ProteoLens in 10 MINUTES

ProteoLens: A Biological Network Visual Data Exploration, Annotation, and Data Mining Tool

http://bio.informatics.iupui.edu/proteolens/

FOR PROTEOLENS VERSION 1.1

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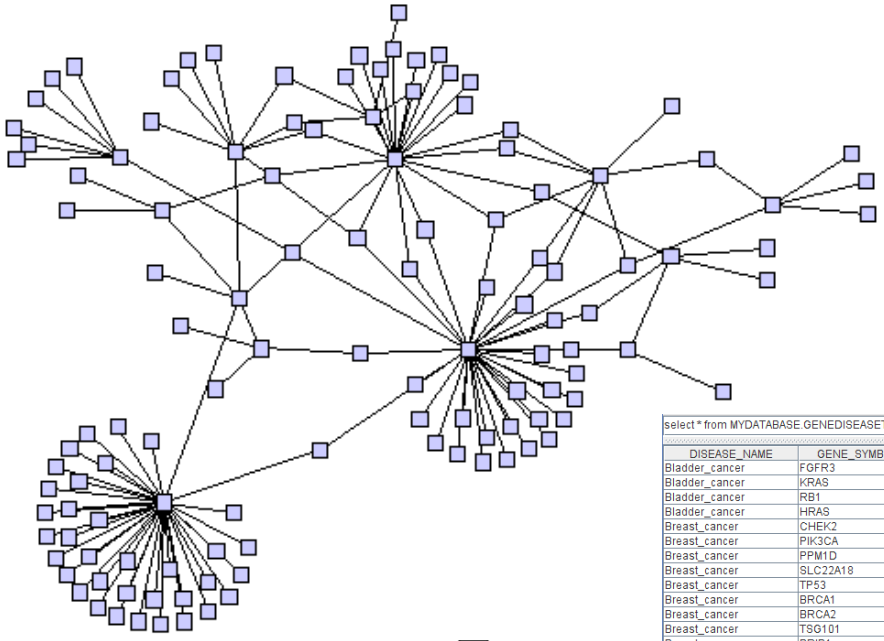

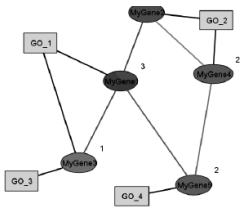


```
select A.DISEASE_NAME DISEASE_A, B.DISEASE_NAME DISEASE_B,
count(B.DISEASE_NAME) NUMLINKS from
MYDATABASE.GENEDISEASETABLE a,
MYDATABASE.GENEDISEASETABLE b
where a.GENE_SYMBOL=B.GENE_SYMBOL and
A.DISEASE_NAME<B.DISEASE_NAME
group by A.DISEASE_NAME , B.DISEASE_NAME
```

DISEASE_A	DISEASE_B	NUMLINKS
Bladder_cancer	Breast_cancer	1
Colon_cancer	Pancreatic_cancer	1
Breast_cancer	Stomach_cancer	1
Bladder_cancer	Stomach_cancer	1
ast_cancer	Lymphoma	1
ast_cancer	Pancreatic_cancer	3
creatic_cancer	Stomach_cancer	1
phoma	Mesothelioma	1
dder_cancer	Colon_cancer	1
dder_cancer	Leukemia	1
kemia	Lung_cancer	1
ast_cancer	Ovarian_cancer	3
anoma	Pancreatic_cancer	2
g_cancer	Pancreatic_cancer	1
kemia	Pancreatic_cancer	1
g_cancer	Stomach_cancer	1
on_cancer	Leukemia	1
on_cancer	Lymphoma	2
ast_cancer	Melanoma	1

```
select * from MYDATABASE.GENEDISEASETABLE
```

DISEASE_NAME	GENE_SYMBOL
Bladder_cancer	FGFR3
Bladder_cancer	KRAS
Bladder_cancer	RB1
Bladder_cancer	HRAS
Breast_cancer	CHEK2
Breast_cancer	PIK3CA
Breast_cancer	PPM1D
Breast_cancer	SLC22A18
Breast_cancer	TP53
Breast_cancer	BRCA1
Breast_cancer	BRCA2
Breast_cancer	TSG101
Breast_cancer	BRIP1
Breast_cancer	RAD54L
Breast_cancer	CDH1
Breast_cancer	AR
Breast_cancer	KRAS
Breast_cancer	RB1CC1
Breast_cancer	PHB
Breast_cancer	ATM
Breast_cancer	BARD1
Breast_cancer	RAD51
Breast_cancer	XRCC3
Colon_cancer	RAD54B
Colon_cancer	RAD54L
Colon_cancer	BCL10
Colon_cancer	PTPN12
Colon_cancer	TGFBR2

Your Very Own Quick 10-Minute Guide to Doing Almost Everything

Table of Contents

Introduction to ProteoLens

Installing ProteoLens is a breeze. All it requires is a java runtime environment. To achieve its maximal range of performance, you may also want to install the free Oracle XE database application onto your system. You are encouraged to print out this guide before getting started.

Biological networks often reveal a wide variety of structures and functions that, when constructed for analysis, may be used to study the development and phenotype of organisms. A challenge has been to find tools that enable multi-scale analyses of biological networks with the right kind of architecture to smoothly and quickly handle diverse types and associations among heterogeneous biological data. ProteoLens has been built as a next-generation biological network visual data exploration, annotation, and mining tool. It has many advanced features that support expert bioinformaticians to perform large-scale network-based integrated data analysis.

This guide has been written to present first-time users with an accelerated experience tour through the features and power of ProteoLens. This guide assumes installation and usage of ProteoLens on a **Windows 95/98/ME/2000/XP/Vista operating system**. For more information, you may also want to consult the more extensive user manual available at: http://bio.informatics.iupui.edu/proteolens/usermanual1.0.pdf.

Getting the ProteoLens Software

ProteoLens can be downloaded in a ready-to-install executable from the website http://bio.informatics.iupui.edu/proteolens/.

Before Installing

To run ProteoLens, you must have Java Runtime Environment version 1.42 or higher installed on your computer. You can get the Java Runtime Environment from http://java.sun.com.

In order to complete the 10-minute case study exercise described in the following pages, **it is also recommended to install Oracle XE on your computer**. Oracle XE is a basic entry-level database, free for download and usage. Oracle XE can be accessed from http://www.oracle.com/technology/products/database/xe/index.html. As an alternative to Oracle XE, **you can also install and use PostgreSQL** with ProteoLens.

Installing ProteoLens and Launching the Application

ProteoLens is released as a standard Windows software installation package. After downloading the ProteoLens installation executable, double-click on the executable, and simply click "OK" to install.

Figure 1 shows the ProteoLens interface. You can navigate both database and file-based input choices from the filesystems window as will be described in subsequent sections. For visualization, a new network window can be opened in the right of the interface through use of the Window menu accessed from the top menu bar of the interface.

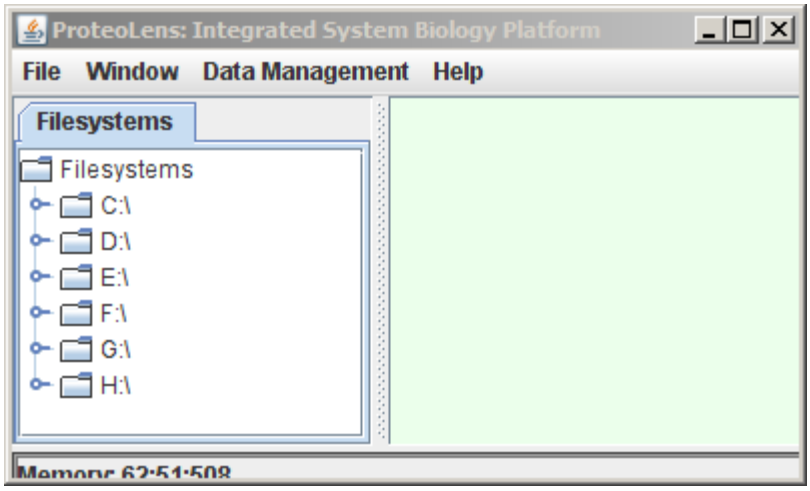

Figure 1. ProteoLens interface. This is what a user sees when first launching the ProteoLens application.

Example Data: Diseases and their Genes

The ProteoLens application comes with various example data sets. In this tutorial guide, the file **gene_disease.txt** is a two-column tab-separated flat file containing content structured in the manner below (based on data from Goh *et al.* 2007):

```
DISEASE_NAME    GENE_SYMBOL
Bladder_cancer  FGFR3
Bladder_cancer  KRAS
Bladder_cancer  RB1
Bladder_cancer  HRAS
Breast_cancer   CHEK2
Breast_cancer   PIK3CA
   .              .
   .              .
   .              .
Pancreatic_cancer     RBBP8
Renal_cell_carcinoma  FLCN
Renal_cell_carcinoma  RNF139
Renal_cell_carcinoma  OGG1
Renal_cell_carcinoma  PRCC
Renal_cell_carcinoma  TFE3
Renal_cell_carcinoma  MET
Renal_cell_carcinoma  VHL
Stomach_cancer  KRAS
```

Optional: Installing and Configuring Oracle XE

A principal advantage of ProteoLens is how it directly connects with a database. To help you get started, brief instructions are provided here for downloading and installing Oracle XE, a free, basic entry-level database. This optional step of installing Oracle XE is a task separate from, but strongly complementary to, the 10-minute tour in this guide.

Oracle XE can be downloaded from:
http://www.oracle.com/technology/products/database/xe/index.html

You will want to install from the OracleXE.exe or the OracleXEUniv.exe file.

You will need to specify three parameters during the installation. The values used for the examples in this manual are indicated.

1) Destination Folder: **C:\oraclexe**

2) HTTP Listener Port: **8081**

3) System administrator password (for both SYS and SYSTEM): *your choice*

Note, the database SID (db_name) for OracleXE is set to "XE" by default.

Viewing the database

A default installation of Oracle XE places the application, Oracle Database 10g Express Edition, in your main start menu list of programs. Selecting the Oracle Database menu item provides you with a link: "Go to Database Home Page." The web interface to Oracle XE is a simple-to-use interface providing a range of options from administration (including the creation and management of non-administrative users), browsing of database objects (such as tables and views), creation and launching of SQL scripts, and utilities that include options for loading external data into the database system.

During installation, configuration, and uploading of content, it is important to make note of five basic parameters:

1) the database user that has permissions to the content you wish to access from ProteoLens – after installation, you may ideally wish to create a non-administrative level user Oracle XE account for connecting to ProteoLens application (you will need to remember the password associated with this account);

2) the SID containing content you wish to connect to – by default this is set to "XE";

3) the table name with content you wish to access and query from ProteoLens;

4) the port number to the Oracle XE application – default value is 1521; and

5) the IP address hosting the Oracle XE application – this will probably be 127.0.0.1 unless you are installing Oracle XE on a computer separate from the one you are using ProteoLens.

This manual presumes the following values for connecting to Oracle XE: user name = MYTESTUSER; SID = XE; table name = GENEDISEASETABLE; port number = 1521; and IP address = 127.0.0.1.

Creating a non-administration level user

Go to the database web interface page (e.g., http://127.0.0.1:8081/apex) and, after logging in with the SYSTEM user, use the Administration link and select the ***Database Users→Create User*** option. You may then create a non-administration level user from the provided interface as shown in Figure 2.

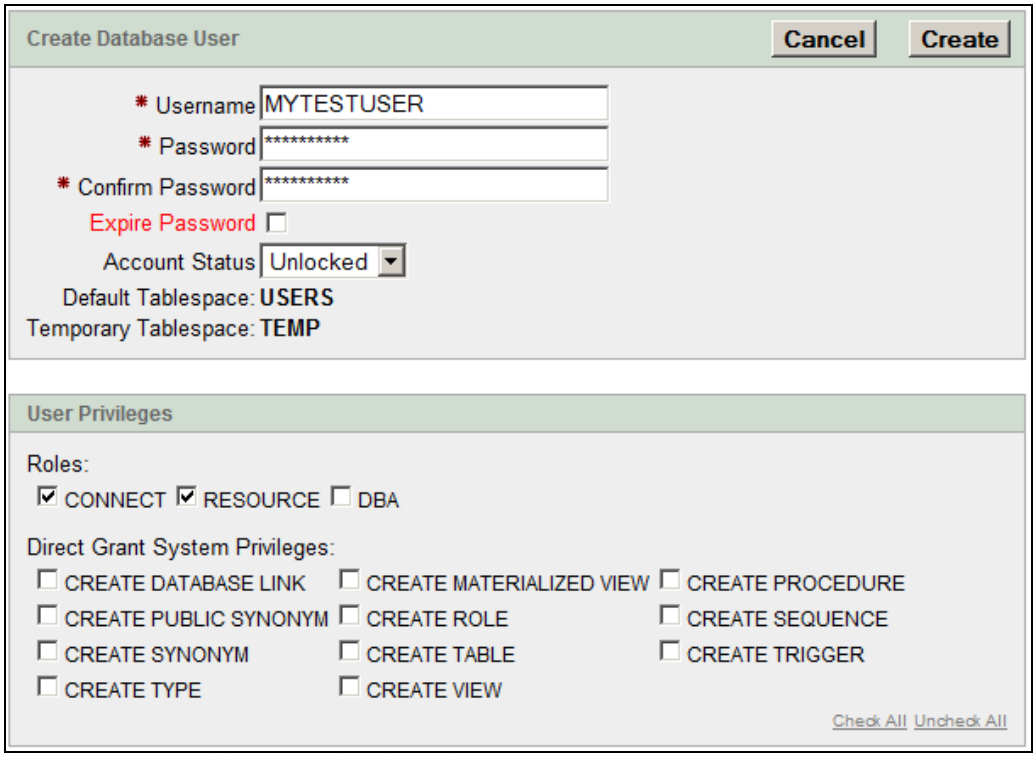

Figure 2. Creating a non-administration level user for Oracle XE.

Uploading File-based Data with SQL*Loader (sqlldr)

You first need to create the table structure you want to load data into. Login as MYTESTUSER and, through the SQL link on the Oracle XE web application, open an SQL command window and enter the following command:

```
CREATE TABLE "GENEDISEASETABLE"
   ("DISEASE_NAME" VARCHAR2(100) NOT NULL ENABLE,
    "GENE_SYMBOL" VARCHAR2(100) NOT NULL ENABLE)
```

The following file, gene_disease_load.ctl, is provided as an example of loading data from a tab-separated file into Oracle XE:

```
OPTIONS (SKIP=1) LOAD DATA INFILE 'C:\Program
Files\IUPUI\ProteoLens_1.1.1\examples\gene_disease.txt' REPLACE
INTO TABLE GENEDISEASETABLE FIELDS TERMINATED BY x'09'
OPTIONALLY ENCLOSED BY '"' TRAILING NULLCOLS (DISEASE_NAME,
GENE_SYMBOL)
```

After you have created the table structure for GENEDISEASETABLE, open a Windows command prompt, and type the following:

```
sqlldr control=C:\Program
Files\IUPUI\ProteoLens_1.1.1\examples\gene_disease_load.ctl
```

After entering this command, you will be prompted to enter the appropriate username (e.g., MYTESTUSER) and password.

Connecting to Database and File-based Input

When using ProteoLens, the general form of input is either a two or three-column relational format.

In the ProteoLens user application, this form of input can be accessed from either a flat file or a supported database type. Supported database types are Oracle and PostgreSQL. Databases can be accessed across the network or hosted on the same computer running the ProteoLens application. The advantage of connecting to a database for input is that you can quickly iterate through different relational associations based on sending SQL queries from the ProteoLens interface directly to the backend database.

A connection begins with using the Filesystems window and viewing a file or database object (right-click with mouse).

It is at this point of the manual that the 10-minute exercise begins. This exercise assumes that you have installed Oracle XE on your system with a user named MYTESTUSER.

Connecting to Database Input

In order to connect to a database object, you must first mount the database. To mount the database, you need to right-click on the root Filesystems node in the Filesystems window and select the ***Mount database…*** option that appears in the submenu as shown in Figure 3. As shown in Figure 4, use the Thin connection type and enter the

parameters as described in the previous section in this manual on installing and configuring Oracle XE.

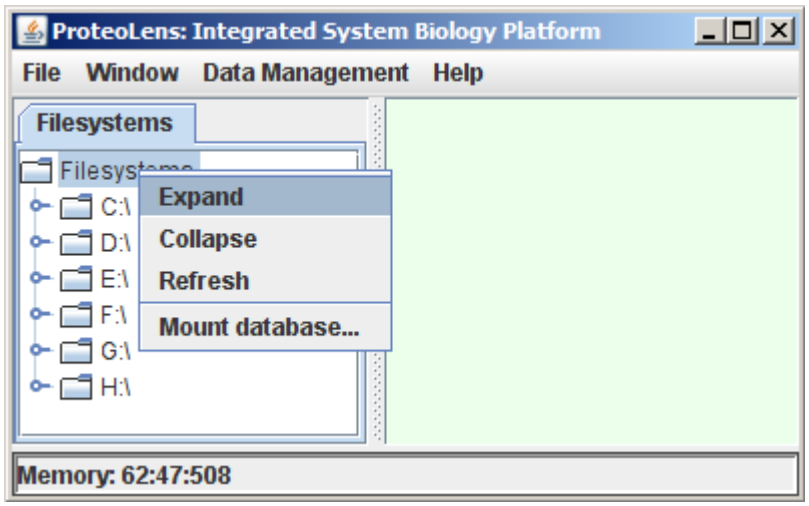

Figure 3. Right-clicking on the root-level Filesystem node presents the Mount Database option.

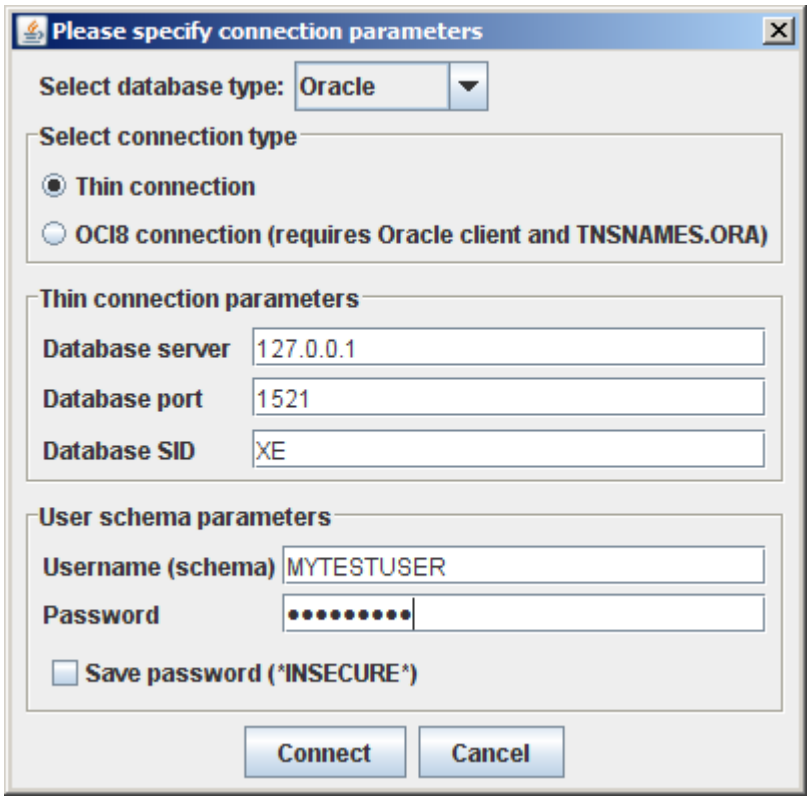

Figure 4. Specifying connection parameters for mounting a database. The settings shown are based on a default installation of Oracle XE and the existence of a username MYTESTUSER.

Use the Filesystem window to navigate to the database (named XE), open the schema named MYTESTUSER and right-click on the table object GENEDISEASETABLE and select ***View*** from the submenu (see Figure 5). The next major section of this manual will describe how you convert the resulting view into a data association.

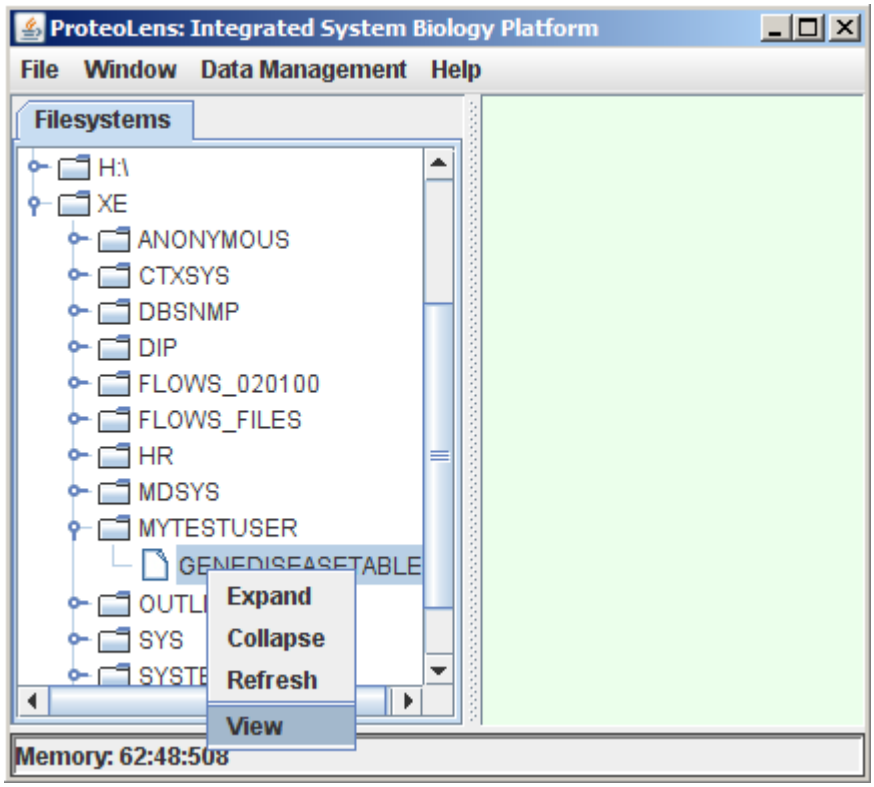

Figure 5. Using the ProteoLens interface to select a table object from an OracleXE database.

Connecting to File-based Input

You may choose to skip this step since the rest of the tutorial exercise relies on the database input connection.

Navigate to a file with the Filesystems window. For purposes of this example, you can use the example **gene_disease.txt** file bundled with the ProteoLens installation. Right-click on the file that contains data you wish to input into ProteoLens, and a submenu will emerge as shown in Figure 6. Click on the ***Table data*** check box. Then select the ***View*** option from the submenu.

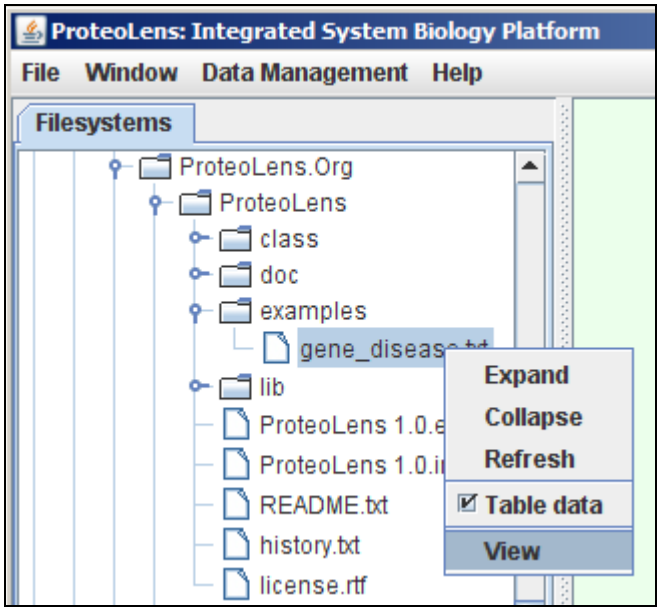

Figure 6. Using a Filesystems submenu to view the table data of a file.

A window then appears as shown in Figure 7 and appropriate options are selected. For this exercise, you should select Tab for the field separator and click on the checkbox for the first row containing column names.

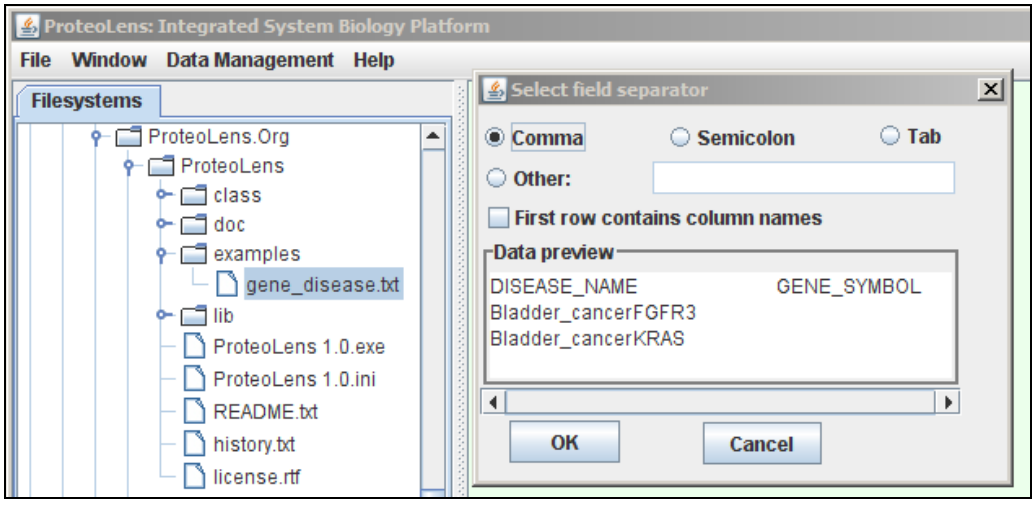

Figure 7. Previewing flat file data for import into the ProteoLens application.

After you have completed the *View* action on your input file, the next step would be to create a data association as described in the next section.

The Fine Art of Data Associations

After completing the steps in the previous section, you can proceed to make a data association as shown in Figure 8 and Figure 9. For this tutorial guide, work with the view that comes from the GENEDISEASETABLE object in the OracleXE database. Figure 8 shows the window that appears in the ProteoLens interface after selecting View as shown in Figure 5.

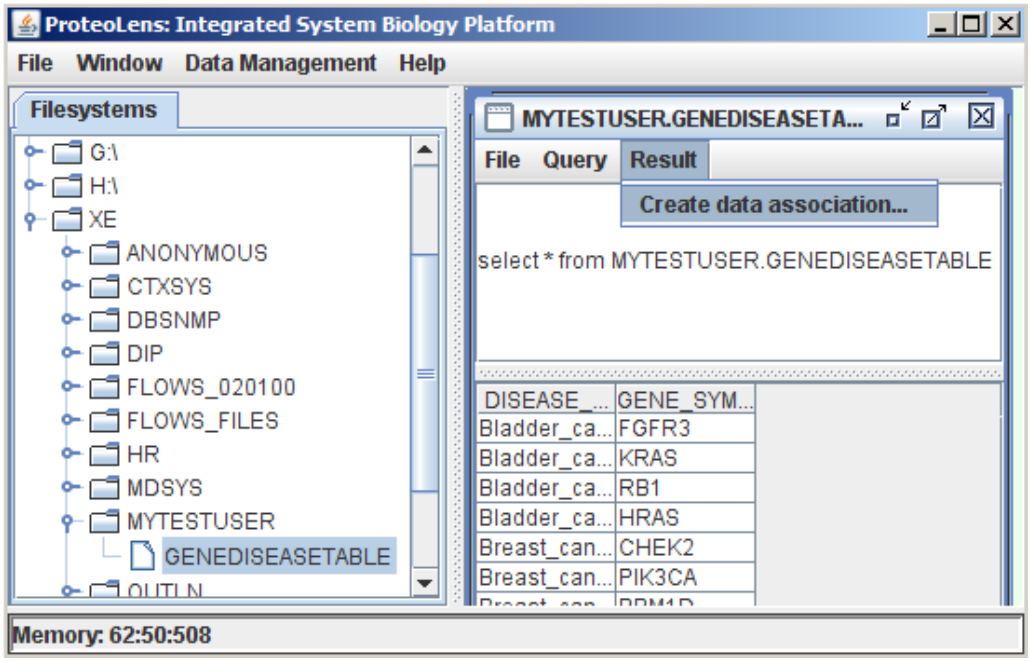

Figure 8. Creating a data association (part 1).

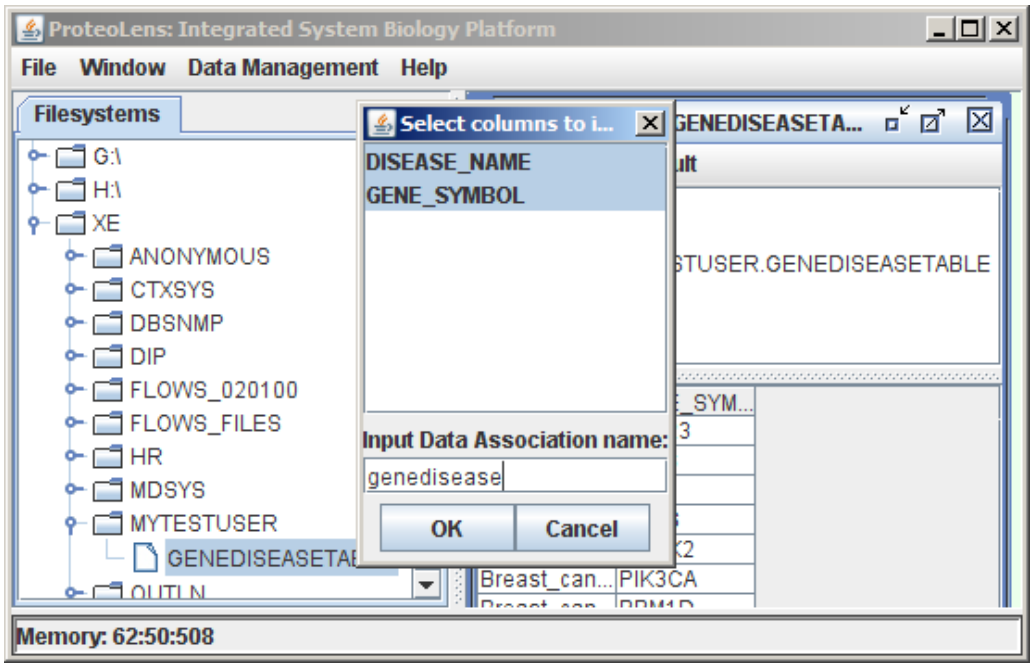

Figure 9. Creating a data association (part 2).

A special note about data associations

Data associations in ProteoLens are the architectural layer that wraps external data from flat files or database tables in a uniform way. Importantly, as described in the user manual:

> The [ProteoLens] application makes no domain-specific assumptions about the nature and meaning of the provided data, which leaves the user with responsibility of using right data at the right place, but also allows for very high flexibility.

As will be described in the next section, data associations can be used for either visualization or annotation.

Viewing and Annotating a Network

Visualizations and annotations are created from data associations. A visualization is the graphical layout of nodes and edges in the network. An annotation is the modification of nodes (e.g., labels, sizes, colors) or edges (e.g., labels, line widths, colors) based on input that links to the identities of the nodes or edges.

Visualization - Showing the Network

Visualization starts with opening a network view through the *Window* menu as shown in Figure 10.

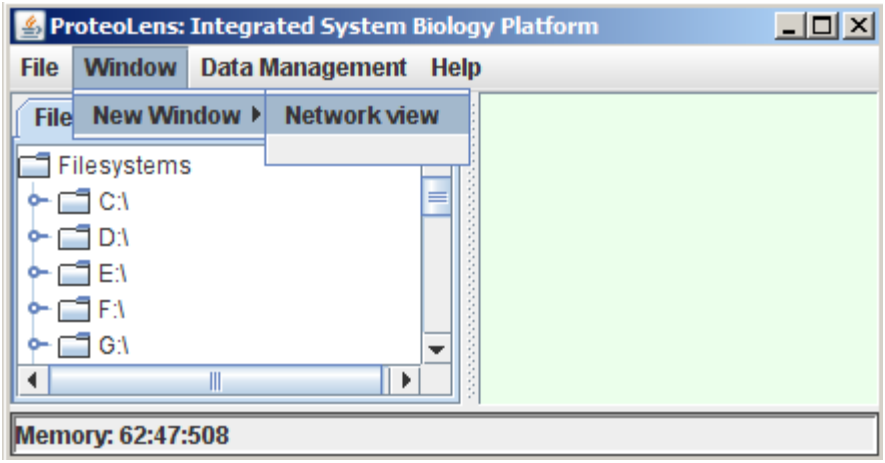

Figure 10. Opening a new network view.

In the newly opened Network View window, the ***Load→Network from data association*** option can be used to construct the network based on the uploaded data association (see Figure 11).

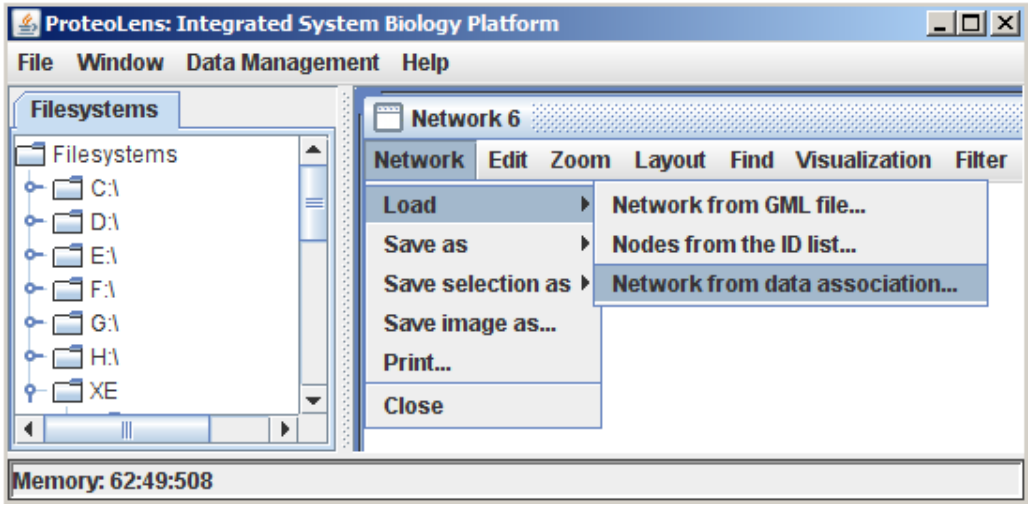

Figure 11. Beginning the process of loading a network from a data association.

Figure 12, Figure 13 and Figure 14 show the process of selecting the network source, specifying loading conditions and receiving the output view respectively. To specify loading conditions from the ***Select network source*** interface, click on either ***Condition…*** button (Figure 12).

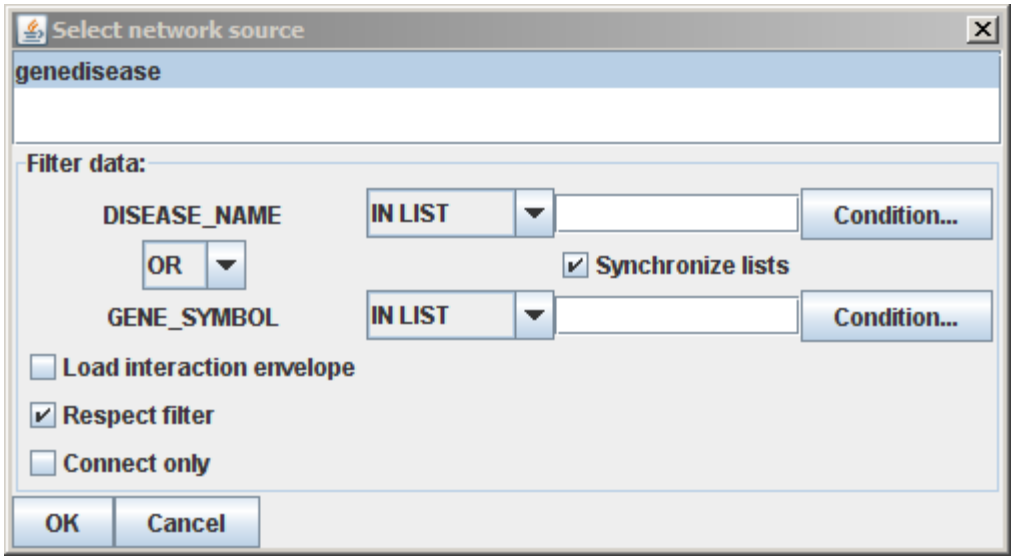

Figure 12. Select network source interface. From this interface, you will need to specify loading conditions using the Condition buttons, prior to clicking on the OK button.

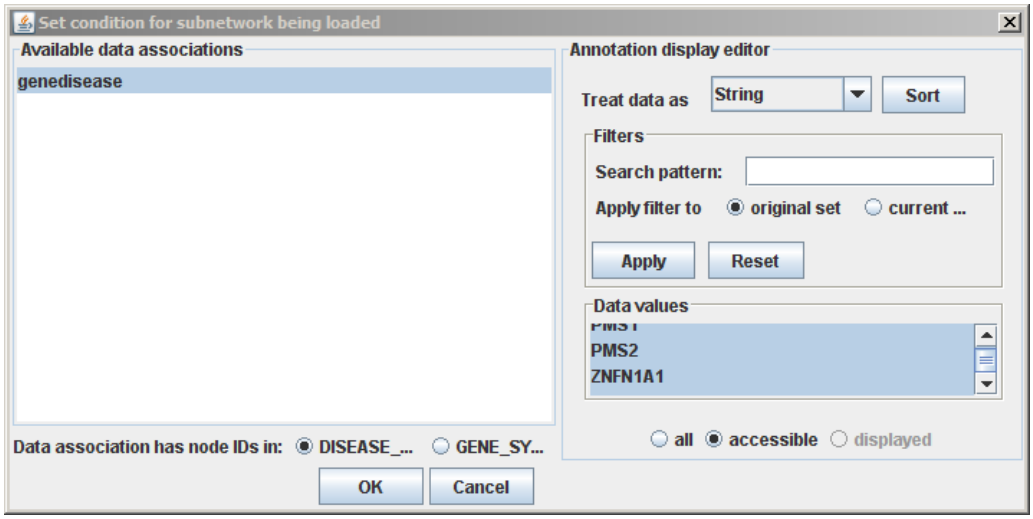

Figure 13. Interface for specifying loading conditions. A basic set of steps for using this interface is: 1) select genedisease from the list of available data associations (upper left); 2) highlight all values that appear in the data values window (lower right); and 3) click the OK button. Upon returning to the 'Select network source" interface shown in Figure 12, click the OK button there also.

After completing the steps of selecting the network source and specifying loading conditions, a network view will appear similar to the network shown on the front cover of this instruction manual. Note however that, as you repeat the exact same procedure, the node-to-node associations will remain the same, but the physical layout of the network on the screen will be somewhat random. The network shown presents how genes link to each other through association with the same disease.

To construct a network that connects diseases directly together based on having a common gene, you can substitute with the following SQL when viewing the

GENEDISEASETABLE object (Figure 5), create a data association, and repeat the steps in Figure 12, Figure 13 and Figure 14:

```
SELECT A.DISEASE_NAME AA, B.DISEASE_NAME BB from
MYTESTUSER.GENEDISEASETABLE
a,MYTESTUSER.GENEDISEASETABLE b
where a.GENE_SYMBOL=B.GENE_SYMBOL and
A.DISEASE_NAME!=B.DISEASE_NAME
group by A.DISEASE_NAME, B.DISEASE_NAME
```

The resulting network view based on the substituted SQL is shown in Figure 14.

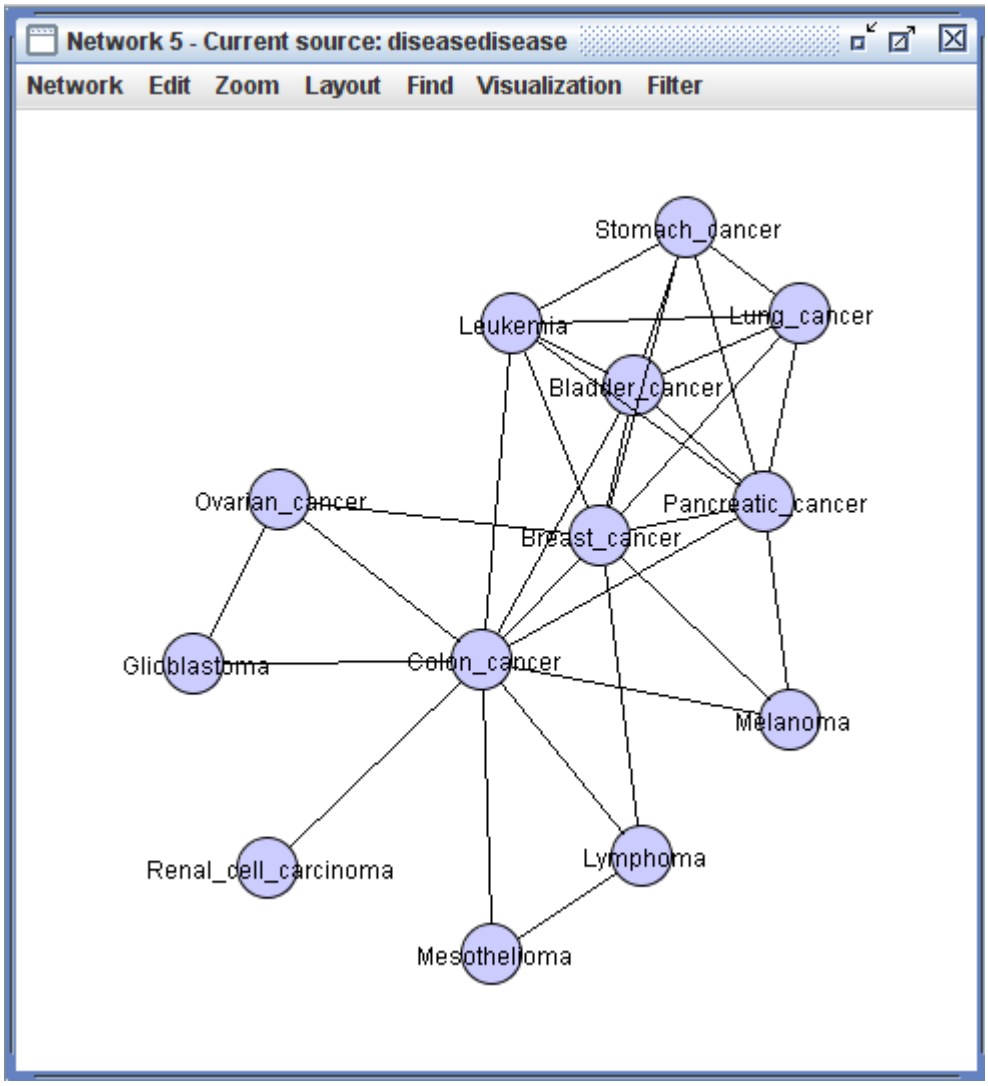

Figure 14. Output view of disease-to-disease associations shown only with defaults for node and edge annotations.

Annotating the Network

Annotating the network also utilizes data associations. For annotating nodes, the specified data association takes the form of an ordered pair: {node_name, annotation_value}. For annotating edges, the specified data association takes the form of an ordered triplet (where node1 and node2 indicate the edge): {node1_name, node2_name, annotation_value}.

With SQL, you can build these annotation tables from your original annotation table (without uploading new tables into your database environment). Follow the steps described in Figure 8 and Figure 9, and use the SQL commands below to define data associations: diseasecount and edgecount.

SQL command for diseasecount:

```
SELECT DISEASE_NAME, count(GENE_SYMBOL) m
FROM MYTESTUSER.GENEDISEASETABLE
GROUP BY DISEASE_NAME
```

For annotating edges, a 3-column table is specified, typically with SQL. Typical usage is to have the first two columns specify the identity of each edge, and the third value (third column) is the annotation for that edge. Here is an example of building an annotation table for edges with SQL as shown in Figure 15, Figure 16 and Figure 17.

SQL command for edgecount:

```
SELECT A.DISEASE_NAME AA, B.DISEASE_NAME BB,
 count(B.DISEASE_NAME) M from MYTESTUSER.GENEDISEASETABLE
 a,MYTESTUSER.GENEDISEASETABLE b
 where a.GENE_SYMBOL=B.GENE_SYMBOL and
 A.DISEASE_NAME!=B.DISEASE_NAME
group by A.DISEASE_NAME, B.DISEASE_NAME
```

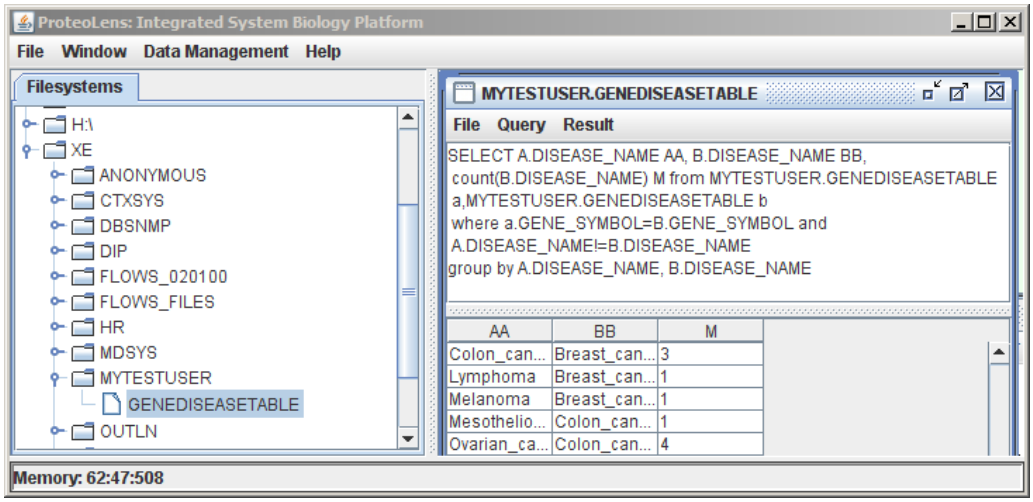

Figure 15. Creating the edgecount annotation (part 1).

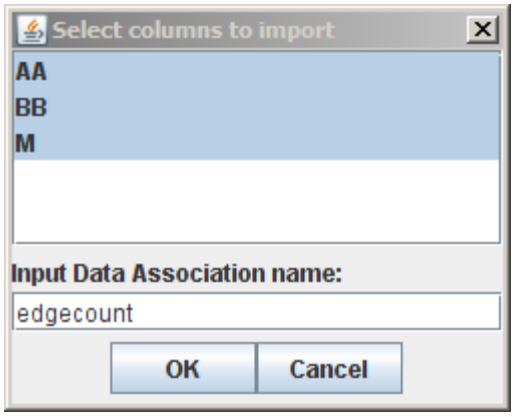

Figure 16. Creating the edgecount annotation (part 2).

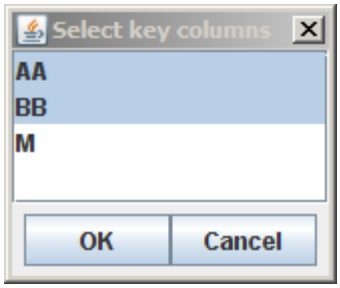

Figure 17. Creating the edgecount annotation (part 3).

From the Visualization menu in the network view, you can choose to ***Add annotation*** to either ***Nodes*** or ***Edges*** as shown in Figure 18.

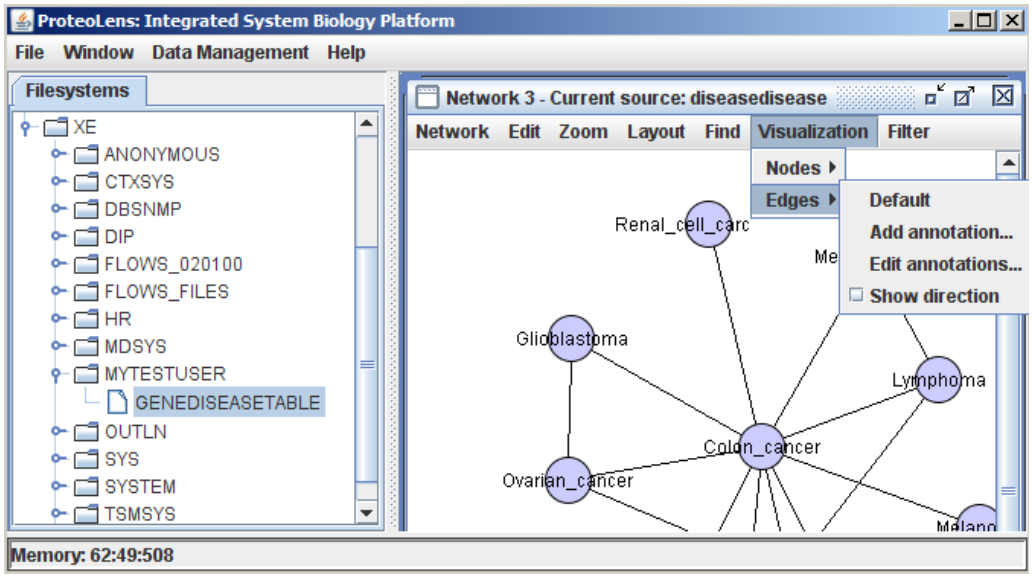

Figure 18. Using Visualization menu of a network view to begin the process of adding an annotation.

Figure 19 and Figure 20 show the specification of a new node annotation and a new edge annotation.

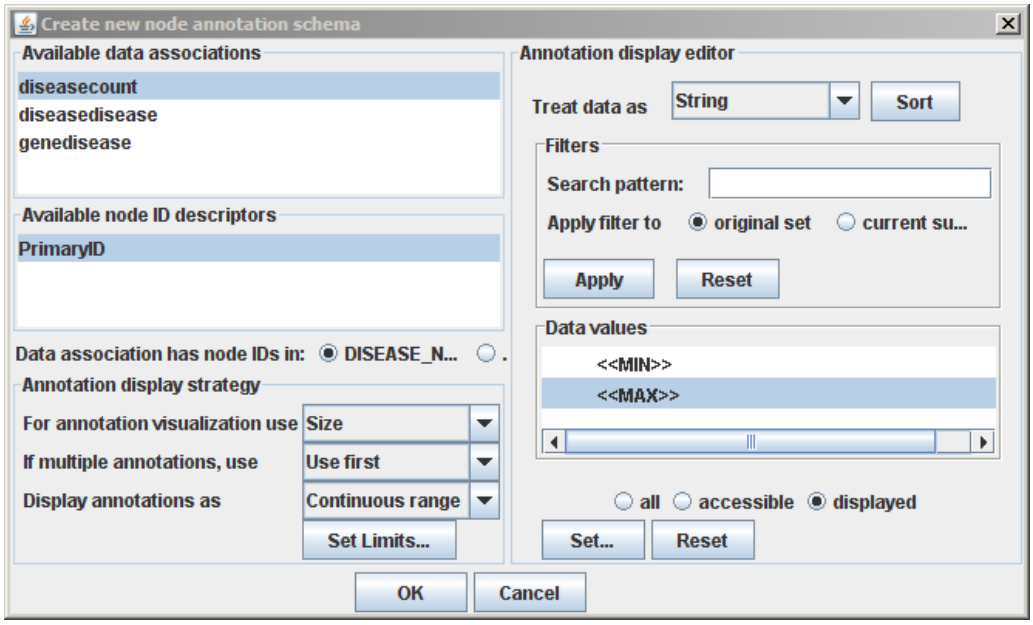

Figure 19. Specifiying a new node annotation with the diseasecount data association.

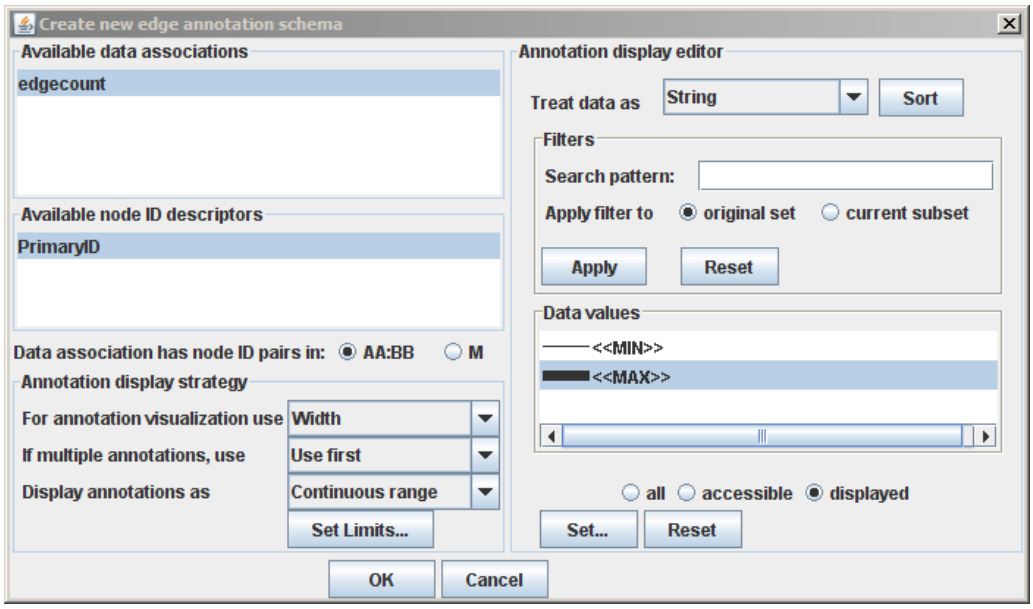

Figure 20. Specifying a new edge annotation with the edgecount annotation.

The resulting, annotated disease-to-disease network is shown in Figure 21.

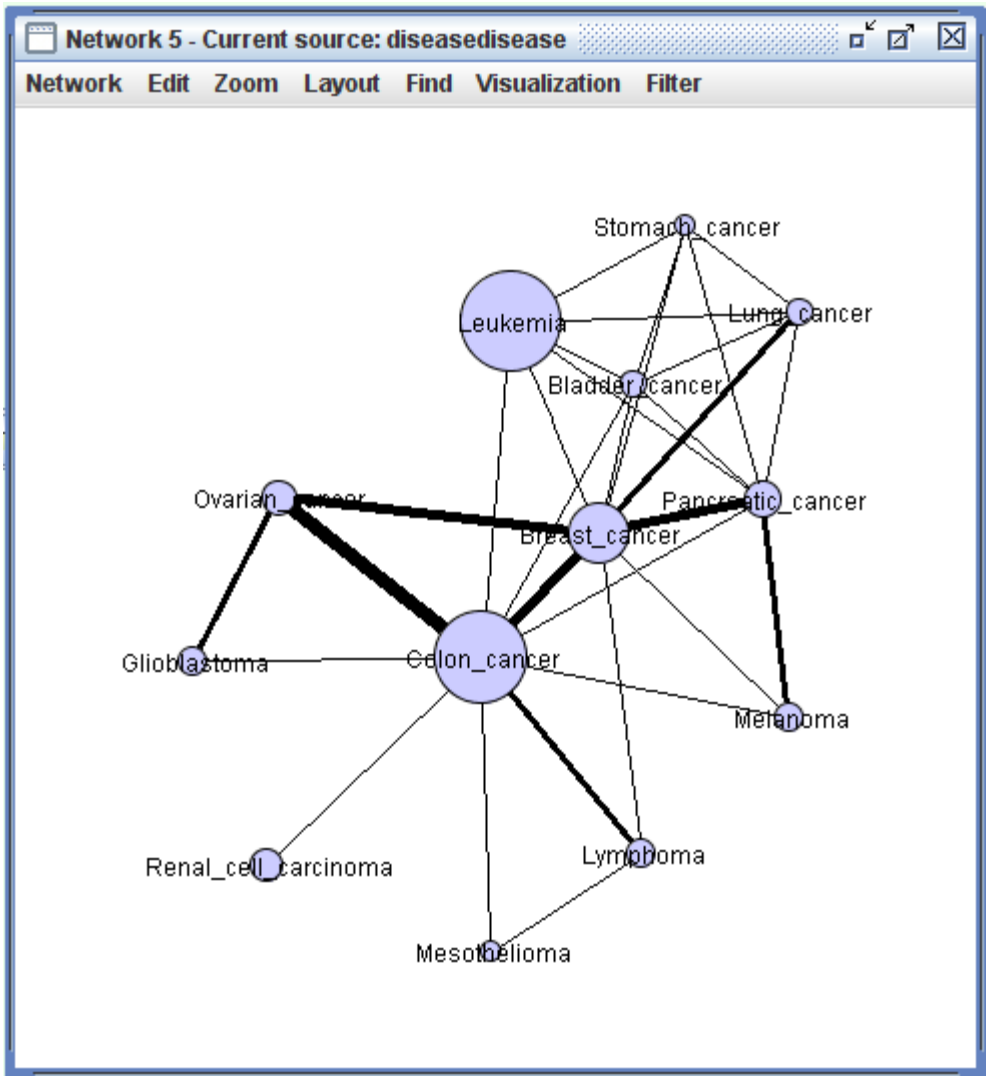

Figure 21. Final output view of annotated nodes and edges of a disease-to-disease network. The thicker lines represent a greater number of genes in common between the corresponding pair of diseases. The enlarged nodes represent those diseases that occur most often in the disease-to-disease association.

From Figure 21, we observe that the colon cancer and leukemia have the highest numbers of listed genes, and that stomach cancer and mesothelioma have the lowest numbers of listed genes.

We can also infer that ovarian cancer has a greater percentage of its listed genes in common with colon cancer than the percentage of listed colon cancer genes that are in common with ovarian cancer.

Managing your Workflow: Sessions, Saving, Export and Printing

Options for exporting and printing network views are provided in the ***Network*** menu of the ***Network*** window as shown in Figure 22.

Sessions and Saving

From the ***File*** menu of the ProteoLens interface, you can save your session. You can then close ProteoLens and reload your session at a later time. Sessions are saved in XML format. A saved session contains your working set of data associations and mounted database connections. Note that the window layout is not saved and, after restarting your session, you will need to regenerate your network views or load them from separately saved GML files.

Saving Network Files with GML Files

Saving and loading of each network view in your session can be done with the standard GML file format (see Figure 22). The exact physical layout of the network is preserved.

Export and Printing

The ***Save image as…*** option allows for exporting the image into jpeg or png graphical file formats.

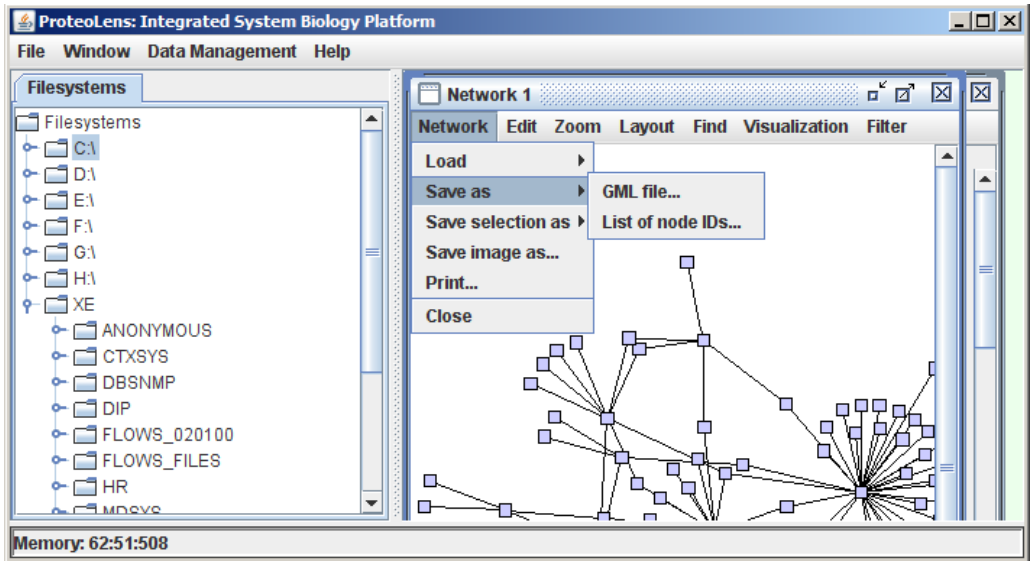

Figure 22. Options for saving and printing network views.

You can also choose the ***Print*** option. The network view is automatically downscaled as needed to fit the print output medium. Note that the zoom level and display window boundaries in the ProteoLens application do not control printing.

Important Notes on Usage

At the time of this writing, to ensure the highest amount of compatibility between database and java resources, we make the following recommendations for character sets used in table names, column names, and data field values:

- Use capital characters and underscores for table names and column names.
- Do not use spaces inside data field values (instead of "Retinal cell carcinoma", use "Retinal_cell_carcinoma").
- Be aware of the 30 character length limitation on table names and column names in Oracle XE.
- In order to avoid appending spaces to data field values, use VARCHAR2 as a column type and not CHAR.

The example data files in the ProteoLens installation and the contents of this guide are consistent with the above recommendations.