

Intrinsically Disordered Proteins and Heterogeneous Complexes

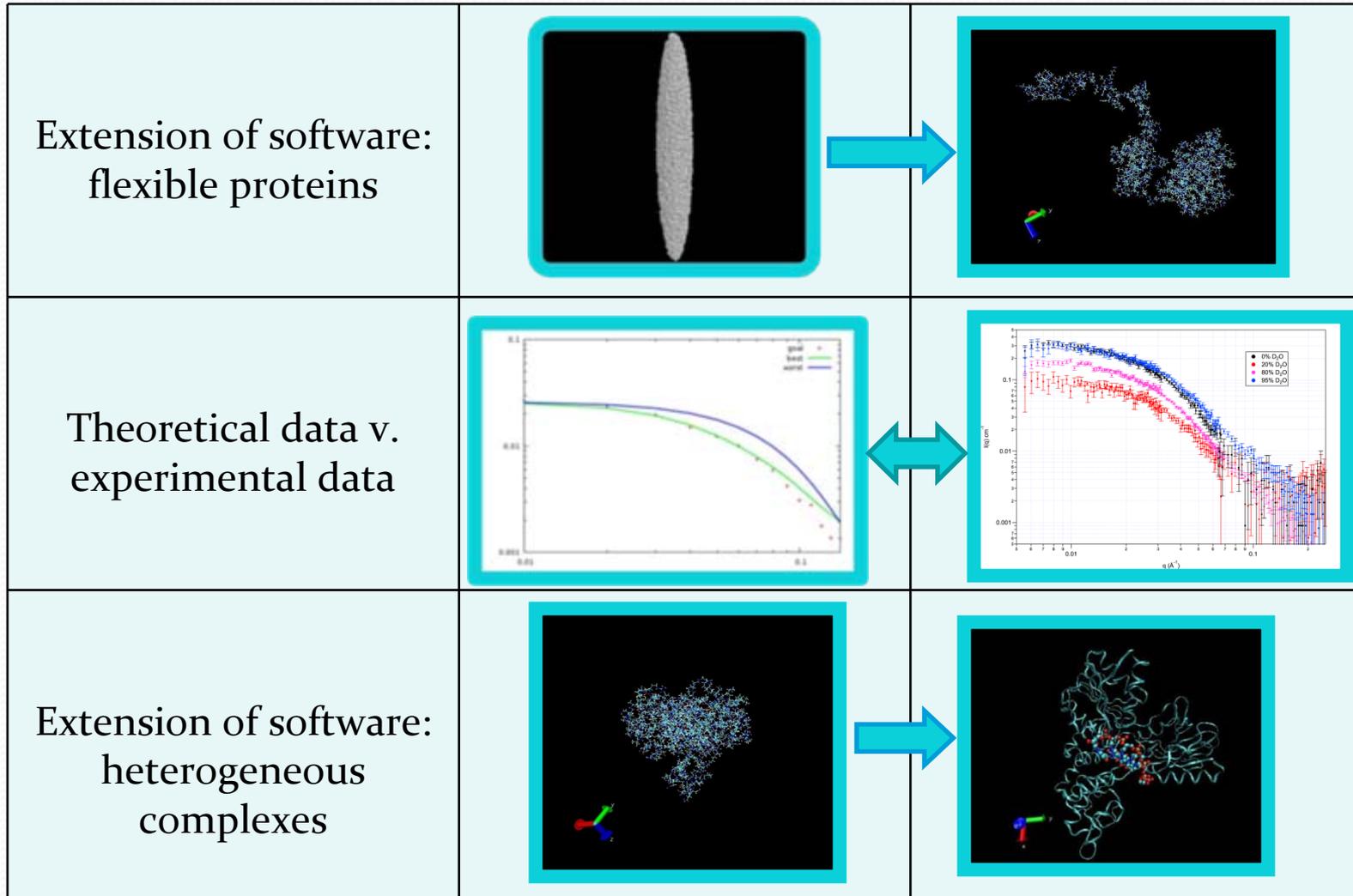
NIST Center for Neutron Research

Advisers: Joseph Curtis, Susan Krueger and Hirsh Nanda

Presented by Sindhu Raghunandan

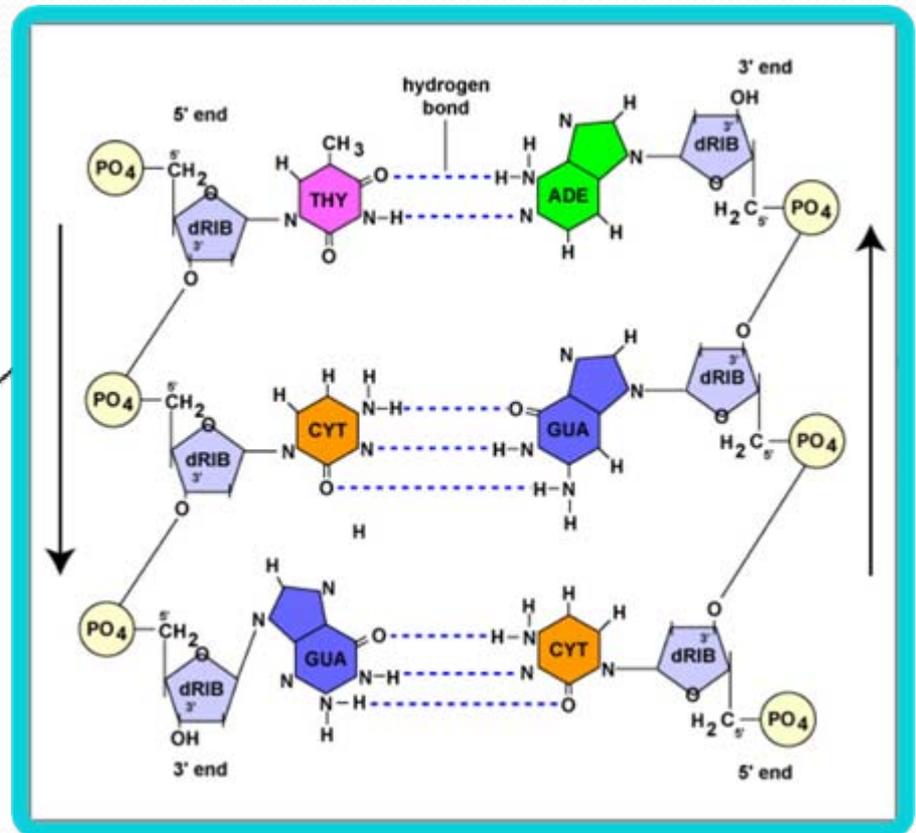
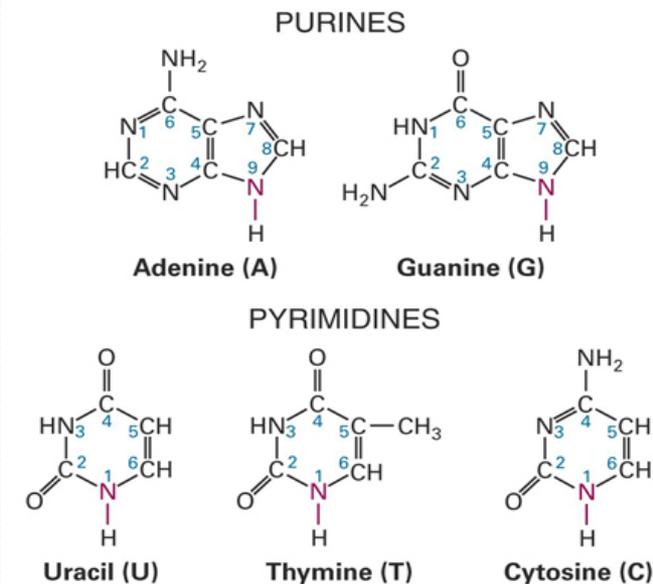


Outline



Protein Structure

- Importance
- Protein Basics
- DNA/RNA

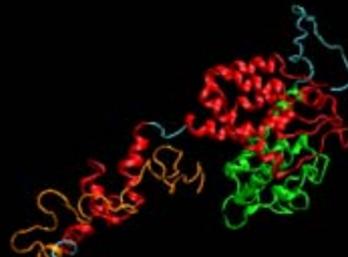
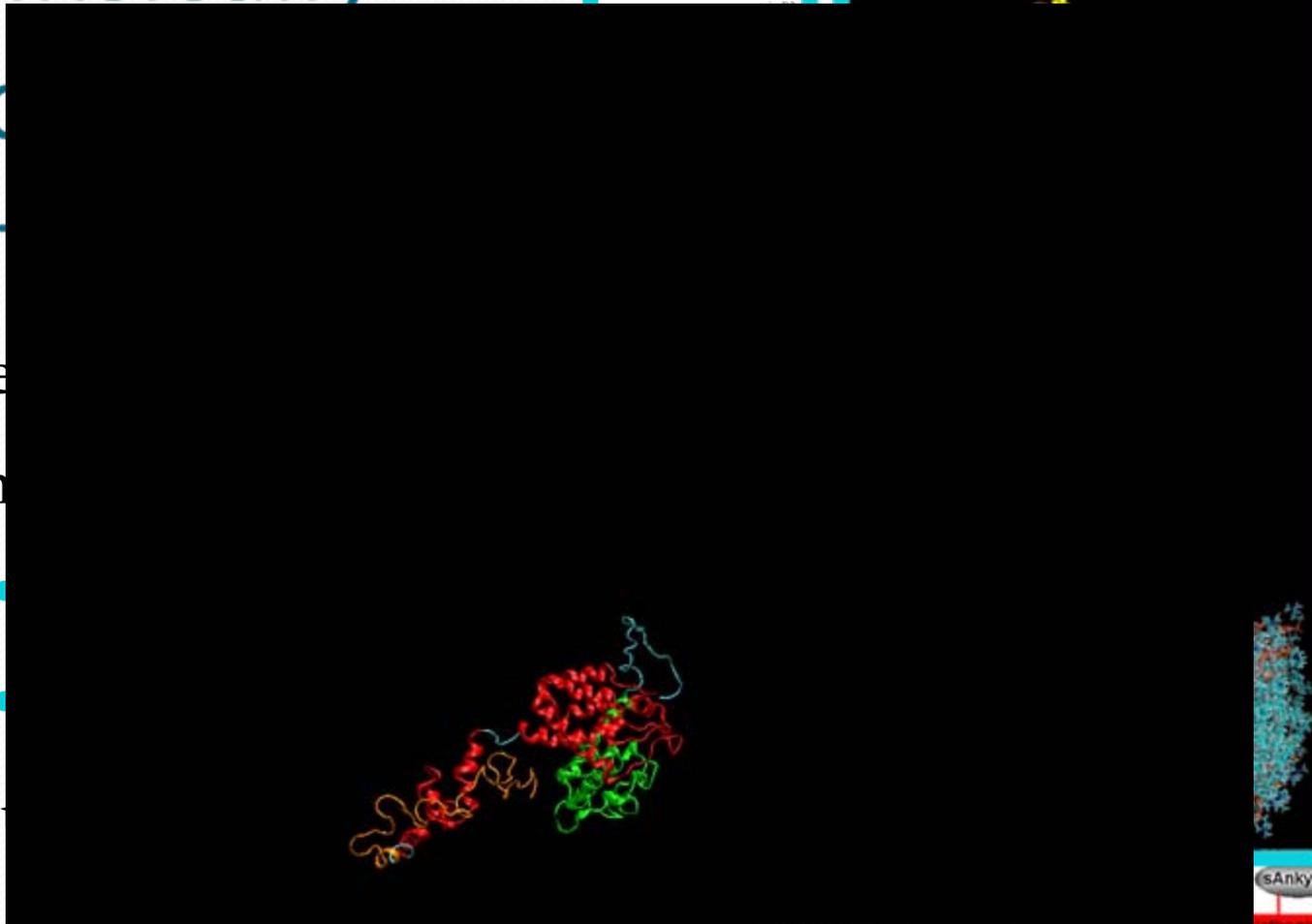


Intrinsically

Diso

Prot

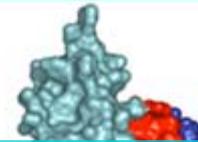
- De
- Im
- Str



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

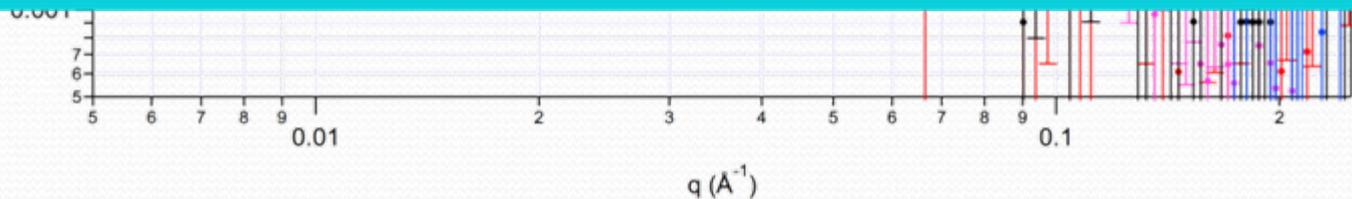
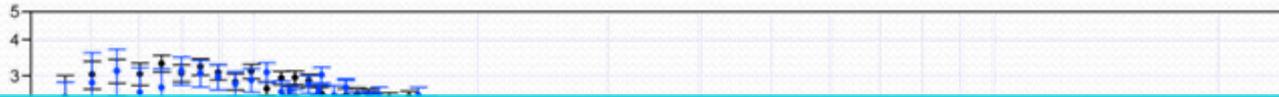
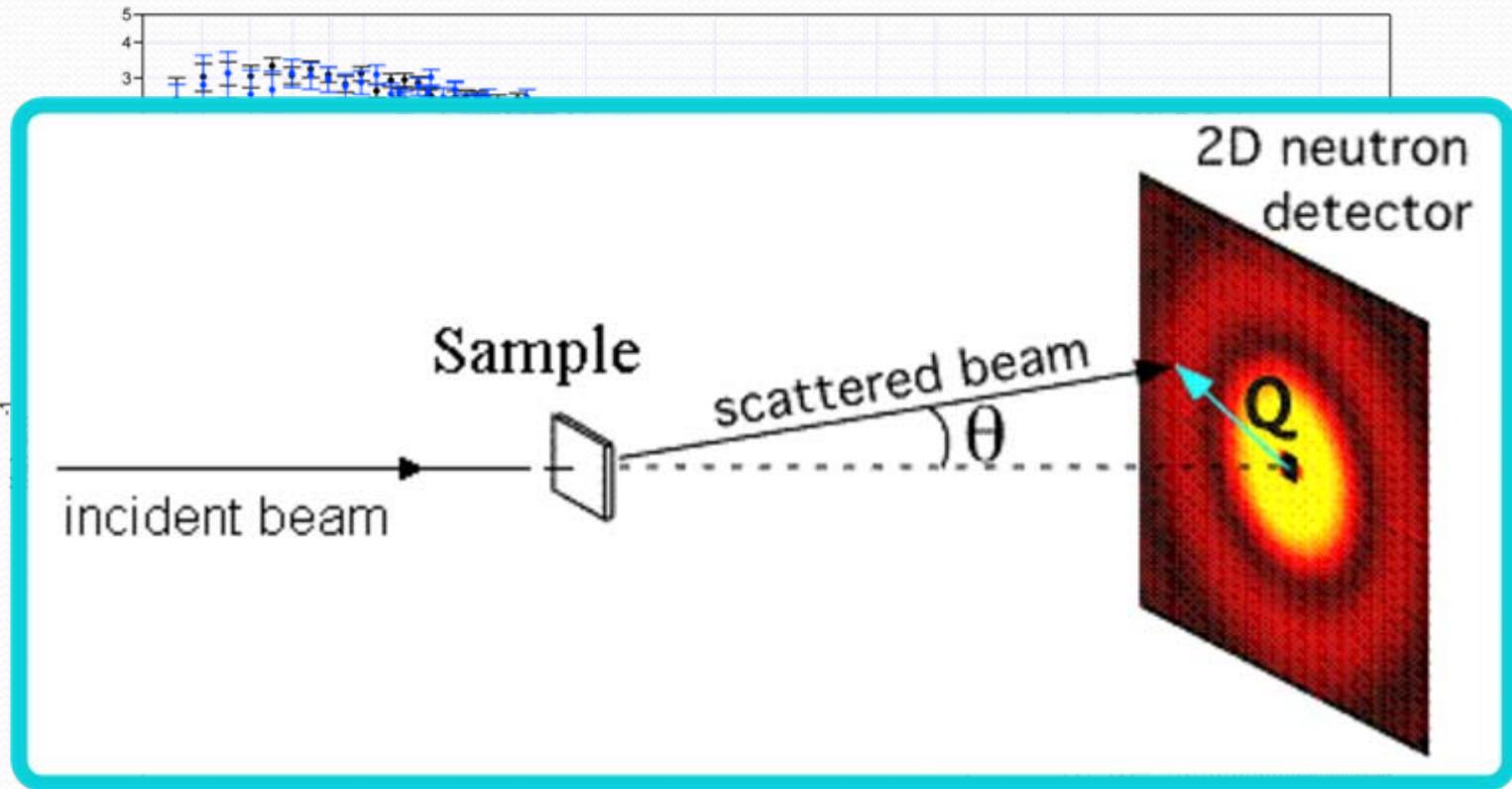
Titin



36 he **Titin 2-disk assembly** **residues** **(variable)** **residues**

37 he

Small Angle Neutron Scattering



SASSIE

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



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

Tools

- Center Frames
- Align Frames
- Modeling (requires graphical VMD)
- Molecular Operations
- Configuration Generators and Minimization
 - Monomer Dihedral Generation
 - Complex Dihedral Generation
- 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

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...

```

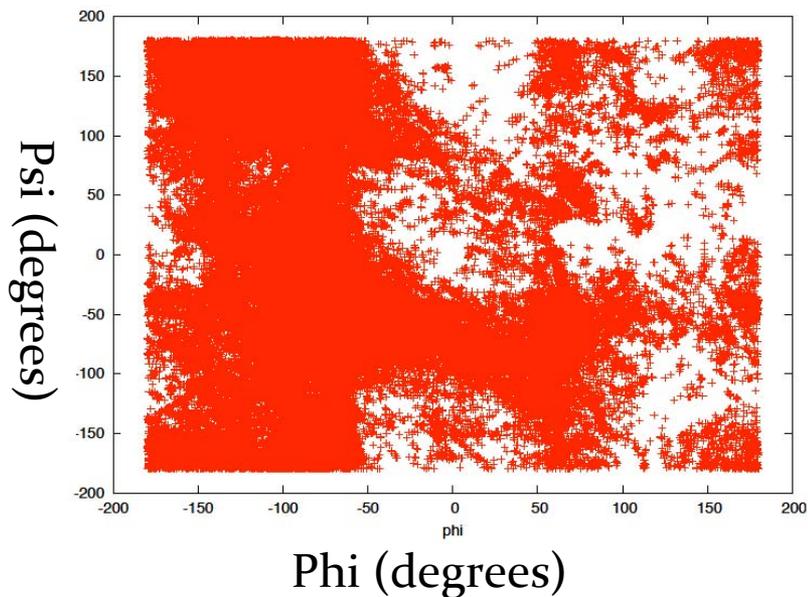
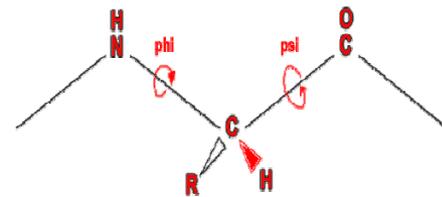
Cnuplot

Rg Results

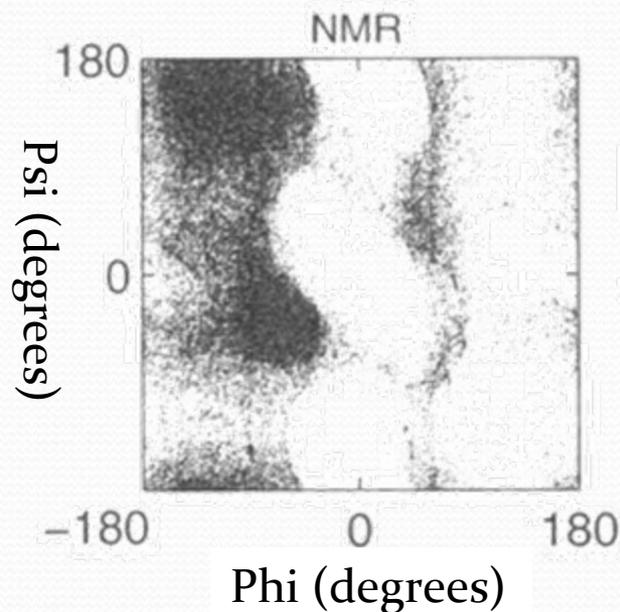
Generating Structures

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

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



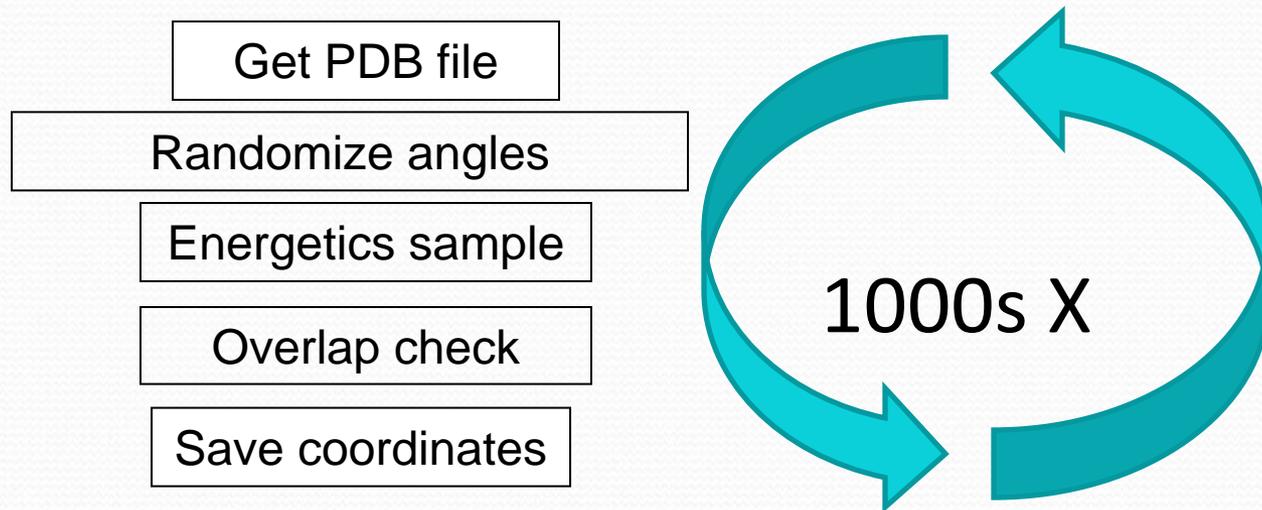
1 protein, 65 residues,
>100,000 configurations



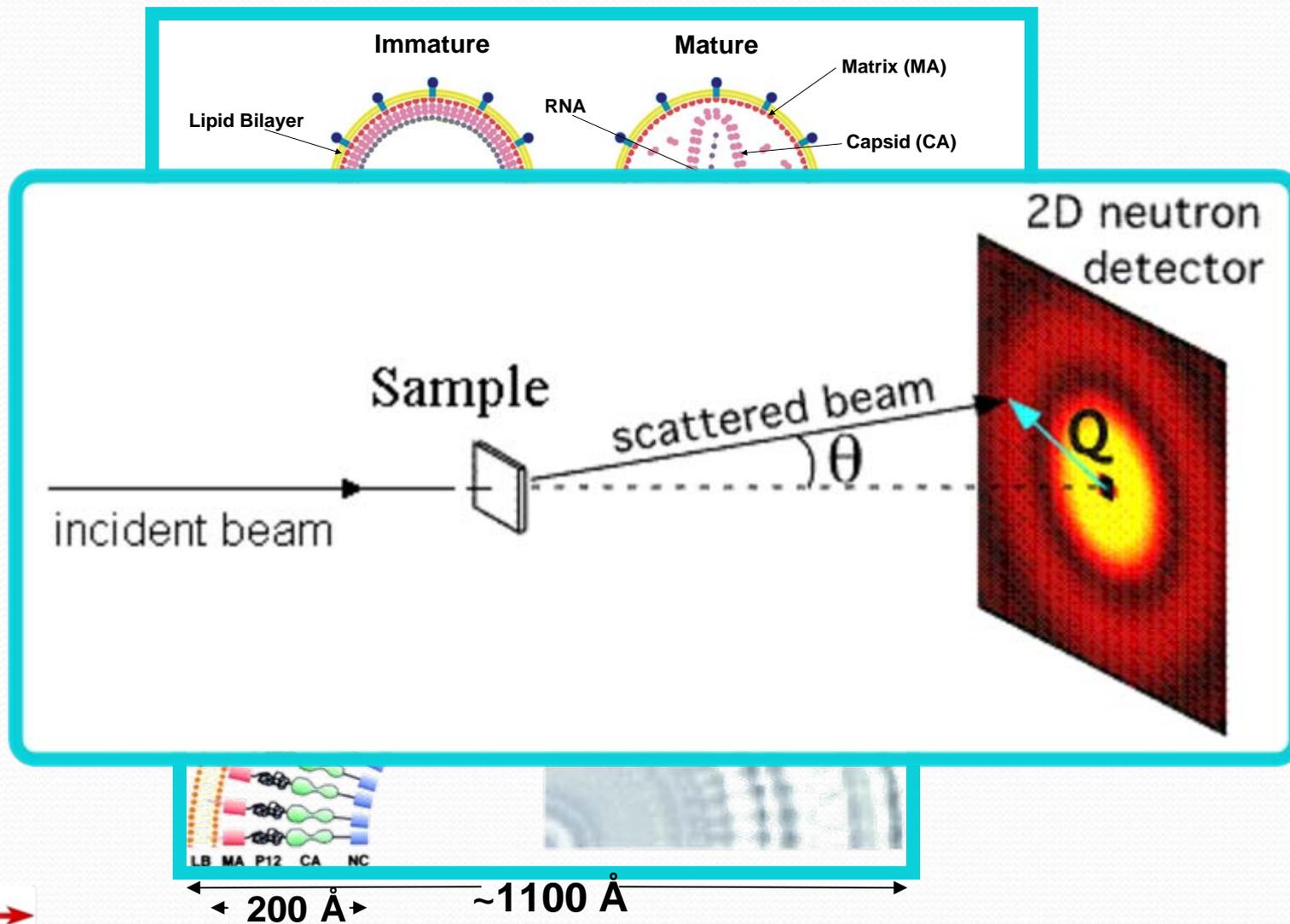
113 proteins, 84719 residues

SASSIE dihedral angle sampling represents experimental data

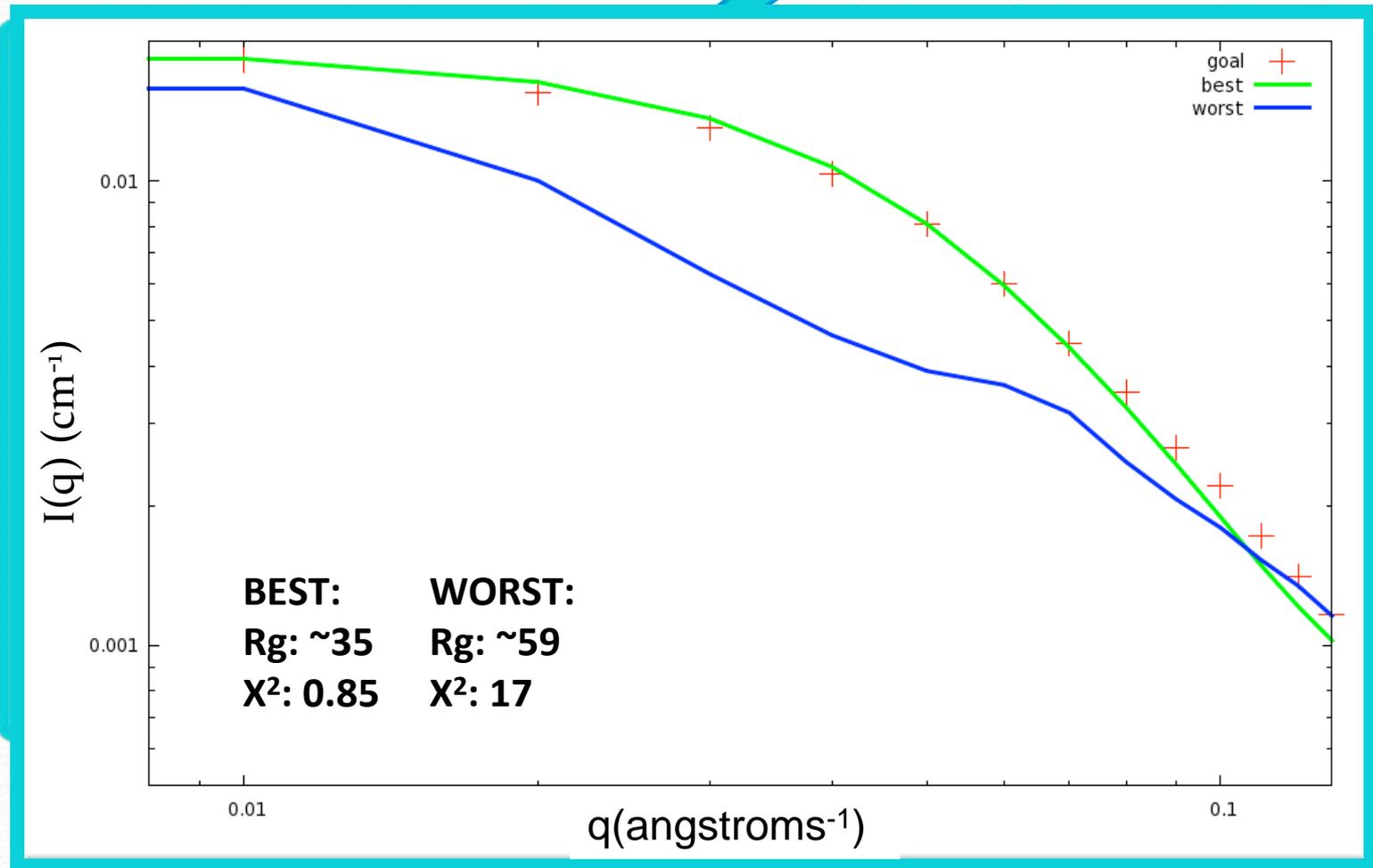
Dihedral Structure Generator Algorithm



Gag: Motivation and Methods

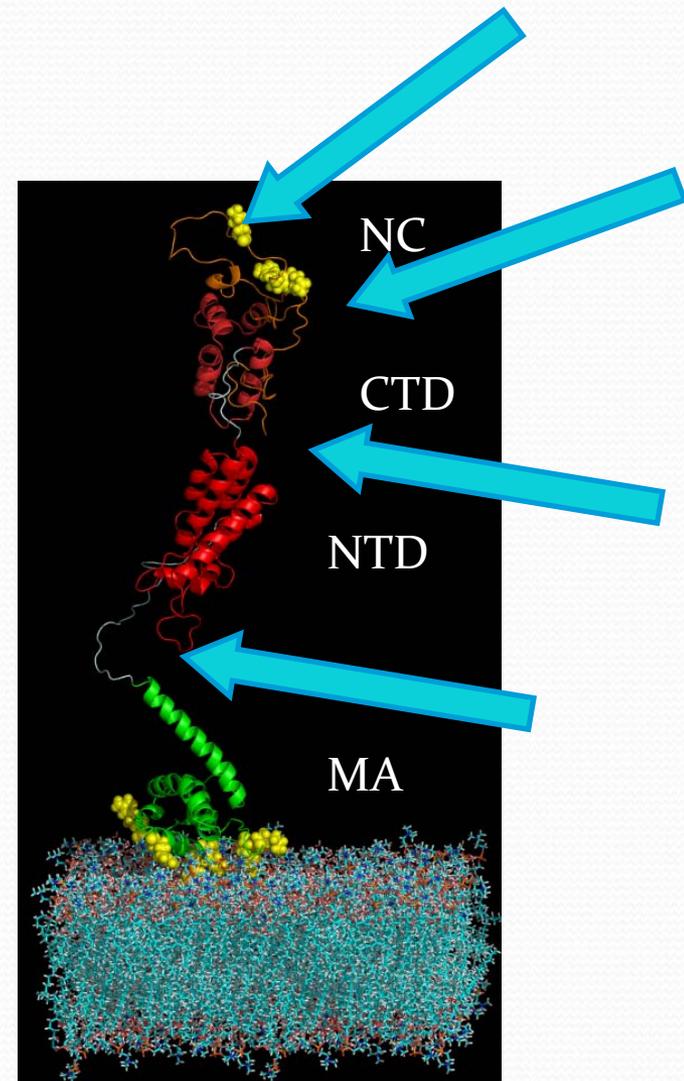


Full Gag

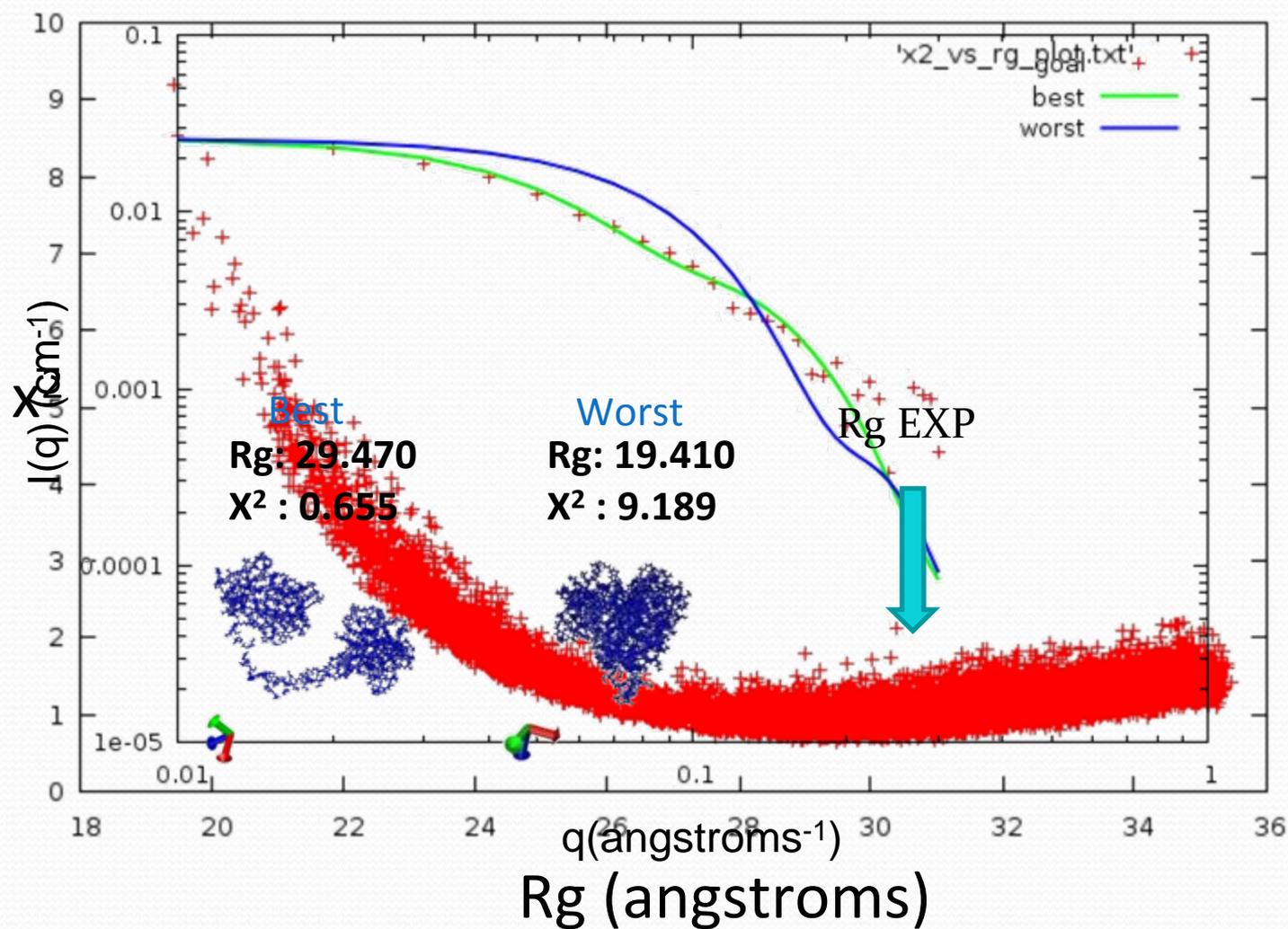


Pieces of Gag

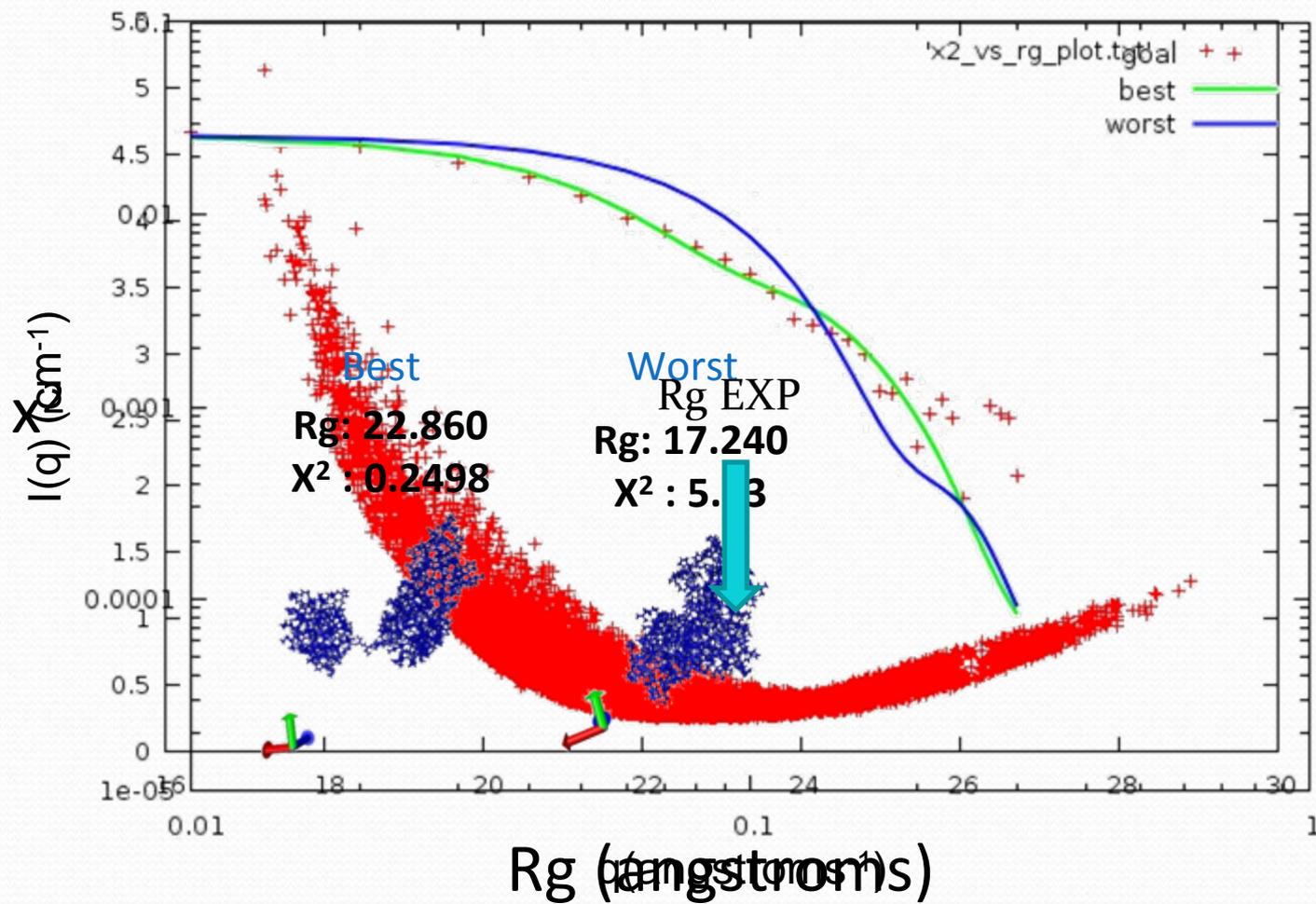
- MA-NTD
 - MA Residues 1-122
 - Linker Residues 123-144
 - 27444 structures
- NTD-CTD
 - NTD Residues 1-133
 - CTD Residues 140-209
 - Linker Residues 134-139
 - 19943 structures
- NTD-CTD-NC
 - P2+NC Residues: 210-287
 - Linker Residues: 134-139
 - 117550 structures



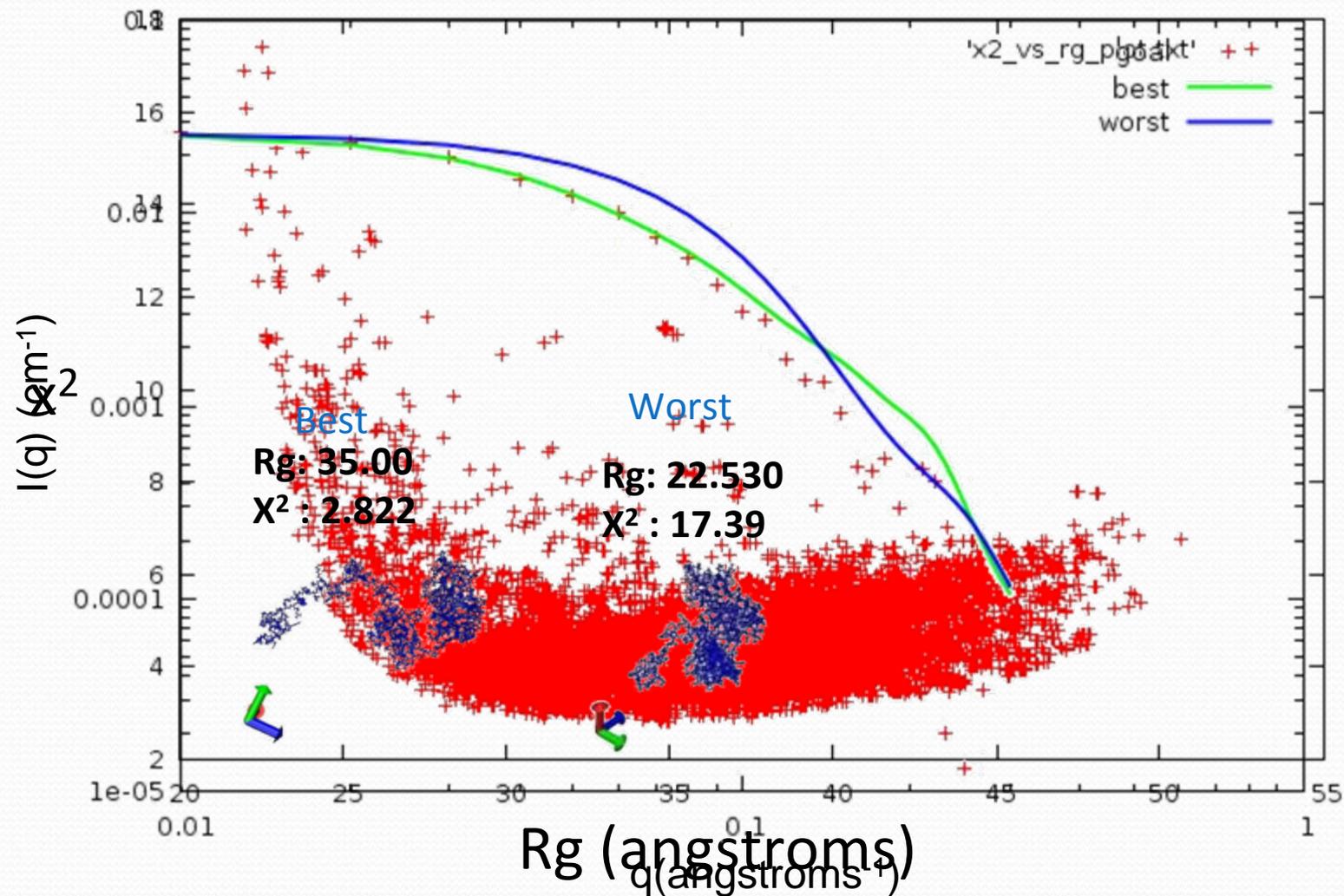
MA-NTD



NTD-CTD

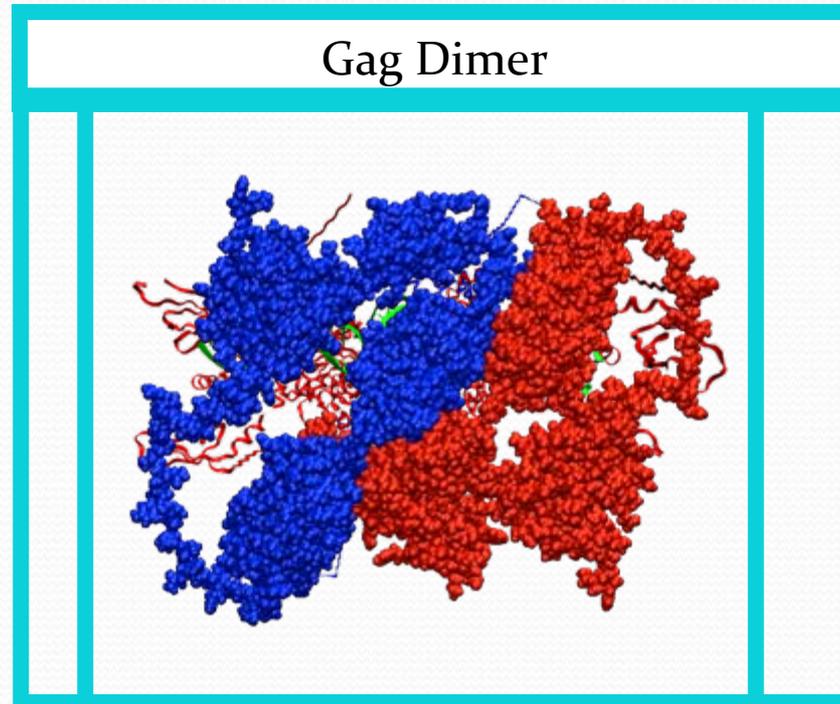


NTD-CTD-NC



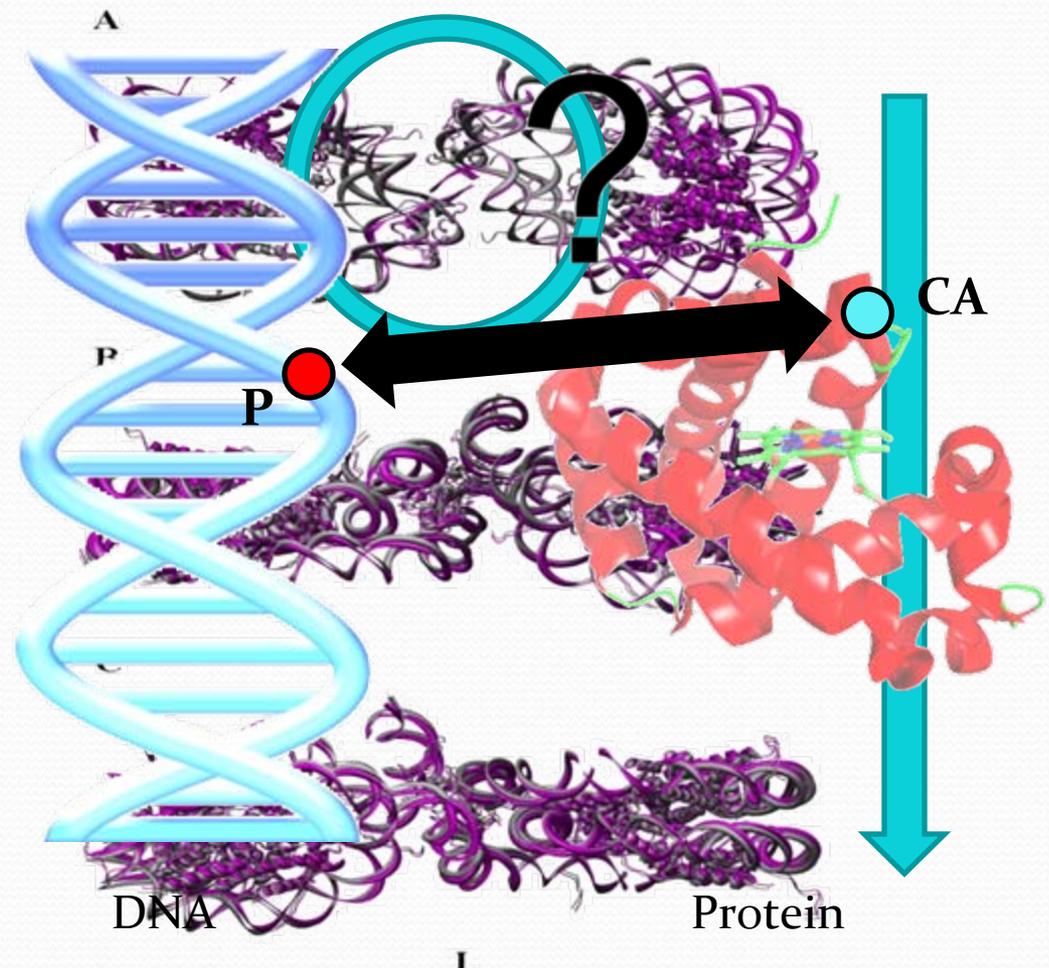
Types of Systems

- Homogenous or Heterogeneous



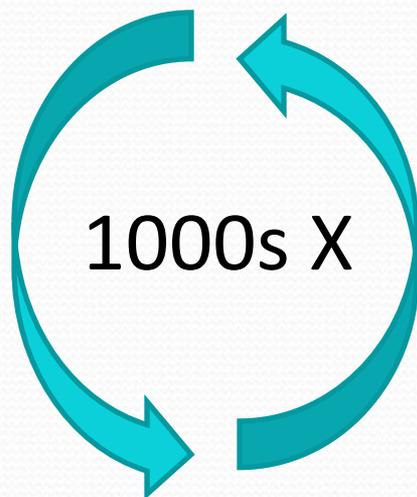
Identifying Interactions

- 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

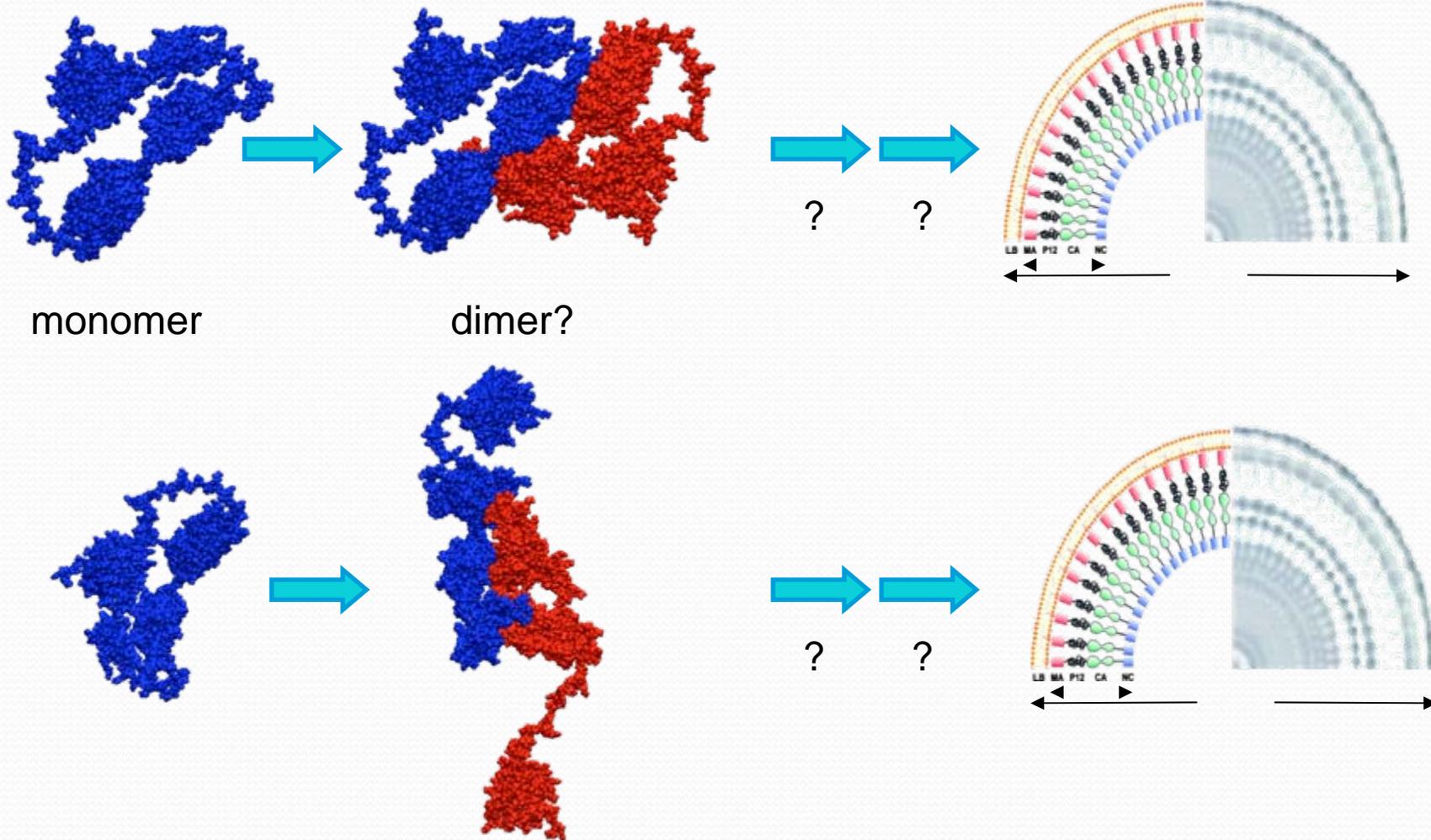
Overlap check

Align

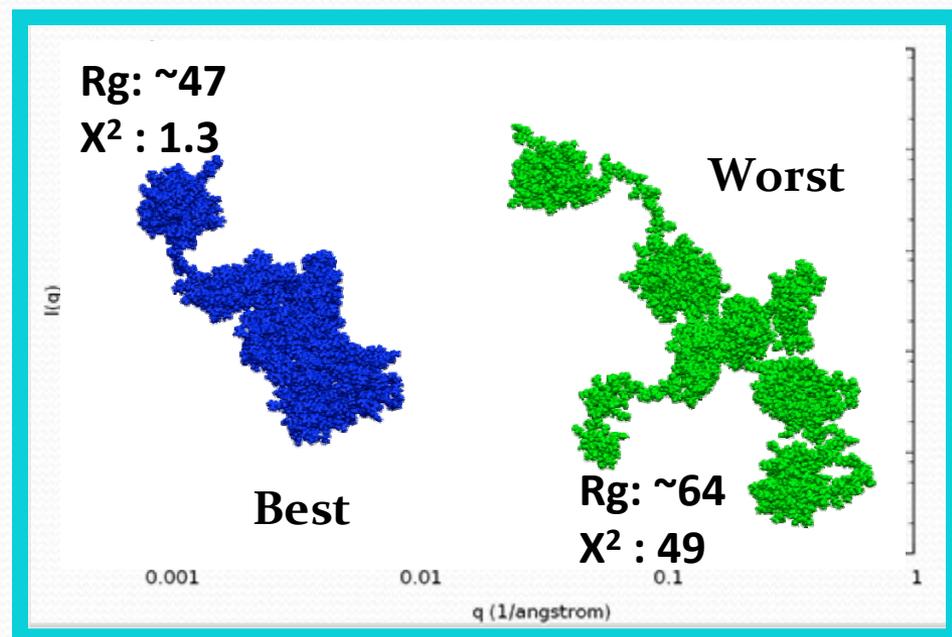
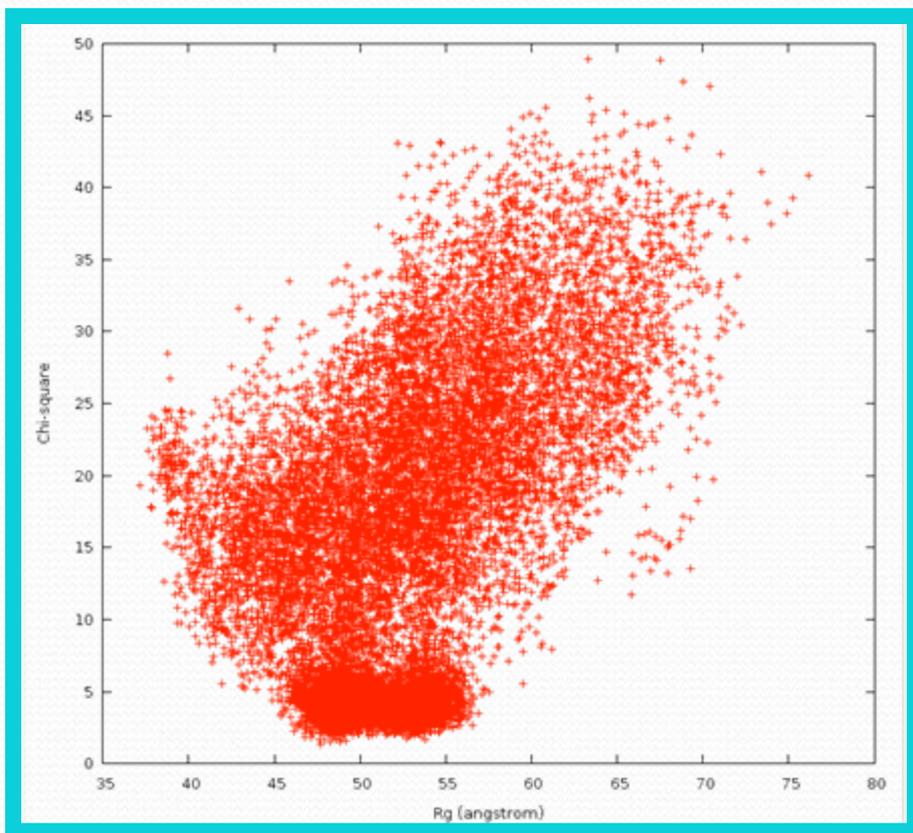
Save coordinates



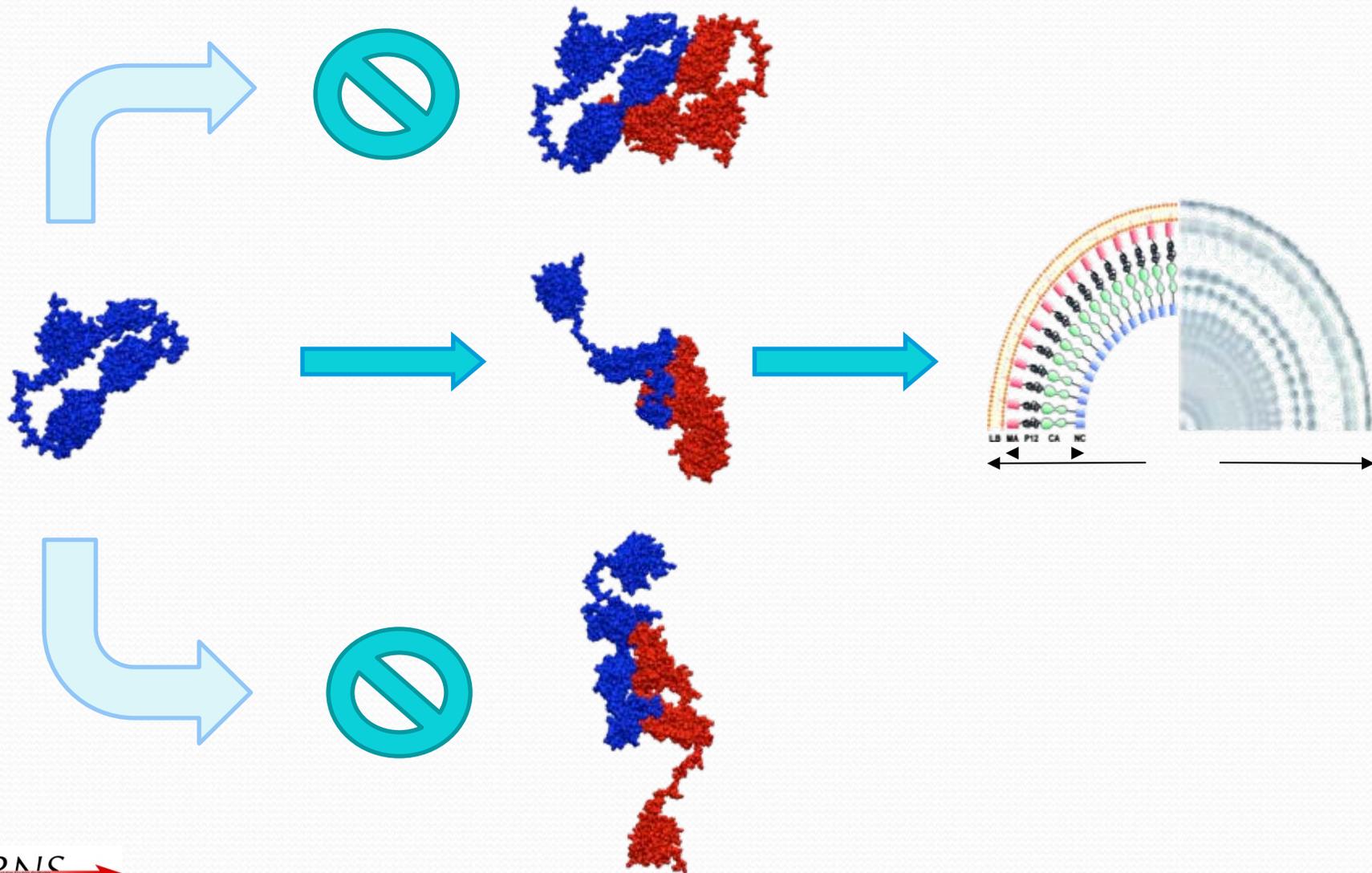
HIV-1 Gag Dimer Assembly



HIV-1 Gag Dimer

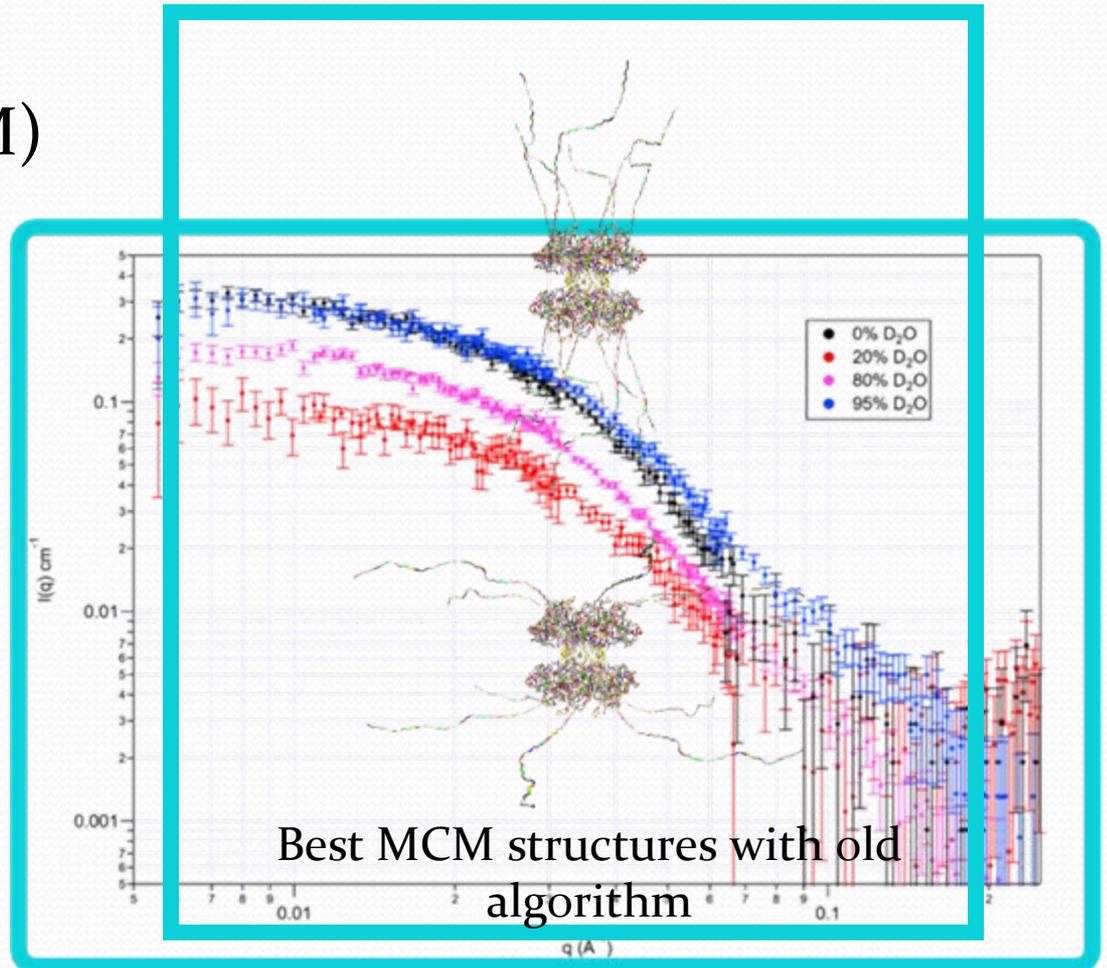
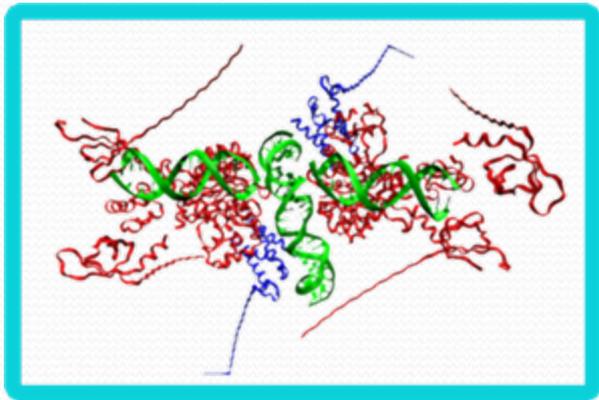


Gag Dimer Assembly: Revisited



Applications:

- Minichromosome maintenance (MCM) proteins
- HIV Integrase



Acknowledgements

Joseph Curtis
Susan Krueger
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Dan Neumann
NCNR
NIST SURF
UMD-CP

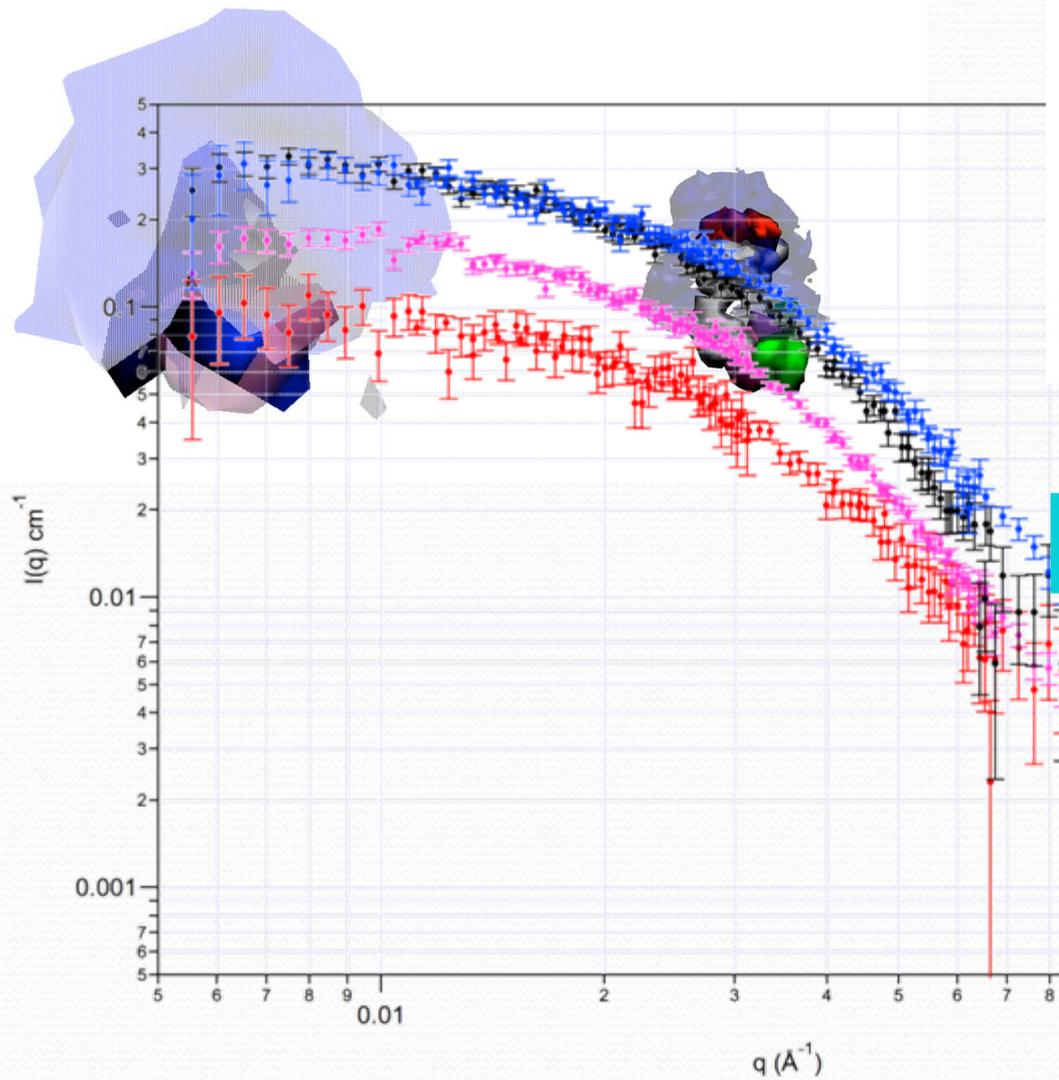


Gag

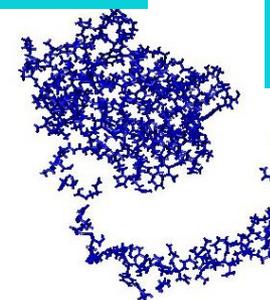


SANS	Sedimentation
$a = b = 13\text{\AA}$	$a = b = 13.5\text{\AA}$
$c = 100\text{\AA}$	$c = 114\text{\AA}$

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



Best



Best

Best



Rg:
X² :

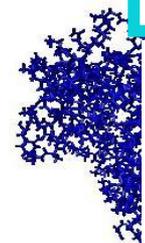


X² : 0.1

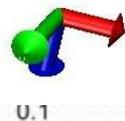
Worst

Worst

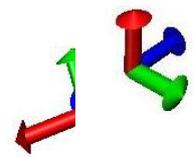
Worst



Rg: 17
X² : 5.1



Rg:
X² :



Rg:
X² :

