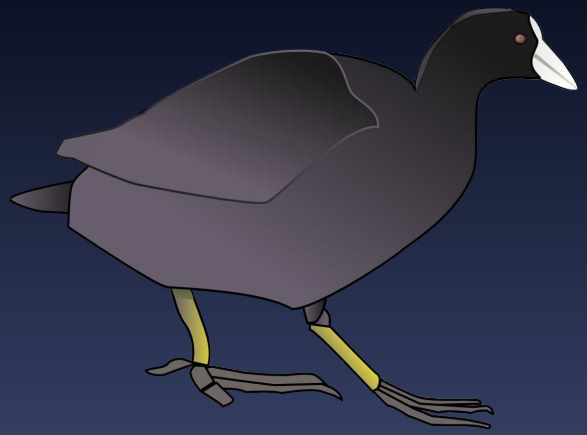
December 2011 Okinawa



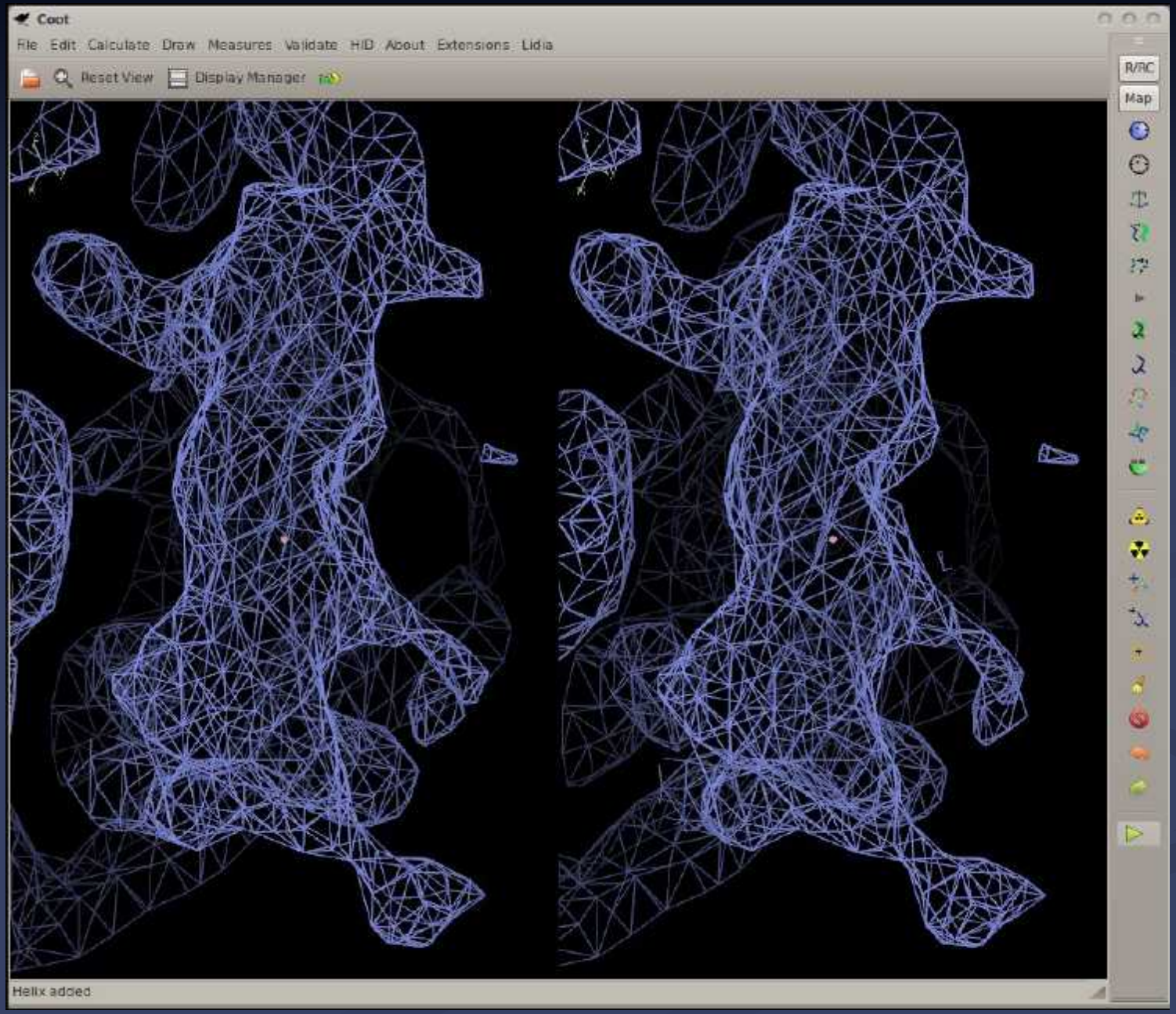
Model-Building with Coot

Secondary structure tools

Bernhard Lohkamp

Karolinska Institutet

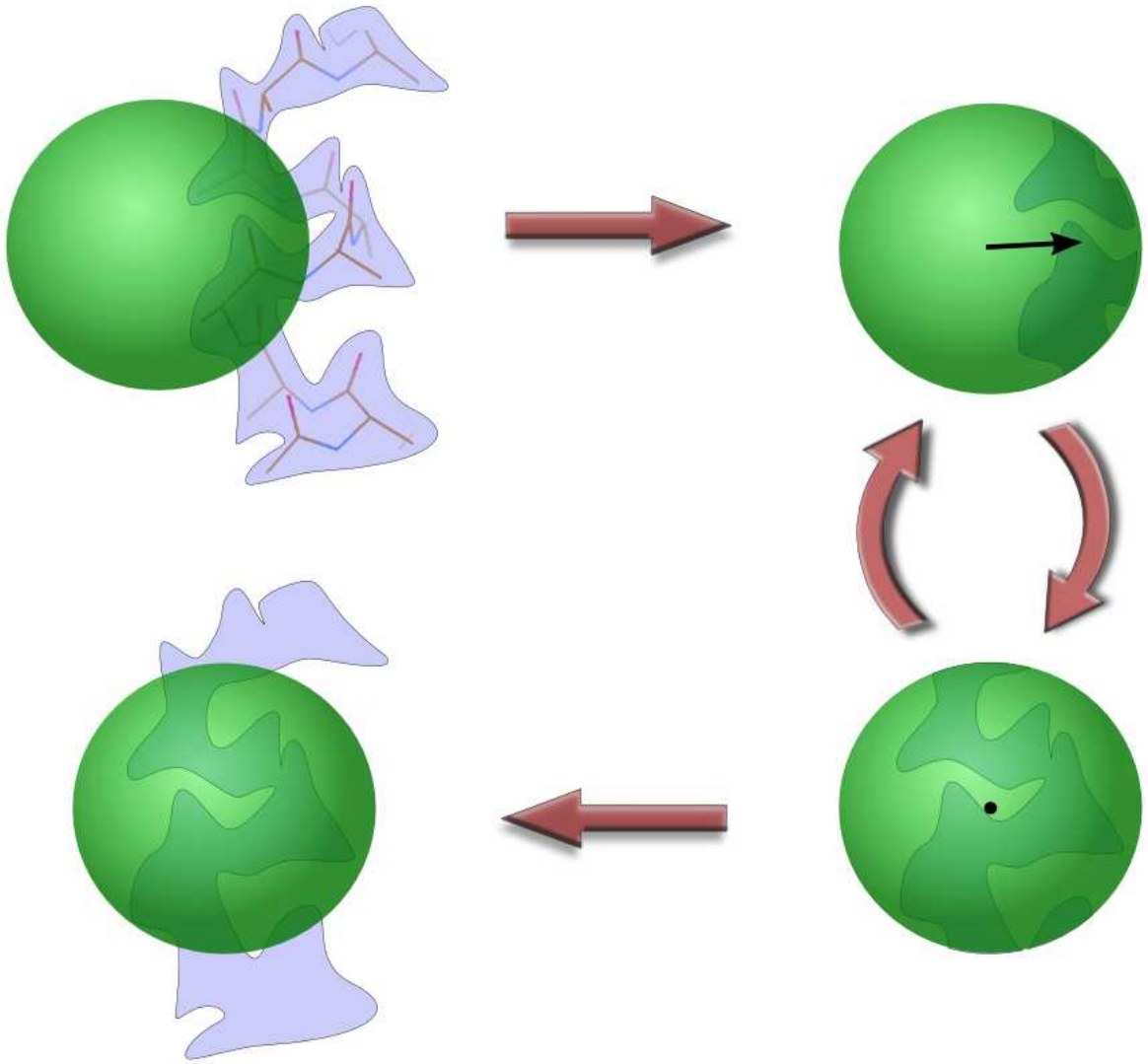
Helix-Building


Coot
File Edit Calculate Draw Measures Validate HID About Extensions Lidia
Reset View
Display Manager
R/RC
Map
Helix added

Alpha Helix Placement

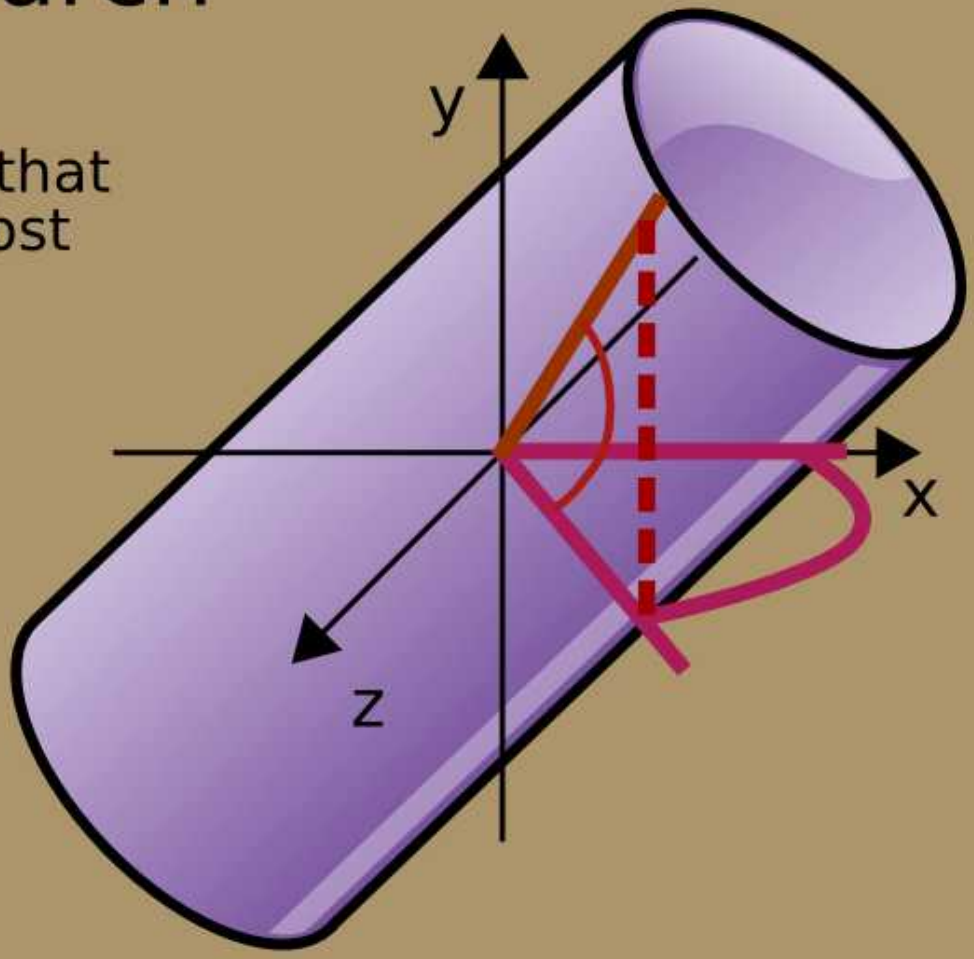
- Scenario: Looking at a new map, not built with automatic tools:
  - “I can see that there’s a helix here - build it for me!”
- From a given point:
  - Move to local averaged maximum
  - Do a 2D MR-style orientation search on a cylinder of electron density
  - Build a helix (both directions)
  - 1D Rotation search to find best fit
  - Score based on density at CB positions
  - Trim ‘n Grow

Centering the Rotation point

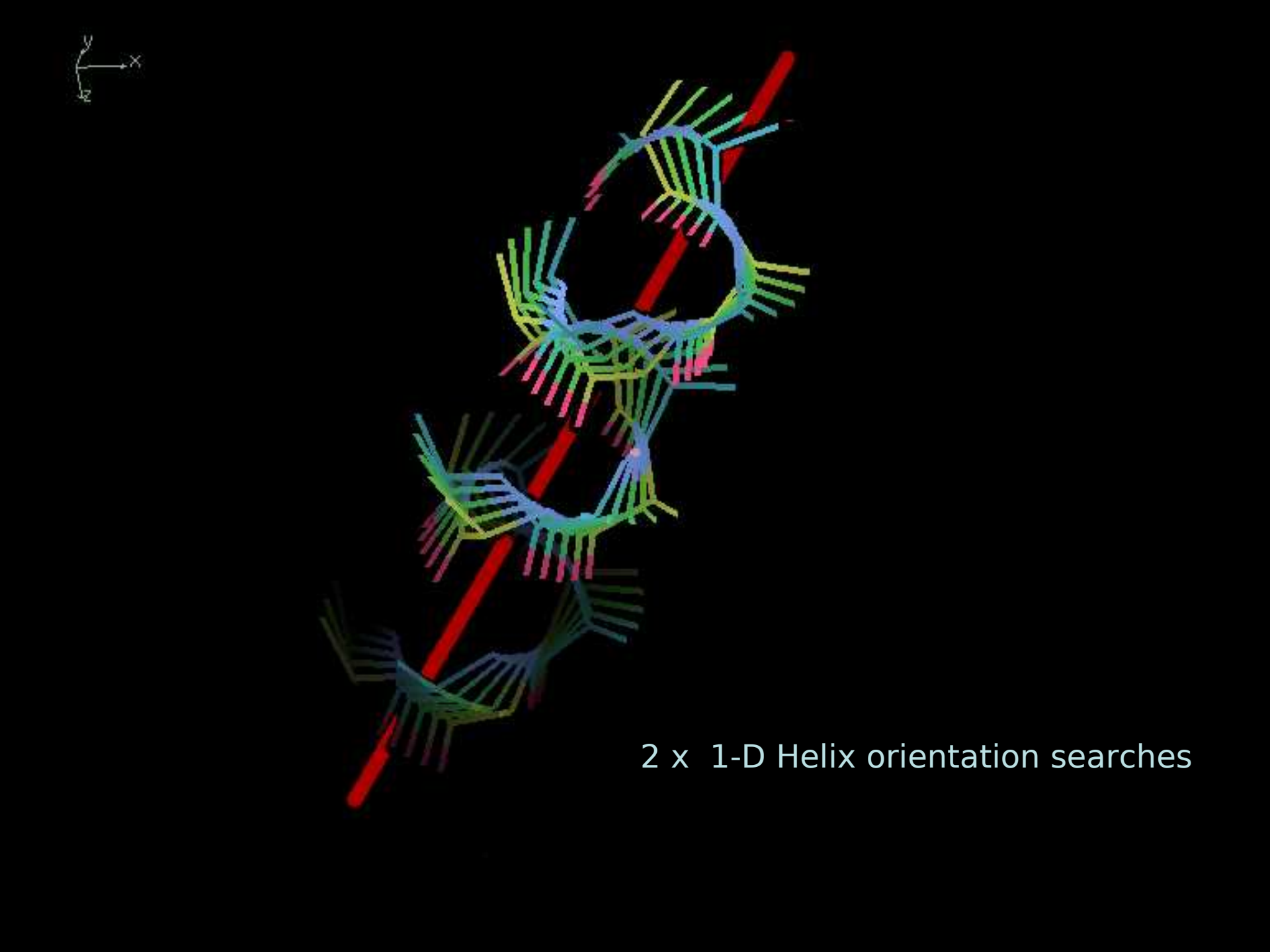


Cylinder Search

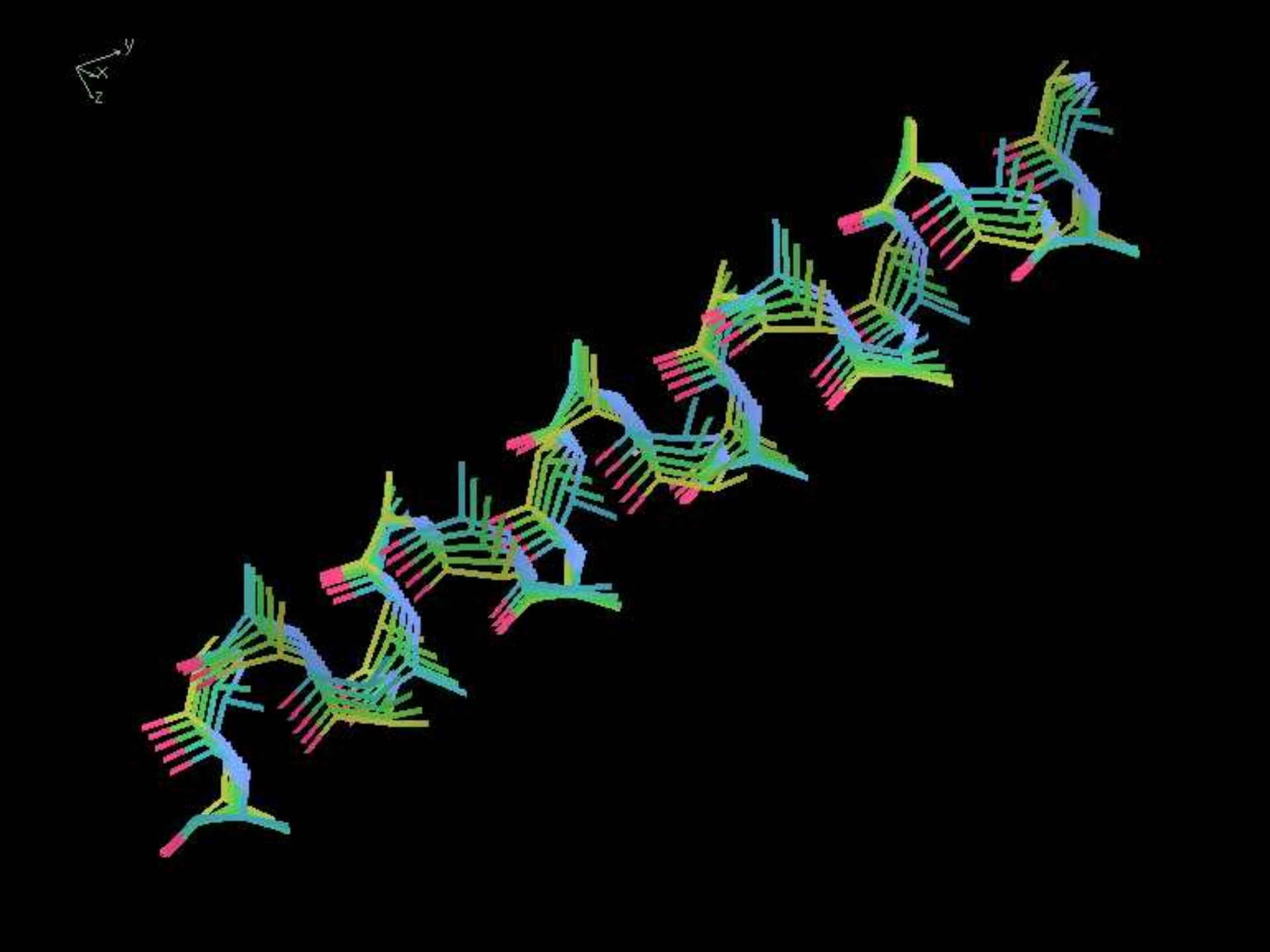
Pick the orientation that encapsulates the most electron density

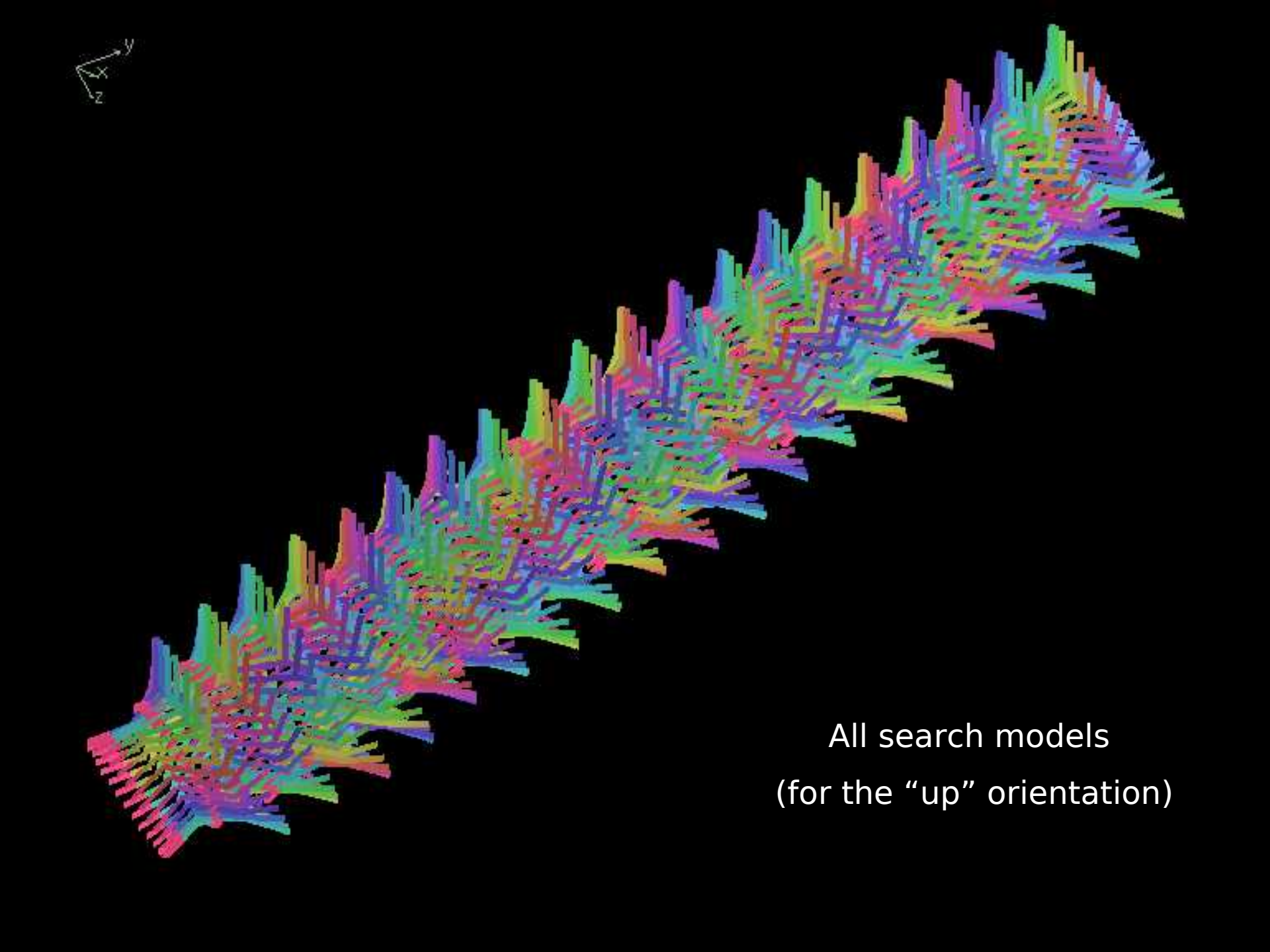


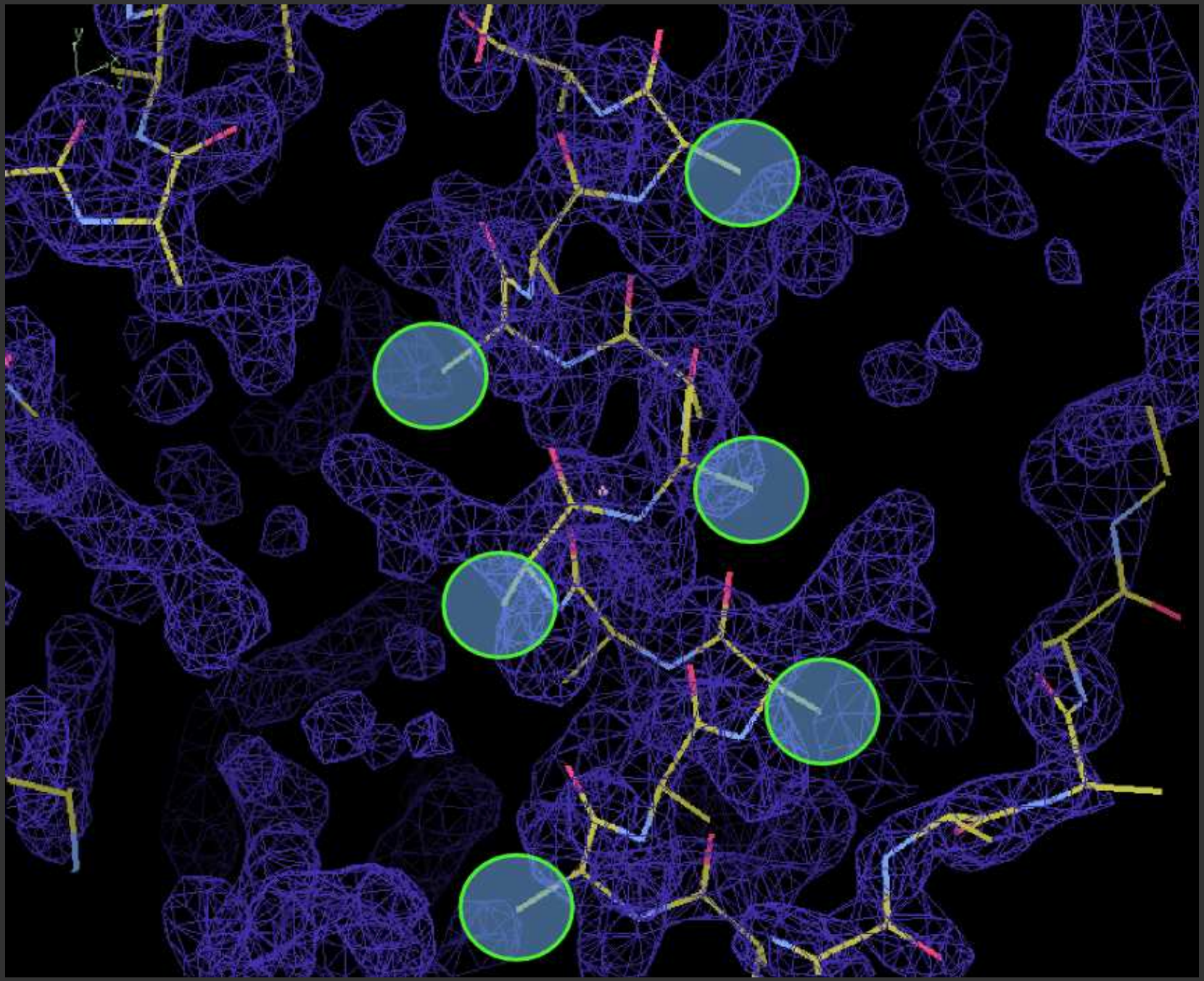
2 orientation axes

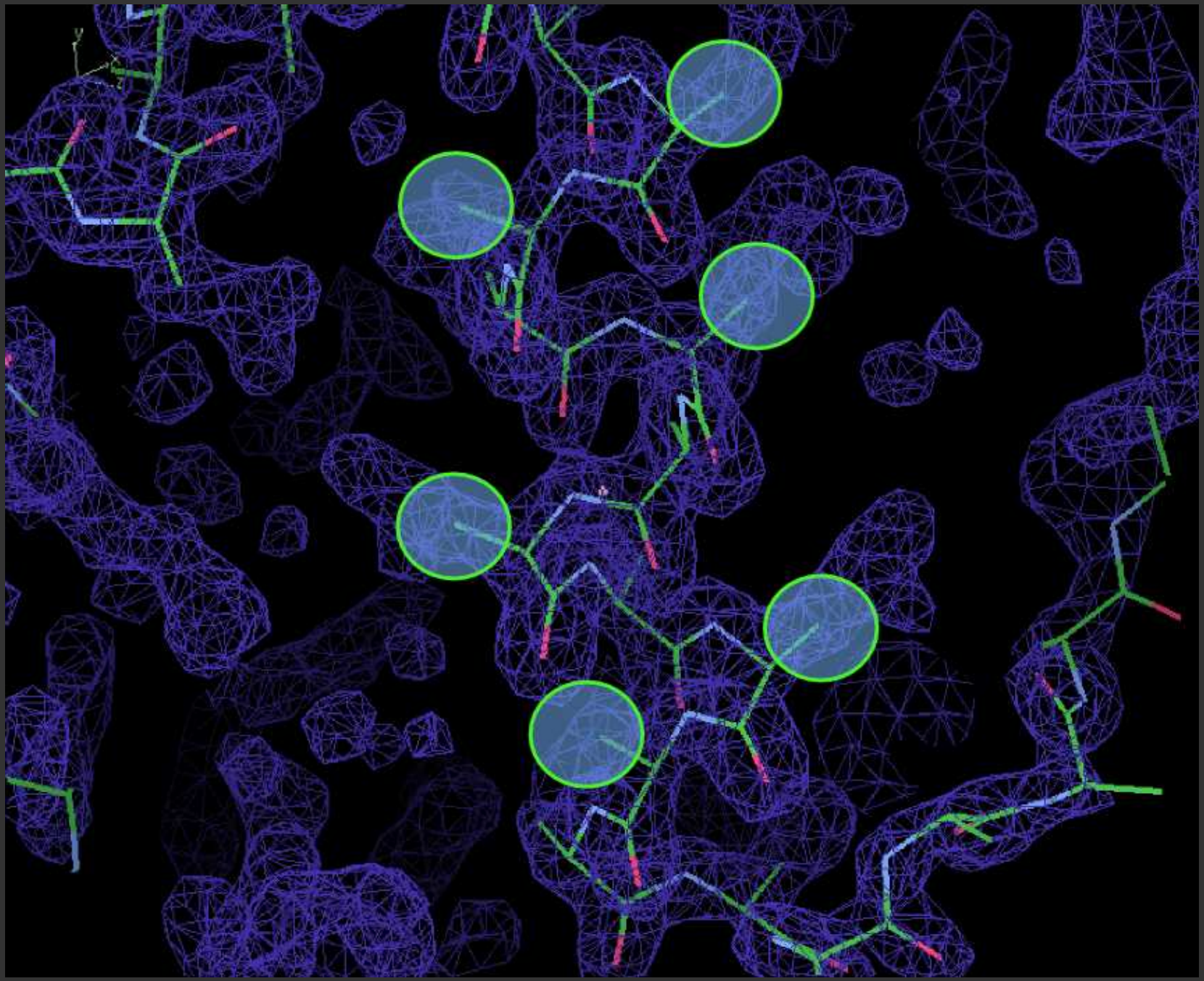


2 x 1-D Helix orientation searches


y
x
z


y
x
z
All search models
(for the “up” orientation)





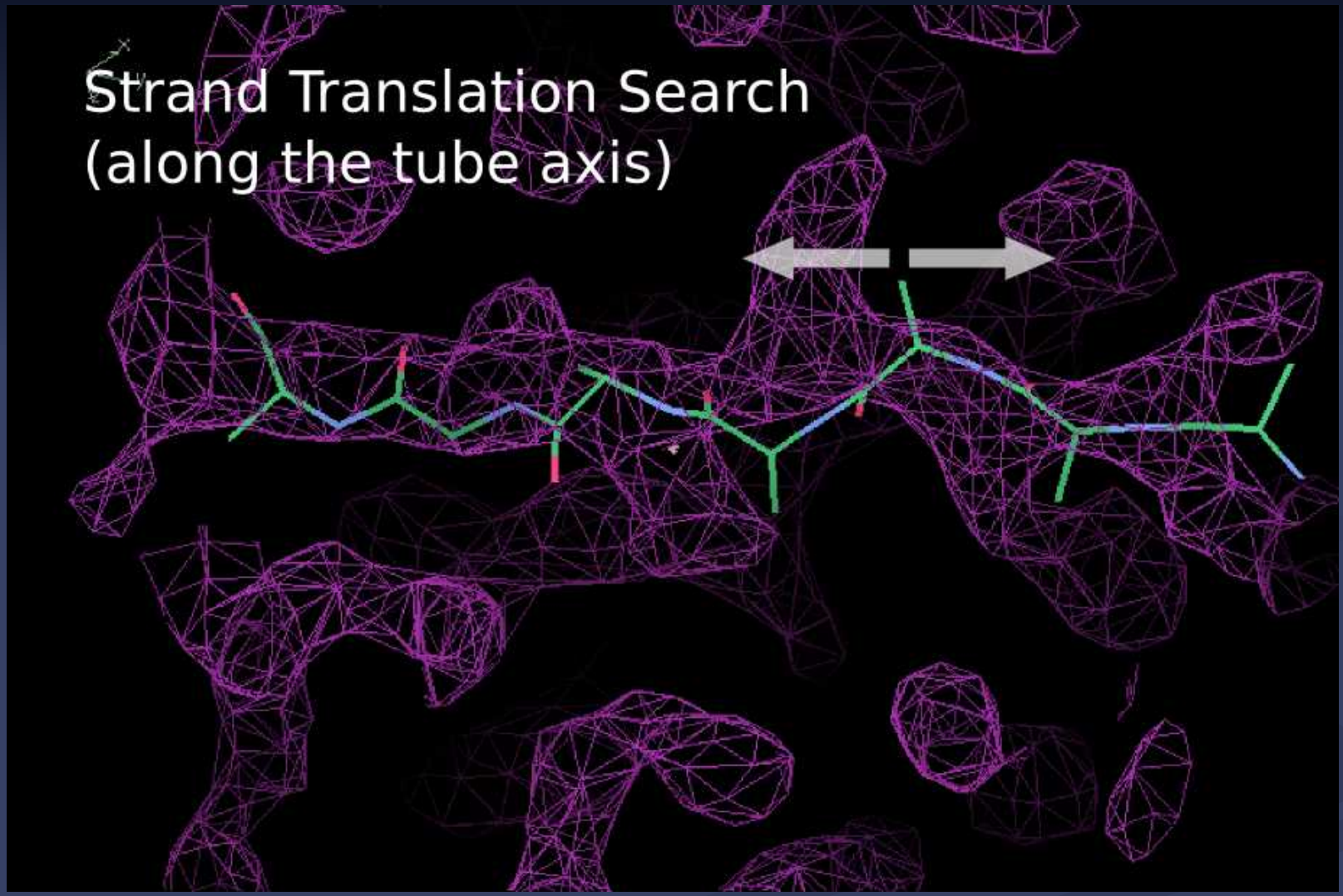
Fitting Strands

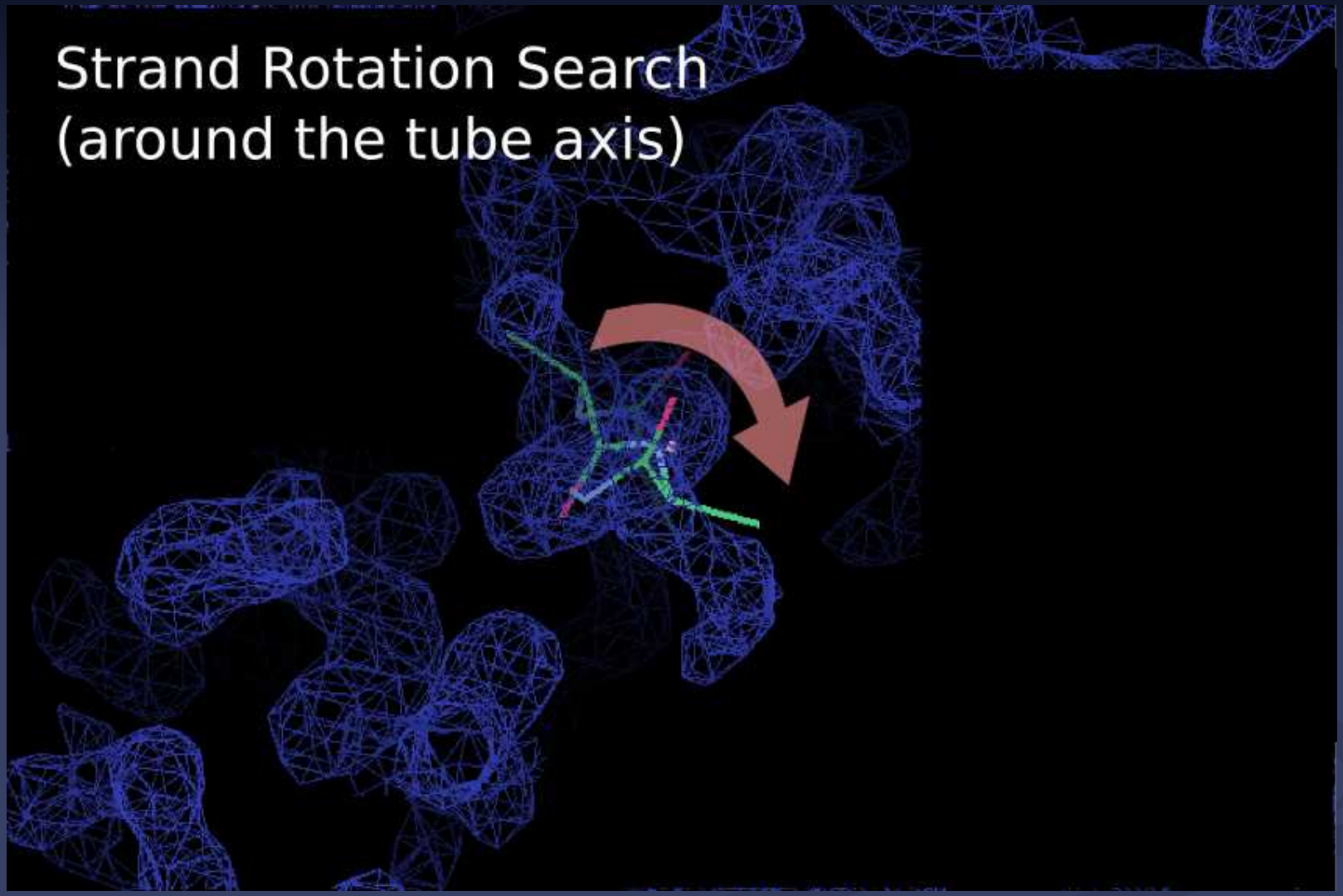
Placing Strands

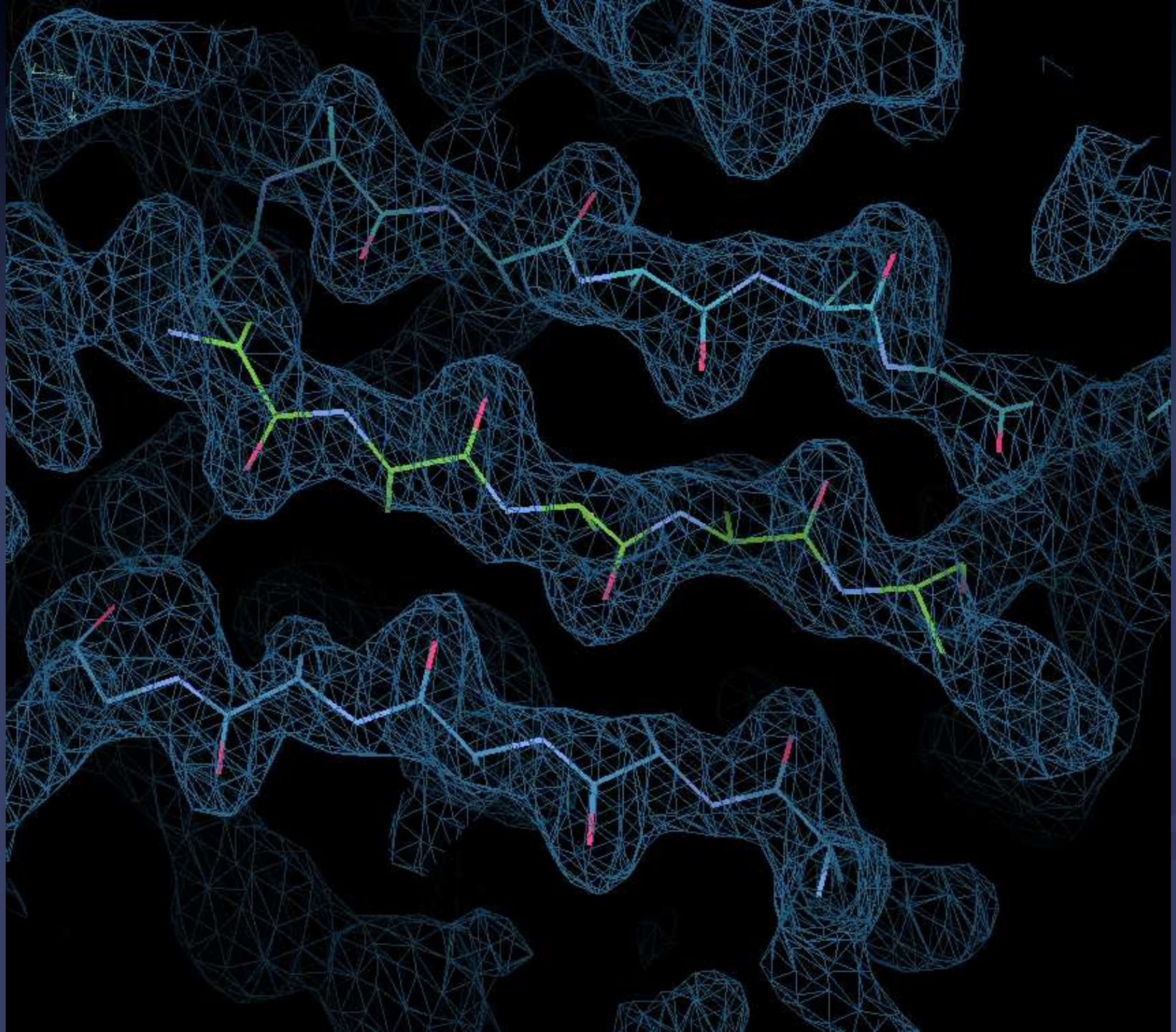
- Unlike Helices, Strands have to be treated as non-idealized
  - Repeating a single phi/psi value doesn't make a structure that fits “real-world” density
- Curvature of strands should be taken into account
  - Use selections from a “database” of good structures

Strand fitting algorithm

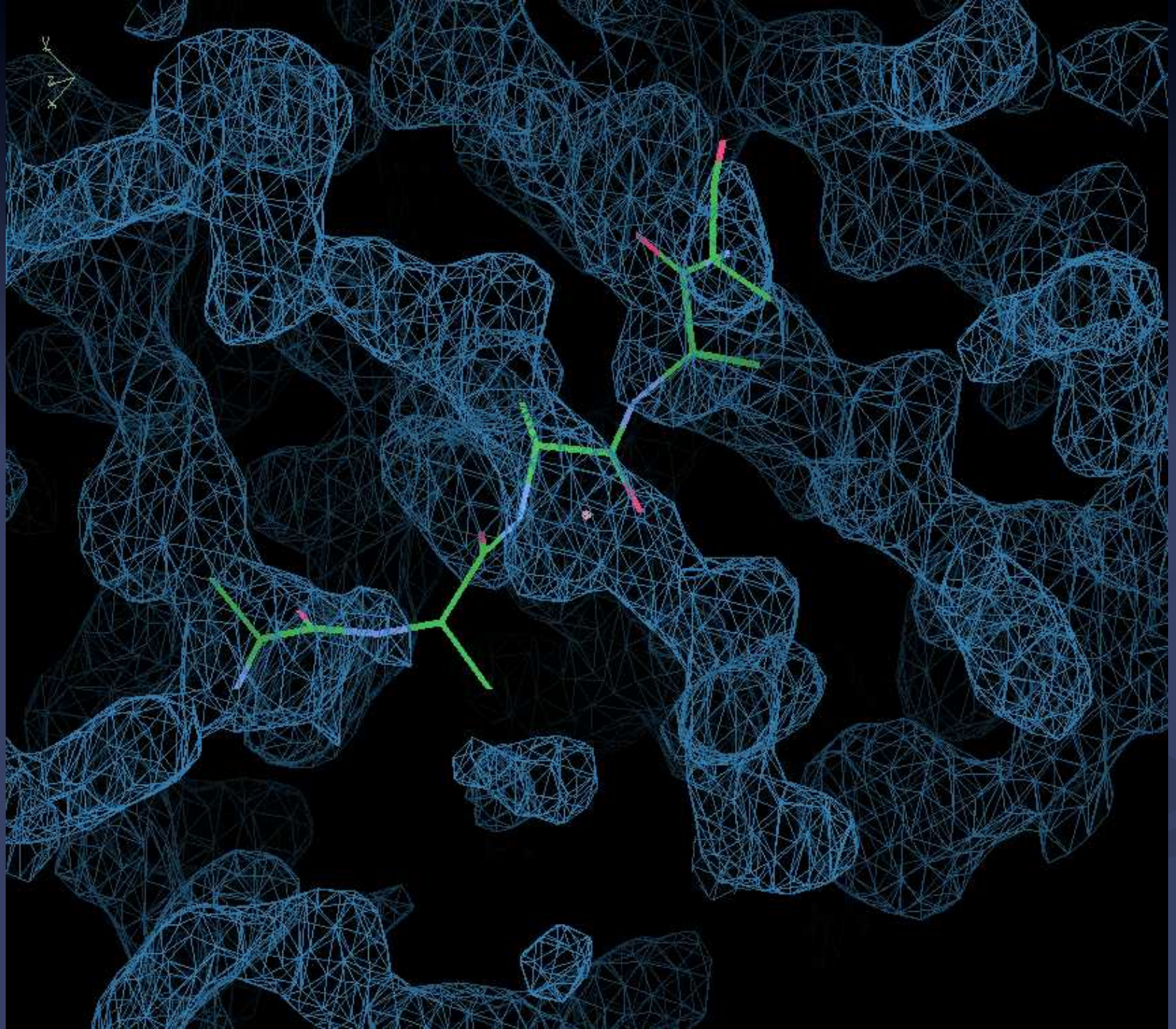
- Cylinder search
- Get N fragments of length l from database
  - 1-D Translation search along the tube
    - 1-D Rotation search around the tube
    - Direction flip search
- Rigid body refine best solutions
- Real-space refine best solution


Strand Translation Search
(along the tube axis)


Strand Rotation Search
(around the tube axis)



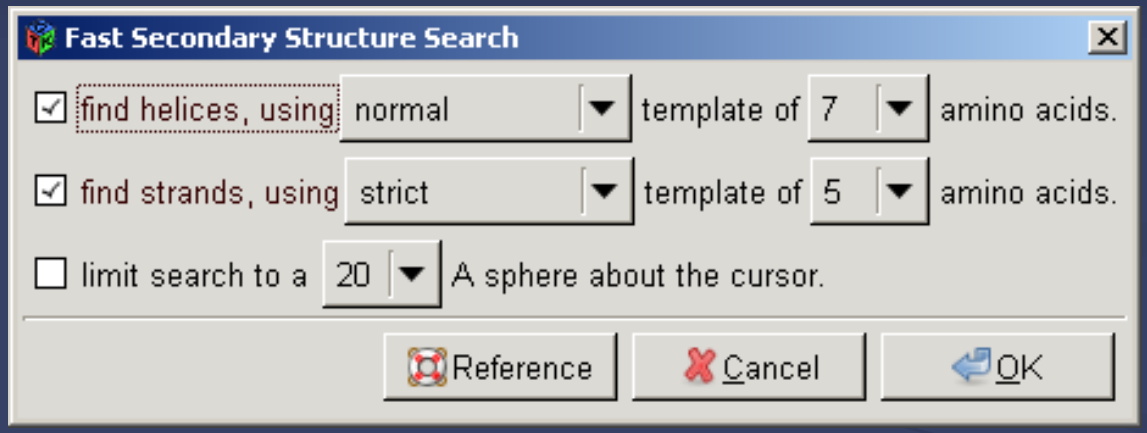
Not all is rosy...

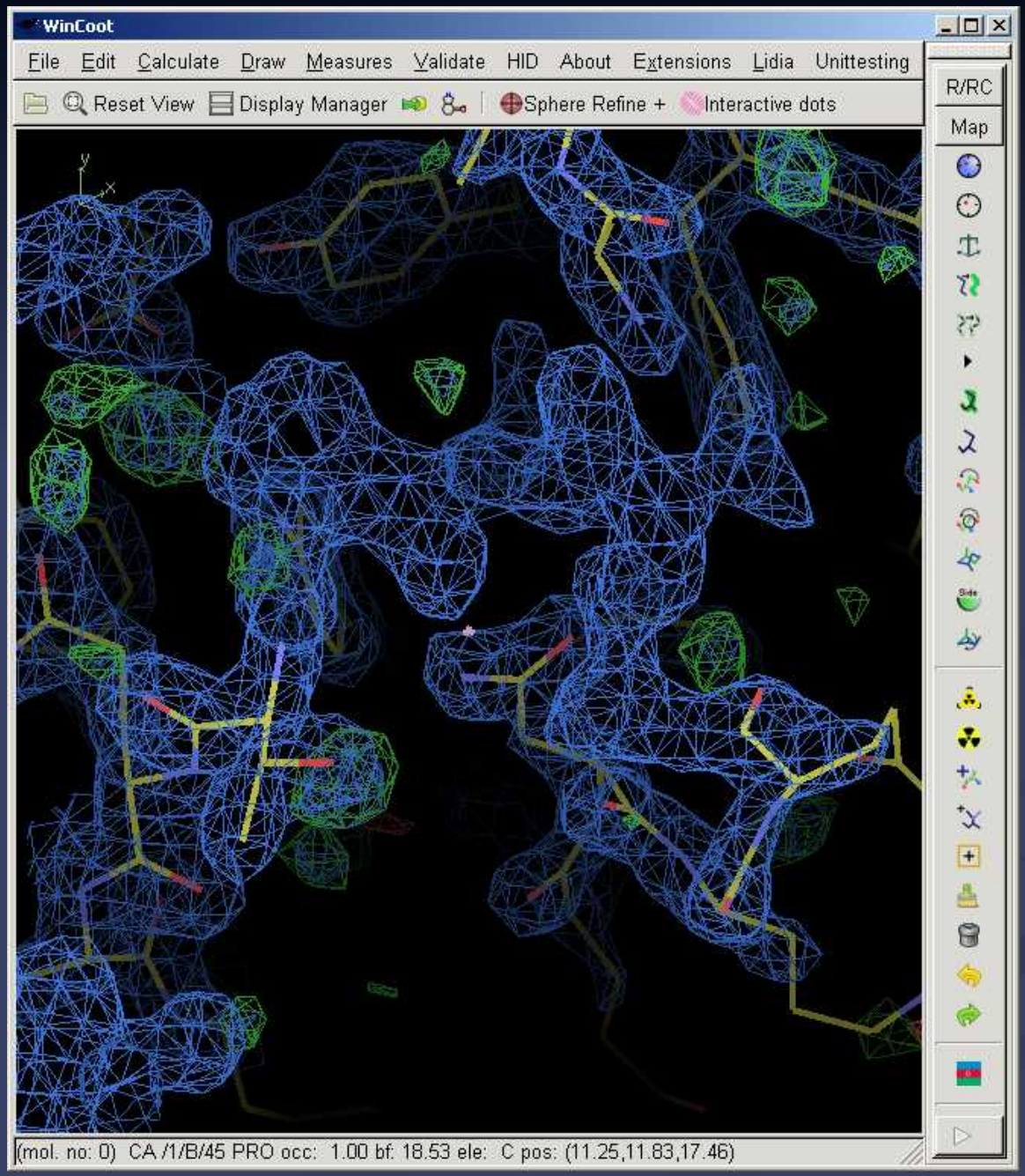


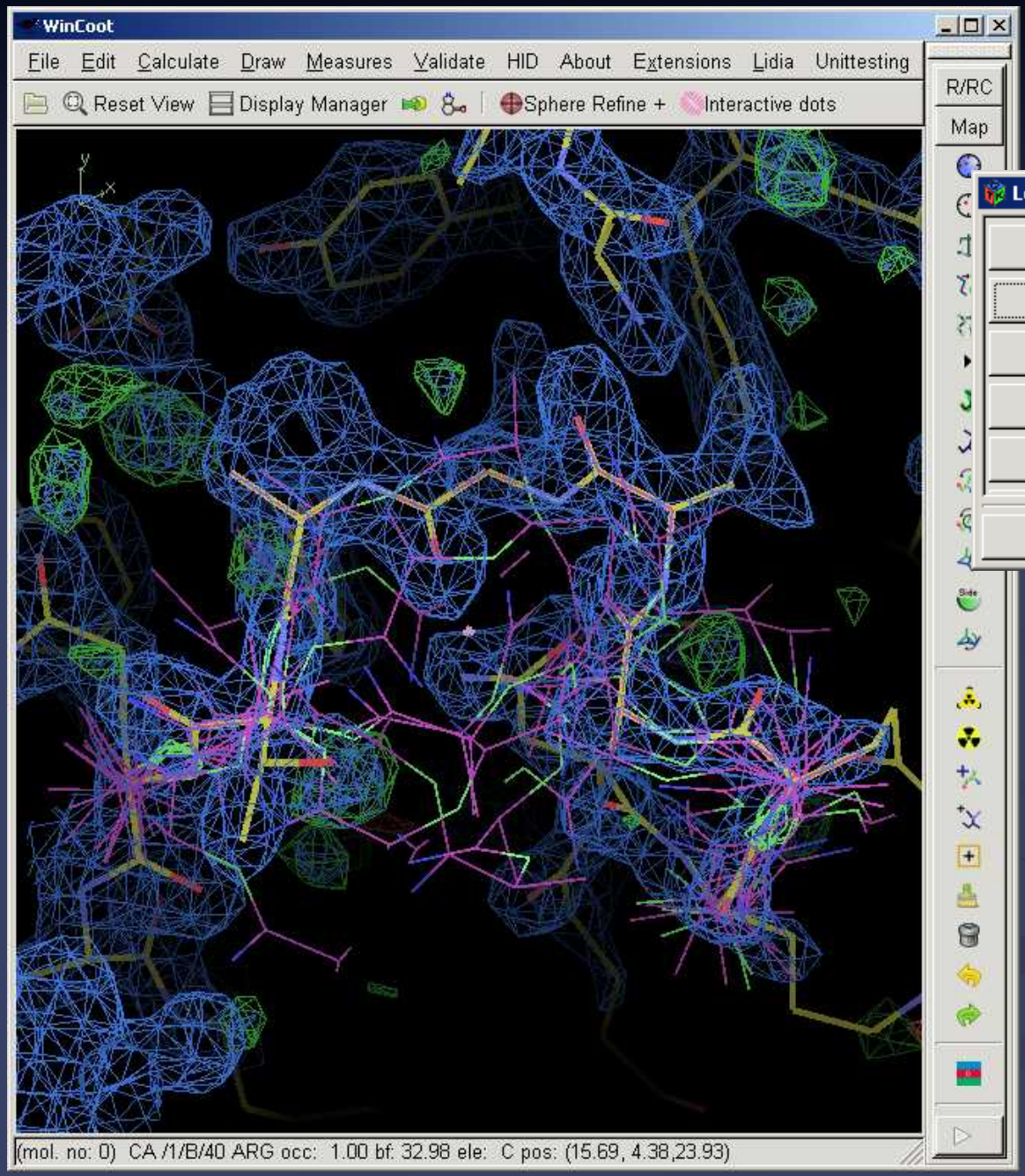
Fitting Strands caveat

- In the case of strand-fitting, the initial translation search centring the cylinder is not performed (the search cylinder is too thin)
- The user is responsible for centring the search point “in the middle of the tube”
- Not at a C-alpha position

Automated Fast Secondary Structure Search



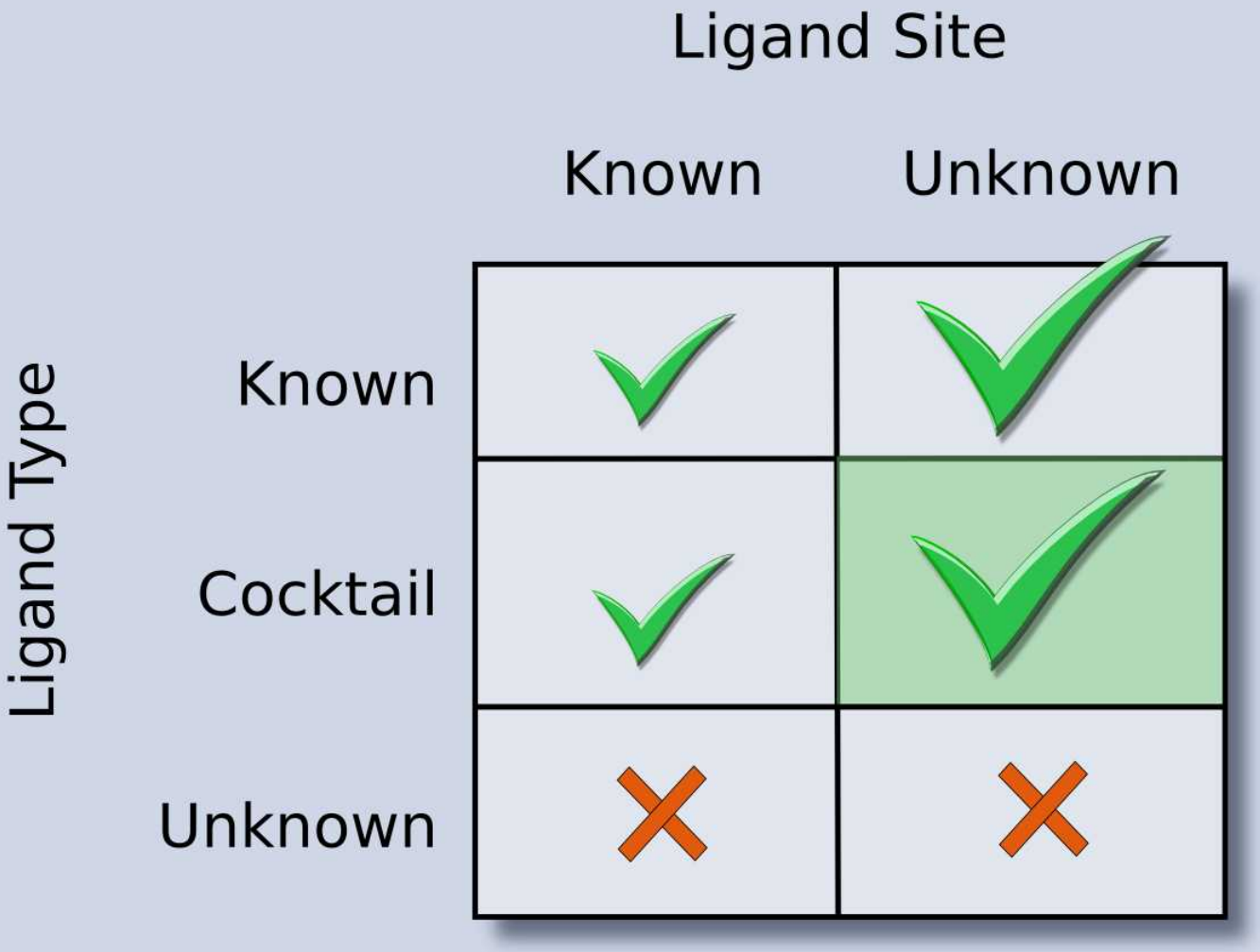

WinCoot
File Edit Calculate Draw Measures Validate HID About Extensions Lidia Unittesting
Reset View
Display Manager
Sphere Refine +
Interactive dots
R/RC
Map
(mol. no: 0) CA /1/B/45 PRO occ: 1.00 bf: 18.53 ele: C pos: (11.25,11.83,17.46)

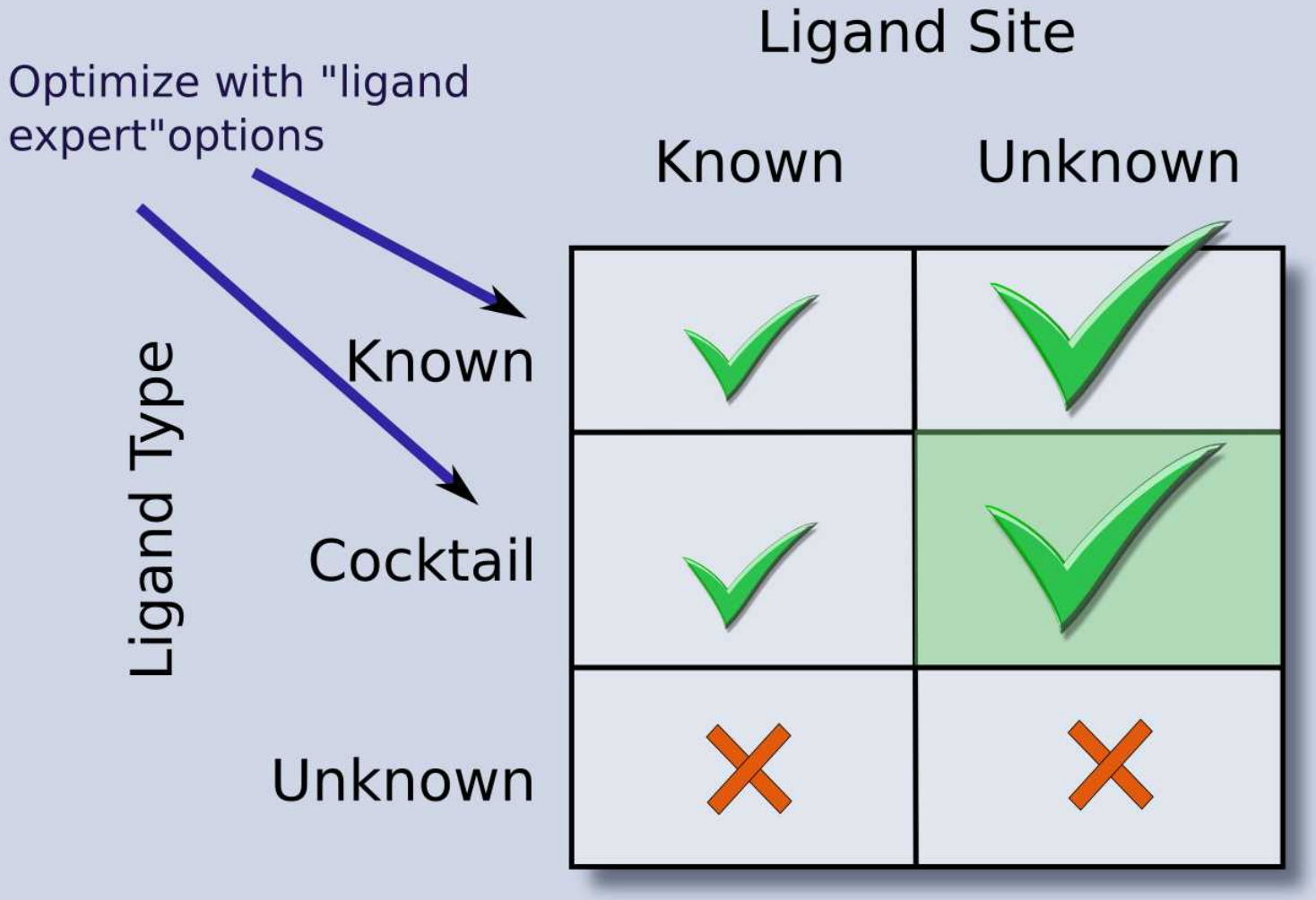

WinCoot
File Edit Calculate Draw Measures Validate HID About Extensions Lidia Unittesting
Reset View
Display Manager
Sphere Refine +
Interactive dots
R/RC
Map
Loop Candidates
Original loop
Toggle All Candidate Loops
3 Loop candidate #1
4 Loop candidate #2
5 Loop candidate #3
Close
(mol. no: 0) CA /1/B/40 ARG occ: 1.00 bf: 32.98 ele: C pos: (15.69, 4.38,23.93)

Fitting Ligands

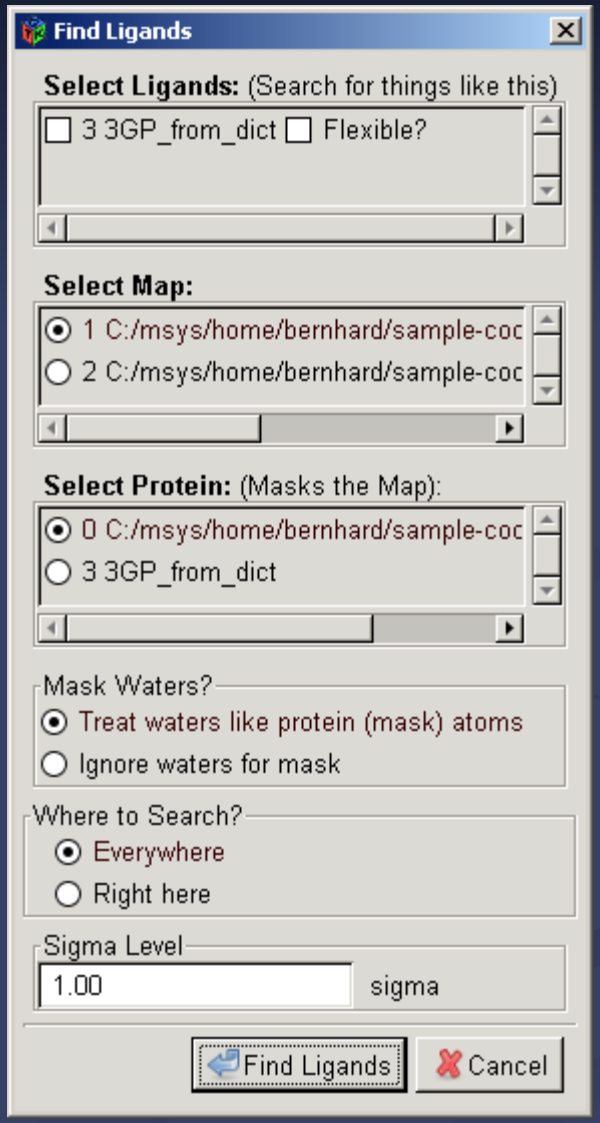
Ligands in Coot

- Fitting ligand
- Ligand validation
- Ligand representation
- Ligand builder


Ligand Site
Known
Unknown
Ligand Type
Known
Cocktail
Unknown


Optimize with "ligand expert"options
Ligand Site
Known
Unknown
Ligand Type
Known
Cocktail
Unknown

Ligand search in Coot



Ligand Fitting

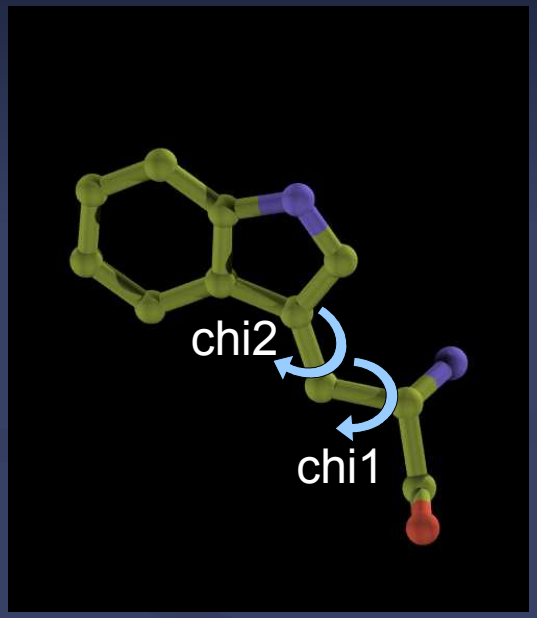
- *c.f.* Oldfield (2001) *Acta Cryst. D* X-LIGAND
- Somewhat different torsion search algorithm
- Build in crystal-space

REFMAC Monomer Library chem_comp_bond

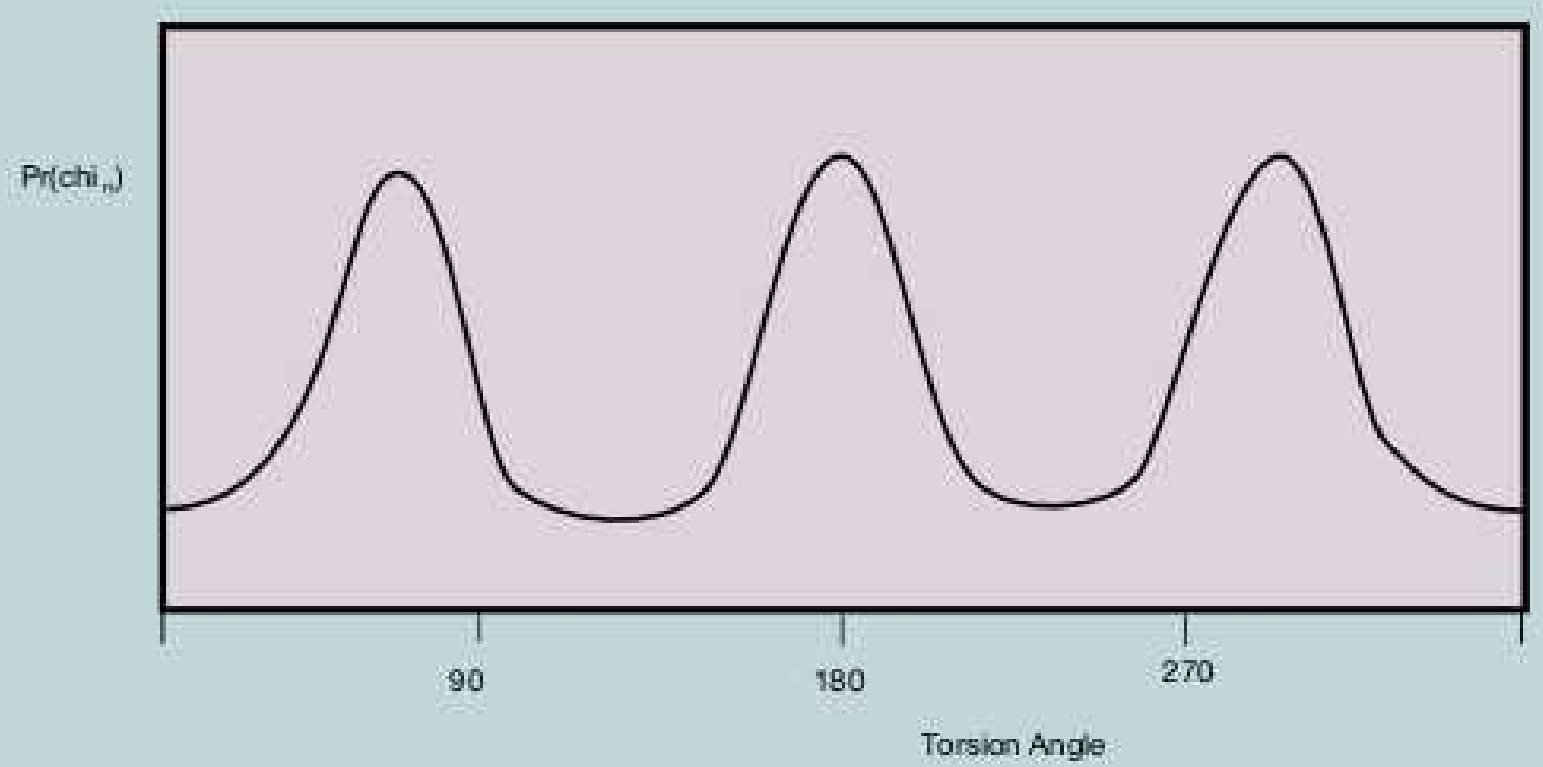
```
loop_
_chem_comp_bond.comp_id
_chem_comp_bond.atom_id_1
_chem_comp_bond.atom_id_2
_chem_comp_bond.type
_chem_comp_bond.value_dist
_chem_comp_bond.value_dist_esd
 ALA      N    H      single    0.860    0.020
 ALA      N    CA     single    1.458    0.019
 ALA      CA   HA     single    0.980    0.020
 ALA      CA   CB     single    1.521    0.033
 ALA      CB   HB1    single    0.960    0.020
 ALA      CB   HB2    single    0.960    0.020
 ALA      CB   HB3    single    0.960    0.020
 ALA      CA   C      single    1.525    0.021
 ALA      C    O      double    1.231    0.020
```

REFMAC Monomer Library chem_comp_tor

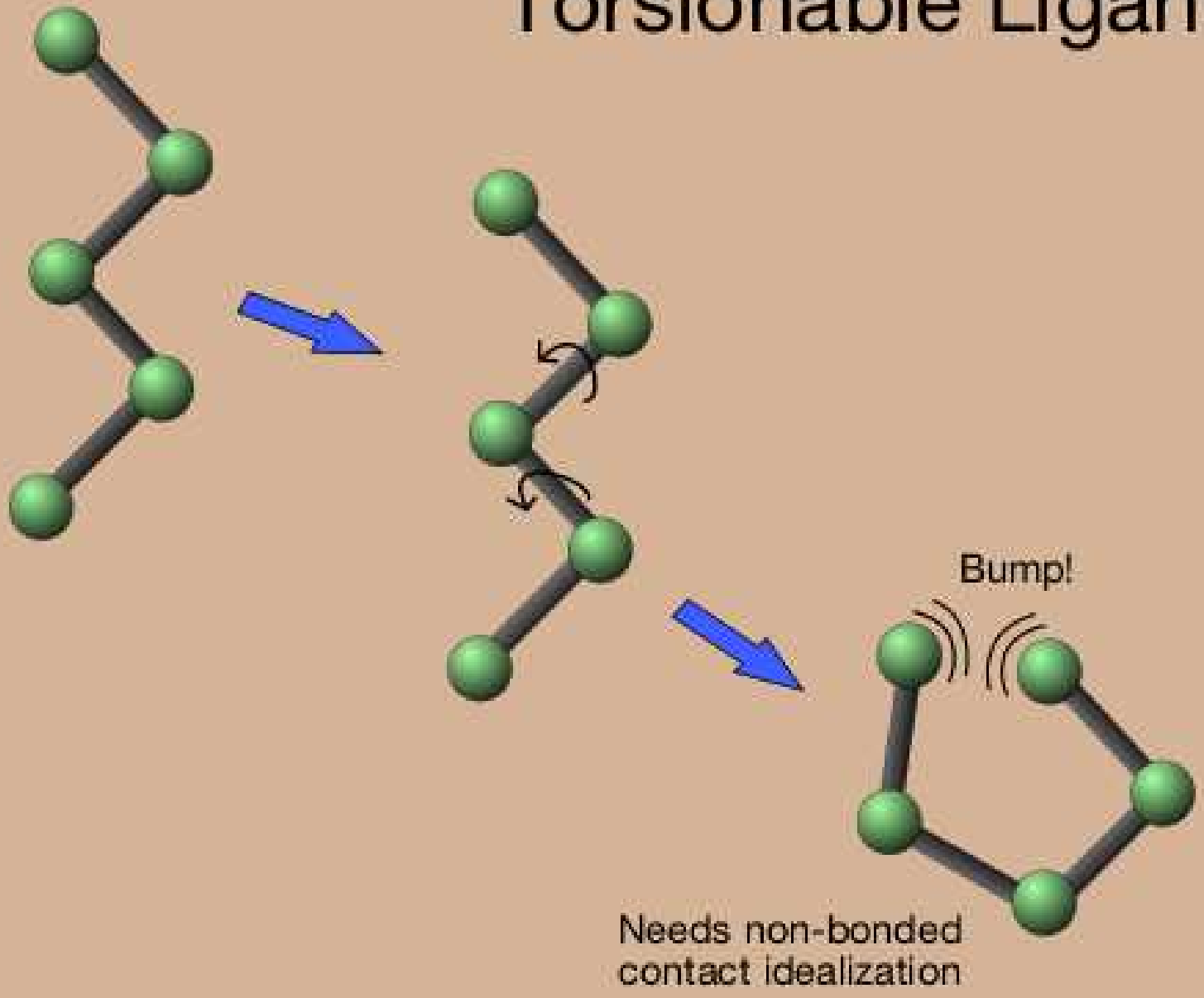
```
loop_
_chem_comp_tor.comp_id
_chem_comp_tor.id
_chem_comp_tor.atom_id_1
_chem_comp_tor.atom_id_2
_chem_comp_tor.atom_id_3
_chem_comp_tor.atom_id_4
_chem_comp_tor.value_angle
_chem_comp_tor.value_angle_esd
_chem_comp_tor.period
 TRP   chi1  N   CA  CB  CG  180.000   15.000   3
 TRP   chi2  CA  CB  CG  CD1  90.000   20.000   2
```



Ligand Torsionable Angle Probability from CIF file



Torsionable Ligands

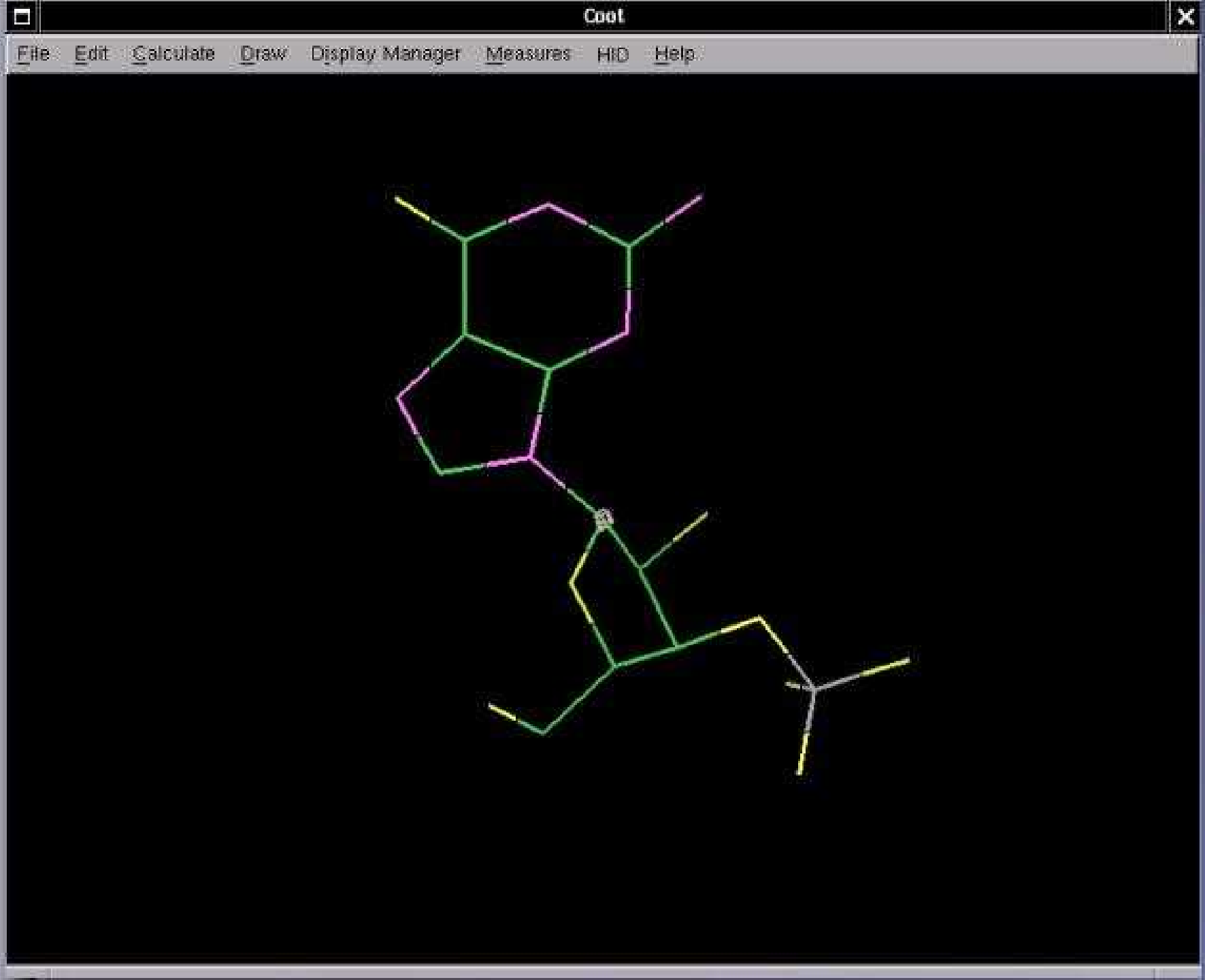


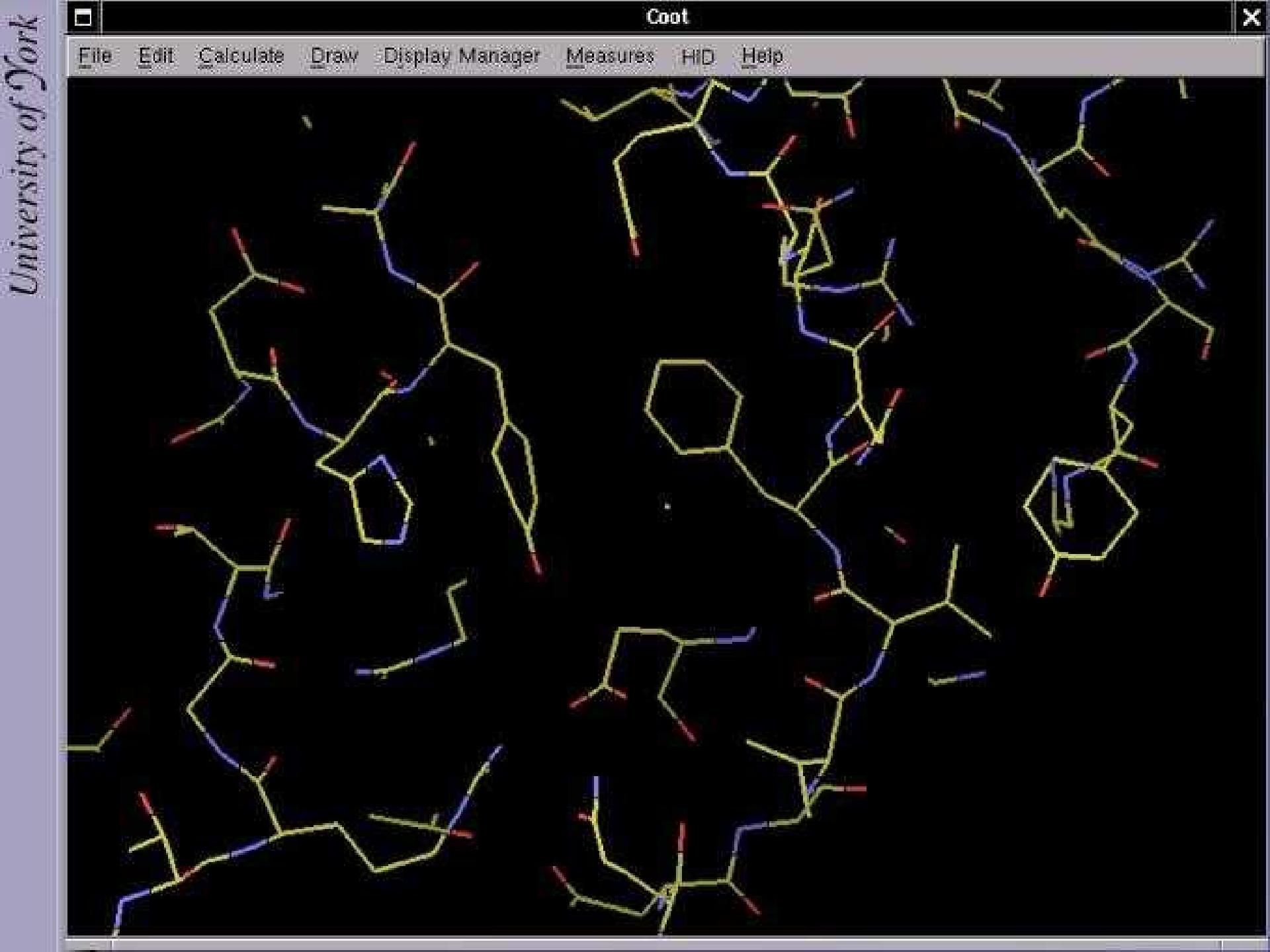
Crystal Space

- Build in “crystal space”
  - Like real-space, but wrapped by crystal symmetry
    - Like “Asteroids”
  - Assures only one real-space representation of map features
    - Build everything only once
    - No symmetry clashing
  - However, more difficult to calculate real space geometries
    - …such as bonds, torsions

Crystal space

- Building in crystal space is good:
  - We don't need to define where the protein is and create an extended map that surrounds it
  - We don't have to worry about the relative position of the ligand and the protein
    - Unknown "BORDER" parameter
  - We find (and fit) each site exactly once
    - No symmetry problems

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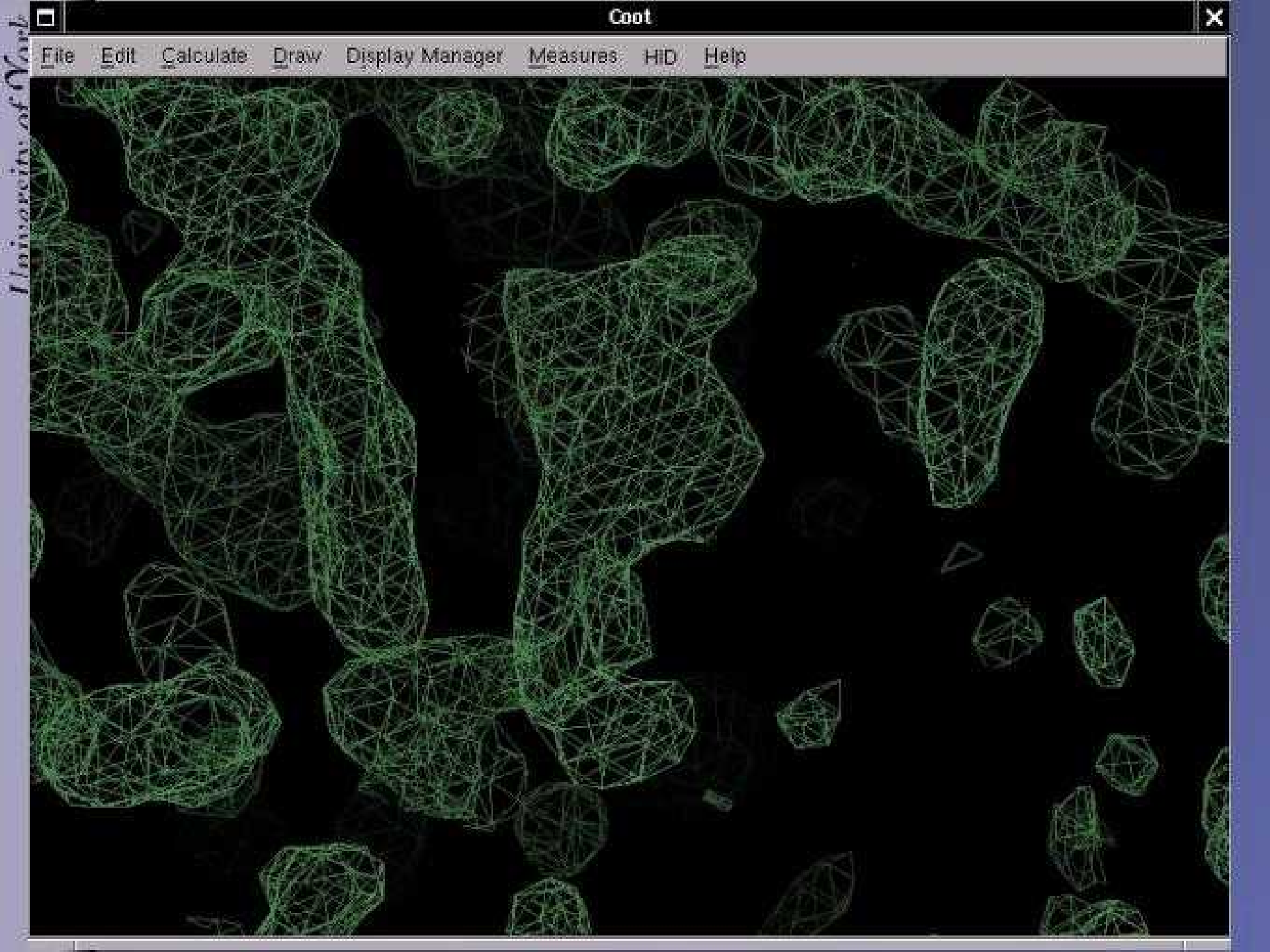
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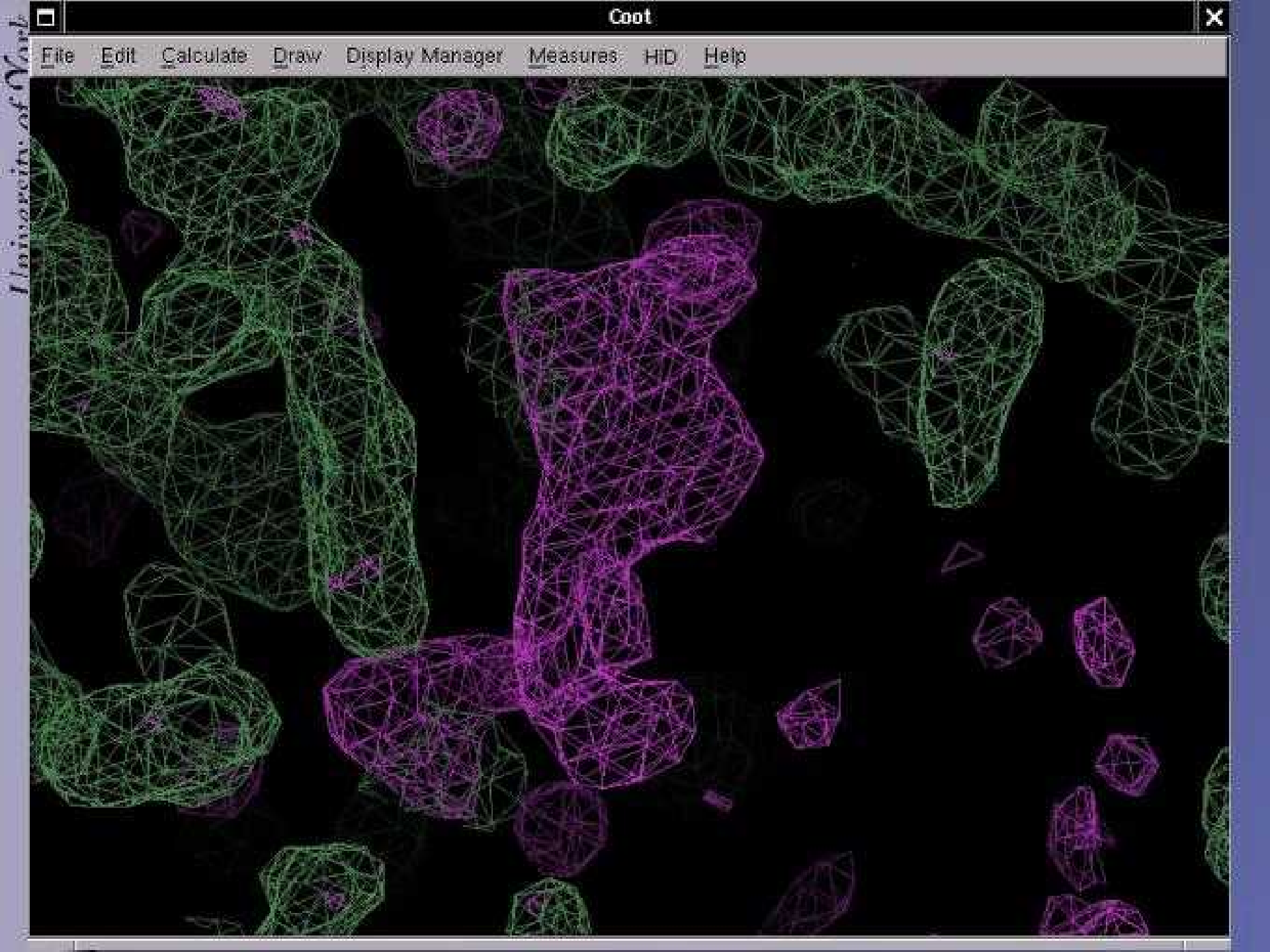
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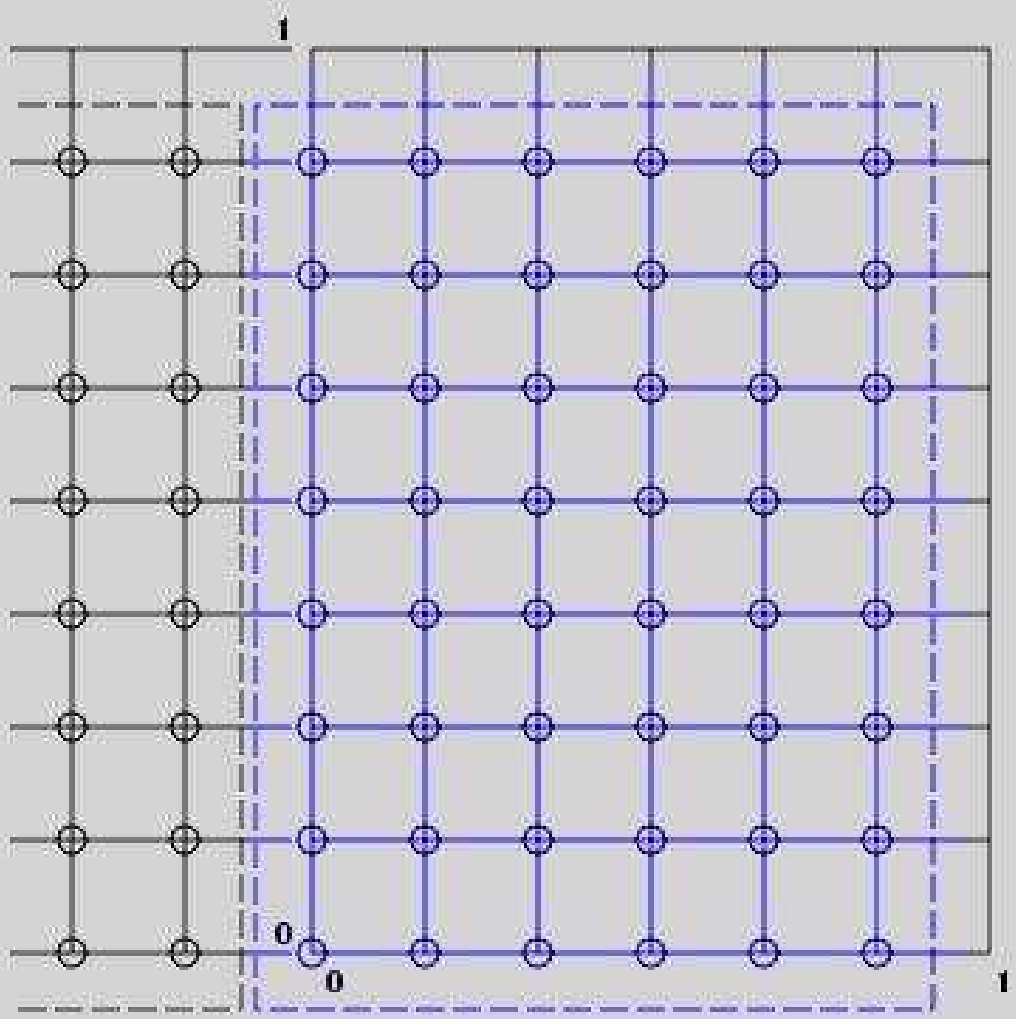
Clipper Map Mapping

- Clipper maps
  - Appear to be “infinite”
  - Density value can be queried anywhere in space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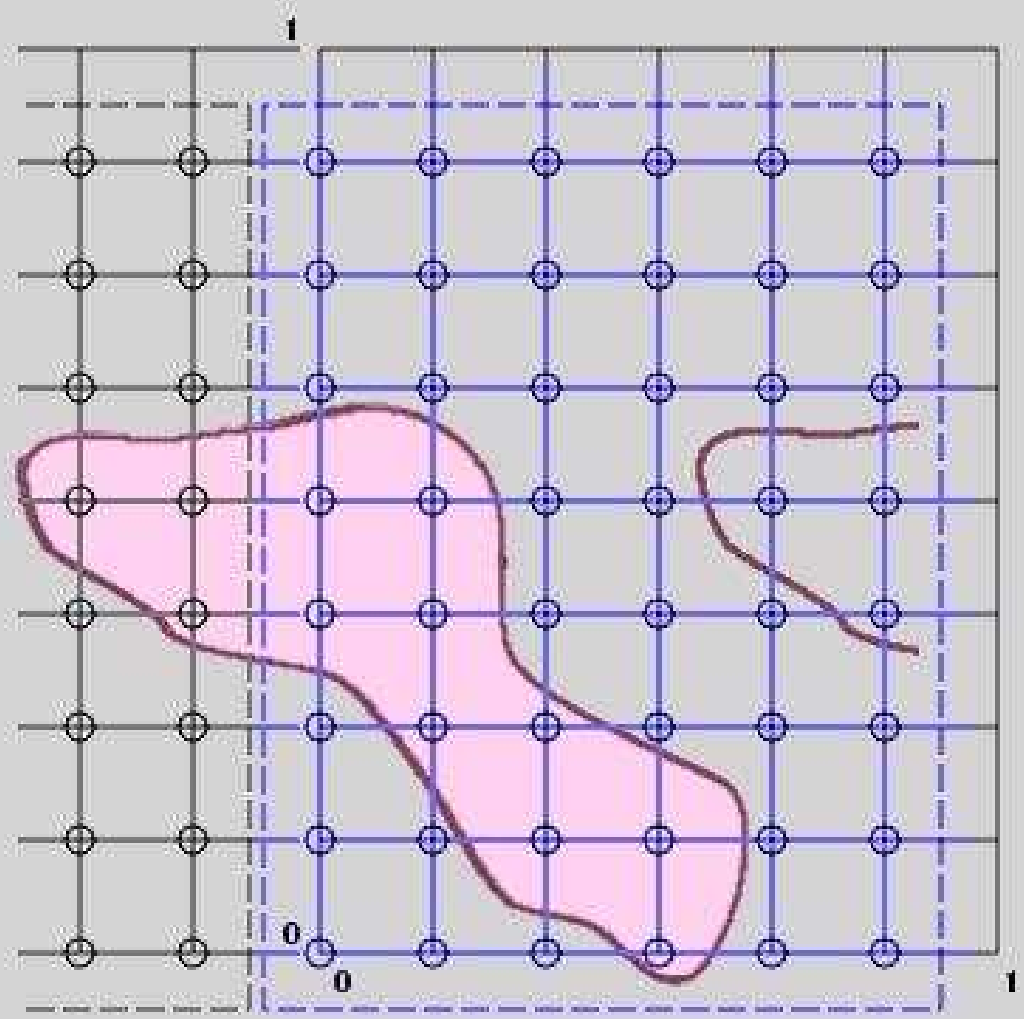
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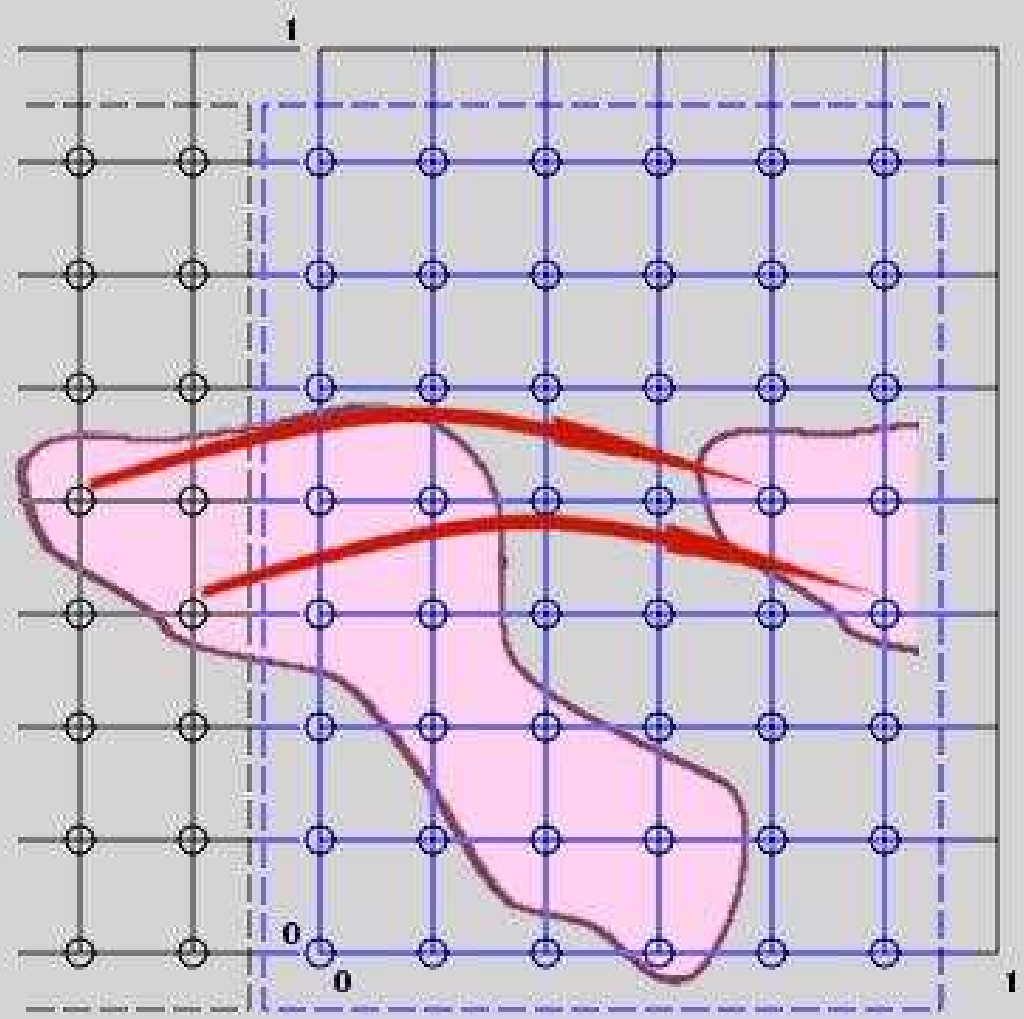
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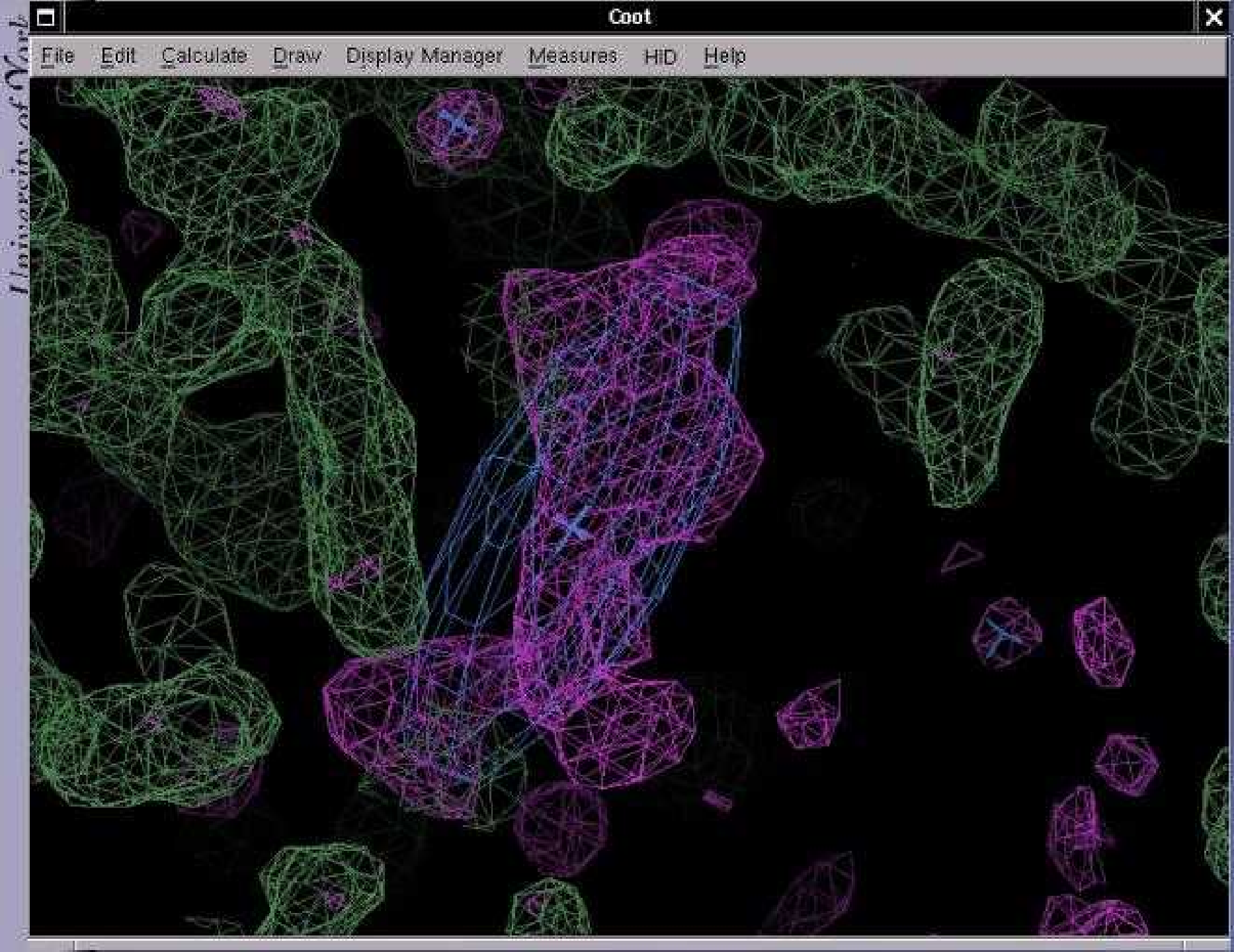
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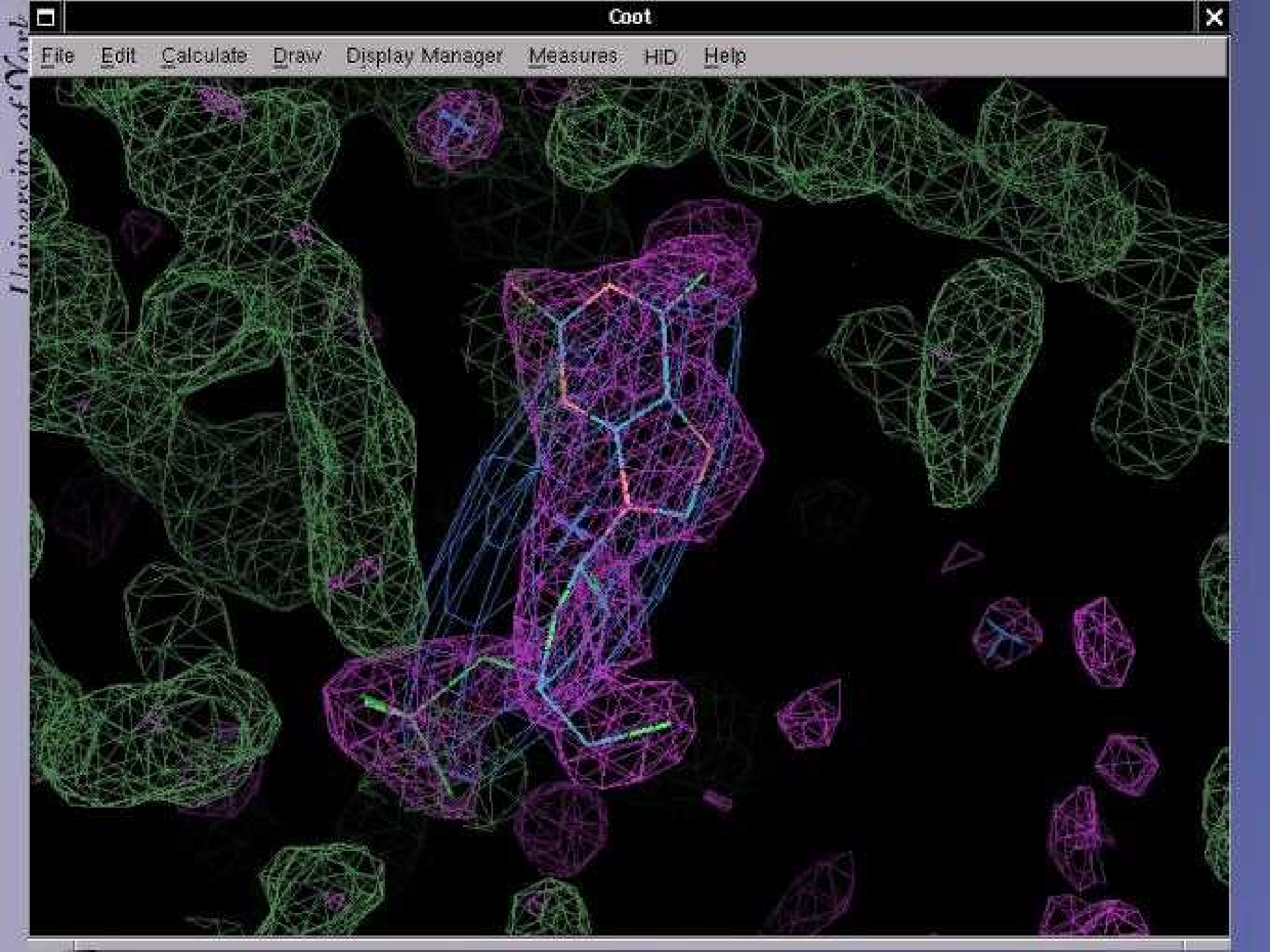
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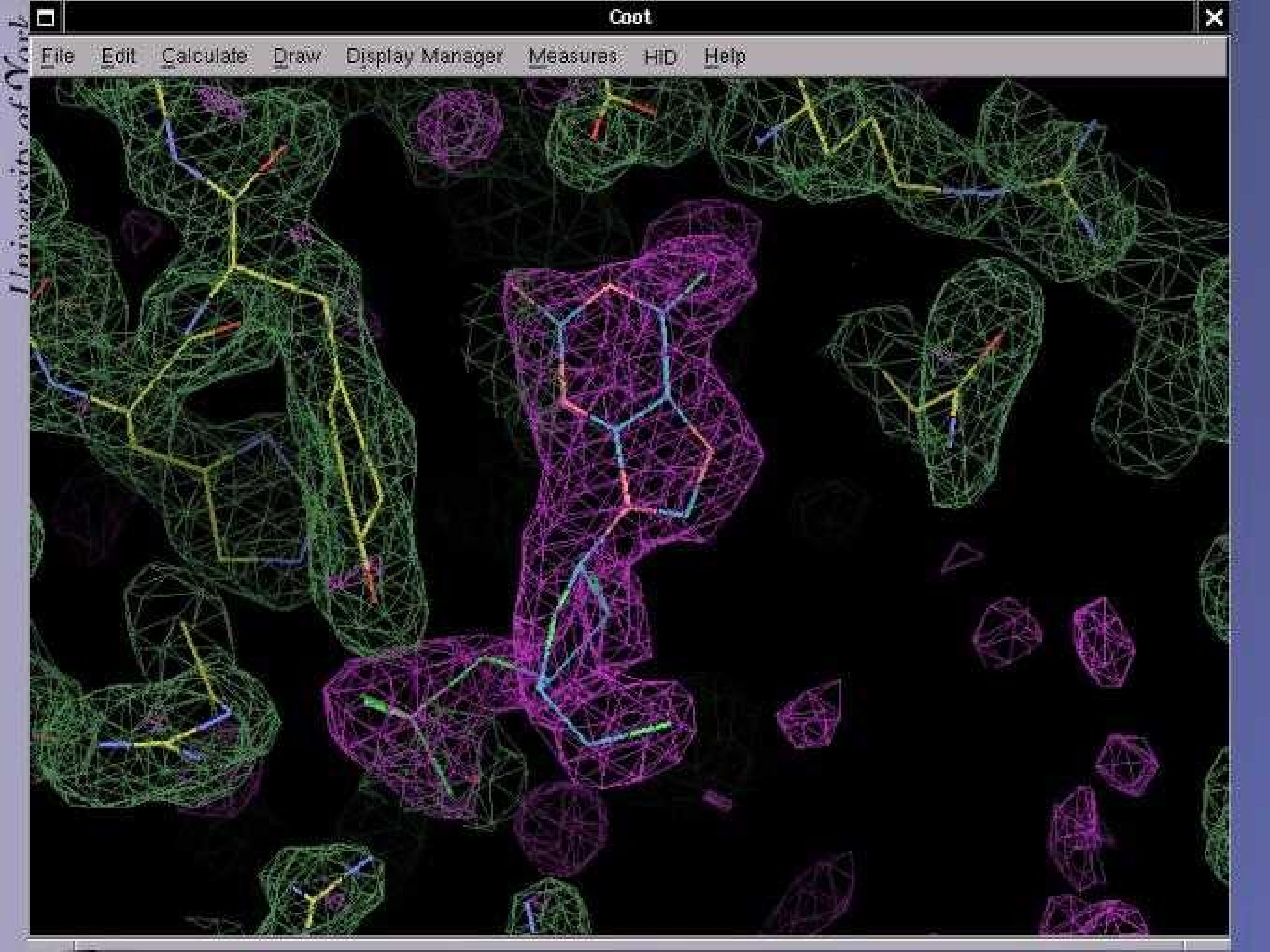
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Display Manager
Measures
HiD
Help
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Conformation Idealization

- Each conformer is passed through the "Regularization" function of Coot
  - Non-bonded terms included
- Better to have hydrogen atoms on the model
- Slows things down a good deal…
  - May not be the best method to explore conformational variability for many rotatable bonds

Scripting

- Python or scheme
- 100s of functions are scriptable
- Accessed via:
  - the command line: `--script`
  - the GUI: Calculate -> Run Script...
  - Interactive: Calculate -> Scripting
- Use `--no-graphics` for “batch mode”

Delete residues by Scripting

- (delete-residue-range *imol chain_id resno_start end_resno*)
- e.g. in scheme
  - (delete-residue-range 0 “A” 10 20)
- e.g. in Python
  - delete_residue_range(0, “A”, 10, 20)
- General command:
  - Scheme: `(scheme-command arg1 arg2 ...)`
  - Python: `python_command(arg1, arg2, ...)`

More on Scripting

- If something is boring, stop it
  - Write a script
  - Or get someone to do it for you
    - Paul, me?
- Scripting available in Python or Scheme (lisp)
- Scripting example available on the mailing list
  - and the Coot Wiki

Some key bindings

- Any function can be bound to a key
  - Allows for personalization/customization
- Here's how you do it:
  - (add-key-binding “Refine residue” "x" (lambda () (refine-active-residue)))
  - add_key_binding(“Refine residue”, "x", lambda: refine_active_residue())
- Makes Coot easy to use
  - (but harder to learn)
- See crib sheet...

Acknowledgements

- Paul Emsley
- Kevin Cowtan
- Eleanor Dodson
- Keith Wilson

http://www.biop.ox.ac.uk/coot/

or

Google: Coot

or for WinCoot

http://www.ysbl.ac.uk/~lohkamp/coot

- Libraries, dictionaries
  - Alexei Vagin, Eugene Krissinel, Stuart McNicholas
  - Dunbrack, Richardsons
- Coot Builders and Testers
  - William Scott, Ezra Peisach
  - York YSBL, Dundee, Glasgow (early adopters)
  - Coot Mailing List subscribers