Pep2Path

Automated mass spectrometry-guided genome mining of peptidic natural products

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1 Installation

1.1 Prerequisites

1.1.1 General prerequisites

Operating system: Mac OS X 10.6+, LINUX or Windows XP/Vista/7.
antiSMASH version 2.x must be installed for the makedb program of Pep2Path to work, and the path to the antiSMASH installation directory should be indicated in the pep2path.cfg file. antiSMASH2 can be downloaded here.
Python 2.7 should be installed as the default Python installation, and the Python installation directory should be added to the $PATH variable. If you are a Windows user, click here for instructions.
When only using Nrp2Path with the supplied genbank.ppd file, or when only using RiPP2Path, it is not necessary to install antiSMASH2.

1.1.2 Prerequisites for antiSMASH2

To be able to run antiSMASH2 on Windows, you will need to install the following packages:
- Microsoft Visual C++ 2008 Redistributable Package:
  http://www.microsoft.com/en-us/download/details.aspx?id=29
- Java: http://www.java.com/en/download/index.jsp
- Python 2.7.X (choosing either the 32- or 64-bits version to match the antiSMASH version): http://www.python.org/ftp/python/2.7.3/python-2.7.3.msi

To be able to run antiSMASH on Mac OS X, you will need to install Cairo and libxml2. These can be acquired by first installing MacPorts. Then, to get Cairo, type 'sudo port install cairo' in the terminal. To get libxml2, type 'sudo port install libxml2' in the terminal. If using a version of OS X older than 10.8, make sure that Python 2.7.3 is installed too.
For more information, see the antiSMASH README file.

1.1.3 Use of makedb with 'light' antiSMASH2 installation

If you do not use antiSMASH2 on your system except as a prerequisite for Pep2Path, it is possible to slightly customize the antiSMASH2 code in order to install and run Pep2Path without having to install the (large) antiSMASH2 ClusterBlast and Pfam databases.

In such a case, one can edit the run_antismash.py file in a text editor (e.g., Notepad/Emacs/Vi) and delete the following lines:

```
#Check prerequisites
if check_prereqs(plugins, options) > 0:
     logging.error("Not all prerequisites met")
     sys.exit(1)
```

1.2 Source code

This package provides the source code of Pep2Path. You are free to modify the source code under the terms of the supplied license and run it using a local Python installation.

1.3 Installation of Pep2Path

Browse to the Pep2Path download page, download the zip file and extract it in a directory to which you have full writing access (e.g., your user home directory).

2 Information for General Use

2.1 Accepted input file formats

2.1.1 NRP2Path: PPD files

NRP2Path uses specialized Pep2Path databases (PPD files), which are generated from antiSMASH2 predictions using the *makedb* program provided with Pep2Path. Multiple PPD files can be merged with the *mergedb* program.

2.1.2 Makedb: GBK/EMBL/FASTA files

The ideal input for the makedb program consists of one or more annotated nucleotide files in Genbank format or EMBL format. The file names must end at either .gbk/.gb or .embl/emb.

General information on the EMBL format is available at http://www.ebi.ac.uk/help/formats.html#EMBL .

General information on the GenBank format is available at http://www.ncbi.nlm.nih.gov/Sitemap/samplerecord.html .

Alternatively, nucleotide FASTA files can also be supplied. In this case, the *ad hoc* gene prediction using Glimmer may lead to slightly lower quality results.

2.1.3 RiPP2Path: GBK/EMBL/FASTA files

RiPP2Path takes in both annotated (Genbank or EMBL format) and unannotated (FASTA format) nucleotide files. One file may contain multiple entries, and multiple files can be analysed simultaneously.

2.2 Database files

For NRP2Path, a PPD database file 'genbank.ppd' containing all NRPS gene clusters predicted by antiSMASH2 on the GenBank database from 10/2013 is shipped with Pep2Path.

2.3 Pep2Path output

All output of your Nrp2Path or RiPP2Path run is saved in a tab-delimited TXT file within the installation directory. The name of the file can be modified using the '-out' parameter from the command-line. The TXT file can be opened in a TXT editor or spreadsheet editor (e.g., MS Excel).

3 Command-line Usage

All Pep2Path programs should be run from the command line using Python, ideally from the Pep2Path installation directory. For information on how to use the command line or terminal, see here (Windows) and here (Linux/Mac). For information on how to run a Python script, see this page.

3.1 Nrp2Path

The general way to run Nrp2Path is

```
python nrp2path.py <options> <sequence tag(s)>
```

The sequence tag is provided as a comma-separated list of amino acids (in three-letter code) or masses (in Da), e.g. "Ala,Gly,Leu,Bht" or "87,113,99,87". For the full list of amino acid three-letter codes, see the contents of the file "NRP_aa.txt". 'Redundant' positions can also be added into an amino acid sequence tag using slashes, e.g. 'Ala,Gly,Ile/Leu,Bht'.

Several options are available from the command line to set up a Nrp2Path run.

In the options below, "<f>" represents a floating number:

```
--db DB               file name of database to search. Default
                      database is genbank.ppd
--out OUTFILE         name of output file to write results to. Default
                      is nrp2path.out
--cpus CPUS           How many CPUs to use in parallel (between 1 and
                      4, default: 1)
--taxonomy TAXONOMY   species/genus/family/order/class/phylum name to
                      delimit taxonomic range to search
--c <f>               confidence parameter c, default=1.0
--x <f>               correction weight parameter x, default=0.01
--eta <f>             strictness parameter eta. default=2.0
--include_subtags     also search for all subtags of provided tags
                      (not just possible N or C termini).
```

An example of a final Nrp2Path call is:

```
python nrp2path.py --db metagenome.ppd --out metagenome_results.txt
--taxonomy Bacillus 57,113,99,99,85,111 83,85,128
```

In this case, all entries in the metagenome.ppd database file that belong to the genus *Bacillus* are searched for two mass shift sequences ("57,113,99,99,85,111" and "83,85,128"). The output is stored in the file “metagenome_results.txt”.

MakeDB

The general way to run makedb is

```
python makedb.py <options> <SEQUENCE FILES>
```

The sequence files are (paths to) file names in GBK/EMBL/FASTA format.

The following options are available:

```
--cpus CPUS       How many CPUs to use in parallel for antiSMASH
--dbname DBNAME   Name for database to write to
--from START      Start antiSMASH analysis at nucleotide specified
                  (only for single input files)
--to END          End antiSMASH analysis at nucleotide specified
                  (only for single input files)
--eukaryotic      DNA is of eukaryotic origin
--all-orfs        Use all ORFs > 60 nt instead of running gene
                  finding
```

An example of a final MakeDB call is:

```
python makedb.py --dbname fungalgenomes.ppd --eukaryotic genome1.gbk
genome2.gbk genome3.fasta
```

Here, the three genome files "genome1.gbk", "genome2.gbk" and "genome3.fasta" are processed with antiSMASH2 into a database called "fungalgenomes.ppd". The '--eukaryotic' tag ensures that eukaryote-specific substrate specificity predictions are performed in antiSMASH2.

3.2 MergeDB

The general way to run mergedb is

```
python mergedb.py <INPUT DATABASE FILES> <OUTPUT DATABASE FILE>
```

An example of a final MergeDB call is:

```
python mergedb.py genbank.ppd my_own_db.ppd genbank_updated.ppd
```

In this case, the custom database "my_own_db.ppd" is appended to the default "genbank.ppd" database, and the combination of the two databases is written to the new database file "genbank_updated.ppd".

3.3 RiPP2Path

The general way to run RiPP2Path is

```
python ripp2path.py --tags <TAGS> --seq <SEQUENCE FILES> <options>
```

Like with Nrp2Path, each sequence tag is provided as a comma-separated list of amino acids (in three-letter code) or masses (in Da), e.g. "Ala,Gly,Ile/Leu,Bht" or "87,113,99,87". For the full list of amino acid three-letter codes, see the contents of the file "RiPP_aa.txt".

Several options are available from the command line to set up a Nrp2Path run:

```
--out OUTFILE         name of output file to write results to
--cutoff CUTOFF       cut-off identity for peptides to be reported,
                      default=0.5
```

An example of a final RiPP2Path call is:

```
python ripp2path.py --tags 57,113,99,99,85,111 83,85,128 --seq
sequence_file1.fasta sequence_file2.gbk --out ripp2path_results.txt
--cutoff 0.4
```

In this case, the six-frame translations of all nucleotide sequences in the files "sequence_file1.fasta" and "sequence_file2.gbk" are searched for short peptides corresponding to the mass shift sequences "57,113,99,99,85,111" and "83,85,128", and all results with identities >40% are reported in the output file "ripp2path_results.txt".

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Version 3, 29 June 2007

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