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Continuum Diffusion Rate of Enzymes by Solving the Smoluchowski Equation

Tutorial Part

Yuhui Cheng

ycheng@mccammon.ucsd.edu

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http://mccammon.ucsd.edu/~ycheng/nbcr0810_tutorial.pdf

Objective

- To learn how to generate and refine simple meshes.
- To learn how to derive the weak form of the diffusion equation and simple potential gradient calculations.
- To implement some preliminary calculations on the simplest spherical and enzyme case.

Tutorial directory guide

- NOTE:

cd /rc/ws/nbcr

- Data structures

./bin all the executable binary files

./cshrc set some necessary environments

./mesh all the mesh files we will use for this tutorial

./pqr all the PQR files for this tutorial

./potential all the potential files and scripts for APBS runs.

./run YOU need to copy it to /var/tmp/nbcr later

./tools Here are all the OpenDX graphic programs and perl scripts

Work directory

- NOTE:

cd /var/tmp

mkdir nbcr

cd nbcr

cp –r /rc/ws/nbcr/run .

source /rc/ws/nbcr/cshrc

Please do your jobs under /var/tmp/nbcr

Sample input files

- NOTE:

There are two input file formats used, the old format was defined by Dr. Nathan Baker.

```
# model parameters
charge 0.0          /* ligand charge */
conc   1.0          /* initial ligand concentration at the outer boundary */
diff   78000.0      /* diffusion coeficient */
temp   300.0        /* temperature, unit: Kelvin */
# potential gradient methods
METHtype BEM                /* you can choose BEM or FEM */
# mapping method
map NONE                    /* you can choose NONE/DIRECT/FEM */
# steady-state or time-dependent
tmkey TDSE          /* you can choose SSSE or TDSE */
# input paths
mol ../../pqr/ion_yuhui.pqr
mesh ../../mesh/sphere_4.m
mgrid ../../potential/pot-0.dx                  /* for APBS input */
dPMF  ../../force/evosphere_4.dat           /* for BEM input */
end 0
```

Manage your input parameters

- NOTE:

${solver}

- the default input file: smol.in

${solver} -ifnam filename

- the default iteration method: CG(lkey=2).

BCG (lkey=4 or 5), BCGSTAB(lkey=6)

${solver} -lkey 2

- default maximal number of iterative steps: 5000

${solver} –lmax 8000

Manage your input parameters (cont.)

- NOTE:
- the default timestep: $5.0*10^{-6}\mu s$

${solver} -dt $5.0*10^{-5}$

- the default number of time steps:500

${solver} –nstep 1000

- the default concentration output frequency: 50

${solver} –cfreq 100

- the default reactive integral output frequency: 1

${solver} –efreq 5

Part I: Simple mesh generation

Our first task is to generate the analytical test for the SMOL diffusion.

software: Netgen (http://www.hpfem.jku.at/netgen/)

software tutorial:
($NBCR_SUMMER_SCHOOL/tutorial/ng4.pdf)

```
cd ./mesh

ng
```

Start from “file”, then “Load Geometry”, then “Generate Mesh”.
Note: The node and element numbers are shown below the software screen

Then you can refine the mesh by choosing “Refinement”. (For example, I have stored a case with 409,886 vertices.)

Finally, from “file”->”Export Mesh”, save the mesh as “born.mesh”

Analytical test: Simple mesh generation

cp born.mesh mesh.neu

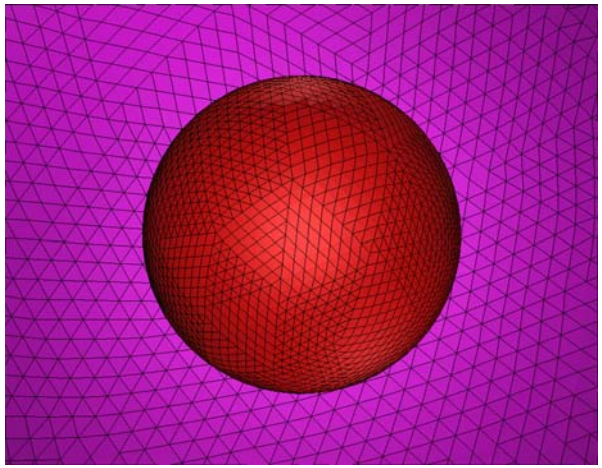
neu2m >& born.m

born.m is exactly the input file we will use for this tutoring.

To visualize your mesh, you can type

mcsf2off --boundary born.m

geomview born.off (OR mcsg born.off)



Analytical test:Potential calculations

We have prepared the potential calculations for various ionic strength cases.

```
mkdir /var/tmp/nbcr/potential

cd /var/tmp/nbcr/potential

cp -r /rc/ws/nbcr/potential/born .

cd born

./submit.csh >& submit.log &
```

Analytical test: Steady-state Diffusion calculations

We have prepared the potential calculations for various ionic strength cases.

cd /var/tmp/nbcr/run/born

Please use any text editor to edit “solve-all.csh” to control your calculations.

AND check your “smol-template.in”, you can use the potential files you calculated if you modify the potential path to your potential directory “/var/tmp/nbcr/potential/born”

./solve-all.csh >& solve-all.log &

Analytical test: Visualization of your calculation

OpenDX is applied to show concentration distribution at steady state.

Please select some tutorials from the below list if you want to know more about OpenDX:

http://ivc.tamu.edu/docs/opendx.pdf

```
cd $NBCR_SUMMER_SCHOOL/run/born
dx -edit ../../tools/visualization/conc.net
```

Sorry, OpenDX doesn’t work on these machines.

mAChE case: mesh and pqr file

- The mAChE mesh file was generated by Mol-LIBIE invented by Chandrajit's group.
- PQR file can be generated from PDB by Nathan's PDB2PQR server
- Assign the reactive boundary

Make sure to set the coordinate of carbonyl carbon of S203 at (0, 0, 0), and align the active site gorge with the y axis.

```
mkdir /var/tmp/nbcr/mesh

cd /var/tmp/nbcr/mesh

cp –r /rc/ws/nbcr/mesh/mache .

cd mache

assignBoundary assignBoundary.in >& assignBoundary.log &
```

mAChE case: mesh and pqr file

If your PDB file doesn’t have the right orientation, you may check the tcl script at $NBCR_SUMMER_SCHOOL/tools/vmd/moveby.tcl

mAChE case: potential calculation

Note: We have these potential files already, you need NOT run them again. But I still prepared a shell command “calc-all-pot.csh” under “$NBCR_SUMMER_SCHOOL/potential/mache”

You can copy “apbs-template0.in”, “apbs-template.in” and “calc-all-pot.csh” to your local machine to do that. It need large memories.

./calc-all-pot.csh >& calc-all-pot.log &

mAChE case: steady-state diffusion calculation

```
cd /var/tmp/nbcr/run/mache

./solve-all.csh >& solve-all.log &
```

mAChE case: Visualization of your calculation

Similarly, you can use gnuplot to plot out your k_on values.

Use OpenDX to plot the concentration distribution.

mAChE tetramer: assign boundaries

```
mkdir /var/tmp/nbcr/mesh

cp /rc/ws/nbcr/mesh/mache4 /var/tmp/nbcr/mesh/.

cd /var/tmp/nbcr/mesh/mache4/asite

./make-asite.csh

cd ..

assignBoundary assignBoundary.in >& assignBoundary.log &
```

Visualization of your mesh files

cd /var/tmp/nbcr/mesh

cd mache4

mcsf2off –boundary mAChE4-bc.m

geomview mAChE4-bc.off

mAChE tetramer: diffusion constant calculation

```
cd /var/tmp/nbcr/run/mache4

./solve-all.csh >& solve-all.log &
```

Additional reading materials

1. http://en.wikipedia.org/wiki/Diffusion
2. Berg, H C. *Random Walks in Biology*. Princeton: Princeton Univ. Press, 1993
3. advanced diffusion materials:

http://www.ks.uiuc.edu/Services/Class/PHYS498NSM/