PuMA

Release 1.1

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Contents

PuMA's code can be found here. PuMA is also available through iMicrobe.

CHAPTER 1

About PuMA

PuMA is a pipeline written in Python3 for papillomavirus genome annotation.

The pipeline was created by utilizing several Python3 and command line packages including Biopython, BLAST, MEME, FIMO, and MUSCLE as well as user defined functions. For more information on how PuMA works, refer to 'How PuMA Works'.

CHAPTER 2

Contents:

2.1 Dependency Information

PuMA has the following dependencies. Install them to run PuMA locally:

- Python3.x
- Biopython
- BLAST
- MEME, FIMO
- MUSCLE
- pandas
- matplotlib

Biopython, pandas, and matplotlib can be installed via *pip*:

```
pip install biopython
pip install pandas
pip install matplotlib
```

Click on each package to be taken to the respective website for detailed installation instructions.

2.2 Local Usage (MacOS or Linux)

Follow the directions below to run PuMA locally without using Docker. If you want to execute PuMA with Docker, refer to the "Usage via Docker" page.

Due to dependencies, PuMA only runs on MacOS or Linux operating systems. Refer to the 'Dependency Information' section for more information.

After the dependencies have been installed, from Github download the 'data_dir' folder and within the 'scripts' directory download 'run_puma.py' and 'puma.py'.

To execute PuMA, make sure 'run_puma.py' is excecutable:

```
chmod +x run_puma.py
```

Minimum PuMA execuation command:

```
./run_puma.py -i HPV16REF.fa -D warning
```

All files and folders need to be in the same location or absolute path needs to be used. For example the input file above (HPV16REF) and the 'data_dir' folder need to be in the same folder as 'run_puma.py' and 'puma.py'.

You can always use '-h' or '–help' on 'run_puma.py' to get a list and description of all inputs.

After execution, it is encouraged to either move, rename, or delete the output folder 'puma_out' before running PuMA again. This way, there are no issues with the existing 'puma_out' folder and the new one that will be generated with each execution.

2.3 Usage via Docker

Download "data_dir" from GitHub, the folder is needed as an input argument.

Be sure you have Docker installed on your machine. No Docker account is needed. Do the following to pull the image locally:

```
docker pull kvdlab/puma:1.2.1
```

Now you should be able to run the image and see the following output:

```
$ docker run --rm -it kvdlab/puma:1.2.1
usage: run_puma.py [-h] -i FILE [-f FORMAT] [-d DIR] [-o DIR] [-e FLOAT]
[-m NUM] [-D STR] [-L FILE]
run_puma.py: error: the following arguments are required: -i/--input
```

To run Puma on your data, you will need to mount your local input and output direc:xtories. For instance, from within this "docker" directory, we can run the program like so:

```
$ docker run --rm \
-v `pwd`/../data_dir:/data \           <1>
-v `pwd`/../input_and_output:/in_out \ <2>
kvdlab/puma:1.2.1 \                    <3>
run_puma.py -i /in_out/BPV2_new.fa -o /in_out/puma_out -d /data <4>
```

1. The "data_dir" dir will be mounted as "/data"
2. The "input_and_output" dir will be mounted as "/in_out"
3. This is the tag of the Docker image to run
4. This is the command to execute Puma with the input and output arguments

Be sure to avoid using a space before or after the colon when mounting the directories using the "-v" argument.

When running PuMA through Docker, the output argument needs to be specified ('-o'). In the above example the "input_and_output" folder represents where the input file and the "puma_out" directory are. The output directory is "puma_out" since part of the command is "-o /in_out/puma_out". For ease of use, it is recommended that there is one folder for the input and output like the above example

Once PuMA executes, the output folder will be in the specified local directory. For the above example, the "puma_out" folder will be in the directory "input_and_output".

2.4 Usage via iMicrobe

PuMA is also available through iMicrobe. You will need to create a Cyverse Account. Once you do this, head to the iMicrobe website and click on 'My Account'-> 'Data Store'. Once you are in the Data Store, you will be able to upload the input files to use for PuMA.

Once you have uploaded the input files in the Data Store, nagivate to 'Tools' -> 'Apps' and click on 'puma-x.x.xux' (most current version). You will then be able to select the input file or copy and paste the contents of the file into the appropriate box.

iMicrobe accesses the Extreme Science and Engineering Discovery Environment (XSEDE) compute resources at Texas Advanced Computing Center (TACC) including Stampede2. **While this offers access to significant compute power, due the large number of users the job might be in the queue for hours.** Once the job runs, it takes a few seconds for execution to complete.

To learn more about iMicrobe and Stampede2:

- iMicrobe Documentation
- Stampede2 Documentation

2.5 Input File formatting

Format for the fasta input file:

```
>Short name|Full name
sequence nucleotides (actg)
```

While the above formatting is standard for a fasta file, it helps with the output of PuMA. Short name is the abbreviation or accession number you want for output files (e.g. HPV16). Full name is what will be printed to the screen (e.g. Human papillomavirus 16).

PuMA can annotate multiple genomes from the same fasta input file. Follow the above formatting for each sequence.

2.6 Output

After execution, a folder 'puma_out' will have been created. Within 'puma_out' there will be a folder named 'Short name' (name used in the input file) for each genome in the input file. Within the 'Short name' folder(s) there will be 'for_user' and 'program_files' folders. Also in 'puma-out' is a log file that is by default called 'puma_execution.log'. This log file has potential notes about the annoation of each genome.

'for_user' contains a .csv file containing indvidual annotations, a .gb file containing annotations in GenBank format, a PDF file that has a visual represntation of the annotated genome, and a 'genbank_submission' folder. 'genbank_submission' has files that will aid in the genbank submission process.

The 'program_files' folder contains all files PuMA generates and uses during execution.

For Local Output:

The 'puma_out' folder will be, by default, in the same folder as all other PuMA files (i.e. 'puma.py' etc.)

For iMicrobe Output:

The 'puma_out' folder will be listed under the 'Output' section on the 'Jobs' page.

2.7 How PuMA Works

The pipeline works in numerous steps. After the sequence data is parsed from the fasta file, each genome is linearlized based on the L1 gene. Next, all main genes are identifed using BLAST (E1, E2, E6, E7, E9, E10, L1, L2). After the main genes are identfied, they are verified by using a database of genes from PaVE by utilizing BLAST and MUSCLE to do sequence identfication, alignment and comparisons. E5 variants (E5_alpha, E5_beta, E5_delta, E5_epsilon, E5_gamma, E5_zeta) are potentially identified by using BLAST to search the genome in the region between the end of E2 and the start of L1. Next, the Upstream Regulatory Region (URR) is identified. Using the URR, E1 and E2 binding sites are identifed via MEME and FIMO. The spliced genes are then identified. The splice acceptor is shared between the E1^E4 and E8^E2 and is embedded with in the E2 gene. MUSCLE is used to align the newly annotated E2 to its closest previously known relative (from BLAST results). For the splice donor site (which is located in E1) a similar approach is used. Once all of the above annotations are created, the various outputs are created. A log file describing the progress of analysis, a 'comma separated values' file (.csv) that contains individual annotation, a 'general features format 3' (.gff3) formated file, a GenBank (.gb) formated file, a PDF file providing a visual representation of the newly annotated genome, and sequin files that are used to streamline the submission process to GenBank are all available after execution.

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CHAPTER 3

Support

For questions, contact Dr. Koenraad Van Doorslaer via vandoorslaer AT arizona DOT edu or visit the KVD Lab website.