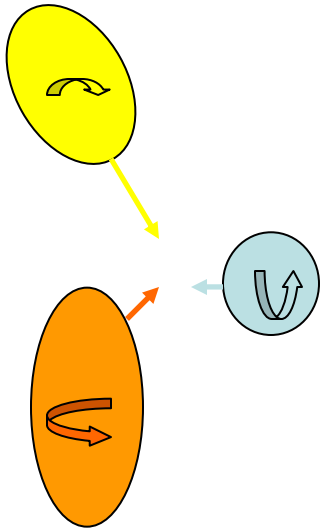
# SASREF: Global Rigid Body Modelling



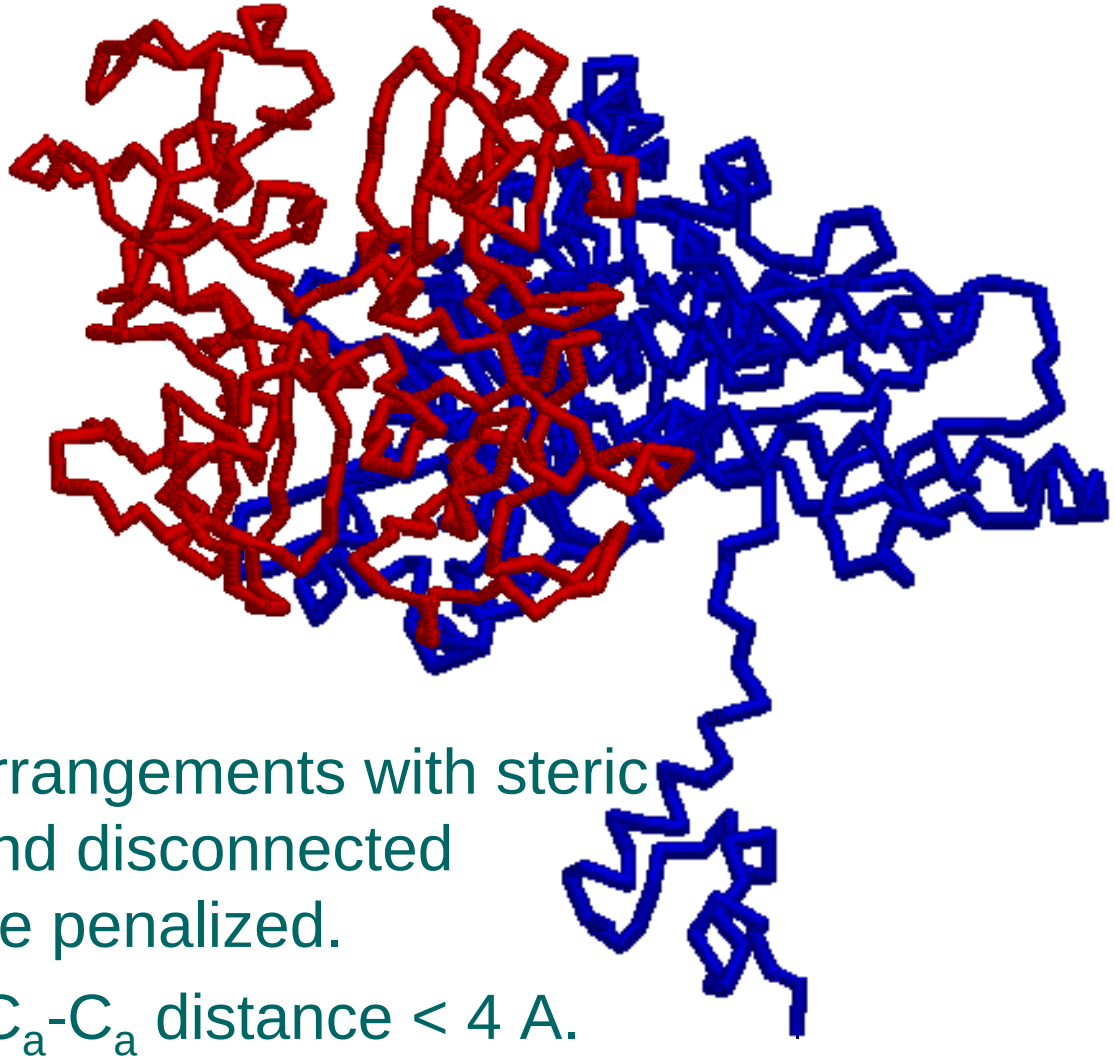
- Starts from arbitrary initial positions and orientations of the subunits
- Employs simulated annealing to search interconnected arrangement of the subunits without clashes
- Random movement/rotation at one SA step
- Fitting the SAXS/SANS data by minimizing the target function
-

$$E(X) = \Sigma\chi^2[I_{exp}(s), I(X,s)] + \Sigma\alpha_i P_i(X)$$

-
- Penalty terms describe additional restraints

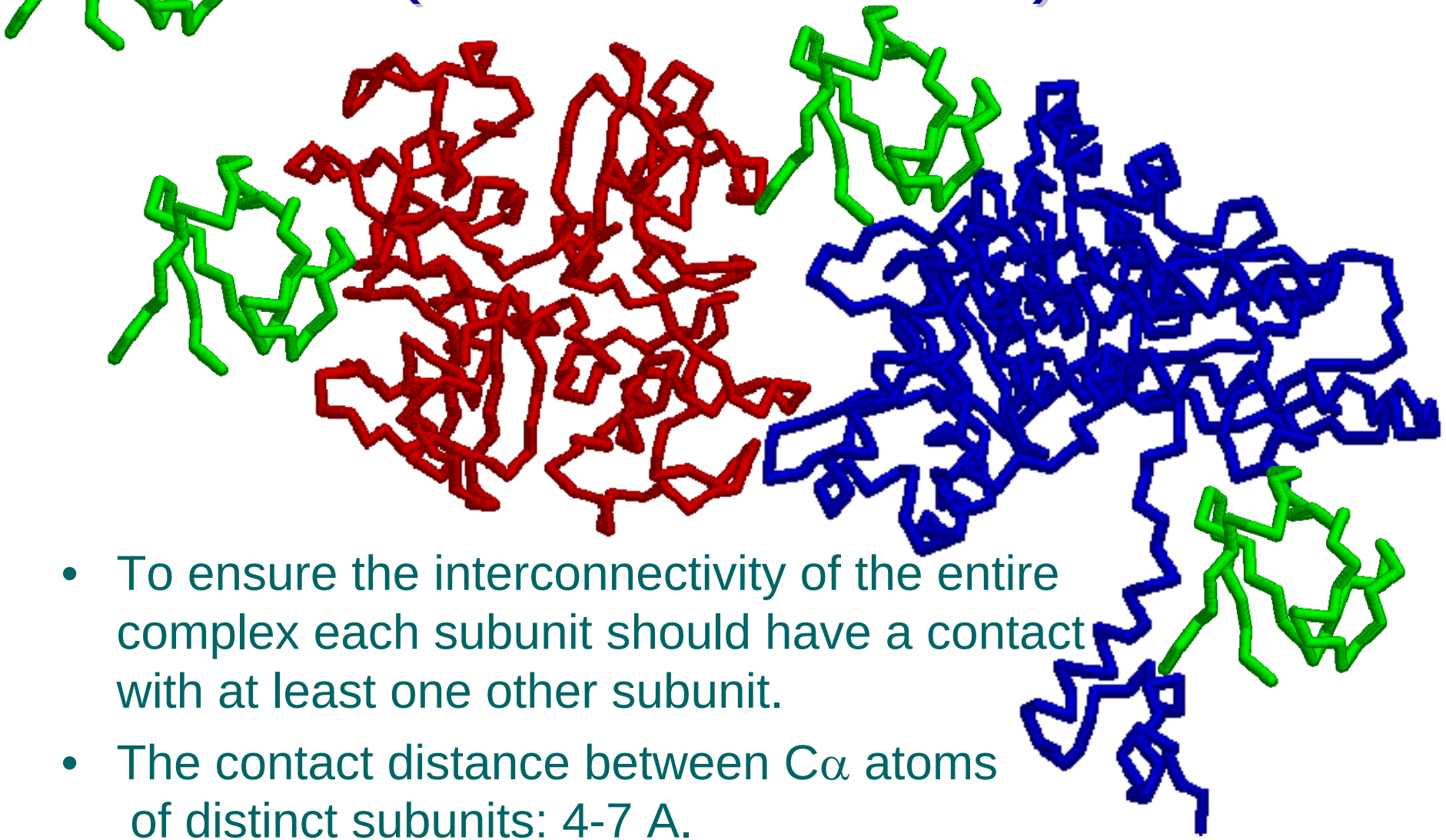
Petoukhov, M. V., and Svergun, D. I. (2006). ***Eur Biophys J.***, 35, 567-576

# Interconnectivity and steric clashes (natural restraints)



- Subunit arrangements with steric clashes and disconnected models are penalized.
- Overlap: $C_a$-$C_a$ distance < 4 A.

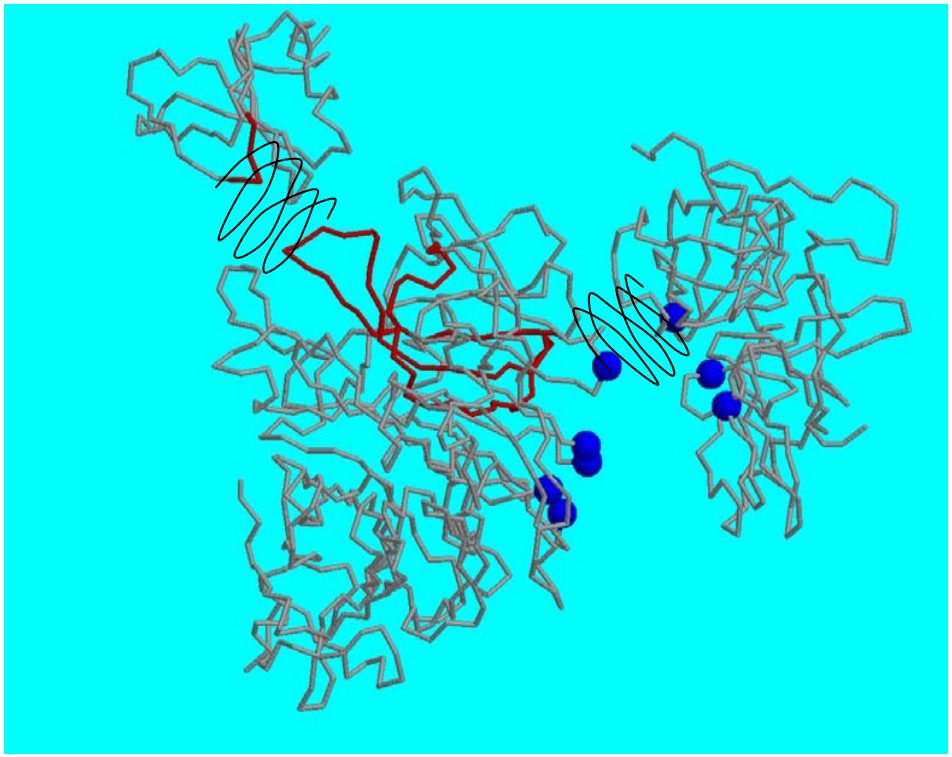
# Interconnectivity and steric clashes (natural restraints)



- To ensure the interconnectivity of the entire complex each subunit should have a contact with at least one other subunit.
- The contact distance between C$\alpha$ atoms of distinct subunits: 4-7 A.

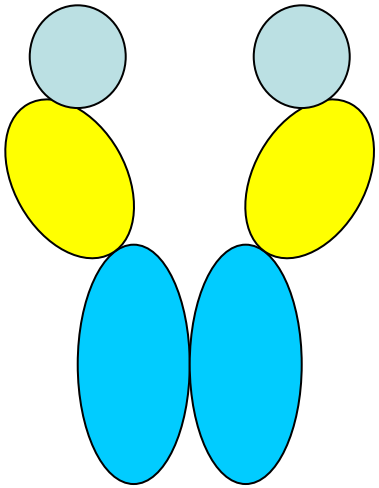
# Contacts restraints

- From binding affinity studies or from mutagenesis data the information on contacting subunits and even individual residues can be available.
- Such information is accounted for by specifying the ranges of residues or nucleotides which can be involved in interactions between the partners.
- Spring force potentials are added as penalties



# Possible constraints

## Symmetry



Groups Pn / Pn2 (n=1..6), P23, P432 and icosahedral symmetry can be taken into account.

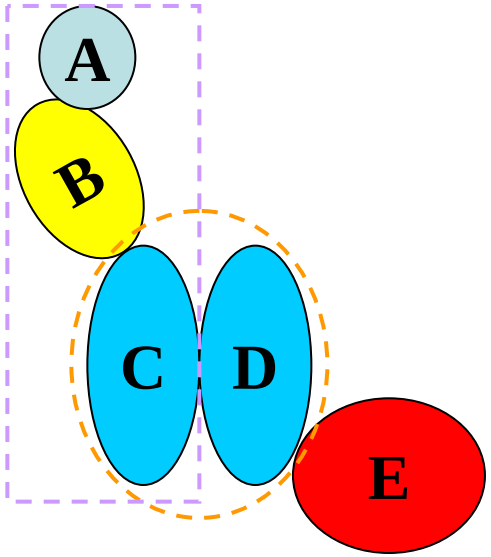
- fewer spatial parameters to describe the model
- selection rules for the partial amplitudes:

  *m* equal to 0 or multiples of n,

  for Pn2, terms of order *l0* with odd *l* and all imaginary parts vanish

## Fixation of subset

Some subunits can be fixed at the initial positions and orientations to keep their mutual arrangement



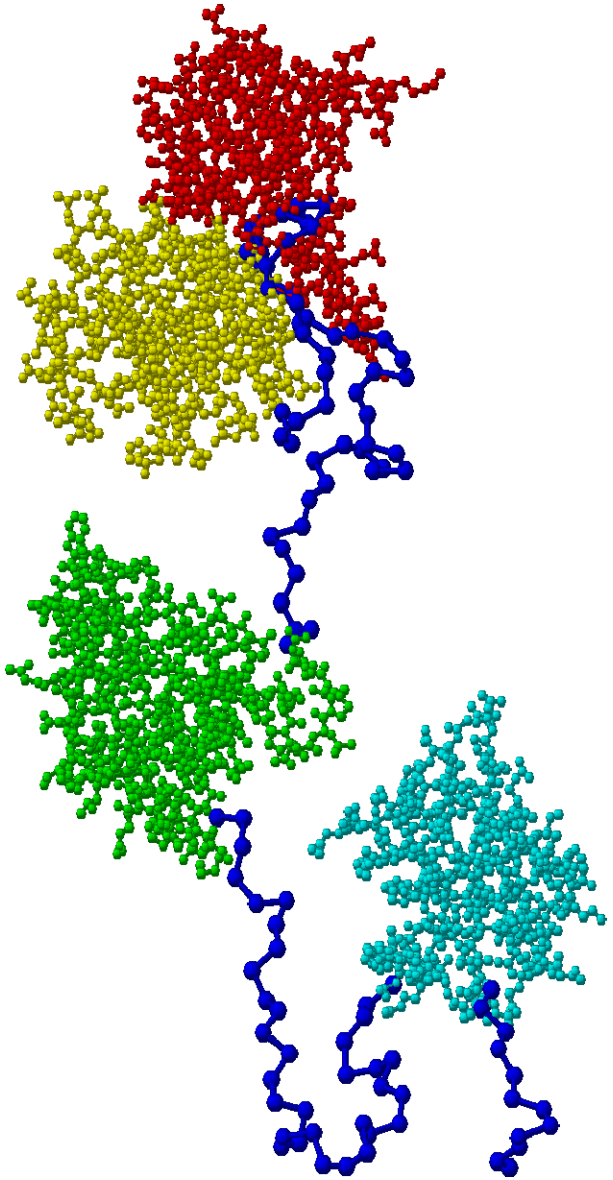
# Test examples

- Symmetric tetramer of pyruvate oxidase
- Dimeric & trimeric functional units of hemocyanin (Patrice)
- TK Met ectodomain - multidomain protein with no extended linkers

# Modelling of multidomain proteins

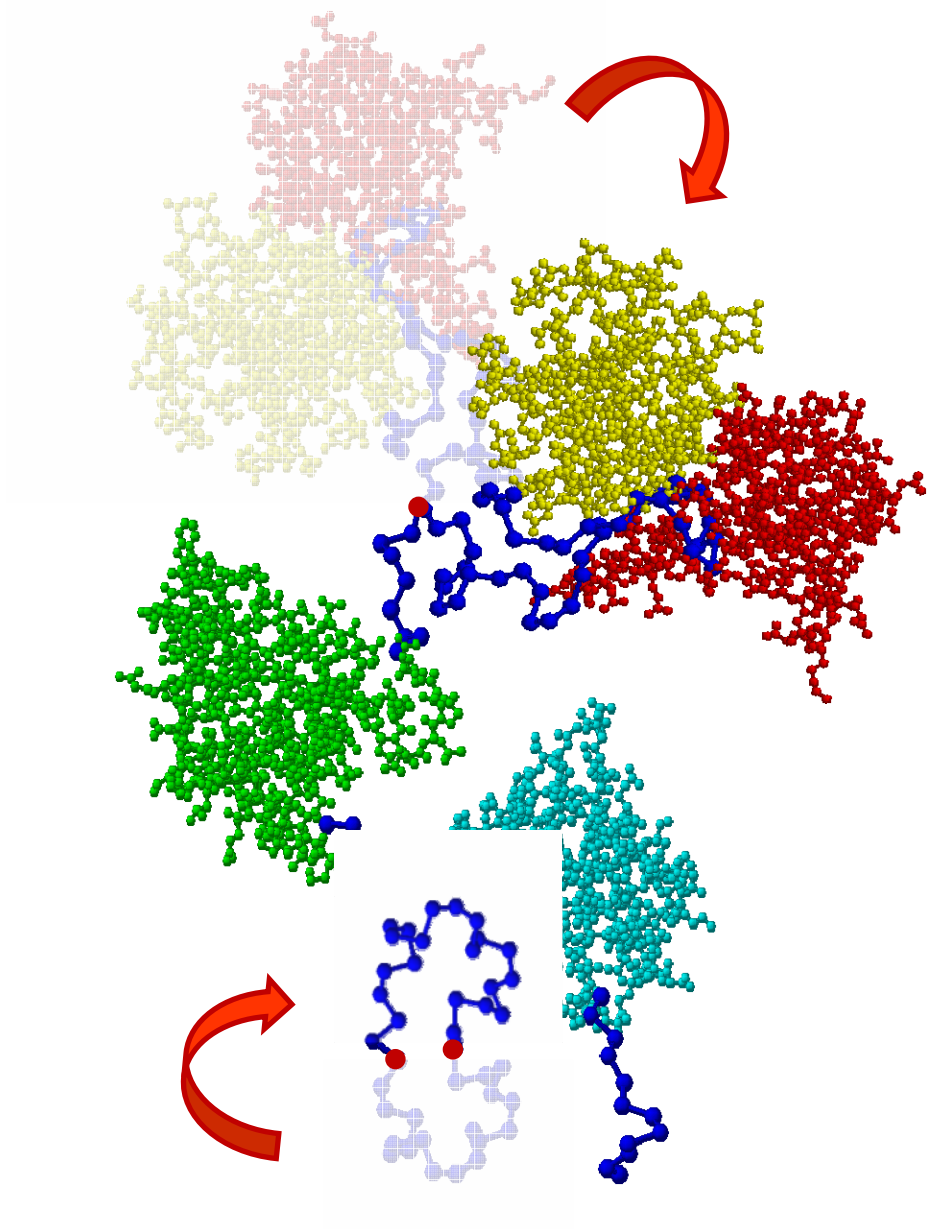
MRGSHHHHHH GSGVPSRVIH IRKLPIDVTE GEVISLGLPF GKVTNLLMLK
GKNQAFIEMN TEEAANTMVN YYTSVTPVLR GQPIYIQFSN HKELKTDSSP
NQARAQAALQ AVNSVQSGNL ALAASAAAVD AGMAMAGQSP VLRIIVENLF
YPVTLDVLHQ IFSKFGTVLK IITFTKNNQF QALLQYADPV SAQHAKLSLD
GQNIYNACCT LRIDFSKLTS LNVKYNNDKS RDYTRPDLPS GDSQPSLDQT
MAAAFGLSVP NVHGALAPLA IPSAAAAAAA AGRIAIPGLA GAGNSVLLVS
NLNPERVTPQ SLFILFGVYG DVQRVKILFN KKENALVQMA DGNQAQLAMS
HLNGHKLHGK PIRITLSKHQ NVQLPREGQE DQGLTKDYGN SPLHRFKKPG

# Modelling of multidomain proteins

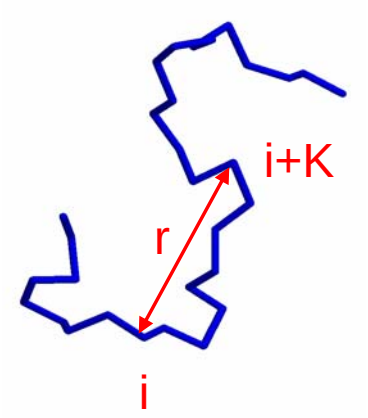


- A combined approach is proposed to built the models of multidomain proteins with large and flexible interdomain linkers
- The latter are represented as DR chains which are attached to the appropriate terminals in rigid domains.
- A single modification of a model is a rotation about one or two randomly selected DR(s).

# Modelling of multidomain proteins

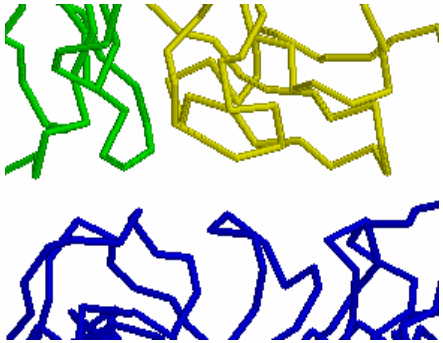


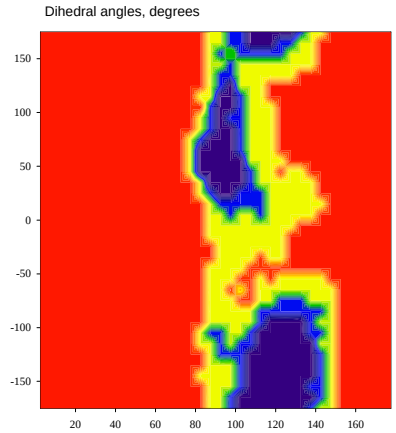
# Building native-like folds of linkers



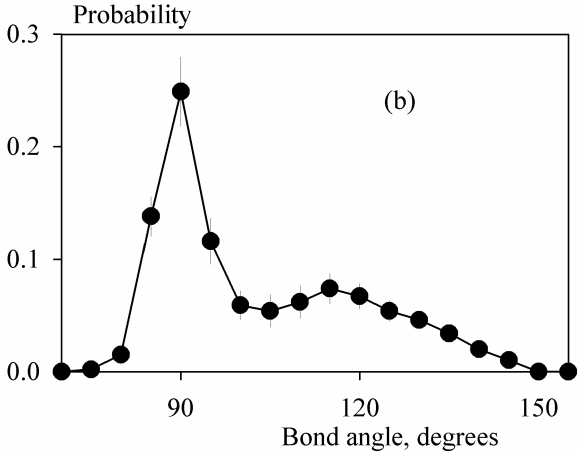

Neighbors distribution along the sequence

Absence of steric clashes



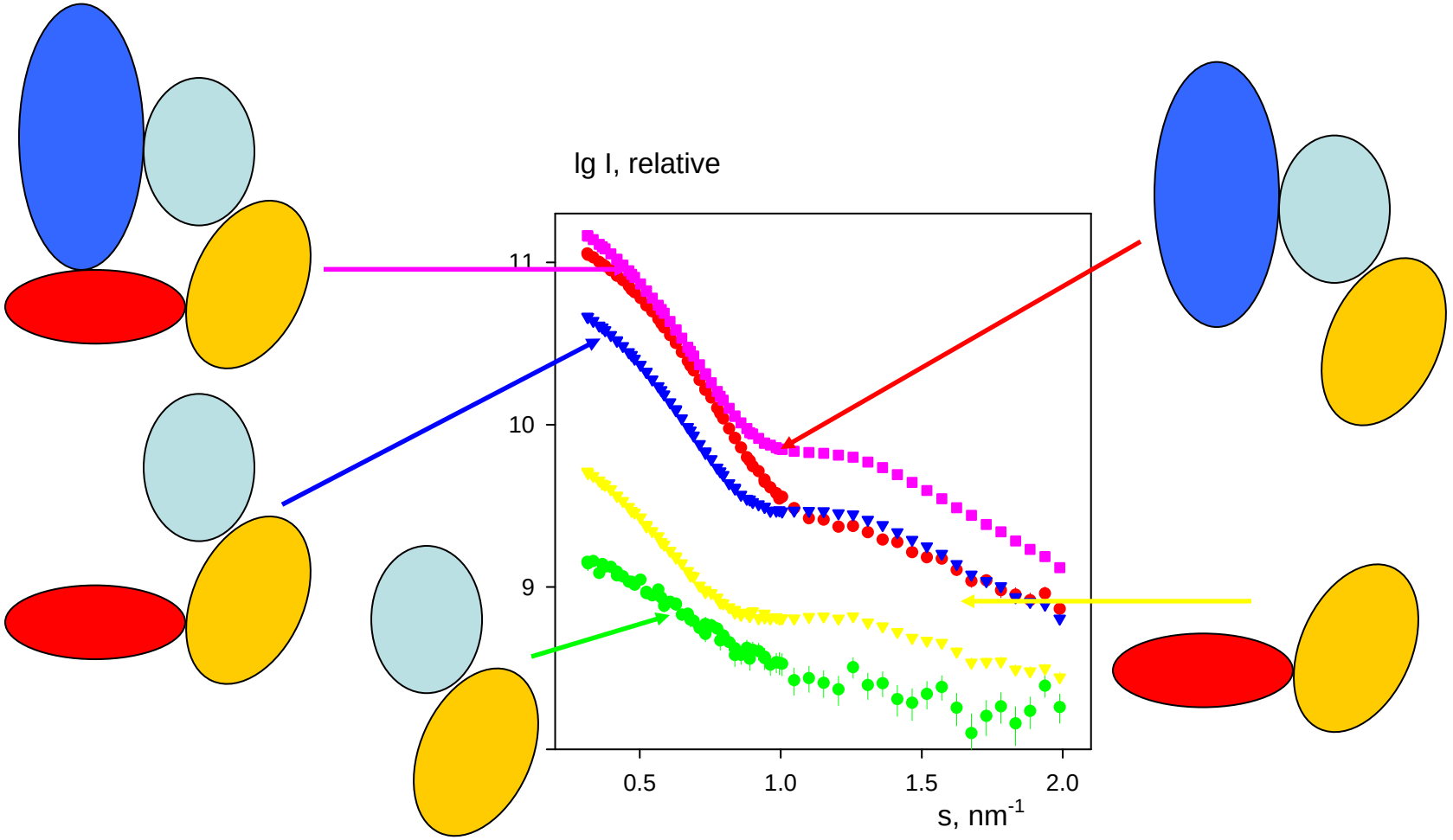



Bond angles & dihedrals distribution




Loop compactness may also be required $Rg_{id} = 3\sqrt[3]{n_l}$

# Simultaneous fitting of multiple data sets from deletion mutants

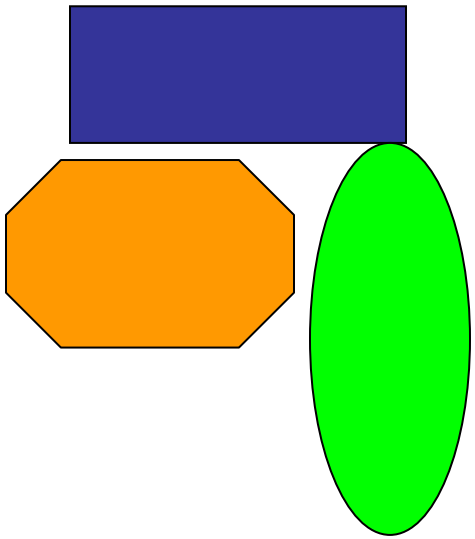


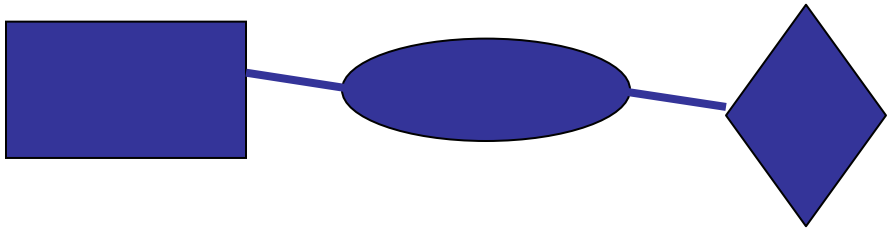
# PTB protein

MRGSHHHHHH GSGVPSRVIH IRKLPIDVTE GEVISLGLPF GKVTNLLM
GKNQAFIEMN TEEAANTMVN YYTSVTPVLR GQPIYIQFSN HKELKTDSS
NQARAQAALQ AVNSVQSGNL ALAASAAAVD AGMAMAGQSP VLRIIVEN F
YPVTLDVLHQ IFSKFGTVLK IITFTKNNQF QALLQYADPV SAQHAKL D
GQNIYNACCT LRIDFSKLTS LNVKYNNDKS RDYTRPDLPS GDSQPSL T
MAAAFGLSVP NVHGALAPLA IPSAAAAAAA AGRIAIPGLA GAGNSVLLVS
NLNPERVTPQ SLFILFGVYG DVQRVKILFN KKENALVQMA DGNQAQLA
HLNGHKLHGK PIRITLSKHQ NVQLPREGQE DQGLTKDYGN SPLHRFKK
SKNFQNIFPP SATLHLSNIP PSVSEEDLKV LFSSNGGVVK GFKFFQKD
MALIQMGSVE EAVQALIDLH NHDLGENHHL RVSFSKSTI

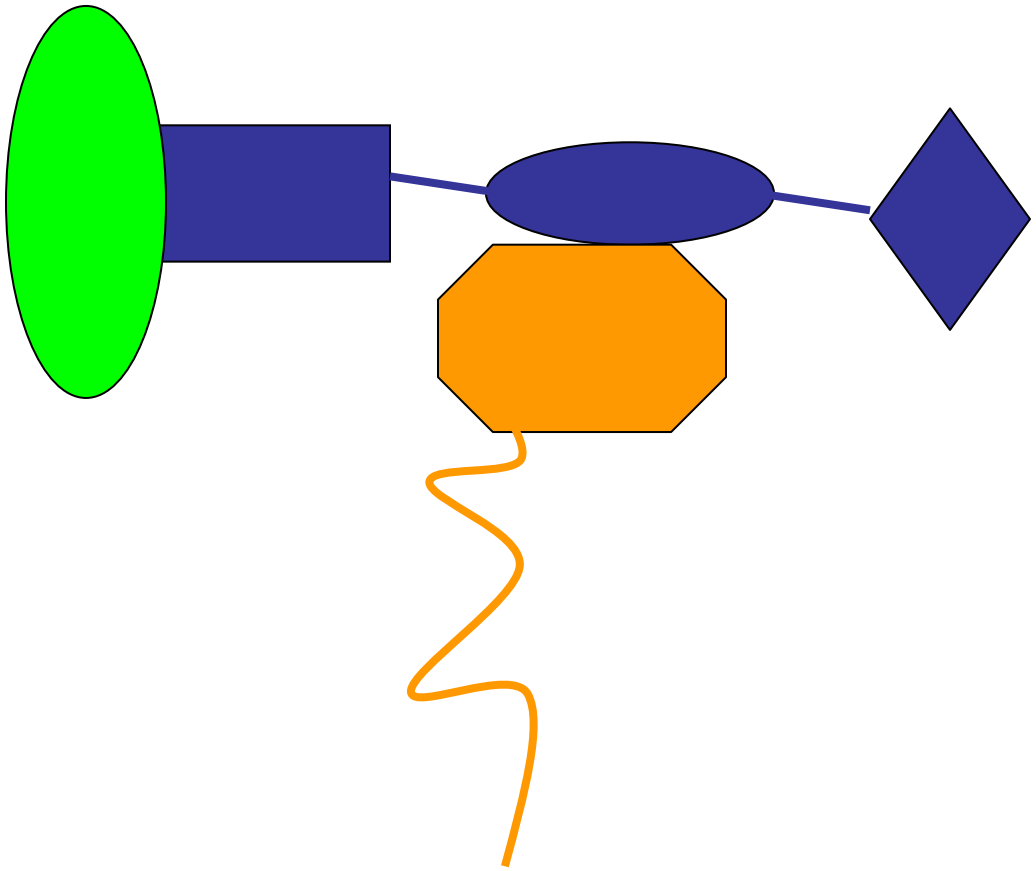
# CORAL: new in ATSAS 2.4

# Sasref vs Bunch



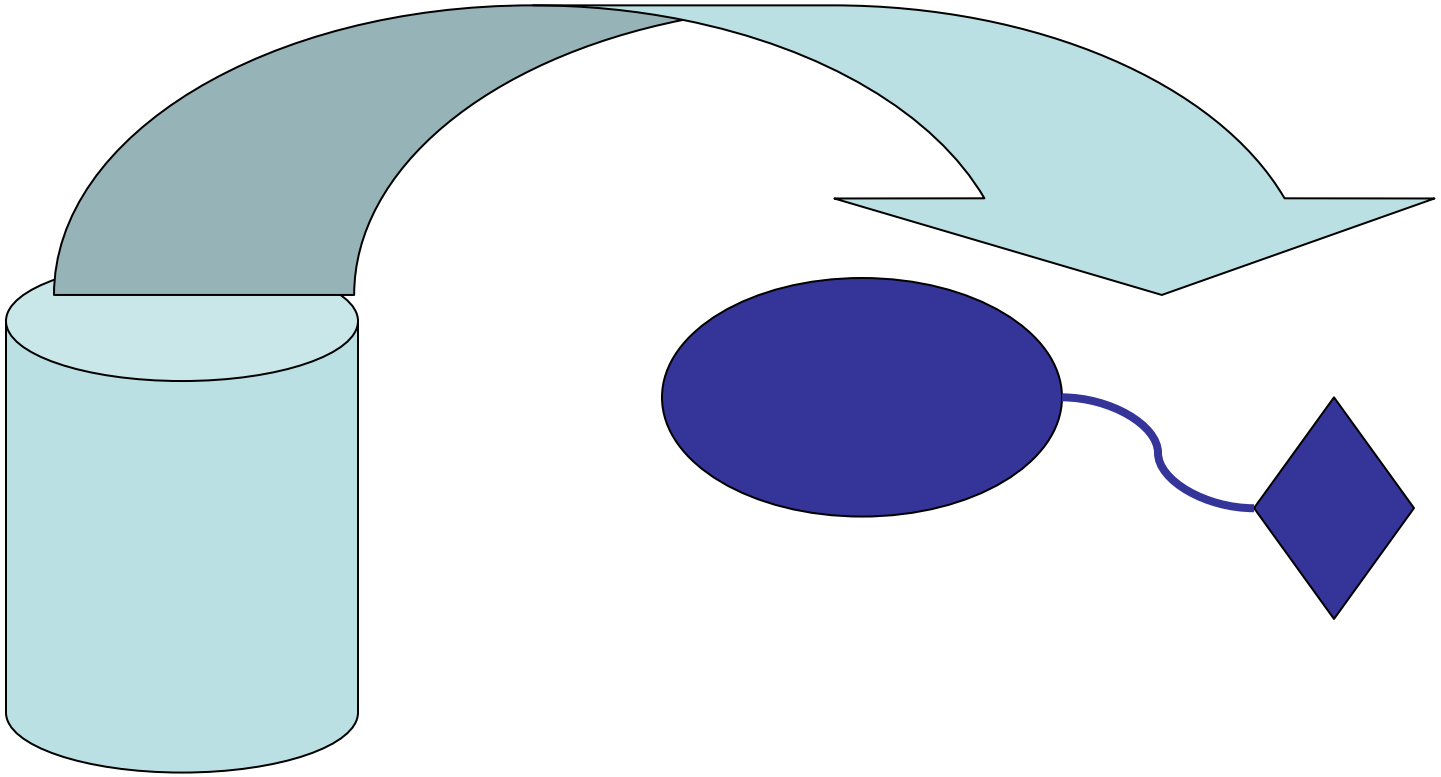


# Merging Sasref and Bunch



CORAL = COmplexes with RAndom Loops

# RanLog library



# Simplified input (config file)

NTER 20
A1.pdb
LINK 25
A2.pdb
CTER 10
.....
NTER 45
B1.pdb
.....
C1.pdb

# Example

- GST-DHFR fusion protein (Kate)