Technical Report

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AFGEN2.0

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AFGEN is a program that generates descriptor spaces for chemical compound(s). The descriptor space consists of graph fragments that can have three different types of topologies: paths (PF), acyclic subgraphs (AF), and arbitrary topology subgraphs (GF).

This manual is divided in the following sections:

- Installation
- Running AFGEN
- Input Files
- Output Files
- Examples
- Limits
- Credits & Contact Information
- Copyright Information

### Installation

AFGEN is provided as a binary distribution with pre-built executables for Linux (both for 32 and 64 bit architectures). Additional binaries can be provided upon request.

Once you download AFGEN, you need to uncompress and untar it using the following commands:

```
> tar -xzf afgem-2.0.tar.gz
```

This will create a directory named `afgen-2.0` with the following structure:

```
afgen-2.0\n  builds\n  Linux-i686\n  Linux-x86_64\n  doc\n  examples\n```

### Running AFGEN

The name of the AFGEN executable is `afgen` and is located in the architecture-specific subdirectory under `builds`. The `afgen` program is invoked at the command-line within a shell window (e.g., xterm, Gnome terminal, etc).

#### Operational Modes

The `afgen` program can be used in two different modes. In the first mode, referred to as the *descriptor-space generation mode* (DSGM), `afgen` reads a library of compounds,
finds all the fragment-based descriptors, and then represents each library compound as a frequency vector in that descriptor space.

In the second mode, referred to as the descriptor-space projection mode (DSPM), afgen takes as input a library of compounds and a previously generated set of afgen descriptors (using the -fragfile option) and then represents each library compound as a frequency vector in that descriptor space. Note that in this second mode, no new fragments (i.e., descriptors) are generated.

**Manpage**

The manpage for afgen is the following (can be obtained by typing afgen -help):

```
Usage
afgen [options] filename

Required parameters
filename
The file containing the library of compounds. The compounds are
specified using MDL's SD file format (http://www.mdl.com) or Tripos's
mol2 format (http://www.tripos.com).
The specific format of the library is determined by the
extension of
the file, which can be either .sdf or .mol2.

Optional parameters
-fragtype=string
Specifies the type of fragment-based descriptors to be
generated.
Supported options are:
gf arbitrary fragments [default]
af acyclic fragments
pf path fragments

-lmin=int
Specifies the minimum length (in terms of bonds) of the
generated
fragments. The default value is 3.

-lmax=int
Specifies the maximum length (in terms of bonds) of the
generated
fragments. The default value is 7.
```
```markdown
|-fmin=int
| Specifies the minimum frequency that a fragment must
| have before it becomes a descriptor. The frequency of a fragment
| is based on the number of distinct compounds that it occurs at.
| The default value is 1 (i.e., all fragments are treated as
| descriptors).

|-noh
| This option forces afgem to remove any hydrogen atoms from the compounds.

|-noatyping
| Forces afgem to ignore the atom typing specified in the input file
| (if any). If this option is used, then only the basic atom types are
| used (e.g., P, N, O, etc.). This option applies only to inputs files
| that use the mol2 format.

|-armark
| Detects aromatic rings in SDF files and relabels the bonds as aromatic.

|-outfile=string
| Specifies the stem of the output files (.out & .frags.[sdf, mol2]).
| If outfile is not specified then the output stem is the same as input
| stem.

|-fragfile=string
| Specifies the file containing previously generated fragments to be used
| for restricting the descriptor representation of the library. If this
| file is specified, the compounds will be represented as vectors in
| that descriptor space and any fragments contained in the compounds
| but not in that file will be ignored.

|-nooutput
| Does not produce any output files and used for testing only.
```
Input Files

The `afgen` program uses two different input files. The first is the file that stores the compound library. At this point `afgen` supports library files in MDL's SD file format (.sdf extension) and Tripos's Mol2 file format (.mol2 extension). These are two of the most widely used structural formats for chemical compounds. Information regarding the SDF format can be found at [http://www.mdl.com](http://www.mdl.com) and information regarding the Mol2 format can be found at [http://www.tripos.com](http://www.tripos.com). If your library is not already in SDF or Mol2 formats, you can use OpenBabel [http://openbabel.org](http://openbabel.org) to convert your input files in one of these two formats.

The second file, supplied via the `-fragfile` optional parameter, is the fragment file generated from a previous run of `afgen`. You should not manually edit this file, unless you have a good understanding of the information stored in it.

Output Files

Depending of the operational model of `afgen`, it will create either two or one files. When `afgen` is used to generate a set of fragment-based descriptors for a library (DSGM) it will produce both a fragment file (extension .frag.sdf or .frag.mol2) containing the SDF/Mol2 representation of the discovered fragments (i.e., descriptors) and the descriptor-based representation of the library (extension .out). When `afgen` is used to generate the descriptor-based representation of a library with respect to a previously discovered set of graph fragments (DSPM), it will only produce the descriptor-based representation of the library.

**Note:**

In addition to these files, while running, `afgen` creates a temporary file with the extension .afgen-temp. Upon successful completion, `afgen` deletes this file.

Format of the Fragment File

The following shows the first few lines of the fragment file generated by executing:

`afgen -lmin=2 -lmax=3 test1.sdf`

(The `test1.sdf` file is in the examples directory).

```
AFGEN
  20AFGEN-GF:2-3:1
```
<table>
<thead>
<tr>
<th>1 0 0 0 0 0 0 0 0 0 999 V2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
</tbody>
</table>

M END
> <AFGEN_NFRAGS>
19

> <AFGEN_VLBLS>
3
000H
001C
0020

$$$$
1
20AFGEN-GF:2-3:1

<table>
<thead>
<tr>
<th>3 2 0 0 0 0 0 0 0 0 999 V2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>1 2 1 0 0 0 0</td>
</tr>
<tr>
<td>1 3 2 0 0 0 0</td>
</tr>
</tbody>
</table>

M END
> <AFGEN_EDGES>
2
0:1:1:1:0
0:1:2:1:1

$$$$
2
20AFGEN-GF:2-3:1

<table>
<thead>
<tr>
<th>4 3 0 0 0 0 0 0 0 0 999 V2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>0.0 0.0 0.0 C 0 0 0 0 0 0</td>
</tr>
<tr>
<td>1 2 2 0 0 0 0</td>
</tr>
<tr>
<td>1 3 1 0 0 0 0</td>
</tr>
<tr>
<td>2 4 1 0 0 0 0</td>
</tr>
</tbody>
</table>

M END
> <AFGEN_EDGES>
3
0:1:1:1:1
The format of the fragment file follows the format of the input file. If the input library is in SDF format then the fragment file is in SDF format. If the input library is in mol2 format, then the fragment file is in mol2 format.

The above example shows the SDF-version of the fragment file. The first compound corresponds to a dummy compound that contains some information related to the number of discovered fragments (AFGEN_NFRAGS) and a mapping of the chemical atoms to internal numbering (AFGEN_VLBLs). The rest of the file contains the SDF format of the fragments that were generated numbered from 1. This fragment numbering is used by the descriptor-based representation file to indicate the set of fragments along with their frequencies that are contained in each compound.

The mol2-version of the fragment file contains similar information.

**Note:**
Besides the standard atoms/bonds information for each fragment, the file also contains the list of bonds in a canonicalized form (AFGEN_EDGES). This information are used by afgen when operating in the DSPM mode and should not be modified.

**Format of the Descriptor-Space Representation File**

The following shows the first few lines of the descriptor-space compound representation file generated by executing: afgen -lmin=3 -lmax=4 -fmin=30 test2.sdf.

```plaintext
>318
14:2 15:2 16:1 17:2 18:2 19:1
3:3 4:11
>332
14:1 15:1 16:1 20:1 21:1
3:1 4:10
>432
3:10 4:20
>656
35:2 36:2 37:2 38:2 39:2 40:1 41:1 42:1 43:1
3:5 4:12
>836
```
The descriptor-space representation file contains three lines for each library compound. The first line (starting with a > character) contains the name of the compound and is obtained from the library file itself.

The second line contains the actual descriptor-space representation. It consists of a sequence of \texttt{fragment-ID:frequency} pairs separated by a space (sorted in increasing fragment-ID order). The fragment-ID corresponds to the name of the fragment as stored in the fragment file and the frequency counts the number of embeddings of this fragment in the compound.

The third line contains a sequence of \texttt{fragment-length:frequency} pairs for those descriptors that are not included in the descriptor-based representation of the compound. These numbers will be non-zero under two scenarios. First, if a value greater than 1 is specified for \texttt{-fmin}, some of the fragments present in the library may be pruned because they do not meet the minimum frequency cutoff. For each fragment that is pruned, their frequencies are added up on a per-length basis and are reported in this line. For example, in the case of the 318 compound in the above example, due to the \texttt{-fmin=30}, it resulted in pruning fragments of length 3 whose total frequency was 3, and fragments of length 4 whose total frequency was 11. The second case in which these frequencies will be non zero are when \texttt{afgen} is used in the \texttt{DSPM} mode. Since the descriptors are restricted to only those provided by the \texttt{-fragfile} option, some of the fragments present in each compound may not have corresponding descriptors. In such cases, the total frequency (on a per fragment length basis) for these ignored fragments is reported in that line.

**Examples**

The following shows the information \texttt{afgen} outputs to the screen by executing: \texttt{afgen -lmin=3 -lmax=4 -fmin=30 test2.sdf}.
Among the information that is printed the most important are that number of fragments that were discovered (nfrags) and the number of non-zeros in the descriptor-based representation of the library (lnnz). The number of non-zeros indicates the space that will be required to store the descriptor-based representation in memory.

Among the other displayed information, ncfraags is the number of fragments read from the file specified via -fragfile and pnfrags is the number of fragments after frequency-based pruning.

**Limits**

The following is a set of limits on the structure/size of the compounds and fragments imposed in the current version of afgem:
<table>
<thead>
<tr>
<th>Property</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of atoms in a compound</td>
<td>511</td>
</tr>
<tr>
<td>Number of bonds in a compound</td>
<td>511</td>
</tr>
<tr>
<td>Number of atoms in a fragment</td>
<td>32</td>
</tr>
<tr>
<td>Number of bonds in a fragment</td>
<td>32</td>
</tr>
<tr>
<td>Degree of an atom in a fragment</td>
<td>5</td>
</tr>
<tr>
<td>Number of atoms types</td>
<td>256</td>
</tr>
<tr>
<td>Number of bond types</td>
<td>8</td>
</tr>
</tbody>
</table>

**Credits & Contact Information**

AFGEN was written by Nikil Wale (version 1.0) and George Karypis (version 2.0).

If you encounter any problems or have any suggestions, please contact George Karypis via email at karypis@cs.umn.edu.

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**Copyright Information**

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```
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