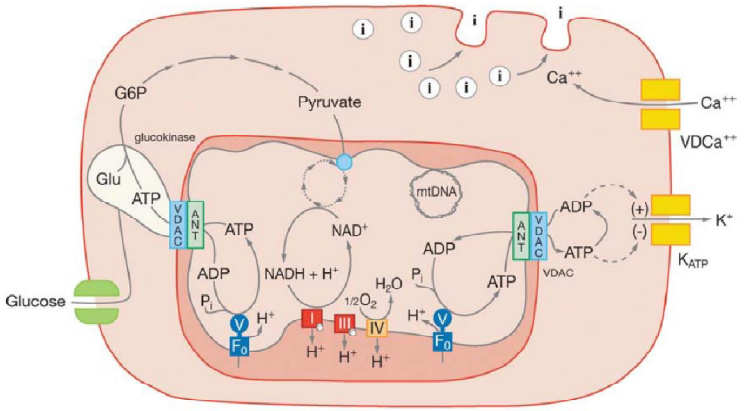
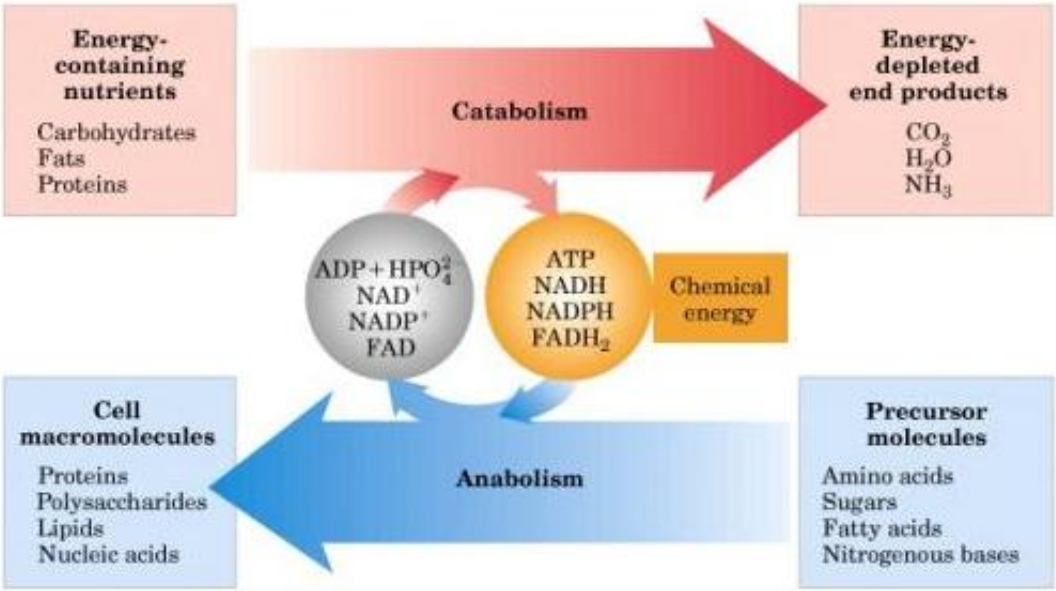
Metabolic Networks

Metabolism

Metabolism is the totality of all the chemical reactions that operate in a living organism.



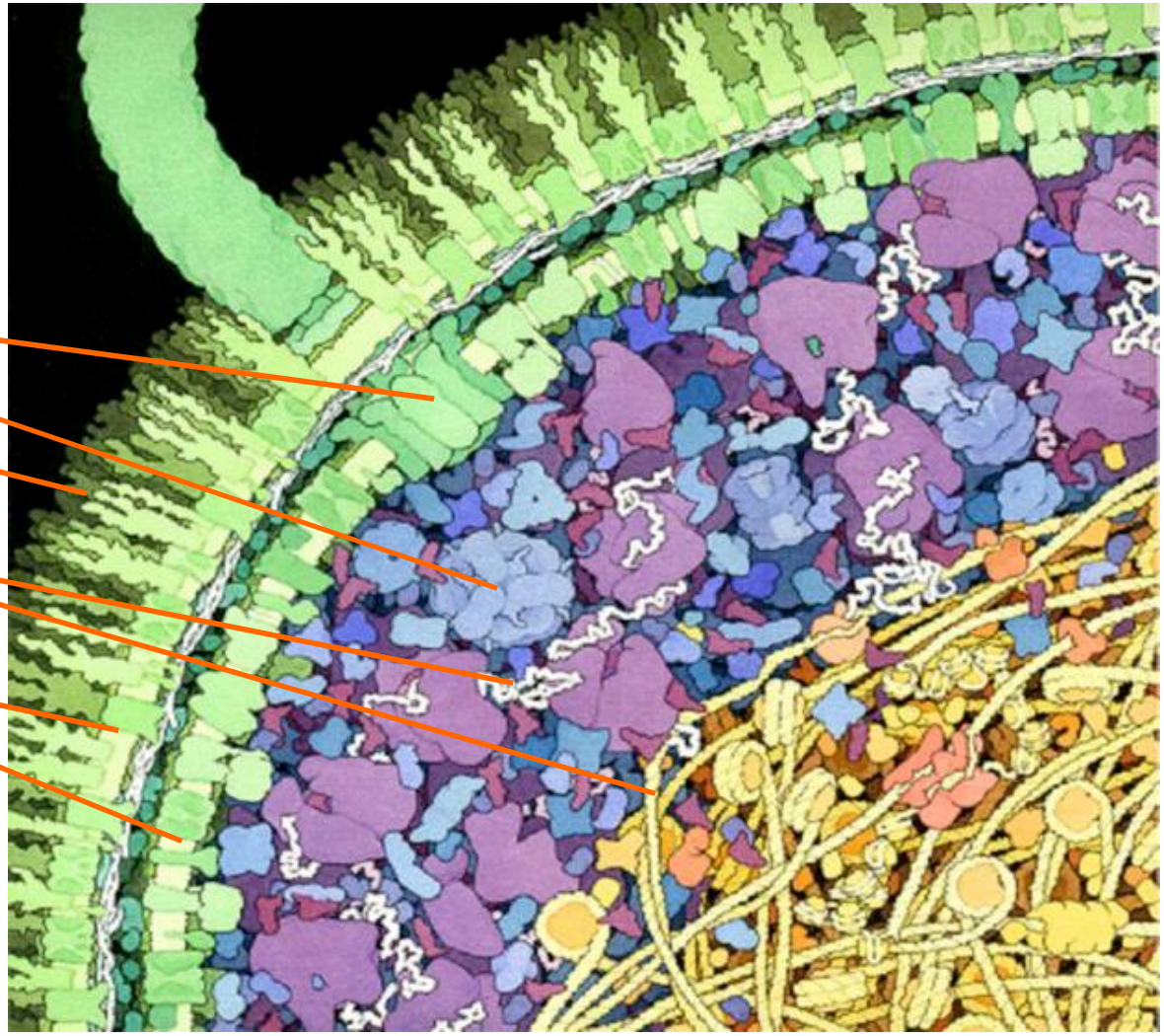


Cells are chemical factories

Metabolism?

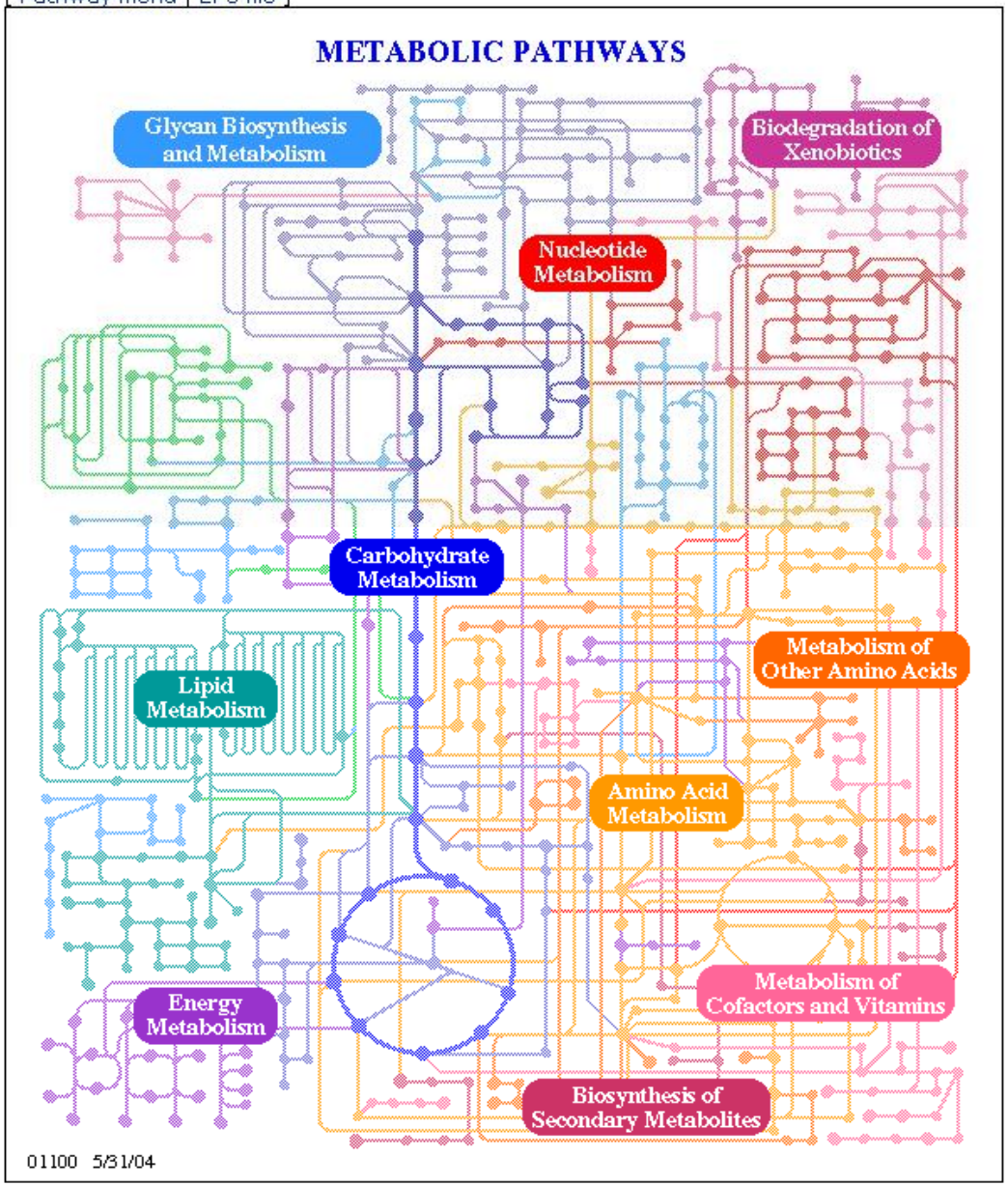
- Key classes of **biochemicals**:

- amino acids
  - proteins
- carbohydrates
  - bacterial envelope
- nucleotides
  - genetic material
- lipids
  - membranes
- coenzymes
  - transfer chemical groups
- minerals
  - assist in biochemical transformations



KEGG Metabolism - Reference pathway

[Pathway menu | EPS file]



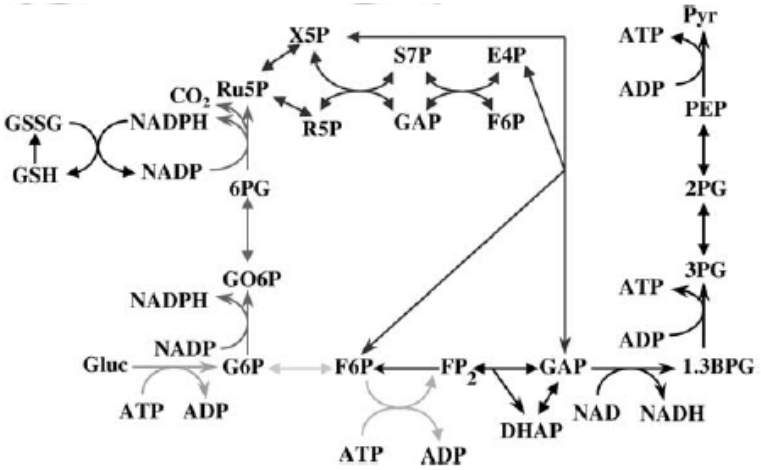
Metabolites and Biochemical Reactions

- Metabolite: an organic substance, e.g. glucose, oxygen
- Biochemical reaction: the process in which two or more molecules (reactants) interact, usually with the help of an enzyme, and produce a product

Glucose + ATP

↓ Glucokinase

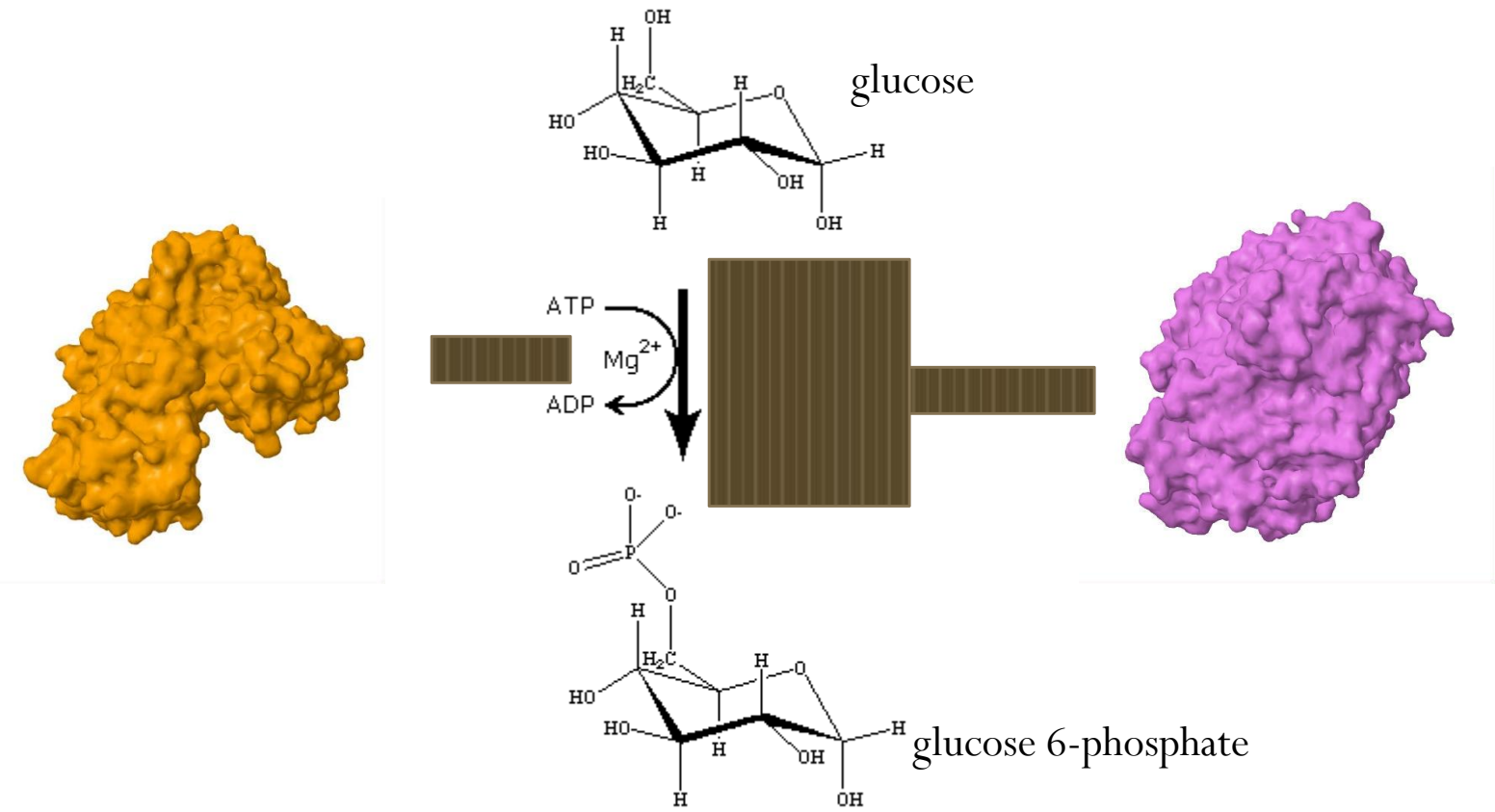
Glucose-6-Phosphate + ADP



- Most of the reactions are catalyzed by enzymes (proteins)

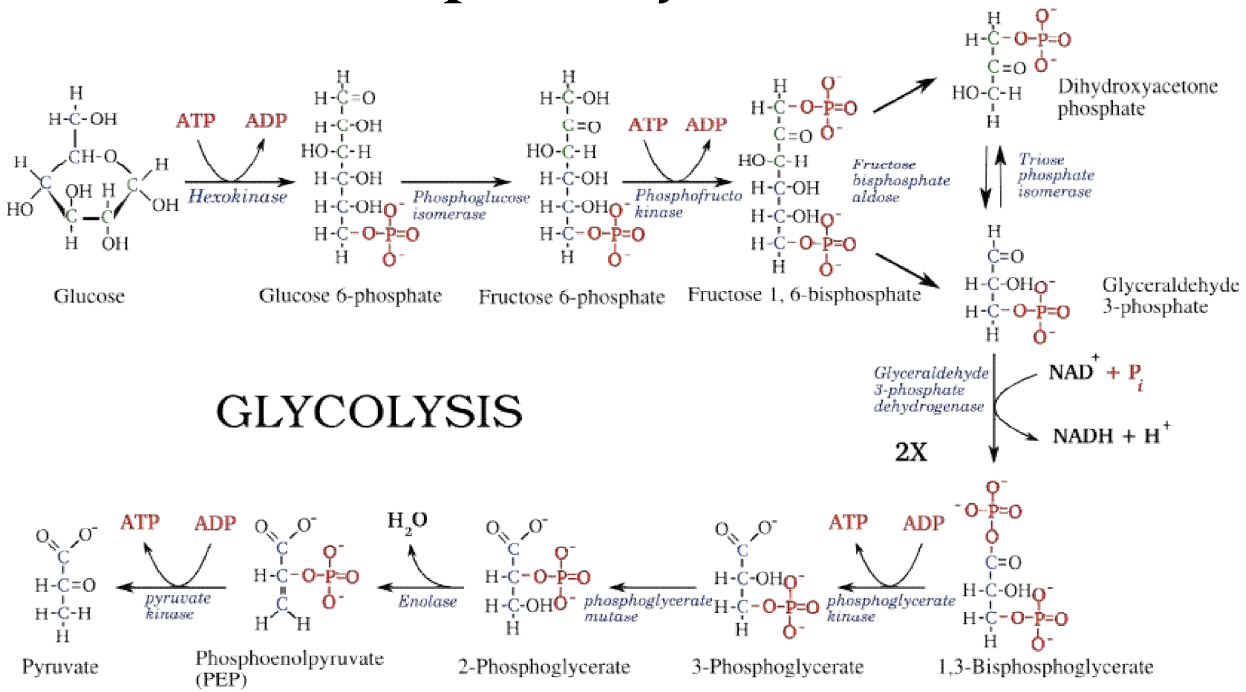
Enzymes

- Metabolic reactions are catalysed by proteins called **enzymes**.



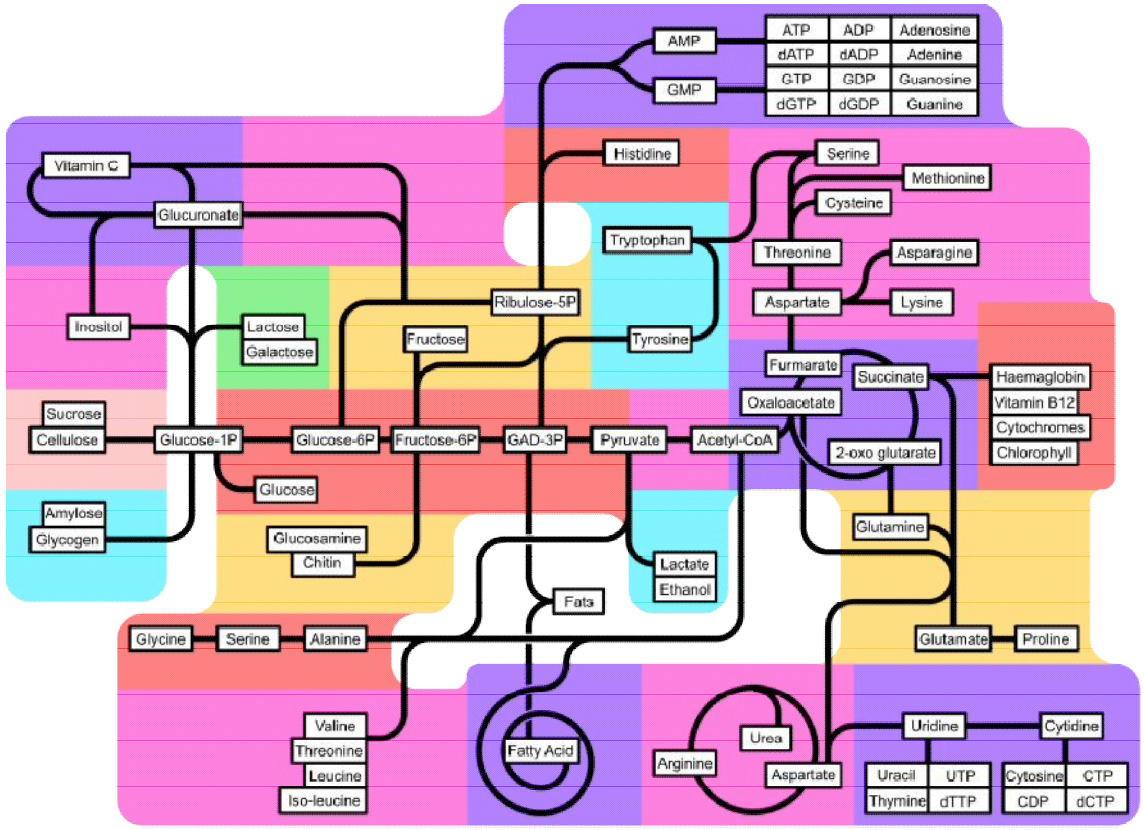
Metabolic pathways

- Traditionally, biochemists consider a series of consecutive metabolic reactions to form a **pathway**.



Metabolic networks

- However, pathways often overlap so much that it is more accurate to consider the set of all metabolic reactions as forming a **network**.



Why should we study metabolic networks?

- ***Fundamental to life***

Since enzymes are encoded in the **genome**, metabolism is one mechanism by which an organism's **genotype** (specific set of genes) is connected to its **phenotype** (how it behaves). Many metabolic processes are common to all forms of life.

- ***Biotechnology***

Deep understanding of the metabolic networks of bacteria is needed if they are to be genetically modified to produce a desired product with maximum yields.

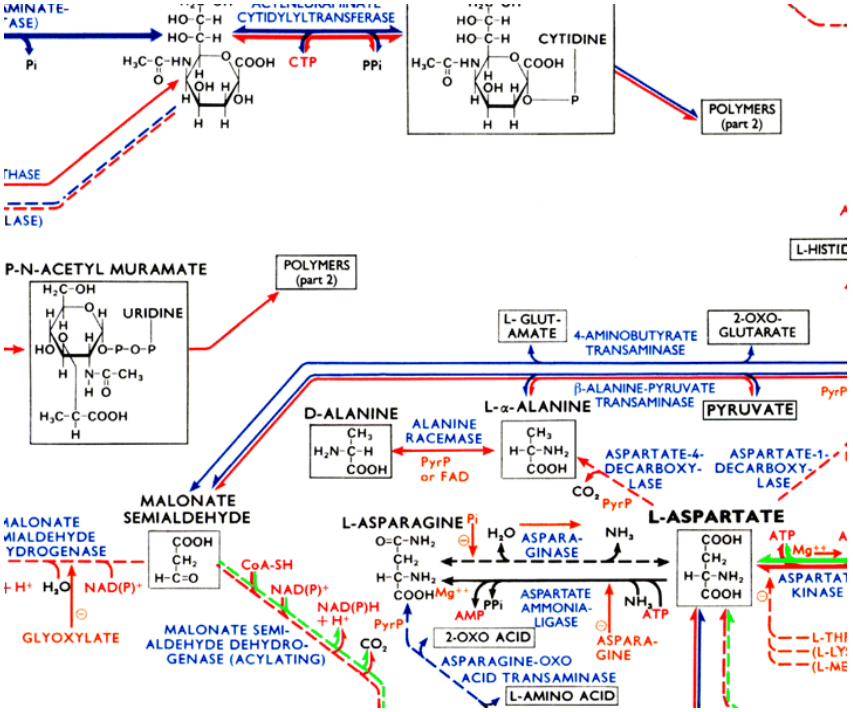
- ***Medicine***

Aberrations in human metabolism are fundamental to diseases such as diabetes and some types of cancer.

Knowledge of the metabolic networks of pathogens and parasites can help to select drug targets (or target combinations) that will be most effective.

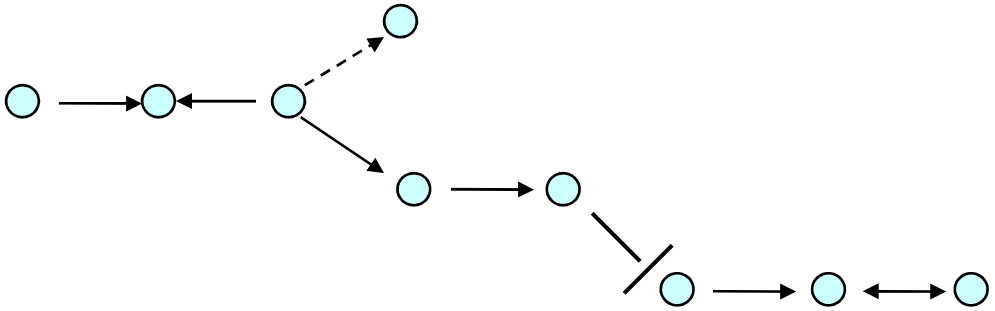
How should we represent metabolic networks?

- **Traditional textbook representation:**
- Compounds are shown as boxes.
- Arrows connect compounds to show interconversions.
- Arrows are labelled with the name of the associated enzyme.
- **Cofactors** (commonly-used compounds) included with curved arrows.



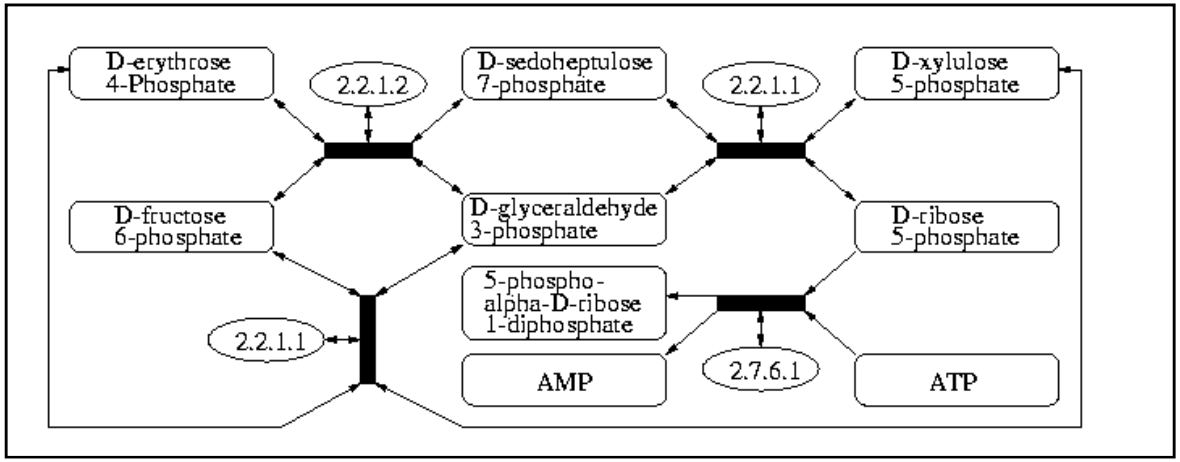
Biological Network Model

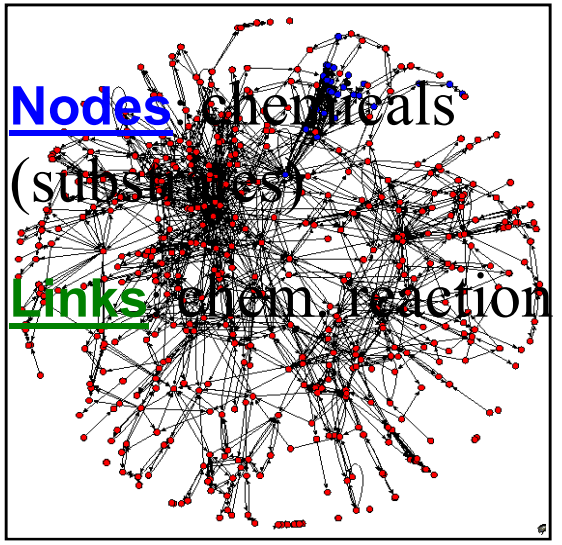
- It is usually represented by a 2-D diagram with characteristic symbols linking the protein and non-protein entities.

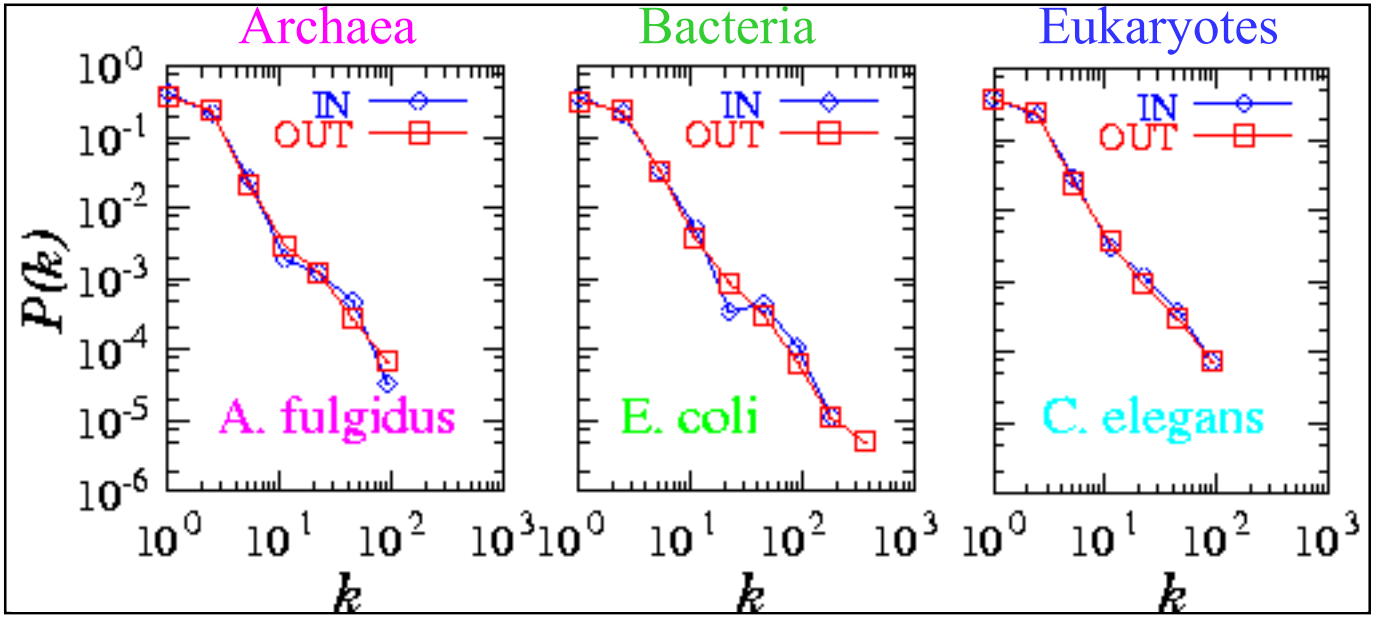


- A circle indicates a protein or a non-protein biomolecule.
- An symbol in between indicates the nature of molecule-molecule process (activation, inhibition, association, disassociation, etc.)

Metabolic Network Structure



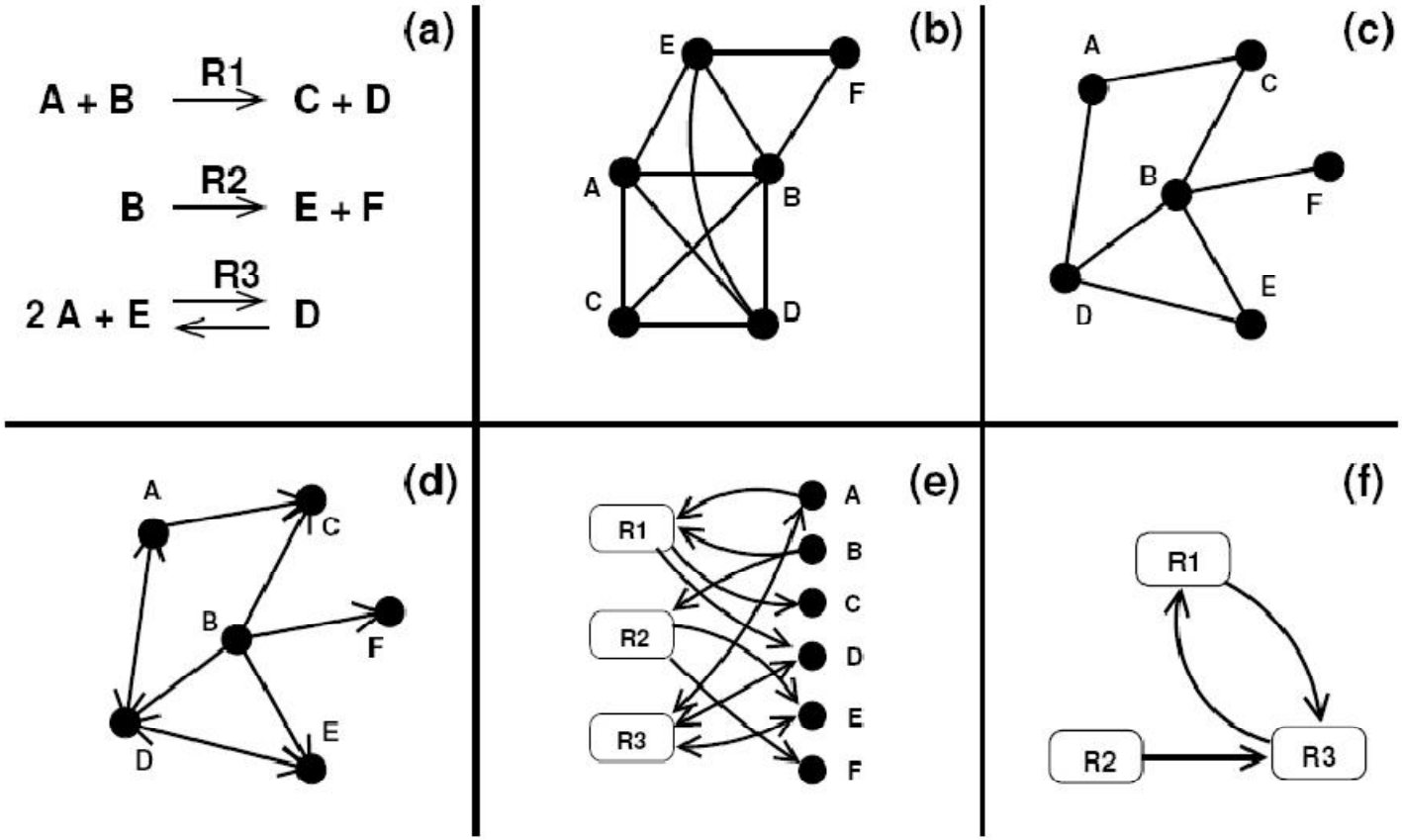




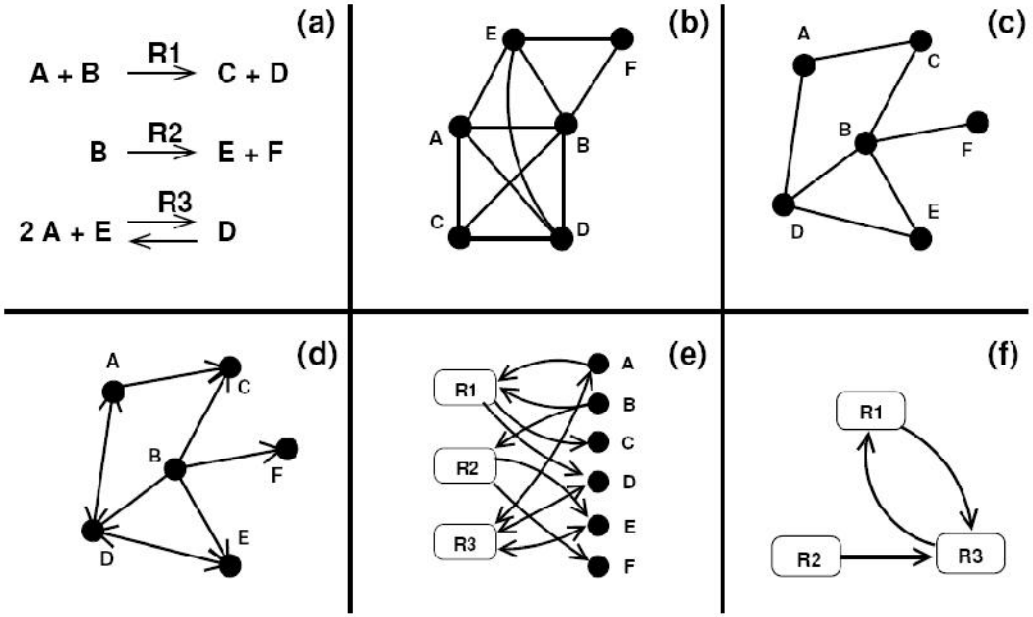
Organisms from all 3 domains of life are **scale-free** networks.

H. Jeong, B. Tombor, R. Albert, Z.N. Oltvai, and A.L. Barabasi, *Nature* **407**, 651 (2000).

Metabolic network representations



Effect of network representations

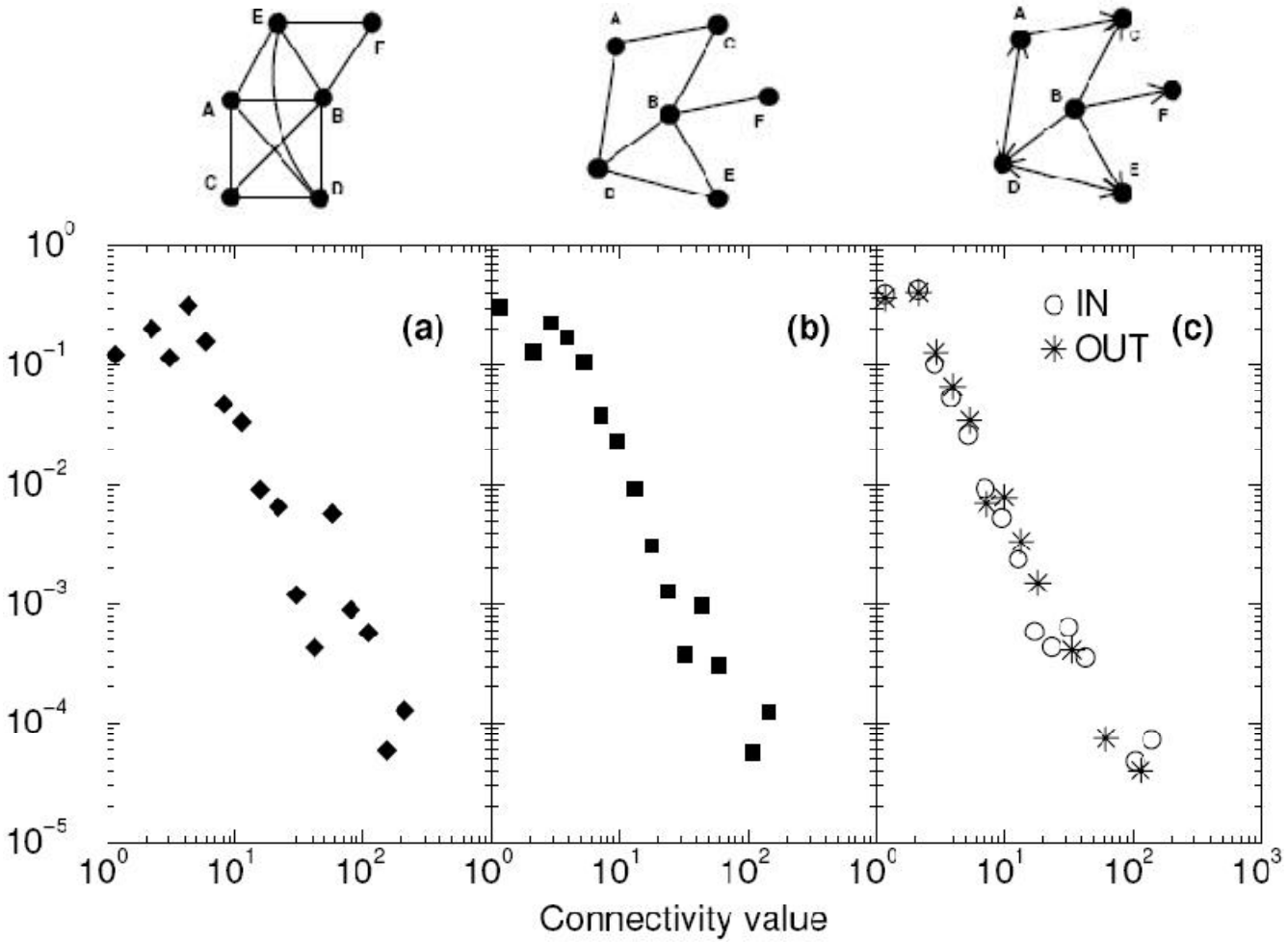


Organism	N	M_b	M_c	$\langle C \rangle_b$	$\langle C \rangle_c$	ρ_b	ρ_c
H. pylori	489	4058	1920	0.72	0.28	-0.285	-0.261
E. coli	540	3753	1867	0.66	0.20	-0.251	-0.217
S. cerevisiae	1064	6941	4031	0.67	0.23	-0.182	-0.150

N nodes
M links.
$\langle C \rangle$ average clustering
ρ assortativity

E. Almaas, *J. Exp. Biol*. **210**, 1548 (2007)

Effect of network representations

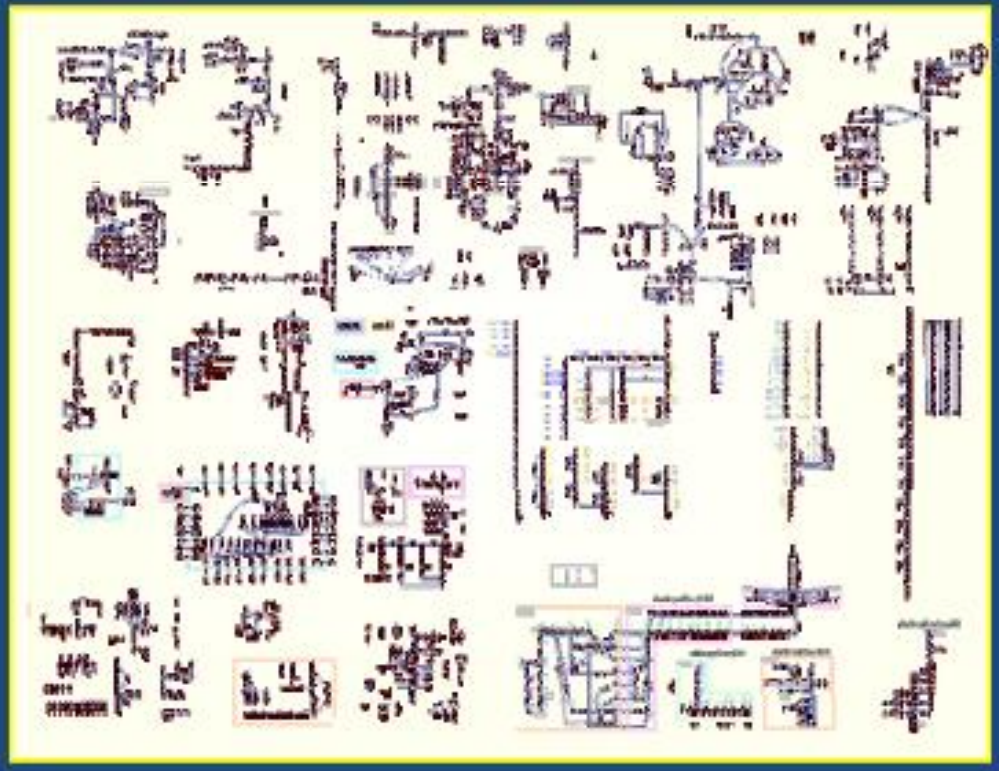


E. Almaas, *J. Exp. Biol*. **210**, 1548 (2007)

Recon 1: A human metabolic network

Duarte *et al*. PNAS, 104(6):1777-82 (2007)

Global Metabolic Map
Comprehensively represents known reactions in human cells



2,712 metabolites

3,311 reactions

7 compartments

1,496 genes total

Genome annotation-based reconstruction

1,134 genes

Gap filling and literature-based reconstruction

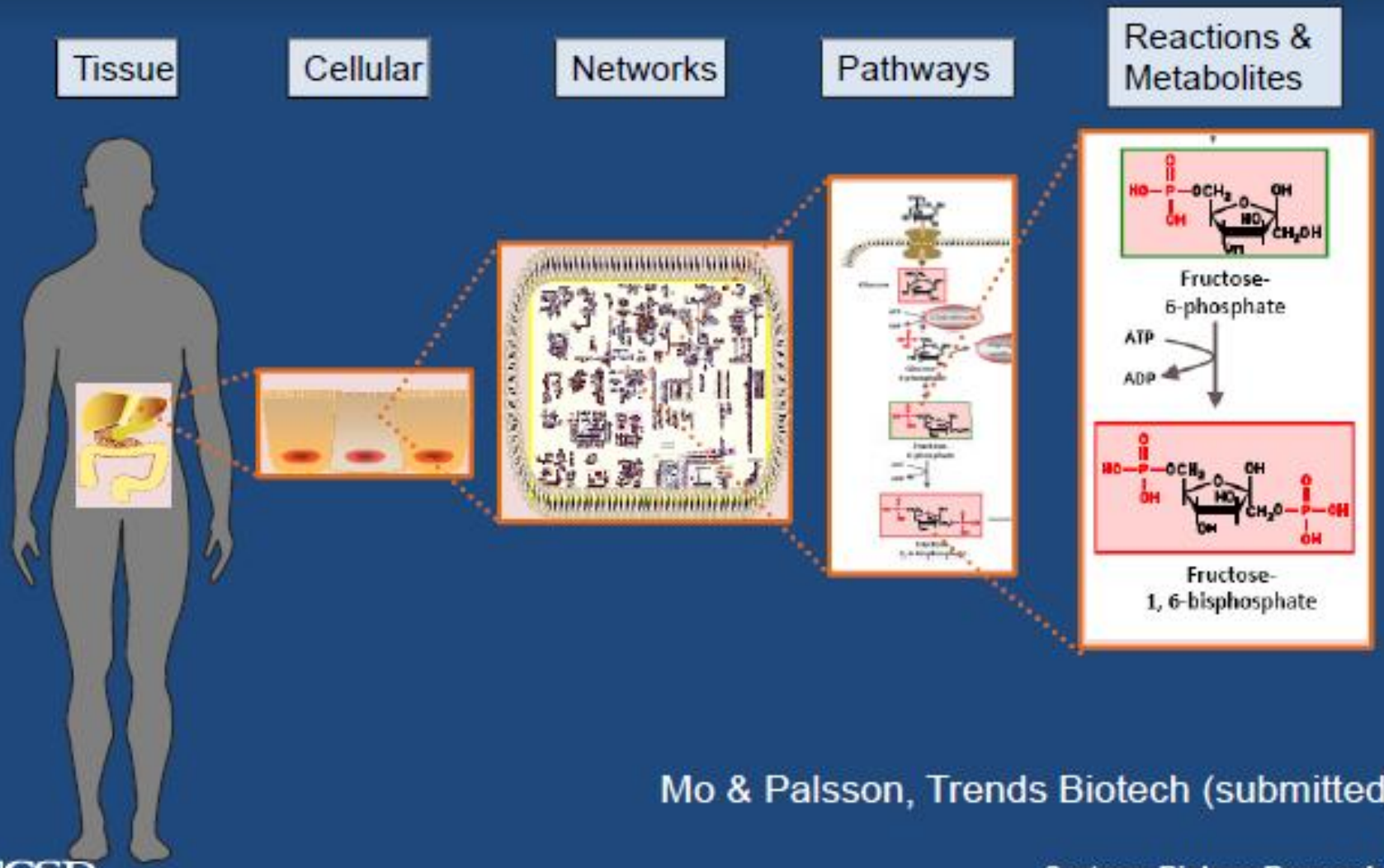
362 genes

http://bigg.ucsd.edu

UCSD Bioengineering

Systems Biology Research Group
http://systemsbiology.ucsd.edu

Human physiology as a multi-scale system



Mo & Palsson, Trends Biotech (submitted)

Network statistics

Component	Number
Genes	1,496
Transcripts*	1,905
Proteins	2,004
Complex-associated reactions*	248
Isozyme-associated reactions*	946
Intrasystem reactions	3,311
Metabolic	2,233
Transport†	1,078
Exchange reactions†	432
Compartment-specific metabolites	2,712
Cytoplasm	995
Extracellular space	388
Mitochondrion	383
Golgi apparatus	279
Endoplasmic reticulum	231
Lysosome	207
Peroxisome	139
Nucleus	90
Citations	1,587
Primary literature	1,378
Review articles	188
Textbooks	21
Validated metabolic functions	288
Knowledge gaps‡	356