

Dictionary of ligands

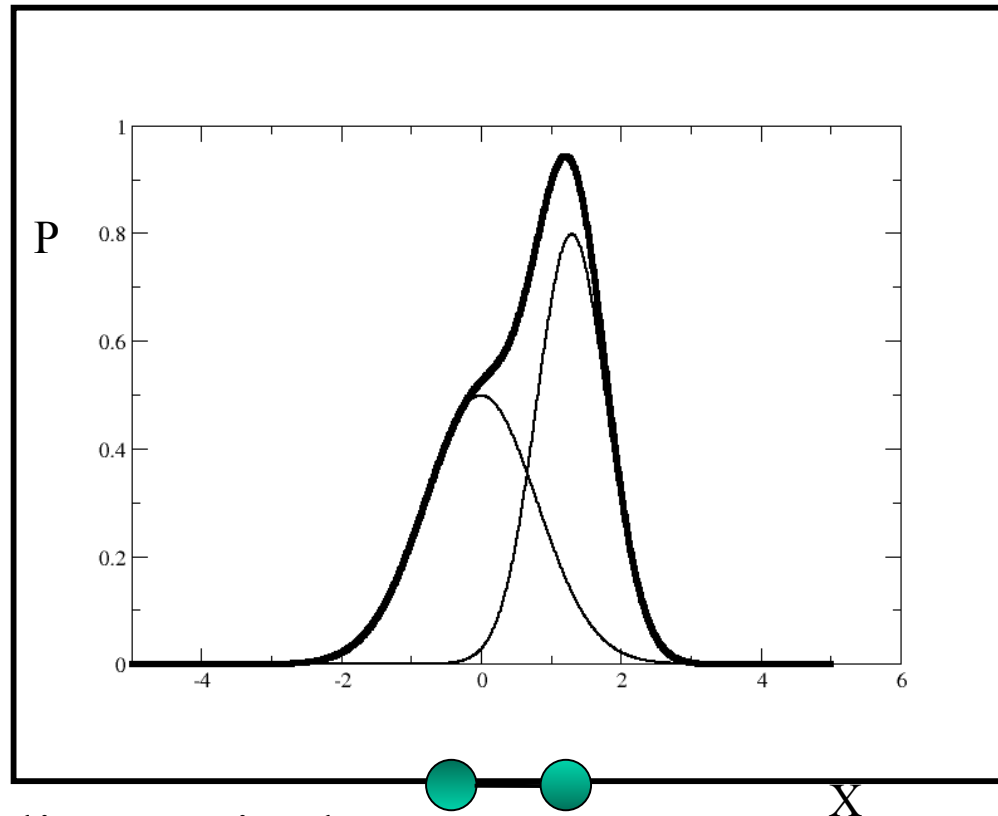
Some of the web and other resources

- Small molecules
- DrugBank: <http://www.drugbank.ca/>
- ZINC: <http://zinc.docking.org/index.shtml>
- PRODRUG: http://www.compbio.dundee.ac.uk/Web_Servers/prodrg_down.html
- CACTVS: <http://www2.chemie.uni-erlangen.de/software/cactvs/>
- Cambridge structural database - CSD: <http://www.ccdc.cam.ac.uk/products/csd/>

- Macromolecules
- PDB:
 - European EBI: <http://www.ebi.ac.uk/msd/>
 - USA RSCB: <http://www.rcsb.org/pdb/download/download.do>
- RASMOL (visualisation tool): <http://rasmol.org/>
- JMOL (Java based visualisation tool): <http://jmol.sourceforge.net/>

Why restraints: Two atoms ideal case

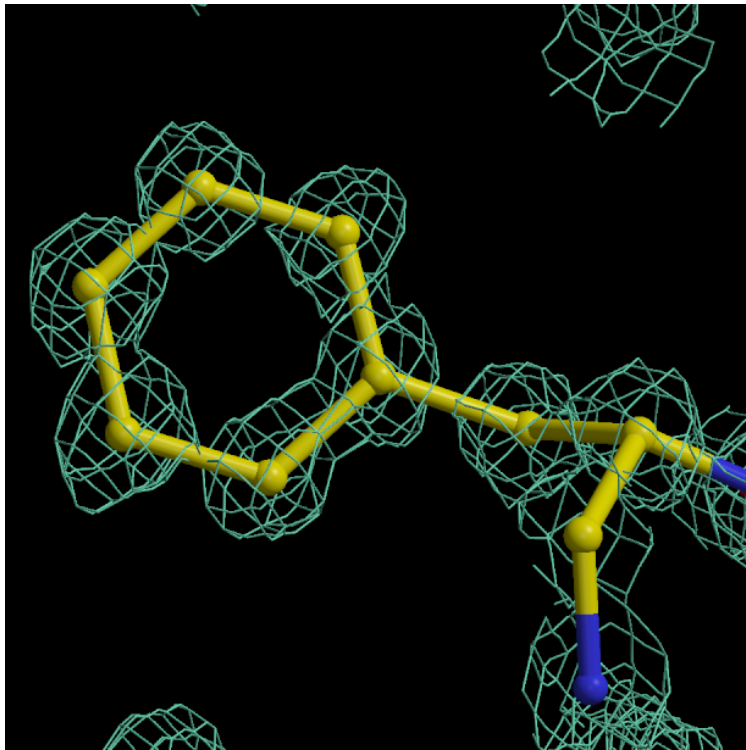
- Distance between atoms 1.3Å. B values 20 and 50



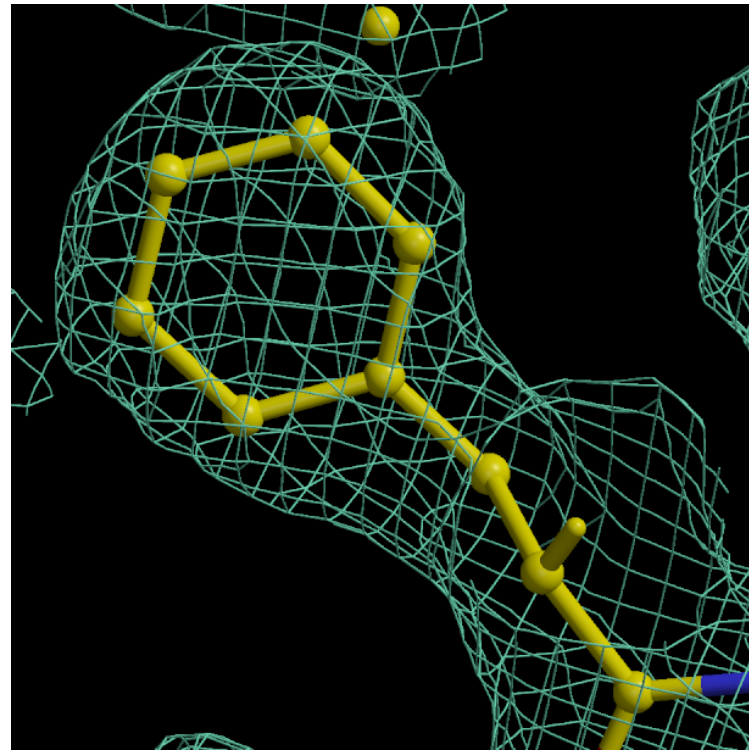
- Thin lines – single atoms
- Bold line - sum of the two atoms

Chemical information: Phe at two different resolutions

- 0.88 Å



2 Å and High mobility



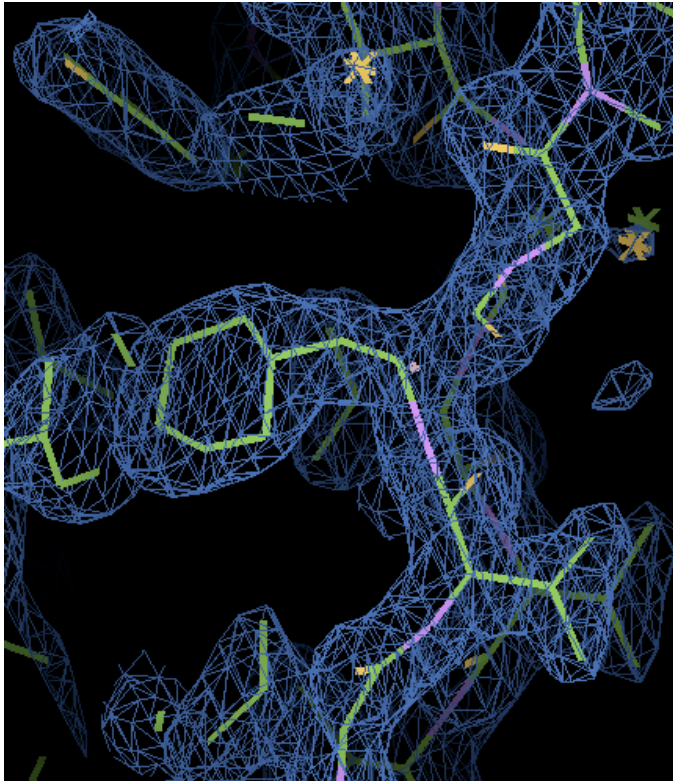
Role of restraints

- When atoms have high B values and/or data are at low resolution then electron density may not show separate peaks
- If restraints would not be used then chemistry of molecule would be unreasonable.
- Role of restraints is that to retain chemistry of atoms and at the same time describe electron density optimally.
- If atoms are close to each other it is unlikely that they will have hugely different B values

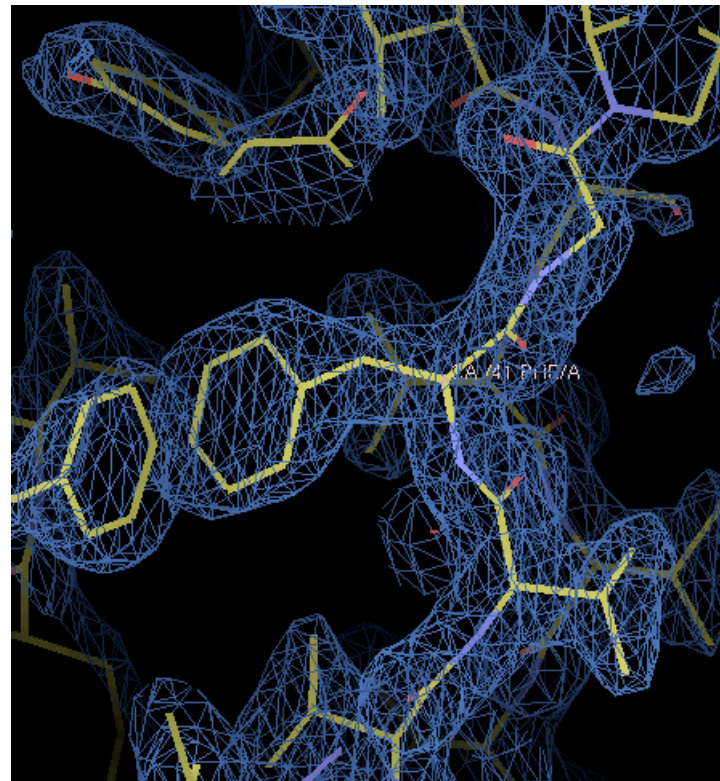
Example

- Data - 1.9Å

Unrestrained

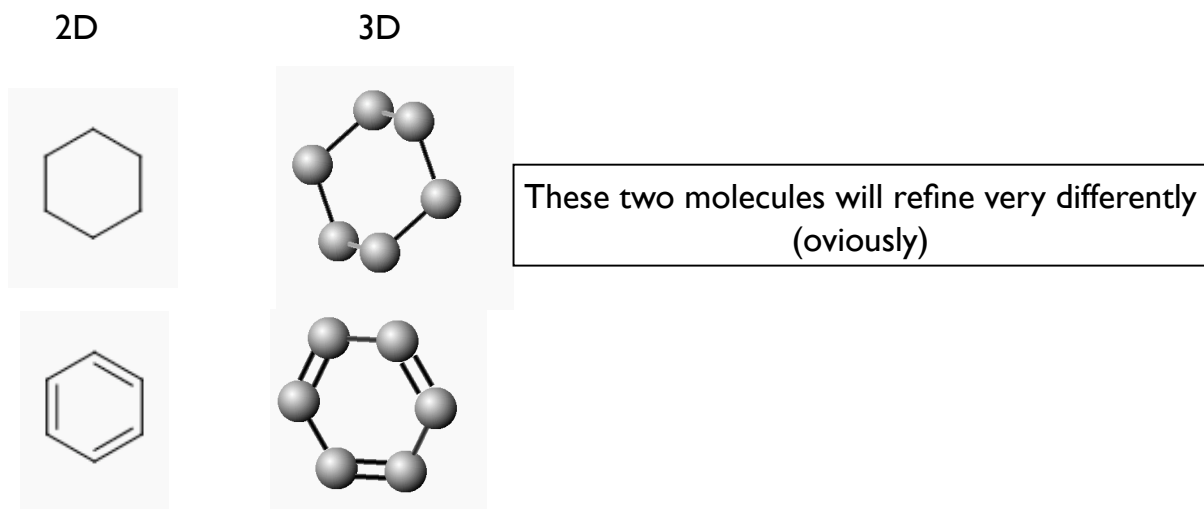


Restrained



Using restraints

- Standard dictionary has description of more than 10000 small molecules. If one of them is in your crystal then the will be used automatically.
- What happens if you have a ligand that is not in the dictionary. Then it is your responsibility to create chemically sensible description.
- Before starting to create a description you need to study bonding structure of your ligand.



DrugBank

There are various options like “Search”, “Download”



Home Browse Search About Downloads Contact Us

Search: Search



The DrugBank database is a unique bioinformatics and cheminformatics resource that combines detailed drug (i.e. chemical, pharmacological and pharmaceutical) data with comprehensive drug target (i.e. sequence, structure, and pathway) information. The database contains nearly 4800 drug entries including >1,350 FDA-approved small molecule drugs, 123 FDA-approved biotech (protein/peptide) drugs, 71 nutraceuticals and >3,243 experimental drugs. Additionally, more than 2,500 non-redundant protein (i.e. drug target) sequences are linked to these FDA approved drug entries. Each DrugCard entry contains more than 100 data fields with half of the information being devoted to drug/chemical data and the other half devoted to drug target or protein data.

DrugBank is supported by [David Wishart](#), Departments of [Computing Science](#) & [Biological Sciences](#), [University of Alberta](#).

[More about DrugBank](#)

What's New?

- We have implemented the [ChemAxon](#) solution for structure searches. You can now perform similarity (tanimoto), substructure, and exact searches via the [ChemQuery](#) function. This system replaces an outdated structure search and should be faster and more accurate. We have only added the most basic features for this release, so if you would like to see more/different features added, please let us know.
- We have added a new page containing links to other useful drug and small molecule databases. The [other databases](#) page

DrugBank

Search can be performed using different tools. One of them is smile string
Search can be exact or substructure

Search:

ChemQuery

Structure Molecular Weight **SMILES** Chemical Formula

Drug Type:


Search Type:

Tanimoto Similarity
Similarity threshold:
A higher similarity threshold results in less hits that are more similar to the query structure.

Substructure

Exact

Molecular Weight Filter:
between and



Query SMILES string:

[Example:](#) NCCCC[C@H](N)C(O)=O

SMILES

SMILES notation is the most popular notation and almost all computational chemical websites, programs use this notation. They can read and write SMILES.

It is based on several simple rules. Full description of SMILES can be find from daylight websites.

<http://www.daylight.com/dayhtml/doc/theory/theory.smiles.html>

SMILES stands for Simplified Molecular Input Line Entry System.

It is concise and widely spread. It is very easy to learn. It was originally designed for manual input using text only editors. SMILES has become as a standard and it is a useful thing to know about.

SMILES

SMILES uses several very simple rules (these rules are sufficient to generate SMILES from structure and structure from SMILES).

Rules:

Atomic symbols used for atoms

Hydrogen atoms as a rule are implicit. They are deduced using valence information about atoms

Neighbouring atoms stand one after another

Single, double, triple and aromatic bonds are denoted using “-”, “=”, “#” and “:” respectively. Single and aromatic bonds are usually not shown.

Branches represented by parentheses

Cycles are added by using matching digits on connecting atoms

Aromatic atoms are denoted using lower cases.

These rules are sufficient to describe most of the cases. Let us consider some examples

PRODRG server

PRODRG Home [FAQ](#) [PRODRG Beta](#) [How to obtain](#) [Usa](#)

The Dundee PRODRG2 Server

Finally, a FAQ is available [here](#), READ it before using this server

Molecular topologies for ... X-ray refinement/MD ... drug design/docking



Funded by:
 The Wellcome Trust

Draw Molecule With JME

... or ...

Paste your input here (PDB coordinates, MDL MOLfile, text drawing). See below for instructions.

Chirality Full charges Energy minimization

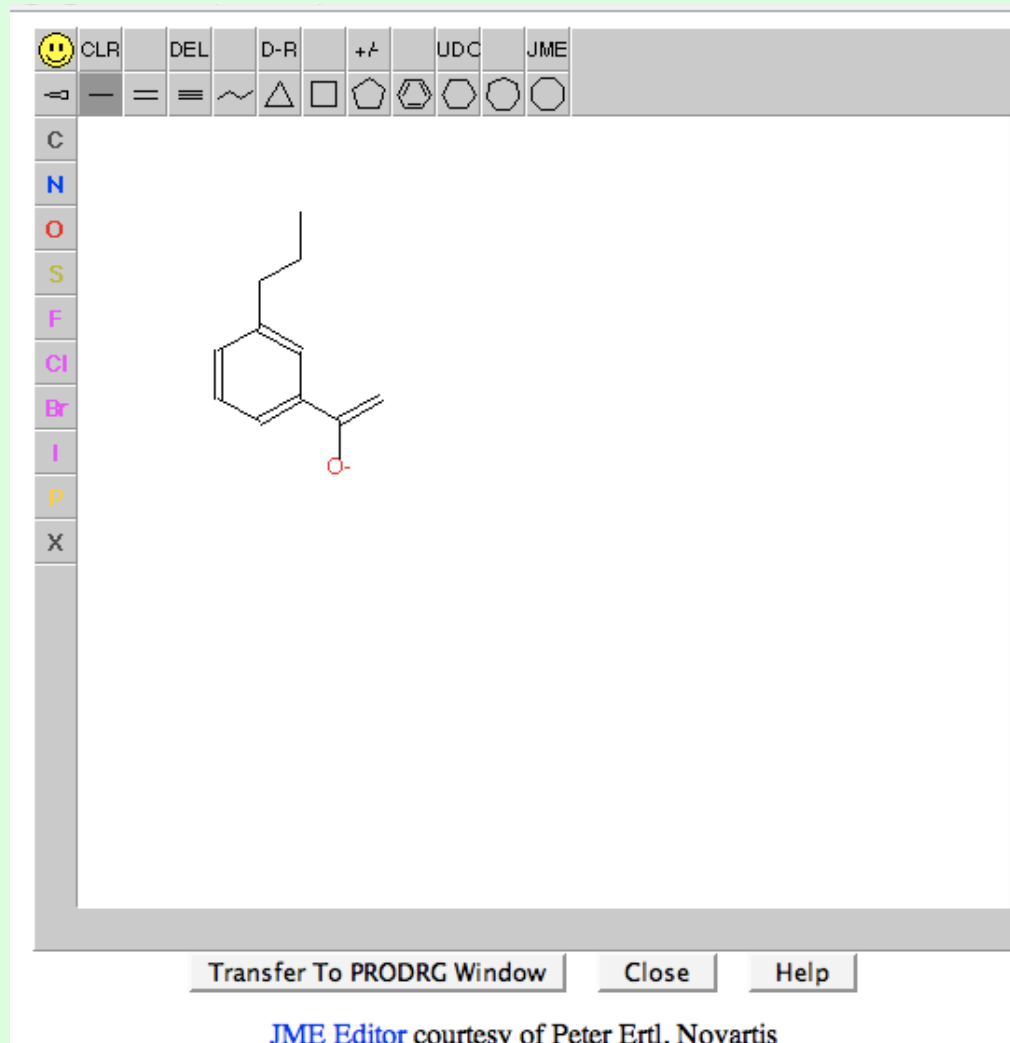
Please be patient, this can take up to 2 minutes

JME

Load your file

PRODRG: JME

JME is java based program for 2D drawing of small compounds. It is used in PRODRG2, MSDchem etc



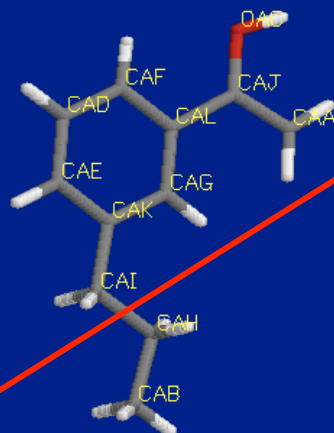
Draw your ligand,
transfer to PRODRG
window and run

PRODRG output

[PRODRG Home](#) [FAQ](#) [PRODRG Beta](#) [How to obtain](#)

```
PRODRG> Starting up PRODRG version 061128.0522
PRODRG> PRODRG written/copyrighted by Daan van Aalten
PRODRG> and Alexander Schuettelkopf
PRODRG>
PRODRG> Questions/comments to dava@davapc1.bioch.dundee.ac.uk
PRODRG>
PRODRG> When using this software in a publication, cite:
PRODRG> A. W. Schuettelkopf and D. M. F. van Aalten (2004).
PRODRG> PRODRG - a tool for high-throughput crystallography
PRODRG> of protein-ligand complexes.
PRODRG> Acta Crystallogr. D60, 1355--1363.
PRODRG>
PRODRG>
PRODRG> MOL mode detected.
PRODRG> No stereo information found in input file.
PRODRG> Molecule complexity index: 2.00.
PRODRG> 1 hydrogen(s) added.
PRODRG> 13 bonds          1 ambiguous
PRODRG> 16 bond angles     3 ambiguous
PRODRG> 9 improper dihedrals 1 ambiguous
PRODRG> 4 dihedrals        0 ambiguous
PRODRG> 2 partial charges  0 ambiguous
PRODRG> Net charge on molecule: 0.000
PRODRG> Using charge groups.
PRODRG> Writing GROMACS topology.
PRODRG> GROMACS topology quality on 0-10 scale: 7.7
PRODRG> Best structure was iteration 841 with 0.70210928
PRODRG> Spawning GROMACS version 3.2.1...
PRODRG> RMSD from GROMOS bond ideality (Angstrom) : 0.017
PRODRG> RMSD from GROMOS angle ideality (degrees) : 2.257
PRODRG> RMSD from GROMOS plane ideality (degrees) : 0.432
PRODRG> Number of improper improper dihedrals : 0
PRODRG> Writing: SCRHWMPG
PRODRG> Normal program end
```

Your molecule + added hydrogens



It can write out representation in various formats suitable for various popular software

Click to go to the following output:

Coordinates

- [PDB \(all H's, polar H's only or no H's\)](#)
- [MDL Molfile \(all H's, polar H's only or no H's\)](#)
- [GROMOS87/GROMACS \(polar H's only\)](#)

X-ray refinement

- [CNS \(parameters and topology\)](#)
- [REFMAC5](#)
- [SHELX](#)
- [O \(pre-9.x torsion entry, pre-9.x refi dictionary and 9.x dictionary\)](#)

Done

PDB

- PDB is Protein Data Bank. It has all macromolecular structures determined experimentally as well as theoretically. There are more than 56000 macromolecular structures available in the PDB.
- In many cases protein structures are determined with some ligands (small molecular compounds). These small molecular structures are available from PDB. There are 8000-9000 such small molecules in the PDB.
- There are websites that allows people to view macromolecular structures as well as small molecular compounds. These sites are located in USA, Europe and Japan.

PDB in Europe: PDBe at EBI, Cambridge

EBI > Databases > Structure Databases > MSD > Services contact msd

Ligand Chemistry ? Energy types ?

Consistent and enriched library of ligands, small molecules and monomers that are referred as residues and hetgroups in any PDB entry (8702 currently in the database - Release:03-2008_02_22)

MSDchem : Molecule

3 letter code

Code

Molecule name

Formula

Non stereo smile

Stereo smile

Fragments

Fingerprint

And Or

Retrieve:

Substructure,
common segment,
exact stereo

Draw Structure [\(how to use editor\):](#)

CLR DEL D-R +/- UDC JME

C
N
O
S
P
Cl
Br
I
P
X

JME 2004.10

or Load File (SDF,MOL,mmCif,PDB e.t.c.)

or give Smile String (i.e. c1ccccc1)

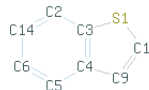
or give Code of Existing Molecule (i.e. ATP)

(Press the Load Button to Load the Molecule with that smile or 3 letter code, or file into the editor)

Fragment
expression

Select chemical fragment pattern

acetylurea	acridine	acridone			
actinophenoxazine	adenine	alkaloid			
barbit	barbiturates	barbiturgroup			
benzimidazole	benzodiazepine	benzofuran			
benzoisoquinoline	benzothiadiazide	benzothiazole			
benzothiophen	benzoxazole	bilirubin			
biotin	carbazole	cephalosporin			
chromen	cinnoline	coumarine			
cyclobutane	cyclohexane	cyclopentane			
cyclopropane	cytosine	deoxyribose			
dibenzofuran	dibenzothiophen	dithiolane			
flavin	furan	furanose			
glycerophos	guanine	imidazole			
indole	inosine	isoquinoline			
isoxadiazole	isoxazole	naphtyridine			
naphthalene	oxadiazole	oxazole			
oxazolinedione	oxepin	peptide			
penicillin	phenanthrene	phenanthridine			
phenanthroline	phenazine	phenothiazine	phenyl	phtalazine	piperazine
porphin	prost	pteridine	pteryl	purine	pyran
pyranose	pyrazine	pyrazole	pyridazine	pyridine	pyrimidine
pyrole	quinazoline	quinoline	quinoxaline	rauwoflia	ribose
steroid	succinimide	thiadiazole	thiazole	thiepin	thiophen
tolol	vitaminAcore	xanthen			



Fragment: min: max: none: any:

Fragment expression

Using resources from ccp4

Sketcher is under Refinement/Restraint Preparation/Monomer library sketcher.

CCP4 Program Suite 6.1.0 CCP4interface 2.0.3 running on snigami.local Project: atwin

List of jobs for project. Double-click on a job displays the log file, shift-double-click reruns the job.

Refinement Project Database Job List - currently no jobs

Directories&ProjectDir

View Any File

View Files from Job

Search/Sort Database..

Graphical View of Project

File Edit

MOUSE BUTTONS Left:rotate Right:drag Control-left:zoom Control-right:Select active atom
Shift-left:Select edit mode from menu first Shift-right:Click bond to change bond type

Run Refmac5 Do nothing

Run NCS Phased R

Model Completion

Undo last edit

Recentre View

Mouse mode

Edit Monomer

Move Fragment

Element	Name	Ox
C	C1	0
C	C2	0
C	C3	0
C	C4	0
C	C5	0
C	C6	0
C	C7	0
C	C8	0
C	C9	0
C	C10	0

Centre Sign B/3 F.

Element	Name	Ox
C	C10	0
H	H101	0
H	H102	0
H	H103	0
C	C9	0
H	H91	0
H	H92	0
C	C8	0
H	H81	0
H	H82	0
Centre	Sign	B/3 F4 1/5 2/6
1	C6	both C1 C5 C7

Edit Table Add Row

Sketch your ligand

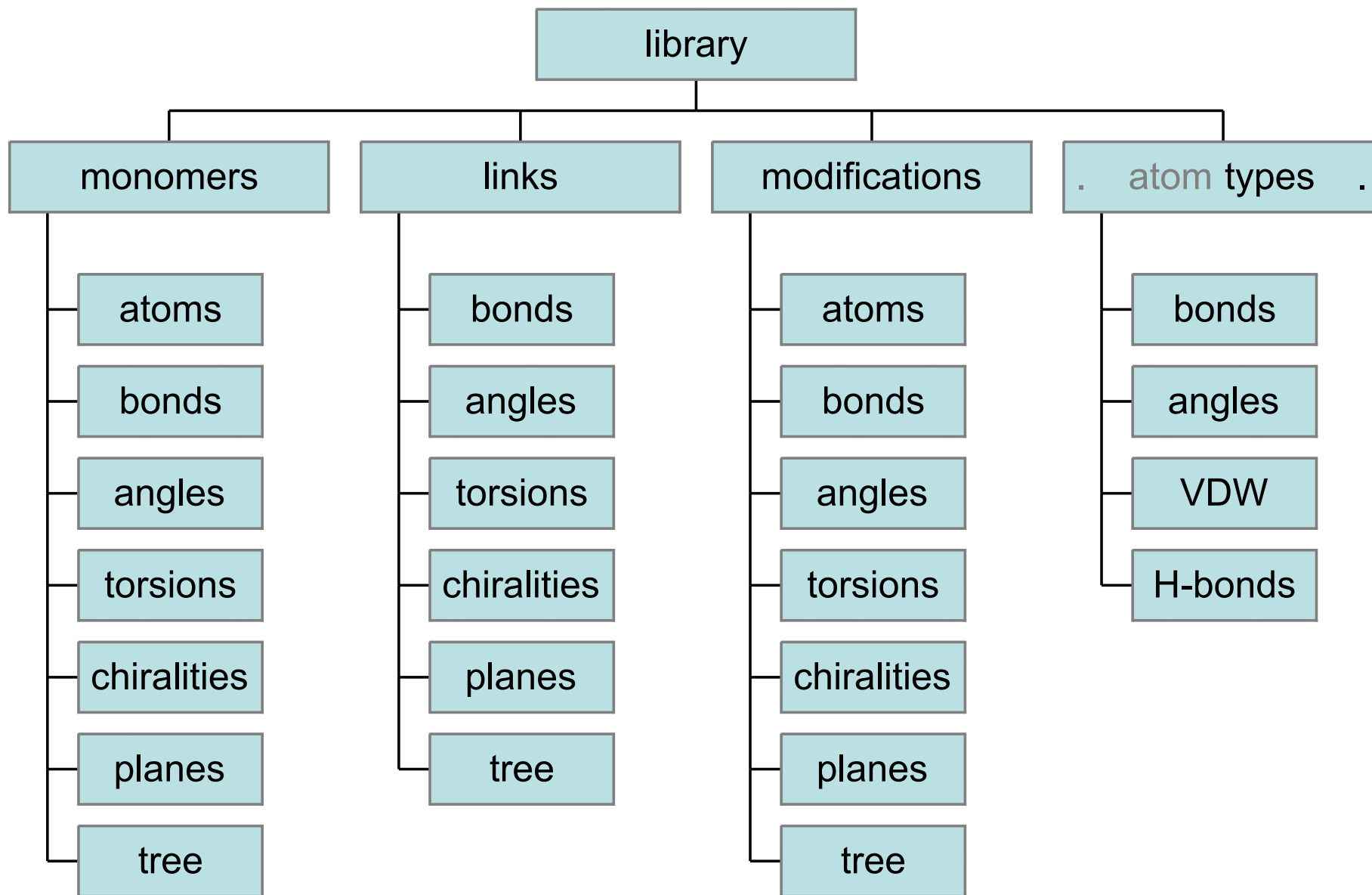
After regularisation

Jligand and Links

CCP4 monomer library: modifications and links

New link description

CCP4 monomer library (library of restraints)



Modifications and links

The idea of this mechanism is that

- while *monomer* records describe individual compounds
- *modifications* and *links* describe changes resulted from chemical reactions

Modification formalism allows to change a monomer

Link formalism allows to join modified monomers together

Generic links for peptides

Generic peptide modification "DEL-OXT":



Generic peptide modification "NH1":

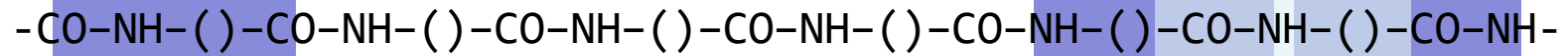


Generic peptide link "TRANS":

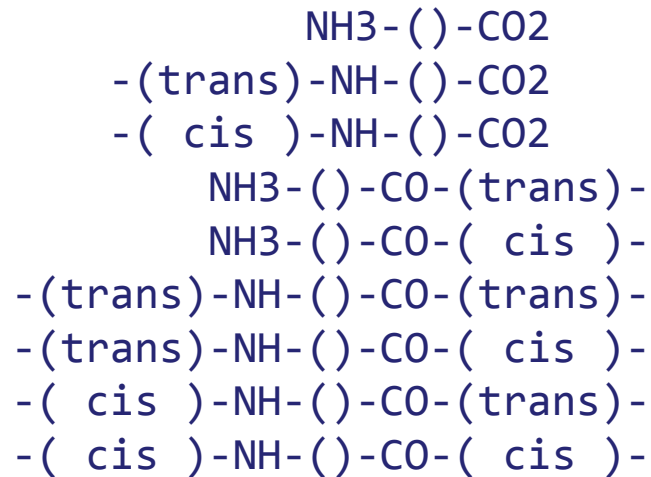


These define: bond length, angles and a plane associated with the bond C-N

Specialised monomers vs. generic links

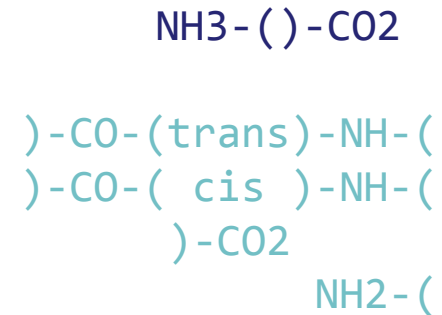


Specialised monomers:



9 versions
 ×
 20 aminoacids
 =
 180 library entries

Generic links:



20 aminoacids
 +
 2 links
 +
 7 modifications
 =
 29 library entries

Links for peptides

generic

– peptide-peptide: TRANS, CIS

generic from one side

– peptide-PRO: PTRANS, NMTRANS, PCIS, NMCIS
– C-terminal modification: FOR_C-C, DFO_N-C, STA_N-C, ...
– N-terminal modification: FOR_C-N, ACE_C-N, DFO_C-N, ...
– pyranose-(ASP, THR, SER): NAG-SER, NAG-THR, NAG-ASN

specialised

– S-S bridge: CYS-CYS
– pyranose-peptide: XYS-SER, XYS-THR, XYS-ASN, ...
– metal-peptide: ZN-CYS, FE-CYS

Standard modifications and links (generic and specialised)

CCP4 library contains modifications for:

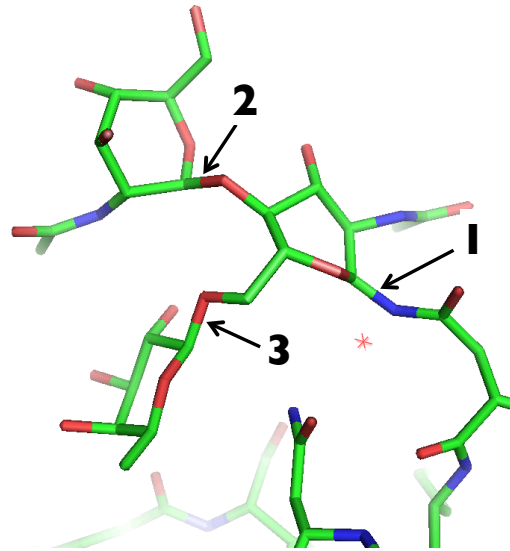
- terminal peptides and nucleotides
- methylated nucleotides
- deprotonated states

CCP4 library contains links and corresponding modifications for:

- polypeptide chains (CIS,TRANS), S-S bridges
- polynucleotide chains
- glycosylated proteins

Generic links for sugars

2xmb



For typical glycosylation cases

- necessary modifications and links are there in the standard ccp4 library
- by default REFMAC uses these library descriptions and does not need any additional instructions

NAG – NAG – ASN

|
FUL

FUL = Beta-L-Fucose
NAG = N-Acetyl-D-Glucosamine

Standard links used here:

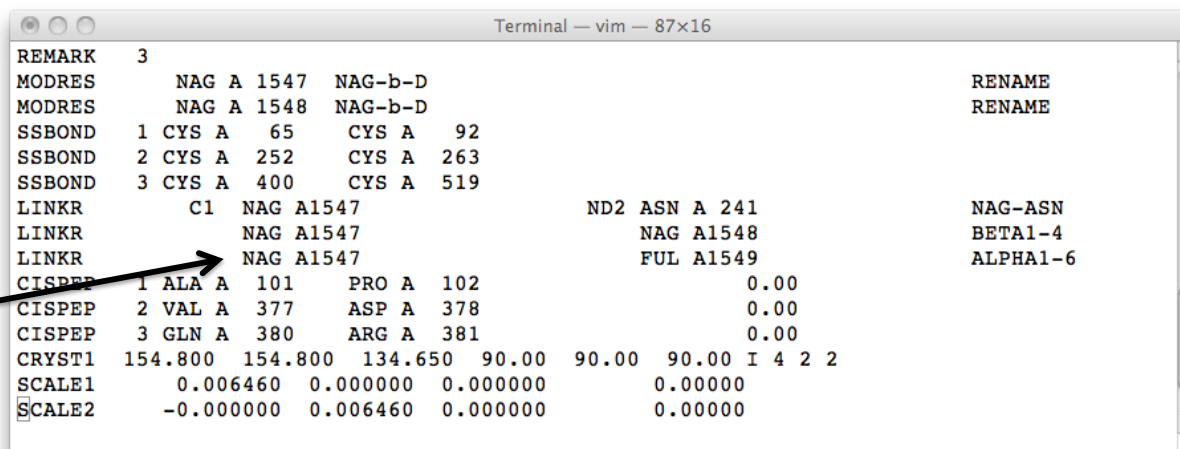
- (1) "NAG-ASN"
- (2) "BETA1-4"
- (3) "ALPHA1-6"

Sugar links: refmac checkpoints

✓ refmac terminated normally

✓ output pdb-file contains expected LINKR records, e.g.

```
LINKR...  
...NAG A1547 FUL  
A1549...  
...ALPHA1-6
```

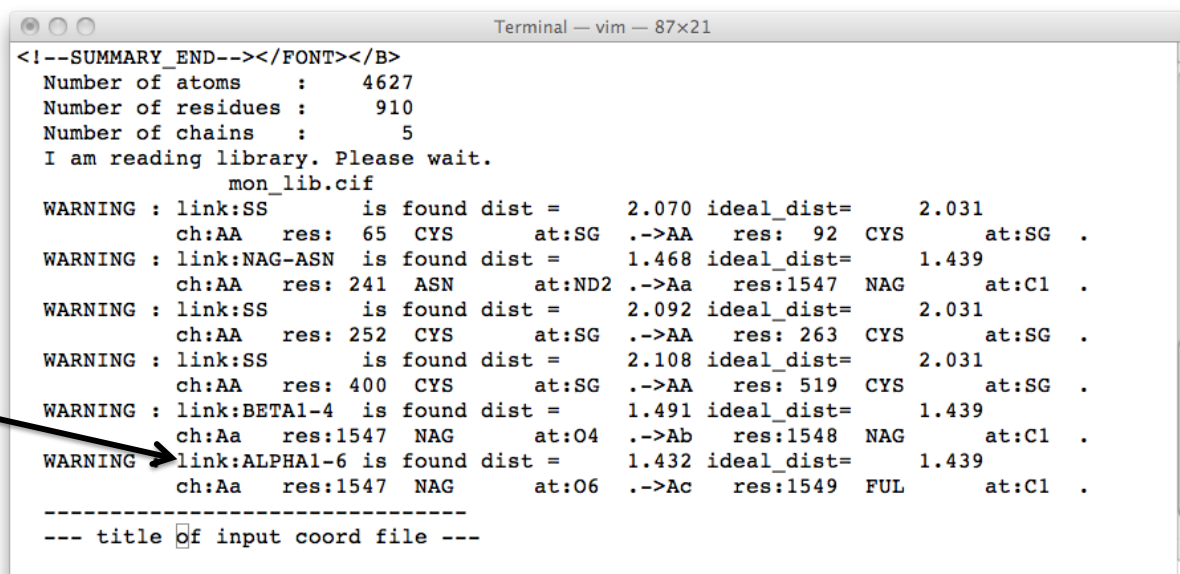


```
Terminal - vim - 87x16  
REMARK      3  
MODRES      NAG A 1547  NAG-b-D  
MODRES      NAG A 1548  NAG-b-D  
SSBOND      1 CYS A   65   CYS A   92  
SSBOND      2 CYS A  252   CYS A  263  
SSBOND      3 CYS A  400   CYS A  519  
LINKR       C1  NAG A1547  
LINKR       NAG A1547  
LINKR       NAG A1547  
CISPEP      1 ALA A  101   PRO A  102  
CISPEP      2 VAL A  377   ASP A  378  
CISPEP      3 GLN A  380   ARG A  381  
CRYST1      154.800 154.800 134.650 90.00 90.00 90.00 I 4 2 2  
SCALE1      0.006460 0.000000 0.000000 0.000000  
SCALE2      -0.000000 0.006460 0.000000 0.000000  
ND2 ASN A 241  
NAG A1548  
FUL A1549  
NAG-ASN  
BETA1-4  
ALPHA1-6
```

✓ log-file contains warnings saying e.g. that

```
... link:ALPHA1-6 is  
found  
... res:1547 NAG ...  
... res:1549 FUL ...
```

(WARNING = OK)



```
Terminal - vim - 87x21  
<!--SUMMARY_END--></FONT></B>  
Number of atoms : 4627  
Number of residues : 910  
Number of chains : 5  
I am reading library. Please wait.  
mon_lib.cif  
WARNING : link:SS is found dist = 2.070 ideal_dist= 2.031  
ch:AA res: 65 CYS at:SG .->AA res: 92 CYS at:SG .  
WARNING : link:NAG-ASN is found dist = 1.468 ideal_dist= 1.439  
ch:AA res: 241 ASN at:ND2 .->Aa res:1547 NAG at:C1 .  
WARNING : link:SS is found dist = 2.092 ideal_dist= 2.031  
ch:AA res: 252 CYS at:SG .->AA res: 263 CYS at:SG .  
WARNING : link:SS is found dist = 2.108 ideal_dist= 2.031  
ch:AA res: 400 CYS at:SG .->AA res: 519 CYS at:SG .  
WARNING : link:BETA1-4 is found dist = 1.491 ideal_dist= 1.439  
ch:Aa res:1547 NAG at:O4 .->Ab res:1548 NAG at:C1 .  
WARNING : link:ALPHA1-6 is found dist = 1.432 ideal_dist= 1.439  
ch:Aa res:1547 NAG at:O6 .->Ac res:1549 FUL at:C1 .  
-----  
--- title of input coord file ---
```

User-defined links

When new link descriptions are needed:

side chain – side chain (e.g. TYR – TYR on the figure)

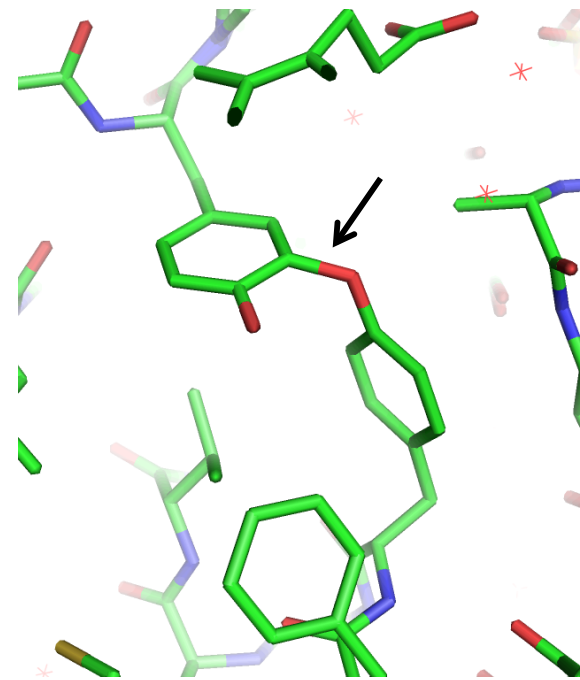
side chain – main chain (e.g. LYS – Ubiquitin)

side chain – ligand (e.g. LYS – PLP)

JLigand:

- new GUI for LIBCHECK
- descriptions of monomers (functionality of SKETCHER)
- descriptions of links and corresponding modifications

TYR–TYR covalent link in
M. tuberculosis Hemoglobin O
PDB id 1ngk



CCP4 monomer library: modifications and links

New link description

New link

Example:

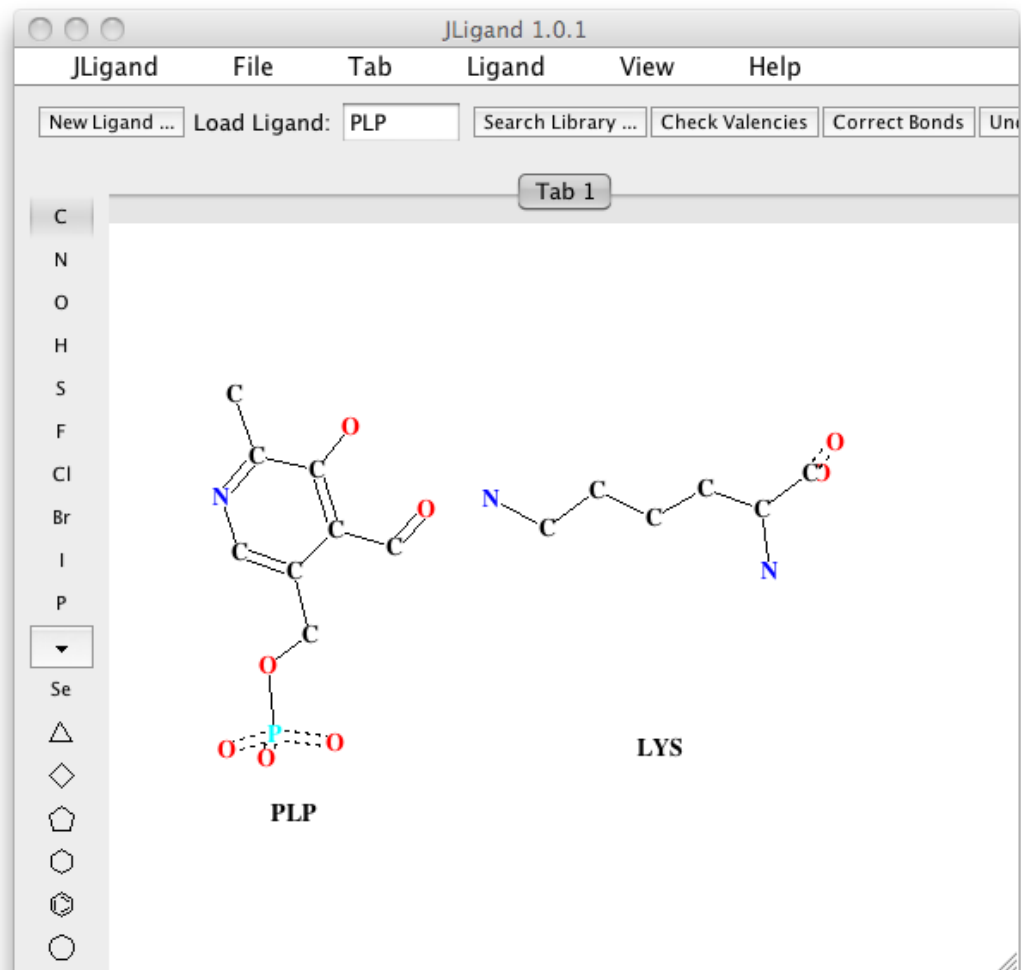
- covalent linkage between LYS and Pyridoxal phosphate (PLP).
- describes PLP forming internal aldimine in aminotransferases.

Given:

- descriptions of LYS and PLP from the standard library

Needed:

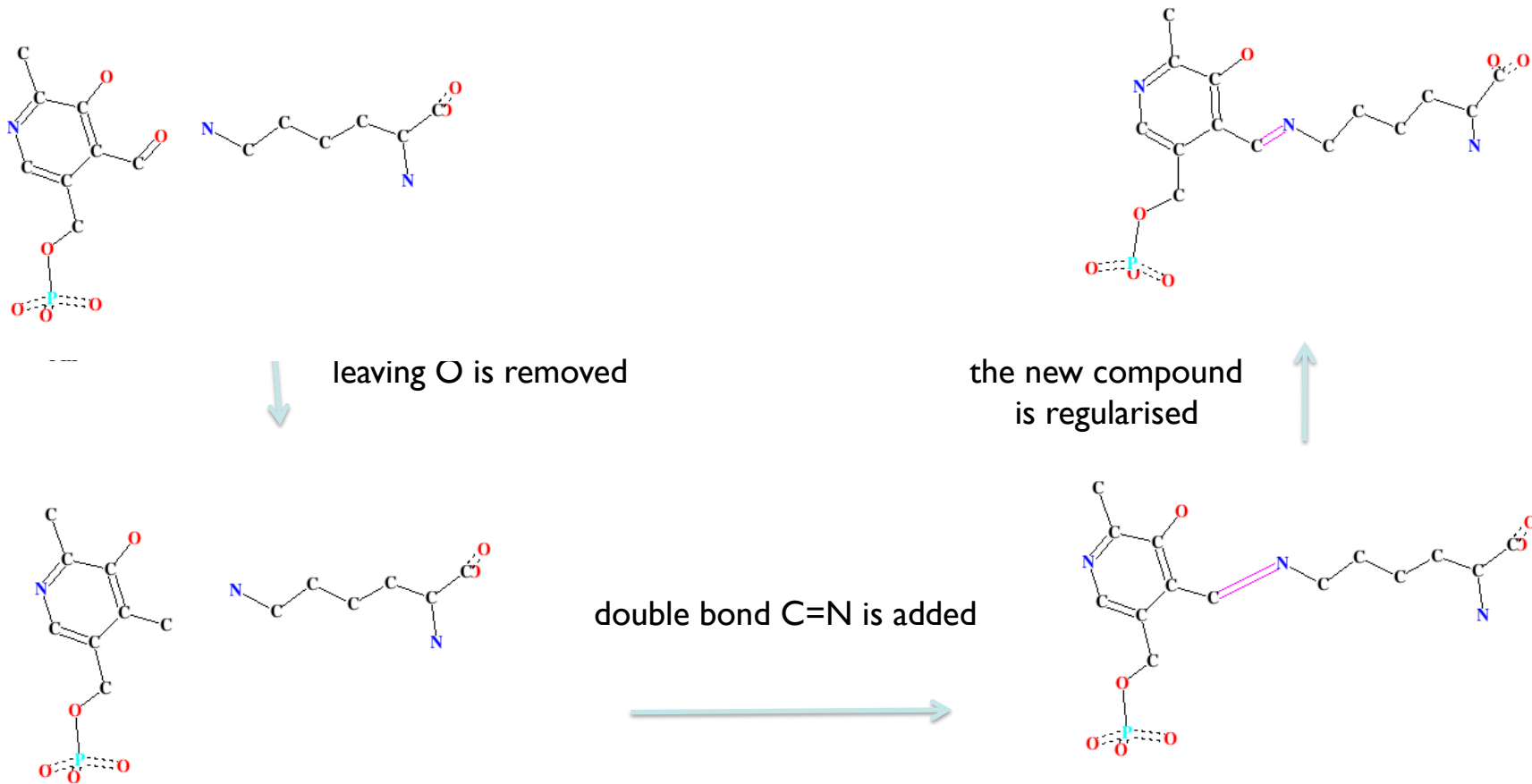
- additional library file with the description of link LYS–PLP



Creating a new link, as seen in JLigand GUI

The two monomers are in effect reacted in silico
Hydrogen atoms are dealt with automatically*)

*) it is also possible to visualise H-atoms and deal with them explicitly



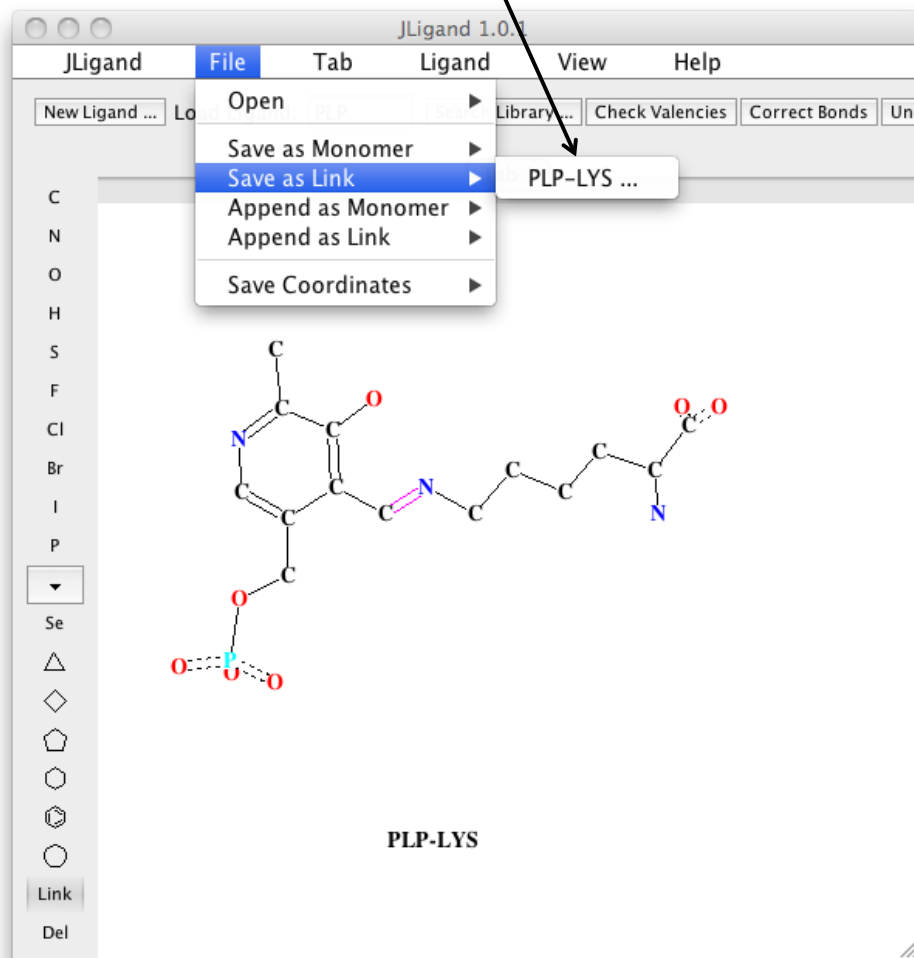
The new link, "file view"

To save into CIF-file (additional library)

Contents:

- (1) modification "PLPmod1"
- (2) modification "LYSmod1"
- (3) link "PLP-LYS"

No monomers

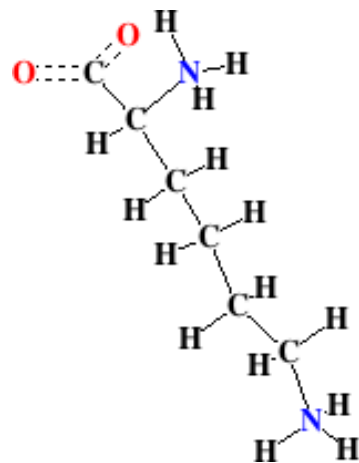


```
data_mod_list
loop_
  _chem_mod.id
  _chem_mod.name
  _chem_mod.comp_id
  _chem_mod.group_id
  PLPmod1 "PYRIDOXAL-5'-PHOSPHATE" . PLP .
  LYSmod1 "LYSINE" . LYS .
data_link_list
loop_
  _chem_link.id
  _chem_link.comp_id_1
  _chem_link.mod_id_1
  _chem_link.group_comp_1
  _chem_link.comp_id_2
  _chem_link.mod_id_2
  _chem_link.group_comp_2
  _chem_link.name
  PLP-LYS PLP PLPmod1 . LYS LYSmod1 .
  PLP-LYS
```

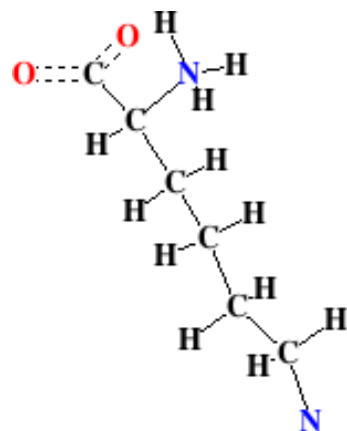
The screenshot shows the content of a CIF file named 'PLP-LYS'. The file contains two main sections: 'data_mod_list' and 'data_link_list'. The 'data_mod_list' section defines two modifications: 'PLPmod1' (PYRIDOXAL-5'-PHOSPHATE) and 'LYSmod1' (LYSINE). The 'data_link_list' section defines a link between these two modifications, named 'PLP-LYS'. Annotations 1, 2, and 3 point to the modification names in the data_mod_list and the link name in the data_link_list.

The new link, "file view"

LYS



LYSmod1



Modification "LYSmod1":
changes to LYS

data_mod_LYSmod1

```

loop_
  _chem_mod_atom.mod_id
  _chem_mod_atom.function
  _chem_mod_atom.atom_id
  _chem_mod_atom.new_atom_id
  _chem_mod_atom.new_type_symbol
  _chem_mod_atom.new_type_energy
  _chem_mod_atom.new_partial_charge
  LYSmod1 change NZ . . N 0.000
  LYSmod1 delete HZ1 . . . .
  LYSmod1 delete HZ2 . . . .
  LYSmod1 delete HZ3 . . . .
  
```

Atoms

```

loop_
  _chem_mod_bond.mod_id
  _chem_mod_bond.function
  _chem_mod_bond.atom_id_1
  _chem_mod_bond.atom_id_2
  _chem_mod_bond.new_type
  _chem_mod_bond.new_value_dist
  _chem_mod_bond.new_value_dist_esd
  LYSmod1 change CE NZ . 1.455 0.020
  LYSmod1 delete NZ HZ3 . . .
  LYSmod1 delete NZ HZ2 . . .
  LYSmod1 delete NZ HZ1 . . .
  
```

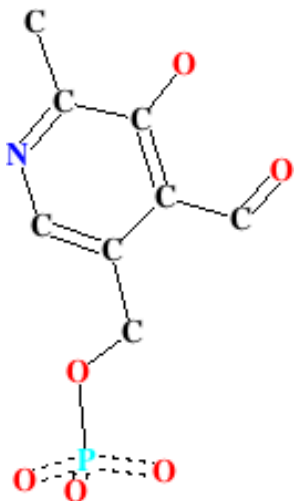
Bonds

Angles

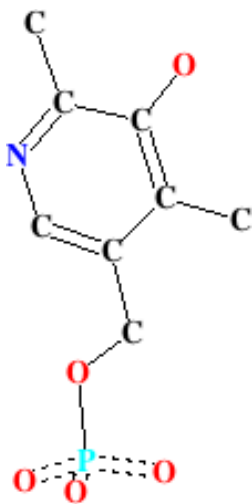
.....

The new link, "file view"

PLP



PLPmod1



Modification "PLPmod1":
changes to PLP

data_mod_PLPmod1

```

loop_
  _chem_mod_atom.mod_id
  _chem_mod_atom.function
  _chem_mod_atom.atom_id
  _chem_mod_atom.new_atom_id
  _chem_mod_atom.new_type_symbol
  _chem_mod_atom.new_type_energy
  _chem_mod_atom.new_partial_charge
  PLPmod1 delete O4A . . . .
  
```

Atom

```

loop_
  _chem_mod_bond.mod_id
  _chem_mod_bond.function
  _chem_mod_bond.atom_id_1
  _chem_mod_bond.atom_id_2
  _chem_mod_bond.new_type
  _chem_mod_bond.new_value_dist
  _chem_mod_bond.new_value_dist_esd
  PLPmod1 delete C4A O4A . . . .
  
```

Bond

```

loop_
  _chem_mod_angle.mod_id
  _chem_mod_angle.function
  _chem_mod_angle.atom_id_1
  _chem_mod_angle.atom_id_2
  _chem_mod_angle.atom_id_3
  _chem_mod_angle.new_value_angle
  _chem_mod_angle.new_value_angle_esd
  PLPmod1 delete H4A C4A O4A . . . .
  PLPmod1 delete C4 C4A O4A . . . .
  
```

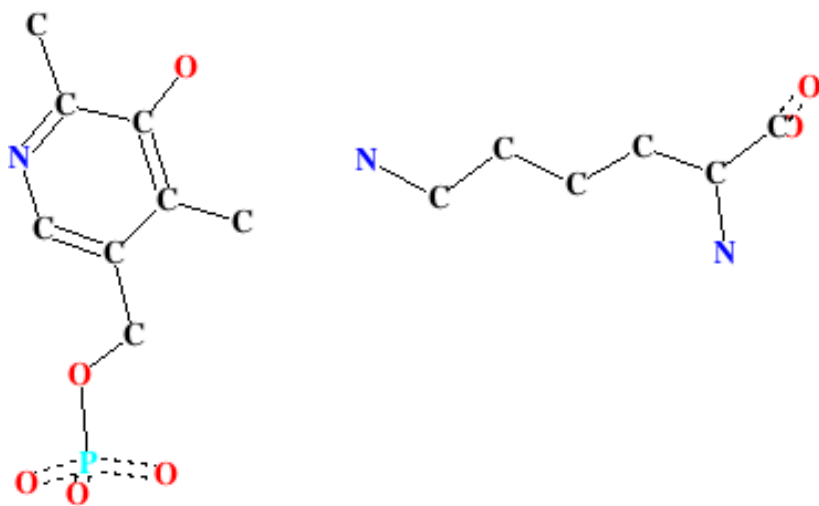
Angles

```

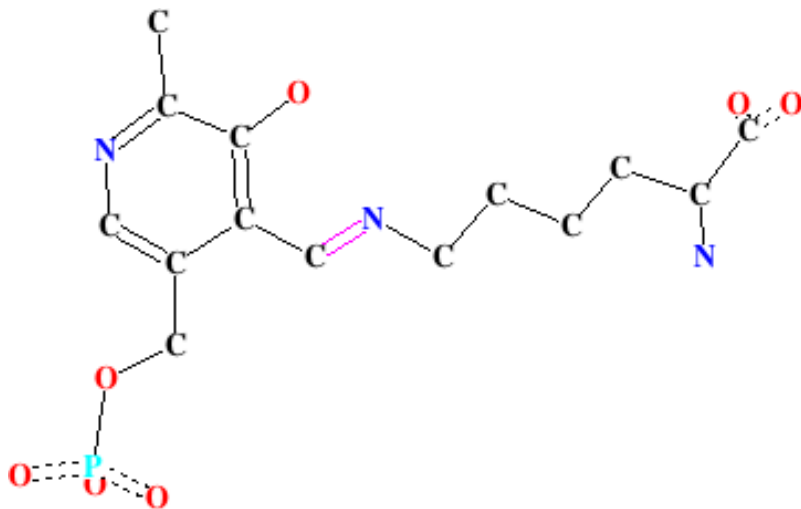
loop_
  _chem_mod_plane_atom.mod_id
  _chem_mod_plane_atom.function
  _chem_mod_plane_atom.plane_id
  _chem_mod_plane_atom.atom_id
  _chem_mod_plane_atom.new_dist_esd
  PLPmod1 delete plan-2 C4 . . . .
  PLPmod1 delete plan-2 C4A . . . .
  PLPmod1 delete plan-2 H4A . . . .
  PLPmod1 delete plan-2 O4A . . . .
  
```

Plane

The new link, "file view"



PLP-LYS



Link "PLP-LYS":
changes associated
with covalent linkage
between modified
PLP and LYS

data_link_PLP-LYS

loop_						
	_chem_link_bond.link_id	_chem_link_bond.atom_1_comp_id	_chem_link_bond.atom_id_1	_chem_link_bond.atom_2_comp_id	_chem_link_bond.atom_id_2	_chem_link_bond.type
	PLP-LYS 1	C4A	2	NZ	double	1.260 0.020

Bond

loop_						
	_chem_link_angle.link_id	_chem_link_angle.atom_1_comp_id	_chem_link_angle.atom_id_1	_chem_link_angle.atom_2_comp_id	_chem_link_angle.atom_id_2	_chem_link_angle.value_angle
	PLP-LYS 1	C4A	2	NZ	2	CE 120.000 3.000
	PLP-LYS 1	H4A	1	C4A	2	NZ 120.000 3.000
	PLP-LYS 1	C4	1	C4A	2	NZ 120.000 3.000

Angles

loop_			
	_chem_link_plane.link_id	_chem_link_plane.plane_id	_chem_link_plane.atom_comp_id
	PLP-LYS	plan-2	1 C4 0.020
	PLP-LYS	plan-2	1 C4A 0.020
	PLP-LYS	plan-2	1 H4A 0.020
	PLP-LYS	plan-2	2 CE 0.020
	PLP-LYS	plan-2	2 NZ 0.020

Plane

Utilising new link description

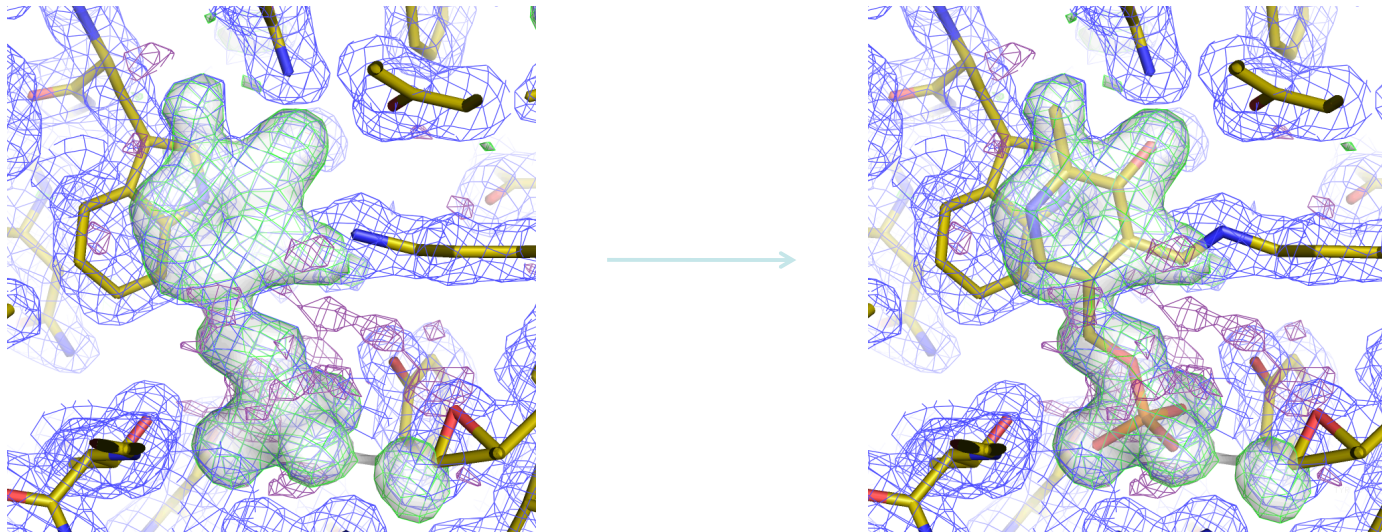
Three remaining steps:

- docking monomer(s) into electron density
- defining link in the pdb-file
- refinement of the structure with linked ligand using additional library

(I) Docking into the electron density

In our example, this is completely independent step: the additional library is not used.

- non-modified monomer is taken from the standard library
- docking is performed, e.g. using coot:



- leaving atoms (O4A of PLP in this example) are removed
- in our example, one of the monomers (LYS) is already in the model

(2) Defining link in the pdb-file

In general case, link cannot be applied automatically.

For example:

- e.g. the same two atoms of the same two compounds can form single or double bond
- H-atom are not defined in the PDB-file

Therefore REFMAC needs additional instructions:

residues to link link to use

```
Terminal - vim - 81x14
CISPEP  1 SER A  137  PRO A  138          0.00
CISPEP  2 ASN A  194  PRO A  195          0.00
CISPEP  3 SER B  137  PRO B  138          0.00
CISPEP  4 ASN B  194  PRO B  195          0.00

LINKR   NZ  LYS B 258
        C4A PLP D  1
        LYS-PLP

CRYST1  125.000  130.800  55.800  90.00  90.00  90.00 P 21 21 21
SCALE1   0.008000  0.000000  0.000000          0.000000
SCALE2  -0.000000  0.007645  0.000000          0.000000
SCALE3   0.000000 -0.000000  0.017921          0.000000
ATOM     1  N  ALA A  1  -76.191 -36.168 -21.452  1.00 49.90  N
ATOM     2  CA ALA A  1  -74.845 -35.859 -20.889  1.00 49.65  C
```

(3) Refinement using additional library

Additional library is defined
here

The screenshot shows the 'Run Refmac5' dialog box. The 'LIB in' field is highlighted with a yellow background and contains the text 'refmac.cif'. An arrow points from the text 'Additional library is defined here' to this field. Other fields include 'Job title' (model with ligands), 'Do' (restrained refinement), 'using' (no prior phase information), 'Input fixed TLS parameters' (no), 'twin refinement' (no), 'MTZ in' (1ajs, data.mtz), 'FP' (FP, Sigma), 'MTZ out' (1ajs, refmac2.mtz), 'PDB in' (1ajs, refmac1-coot-0.pdb), 'PDB out' (1ajs, refmac2.pdb), 'Output lib' (1ajs, refmac2.cif), and 'Include keyword file' (1ajs). There are 'Browse' and 'View' buttons for most file fields, and a 'Merge LIBINs' button next to the 'LIB in' field. At the bottom, there are 'Run', 'Save or Restore', and 'Close' buttons.

Job title	model with ligands	
Do	restrained refinement	using no prior phase information input
<input type="checkbox"/> Input fixed TLS parameters	no	
<input type="checkbox"/> twin refinement	no	
MTZ in	1ajs	data.mtz
FP	FP	Sigma
MTZ out	1ajs	refmac2.mtz
PDB in	1ajs	refmac1-coot-0.pdb
PDB out	1ajs	refmac2.pdb
LIB in	1ajs	refmac.cif
Output lib	1ajs	refmac2.cif
Include keyword file	1ajs	

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Jligand is available from CCP4 or from York's ftp site:

www.ysbl.york.ac.uk/mxstat/JLigand

or google jligand

This and other presentations can be found on:

www.ysbl.york.ac.uk/refmac/Presentations/

