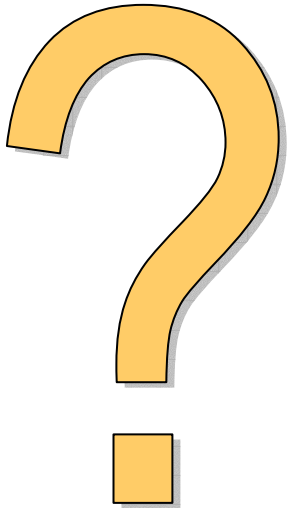
What is Systems Biology



M. Arsenakis

School of Biology

Aristotle University of |Thessaloniki

Systems Biology: A New Science (?)

"***Systems biology*** *is the science of discovering, modeling, understanding and ultimately engineering at the molecular level the dynamic relationship between the biological molecules that define living organisms.*"

Leroy Hood, President ISB
(from systemsbiology.org)

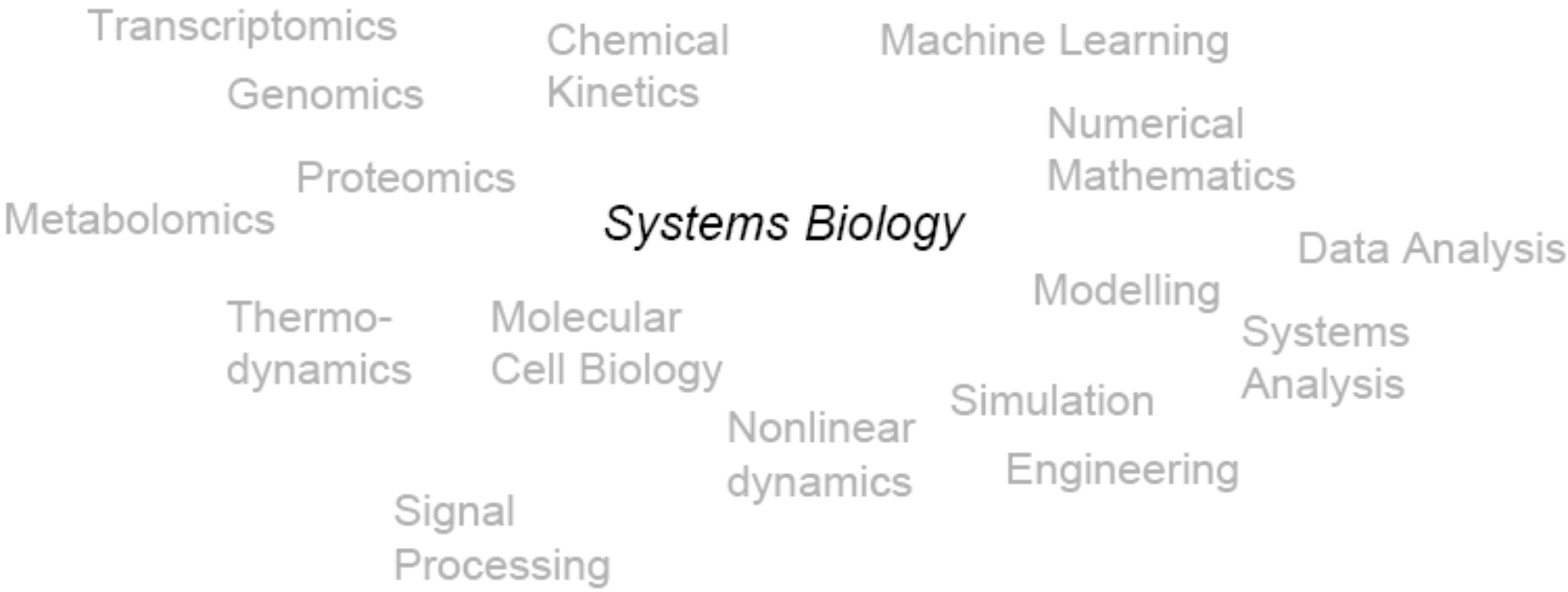
"*Organisms function in an integrated manner[…] But biologists have historically studied organisms part by part and celebrated the modern ability to study them molecule by molecule, gene by gene.*"
Systems biology is "*a new science, a critical sciences of the future that seeks to understand the integration of the pieces to form biological systems.*"

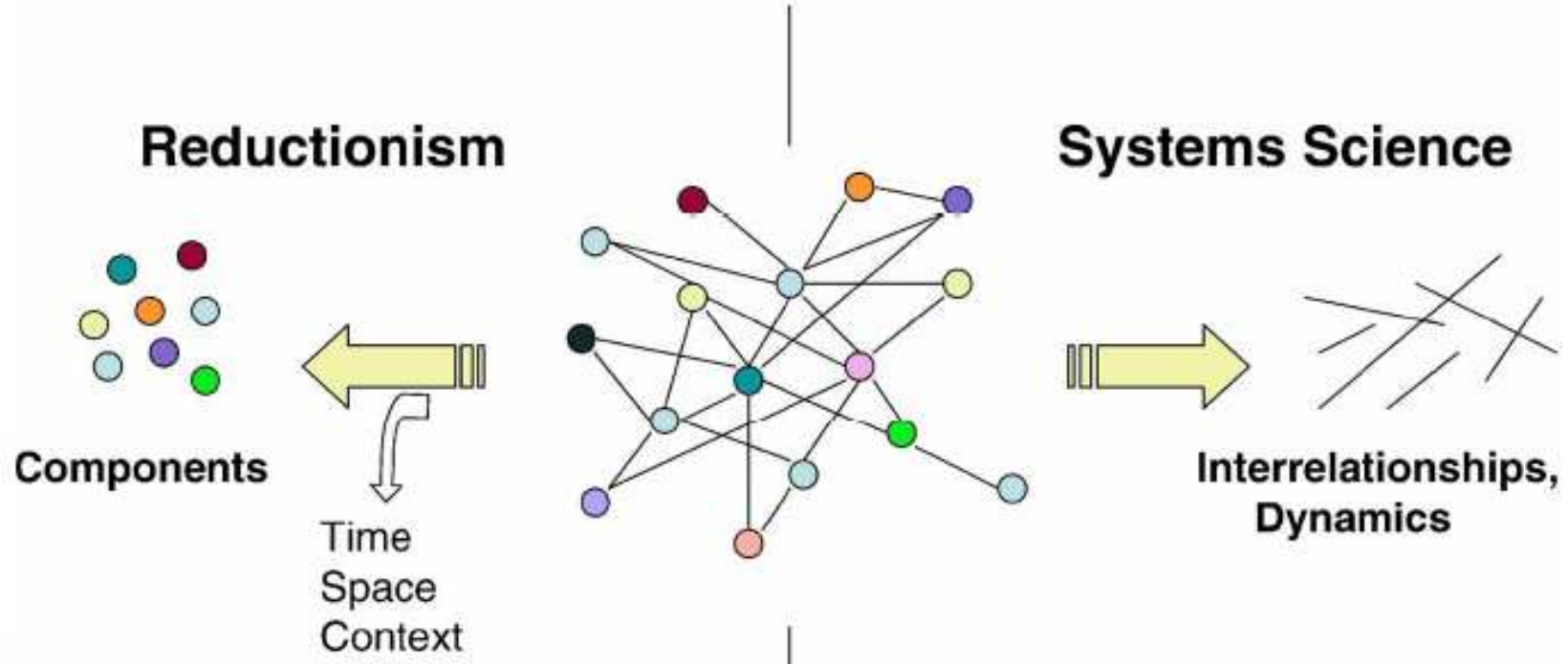
David Baltimore, Nobel Laureate, President CalTech
(from systemsbiology.org)

Systems Biology: An Integrative Approach

"***Systems biology*** *is an academic field that seeks to integrate different levels of information to understand how biological systems function. By studying the relationships and interactions between various parts of a biological system […] it is hoped that eventually an understandable model of the whole system can be developed.*"

Wikipedia





Medical Treatments

Disease-driven
Aimed for normalcy (normal range)
Additive

Medical Treatments

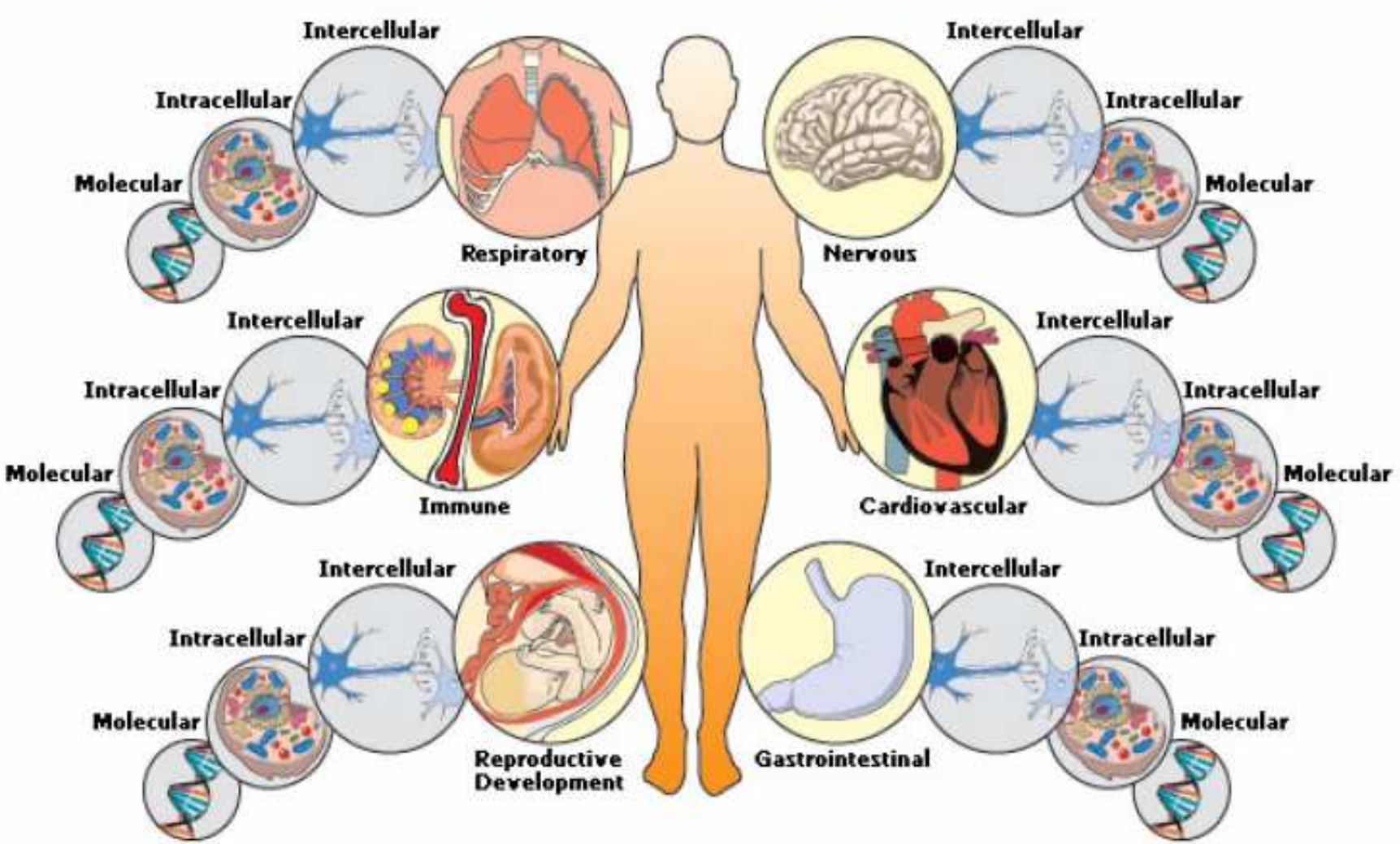
Individualized
Multidimensional use of drugs
Time-sensitive
Space-sensitive
Synergistic

Ahn et al. PLoS Med. 2006.e209.

- 20th Century has been often called the “great century of Biology” due to the great advances of Molecular Biology
- **but** was dominated by a ***reductionist approach*** influenced by 19th Century physics
- mixed blessing
  - On the positive side, problems amenable to a reductionist approach benefited from the experimental power of molecular biology
  - On the negative side, biology’s holistic problems, remained relatively or completely undeveloped

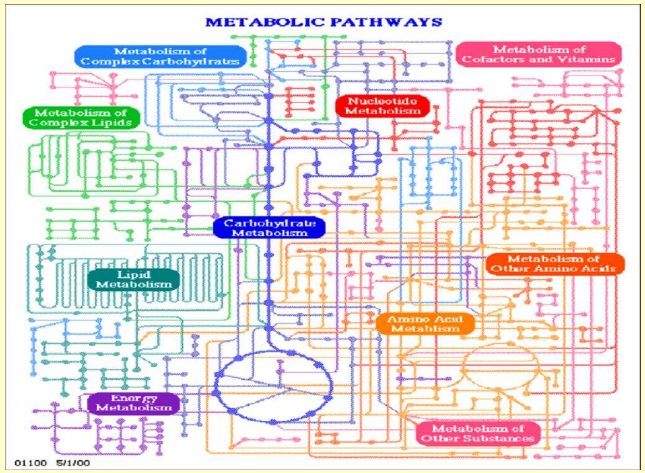
- **“... a biology viewed through the eyes of fundamentalist reductionism is an incomplete biology. Knowing the parts of isolated entities is not enough. A musical metaphor expresses it best: molecular biology could read the notes in the score, but it couldn’t hear the music.”**

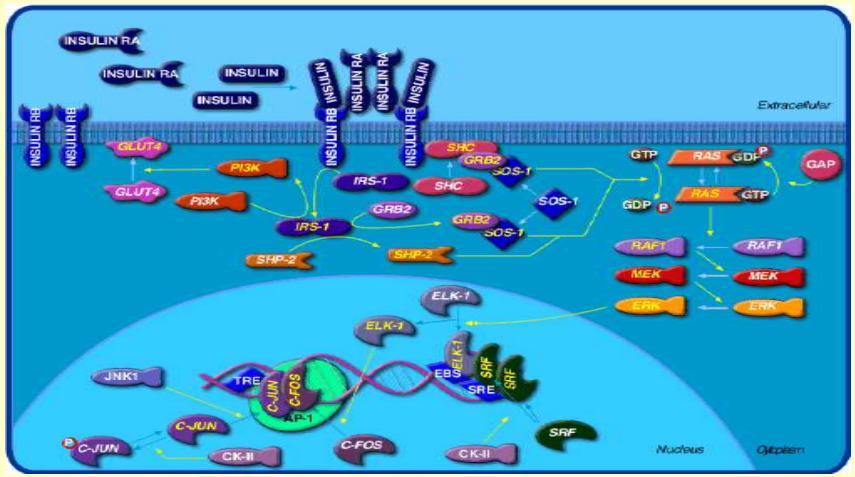
(Woese, 2004)


Intercellular
Intracellular
Molecular
Respiratory
Nervous
Intercellular
Intracellular
Molecular
Intercellular
Intracellular
Molecular
Immune
Cardiovascular
Intercellular
Intracellular
Molecular
Intercellular
Intracellular
Molecular
Reproductive
Development
Gastrointestinal
Intercellular
Intracellular
Molecular

Molecular biology

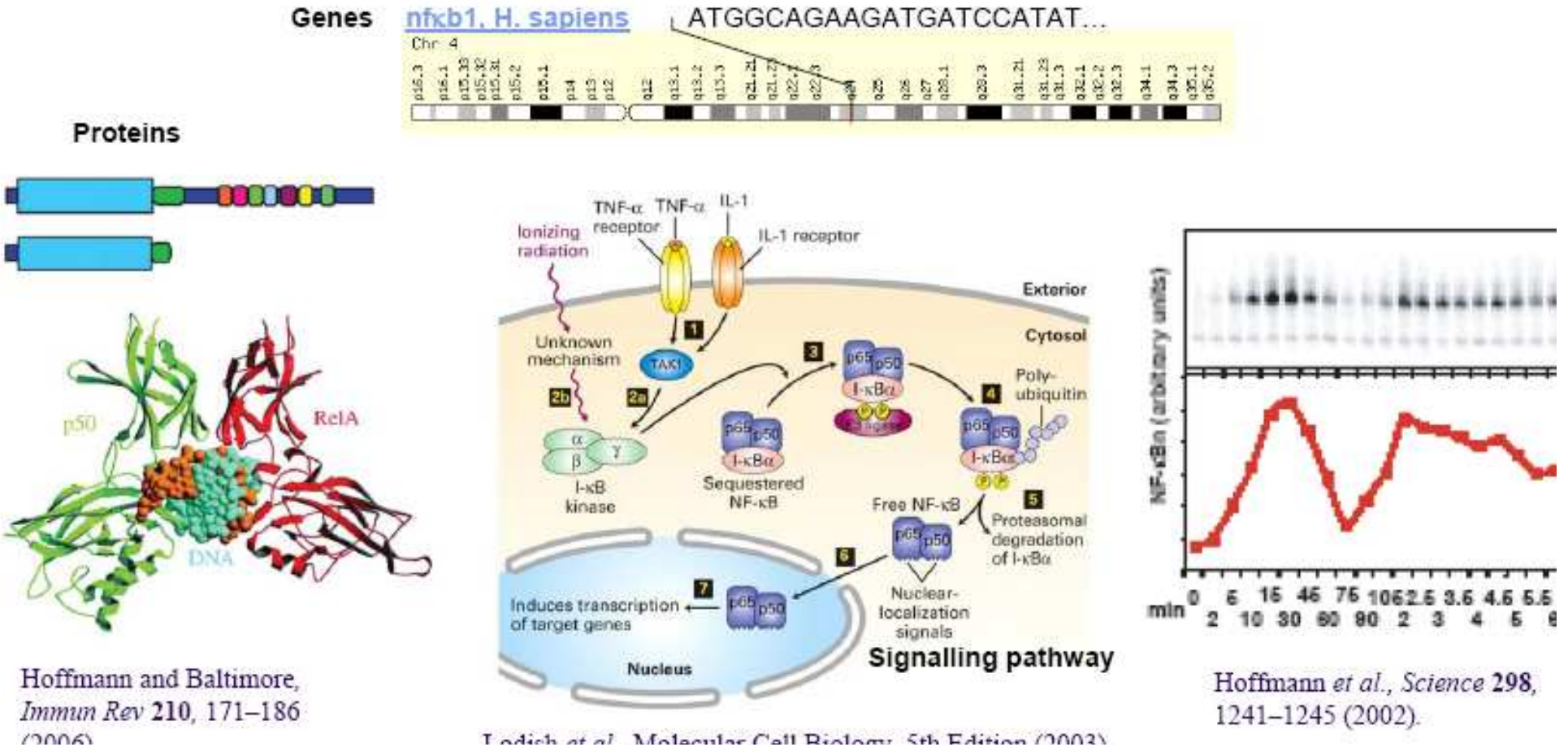
- qualitative and descriptive
- focused on **individual components and their (individual) interaction**
- focused on understanding of molecular details
- **<u>not</u>** focused on **complex networks** behavior





Systems Biology: Key Aspects

- Interacting *network* of components and processes (spatiotemporal);
- *Integrative* approach (sources of data on different levels/scales, such as genomic, proteomic, metabolic, etc.);



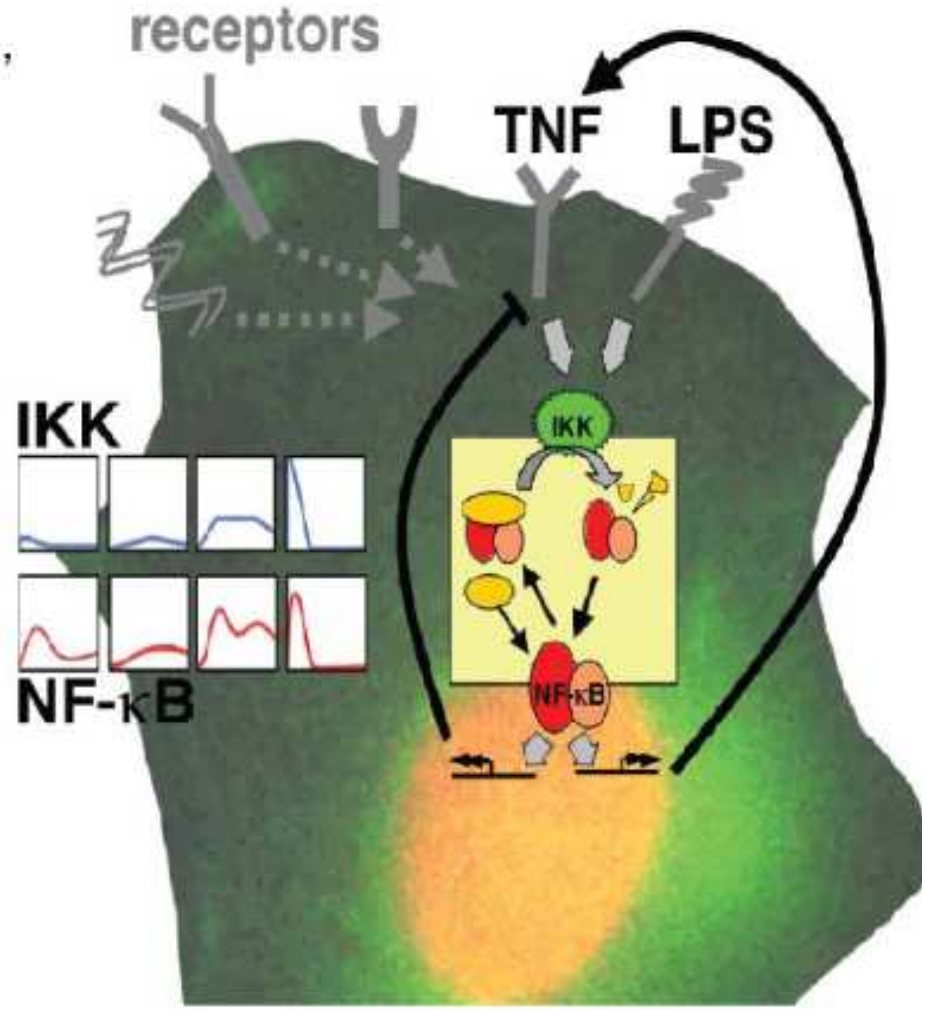
Hoffmann and Baltimore, *Immun Rev* **210**, 171–186 (2006)

Lodish *et al.*, Molecular Cell Biology, 5th Edition (2003)

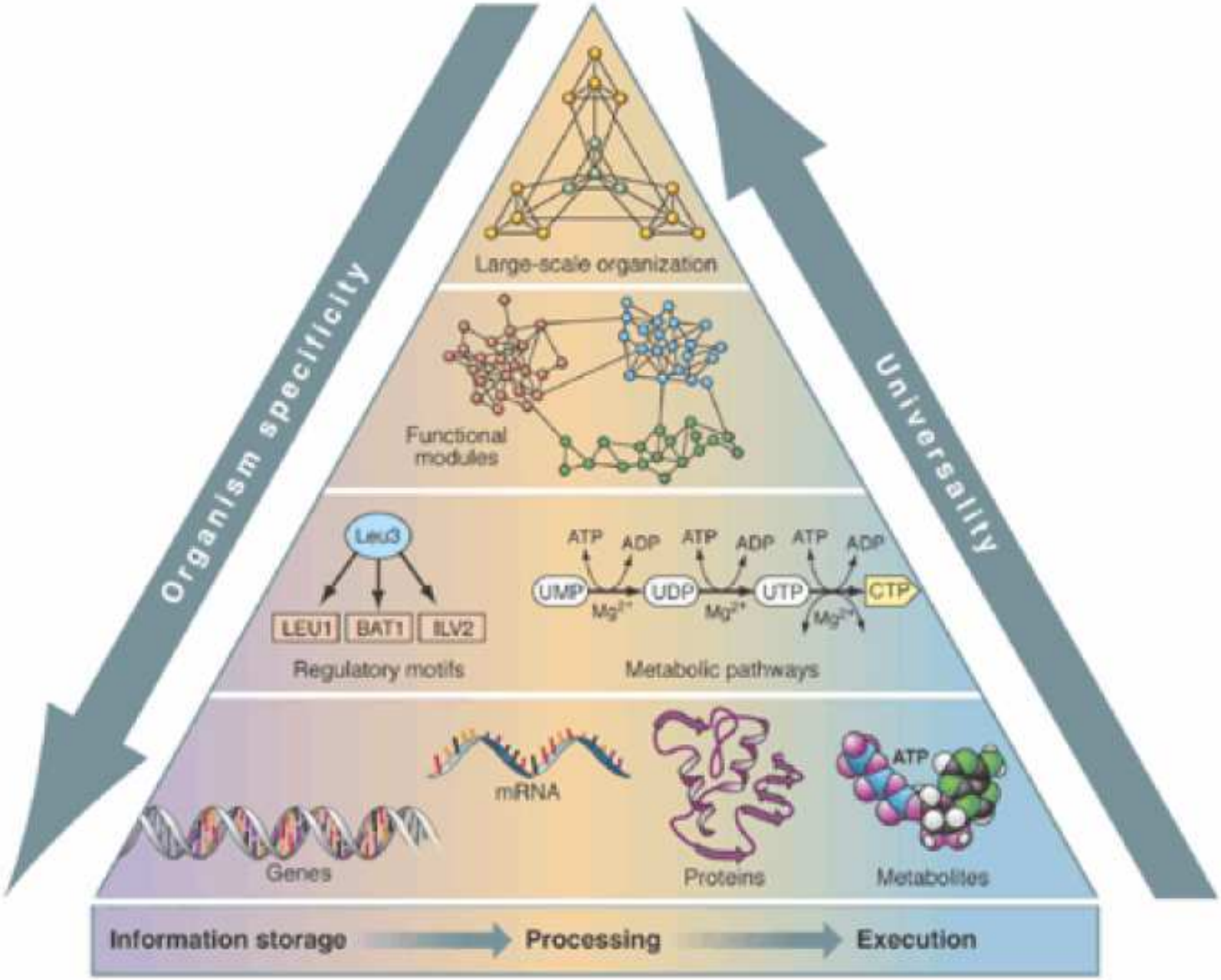
Hoffmann *et al.*, *Science* **298**, 1241–1245 (2002).

Systems Biology: Key Aspects (cont.)

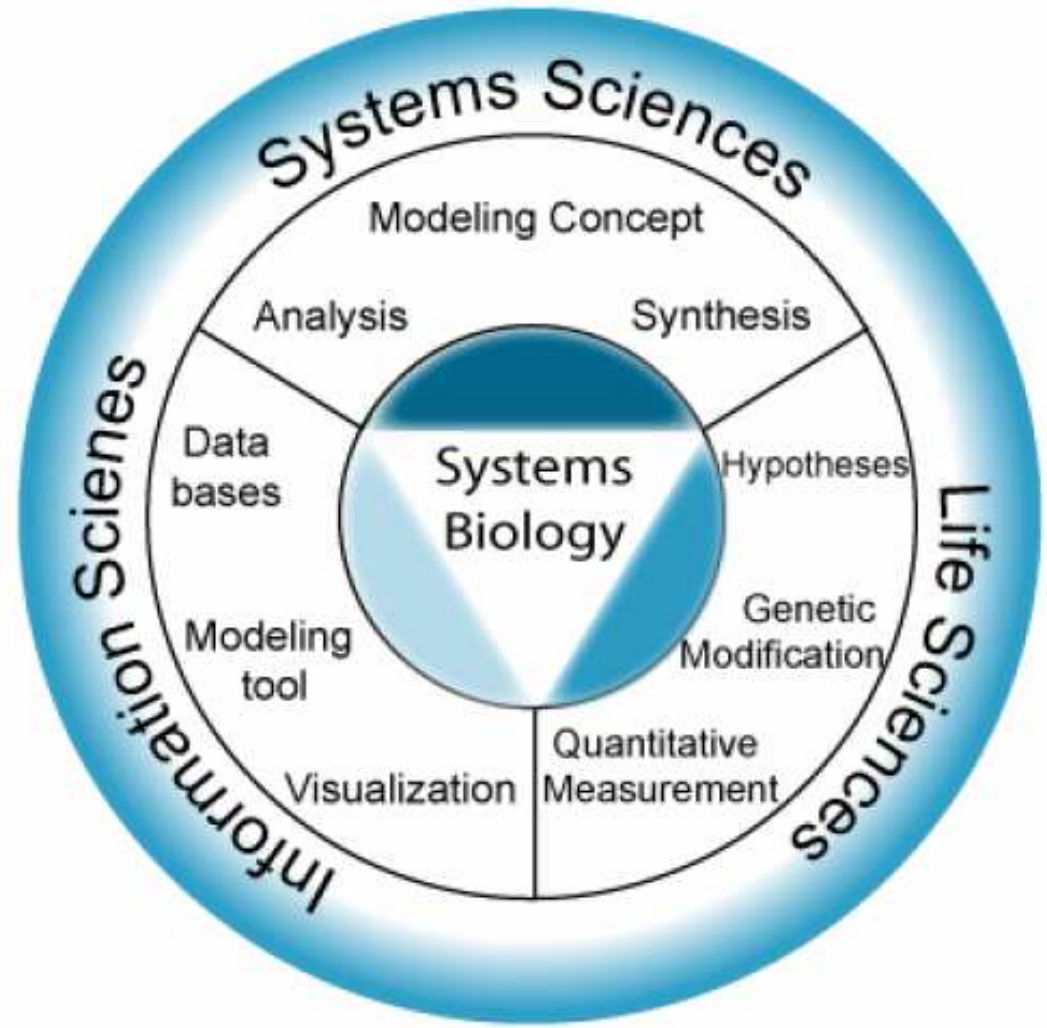
- Aimed at a *quantitative* understanding of the function;
- Ultimate goal: understanding structure, development, dynamics, functioning and **control** of cells and entire organisms (→ medical applications).



Hoffmann and Baltimore, *Immun Rev* **210**, 171–186 (2006).


Organism specificity
Universality
Large-scale organization
Functional modules
Leu3
LEU1
BAT1
ILV2
Regulatory motifs
ATP
ADP
UMP
UDP
UTP
CTP
Metabolic pathways
mRNA
Genes
Proteins
ATP
Metabolites
Information storage
Processing
Execution

Multidisciplinarity in Systems Biology



Success is dependent on:

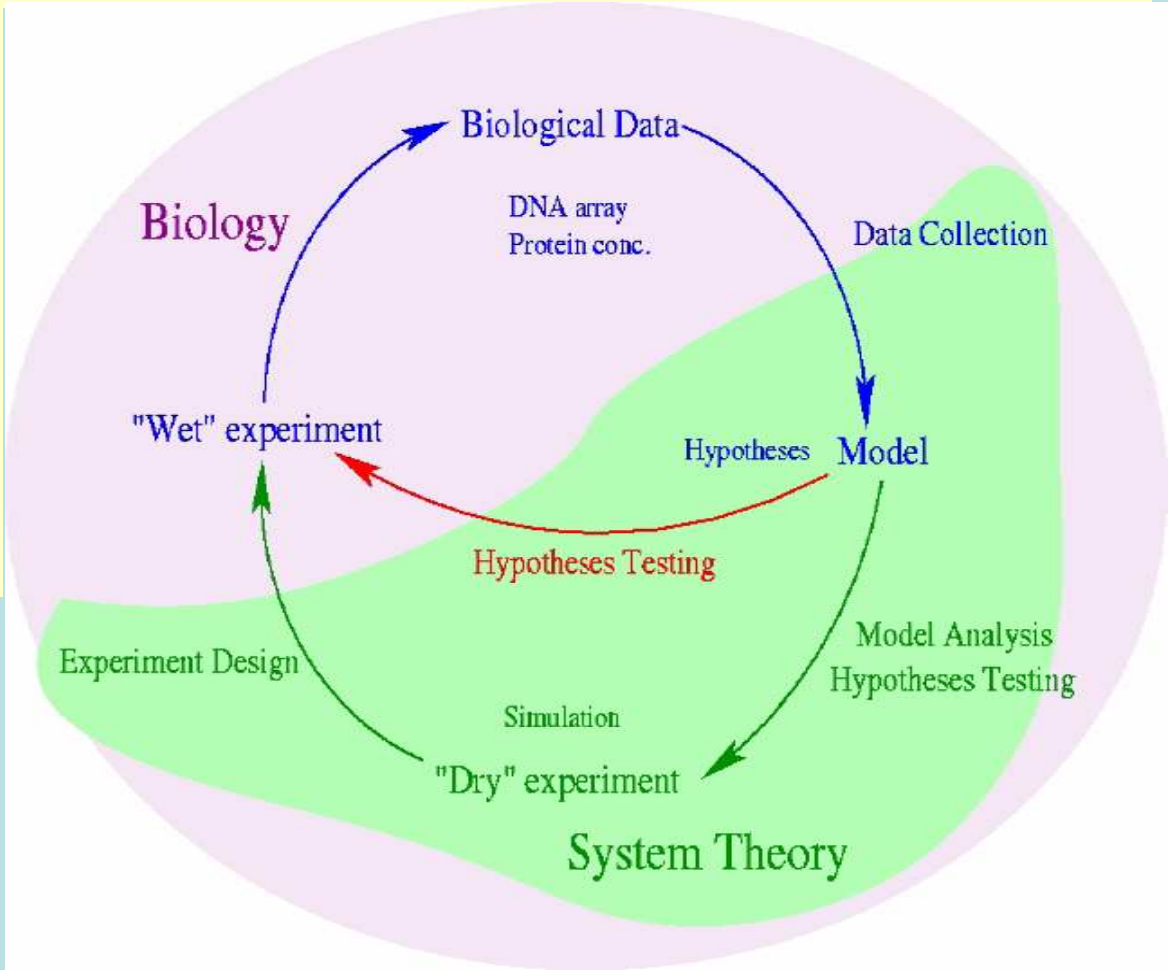
A systematic multidisciplinary approach combining:

- **Life sciences**
- **System sciences**
- **Information sciences**

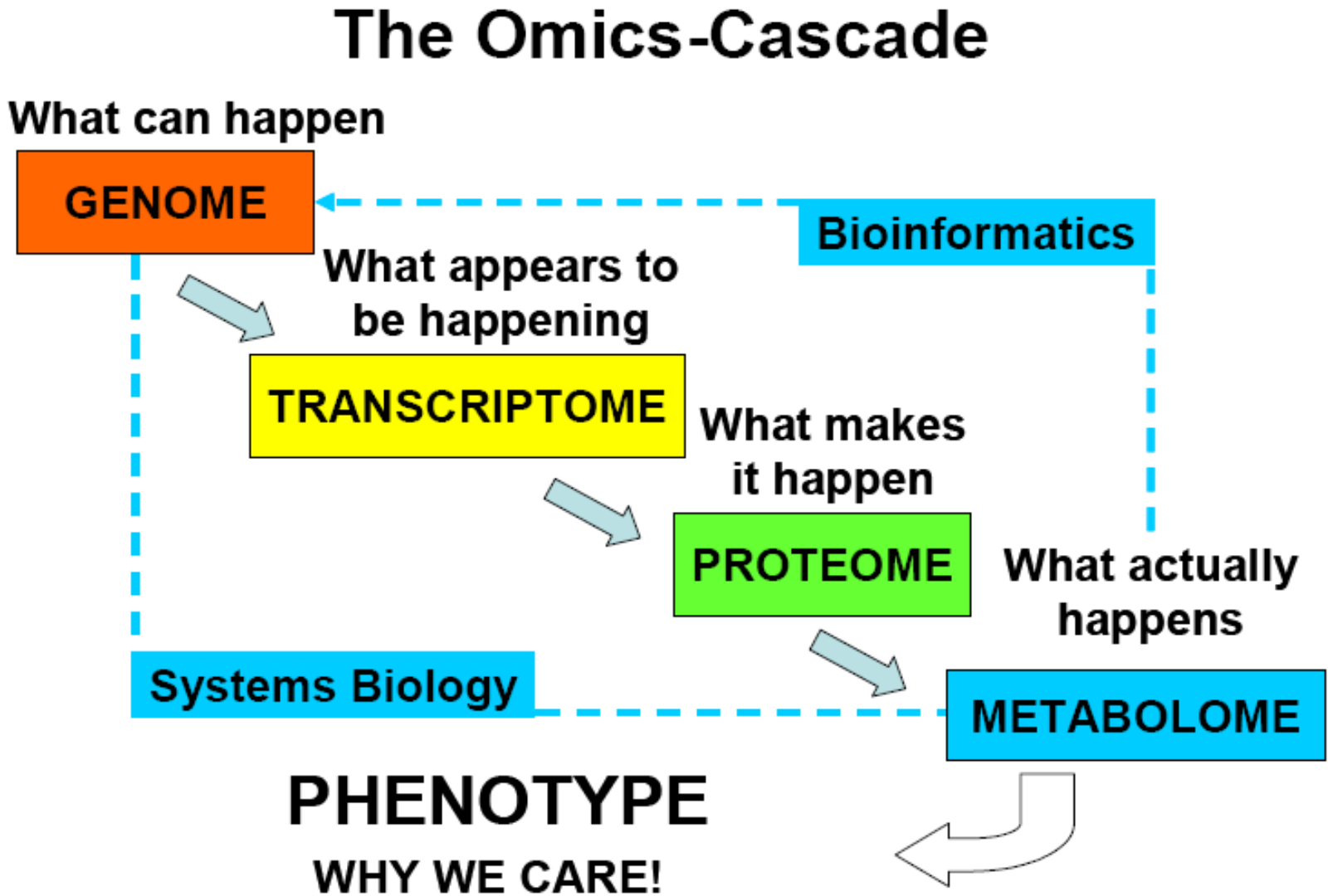
Systems Biology - Holistic Understanding

Increasing knowledge via Cycling through:

1. Experiment
2. Data Processing
3. Modeling
4. Analysis
5. Experimental design

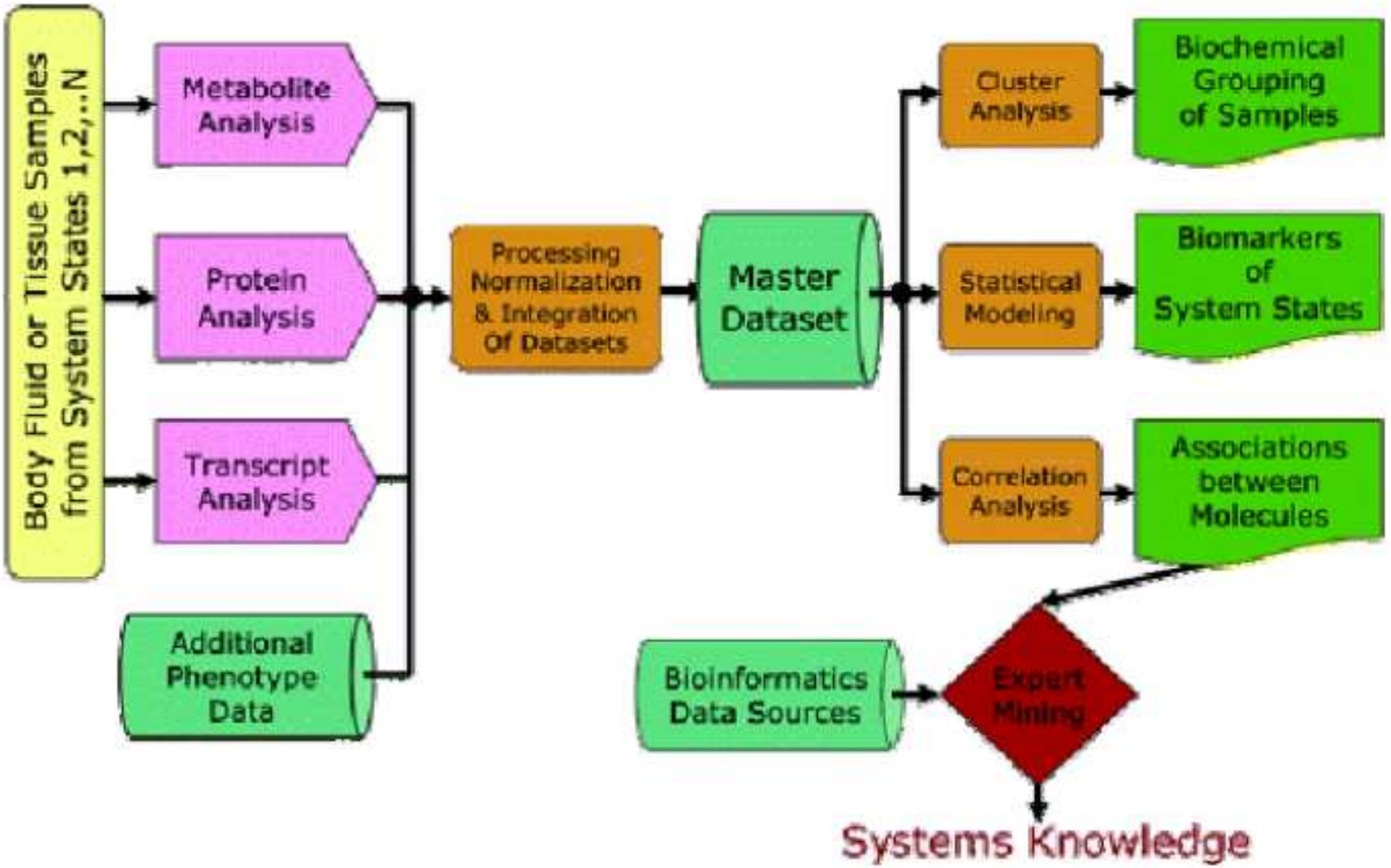


High throughput technologies



What are “omics” sciences

- “omics” implies the integration of biology with information sciences
- “omics” conveys a systems approach
- It implies large scale biology
- Involves large scale data acquisition


Body Fluid or Tissue Samples from System States 1,2,..N
Metabolite Analysis
Protein Analysis
Transcript Analysis
Additional Phenotype Data
Processing Normalization & Integration Of Datasets
Master Dataset
Cluster Analysis
Statistical Modeling
Correlation Analysis
Biochemical Grouping of Samples
Biomarkers of System States
Associations between Molecules
Bioinformatics Data Sources
Expert Mining
Systems Knowledge

Challenges of Systems Biology

- Systems biology research is still in its infancy. Maturation of the field will proceed as the many challenges that it faces are addressed and successfully solved. The most pressing challenges fall roughly into the following four categories:

1. *Experimental* (data volume/quality/noise)
2. *Technological* (miniaturize,integrate,automate)
3. *Computational* (models, mathematics)
4. *Sociological* (interdisciplinary teams/roles)

Promise of Systems Biology

"Systems biology promises to transform how biology is done—away from a reductionist focus on a limited number of molecular components to a comprehensive understanding of how large numbers of interrelated components of a system comprise modules or networks whose functional properties emerge as definable phenotypes".

The benefits of systems biology can be classified into three broad areas:

1. **Technology development**
2. **Advances in basic concepts of biology**
3. **Real-world practical applications (e.g. predictive and preventive medicine)**

Systems Biology expected benefits?

- **Basic research**
  - How do biological systems operate?
  - Understand basic principles of life
- **Biomedical**
  - Modeling and analysis of diseases
  - Development of pharmaceuticals
- **Chemical and biochemical industry**
  - Production of chemicals/biochemicals
- **General engineering and system sciences**
  - Reverse engineering
  - How does nature achieve robustness

n=1 clinical trials???