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# Introduction to Systems Biology

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**What is Systems Biology?**

Biology itself is a very broad term… in the context of this course biology encompasses

Molecular → Cellular → Tissue Organ → Physiological Function

**Systems biology** is the study of how molecules interact and come together to give rise to subcellular machinery that form the functional units capable of operations that are needed for cell, tissue/organ level physiological functions

# Introduction to Systems Biology
## Lecture 1 - Part A -2a Iyengar

The term “Systems Biology” started being widely used in the early 2000s. Prior to that this field was often called Complex Systems - an even vaguer term

Key papers in the late 90s set the stage

Iyer VR, Eisen MB, Ross DT, Schuler G, Moore T, Lee JC, Trent JM, Staudt LM, Hudson J Jr, Boguski MS, Lashkari D, Shalon D, Botstein D, Brown PO. (1999) **The transcriptional program in the response of human fibroblasts to serum.** Science. 283:83-7. PMID: 9872747

*Experimentally - development of microarrays to measure the levels of thousands of mRNAs simultaneously allowed us to see how many components in a cell change in response to stimuli*

# Introduction to Systems Biology
## Lecture 1 - Part A -2b Iyengar

Key papers in 1999

Bhalla US, Iyengar R. (1999) **Emergent properties of networks of biological signaling pathways**. Science. 283:381-7. PMID: 9888852

*Computationally - simulations showed how interaction between components give rise to functional capabilities (in this case switching behavior) that the individual components do not have.*

Alon U, Surette MG, Barkai N, Leibler S. (1999) **Robustness in bacterial chemotaxis**. Nature. 397:168-71. PMID: 9923680

*Experiments and Computation - together showed how certain system behavior such as adaptation in bacterial chemotaxis is robust …that is insensitive to variation of concentrations of protein components in the network*

***Isn't Systems Biology just physiology with a new name?***

Yes … up to a point

Physiology has provided description of functions at tissue/organ level, most often from a phenomenological perspective… a very useful and essential starting point

Often molecular biology and biochemistry are not fully considered in physiological descriptions

Systems Biology uses molecular biology and biochemistry of cellular components to understand **HOW** physiological functions at the cell/tissue and organ level arise.

# Introduction to Systems Biology
## Lecture 1 - Part A -4

Iyengar

**Systems Biology and Genomics**

**Genome** - A set of chromosomes, Winkler in 1920s

**Genomics** - considering genes in the context of the whole genome
*provides a understanding of how genes are organized within chromosomes and the whole genome*
*Characteristics of genes – sequence and single nucleotide polymorphisms, mutations, copy number variations*

**Epigenomics** - DNA methylation of genes

**Transcription** - Regulation of gene expression and patterns of mRNA expression

If *genomics* is one book-end of systems biology ------ *physiological functions* are the other book end.

**Multiscale systems**

In the context of this course multiscale refers to the scales of organizations

Molecular components to subcellular machines -- Transcriptional machinery, Cell motility machinery

Subcellular Machines to Cells

Cells to Tissues and Organs

Organs to whole Organisms

**Increasing levels of organization give rise to new properties and capabilities**

Sometimes multiscale also refers functions in different time scales: millisecs -- secs -- mins -- days

## Top-Down and Bottom-up Approaches

**Top-Down:** Starting from a description of the system as a whole -- understand system characteristics and capabilities

Typically the top-down models provide a big and sometimes comprehensive picture…

However, relations are typically identified by correlation, and causal inference is often not possible

**Bottom-Up:** Starting with cellular components (e.g., genes, proteins , lipids, sugars) develop an understanding of how functional systems such as subcellular machines are assembled, controlled and operated

Bottom-up models can provide mechanistic understanding -- how things work…

but as the systems get bigger one can be lost in the detail

*A case of "can't see the forest by just looking at the leaves"*