



**Led by Arup K. Chakraborty, Ph.D.**

**Sponsored by Boston University, the Ragon Institute of MIT, MGH, and Harvard, and Massachusetts Green High Performance Computing Center (MGHPCC) Holyoke, MA**

## About the Instructor

Arup K. Chakraborty is the Robert T. Haslam Professor of Chemical Engineering, Chemistry, and Biological Engineering at MIT, and a founding member of the Ragon Institute of MIT, MGH, and Harvard. After obtaining a PhD in chemical engineering at the University of Delaware, and completing his post-doctoral studies at the University of Minnesota, he joined the faculty at the University of California at Berkeley in December 1988. He rose through the ranks and ultimately served as the Warren and Katherine Schlinger Distinguished Professor and Chair of Chemical Engineering, Professor of Chemistry, and Professor of Biophysics at Berkeley. He was also Head of Theoretical and Computational Biology at Lawrence Berkeley National Laboratory. In September of 2005, Dr. Chakraborty moved to MIT. The central theme of his research over the past 10 years has been the development and application of theoretical/computational approaches to study how T lymphocytes, orchestrators of the adaptive immune response, function. A characteristic of his work is its experimental impact; he collaborates extensively with leading immunologists. Dr. Chakraborty's work at the interface of the physical, life, and engineering sciences has been recognized by many honors that include a *NIH Director's Pioneer Award*, the *E.O. Lawrence Memorial Award for Life Sciences*, the *Allan P. Colburn* and *Professional Progress Awards of the American Institute of Chemical Engineers*, a *Camille Dreyfus Teacher-Scholar Award*, a *Miller Research Professorship*, and a *National Young Investigator Award*. Dr. Chakraborty is also a member of the *National Academy of Engineering* and *Fellow of the American Academy of Arts & Sciences* and the *American Association for the Advancement of Science*.

## Course Objective

This three-day course is intended to educate physicists, physical chemists, and engineers about the basic concepts in immunology and describe how approaches rooted in the physical sciences can help address important immunological questions. The ultimate goal of the course is to inspire physical and engineering scientists to work together with immunologists and virologists to advance our understanding of the immune response to pathogens and to harness that understanding in order to develop therapeutic protocols (such as vaccines). No background in immunology is assumed; the course is appropriate for graduate students, postdoctoral scholars, and faculty members in physics, chemistry, or engineering departments.

## Course Overview

Various types of cells and organs of the immune system serve as the sentinels and armed forces that enable humans to survive in a world full of infectious pathogens. Higher organisms, like humans, have an adaptive immune system that allows them to mount pathogen-specific immune responses to combat a diverse and evolving world of pathogens for which they are not pre-programmed. The importance of adaptive immunity is made vivid when it is compromised (e.g., upon HIV infection). Also, many autoimmune diseases are the direct consequence of the adaptive immune system failing to discriminate between markers of "self" and "non-self." The toll of infectious diseases and autoimmune disorders has motivated a great deal of experimental research aimed toward understanding how the adaptive immune response is regulated, and indeed, some spectacular discoveries have been made. Yet, an understanding of the principles that govern the emergence of immune or autoimmune responses has proven to be elusive. An example of a practical consequence of this missing knowledge is that a quarter of a century after the discovery of HIV, a vaccine is not yet available. An important barrier to the quest for mechanistic principles is that the pertinent processes involve multi-scale, stochastic, and collective dynamic phenomena with many participating components, features that can confound an intuitive interpretation of experimental observations. Theoretical, computational, and quantitative approaches rooted in the physical and engineering sciences, are beginning to play an important role in confronting this challenge. The goal of this course is to introduce students to basic immunology, and then lead them to such leading-edge research at an intersection of the physical, life, and engineering sciences.

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MGHPCC: Massachusetts Green High Performance Computing Center



## Wednesday, September 8, 2010

9:30 - 10:00

Registration and continental breakfast

10:00 - 12:00

**Basic concepts in immunology:**

- The innate and adaptive immune systems and how they interact
- A focus on adaptive immunity
- Humoral immunity (e.g., B lymphocytes)
- Cellular immunity (e.g., T lymphocytes)

12:00 - 1:30

Lunch and interaction time (lunch provided)

1:30 - 5:00

**Cellular immune responses mediated by T lymphocytes (T cells) I:**

- How T cells recognize the presence of a foreign pathogen
- How signaling in T cells translates recognition to function
- Challenges in understanding T cell signaling and its aberrant regulation
- Deterministic mathematical models for the T cell signaling network
- Importance of stochastic fluctuations, master equation-based models, and algorithms
- Case study showing the discovery of new aspects of the T cell signaling machinery by bringing together computational and experimental studies

5:00 – 5:30 **Break**

5:30 – 6:30

**Challenges in understanding signaling in cells of the immune system**, *Dr. Andrey Shaw, Chair*, Department of Immunology, Washington University, St. Louis.

## Thursday, September 9, 2010

9:30 - 10:00

Registration and continental breakfast

10:00 - 12:00

**Cellular immune responses mediated by T lymphocytes (T cells) II:**

- How many types of T cells do you need to recognize diverse pathogens
- How long must the peptides be to cover self and foreign antigens
- Development of the T cell repertoire in the thymus
- How is T cell recognition of pathogens both specific and degenerate
- Theoretical and computational models for development of the T cell repertoire
- Case study on specific/degenerate T cell recognition of pathogens by bringing together concepts from spin glass physics, extreme value distributions, and experiments

12:00 - 1:30

Lunch and interaction time (lunch provided)

1:30 - 5:00

**Cellular immune responses mediated by T lymphocytes (T cells) II cont'd.; and Humoral immune responses mediated by B lymphocytes and Antibodies:**

- Development of B cells
- Germinal center reactions and evolution of antibodies (affinity maturation)
- Mathematical models, continuum and stochastic, for antibody maturation

5:00 – 5:30 **Break**

5:30 – 6:30

**Challenges in understanding T cell repertoire development**, *Dr. Eric Huseby*, Department of Immunology and pathology, University of Massachusetts Medical School, Worcester.

## Friday, September 10, 2010

9:30 - 10:00

Registration and continental breakfast

10:00 – 12:00

**Host-pathogen dynamics:**

- Basic concepts in host-pathogen interactions
- Dynamical equations for host-pathogen dynamics
- Virus evolution, stochastic and deterministic models

12:00 – 2:00

Lunch and interaction time (lunch provided)

2:00 – 5:00

**Case studies focused on adaptive immune response to human immunodeficiency virus (HIV)**

5:00 – 5:30 **Break**

5:30 – 6:30

**Challenges and Opportunities in the Quest for an HIV Vaccine**, *Dr. Bruce D. Walker*, Harvard Medical School, Ragon Institute of MGH, MIT, and Harvard.