
# Oxidative Phosphorylation and Transfer of Reducing Equivalents



Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



# Electron Transport Chain



[https://en.wikipedia.org/wiki/Electron\\_transport\\_chain](https://en.wikipedia.org/wiki/Electron_transport_chain)



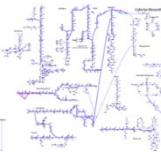
# Metabolites & Reactions

Oxidative Phosphorylation and Transfer of Reducing Equivalents

Abbr.	Name	Formula	Charge
q8	Ubiquinone-8	C <sub>49</sub> H <sub>74</sub> O <sub>4</sub>	0
q8h2	Ubiquinol-8	C <sub>49</sub> H <sub>76</sub> O <sub>4</sub>	0
nad	Nicotinamide-adenine-dinucleotide (NAD <sup>+</sup> )	C <sub>21</sub> H <sub>26</sub> N <sub>7</sub> O <sub>14</sub> P <sub>2</sub>	-1
nadh	Nicotinamide-adenine-dinucleotide-reduced	C <sub>21</sub> H <sub>27</sub> N <sub>7</sub> O <sub>14</sub> P <sub>2</sub>	-2
nadp	Nicotinamide-adenine-dinucleotide-phosphate	C <sub>21</sub> H <sub>25</sub> N <sub>7</sub> O <sub>17</sub> P <sub>3</sub>	-3
nadph	Nicotinamide-adenine-dinucleotide-phosphate-reduced	C <sub>21</sub> H <sub>26</sub> N <sub>7</sub> O <sub>17</sub> P <sub>3</sub>	-4
atp	Adenosine-5'-triphosphate	C <sub>10</sub> H <sub>12</sub> N <sub>5</sub> O <sub>13</sub> P <sub>3</sub>	-4
adp	Adenosine diphosphate	C <sub>10</sub> H <sub>12</sub> N <sub>5</sub> O <sub>10</sub> P <sub>2</sub>	-3
amp	Adenosine monophosphate	C <sub>10</sub> H <sub>12</sub> N <sub>5</sub> O <sub>7</sub> P	-2
h	Proton	H	+1

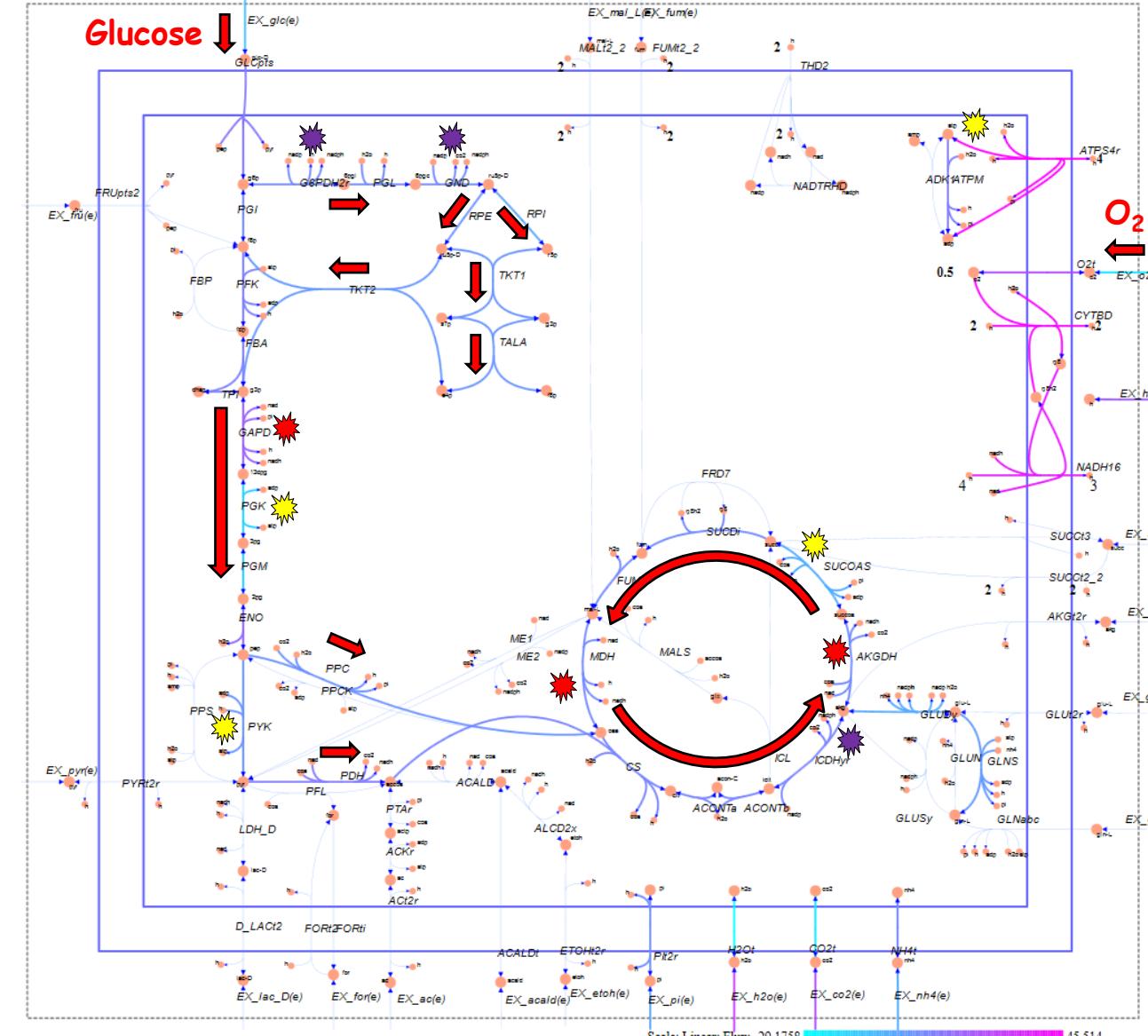
Abbr.	Name	Equation
NADH16	NADH dehydrogenase (ubiquinone-8 & 3 protons)	4 h + nadh + q8 → 3 h[e] + nad + q8h2
CYTBD	cytochrome oxidase bd (ubiquinol-8: 2 protons)	2 h + $\frac{1}{2}$ o <sub>2</sub> + q8h2 → h <sub>2</sub> o + 2 h[e] + q8
O2t	o <sub>2</sub> transport via diffusion	o <sub>2</sub> [e] ⇌ o <sub>2</sub>
ATPS4r	ATP synthase (four protons for one ATP)	adp + 4 h[e] + pi ⇌ atp + h <sub>2</sub> o + 3 h
ATPM	ATP maintenance requirement	atp + h <sub>2</sub> o → adp + h + pi
ADK1	adenylate kinase	amp + atp ⇌ 2 adp
THD2	NAD(P) transhydrogenase	2 h[e] + nadh + nadp → 2 h + nad + nadph
NADTRHD	NAD transhydrogenase	nad + nadph → nadh + nadp

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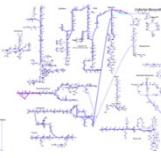


## Aerobic Conditions Carbon Source: Glucose

ATP = ☀  
 NADPH = ⚡  
 NADH = ⚡

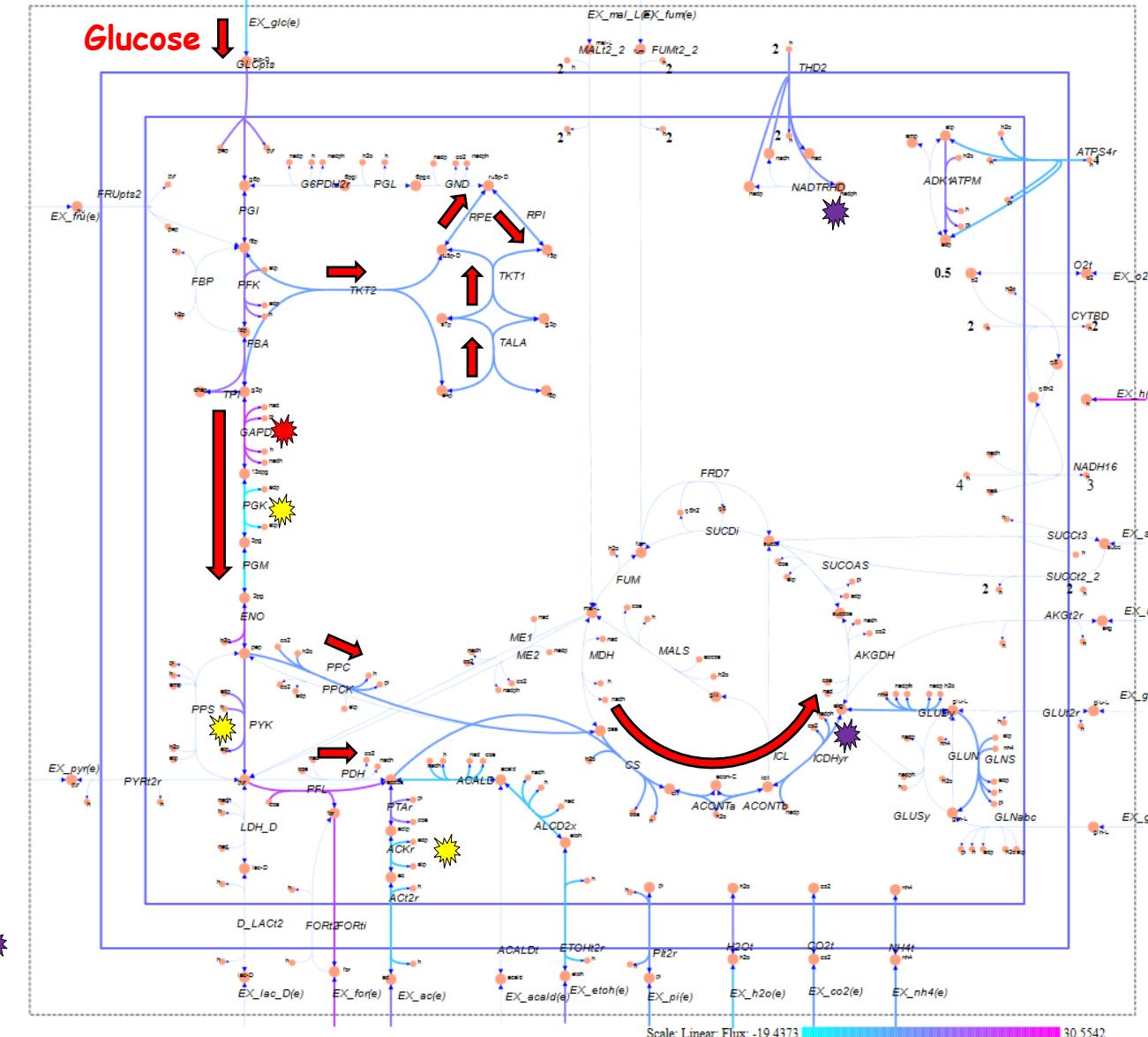


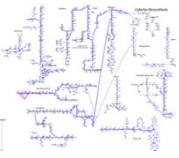
AerobicGlucoseBioMass.m



## Anaerobic Conditions Carbon Source: Glucose

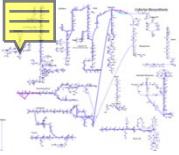
ATP =   
 NADPH =   
 NADH =





# *E.coli* Core Model

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- Fermentation
- Nitrogen Metabolism

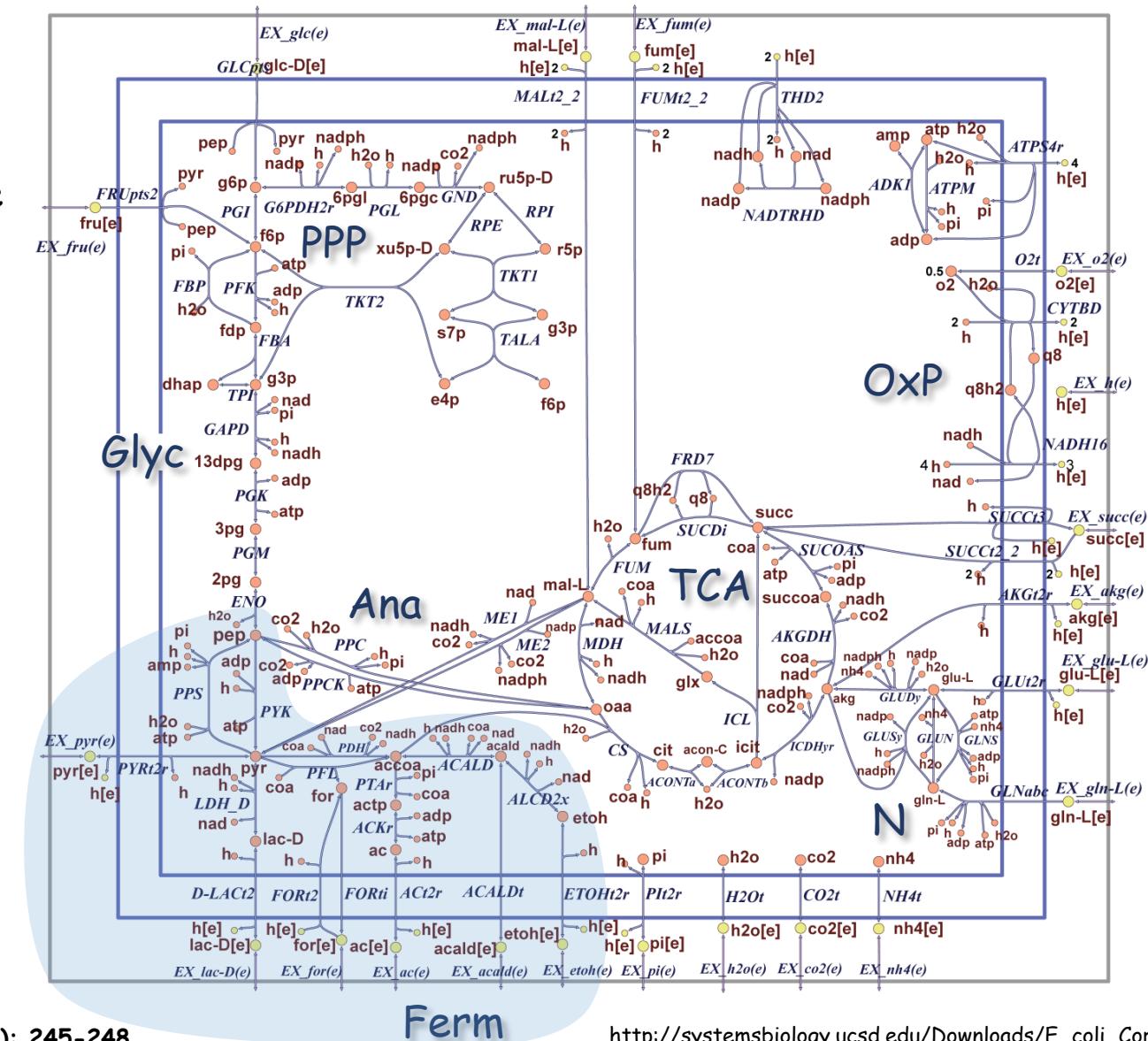


# Fermentation

## *E.coli* Core Model

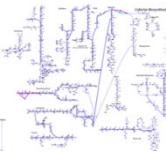
Fermentation is the process of extracting energy from the oxidation of organic compounds, such as carbohydrates, using an endogenous electron acceptor (not oxygen), which is usually an organic compound.

Glycolysis results in the net production of 2 ATP per glucose by substrate level phosphorylation, but this is low compared to 17.5 ATP per glucose for aerobic respiration. The substrates of fermentation are typically sugars, so during fermentative growth, each cell must maintain a large magnitude flux through glycolysis to generate sufficient ATP to drive the constitutive biosynthesis, polymerization, and assembly reactions required for growth. This necessitates a large magnitude efflux of fermentative end products since there is insufficient ATP to assimilate all carbon as biomass. Approximately 10% of carbon substrate is assimilated due to the poor energy yield of fermentation.

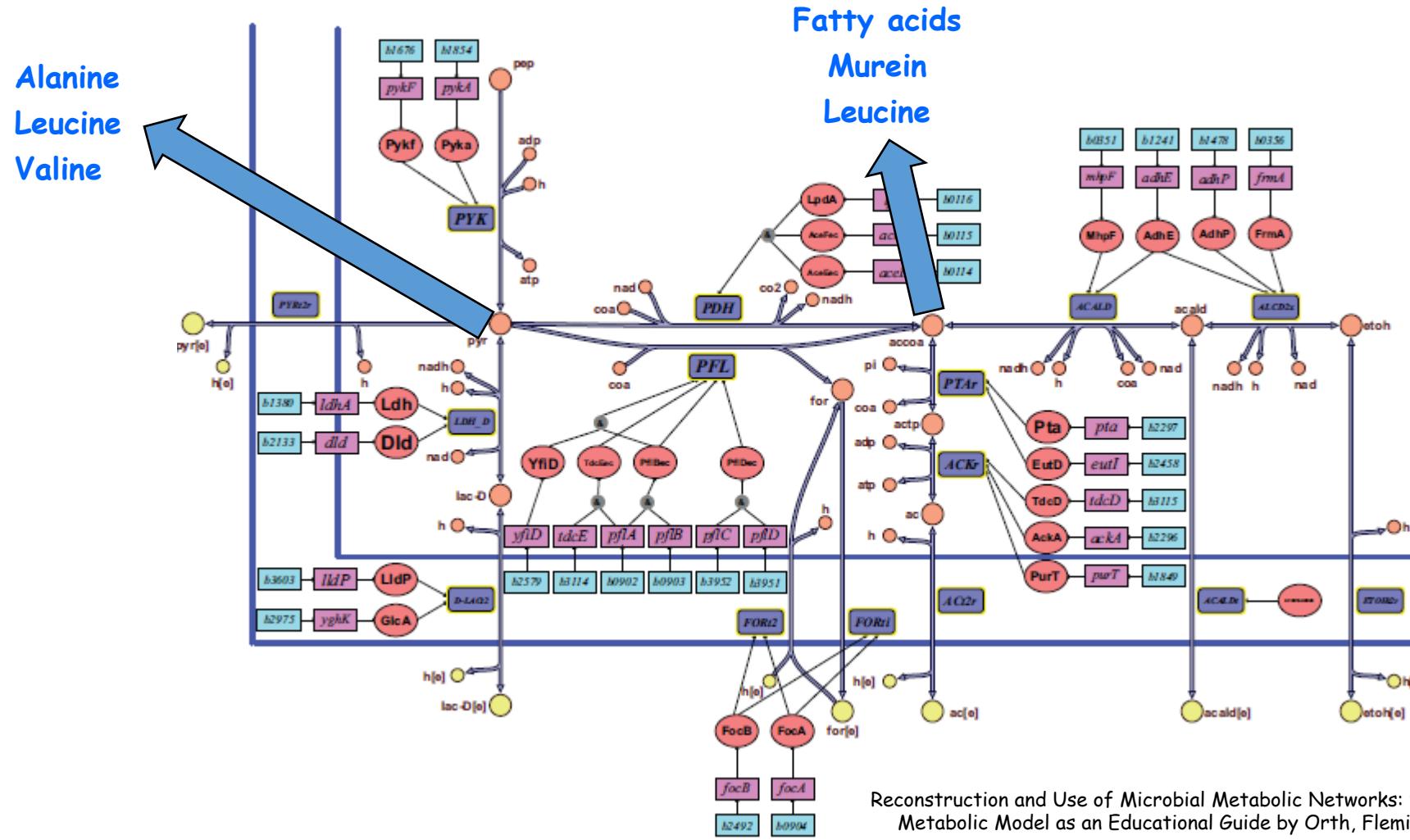


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# Fermentation



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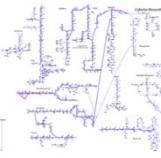
# Metabolites & Reactions

## Fermentation

Abbr.	Metabolite	Formula	Charge
lac-D	D-Lactate	C <sub>3</sub> H <sub>5</sub> O <sub>3</sub>	-1
for	Formate	CHO <sub>2</sub>	-1
actp	Acetyl-phosphate	C <sub>2</sub> H <sub>3</sub> O <sub>5</sub> P	-2
ac	Acetate	C <sub>2</sub> H <sub>3</sub> O <sub>2</sub>	-1
acald	Acetaldehyde	C <sub>2</sub> H <sub>4</sub> O	0
etoh	Ethanol	C <sub>2</sub> H <sub>6</sub> O	0

Abbr.	Reaction	Equation
LDH_D	D lactate dehydrogenase	lac-D + nad ⇌ h + nadh + pyr
D_LACt2	D-lactate transport via proton symport	h[e] + lac-D[e] ⇌ h + lac-D
PDH	pyruvate dehydrogenase	coa + nad + pyr → accoa + co2 + nadh
PFL	pyruvate formate lyase	coa + pyr → accoa + for
FORti	formate transport via diffusion	for → for[e]
FORt2	formate transport via proton symport	for[e] + h[e] → for + h
PTAr	phosphotransacetylase	accoa + pi ⇌ actp + coa
ACKr	acetate kinase	ac + atp ⇌ actp + adp
ACALD	acetaldehyde dehydrogenase (acetylating)	acald + coa + nad ⇌ accoa + h + nadh
ALCD2x	alcohol dehydrogenase (ethanol)	etoh + nad ⇌ acald + h + nadh
ACt2r	acetate reversible transport via proton symport	ac[e] + h[e] ⇌ ac + h
ACALDt	acetaldehyde reversible transport	acald[e] ⇌ acald
ETOHt2r	ethanol reversible transport via proton symport	etoh[e] + h[e] ⇌ etoh + h

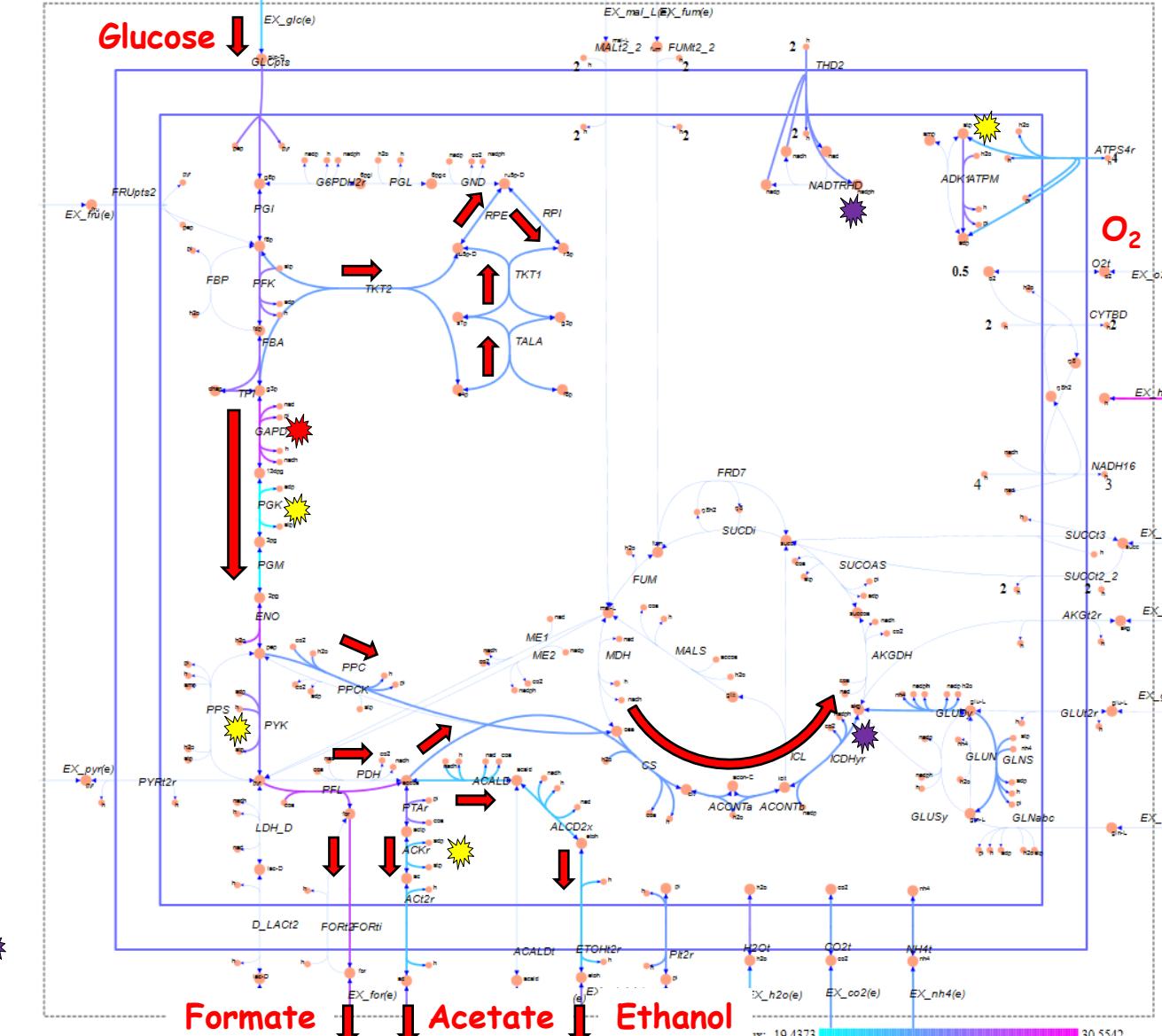
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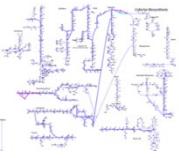


# Mixed Acid Fermentation

Anaerobic Conditions  
Carbon Source: Glucose

ATP =   
NADPH =   
NADH =

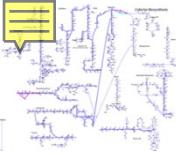




# *E.coli* Core Model

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- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism





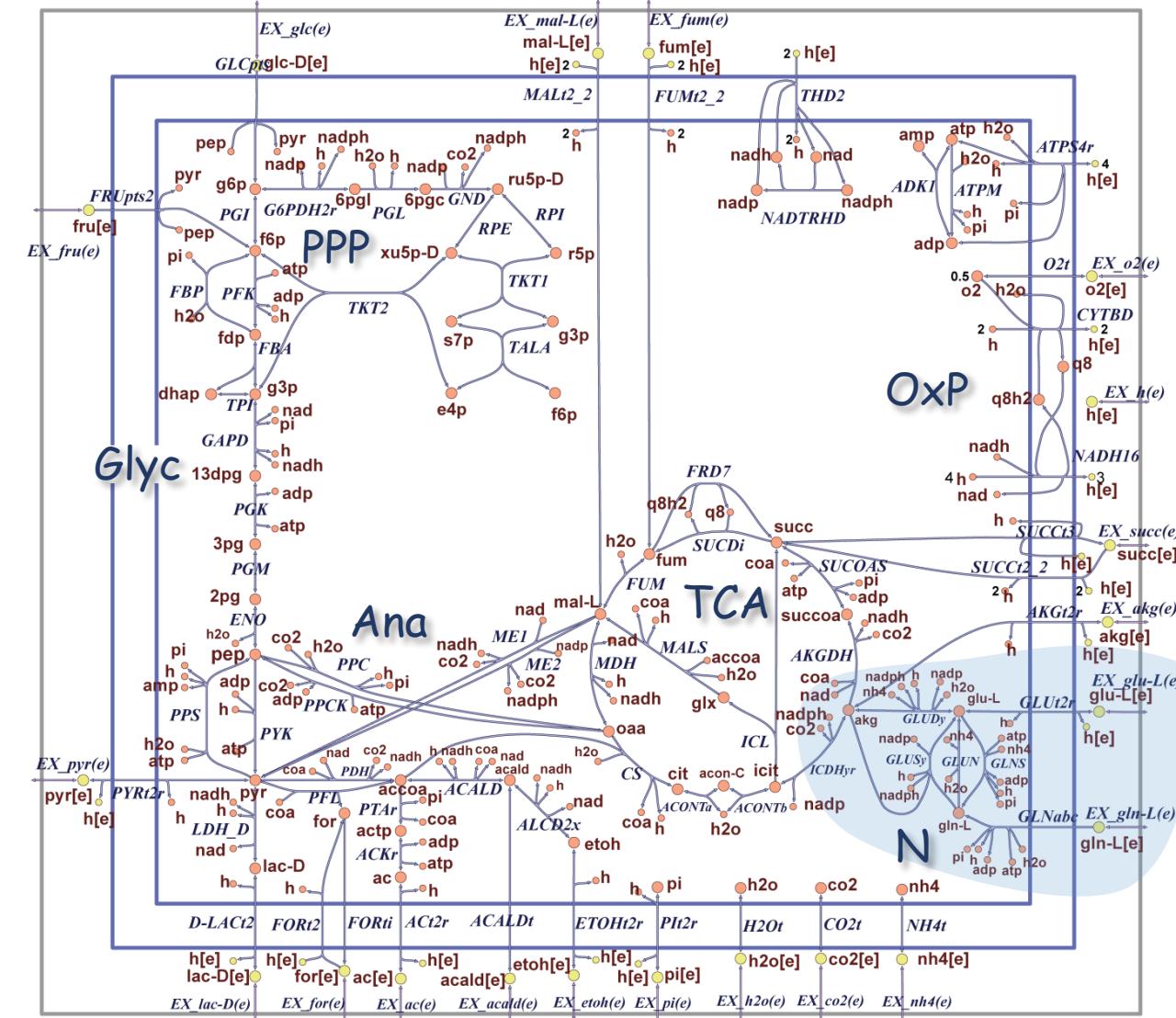
# Nitrogen Metabolism

## *E.coli* Core Model

Nitrogen is the fourth most abundant atom in *E. coli* and enters the cell either by ammonium ion uptake, NH<sub>4</sub><sup>+</sup>, or as a moiety within organic molecules, such as glutamine or glutamate.

The *E.coli* core model covers the pathways between 2-oxoglutarate, L-glutamate, and L-glutamine.

Orth, J. D., I. Thiele, et al. (2010). "What is flux balance analysis?" *Nature biotechnology* 28(3): 245-248.

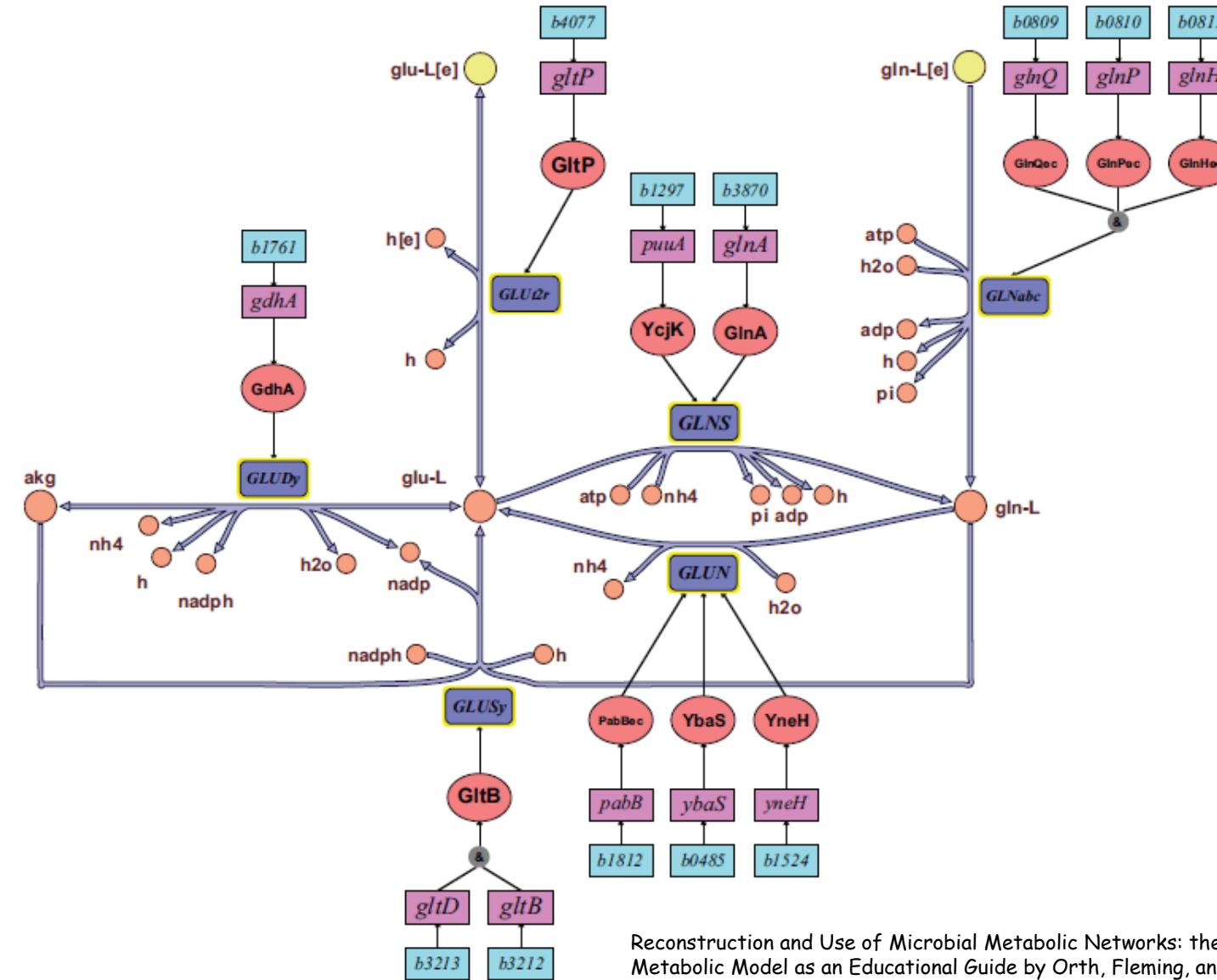


Ferm

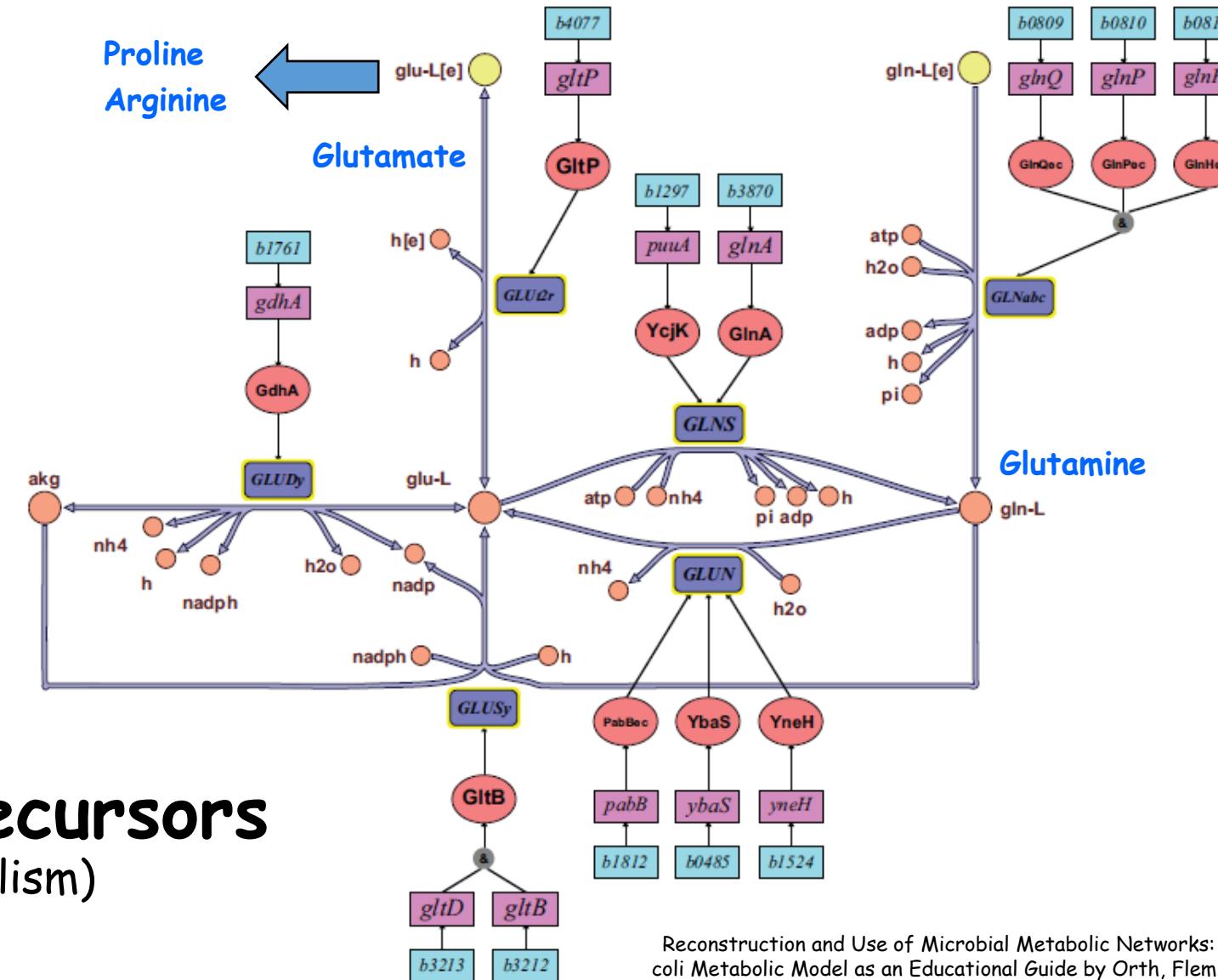
[http://systemsbiology.ucsd.edu/Downloads/E\\_coli\\_Core](http://systemsbiology.ucsd.edu/Downloads/E_coli_Core)



# Nitrogen Metabolism



## Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



## Biosynthetic Precursors (Nitrogen Metabolism)

Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)



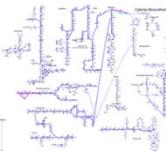
# Metabolites & Reactions

## Nitrogen Metabolism

Abbr.	Metabolite	Formula	Charge
glu-L	L-Glutamate	C <sub>5</sub> H <sub>8</sub> NO <sub>4</sub>	-1
gln-L	L-Glutamine	C <sub>5</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub>	0
nh4	Ammonium	H <sub>4</sub> N	+1

Abbreviation	Reaction	Equation
GLNabc	L-glutamine transport via ABC system	atp + gln-L[e] + h <sub>2</sub> o → adp + gln-L + h + pi
GLUT2r	L-glutamate transport via proton symport	glu-L[e] + h[e] ⇌ glu-L + h
GLUDy	glutamate dehydrogenase (NADP)	glu-L + h <sub>2</sub> o + nadp ⇌ akg + h + nadph + nh4
GLNS	glutamine synthetase	atp + glu-L + nh4 → adp + gln-L + h + pi
GLUSy	glutamate synthase (NADPH)	akg + gln-L + h + nadph → 2 glu-L + nadp
GLUN	glutaminase	gln-L + h <sub>2</sub> o → glu-L + nh4

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)

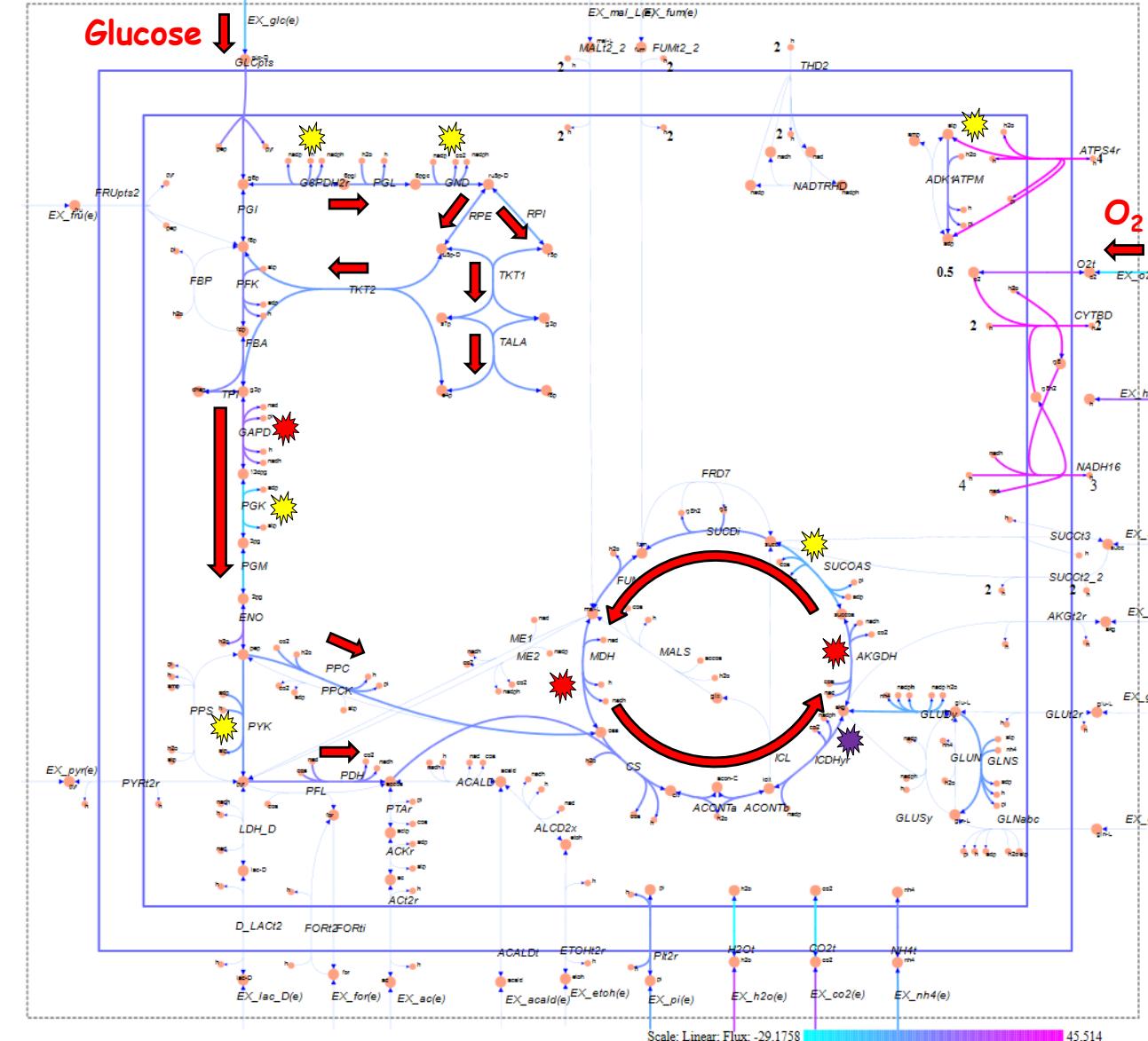


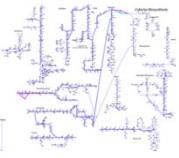
## Aerobic Conditions Carbon Source: Glucose

ATP = 

NADPH = \*

NADH = \*





# *E.coli* Core Model

- Component Parts of the *E. coli* Core Model
- Glycolysis
- Pentose Phosphate Pathway
- Tricarbonoxylic Acid (TCA) Cycle
- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism



# References

1. Reconstruction and Use of Microbial Metabolic Networks: the Core *Escherichia coli* Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
2. Jan Koolman and Klaus-Heinrich Roehm, "Color Atlas of Biochemistry", 2nd Edition, 2005.