Introduction to Systems Biology

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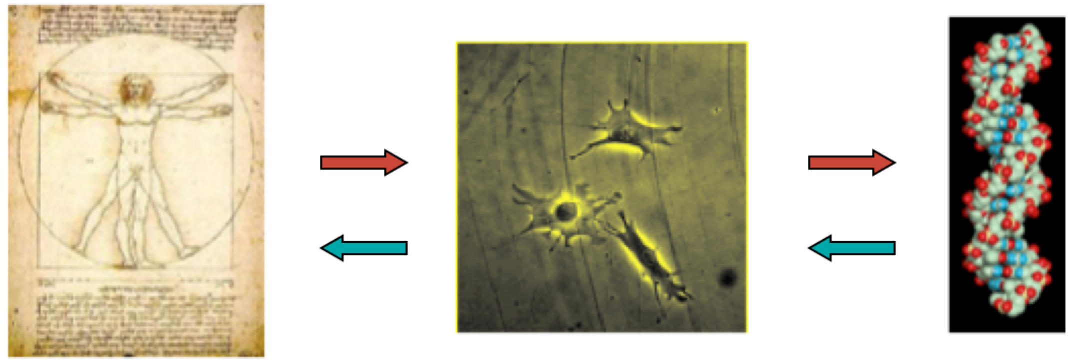
> "Biology-the study of life-has a long and distinguished history dating back millennia, but our understanding of the *mechanisms* by which living things operate is fairly recent, and is still developing."
>
> - Ingalls

Introduction to Quantitative Biology, Fall 2016

Reductionism vs. Systems Biology



The driving force in 20th century biology has been reductionism:

From the population to the individual
From the individual to the cell
From the cell to the biomolecule
From the biomolecule to the genome
From the genome to the genome sequence
With the publication of genome sequences, reductionist biology has reached its endpoint

The driving force for 21st century biology will be integration:

Integrating the activity of genes and regulators into regulatory networks
Integrating the interactions of amino acids into protein folding predictions
Integrating the interactions of metabolites into metabolic networks
Integrating the interactions of cells into organisms
Integrating the interactions of individuals into ecosystems

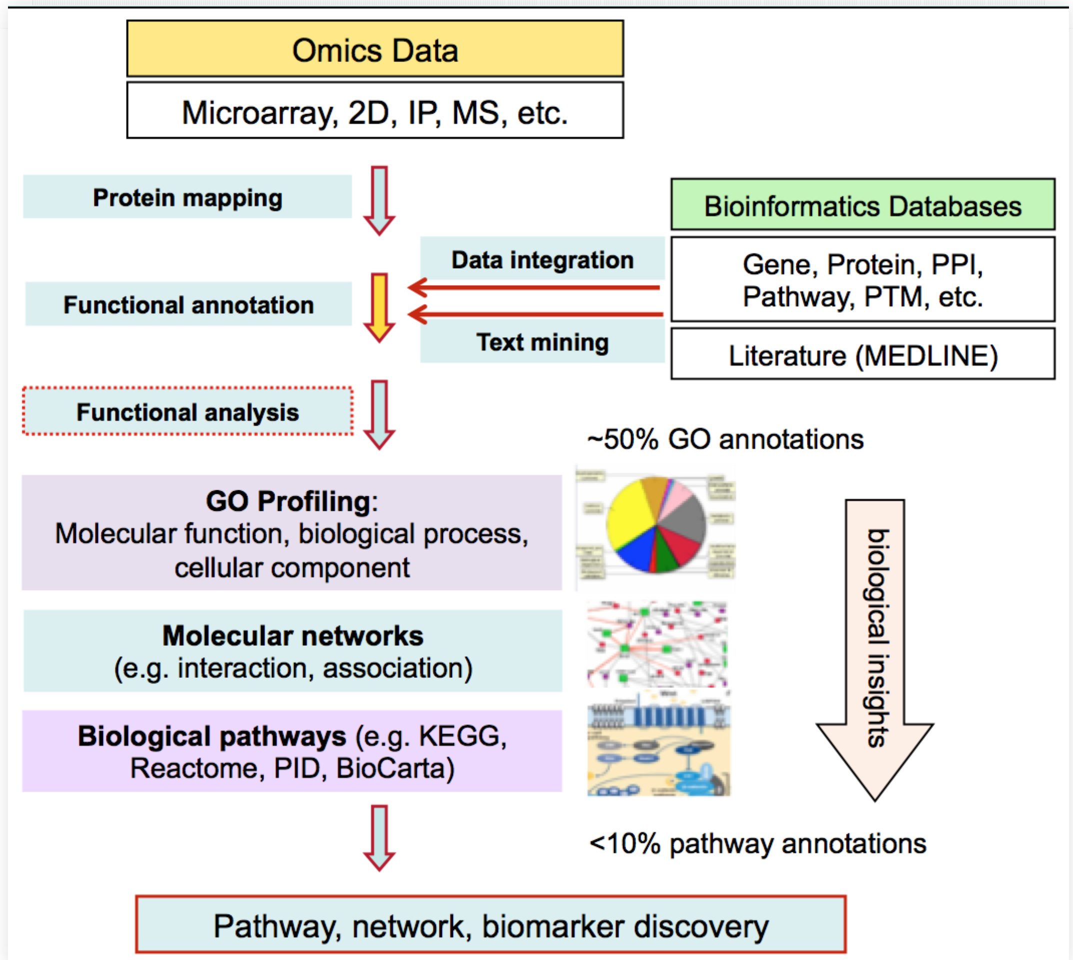
The Role of Computation

"A key feature of present-day biological studies is a reliance on computation."

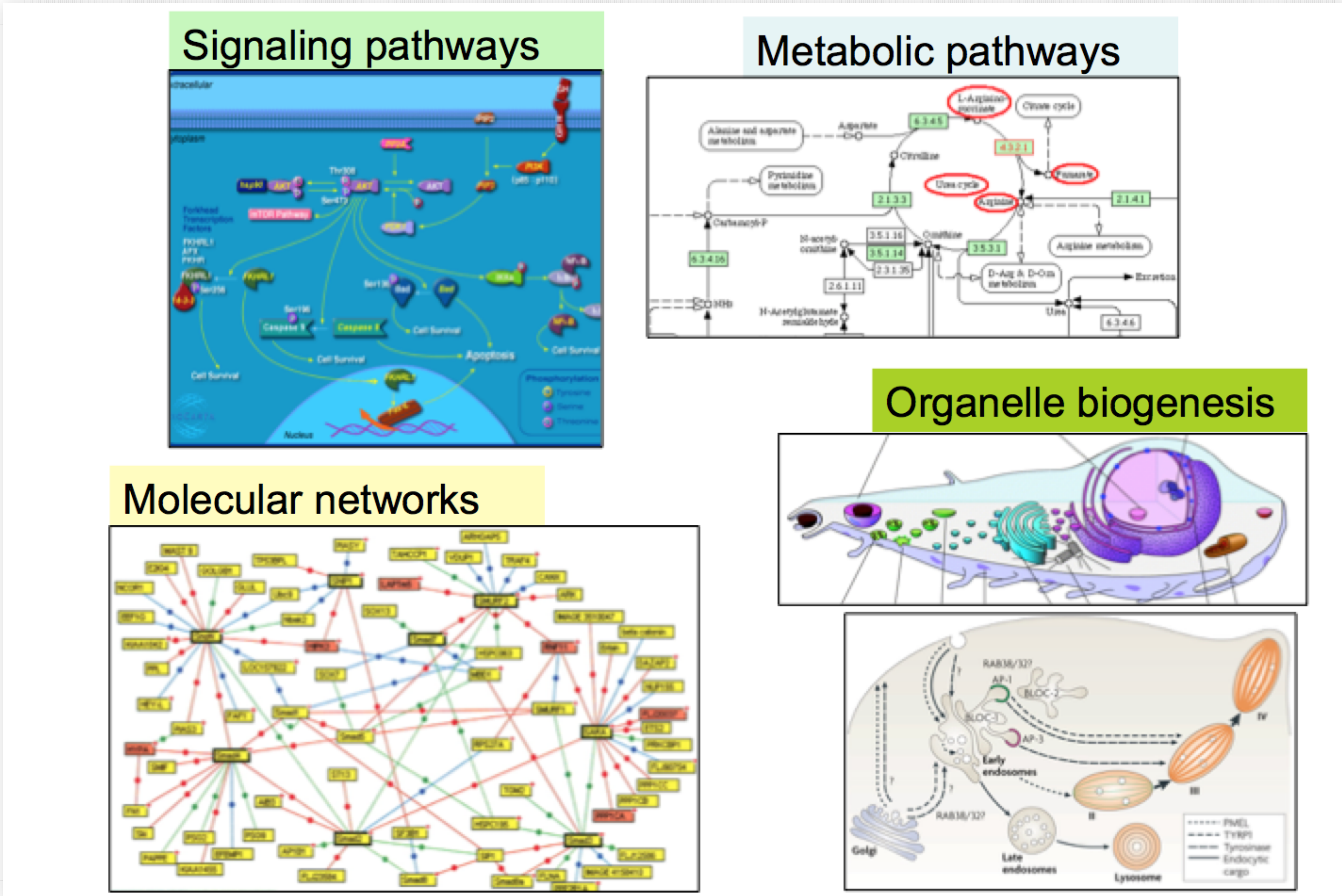
- Ingalls

Bioinformatics vs. mechanistic modeling

Bioinformatics: Omics and System States



Biological Pathways and Networks



Dynamic Systems

We are not going to explore bioinformatics. We we investigate "intracellular processes as dynamic systems."

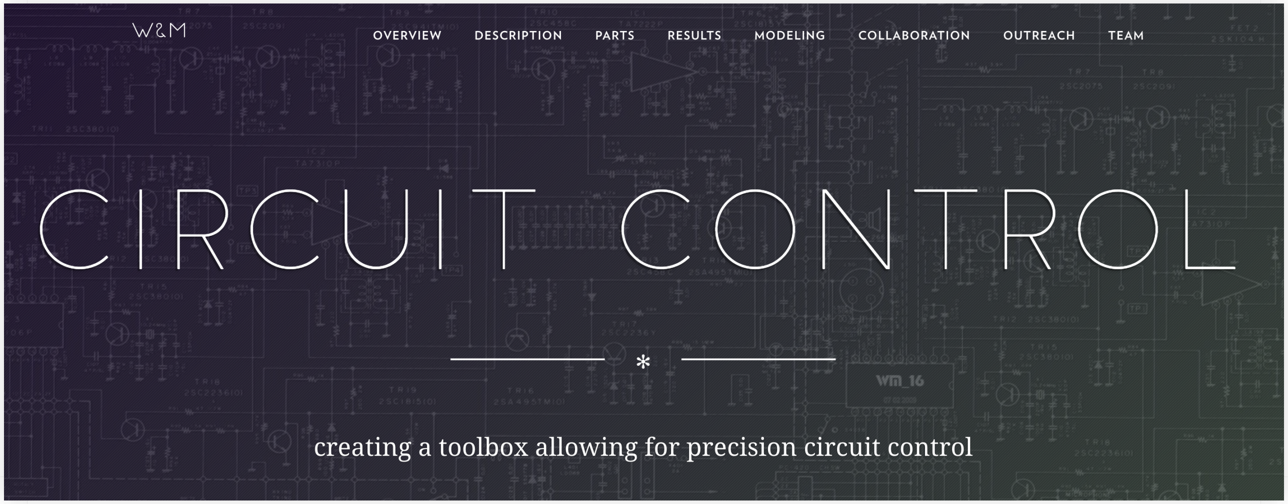
"The use of such models in molecular biology has been, in the past, hampered by the absence of experimental observations of system behaviour; that is no longer the case."

- Ingalls

Question: How do you estimate paramaters for a system with hundreds of molecular species and thousands of interactions?

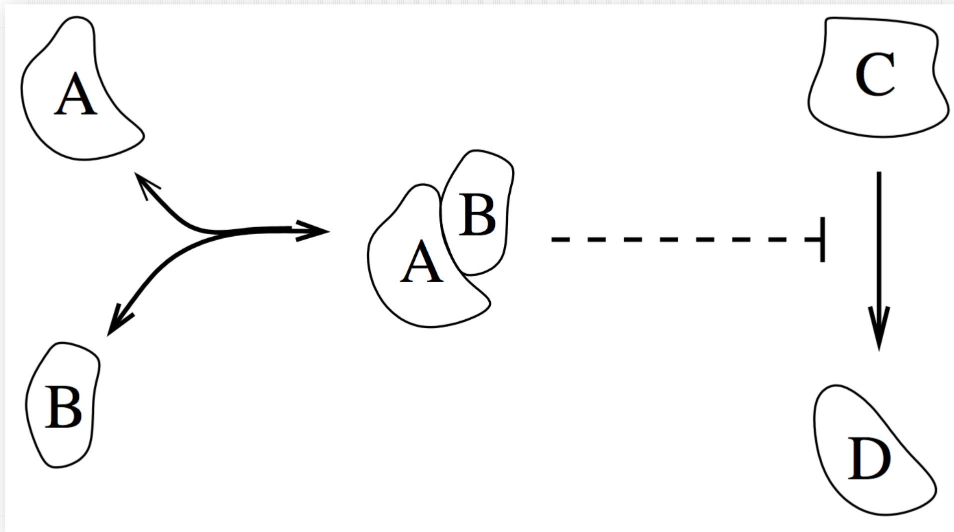
Reverse vs. Forward Engineering

International Genetically Engineered Machine (iGEM) competition



What is a Dynamic Mathematical Model?

...in systems biology



Definition: A ***model*** is a simplified, abstract (or concrete) representation of objects and their relationships and/or processes in the real world.

What is a Dynamic Mathematical Model?

"Quantitative descriptions of molecular interactions typically invoke the laws of physics and chemistry. The resulting models are thus mechanistic - they describe the mechanisms that drive the observed behaviour."

- Ingalls

Question: What can I do with a dynamic model?

Answer: Simulation and analysis.

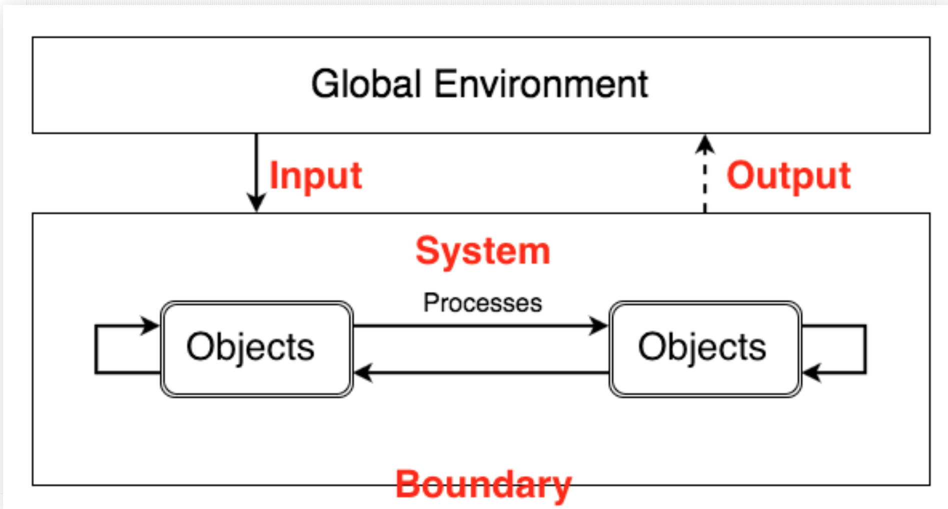
"Whereas *simulations* indicate how a system behaves, *model analysis* reveals why a system behaves as it does."

- Ingalls

What is a system?

Definition: In his book Out of Control (Kelly, 1995), Kevin Kelly defines a system as "anything that talks to itself."

A system also must have a ***boundary***.



What is a complex system?

Definition: Most would agree that a system qualifies as ***complex*** if the overall behaviour of the system cannot be intuitively understood in terms of the individual components or interactions.

Sound familiar? Concept of emergence!

Two essential features of complex systems:

- Nonlinear interactions or processes
- Feedback loops

Positive Feedback

Definition: ***Positive feedback*** is exhibited when system components increase (*excite*) their own activity.

Result: Unstable divergent behaviour, but when the mechanism is constrained by saturating effects, can lead to 'locked-in' states and memory.

Examples:

- Exponential growth

Negative Feedback

Definition: ***Negative feedback*** is exhibited when system components inhibit their own activity.

Result: Stabilization (generally), but can lead to instability and oscillations if there is a *time lag* in the feedback.

Examples:

- Thermostat
- Logistic growth