Network Biology- part I

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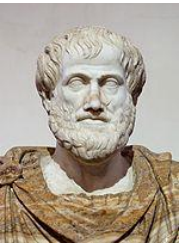
Outline

- **Part I: Fundamental theories of network biology**
- **Part II: Overview of association and causal networks**
- **Part III: Application of network biology in human diseases**

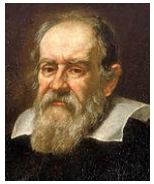
History of Physics

Observation-> description-> explanation-> prediction

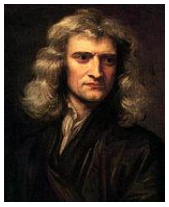
The philosopher **Thales** (624 BCE – 546 BCE) , “the Father of Science”, every event had a natural cause.



Aristotle (384 – 322 BCE): observation of physical phenomena could ultimately lead to the discovery of the natural laws governing them.



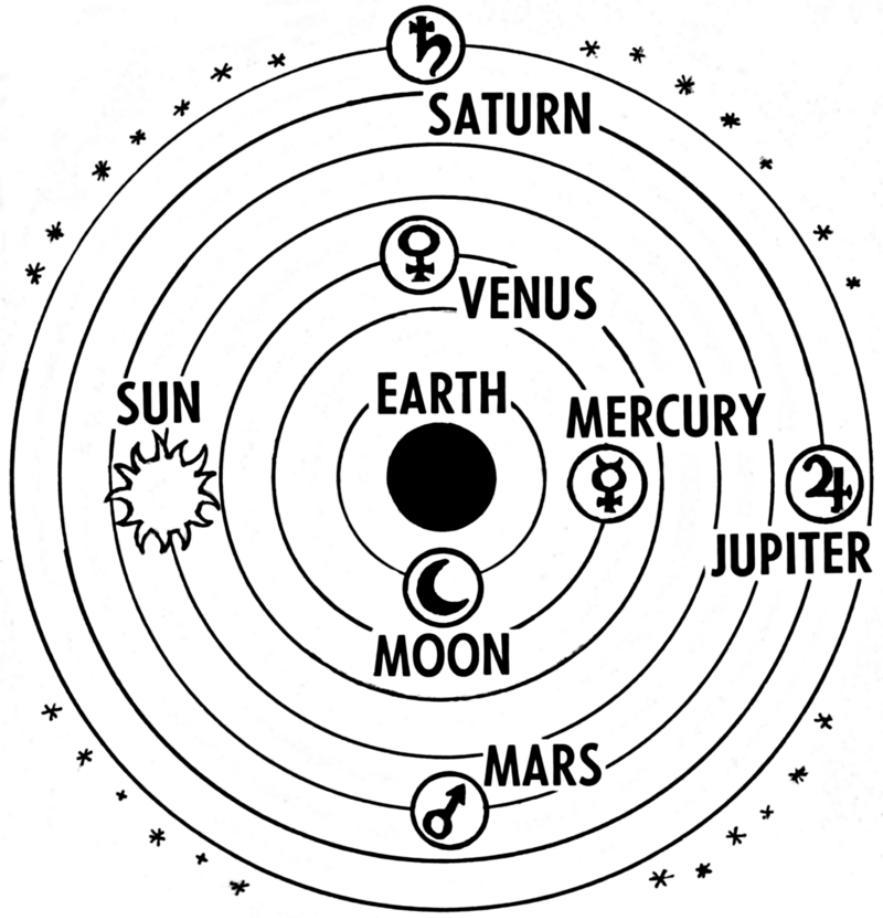
Galileo (1564-1642): **mathematical description**

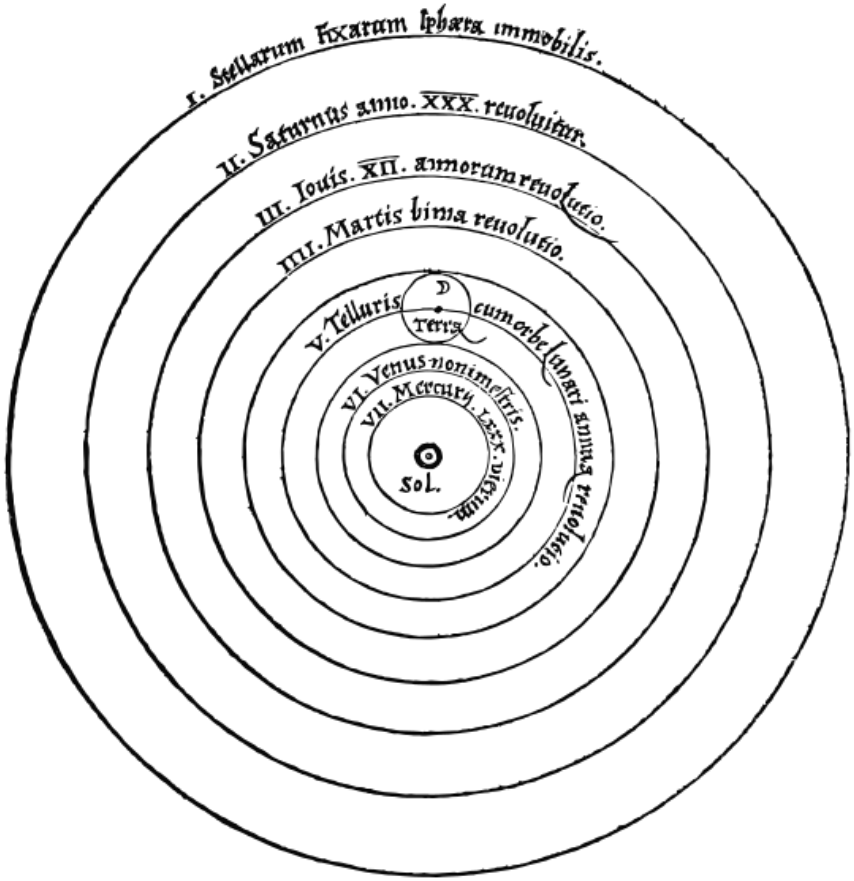


Newton (1642-1726): mathematical principles of natural philosophy

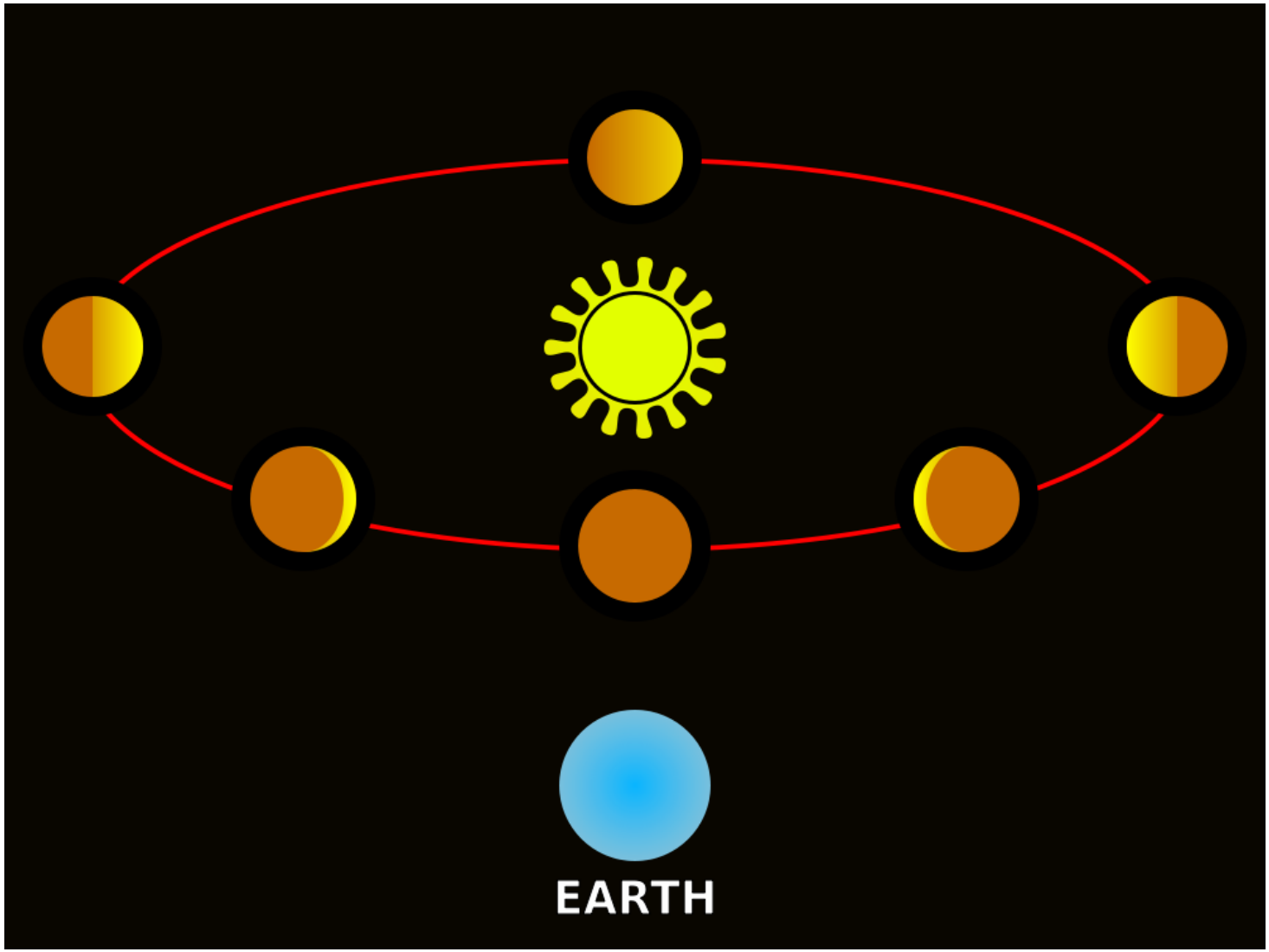
Geocentric model vs heliocentric model

Observation-> description-> explanation-> prediction



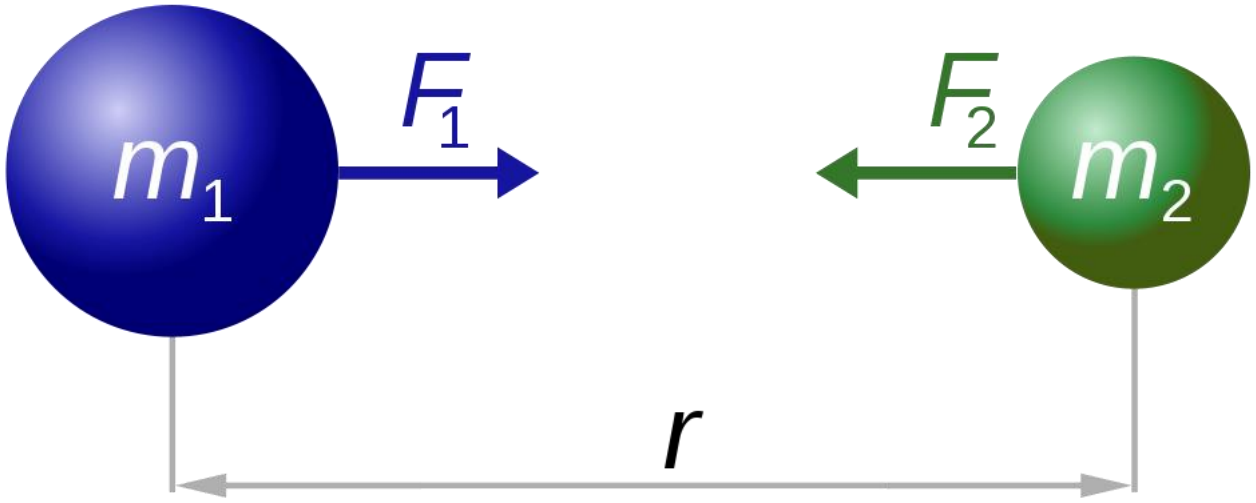


Geocentric model vs heliocentric model



How to explain phases of Venus?

Newton's law of universal gravitation



$$F_1 = F_2 = G\frac{m_1 \times m_2}{r^2}$$

Classic Mechanics/thermodynamics (~1700) -> quantum mechanics (~1900)

In contrast, it took over 2000 years to develop classic mechanics.

What about Biological sciences?

Biology → cell biology→molecular biology

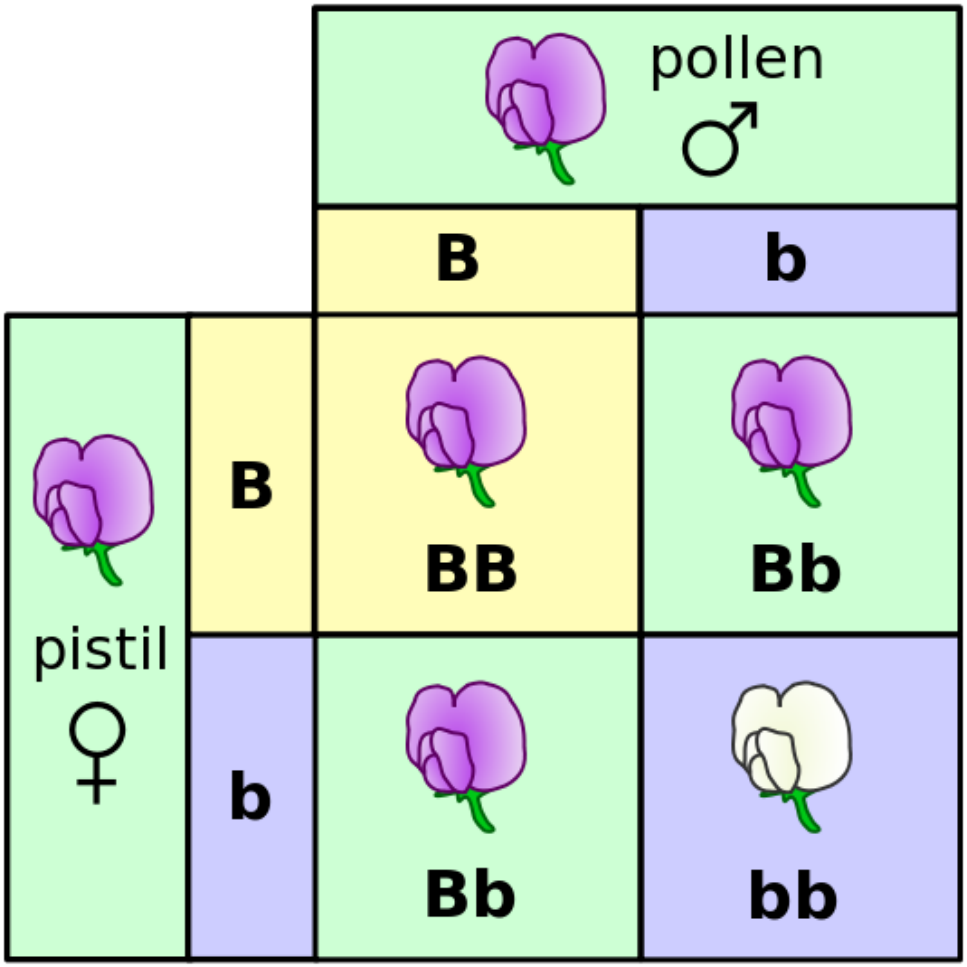
- Observation
- Description
- Explanation
- prediction

Mathematical description!

History of genetics

- Observation->mathematic description
- Mendel: heredity
- DNA
- Genome
- Where are we now?

Modern genetics: Mendel's pea paper (1866)



Mendelian inheritance

Genes: factors

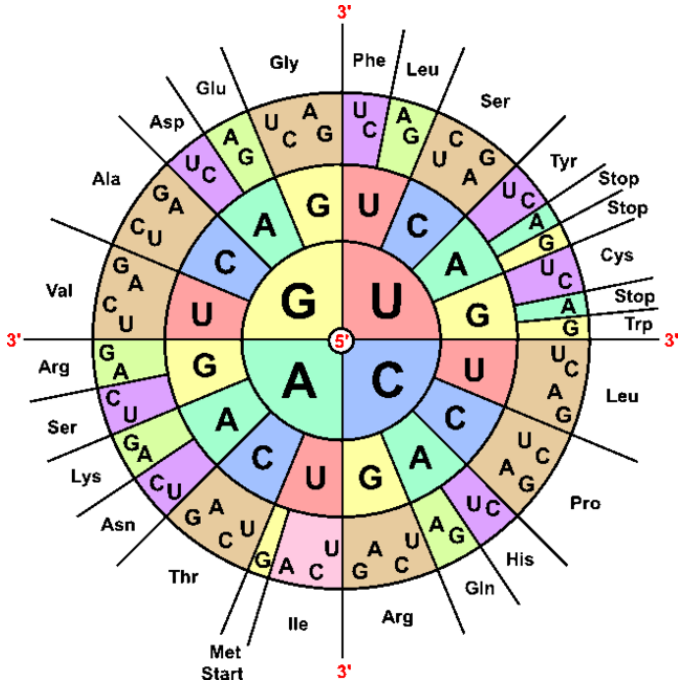
Alleles, Dominant, recessive homozygous, heterozygous

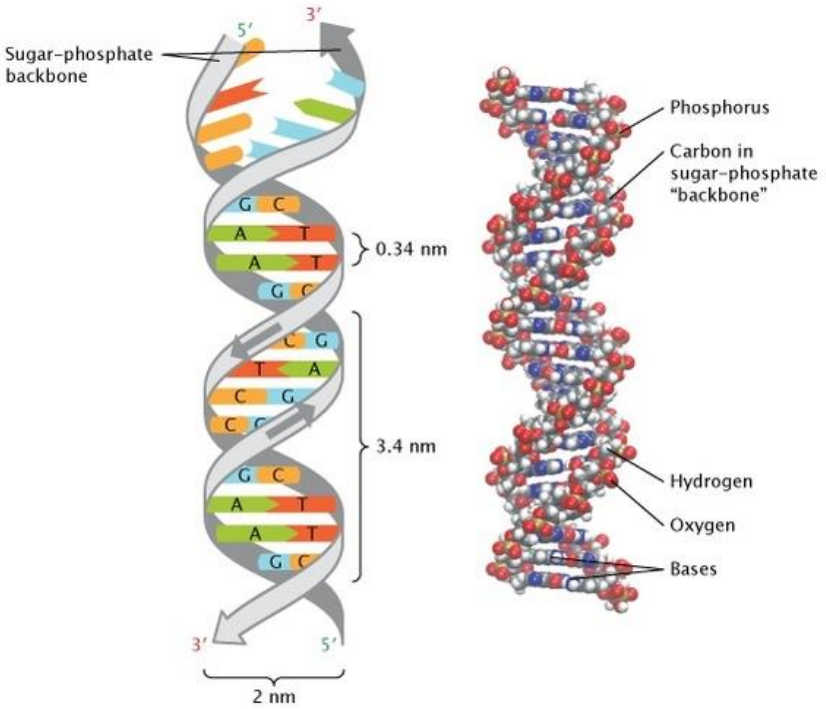
Ratio of genotype:

¼, ½, ¼

Inheritance: through DNA (1940s)

- One gene-> one protein -> one enzyme
- DNA structure in double helix:
  - 1952 Rosalind Franklin and Raymond Gosling
  - 1953 James Watson and Francis Crick
- Genetic code: 3 nucleotides (1961)



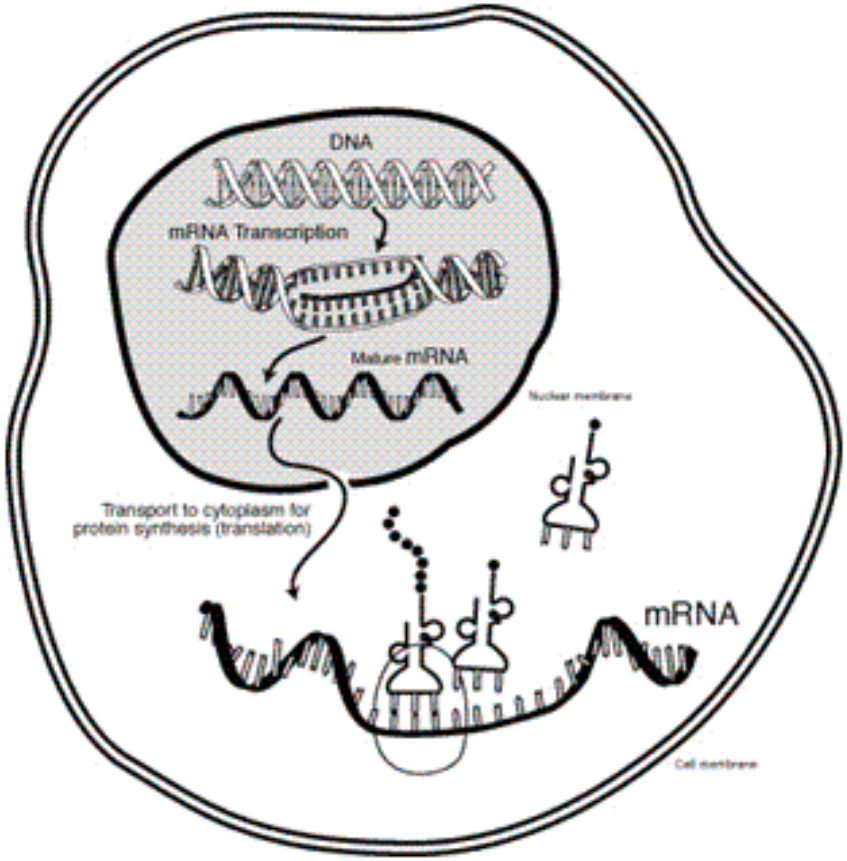


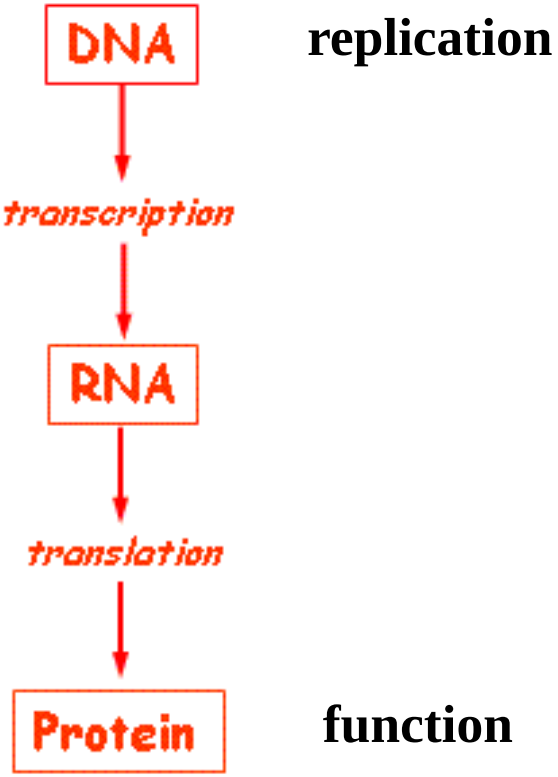
Genomics: determine the sequence of a gene (1972)

- DNA sequence: Fred Sanger, 1977
- First human genome, 2001

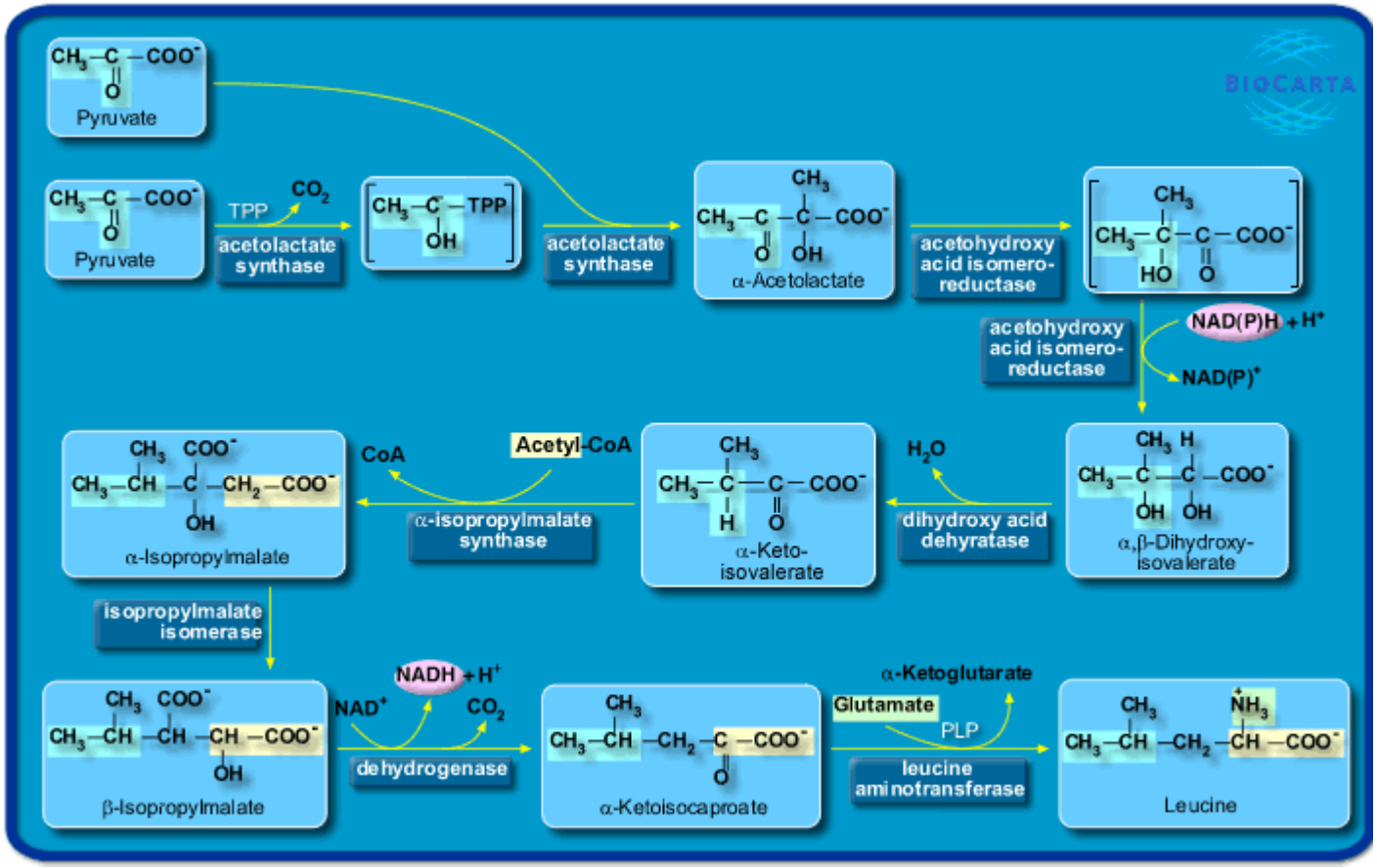
Central dogma of biology

Observation-> description-> explanation-> prediction





Theory of network biology: how biological processes are regulated?



Leucine biosynthesis

Darwin's evolution theory: natural selection (1859)

Entropy and fundamental assumptions in network biology

- Components in a system are coordinated to conserve energy
- Components in a system are coordinated to respond changes

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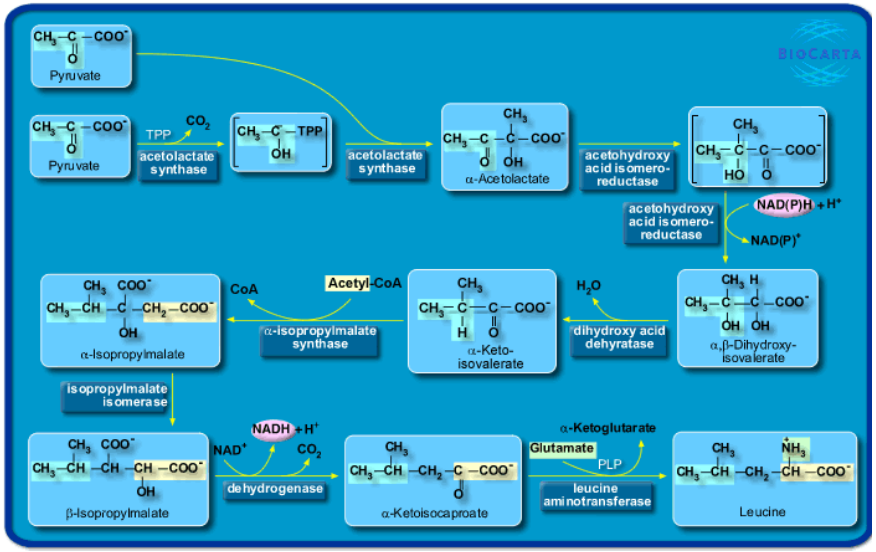
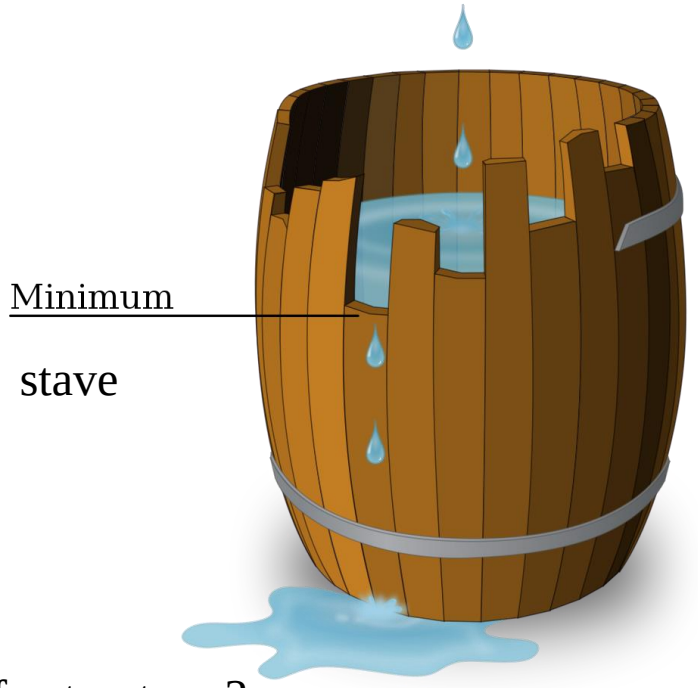
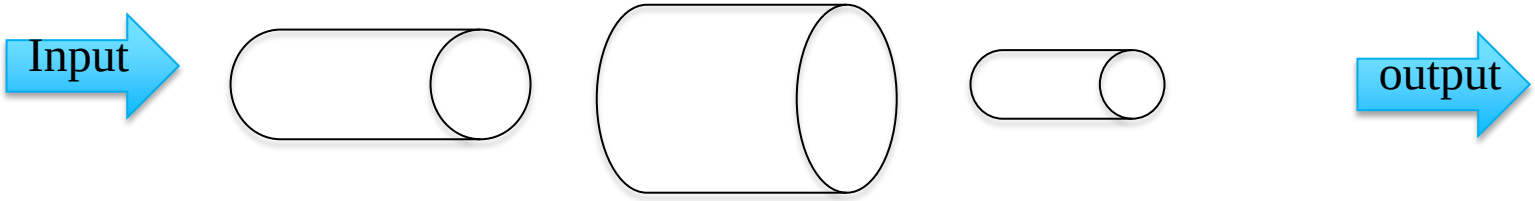




Infrastructure 1 Infrastructure 2 Infrastructure 3



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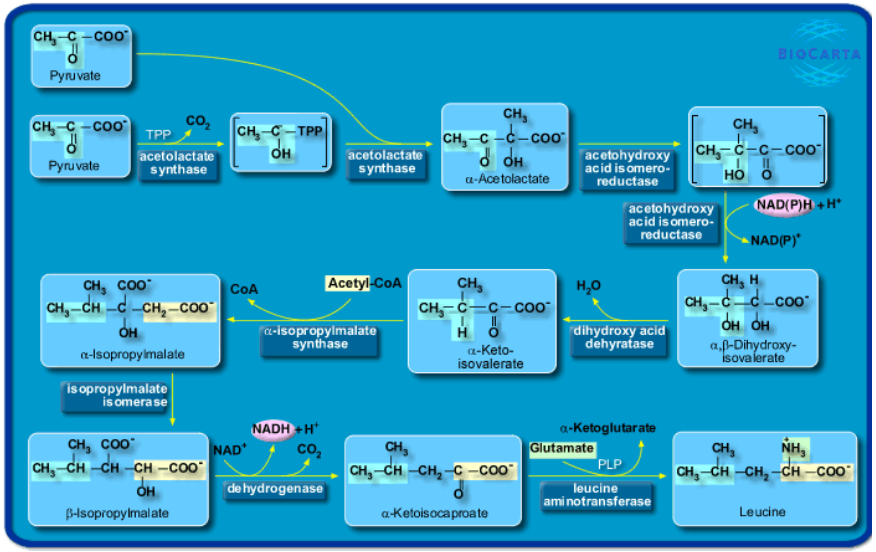
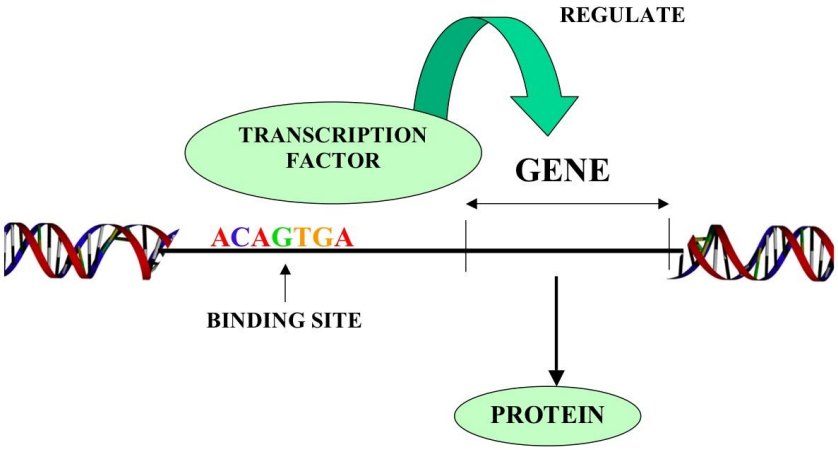
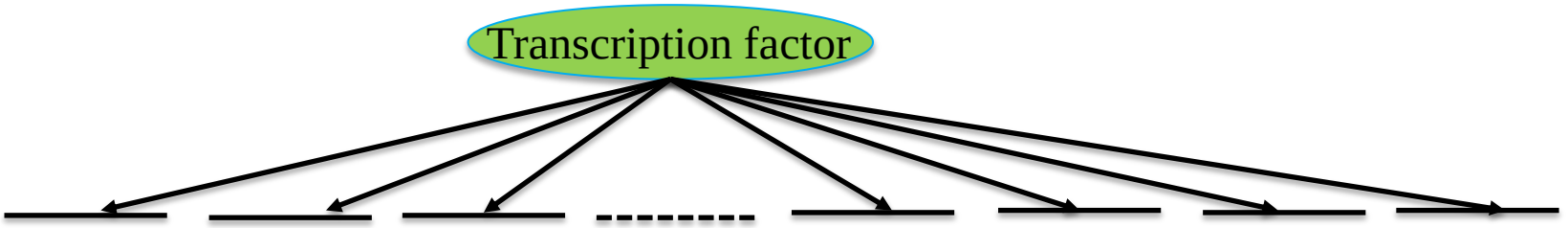


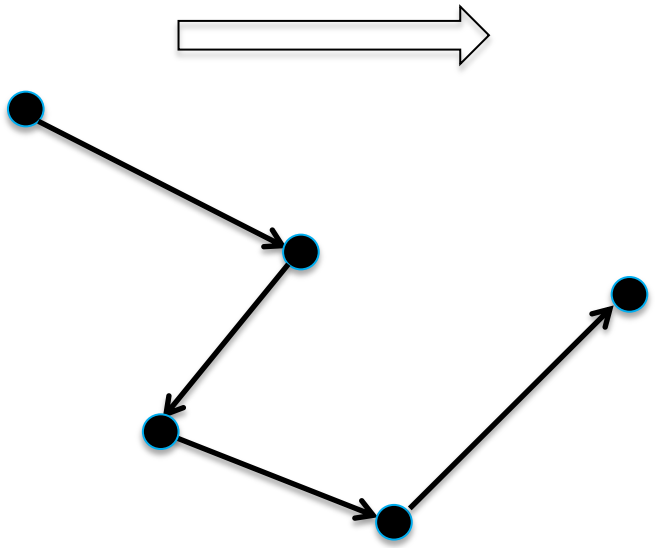
Legend: A transcription factor molecule binds to the DNA at its binding site, and thereby regulates the production of a protein from a gene.

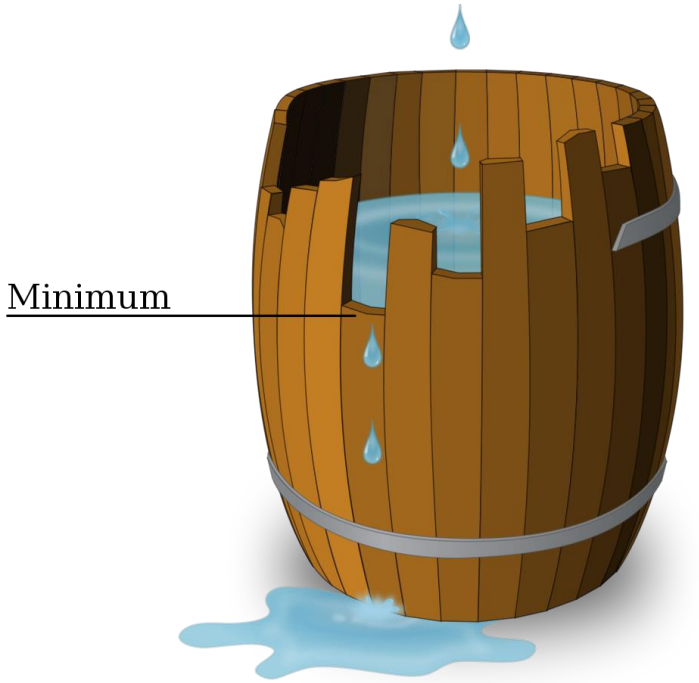




Multiple genes

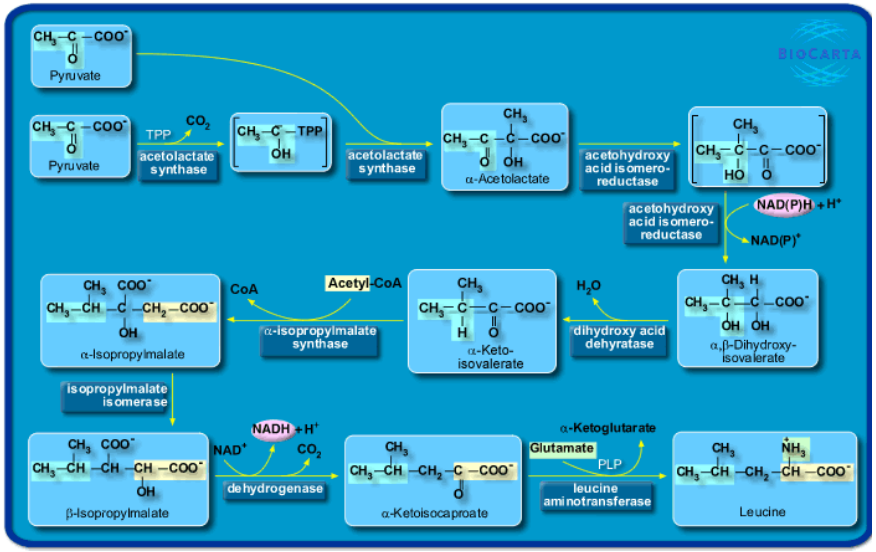
Thermodynamics -> stochastic variation





What is the most efficient way to adapt to changes?

Theory of network biology: to respond quickly?



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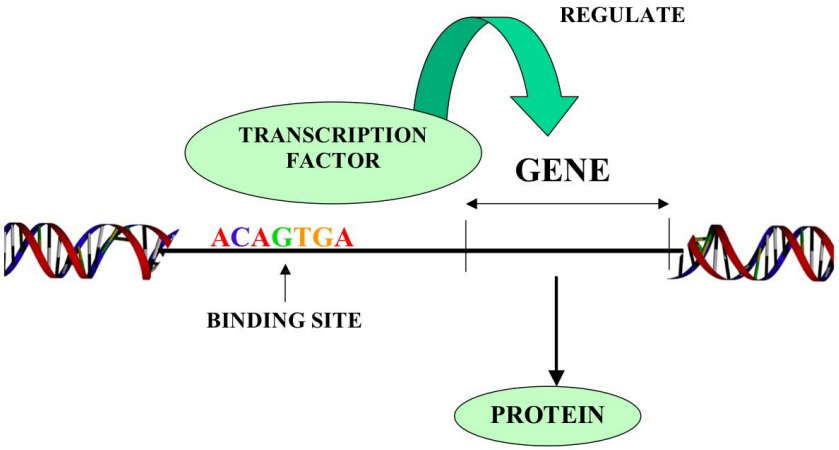


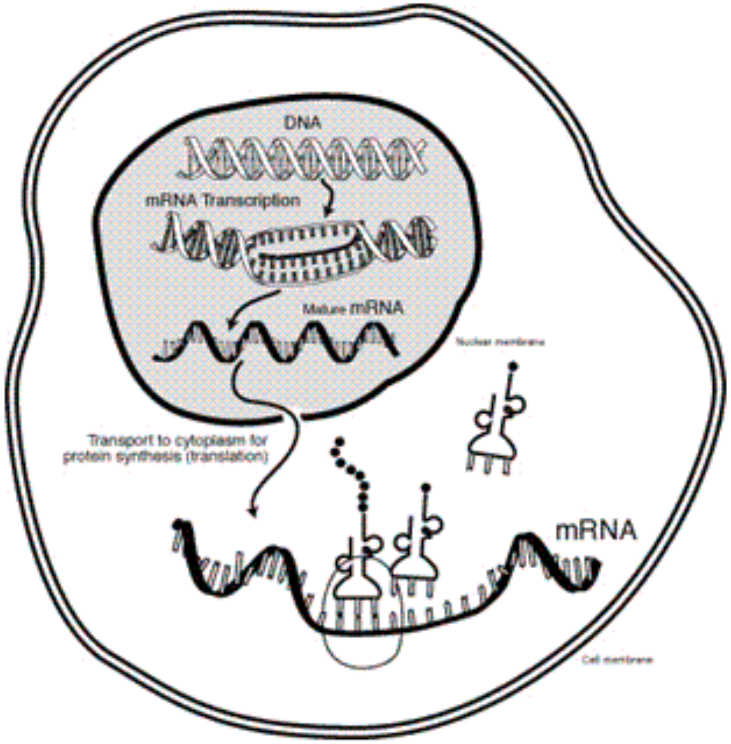
mRNA degradation lifetime > 5 minutes

Protein degradation lifetime >10 minutes

Protein phosphorylation ~ microsecond

Why it is so hard to model biological systems?

- The more we learn, the more complicated it becomes!



Epigenetic regulation : heritable changes in gene function that cannot be explained
by changes in DNA sequence

- DNA methylation
- Chromatin structure

Junk DNA?

Post transcriptional regulation

- Splicing (1981)
- RNA editing (1986)
- miRNA mediated regulation (1993)

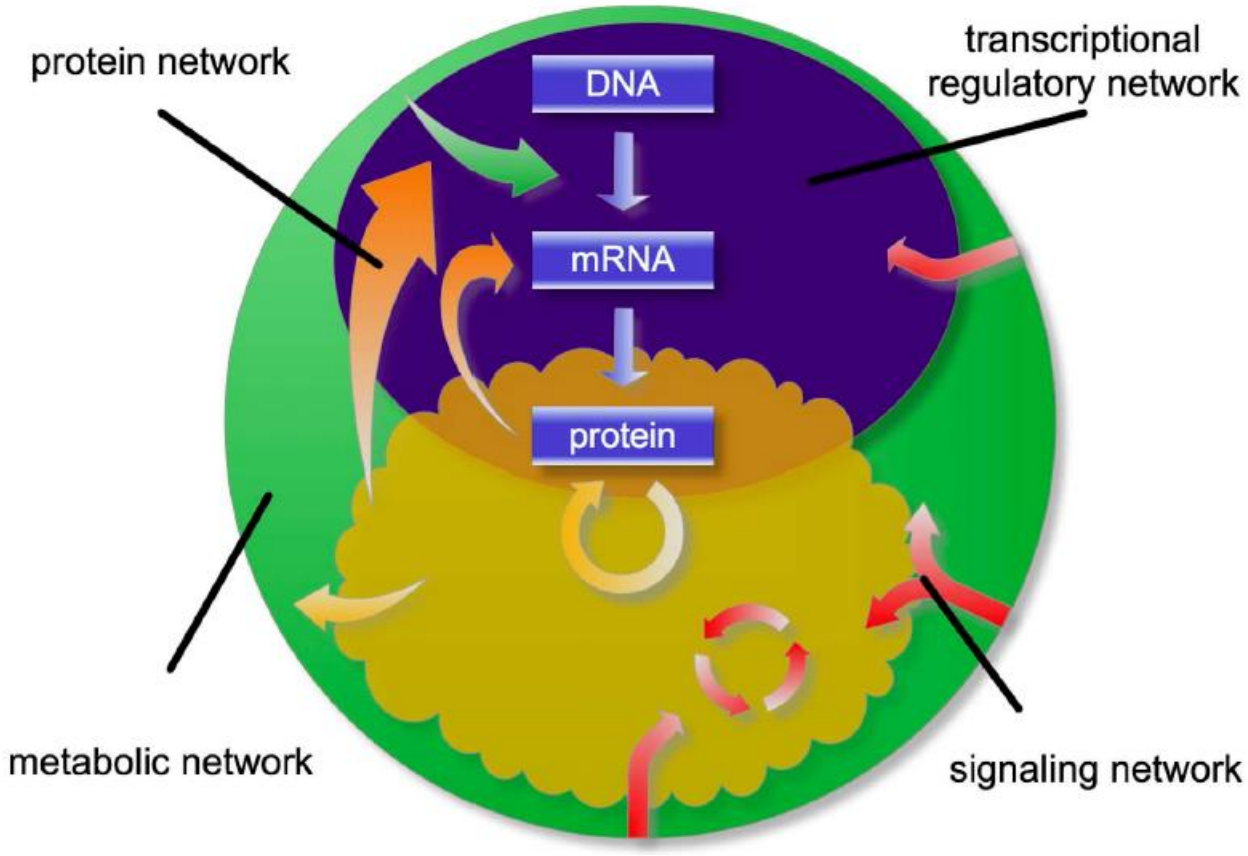
Post translational regulation

- Phosphorylation
- Glycosylation
- acetylation

It is not one gene to one protein anymore!

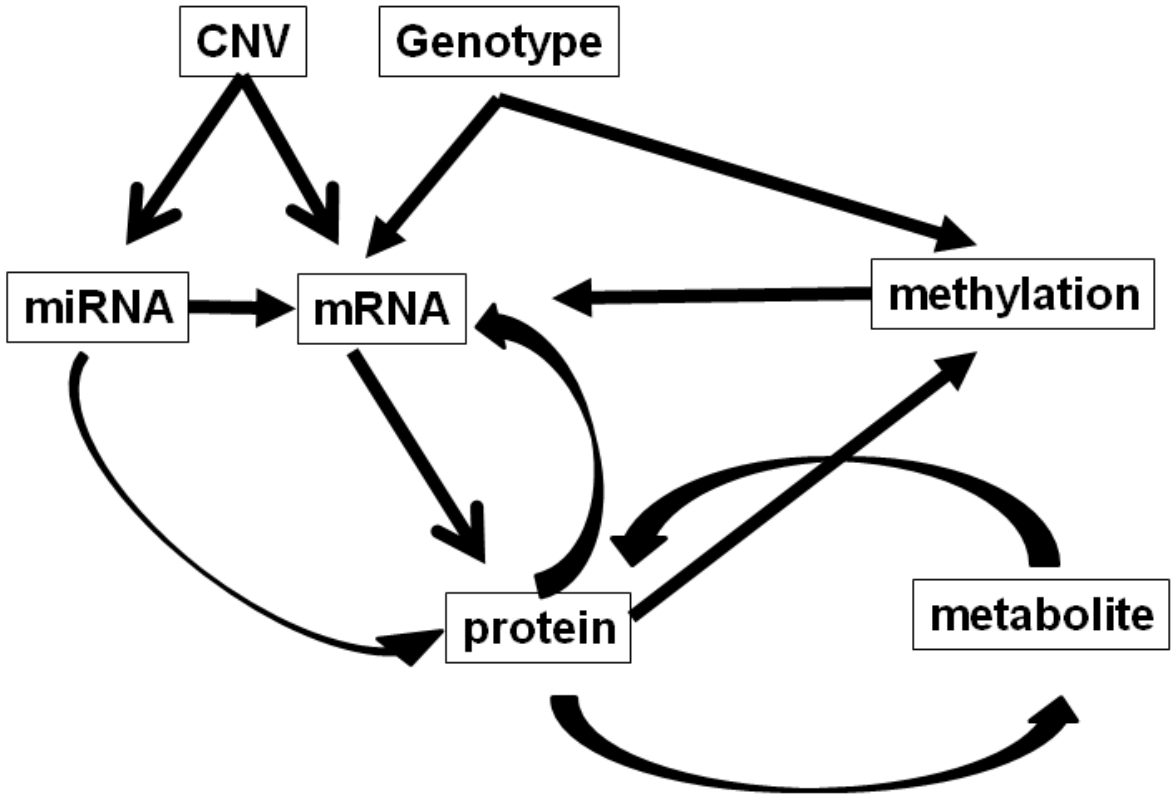
Network models of cells

Observation-> description-> explanation-> prediction



Complex diseases: observations to models

perturbations



perturbations

diseases

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