**Sub-cellular and Multicellular Modeling Workshop
at The Hamner Institutes for Health Sciences
Research Triangle Park, NC USA**

**Instructors: Herbert M. Sauro (Univ. Washington),
Maciej Swat, James Glazier, Julio Belmonte, Jim Sluka (Indiana Univ.)**

**The following materials will be provided to Participants during the Course:**

1. Discounted copy of Text Book on Enzyme and Gene Regulatory Kinetics (Paper and ebook)
2. CompuCell3D Introduction (all other manuals including CC3D reference, Python scripting etc… will be available in the electronic form)
3. PowerPoint/PDF copies of lecture slides
4. Folder with simulation notes and other materials
5. Model Files from the course web site
6. Selected readings and background material

*July 30th, 2012 (Monday)*

**Day 1: Course: 9AM – 6.00PM:**

**9.00 – 9.10:** *Welcome note (Jim Sluka, Indiana Univ.)*

**9.10 – 9.20:** *Welcome note (Sudin Bhattacharya, The Hamner Institute)*

**9.20 – 10.00:** *Lecture:*

 *a) Introduction to Modeling with JDesigner and Jarnac*

 *b) Definitions of: Stoichiometry, Rate Laws,*

 *Boundary Species, Steady States and Transients*

**10.05-10.30:**  *Hands on exercises*

 *a) Getting Help: Documentation and tutorials*

 *b) Simple Closed Systems*

 *c) Rate Law Selection*

**10.30 – 11.00:** *Break*

**11:00 – 12:30:** *Hands on exercises*

 *a) Simple Open Systems*

*b) Applying Perturbations
 c) Plotting Simulations*

 *d) SBW Simulation Tool*

**12.30 – 1.30:** *Lunch*

**1.30 – 2.30:** *Lecture:*

 *SBML, Sensitivity Analysis, Parameter Scans*

**3.30 – 4.00:** *Break*

**4:00 – 5:40:** *Hands on exercises*

a) Exchanging models, SBML, Matlab

b) Using other models, obtaining model components

 c) Sensitivity Analysis, Interactive Modeling and Parameter Scans

**5.40 – 6.00:** *Road map for 2012-2014 and developer information*

*July 31st, 2012 (Tuesday)*

**Day 2: Course: 9AM – 5.30PM:**

**9.00 – 9.30:** *Generalized**enzyme kinetic rate laws*

**9.35 – 10.30:** *Mini Project: Build a Signaling Pathway*

**10.30 – 11.00:** *Break*

**11:00 – 12:30:** *Mini Project*

**12.30 – 1.30:** *Lunch*

**1.30 – 2.30:** *Overview of multi-cell modeling (James Glazier, Indiana Univ.)*

**2.30 – 3.30:** *Introduction to CompuCell3D (Maciej Swat, Indiana Univ.)*

**3.30 – 4.00:** *Break*

**4:00 – 5.30:** *CompuCell3D 101 tutorials*

*August 1st, 2012 (Wednesday)*

**Day3: Course: 9AM – 5.30PM:**

**9.00 – 12.30:** *CompuCell3D (Introduction to Python-based Simulations-Mastering Twedit++, Python Mini-Tutorial, CC3D-Hands-on Exercises - Maciej Swat, Indiana Univ.)*

**10.30 – 11.00:** *Break*

**11:00 – 12:30:** *CC3D-Hands-on Exercises - Maciej Swat, Indiana Univ.*

**12.30 – 1.30:** *Lunch*

**1:30 – 2:15:** *Invited talk***-** *Tom Knudsen EPA*

**2.15 – 3.30:** *CompuCell3D (Fields, Basic Diffusion-based PDEs, Chemotaxis, Hands-on Tutorials - Maciej Swat, Indiana Univ.)*

**3.30 – 4.00:** *Break*

**4.00 – 5.30:** *CompuCell3D (continue Hands-on Tutorial - Maciej Swat, Indiana Univ.)*

*August 2nd, 2012 (Thursday)*

**Day 4: Course: 9AM – 5.30PM:**

**9.00 – 10.30:** *CompuCell3D (Advanced Python Scripting in CC3D –Attaching Extra Cell Attributes, Mitosis-Based Simulations, Cell Shape Constraints etc… ,Hands-on Tutorials - Maciej Swat, Indiana Univ.)*

**10.30 – 11.00:** *Break*

**11:00 – 12:30:** *CompuCell3D (continue Hands-on Tutorial - Maciej Swat, Indiana Univ.)*

**12.30 – 1.30:** *Lunch*

**1:30 – 2:15:** *Invited talk***-** *Imran Shah EPA*

**2.15 – 3.30:** *CompuCell3D (Advanced Python Scripting in CC3D Part 2 – using third party modules in Python, File operations, Post Processing, Simulation Steering – changing CC3DML on-the-fly - Maciej Swat, Indiana Univ. )*

**3.30 – 4.00:** *Break*

**4.00 – 5.30:** *CompuCell3D (Plots and Graphs, configuring CC3D GUI from Python/XML, continue Hands-on Tutorial - Maciej Swat, Indiana Univ.)*

*August 3rd , 2012 (Friday)*

**Day 5: Course: 9AM – 5.30PM:**

**9.00 – 10.30:** *CompuCell3D (SBML-Based Models in CC3D – Reaction Kinetics, ODE, PBPK models, Hands On Tutorials – Julio Belmonte, Indiana Univ. )*

**10.30 – 11.00:** *Break*

**11:00 – 12:30:** *CompuCell3D (continue Hands-on Tutorial - Julio Belmonte, Indiana Univ.)*

**12.30 – 1.30:** *Lunch*

**1:30 – 2:15:** *Invited talk***-** *Dr. Jeff Woodhead, The Hamner.*

*Title: "The DILIsym Model and its Application to Hepatotoxicity Testing in Drug Development." (It will include their work on APAP toxicity modeling.)*

**2.15 – 3.30:** *CompuCell3D (Developing CC3D extension modules in C++ using Twedit++ - demo, Questions-And-Answers session – Suggestions For Future CC3D improvements - Maciej Swat, James Glazier, Jim Sluka, Julio Belmonte, Indiana Univ.)*

**3.30 – 4.00:** *Break*

**4.00 – 5.30:** *CompuCell3D (continue Hands-on Tutorial - Maciej Swat, Indiana Univ.)*

**7.00 – 9.30: *Hackathon:*** *Combining a PBPK (as SBML) whole body, CompuCell3D multi-cellular and sub-cellular metabolic modeling (SBML) to create a multi-scale model of Acetaminophen (Paracetamol) liver toxicity and therapeutic effects. (CC3D group and The Hamner group but everyone is invited.)*

*August 3rd , 2012 (Friday) 7.00PM – 9.30PM*

***Hackathon***

*Combining a PBPK (as SBML) whole body, CompuCell3D multi-cellular and sub-cellular metabolic modeling (SBML) to create a multi-scale model of Acetaminophen (Paracetamol) liver toxicity and whole-body therapeutic effect. (CC3D group, The Hamner group but everyone is invited.)*

*Create a single publishable model that includes:*

1. *Whole body adsorption, distribution, metabolism and elimination of Acetaminophen*
2. *Movement of Acetaminophen through a sinusoid and diffusion into/out of adjacent hepatocytes*
3. *Hepatic metabolism of Acetaminophen, peripheral metabolism of Phase II products*
4. *Hepatic toxicity of Acetaminophen (with zonation imposed?)*

*Need:*

1. *CC3D model of Sinusoid with blood flow (Sluka)*
2. *SBML model of Acetaminophen hepatocyte metabolism (Sluka)*
3. *SBML PBPK whole body model of Acetaminophen ADME (Hamner?)*
4. *Integration technique for representing the whole body PBPK model in CC3D (Swat)*

***August 4th, 2012 (Saturday) (for vLiver participants only)***

**Day 6: Virtual Liver Consortium meeting: 9AM – 4.00PM:**

**9.00 – 9.45:** *Padma Rajagopalan & T. M. Murali, Virginia Tech*

**9.45 – 10:30:** *Alexander Tropsha, University of North Carolina at Chapel Hill*

**10.30 – 10:45:** *break*

**10.45 – 11.30:** *Sudin Bhattacharya, The Hamner Institute*

**11.30 – 12.15:** *Jim Sluka, James Glazier, Indiana University*

**12.15 – 1.15:** *Lunch*

**1.15 – 2.15:** *Pasky Pascual, Imran Shah, EPA*

**2.15 – 3.15:** *Group Discussion: Plans for the upcoming year for each group*

**3.15 – 4.00:** *Group Discussion: Data sharing plans*