NAME

Psi4GenerateConformers.py - Generate molecular conformations

SYNOPSIS

Psi4GenerateConformers.py [--basisSet <text>] [--confParams <Name,Value,...>] [--energyOut <yes or no>] [--energyDataFieldLabel <text>] [--energyUnits <text>] [--energyRMSDCalcMode <RMSD or BestRMSD>] [--energyRMSDCutoff <number>] [--energyRMSDCutoffMode <All or Lowest>] [--energyWindow <number>] [--infileParams <Name,Value,...>] [--maxIters <number>] [--methodName <text>] [--mp <yes or no>] [--mpLevel <Molecules or Conformers>] [--mpParams <Name, Value,...>] [--outfileParams <Name,Value,...>] [--overwrite] [--precision <number>] [--psi4OptionsParams <Name,Value,...>] [--psi4RunParams <Name,Value,...>] [--quiet <yes or no>] [--reference <text>] [--recenterAndReorient <yes or no>] [--symmetrize <yes or no>] [--symmetrizeTolerance <number>] [-w <dir>] -i <infile> -o <outfile>

Psi4GenerateConformers.py -h | --help | -e | --examples

DESCRIPTION

Generate 3D conformers of molecules using a combination of distance geometry and forcefield minimization followed by geometry optimization using a quantum chemistry method. A set of initial 3D structures are generated for a molecule employing distance geometry. The 3D structures in the conformation ensemble are sequentially minimized using forcefield and a quantum chemistry method.

A Psi4 XYZ format geometry string is automatically generated for each molecule in input file. It contains atom symbols and 3D coordinates for each atom in a molecule. In addition, the formal charge and spin multiplicity are present in the the geometry string. These values are either retrieved from molecule properties named 'FormalCharge' and 'SpinMultiplicty' or dynamically calculated for a molecule.

The supported input file formats are: Mol (.mol), SD (.sdf, .sd), SMILES (.smi, .csv, .tsv .txt)

The supported output file formats are: SD (.sdf, .sd)

OPTIONS

-b, --basisSet <text> [default: auto]

Basis set to use for energy minimization. Default: 6-31+G** for sulfur containing molecules; Otherwise, 6-31G** [Ref 150]. The specified value must be a valid Psi4 basis set. No validation is performed.

The following list shows a representative sample of basis sets available in Psi4:

```
STO-3G, 6-31G, 6-31+G, 6-31++G, 6-31G*, 6-31+G*,  6-31++G*,
6-31G**, 6-31+G**, 6-31++G**, 6-311G, 6-311+G, 6-311++G,
6-311G*, 6-311+G*, 6-311++G*, 6-311G**, 6-311+G**, 6-311++G**,
cc-pVDZ, cc-pCVDZ, aug-cc-pVDZ, cc-pVDZ-DK, cc-pCVDZ-DK, def2-SVP,
def2-SVPD, def2-TZVP, def2-TZVPD, def2-TZVPP, def2-TZVPPD
```

--confParams <Name,Value,...> [default: auto]

Generate an initial 3D conformation ensemble using distance geometry and forcefield minimization before final geometry optimization by a specified method name and basis set. Possible values: yes or no.

A comma delimited list of parameter name and value pairs for generating initial sets of 3D conformations for molecules. The 3D conformation ensemble is generated using distance geometry and forcefield functionality available in RDKit. The 3D structures in the conformation ensemble are subsequently minimized by a quantum chemistry method available in Psi4.

The supported parameter names along with their default values are shown below:

```
confMethod,ETKDGv2,
forceField,MMFF, forceFieldMMFFVariant,MMFF94,
enforceChirality,yes,alignConformers,yes, embedRMSDCutoff,0.5,
maxConfs,50,maxIters,250,randomSeed,auto

confMethod,ETKDGv2   [ Possible values: SDG, KDG, ETDG,
    ETKDG , or ETKDGv2]
forceField, MMFF   [ Possible values: UFF or MMFF ]
forceFieldMMFFVariant,MMFF94   [ Possible values: MMFF94 or MMFF94s ]
enforceChirality,yes   [ Possible values: yes or no ]
```

```
    alignConformers,yes   [ Possible values: yes or no ]
    embedRMSDCutoff,0.5   [ Possible values: number or None]
```

confMethod: Conformation generation methodology for generating initial 3D coordinates. Possible values: Standard Distance Geometry (SDG), Experimental Torsion-angle preference with Distance Geometry (ETDG), basic Knowledge-terms with Distance Geometry (KDG) and Experimental Torsion-angle preference along with basic Knowledge-terms with Distance Geometry (ETKDG or ETKDGv2) [Ref 129, 167] .

forceField: Forcefield method to use for energy minimization. Possible values: Universal Force Field (UFF) [Ref 81] or Merck Molecular Mechanics Force Field [Ref 83-87] .

enforceChirality: Enforce chirality for defined chiral centers during forcefield minimization.

alignConformers: Align conformers for each molecule.

maxConfs: Maximum number of conformations to generate for each molecule during the generation of an initial 3D conformation ensemble using conformation generation methodology. The conformations are minimized using the specified forcefield and a quantum chemistry method. The lowest energy conformation is written to the output file.

embedRMSDCutoff: RMSD cutoff for retaining initial set of conformers embedded using distance geometry and before forcefield minimization. All embedded conformers are kept for 'None' value. Otherwise, only those conformers which are different from each other by the specified RMSD cutoff, 0.5 by default, are kept. The first embedded conformer is always retained.

maxIters: Maximum number of iterations to perform for each conformation during forcefield minimization.

randomSeed: Seed for the random number generator for reproducing initial 3D coordinates in a conformation ensemble. Default is to use a random seed.

--energyOut <yes or no> [default: yes]

Write out energy values.

--energyDataFieldLabel <text> [default: auto]

Energy data field label for writing energy values. Default: Psi4_Energy (<Units>).

--energyUnits <text> [default: kcal/mol]

Energy units. Possible values: Hartrees, kcal/mol, kJ/mol, or eV.

--energyRMSDCalcMode <RMSD or BestRMSD> [default: RMSD]

Methodology for calculating RMSD values during the application of RMSD cutoff for retaining conformations after the final energy minimization. Possible values: RMSD or BestRMSD. This option is ignore during 'None' value of '--energyRMSDCutoff' option.

During BestRMSMode mode, the RDKit 'function AllChem.GetBestRMS' is used to align and calculate RMSD. This function calculates optimal RMSD for aligning two molecules, taking symmetry into account. Otherwise, the RMSD value is calculated using 'AllChem.GetConformerRMS' without changing the atom order. A word to the wise from RDKit documentation: The AllChem.GetBestRMS function will attempt to align all permutations of matching atom orders in both molecules, for some molecules it will lead to 'combinatorial explosion'.

--energyRMSDCutoff <number> [default: 0.5]

RMSD cutoff for retaining conformations after the final energy minimization. By default, only those conformations which are different from the lowest energy conformation by the specified RMSD cutoff and are with in the specified energy window are kept. The lowest energy conformation is always retained. A value of zero keeps all minimized conformations with in the specified energy window from the lowest energy.

--energyRMSDCutoffMode <All or Lowest> [default: All]

RMSD cutoff mode for retaining conformations after the final energy minimization. Possible values: All or Lowest. The RMSD values are compared against all the selected conformations or the lowest energy conformation during 'All' and 'Lowest' value of '--energyRMSDCutoffMode'. This option is ignored during 'None' value of --energyRMSDCutoff.

By default, only those conformations which all different from all selected conformations by the specified RMSD cutoff and are with in the specified energy window are kept.

--energyWindow <number> [default: auto]

Psi4 Energy window for selecting conformers after the final energy minimization. The default value is dependent on '--energyUnits': 20 kcal/mol, 83.68 kJ/mol, 0.8673 ev, or 0.03188 Hartrees. The specified value must be in '--energyUnits'.

-e, --examples

Print examples.

-h, --help

Print this help message.

-i, --infile <infile>

Input file name.

--infileParams <Name,Value,...> [default: auto]

A comma delimited list of parameter name and value pairs for reading molecules from files. The supported parameter names for different file formats, along with their default values, are shown below:

```
SD, MOL: removeHydrogens,no,sanitize,yes,strictParsing,yes
SMILES: smilesColumn,1,smilesNameColumn,2,smilesDelimiter,space,
    smilesTitleLine,auto,sanitize,yes
```

Possible values for smilesDelimiter: space, comma or tab.

--maxIters <number> [default: 50]

Maximum number of iterations to perform for each molecule or conformer during energy minimization by a quantum chemistry method.

-m, --methodName <text> [default: auto]

Method to use for energy minimization. Default: B3LYP [Ref 150]. The specified value must be a valid Psi4 method name. No validation is performed.

The following list shows a representative sample of methods available in Psi4:

```
B1LYP, B2PLYP, B2PLYP-D3BJ, B2PLYP-D3MBJ, B3LYP, B3LYP-D3BJ,
B3LYP-D3MBJ, CAM-B3LYP, CAM-B3LYP-D3BJ, HF, HF-D3BJ,  HF3c, M05,
M06, M06-2x, M06-HF, M06-L, MN12-L, MN15, MN15-D3BJ,PBE, PBE0,
PBEH3c, PW6B95, PW6B95-D3BJ, WB97, WB97X, WB97X-D, WB97X-D3BJ
```

--mp <yes or no> [default: no]

Use multiprocessing.

By default, input data is retrieved in a lazy manner via mp.Pool.imap() function employing lazy RDKit data iterable. This allows processing of arbitrary large data sets without any additional requirements memory.

All input data may be optionally loaded into memory by mp.Pool.map() before starting worker processes in a process pool by setting the value of 'inputDataMode' to 'InMemory' in '--mpParams' option.

A word to the wise: The default 'chunkSize' value of 1 during 'Lazy' input data mode may adversely impact the performance. The '--mpParams' section provides additional information to tune the value of 'chunkSize'.

--mpLevel <Molecules or Conformers> [default: Molecules]

Perform multiprocessing at molecules or conformers level. Possible values: Molecules or Conformers. The 'Molecules' value starts a process pool at the molecules level. All conformers of a molecule are processed in a single process. The 'Conformers' value, however, starts a process pool at the conformers level. Each conformer of a molecule is processed in an individual process in the process pool. The default Psi4 'OutputFile' is set to 'quiet' using '--psi4RunParams' for 'Conformers' level. Otherwise, it may generate a large number of Psi4 output files.

--mpParams <Name,Value,...> [default: auto]

A comma delimited list of parameter name and value pairs to configure multiprocessing.

The supported parameter names along with their default and possible values are shown below:

```
chunkSize, auto
inputDataMode, Lazy   [ Possible values: InMemory or Lazy ]
numProcesses, auto   [ Default: mp.cpu_count() ]
```

These parameters are used by the following functions to configure and control the behavior of multiprocessing: mp.Pool(), mp.Pool.map(), and mp.Pool.imap().

The chunkSize determines chunks of input data passed to each worker process in a process pool by mp.Pool.map() and mp.Pool.imap() functions. The default value of chunkSize is dependent on the value of 'inputDataMode'.

The mp.Pool.map() function, invoked during 'InMemory' input data mode, automatically converts RDKit data iterable into a list, loads all data into memory, and calculates the default chunkSize using the following method as shown in its code:

```
chunkSize, extra = divmod(len(dataIterable), len(numProcesses) * 4)
if extra: chunkSize += 1
```

For example, the default chunkSize will be 7 for a pool of 4 worker processes and 100 data items.

The mp.Pool.imap() function, invoked during 'Lazy' input data mode, employs 'lazy' RDKit data iterable to retrieve data as needed, without loading all the data into memory. Consequently, the size of input data is not known a priori. It's not possible to estimate an optimal value for the chunkSize. The default chunkSize is set to 1.

The default value for the chunkSize during 'Lazy' data mode may adversely impact the performance due to the overhead associated with exchanging small chunks of data. It is generally a good idea to explicitly set chunkSize to a larger value during 'Lazy' input data mode, based on the size of your input data and number of processes in the process pool.

The mp.Pool.map() function waits for all worker processes to process all the data and return the results. The mp.Pool.imap() function, however, returns the the results obtained from worker processes as soon as the results become available for specified chunks of data.

The order of data in the results returned by both mp.Pool.map() and mp.Pool.imap() functions always corresponds to the input data.

-o, --outfile <outfile>

Output file name.

--outfileParams <Name,Value,...> [default: auto]

A comma delimited list of parameter name and value pairs for writing molecules to files. The supported parameter names for different file formats, along with their default values, are shown below:

```
SD: kekulize,yes,forceV3000,no
```

--overwrite

Overwrite existing files.

--precision <number> [default: 6]

Floating point precision for writing energy values.

--psi4OptionsParams <Name,Value,...> [default: none]

A comma delimited list of Psi4 option name and value pairs for setting global and module options. The names are 'option_name' for global options and 'module_name__option_name' for options local to a module. The specified option names must be valid Psi4 names. No validation is performed.

The specified option name and value pairs are processed and passed to psi4.set_options() as a dictionary. The supported value types are float, integer, boolean, or string. The float value string is converted into a float. The valid values for a boolean string are yes, no, true, false, on, or off.

--psi4RunParams <Name,Value,...> [default: auto]

A comma delimited list of parameter name and value pairs for configuring Psi4 jobs.

The supported parameter names along with their default and possible values are shown below:

```
MemoryInGB, 1
NumThreads, 1
OutputFile, auto   [ Possible  values: stdout, quiet, or FileName ]
ScratchDir, auto   [ Possivle values: DirName]
RemoveOutputFile, yes   [ Possible values: yes, no, true, or false]
```

These parameters control the runtime behavior of Psi4.

The default file name for 'OutputFile' is <InFileRoot>_Psi4.out. The PID is appended to output file name during multiprocessing as shown: <InFileRoot>_Psi4_<PIDNum>.out. The 'stdout' value for 'OutputType' sends Psi4 output to stdout. The 'quiet' or 'devnull' value suppresses all Psi4 output. The 'OutputFile' is set to 'quiet' for 'auto' value during 'Conformers' of '--mpLevel' option.

The default 'Yes' value of 'RemoveOutputFile' option forces the removal of any existing Psi4 before creating new files to append output from multiple Psi4 runs.

The option 'ScratchDir' is a directory path to the location of scratch files. The default value corresponds to Psi4 default. It may be used to override the deafult path.

-q, --quiet <yes or no> [default: no]

Use quiet mode. The warning and information messages will not be printed.

-r, --reference <text> [default: auto]

Reference wave function to use for energy calculation. Default: RHF or UHF. The default values are Restricted Hartree-Fock (RHF) for closed-shell molecules with all electrons paired and Unrestricted Hartree-Fock (UHF) for open-shell molecules with unpaired electrons.

The specified value must be a valid Psi4 reference wave function. No validation is performed. For example: ROHF, CUHF, RKS, etc.

The spin multiplicity determines the default value of reference wave function for input molecules. It is calculated from number of free radical electrons using Hund's rule of maximum multiplicity defined as 2S + 1 where S is the total electron spin. The total spin is 1/2 the number of free radical electrons in a molecule. The value of 'SpinMultiplicity' molecule property takes precedence over the calculated value of spin multiplicity.

--recenterAndReorient <yes or no> [default: yes]

Recenter and reorient a molecule during creation of a Psi4 molecule from a geometry string.

The 'No' values allows the minimization of a molecule in its initial 3D coordinate space generated by RDKit.

--symmetrize <yes or no> [default: auto]

Symmetrize molecules before energy minimization. Default: 'Yes' during 'Yes' value of '--recenterAndReorient'; Otherwise, 'No'. The psi4 function, psi4mol.symmetrize(SymmetrizeTolerance), is called to symmetrize the molecule before calling psi4.optimize().

The 'No' value of '--symmetrize' during 'Yes' value of '--recenterAndReorient' may cause psi4.optimize() to fail with a 'Point group changed...' error message.

--symmetrizeTolerance <number> [default: 0.01]

Symmetry tolerance for '--symmetrize'.

-w, --workingdir <dir>

Location of working directory which defaults to the current directory.

EXAMPLES

To generate an initial conformer ensemble of up to 50 conformations using a combination of ETKDGv2 distance geometry methodology, applying embed RMSD cutoff of 0.5 and MMFF forcefield minimization, followed by energy minimization using B3LYP/6-31G** or B3LYP/6-31+G** (sulfur containing), selecting a final set of minimized conformers for molecules in a SMILES file, applying energy RMSD cutoff of 0.5 and energy window value value of 20 kcal/mol, and write out a SD file containing minimized conformers, type:

```
% Psi4GenerateConformers.py -i Psi4Sample.smi -o Psi4SampleOut.sdf
```

To run the first example in a quiet mode and write out a SD file, type:

```
% Psi4GenerateConformers.py -q yes -i Psi4Sample.smi -o
  Psi4SampleOut.sdf
```

To run the first example in multiprocessing mode at molecules level on all available CPUs without loading all data into memory and write out a SD file, type:

```
% Psi4GenerateConformers.py --mp yes -i Psi4Sample.smi -o
  Psi4SampleOut.sdf
```

To run the first example in multiprocessing mode at conformers level on all available CPUs without loading all data into memory and write out a SD file, type:

```
% Psi4GenerateConformers.py --mp yes --mpLevel Conformers
  -i Psi4Sample.smi -o Psi4SampleOut.sdf
```

To run the first example in multiprocessing mode at molecules level on specific number of CPUs and chunk size without loading all data into memory and write out a SD file, type:

```
% Psi4GenerateConformers.py  --mp yes --mpParams "inputDataMode,Lazy,
  numProcesses,4,chunkSize,8" -i Psi4Sample.smi -o Psi4SampleOut.sdf
```

To run the first example by using an explicit set of specific parameters, and write out a SD file, type

```
% Psi4GenerateConformers.py --confParams "confMethod,ETKDGv2,
  forceField,MMFF, forceFieldMMFFVariant,MMFF94s, maxConfs,20,
  embedRMSDCutoff,0.25" --energyUnits "kJ/mol" -m B3LYP
  -b "6-31+G**" --maxIters 20 -i Psi4Sample.smi -o Psi4SampleOut.sdf
```

To run the first example for molecules in a CSV SMILES file, SMILES strings in column 1, name column 2, and write out a SD file, type:

```
% Psi4GenerateConformers.py --infileParams "smilesDelimiter,comma,
  smilesTitleLine,yes,smilesColumn,1,smilesNameColumn,2"
  -i Psi4Sample.csv -o Psi4SampleOut.sdf
```

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SEE ALSO

Psi4CalculateEnergy.py, Psi4CalculatePartialCharges.py, Psi4PerformMinimization.py

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The functionality available in this script is implemented using Psi4, an open source quantum chemistry software package, and RDKit, an open source toolkit for cheminformatics developed by Greg Landrum.

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