Summer School Introduction and Overview: Benefits for Immunologists to Use "Modeling" Approaches

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Outline

- Introduction: computational immunology
  - Basic concepts and scope
  - Multidisciplinary interplay
- Benefits for immunologists to use modeling approaches
- Summer school overview
- Symposium overview

Definitions and Concepts

- Computational biology
- Bioinformatics
- Systems biology
- Computational immunology

Definitions and Concepts

- Computational biology: An interdisciplinary field that applies the modeling, analysis and computing techniques from
  - ✓Computer science
  - ✓Mathematics
  - ✓Statistics
  - ✓Informatics
  - ✓Physics and engineering

  to address biological problems.

Definitions and Concepts

- Bioinformatics: An interdisciplinary field that applies
  - ✓Computer science
  - ✓Statistics
  - ✓Information technologies

  to the field of biology and biomedicine, particularly to analysis and annotation of genomics, genetics and other high-throughput "-omics" data.

Definitions and Concepts

- Bioinformatics: includes development and application of
  - Computing algorithms, software engineering, databases, artificial intelligence, web technologies, computer simulations, data and text mining techniques, machine learning
  - Statistical data analysis: pattern recognition
  - Mathematical or computational modeling

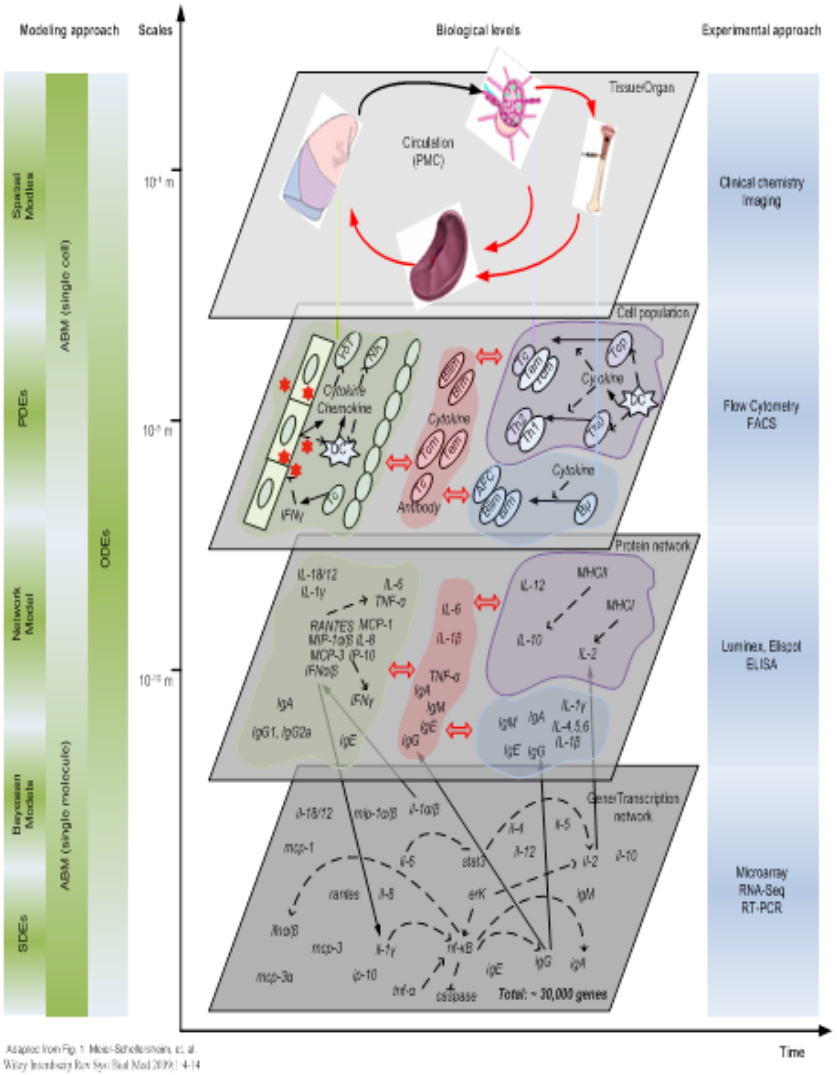
  to deal with management, processing and analysis of biological information and data at genetic, molecular/protein and cellular levels

Definitions and Concepts

- Systems biology: an interdisciplinary study field that focuses on the systematic study of
  - complex interactions between the components of a biological system, and
  - how these interactions give rise to the function and behavior of that system

  using the integration rather than reduction approach.

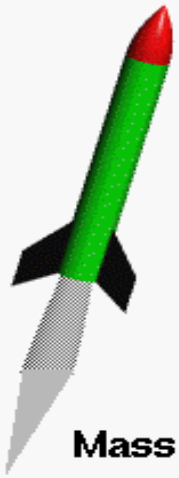
Two Complex Systems



A Rocket System

A Rocket System: Tsiolkovsky Rocket Equation

Ideal Rocket Equation



M = instantaneous mass of rocket
u = velocity of rocket
t = time
F = net force = thrust = $\dot{m}\, V_{eq}$
V_{eq} = equivalent engine exhaust velocity = Isp g_0

mf = full mass
me = empty mass
mp = mass of propellant
Isp = specific impulse

Newton's second law of motion: $\frac{d\,Mu}{dt} = F = V_{eq}\frac{d\,mp}{dt}$

$M\,du + u\,dM = V_{eq}\,dmp$

Assume we move with rocket --> u = 0

$M\,du = -V_{eq}\,dM$

Mass of rocket varies with time:

$M(t) = me + mp(t) \quad dM = -dmp$

$du = -V_{eq}\frac{dM}{M}$

MR = propellant mass ratio = $\frac{mf}{me}$

$\Delta u = -V_{eq}\,\ln(M)\Big|_{mf}^{me}$

$$\Delta u = V_{eq}\ln\left(\frac{mf}{me}\right) = V_{eq}\ln MR = Isp\; g_o \ln MR$$

Definitions and Concepts

- Systems biology: includes development and application of
  - Control theory and systems theory
  - Quantitative modeling of biological processes: mathematics, engineering and physics etc.
  - Statistical data integration methods

  to study complex interactions between the components of a biological system using the integration rather than reduction approach.

Definitions and Concepts

- Systems biology study: key features and careful experimental design
  - Study the interactions: Capture the dynamics feature of the system-need time course data
  - Integration rather than reduction: measure key elements of the system simultaneously
  - Need advanced data analysis methods integrated with mechanism-based models
  - More expensive

Definitions and Concepts

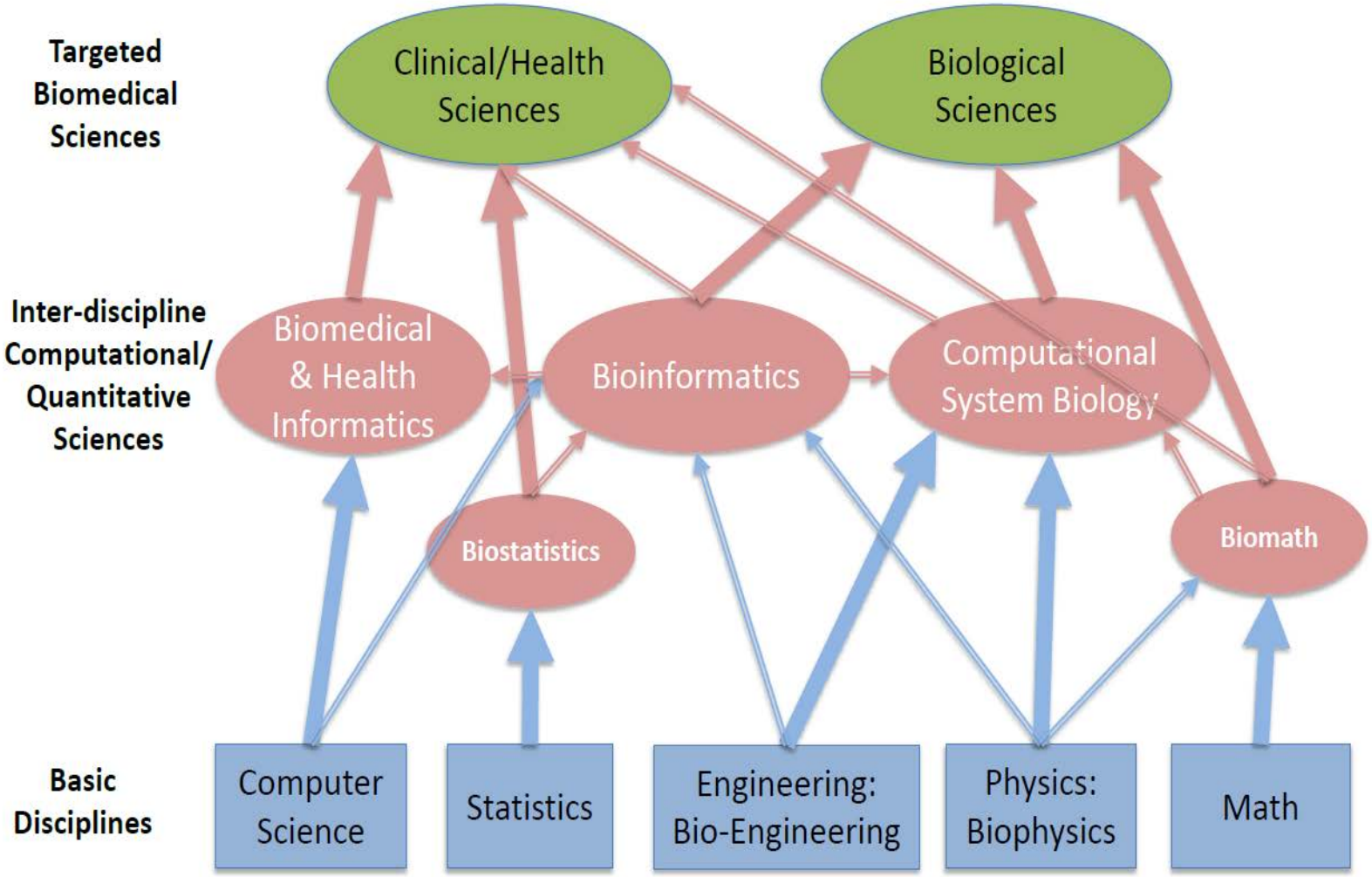
- Computational immunology and immuno-informatics: use mathematical/computational models or representations, derived from immunological/biological concepts and mechanisms based on experimental data to query or address immunological problems by employing computational methods, bioinformatics and/or systems biology approaches

Definitions and Concepts

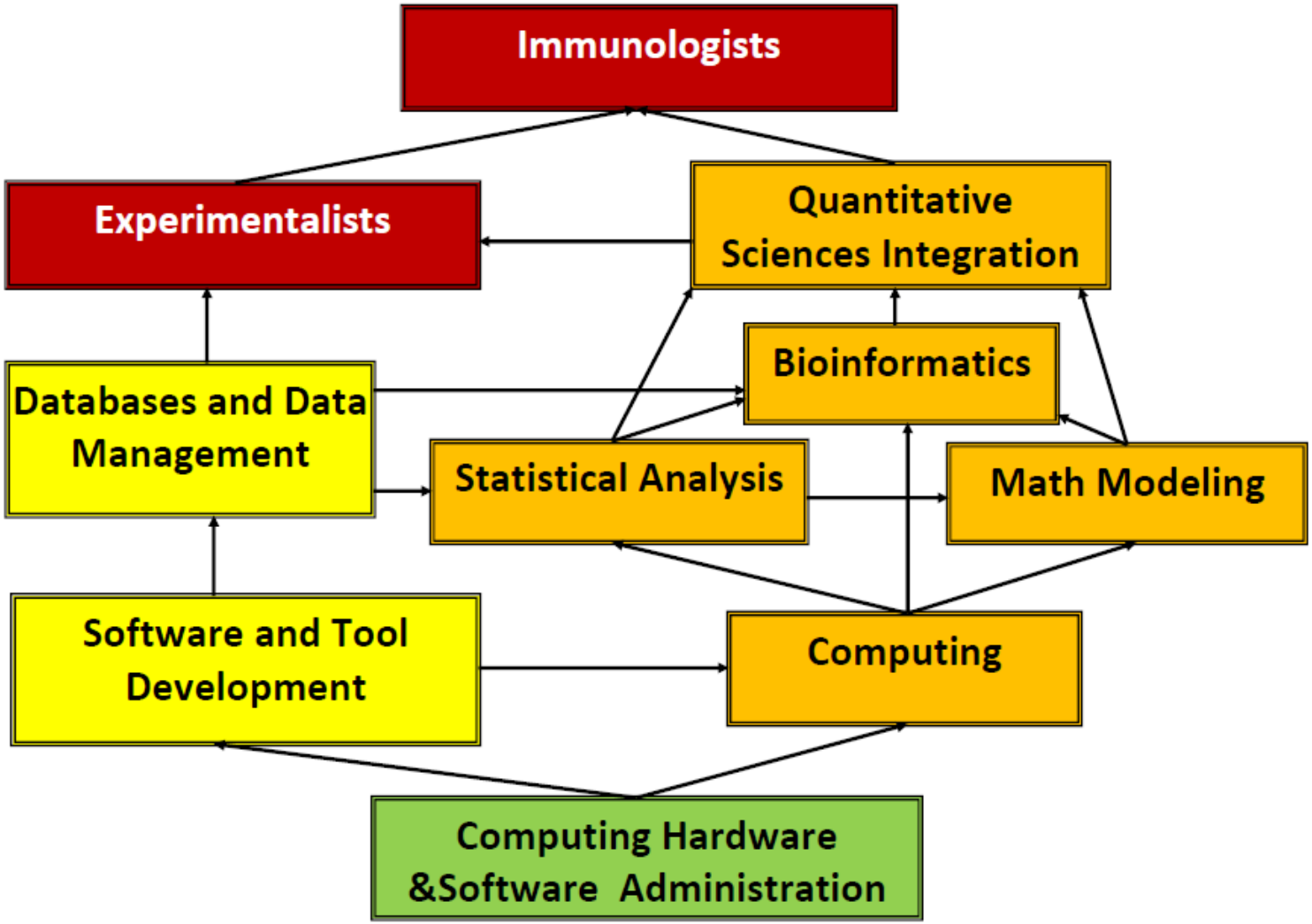
- Computational immunology and immuno-informatics: need to develop and apply methods of
  - ✓Computer science
  - ✓Mathematics/physics/engineering modeling
  - ✓Statistics
  - ✓Informatics

to address immunological problems

Who Are Doing These?



Computational Immunology: Multidisciplinary Interactions



Why Modeling for Immunology?

- Quantify immune responses
- Model immune systems in a system way
- Design more efficient experiments
- Extract more information from experimental data
- Integrate and interpret complex experimental data in a system way
- Simulations and predictions
- Identify therapeutic targets and design new drugs/vaccines

NIH Grant Review Criteria

- Significance
- Innovation
- Approach
- Investigator
- Environment

The first three criteria: also used for peer-review of papers

Modeling Approaches Can Help

- Propose novel aims and address complex scientific problems that require complex quantitative and modeling approaches.
- Design novel and efficient experiments to generate unique data: cost-effective
- Use novel analysis methods and modeling approaches to extract more and unique information from complex experimental data?

Summary

- Computational modeling: important and useful for immunology research
- Need multidisciplinary collaborations:
  - ✓Computer sciences
  - ✓Information technologies
  - ✓Statistics
  - ✓Mathematics
  - ✓Engineering/physics
  - ✓Bioinformatics and systems biology
  - ✓Immunology and biology

Multidisciplinary Collaboration Challenges

- Among computational and quantitative scientists
- Between computational/quantitative scientists and immunologists/biologists
- Lack of common languages and cultures
- Lack of integration leaders and experts
- Summer school training purpose: bridge between computational/quantitative scientists and immunologists/biologists

Summer School Goals

- Introduction of computational modeling concepts and analysis methods to immunologists and biologists
- Learn importance and usefulness of modeling approaches in immunology research
- Learn how to collaborate with computational and quantitative scientists to use modeling approaches to tackle complex immunological problems

Summer School Schedule

- Day 1: Basic concepts of computational modeling analysis approaches and Software introduction-R
- Day 2: ODE models—bridging immunology and mathematics
- Day 3: Basic statistical data analysis methods—bridging mathematical models and experimental data
- Day 4: Flow cytometry data processing

Summer School Speakers

- Martin Zand, MD/PhD, Professor of Medicine (Nephrology) and Co-Director, CBIM, University of Rochester Medical Center (URMC)
- Hongyu Miao, PhD, Associate Professor of Biostatistics & Computational Biology and Core Director of CBIM, URMC
- Xing Qiu, PhD, Assistant Professor of Biostatistics & Computational Biology, URMC
- Tim Mosmann, PhD, Professor and Michael and Angela Pichichero Director's Endowed Chair and Director, Center for Vaccine Biology and Immunology, URMC
- Hulin Wu, PhD, Dean's Professor of Biostatistics & Computational Biology and Co-Director, CBIM, URMC

Symposium Goals: June 4-5, 2015

- Leading scientists present successful examples and evidences to use computational modeling approaches in immunological and biological research
- Sessions (Thur afternoon and Fri):
  - Immunology Big Data
  - Mathematical Modeling of Immunity and Pathogens
  - Bioinformatics Modeling in Immunology
  - Network Modeling for Systems Immunology and Biology
  - Modeling Ebola and Other Emerging Viruses

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Acknowledgement

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  - Martin Zand (Co-Chair)
  - Alan Perelson
  - Alexandra Livingstone
  - Hongyu Miao
  - Juilee Thakar
  - Jeanne Holden-Wiltse
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