1 Purpose of *lmw4amber*

lmw4amber is used to generate Amber-related files for low-molecular-weight compounds. It was mainly created to generate files to be used in cases where more than one ligand is complexed in a protein (e.g. co-factors, ATP, and alike). It also creates a "library file" allowing to use the low-molecular-weight compound directly in PDB files. It requires AmberTools17 or later and will probably **not** work with earlier versions.

NOTE: The generated files do not include explicit solvation! For running Amber simulations on low-molecular-weight compounds in a water box, use the *files4amber* tool and read in the molecule with the `--lig` option, without specifying protein or complex. This will yield a TIP3P-water solvated system that can be used directly for explicit-water simulation.

2 File types required or generated by *files4amber*

***.sdf: input** standard SDF (MDL) file, with all hydrogens and bond orders correctly included;

***.leap.pdb: output** standard PDB file; the ".leap" indicates that it was created via *tleap*; the file has all hydrogens attached;

***.leap.crd: output** Amber format coordinate file;

***.leap.prm: output** Amber parameter-topology file;

***.lib: output** Amber "library" file; useful for special purposes (see 5);

***.frcmod: output** file that contains force field parameters (generated automatically) that are not part of the original parameter files;

***.ac.mol2: output** generated by *lmw4amber* (internally via the *antechamber* module); it has SYBYL mol2 format, but atoms have GAFF/GAFF2 force field atom types; it also contains the partial charges generated via the AM1/BCC method;

sqm.*: output left overs from the *sqm* module used to compute partial charges; useful for debugging only;

***.leap.cmd: output** file containing the commands submitted to the *tleap* module; useful for debugging only;

3 Running *lmw4amber*

For help, just type lmw4amber and RETURN. You then get this:

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 lmw4amber version 0.2
 Romain M. Wolf (February 2019)
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Usage: lmw4amber [options]

Options:
  -h, --help      show this help message and exit
  --lmw=FILE      ligand SD file (sdf)           (no default)
  --name=STRING   3-letter code for lmw          (default = XYZ)
  --lfrc=STRING   ligand force field             (default: gaff2)
  --chrg=INTEGER  formal charge on ligand        (default: 0)
  --rad=STRING    radius type for PB/GB          (default: mbondi2)
```

4 Command line options

`--lmw` must be followed by an SDF file, including all hydrogens and reflecting the correct bond order, tautomeric and protonation state; if intended to be directly integrated into a complex, the coordinates must correspond to the precise location, orientation, and conformation in that complex (*lmw4amber* does not "dock");

`--name` must be followed by a **3-letter** "residue" name for the low-molecular-weight compound (no extension); this feature is described in more detail below (see 5);

`--lfrc` selects the (small molecule) force field; the latest GAFF (*gaff2*) is the default, the only other option would be *gaff*;

`--chrg` must be specified if the molecule has a formal charge; omitting this option with a charged structure leads to a failure of the partial charges computations via AM1/BCC and the routine stops;

`--rad` can be used to change the default selection for radii used in GB and PB computations; the `mbondi2` default is a good choice is the GB settings `igb=5` are used; keep the default if in doubt what to use;

continued on the next page...

5 Remarks to *lmw4amber* output files

All generated files specific to the low-mol-weight compound entered under `--lmw` will start with the 3-letter name given under `--name`.

- `*.leap.prm`, `*.leap.crd`), and the corresponding `*.leap.pdb`) are created by *tleap* and must be kept together; do not change the order of atoms in the files via an external application or editor;
- `*.ac.mol2` and `*.frcmod` are the same kind of files generated also for ligands with the *files4amber* routine (see that documentation sheet); they are required when the molecule is later used as a "co-ligand" in a protein/ligand complex;
- `*.lib` is an Amber "library" file; it can be used for more advanced features, e.g., including the `*.leap.pdb` file directly into a large PDB file (of a protein, for example), provided that the atom order, atom names, and residue name (from the `--name` option) are not altered; in that case, reading the library file via the *tleap* `loadoff` command will recognize the PDB sequence and the low-mol-weight compound is treated like a "natural" residue; the corresponding `*.frcmod` must also be loaded in *tleap* via `frcmod = loadamberparams` followed by the `frcmod` file name; the `*.lib` file type is also required to build systems with various low-mol-weight compounds, mixed solvents, etc. with programs like *packmol* (going beyond the "simple" simulations treated here...);