

# Glycolysis and Gluconeogenesis

## Introduction

Production of **two molecules of ATP** from **one molecule of glucose** with concomitant production of two molecules of **ATP**

It's **anaerobic** - it evolved before the accumulation of O<sub>2</sub> in the atmosphere

Buchner, in 1897 discovered that fermentation was not inextricably linked to the cell - it's chemistry

**Glucose**

- Does not expose a **carbonyl group**
- Tends to exist in a **ring**
  - This could **nonselectively glycosylate proteins**
  - Thereby deactivating them, forming **Schiff bases**
- One of several **monosaccharides** formed from **formaldehyde** in **prebiotic conditions** - might have been available to **primitive biochemical systems**

## Misc. points on glycolysis

Three steps in glycolysis have a large change in free energy and are nearly irreversible

- G → G6P
- F6P → F-1,6-BP
- PEP → Pyr

Yields only a **fraction** of energy available in glucose, but often needed

- If **no oxygen available**
- If **lacking mitocs (retina, RBC)**
- If **burst of activity is required, faster than ability to provide O<sub>2</sub>**

Oxygen debt must be repaid

- Increase TCA cycle rate to oxidise lactate produced
- If conc. rises above 5mM, buffering capacity of the blood is overpowered and pH drops → burning sensation

**Binding site for NAD<sup>+</sup>** is similar in all the **dehydrogenases**

**Rossmann Fold**

- four ALPHA-helices
- six parallel BETA-strands

**Classic galactosemia**

- Inherited deficiency in **galactose 1-phosphate uridyl transferase** activity
- Lots of symptoms (vomiting after milk, cataract, jaundice, lethargy, retarded mental development)

**Cataract**

- If not active in eye, **aldose reductase** causes **accumulating galactose** to convert to **galactitol**
- Osmotically active** and water **diffuses into lens**

## Gluconeogenesis

**Maintaining glucose levels** is important because it is a major source of fuels (for RBCs, the **only source**)

Direct reserves are sufficient for about a day, but gluconeogenesis becomes important over longer periods of time or starvation

Mostly occurs in the **liver**, and somewhat in the kidney

**Lactate** by the action of **lactate dehydrogenase**

**Amino acids** as **pyruvate** or **oxaloacetate**

Other compounds can also be introduced into the cycle

**Glycerol [see card]**

Glycolysis equilibrium well on pyruvate side - must bypass the problematic reactions to make it produce glucose

**PYRUVATE CARBOXYLASE** (in **mitochondria**)

**GLUCOSE 6-PHOSPHATASE** (membrane bound in the **ER**)

All enzymes are in **cytoplasm** except for