What is Systems Biology?

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What is Systems Biology?

• Hiroaki Kitano (Nature 2002, Science 2002) - Systems biology is an emerging field that enables us to achieve in-depth understanding (of biology) at the system level.

• Marc W. Kirschner (Cell 2005) – Systems biology is the study of the behavior of complex biological organization and processes in terms of the molecular constituents.
A historic perspective

- The “old fashioned” biology era
- The information era (> 1990)
- The systems era (> 2000)
The “old fashioned” biology era

• Rise of molecular biology 1953

• Single element issues – structure and function proteins & genes

• Many, many techniques invented and developed in 2nd half of 20th century
The information era

- Human genome project (>1990) led to avalanche of data
- Bioinformatics - creation and advancement of algorithms, computational and statistical techniques, management and analysis of biological data.
- Computational biology - hypothesis-driven investigation of a specific biological problem using computers towards discovery and the advancement of biological knowledge.
The systems era


- Systems issues: signaling, network, pathway, dynamics

- Integration of biological experiment, bioinformatics and hypothesis driven model analysis towards systems-level understanding
The interdisciplinary nature of systems biology

• The “old fashioned” biology era
  – Biology
  – Biostatistics – biological data\+ statistics

• The information era (> 1990)
  – Bioinformatics – biological data\+ computer
  – Theoretical/computational biology – biology\+ physics/models

• The systems era (> 2000)
  – Systems biology – biology\+ data\+ computer\+ statistics\+ physics/models
The section of DNA encoding a protein is a **GENE** (基因). When the protein is produced through transcription and translation the gene is **EXPRESSED** (表現).
Genome (基因組) and the computer have similar design concepts

Chromosome \leftrightarrow \text{Hard Disc}

Genes & other codes \leftrightarrow \text{Programs & documents}

Transcribe gene \leftrightarrow \text{Run program copy document}
A cell and a very large factory

Membrane ↔ Building
Genome ↔ Blueprint
Proteins ↔ Machines & workers
Chemical material ↔ Energy & supplies
Networks & pathways ↔ Physical plant
Regulatory system ↔ Switches & controls
Self supervised* ↔ Engineers/Supervisors
Proteins, energy, functions, etc. ↔ Products & services

*Regulatory and control system in cell is necessarily MUCH more complex than in any factory
A transcription factor (a protein) binds to the DNA at its binding site, thereby regulating the production of a protein from a gene.
There are positive and negative regulations

**Negative regulation**
Boudd repressor TF prevents txn

**Positive regulation**
Bound activator TF promotes txn

Life is self-organized, hence must have feedback mechanisms.
A regulatory gene network

Regulatory gene network for endomesoderm specification (from Eric Davidson)
Systems approaches to disease: In diseased cell, protein and gene regulatory networks DIFFER from their normal counterparts

A network perturbation model of galactose utilization in yeast

High-throughput experiments

• Microarray
  – clustering of expression profiles
  – gene-disruption data
• (protein–protein interaction) yeast two-hybrid data
• Many high-throughput experimental methods and equipments developed since Kitano’s 2002 paper
  – Mass spectrometry
  – Protein microarray
DNA Microarray

Revolutionized bio-technology; can simultaneously study the aberrant expression levels of thousands of genes.
Microfluidic and nanotechnology platforms for systems biology studies

(A) An integrated microfluidics environment for single-cell gene expression studies. (B) Array of nanomechanical biomolecular sensors. (C) An electron micrograph showing a library of 16-nm-wide silicon nanowire biomolecular sensors.
What can physicists do in Systems Biology?

- **Experimental**
  - Design of new methods for *in vivo* and *in vitro* measurement of biological systems
  - Studies of signaling and regulation
  - Life on chips; nano-biosensors

- **Theoretical**
  - Quantitative biology
  - High-throughput data analysis
  - Network classification and dynamics
  - Model and hypothesis concerning disease

- Many, many more ...
An Integrative Research Project @ SyBBi

Integrating DNA-array, protein-array, informatics, computation, and modeling for cancer diseases research

- Develop & manufacture new protein-probe chip for high-throughput application
- Study dynamics of and disease-induced aberration in biological pathways
- Develop integration research protocol
- Model: colon cancer cell line

國科會自然處跨領域整合型計畫（2009－2012）
Connections among components

- Initial probe list
- Initial TF binding sites
  - Protein microarray Fabrication & application (SP3)
  - CCPC
  - TF sites
  - PPIN

- Bioinformatics Analysis (SP1)
- Literature
- Data analysis
- Database

- Colorectal cancer cell pathways & aberrations
  - Pathways
  - Aberration
  - Model/Dynamics

- Systems biology Application (SP4)

- Exon microarray Experiments (SP2)
  - Exon expression
  - Stress induced changes
  - Time course data

- Essay proteins
  - “Internet”

Data

Validation

Verification/integration

Data

Data analysis

Database

Literature

Pathways Aberration Model/Dynamics

Initial PPIN/pathways

Initial probe list

Initial TF binding sites
Website for many papers on systems biology

http://sansan.phy.ncu.edu.tw/~hclee/SB_course/index.htm
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