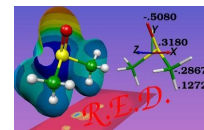




HowTo The R.E.D.-III.5 tools



About using Ante_R.E.D., R.E.D. and X R.E.D.
<http://q4md-forcefieldtools.org/RED/>

For more information: Tutorials @ <http://q4md-forcefieldtools.org/Tutorial/>
R.E.DD.B. <http://q4md-forcefieldtools.org/REDDB/>
R.E.D. Server <http://q4md-forcefieldtools.org/REDS/>



Distribution of the R.E.D. III.5 tools under the GNU General Public License.



The examples presented in this distribution are similar to those available in the R.E.D.-III.3/4 tools version.
Most of the presented examples are available in R.E.DD.B.

Last update of this document: February 20th, 2012

-1- Installation of the R.E.D. tools

See the different manuals in the pdf file format @ <http://q4md-forcefieldtools.org/RED/documentation.php>

-2- Executing Ante_RED-1.5

To execute Ante_R.E.D., use “perl” as it follows:

```
perl Ante_RED-1.5.pl PDB-file          or
perl Ante_RED-1.5.pl PDB-file > Ante_RED.log &          PDB-file = a PDB file
```

```
- For multiple Ante_RED executions, create a csh script:
#!/bin/csh
#
touch Ante_RED.log
foreach PDBFILE (*.pdb)
    perl Ante_RED-1.5.pl $PDBFILE >> Ante_RED.log
end
```

- Remark: The PDB-file(s) & Ante_RED-1.5.pl have to be in the working directory.

* Example-A

Using the “DMSO.pdb” file provided in the R.E.D.-III.5 tools distribution (available in the HowTo/2-Dimethylsulfoxide directory), execute:

```
cp Ante_RED-1.5.pl HowTo/2-Dimethylsulfoxide
cd HowTo/2-Dimethylsulfoxide
perl Ante_RED-1.5.pl DMSO.pdb > Ante_RED.log
```

Then, compare the “DMSO-out.p2n” file generated using Ante_R.E.D. with the “Mol_red1.p2n” file (available in the HowTo/2-Dimethylsulfoxide directory). The “Mol_red1.p2n” file is an example of input file to be used with R.E.D.-III.5.

* Example-B

Using the “EtOH*\$i*.pdb” files provided in the R.E.D.-III.5 tools distribution (conformations: *\$i*=2; available in the HowTo/1-Ethanol directory), execute:

```
cp Ante_RED-1.5.pl HowTo/1-Ethanol
cp Scripts/@Multi-Ante-RED.csh HowTo/1-Ethanol
cd HowTo/1-Ethanol
csh @Multi-Ante-RED.csh
```

Then, compare the “EtOH*\$i*-out.p2n” files generated using Ante_R.E.D. with the “Mol_red1.p2n” file. The “Mol_red1.p2n” is an example of input file for R.E.D.-III.5 (charge derivation & force field library building involving two conformations).

-3- Executing RED-vIII.5

To execute R.E.D. and modify R.E.D. variables, see the "MAIN PROGRAM" section in the source code:
i. e. lines 7269-7310.

Those options are summarized below:

```
$XRED = "Off";           # If XRED="ON", R.E.D. is executed using the X R.E.D. graphical interface (see below).

$NP = "1";              # Number of cpu(s)/core(s) used in parallel in QM calculations; used only if XRED="OFF".

$QMSOFT = "FIREFLY";   # "GAMESS" (GAMESS-US or WinGAMESS), "FIREFLY", or
                       # "GAUSSIAN" (g09, g03, g98 or g94, the latest version found is used) is interfaced in QM calculations;
                       # used only if XRED="OFF".

$DIR = "Data-RED";     # Directory name where data generated by R.E.D. are stored; useful only if XRED="OFF".
                       # If $DIR = "", $DIR is automatically set to "Data-RED".
                       # When using $Re_Fit = "On" do not change $DIR between the first R.E.D. job & the re-fit job(s).

$OPT_Calc = "Off";     # Geometry optimization is carried out only if $OPT_Calc = "ON"; used only if XRED="OFF".

$MEPCHR_Calc = "On";   # MEP computation & charge fitting are carried out if $MEPCHR_Calc = "ON";
                       # used only if XRED="OFF".

$Re_Fit = "Off";      # Charges are re-fitted & force field (FF) library(ies) re-built from a previous R.E.D. job;
                       # used only if XRED="OFF".
                       # If $Re_Fit = "On", $OPT_Calc & $MEPCHR_Calc are automatically set to "Off"

$CHR_TYP = "RESP-A1"; # Charge models available:
                       # "RESP-A1, RESP-A2, RESP-C1, RESP-C2, ESP-A1, ESP-A2, ESP-C1, ESP-C2";
                       # -1- RESP-A1: HF/6-31G* Connolly surface algo., 2 stage RESP fit qwt=.0005/.001
                       # Used in the Cornell et al., Kollman et al., Cheatham et al., Wang et al. & Hornak et al. AMBER force fields.
=> You could execute the "Corn2Duan.csh" script to modify RED-III.5 so that the RESP-A1 charge model can be used to handle the charge model
developed by Duan et al. [i.e. B3LYP/cc-pVTZ SCRF(IEFPCM,Solvent=Ether)//HF/6-31G**, using the Gaussian 2003 program] or the charge model
developed by Cornell et al.
                       # -2- RESP-A2: HF/6-31G* Connolly surface algo., 1 stage RESP fit qwt=.01
                       # Created by analogy to the RESP-C2 charge model.
                       # -3- RESP-C1: HF/6-31G* CHELPG algo., 2 stage RESP fit qwt=.0005/.001
                       # Created by analogy to the RESP-A1 charge model.
                       # -4- RESP-C2: HF/6-31G* CHELPG algo., 1 stage RESP fit qwt=.01
                       # Used in the GLYCAM force fields.
                       # -5- ESP-A1: HF/6-31G* Connolly surface algo., 1 stage RESP fit qwt=.0000
                       # Used in some AMBER, OPLS & CHARMM force field based simulations.
                       # -6- ESP-A2: HF/STO-3G Connolly surface algo., 1 stage RESP fit qwt=.0000
                       # Used in the old Weiner et al. AMBER force field.
                       # -7- ESP-C1: HF/6-31G* CHELPG algo., 1 stage RESP fit qwt=.0000
                       # Used in some OPLS & CHARMM force field based simulations
                       # -8- ESP-C2: HF/STO-3G CHELPG algo., 1 stage RESP fit qwt=.0000
                       # Created by analogy to the ESP-A2 charge model.
                       # -9- DEBUG: Do not use the DEBUG mode for generating correct charge values !!!
                       # The DEBUG mode could be used to (I) quickly get an idea of "what is done", (ii) debug the source code
                       # & (iii) create new functionalities.
                       # useful only if XRED="OFF".

$COR_CHR = "4";        # Correct charge value rounding off errors at an accuracy defined by the user NEW
                       # 0 : no correction is performed
                       # 6 : correction at ± 1.10-6 e           # 3 : correction at ± 1.10-3 e (pay attention)
                       # 5 : correction at ± 1.10-5 e           # 2 : correction at ± 1.10-2 e (pay attention)
                       # 4 : correction at ± 1.10-4 e (default) # 1 : correction at ± 1.10-1 e (pay attention)
```

To execute R.E.D., use "perl" as it follows:

```
perl RED-vIII.5.pl           OR
perl RED-vIII.5.pl > RED-vIII.log &    OR
time perl RED-vIII.5.pl (to get the time required for this command)
```

R.E.D. can be executed in three modes:

- Mode 1

```
$OPT_Calc      = "On";  
$MEPCHR_Calc  = "On";  
$Re_Fit       = "Off";
```

Let's use the default RESP-A1 charge model in the example below.

In this mode the geometry optimization, MEP computation and charge fitting steps are handled by the R.E.D. program.

“Mode 1” only requires the P2N-file(s) & RED-vIII.5.pl to be in the working directory. The name(s) of the P2N-file(s) has(have) to be “mol_red\$n.p2n” (“\$n” is the number of molecules involved in charge derivation and force field library building). Although “Mode 1” seems simpler than “Mode 2”, such an approach is not recommended when deriving RESP or ESP charge values involving multiple conformations and multiple molecules. Indeed, it is unlikely that all the geometry optimization jobs for the different conformations and molecules converge. This leads to a failed R.E.D. execution (see the R.E.D. tools tutorial for more information @ <http://q4md-forcefieldtools.org/Tutorial/>).

* Example-1

Using the “mol_red1.p2n” file provided in the R.E.D.-III.5 tools distribution (directory HowTo/1-Ethanol), execute:

```
cp RED-vIII.5.pl HowTo/1-Ethanol  
cd HowTo/1-Ethanol  
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation involving two conformations of a single molecule (as defined in the Cornell *et al.* force field) and force field library building are carried out by R.E.D.

See the corresponding "W-10" R.E.D.D.B. project @ <http://q4md-forcefieldtools.com/REDDB/Projects/W-10/> as well.

- Mode 2

```
$OPT_Calc      = "Off";  
$MEPCHR_Calc  = "On";  
$Re_Fit       = "Off";
```

Let's use the default RESP-A1 charge model in the following examples.

In this mode only the MEP computation and charge fitting steps are handled by the R.E.D. program.

“Mode 2” requires the P2N & QM geometry optimization output file(s) and RED-vIII.5.pl to be in the working directory. The name(s) of the P2N-file(s) has(have) to be “mol_red\$n.p2n” (“\$n” is the number of molecules involved in charge derivation and force field library building). The names of the corresponding QM geometry optimization outputs have to be “mol_red\$n.log”.

Modify the \$QMSOFT & \$NP variables in the R.E.D. source code according to your choice as well.

* Example-2a

Using the “mol_red1.p2n” and “mol_red1.log” files provided in the R.E.D.-III.5 tools distribution (directory HowTo/2-Dimethylsulfoxide), execute:

```
cp RED-vIII.5.pl HowTo/2-Dimethylsulfoxide  
cd HowTo/2-Dimethylsulfoxide  
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation (as defined in the Cornell *et al.* force field) involving a single molecule and force field library building in the Tripos mol2 file format are carried out by R.E.D. The force field library generated “mol_m1-o1.mol2”. See the corresponding "W-4" R.E.D.D.B. project @ <http://q4md-forcefieldtools.com/REDDB/Projects/W-4/>.

** Example-2b*

Use of multiple rigid-body transformations before MEP computation:

Using the "Mo1_red\$n.p2n" and "Mo1_red\$n.log" files provided in the R.E.D.-III.5 tools distribution (\$n = 4; directory HowTo/2-Dimethylsulfoxide-new), execute:

```
cp RED-vIII.5.pl HowTo/2-Dimethylsulfoxide-new
cd HowTo/2-Dimethylsulfoxide-new
perl RED-vIII.5.pl > RED-vIII.log &
```

The P2N files only differ by the transformation procedure applied before MEP computation:

- No rigid-body transformation is requested in Mo1_red1.p2n
- "REMARK TRANSLATE 1 1 1 | -1 0 1.5" in Mo1_red2.p2n
- "REMARK REORIENT 1 5 6 | 6 5 1" in Mo1_red3.p2n
- "REMARK ROTATE 1 5 6 | 6 5 1" in Mo1_red4.p2n

Compare the charge values in the four Mo1_MM/Mo1_m\$n-o1-mm2.mol2 files generated (\$n = 1-4). Your conclusion?

Answer: Using the rigid-body re-orientation, rotation and translation algorithms implemented in R.E.D. III.5 any user can demonstrate that (i) translation does not affect charge values, and applying the rigid-body translation algorithm or the QMRA algorithm leads to identical charge values, (ii) applying the rigid-body rotation algorithm or rigid-body re-orientation algorithm leads to identical charge values.

Please, read <http://q4md-forcefieldtools.org/Tutorial/Tutorial-1.php#REORIENT> for more information.

** Example-3*

Use of multiple molecule charge derivation:

Using the "Mo1_red\$n.p2n" and "Mo1_red\$n.log" files provided in the R.E.D.-III.5 tools distribution (\$n = 3; directory HowTo/3-Solvents), execute:

```
cp RED-vIII.5.pl HowTo/3-Solvents
cd HowTo/3-Solvents
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation involving three molecules and force field library building are carried out by R.E.D. See the corresponding "W-46" R.E.D.D.B. project @ <http://q4md-forcefieldtools.org/REDDB/Projects/W-46/>.

Execute "xleap -f LEaP-script.cmd" to load those three force field libraries in LEaP.

** Example-4*

Use of intra-molecular charge constraint during the fitting step for an amino acid fragment:

Using the "Mo1_red1.p2n" & "Mo1_red1.log" files provided in the R.E.D.-III.5 tools distribution (directory HowTo/4-Fragment-1), execute:

```
cp RED-vIII.5.pl HowTo/4-Fragment-1
cd HowTo/4-Fragment-1
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation involving a single molecule (as defined in the Cornell *et al.* force field) and force field library building for the central fragment of the α -aminoisobutyric acid are carried out by R.E.D. The force field library generated is "Mo1_m1-o1-sm.mol2".

Execute "xleap -f LEaP-script-4-F.cmd" to load this force field library in LEaP.

See the corresponding "F-3" R.E.D.D.B. project @ <http://q4md-forcefieldtools.com/REDDB/Projects/F-3/>.

** Example-5*

Use of inter-molecular charge constraint during the fitting step for an amino acid fragment:

Using the "Mo1_red\$n.p2n" and "Mo1_red\$n.log" files provided in the R.E.D.-III.5 tools distribution ($n = 2$; directory HowTo/5-Fragment-2), execute:

```
cp RED-vIII.5.pl HowTo/5-Fragment-2
cd HowTo/5-Fragment-2
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation involving two molecules and force field library building for the $(^+)NH_3$ -terminal fragment of the α -aminoisobutyric acid are carried out by R.E.D. The force field library generated is "Mo1_MM/Mo1_m2-o1-mm1.mo12".

A similar approach can be followed for the $COO^{(-)}$ -terminal fragment.

Please, read <http://q4md-forcefieldtools.org/Tutorial/Tutorial-1.php#19> & <http://q4md-forcefieldtools.org/Tutorial/leap.php>. Compare the Mo1_MM/Mo1_m2-o1-mm1.mo12 file generated by R.E.D.-III.5 with that generated with R.E.D.-III.3: Which geometry do you prefer? This represents a major improvement in the R.E.D. III.5 tools...

Execute "xleap -f LEaP-script-5-F.cmd" to load this force field library in LEaP.

See the corresponding "F-7" R.E.D.D.B. project @ <http://q4md-forcefieldtools.com/REDDB/Projects/F-7/>.

** Example-6*

Use of inter-molecular charge constraint during the fitting step for a nucleotide fragment:

Using the "Mo1_red\$n.p2n" and "Mo1_red\$n.log" files provided in the R.E.D.-III.5 tools distribution ($n = 2$; directory HowTo/6-Fragment-3), execute:

```
cp RED-vIII.5.pl HowTo/6-Fragment-3
cd HowTo/6-Fragment-3
perl RED-vIII.5.pl > RED-vIII.log &
```

RESP charge derivation involving two molecules and force field library building for the central fragment of the deoxyadenosine nucleotide are carried out by R.E.D. The force field library generated is "Mo1_MM/Mo1_m2-o1-mm1.mo12".

Please, read <http://q4md-forcefieldtools.org/Tutorial/Tutorial-1.php#19> & <http://q4md-forcefieldtools.org/Tutorial/leap.php>. Compare the Mo1_MM/Mo1_m2-o1-mm1.mo12 file generated by R.E.D.-III.5 with that generated with R.E.D.-III.3: Which geometry do you prefer? This represents a major improvement in the R.E.D. III.5 tools...

Execute "xleap -f LEaP-script-6-F.cmd" to load the force field library in LEaP.

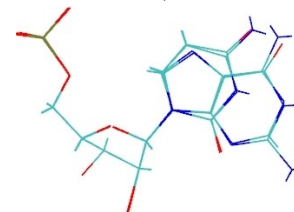
This example is not available in R.E.D.D.B. but this fragment belongs to several R.E.D.D.B. projects ("F-45" and "F-60" for instance) with a different set of atom charges (as the charge derivation procedure used is different).

** Example-7:*

Use of inter-molecular charge constraint and inter-molecular charge equivalencing during the fitting step for a set of nucleotide fragments:

Using the "Mo1_red\$n.p2n" and "Mo1_red\$n.log" files provided in the R.E.D.-III.5 tools distribution ($n = 4$; directory HowTo/7-Fragment-4-new), execute:

```
cp RED-vIII.5.pl HowTo/7-Fragment-4-new
cd HowTo/7-Fragment-4-new
perl RED-vIII.5.pl > RED-vIII.log &
```



Superimposition of 4 central fragments

Look at the four generated files Data-RED/Mo1_MM/Mo1_m\$n-o1-mm1.mo12 ($n = 4$) in a graphical program (see Fig. above). Execute "xleap -f LEaP-script-7.cmd" to load the corresponding force field libraries in LEaP.

This example is not available in R.E.D.D.B. but the fragments belongs to several R.E.D.D.B. projects ("F-45" and "F-60" for instance) with a different set of atom charges (as the charge derivation procedure used is different).

- Mode 3

Charge re-fitting and force field library re-building from a previous R.E.D. job

```
$Re_Fit = "On";
```

If \$Re_Fit = "On", then \$OPT_Calc and \$MEPCHR_Calc are automatically set to "Off".

A previous R.E.D. job has to be available in the working directory to be able to execute this Mode 3.

* Example-8

First execute "Example-3" (\$CHR_TYP = "RESP-A1" is set - run R.E.D. using "Mode 2" as previously shown).

Then, set \$CHR_TYP = "ESP-A1" and \$Re_Fit = "On" in RED-vIII.5.pl

```
Re-execute R.E.D.: perl RED-vIII.5.pl > RED-vIII.log2 &
```

MEP files generated in the first R.E.D. job available in the "Data-RED" directory are used in the re-fitting job.

The directory corresponding to the first R.E.D. job is then renamed into "Data-RED-1"

The data corresponding to the "Re_Fit" job are available in a new "Data-RED" directory.

See the corresponding "W-48" R.E.D.D.B. project @ <http://q4md-forcefieldtools.com/REDDB/Projects/W-48/>.

* Example-9

First execute "Example-6" (\$CHR_TYP = "RESP-A1" is set - run R.E.D. using "Mode 2" as previously shown).

Then, set \$Re_Fit = "On", \$RESTD = "ON" and \$resInterval = 3 - line 5757 in RED-vIII.5.pl

```
Re-execute R.E.D.: perl RED-vIII.5.pl > RED-vIII.log2 &
```

Compare the geometry of the two fragments generated: Which one do you prefer ?

```
diff Data-RED/Mol_MM/Mol_m2-01-mm1.mol2 Data-RED-1/Mol_MM/Mol_m2-01-mm1.mol2
```

Re-do the fit and force field library building using: \$Re_Fit = "On", \$RESTD = "ON" and \$resInterval=4, etc...

This re-fitting mode has several other applications. It allows:

-1- ESP-A1 (or RESP-A2) charge fitting after a previous RESP-A1 job (see above),

-2- modifying atom names and/or adding/removing INTRA-MCC, INTER-MCC and/or INTER-MEQ keywords in P2N files before re-running the fitting step and force field library building,

-3- correcting errors in P2N files after a first R.E.D. run and re-running the fitting step and force field library building,

-4- re-generating the charge fitting step after finding and correcting a bug in the R.E.D. source code.

The key point in those examples is that MEP files used in a first R.E.D. job and those in a re-run job have to be identical!

Thus, Mode 3 does neither allow "RESP-C2" charge fitting after a previous "RESP-A1" run (required MEP files are different *i. e.* based on the CHELPG or Connolly surface algorithm) nor changing the number of molecules, conformations or orientations after a first R.E.D. run (the number of MEP files is different). In those two cases, a full R.E.D. job should be ran (*i. e.* using Mode 1 or 2).

Warning: R.E.D. does not check MEP files when using the "Re_Fit" mode!

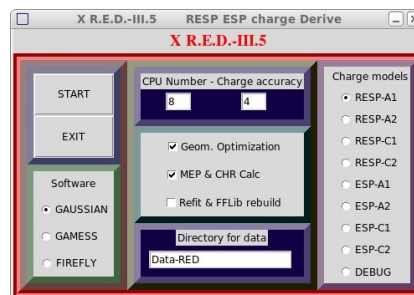
-4- Executing XRED-III.5

Modify the "XRED" variable in RED-vIII.5.pl:

Set XRED="ON" (instead of XRED="OFF", which is the default).

To execute X R.E.D., use "wish" as it follows:

```
wish XRED-III.5.tcl &
```



You can execute R.E.D. in its three different modes and affect the R.E.D. variables previously described without modifying the R.E.D. source code.

-5- Benchmark & checking procedure

De-activate the XRED variable (if activated), define the QM program you wish to interface as well as the number of cores/cpus to be used in the QM computations in RED-vIII.5.pl. Then, run the "check-1.01.csh" shell script as it follows:

```
csh check-1.01.csh          or
time csh check-1.01.csh    (to get the time required for this command)
```

This script needs the data available in the "HowTo" directory and the R.E.D. program belonging to the R.E.D.-III.5 tools distribution. It automatically (i) executes R.E.D. on your machine and (ii) compares the force field libraries derived on your machine to those we have generated using Gaussian 2003 E.01 (available in HowTo/FFLib).

When setting \$COR_CHR = "4" (or "0") the maximum charge difference observed for an atomic charge should not be above $\pm 0.0002/0.0003$ e independently of the QM program used. Setting qtol = 0.1d-5 in "resp.f" could help to slightly lower these differences.

This "check-1.01.csh" job took around:

- 5 min. using Gaussian 2009 A.02 & 8 cores Xeon E5430 @ 2.66GHz (Linux CentOS 5.2).
- 10 min. using GAMESS-US Jan 09 (R1) & 8 cores Xeon E5430 @ 2.66GHz (Linux CentOS 5.2).
- 12 min. using Gaussian 2003 E.01 & 4 cores Core 2 Quad Q6600 @ 2.40GHz (Linux CentOS 5.3).
- 14 min. using PC-GAMESS 7.1.F & 4 cores Xeon X5365 @ 3.00GHz (Leopard/Darwin).
- 17 min. using PC-GAMESS 7.1.F & 4 cores Core 2 Quad Q8200 @ 2.33GHz (Vista 64-bit SP1/Cygwin).
- 30 min. using PC-GAMESS 7.1.F & 2 cores Core 2 Duo P8600 @ 2.40GHz (Windows 7/Cygwin).
- 70 min. using WinGamess Jan 09 (R3) & 1 core Core 2 Duo P8600 @ 2.40GHz (Windows 7/Cygwin).

-6- Additional programs in this distribution

- resp-2.2/resp.f: The version 2.2 of the RESP program with an updated documentation.
- Scripts/0Multi-Ante-RED.csh: An example of csh script to generate multiple P2N files.
- Scripts/check-1.01.csh: The csh script to perform the benchmark and the checking procedure.
- Scripts/Corn2Duan-1.01.csh: A csh script to derive charge values for the Duan *et al.* force field with the "RESP-A1" charge model defined in R.E.D.-III.5.
- Scripts/check-TotalCharge.csh: A csh script to compute the total charge values of the mol2 files belonging to a R.E.D. or R.E.D. Server job (it is complementary to the approach used when \$COR_CHR = "4" in R.E.D.).
- Scripts/Script1-101-REDDB.pl and Scripts/Script2-101-REDDB.pl: Two PERL scripts to help submitting in R.E.D.D.B. the data generated by using the R.E.D. tools or R.E.D. Server.

Do you need a new feature which is not yet implemented in R.E.D.-III.5 ?
contact the q4md force field tools team at contact@q4md-forcefieldtools.org
We will try to help you as much as possible...

Regularly look for bug fixes at the R.E.D. home page.

Need to perform more complex charge derivation and/or force field library building ?
See R.E.D. Server @ <http://q4md-forcefieldtools.org/REDS/> to be able to interface R.E.D.-IV.

Please, submit your force field library(ies) to R.E.D.D.B. at <http://q4md-forcefieldtools.org/REDDB/>
to **freely review & share** your results within the scientific community.

Need help about the q4md force field tools ?
Please, ask your queries to the q4md-forcefieldtools mailing list @ <http://lists.q4md-forcefieldtools.org/>

We hope you will find the R.E.D.-III.5 tools useful...
The q4md force field tools team