DockEM2 (and ShapeEM)

Part 1 - today
Introduction

Using with UCSF Chimera
UCSF Chimera options

Practical example
Run you own domain

Part 2 –tomorrow-more detailed analysis of solutions
Bacterial chaperonins GroEL and GroES
ATP drives cycles of binding and release of GroES and substrate protein that promote critical steps in protein folding.
Interacts with 30% of *E. coli* soluble proteins.
Analogues from human and archaea are CCT and the thermosome.
Docking

unliganded GroEL

GroEL(D398A)-ATP

GroES-ADP$_7$-GroEL-ATP$_7$
Apo GroEL at 8 Å resolution
DockEM uses the FLCF

- Fourier implemented Fast Local Correlation Function, or locally normalised correlation coefficient.

As described in:
Locally normalised cross correlation coefficients

<table>
<thead>
<tr>
<th>SNR</th>
<th>1</th>
<th>0.2</th>
<th>0.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84</td>
<td>0.30</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>0.91</td>
<td>0.42</td>
<td>0.24</td>
<td></td>
</tr>
</tbody>
</table>
The Eukaryotic Translation Initiation Factors eIF1 and eIF1A Induce an Open Conformation of the 40S Ribosome

Lori A. Passmore,1 T. Martin Schmeing,1 David Maag,2,3 Drew J. Applefield,2,4 Michael G. Acker,2 Mikkel A. Algire,2,5 Jon R. Lorsch,2,* and V. Ramakrishnan1,*

1 MRC-Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK
2 Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, 725 N. Wolfe Street, Baltimore, MD 21205, USA

Molecular Cell
eIF1 and eIF1A Promote an Open 40S Conformation
\[ C = \frac{1}{N} \sum_{i=1}^{N} \frac{(S_i - \bar{S})(T_i - \bar{T})}{\sigma_S \sigma_T} \]

\[ C(x) = \frac{1}{N} \sum_{i=1}^{N} \frac{(S_i - \bar{S})(T_{i+x} - \bar{T})}{\sigma_S \sigma_T} \]
\[ T_{M}(x) = \frac{1}{P} \sum_{i=1}^{N} M_{i} T_{x-i} \]

\[ \sigma_{MT}^{2}(x) = \frac{1}{P} \sum_{i=1}^{N} M_{i} T_{x-i}^{2} - \bar{T}_{M}^{2}(x) \]
1.1 Search Object

1.2 Mask
1.3 Target Map

1.4 Noisy Target Map
Figure 1.

1.1 Search Object

1.2 Mask

1.3 Target Map

1.4 Noisy Target Map

1.5 CCF

1.6 CCF (with noisy map)

1.7 LCF

1.8 LCF (with noisy map)
3D objects, 3D masks
Target map, 8.5 Å GroEL (emdb:1997)

Saibil Lab, Birkbeck College
Search object pdb
Target map 8.5 Å GroEL
Search object density ff8
Search object density ff8, with pdb
Search object, not ff
Search object pdb, density ff8
Mask around search object density
Mask around search object pdb
Mask around search object density
Mask around search object density
Docked domains, with oligomer pdb:1grl
Fig 1. Selecting the intermediate domain in Chimera (from pdb:1AON)
Some start position, by fit in Chimera
Fig 2a. Show outline box of map extent
Fig 2b. Show outline box of map extent
Fig 3. Move domain. Save relative to map.
DockEM2 solution compared to the full heptamer, pdb coordinates 1grl
ShapeEM

- Same algorithm and concepts
- Entry point is density object
- Output is extracted densities aligned to match the search object.
Important factors

• Correct magnification scale for target map and search objects (DockEM2 can do a scale search)
• Match resolution ranges
• Fourier amplitude scaling check, match (DockEM2 will have a utility for this in the next release)
Notes will be provided in the work directories

Documents

- Slides.pdf
- INSTRUCT-tutorial.pdf
- DockEM2.0-Instructions.pdf
Summary

• Normalised fast local correlation function is a Fourier real space method
• Costs 3 x (in speed, vs. basic cross-correlation)
• Advantages are flying mask and optimal local normalisation
• Don't need to define boundaries
• Equivalent to least squares or weighted least squares