Design of Metabolism
or How Biological Order Comes About

What is Metabolism?

It is catalytic reactions (run by enzymes) in cells.....

2 Categories catalytic reactions -

CATABOLISM - Cell respiration : oxidation of food stuffs

3 steps: 1) digestion of polymers (foods)

2) GLYCO-LYSIS ---> AcoA [splitting of sugar]

3) oxidation of AcoA ---> CO_2 + NADH --> H_2O

ADP + P ---> ATP

ANABOLISM - biosynthesis

coupled reaction - energetically unfavored w favored

ENERGY - capacity or ability to do work - kinds:

KINETIC – motion

HEAT - assoc w movement molecules in a body of matter; most random form of energy (wasted)

POTENTIAL - stored energy; capacity to do work eventually

molecules in living cell have potential energy to do work because of the arrangement (orientation) of their atoms in space... we call this chemical energy & the energy is stored in the covalent bonds of the molecules.

EXAMPLES: general: heat, light, sound, mechanical

biological: synthetic, osmotic, mechanical,

HOMEOSTASIS = energy needed to maintain steady state

BIOENERGETICS - study of energy transformations (changes)

EQUILIBRIUM THERMODYNAMICS

1st LAW = Conservation of Energy

energy is a constant,
energy can't be created or destroyed,
only transformed.
caloric data says 1st law is true

2nd LAW = energy transformations reduce order of universe
directional
moves toward equilibrium (maximize disorder)
ENTROPY = amount of disorder in a system

The Rules of Universe are :

Cities crumble, Stars go Supernova, &
we're all dying.... (Equilibrium…izing)

Degree of disorder of the Universe
(its randomness - its ENTROPY)
can only increase.

There are no unique laws covering cells…

Cells do obey Laws of Chemistry & Physics

yet CELLS... WOW ! ... become highly ORDERED...

wing of bird, a spider's web, the human eye, ...etc
& cells Feed, Grow, & Differentiate = HOW?

for a system to become more ordered [lose entropy]
(such as a cell),
its surroundings must become more disordered
(gain entropy)

FOODs (light & covalent bond energy)

→ cell reactions give increased order within cell

→ with release of HEAT

ENERGY IN ----> CELL STRUCTURE ----> ENERGY OUT

FREE ENERGY $\Delta G = \Delta H - T\Delta S$

ΔG is then a numerical measure of
how far a reaction is from equilibrium

ΔG is measure amount energy in system able to do work...

Disorder increases (entropy increases) when useful energy, that which could be used to do work, is dissipated as heat

PREDICTS .....the Direction of Cellular Reactions.....
TOWARD EQUILIBRIUM... Towards Maximum ENTROPY

CHEMICAL REACTON..... A <---> B Which Way?

$$\Delta G = \Delta G^{0'} + RT \ln [p]/[r]$$

change in free energy content of a reaction...depends upon:

1. **energy is stored in molecule's covalent bonds**
2. **temperature is negligable... ells are isothermal, i.e., function within narrow range (4o to 99o)**

ΔG	**=**	**actual free energy**
$\Delta G^{0'}$	**=**	**standard free energy**
R	**=**	**gas constant (2 x 10-3 Kc/mol)**
T	**=**	**absolute temp (-273OK)**
ln	**=**	**natural log (conversion log10 = 2.303)**

at equilibrium ΔG = 0 and we call [p]/[r] = Keq

solve above equation to see relationship of Keq to ΔG0'

Free Energy Equation

$\Delta G = \Delta G0' + RT \ln [P] / [R]$

@ equilibrium $\Delta G = 0$ ....

thus rearranging $\Delta G0' = -RT \ln [P]/[R]$

@ equilibrium $[P] / [R] = Keq$

& @ 25^0C... $-RT \ln Keq =$

$-(2.0)(298)(2.303)lg^{10} Keq = -[1372] lg^{10} Keq$

thus..... $\Delta G0' = - [1372] lg10 Keq$

Products / Reactants	Keq	log10	dG0' cal/mole*
[R] > [P]			[lg10 x -1372]
1/1000	0.001	-3	+4116
1/100	0.01	-2	+2744
1/10	0.1	-1	+1372
1/1			
10/1	10	1	-1372
100/1	100	2	-2744
1000/1	1000	3	-4116
[P] > [R]			

CHEMICAL REACTIONS **A <----> B** **Which way & Why?**

EXERGONIC REACTION - is one which releases energy

Product (B) << Reactant (A) [stored in covalent bonds]

ex: burning wood (cellulose)

glucose monomers= potential energy

breaks bonds, release heat & light ---> CO_2 & H_2O

cell respiration - cellular burning of glucose

slower, multi-step process to capture released energy.... as ATP

ENDERGONIC REACTION - requires input of energy A-->B

Product (B) >> Reactant (A)

ex: photosynthesis (autotrophy)

glucose made from CO_2 + H_2O --light---> $C_6H_{12}O_6$

energy poor energy rich

CELL METABOLISM is then...

Exergonic & Endergonic reactions that occur in cells

How does metabolism really work energetically?

COUPLED REACTIONS:

for RX's which share one or more intermediates....
the free energy change ΔG is the sum of indiv ΔG's

Glu + Fruc ---> Suc ΔG= + 5.5 Kc/m
ATP --> ADP + P ΔG = - 7.3 Kc/m
Glu + ATP ---> G-1-P + Fruc ---> Suc + P ΔG= -1.8Kc/m

COUPLED REACTIONS - linking hydrolysis of ATP
(a favored rx) to a thermodynamically unfavored reaction
creates biological order (greater molecular structure).

WHY ATP ? ? ? and not other nucleotides.

the ENERGY MOLECULE of CELLS is ATP
over evolution... cells favored enzymes that bind
ATP & use its hydrolysis to drive endergonic reactions

adenosine triphosphate
- **its structure**
- **how it works**
- **phosphorylation, energy coupling**

HYDROLYSIS of ATP

ATP ----------> ADP + P (exergonic)
$\Delta G^{0'}$ = -7.3 Kc/m

So how do cells make ATP?

By PHOSPHORYLATION... adding phosphate to ADP

ADP + P ----------> ATP

a) substrate level phosphorylation –
where a substrate molecule (X-p) donates its P to ADP making ATP

b) Chemiosmosis - [oxidative phosphorylation]...
food substrates donate e- & protons to acceptors
protons are pumped out of mito/chlp
protons diffuse back into mito thru ATP synthase
ATP synthase makes ATP

c) photophosphorylation –
e- of light energy are captured to make a proton gradient across the chloroplast membranes
protons move through chloroplast ATP synthase to make ATP

Heterotrophic Metabolism organisms that consume foods

we say our bodies oxidize (consume) foods to make energy
where is energy in foods? it's in covalent bonds (& e^-s)

OXIDATIVE METABOLISM…

Metabolism is then, cells capturing e^- from food to make ATP

REDOX Reaction –

e^- passed from one molecule to another in chemical rx's
called REDOX rx .....energy transferred into new molecule

OXIDATION = removal of electron &/or proton
removes an e^- from a food molecule
REDUCTION = gaining electron &/or proton
adds an e^- to an acceptor molecule

A-H	+	B-O	<----->	A	+	B-O-H
donor		acceptor	:H	acceptor		donor
reducing		oxidizing		becomes		becomes
agent		agent		oxidized		reduced

Thus : heterotrophic metabolism is stepwise oxidation of foods
if aerobic - requires oxygen as electron acceptor
if anaerobic - requires no oxygen (other e^- acceptor)

CELL RESPIRATION…

oxidation of GLUCOSE to $CO_2 + H_2O$ & reduction O_2 to H_2O

$C_6H_{12}O_6 + 6O_2 \text{ <----> } 6\,CO_2 + 6\,H_20 + e^- \text{ ---> } 36\ ATP$

- 686 Kc/mole

called oxidation.....because e- are removed from glucose

called reduction.....because e- passed to O_2 making water

Fuller definition :

series of enzyme rx's (pathways) in cytoplasm & mitochondria which...

- remove e- from chemical bonds of substrates (as glucose)

- pass e- to acceptor molecules [CoE's] as NAD+ & FAD which become reduced [NADH & FADH2]

- reduced CoE [NADH & FADH2] pass e- to other acceptors a series of protein electron carriers [cytochromes]

- electron carriers [cytochromes] pass e- to O_2---> H_2O

- cytochromes also pump protons (H+) out of mito into space between membranes

- protons move back into mitochondria thru a special enzyme protein (ATP synthase) & make ATP

METABOLIC PATHWAYS OF CELL RESPIRATION…

Glyco-lysis

converts glucose (C6) to pyruvate (C3)
makes 2 pyruvate , 2 NADH & 2 ATP (net)
in cytoplasm
alcoholic fermentation = glucose --> alcohol
lactic acid fermentation = glucose --> lactic acid

KREBs Cycle

converts 2 pyruvate to $CO_2 + H_2O$
makes 8 NADH, 2 ATP, 2 $FADH_2$
releases 6 CO_2
in mitochondria

ETC - Electron Transport Chain

passes e^- & H^+ from NADH & $FADH_2$ to O_2
to make water
generates a proton gradient (chemiosmosis)
in mitochondria

ATP synthase

enzyme of mitochondrial membrane
that lets H^+ back into mitoplasm & makes ATP

KEY REACTIONS of GLYCOLYSIS -

substrate level phosphorylation

Redox reaction involving NAD

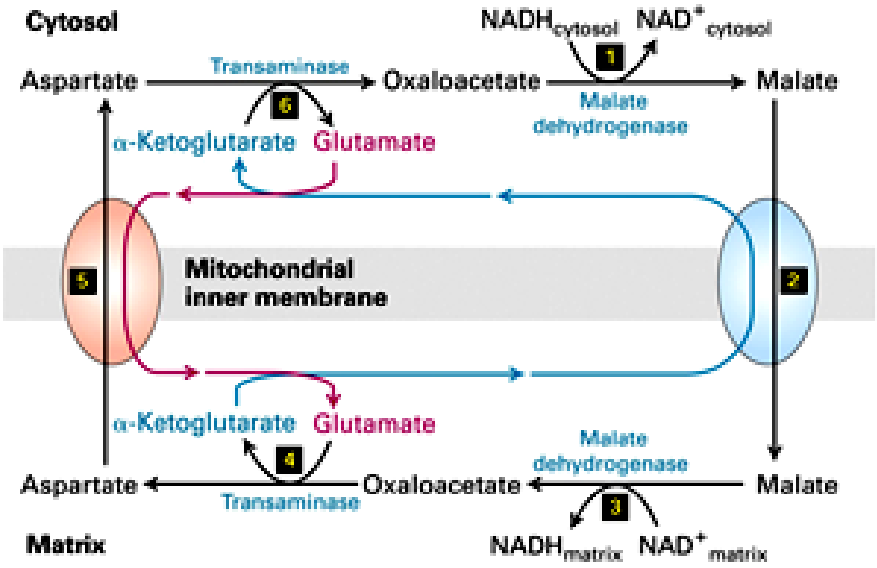
Fates of NADH -

alcoholic ferementation

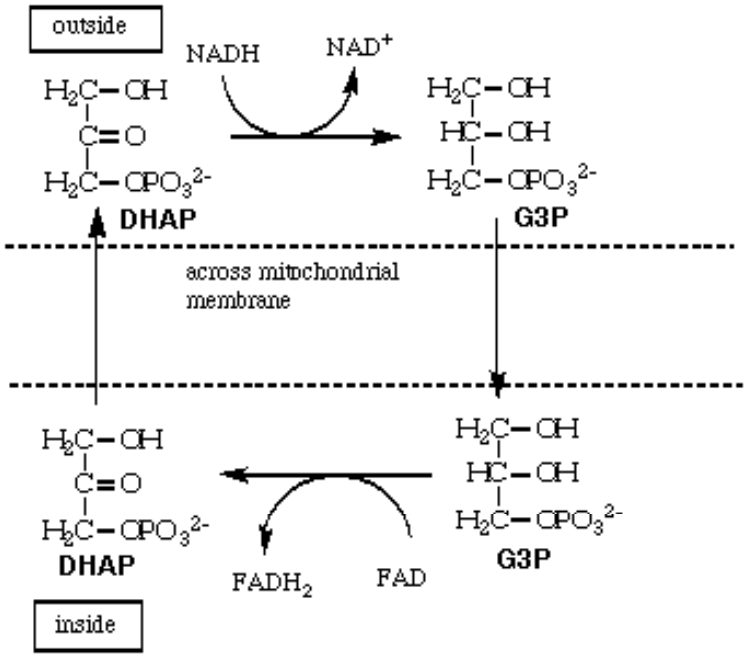
lactic acid respiration (fermenation)

shuttles

malate shuttle (liver, kidney, heart) = NADH



Glycero-P shuttle (muscle/brain) = $FADH_2$



Fates of PYRUVATE -

if anaerobic

alcoholic fermentation

lactic acid respiration (fermentation)

if aerobic

Krebs Cycle

Summary of GLYCOLYSIS

- 2 ATP to initiate

2 substrate level phosphorylations

makes 2 ATP (net), 2 NADH, and 2 PYRUVATES

Fermentations & Shuttles

PYRUVATE DEHYDROGENASE Reaction

in mitoplasm

involves CoASH -----> acetyl coenzyme A [AcoA]

decarboxylation $-CO_2$

Key Reactions of KREBS CYCLE

NAD is reduced

substrate level phosphorylation occurs

decarboxylation [-COOH]

acylation via CoASH

OXIDATIVE PHOSPHORYLATION & ELECTRON TRANSFER

coupling of oxidation of substrates (-e) to the
phosphorylation of ADP to make ATP
involves "protein carriers" - gain/lose e-'s & protons
occurs in 3 submitochondrial cell membrane complexes:

a) NADH Reductase,
b) Cytochrome Reductase, &
c) Cytochrome Oxidase

Chemiosmosis & ATP Synthase

- creation of a hydrogen ion gradient (H+)
as e- flow thru the ETC
- some carriers release protons to outside
- H+ diffuse back into mitoplasm thru ATP synthase --> ATP

OVERVIEW of Cell Respiration

How much ATP is made per Glucose ?
Substrates & Regulation

Summation: cell respiration & heterotrophic metabolism

1. Substrates = sugars, amino acids acids, fatty acids

2. Glyco-lysis, Krebs Cycle, & ETC are Universal to all cells

3. Products = $C0_2$, H_20, and energy as NADH, $FADH_2$, & ATP

4. Process is anaerobic respiration (-0_2 ; GLYCO-LYSIS)
   alcohol & lactate fermentation (anaerobic)
   & aerobic ($+0_2$; glycolysis & Krebs Cycle)

5. Reactions include:
   oxidation, reduction, decarboxylation, phosphorylation,
   & hydrolysis (dephosphorylation)

6. Energy capture is via electron transfers & proton pumps

7. Regulation is by:
   feedback inhibition & allosteric modulation of
   key enzymes as phospho-fructokinase

8. Intracellular compartmentation:
   glycolysis is in the cytoplasm
   Krebs Cycle is mostly in the matrix of mitochondria
   ETC is in the cristae membranes of mitochondria