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RAVI RADHAKRISHNAN

EB PPT

BIOGRAPHY

RAVI RADHAKRISHNAN (ASSOCIATE PROFESSOR) OBTAINED HIS PHD IN CHEMICAL PHYSICS FROM THE DEPARTMENT OF CHEMICAL ENGINEERING AT CORNELL UNIVERSITY IN 2001. AFTER TWO POSTDOCTORAL ASSIGNMENTS IN CHEMICAL PHYSICS AND BIOPHYSICS AT MIT AND NYU/HHMI, HE JOINED THE UNIVERSITY OF PENNSYLVANIA FACULTY IN 2005. DR. RADHAKRISHNAN HAS APPOINTMENTS IN THE DEPARTMENTS OF BIOENGINEERING, CHEMICAL ENGINEERING, AND BIOCHEMISTRY AND BIOPHYSICS. HIS LABORATORY IS INVOLVED IN DEVELOPING MODELING AND SIMULATION PROTOCOLS USING PRINCIPLES FROM APPLIED MATHEMATICS, CHEMICAL PHYSICS, AND MOLECULAR BIOPHYSICS IN ORDER TO PREDICT SINGLE MOLECULE PROPERTIES AS WELL AS SIGNAL TRANSDUCTION MECHANISMS RELATED TO CANCERS. ONGOING PROJECTS IN DR. RADHAKRISHNAN'S LAB INCLUDE FINDING A MOLECULAR BASIS FOR DNA REPAIR AND REPLICATION IN OXIDATIVELY DAMAGED DNA, SEARCHING FOR NEW PARADIGMS IN DRUG RESISTANCE IN CANCER THERAPEUTICS, AND OPTIMIZING DRUG DELIVERY PROTOCOLS BY A RATIONAL DESIGN OF MICROCARRIERS. HIS LABORATORY IS CURRENTLY FUNDED BY US NATIONAL SCIENCE FOUNDATION AND NATIONAL INSTITUTES OF HEALTH. DR. RADHAKRISHNAN IS THE RECIPIENT OF THE HEWLETT PACKARD YOUNG INVESTIGATOR AWARD AND SERVERS ON THE EDITORIAL BOARD OF THE JOURNAL OF BIOMEDICAL SCIENCE AND BIOENGINEERING.

RESEARCH INTEREST

STATISTICAL MECHANICS; MOLECULAR SYSTEMS BIOLOGY; MULTISCALE MODELING

WHY SYSTEMS BIOLOGY?

On the technology side (PUSH): Capabilities for high-throughput data gathering that have made us aware that biological networks have many more components than we previously surmised.

On the biology side (PULL): The realization that to the extent that we don't characterize biological systems quantitatively in their full complexity, the scope and accuracy of our understanding of those systems will be compromised. (in classical experimental terms, the uncontrolled variables in the system will undermine our confidence in the conclusions we draw from our experiments and observations)

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SYSTEMS BIOLOGY VS. TRADITIONAL CELL AND MOLECULAR BIOLOGY

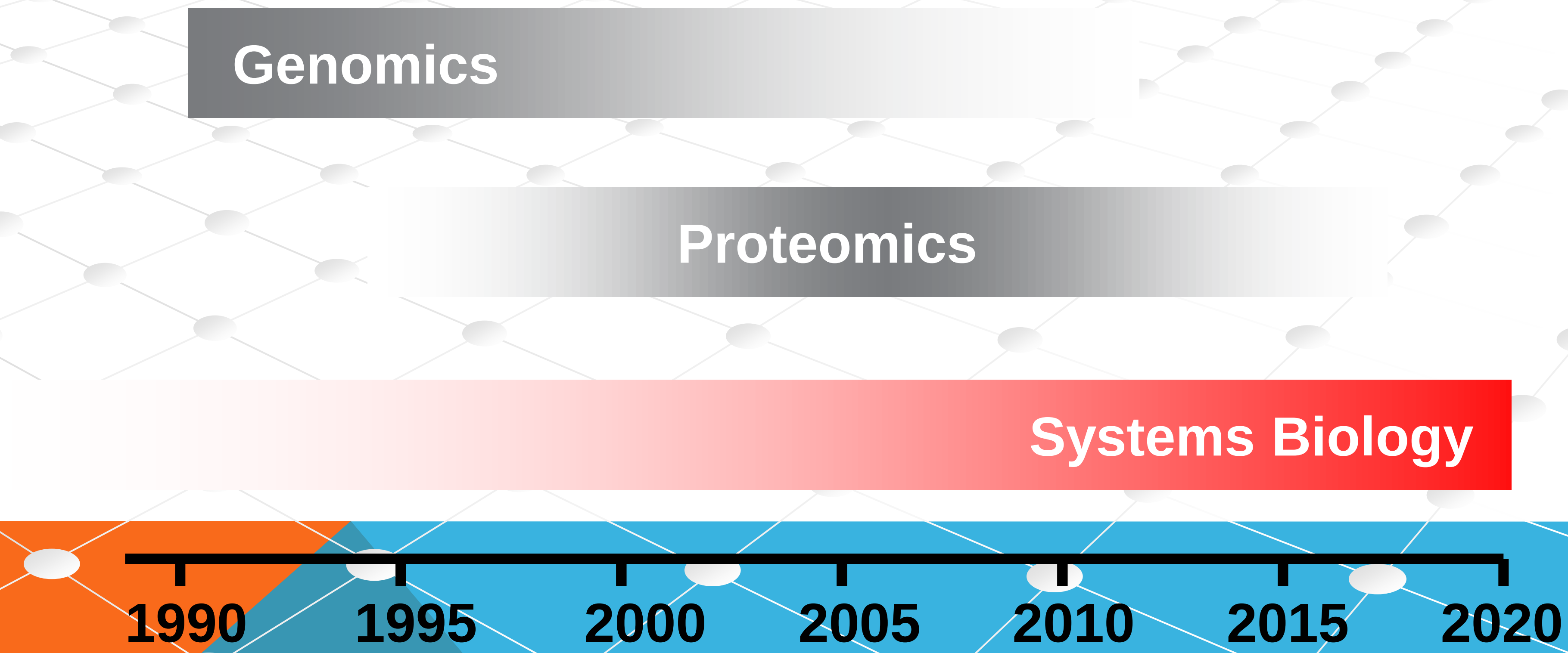
Experimental techniques in systems biology are high throughput.

Intensive computation is involved from the start in systems biology, in order to organize the data into usable computable databases.

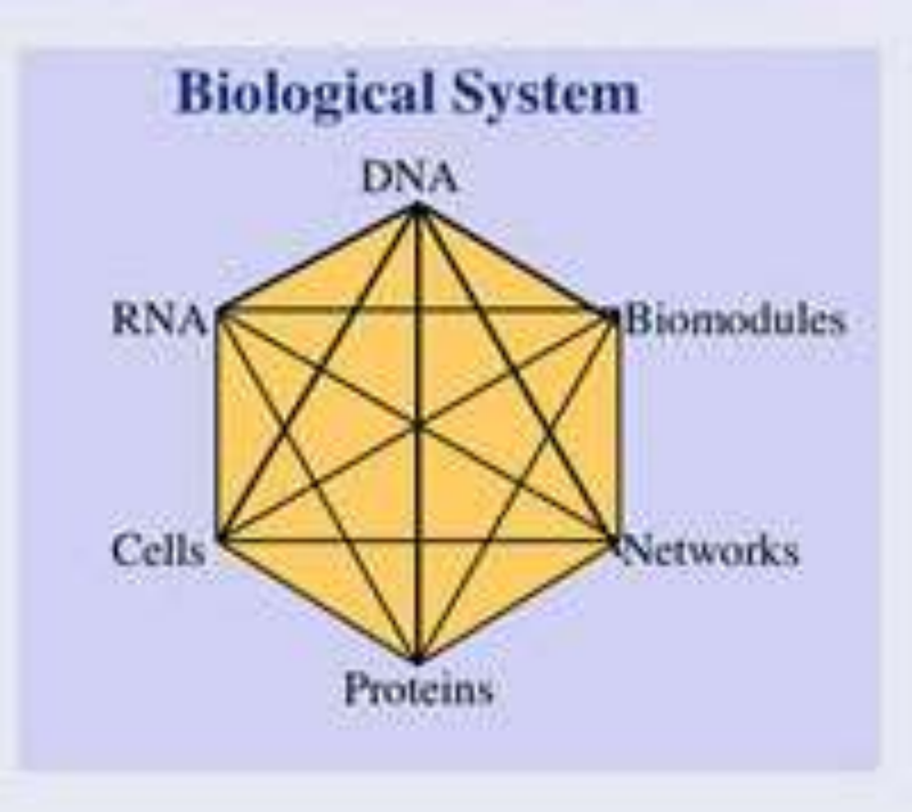
Exploration in traditional biology proceeds by successive cycles of hypothesis formation and testing; data accumulates during these cycles.

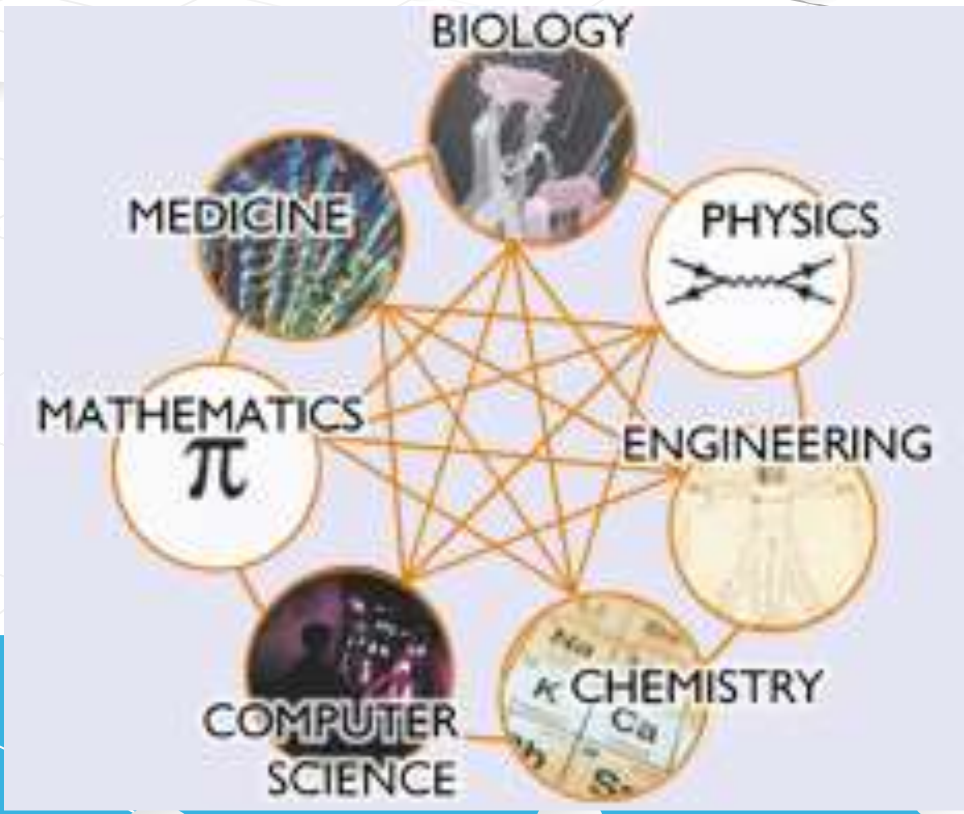
***Systems biology initially gathers data without prior hypothesis formation*; hypothesis formation and testing comes during post-experiment data analysis and modeling.**

GENOMICS, PROTEOMICS & SYSTEMS BIOLOGY



SYSTEMS BIOLOGY IS AN INTEGRATION OF DATA & APPROACHES

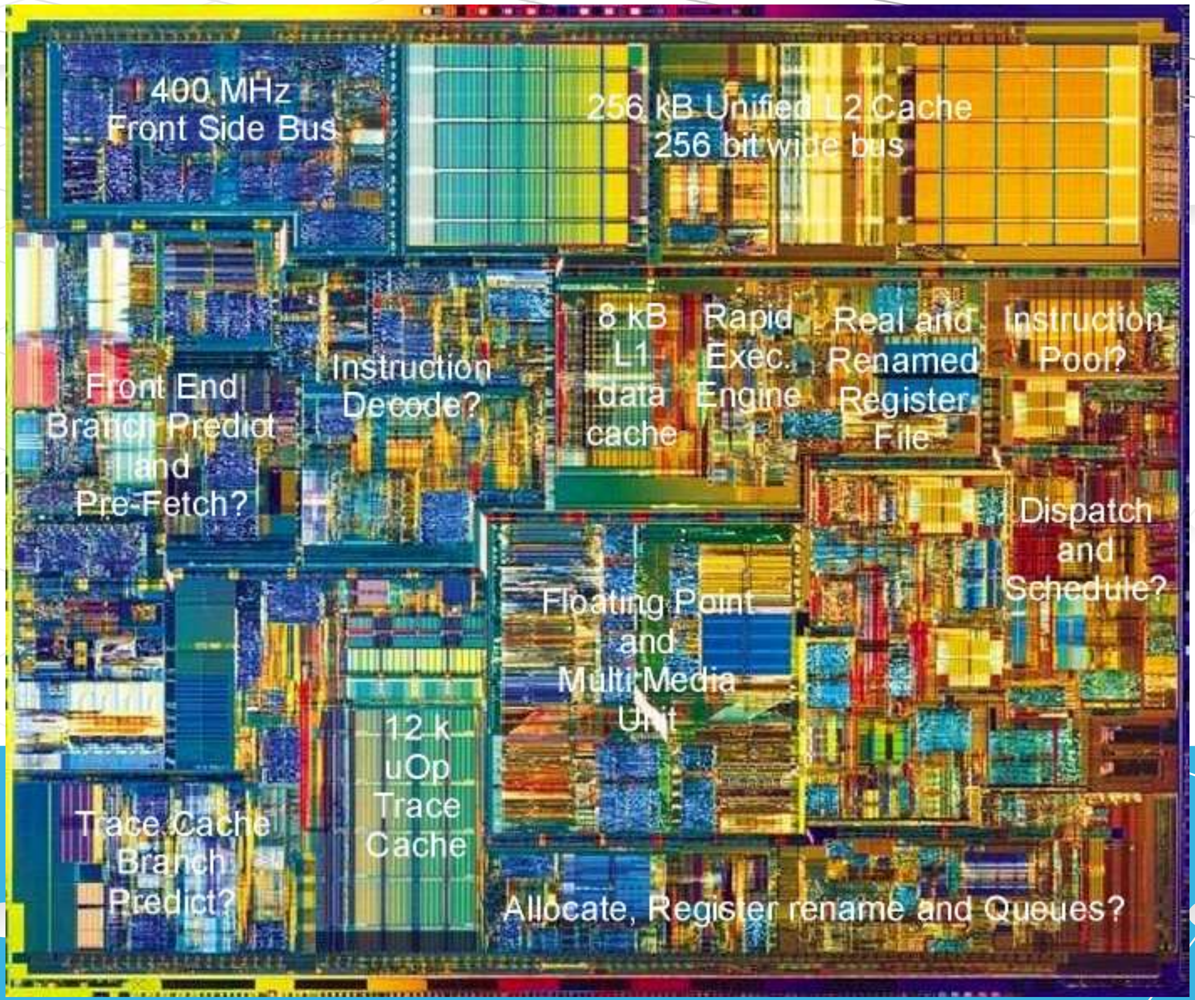




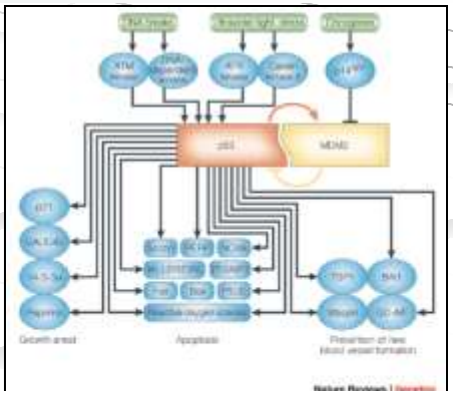
MAN-MADE COMPLEX DEVICES

Intel Pentium 4

42 million transistors



AIMS OF SYSTEMS BIOLOGY



Tier 1: Interactome

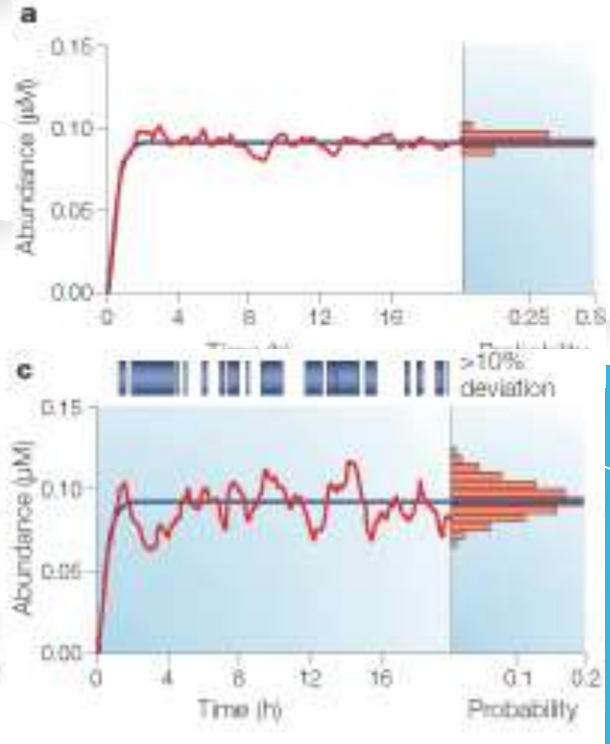
- Which molecules talk to each other in networks?

Tier 2: Deterministic

- What is the average case behavior?

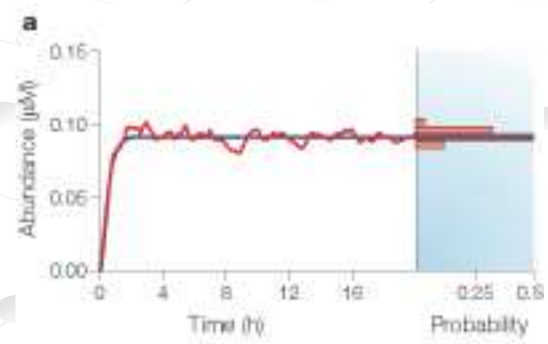
Tier 3: Stochastic

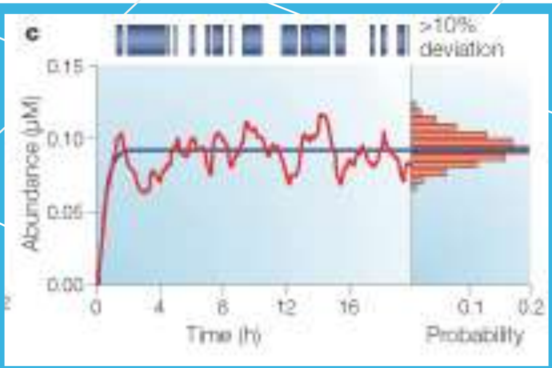
- What is the variance of the system?



AIMS OF SYSTEMS BIOLOGY

- **Tier 2 & 3**
  - **Deterministic:** Behavior of system with respect to time is predicted with certainty given initial conditions
  - **Stochastic:** Dynamics cannot be predicted with certainty given initial conditions





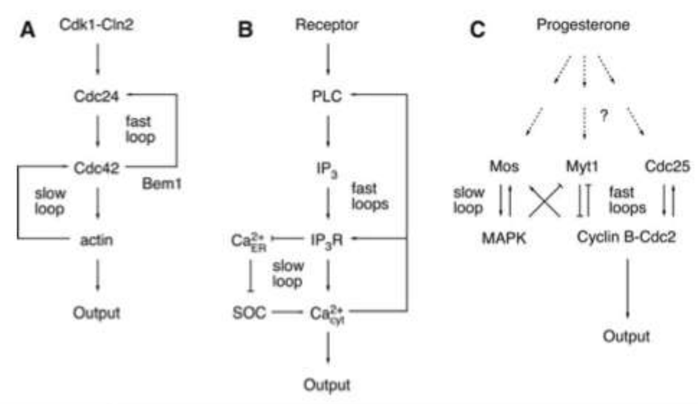
AIMS OF SYSTEMS BIOLOGY

Tier 2 & 3

- Enumerate biochemistry
- Define network/mathematical relationships
- Compute numerical solutions

Table 1. Examples of interlinked positive feedback loops in biological regulation.

System	Positive feedback loops
Mitotic trigger	Cdc2 → Cdc25 → Cdc2 Cdc2 -| Wee1 -| Cdc2 Cdc2 -| Myt1 -| Cdc2
p53 regulation	p53 → PTEN -| Akt → Mdm-2 -| p53 p53 → p21 -| CDK2 -| Rb -|Mdm-2 -| p53
Xenopus oocyte maturation	Cdc2 → Mos → Cdc2 Cdc2 → Cdc25 → Cdc2 Cdc2 → Myt1 → Cdc2



1) One loop

$$\frac{dOUT}{dt} = k_{out\_on} * A * (1 - OUT) - k_{out\_off} * OUT + k_{out\_min}$$

$$\frac{dA}{dt} = [stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - A) - A + k_{min}] * \tau_A$$

2) Two loops

$$\frac{dOUT}{dt} = k_{out\_on} * (A + B) * (1 - OUT) - k_{out\_off} * OUT + k_{out\_min}$$

$$\frac{dA}{dt} = [stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - A) - A + k_{min}] * \tau_A$$

$$\frac{dB}{dt} = [stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - B) - B + k_{min}] * \tau_B$$

AIMS OF SYSTEMS BIOLOGY

Deterministic

- Ordinary differential equations (ODE's)
  - Concentration as a function of time only
- Partial differential equations (PDE's)
  - Concentration as a function of space and time

$$\frac{d\vec{x}}{dt} = f(\vec{x})$$

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} - \nu\frac{\partial C}{\partial x} + R$$

Stochastic

- Stochastic update equations
  - Molecule numbers as random variables
  - functions of time

$$\frac{\partial}{\partial t}P(Y,t|Y_0,t_0) = \sum_{\mu}^{M}[c_\mu h_\mu(Y-\alpha_\mu) \times P(Y-\alpha_\mu,t|Y_0,t_0) - c_\mu h_\mu(Y)P(Y,t|Y_0,t_0)]$$

Y = # molecules at time t

Journals

1.Analytical & Bioanalytical Techniques
http://omicsonline.org/analytical-bioanalytical-techniques.php
2.Chromatography & Separation Techniques
http://omicsonline.org/chromatography-separation-techniques.php

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