I. 1. PROGRAMMING DETAILS

The program is written in fortran 77. Its code and manual are available for download at http://www.chem.duke.edu/∼yang/software.html

A. Input

The input is keyword oriented and free-format. A maximum dimension is defined for the number of atoms that can be analyzed. Currently, up to 500 atoms are supported from SCF densities, and up to 10000 for promolecular densities.

The following notation is used for variables within the input specification:

- r stands for real.
- x,y,z stand for positions in space (real)
- n stands for integer
- `name` stands for any character string

Comments must be preceded by #

a. Required input

- The first line must contain the number of files to be analyzed. Currently, from 1 to 3 files are supported for xyz files, so that, if interactions between different molecules are to be analyzed, the molecules can be uploaded in different files. Only one wfn file can be analyzed at one time.
- The second line must contain the name of the molecular file. It accepts two different types of file format, depending on the level of approximation. They must have the following extensions, depending on the desired calculation:
  - `name.xyz` coordinate specification in the xyz format (Promolecular approximation), recommended for large systems [default]
  - `name.wfn` wavefunction file in the `AIMPAC WFN` format (SCF calculation)

b. Optional keywords (in order)

- `LIGAND n r`

  `n` is the number of the file (in the order of introduction in the input) and `r` is a distance in Å. This option will only plot intermolecular interactions within a radius `r` of file #`n`. This option is especially designed for protein-ligand interactions and is only available for promolecular densities.

- `INTERMOLECULAR r`

  `r` may vary from 0 to 1. For good results, `r` should be in the range 0.8-0.95. This option will eliminate all interactions where at least a fraction r of the density at a point in space comes from a single molecule. This enables only intermolecular, and not intramolecular, interactions to be plotted. The default is set so that an interaction is discarded if 0.95 of the density at each point comes from a single molecule. Note that this option is only available for promolecular densities.

- `RADIUS x y z r`

  `x y z` determine the position around which interactions are represented for a radius `r` (all in Å)

- `ONAME name`

  `name` is the string to be passed for use as the output file names (otherwise the default is taken from the input file name). The name used will be output in capital letters.

- `OUTPUT n`, where `n` is an integer running from 1 to 3.

  - 1 will only print the .dat file
  - 2 will only print the .cube files
  - 3 will print all three output files [default]

- `CUBE x0 y0 z0 x1 y1 z1`

  This option will set the cube within which NCI is analyzed (atomic units). The lower left corner of the cube is located at the Cartesian coordinate (`x0,y0,z0`) and the top right corner is at (`x1,y1,z1`). The default is produced in terms of molecular

coordinates. In order to ensure a correct cube in planar or linear molecules, a minimum distance of +/- 2a.u. is added to the axes in all directions.

- `INCREMENTS r1 r2 r3` This option sets the increments along the `x,y,z` directions of the cube (atomic units). The default is set to 0.1,0.1,0.1

- `CUTOFFS r1 r2`

  Density (`r1`) and RDG (`r2`) cutoffs used to create the dat file. The default density cutoff is set to 0.2. The RDG cutoff depends on the level of calculation:

  - In the promolecular case it is set to 1.0.
  - In the SCF case it is set to 2.0.

- `CUTPLOT r1 r2`

  Density (`r1`) and RDG (`r2`) cutoffs used when creating the cube files. `r1` will set the density cutoff that must be met for the RDG to be registered in the cube files, whereas `r2` will be used in the `VMD` script for the plotting of isosurfaces. The default values are:

  - In the promolecular case: r1=0.07, r2=0.3.
  - In the SCF case: r1=0.05, r2=0.5.

B. Output

The NCI output thus consists of 4 files:

- a data file that collects ρ vs s values
- a cube file with s' values (only s values above the cutoff are collected)
- a cube file with $\text{sign}(\lambda_2)\rho$
- a script for visualization of the results in vmd, subject to the cutoffs used in the run.

II. INPUTS FOR THE EXAMPLES

This section collects the inputs necessary to reproduce the results of the paper. They include both the input for `NCIPLOT` and the geometry used. In the case of SCF calculation, the geometry is provided as it appears in the wfn file. In the promolecular case, the XYZ file is given. If the geometry is already available in the literature, the source is provided.

A. S-S bond in S_4N_4

Calculation details

Method: B3LYP

Basis set: 6-31G*

1. Boat

Input

```
1
boat.wfn
```

Geometry

Geometry taken from: Pritchina, E. A.; Gritsan, N. P.; Zibarev, A. V.; Bally, T. *Inorganic Chemistry* **2009**, *48*, 4075.

```
N    1    (CENTRE  1)   2.14447607 -2.43213755  0.00000000  CHARGE =  7.0
N    2    (CENTRE  2)   0.29551853  3.46824219  0.00000000  CHARGE =  7.0
N    3    (CENTRE  3)  -0.62783827 -0.17448644  3.65514230  CHARGE =  7.0
N    4    (CENTRE  4)  -0.62783827 -0.17448644 -3.65514230  CHARGE =  7.0
S    5    (CENTRE  5)   0.36876869 -2.83230297  2.55367196  CHARGE = 16.0
S    6    (CENTRE  6)   0.36876869 -2.83230297 -2.55367196  CHARGE = 16.0
S    7    (CENTRE  7)  -0.62783827  2.68199289 -2.80793650  CHARGE = 16.0
S    8    (CENTRE  8)  -0.62783827  2.68199289  2.80793650  CHARGE = 16.0
```

2. Cage

Input

```
1
cage.wfn
```

Geometry

Geometry taken from: Pritchina, E. A.; Gritsan, N. P.; Zibarev, A. V.; Bally, T. *Inorganic Chemistry* **2009**, *48*, 4075.

```
N    1    (CENTRE  1)   2.47571131  2.47571131  0.00000000  CHARGE =  7.0
N    2    (CENTRE  2)  -2.47571131  2.47571131  0.00000000  CHARGE =  7.0
N    3    (CENTRE  3)  -2.47571131 -2.47571131  0.00000000  CHARGE =  7.0
N    4    (CENTRE  4)   2.47571131 -2.47571131  0.00000000  CHARGE =  7.0
S    5    (CENTRE  5)   0.00000000  2.59961498  1.84258125  CHARGE = 16.0
S    6    (CENTRE  6)  -2.59961498  0.00000000 -1.84258125  CHARGE = 16.0
S    7    (CENTRE  7)   0.00000000 -2.59961498  1.84258125  CHARGE = 16.0
S    8    (CENTRE  8)   2.59961498  0.00000000 -1.84258125  CHARGE = 16.0
```

B. Metal complexes: along Hg series

Calculation details

Method: B3LYP

Basis set: SDD for Hg, 6-31++G** for the ligands

1. $[Hg(H_2O)_3]^{2+}$

Input

```
1
hghoh3.wfn
```

Geometry

```
Hg   1    (CENTRE  1)  -0.09271993 -0.21375982  0.00419875  CHARGE = 20.0
O    2    (CENTRE  2)  -4.18390197 -0.42267499 -0.08472427  CHARGE =  8.0
H    3    (CENTRE  3)  -5.24420024  0.67915034  0.94936888  CHARGE =  1.0
H    4    (CENTRE  4)  -5.09124849 -1.99525591 -0.41987790  CHARGE =  1.0
O    5    (CENTRE  5)   3.67654291 -1.86909391  0.06484495  CHARGE =  8.0
H    6    (CENTRE  6)   3.98657702 -3.67767805  0.26289841  CHARGE =  1.0
H    7    (CENTRE  7)   5.07428067 -1.11487402 -0.87463946  CHARGE =  1.0
O    8    (CENTRE  8)   1.25020912  3.94010262 -0.02780957  CHARGE =  8.0
H    9    (CENTRE  9)   0.77384130  5.19667456 -1.28543005  CHARGE =  1.0
H   10    (CENTRE 10)   1.97554381  4.82609920  1.41329105  CHARGE =  1.0
```

2. *$[Hg(F)_3]^-$*

Input

```
1
HgF3.wfn
```

Geometry

```
Hg   1    (CENTRE  1)   0.00274765 -0.00613533 -0.00002901  CHARGE = 20.0
F    2    (CENTRE  2)  -0.66374794  3.96404083  0.00008485  CHARGE =  9.0
F    3    (CENTRE  3)   3.78129357 -1.39417921  0.00008676  CHARGE =  9.0
F    4    (CENTRE  4)  -3.14196915 -2.51532535  0.00008626  CHARGE =  9.0
```

3. *$[Hg(Cl)_3]^-$*

Input

```
1
HgCl3.wfn
```

Geometry

```
Hg   1    (CENTRE  1)   0.00658792 -0.01360068 -0.00016745  CHARGE = 20.0
Cl   2    (CENTRE  2)  -0.69821368  4.64157150  0.00025851  CHARGE = 17.0
Cl   3    (CENTRE  3)   4.38967792 -1.70098222  0.00026587  CHARGE = 17.0
Cl   4    (CENTRE  4)  -3.72246622 -2.87658607  0.00026364  CHARGE = 17.0
```

4. $[Hg(Br)_3]^-$

Input

```
1
HgBr3.wfn
```

Geometry

```
Hg   1    (CENTRE  1)   0.00471421 -0.00268653 -0.00015930  CHARGE = 20.0
Br   2    (CENTRE  2)   4.92465831 -0.32089631  0.00012180  CHARGE = 35.0
Br   3    (CENTRE  3)  -2.18721415  4.41903634  0.00012098  CHARGE = 35.0
Br   4    (CENTRE  4)  -2.74821948 -4.09199939  0.00012134  CHARGE = 35.0
```

C. BH_3NH_3 and the dihydrogen bond

Calculation details

Method: B3LYP

Basis set: 6-31G*

1. Gas-phase geometry

Optimization: Full

Input

```
1
diHB-B3LYP.wfn
```

Geometry

```
B    1    (CENTRE  1)  -0.01488593  3.36268955 -2.66219498  CHARGE =  5.0
H    2    (CENTRE  2)   1.89147870  2.10623554 -2.34229548  CHARGE =  1.0
H    3    (CENTRE  3)  -1.91373108  2.09957575 -2.32362575  CHARGE =  1.0
H    4    (CENTRE  4)  -0.02643338  4.43154308 -4.67776626  CHARGE =  1.0
N    5    (CENTRE  5)  -0.00827884  5.48391306 -0.44315913  CHARGE =  7.0
H    6    (CENTRE  6)   0.00240783  4.65636332  1.33078996  CHARGE =  1.0
H    7    (CENTRE  7)  -1.56355038  6.62076684 -0.54259965  CHARGE =  1.0
H    8    (CENTRE  8)   1.54159877  6.62667230 -0.55791006  CHARGE =  1.0
B    9    (CENTRE  9)   0.04192809  1.80936252  4.48636635  CHARGE =  5.0
H   10    (CENTRE 10)   1.95964652  2.91310447  3.82319206  CHARGE =  1.0
H   11    (CENTRE 11)  -1.88396404  2.92680093  3.87121362  CHARGE =  1.0
H   12    (CENTRE 12)   0.06772139  1.34214654  6.71830295  CHARGE =  1.0
N   13    (CENTRE 13)   0.01343331 -0.84567352  2.94732020  CHARGE =  7.0
H   14    (CENTRE 14)  -0.01122461 -0.57326863  1.03540129  CHARGE =  1.0
H   15    (CENTRE 15)  -1.55692012 -1.91406023  3.31782461  CHARGE =  1.0
H   16    (CENTRE 16)   1.58706100 -1.92302535  3.27769640  CHARGE =  1.0
B   17    (CENTRE 17)  -5.33956114 -3.55156005  0.23080100  CHARGE =  5.0
H   18    (CENTRE 18)  -3.28151035 -4.46700043 -0.19714943  CHARGE =  1.0
H   19    (CENTRE 19)  -5.40156597 -2.26693342  2.13568831  CHARGE =  1.0
H   20    (CENTRE 20)  -4.47674474 -0.19200344 -2.23885083  CHARGE =  1.0
N   21    (CENTRE 21)  -5.85189932 -1.55483564 -2.11782510  CHARGE =  7.0
H   22    (CENTRE 22)  -7.54740268 -0.65958327 -1.91117831  CHARGE =  1.0
H   23    (CENTRE 23)  -7.04407009 -5.07044693  0.13240883  CHARGE =  1.0
H   24    (CENTRE 24)  -5.89218877 -2.48300334 -3.80782604  CHARGE =  1.0
B   25    (CENTRE 25)   5.32337295 -3.58013626  0.18368396  CHARGE =  5.0
H   26    (CENTRE 26)   3.26078695 -4.47917195 -0.25644036  CHARGE =  1.0
H   27    (CENTRE 27)   7.02203500 -5.10300946  0.05232618  CHARGE =  1.0
H   28    (CENTRE 28)   5.39570478 -2.33317456  2.11328947  CHARGE =  1.0
N   29    (CENTRE 29)   5.83812816 -1.54028369 -2.12691435  CHARGE =  7.0
H   30    (CENTRE 30)   5.87796175 -2.43719186 -3.83372979  CHARGE =  1.0
H   31    (CENTRE 31)   7.53455562 -0.65081924 -1.90339829  CHARGE =  1.0
```

```
H   32    (CENTRE 32)   4.46439498 -0.17413693 -2.22459633  CHARGE =  1.0
```

2. Crystal geometry

Optimization: Heavy atoms frozen, hydrogen-atom positions optimized

Input

```
1
diHB-crystal.wfn
```

Geometry

```
N    1    (CENTRE  1)   0.00000150  4.86874151 -0.14750490  CHARGE =  7.0
N    2    (CENTRE  2)  -0.00000179 -4.08300818  2.11977450  CHARGE =  7.0
N    3    (CENTRE  3)  -5.09718264 -1.03226134 -3.51270679  CHARGE =  7.0
N    4    (CENTRE  4)   5.09718309 -1.03226424 -3.51270594  CHARGE =  7.0
B    5    (CENTRE  5)   0.00000181  6.04274229  2.60718755  CHARGE =  5.0
B    6    (CENTRE  6)  -0.00000149 -2.91013112  4.87459459  CHARGE =  5.0
B    7    (CENTRE  7)  -5.09834255 -0.75459226 -0.53126239  CHARGE =  5.0
B    8    (CENTRE  8)   5.09834188 -0.75459516 -0.53126154  CHARGE =  5.0
H    9    (CENTRE  9)   1.56740642  5.39762028 -1.13615868  CHARGE =  1.0
H   10    (CENTRE 10)   1.58073316 -3.47916018  1.18258505  CHARGE =  1.0
H   11    (CENTRE 11)  -6.72971140 -1.87031055 -4.12082948  CHARGE =  1.0
H   12    (CENTRE 12)   3.64219315 -2.11138035 -4.17882849  CHARGE =  1.0
H   13    (CENTRE 13)  -3.64219140 -2.11137581 -4.17882919  CHARGE =  1.0
H   14    (CENTRE 14)   6.72971282 -1.87031168 -4.12082851  CHARGE =  1.0
H   15    (CENTRE 15)  -1.56737305  5.39766832 -1.13618107  CHARGE =  1.0
H   16    (CENTRE 16)  -1.58073679 -3.47916026  1.18258515  CHARGE =  1.0
H   17    (CENTRE 17)   1.91229178  5.29605486  3.61378198  CHARGE =  1.0
H   18    (CENTRE 18)   1.91007610 -3.68342743  5.89513783  CHARGE =  1.0
H   19    (CENTRE 19)  -6.89888730  0.53616146 -0.00036571  CHARGE =  1.0
H   20    (CENTRE 20)   3.09702624  0.23956311 -0.01463887  CHARGE =  1.0
H   21    (CENTRE 21)  -3.09702831  0.23956822 -0.01463862  CHARGE =  1.0
```

```
H   22    (CENTRE 22)   6.89888532  0.53616047 -0.00036459  CHARGE =  1.0
H   23    (CENTRE 23)  -1.91232474  5.29611317  3.61375691  CHARGE =  1.0
H   24    (CENTRE 24)  -1.91007866 -3.68342783  5.89513836  CHARGE =  1.0
H   25    (CENTRE 25)  -0.00002780  2.93972143 -0.00577422  CHARGE =  1.0
H   26    (CENTRE 26)   0.00003824  8.32687698  2.29184998  CHARGE =  1.0
H   27    (CENTRE 27)  -0.00000176 -6.00978890  2.15885598  CHARGE =  1.0
H   28    (CENTRE 28)  -0.00000178 -0.63803101  4.60552116  CHARGE =  1.0
H   29    (CENTRE 29)  -4.99999818  0.67964776 -4.40151662  CHARGE =  1.0
H   30    (CENTRE 30)  -5.26213377 -2.89699843  0.27348384  CHARGE =  1.0
H   31    (CENTRE 31)   4.99999681  0.67964465 -4.40151596  CHARGE =  1.0
H   32    (CENTRE 32)   5.26213548 -2.89700122  0.27348468  CHARGE =  1.0
```

D. High affinity host-guest complexes

Calculation details

Promolecular density

Docking performed by AutoDock and optimization of the geometry performed with NAMD.

Input

```
2
cb7.xyz
bcb.xyz
LIGAND 2 5
```

Geometry

Geometry taken from : Moghaddam, S.; Inoue, Y.; Gilson, M. K. *J. Am. Chem. Soc.* **2009**, *131*, 4012.

- BCB

30

C 11.92700 7.10200 10.39300
C 13.24600 7.04800 11.17100
H 13.64400 8.05200 11.30800
H 13.05900 6.64300 12.16500
C 14.26600 6.16900 10.43900
H 14.99000 6.79600 9.91700
H 14.83200 5.55800 11.14200
C 13.53800 5.28300 9.42500
C 12.34400 4.64900 10.13700
H 12.70000 4.19000 11.06000
H 11.91300 3.85100 9.53300
C 11.29400 5.71200 10.46000
H 10.86500 5.52800 11.44200
H 10.48900 5.65400 9.73200
C 13.01000 6.20300 8.31500
H 12.35200 5.63900 7.65400
H 13.83700 6.57000 7.71100
C 12.25300 7.39100 8.92500
H 11.34400 7.58900 8.35600
H 12.85800 8.29500 8.86200
C 11.00000 8.16900 10.99700
H 11.51200 9.13200 11.04400
H 10.73900 7.89700 12.01800
O 9.79900 8.35100 10.28200
H 9.40100 7.48600 10.19000
C 14.43100 4.15800 8.87400
H 14.38300 3.28900 9.53200
H 14.07100 3.83900 7.89600
O 15.78500 4.51500 8.74000
H 15.87200 4.93600 7.89100

- CB7

```
126

O 7.99900 6.25900 9.66100
C 7.97600 5.06000 9.47400
N 7.99200 4.44600 8.27100
N 7.82800 4.11500 10.43300
C 7.99300 2.99600 8.37800
C 7.88900 2.76700 9.89500
H 7.17000 2.54700 7.82300
H 7.01100 2.17600 10.17700
N 9.27500 2.38400 8.04600
N 9.13200 2.08200 10.21700
C 9.89600 1.86900 9.12100
O 10.92800 1.21200 9.09100
C 7.42700 4.39600 11.81000
H 6.87600 5.33800 11.84600
H 6.72200 3.62800 12.13200
C 9.37700 1.49800 11.53200
H 10.04800 0.63900 11.44400
H 8.43900 1.10900 11.93100
O 8.73500 6.70000 12.95700
C 9.04600 5.57400 13.28100
N 8.54400 4.43600 12.75700
N 9.92000 5.24400 14.26200
C 9.09000 3.23800 13.37500
C 10.09300 3.80600 14.39300
H 8.31600 2.62900 13.83800
H 9.89600 3.46800 15.41500
N 9.93700 2.46200 12.48100
N 11.37400 3.31600 13.90400
```

C 11.23900 2.56500 12.78600

O 12.15100 2.00300 12.19700

C 10.43800 6.20000 15.24200

H 9.82000 7.10000 15.24100

H 10.32600 5.77000 16.23700

C 12.58700 3.36100 14.71500

H 12.32500 3.15400 15.75400

H 13.26600 2.55700 14.41400

O 11.53600 8.67000 14.20500

C 12.24900 7.79600 14.64100

N 11.84700 6.57300 15.05600

N 13.58400 7.89700 14.85000

C 12.94400 5.74900 15.53600

H 12.78400 5.41400 16.55800

C 14.16000 6.68200 15.39300

H 14.66400 6.86400 16.34600

N 13.29100 4.64400 14.65200

N 15.02100 5.98000 14.45700

C 14.45500 4.83400 14.01200

O 14.96400 4.05500 13.22100

C 14.32800 9.15300 14.75600

H 14.93900 9.25700 15.65000

H 13.63700 9.99600 14.77700

C 16.43300 6.31200 14.30200

H 16.81800 6.66400 15.26000

H 17.00000 5.40900 14.06500

O 13.84800 10.54400 12.26400

C 14.91000 10.01900 12.49900

N 15.20000 9.26100 13.58100

N 16.03800 10.13600 11.75000

C 16.56400 8.76000 13.57500

H 17.09800 9.03200 14.48100

C 17.16000 9.40300 12.30900

H 18.00300 10.06500 12.53200

N 16.67900 7.33500 13.28500

N 17.56900 8.26200 11.50800

C 17.24500 7.08700 12.09300

O 17.51400 5.98300 11.64600

C 16.17800 11.06400 10.62800

H 15.39700 11.82600 10.67900

H 17.11800 11.60400 10.73600

C 18.46400 8.38600 10.36100

H 19.14000 9.22700 10.52200

H 19.09700 7.49700 10.28200

O 13.97100 10.82900 8.77800

C 15.08300 10.46900 8.47900

N 16.15300 10.42800 9.30600

N 15.49600 10.09200 7.24200

C 17.35100 9.91600 8.65600

H 18.17600 10.62000 8.70800

C 16.87500 9.65200 7.21600

H 17.46000 10.20200 6.47300

N 17.73700 8.58800 9.10800

N 17.03200 8.21500 7.06100

C 17.54300 7.64000 8.17500

O 17.85800 6.46500 8.27800

C 14.72600 10.32200 6.02300

H 13.99200 11.11200 6.19500

H 15.39600 10.70000 5.25300

C 16.92600 7.54500 5.76600

H 17.35700 8.19000 5.00100

H 17.53000 6.63600 5.76500

O 11.95300 9.59600 6.26600

C 12.72300 8.93800 5.60200

N 14.05200 9.13100 5.51200

N 12.39300 7.91800 4.78000

C 14.71700 8.16000 4.65400

H 15.25300 8.63400 3.83900

C 13.54700 7.28000 4.17700

H 13.46600 7.24100 3.08600

N 15.55000 7.21700 5.38500

N 13.85000 5.97200 4.74300

C 15.01000 5.98900 5.44500

O 15.51900 5.02100 5.98900

C 11.02700 7.63000 4.36600

H 10.39700 8.51000 4.52000

H 11.02100 7.44300 3.29100

C 13.15800 4.75000 4.31700

H 13.81800 3.88900 4.45100

H 12.97500 4.81300 3.24300

O 9.27800 7.57600 6.67800

C 9.56100 6.57100 6.05800

N 10.46000 6.47800 5.05800

N 8.98300 5.35900 6.21900

C 10.63200 5.12300 4.56200

H 10.49900 5.06400 3.48400

C 9.56200 4.34900 5.34900

H 8.81000 3.89500 4.69900

N 11.87600 4.49200 4.99500

N 10.33000 3.34800 6.06600

C 11.66300 3.49100 5.86900

O 12.52000 2.76100 6.34400

C 7.77100 5.13800 7.00000

H 7.27000 6.09000 7.18300

H 7.07200 4.55300 6.40000

C 9.70300 2.17300 6.66300

H 10.38800 1.32300 6.61500

H 8.83300 1.89500 6.06600

E. Protein-ligand

Calculation details

Promolecular density

Input

```
2
v5x.xyz
2v5x.xyz
LIGAND 1 5.
INCREMENTS 0.2 0.2 0.2
```

Geometry

Obtained from 2v5x.pdb