Out line

- Protein dynamic and TEM
- Electron Microscopy Cryo-Tomography
- Individual-particle Electron Tomography method
- Goals for GPU implementation
The dynamic nature and structural heterogeneity of proteins is essential for their functions.

Dynamic proteins, like antibody, have a big conformation space.
However, conventional structural determination technologies, such as X-ray, NMR and single-particle electron cryo-microscopy (cryo-EM) are limited by structural heterogeneity because they all involved in averaging process of hundreds to thousands of different particles.
Electron Microscopy Cryo-Tomography (ET)
Negative stain and Cryo-EM

View unaltered macromolecular assemblies by freezing them
Sample is studied at cryogenic temperatures
Show biological specimen in their native environment
Improving steadily since vitreous ice can be produced
Tomography 3D Reconstruction
3D reconstruction is a challenge with Cryo-TEM data for small protein

- Low dose, low contrast
- High noise ratio 0.05
- Distortion in large area

- How to make good alignment and reduce noise lever?
Individual-particle Electron Tomography (IPET)

Lei Zhang, Gang Ren  PLoS ONE January 2012 | Volume 7 | Issue 1 | e30249
The Core Algorithm of the Local Refinement Program

Original tilt series

Translated tilt series

3D reconstruction

Filtered and masked Tilt series

FSC

Dynamic Gaussian low-pass filter

Dynamic 3D & 2D masks

Filtered and masked projections as references

Translation parameters
The Flow Diagram of Our Local Refinement Program

Align the ET micrographs

Correct the CTF

Window the target particle

Generate initial 3D

Refine the trans. param. of tilt series

2D cross-correlation

Project the 3D

Generate initial 3D

Refine the center of tilt-series

Interpolation

Low-pass filter & 2D Corr.

Round one

Back-project to 3D

2D circle mask

Refine the center of tilt-series

Interpolation

Round two

Back-project to 3D

3D particle-shape mask

Back-project to 3D

Project the 3D

Final 3D

2D particle-shape mask

Round three
Creating a Series of Simulating Cryo-ET Tilt Images of One Individual Particle - A 100kDa Transporter

Projections of the Model

CTF effects

Translation Errors

Add Noise S:N=1:5
The 3D reconstruction by IPET method
Antibody 3D reconstruction

Raw Images of One Individual Antibody
Antibody Dynamic

Unconjugated Antibody #1
GPU implementation?
The 3D reconstruction is very time consuming

To finish one 3D construction by IPET method need hundreds of iterations which means more than 5 hours, just for 120 tilted images (400*400 pixel)

Key algorithm(s) involved in traditional CPU approach

Pixel by pixel matrix operations, Fourier transform, Cross-Correlation calculation, interpolation and function fitting calculation

GPU acceleration

Imaging processing is very suit for GPU implementation, because their internal parallel property
Goals

- Increase calculation speed by verify SPIDER code and apply GPU accelerate
- The speed limiting steps: 3D volume rotation, FFT, Cross-Correlation calculation, Fourier space interpolation
Our Group member:

Gang (Gary) Ren, Ph.D.
Staff Scientist, Molecular Foundry
Principal Investigator

Dr. Lei Zhang
Dr. Bo Peng
Dr. Huimin Tong
Mr. Xing Zhang (ME)
Mr. Zhuoyang Lu
Mr. Meng Zhang
Mr. Dongsheng Lei
Mr. Matthew J. Rames

Group home page:
http://foundry.lbl.gov/rengroup/index.html