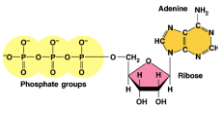
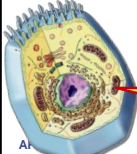



# AP Biology

## Making energy!



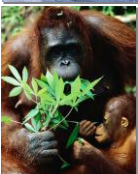


The point is to make ATP!

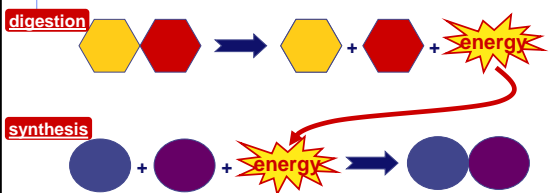
## The energy needs of life

- Organisms are **endergonic** systems
  - What do we need energy for?
    - synthesis
      - building biomolecules
    - reproduction
    - movement
    - active transport
    - temperature regulation

## Where do we get the energy from?

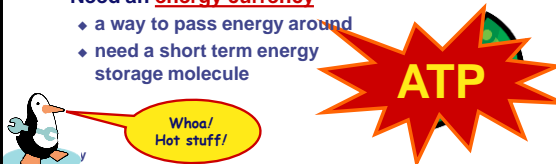
- Work of life is done by **energy coupling**
  - use **exergonic** (catabolic) reactions to fuel **endergonic** (anabolic) reactions



AP Biology

## Living economy

- Fueling the body's economy
  - eat high energy **organic molecules**
    - food = carbohydrates, lipids, proteins, nucleic acids
  - break them down
    - digest = **catabolism**
  - capture released energy in a form the cell can use
- Need an **energy currency**
  - a way to pass energy around
  - need a short term energy storage molecule

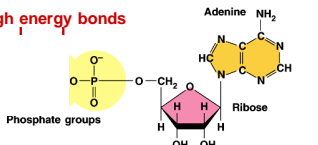


## ATP

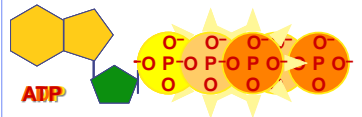
- Adenosine TriPhosphate**
  - modified nucleotide
    - nucleotide = adenine + ribose +  $P_i \rightarrow$  AMP
    - AMP +  $P_i \rightarrow$  ADP
    - ADP +  $P_i \rightarrow$  ATP
  - adding phosphates is **endergonic**

How efficient! Build once, use many ways

high energy bonds



## How does ATP store energy?



I think he's a bit unstable... don't you?

- Each negative  $PO_4$  more difficult to add
  - a lot of stored energy in each bond
    - most energy stored in 3rd  $P_i$
    - 3rd  $P_i$  is hardest group to keep bonded to molecule
- Bonding of negative  $P_i$  groups is unstable
  - spring-loaded**
  - $P_i$  groups "pop" off easily & release energy

AP B Instability of its P bonds makes ATP an excellent energy donor

# AP Biology

## How does ATP transfer energy?

- ATP → ADP
  - releases energy
    - $\Delta G = -7.3$  kcal/mole
- Fuel other reactions
- Phosphorylation
  - released  $P_i$  can transfer to other molecules
    - destabilizing the other molecules
  - enzyme that phosphorylates = "**kinase**"

## An example of Phosphorylation...

- Building polymers from monomers
  - need to destabilize the monomers
  - phosphorylate!**

## Another example of Phosphorylation...

- The first steps of **cellular respiration**
  - beginning the breakdown of glucose to make ATP

## ATP / ADP cycle

**Can't store ATP**

- good energy donor, not good energy storage
  - too reactive
  - transfers  $P_i$  too easily
  - only short term energy storage
  - carbohydrates & fats are long term energy storage

A working muscle recycles over 10 million ATPs per second

## Cells spend a lot of time making ATP!

## ATP synthase

Enzyme channel in mitochondrial membrane

- permeable to  $H^+$
- $H^+$  flow down concentration gradient
  - flow like water over water wheel
  - flowing  $H^+$  cause change in shape of ATP synthase enzyme
  - powers bonding of  $P_i$  to ADP:  $ADP + P_i \rightarrow ATP$

# AP Biology

That's the rest of *my* story!  
Any Questions?

AP Biology 2008-2009

Cellular Respiration  
Harvesting Chemical Energy

ATP

AP Biology

What's the point?

The point is to make ATP!

ATP

AP Biology

### Harvesting stored energy

- Energy is stored in organic molecules
  - carbohydrates, fats, proteins
- Heterotrophs eat these organic molecules → food
  - digest organic molecules to get...
    - raw materials for synthesis
    - fuels for energy
      - controlled release of energy
      - "burning" fuels in a series of step-by-step enzyme-controlled reactions

### Harvesting stored energy

- Glucose is the model
  - catabolism of glucose to produce ATP

respiration

glucose + oxygen → energy + water + carbon dioxide

$$C_6H_{12}O_6 + 6O_2 \rightarrow ATP + 6H_2O + 6CO_2 + \text{heat}$$

COMBUSTION = making a lot of heat energy by burning fuels in one step

RESPIRATION = making ATP (& some heat) by burning fuels in many small steps

fuel (carbohydrates) + O<sub>2</sub> → CO<sub>2</sub> + H<sub>2</sub>O + heat

glucose + O<sub>2</sub> → CO<sub>2</sub> + H<sub>2</sub>O + ATP (+ heat)

### How do we harvest energy from fuels?

- Digest large molecules into smaller ones
  - break bonds & move electrons from one molecule to another
    - as electrons move they "carry energy" with them
    - that energy is stored in another bond, released as heat or harvested to make ATP

loses e<sup>-</sup> + gains e<sup>-</sup> → oxidized + reduced


oxidation reduction

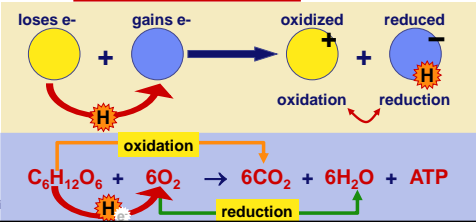
redox

AP Bi

# AP Biology


## How do we move electrons in biology?

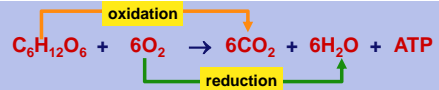
- Moving electrons in living systems
  - electrons cannot move alone in cells
    - electrons move as part of **H atom** 
    - move H = move electrons



AP BI

## Coupling oxidation & reduction

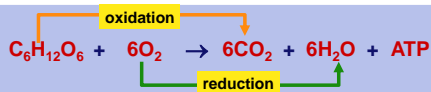
- REDOX reactions in respiration
  - release energy as breakdown organic molecules
    - break C-C bonds
    - strip off electrons from C-H bonds by removing H atoms
      - $C_6H_{12}O_6 \rightarrow CO_2$  = the fuel has been **oxidized**
    - electrons attracted to more electronegative atoms
      - in biology, the most electronegative atom? 
      - $O_2 \rightarrow H_2O$  = oxygen has been **reduced**
  - couple REDOX reactions & use the released energy to synthesize ATP



AP E

## Oxidation & reduction

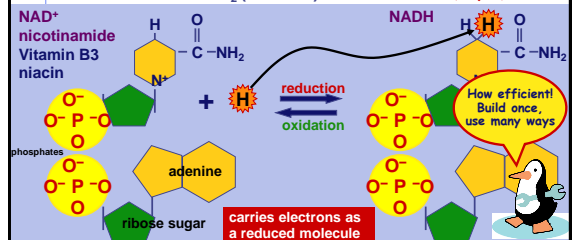
- |  |   |
|--|---|
| <ul style="list-style-type: none"> <li><b>Oxidation</b> <ul style="list-style-type: none"> <li>adding O</li> <li>removing H</li> <li>loss of electrons</li> <li>releases energy</li> <li><b>exergonic</b></li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li><b>Reduction</b> <ul style="list-style-type: none"> <li>removing O</li> <li>adding H</li> <li>gain of electrons</li> <li>stores energy</li> <li><b>endergonic</b></li> </ul> </li> </ul> |
|--|---|



AP Biology

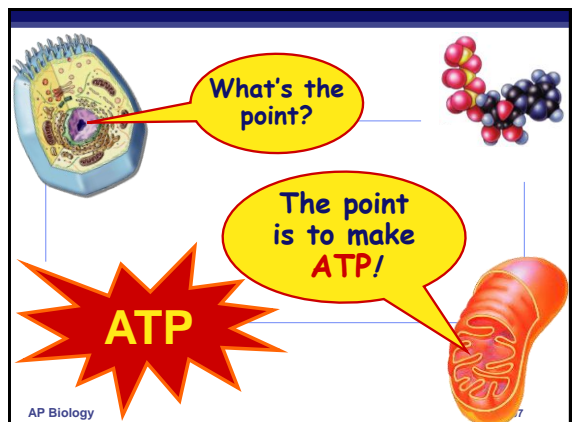
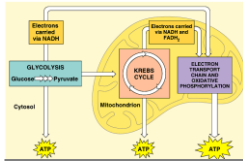
## Moving electrons in respiration

- Electron carriers** move electrons by shuttling H atoms around
  - $NAD^+ \rightarrow NADH$  (reduced)
  - $FAD^{+2} \rightarrow FADH_2$  (reduced)



## Overview of cellular respiration

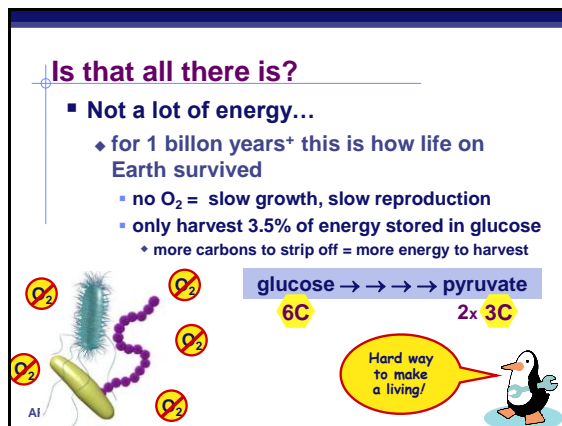
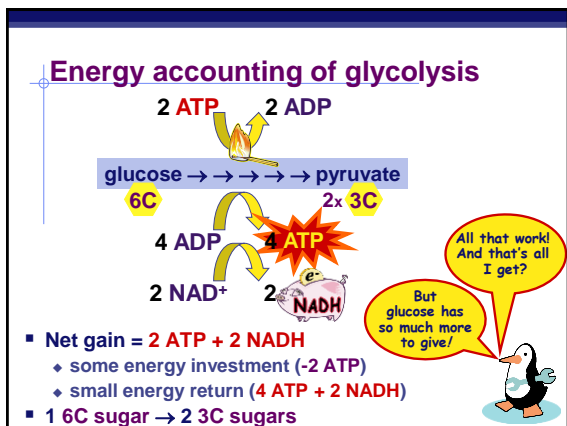
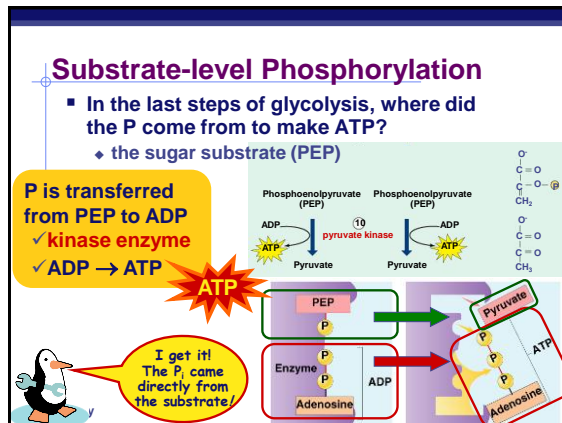
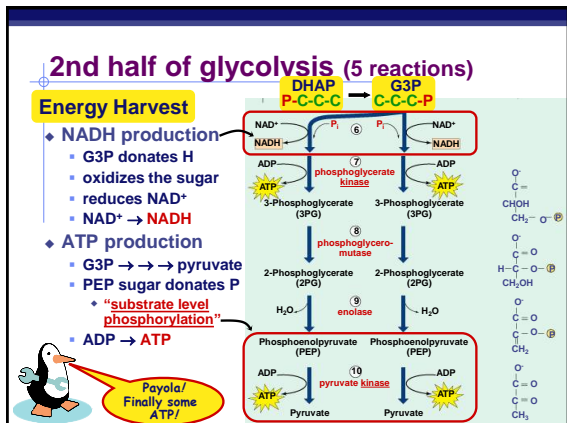
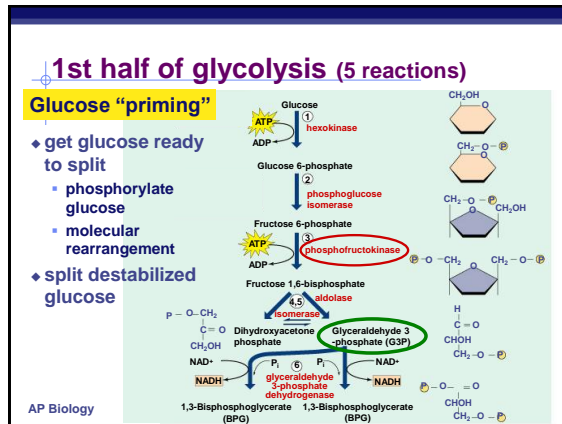
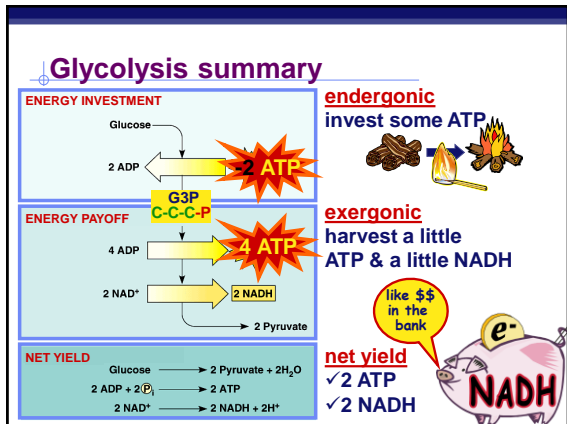
- 4 metabolic stages
    - Anaerobic respiration**
      - Glycolysis**
        - respiration without  $O_2$
        - in cytosol
    - Aerobic respiration**
      - respiration using  $O_2$
      - in mitochondria
- Pyruvate oxidation**
  - Krebs cycle**
  - Electron transport chain**



AP Biology



# AP Biology



# AP Biology

**But can't stop there!**

raw materials → products

**Glycolysis**  
 $\text{glucose} + 2\text{ADP} + 2\text{P}_i + 2\text{NAD}^+ \rightarrow 2\text{ pyruvate} + 2\text{ATP} + 2\text{NADH}$

Going to run out of  $\text{NAD}^+$

- without regenerating  $\text{NAD}^+$ , energy production would stop!
- another molecule must accept H from  $\text{NADH}$ 
  - so  $\text{NAD}^+$  is freed up for another round

**How is NADH recycled to  $\text{NAD}^+$ ?**

Another molecule must accept H from  $\text{NADH}$

with oxygen: **aerobic respiration**  
 without oxygen: **anaerobic respiration "fermentation"**

pyruvate

recycle  $\text{NADH}$

which path you use depends on who you are...

Krebs cycle

acetyl-CoA

lactate  
lactic acid fermentation

ethanol  
alcohol fermentation

$\text{CO}_2$

**Fermentation (anaerobic)**

Bacteria, yeast

$\text{pyruvate} \rightarrow \text{ethanol} + \text{CO}_2$   
 $3\text{C} \rightarrow 2\text{C} + 1\text{C}$

beer, wine, bread

back to glycolysis →

Animals, some fungi

$\text{pyruvate} \rightarrow \text{lactic acid}$   
 $3\text{C} \rightarrow 3\text{C}$

cheese, anaerobic exercise (no  $\text{O}_2$ )

**Alcohol Fermentation**

pyruvate → ethanol +  $\text{CO}_2$

bacteria yeast

recycle  $\text{NADH}$

Dead end process

- at ~12% ethanol, kills yeast
- can't reverse the reaction

Count the carbons!

2 Ethanol

2 Acetaldehyde

2 Pyruvate

2  $\text{CO}_2$

2  $\text{NAD}^+$

2  $\text{NADH} + 2\text{H}^+$

2  $\text{ADP} + 2\text{P}_i$

2 ATP

GLYCOLYSIS

Glucose

Acetyl CoA

KREBS CYCLE

**Lactic Acid Fermentation**

pyruvate ↔ lactic acid

animals some fungi

recycle  $\text{NADH}$

Reversible process

- once  $\text{O}_2$  is available, lactate is converted back to pyruvate by the liver

Count the carbons!

2 Lactate

2 Pyruvate

2  $\text{NAD}^+$

2  $\text{NADH} + 2\text{H}^+$

2  $\text{ADP} + 2\text{P}_i$

2 ATP

GLYCOLYSIS

Glucose

Acetyl CoA

KREBS CYCLE

**Pyruvate is a branching point**

Pyruvate

fermentation anaerobic respiration

mitochondria

Krebs cycle

aerobic respiration

Glucose

Cytosol

Pyruvate

No  $\text{O}_2$

$\text{O}_2$

Ethanol or lactate

Acetyl CoA

Mitochondrion

KREBS CYCLE

AP Biology

# AP Biology

What's the point?

The point is to make **ATP!**

**ATP**

AP Biology

And how do we do that?

- ATP synthase
  - set up a  $H^+$  gradient
  - allow  $H^+$  to flow through ATP synthase
  - powers bonding of  $P_i$  to ADP

$ADP + P_i \rightarrow ATP$

But... Have we done that yet?

AP Biology

**Overview**

10 reactions

- convert **glucose (6C)** to **2 pyruvate (3C)**
- produces: **4 ATP & 2 NADH**
- consumes: **2 ATP**
- net: **2 ATP & 2 NADH**

glucose C-C-C-C-C-C

fructose-1,6bP P-C-C-C-C-C-P

DHAP P-C-C-C G3P C-C-C-P

2P<sub>i</sub> 2H<sup>+</sup> 2NAD<sup>+</sup> 2NADH

2P<sub>i</sub> 4ADP 4ATP

pyruvate C-C-C

AP Biology

**Cellular Respiration**

Stage 2 & 3:

**Oxidation of Pyruvate**

**Krebs Cycle**

AP Biology

**Glycolysis is only the start**

- Glycolysis
  - glucose  $\rightarrow \rightarrow \rightarrow \rightarrow$  pyruvate
  - 6C  $\rightarrow$  2x 3C
- Pyruvate has more energy to yield
  - 3 more C to strip off (to **oxidize**)
  - if  $O_2$  is available, pyruvate enters mitochondria
  - enzymes of Krebs cycle complete the full oxidation of sugar to  $CO_2$

pyruvate  $\rightarrow \rightarrow \rightarrow \rightarrow$   $CO_2$

3C  $\rightarrow$  1C

AP Biology

**Cellular respiration**

Electrons carried via NADH

Electrons carried via NADH and  $FADH_2$

GLYCOLYSIS: Glucose  $\rightarrow$  Pyruvate

KREBS CYCLE

ELECTRON TRANSPORT CHAIN AND OXIDATIVE PHOSPHORYLATION

Cytosol

Mitochondrion

ATP Substrate-level phosphorylation

ATP Substrate-level phosphorylation

ATP Oxidative phosphorylation

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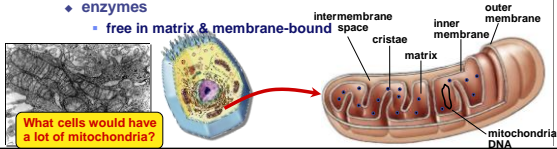
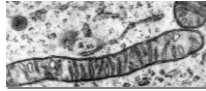


# AP Biology

## Mitochondria — Structure

### Double membrane energy harvesting organelle

- smooth outer membrane
- highly folded inner membrane
  - cristae
- intermembrane space
  - fluid-filled space between membranes
- matrix
  - inner fluid-filled space
- DNA, ribosomes
- enzymes
  - free in matrix & membrane-bound



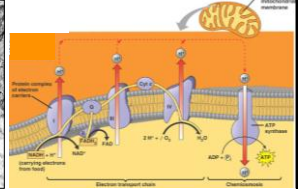
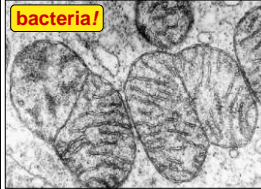
## Mitochondria – Function

Oooooh!  
Form fits  
function!



### Dividing mitochondria Who else divides like that?

### Membrane-bound proteins Enzymes & permeases

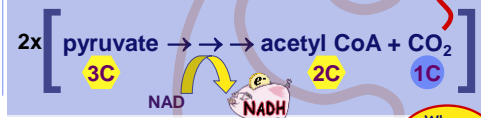


What does this tell us about the evolution of eukaryotes?  
**Endosymbiosis!**

Advantage of highly folded inner membrane?  
**More surface area for membrane-bound enzymes & permeases**

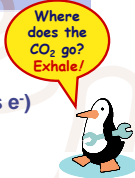
## Oxidation of pyruvate

### Pyruvate enters mitochondrial matrix

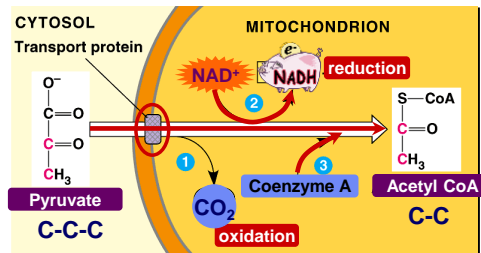


- 3 step oxidation process
- releases 2 CO<sub>2</sub> (count the carbons!)
- reduces 2 NAD → 2 NADH (moves e<sup>-</sup>)
- produces 2 acetyl CoA

### Acetyl CoA enters Krebs cycle



## Pyruvate oxidized to Acetyl CoA



## Krebs cycle

1937 | 1953

### aka Citric Acid Cycle

- in mitochondrial matrix
- 8 step pathway
  - each catalyzed by specific enzyme
  - step-wise catabolism of 6C citrate molecule

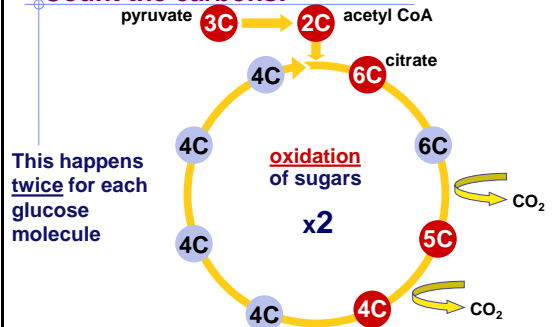


Hans Krebs  
1900-1981

### Evolved later than glycolysis

- does that make evolutionary sense?
  - bacteria → 3.5 billion years ago (glycolysis)
  - free O<sub>2</sub> → 2.7 billion years ago (photosynthesis)
  - eukaryotes → 1.5 billion years ago (aerobic respiration = organelles → mitochondria)

## Count the carbons!



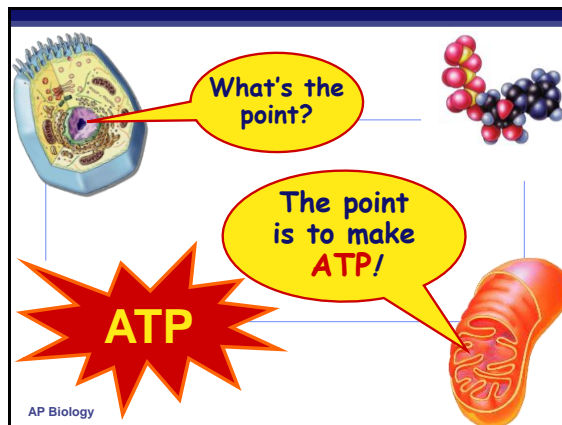
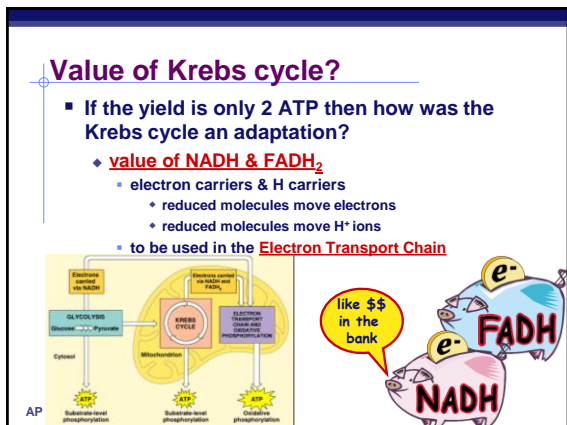
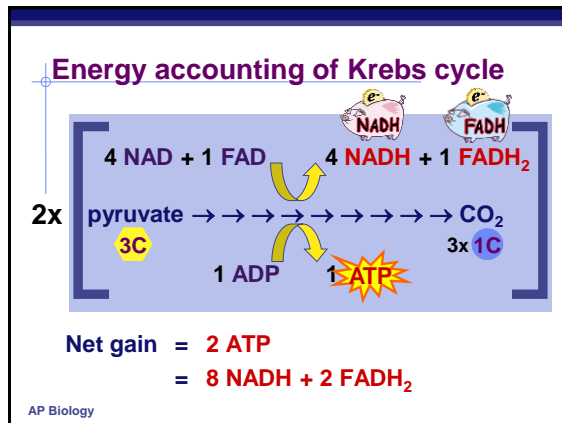
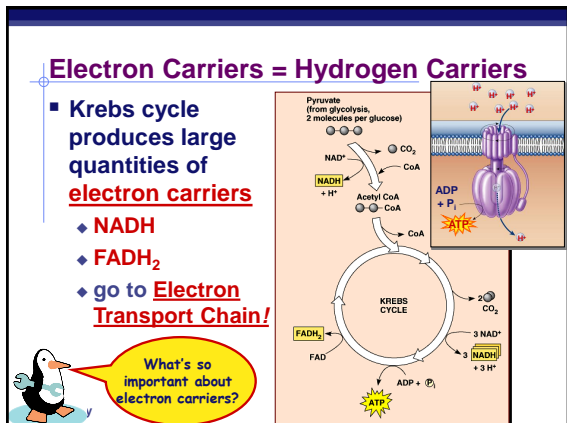
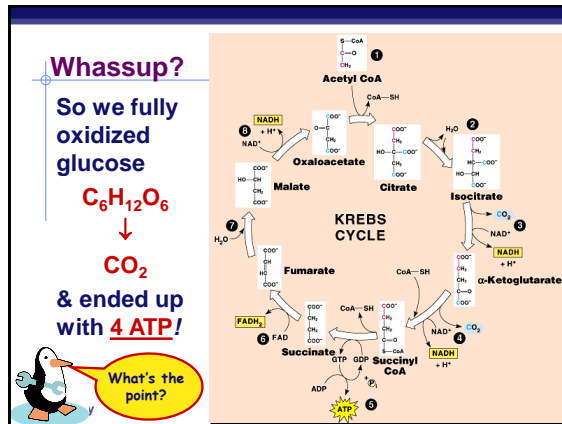
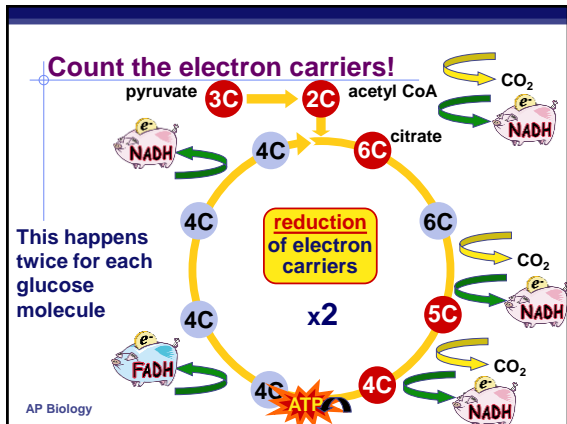
This happens twice for each glucose molecule

AP Biology

AP Biology

AP Biology

# AP Biology

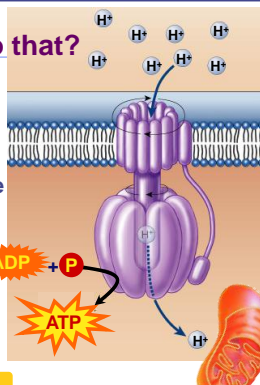


# AP Biology

And how do we do that?


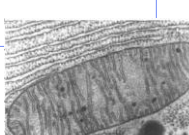
- ATP synthase
  - set up a  $H^+$  gradient
  - allow  $H^+$  to flow through ATP synthase
  - powers bonding of  $P_i$  to ADP

$ADP + P_i \rightarrow ATP$



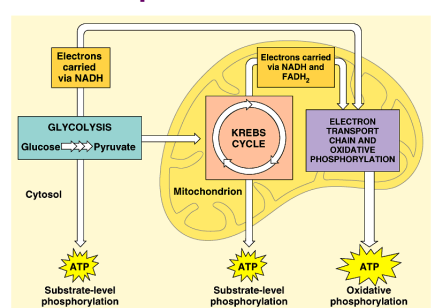
But... Have we done that yet?

## Cellular Respiration Stage 4: Electron Transport Chain

AP Biology

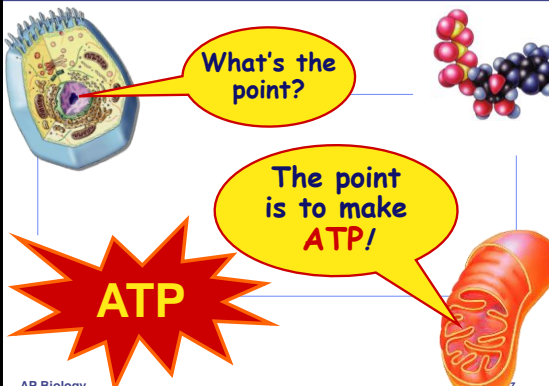
## Cellular respiration



AP Biology

What's the point?

The point is to make ATP!





ATP

AP Biology

## ATP accounting so far...

- Glycolysis  $\rightarrow$  2 ATP
- Kreb's cycle  $\rightarrow$  2 ATP
- Life takes a lot of energy to run, need to extract more energy than 4 ATP!

There's got to be a better way!

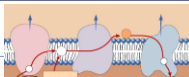




A working muscle recycles over 10 million ATPs per second

AP Biology

## There is a better way!

- Electron Transport Chain
  - series of proteins built into **inner mitochondrial membrane**
    - along **cristae**
    - transport proteins & enzymes
  - transport of electrons down ETC linked to pumping of  $H^+$  to create  $H^+$  gradient
  - yields  **$\sim 36$  ATP** from 1 glucose!
  - only in presence of  $O_2$  (**aerobic respiration**)

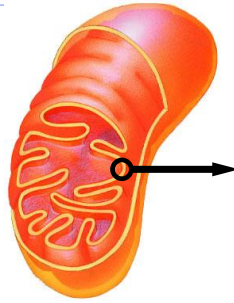
$O_2$

AP Biology

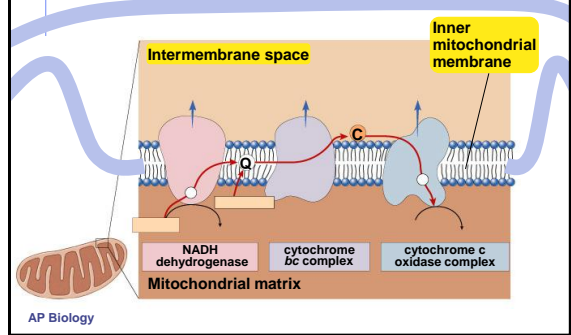
# AP Biology

## Mitochondria

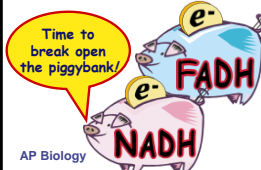
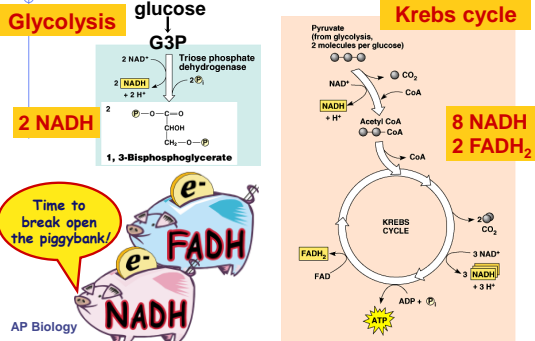
- Double membrane
  - outer membrane
  - inner membrane**
    - highly folded **cris**tae
    - enzymes & transport proteins
  - intermembrane space**
    - fluid-filled space between membranes



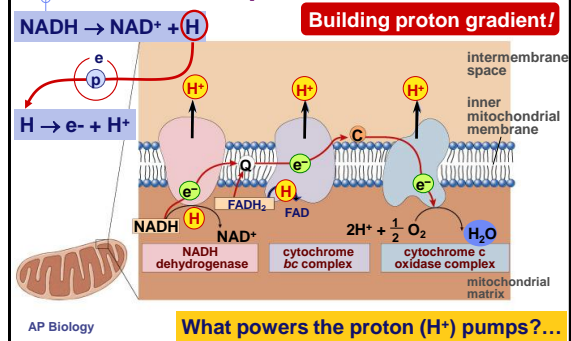
## Electron Transport Chain



## Remember the Electron Carriers?



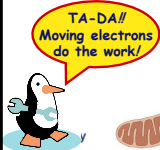
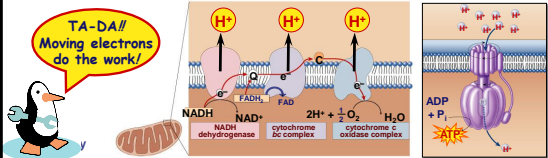
## Electron Transport Chain



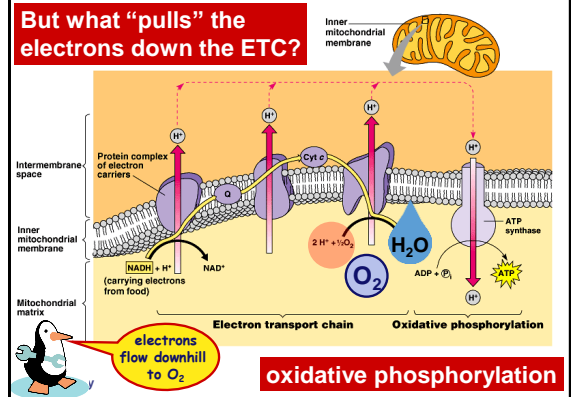
What powers the proton (H<sup>+</sup>) pumps?...

## Stripping H from Electron Carriers

- Electron carriers pass electrons & H<sup>+</sup> to ETC
  - H cleaved off NADH & FADH<sub>2</sub>
  - electrons** stripped from H atoms → H<sup>+</sup> (protons)
    - electrons passed from one electron carrier to next in mitochondrial membrane (ETC)
    - flowing electrons = energy to do work
  - transport proteins in membrane pump H<sup>+</sup> (protons) across inner membrane to **intermembrane space**



## But what "pulls" the electrons down the ETC?



electrons flow downhill to O<sub>2</sub>

oxidative phosphorylation



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## Summary of cellular respiration

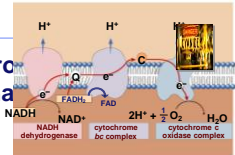


- Where did the glucose come from?
- Where did the  $O_2$  come from?
- Where did the  $CO_2$  come from?
- Where did the  $CO_2$  go?
- Where did the  $H_2O$  come from?
- Where did the ATP come from?
- What else is produced that is not listed in this equation?
- Why do we breathe?

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## Taking it beyond...

- What is the final electron acceptor in the Electron Transport Chain?



- So what happens if  $O_2$  unavailable?
  - ETC backs up
    - nothing to pull electrons down chain
    - $NADH$  &  $FADH_2$  can't unload H
  - ATP production ceases
  - cells run out of energy
  - and you die!

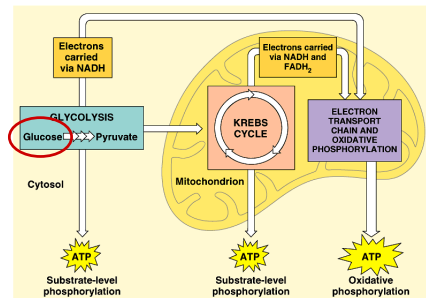


## Cellular Respiration Other Metabolites & Control of Respiration



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## Cellular respiration



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## Beyond glucose: Other carbohydrates

- Glycolysis accepts a wide range of carbohydrates fuels



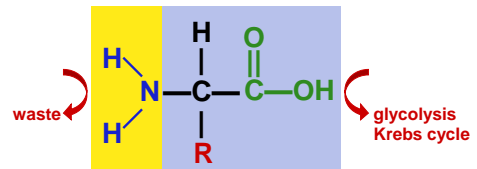
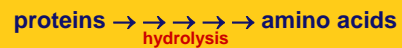
- ex. starch, glycogen



- ex. galactose, fructose

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## Beyond glucose: Proteins



amino group = waste product excreted as ammonia, urea, or uric acid

2C sugar = carbon skeleton = enters glycolysis or Krebs cycle at different stages

AF

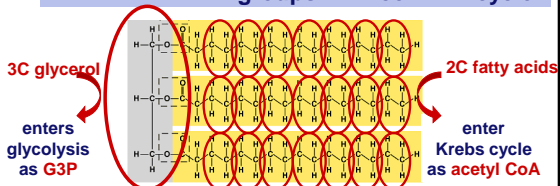
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## Beyond glucose: Fats

fats → → → → glycerol + fatty acids  
hydrolysis

glycerol (3C) → → G3P → → glycolysis

fatty acids → 2C acetyl → acetyl → Krebs cycle  
groups coA

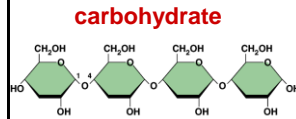


## Carbohydrates vs. Fats

Fat generates 2x ATP vs. carbohydrate

- more C in gram of fat
  - more energy releasing bonds
- more O in gram of carbohydrate
  - so it's already partly oxidized
  - less energy to release

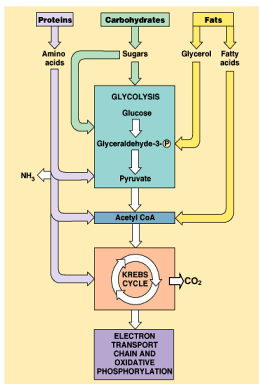
That's why it takes so much to lose a pound a fat!



## Metabolism

Coordination of chemical processes across whole organism

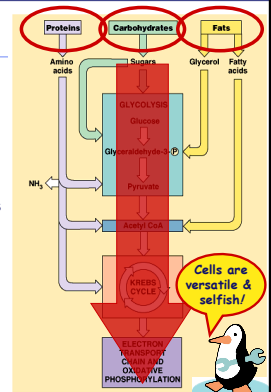
- digestion**
  - catabolism when organism needs energy or needs raw materials
- synthesis**
  - anabolism when organism has enough energy & a supply of raw materials
- by **regulating enzymes**
  - feedback mechanisms
  - raw materials stimulate production
  - products inhibit further production



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## Metabolism

- Digestion**
  - digestion of carbohydrates, fats & proteins
  - all catabolized through same pathways
  - enter at different points
- cell extracts energy from every source



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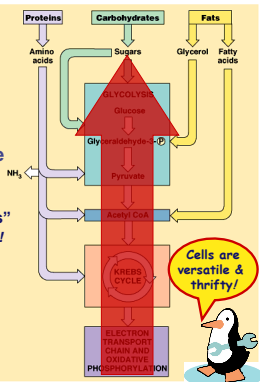
## Metabolism

- Synthesis**
  - enough energy? **build stuff!**
  - cell uses points in glycolysis & Krebs cycle as links to pathways for synthesis
    - run pathways "backwards"
      - have extra fuel, build fat!

pyruvate → → glucose

Krebs cycle intermediaries → → amino acids

acetyl CoA → → fatty acids

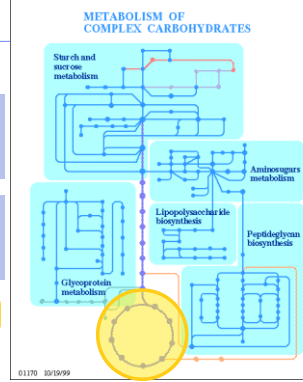


## Carbohydrate Metabolism

The many steps on the Carbohydrate Line

from Krebs cycle back through glycolysis

"gluconeogenesis"



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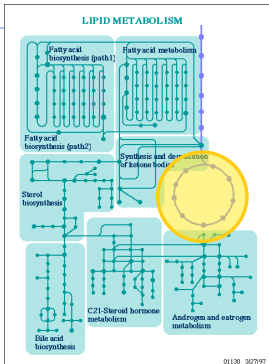
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## Lipid Metabolism

The many steps on the Lipid Line

from Krebs cycle (acetyl CoA) to a variety of lipid synthesis pathways



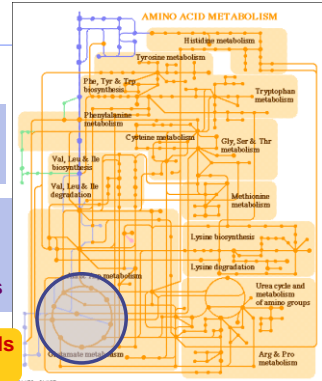
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## Amino Acid Metabolism

The many steps on the Amino Acid Line

from Krebs cycle & glycolysis to an array of amino acid synthesis pathways

8 essential amino acids  
12 synthesized aa's

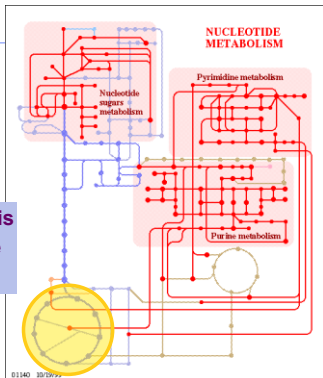


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## Nucleotide Metabolism

The many steps on the GATC Line

- sugar from glycolysis
- phosphate & N-base from Krebs cycle

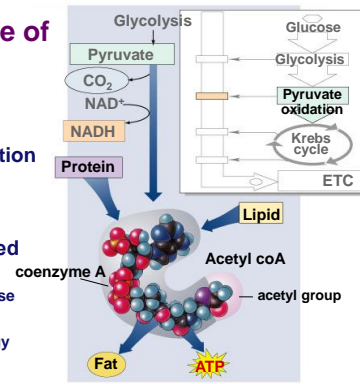


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## Central Role of Acetyl CoA

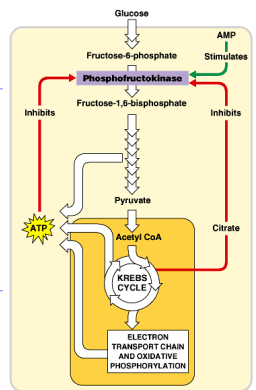
- Acetyl CoA is central to both energy production & biomolecule synthesis
- Depending on organism's need
  - ♦ build ATP
    - immediate use
  - ♦ build fat
    - stored energy



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## Control of Respiration

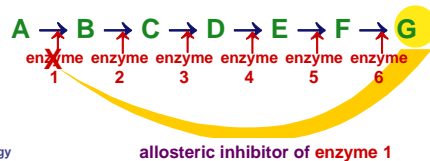
Feedback Control



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## Feedback Inhibition

- Regulation & coordination of production
  - ♦ final product is inhibitor of earlier step
    - allosteric inhibitor of earlier enzyme
  - ♦ no unnecessary accumulation of product
  - ♦ production is self-limiting



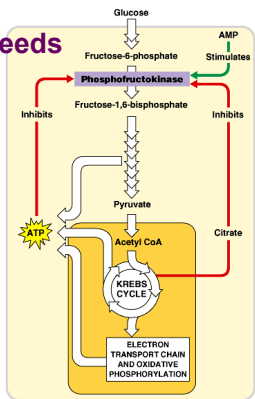
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## Respond to cell's needs

- Key point of control
  - phosphofruktokinase
    - allosteric regulation of enzyme
      - why here?
        - "can't turn back" step before splitting glucose
    - AMP & ADP stimulate
    - ATP inhibits
    - citrate inhibits



Why is this regulation important?

Balancing act: availability of **raw materials** vs. **energy demands** vs. **synthesis**

## A Metabolic economy

- Basic principles of **supply & demand** regulate metabolic economy
  - balance the supply of **raw materials** with the **products** produced
  - these molecules become **feedback regulators**
    - they **control enzymes** at strategic points in glycolysis & Krebs cycle
      - levels of **AMP, ADP, ATP**
        - regulation by **final products** & **raw materials**
      - levels of **intermediates compounds** in pathways
      - regulation of **earlier steps** in pathways
      - levels of **other biomolecules** in body
        - regulates rate of siphoning off to **synthesis pathways**

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## It's a Balancing Act

- Balancing **synthesis** with availability of both **energy & raw materials** is essential for survival!
  - do it well & you survive longer
  - you survive longer & you have more offspring
  - you have more offspring & you get to "take over the world"

