CompuCell3D Modeling 2020 Summer School

August 3-6, 2020 (Monday-Thursday)
Python Intro Courses on Sunday July 26 and Sunday August 2
https://compucell3d.org/Workshop20

First we will have 2 days of **optional** Python training. These will be on Sunday July 26 and Sunday August 2 day.

Part 0a: Introduction to Python I, Sunday July 26

> **Basics of Python: Use nanHUB Tellurium as the IDE for the class.** Installing, running), uploading and downloading files from nanoHUB to from google drive and desktop, loops, conditionals, slicing & stacking, functions, loops, conditionals, lists, Numpy, Scipy, Matplotlib, file input/output, objects (but not classes)
> *We will record and make the session available on YouTube*

Part 0b: Introduction to Python II, Sunday August 2

> **More advanced python:** Including dictionaries, classes
> (note that this date was not included on the class' fliers)
> *We will record and make the session available on YouTube*

For the CompuCell3D course we have allocated five days. These days will follow a similar though not exact schedule. Each day will start at 11AM **Eastern Daylight Time EDT** (8am PDT, 4pm BST, 8.30pm IST). Each day will end at 6pm Eastern Daylight Time.

Adjustments for other parts of the world:

- Add 5 hours for UK
- Add 6 hours for Germany
- Add 9 hours for India
- Add 12 hours for Japan
- Add 16 hrs for New Zealand

Telecom / Zoom Info:

Zoom for Python course:
https://iu.zoom.us/meeting/register/tJ0kdOmorjgoH9f9I8iQG_Ykj6iRdoMI68LK
Zoom for CC3D course:
https://iu.zoom.us/meeting/register/tJMufuioqT8pHdYPowlohg6d_fivXftFu_jR
Slack: https://app.slack.com/client/T017HE055JN
CC3D Website: https://compucell3d.org/Workshop20
CC3D Website Class Files: https://compucell3d.org/CC3D_2020_class_files

Instructors:

1. Prof. James A Glazier, IUB, jaglazier@gmail.com
2. Dr. Gilberto L Thomas, Univer. Federal do Rio Grande do Sul, Brazil, glt@if.ufrgs.br
3. Dr. Bobby Madamanchi, Purdue University, akmadamanchi@gmail.com
4. Dr. Andy Somogyi, IUB, somogyie@indiana.edu
5. Dr. TJ Sego, IUB, tjsego@gmail.com
6. Dr. Jim Sluka, IUB, jsluka@iu.edu
7. Dr. Javier Toledo, IUB, toledom@iu.edu
8. Mr. Joshua Aponte-Serrano, IUB, joaponte@iu.edu
9. Mr. Juliano Ferrari Gianlupi, IUB, jferrari@iu.edu

(IUB: Indiana University, Bloomington, Indiana USA)

Cheat Sheets:

Available in the Slack folder at: https://app.slack.com/client/T017HE055JN/browse-files

1. Python 3
   https://compucell3d.org/CC3D_2020_class_files?action=AttachFile&do=get&target=python_cheat_sheet_py3.pdf
2. CC3D
   https://compucell3d.org/CC3D_2020_class_files?action=AttachFile&do=get&target=cc3d_quick_reference_guide.pdf
3. Twedit++
4. Player
5. Tellurium
   https://compucell3d.org/CC3D_2020_class_files?action=AttachFile&do=get&target=TellRoadCheatSheet.pdf

Standard Project:

1. Covid-19 modeling

Sunday July 26: Python Introduction 1
11AM EDT - 6PM ED

Sunday August 2: Python Introduction 2
11AM EDT - 6PM EDT

Class files and YouTube recordings are available at
https://compucell3d.org/Python2020_class_files

1: Monday August 3rd, 2020
11AM EDT-6PM EDT

Module 1.0: 11:00AM-11:15AM

Title: Welcome and Setup--Make Sure everyone is on the same page

Instructor: James Glazier

Module 1.1: 11:15AM-12:00AM

Title: 1.1 Intro To running CC3D (use Angiogenesis as demo) uploads, downloads, Twedit++ and Player

Instructor: Juliano Gianlupi Ferrari

Educational Aims: Make sure everyone can run CC3D and Tellurium Locally and on nanoHUB.

Where are course resources? (Cheat Sheets, exercises, sample code, links to manuals, where are videos and slide decks available)

Navigating nanoHUB (dashboard, workspace)

Uploading and downloading files from nanoHUB (open and download)

0-th order introduction to Twedit++ and Player(zipping and unzipping packages, where CC3D saves things, moving back and forth between Player and Twedit++)

Exercises: Run CC3D simulation (Colonic Crypt)

Configure display in player. Upload and download a CC3D file from nanohub and run it. Rename and save a file.

Module 1.2: 12:00AM-12:45PM

Title: Sample CC3D applications

Instructor: James Glazier

Exercise: brief description of student problems

Domain (e.g., disease or overall bio process), agents (cell types, ECM, molecules), processes

Module 1.3/1.4: 12:45AM-2:30PM

Title: COVID Big model, exercises, using Player and Twedit++

Exercise: tbd (perhaps run Nanohub model with minimal setup to start)

Instructor: TJ Sego

We want to answer the question how does a change in viral-ACE2 receptor affinity affect the spread of the infection in our tissue?

What happens when the number of virus particles produced by an infected cell before it dies changes?

We will show you the basic things you need to answer these questions and begin to learn how to use the main CC3D tools--Player, for executing and visualizing models and Twedit++ for editing model specifications….

Educational Aims: ? Can you get people changing model parameters here? Introduce using Twedit++ and Player?

Running the code. Where are things saved? What is saved? Setting screen configurations, setting screenshot frequencies. Creating new visualization windows. Tile, Setting colors, setting ranges for fields. Saving time series using export image and export CSV on right-click. Changing lin/log on time series.

Exercise:

Modifying model parameters and observing the simulations' response.

Lunch Break 2:30PM - 3:00PM

Module 1.5: 3:00PM-4:30PM

Title: Reminder on Tellurium and nanoHUB, ODE model text and examples

Instructor: James Glazier

We look at the flu virus time course, we see the eclipse phase, rapid exponential growth, slow exponential clearance (associated with innate immunity) followed by rapid clearance (associated with adaptive immunity). We have already built a very simple model of this using ODEs. We want to understand what changes when we think about the tissue-level context in which epithelial cells, chemical signals, virus and immune cells operate.

Educational Aims: How to interpret models. Run models in Tellurium

Quick review of Antimony—Model specification and in Tellurium (using nanoHUB Tellurium). Biologically meaningful metrics: Maximum viral load. Time of viral maximum. Time for clearance. [Number of surviving cells]

Exercise:

Run simulation, select outputs, change some parameters. Have participants look for data sets, existing ODE models and spatial models. Ask for questions to answer? Identify models to replicate. What components should be in a model of Viral replication and clearance? Different viruses, tissues, hosts, in vitro organoid and in vivo. Types of available data?

Module 1.6: 4:30PM-6:00PM

Title: Version 0 of Cellularization -- getting Tellurium model running in CC3D, converting timescales, plots and saving data

Instructor: Joshua Aponte-Serrano

Goal--eventually want to be able to run ODE model and spatial model inside the SAME framework and compare them. TO do this we need first to be able to run our tellurium model inside of Compucell3D and plot the results. Since time stepping and plotting are somewhat different in CC3D and Tellurium, we will learn:

a) How to build a minimal CC3D simulation that allows us to run an antimony model. Using Wizard to create a template model.
b) How to load and run an Antimony model inside a CC3D simulation and execute it.

c) How to relate the time steps between CC3D steps and Antimony steps
d) How to plot the results.

CC3D model structure: plugins, steppables, file structure, wizard

Exercises:

for Above, Twedit++ to a basic simulation using the Wizard, saving the project, create a notes page in the CC3D projects to put comments

Running tellurium model inside of CC3D

Module 1.end: 5:45PM - 6:00PM EDT

Title: Wrap Up, Introduction to next day

2: Tuesday August 4: CompuCell3D Day 2 11AM EDT-6PM EDT

Module 2.0: 11:00AM-11:15AM

Title: Welcome, day's plan

Module 2.1: 11:15AM-12:15PM

Title: Version 1 -- Creating Epithelial Layer, Cell Type Transitions, Issue of Poisson Rules

Instructor: Joshua Aponte-Serrano

ODE□Spatial models PART 2a: How to do spatialization and when it is needed at all.? We think of infection in an epithelial tissue. In our ODE model, the number of cells of different types and the virus are all continuous scalar quantities. In reality cells are discrete objects (as is virus) and infection follows specific spatial patterns. Does this discretization make a difference? How?

How do we create a field of epithelial cells in Twedit++/wizard?

How do we define cell types and state transitions?

How do we translate ODE terms into CC3D transitions?

Conceptualization of Cellularization: Explain what the purpose of cellularization is and its limitations and advantages Importance of breaking feedback loops to keep ODEs and spatial models in register
Need to reproduce ODEs term by term (remember we will have to keep breaking the feedback in the ODEs)

Basics of using CC3D. Introduction to Twedit++: Creating a model, editing functions (Juliano needs to identify these and prep) CC3D Model architecture and files (steppables and plotting).

Basics of CC3D Running a model using Player: Reminders Key features and functions. We will run COVID model together. Use Twedit++ to change parameters. How to save data series and screenshots in CC3D. Where does CC3D store things? Basic controls of CC3D—duration of simulation and multithreading

Running a tellurium model in CC3D. Creating a blank template model for Glazier's model. Time unit conversions.

Plotting functions in CC3D. Saving plotting data sets. Does JAG's model in CC3D agree with Tellurium?

Exercises:

At the end of this they can take a tellurium model, run it inside cc3d, plot and save results, and change timescales.

Module 2.2: 12:15PM - 1:15PM EDT

Title: Version 2 -- Spatializing the virus, diffusion as an idea, diffusion solver, secretion and absorption, adding chemokine

Instructor: Joshua Aponte-Serrano

Module: CompuCell Cells and Types: Spatializing Glazier's model: Introducing a cell field. Creating Cells, how to specify, what is required. How rate laws map to transition probabilities. Using Wizard. Cell types, CC3D ML. Frozen cells and uniform initializer. Idea of infection. Changes of cell type. Numpy in CC3D and random. Implement infection of cells by scalar viral concentration (key idea of virus per cell). Check that infected cells match Glazier's infected cells. Why or why not? What can we learn from it?

Exercises:

Module 2.3: 1:15PM-2:15PM

Title: Version 3 -- Immune Cell Spatialization model, links, creating cells, saving data?

Instructor: TJ

Virus production as scalar; Same process. Should all cells produce virus at a constant rate? Consequences of choice. Key issues—eliminate decay terms to match growth phase before trying to match growth and decay together (issues of undecidability in models)

Cell death equation (start with linear version, then add the “immune response”)

How to tell whether the ODE and the spatial model match?

Note that so far we are stochastic but not really taking meaningful advantage of spatiality

Exercises:

Lunch Break: 2:15PM-2:45PM

Module 2.4: 2:45PM-3:45PM

Title: Version 4 -- Exercises on cell motility, chemotaxis and random motility and dependence on parameters

Instructor: TJ

Virus isn’t everywhere at once. It is transmitted locally from the releasing cell by diffusion and active transport by mucus and in the mesenchymal ECM. What is the consequence of the local transmission of virus?

Spatializing the Virus: Module: Fields and Diffusion. We now have a non-spatial stochastic model. Turning virus into a field. Issues on the analysis end. How CC3D represents and solves diffusion fields. Implementing diffusion fields using Twedit++. What happens to secretion rates and decay rates? Reading and writing chemical fields. Displaying chemical fields.

Boundary conditions on fields, limits of decay rates, Reminder on displaying concentrations.

> Josh, when you cellularize my model use new reporters for the amount of virus in the entire field and in cell volume.

Introduction to the physics and biology of diffusion. Field absorption and secretion. Does the total amount of secreted virus and amount of virus per cell match Amber's model? Why or why not? Does diffusion make sense for a respiratory virus?

Closing the feedback loop. Have cells infected by viral fields. How do I relate concentrations to scalar quantities? Does the model work? Start to reduce the diffusion constant. Now we can be sure that any differences between the models are ONLY due to spatial effects.

Congratulations! We have now converted an ODE model into a matching CC3D Model

Creating a new cell type

Adding and removing immune cells from the cell field

What do they do? Disappear? Now discuss Cell volume control, contact energies

> Creating and destroying cells in CC3D. Controlling motile cells. Contact energies, volume constraints, surface constraints.
>
> Some immune cells stick to each other some don't want these to stick to epithelial cells and not to each other.

How many immune cells are there in time vs E in ODE?

Chemotaxis--immune cells move in response to cytokines

Added parameters and considerations (a lot) Log scaled chemotaxis

How do immune cells move in response to cytokine?

How fast does a T-cell move?

Chemotaxis and response to a field. How do our immune cells move? Defining chemotaxis. Speed limits in CC3D. Logarithmic responses to chemical field—how to implement

Exercise: how cells move

Random motility plug in (Juliano) how fast do cells move? Is it realistic? What are the limits of the time step in CC3D vs wall clock time (if immune cells move at 2 microns/minute?)

Break: 3:45PM-4:00PM

Module 2.5: 4:00PM-5:45PM

Title: Overage time

Module 2.end: 5:45PM - 6:00PM EDT

Title: Wrap Up, Introduction to next day

3: Wednesday August 5: CompuCell3D Day 3 11AM EDT-6PM EDT

Module 3.0: 11AM-11:15AM

Title: Welcome and Setup

Module 3.1: 11:15AM - noon EDT

Title: Version 5 -- Contact killing -- contact area plug-in and links

Adding tissue recovery (simple case).

Finding cell-cell contact in CC3D and having a cell kill another cell. How long does a T-cell take to kill?

Ways to keep an immune cell attached to its target? Change lambda_vol to reduce motility, change lambda chemo. Add links?

How does the cellularized model differ? What are the new parameters (chemotaxis rate, diffusion constant of virus)? Explore parameter space. Is the cellularized model worth the effort?

Exercises:

Module 3.2: 12:00PM - 1:00PM EDT

Title: Version 6 -- Adding Tissue Recovery and Cell Division

Exercises:

Module 3.3: 1:00PM - 2:00PM EDT

Title: Version 7 -- Adding viral replication model in individual cells

Keeping average
viral production per cell in register with ODE.
Tissue recovery or cell division when SBML is included. Exercises:

Lunch Break 2:00PM - 2:30PM EDT

Module 3.4: 2:30PM - 3:30PM EDT

Title: Version 8 -- Adding INF induced viral resistance, macrophages and phagocytosis

INF-induced viral resistance. Biology and unknowns. Planning a model and exploring together. Infection resistance vs reduced production vs faster death. Internal, autocrine and paracrine signaling. Break up into groups and implement different model structures. Compare results.

Exercises:

Module 3.5: 4:30PM - 5:45PM EDT

Title: Principles of operation of CompuCell3D

Instructor: Maciej Swat

Exercises:

Walk through complete model creation from scratch using Twedit

Module 3.end: 5:45PM - 6:00PM EDT

Title: Wrap Up, Introduction to next day

4: Thursday August 6: CompuCell3D Day 4
11AM EDT-6PM EDT

Module 4.0: 11AM - 12:30PM EDT

Title: Welcome and Setup, and practical operation of CompuCell3D

Continuing basics of CC3d, Potts, …

Exercises:

Using Twedit helpers to modify the simulation created last session
Use the Twedit++ helpers to modify and extend the model each student created in the AM. Add steppable, plots, cell behaviors (division, death, phenotype change, ..), writing data to files

Module 4.1: 12:30PM - 1:15PM EDT

Title: Delta Notch Contact signaling between SBML models and Colonic Crypt Model

Instructor: Julio Belmonte

Exercises:

Module 4.2: 1:15PM - 2:00PM EDT

Title: Cell Crawling -- Compartmental Cells

Instructor: Gilberto Thomas

Exercises:

Lunch Break 2:00PM - 2:30PM EDT

Module 4.3: 2:30PM - 3:15PM EDT

Title: Cluster and Parameter Scan execution

Instructor: Maciej Swat

May not have access to a cluster
Parameter scans can be done on laptops.
Parameter scans as a hack to do sensitivity. Does single parameters, paired parameters, up to all parameters in a single run)

Exercises: PScan on the CV19 model.

3 parameters, 2 values/parameter. Can extract sensitivity. Challenge: CC3D simulations are often stochastic; are the run to run changes in output from the parameter changes or from stochasticity of the model? Can you think of a way to get the PScan tool to do multiple replicates for each parameter set? (How can you use PScan to just manage running a large number of replicates with a single set of parameters?)

Module 4.4: 3:15PM - 4:00PM EDT

Title: Segmentation and Links

Instructor Priyom Adhyapok

Exercises:

Module 4.5: 4:00PM - 4:45PM EDT

Title: Deploying CC3D simulation on NanoHub

Instructor: Juliano Gianlupi Ferrari

Exercises:

Module 4.6: 4:45PM - 5:30PM EDT

Title: CompuCell3D Best Practices

Instructor Jim Sluka

Exercises:

Add a parameter file to a CC3D project, including biological and computational parameters. Set project so that it does a reasonable job of rescaling a simulation with either 3x3 pixel cells or 10x10 pixel cells.

Module 4.7: if needed

Title: Turning unitary model into modules

Exercises:

Module 4.end: 5:30PM - 6:00PM

Title: Wrap Up

Further work, collaborations?
Feedback survey.

5: Friday August 7: Hackathon Day 1
11:00AM EDT - 6:00PM EDT

Possible subjects to cover: parameter fitting (gradient based, perhaps with Python fitting tools and callable CC3D), Particle swarm optim, sensitivity, parameter sweeps, command line runs, batch runs (slurm or other job scheduler), file io, movies, other useful things?

Also, possibly just do what students want; for example help them start developing a model of their own.

Module 7.0: 11:00AM - 11:15AM EDT

Title: Welcome, start, day's plan

Module 7.1: 11:15 AM - 2:00 PM EDT

Title: Team Assignments

Opportunity for each group to present 2 slides and look for partners

Title: First Breakout Sessions--Problem Definition

Lunch Break: 2:00 PM - 2:30 PM EDT

Module 7.2: 2:30 PM - 6:00 PM EDT

Title: Second Breakout Sessions--Complete Problem Definition

Title: Lightning Review of Problem Definitions

Title: Refine Problem Definitions/Begin Coding

Title: Coding Models

Title: Lightning presentations problem solving, define overnight tasks

6: Saturday August 8: Hackathon Day 2
11:00AM EDT - 6:00PM EDT

Module 8.0: 11:00AM - 11:15AM EDT

Title: Start, day's plan

Module 8.1: 11:15AM - 2:00PM EDT

Title: Update on Overnight Progress, Questions and Problems

Opportunity for each group to present 2 slides and look for partners

Lunch Break: 2:00 PM - 2:30 PM EDT

Module 8.2: 2:30PM - 5:00PM EDT

Title: Coding Session

Module 8.2: 5:00PM - 6:00PM EDT

Title: Closing

- Final presentations
- Future work
- Collaborations