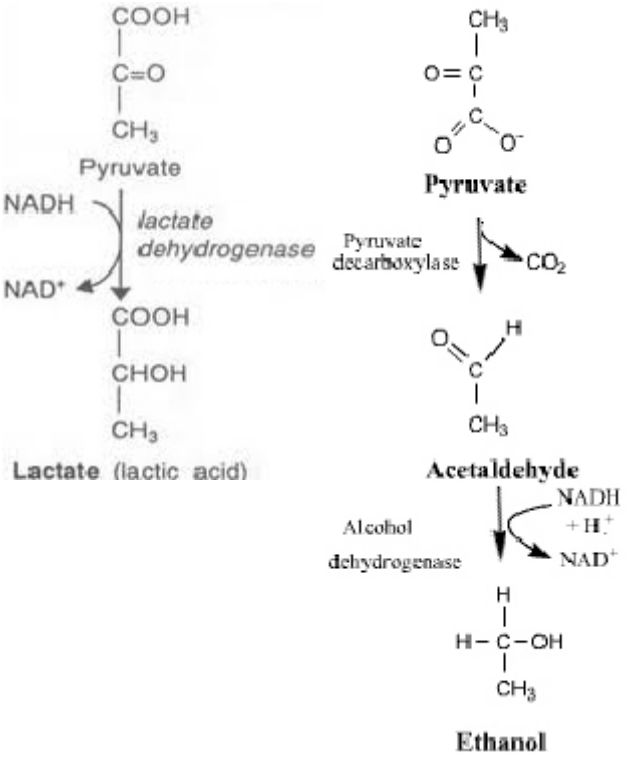
FERMENTATION, REGULATION

10/30/91, rvsd 11/3/93, 11/8/94, 5 Nov 99, 6 Nov 00, 5 Nov 01, 7 Nov 03, 5 Nov 04, 27Oct08, 27OOct10
BKH: pp. 382-401, BKH 5th: 378-393, bkhb 7TH: PP229-246



WHY FERMENTATION?

NAD^+ is required for glycolysis.
It can be regenerated from accumulated NADH:

pyruvate can accept H, produce lactate.
Lactate can be carried to liver, gluconeogenesis

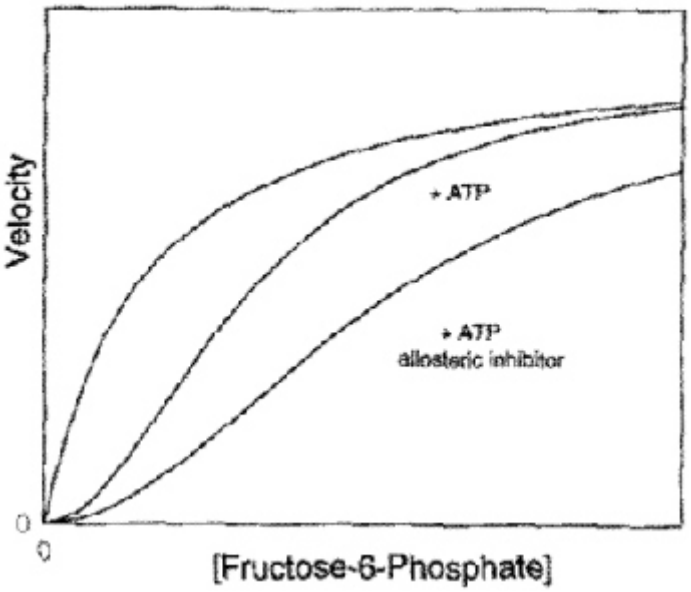
Microorganisms alternative:
Ethanol formed by decarboxylation, reduction

ATP from glycolysis only traps about 7% of energy in glucose

STARCH CATABOLISM:
Phosphorolysis of starch produces G-1-PO_4,
phosphoglucomutase changes to G-6-PO_4

Regulation of Glycolysis: THREE intrinsic mechanisms:

1. **hexokinase**
   inhibited by Glucose-6-PO_4
2. **phosphofructokinase** (p 250**)**
   inhibited by ATP allosterically (also a substrate): forms *sigmoidal* curve enzyme conc vs reaction velocity (active site has higher affinity for ATP than allosteric site.) (Show rate vs [F-6-PO_4] at low vs high ATP.)
   also inhibited by citrate and by fatty acids
3. **pyruvate kinase**
   inhibited by ATP and acetyl coenzyme A



A second phosphofructokinase (PFK-2) synthesizes in the unphosphorylated state:

HORMONAL REGULATION of glycolysis versus gluconeogenesis by glucagon: (p 245)

Fructose-2,6-bisphosphate activation of phosphofructokinase: stimulates glycolysis *vs* inhibits gluconeogenesis

1) Glucagon triggers cAMP production in the cytoplasm
2) cAMP activates a kinase which phosphorylates PFK-2.
   a) unphosphorylated, PFK-2 makes **Fructose-2,6-bisphosphate which activates phosphofructokinase**, and stimulates **glycolysis**. (F 2,6 bisPO_4 also inhibits fructose-1,6-bisPase
   b) when phosphorylated, PFK-2 acts as a **phosphatase**. Removing the 2 PO_4 from F2,6 bisPO_4 which inhibits phosphofructokinase (and glycolysis), stimulates **gluconeogenesis**.