Topic To Be Covered	Reading
Gluconeogenesis.	599-606
Glycogen metabolism.	484-498
Glycoprotein synthesis	608-617
Pentose Phosphate Pathway.	617-622

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The Conc. Of Serum Glucose is constant!

Before eating: 5 mM
After eating: 10 mM.

The conc. of glucose is buffered.

WHY?

Brain, CNS & RBC use glucose exclusively as energy source.

Brain consumes ~ 120 gm glucose/day

Glycogen reserves: ~ 190 gm.

During Fasting and extreme exertion (e.g. marathon) the available glucose is rapidly depleted.

So:

Glucose is kept available for energy!

In addition:

Glucose is main precursor of
- Amino sugars
- Complex polysaccharides
- Glycoproteins
- Glycolipids

The buffering mechanism

High Glucose

Glycogen Glucose Pyruvate Acetyl CoA Fatty Acids

Low Glucose

Glycogen Glucose non–sugar precursors

(but not fatty acids)

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A Problem.

Glycolysis is EXERGONIC!

(ΔG' ~ –96 kJ/mole {-23 kcal}).

3 Reactions of Glycolysis are irreversible!

Reaction	ΔG' (kJ/mole)
Hexokinase	« 0
Phosphoglucoisomerase	~0
Phosphofructokinase	« 0
Aldolase	~0
Triose P isomerase	~0
Glyceraldehyde-3-P dehydrogenase	~0
Phosphoglycerate kinase	~0
Phosphoglycerate mutase	~0
Enolase	~0
Pyruvate kinase	« 0

Gluconeogenesis is not Glycolysis in Reverse!

The secret of gluconeogenesis

a) Hexokinase is replaced by Glucose-6-Phosphatase

$$G + ATP \xrightarrow[HK]{} G6P + ADP$$

$$G6P \xrightarrow[G6Pase]{} G + P$$

b) Phosphofructokinase is replaced by Fructose1,6 bisphosphatase

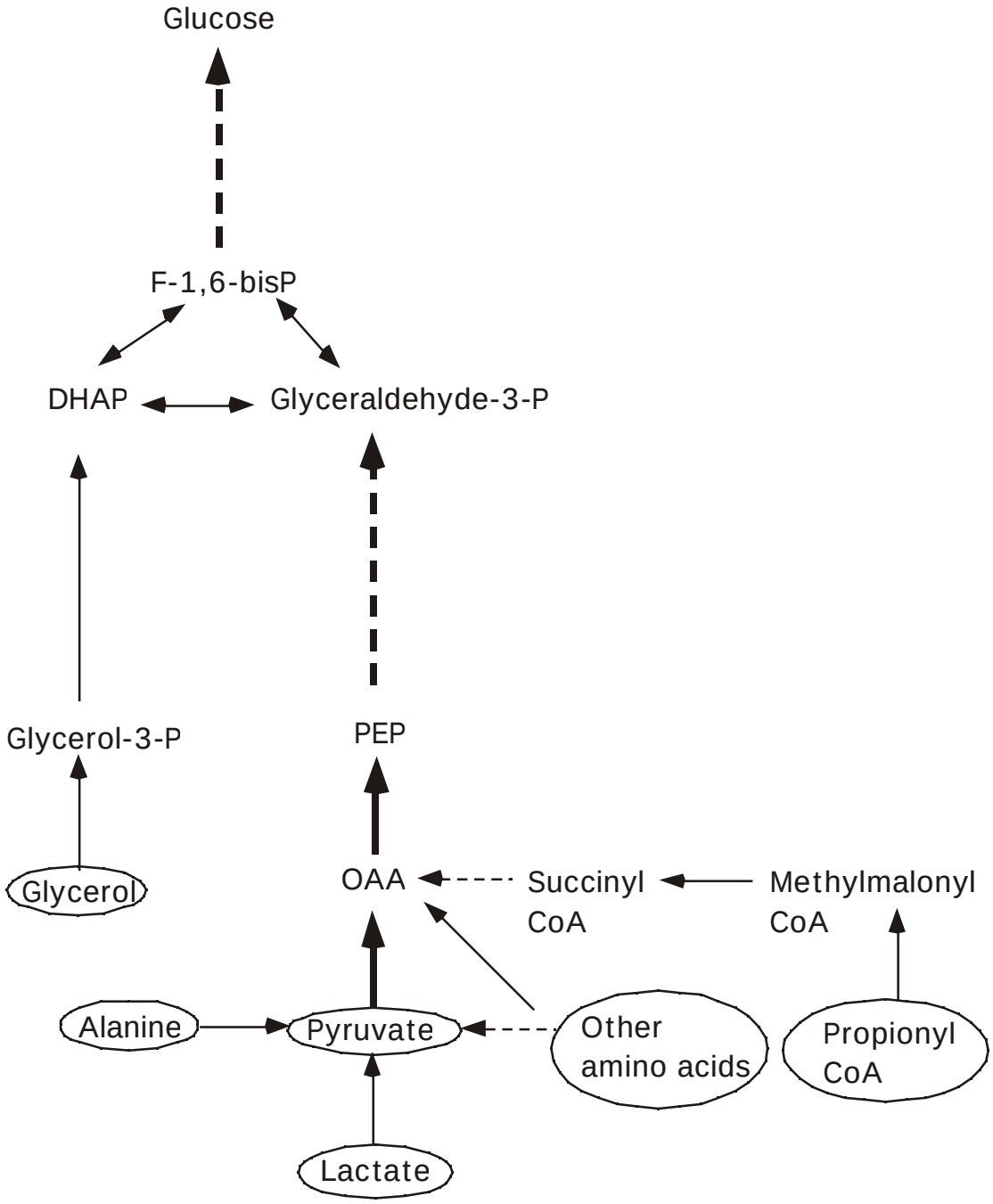
$$F6P + ATP \xrightarrow[PFK1]{} F1,6P + ADP$$

$$F1,6P \xrightarrow[FBPase]{} F6P + P$$

c) Pyruvate kinase is replaced by a complex sequence!

1. Make oxalacetate (by a variety of ways).
2. Convert OAA to PEP (PEPCK (anapleroptic reactions)

These reactions occur mainly in the liver.


Glucose
F-1,6-bisP
DHAP
Glyceraldehyde-3-P
Glycerol-3-P
PEP
Glycerol
OAA
Succinyl CoA
Methylmalonyl CoA
Alanine
Pyruvate
Other amino acids
Propionyl CoA
Lactate

MAIN REACTIONS.

Pyruvate Oxalacetate

CH_3-CO-COOH + ATP + CO_2 ⇔ COOH-CH_2–CO-COOH + ADP + Pi

Pyruvate carboxylase

(biotin)

Oxalacetate PEP

COOHCH_2COCOOH + GTP ⇔ CH_2=OP-COOH + GDP + Pi + CO_2

PEPCK (Mn; mito or cyto)

Both PC & PEPCK were covered in anapleroptic reactions!

Glycerol DHAP Glyceraldehyde-3-P

Consider

G + ATP G6P G + P.

A machine for burning ATP-a futile cycle.

So…..Enable

glycolysis

OR

gluconeogenesis

but not both.

The control of glucose metabolism.

Organizing Principles

1. Molecules are synthesized by different pathways (tho many shared reactions).
2. Corresponding pathways controlled by 1 (or more) early steps.

3. Synthesis rendered exergonic via excess ATP & NADPH

Three mechanisms.

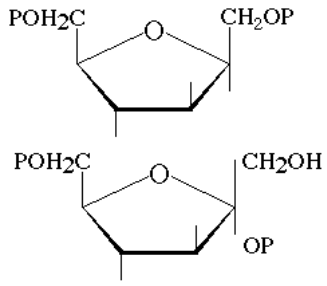
Allosteric activators/inhibitors

Covalent Modification (phosphorylation).

Protein synthesis.

Allosteric Controls

	Activated by:	Inhibited by:
Hexokinase	-------	G6P
G6Pase	-------	
PFK-1	AMP, ***F2,6P***	ATP, citrate
FBPase	-------	AMP, ***F2,6P***
Pyruvate kinase	F1,6P	Alanine, ATP
Pyruvate carboxylase	acetyl CoA	
PEPCK	___	___
PFK-2	AMP, F6P	citrate
FBPase-2	glycerol-3-P	F6P



F2,6P a potent regulator of the interconversion of F6P and F1,6P.

Product of phosphofructokinase-2

F6P + ATP F2,6bisP + ADP

PFK–2…….An enzyme with 2 activities

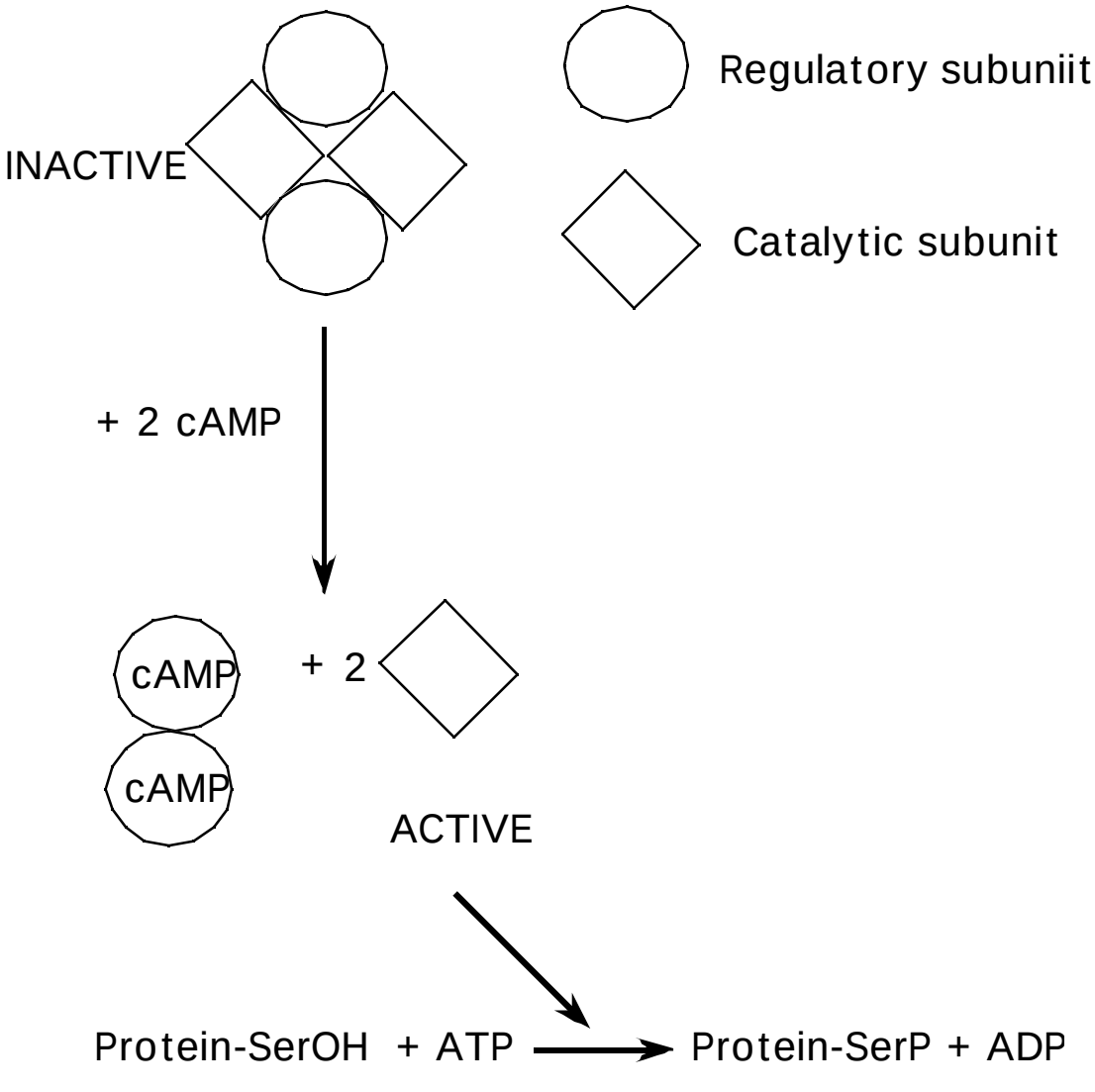
Enz: KINASE
Enz-P: PHOSPHATASE

Enz + ATP ⇔ Enz-P + ADP
Protein kinase

Low blood sugar Glucagon cAMP

Enzyme modification caused by Protein Kinase

Specific PKs controlled by cAMP/Insulin



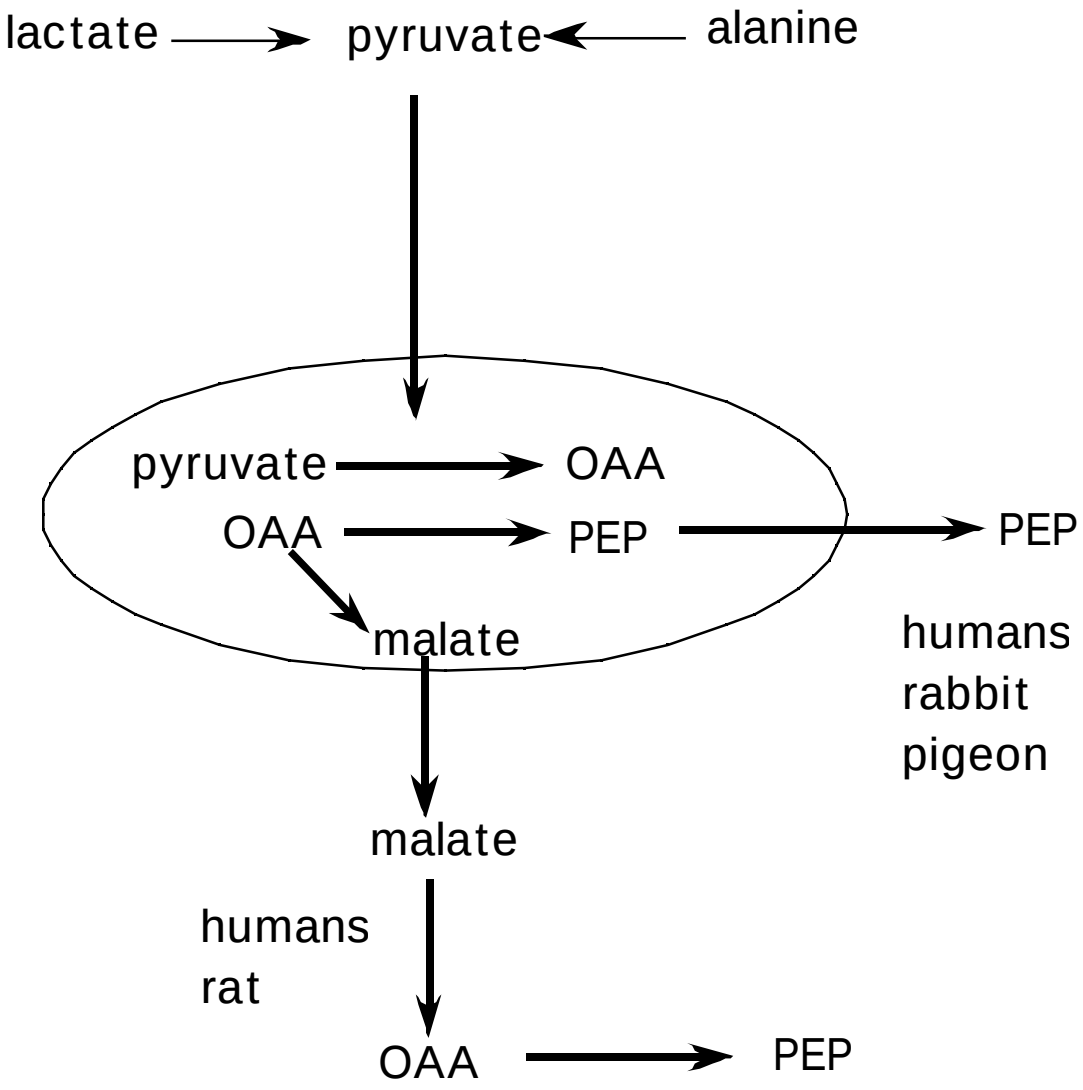
Enzyme Phosphorylation

Inactivates

Pyruvate Kinase.
PFK-2

Activates

FBPase-2


lactate
pyruvate
alanine
pyruvate
OAA
OAA
PEP
PEP
malate
humans
rabbit
pigeon
malate
humans
rat
OAA
PEP