========

Overview

========

Lattice Microbes (LM) is a software package for efficiently sampling trajectories from the chemical and reaction-diffusion master equations (CME/RDME) [#LM1] . LM computes CME/RDME using Graphics Processing Units (GPU) and even multiple GPUs [#LM2] . LM is recently used for the simulation of mRNA splicing in a HeLa cell [#LM3]\_.

LM has been designed for building geometrically-shaped cells. However, LM essentially can incorporate any shapes of cells and cellular structure, as demonstrated in a previous study [#LM4]\_.

LM is designed to simulate cells with geometric shapes, because of limited availability of information on cellular shapes. However, LM originally can incorporate any shapes of cellular boundary or the other cellular structure, as demonstrated in a previous study [#LM4] .

We here developed an extension of LM, which is named Lattice Dendrites (LD), for the efficient incorporation of realistic cellular shapes. In particular, LD is designed to incorporate shapes of segmented images from electron microscopy (EM). LD provides a variety of utility classes/functions for:

#. Conversion of segmented shapes from a software for EM segmentation (reconstruct).

#. Object rotation to minimize their volume in a rectangular solid.

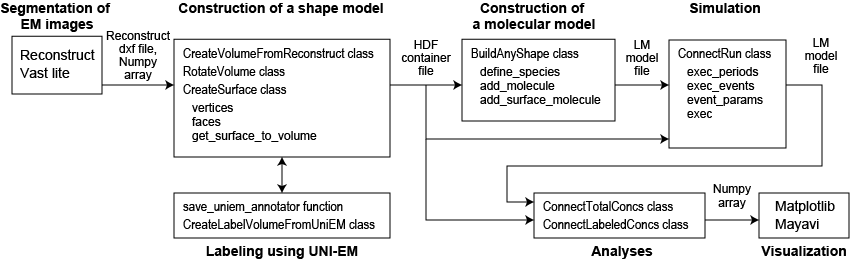
#. Manual annotation using UNI-EM annotator.

#. Surface molecules distribution proportional to surface area.

#. Simulation with events

#. Data analyses for visualization.

Users can use a variety of functions below for their model development, simulation, and analyses. Their usages are described in Tutorials 1 and 2.



.. [#LM1] Roberts E, Stone JE, and Luthey-Schulten Z (2013) Lattice Microbes: high-performance stochastic simulation method for the reaction-diffusion master equation, J. Comput. Chem. 34(3):245-255, http://faculty.scs.illinois.edu/schulten/lm/ , http://faculty.scs.illinois.edu/schulten/Software2.0.html#1

.. [#LM2] Hallock MJ, Stone JE, Roberts E, Fry C, Luthey-Schulten Z (2014) Simulation of reaction diffusion processes over biologically-relevant size and time scales using multi-GPU workstations, Parallel Comput. 40:86-99

.. [#LM3] Ghaemi Z, Peterson JR, Gruebele M, and Luthey-Schulten Z (2020) An in-silico human cell model reveals the influence of organization on RNA splicing, PLOS Comput. Biol. 16(3): e1007717, https://eukaryoticcellbuilder.github.io/HeLa\_Builder/

.. [#LM4] Earnest, TM, Watanabe, R, Stone, JE, Mahamid, J, Baumeister, W, Villa, E, & Luthey-Schulten, Z (2017) Challenges of integrating stochastic dynamics and cryo-electron tomograms in whole-cell simulations. J. Phys. Chem. B, 121(15):3871-3881

==============================

Tutorial 1: schematic dendrite

==============================

We would introduce how to use LD and LM through two tutorials. In this tutorial (tutorial 1), we first build a dendritic spine that is represented by a schematic shape (ball and stick), then two types of simulation are conducted: Ca2+ influx through NMDA receptors and fluorescence recovery after photobleaching (FRAP). Through these simulations, users can understand how to build a spiny dendrite, label the spine, run simulation, and visualize the simulation results.

.. toctree::

tut1/create\_spiny\_dendrite

tut1/label\_spine

tut1/set\_reactions

tut1/run\_simulation

tut1/visualization1\_matplotlib

tut1/visualization2\_mayavi

All tutorial programs are located in $LD\_DIRECTORY/tutorial. Find the following script in the subdirectory "1". It provides utility functions that are used in tutorial 1. The function "make\_cylinder" makes a cylinder with an indicated radius and length. The function "add\_shape" locates a geometric object into a volume space. The function "show\_dendrite" loads and displays the surface objects of cellular boundary, postsynaptic density (PSD), mitochondrion, and endoplasmic reticulum (ER).

All tutorial programs are located in $LD\_DIRECTORY/tutorial. Find the following script in the subdirectory "1". It includes utility functions for tutorial 1. The function "make\_cylinder" makes a cylinder with a indicated radius and length. The function "add\_shape" locates such a geometric object in a volume space. The function "show\_dendrite" loads and displays the surface objects of cellular boundary, postsynaptic density (PSD), mitochondrion, and endoplasmic reticulum (ER).

.. literalinclude:: ../tutorial/1/tut1\_functions.py

:language: python

:linenos:

:caption: tut1\_functions.py

==============

Create a shape

==============

We would first draw a blueprint of a schematics shape of spiny dendrite (Figure below), and embed the designed shape in a numpy 3D array. First, a voxel space of 96 |times| 60 |times| 96 voxels (20 nm/voxel) is set (vol\_dend; Line 14 in 11\_create\_dend.py), and a sphere with a radius of 0.25 |mgr| m (12 voxels) is generated as a spine head. We used a Python module function morphology.ball (skimage) to create the spine head (Line 10), which is added to the voxel space “vol\_dend” (add\_shape; Line 15). Similarly, we make a spine neck and dendrite (Lines 11 and 12, respectively), and add them to “vol\_dend” (Lines 16 and 17, respectively). The in-house function “add\_shape,” simply overlays overwrapped regions, and represents the filled areas as 1 (cytosolic region), and void areas as 0 (extracellular region).