

Network Analysis Tools

Web server installation

Sylvain Brohée
sbrohee@ulb.ac.be

Karoline Faust
kfaust@ulb.ac.be

Jacques van Helden
jvhelden@ulb.ac.be

Laboratoire de Bioinformatique des Génomes et des Réseaux (BiGRe)
Laboratory of Genome and Network Biology
Université Libre de Bruxelles, Belgium
<http://www.bigre.ulb.ac.be/>

October 20, 2017

Contents

0.1	Installation of stand-alone programs required for NeAT	4
0.1.1	Compiling stand-alone programs provided in the RSAT/NEAT distribution	4
1	NeAT Web server installation	5
1.1	Installing a local web server	5
1.1.1	Web server pages	5
1.1.2	Apache modules	5
1.1.3	Tomcat	6
1.1.4	Java tools server	8
1.1.5	Metabolic Pathfinder and Pathway extraction	10
1.1.6	Web services	12

Description

This document describes the installation procedure for the web server of the **Network Analysis Tools (NeAT)**.

It assumes that you already installed the stand-alone version of the software suite **Regulatory Sequence Analysis Tools (RSAT)**, as described in the **RSAT** installation guide, and that you configured a local web server, as described in the **RSAT** webserver install guide.

0.1 Installation of stand-alone programs required for NeAT

For the Network Analysis Tools (NeAT), we need to install a set of programs developed by third-parties. Some of these programs come in the contrib directory of the **NeAT** distribution. Some others have to be downloaded from their original distribution site.

0.1.1 Compiling stand-alone programs provided in the RSAT/NEAT distribution

```
make -f makefiles/init_RSAT.mk compile_pathway_tools
```

Checking and configuring kwalks for NeAT

You can test that the compilation worked by running the following command.

```
$RSAT/contrib/kwalks/bin/lkwalk
```

This should display the help message of **lkwalk**.

Check that the KWALKS_ROOT variable in the RSAT config file (*\$RSAT/RSAT_config.props*) points to the correct path (it should be the absolute path of *\$RSAT/contrib/kwalks/bin/*).

Checking and configuring REA for NeAT

You can test that the compilation worked by running the following command.

```
$RSAT/contrib/REA/REA
```

This should display the help message of **REA**.

Check that the REA_ROOT variable in the RSAT config file (*\$RSAT/RSAT_config.props*) points to the correct path (it should be the absolute path of *\$RSAT/contrib/REA/*).

Chapter 1

NeAT Web server installation

1.1 Installing a local web server

As the Regulatory Sequence Analysis Tools, **NeAT** includes a web server, which offers a user-friendly interface for biologists. The main server is available for academic users at <http://rsat.ulb.ac.be/neat/>. A few additional mirrors have been installed in different countries.

1.1.1 Web server pages

The web pages are located in the directory *rsat/public_html*. This directory contains both the HTML help pages, and the PHP and CGI scripts.

1.1.2 Apache modules

The **NeAT** interface mainly relies on PHP (and CGI only for the roc-stats tool). These modules should be installed on the web server, and activated in the Apache configuration files. The installation and configuration of CGI is described in manual of the web server of **RSAT**.

To perform the following steps, you might dispose of the administrator permissions.

PHP module for Mac OSX

If your server is running under Mac OSX, you need to install a recent version (at least v5) of the php module, which can be found at the following site.

<http://www.entropy.ch/software/macosx/php/>

PHP module for LINUX

Generally, **PHP5** is included with the Linux distribution or can easily be installed using the installer (YAST, YUM, etc). Take care that the PHP5 Module for Apache 2.0 (apache2-mod_php5) is installed.

PHP5 can also be installed manually from the PHP website
<http://www.php.net/downloads.php>

In addition, you will need to install the module **php5-SOAP**.

Modification of `php.ini`

In order for the server to work with **NeAT**, you have to edit the main PHP configuration file `php.ini`. Depending on your PHP installation, this file might be in different directory. On Linux computers, it is usually found here:
`/etc/php5/apache2/php.ini` directory. In this file, you must modify the following fields accordingly.

```
soap.wsdl_cache_enabled=0
max_execution_time = 3600
max_input_time = 1800
memory_limit = 1G
error_reporting = E_ALL & ~E_NOTICE
post_max_size = 100M
upload_max_filesize = 100M
default_socket_timeout = 1800
upload_tmp_dir = "/tmp/php/"
```

Pay attention to the location of php5 extension libraries. Indicate the correct directory, e.g.:

```
extension_dir=/usr/lib/php5/extensions
```

You must change permissions so that the directory `/tmp/php/` for temporary upload is writable by everybody. To do this, type:

```
sudo mkdir -p /tmp/php;
sudo chmod 777 /tmp/php
```

1.1.3 Tomcat

The path finding and pathway extraction tools are using axis web services, JSP and Java servlet pages and needs Tomcat (<http://tomcat.apache.org/>) or an equivalent servlet engine to run.

Tomcat can be easily installed on SUSE with yast and is usually located in `/usr/share/tomcat` after installation.

On MacOS, you need to install TomCat (<http://tomcat.apache.org/>).

Make sure to install at least Tomcat version 5. We noticed however that Tomcat version 6 is more stable.

We will refer from now on to the Tomcat root directory as `$CATALINA_HOME` (for example, `/usr/share/tomcat7`).

Tomcat configuration

If you would like to use the Tomcat manager, make sure to configure the file `tomcat-users.xml` located in `$CATALINA_HOME/conf`.

Add a manager role with a special login and password, e.g.

```
<tomcat-users>
  <role rolename="tomcat"/>
  <role rolename="manager"/>
  <user username="tomcat" password="tomcat" roles="tomcat"/>
  <user username="metheadmin" password="mypassword" roles="manager"/>
</tomcat-users>
```

Make sure that tomcat-users.xml cannot be read by anyone else than tomcat or root.

By default, Tomcat takes a lot of memory. You can reduce this amount by modifying the file tomcat.conf in \$CATALINA_HOME/conf. Adjust the variable JAVA_OPTS as follows:

```
JAVA_OPTS="-Xmx800m"
```

You can start Tomcat on SUSE with

```
/etc/init.d/tomcat6 start
```

and stop it with

```
/etc/init.d/tomcat6 stop
```

More advice for the installation and configuration of Tomcat on unix systems can be found at: http://linux-sxs.org/internet_serving/book1.html

Optional: Mod_jk

The installation of Mod_jk is optional. If you do not want to install it, skip this section.

Mod_jk forwards requests for defined contexts from Apache to Tomcat. Users that have a strict firewall configuration blocking the Tomcat port will be able to access the web services through the Apache default port.

To install and configure mod_jk, you can follow the steps below:

1. Install the mod_jk module from <http://tomcat.apache.org/connectors-doc/> or via installation systems like yast.
2. In the Apache configuration folder (e.g. `/etc/apache2/conf.d`), add two configuration files: `workers.properties` and `tomcat.conf`
3. Content of `workers.properties`

```
# Define 1 real worker using ajp13
# this could be al list in the format
# worker.list=worker1, worker2, worker3, worker4
worker.list=worker1
# Set properties for worker1 (ajp13)
worker.worker1.type=ajp13
worker.worker1.host=localhost
worker.worker1.port=8009
```

4. Content of `tomcat.conf`

```
# Update this path to match your modules location
LoadModule jk_module /usr/lib/apache2/mod_jk.so
# Where to find workers.properties
# Update this path to match your conf directory location
```

```
JkWorkersFile /etc/apache2/conf.d/workers.properties
# Where to put jk shared memory
# Update this path to match your local log directory
# JkShmFile /var/log/apache2/mod_jk.shm
# Where to put jk logs
# Update this path to match your logs directory location
JkLogFile /var/log/apache2/mod_jk.log
# Set the jk log level [debug/error/info]
JkLogLevel error
# Send everything for context to worker named worker1 (ajp13)
JKMount /be.ac.ulb.bigre.graphtools.server/* worker1
JKMount /metabolicpathfinding/* worker1
```

5. Reload Apache (on SUSE `/etc/init.d/apache2 reload`).

An alternative to `mod_jk` is `mod_proxy`, which requires less configuration.

Preparation of folders for Tomcat

In Linux, a tomcat user is created if Tomcat is installed via yast. Make sure that this user has read, write and execution rights for the following folders:

```
$RSAT/contrib/REA
$RSAT/contrib/kwalks/bin
$RSAT/public_html/data/KEGG
$RSAT/public_html/data/Stored_networks
$RSAT/java/lib
```

If any of these folders does not yet exist, create them.

For installation of REA and kwalks see the section on third-party programs in the RSAT install guide.

1.1.4 Java tools server

The graphtools server contains the java web services of NeAT.

Installation of Java tools server

The graphtools server is stored as a war file in `$RSAT/java/web`.

1. Open the RSAT configuration file `RSAT_config.props` located in `$RSAT`. Set the value of the parameter `neat_java_ws` to `web_services/GraphAlgorithms.wsd`
2. If `mod_jk` or equivalent has not been installed, open the RSAT configuration file and set the parameter `tomcat_port` to the port on which Tomcat runs (by default 8080).
3. There are two ways to deploy a war file. If you do not use the Tomcat manager, make sure Tomcat can open the war file with the command:

```
chown tomcat:tomcat be.ac.ulb.bigre.graphtools.server.war
```

Then place the war file `be.ac.ulb.bigre.graphtools.server.war` in `$CATALINA_HOME/webapps` and

start Tomcat. If you use the Tomcat manager, open (<http://localhost:8080/manager/html>) and go to option *Select WAR file to upload*. After having selected the war file to upload, click *Deploy*.

4. Go to `$CATALINA_HOME/webapps/be.ac.ulb.bigre.graphtools.server/WEB-INF`
5. Open `serverConfig.txt` and set the value of `RSAT_ROOT` to the value of `$RSAT`.
6. Run `install.sh` with the following commands:

```
chmod 755 install.sh
./install.sh
```

You are done. You may read the section "Configuration remarks" for additional information. If you want to install the metabolic pathfinder, continue with section "Metabolic Pathfinder and Pathway extraction".

Configuration remarks

The directory `$RSAT/public_html/data/Stored_networks` allows to store graph files for longer time (since `$RSAT/public_html/tmp` is cleaned regularly).

Note that the Kegg network provider accesses the metabolic database to add attributes such as compound name or EC number to networks. In order to install the database, see the installation of the metabolic pathfinder. The name of this database, its IP address, its owner and password may be modified. These parameters may be set in `serverConfig.txt` located at `$CATALINA_HOME/webapps/be.ac.ulb.bigre.graphtools.server/WEB-INF`.

Update the KEGG network provider

The KEGG network provider places organism-specific KGML files in `$RSAT/public_html/data/KEGG` in a folder with the KEGG organism name (e.g. `sce`). You may place KGML folders for organisms yourself or you may let the program download required KGML files on the fly. In the latter case, make sure that the KGML version is set correctly. To change the KGML version displayed in the web interface, go to

`$CATALINA_HOME/webapps/be.ac.ulb.bigre.graphtools.server/WEB-INF`

Open `serverConfig.txt` with a text editor, and modify the value of the parameter `KGML_VERSION`.

The Kegg network provider queries a metabolic database in order to annotate the network with certain compound and reaction attributes.

To install and update the metabolic database, use the

`KeggLigandDataManager`

command line tool. For details, type:

```
java graphtools.parser.KeggLigandDataManager -h
```

The KEGG network provider is also using the file `rpairs.tab` located in `$RSAT/data/KEGG` to convert reaction into RPAIR graphs. To update this file, use the `KeggLigandDataManager` command line tool.

Finally, the KEGG network provider displays a list of KEGG organisms. To obtain the organism list for the recent KEGG version, use the `MetabolicGraphProvider` command line tool. For details on this tool, type: `java graphtools.util.MetabolicGraphProvider -h` Place the updated list in the folder `$RSAT/data/KEGG` to replace the old list.

1.1.5 Metabolic Pathfinder and Pathway extraction

After successful installation of the Java web services, you may install metabolic pathfinder and Pathway extraction, which are clients of the pathfinder and pathwayinference web services respectively.

Requirements of metabolic pathfinder and pathway extraction

Metabolic pathfinder and pathway extraction have a number of additional requirements.

1. Dot

Dot is needed to draw graphs and can be obtained freely from <http://www.graphviz.org/>.

2. Postgres

(a) Installation

Postgres (version 8.2 or later) is needed to store KEGG and MetaCyc data. Postgres can be obtained freely from <http://www.postgresql.org/>. For MacOS, you can use Darwinports to install postgres. On SUSE, you may install it with `yast` (`install postgresql` and `postgresql-server`). Usually, a postgres user is created during installation of postgres.

(b) Postgres configuration

You may need to configure the postgres server. You can simply allow all users on your machine (but not from outside) to access all postgres databases. This can be achieved by modifying the `pg_hba.conf` file located in the postgres home directory. Paste the following in this file:

host	all	all	127.0.0.1/32	trust
# IPv6 local connections:				
host	all	all	:::1/128	trust
host	all	all	127.0.0.1	trust

For more details on postgres configuration, check the postgres manual on the `pg_hba.conf` and `pg_ident.conf` files.

(c) Start the server

On SUSE, you may start the postgres server with `/etc/init.d/postgresql start`. On MacOS, you may start the postgres server using a command similar to `pg_ctl -D /usr/local/pgsql/data/ -l logfile start`.

(d) Obtain the data file

Download the postgres backup file `metabolicdb_dump_day_month_year.backup` from the data section of the official NeAT web site.

- (e) Load data into postgres

Load the *metabolicdb_dump_day_month_year.backup* file into postgres as follows:

- i. Start postgres by typing the following on command line:
psql -U postgres
- ii. In postgres, do:
create user metabolic with password 'metabolic';
create database "metabolicdb" with owner "metabolic" encoding='UTF8';
- iii. Quit postgres and type the following command in one line:
pg_restore -d metabolicdb metabolicdb_dump_day_month_year.backup -U postgres

Installation of metabolic pathfinder and pathway extraction

Either place the war file *metabolicpathfinding.war* located in *\$RSAT/java/web* in *\$CATALINA_HOME/webapps* and then start Tomcat or use the Tomcat manager to deploy the war file.

Configuration of metabolic pathfinder and pathway extraction

1. Go to the folder *\$CATALINA_HOME/webapps/metabolicpathfinding/WEB-INF*.
2. If you are not the rsat user, set the RSAT environment variable, e.g.:
export RSAT=/home/rsat/rsat Run the configuration script with the following commands:
chmod 755 configureWebxml.pl
./configureWebxml.pl
3. Reload the metabolic pathfinding web application using the Tomcat manager or on command line, restart Tomcat.

Update of metabolic pathfinder

The metabolic pathfinder contains by default data from KEGG version 49.0. In order to update it, you can follow the steps below:

1. Load KEGG LIGAND compound and reaction file into the metabolic database. The command line tool *KeggLigandDataManager* can be used for this. If present, delete previous KEGG data in the database. You may change the name, the location, owner and password of the metabolic database. In this case, change the default values in the web.xml file located at
\$CATALINA_HOME/webapps/metabolicpathfinding/WEB-INF.
2. Generate the preloaded networks with the *KeggLigandDataManager* command line tool. Place those networks in *\$RSAT/data/Stored_networks* replacing the old ones.

3. In point 2, example networks have been generated as well.

Copy them to `$CATALINA_HOME/webapps/metabolicpathfinding/networks`, replacing the old ones.

4. Set the parameter `keggVersion` in the `web.xml` file to the updated KEGG version.
5. Reload the metabolicpathfinding web application in tomcat.

Update of pathway extraction

This section only describes how to update MetaCyc data. See the section on the update of metabolic pathfinder for the KEGG data.

1. Load the MetaCyc OWL file into the metabolic database. The command line tool *MetabolicXMLFilesParser* can be used for this. If present, delete previous MetaCyc data in the database. You may change the name, the location, owner and password of the metabolic database. In this case, change the default values in the `web.xml` file located at
`$CATALINA_HOME/webapps/metabolicpathfinding/WEB-INF`.
2. Generate the preloaded networks with the *MetabolicGraphProvider* command line tool. Place those networks in `$RSAT/data/Stored_networks` replacing the old ones.
3. In point 2, an example network has been generated as well.
Copy it to `$CATALINA_HOME/webapps/metabolicpathfinding/networks`, replacing the old one.
4. Set the parameter `metacycVersion` in the `web.xml` file to the updated MetaCyc version.
5. Reload the metabolicpathfinding web application in tomcat.

1.1.6 Web services

Edit the WSDL file

The web interface consists in web services that are called by the PHP web pages. Your computer must thus act as web service server.

First, edit the file `RSATWS.wsdl` located in the `$RSAT/public_html/web_services/` directory. At the very end of the file, the line

```
<soap:address location="http://rsat.bigre.ulb.ac.be/rsat/web_services/RSATWS.cgi"/>
```

must be replaced by

```
<soap:address location="url_of_the_cgi_file_on_your_server"/>
```

The URL can be `http://127.0.0.1/rsat/web_services/RSATWS.cgi`.

Edit the NeAT config file

Edit the *RSAT_config.props* present in the main RSAT directory and edit the following fields so that they correspond to your local configuration.

```
neat_supported=1
neat_ws=web link to the WSDL file on your computer
(e.g. http://127.0.0.1/rsat/web_services/RSATWS.wsdl)
```

Change permissions of the temporary files and log files directories

The directories *\$RSAT/public_html/logs/* and *\$RSAT/public_html/tmp/* must be writable. So, change the permissions

```
chmod 777 \ $RSAT/public\_html/logs/
chmod 777 \ $RSAT/public\_html/tmp/
```