Session 1: Working with PhysiCell Projects



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• @MathCancer

PhysiCell Project

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Goals

- Learn how to work with sample projects
 - Get a list of sample projects
 - Populate a project
 - Look at typical project structure
 - Modify settings
 - Compile and run a populated project
 - See typical model outputs
 - Clear out data and reset

Sample projects

- It's inefficient (and a little insane) to code new projects entirely from scratch.
- So, we provide sample projects:
 - 2D/3D template project
 - Cancer models
 - Synthetic multicellular systems
 - Viral dynamics in tissue
 - and more ...
- make [project-name]: populate a sample project (puts all the source files where they belong)
 - Then use make to compile it
- make data-cleanup: clean up the output data
- make reset: return to a "clean slate" (depopulate the project)
- make list-projects: display all available sample projects

Documentation: User Guide Sections 6, 7.

PhysiCell Project Essentials (1)

- Each PhysiCell release includes sample projects. To list them:
 - make list-projects

- Your first step is to populate a project.
 - make project_name>
 - Let's use biorobots-sample:
 - ♦ make biorobots-sample
 - This copies source code, a tailored make file, and configuration files

```
C:\Physicell>make list-projects
Sample projects: template2D template3D biorobots-sample cancer-biorobots-sample heterogeneity-sample cancer-immune-sample virus-macrophage-sample

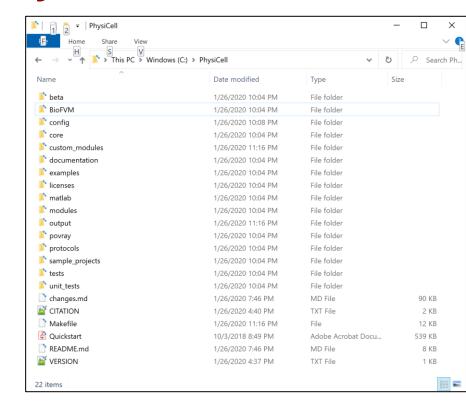
c:\Physicell>
c:\Physicell>make biorobots-sample
cp./sample_projects/biorobots/custom_modules/*./custom_modules/
touch main.cpp && cp main.cpp main-backup.cpp
cp./sample_projects/biorobots/main-biorobots.cpp./main.cpp
cp./sample_projects/biorobots/main-biorobots.cpp./main.cpp
cp./sample_projects/biorobots/main-biorobots.cpp
cp./sample_projects/biorobots/main-biorobots.cpp
cp./sample_projects/biorobots/main-biorobots.cpp
cp./sample_projects/biorobots/main-biorobots.cpp
cp./sample_projects/biorobots/config/Physicell_settings-backup.xml
cp./sample_projects/biorobots/config/*./config/
c:\PhysiCell>
```

Let's look at the project structure ...

Project directory structure

- · (key) directories:
 - ./ (root): main source, Makefile, and executable go here
 - ./beta: for beta-testing (don't use)
 - ./BioFVM: diffusion solver
 - ./config: configuration files
 - ./core: PhysiCell core functions
 - ./custom_modules: put custom code for your project here.
 - ./documentation: user guide, etc.
 - ./examples: deprecated
 - ./licenses: yep
 - ./matlab: scripts and functions to load data in matlab
 - ./modules: standard add-ons for PhysiCell
 - ./addons: officially supported addons like PhysiBoSS and libRoadrunner
 - ./output: where data are stored (by default, but can be changed)
 - ./povray: deprecated
 - ./protocols: instructions mostly for maintainers (e.g., release protocols)
 - ./sample_projects: where we add sample projects
 - ./tests: for automated testing (WIP)
 - ./unit_tests: for automated testing (WIP)

Most of your work will be in the red directories



Project structure: config files

- Configuration files (XML)
 - domain: domain size and resolution
 - overall: general options
 - ♦ Final simulation time
 - ◆ Time step sizes
 - parallel: parallelization options
 - Number of threads
 - save: save options
 - ♦ Save where?
 - Save SVGs? (how often?)
 - Save full data? (how often?)
 - Save legacy data (don't)
 - microenvironment_setup: diffusion settings
 - more later
 - cell_definitions: define different cell types and starting parameters
 - more later
 - user_parameters: simulation-specific settings
 - more later

```
🔚 PhysiCell_settings.xml 🔀
75 ⊟<PhysiCell settings version="devel-version">
              <x min>-750</x min>
              <x max>750</x max>
              <y min>-750</y min>
              <y max>750</y max>
              <z min>-750</z min>
              <z max>750</z max>
              <dx>20</dx>
              <dy>20</dy>
              <dz>20</dz>
              <use 2D>false</use 2D>
       ----</domain>
<max time units="min">30240</max time> <!-- 21 days * 24 h * 60 min -->
              <time units>min</time units>
              <space units>micron</space units>
              <dt diffusion units="min">0.01</dt diffusion>
              <dt mechanics units="min">0.1</dt mechanics>
              <dt phenotype units="min">6</dt phenotype>
       ----</overall>
              ><omp num threads>8</omp num threads>
102 <del>□</del> → < save >
              <folder>output</folder> <!-- use . . for root -->
                  ><interval units="min">360</interval>
                 →<enable>true</enable>
              </full data>
                  <interval · units="min">60</interval>
                  <enable>true</enable>
              <legacy data>
                 →<enable>false</enable>
              </legacy data>
          <microenvironment setup;</pre>
          <user parameters>
```

Project structure: custom modules

- Custom Modules
 - Setup functions
 - Cell definitions
 - Custom functions
 - any other modeling
 - Custom coloring functions

```
hysiCellacd custom module
C:\GitHub\engr-MCSB\lectures\Lecture2 source\PhysiCell\custom modules\custom.h - Notepad++
<u>File Edit Search View Encoding Language Settings Tools Macro Run Plugins Window</u>
     PhysiCell settings.xml 🗵 📙 custom.cpp 🗵 📙 custom.h 🗵
         # CONSEQUENTIAL DAMAGES (INCLUDING, BUT NOT LIMITED TO, PROCUREMENT OF
        # SUBSTITUTE GOODS OR SERVICES; LOSS OF USE, DATA, OR PROFITS; OR
        # INTERRUPTION) HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER
         # CONTRACT, STRICT LIABILITY, OR TORT (INCLUDING NEGLIGENCE OR OTHERWISE)
        #include ... / core / PhysiCell.h"
         #include . ".. / modules / PhysiCell standard modules.h"
        using namespace BioFVM;
        using namespace PhysiCell;
        void tumor cell phenotype with oncoprotein ( Cell* pCell, Phenotype & phenotype, double dt );
        // any additional cell types (beyond cell defaults)
        extern Cell Definition motile cell;
        // custom cell phenotype functions could go here
        // setup functions to help us along
        void create cell types( void );
        void setup tissue( void );
        // set up the BioFVM microenvironment
        void setup microenvironment( void );
        // custom pathology coloring function
         std::vector<std::string> my coloring function( Cell* );
```

Project structure: custom modules

- Custom Modules
 - Any user-defined globals (at top)
 - ◆ Declared cell types
 - Setup functions
 - ♦ create cell types()
 - » Do all setup on all cell types
 - Adjust phenotype
 - o Add / adjust custom data
 - Set functions
 - - » Place initial cells in microenvironment
 - » Modify each cell as needed
 - Custom functions
 - any other modeling
 - Custom coloring functions

```
hysiCell>cd custom_modules
C:\GitHub\engr-MCSB\lectures\Lecture2 source\PhysiCell\custom modules\custom.h - Notepad++
File Edit Search View Encoding Language Settings Tools Macro Run Plugins Window
     PhysiCell settings.xml 🗵 📙 custom.cpp 🗵 📙 custom.h 🗵
         # CONSEQUENTIAL DAMAGES (INCLUDING, BUT NOT LIMITED TO, PROCUREMENT OF
        # SUBSTITUTE GOODS OR SERVICES; LOSS OF USE, DATA, OR PROFITS; OR
        # INTERRUPTION) HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETH
         # CONTRACT, STRICT LIABILITY, OR TORT (INCLUDING NEGLIGENCE OR OTHERWISE)
        #include ... / core / PhysiCell.h"
        #include "../modules/PhysiCell standard modules.h"
        using namespace BioFVM;
        using namespace PhysiCell;
        void tumor cell phenotype with oncoprotein ( Cell* pCell, Phenotype & phenotype, double dt );
        // any additional cell types (beyond cell defaults)
        extern Cell Definition motile cell;
        // custom cell phenotype functions could go here
        // setup functions to help us along
        void create cell types( void );
         void setup tissue( void );
        // set up the BioFVM microenvironment
        void setup microenvironment( void );
        // custom pathology coloring function
         std::vector<std::string> my coloring function( Cell* );
```

Project structure: main.cpp

- main.cpp
 - (in the root directory)
 - calls the setup functions

```
C:\GitHub\engr-MCSB\lectures\Lecture2_source\PhysiCell\main.cpp - Notepad++
File Edit Search View Encoding Language Settings Tools Macro Run Plugins Window ?
           😼 😘 🚔 🕹 😘 🛍 🗩 🗷 📾 🚱 💌 🤏 🕞 🏗 🏗 🏗 🖫 💯 🕮 👁 💌 🗎 🖼 🕬
             setup microenvironment(); // modify this in the custom code
             // set mechanics voxel size, and match the data structure to BioFVM
            Cell Container* cell container = create cell container for microenvironment( microenvironment, mechanics voxel size );
             /* Users typically start modifying here. START USERMODS */
             create_cell_types();
           →//·set·MultiCellDS·save·options
            →set_save_biofvm_mesh_as_matlab( true );
            -set save biofvm data as matlab( true );
            →set_save_biofvm_cell_data( true );
            >set_save_biofvm_cell_data_as_custom_matlab( true );
           →//·save·a·simulation·snapshot
             sprintf( filename ., "%s/initial" ., PhysiCell_settings.folder.c_str() );
             save PhysiCell_to MultiCellDS_xml_pugi( filename , microenvironment , PhysiCell globals.current time );
            -// save a quick SVG cross section through z = 0, after setting its
           →//·length·bar·to·200·microns
            PhysiCell_SVG_options.length_bar = 200;
```

Project structure: main.cpp (continued)

- main.cpp
 - set coloring function

```
C:\GitHub\engr-MCSB\lectures\Lecture2_source\PhysiCell\main.cpp - Notepad++
 Edit Search View Encoding Language Settings Tools Macro Run Plugins Window ?
        🗟 😘 🔝 🖟 🐚 🖍 🐚 🖍 🗩 🗷 🕍 🛬 🔍 🤏 🕞 📑 🖺 🏗 🖫 🔑 📾 💿 💌 🗈 🕟 🕪 🔀
          std::vector<std::string> (*cell_coloring_function)(Cell*) = my_coloring_function;
          sprintf( filename , "%s/initial.svq" , PhysiCell settings.folder.c str() );
          SVG_plot(filename, microenvironment, 0.0., Physicell_globals.current_time, cell_coloring_function);
         display citations();
          BioFVM::RUNTIME_TIC();
         →BioFVM::TIC();
          std::ofstream report file;
          if ( PhysiCell settings.enable legacy saves == true )
              sprintf( filename , "%s/simulation report.txt" , PhysiCell settings.folder.c str() );
              report file<<"simulated time\tnum cells\tnum division\tnum death\twall time"<<std::endl;
       →//·main·loop
              while ( PhysiCell globals.current time < PhysiCell settings.max time + 0.1*diffusion dt )
                  pif( fabs( PhysiCell globals.current time - PhysiCell globals.next full save time ) < 0.01 * diffusion dt )</pre>
                     display_simulation_status( std::cout );
                     >if( PhysiCell settings.enable legacy saves == true )
```

Project structure: main.cpp (continued)

- main.cpp
 - insert custom routines
 - This would be a good place to put extensions.

```
C:\GitHub\engr-MCSB\lectures\Lecture2_source\PhysiCell\main.cpp - Notepad++
   Edit Search View Encoding Language Settings Tools Macro Run Plugins Window ?
                          PhysiCell globals.full output index++;
                          PhysiCell globals.next full save time += PhysiCell settings.full save interval;
                      if ( fabs ( PhysiCell globals.current time - PhysiCell globals.next SVG save time ) < 0.01 * diffusion dt )
                          if ( PhysiCell settings.enable SVG saves == true
                              sprintf(filename, "%s/snapshot%08u.svg", PhysiCell settings.folder.c str(), PhysiCell globals.SVG output index);
                              SVG plot (filename, microenvironment, 0.0, Physicell globals current time, cell coloring function);
                              PhysiCell globals.SVG output index++;
                              PhysiCell_globals.next_SVG_save_time -+= PhysiCell_settings.SVG_save_interval;
                      microenvironment.simulate diffusion decay( diffusion dt );
                      ((Cell Container *)microenvironment.agent container) -> update all cells( PhysiCell globals.current time );
                      PhysiCell globals.current time += diffusion dt;
                  if( PhysiCell settings.enable legacy saves == true )
                      log output (PhysiCell globals.current time, PhysiCell globals.full output index, microenvironment, report file);
                     report file.close();
                                                                      length: 10,848 lines: 241
                                                                                                Ln:157 Col:95 Sel:0|0
```

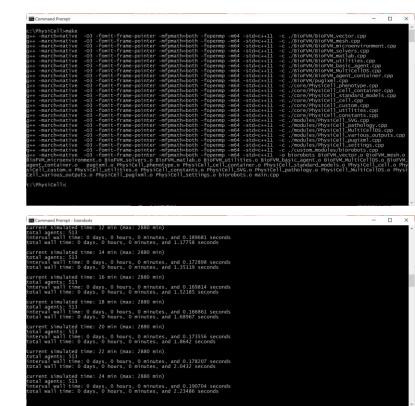
Now, let's get back to working with sample projects.

PhysiCell Project Essentials (2)

- Now, compile the project
 - make

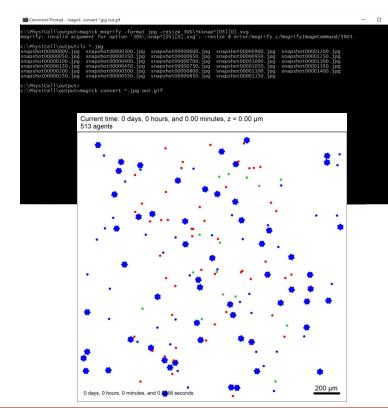
- Then, run the project
 - ./biorobots (Linux, MacOS)
 - biorobots.exe (Windows)

This should take about 5 minutes



PhysiCell Project Essentials (3)

- Look at saved data
 - Most projects save data to ./output
 - ◆ XML files give metadata, mesh, and substrate info
 - ◆ MAT file save (compressed) substrate and cell data
 - ♦ SVG files are visual quick snapshots
 - ♦ More on loading XML / MAT files in Python later
- Let's convert SVG to rescaled JPEG
 - magick mogrify -format jpg -resize 30% snap*.svg
 - ◆ Convert snapshot00000000.svg, snapshot00000001.svg, ...
 - magick mogrify -format jpg -resize 30% snap*[05][0].svg
 - ◆ Convert snapshot00000000.svg, snapshot00000050.svg, ...
- Now, let's create an animated GIF
 - magick convert *.jpg out.gif



Working with the images

- To convert all the SVG files to PNG format magick mogrify -format png snap*.svg
- To convert every SVG file ending in 0 or 5 to JPG format magick mogrify -format jpg snap*[05].svg
- To convert the JPG files to an animated GIF magick convert *.jpg out.gif

To create an mp4 movie:

```
Handy tricks!
```

Use make jpeg to create a full set of JPGs

Use make movie easily create the mp4.

```
ffmpeg -r 24 -f image2 -i snapshot%08d.jpg -vcodec libx264 -pix fmt yuv420p -strict -2 -tune
animation -crf 15 -acodec aac out.mp4
```

PhysiCell Project Essentials (4)

Data cleanup

- Clean up data to get ready for another run
- make data-cleanup

- Reset to a clean slate
 - De-populate the project
 - Get ready for another project
 - make reset

```
c:\Physicell>make data-cleanup
rm = f *.mat
rm = f *.mat
rm = f *.xml
rm = f *.xml
rm = f *.xml
rm = f *.xml
rm = f *.svg
rm = f .Output/*
touch ./Output/empty.txt

c:\Physicell>make reset
rm = f *.cpp
rouch ./output/empty.txt

c:\Physicell>make reset
rm = f *.cpp
rouch ./custom_modules/empty.txt
touch .ALL_CITATIONS.txt
rm ALL_CITATIONS.txt
couch AIL_CITATIONS.txt
cp ./config/Physicell_settings-backup.xml ./config/Physicell_settings.xml
c:\PhysiCell>|
```

Changing settings in a project

XML Refresher (1)

- XML stands for eXtensible Markup Language
 - (Think of it as a generalization of HTML.)
- Information in XML are stored in elements. Key elements are:
 - element name in a start tag
 - attributes and values
 - element value
- If an element has a value, it must have a matching end tag:



• If an element has attributes but no value, you can use a more compact form:

<element name attribute1="attribute 1 value" attribute2="attribute 2 value" />



XML Refresher (2)

Just like HTML, XML can have sub-elements:

- By convention:
 - the name of the element is a parameter name
 - the element's value is the parameter value
 - attributes are used to store metadata or other clarifications (e.g., units)

<diffusion_coefficient units="micron/min^2">1000</diffusion_coefficient>

First, populate the cancer heterogeneity project

List all available sample projects

 Populate the cancer heterogeneity project

Build the project

• Change some settings (next slide)

```
PowerShell 7 (x64)
 C:\Users\PaulT\Downloads\PhysiCell-1.7.1\PhysiCell-1.7.1> make list-projects
ample projects: template2D template3D biorobots-sample cancer-biorobots-sample heterogeneity-sample
                cancer-immune-sample virus-macrophage-sample template
 C:\Users\PaulT\Downloads\PhysiCell-1.7.1\PhysiCell-1.7.1> make heterogeneity-sample
   /sample_projects/heterogeneity/custom_modules/* ./custom_modules/
    main.cpp && cp main.cpp main-backup.cpp
   /sample_projects/heterogeneity/main-heterogeneity.cpp ./main.cpp
   /sample_projects/heterogeneity/Makefile .
   config/PhysiCell settings.xml ./config/PhysiCell settings-backup.xml/
  /sample projects/heterogeneity/config/* ./config/
 C:\Users\PaulT\Downloads\PhysiCell-1.7.1\PhysiCell-1.7.1> make _
```

How to change settings in XML

- Open config/PhysiCell_settings.xml
- Major sections:
 - domain -- how big of a region to simulate
 - overall -- how long to simulate, time step sizes
 - parallel -- OpenMP settings
 - save -- how often to save SVG images and full data
 - microenvironment -- settings on diffusing substrates
 - user_parameters -- model-specific settings
 - cell_definitions -- set baseline cell properties

Exercise: change settings and run

Let's set the maximum simulation time to 2160 minutes

• Let's set the domain to [-500,500] x [-500,500] to speed it up

- Let's set the oncoprotein standard deviation to 3
- Let's set the max oncoprotein to 10 (mean + 3 standard deviations)
- Compile and run as before.

Let's set options and run (1)

- Open ./config/PhysiCell-settings.xml
- Let's set the domain size in the domain block
 - Switch to [-500,500] x [-500,500] x [-10,10] to speed it up

Let's set options and run (2)

- Let's also look at the user_parameters block
 - Let's change the oncoprotein standard deviation (oncoprotein_sd) to 3 (more variation)
 - Let's change the max oncoprotein (oncoprotein_max) to mean + 3 sds = 1 + 9 = 10

Let's set options and run (3)

- Let's look at the overall block
 - Set max time to 1.5 days = 1.5 x 24 x 60 = 2160 minutes

- Let's look at the save block
 - Set the full save interval to 6 hours = 360 minutes

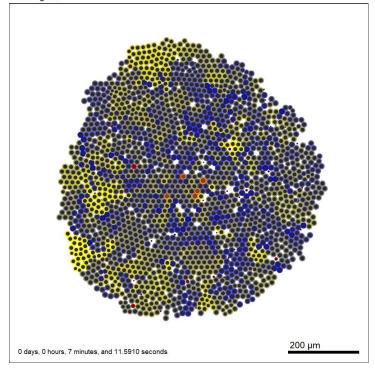
• Now, run! (./heterogeneity)

Let's do a quick visualization

• make gif

- We can see that the yellow cells eventually "win": they grow faster and form microcolonies within the tumor
- The effect is greatest on the outside edge: They have access to more O₂ here

Current time: 5 days, 0 hours, and 0.01 minutes, z = 0.00 μ m 1996 agents



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