



**SBCNY FALL 2008 WORKSHOP:**  
**SPECIFICATION OF RATE CONSTANTS FOR KINETIC  
MODELS**

**WEDNESDAY NOVEMBER 19, 2008**

**10:00AM TO 5:00PM**

**MOUNT SINAI SCHOOL OF MEDICINE**

**ICAHN MEDICAL INSTITUTE**

**1425 MADISON AVENUE**

**12TH FLOOR RM 12-84**

## Participants:

### *Invited Participants*

**Walter Kolch**  
**Boris Kholodenko**  
**Dean Bottino**  
USA

The Beatson Institute for Cancer Research, Glasgow, UK  
Thomas Jefferson University, Philadelphia, PA, USA  
Novartis Pharmaceuticals Corporation, East Hanover, NJ,

### *SBCNY- MSSM Participants*

**Ravi Iyengar**  
**Fernand Hayot**  
**Susana Neves**  
**Eric Sobie**  
**Avi Maayan**  
**Simon Hardy**  
**Azi Lipshtat**  
**Anamika Sarkar**  
**Padmini Rangamani**  
**Seth Berger**  
**Michael Chary**

## **Goals of the Workshop**

This workshop is a follow up on our Spring 2008 workshop where we discussed the feasibility of experimentally obtaining kinetic constants for cellular interactions between all of the proteins encoded by the human genome. This workshop will assess the currently available kinetic data for the development of quantitative models of signaling pathways. Approaches to organize the data in a format useful for modeling in standard modeling platforms such as MatLab, Mathematica and Virtual Cell will be discussed. Currently available databases of metabolic pathways will also be analyzed. The workshop will focus on identifying the types of kinetic data that will be most useful for development of models with the ultimate goal of drug targets discovery and drug action analyzes. The cost vs. benefits of obtaining equilibrium constants vs. rate parameters will be discussed. Specification of initial concentrations of reactants in different cell types will be considered. Development of simple yet useful databases for storage of quantitative information will be discussed.

## **Format**

The workshop will be conducted as an open discussion forum. There will be no formal presentations, although participants are free to present a few slides to illustrate points they want to make. The proceedings of the workshop will be recorded and at the end

we will produce a document reporting the discussed points and the final recommendations. Enclosed are a few starting questions to facilitate discussion.

### **Major Questions:**

How can we compare and integrate kinetic constants obtained from standardized measurements with those obtained (or estimated) from the literature into a database that can be used for development of kinetic models?

How can we annotate the kinetic constants within a database so that they can be used for a wide variety of contexts (e.g. different cell types/ tissue/ organism) specific models?

### **Issues to be discussed**

1. Kinetic data resources already available for modeling cell signaling networks.
  - 1a. Quality usability and limitations*
  
2. Types of kinetic data geared for modeling for drug discovery and drug action
  - 2a. small molecule-protein targets  $K_d$*
  - 2b. small molecules  $IC_{50}$*
  
3. Specifics related to handling of certain types of biochemical reactions.
  - 3a. The handling of multi-component complexes (AB binds to C)*
  - 3b. Annotation of kinetic parameters when dealing with different species of the same protein (phosphorylated activity vs. non phosphorylated activity)*
  - 3c.  $V_{max}$  issue for enzymes: reported  $V_{max}$  usually lacks enzyme concentration used in vitro to convert to  $K_{cat}$ . A standard measure for  $K_{cat}$  estimation*
  
4. Organizing experimental input/output relationships to constrain models.
  - 4a. Converting published experimental data into computationally usable and indexable formats.*
  
5. Amount of experimental detail that should be included with the kinetic data
  - 5a. Purification method, source of protein, presence/absence of key modulators, temperature of assay.*
  
6. Organization of Kinetics database:
  
7. Consolidation of all the freely available quantitative resources into a meta-database

## 8. Relationship between quantitative interaction database and qualitative databases

### **Currently Available.**

#### *Databases of kinetic parameters:*

KDBI <http://bioinf.xmu.edu.cn/databases/kdbi/kdbi.php>

BIND <http://bond.unleashedinformatics.com/Action>

BRENDA <http://www.brenda-enzymes.info/>

Kmed <http://sysbio.molgen.mpg.de/KMedDB>

#### *Databases of kinetic models:*

BioModels <http://www.ebi.ac.uk/biomodels-main/static-pages.do?page=home>

DOQCS <http://doqcs.ncbs.res.in/>

JWS <http://jjj.biochem.sun.ac.za/>

SABIO-RK <http://sabio.villa-bosch.de/>