คม 324
สารออกฤทธิ์ทางชีวภาพ

โดย อ.ดร. เอกวิทย์ ตรีเนตร

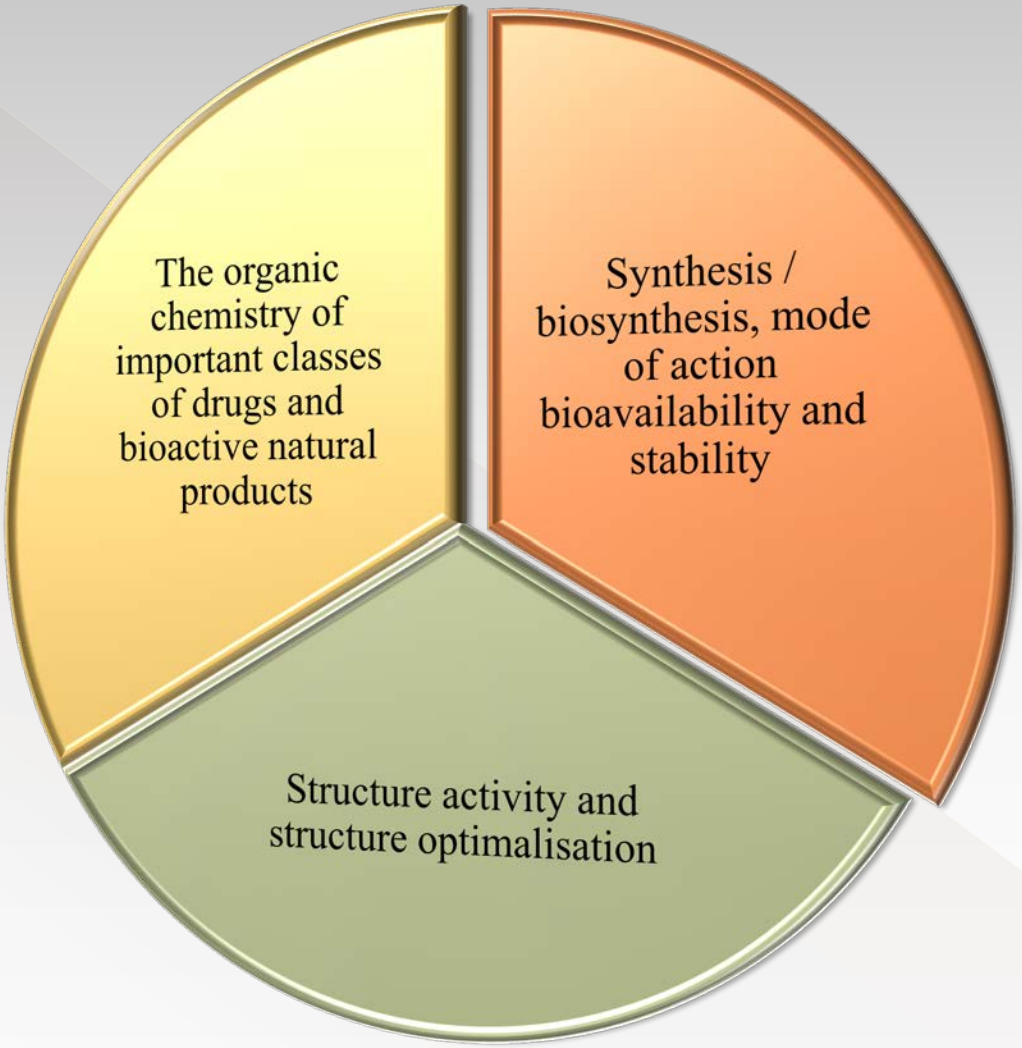
สารออกฤทธิ์ทางชีวภาพ

bioactive compounds เป็นสารออกฤทธิ์ทางชีวภาพ หมายถึง สารประกอบที่มี biological activity หรือมีกิจกรรม (activity) ต่อสิ่งที่มีชีวิต การออกฤทธิ์อาจให้ผลดี (beneficial) หรือให้ผลเสีย (adverse) ขึ้นอยู่กับชนิดของสารและปริมาณสารที่ได้รับ

Bioactive compounds are experiencing a growing interest in wide range of applications:

- **geo-medicine**
- **plant science**
- **modern pharmacology**
- **agrochemicals cosmetics**
- **food industry**
- **nano bio-science**
- **etc**

Bioactive Molecules



Study

- **Natural Products**
- **Drug Design**
- **Reseptors - Drug Action**
- **Drug Metabolism**

Results

- **Antibiotics/ Antimicrobial Agents**
- **Antiparasitic Agents**
- **Antifungal Agents**
- **Antimycobacterial Agents**
- **Anticancer Agents**
- **Antiviral Agents**

Study of Drugs / Bioactive Compounds

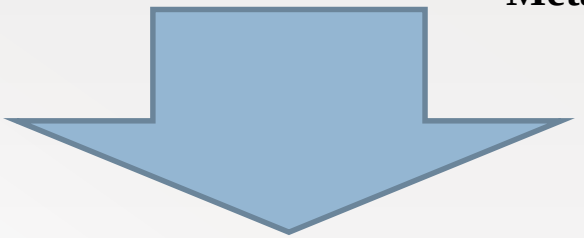
- **Natural Products / Natural Product Derivatives**
- **Random testing, serendipity***
- **Screening of Libraries**
- **(Rational) Drug Design** **(1. mentioned SciFinder 1970, most papers after 1990)**

- **Screening/Design/Serendipity**
- **Design/Structure Optimisation**
- **Actual Drug**

→

- **Activity**
- **Toxicity**
- **Bioavailability**
- **Metabolism**

in vitro
***in vivo* animals**
***in vivo* humans**



Properties

- **Resistance**
- **New diseases (Aging, life style)**
- **Less tollerance for side effects**

Origin of Drugs / Bioactive Compounds: History

Before 1800: Plants, plant extracts, inorganic material

1805: Morphine isolated from opium (sructure proposed 1935, prooved by synth. 1952)

1828: First organic synthesis (urea)

1840-1850: First synthesized org. compds used in medicine: $CHCl_3$, Et_2O anestechia)

Ex of early synthetic drugs:

- **Choral hydrate (sleeping pill) 1869**
- **Acetyl salicylic acid synth 1853, clin trials 1893**
- **Phenazone synth 1884**
- **Benzocaine 1902**
- **Prontocil 1932**

Ex of early isolated nat. prod.

- **Quinine ca 1825**
- **Digitoxin 1841 (structure 1928)**
- **Salicylic acid, antipyretic 1875**
- **Cocaine isol. 1860, local anestethic 1884**
- **Benzylpenicillin 1941**

Traditional medicine
Screening
Serendipity

Natural Products

- **Only source of drugs before last part of 19th century**
- **Antibiotics 1940 - 1960**
- **Cyclosporin (immunomodulator) isolated from soil fungus Hardangervidda 1971**
- **Taxol isolated 1960s, approved drug USA 1992**

Natural Products

Sources

1. Microorganisms (bacteria, fungus) - Antibiotics
2. Higher plants, ex. morphine, quinine, taxol
3. Sponges (polycellular "animals", no real organs or cell tissue)

   ex. agelasines

No immune system, produce their own antibiotics as defence

Secondary metabolites with great structural diversity, stereochemistry!

Secondary metabolites have no known metabolic role in cells

Three main classes: alkaloids, terpenoids, phenolics

4. Higher animals, fewer examples, epibatidine from South American tree frog

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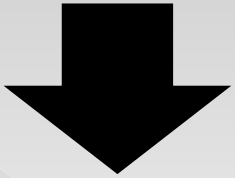
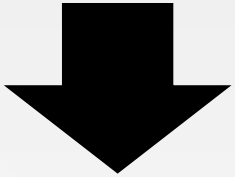
Principle of Metabolism



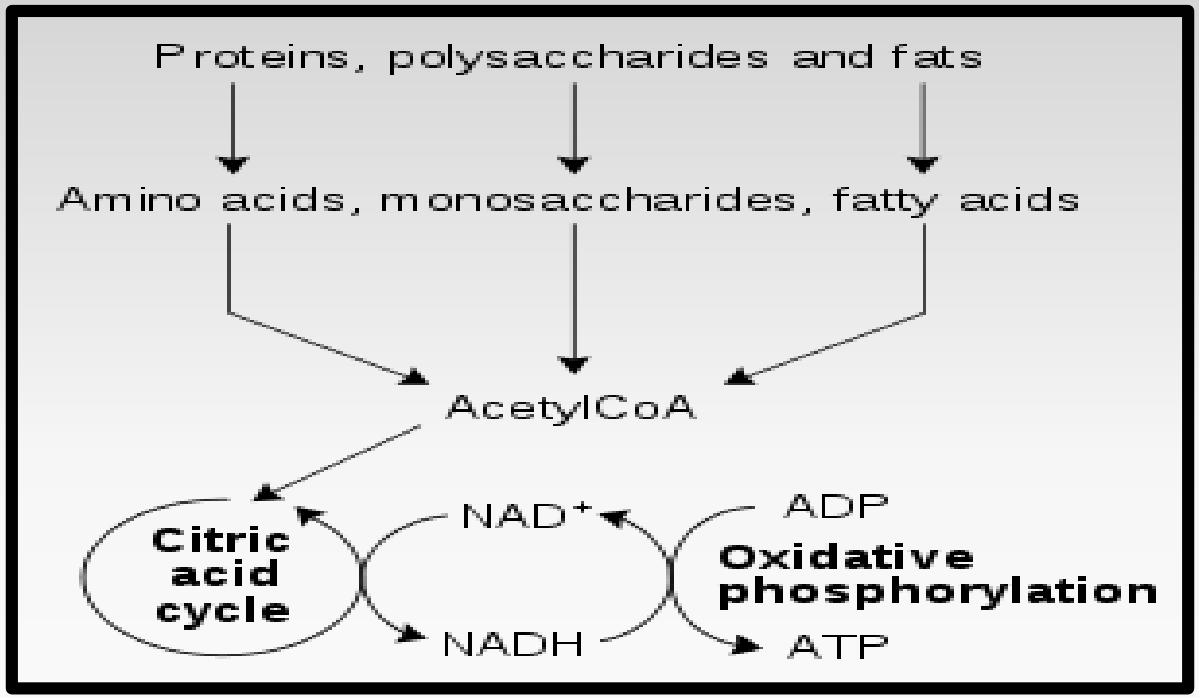
Specific Metabolism

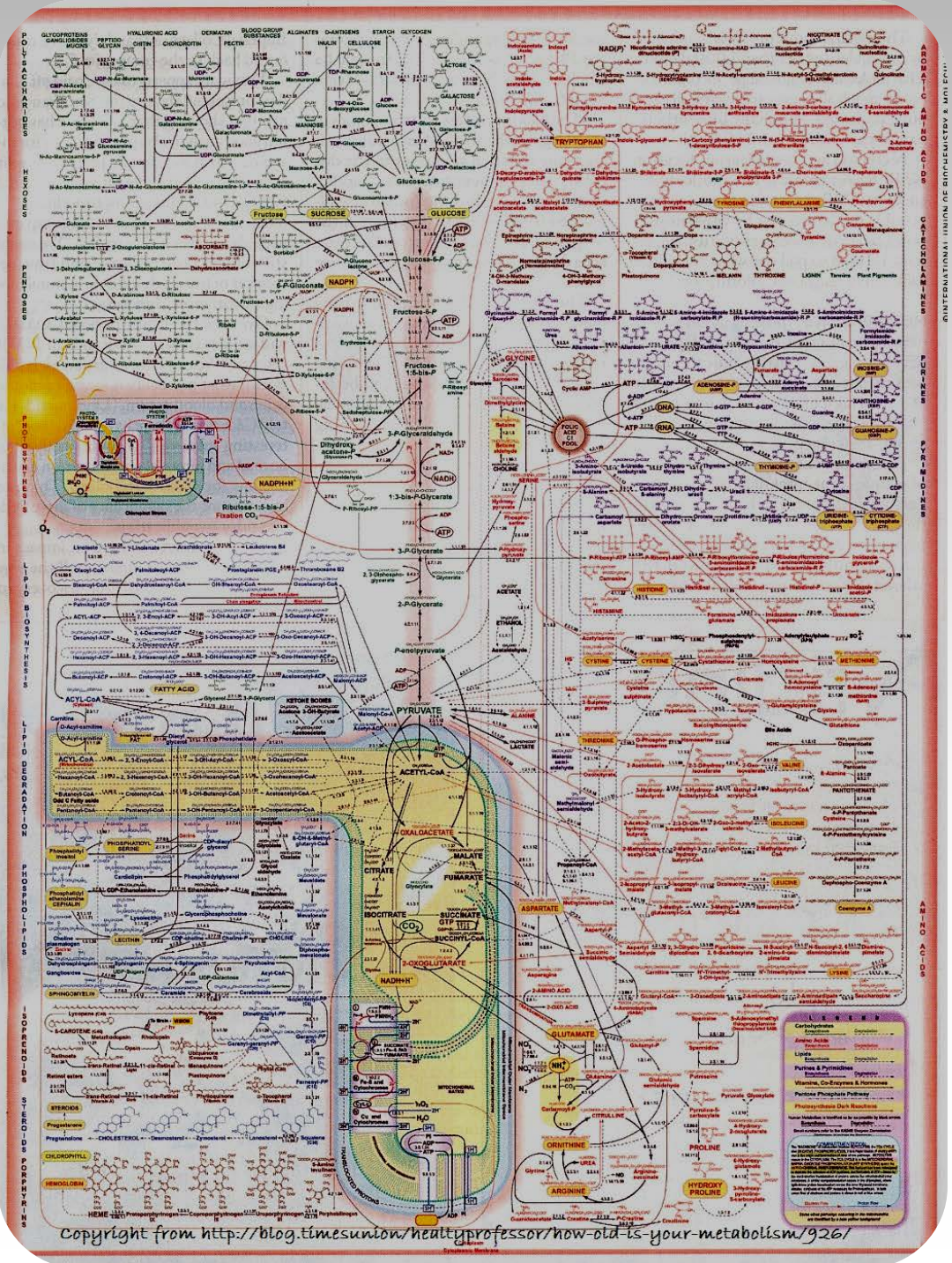
Xenobiotic Metabolism



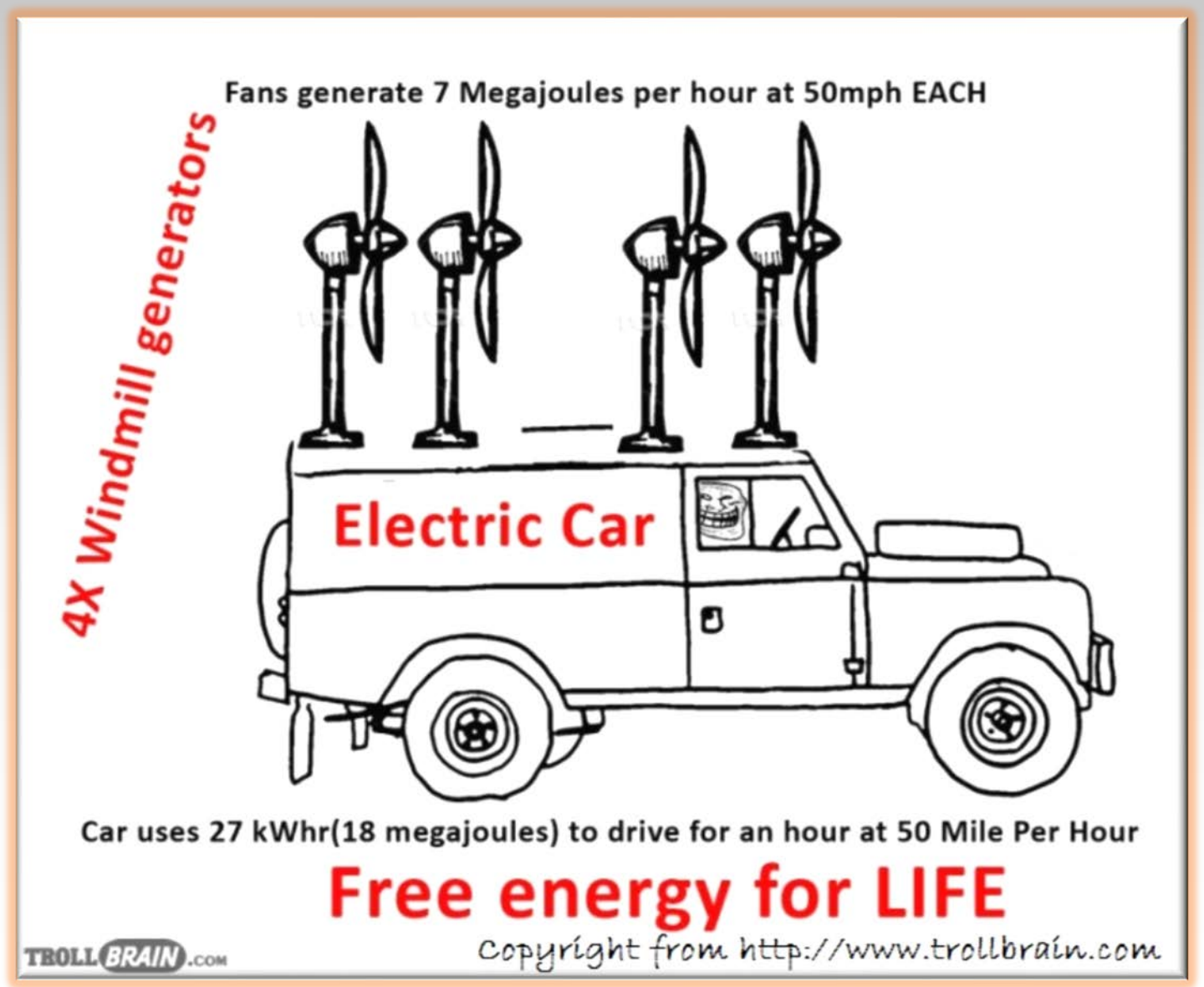
Mechanism of Cell response

หลักการของเมแทบอลิซึม
(Principle of Metabolism)

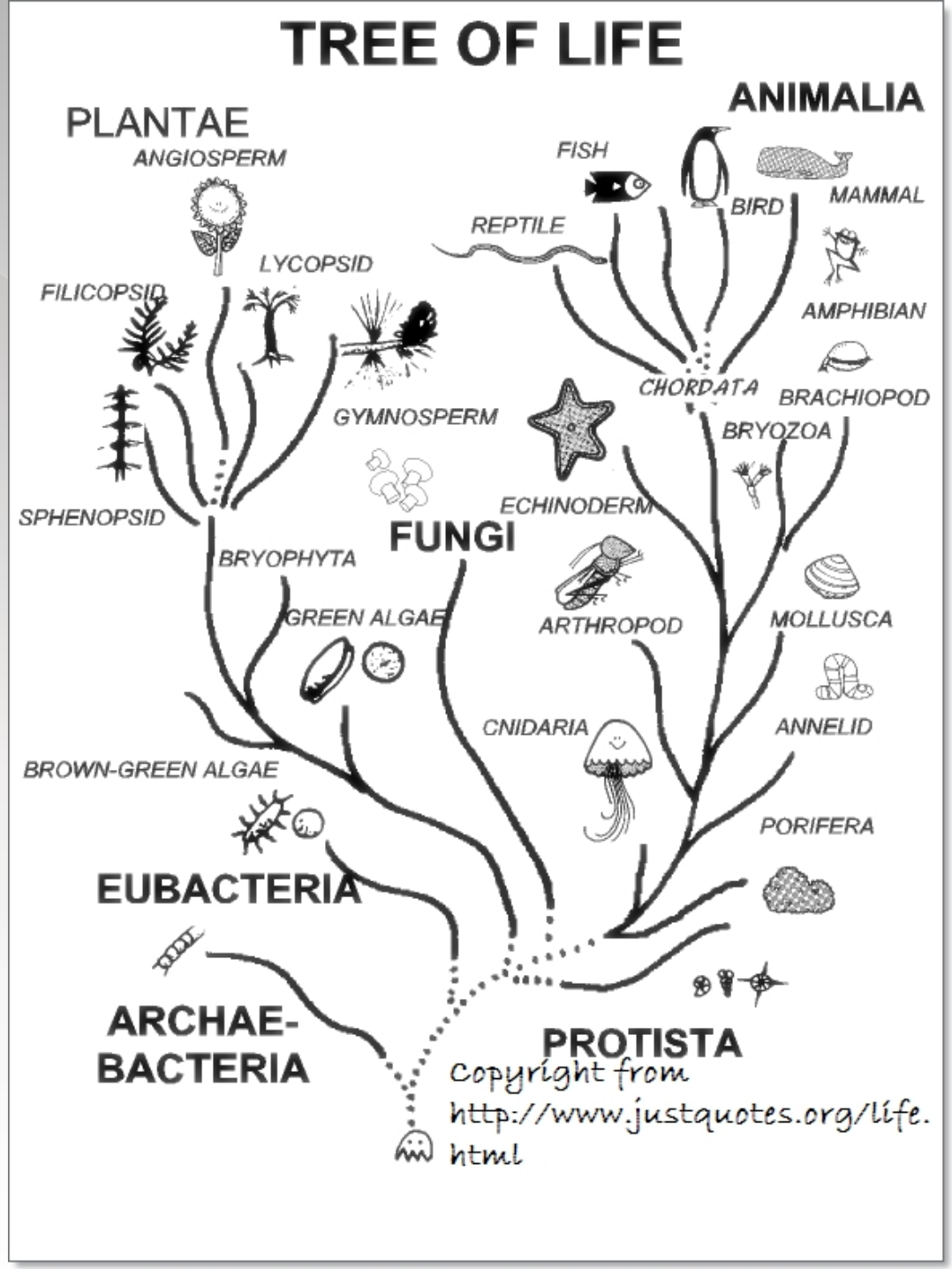



POLYSACCHARIDES
HEXOSES
PENTOSES
PHOTOSYNTHESIS
LIPID BIOSYNTHESIS
LIPID DEGRADATION
PHOSPHOLIPIDS
ISOPRENOIDS
STEROIDS
PORPHYRINS
AROMATIC AMINO ACIDS
CARCINOGENS
PURINES
PYRIMIDINES
AMINO ACIDS
INTERNATIONAL UNION OF BIOCHEMISTRY & MOLECU
GLUCOSE
SUCROSE
Fructose
PYRUVATE
ACETYL-CoA
CITRATE
ISOCITRATE
2-OXOGLUTARATE
SUCCINATE
FUMARATE
MALATE
OXALOACETATE
TRYPTOPHAN
TYROSINE
PHENYLALANINE
GLUTAMATE
ASPARTATE
ALANINE
GLYCINE
SERINE
CYSTEINE
METHIONINE
THREONINE
VALINE
ISOLEUCINE
LEUCINE
LYSINE
PROLINE
HYDROXY PROLINE
ARGININE
ORNITHINE
CITRULLINE
HISTIDINE
THYMIDINE-P
URIDINE triphosphate (UTP)
CYTIDINE triphosphate (CTP)
ADENOSINE-P
GUANOSINE-P
XANTHOSINE-P
INOSINE-P
FATTY ACID
ACYL-CoA
KETONE BODIES
PHOSPHATIDYL-SERINE
LECITHIN
CEPHALIN
CHOLESTEROL
HEME
CHLOROPHYLL
HEMOGLOBIN
Ribulose-1:5-bis-P
Fixation CO2
NADPH+H+
NADH+H+
ATP
ADP
NADPH
NADH
Copyright from http://blog.timesunion/healthprofessor/how-old-is-your-metabolism/926/

Life and Energy



Life


TREE OF LIFE
ANIMALIA
PLANTAE
ANGIOSPERM
FISH
MAMMAL
BIRD
REPTILE
LYCOPSID
FILICOPSID
AMPHIBIAN
CHORDATA
BRACHIOPOD
GYMNOSPERM
BRYOZOA
ECHINODERM
SPHENOPSID
FUNGI
BRYOPHYTA
ARTHROPOD
MOLLUSCA
GREEN ALGAE
CNIDARIA
ANNELID
BROWN-GREEN ALGAE
PORIFERA
EUBACTERIA
ARCHAE-
BACTERIA
PROTISTA
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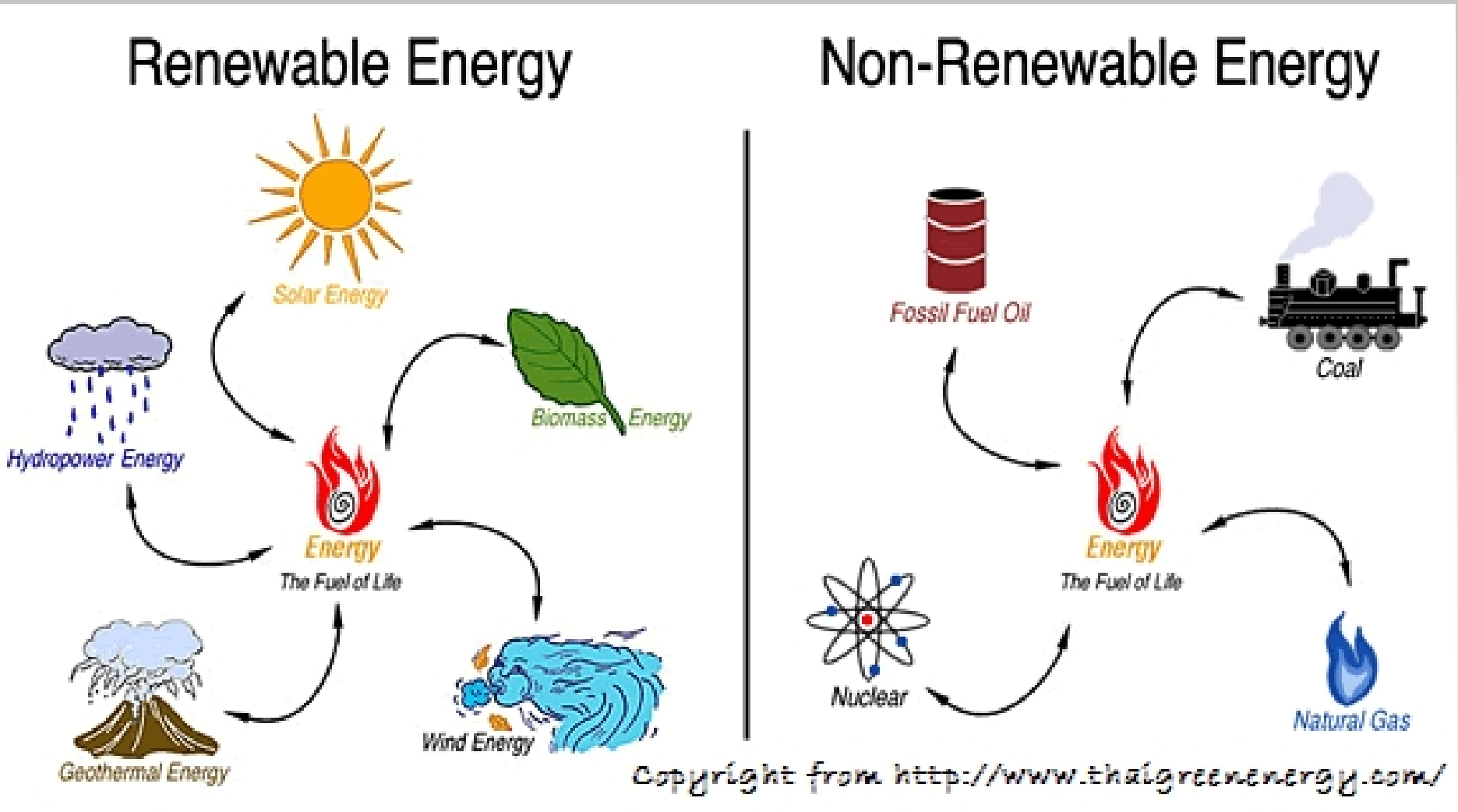
http://www.justquotes.org/life.html

Energy


Renewable Energy
Non-Renewable Energy
Solar Energy
Hydropower Energy
Biomass Energy
Energy
The Fuel of Life
Geothermal Energy
Wind Energy
Fossil Fuel Oil
Coal
Energy
The Fuel of Life
Nuclear
Natural Gas
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Units of Energy

Joule (J) = พลังงานที่ใช้ในการเคลื่อนย้ายมวล 1 kg ให้เคลื่อนที่ไปได้เป็นระยะทาง 1 m

$$\mathrm{J} = \frac{\mathrm{kg} \cdot \mathrm{m}^2}{\mathrm{s}^2} = \mathrm{N} \cdot \mathrm{m} = \mathrm{Pa} \cdot \mathrm{m}^3 = \mathrm{W} \cdot \mathrm{s}$$

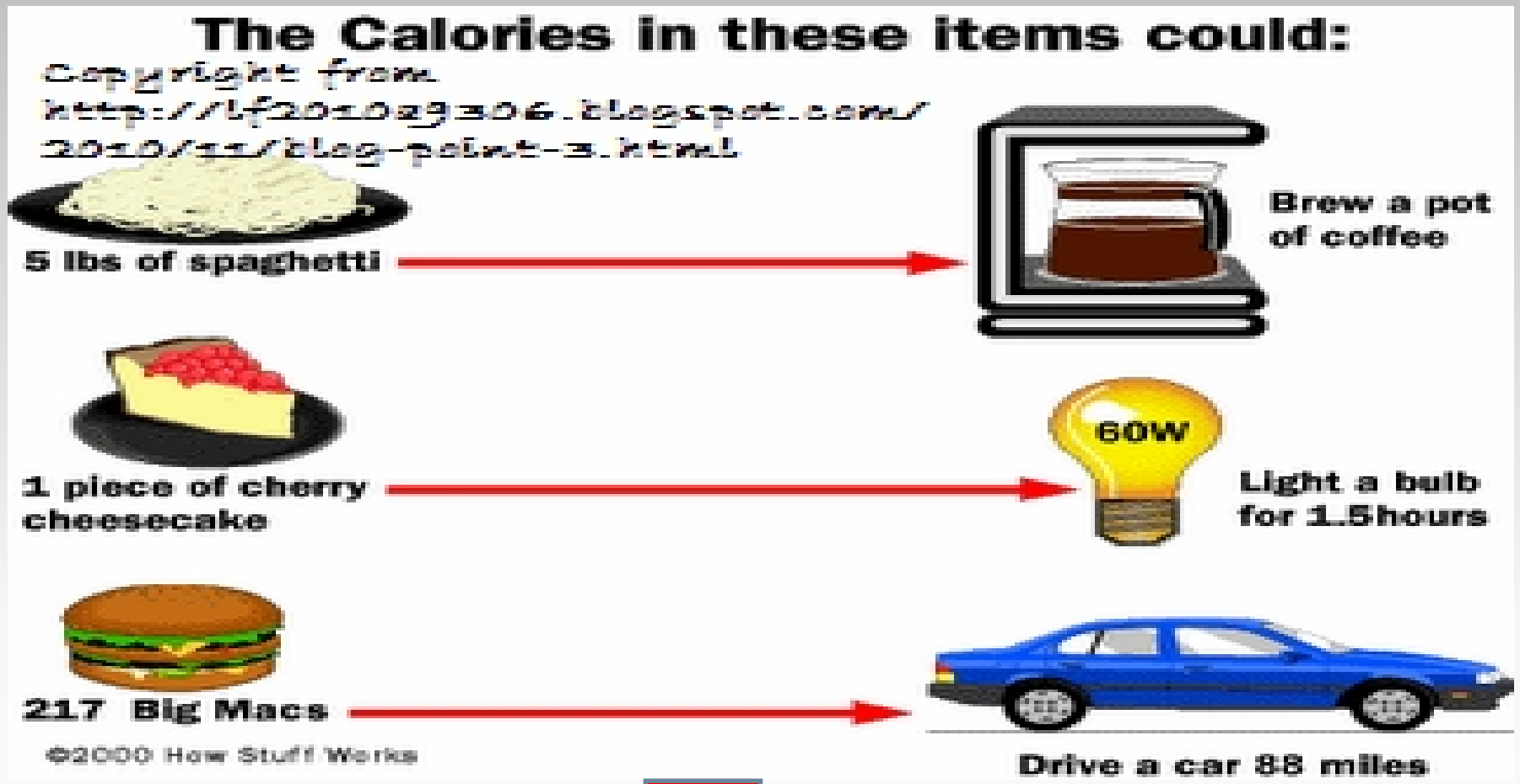
N (newton), m(metre), Kg(kilogram), s (second), Pa (Pacal), and W (watt)

Calory (Cal) = พลังงานความร้อนที่ทำให้น้ำหนึ่ง 1 กรัมที่ทำให้อุณหภูมิของน้ำ 1 กรัมเพิ่มขึ้น 1 องศาเซลเซียส 1 cal= 4.12 J

* สังเกต ตัว C พิมพ์ใหญ่ มีค่าเท่ากับ 1000 cal

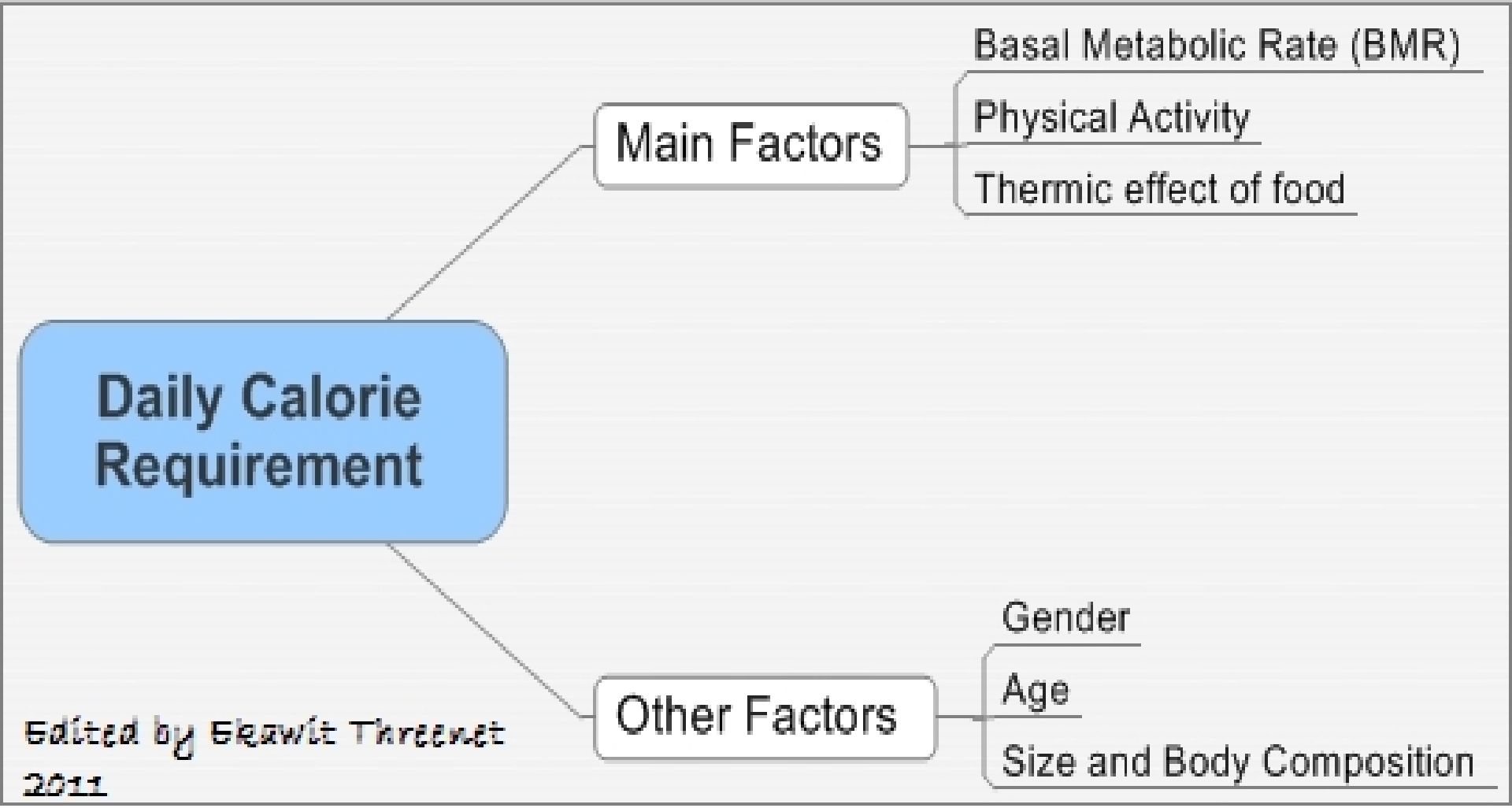
** ดังนั้น 1 Cal = 1000 cal = 1 kcal

Units of Energy



Living cells unavoidably convert organized forms of energy to heat

Calorie Requirement



Basal metabolic rate

Body-Mass Index (BMI)
Waist-to-Height Ratio (WHtR)
Basal Metabolic Rate (BMR)
Body Fat & Surface Area
Willoughby Ideal Weight & Waist

Enter your weight (in lbs), height (in feet and inches), waist (in inches), sex and age. Then, press the Calculate! button.

Weight	150	lbs
Height	5	ft
	10	in
Waist	34	in
Sex	Male	
Age	50	yrs

Calculate!

Body-Mass Index (BMI)	21.6	kg/m^2
Waist-to-Height Ratio (WHtR)	48.6	%
Body Fat	20.3	%
Basal Metabolic Rate (BMR)	1555	kcals/day
Surface Area	1.83	m^2
Willoughby Athlete Weight	180	lbs
Willoughby Athlete Waist	32.1	in

พลังงานของอาหารอีสานรสแซบ

95 kcal
ลาบเลือด (100 กรัม)

97 kcal
ข้าวเหนียว (100 กรัม)

72 kcal
ชุบหน่อไม้ (100 กรัม)

182 kcal
ไก่ย่างวิ้นเจ๋ว (100 กรัม)

108 kcal
ส้มตำพลไม้ (100 กรัม)

เปรียบเทียบจากปริมาณอาหาร **50** กรัม

พลังงานของว่างแบบไทยๆ

ลูกชิ้นหมูปิ้ง

กะหรี่พัฟไส้ไก่

ไส้กรอกอีสาน

ข้าวต้งหน้าตั้ง

ปั้นสินปลา

ขนมปังหน้าหมู

ข้อมูล : Shape Tested SHAPE Magazine
ภาพประกอบจากอินเตอร์เน็ต

Fit with the Brain www.facebook.com/lovefittpage | www.lovefitt.com

Design by: designblahbalah.com

LOW-CALORIE FOODS

*all calories are per 100 gr

@thoresenfitness

Cucumber
15 cals

Lettuce
13 cals

Broccoli
33 cals

Celery
15 cals

Bell Pepper
33 cals

Strawberries
34 cals

Watermelon
35 cals

Tomato
18 cals

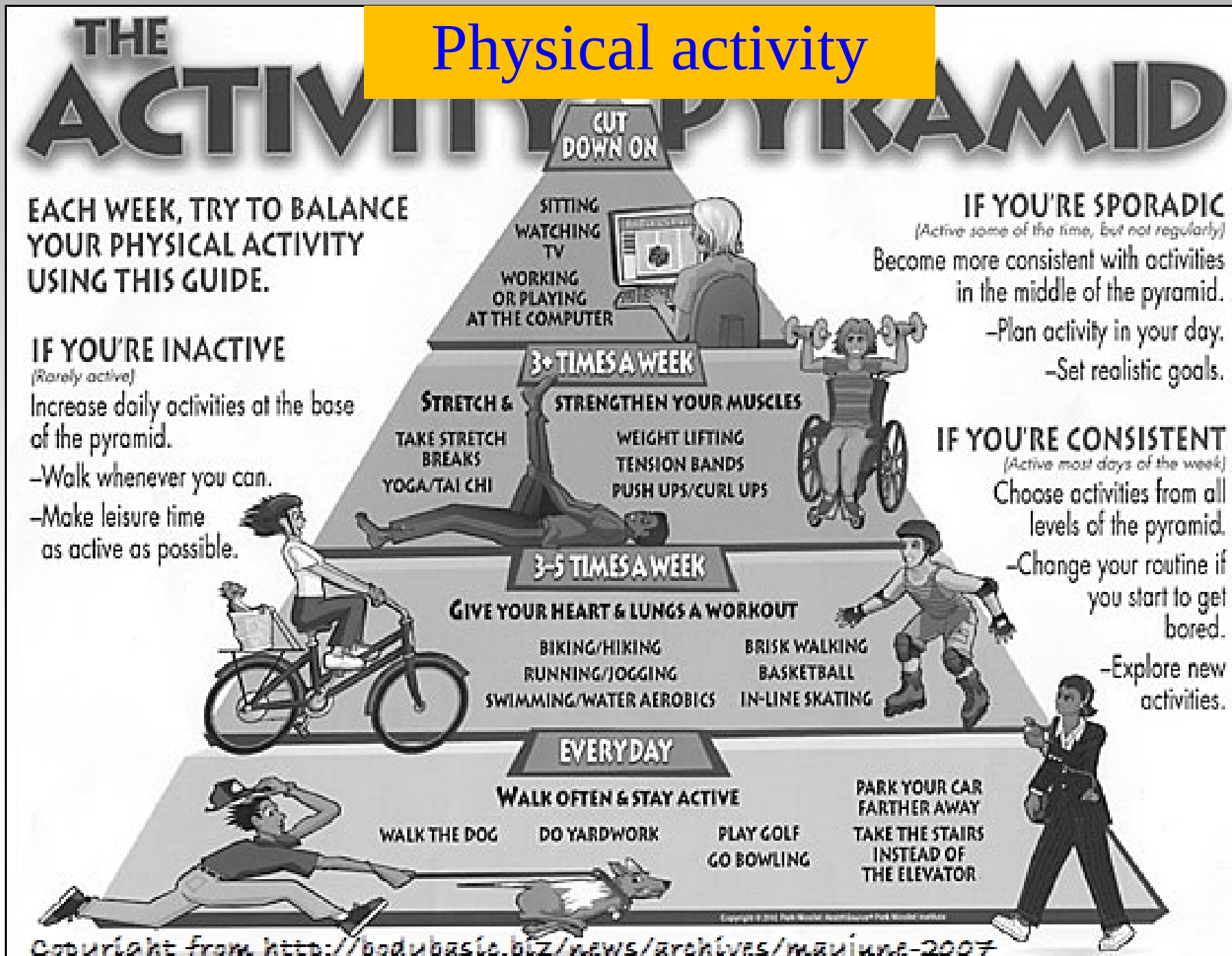
Pineapple
50 cals

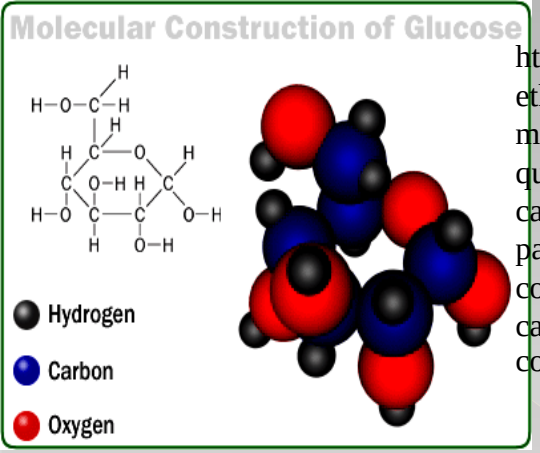
Lemon
23 cals

Honey melon
35 cals

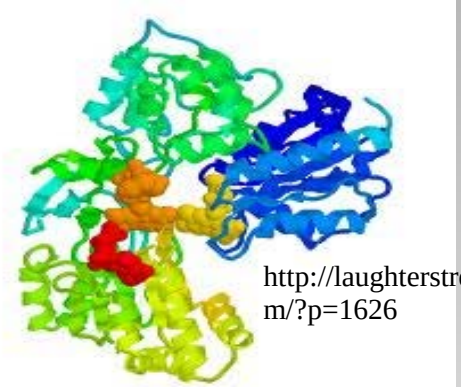
Peach
39 cals

Physical activity

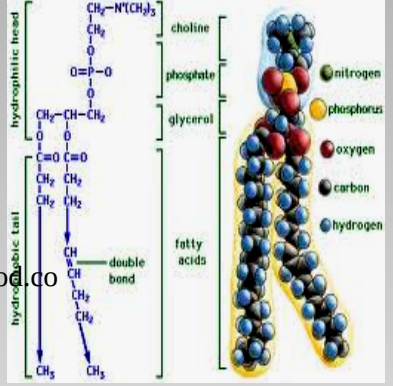




http://getfitnesstogether.wordpress.com/2011/08/31/conquering-carbohydrates-part-3-the-complex-carbohydrate-conundrum/

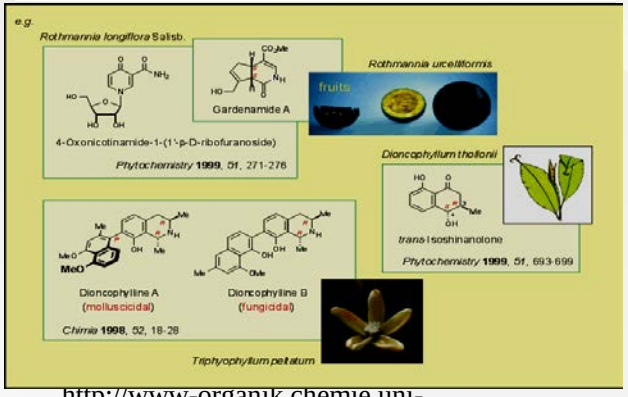


http://laughterstrengthfood.com/?p=1626

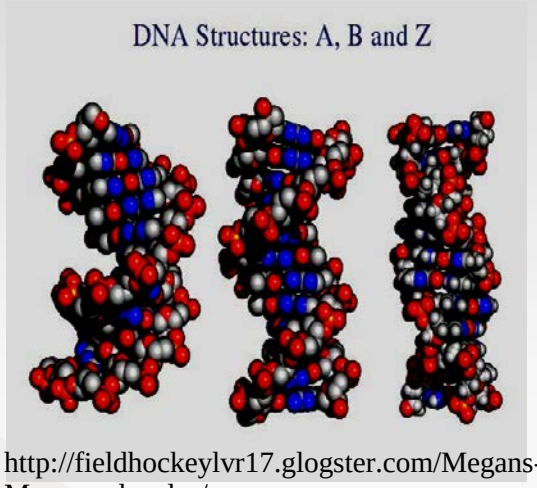


http://schoolworkhelper.net/2010/06/biological-molecules/

Thermal effect of food



http://www-organik.chemie.uni-wuerzburg.de/lehrstuehlearbeitskreise/bringmann/fields_of_research/tropical_plant_compounds/



http://fieldhockeylvr17.glogster.com/Megans-Macromolecules/

Form of energy

- **Kinetic energy** is energy associated with motion
- **Heat (thermal energy)** is kinetic energy associated with random movement of atoms or molecules
- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction
- Energy can be converted from one form to another

Form of energy

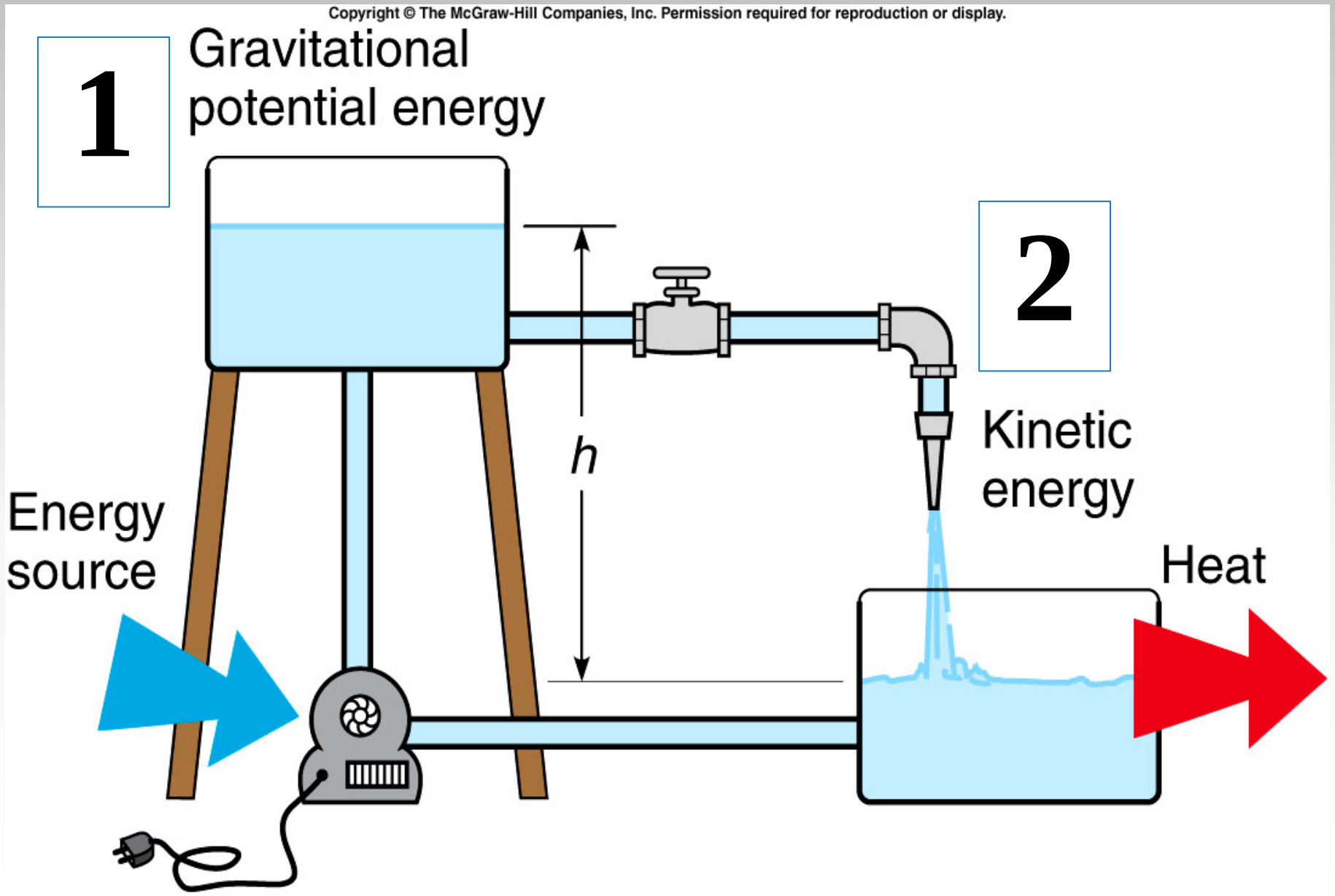


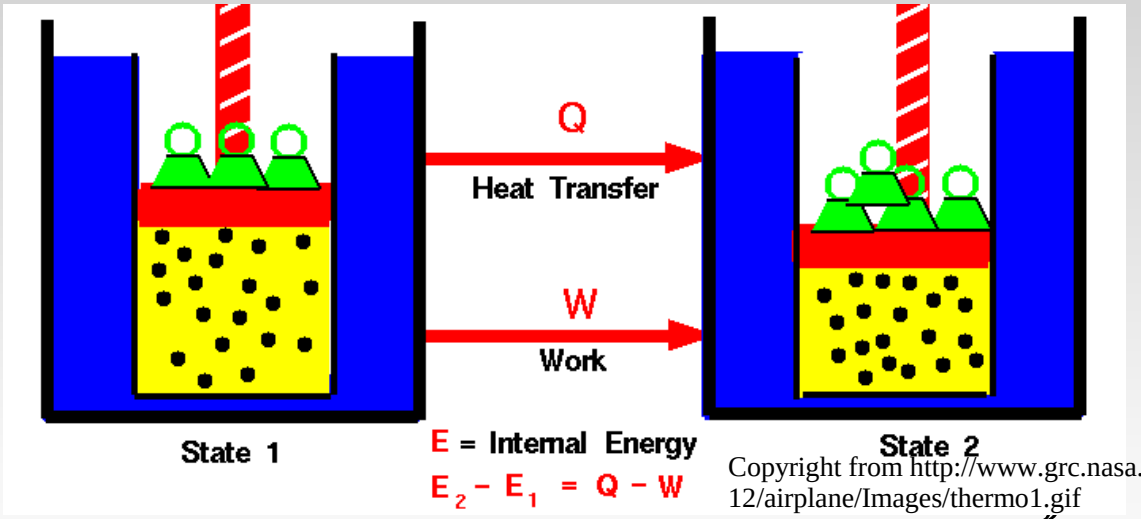
Figure 8.2

The Laws of Thermodynamics

1. กฎอนุรักษ์พลังงาน

:พลังงานไม่เคยถูกสร้างขึ้น หรือ ถูกทำลาย แต่มีการเปลี่ยนรูปไปมาเท่านั้น

$$\Delta E = q + w$$



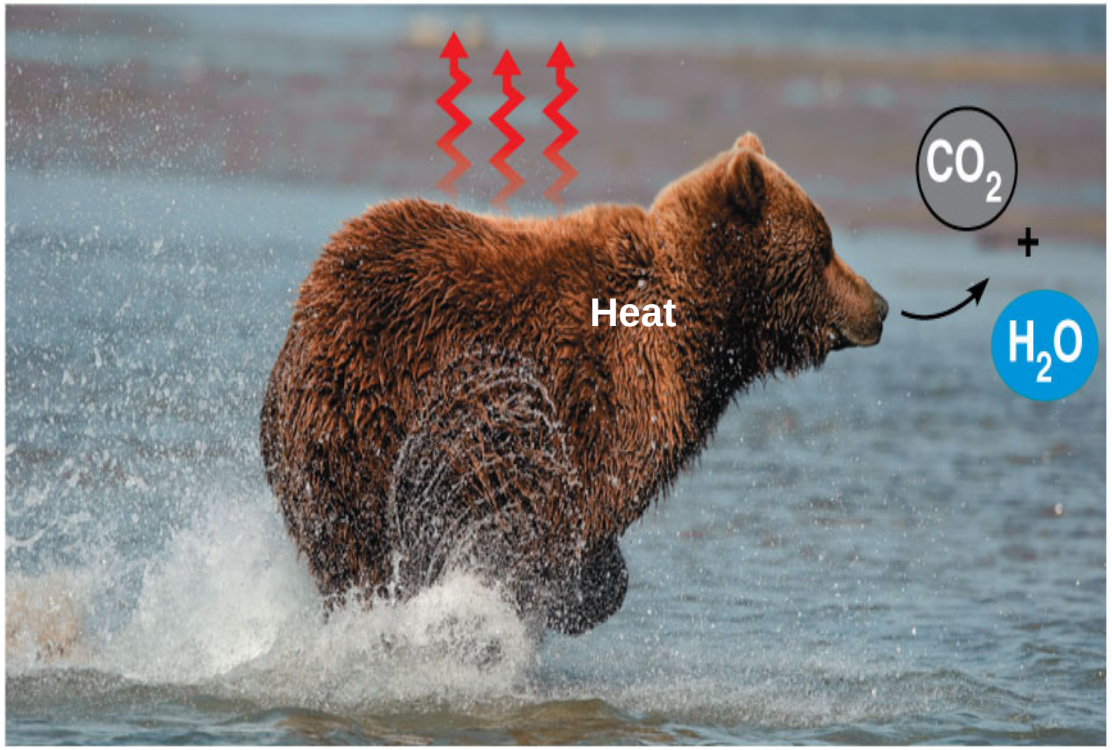
Copyright from http://www.grc.nasa.gov/WWW/k-12/airplane/Images/thermo1.gif

2. การเปลี่ยนสภาพของพลังงานจะมีผลให้เกิดความร้อนเกิดขึ้น เป็นการเพิ่มความไร้ระเบียบของระบบ

$$\Delta S = \text{ความไร้ระเบียบ (entropy)}$$

$$\Delta S_{Total} = \Delta S_{system} + \Delta S_{surroundings} > 0$$

(a) First law of thermodynamics

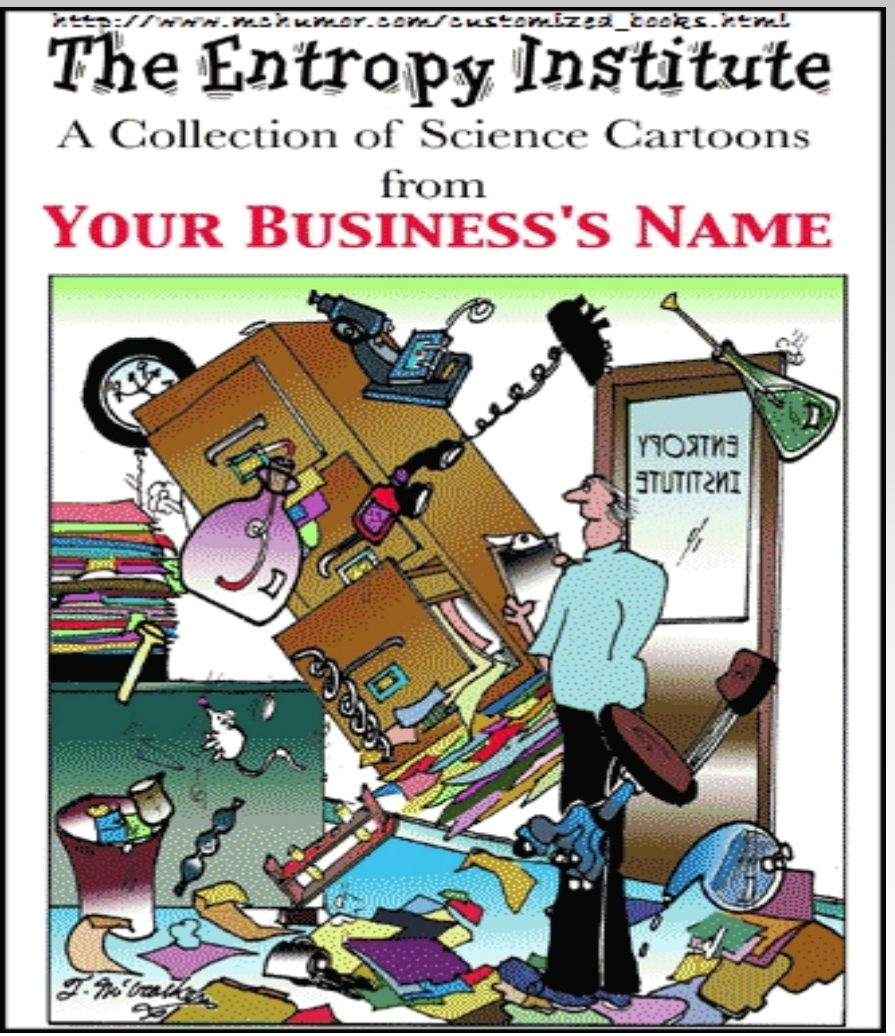


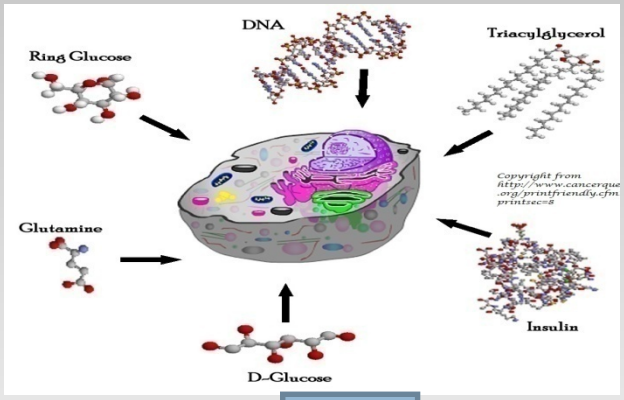
(b) Second law of thermodynamics

The evolution of more complex organisms does not violate the second law of thermodynamics

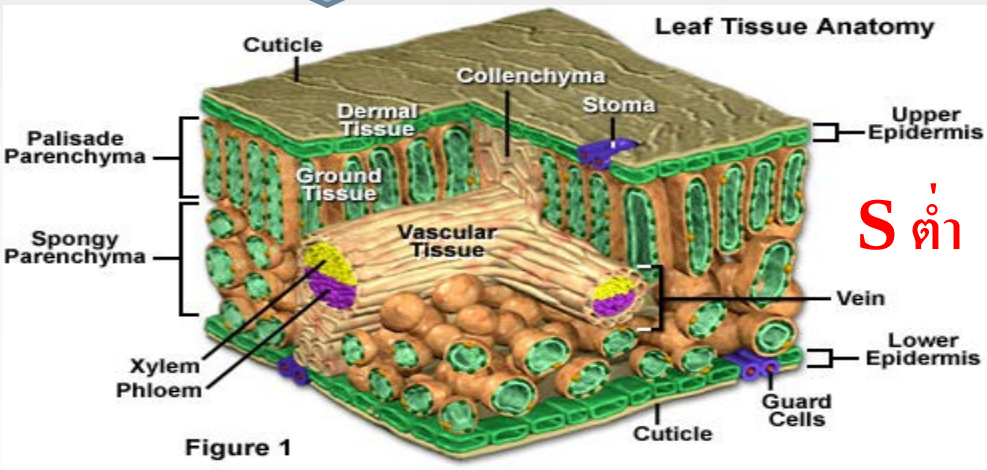
- กระบวนการตามปกติที่เกิดขึ้นเอง (sapontaneous process) จะเพิ่มค่า ΔS

- กระบวนการในสิ่งมีชีวิต มักจะ ลดค่า ΔS





S สูง

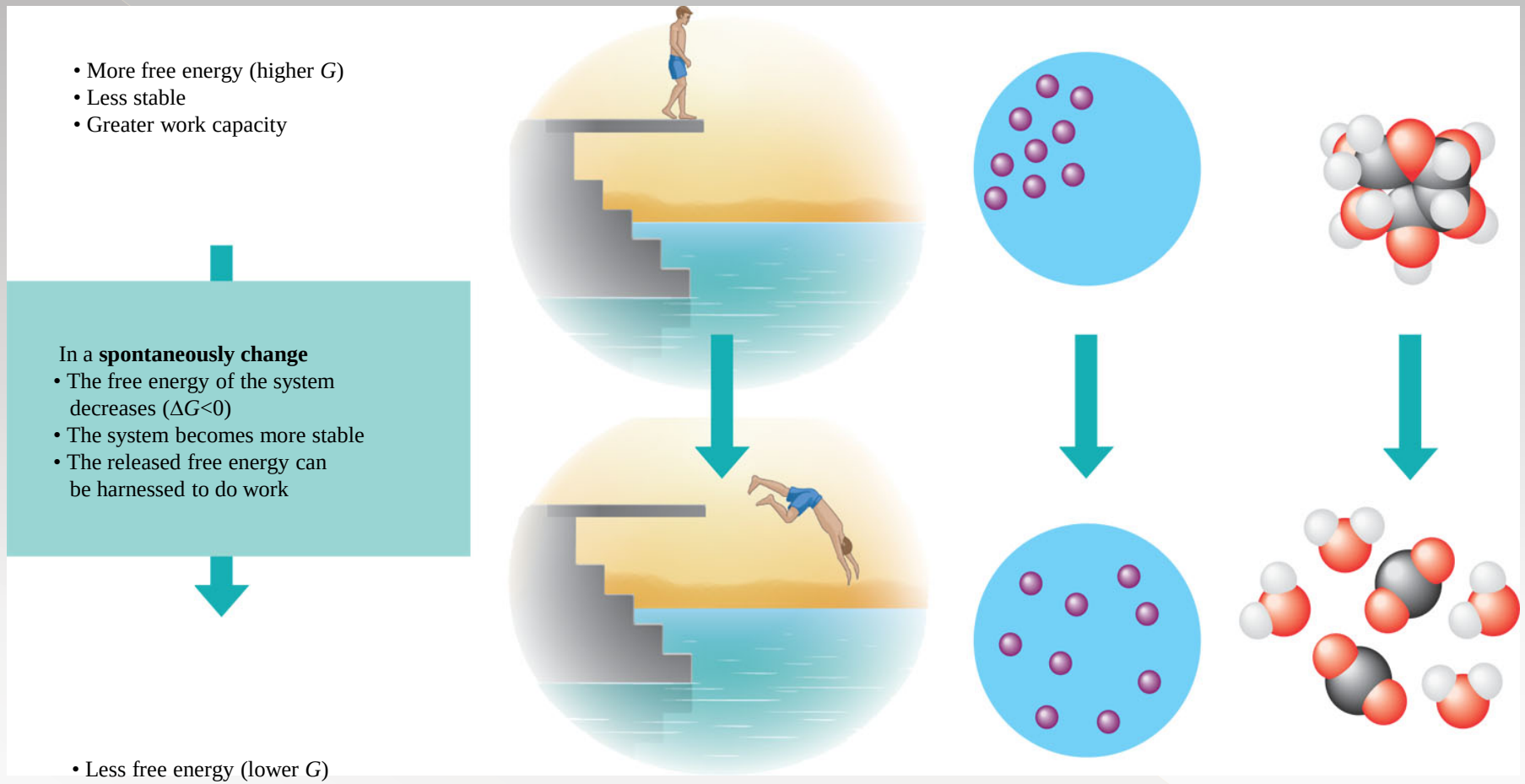


S ต่ำ

http://micro.magnet.fsu.edu/cells/leaftissue/images/leafstructurefigure1.jpg

Entropy (disorder) may decrease in an organism, but the universe's total entropy increases

Sapontaneous process



(a) **Gravitational motion.** Objects move spontaneously from a higher altitude to a lower one.

(b) **Diffusion.** Molecules in a drop of dye diffuse until they are randomly dispersed.

(c) **Chemical reaction.** In a cell, a sugar molecule is broken down into simpler molecules.

Metabolism

คือ ปฏิกิริยาเคมีที่เกิดขึ้นในร่างกายเพื่อการสร้างพลังงานในสิ่งมีชีวิต เพื่อใช้ในการดำรงชีวิต หรือนำมาสร้างโครงสร้างใหม่

Bioenergetics

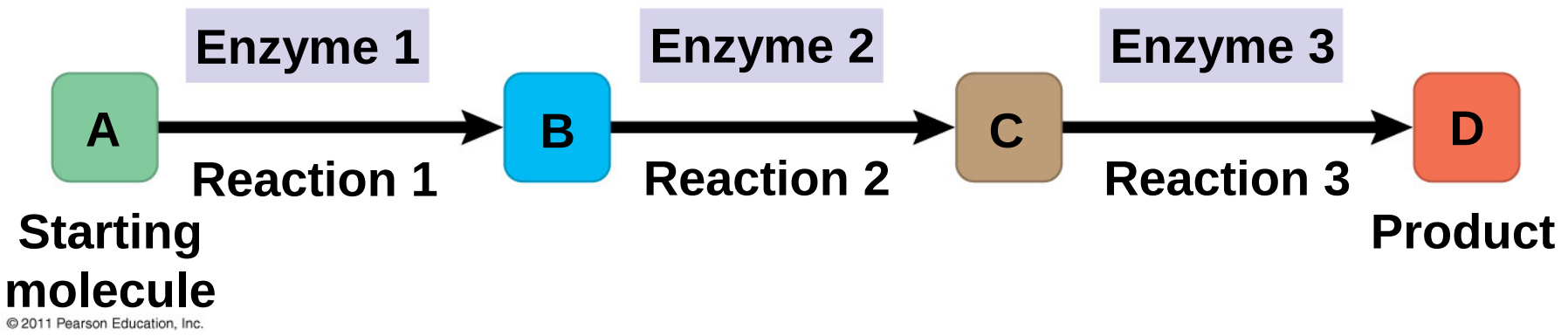
คือ การศึกษาเรื่องราวเฉพาะของพลังงานในสิ่งมีชีวิต

Metabolic pathway

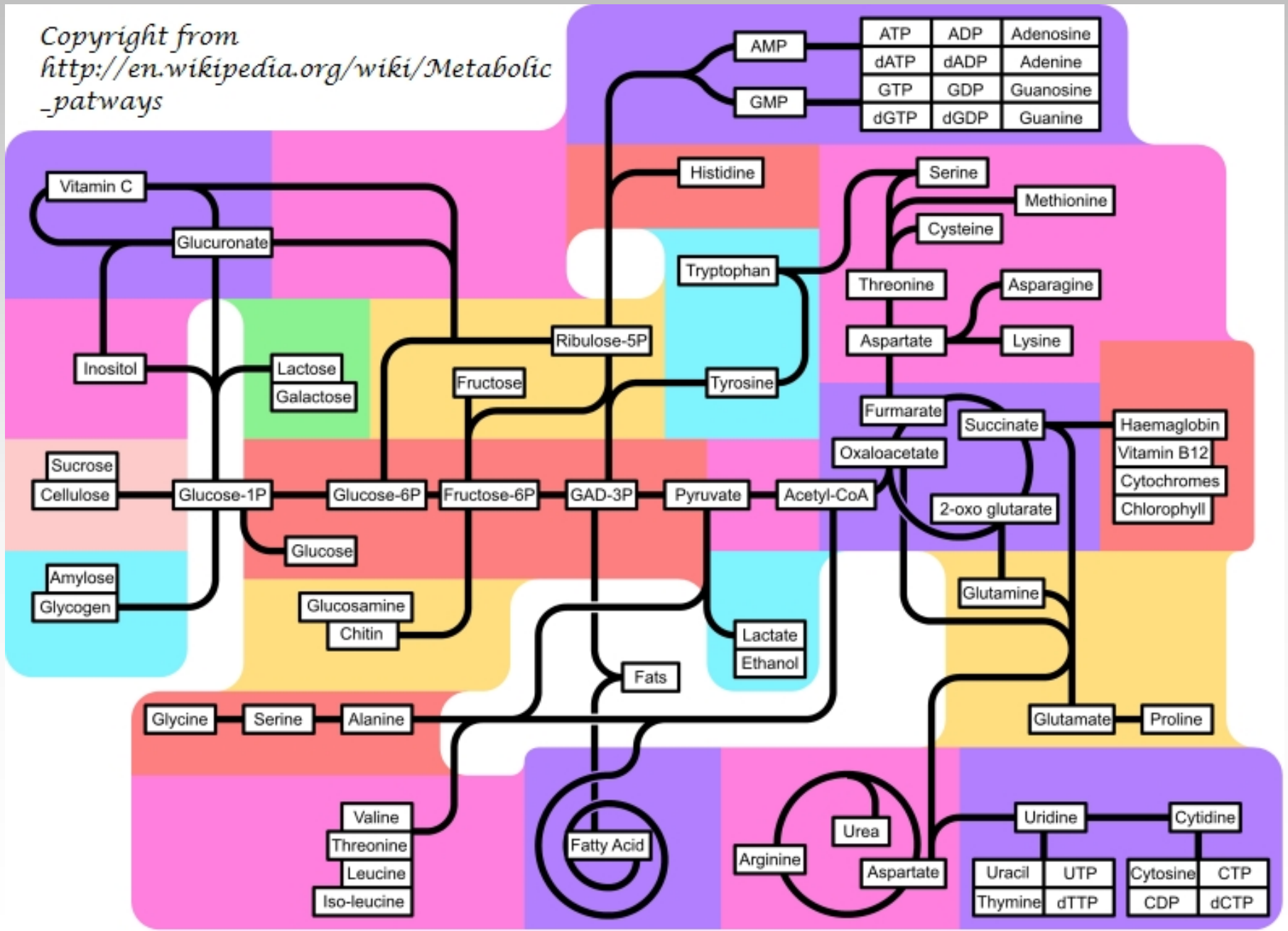
คือ ปฏิกิริยาเคมีที่เกิดขึ้นในขบวนการเมทาบอลิซึม จะมีลักษณะเป็นขั้นตอนตามลำดับ

Metabolic Pathways

- A **metabolic pathway** begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme



Metabolic pathway



Types of Metabolism

Anabolism

เป็นปฏิกิริยาเคมีที่เกิดขึ้นในร่างกายเพื่อการสังเคราะห์สารหรือการเปลี่ยน สภาพสารที่มีโมเลกุลเล็กให้เป็นสารที่มีโมเลกุลใหญ่ขึ้น

เพื่อ ให้เกิดการเจริญเติบโตและซ่อมแซมส่วนที่สึกหรอ

เป็น ใช้พลังงานที่มีอยู่ภายในเซลล์ซึ่งส่วนใหญ่ ได้จากการสลายโมเลกุลของสารเคมีพลังงานสูงพวก **adenosine triphosphate (ATP)**

The synthesis of protein from amino acids is an example of anabolism

Types of Metabolism

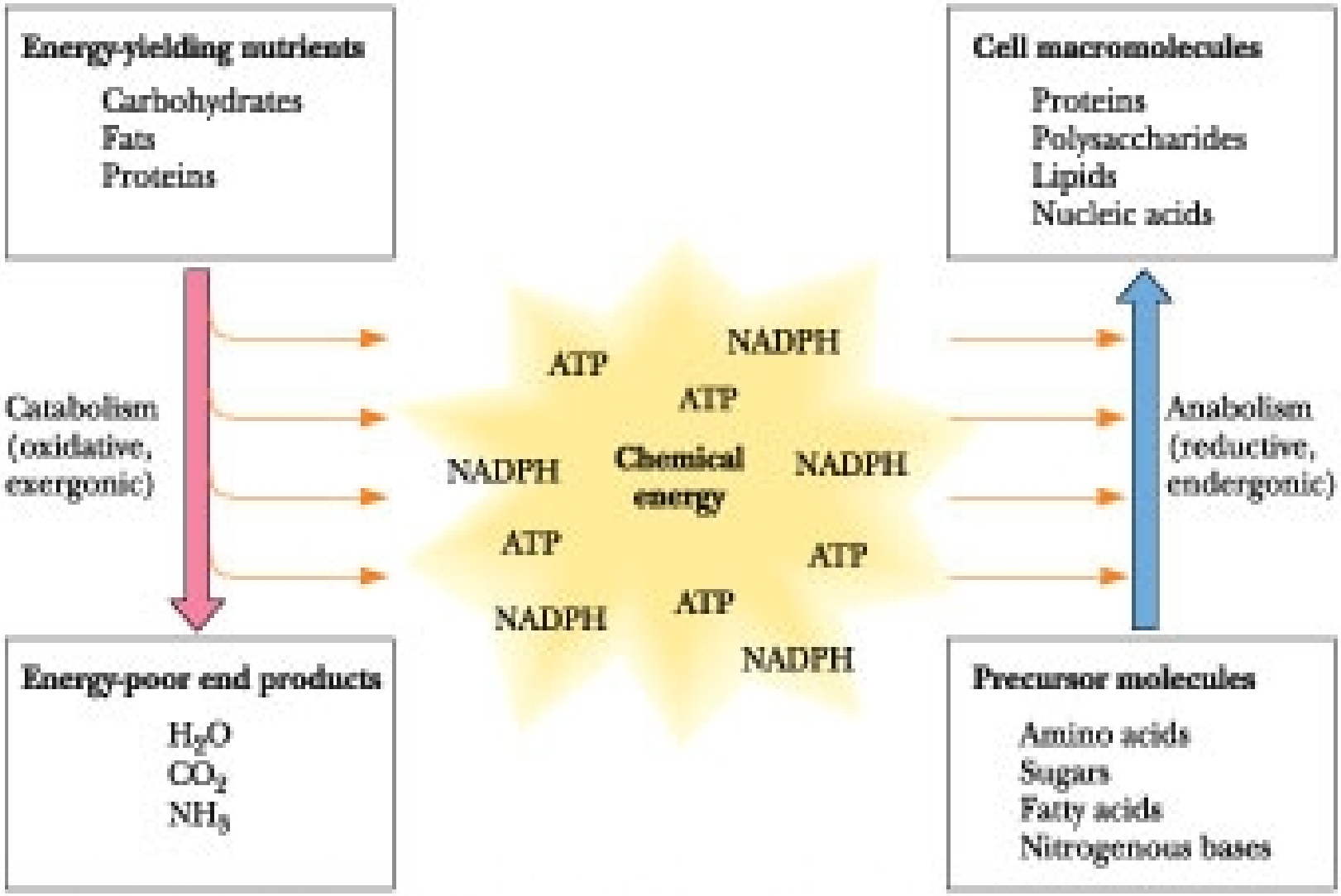
Catabolism

เป็นปฏิกิริยาเคมีที่เกิดขึ้นในร่างกายที่มีการสลายสาร คือเปลี่ยนสภาพจากสารที่มีโมเลกุลขนาดใหญ่ให้มีโมเลกุลขนาดเล็กลง

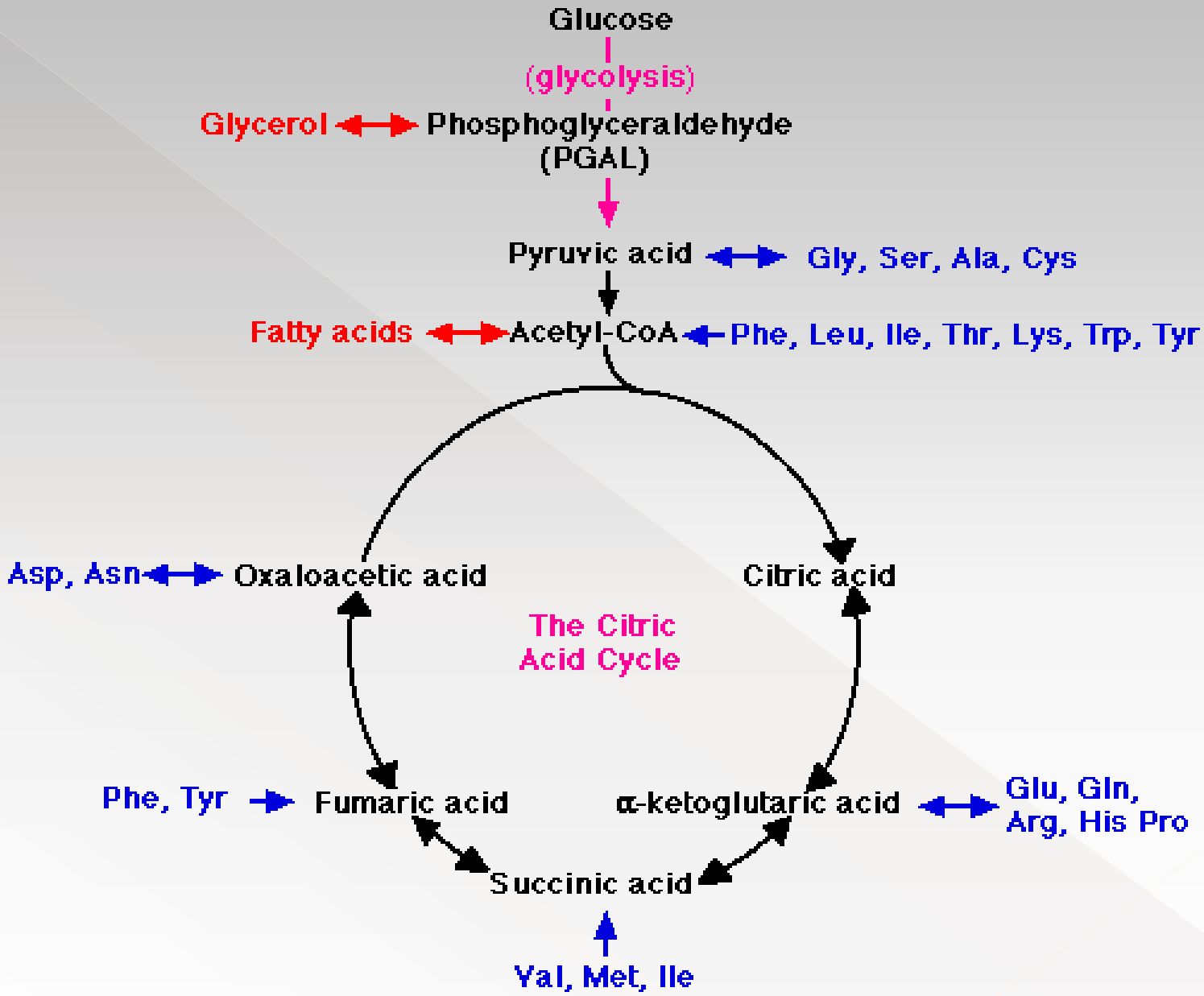
ผลจากการสลายสารดังกล่าว จะได้ พลังงาน **(ATP)** และของเสียออกมา

Cellular respiration, the breakdown of glucose in the presence of oxygen, is an example of a pathway of catabolism

Relative between anabolism and catabolism



Krebs Cycle connects the catabolic and anabolic pathways

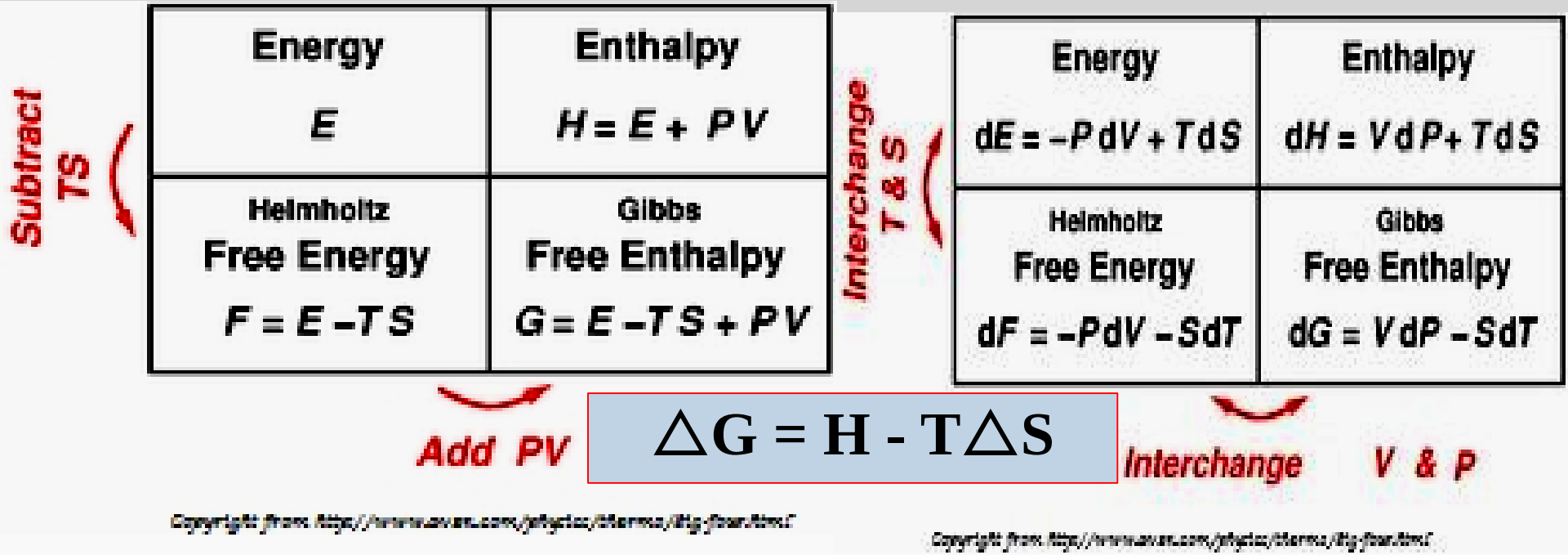


http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/I/IntermediaryMetabolism.html

Enthalpy (H)

คือ ปริมาณความร้อนที่ผ่านเข้าหรือออกจากระบบในกระบวนการที่ความดันคงที่

$$H = E + PV$$



F = free energy (พลังงานในระบบที่นำไปใช้ในการสร้างงานในสิ่งมีชีวิต)

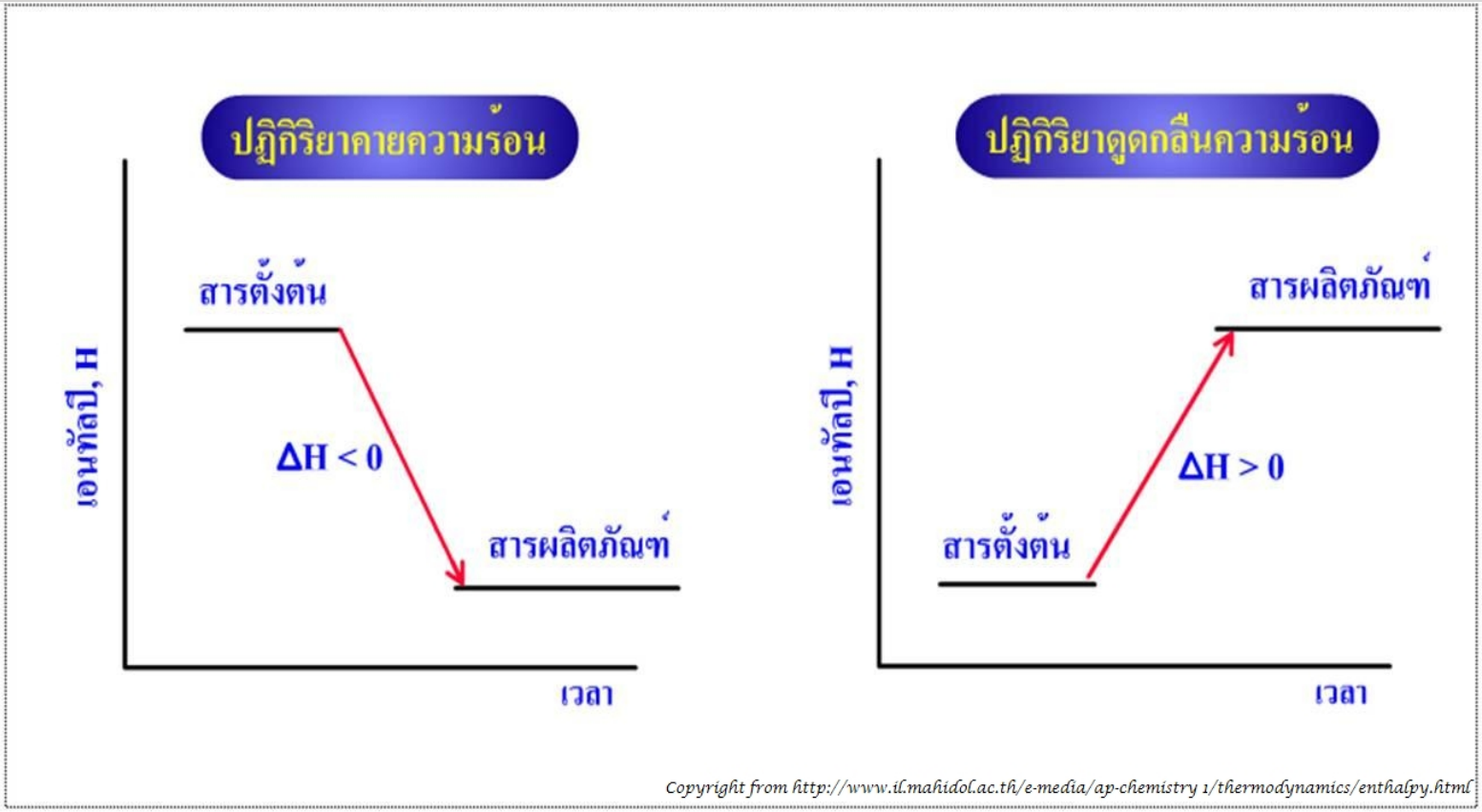
, *E* = the energy, *S* = the entropy, and *T* = temperature of the parcel

Enthalpy (H)

ทางปฏิริยาเคมี

enthalpy = พลังงานความร้อนที่อยู่ภายในพันธะเคมีของแต่ละโมเลกุล

$$\Delta H = H_{\text{สารผลิตภัณฑ์}} - H_{\text{สารตั้งต้น}}$$



$\Delta H < 0$ สำหรับกระบวนการคายความร้อน $\Delta H > 0$ สำหรับกระบวนการดูดความร้อน

The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously

- Biologists want to know which reactions occur spontaneously and which require input of energy
- To do so, they need to determine energy changes that occur in chemical reactions

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

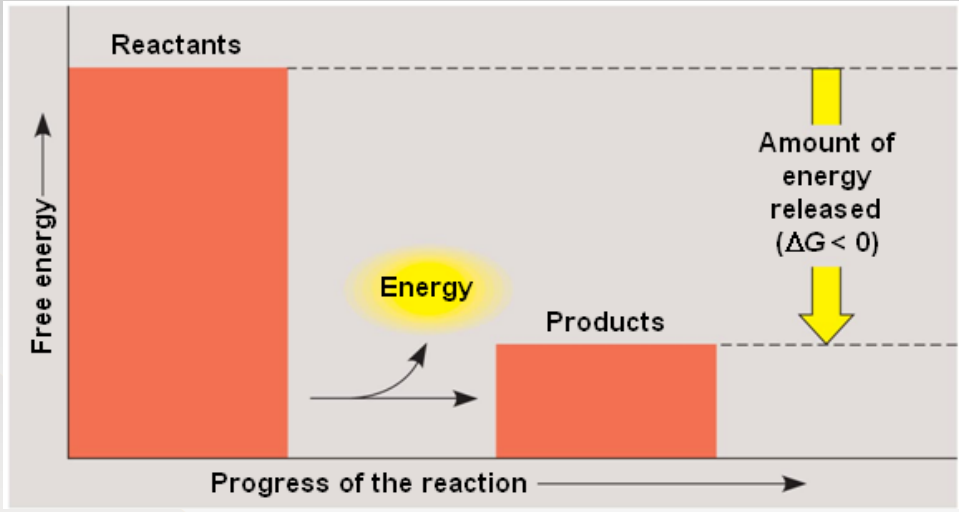
- *Free Energy* = *Total Energy – Unusable Energy*
- Only processes with a negative ΔG are spontaneous

Free energy (G)

พลังงานในระบบที่นำไปใช้ในการสร้างงานในสิ่งมีชีวิต

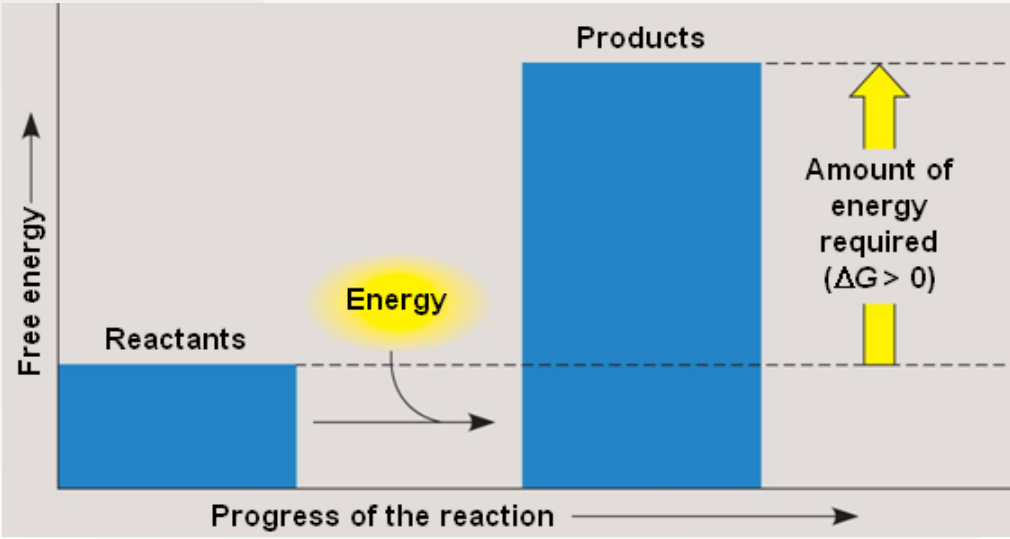
Exergonic and Endergonic Reactions in Metabolism

- EXERGONIC reactions (- ΔG)
- Release energy
- are spontaneous

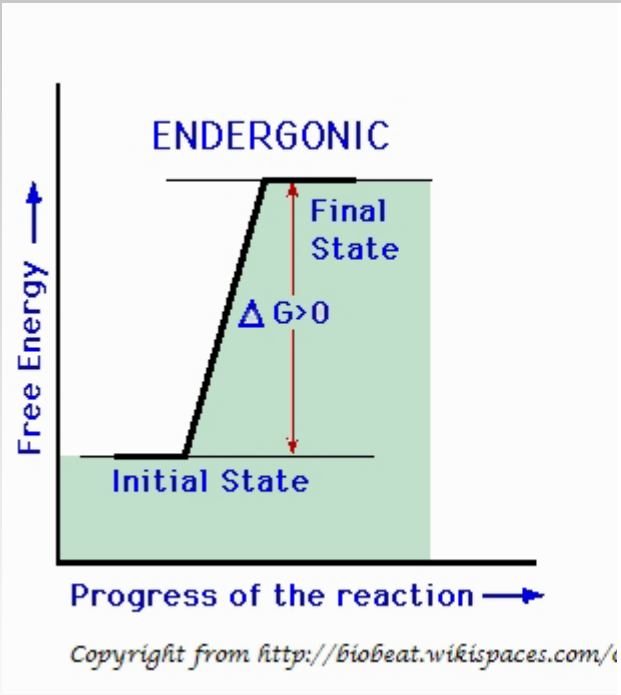


ENDERGONIC reactions (+ ΔG)

- Absorb energy from their surroundings
- are non-spontaneous



Free energy (G)



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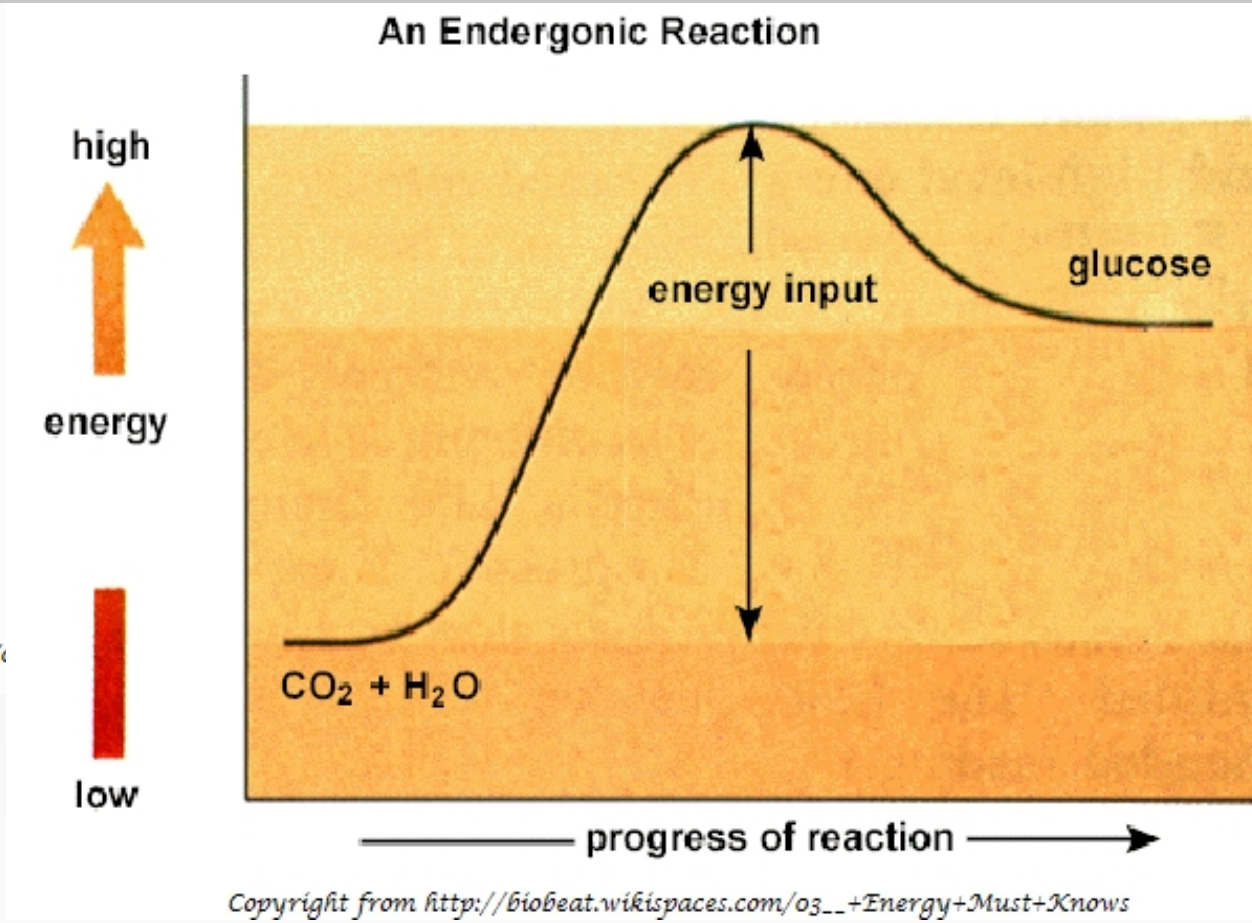

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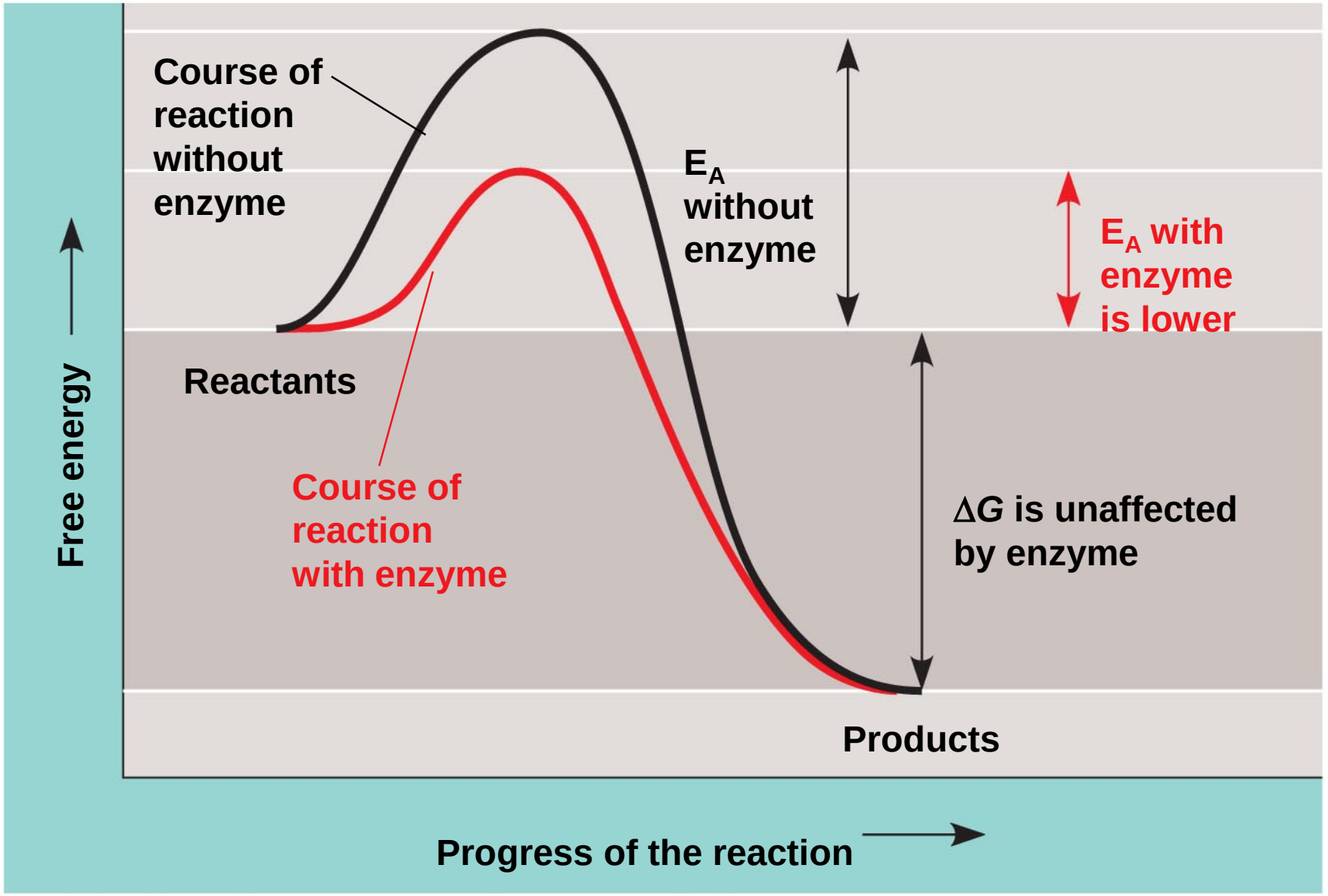
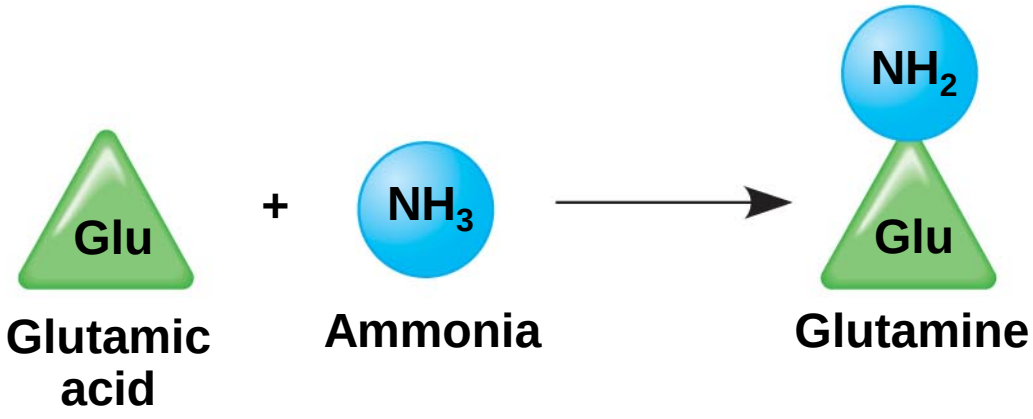
- An **exergonic reaction** proceeds with a net release of free energy and is spontaneous
- An **endergonic reaction** absorbs free energy from its surroundings and is nonspontaneous



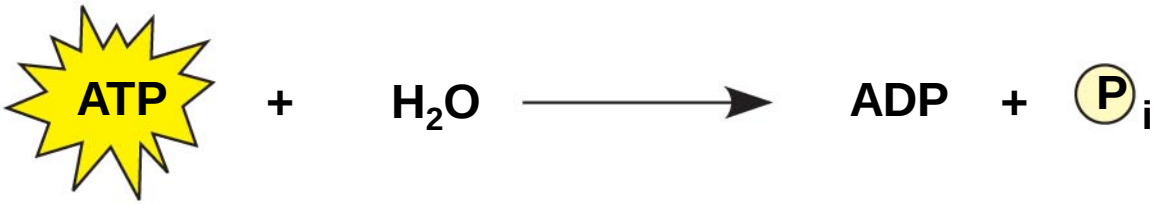
ENZYMES work by LOWERING ACTIVATION ENERGY;

Endergonic reaction:
DG is positive, reaction is not spontaneous



$\Delta G = +3.4$ kcal/mol

Exergonic reaction:
DG is negative, reaction is spontaneous



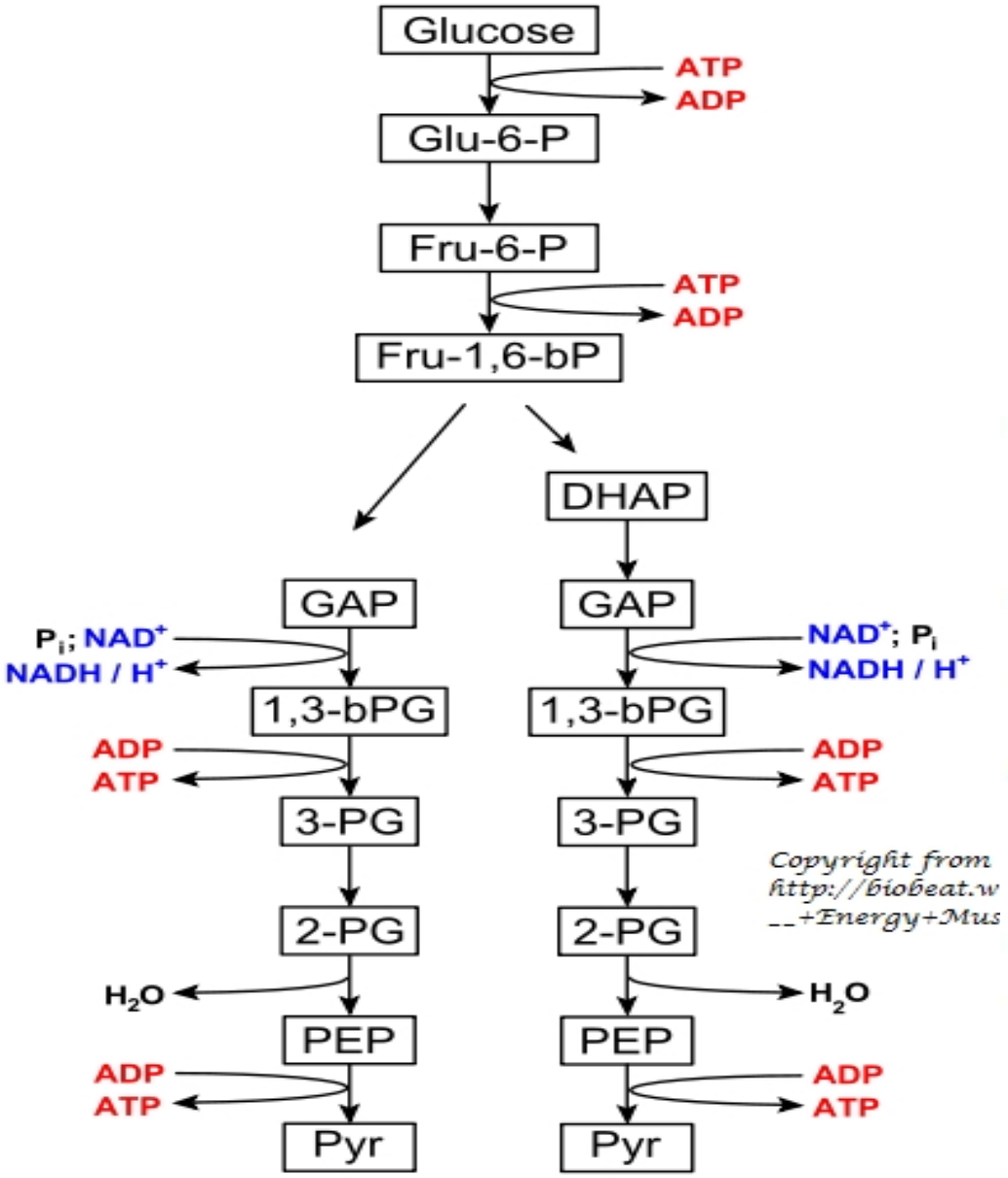
$\Delta G = -7.3$ kcal/mol

Coupled reactions:
Overall DG is negative;
Together, reactions are spontaneous

$\Delta G = -3.9$ kcal/mol

Free enery (G)

พลังงานในระบบที่นำไปใช้ในการสร้างงานในสิ่งมีชีวิต



EXERGONIC

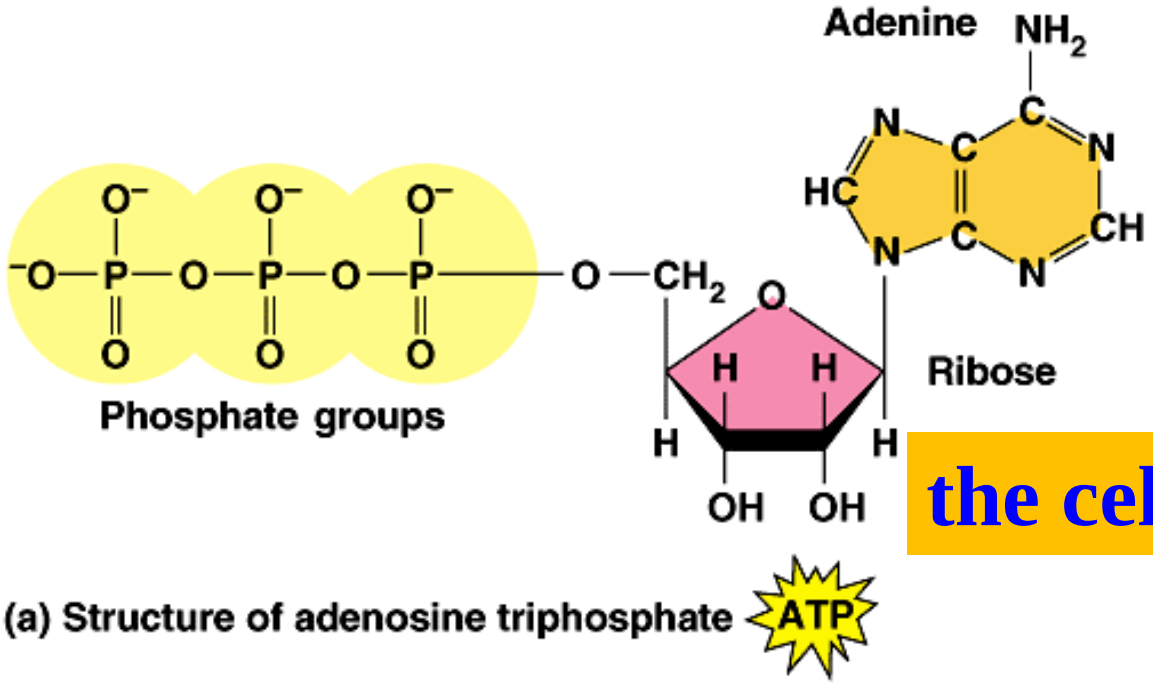
Change in free energy for each step of glycolysis[7]

Step	Reaction	ΔG / (kJ/mol)
1	glucose + ATP^{4-} → glucose-6-phosphate^{2-} + ADP^{3-} + H^+	-34
2	glucose-6-phosphate^{2-} → fructose-6-phosphate^{2-}	-2.9
3	fructose-6-phosphate^{2-} + ATP^{4-} → fructose-1,6-bisphosphate^{4-} + ADP^{3-} + H^+	-19
4	fructose-1,6-bisphosphate^{4-} → dihydroxyacetone phosphate^{2-} + glyceraldehyde-3-phosphate^{2-}	-0.23
5	dihydroxyacetone phosphate^{2-} → glyceraldehyde-3-phosphate^{2-}	2.4
6	glyceraldehyde-3-phosphate^{2-} + P_i^{2-} + NAD^+ → 1,3-bisphosphoglycerate^{4-} + NADH + H^+	-1.29
7	1,3-bisphosphoglycerate^{4-} + ADP^{3-} → 3-phosphoglycerate^{3-} + ATP^{4-}	0.09
8	3-phosphoglycerate^{3-} → 2-phosphoglycerate^{3-}	0.83
9	2-phosphoglycerate^{3-} → phosphoenolpyruvate^{3-} + H_2O	1.1
10	phosphoenolpyruvate^{3-} + ADP^{3-} + H^+ → pyruvate$^-$ + ATP^{4-}	-23.0

ATP powers cellular work by coupling exergonic reactions to endergonic reactions

- A cell does three main kinds of work
  - Chemical
  - Transport
  - Mechanical
- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP

Adenosine triphosphate(ATP)



the cell's energy shuttle

(a) Structure of adenosine triphosphate ATP

Adenosine triphosphate (ATP)

Inorganic phosphate

Adenosine diphosphate (ADP)

(b) Hydrolysis of ATP

3 types of cellular work by the hydrolysis of ATP

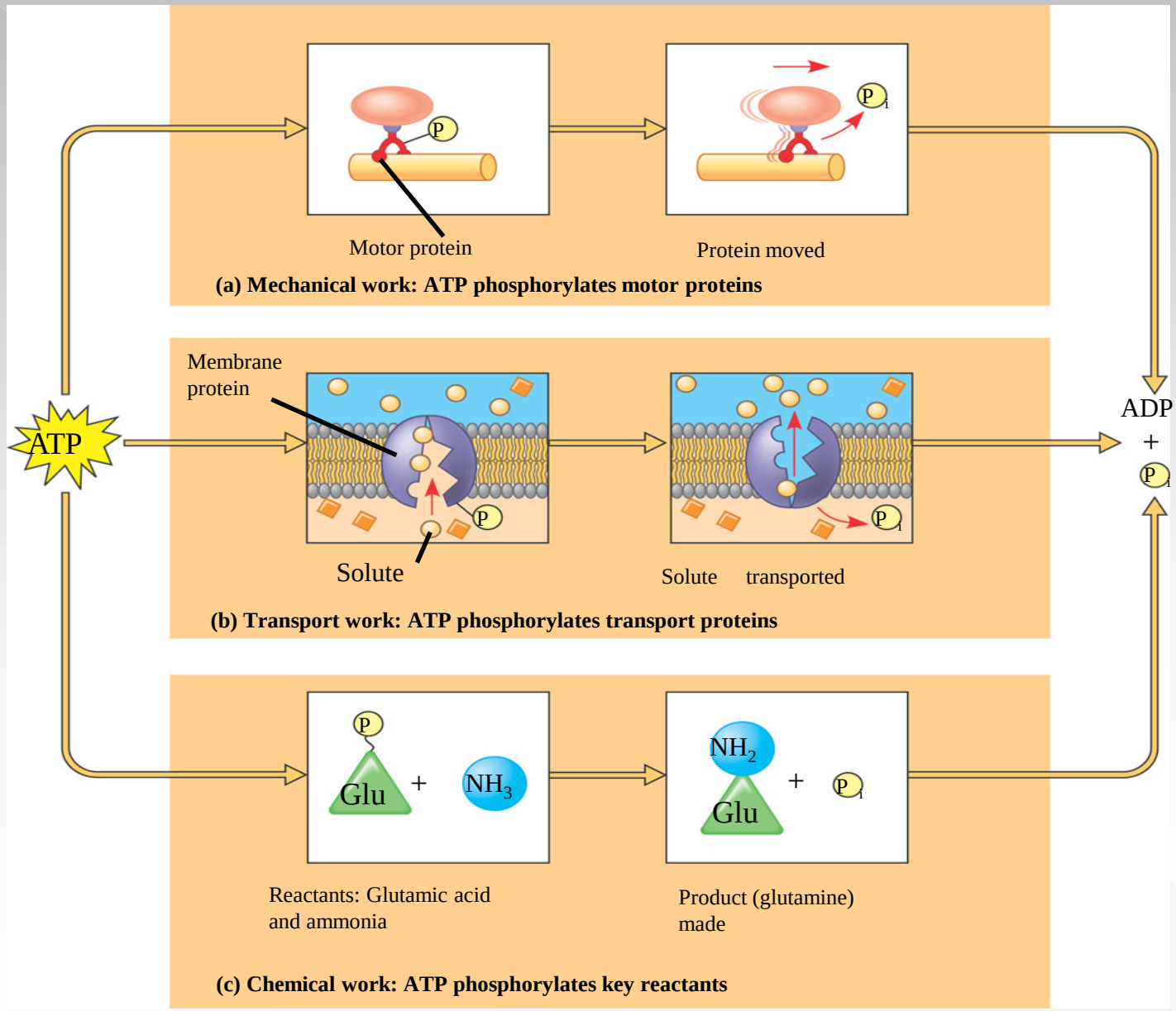
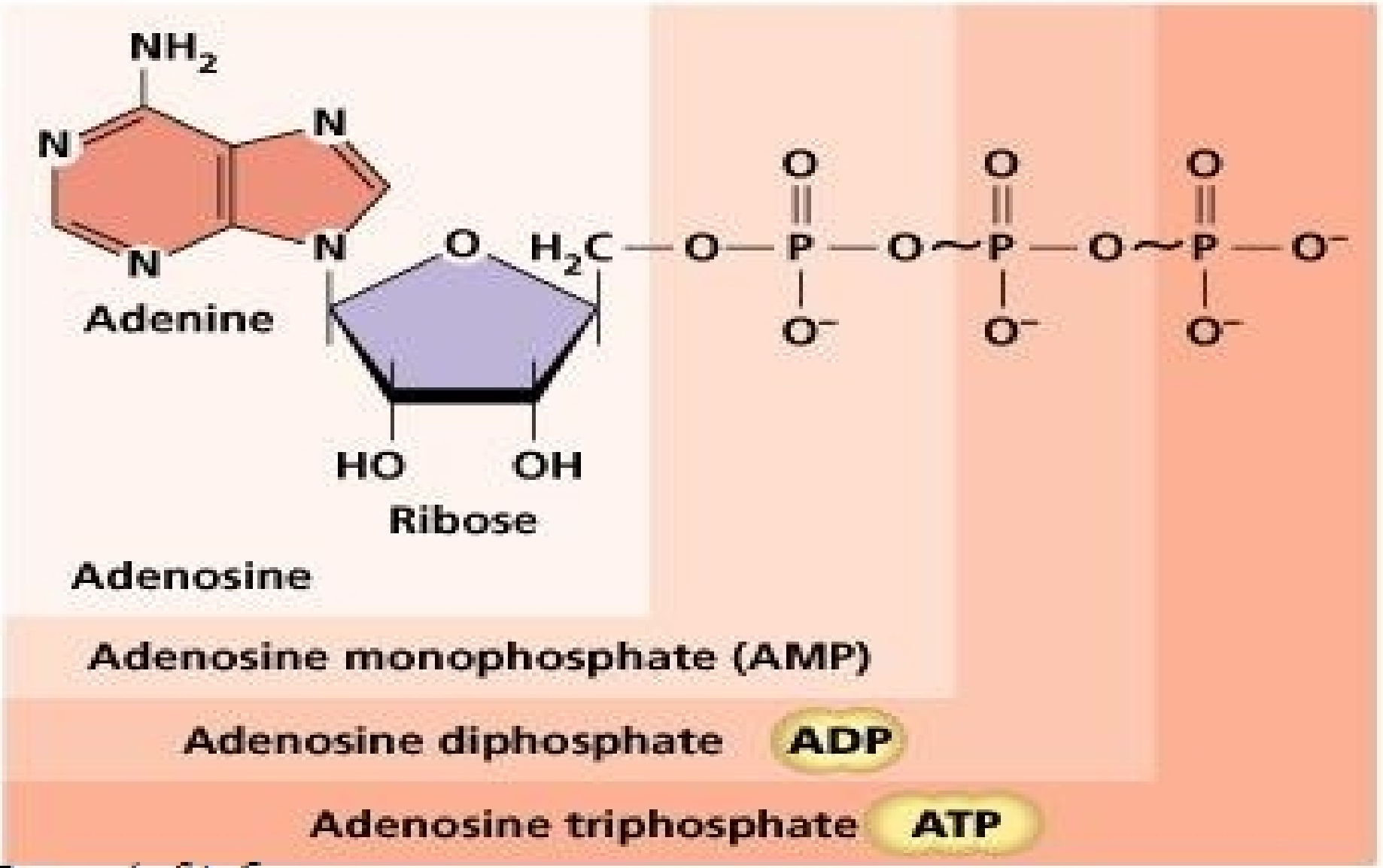
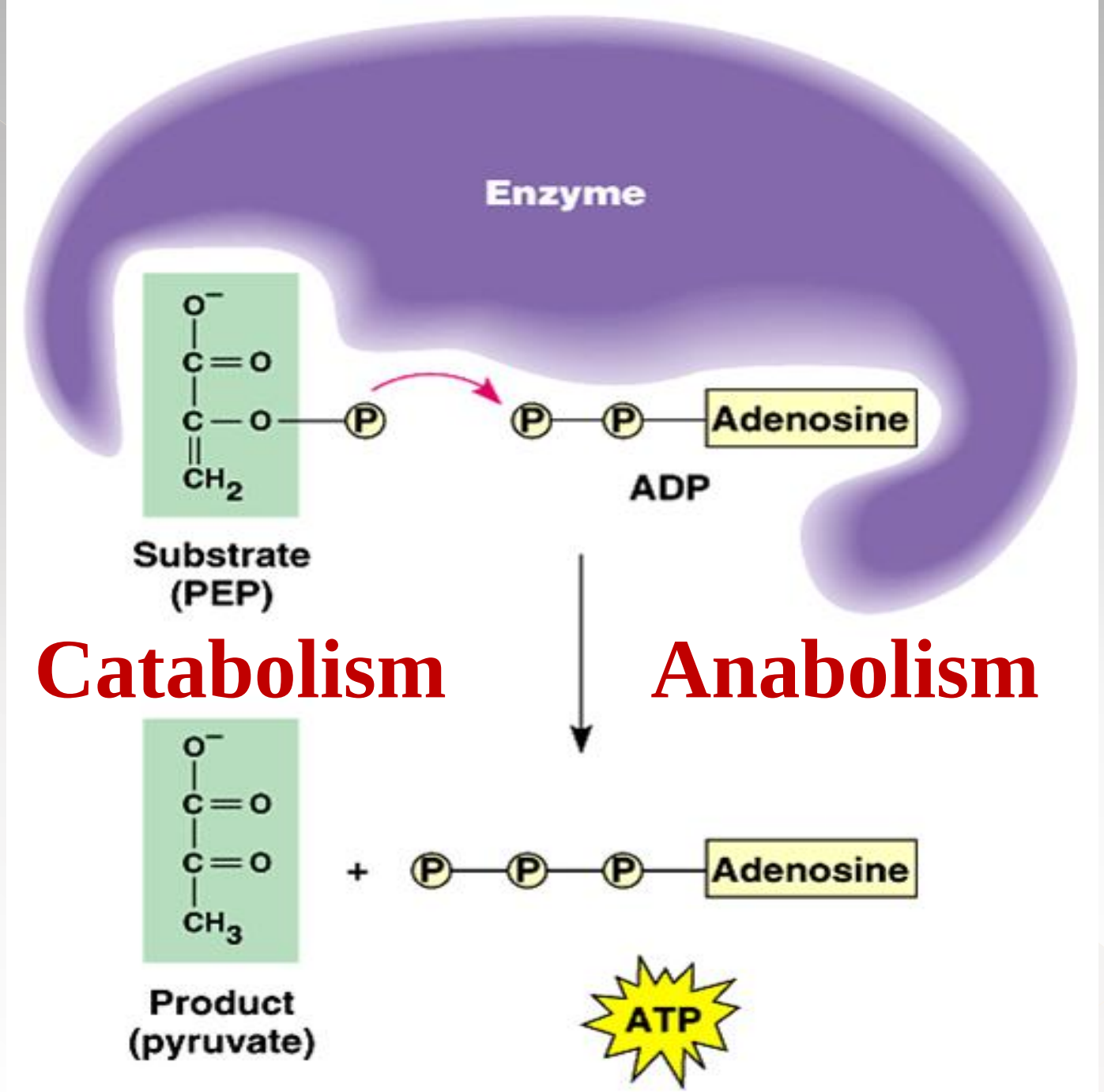


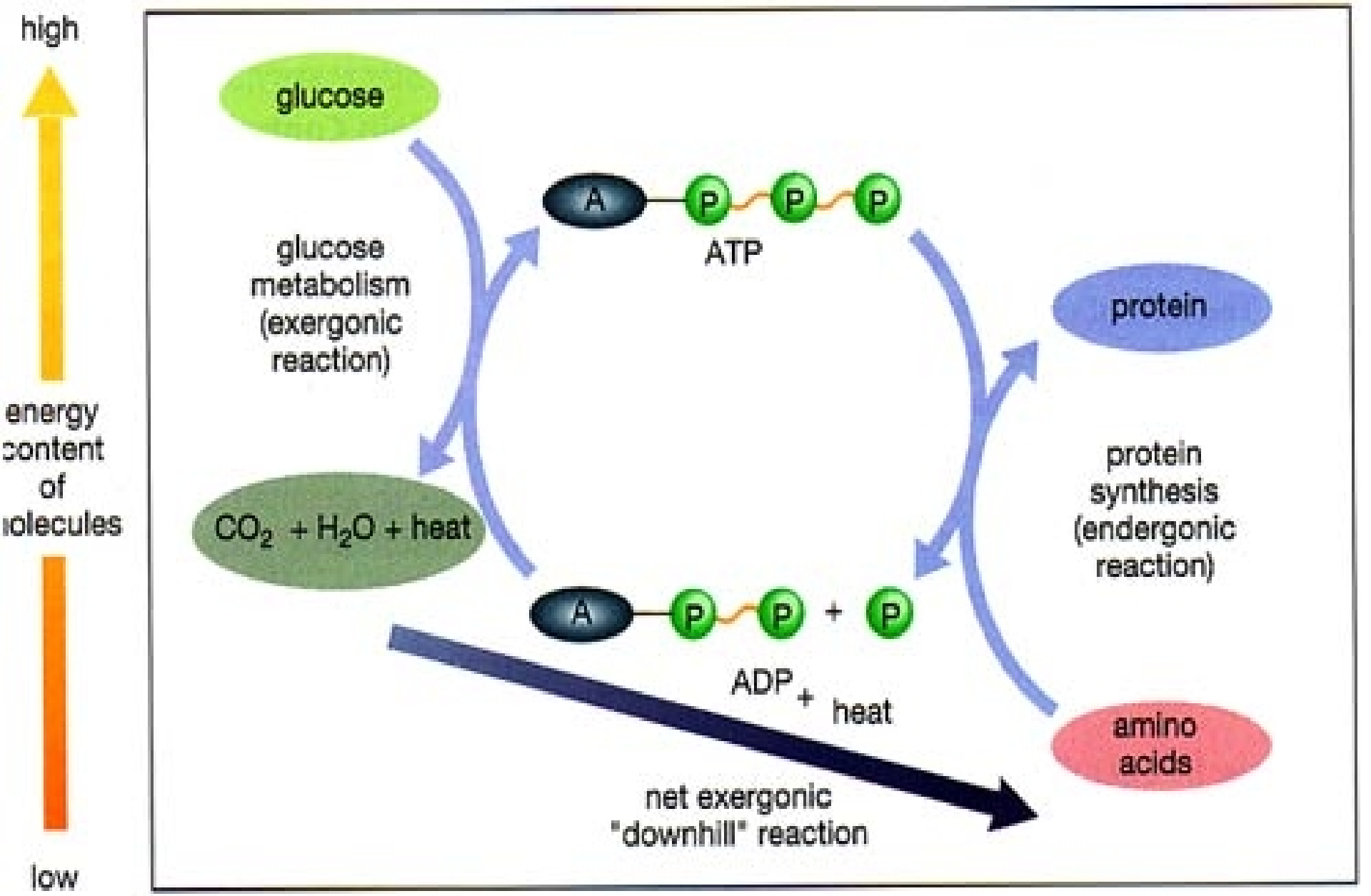
Figure 8.11

Adenosine triphosphate(ATP)



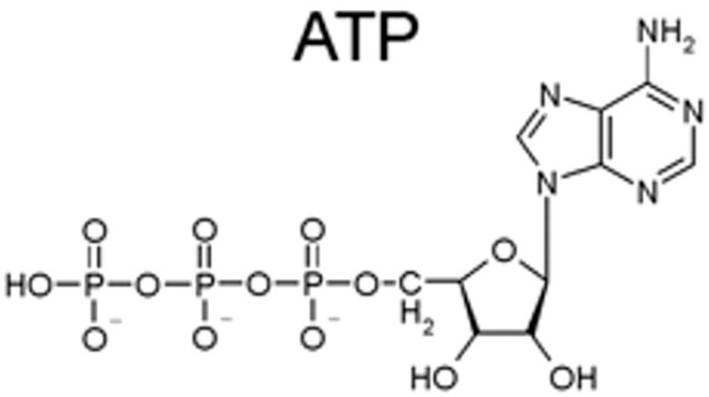


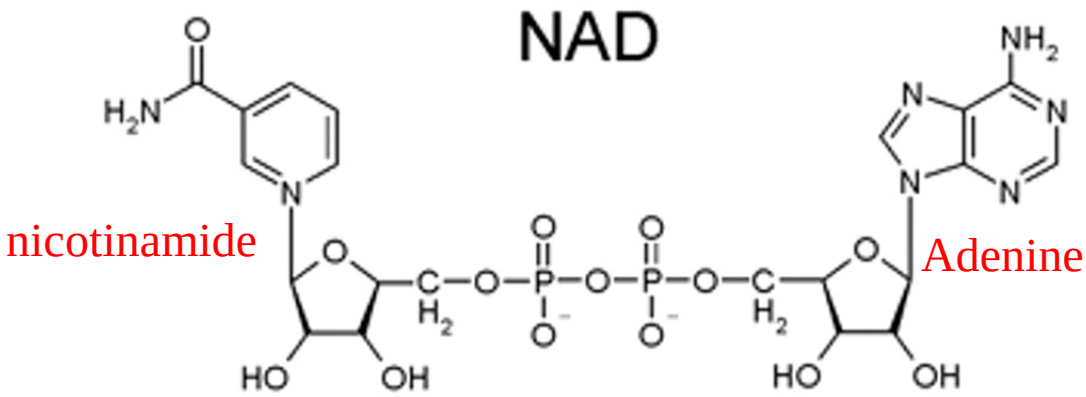
Coupled Reaction



Enery substrats

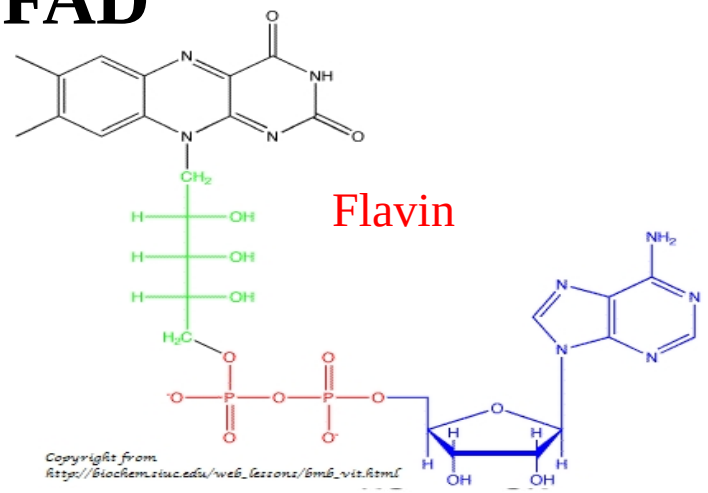
Nicotinamide adenine dinucleotide



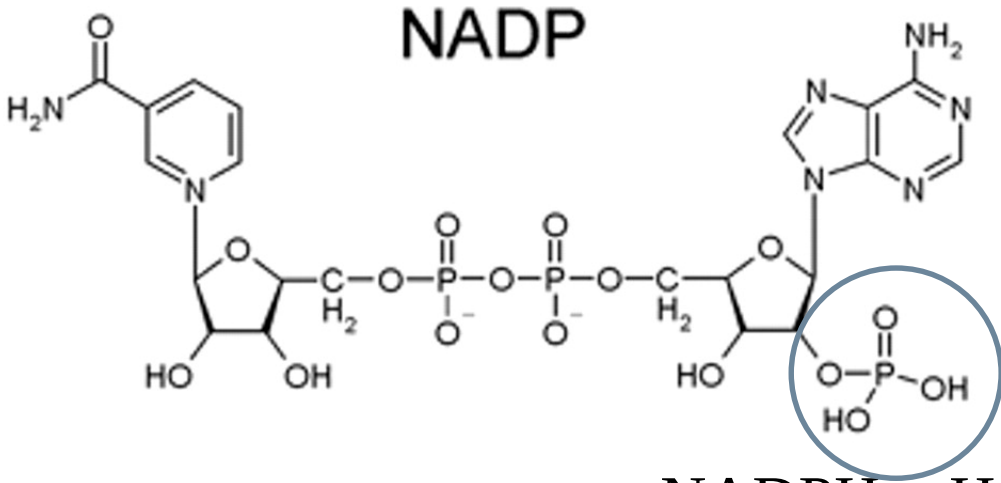


$NAD^+ + 2e^- + 2H^+ \rightarrow NADH + H^+$

FAD



$NAD^+ + 2e^- + 2H^+ \rightarrow FADH_2$



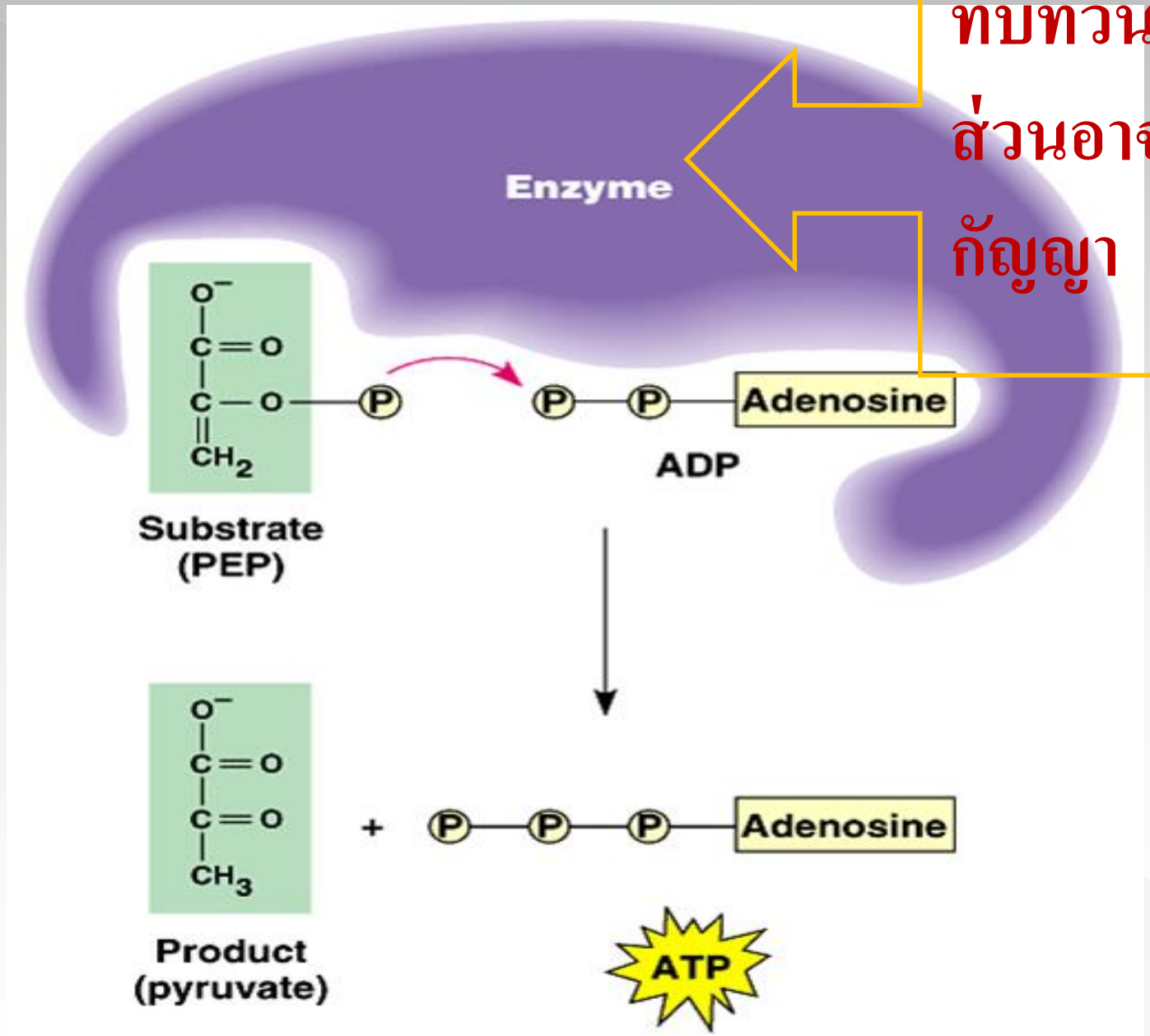
$NADP^+ + 2e^- + 2H^+ \rightarrow NADPH + H^+$

Flavin adenine dinucleotide

Nicotinamide adenine dinucleotide phosphate

Enzyme

ทบทวนเนื้อหา
ส่วนอาจารย์
กัญญา

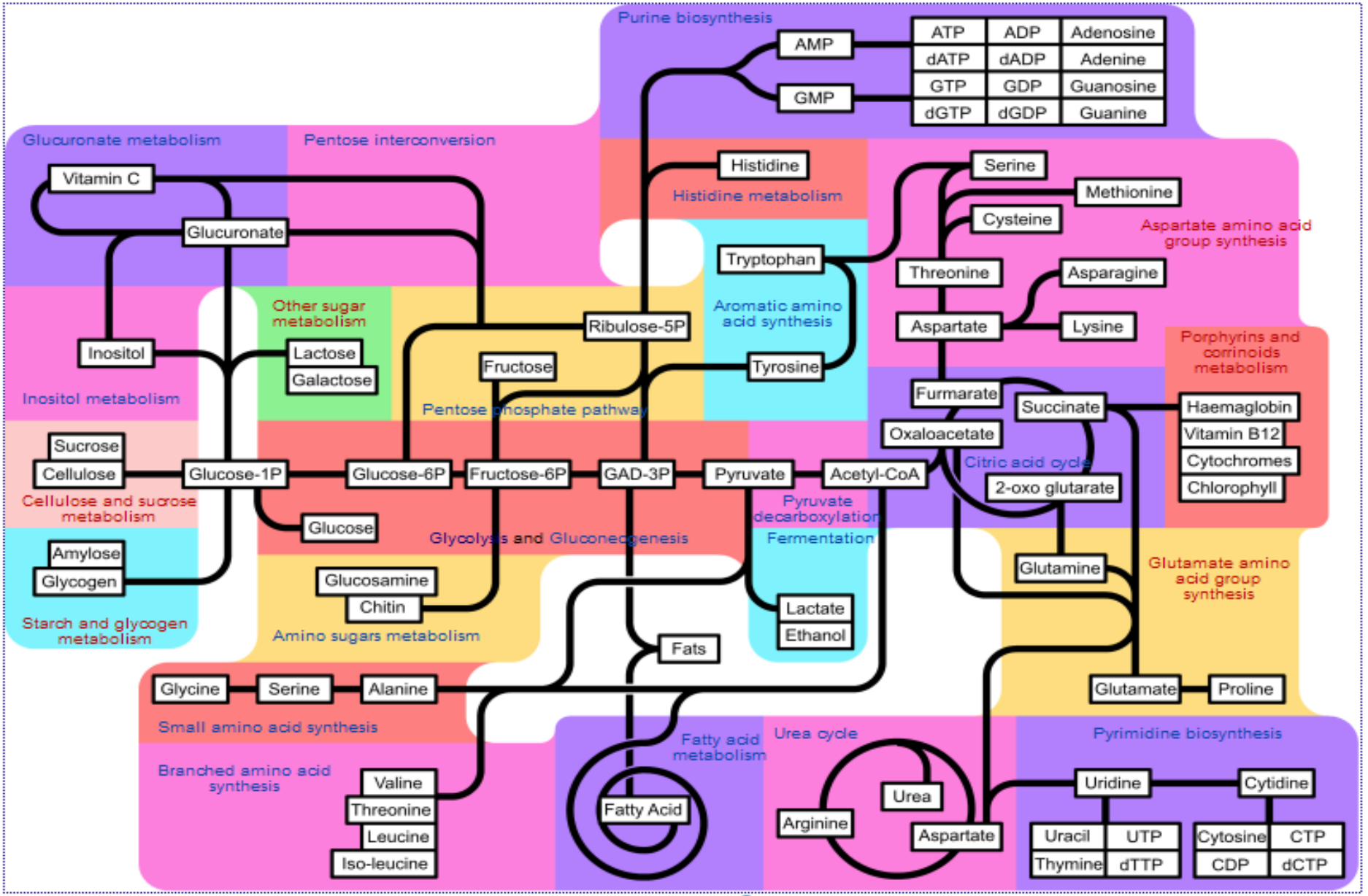


Study of metabolic pathway

1. ***Major metabolic pathway***
   (เทอม ที่ 2 ในรายวิชา คม 325)

2. ***Specific metabolic pathway***
   (ในบาง pathways ที่น่าสนใจ)

Major metabolic pathway



v · d · e

All pathway labels on this image are links, simply click to access the article.

Main pathways (all living organisms)

- Glycolysis
- Aerobic respiration and/or Anaerobic respiration
- Citric acid cycle / Krebs cycle
- Oxidative phosphorylation

Other pathways (most) :

- Fatty acid oxidation (β-oxidation)
- Gluconeogenesis
- Amino acid metabolism
- Urea cycle / Nitrogen metabolism
- Nucleotide metabolism
- Glycogen synthesis / Glycogen storage
- Pentose phosphate pathway (hexose monophosphate shunt)
- Porphyrin synthesis (or heme synthesis) pathway
- Lipogenesis
- HMG-CoA reductase pathway
  (isoprene prenylation chains, see cholesterol)

Synthesis of energetic compounds from non-living matter:

- Photosynthesis (plants, algae, cyanobacteria)
- Chemosynthesis (some bacteria)