

# Intrinsically Disordered Proteins and Heterogeneous Complexes

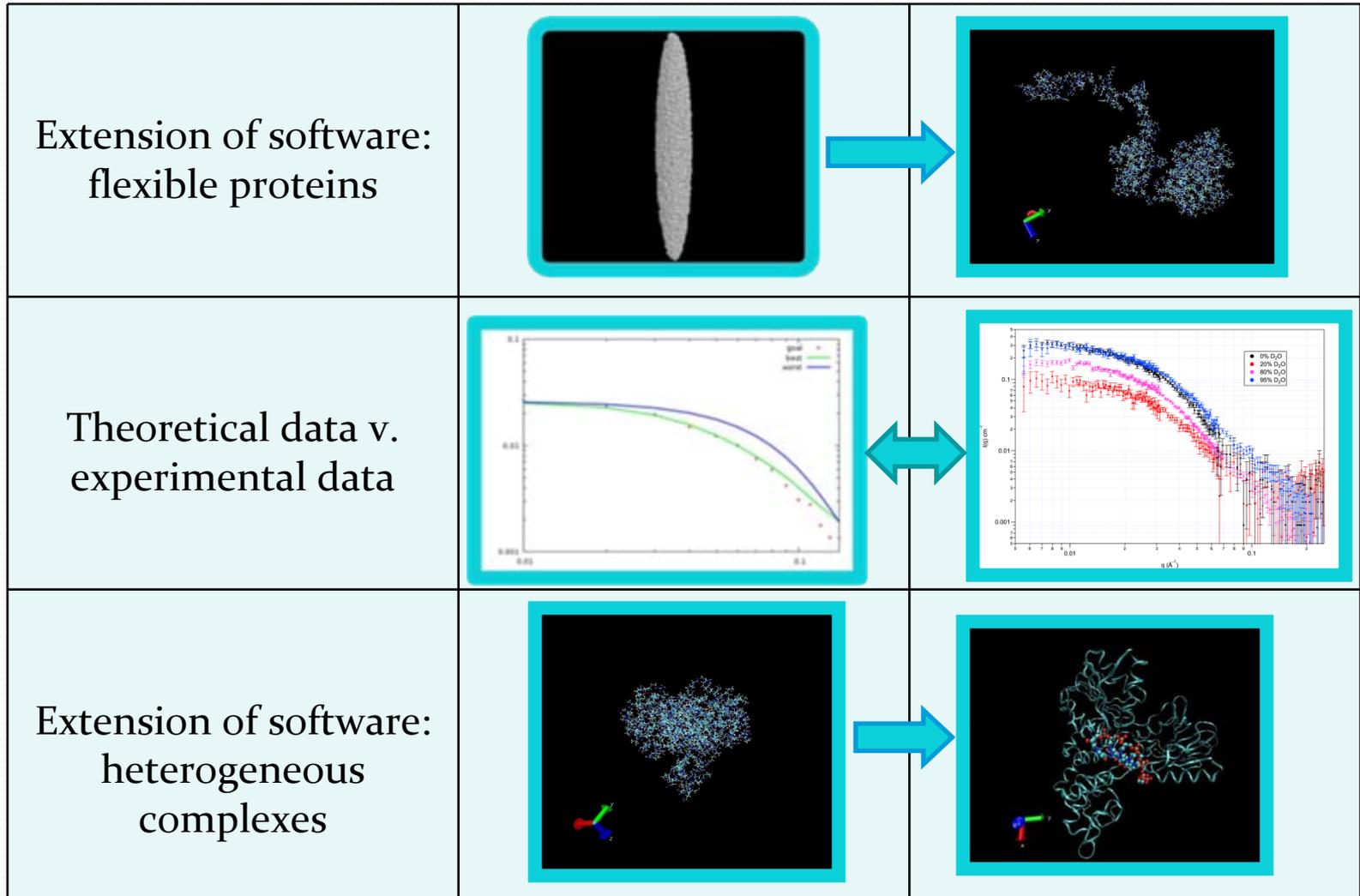
NIST Center for Neutron Research

Advisers: Joseph Curtis, Susan Krueger and Hirsh Nanda

Presented by Sindhu Raghunandan

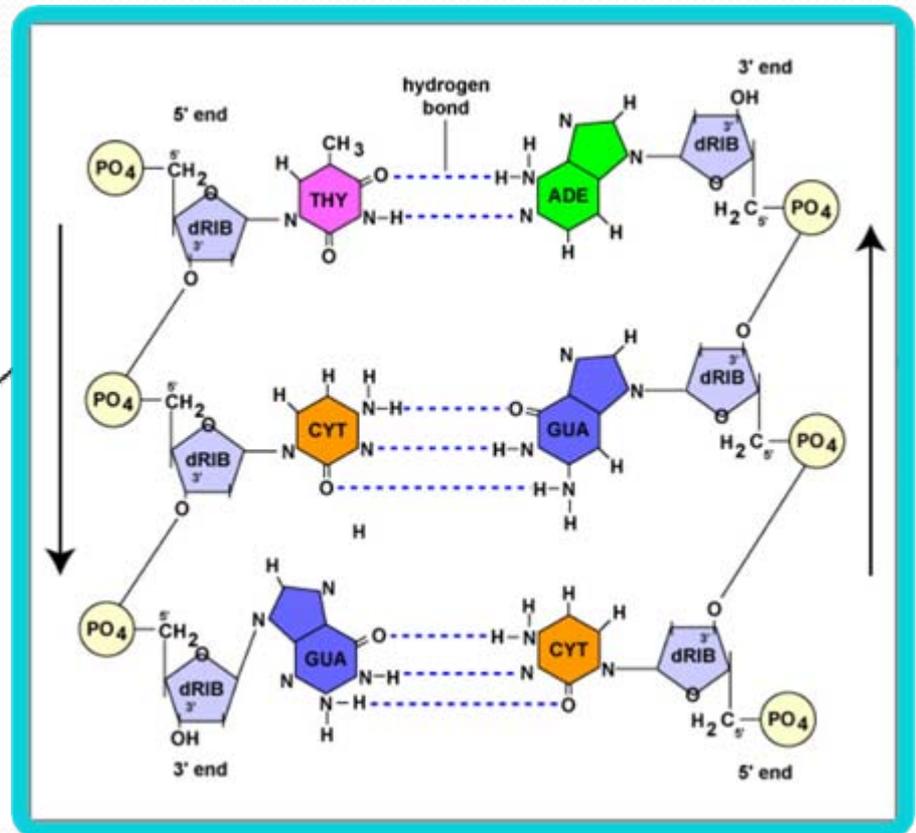
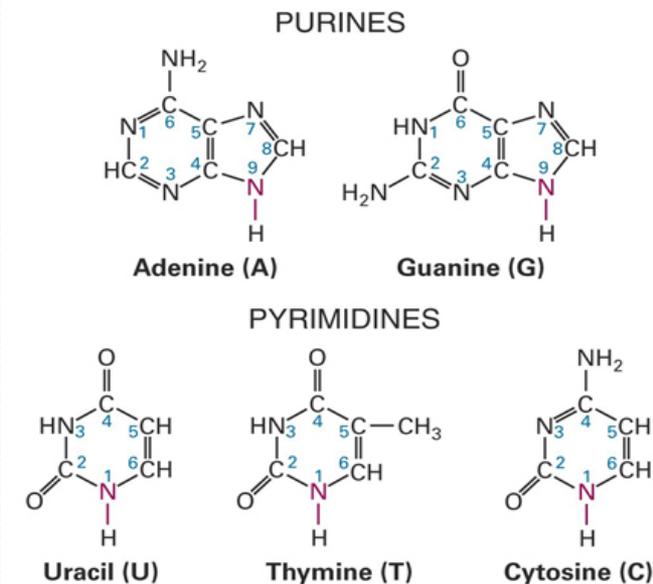


# Outline



# Protein Structure

- Importance
- Protein Basics
- DNA/RNA

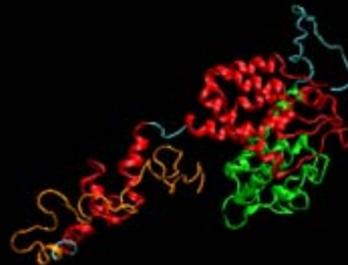
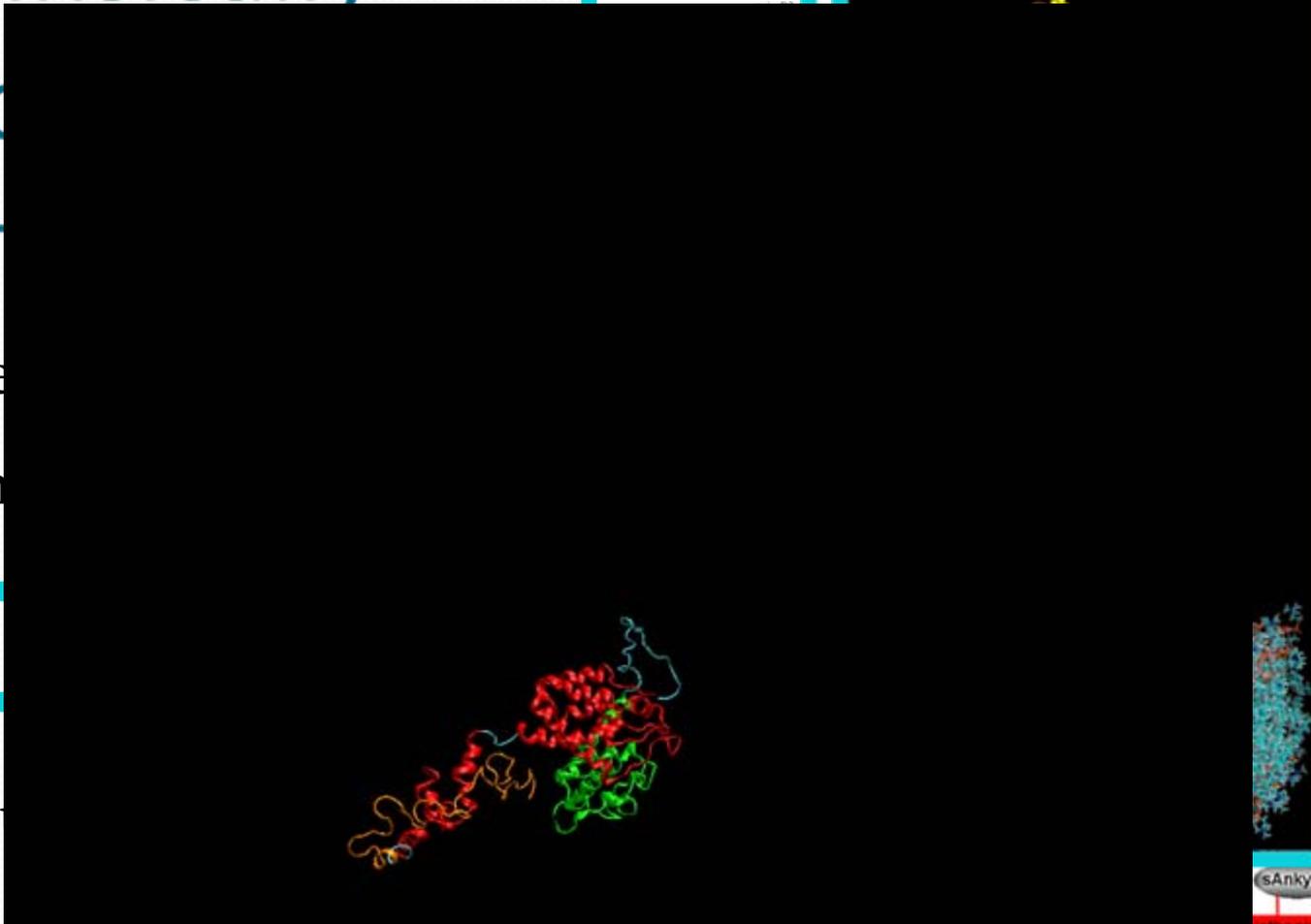


# Intrinsically

# Diso

# Prot

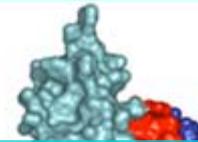
- De
- Im
- Str



### Current Topics

Table 1: Intrinsically

	protein
1a	acidic ribosome protein P11
1b	acidic ribosome



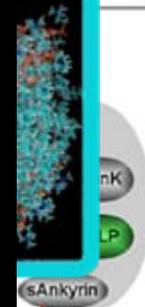
21, 2002 6575

### refs

- (25, 27-29)
- (30-32)
- (33)
- (34, 35)
- (36)
- (37-39)
- (40)
- (41-43)
- (42, 44-47)
- (48, 49)
- (50)
- (51, 52)
- (53)
- (54, 55)
- (56)
- (57-59)
- (60, 61)
- (62)

Titin

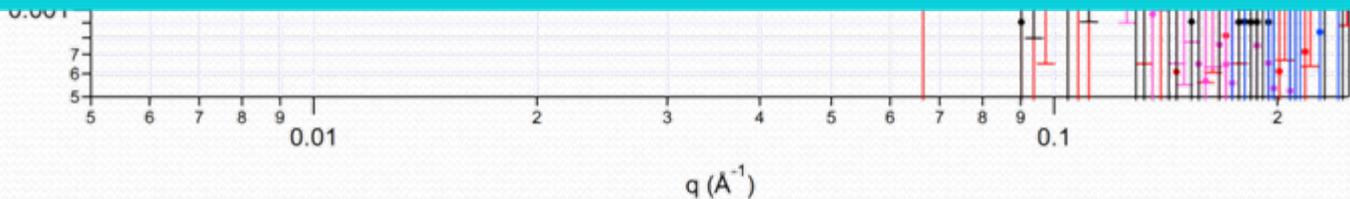
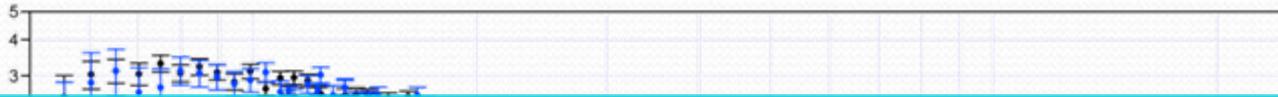
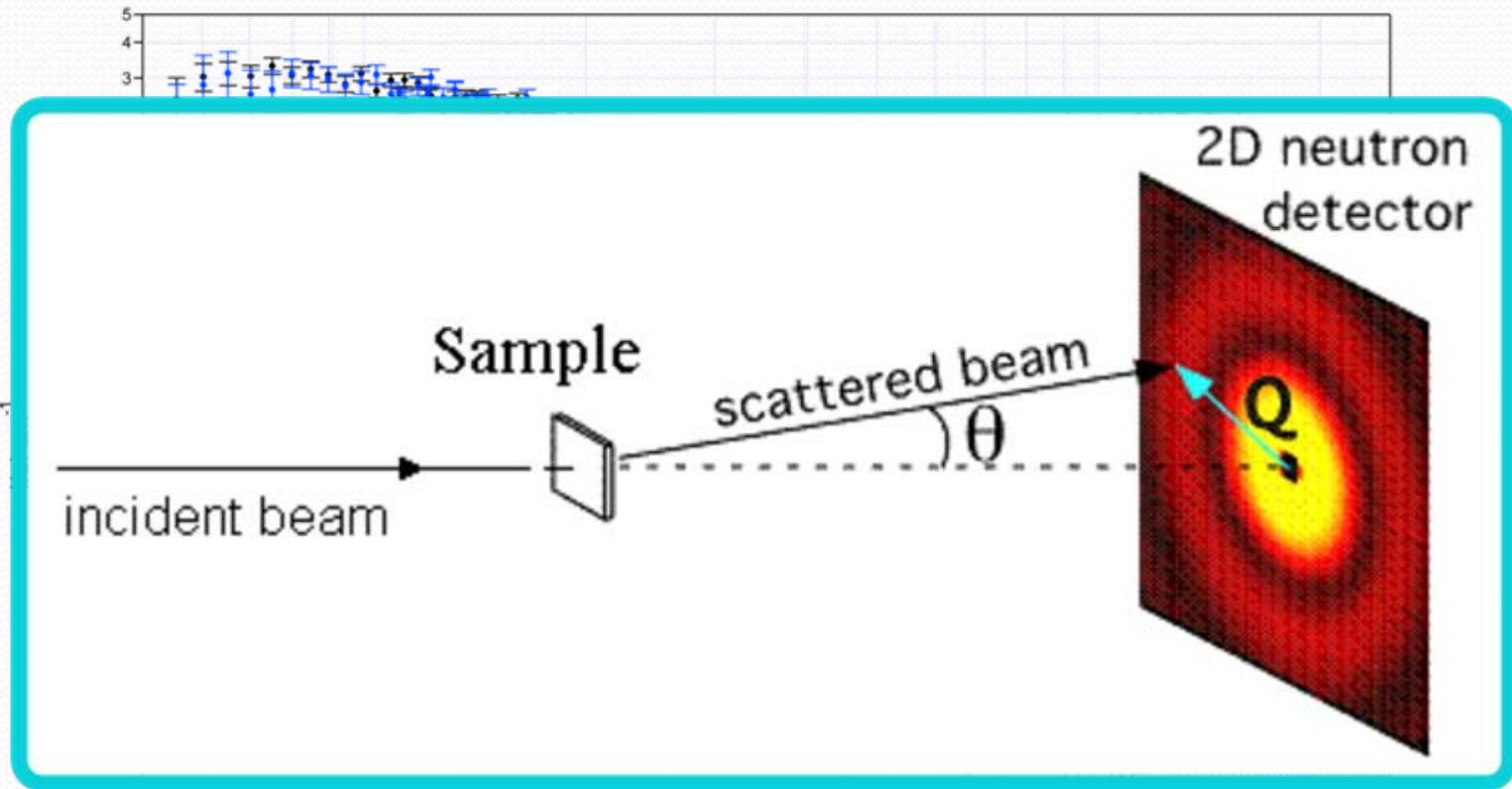
Titin



36 he  
37 he

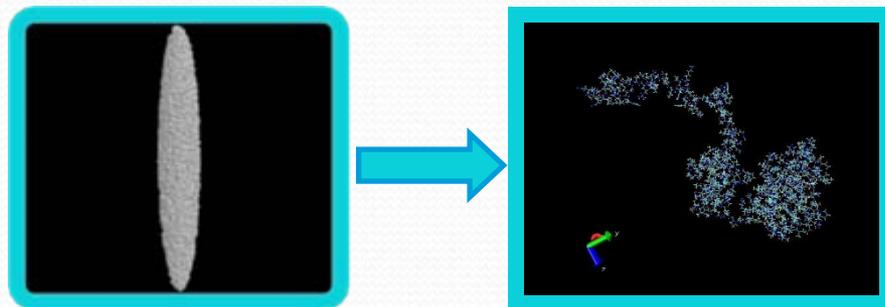
protein assembly  
residues  
(variable)  
residues

# Small Angle Neutron Scattering



# SASSIE

- Dihedral Structure Generator
- Cryson (SAS Calculator)
- Chi-square filtering
- Density Plot



```
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SASSIE
version cpc_0.9 : 11/06/06 : jc
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Tools

Center Frames

Align Frames

Modeling (requires graphical VMD)

Molecular Operations

SAS Data Analysis & Visualization Methods

Configuration Generators and Minimization
Monomer Dihedral Generation
Complex Dihedral Generation
SAS Data Minimization

SAS Calculators

Xtal2sas

Cryson

Crysol

EM Calculators

EM to SANS

SAS Data Analysis & Visualization Methods

Chi-Square Filtering

Density Plot

Quit

Thu Jul 30 11:23:51 2009
```

**SASSIE**  
version cpc\_0.3 : 11.06.06 : jc

Tools

- Center Frames
- Align Frames
- Modeling
- SAS Explorer
- Configuration Generator and Minimization
- Monomer Dihedral Generation
- Structure Minimization
- SAS Calculators
- Xtal2nan
- Cryson
- Cryool
- Data Analysis & Visualization Methods
- Chi-Square Filtering
- Density Plot
- Quit

Mon Sep 15 12:12:53 2008

**Dihedral Structure Generator**

input pdb filename :	min3.pdb	run name :	run_42/
Return to last accepted structure :	50	input file path :	/
output filename (dcd) :	run42.dcd	low Rg cutoff :	0.0
overlap basis :	alpha	high Rg cutoff :	400.0
number of trial attempts :	10000	overlap cutoff :	3.0
number of ranges :	5	enter MAX [theta] :	30 0,30 0,30 0,30 0,30 0
enter low residues :	123,278,354,378,408	number contiguous :	21,5,24,11,4
align frames (1--yes) :	1	save unaligned frames (1--yes) :	0
low residue :	204	high residue (K) :	350
Manual H/C Terminal(s) (0--no, 1--yes) :	0	temperature (K) :	300.0

version 0.3 : 11.02.05 : jc

```

-> found 431 alpha-carbon atoms (and residues)
first - 123 last - 144
first - 278 last - 283
first - 354 last - 378
first - 378 last - 389
first - 408 last - 412

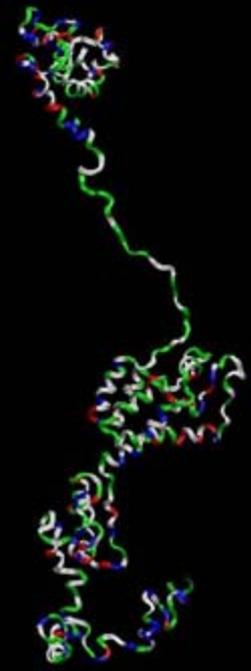
RESULTS
lowest Rg = 41.230372   highest Rg = 71.104557
accepted 335 out of 1000 : 33.500000 percent
overlapped 665 out of 1000 moves : 66.500000 percent
bad rg2 0 out of 1000 moves : 0.000000 percent
average accepted rg2 = 60.623295

Configurations and statistics saved in run_42/generate/ directory
average total rg2 of ensemble = 58.732522
DATA FROM RUN:
Reference structure used : run_42/generate/min3.pdb
Reference basis used : alpha
Aligned structures written to : run_42/generate/aligned_min3.pdb_run42.dcd.pdb

```

Run Dihedral Program

**VMD 1.8.3 OpenGL Display**



**VMD Main**

File Molecule Graphics Display Mouse Extensions Help

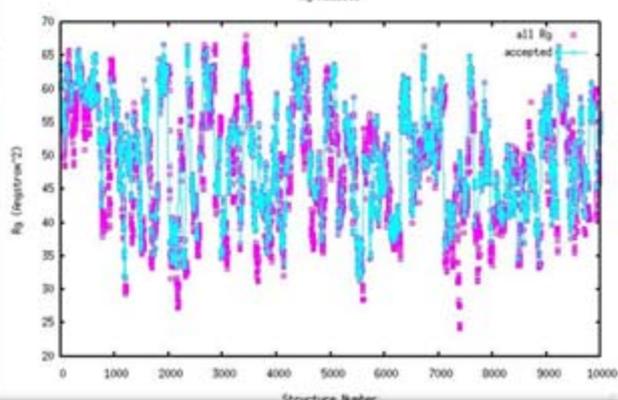
ID	T	A	D	F	Molecule	Atoms	Frames	Vol
2	T	A	D		molecule	6732	335	0

334

zoom | Loop | stop | speed

**Cnuplot**

Rg Results



**vmd console**

```

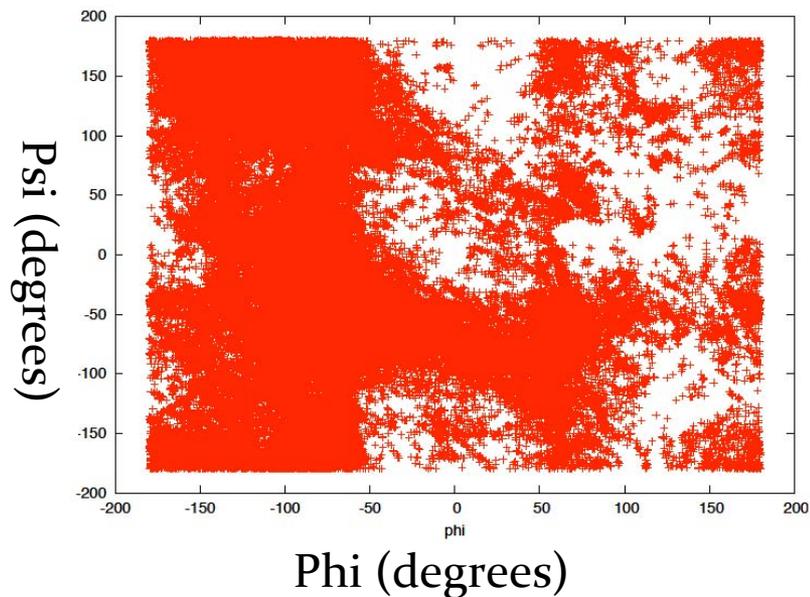
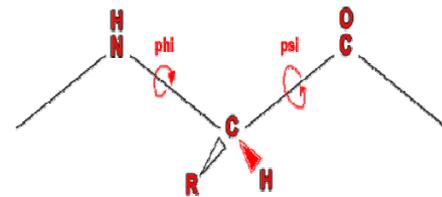
[Info] Opened coordinate file run_42/generate/aligned_min3.pdb_run42.dcd
for writing.
DCD data (n=4746) were written to run_42/generate/aligned_min3.pdb_run42.dcd
I am done
alignment done
Press return to clear plot and finish...

```

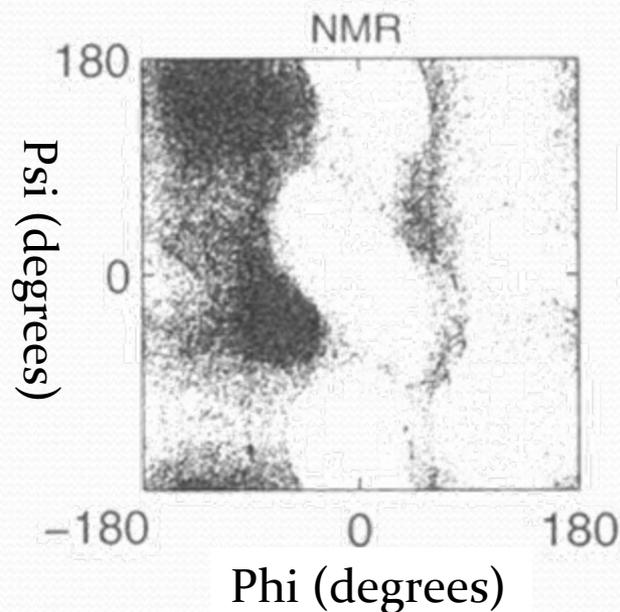
# Generating Structures

$$V \cong V(\text{VDW}) + V(\text{Dihedral})$$

$$V(\text{Dihedral}) = K_1(1 + \cos(n_1\Theta - \Delta_1)) + K_2(1 + \cos(n_2\Theta - \Delta_2))$$



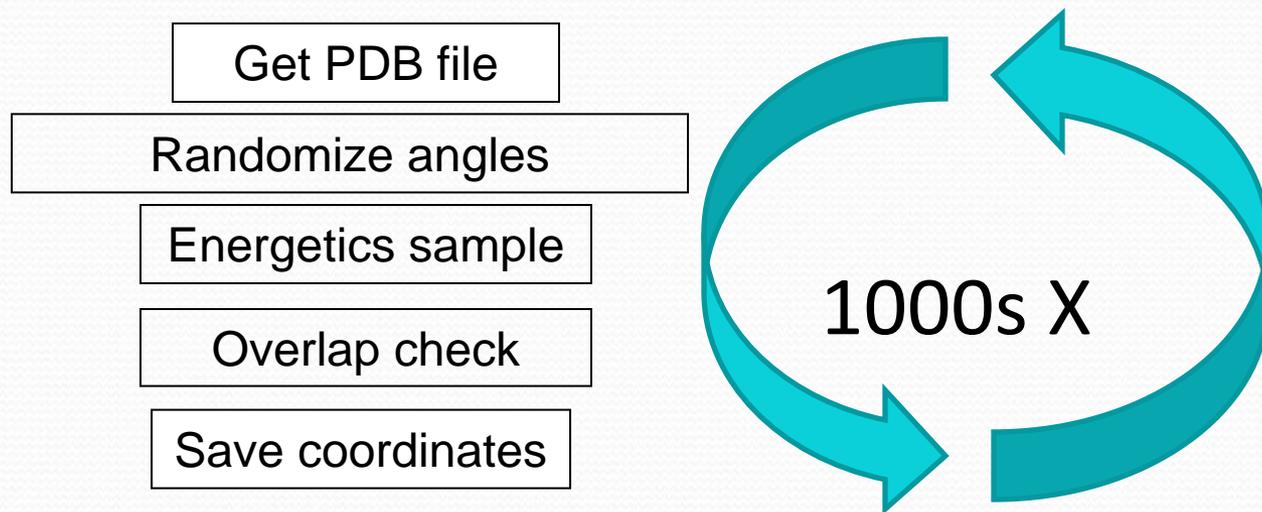
1 protein, 65 residues,  
>100,000 configurations



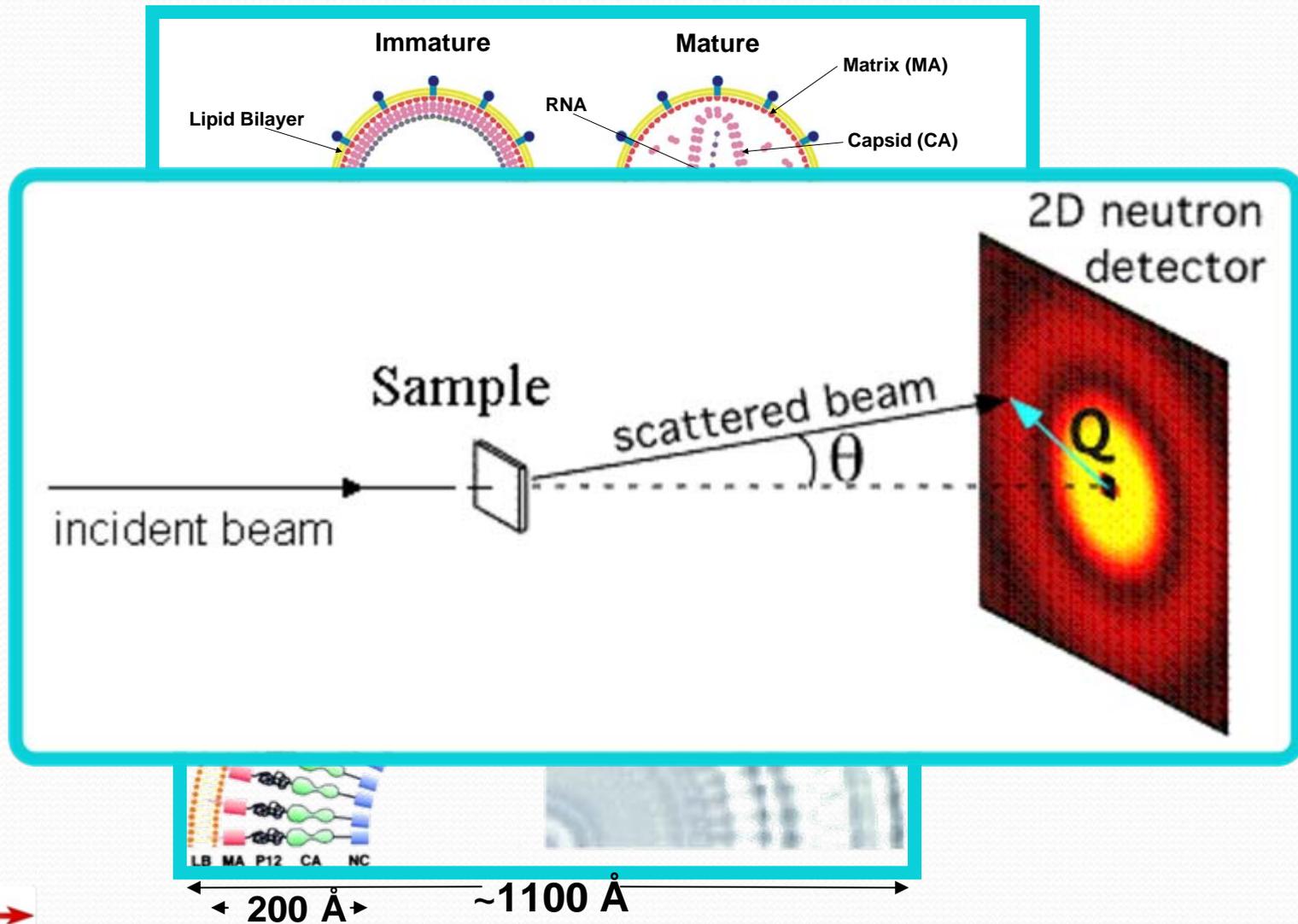
113 proteins, 84719 residues

SASSIE dihedral angle sampling represents experimental data

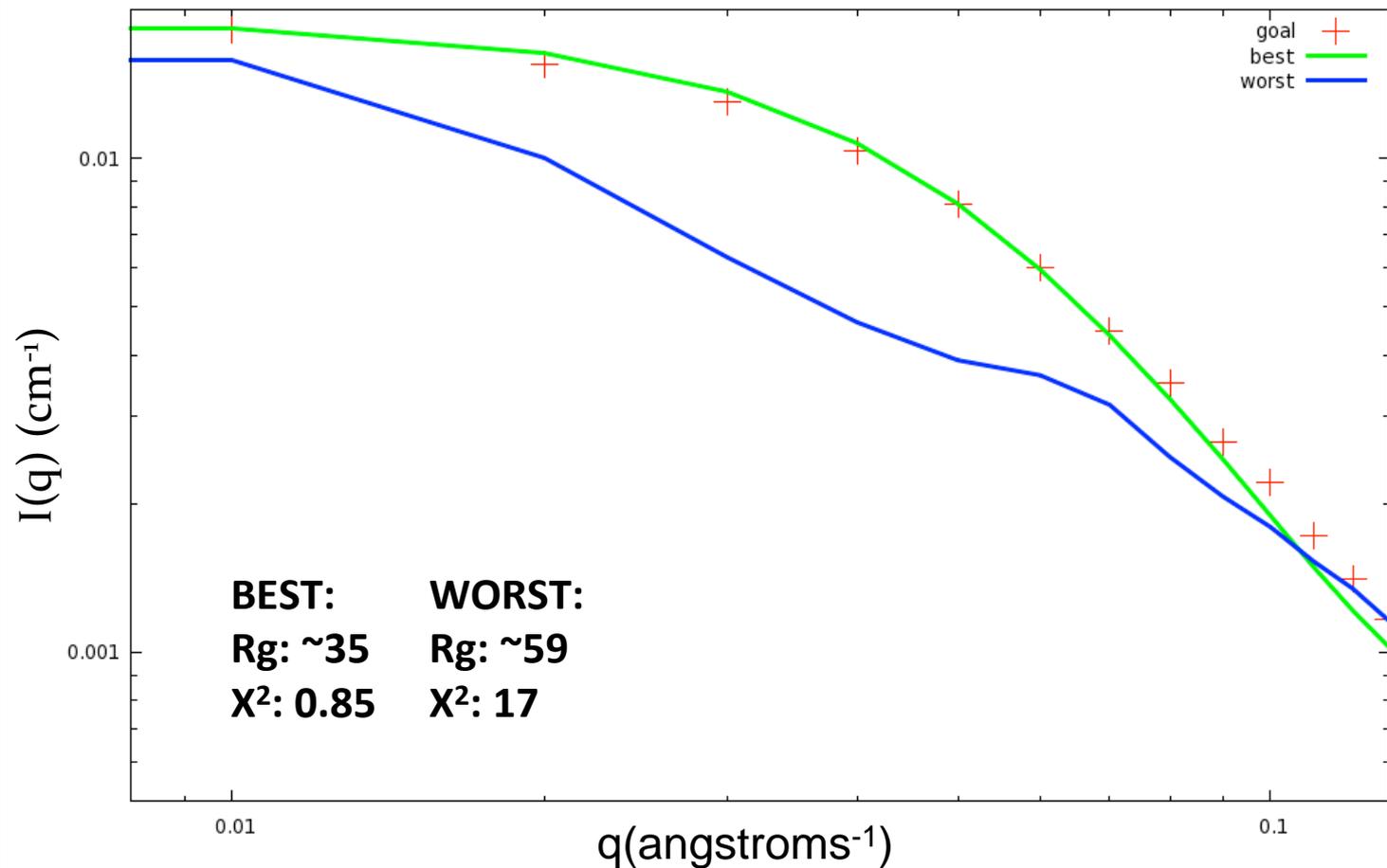
# Dihedral Structure Generator Algorithm



# Gag: Motivation and Methods

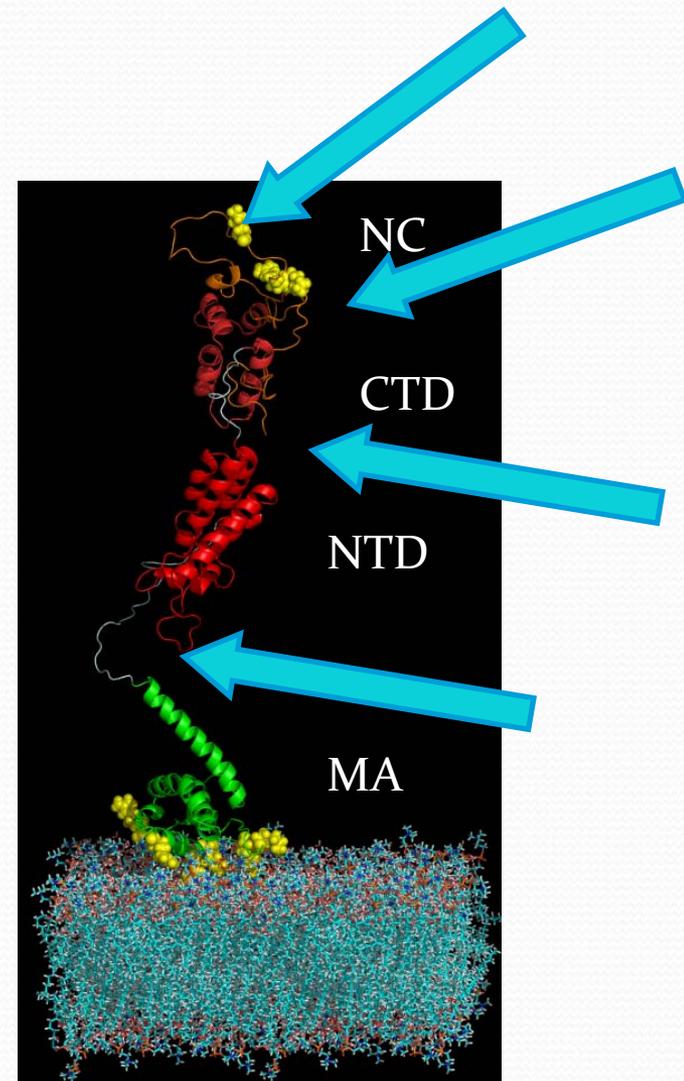


# Full Gag

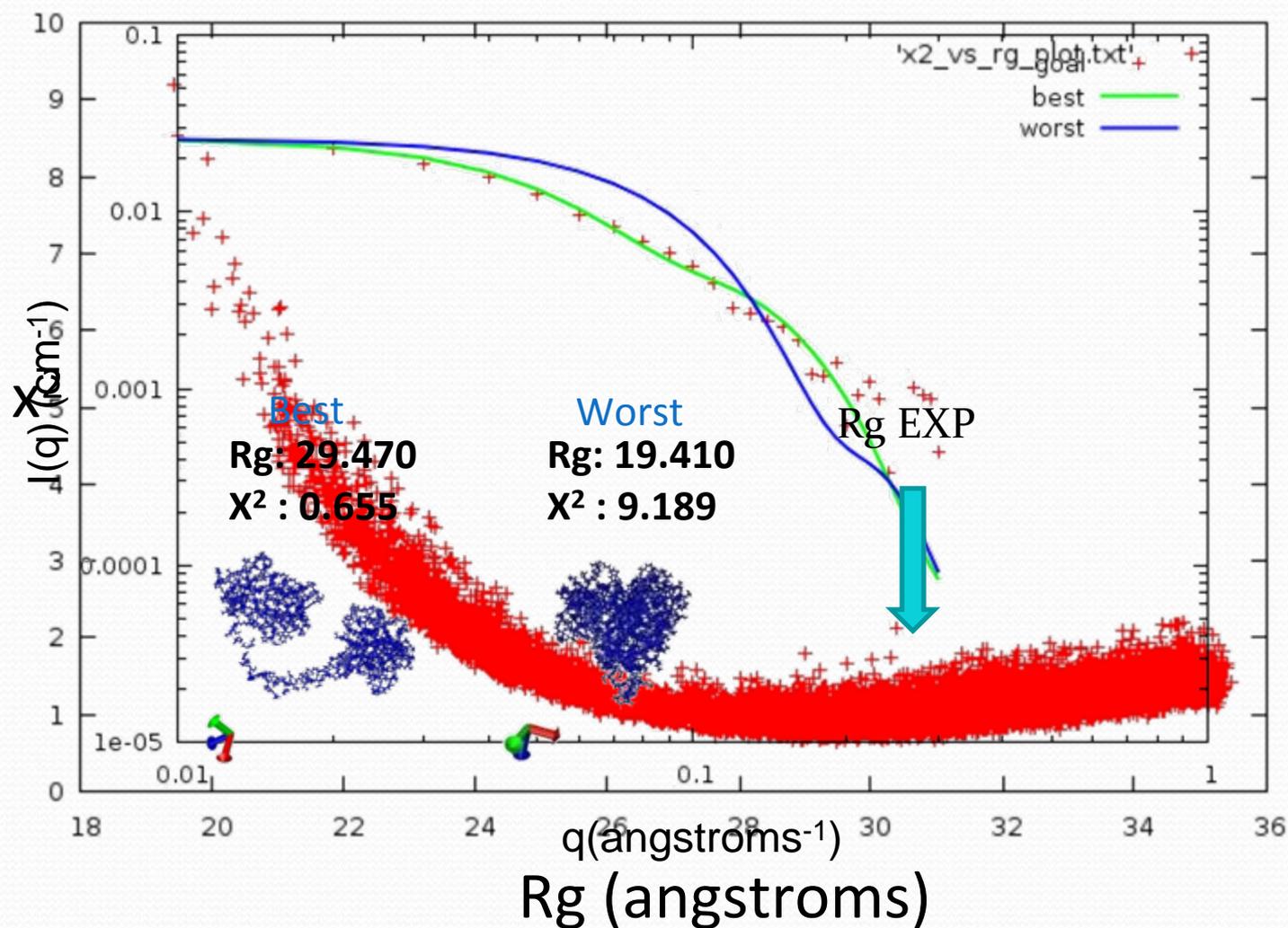


# Pieces of Gag

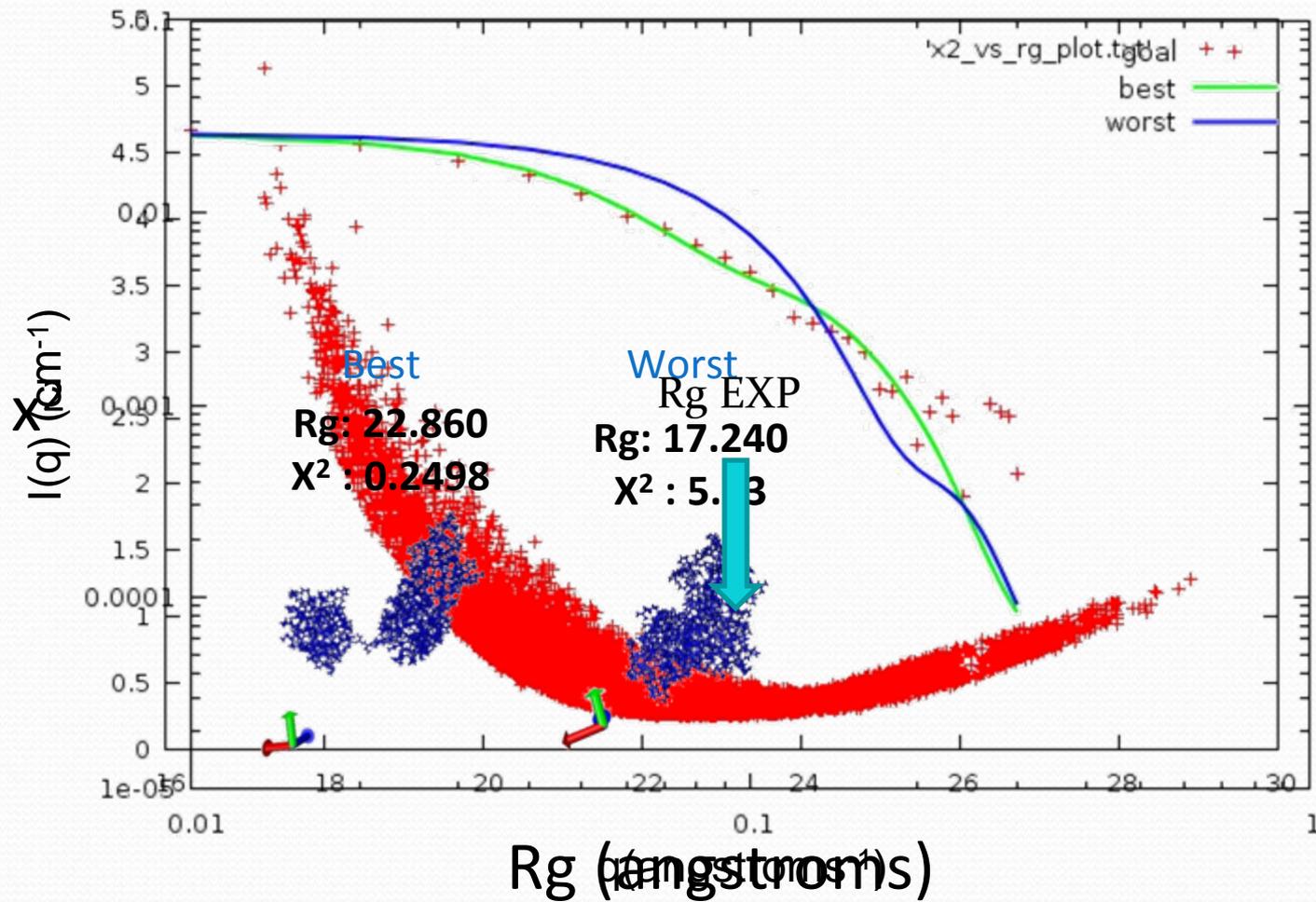
- MA-NTD
  - MA Residues 1-122
  - Linker Residues 123-144
  - 27444 structures
- NTD-CTD
  - NTD Residues 1-133
  - CTD Residues 140-209
  - Linker Residues 134-139
  - 19943 structures
- NTD-CTD-NC
  - P2+NC Residues: 210-287
  - Linker Residues: 134-139
  - 117550 structures



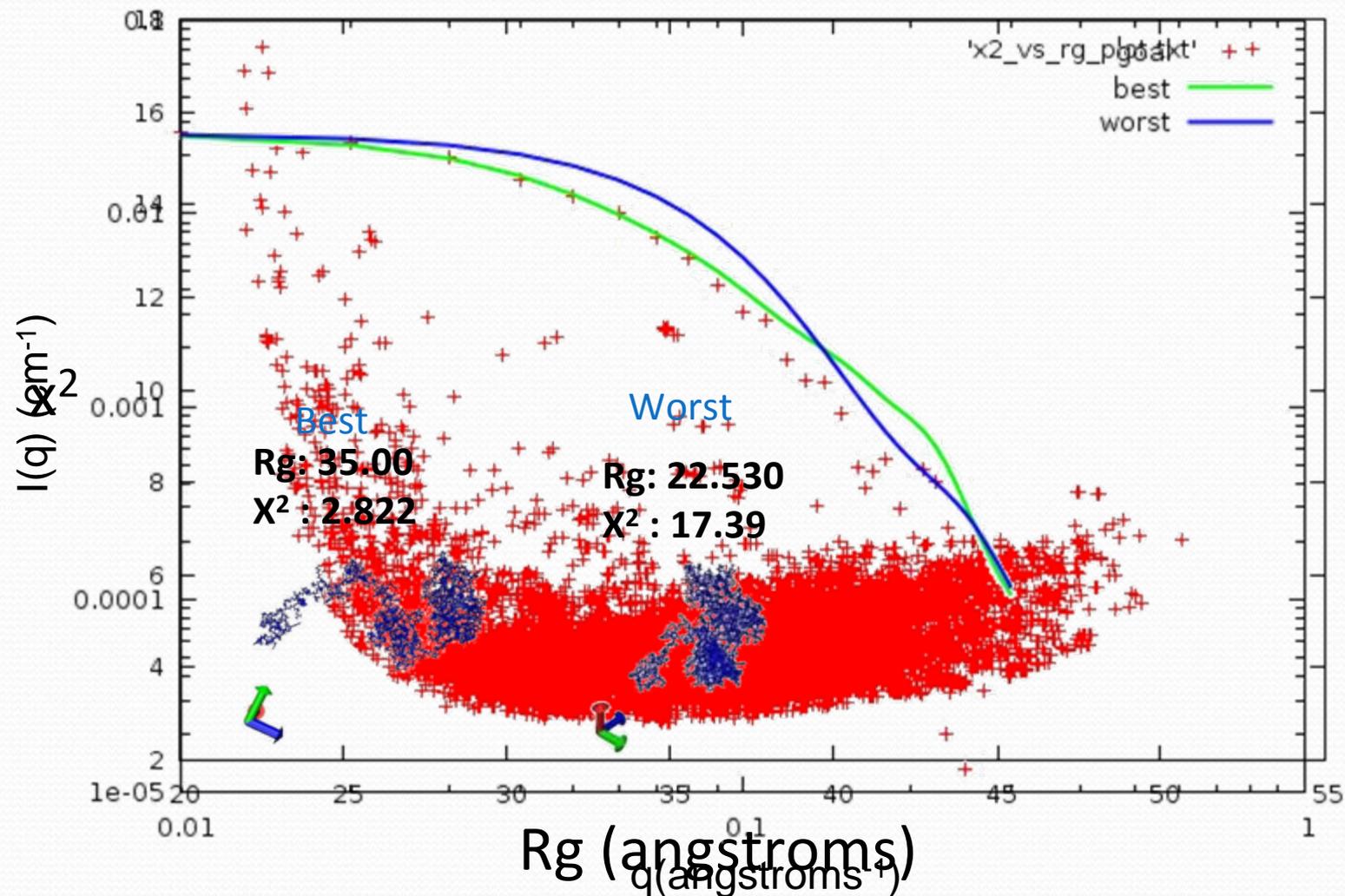
# MA-NTD



# NTD-CTD

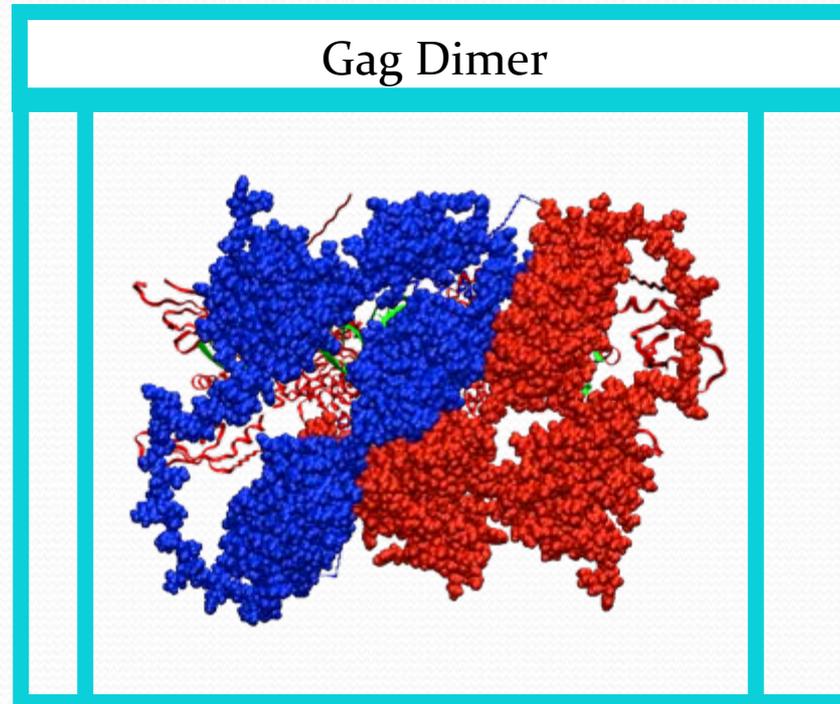


# NTD-CTD-NC



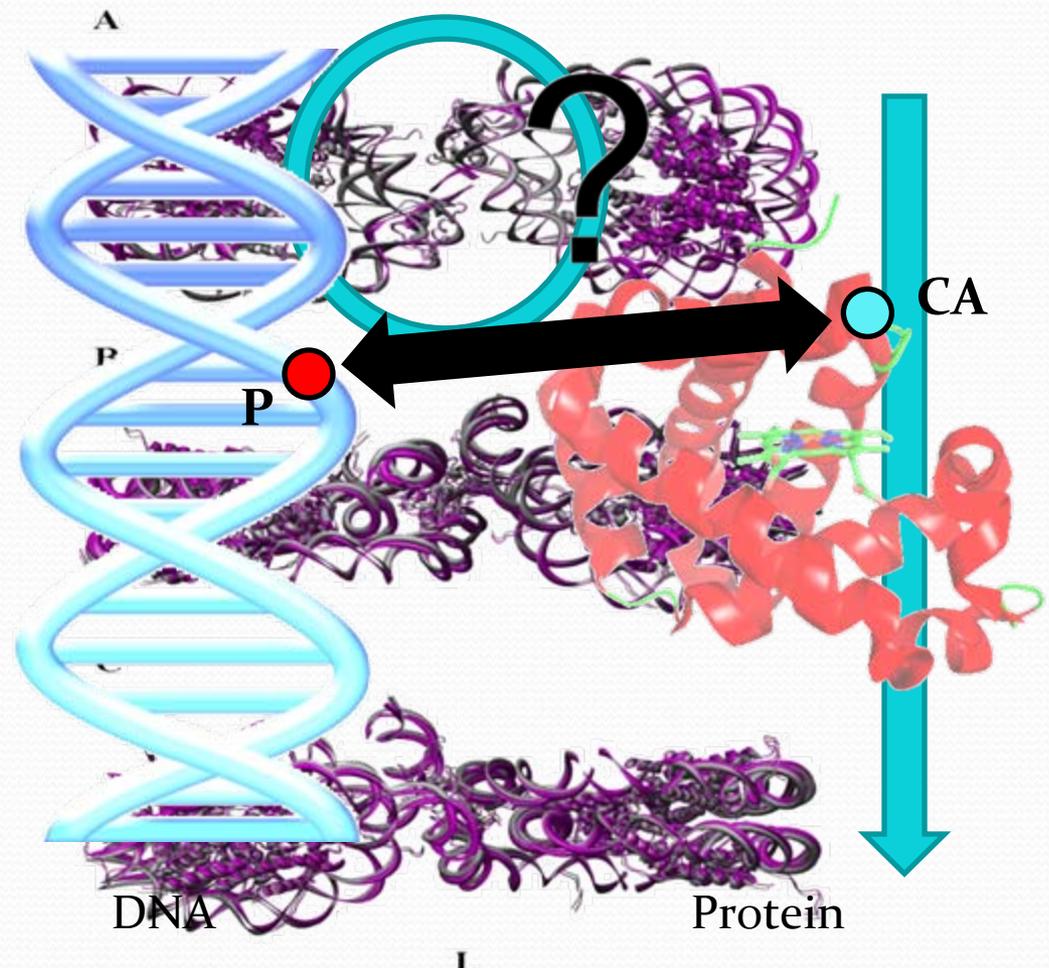
# Types of Systems

- Homogenous or Heterogeneous



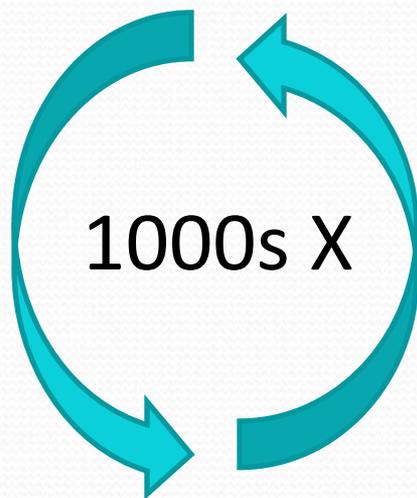
# Identifying Interactions

- 3D plotting
- Representative Atoms
- Distance measurements
- Cutoff



# SASSIE: Complex Dihedral Generate

- Algorithm
- Changes in code
  - Types of overlap
  - Align



Get PDB file

ID segments

ID interaction

Randomize angles

Energetics check

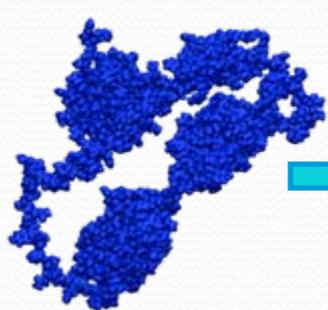
Overlap check

Align

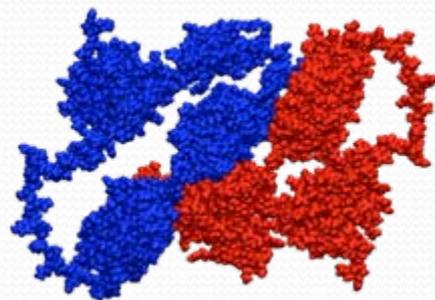
Save coordinates



# HIV-1 Gag Dimer Assembly



monomer

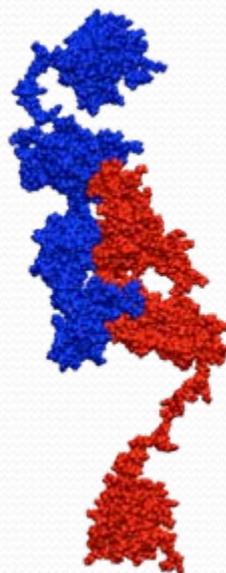
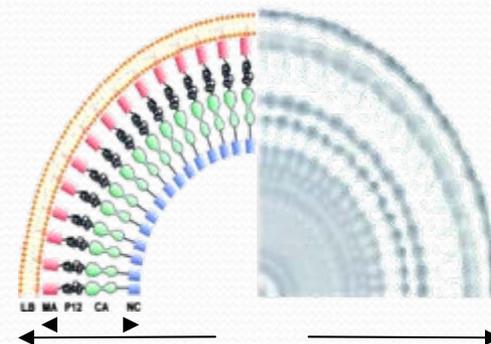


dimer?



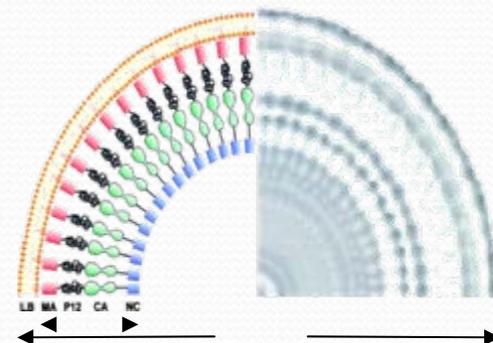
?

?

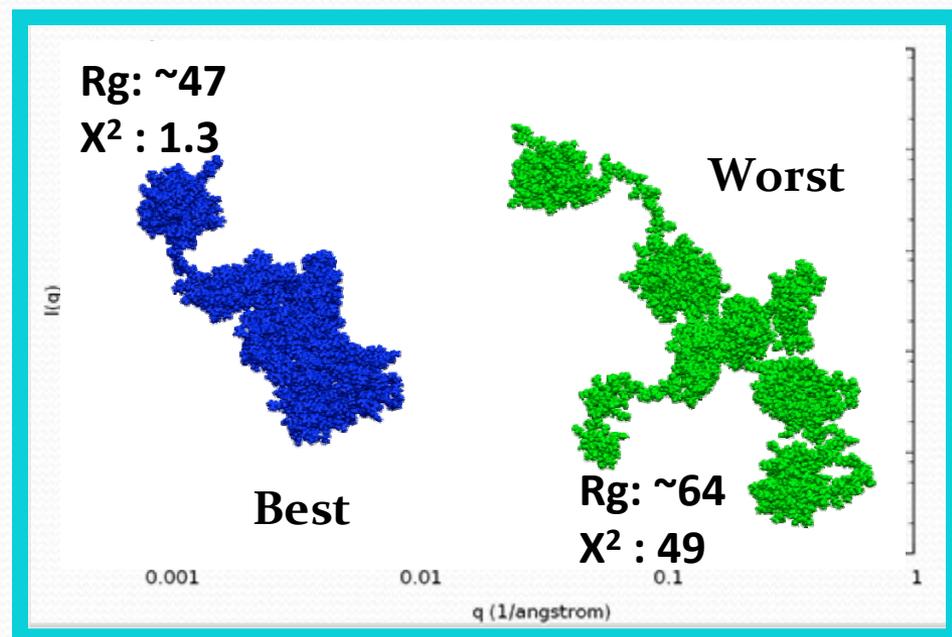
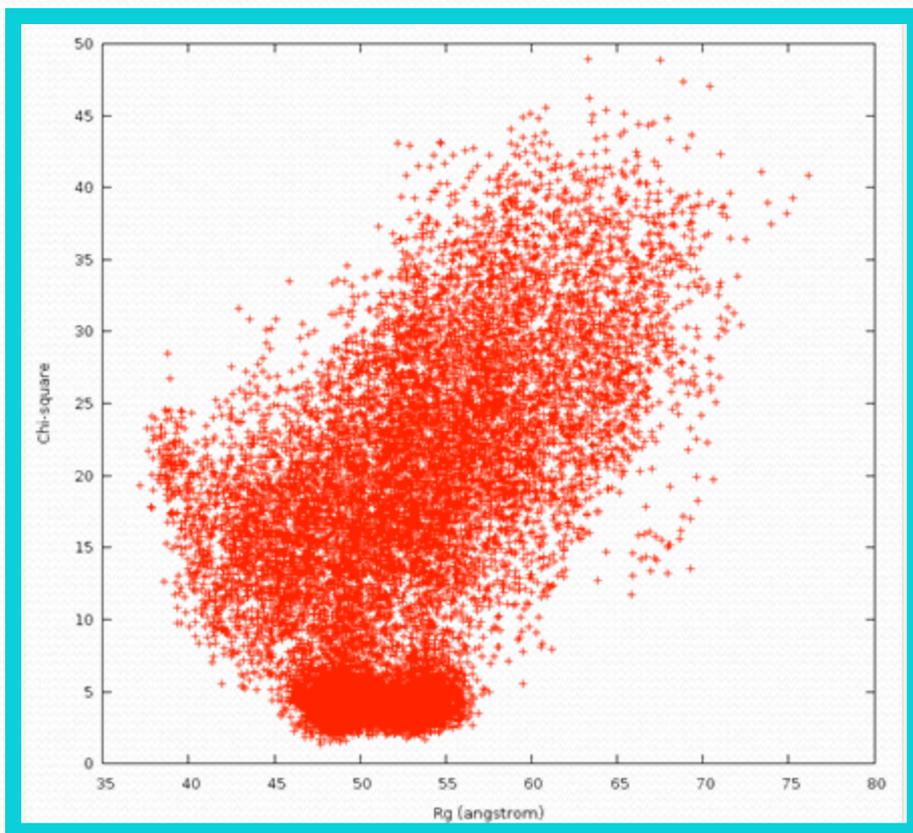


?

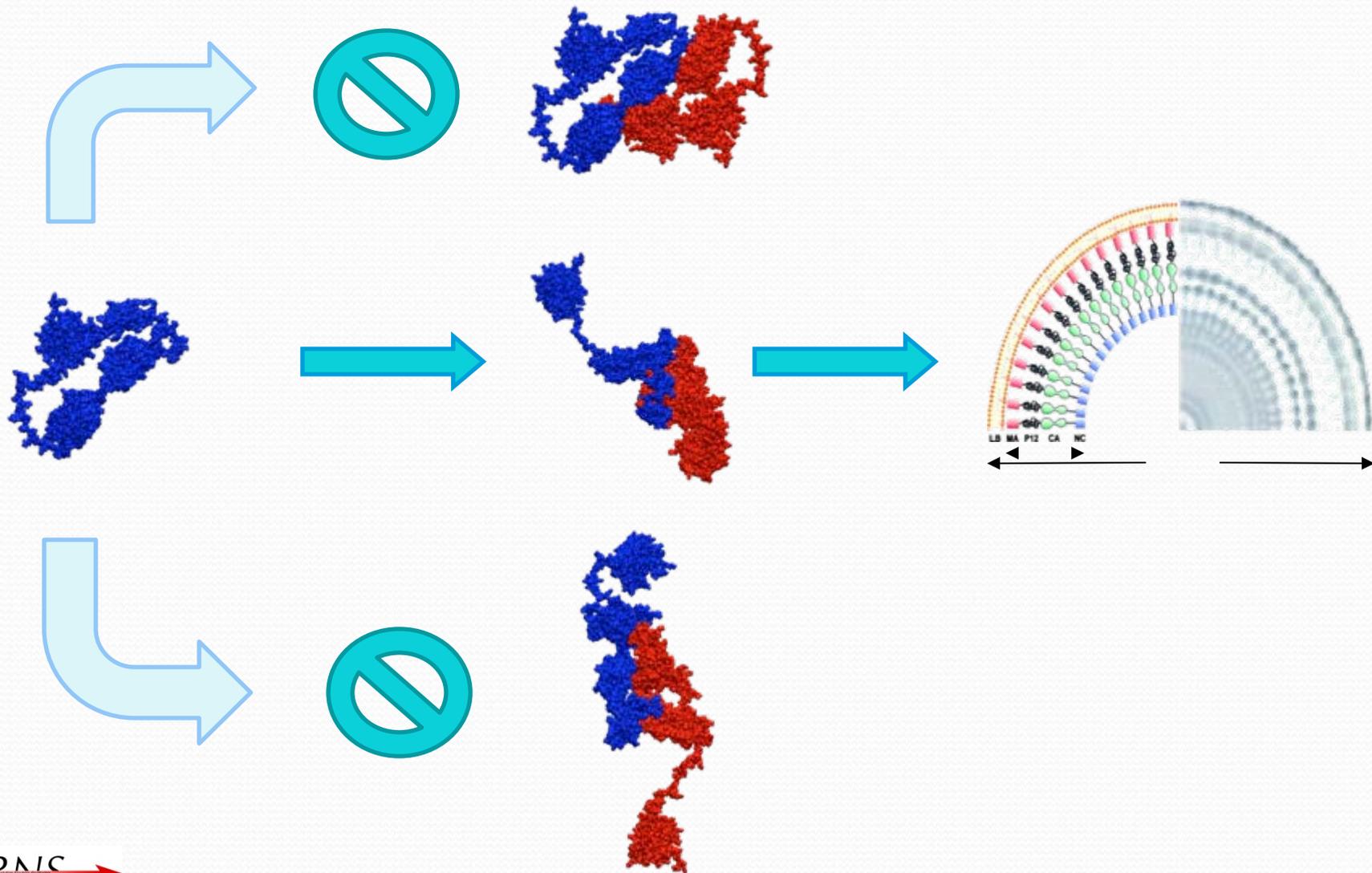
?



# HIV-1 Gag Dimer

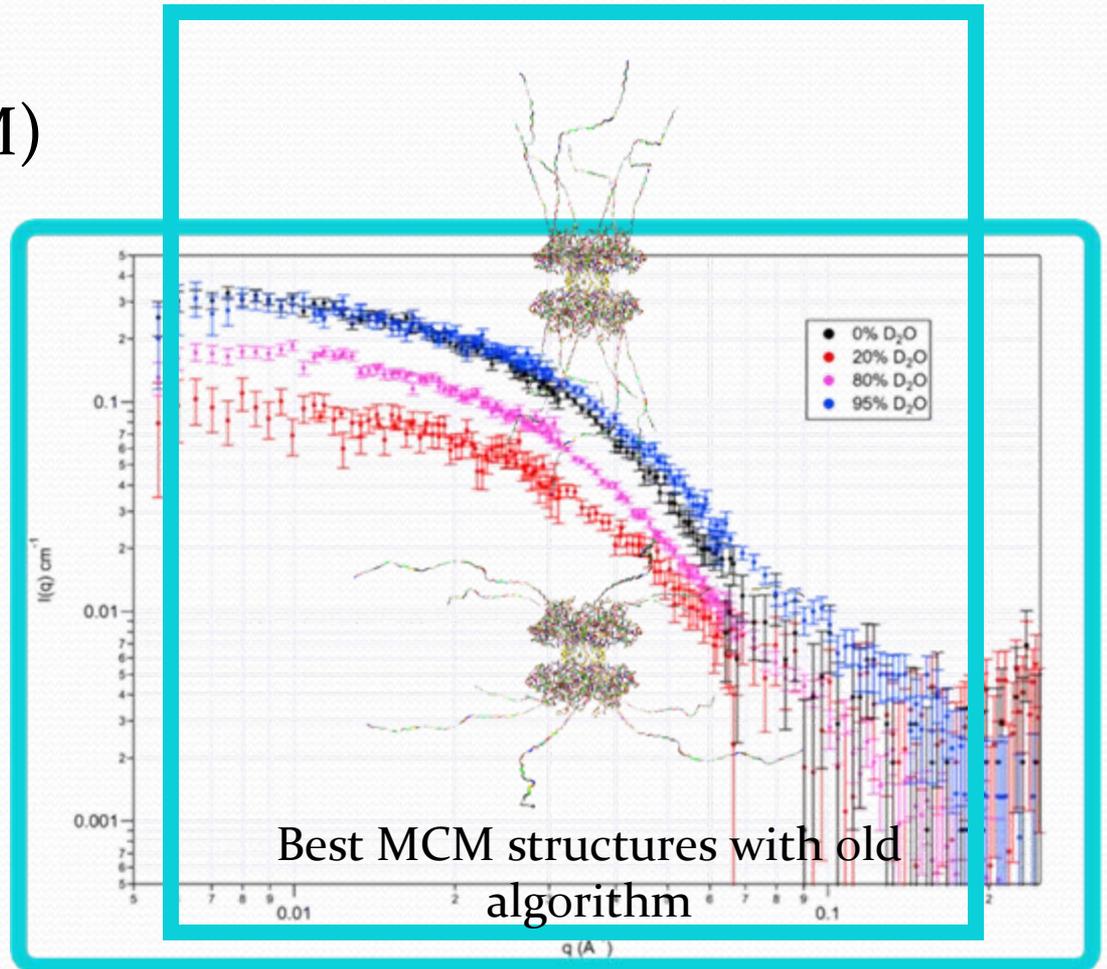
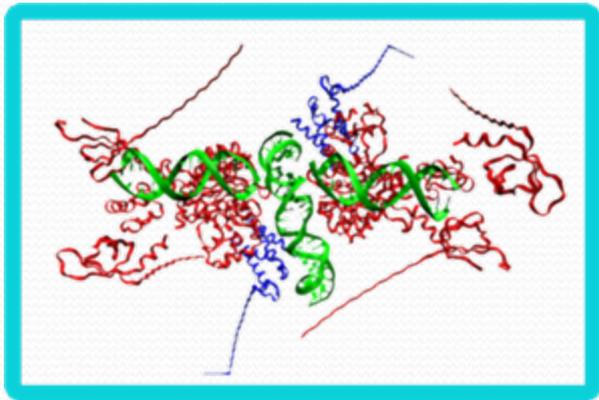


# Gag Dimer Assembly: Revisited



# Applications:

- Minichromosome maintenance (MCM) proteins
- HIV Integrase



# Acknowledgements

Joseph Curtis  
Susan Krueger  
Hirsh Nanda  
Julie Borchers  
Dan Neumann  
NCNR  
NIST SURF  
UMD-CP

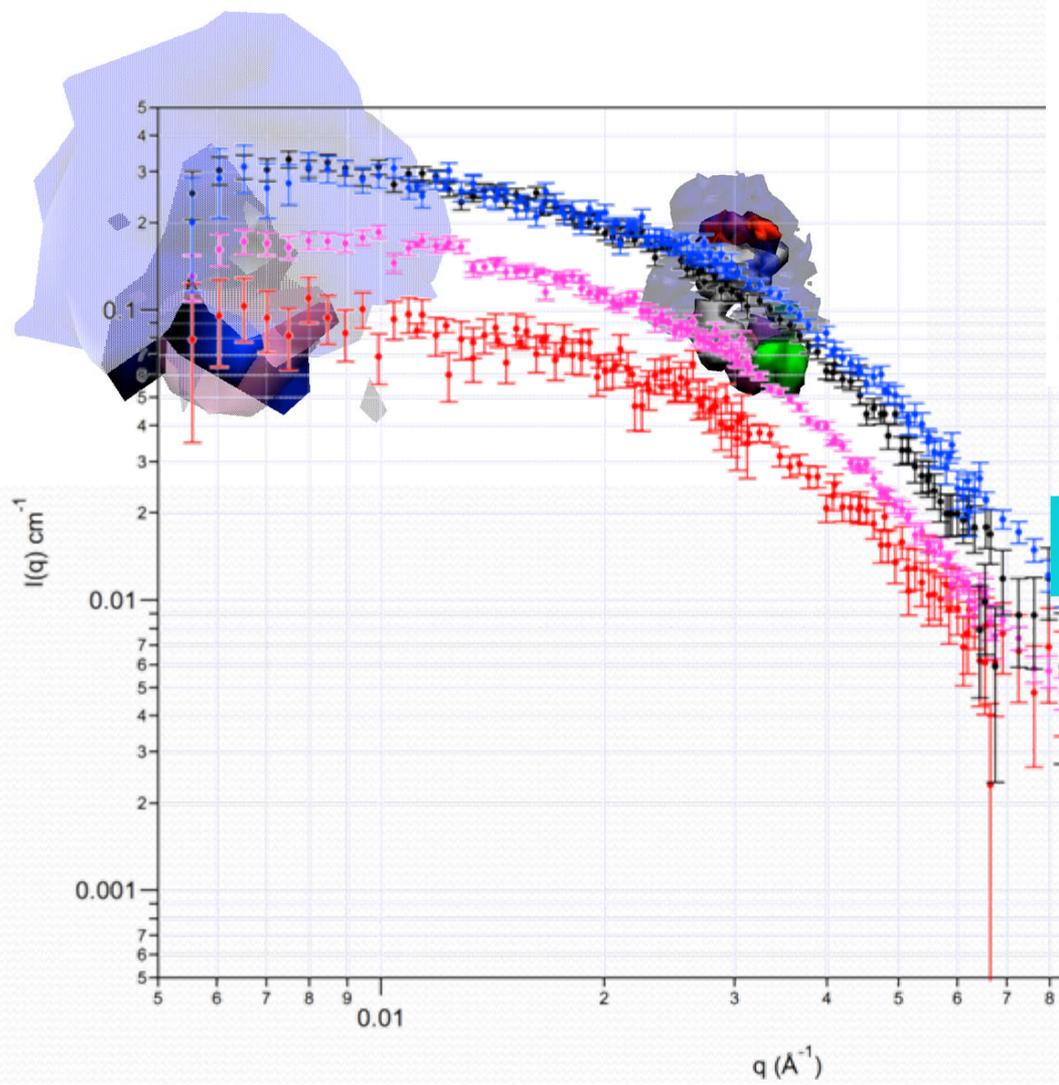


# Gag

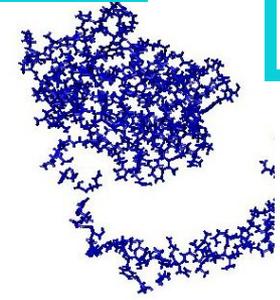


SANS	Sedimentation
$a = b = 13\text{\AA}$	$a = b = 13.5\text{\AA}$
$c = 100\text{\AA}$	$c = 114\text{\AA}$

SANS
$a = b = 47\text{\AA}$
$c = 5\text{\AA}$ (thickness)



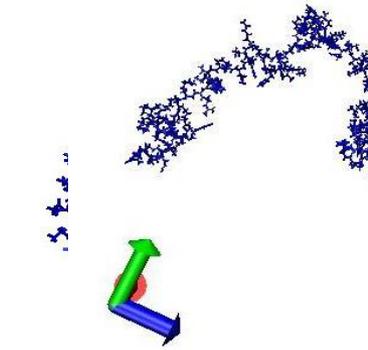
Best



$R_g:$   
 $\chi^2:$

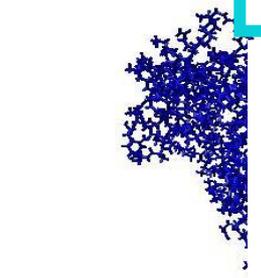


Best



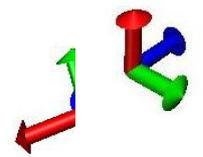
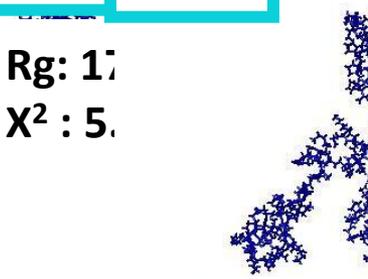
$\chi^2: 0.1$

Worst

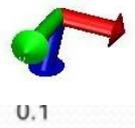


$R_g: 17$   
 $\chi^2: 5.1$

Worst



$R_g:$   
 $\chi^2:$



0.1

