I. Introduction:

A. Background of the Study

All cancers are deadly whether you are man or woman. But for women "breast cancer" is the second leading cancer cause-death. Exact cause is unknown but there are some factors may alter an individual risk of having these, like age, race, smoking, family history or genetics, personal history and number of pregnancies. When single cell containing altered genetic material has disrupted normal cellular regulation, the gene expression will be not sufficient, cell death increases, or uncontrolled cell growth. This is how cancer started. [1].

Within an organism certain metabolites are consumed in a series of enzymatic reactions, this is a metabolic pathway. Complex network reactions are formed when metabolites participate in more than one metabolic pathway. Metabolic intermediates and their properties, biochemical reactions, properties of enzymes from different sources regulation of gene expression are some of the cell physiology that involves in the analysis of complex network. Also, the enormous amount of data from biochemistry included, as well as principles from physical sciences [2].

The existence of large number of experiments, research study and proteomic sequence of data has resulted to different pathway databases such as PGDB: Pathway/Genome Database and KEGG PATHWAY: Kyoto Encyclopedia of Genes and Genomes. These databases provide data-mining that has a means of trying to associate protein annotations to pathway templates to derive a specific pathways of an organism.

B. Statement of the Problem

Information contained in databases and in experiments are rapidly growing making it difficult to understand and making it hard to generate the desired results. There are also databases which do not contain pathways among species. For instance, "*The Protein Kinase Resource (Smith 1997), a well known and useful database related to protein kinases, provides various types of information such as protein conformations, all members of the protein kinases, and mutations. However, it does not provide pathways that include protein kinases and ortholog tables among species*"[22]. There are available databases that are complicated and extensive that sometimes it takes time for the result to be generated. Such databases are "*Transpath (Schacherer et al. 2001), KEGG (Kanehisa et al. 2002), and DIP (Xenarios et al. 2002) that provide biological pathways and/or protein–protein interaction information, which can be summarized quite well manually and is thus useful in many respects. However,*

manual information extraction is very time-consuming and costly. Consequently, recent information that is relevant is not likely to be accumulated in such databases due to the rapid progress in molecular biology"[22]. Others do not provide the tool for generating a pathway and sometimes gives the final result without showing the interaction between BRCA1 gene to other gene, protein, enzyme, etc. There are pathway databases that do not provide a clear statement of the pathway conceptualization that they use. We are unaware of how these pathways are formed. For such case, "*PathDB which the cross-references within the pathway representation to other connected pathways are missing and ExPASY (Expert Protein Analysis System) does not offer any tools to navigate on the pathway map or to search for reactions or pathways by defining substrates, etc.*"[23].

C. Objectives

1. The primary objective of this study is to provide a user-friendly and a detailed website showing the pathway of BRCA1.

2. To provide the different users the following functionalities:

    a. Allows the unregistered user (i.e. guest viewer) to:

        i. Sign-up for membership

ii. Search and View other research study about BRCA1 metabolic pathway by experiment name, experimenter or researcher who conducted that experiment

iii. Choose a BRCA1 experiment (i.e. by experiment name) to combine with other experiment stored in the database (gene, enzyme, protein, etc.) to generate and view the graph of BRCA1 pathway

iv. Use the external search of the system which search in MetaCyc and KEGG (Kyoto Encyclopedia of Genes and Genomes)

b. Allows the registered user to:

i. Edit user Account

ii. Submit project information requesting as a project leader to the system administrator

iii. Submit experiment information requesting as a project member of a particular project

iv. Search and View other research study about BRCA1 metabolic pathway by experiment name, experimenter or researcher who conducted that study / experiment

v. Use the external search of the system which search in MetaCyc and KEGG (Kyoto Encyclopedia of Genes and Genomes)

vi. Choose a BRCA1 experiment (i.e. by experiment name) to combine with other experiment stored in the database (gene, enzyme, protein, etc.) to generate and view the graph of BRCA1 pathway

c. Allows the project leader to:

i. Accept or reject a user's project membership request

ii. Edit or delete a project that he added

iii. Add new members in the project created

iv. Add, edit or delete an experiment under a project he created

v. Add new parameters to a project created

vi. Accept or reject a user's project parameter request

vii. Use the external search of the system which search in MetaCyc and KEGG (Kyoto Encyclopedia of Genes and Genomes)

viii. Choose a BRCA1 experiment (i.e. by experiment name) to combine with other experiment stored in the database

(gene, enzyme, protein, etc.) to generate and view the graph of BRCA1 pathway

d. Allows the project member to:

   i. Edit or delete an experiment under a project in which he is a member

   ii. Request for new parameter for project

   iii. Search and View other research experiment about BRCA1 metabolic pathway by experiment name, experimenter or researcher who conducted that study / experiment

   iv. Use the external search of the system which search in MetaCyc and KEGG (Kyoto Encyclopedia of Genes and Genomes)

   v. Choose a BRCA1 experiment (i.e. by experiment name) to combine with other experiments stored in the database with (gene, enzyme, protein, etc.) to generate and view the graph of BRCA1 pathway

e. Allows the system administrator to:

   i. Edit the users' account

   ii. Accept or reject the user's membership request

   iii. Accept or reject the request for new project

iv. Enable or disable the users' account

D. Significance of the Study

The system will help the user especially the researcher or expert in studying the BRCA1 gene or breast cancer for their experiments. This system is also useful for the users who wanted to study the BRCA1 gene interaction to other gene, protein, enzyme, etc. It is also used in understanding the BRCA1 gene behavior of how it reacts to different factors. This can provide a repository for the experiments or studies concerning BRCA1 gene. The system is specific only to BRCA1 gene and focuses only to the construction of its metabolic pathway which can ensure that the result derived will be precise and rigorous. The information stored in the database can be a relation type, process, etc. that will greatly aid in building the complete BRCA1 pathway.

E. Scope and Limitation

1. The system will only concern in experiments or studies about BRCA1 gene.

2. The verification and validation of the data will not be the concern of the system.

3. Approval for a new user account request is subject to the administrator consent.

4. The graph generated by the system is only based on the pathway/rules created by the researcher.

F. Assumption

i. The input data of the researcher is assumed to be valid.

ii. The users of the system are assumed to be an expert in BRCA1 metabolic pathway.

II. Review of Related Literature:

Molecular complexes, interactions and pathways are the information stored in the Biomolecular Interaction Network Database (BIND) (Bader, G., Betel, D., et.al, 2008). [3]

According to Collado-Vides, J. et.al. EcoCyc system is used to contain both computable descriptions and detailed comments describing all genes, proteins, pathways and molecular interactions in Ecoli. [4]

On the other hand, one of the uniquely high-quality resources for metabolic pathways and enzymes is the MetaCyc, which is called the universal database (Caspi, R., Foerster, H., et.al., 2007). [5]

Based on Cakmak, A. et.al. the functional relationships between molecules are illustrated by pathways, for instance, the identity of substrate(s), product(s), cofactors, activators, inhibitators, enzymes or other processing molecules, RNA and protein expression patterns, reaction kinetics, and associated phenotypic variation and diseases. [6]

Caspi, R. et.al. states that From Metabolite to Metabolite (FMM) was created for the purpose of reconstructing metabolite pathways from one metabolite to another with different species. [7]

The study of Caspi, R. et.al. states that MetaCyc contains metabolic pathways, enzymatic reactions, enzymes, chemical compounds genes, and review-level comments. [8]

Khan, M. et.al. found that distribution of chromosomal in cancer metasignature genes does not show any relation to the genomic length and gene density of the chromosomes and these genes are scattered throughout the human genome. [9]

The Meta-All software is populated with sufficient amounts of data and a variety of complex queries is possible for detailed structure of the database schema (Grosse, I., 2006). [10]

Holford, M. et.al. states that VitaPad develops existing software in the following areas. By creating diagrams, it is open source and uses an open XML format and it features a cutting edge user interface with intuitive controls, high resolution graphics and fully customizable appearance. [11]

According to Viswanathan, G. et.al building the pathway includes the process of identifying and integrating the entities, interactions, and associated annotations, and populating the knowledgebase. The construction of pathway consists of either a data-driven objective which is used to generate relationship information of genes or proteins identified in a specific experiment such as a microarray study, or a knowledge-driven objective which entails development of a detailed pathway knowledgebase for particular domains of interest such as cell type, disease, or system. [12]

III. Theoretical Framework:

BRCA1 Metabolic Pathway

Mutations in the BRCA1 breast cancer gene appear to be linked with the loss of a protein important for putting the brakes on cell growth. Researchers at Columbia, working with a team at Sweden's Lund University, now believe mutations in the BRCA1 gene can leave cells incapable of repairing routine DNA damage. When such damage occurs in a protein called PTEN, which regulates the growth of cells, cell growth is unchecked and tumors form. Women with faulty copies of BRCA1 or BRCA2 have a 50 to 85% chance of getting breast cancer. Mutations in these genes account for 5 to 10% of breast cancer cases. Most breast tumors are called estrogen-receptor positive, because they are fueled by the hormone estrogen. About 20% are HER2-positive, because a protein called HER2 is involved. A third type is driven by the hormone progesterone. These types of cancer have good treatments. Then there are basal-like or triple-negative

tumors, so named because they lack estrogen, progesterone or HER2 receptors needed for most breast cancer drugs to work. [18]

The basic idea is that BRCA1 is a repair enzyme that is involved in coordinating the repair of double strand DNA breaks. When it is mutated, it is no longer present in a cell. If a cut occurs in PTEN, there is no way for this cell to fix it. It is like cutting the brake cable on a car. If PTEN is broken, you turn on a pathway that tells the cell to grow. It tells the cell to start dividing. It tells the cell, don't die. The loss of the protein PTEN is how breast cancer gets started in women who have inherited the BRCA1 gene mutation (Mr. Parsons, Nature Genetics). [18]

His team made the connection between BRCA1 and PTEN by searching for chromosome breaks within the PTEN gene. They scanned 34 biopsies taken from women with BRCA1 tumors. The PTEN gene had been split in two, but inadequately repaired in about one-third of the cancers. In some cases, entire sections of the gene were missing. They said these chromosomal mistakes trace back to the tumor's lack of BRCA1, which is charged with cell repair. He estimates that about 50% of BRCA1 breast cancers harbor mutated PTEN. [18]

According to Mr. Parsons, these tumors have very high frequency loss of the PTEN protein. In breast cancers from women with normal BRCA1, they rarely found large mutations in PTEN. There is reasonably good hope that this approach will improve therapy for patients. Basal-like breast tumors are also found in 10% to 20% of women whose cancer was not caused by BRCA1 or

another gene. The researchers found PTEN is lost in most of these breast tumors as well. [18]

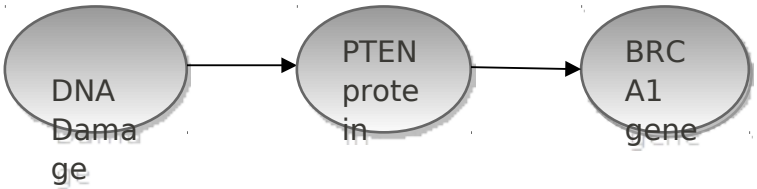


Figure 1: One example of pathway in BRCA1 metabolic pathway. Parameters and their corresponding values are type of damage: DNA damage, Protein affected: PTEN and gene affected: BRCA1.

Metabolic Pathways *within an organism is a series of enzymatic reactions consuming certain metabolites and producing others. Often these metabolites participate in more than one metabolic pathway, forming a complex network of reactions. The analysis of this complex network involves an enormous amount of data from biochemistry and cell physiology, such as metabolic intermediates and their properties, biochemical reactions, properties of enzymes from different sources, regulation of gene expression, etc., as well as principles from physical sciences* [2].

GraphViz *is an open source visualization tool that is capable of reading a state diagram definition, provided in the form of a specially formatted text file, and creating a graphical output file showing each state and the relationships it has with other states* [24].

The Graphviz layout programs take descriptions of graphs in a simple text language, and make diagrams in several useful formats such as images and SVG for

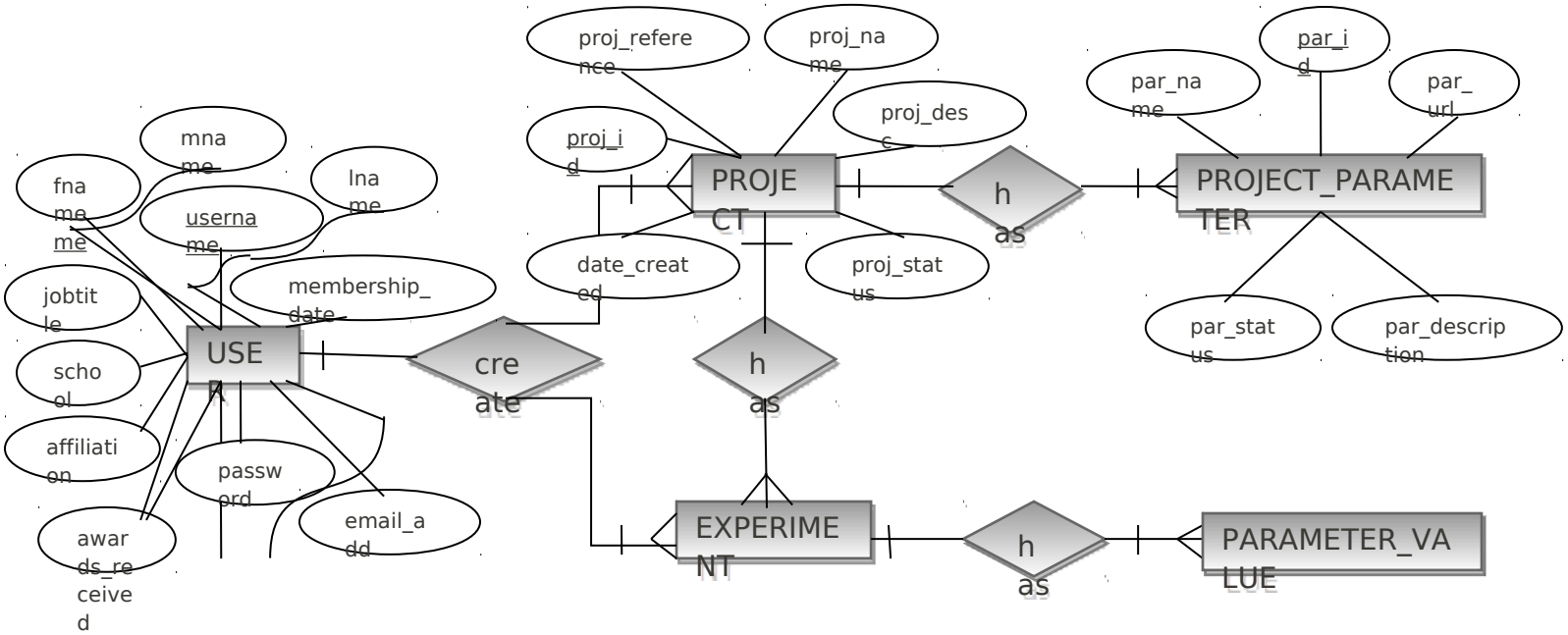
web pages, Postscript for inclusion in PDF or other documents; or display in an interactive graph browser [26].

DBMS (Database Management System**)** *is a suite of programs which typically manage large structured sets of persistent data, offering ad hoc query facilities to many users. A database management system (DBMS) can be an extremely complex set of software programs that controls the organization, storage and retrieval of data (fields, records and files) in a database. It controls the security and integrity of the database. The DBMS accepts requests for data from the application program and instructs the operating system to teacher the appropriate data. When a DBMS is used, information systems can be changed much more easily as the organization's information requirements change without disruption to the existing system* [14].

IV. Design and Implementation:

A. Entity Relationship Diagram

Figure 1 show the entity relationship diagram of the system which is composed of entities and association between entity types. USER, PROJECT, EXPERIMENT, PROJECT_PARAMETER, PARAMETER_VALUE and RULES are the entities of the system which is equivalent to a relational table. The primary keys are the username, proj_id, exp_id and par_id which are linked to other database tables.



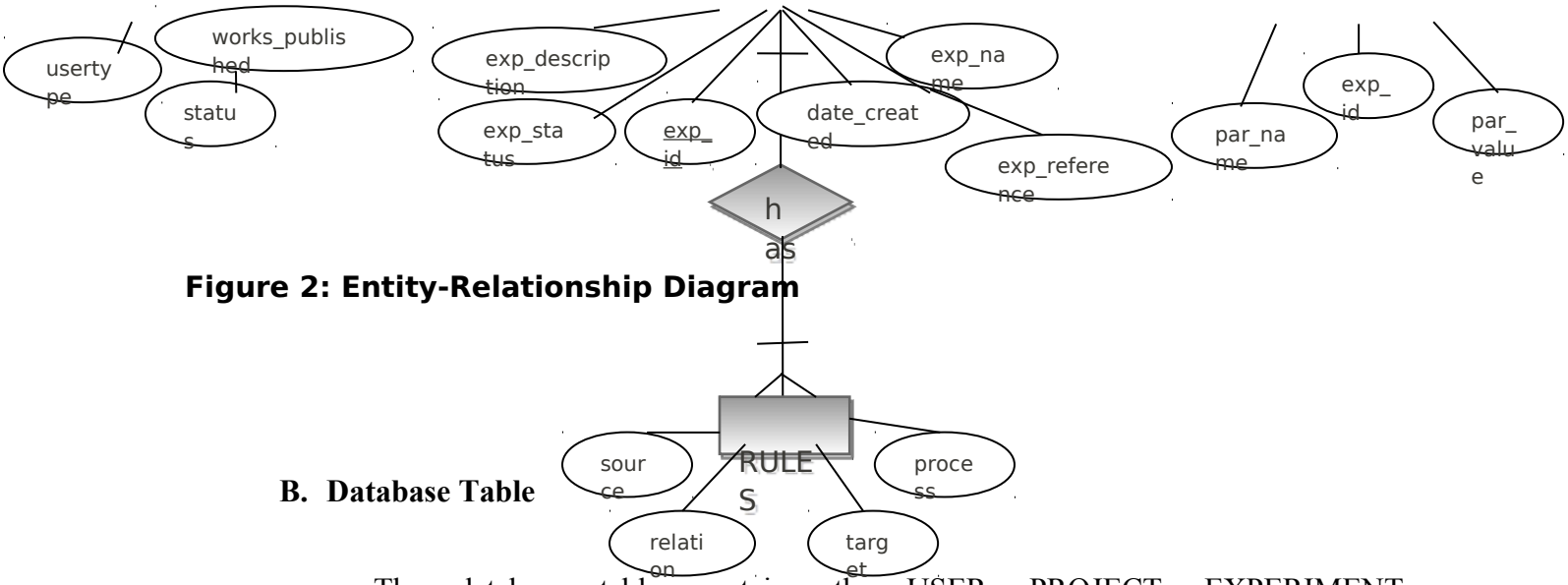


Figure 2: Entity-Relationship Diagram

B. Database Table

The database table contains the USER, PROJECT, EXPERIMENT, PROJECT_PARAMETER, PARAMETER_VALUE and RULES entities shown in Figure 2. The database contains information about the user, project, experiment and parameter. Each of the primary key in the table is underlined whereas the foreign key in the table is marked with asterisk (*). The tables are listed below as well as their respective data fields and descriptions.

USER table: This table contains the information about the users of the system. The data it contains are being retrieved whenever the user wants to view the information such as first name, middle name, last name, etc.

Datafield	**Data Type**	**Description**
username	varchar(30)	unique username for logging in the system
password	varchar(32)	password of the user
usertype	varchar(30)	type of user
fname	varchar(30)	first name of the user
mname	varchar(30)	middle name of the user
lname	varchar(30)	last name of the user

status	varchar(30)	status of the user (enable, disable)
membership_date	timestamp	date and time when the membership request of user was created
job_title	text	job title of the user
affiliation	text	user affiliation
school	text	college or university where the user studied
awards	text	awards received by the user
works_published	text	works published by the user
email_add	varchar(30)	email address of the user

PROJECT table: This table contains the general information about the project**.** The data it contains are being retrieved whenever the user wants to view the information about a project such as project name, project description, project reference, etc.

Datafield	Data Type	Description
proj_id	int(5)	system generated unique project id
*username	varchar(30)	user's username who created the project
*exp_id	int(5)	experiment id under a project
proj_name	varchar(50)	name of the project
proj_desc	text	description of the added project
proj_reference	text	reference of the project added
proj_status	varchar(7)	status of the project (i.e. approve, private, public, decline, delete)
date_created	timestamp	date and time when the project was created

EXPERIMENT table: This table contains the general information about the experiment. The data it contains are being retrieved whenever the user wants to

view the information about an experiment such as experiment name, experiment description, experiment reference etc.

Datafield	Data Type	Description
exp_id	int(5)	system generated unique experiment id
*proj_id	int(5)	project id to which the experiment is under
*username	varchar(30)	user's username who created the experiment
exp_name	varchar(50)	name of the experiment
exp_description	text	description of the added experiment
exp_reference	text	source or reference of the experiment added
exp_status	varchar(7)	status of the experiment (i.e. delete, decline, approve, accept)
date_created	timestamp	date and time when the experiment created

PROJECT_PARAMETER table: This table contains the information about the parameters in a particular project. The data it contains are being retrieved whenever the user wants to create or edit an experiment.

Datafield	Data Type	Description
par_id	int(5)	system generated unique parameter id
*proj_id	int(5)	project id to which the parameter is under
*username	varchar(30)	user's username who created the parameter
par_name	varchar(50)	name of the parameter that is part of the project and will be used in pathway generation
par_description	text	description of the parameter
par_url	text	url of the parameter
par_status	varchar(7)	the parameter status (e.g. approve, decline, accept)

PARAMETER_VALUE table: This table defines the values of the parameters in an experiment. The data it contains are being retrieved whenever the user wants to create or edit an experiment.

Datafield	Data Type	Description
*exp_id	int(5)	experiment id to which the parameter is under
par_name	varchar(100)	name of the parameter
par_value	varchar(100)	value of the parameter

RULES table: This table contains the information in generating the graph of an experiment. The data it contains are being retrieved whenever the user wants to view the graph of the experiment's pathway.

Datafield	Data Type	Description
*exp_id	int(5)	experiment id to which the rules are under
source	varchar(100)	source would be the starting node of the pathway
target	varchar(100)	target would be the ending/result node of the pathway
relation	varchar(100)	relation values and their equivalent arrow in the graph are the following: acts / produce / cause = --->; connected to = --- (solid black) attached to =--- (dashed red) reversible to = <-->
process	text	process that undergone by the source or target values

C. Context Diagram

The users of the system are the unregistered user (i.e. guest viewer), the registered user, the project leader, the project member and the system administrator. The unregistered user can query the available experiments in the internal database, generate BRCA1 pathway found in the internal database, query information from other databases in the external search and can be registered in the system by filling-up the registration form. The registered user can apply as project leader or project member by creating project or experiment respectively. The project member can add, delete or update an experiment under a particular project. The project leader can add, delete or update a project and an experiment. Also, the project leader can add members, accept or deny request for membership in a particular project. The system administrator is responsible for maintaining the system. He / She can accept or reject the user's request for membership or the user's request for new project.

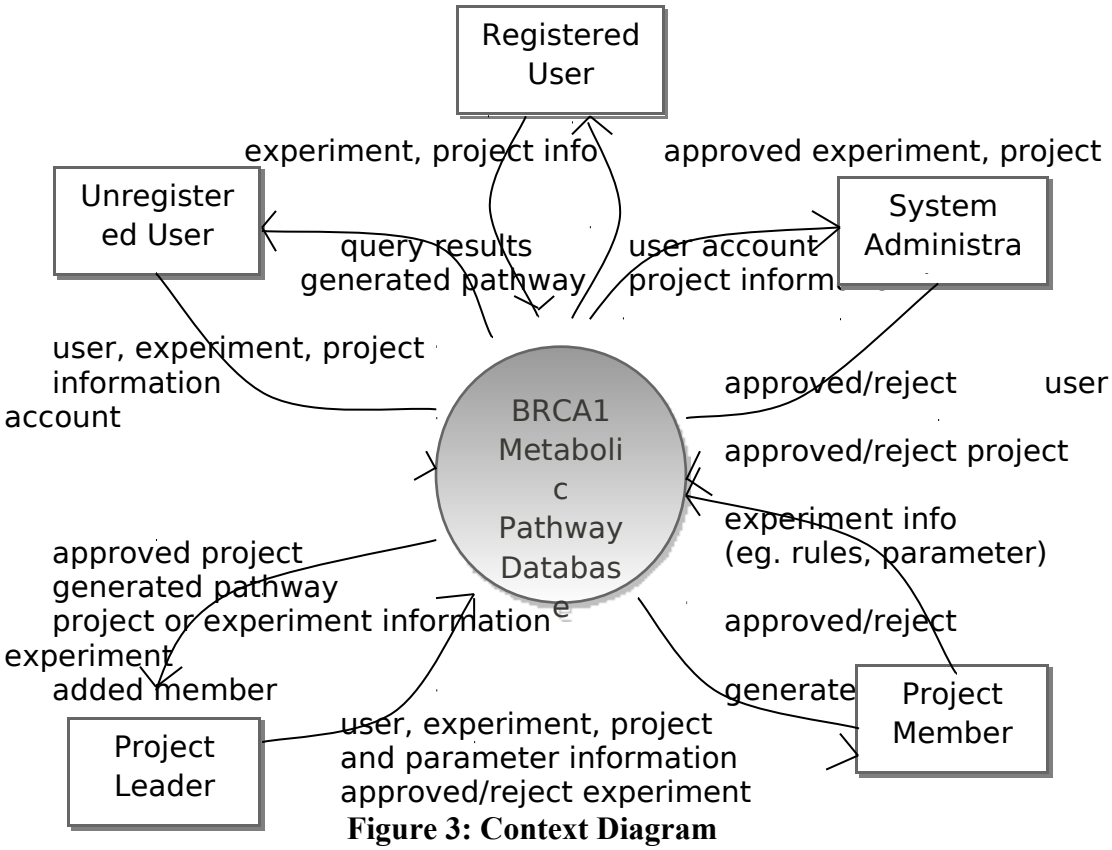
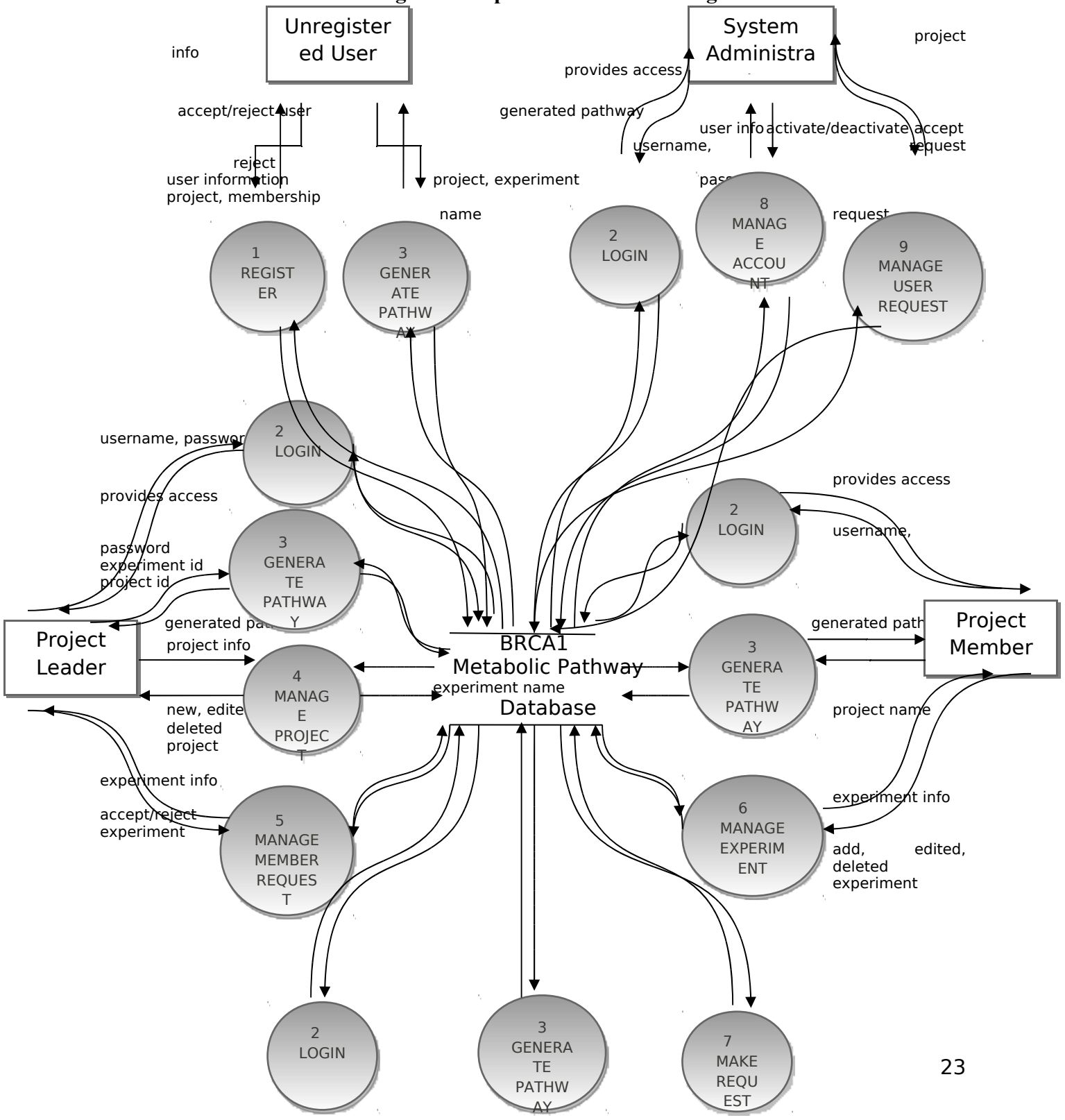


Figure 3: Context Diagram

Figure 4: Top Level Data Flow Diagram



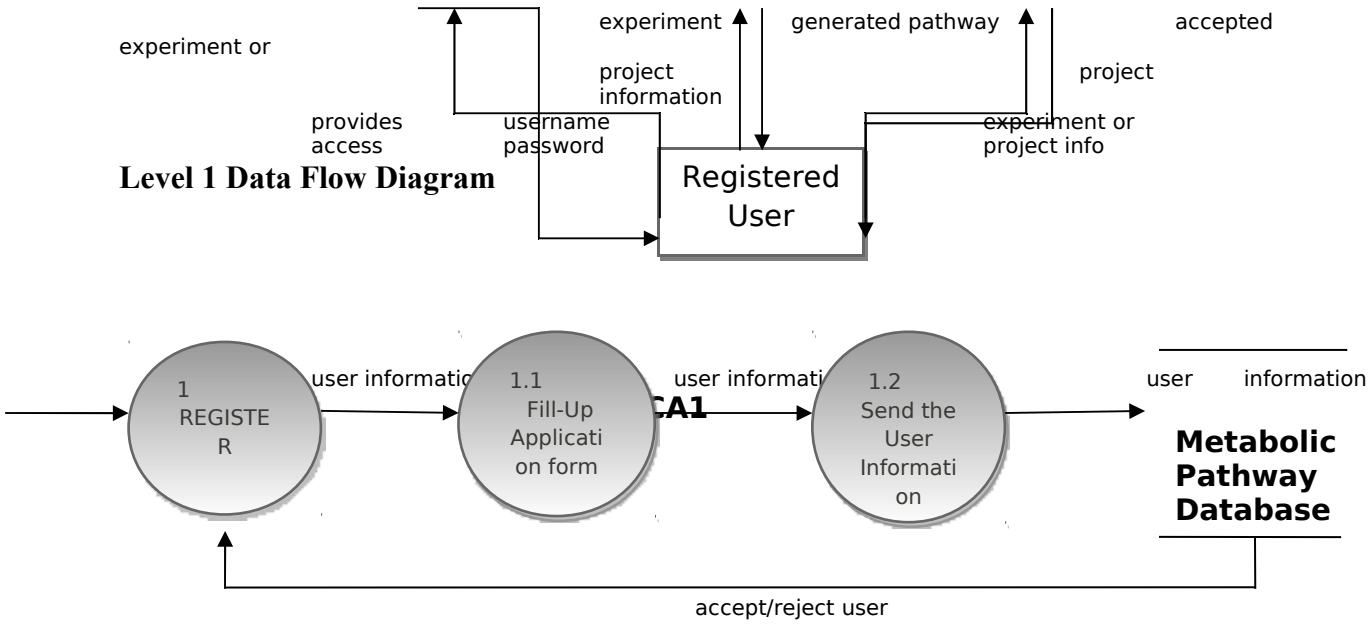


Figure 5.1 Level 1 DFD for REGISTER

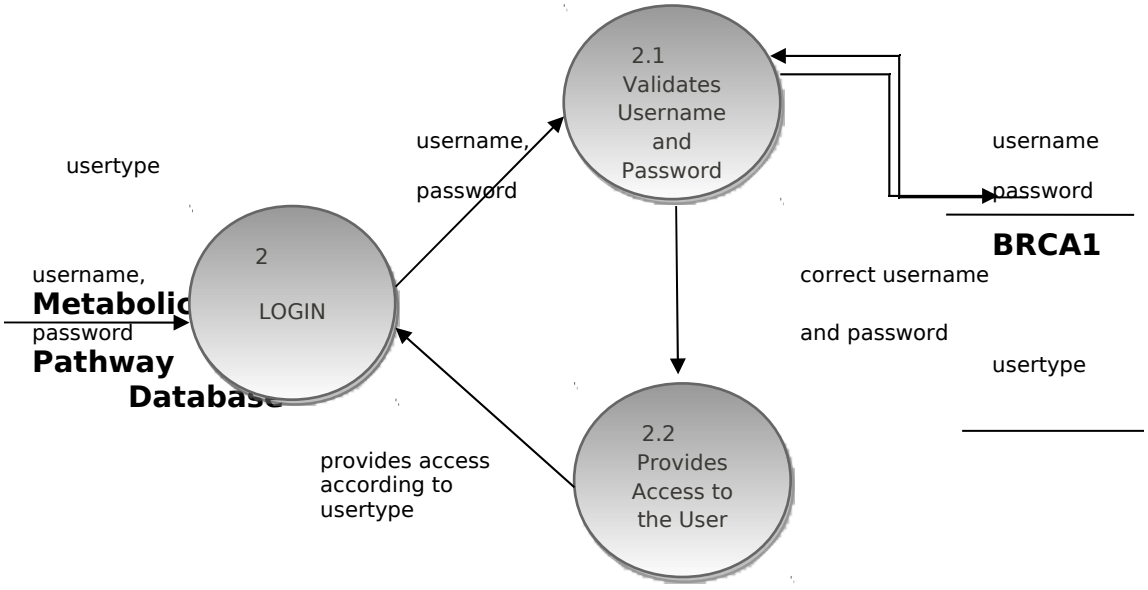


Figure 5.2 Level 1 DFD for LOGIN

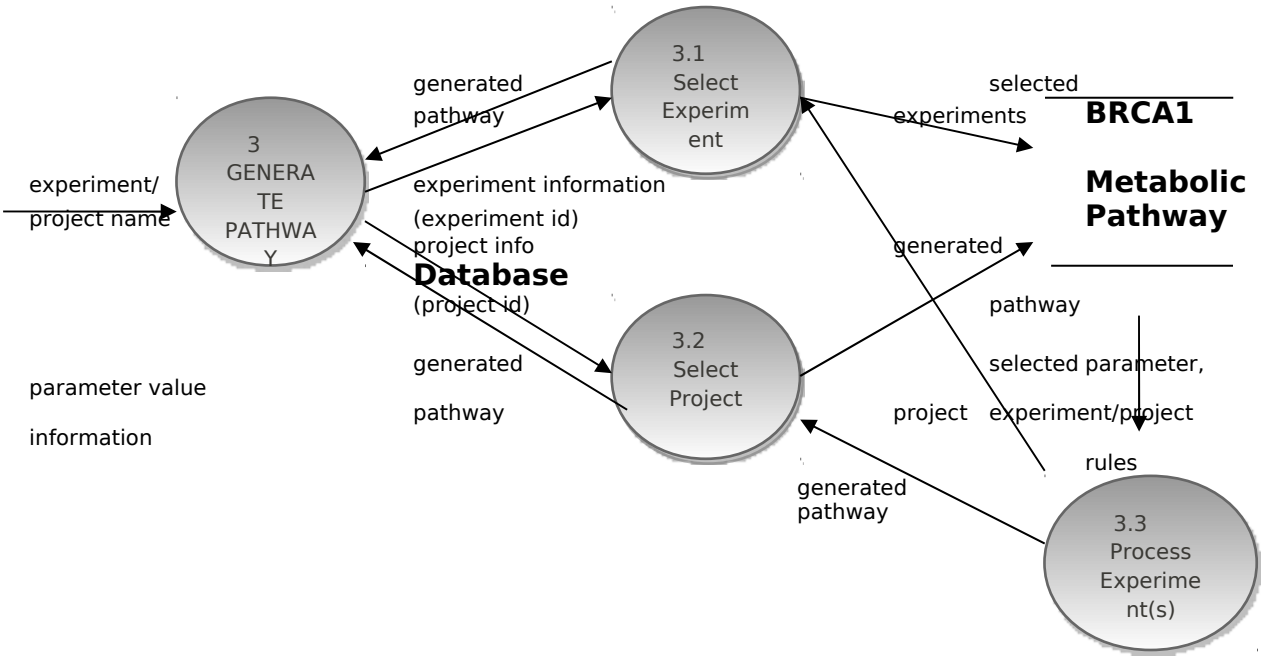


Figure 5.3 Level 1 DFD for GENERATE PATHWAY

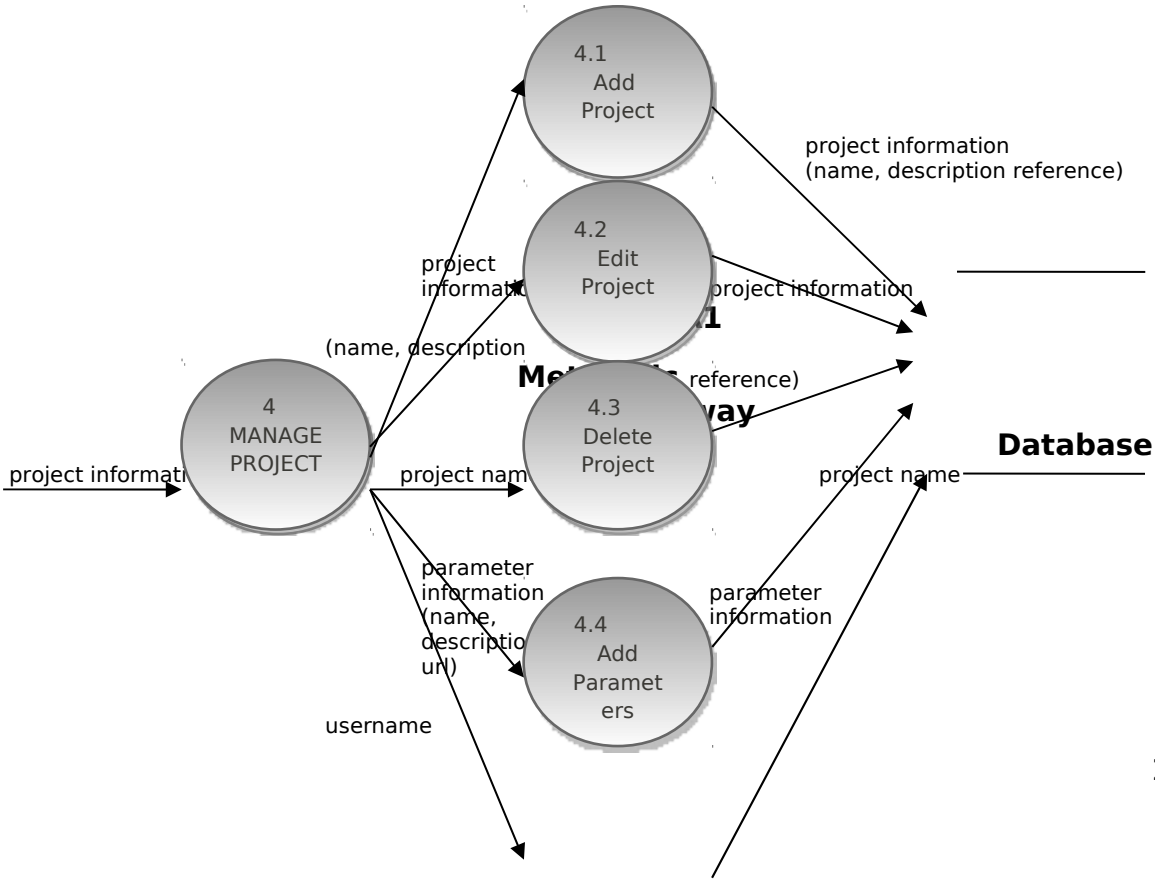


Figure 5.4 Level 1 DFD for MANAGE PROJECT

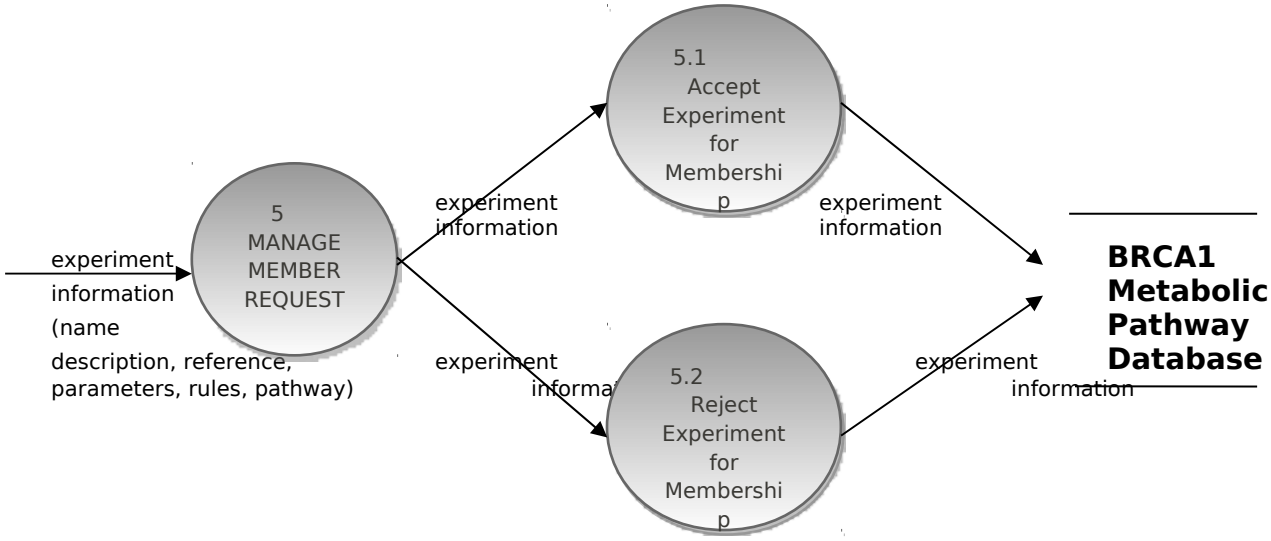


Figure 5.5 Level 1 DFD for MANAGE MEMBER REQUEST

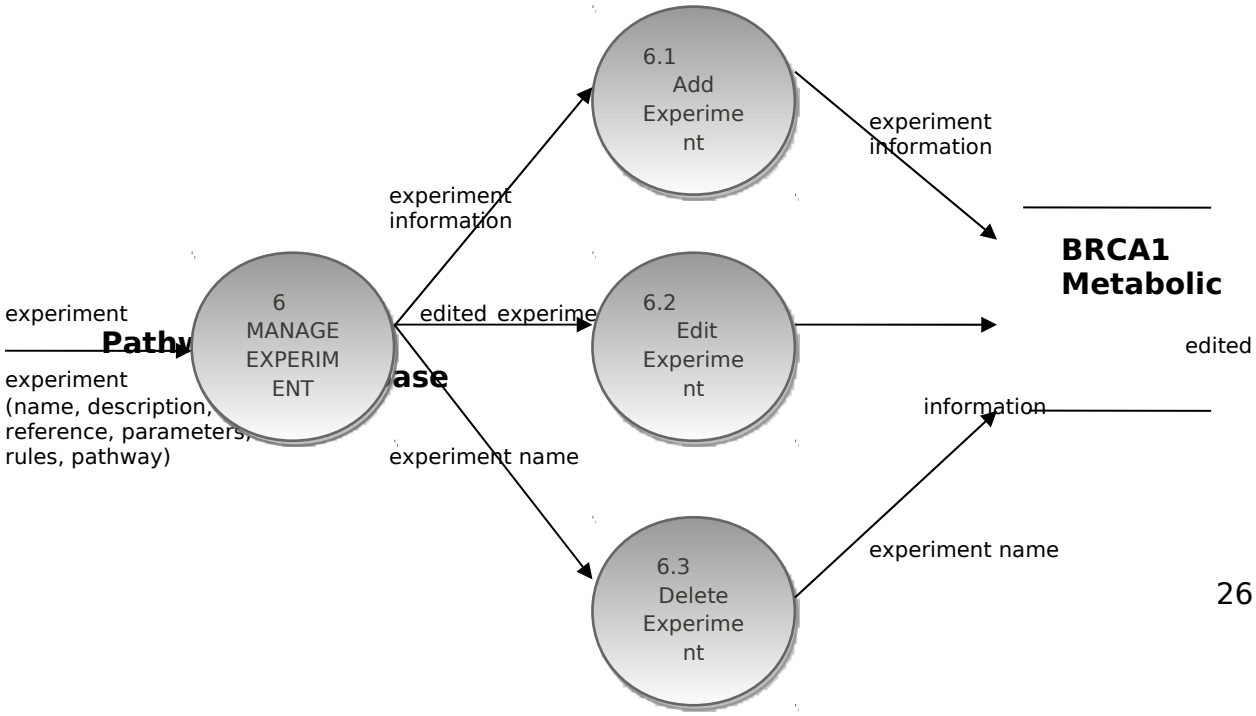


Figure 5.6 Level 1 DFD for MANAGE EXPERIMENT

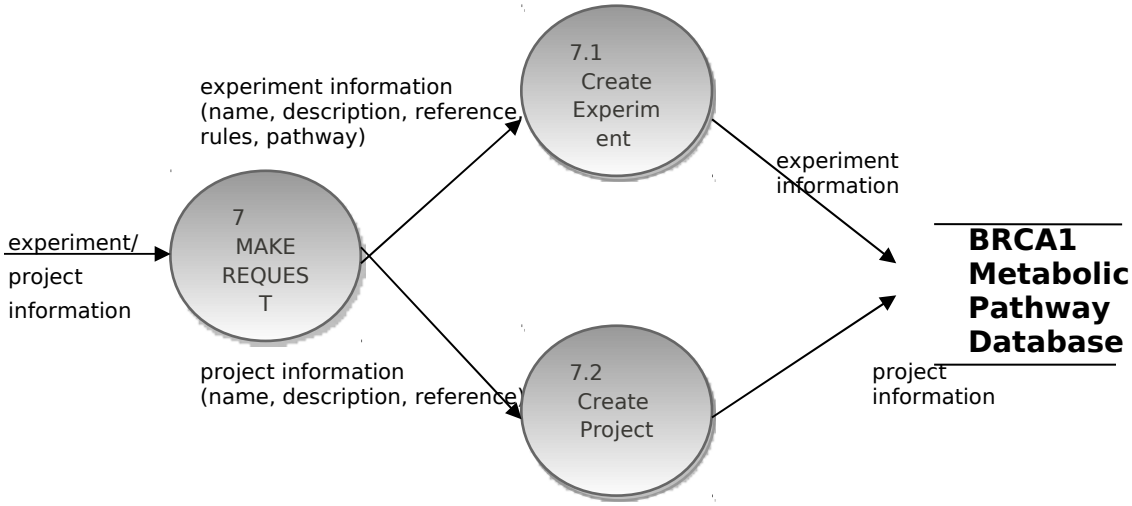


Figure 5.7 Level 1 DFD for MAKE REQUEST

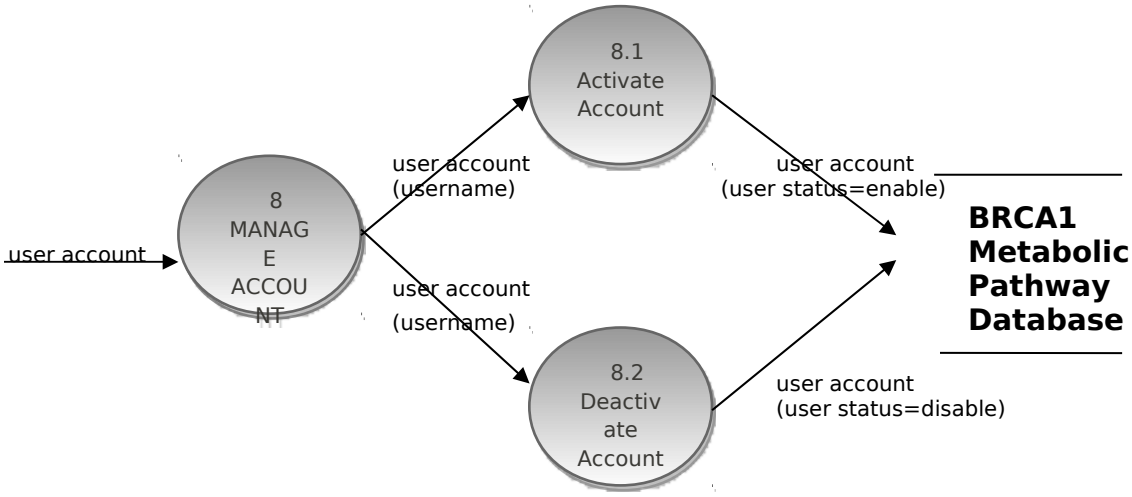


Figure 5.8 Level 1 DFD for MANAGE ACCOUNT

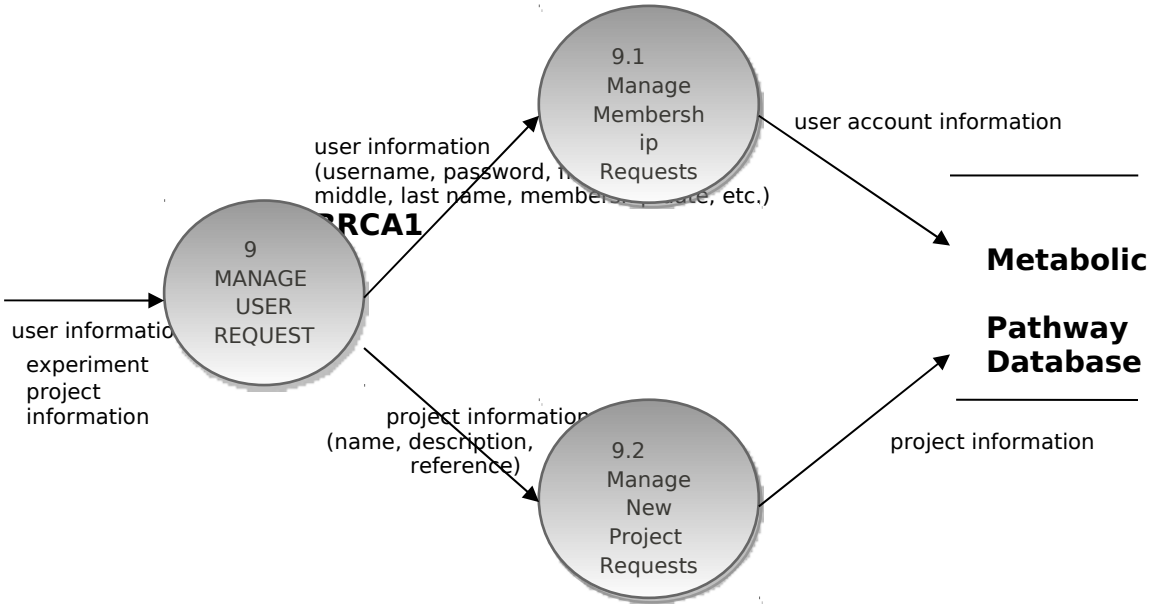


Figure 5.9 Level 1 DFD for MANAGE USER REQUEST

Level 2 Data Flow Diagram

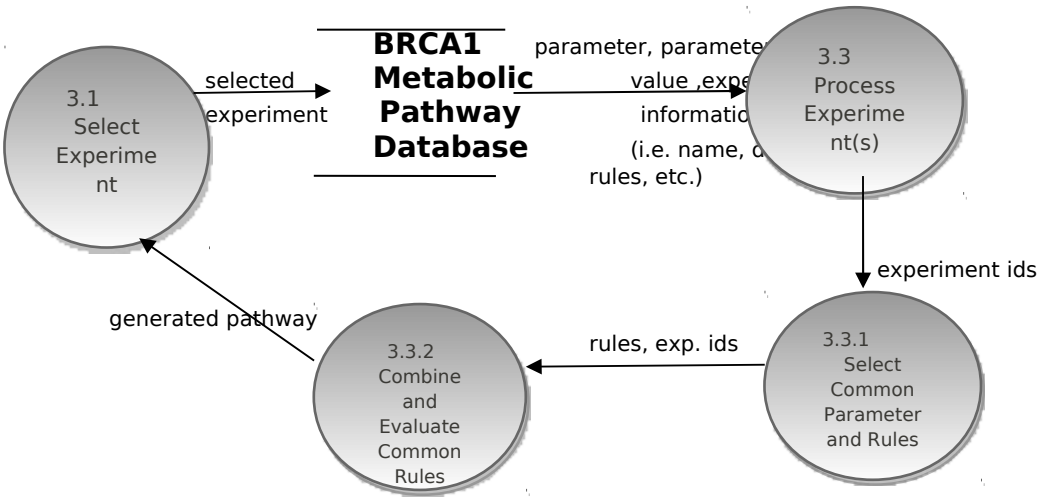


Figure 6.1 Level 2 DFD for SELECT EXPERIMENT

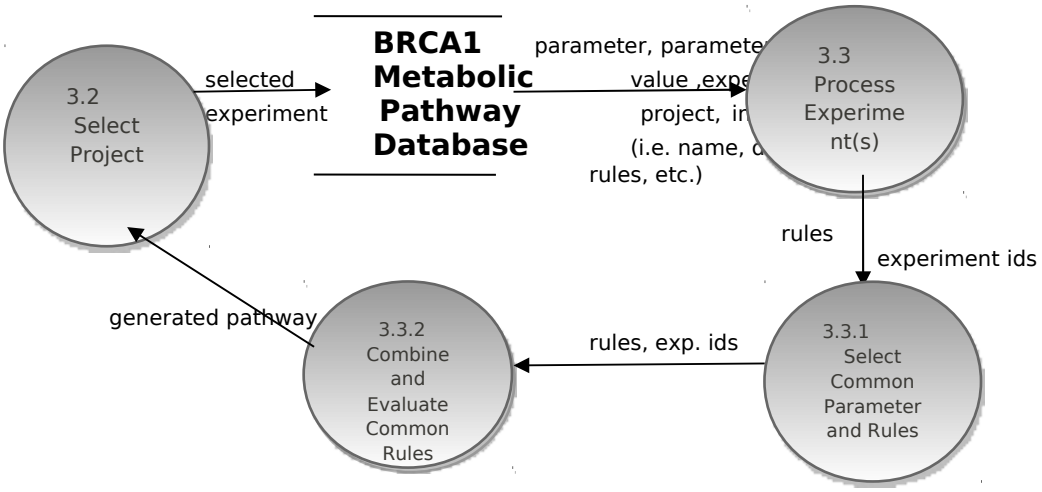


Figure 6.2 Level 2 DFD for SELECT PROJECT

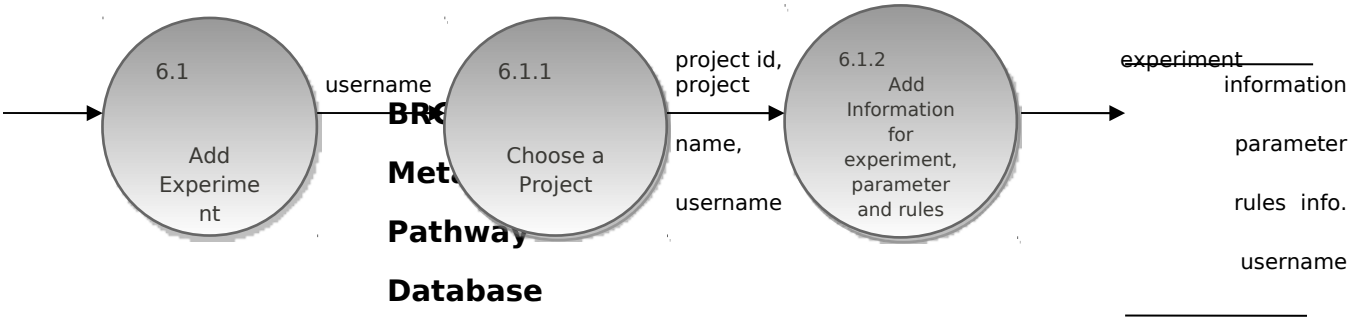


Figure 6.3 Level 2 DFD for ADD EXPERIMENT

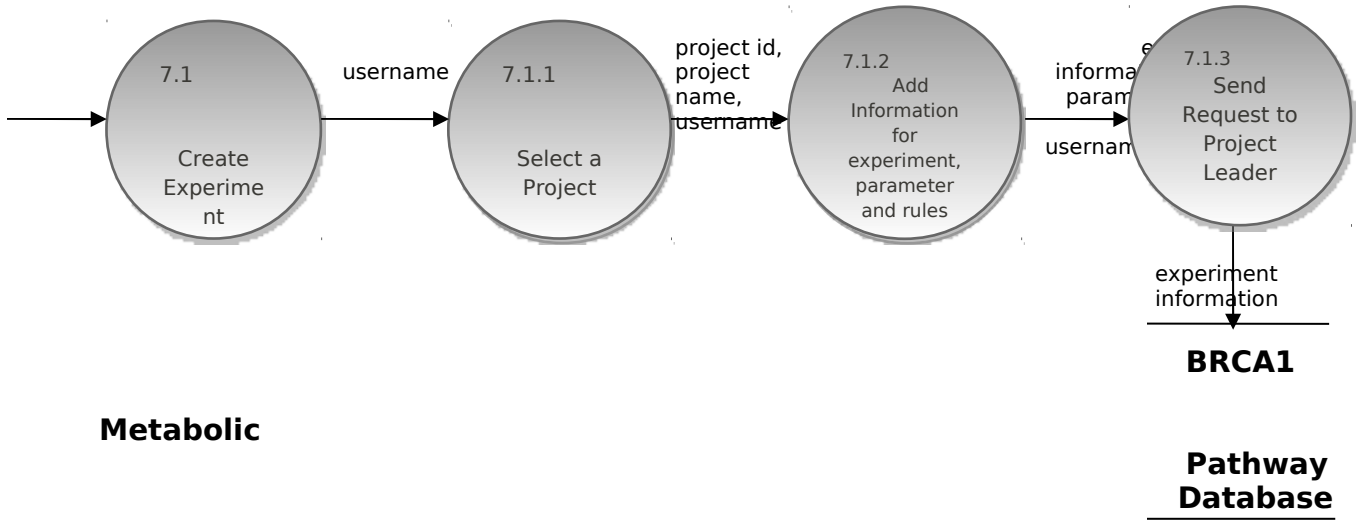


Figure 6.4 Level 2 DFD for CREATE EXPERIMENT

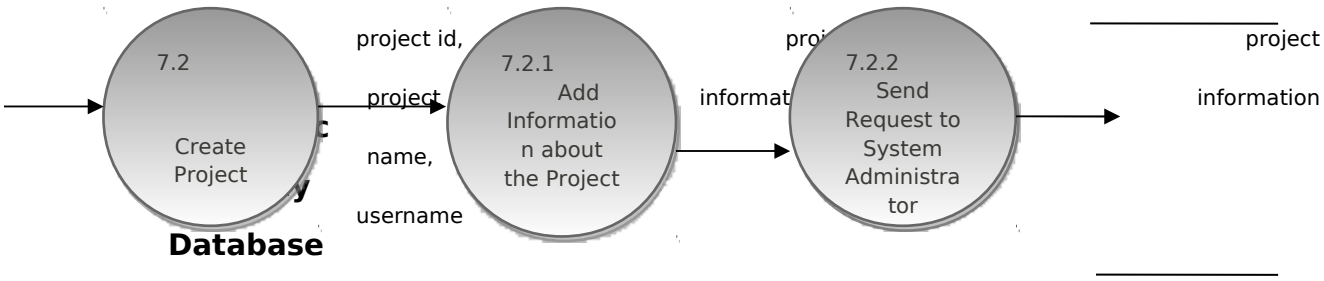


Figure 6.5 Level 2 DFD for CREATE PROJECT

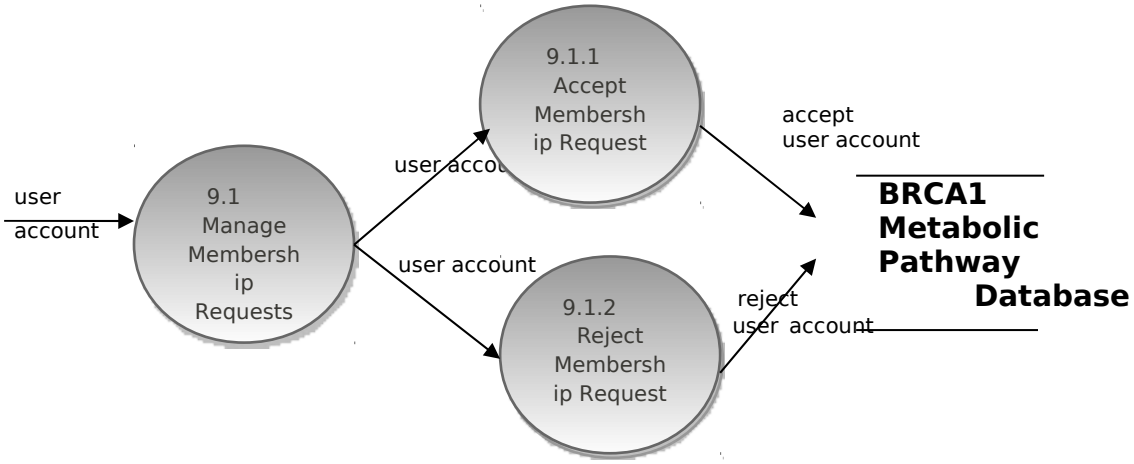


Figure 6.6 Level 2 DFD for MANAGE MEMBERSHIP REQUESTS

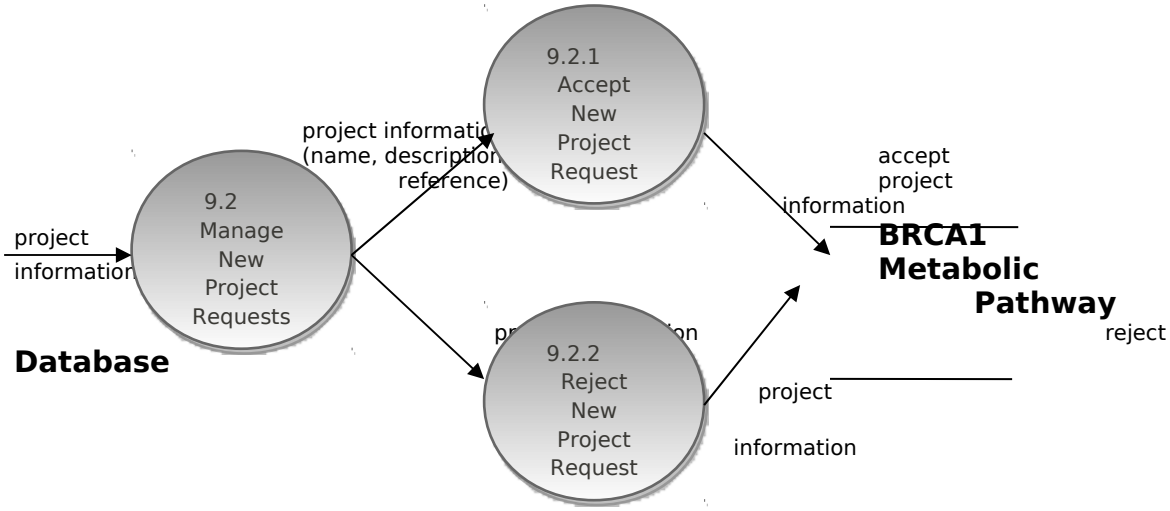


Figure 6.7 Level 2 DFD for MANAGE PROJECT LEADER REQUESTS

D. Technical Architecture

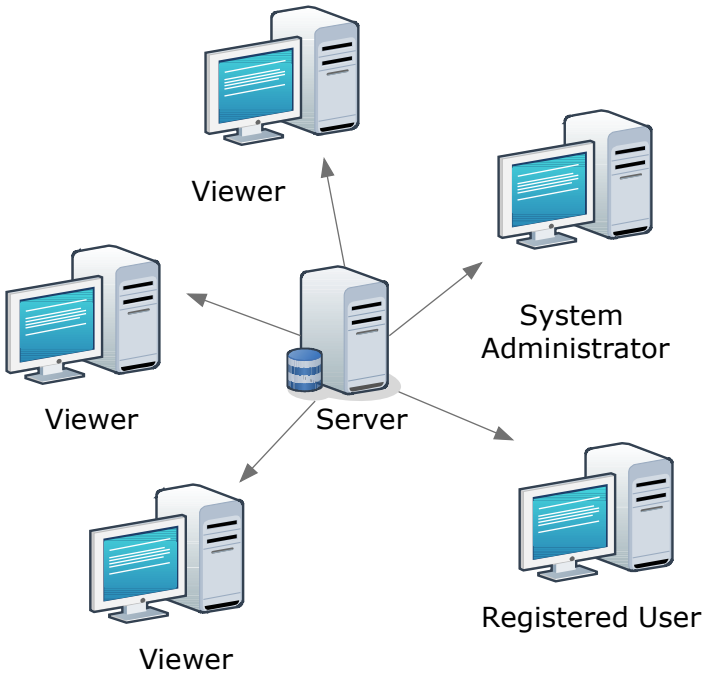


Figure 7:

Client-Server Architecture

The system uses the client-server architecture. In which the client makes a service request from another program, the server, which fulfills the request. In a network, the client/server model provides a convenient way to interconnect programs that are distributed efficiently across different locations [25].

The programming language used in the system is PHP v.5.2.5. The graphviz tool v.2.26 is also used in the system to graph the pathway. An internet connection is needed in order to access the system. It can run on Windows XP operating system. The graph generated by the system is best viewed using Mozilla Firefox. XAMPP v.1.6.6a is also used by the system.

V. Results and Discussions:

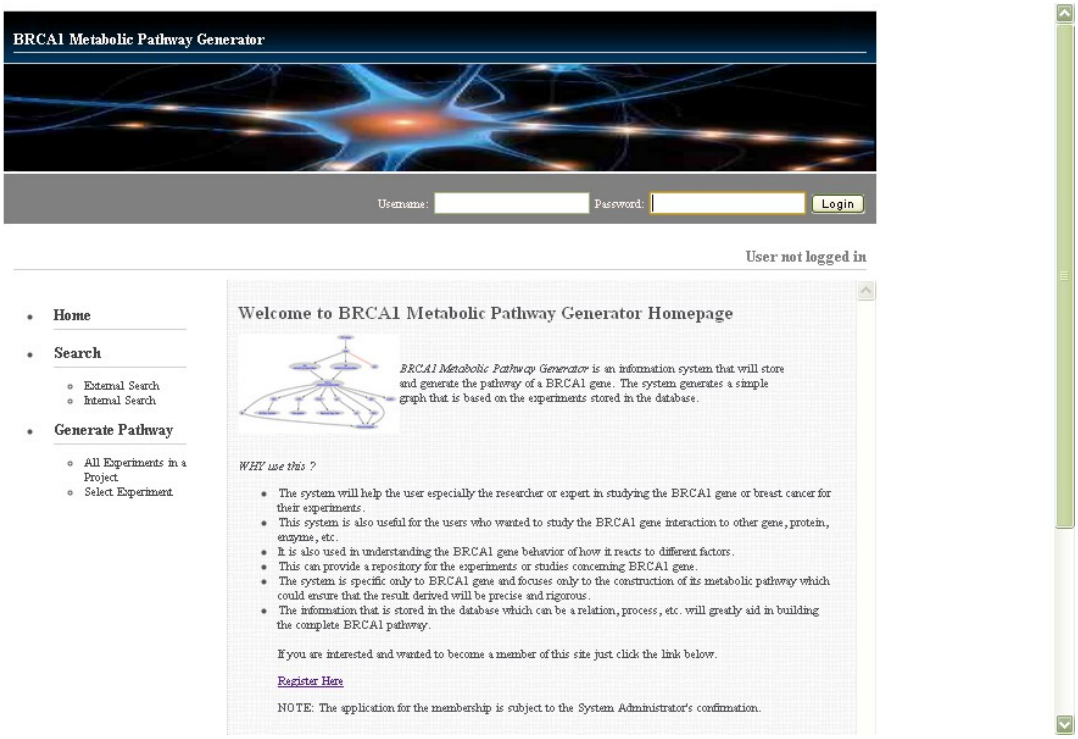


Figure 8 Main Page

The figure shows the system's main page interface. The unregistered users can query the available experiments and generate pathway found in the internal database by accessing the internal search link provided. They can also query information from MetaCyc and KEGG databases in the external search link. They are also allowed to register in the system by filling-up the registration form that can be found by accessing the register here link.

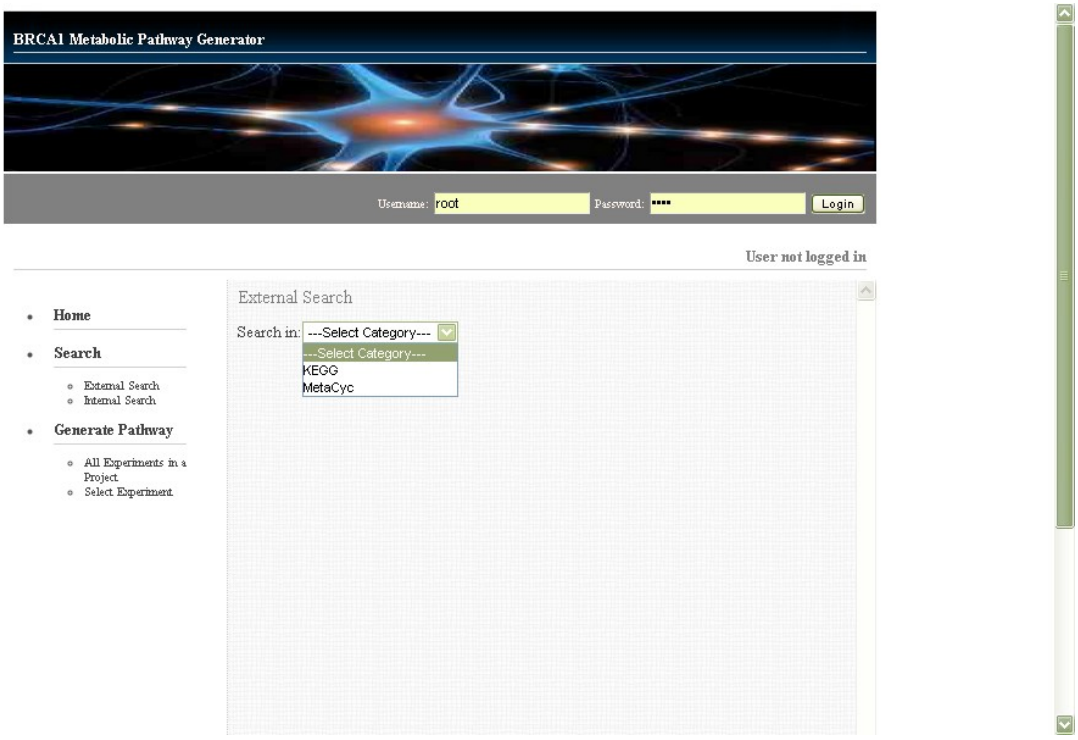


Figure 9 External Search

The figure shows the external search interface of the system. The system provides the user an option to choose what database to search in (i.e. KEGG or MetaCyc).

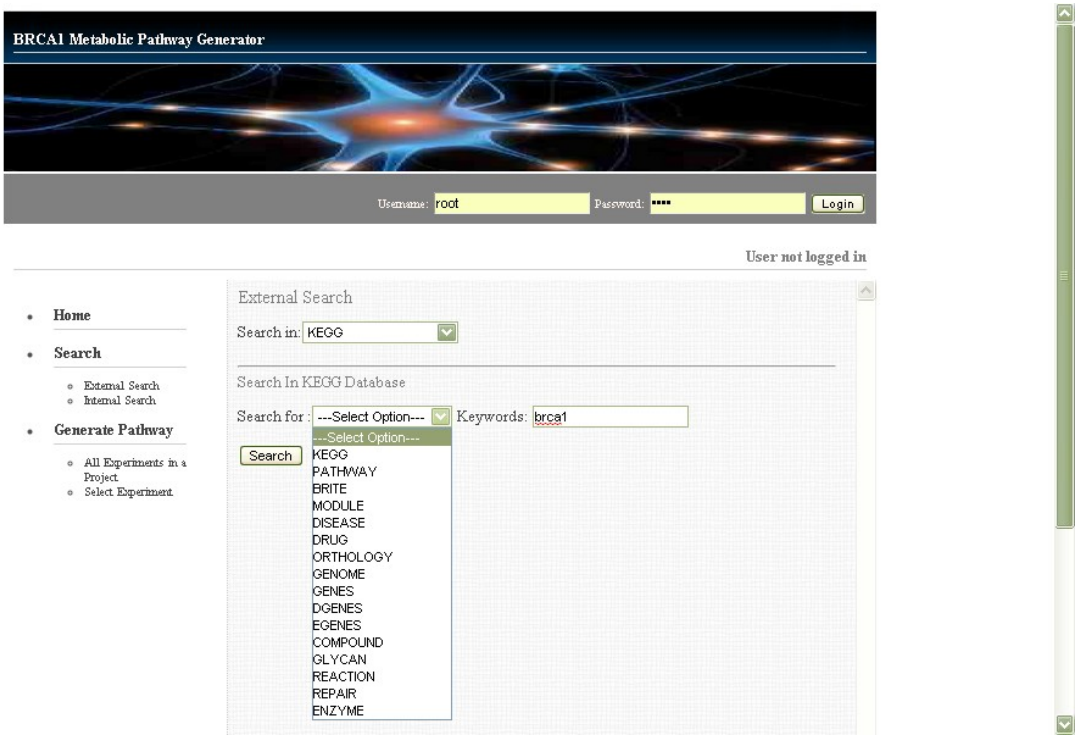


Figure 10 External Search in KEGG

The figure shows the search interface in KEGG database section. The system provides the user an option to choose what information (i.e. KEGG, PATHWAY, BRITE etc.) and keywords to search.

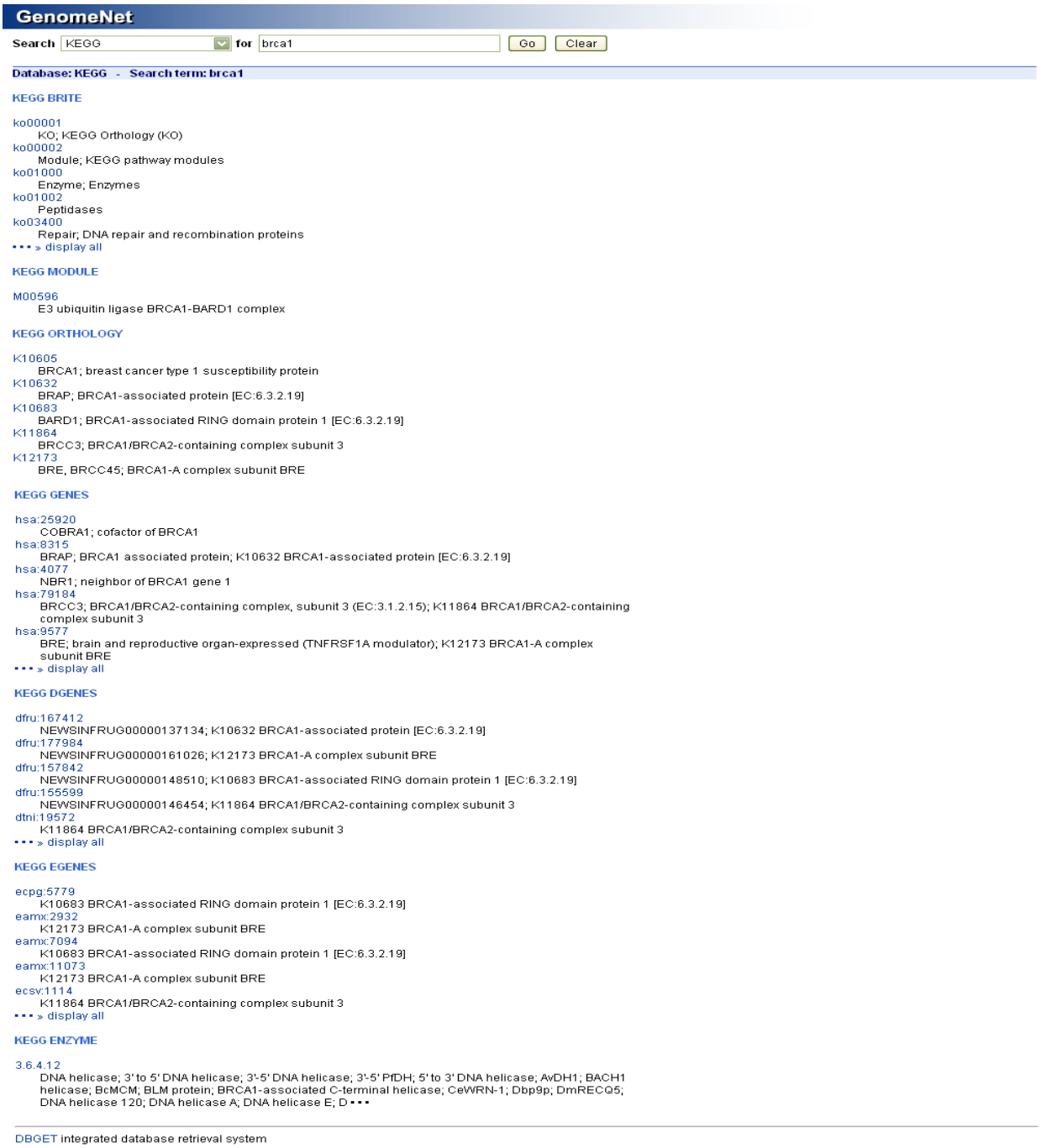


Figure 11 External Search in KEGG Results

Sample results found in the KEGG database based on the previous input of the user that searches KEGG for brca1 keyword.

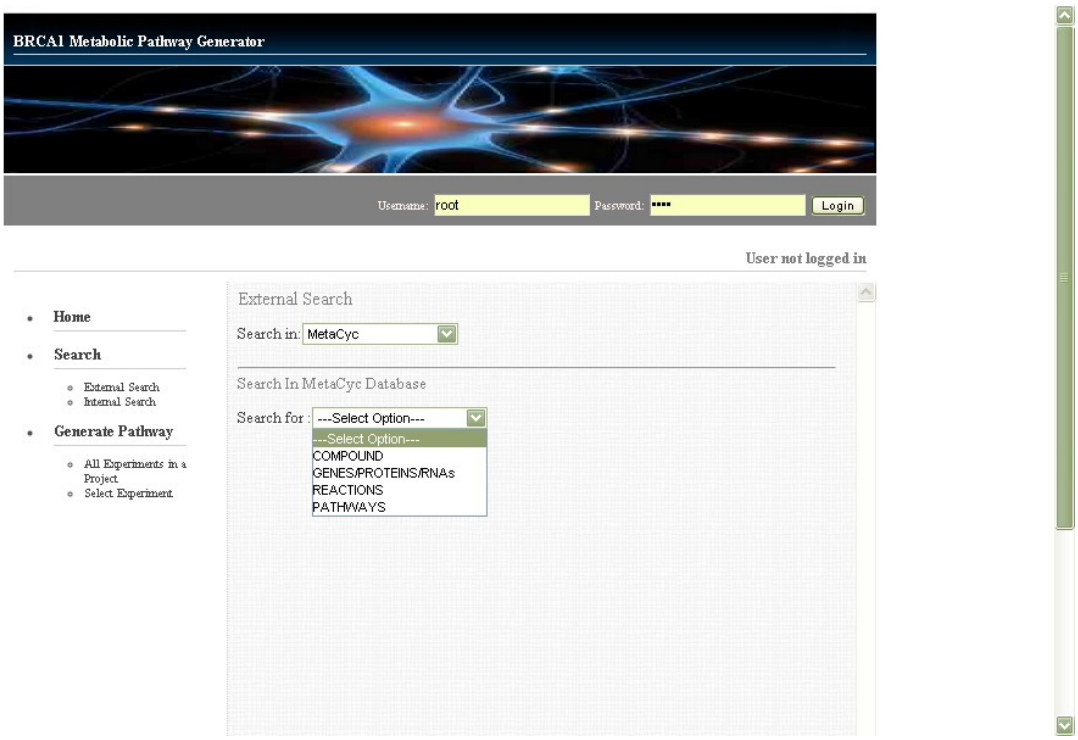


Figure 12 External Search in MetaCyc

The figure shows the search interface in MetaCyc database section. The system provides the user an option to choose what information to search (i.e. COMPOUND, GENES/PROTEINS/RNAs, REACTIONS, and PATHWAYS)

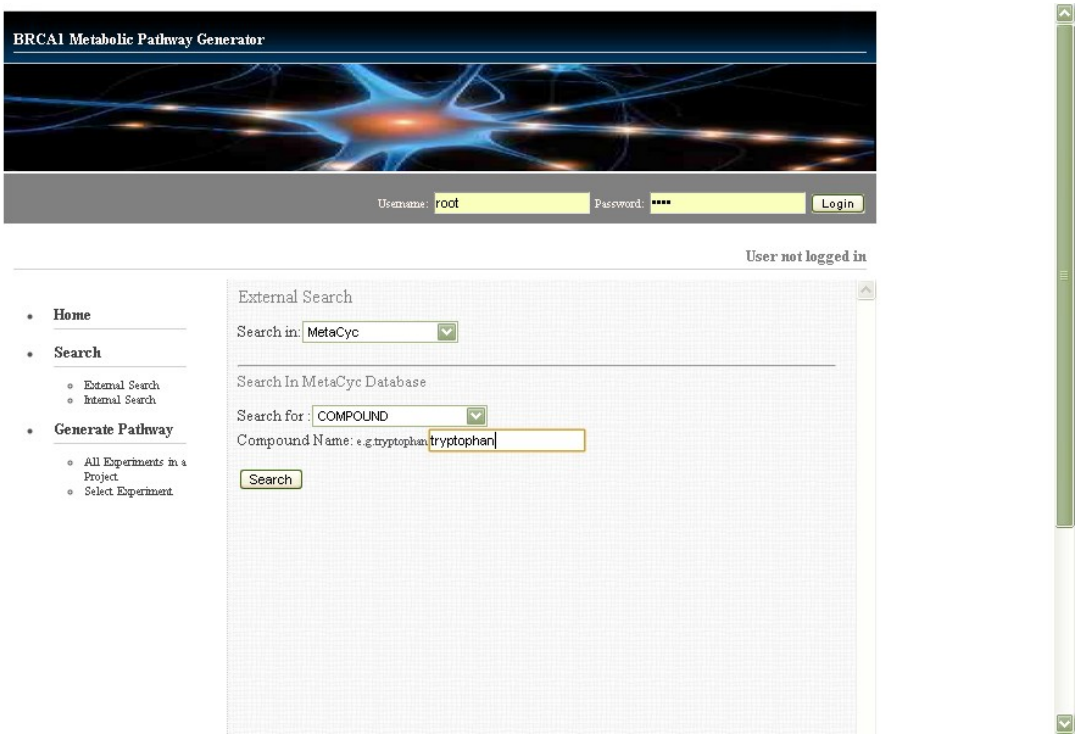


Figure 13 Search for COMPOUND

This figure shows the search interface for compound section in MetaCyc database. The system asks the user for the compound name to search.

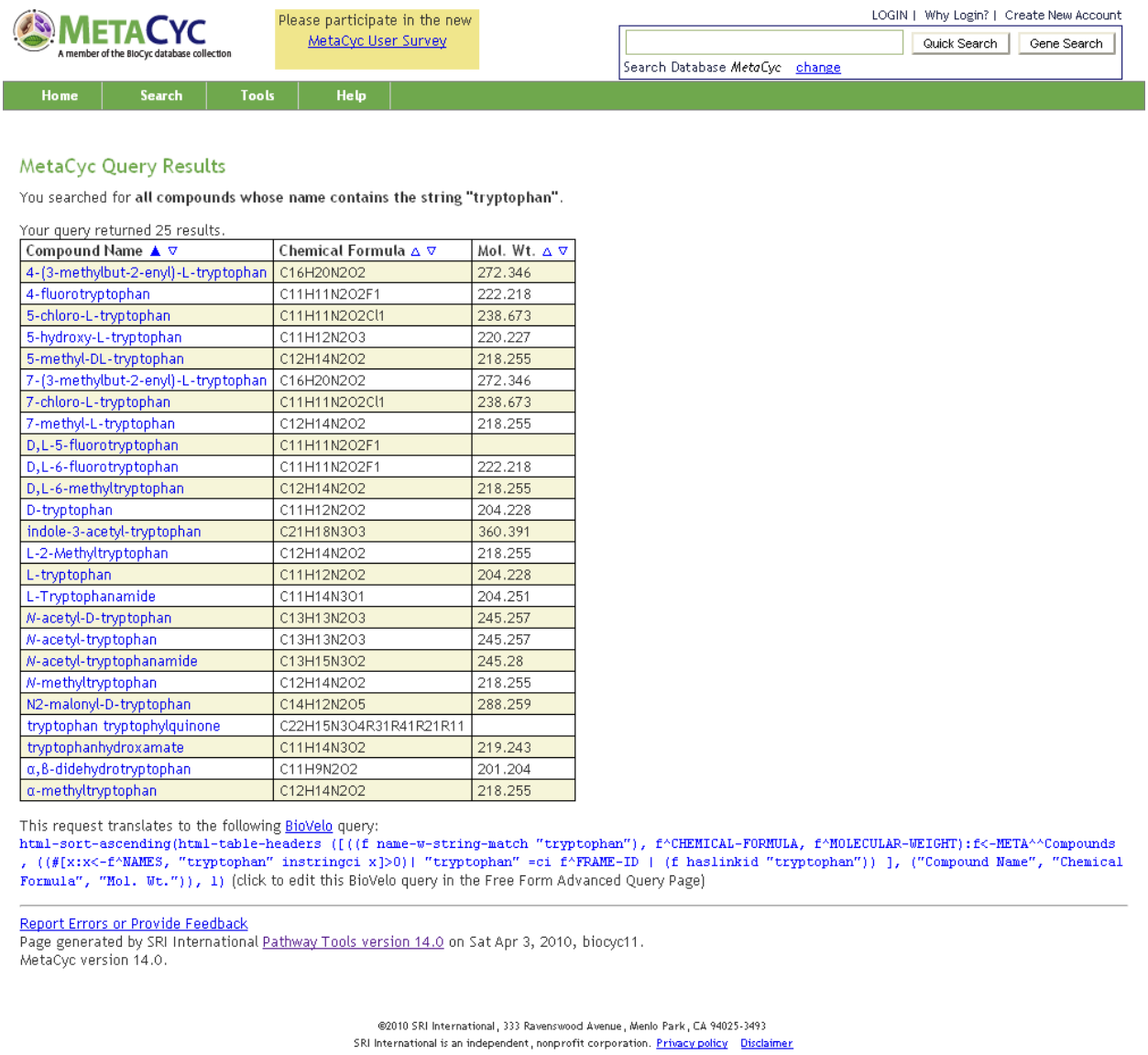


Figure 14 Search for COMPOUND Results

Sample results found in the MetaCyc database based on the previous input of the user that searches for compound whose name contains tryptophan.

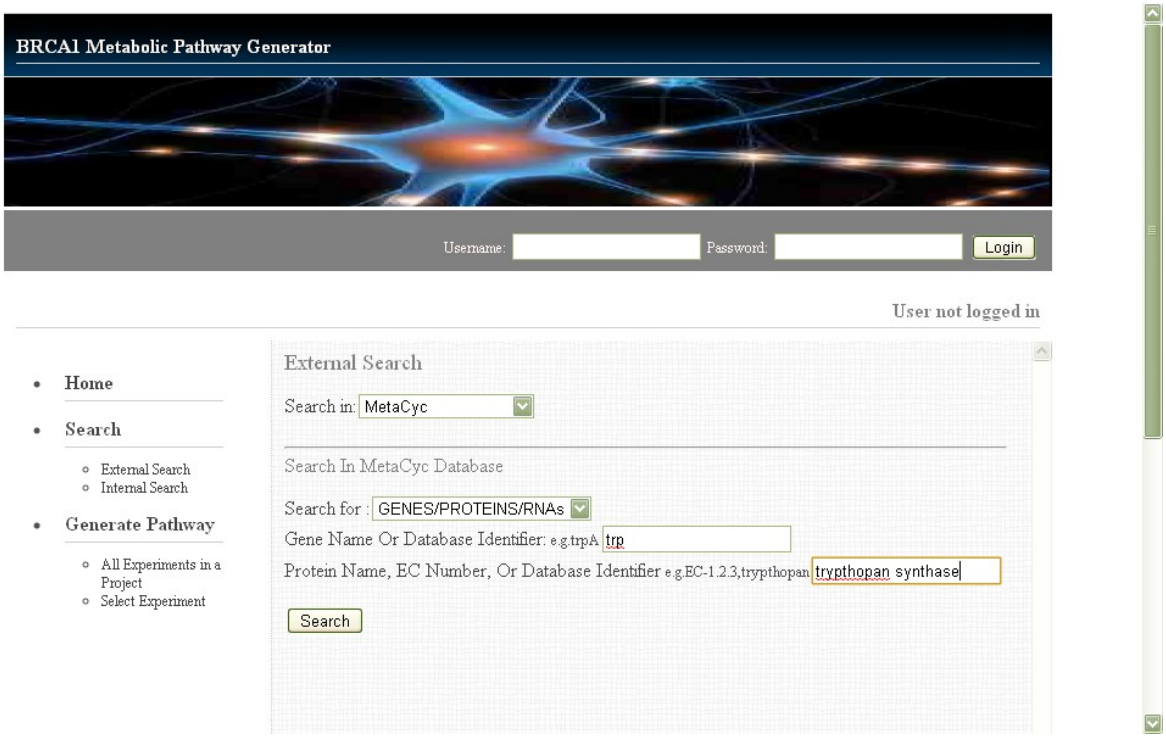


Figure 15 Search for GENES/PROTEINS/RNAs

The figure shows the search interface for genes/proteins/RNAs section in MetaCyc database. The system asks the user for the gene name, protein name, EC number, or database identifier to search.

Figure 16 Search for GENES/PROTEINS/RNAs Results

Sample results found in the MetaCyc database based on the previous input of the user that searches for genes/proteins/RNAs whose name contains trpA and whose product contains trypthopan synthase.

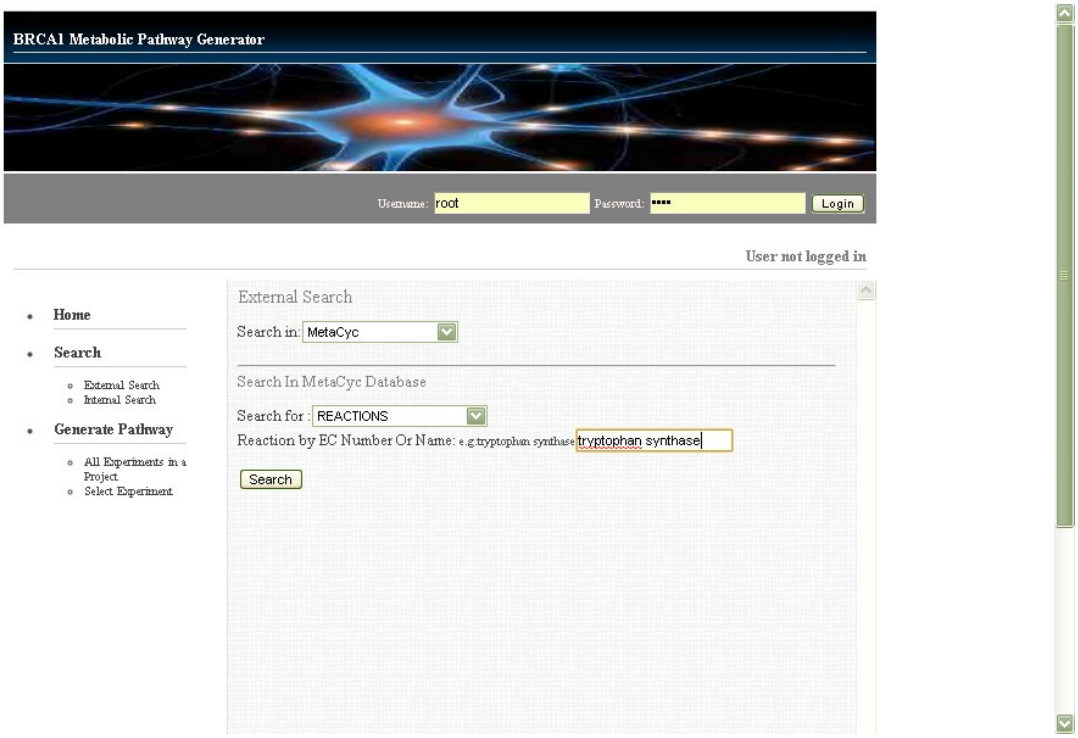


Figure 17 Search for REACTIONS

The figure shows the search interface for reactions section in MetaCyc database. The system asks the user for the EC number, or reaction name to search.

Figure 18 Search for REACTIONS Results

Sample results found in the MetaCyc database based on the previous input of the user that searches for reactions whose name contains tryptophan synthase.

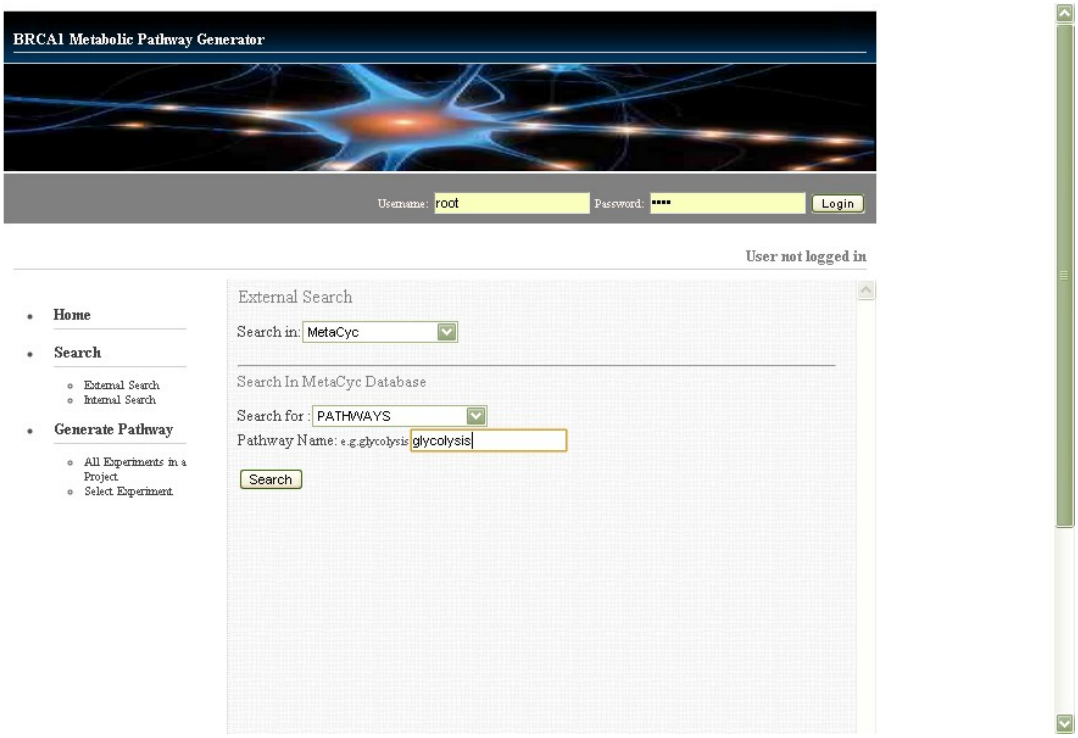


Figure 19 Search for PATHWAYS

This figure shows the search interface for pathways section in MetaCyc database. The system asks the user for the pathway name to search.

Figure 20 Search for PATHWAYS Results

Sample results found in the MetaCyc database based on the previous input of the user that searches for pathways whose name contains glycolysis.

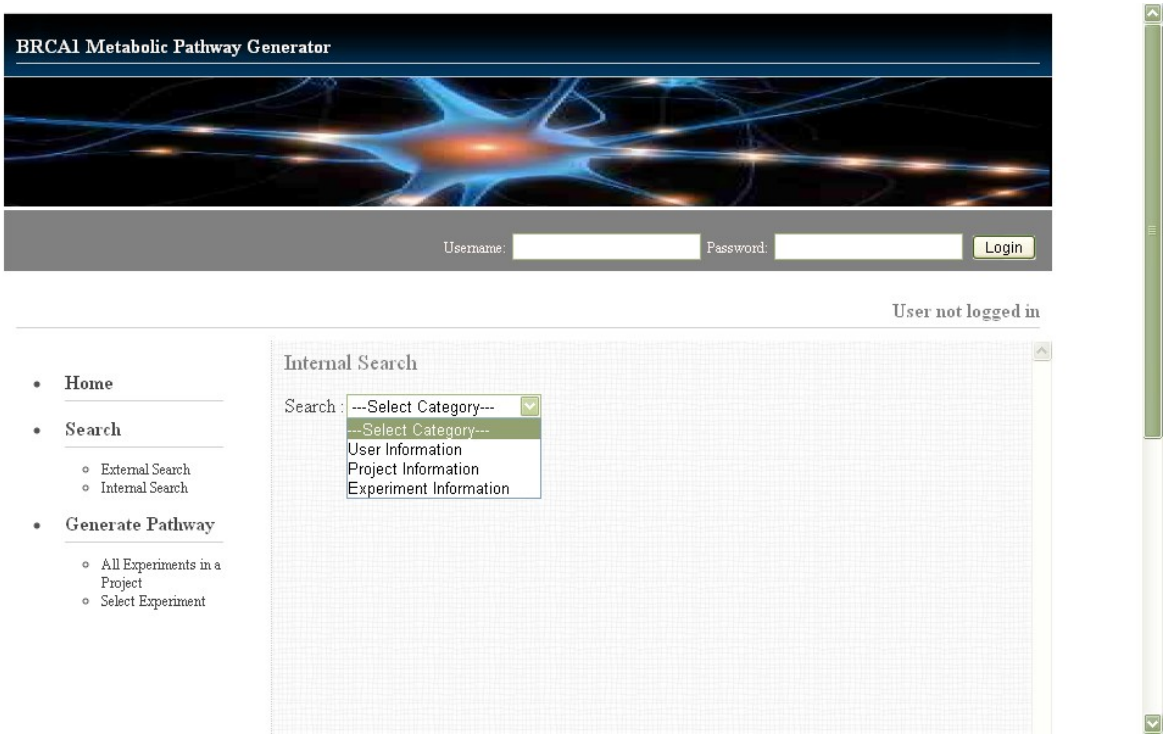


Figure 21 Internal Search

The figure shows the internal search interface of the system. The system provides the user an option to choose what information to search in (i.e. user, project and experiment information).

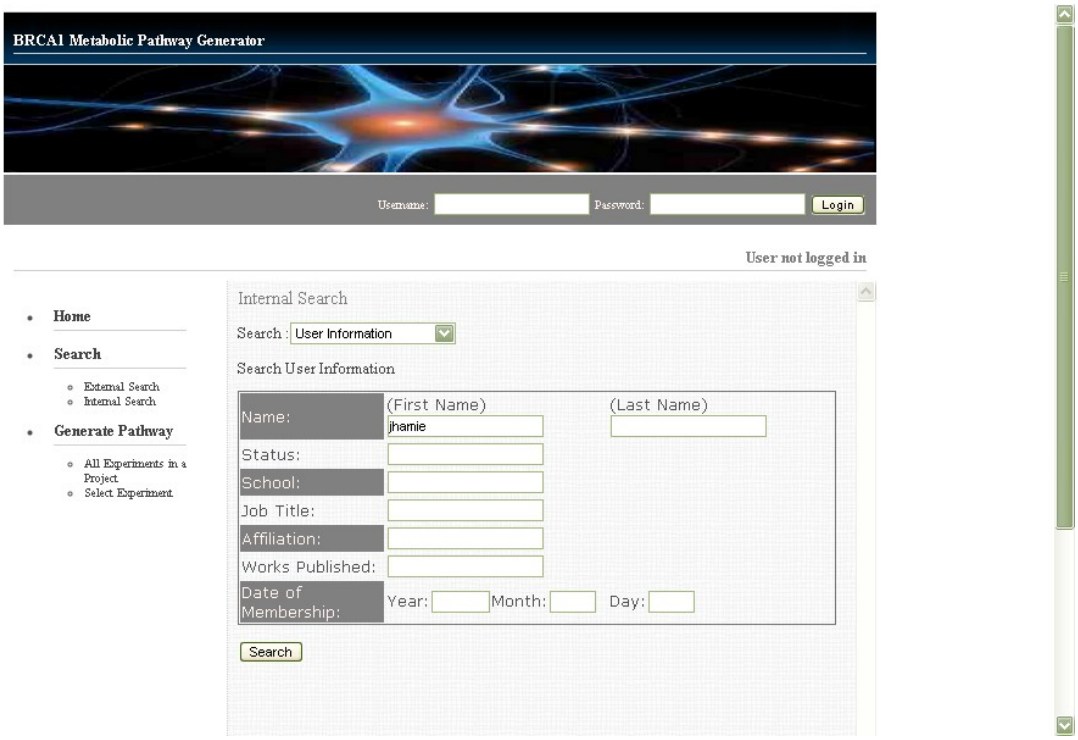


Figure 22 Search for User Information

The figure shows the search interface for user information. The system asks the user for first or last name, status, school, job title, affiliation, works published, or date of membership. The user is not required to fill-up all the fields in the form. He/She can fill-up the field(s) that he/she thinks that is/are necessary for his/her search.

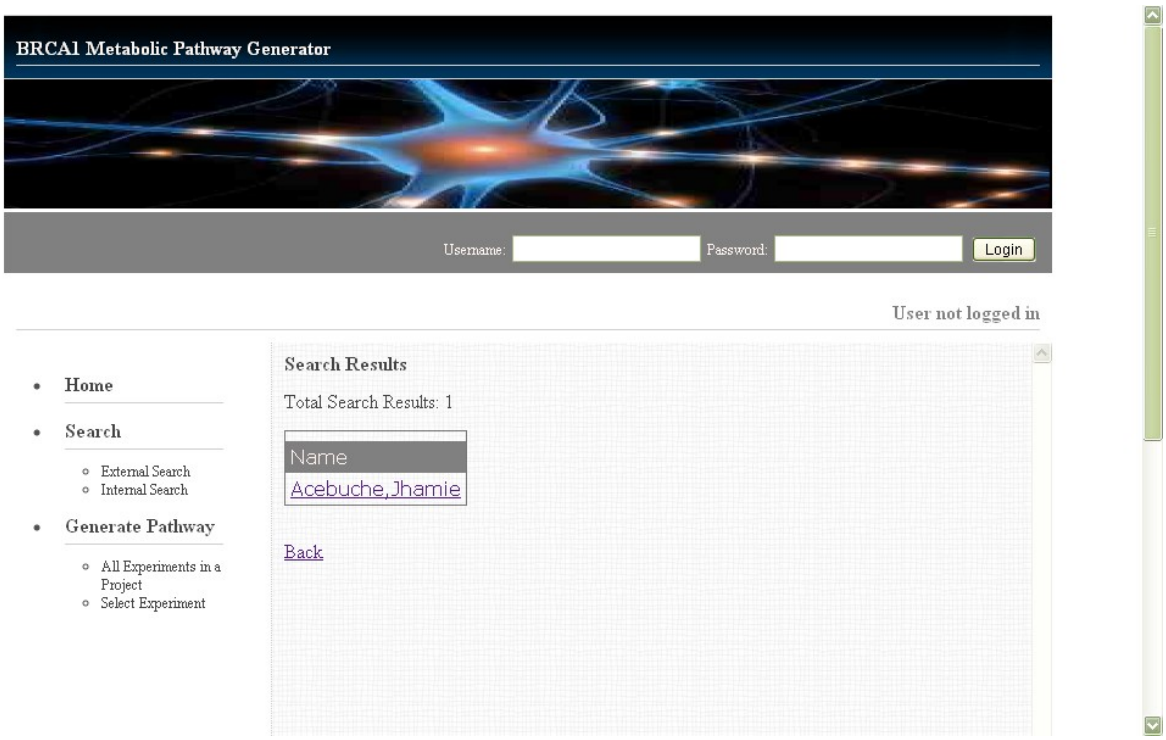


Figure 23 Search for User Information Results

Sample result found in the system's database based on the information entered previously by the user. The result is made clickable to view the profile of the searched user.

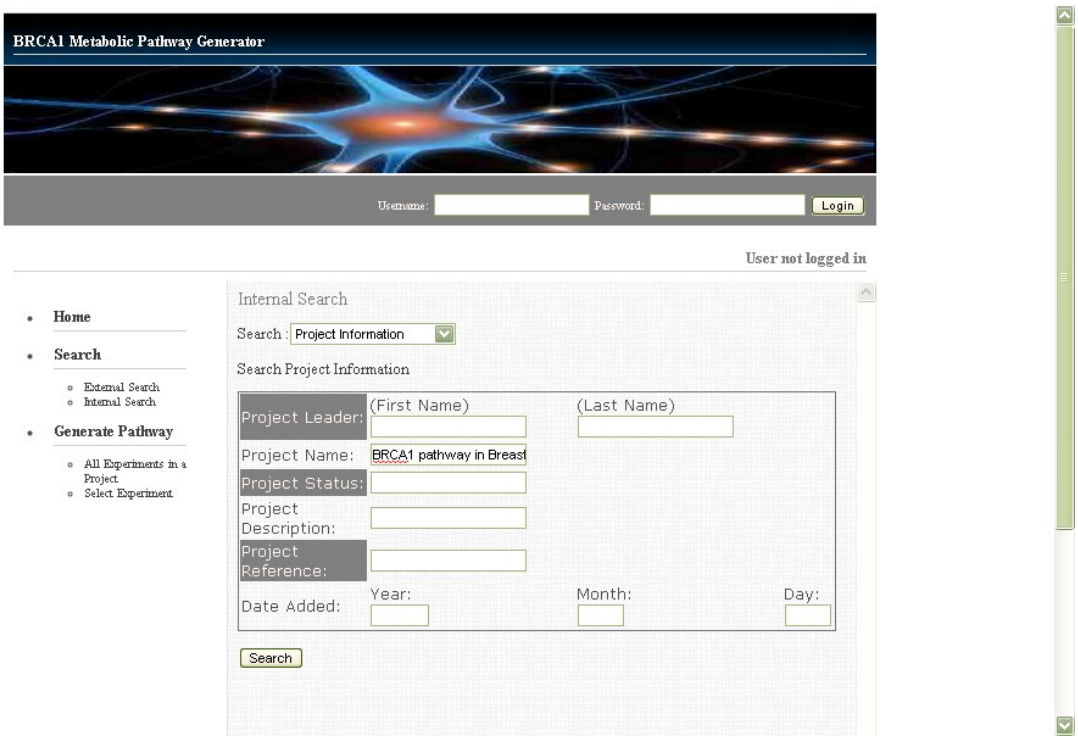


Figure 24 Search for Project information

The figure shows the search interface for project information. The system asks the user for project leader's first or last name, project name, project status, project description, project reference or date where the project is added. The user is not required to fill-up all the fields in the form. He/She can fill-up the field(s) that he/she thinks that is/are necessary for his/her search.

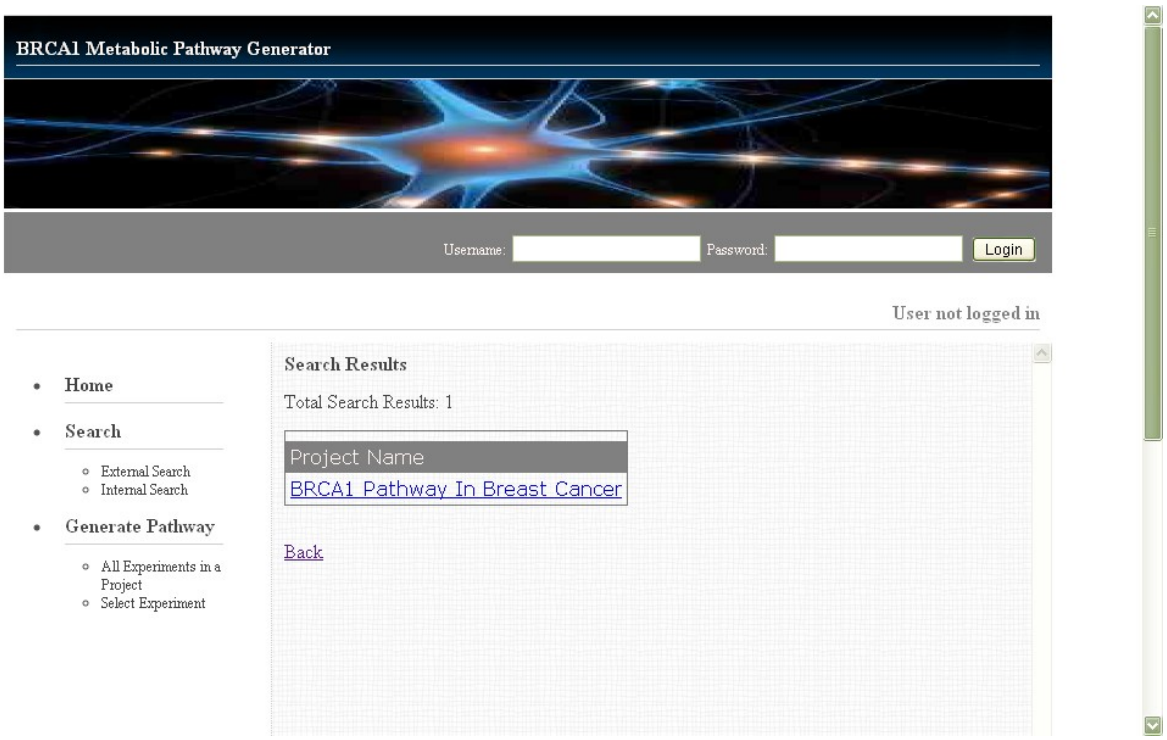


Figure 25 Search for Project Information Results

Sample result found in the system's database based on the information entered previously by the user. The result is made clickable to view the information about the searched project.

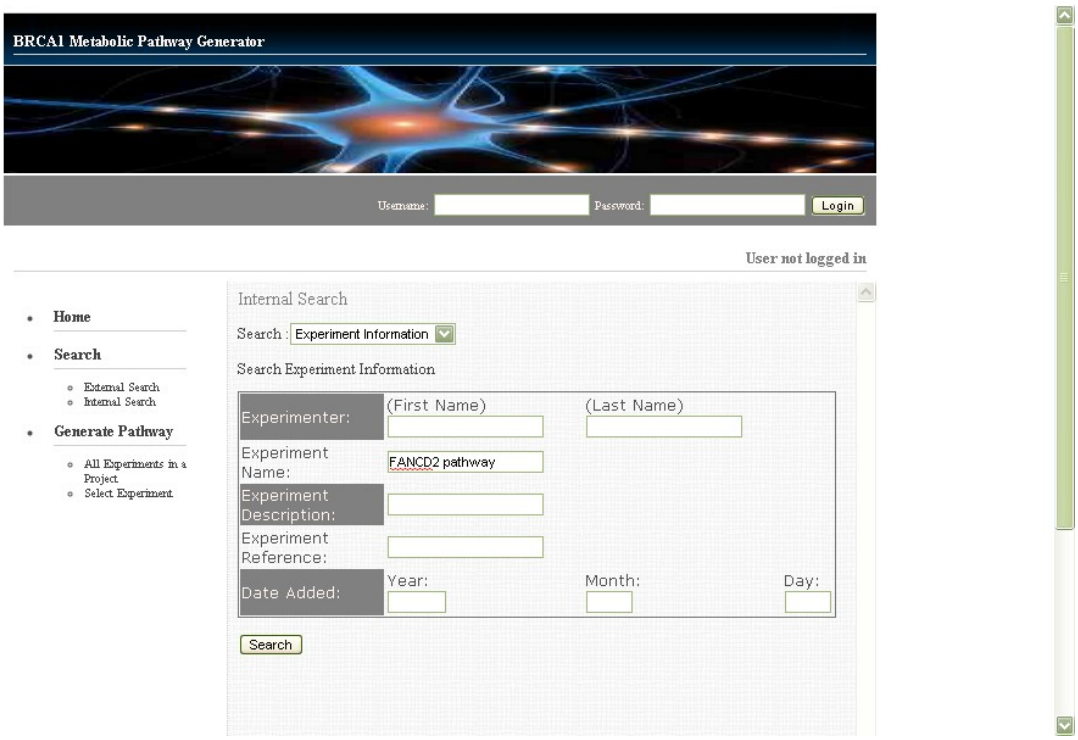


Figure 26 Search for Experiment Information

The figure shows the search interface for experiment information. The system asks the user for experimenter's first or last name, experiment name, experiment description, experiment reference or date when the experiment is added. The user is not required to fill-up all the fields in the form. He/She can fill-up the field(s) that he/she thinks that is/are necessary for his/her search.

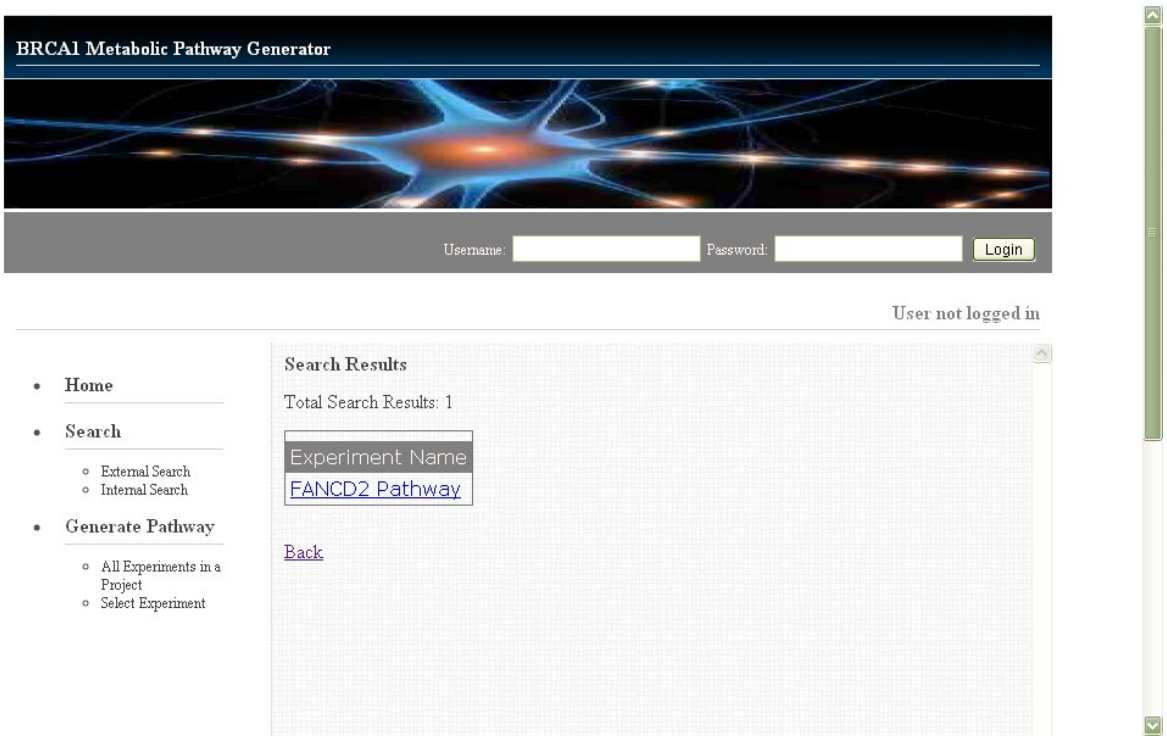


Figure 27 Search for Experiment Information Results

Sample result found in the system's database based on the information entered previously by the user. The result is made clickable to view the information about the searched experiment.

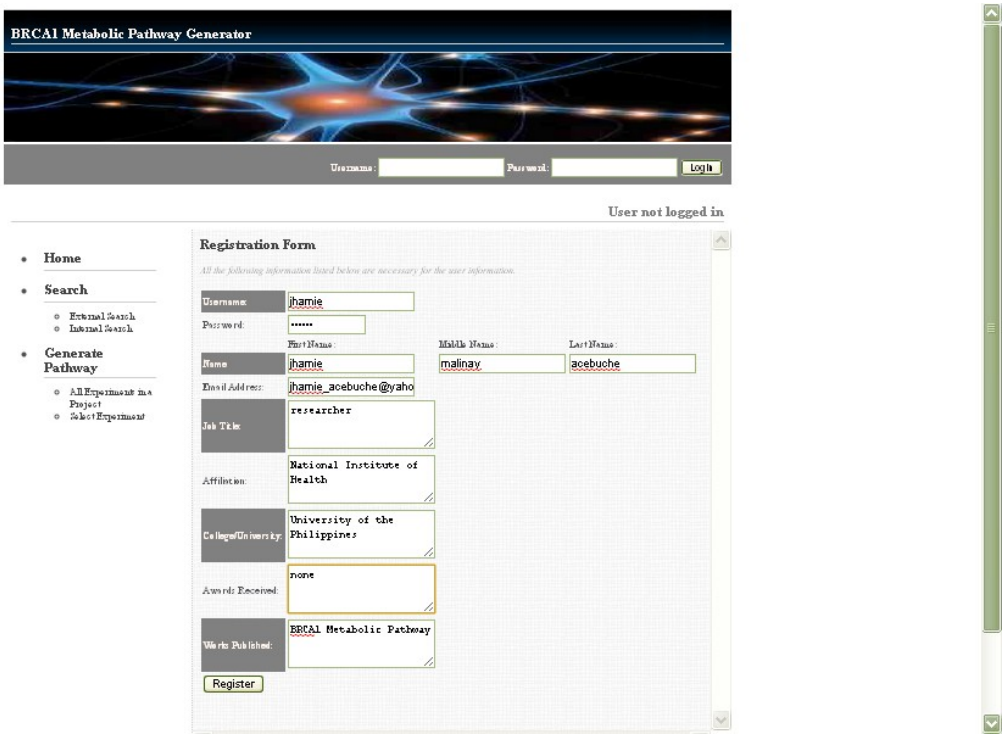
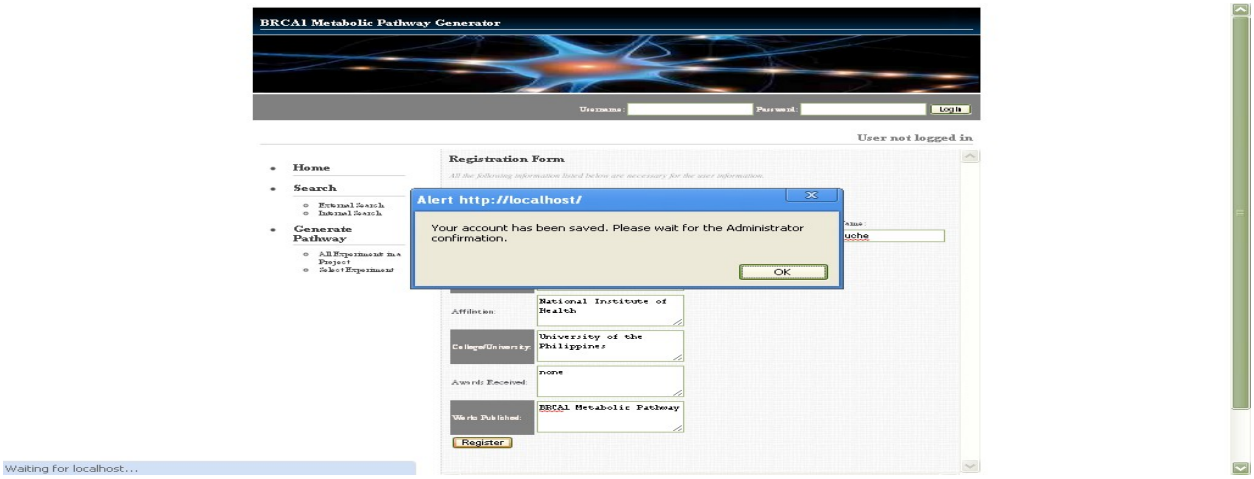


Figure 28 Registration Form

This figure shows the registration interface of the system. Registration form consist of the following fields: username, password, first name, middle name, last name, email address, job title, college/university, awards received and works published. After clicking the register button, the system will show an alert message to notify the user if the information is send successfully or if there are unfilled fields.



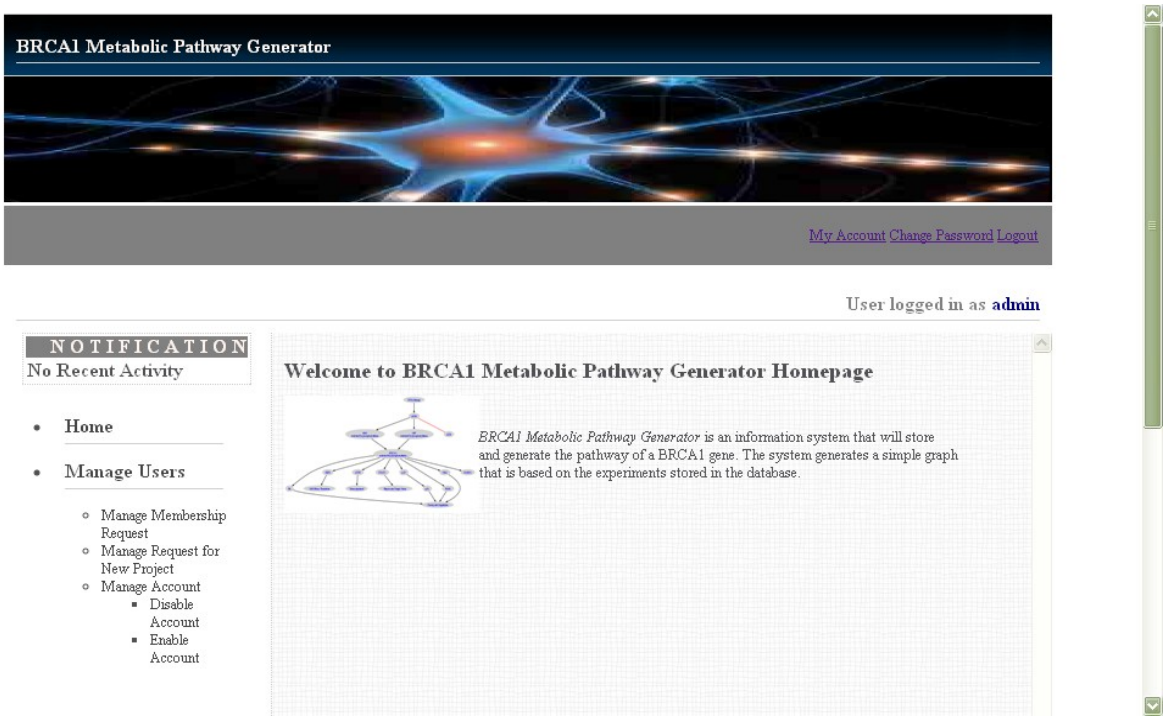


Figure 29 Admin Page

This figure shows the admin page interface. On the left side of the page you can find the notification table indicating the number of request application for membership and the number of request application for new project. You can also find the functionalities offered to the system administrator which are the manage membership request, manage request for new project and manage account links. On the upper right side of the page you can find the “my account” link, the “change password” link and the “logout” link.

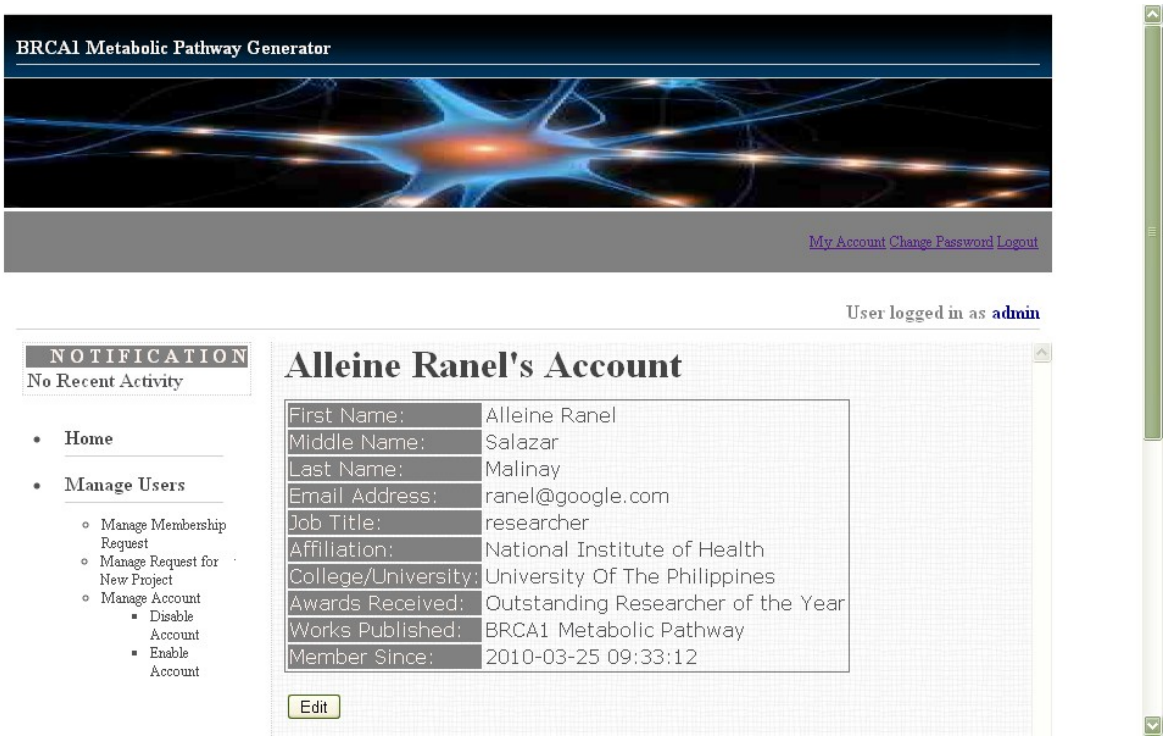


Figure 30 System Administrator's Account

This figure shows the admin's account interface. It contains information like email address, job title, affiliation, college/university, awards received, works published, date and time of membership and the first and last name of system administrator.

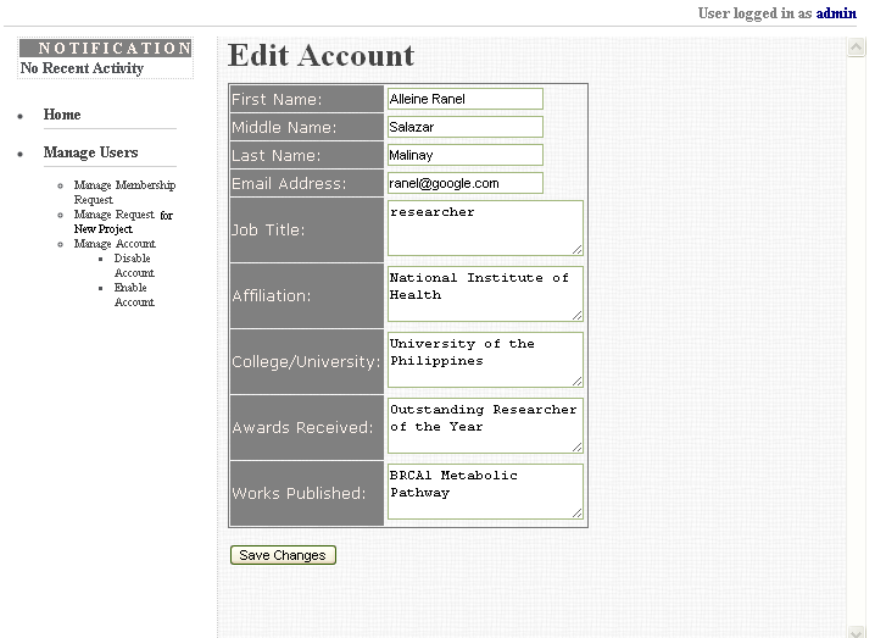
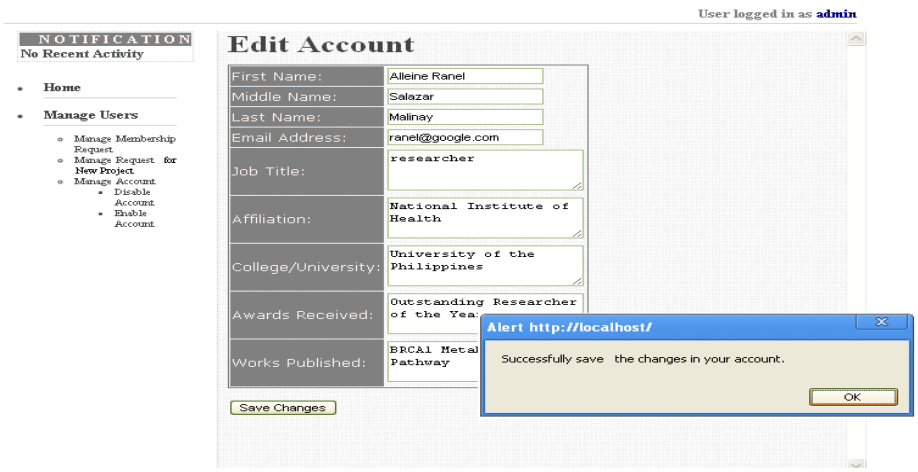


Figure 31 System Administrator's Edit Account

This figure shows the admin's edit account section. The system administrator can edit the information about the email address, job title, affiliation, college / university, awards received, works published and name fields. After clicking the save changes button, the system will show an alert message to notify the user that it has been save successfully.



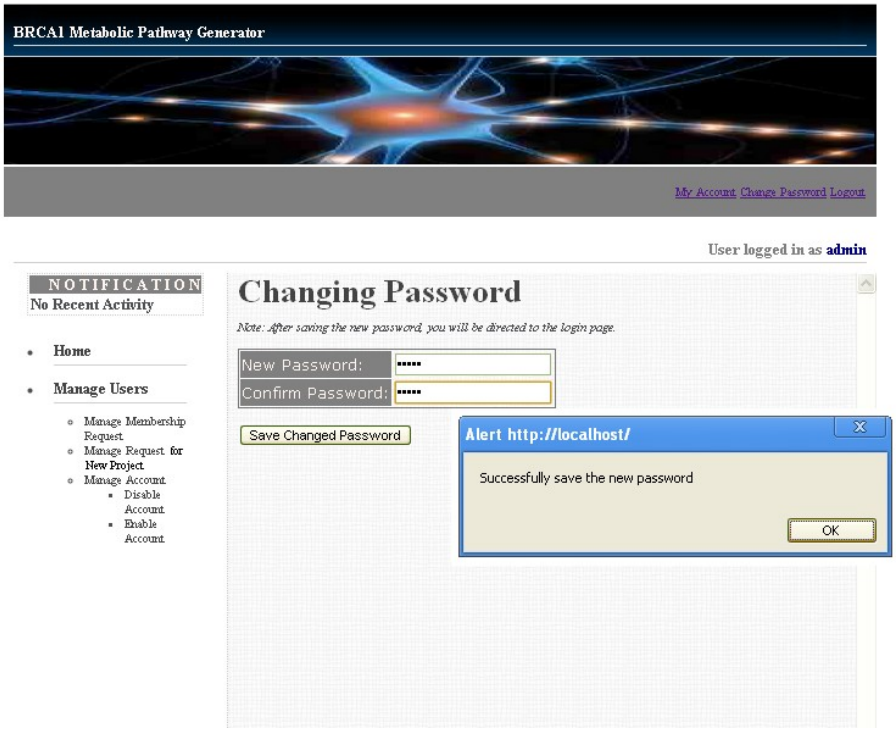


Figure 32 System Administrator's Changing Password

This figure shows the admin's changing password section. It includes the "new password" and "confirm password" fields. The input value in "confirm password" field should match to the input value in "new password" field. After changing the password, the system will show an alert message to notify the user that it has been save successful and then logout the user and redirect to the main page.

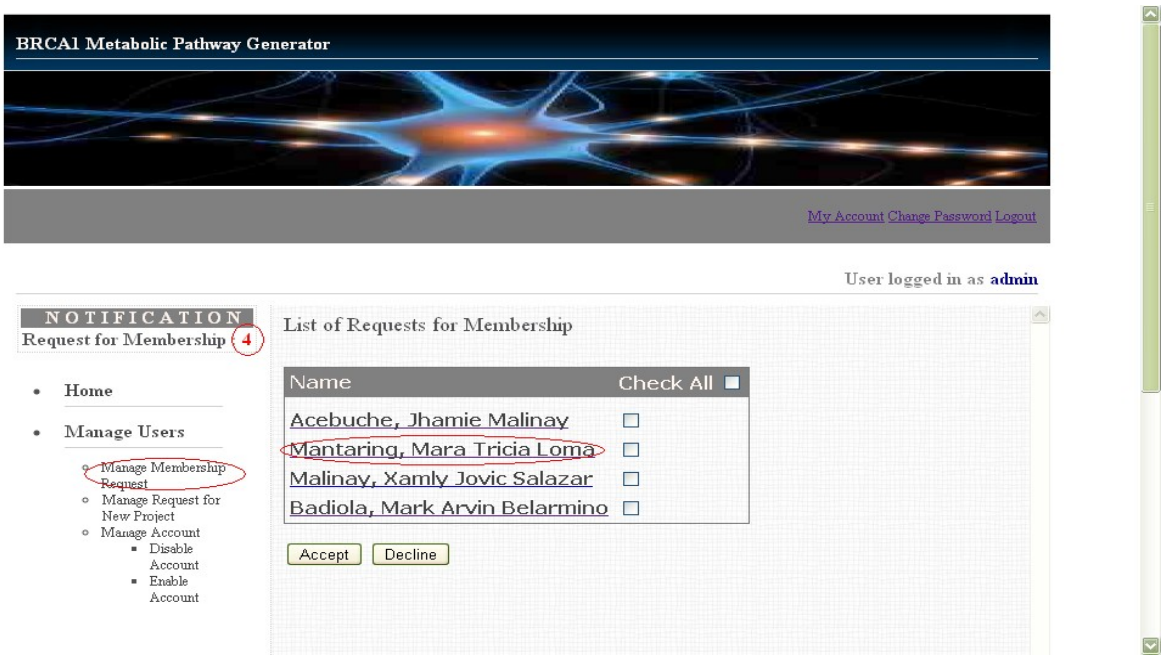
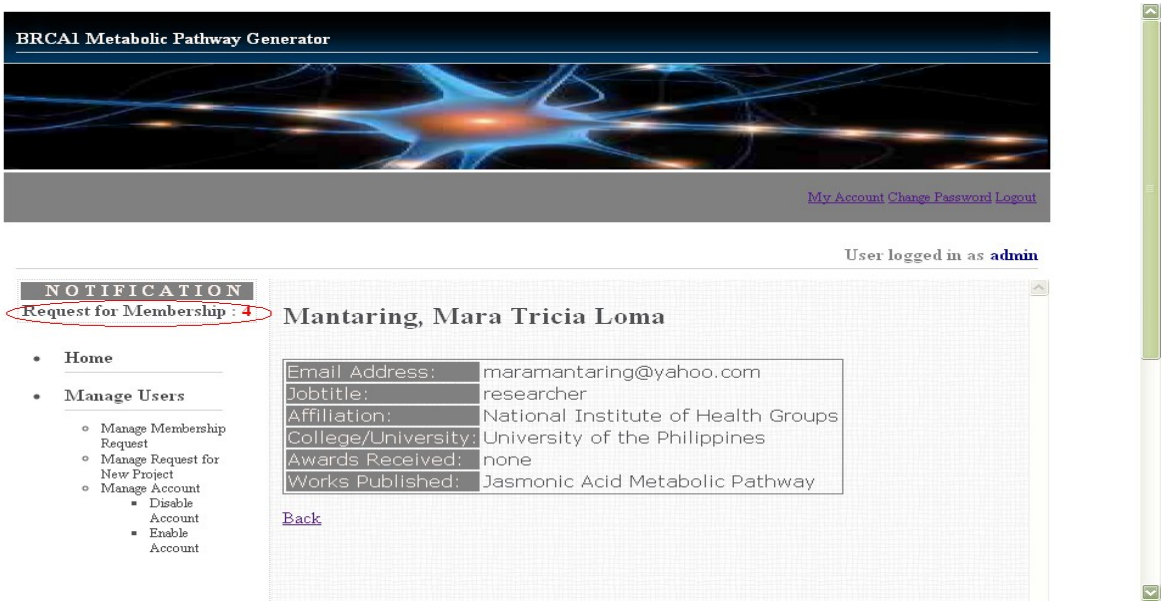


Figure 33 Manage Membership Request(s)

This figure shows how to manage the membership request(s). By clicking the number of request or the link "manage membership request", the system will show the list of names requesting for membership. Clicking a name in the list, the system will show the information about that requester. The figure below shows the requester's profile.



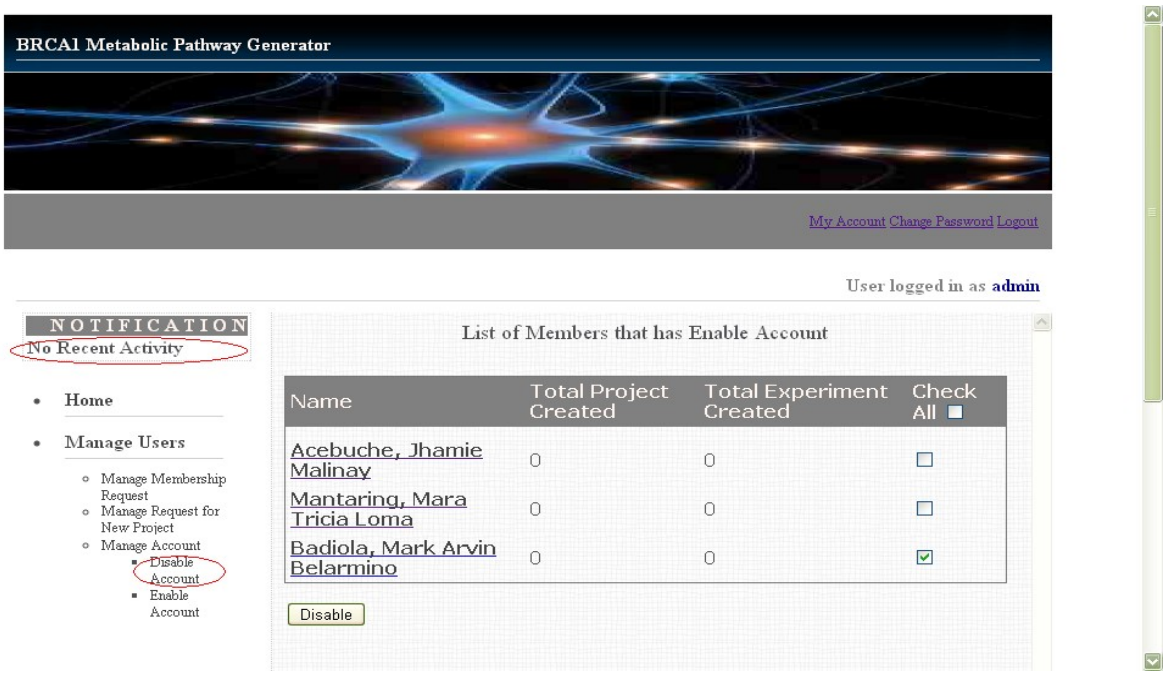


Figure 34 Manage User Account – Disabling an Account

This figure shows the interface for disabling an account. Since all the requests were already handled by the system administrator the notification was changed into "No Recent Activity". To disable the account of user(s) simply click the "disable account" link and the system will show the list of account that was currently active/enable. After disabling an account, the name that was being disabled will be removed from the list of enable account that is shown in the figure below.

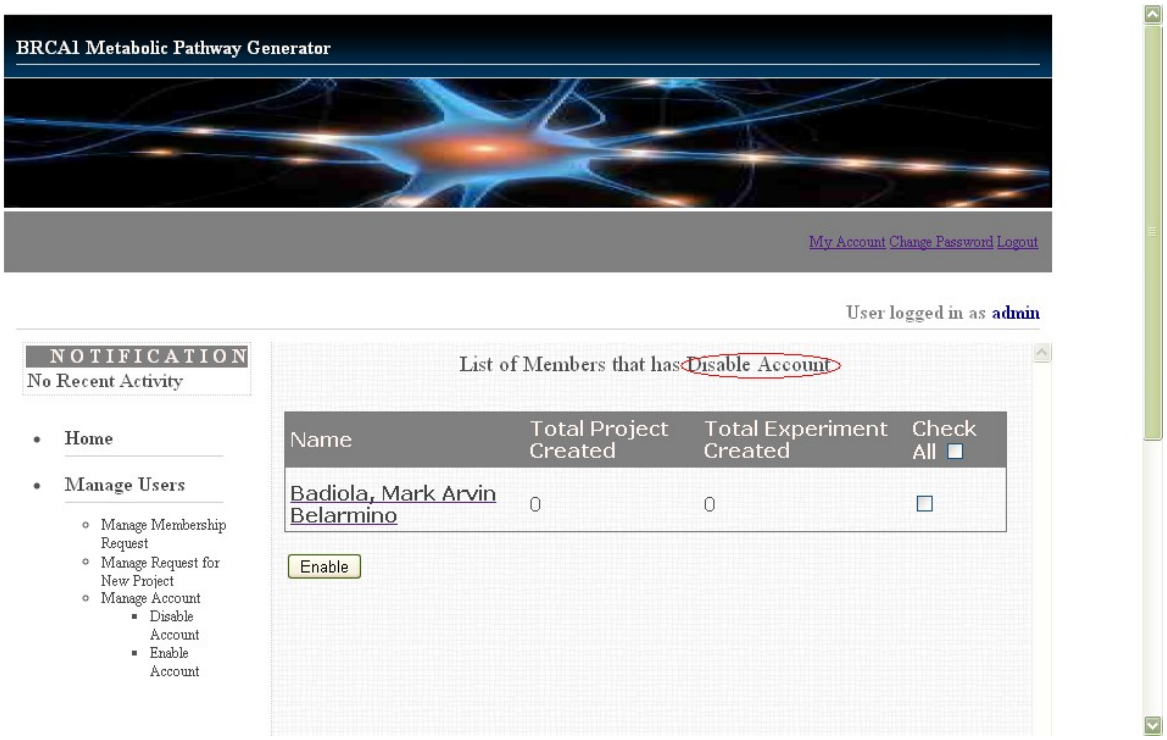


Figure 35 Manage User Account – Enabling an Account

This figure shows the interface for enabling an account or for viewing the name of user with disabled account. If you want to see the names of the users with disabled status or if you want to enable an account just click the "Enable Account" link and the system will show the list of names with disabled account/status. The process of enabling an account is similar to the process of disabling an account.

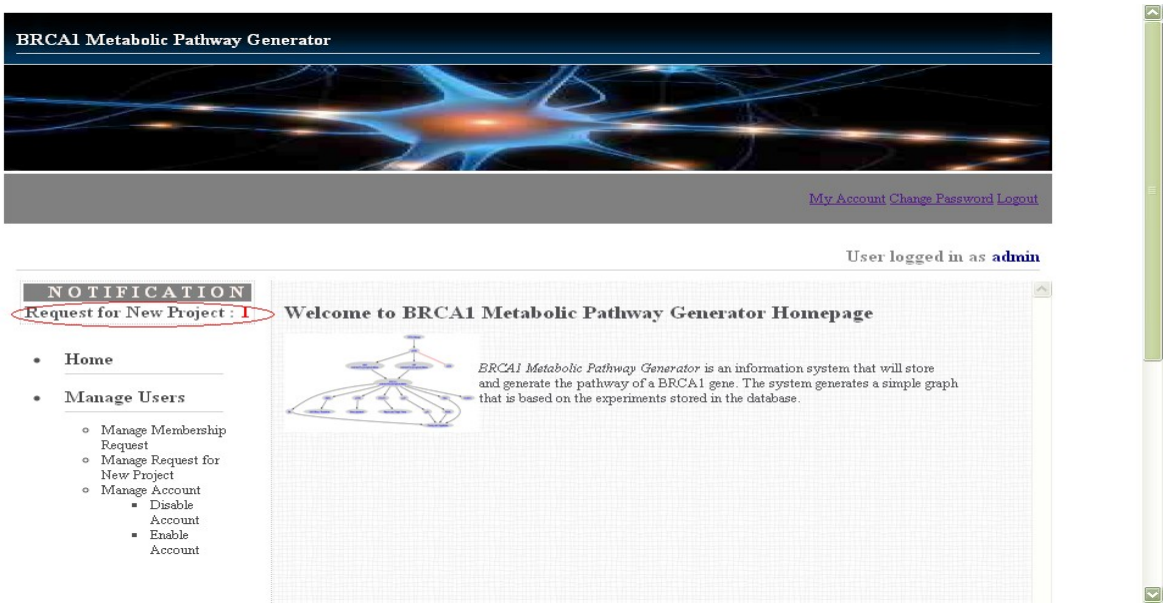


Figure 36 Manage New Project Request(s)

This figure shows how to manage new project request(s). The notification table shows the number of request for new project. By clicking the number of request for new project or the "manage request for new project" link, the system will show the name of the project and the name of the creator of that project. After managing the request(s), the name of the managed project will be removed in the list. By clicking the name of the project, the system will show the information about that project.

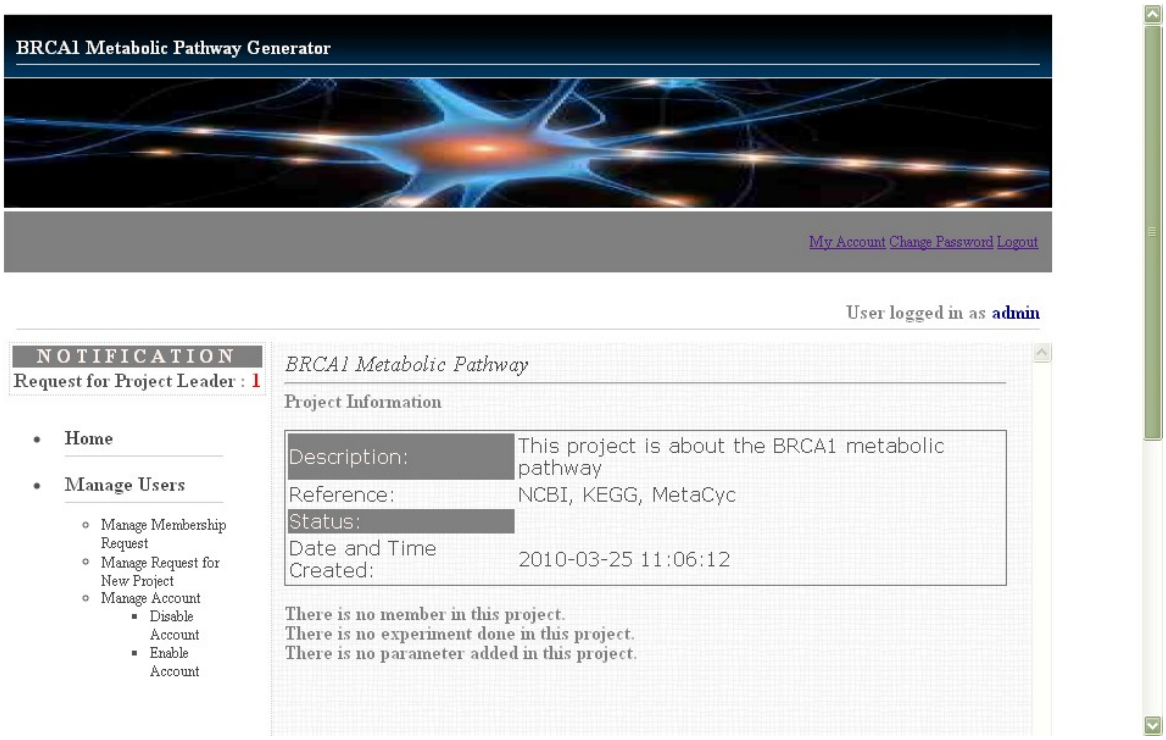


Figure 37 Manage New Project – View Project's Information

This figure shows the interface for viewing the project's information. It consists of information about the project's description, reference, date and time created, members, experiments, and parameters.

Figure 38 Registered User Main Page

This figure shows the registered user main page interface. The registered user has no project and experiment created. As this user logged in, the system will provide additional functionalities: Manage Project, Manage Experiment and Manage Requests. On the upper left side of the page you can find the notification table indicating the number of pending request for new project and new experiment, the number of requests from Project Leader, Approved and Declined Project, Deleted, Approved and Declined Experiment, Approved and Declined Parameter.

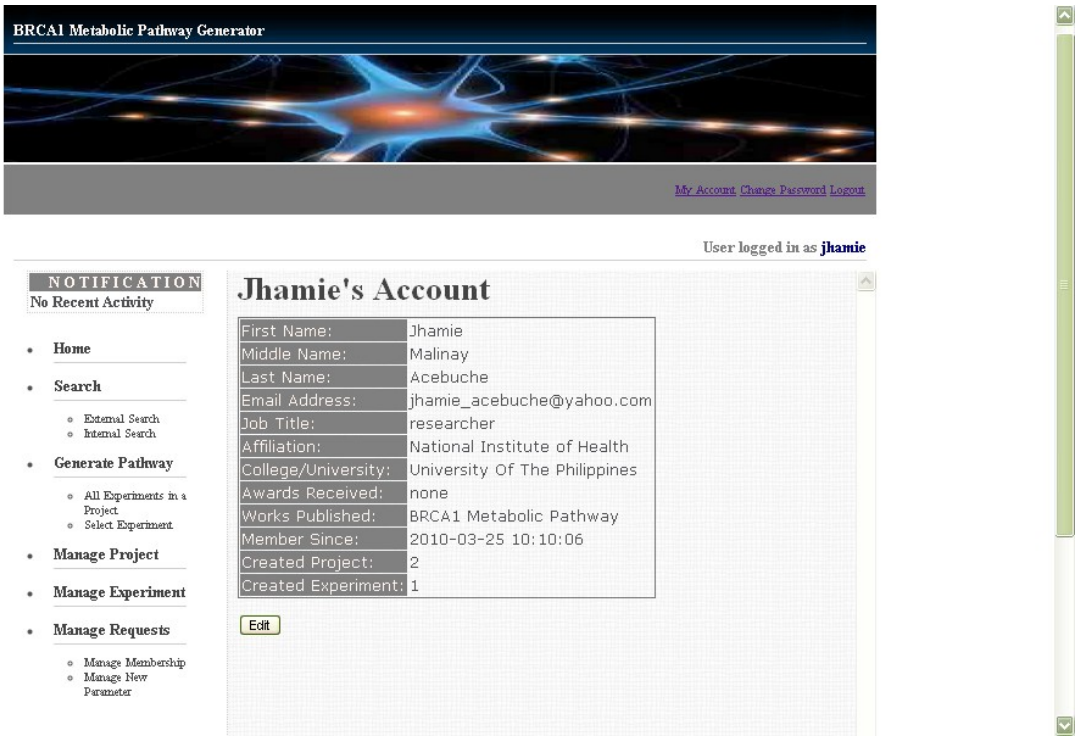


Figure 39 User's Account

This figure shows the user's account interface. It contains information like email address, job title, affiliation, college/university, awards received, works published, date and time of membership and the first and last name of logged in user.

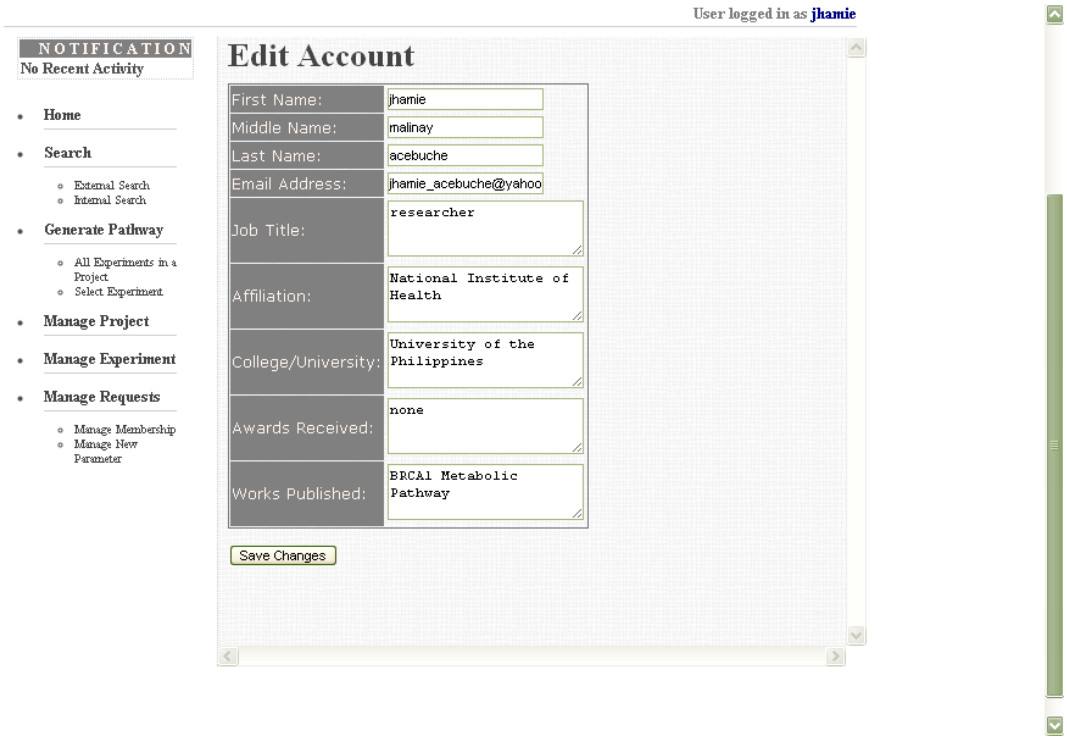
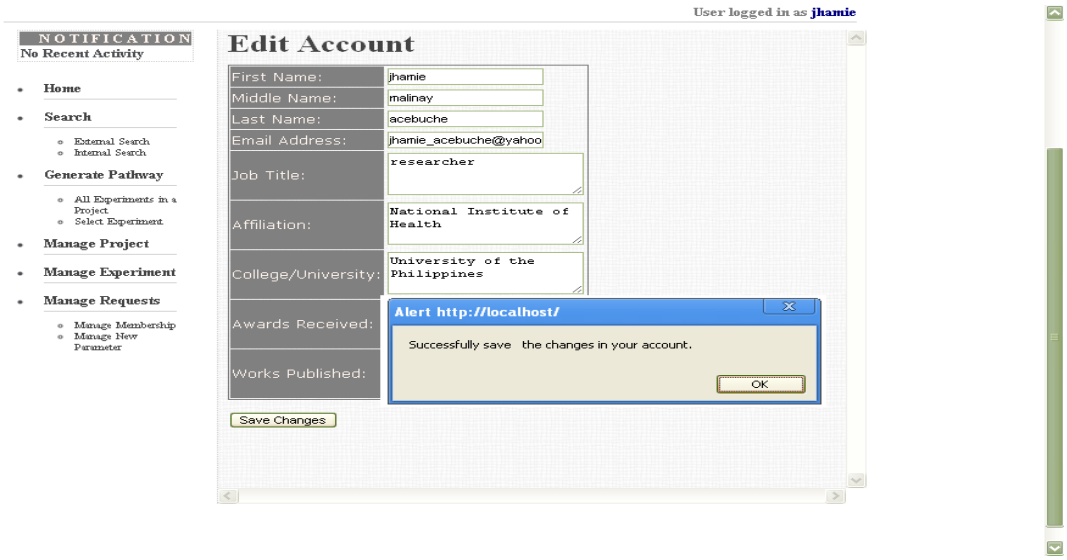


Figure 40 User's Edit Account

This figure shows the user's edit account section. The logged in user can edit the information about the email address, job title, affiliation, college / university, awards received, works published and name fields. After clicking the save changes button, the system will show an alert message to notify the user if it has been save successfully.



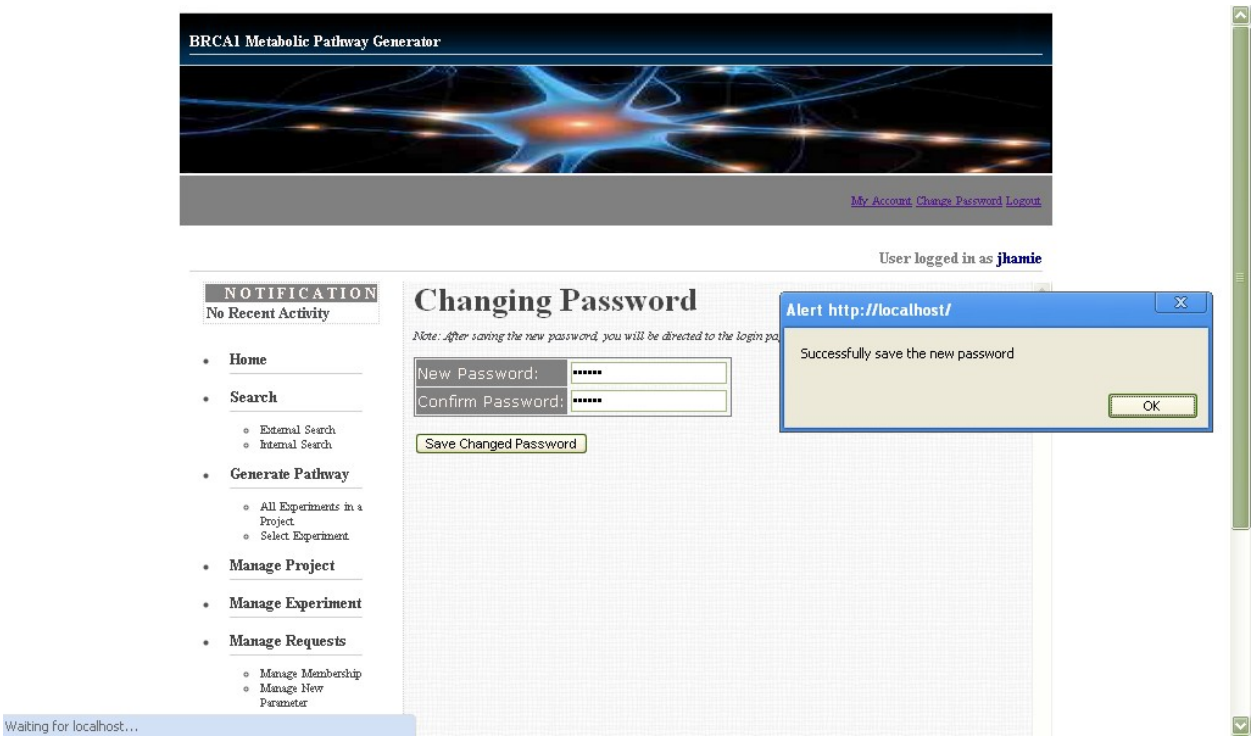


Figure 41 User's Changing Password

This figure shows the user's changing password section. It includes the "new password" and "confirm password" fields. The input value in "confirm password" field should match to the input value in "new password" field. After changing the password, the system will show an alert message to notify the user that it has been save successful and then logout the user and redirect to the main page.

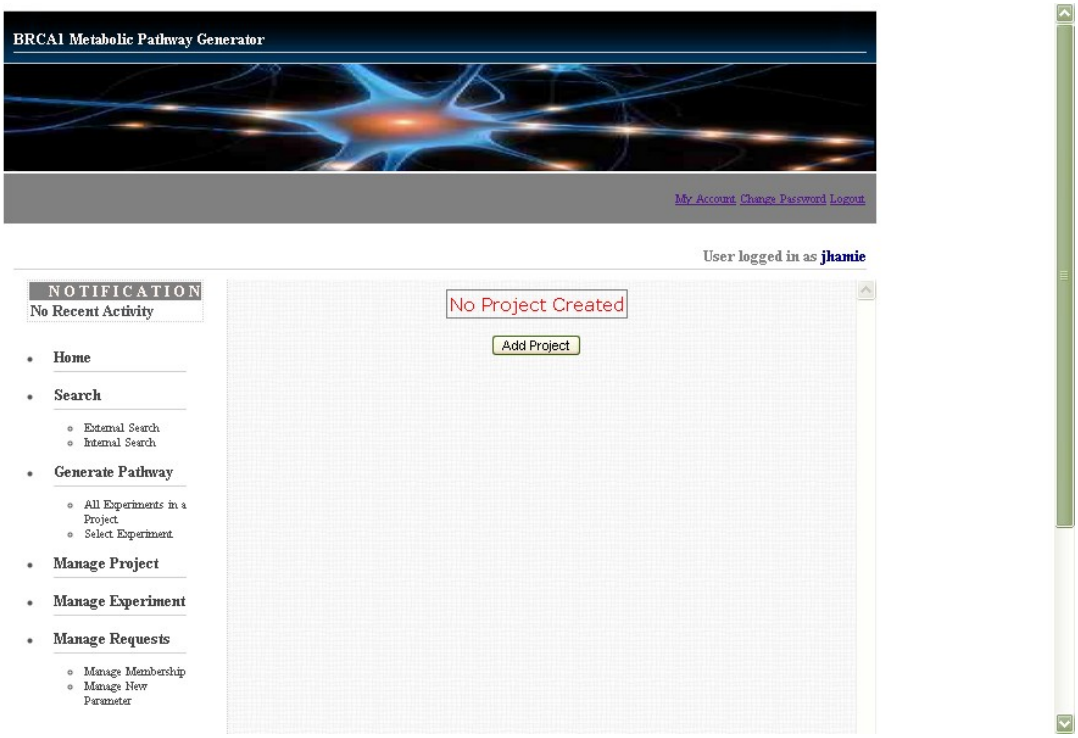


Figure 42 Manage Project

This figure shows the interface for managing a project. Manage project section consists of functionalities which are add project, edit, delete, add members and add parameters. Since there is no created/approved project the system only offers the add project function.

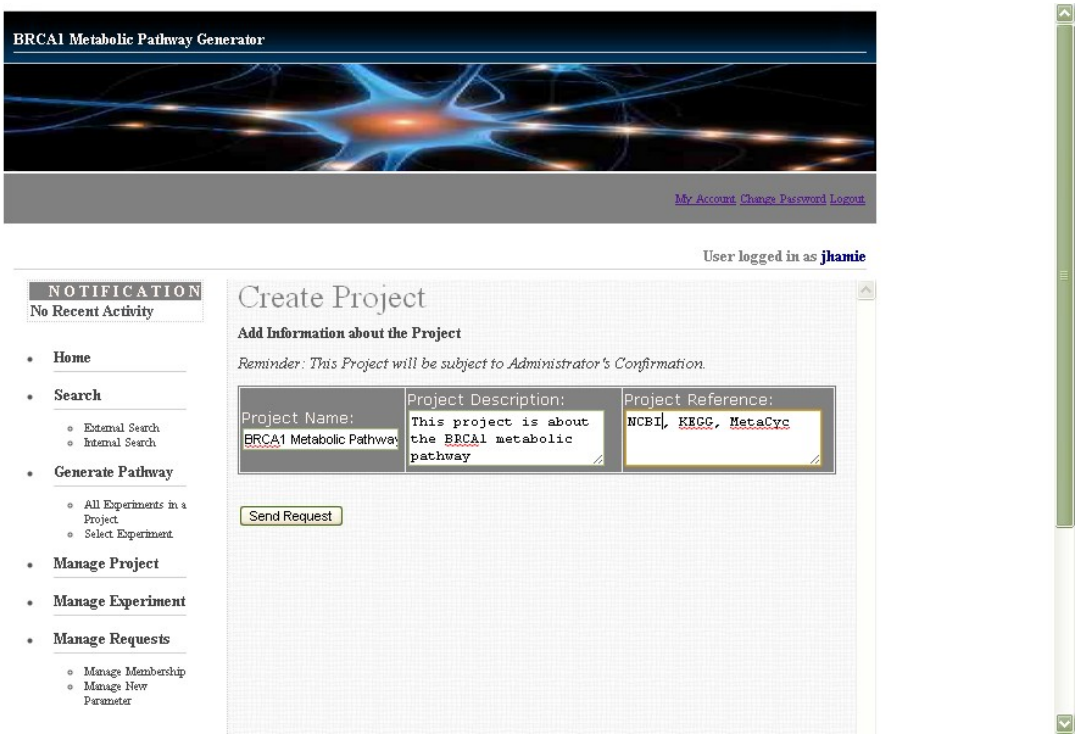
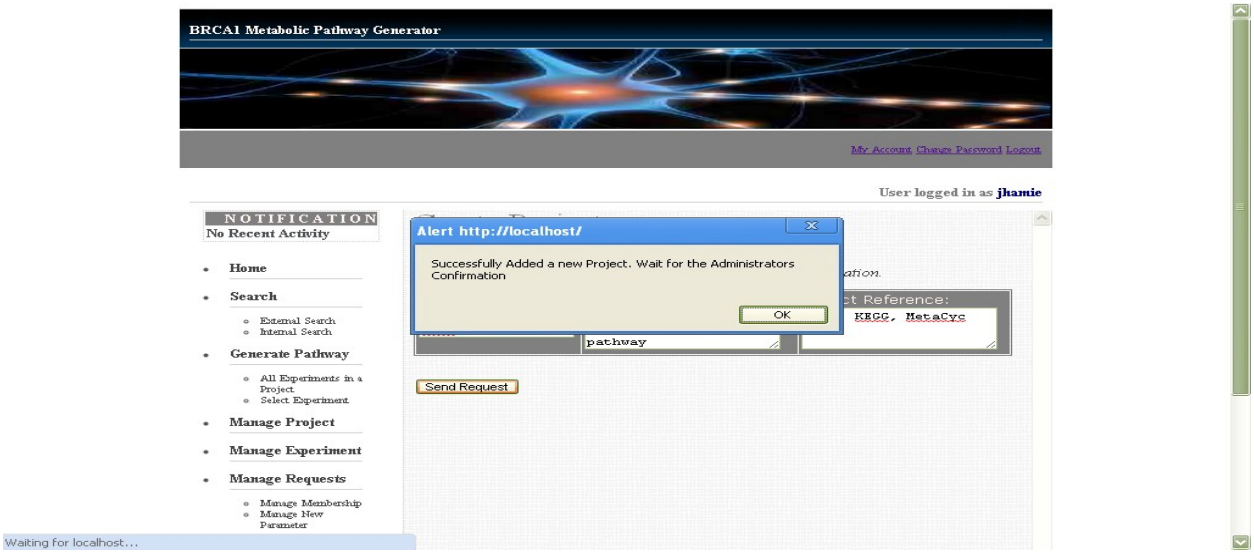
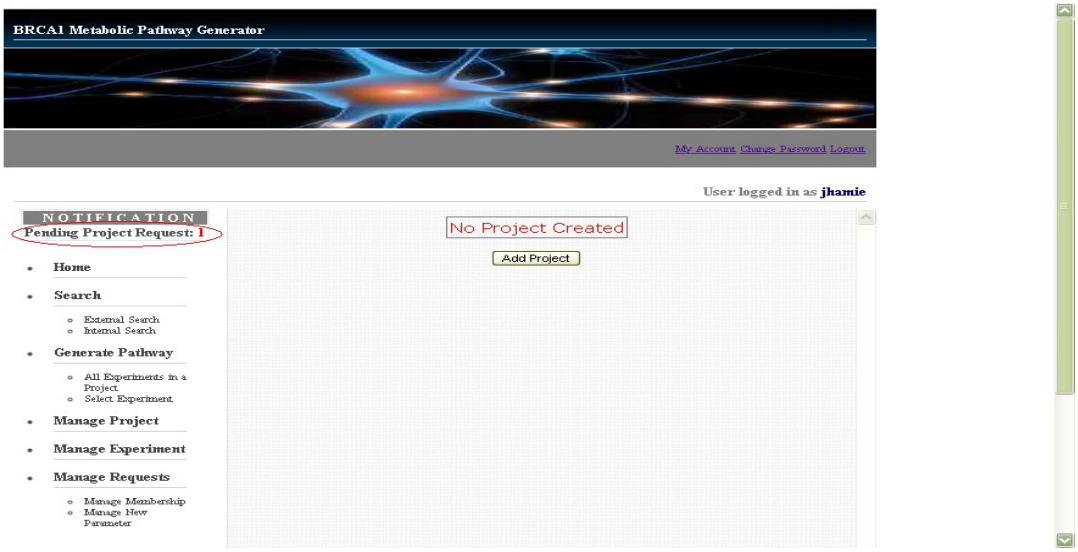


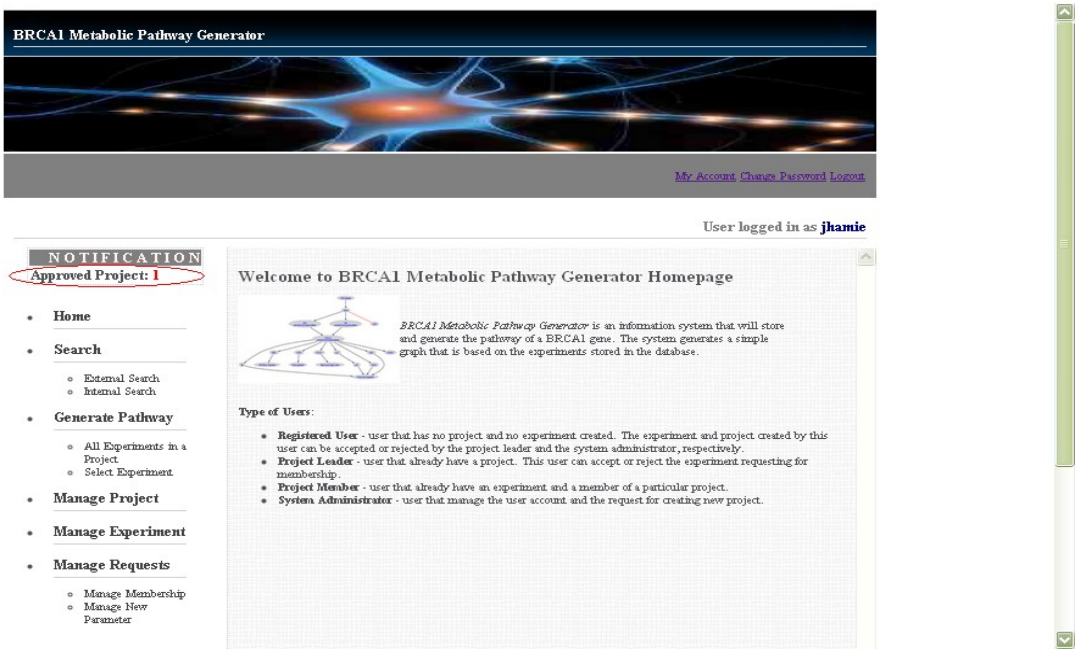
Figure 43 Manage Project – Create New project

The figure shows how to add information in the field of project name, project description and project reference. This project will be send to the system administrator for confirmation. The system will display an alert message to inform the user that the project created was successfully sent to the system administrator.

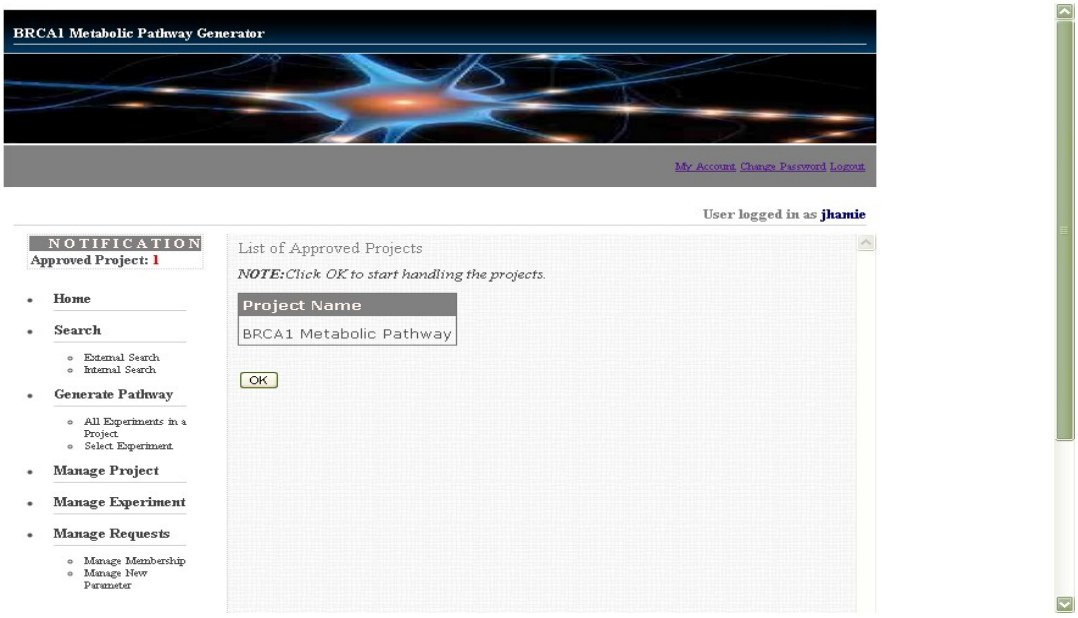




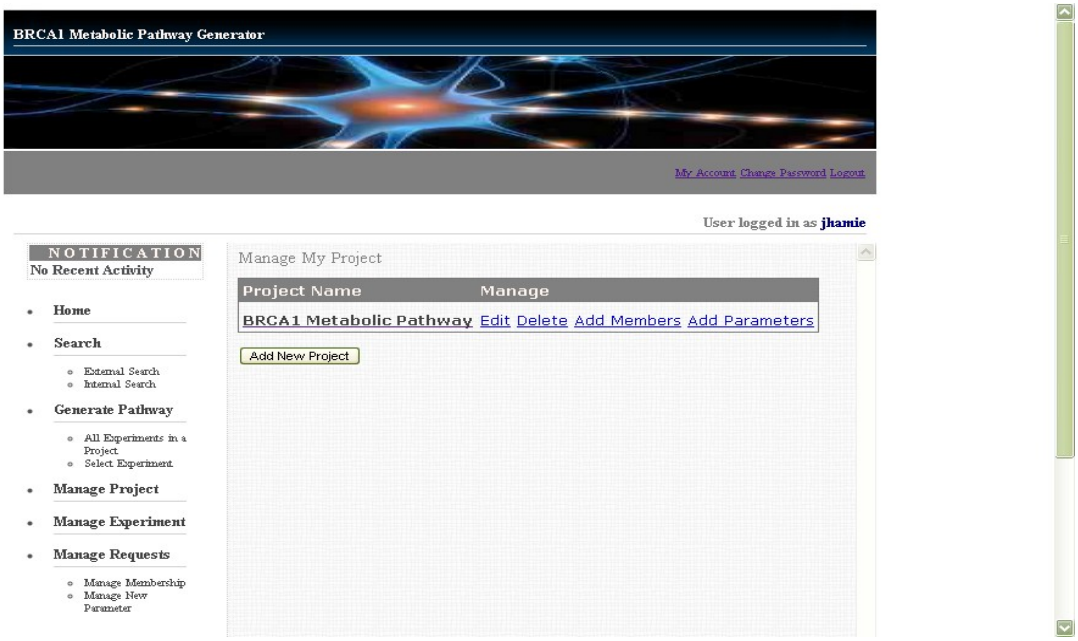
The notification table will display the number of project that is not yet confirmed by the system administrator.



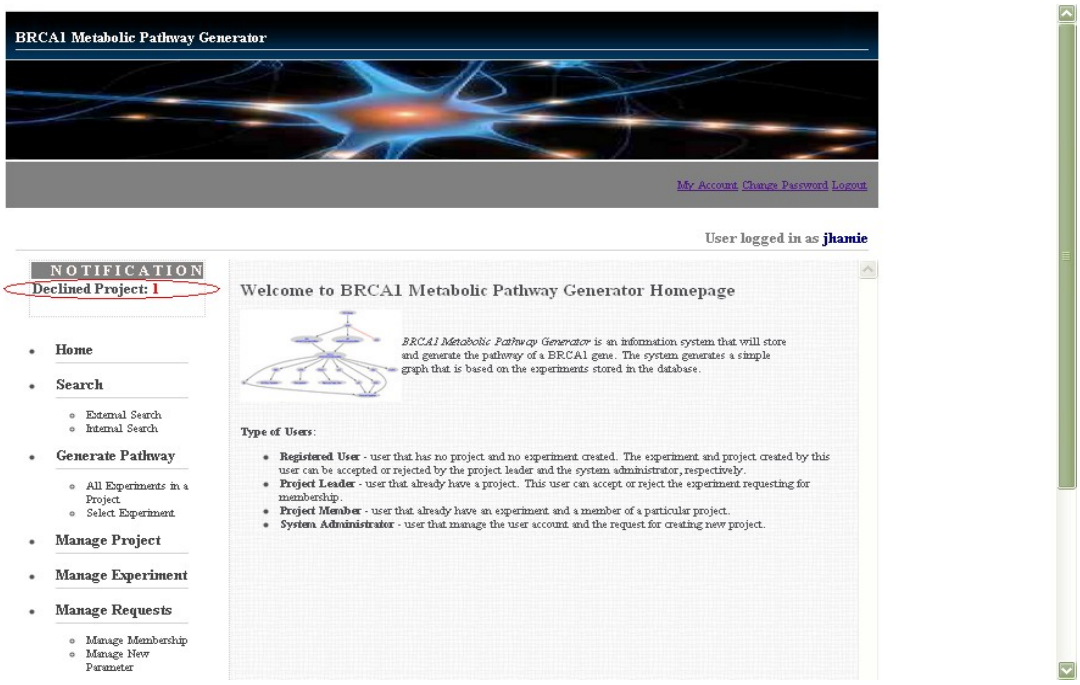
The notification table will display the number of approved/rejected projects. If the system administrator accepts the project then the registered user will become the project leader of that project.



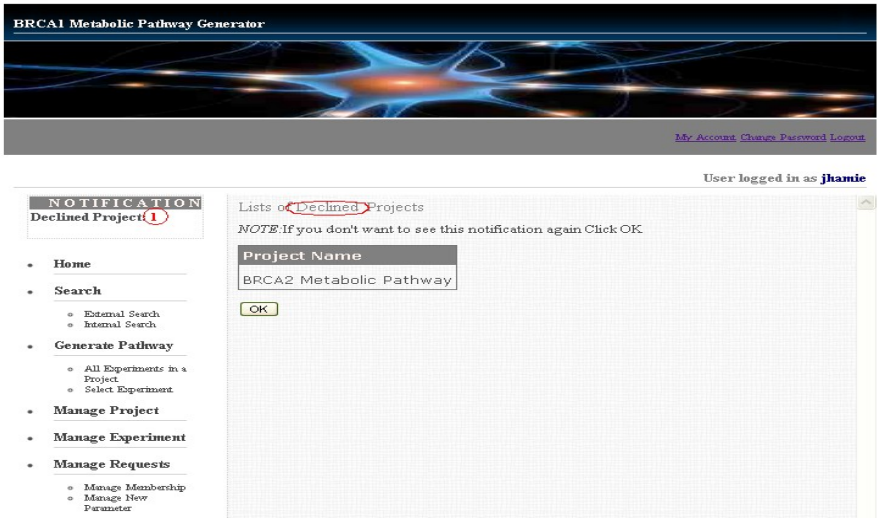
The system will display the list of names of projects accepted by the system administrator. The project leader must confirm the accepted project to continue handling the projects. The current status of that project was private. Clicking the ok button, the system will now display the name of the added project and the functionalities that can be done to that project namely: Edit, Delete, Add Members, and Add Parameters.



On the other hand, if the system administrator didn't accept the request for the new project. The system will notify the user that the application for the new project was rejected.



By clicking the number of rejected project the system will display the list of project names that have been rejected. The user is also allowed to remove the notification by clicking the ok button found after clicking the number of rejected project.



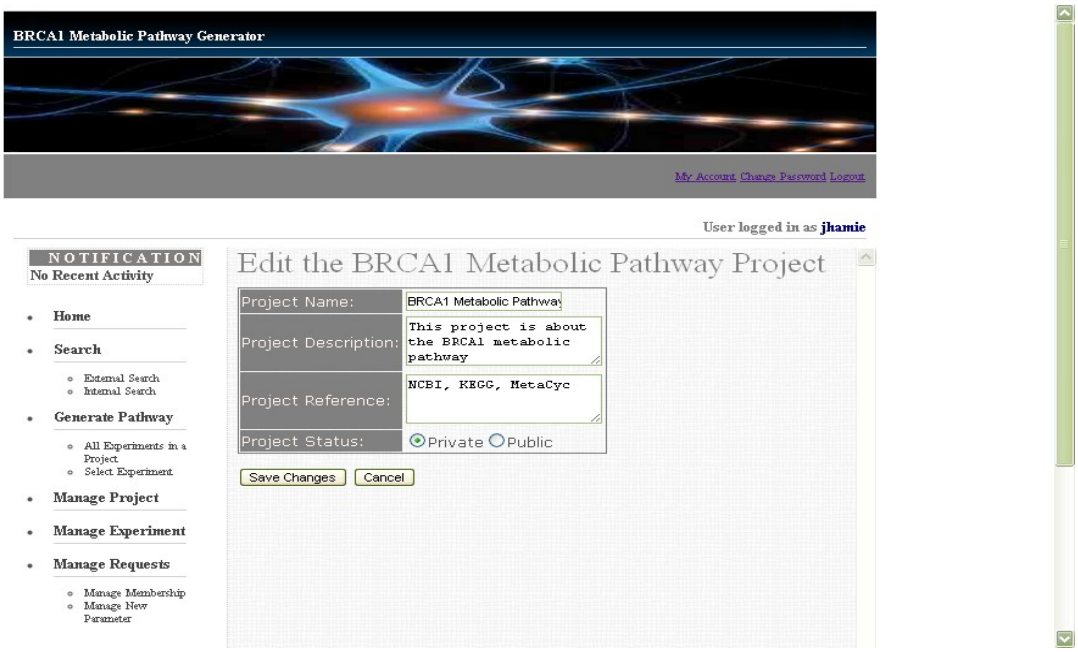


Figure 44 Manage Project – Edit Project

This figure shows the interface for editing a project. The user is allowed to edit the information about the project's name, description, reference and status.

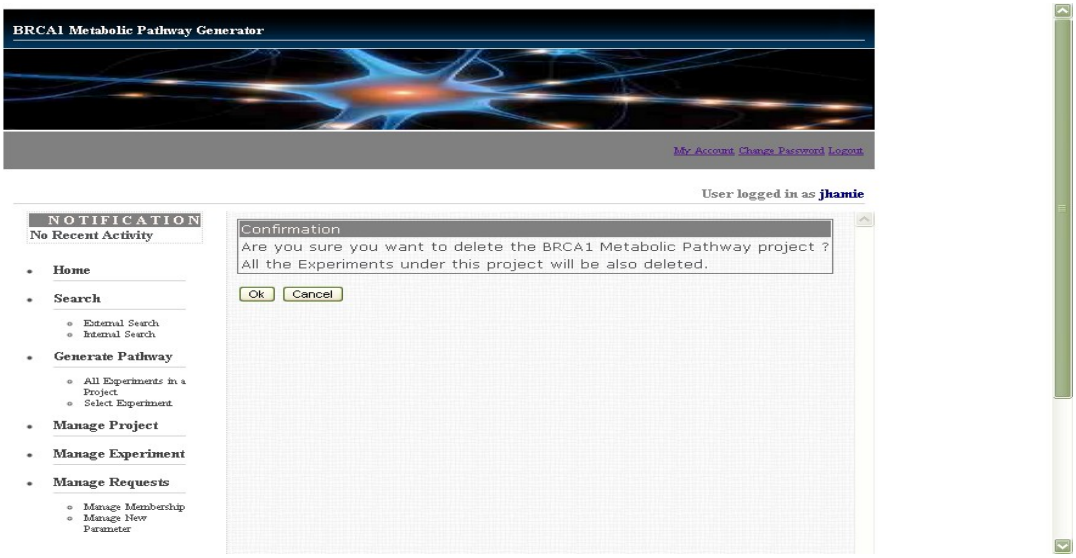


Figure 45 Mange Project – Delete Project

This figure shows the interface for deleting a project. The delete project section can be found by clicking the delete link. It displays a verification note to the user before finally deleting a project.

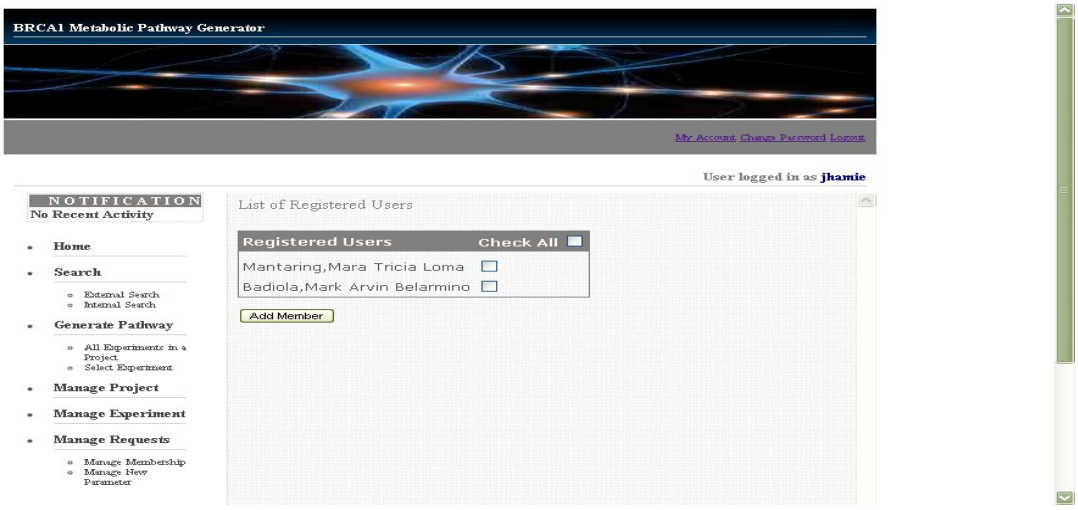


Figure 46 Manage Project – Add Members

This figure shows the interface for adding a member. Add member section can be found when the "add members" link was clicked. It consists of names of nonmember registered user in a project.

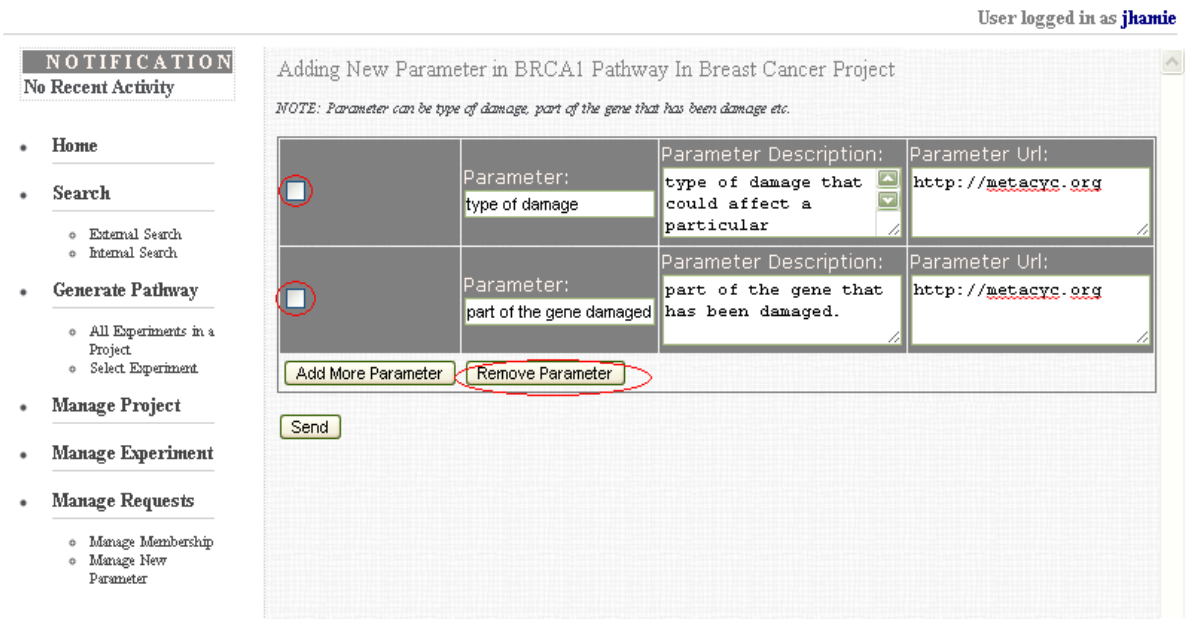
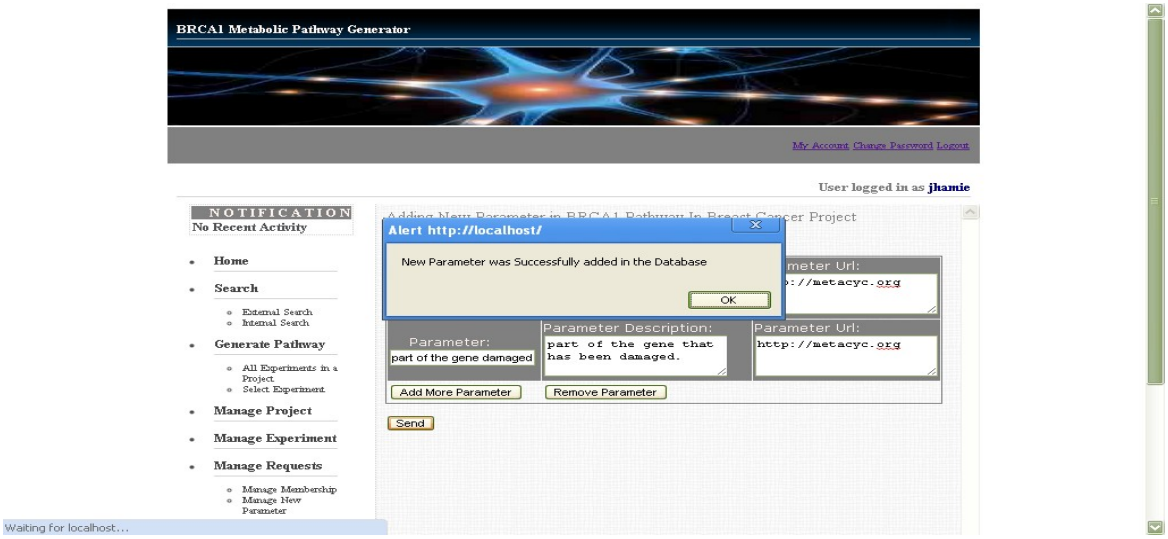


Figure 47 Manage Project – Add Parameters

This figure shows the interface for adding a parameter. Since the project leader is the one who adds new parameters then there will be no confirmation for the acceptance of those parameters and it will be directly added to that project. The checkbox besides the parameter field will be use if the user wants to delete a set of parameter. After adding new parameters, the system will display an alert message to inform the user that new added parameters were successfully added.



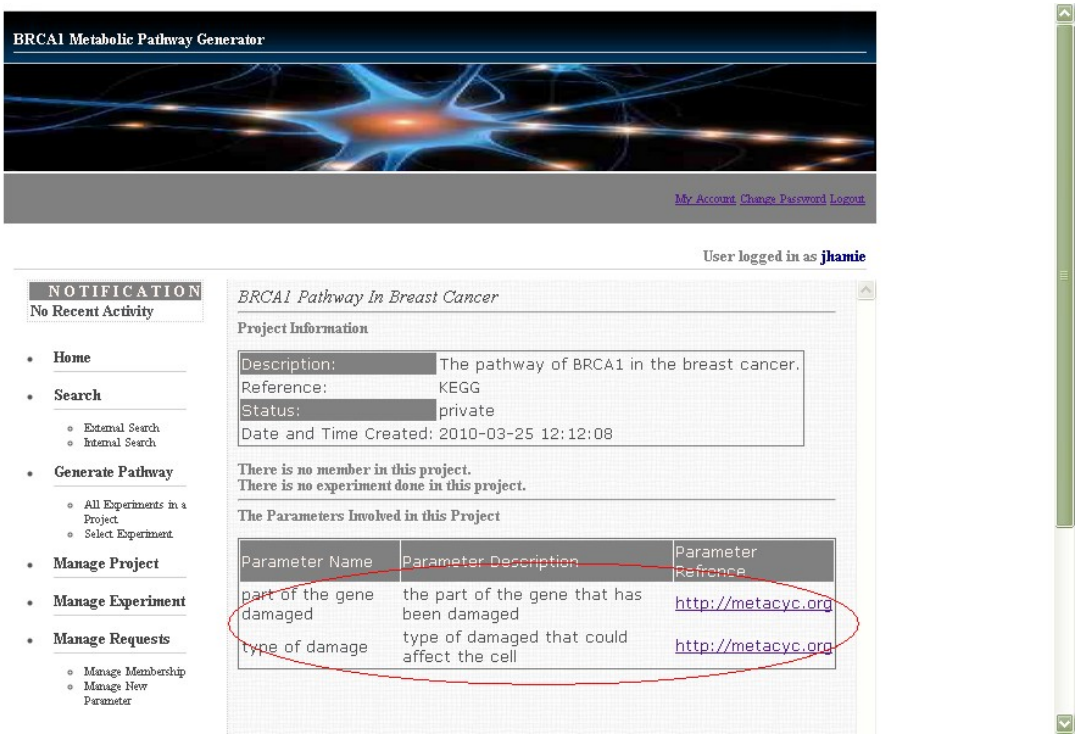


Figure 48 Manage Project – View Parameter's Information

This figure shows the interface for viewing the parameter's information. View parameter's information section can be found after adding new parameters or by clicking a name of a project. It consists of information about the parameter's name, description and reference.

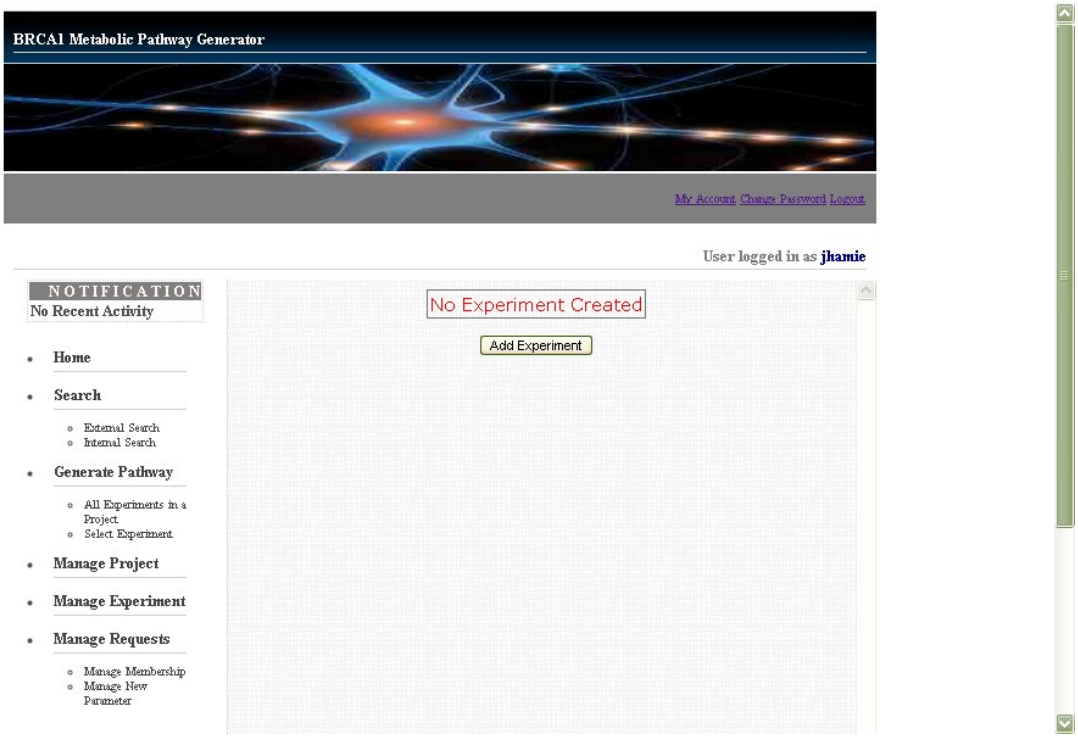


Figure 49 Manage Experiment

This figure shows the interface for managing an experiment. The registered user (i.e. project leader or project member) can add an experiment to his/her project. In this figure the logged in user has not yet created an experiment therefore the system only offers the add experiment function. There are three steps in creating new experiment. First, choosing what project the new experiment would be included. Second, adding information about the experiment (i.e. name, description, and reference) and giving values to the parameters selected. Lastly, creating set of pathway that will serves as a rule for the system in generating the graph.

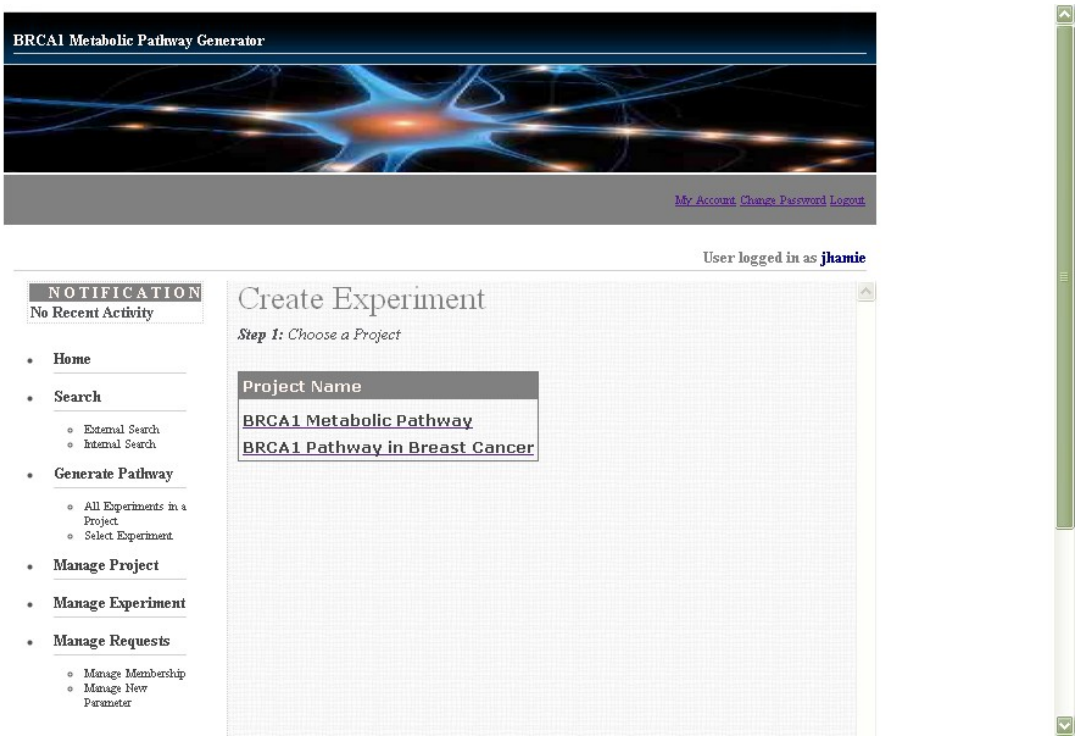
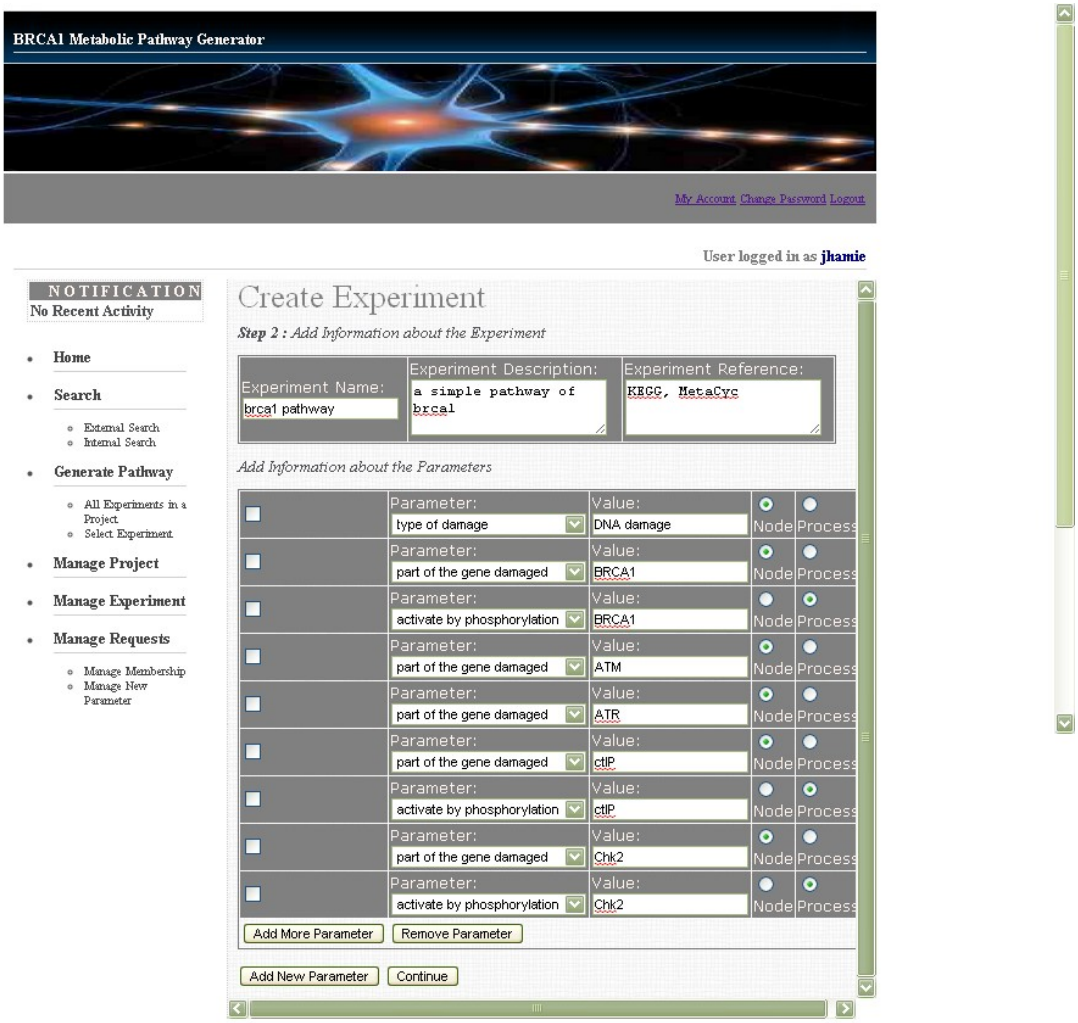


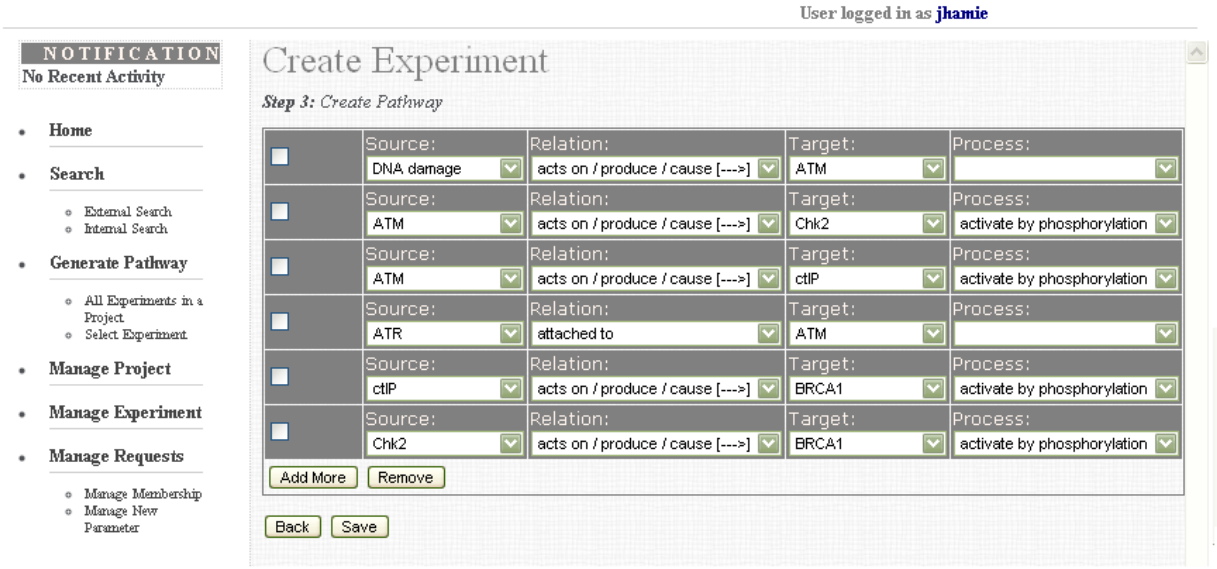
Figure 50 Manage Experiment – Add New Experiment

This figure shows the interface for adding an experiment in which at the start the user must choose a project. The user is required to choose in what project he/she wants to add his/her new experiment. The list of project name displayed was the name of project with public status, project that he/she created, or project that he/she was a member of.

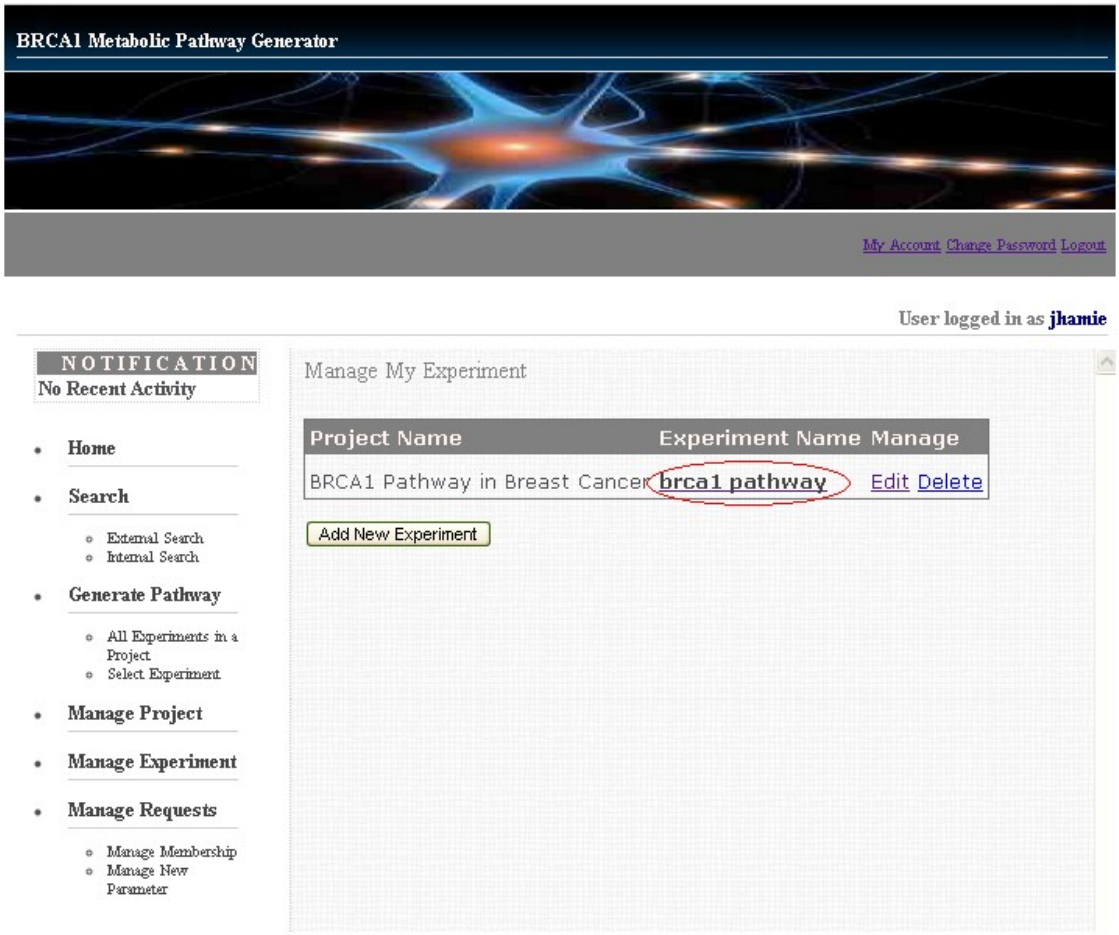


This figure shows adding an experiment under a project that already has parameters. This figure also shows adding information about the experiment, giving values for the parameters in that project, assigning the nodes and process of the graph. If you assign a parameter as a process then the value for that parameter must be a value of a parameter that is assigned as a node. For instance the parameter: part of the gene damaged has a value: BRCA1 assigned as a node,

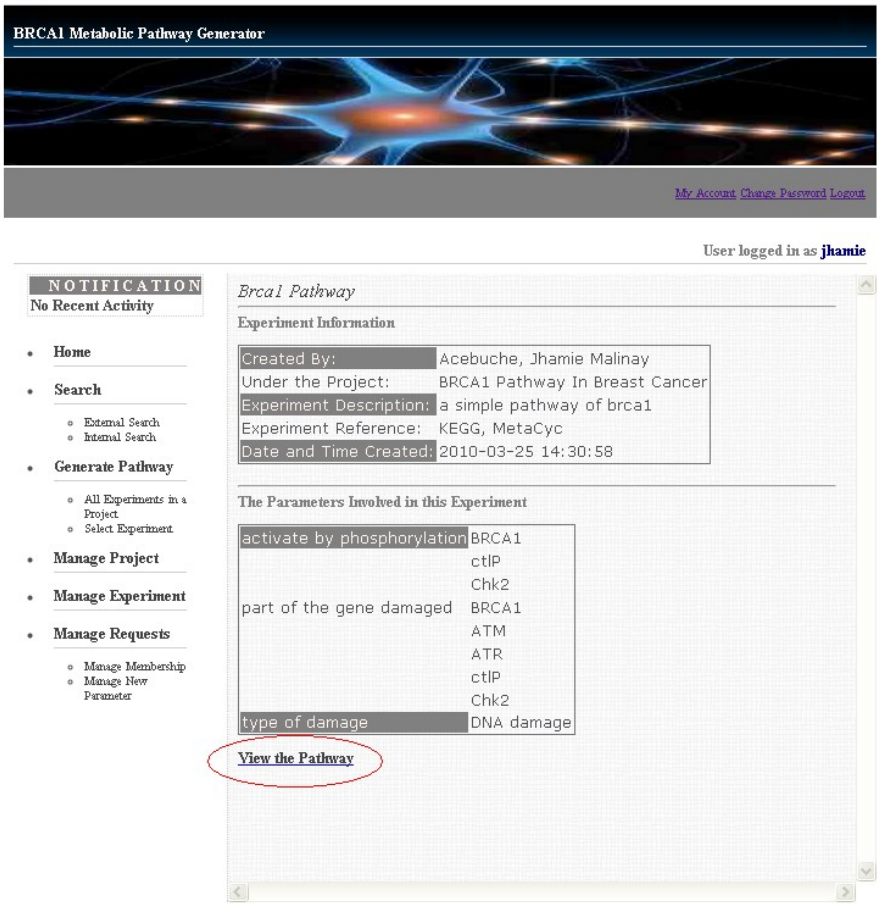
parameter: part of the gene damaged has a value: Chk2 assigned as a node, parameter: part of the gene damaged has a value: ctlP assigned as a node, then if you want to create the parameter: activate by phosphorylation as a process you can choose the value BRCA1, Chk2 or ctlP as its value. This is done to know what node value undergo that process.



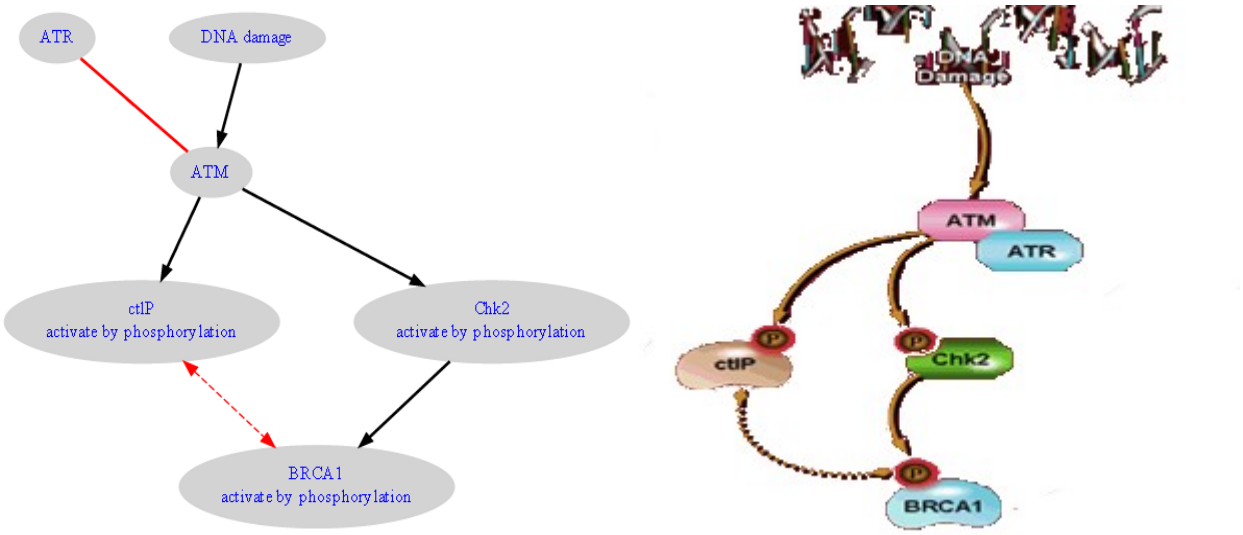
The figure shows how to make a simple graph by choosing the values for the source, relation, target and process. The value for the source and target fields was the parameter values that were entered previously as a node whereas the value for the process field was the parameter that was entered previously as a process. For instance the *parameters* earlier were the type of damage, part of gene damaged and activate by phosphorylation and the *parameter values* were DNA damage, ATM, ATR, ctlP and Chk2. Since the "activate by phosphorylation" was the only parameter assigned as process hence it was the only value for the process field. The relation field was fixed to the values acts on / produce / cause (->), connected to (-), attached to (-) and reversible to (<->). These created pathways will then serve as the rule for generating the graph.



The system will now display the name of the new added experiment and functionalities that can be done to that experiment namely: Edit and Delete. The information about the experiment and the generated pathway can be viewed by clicking the name of the experiment. As you click the name of the experiment, the system will produce .dot and .svg files.



This figure shows the information about the experiment. The graph generated by the system can be viewed by clicking the link “View the Pathway”. The system will then open a new window to enable the user to view the entire graph.



The left figure was the graph representation of the system for the figure on the right which is from http://www.sabiosciences.com/pathway.php?sn=BRCA1_Pathway. The red line connecting the two nodes represents the relation “attached to”, the black arrow (i.e. the head of the arrow pointing to the target) represents the relation “acts on / produce / cause” and the red dashed arrow with heads at both ends represents the relation “reversible to”. The “p” node that was attached to the ctlP, Chk2 and BRCA1 node on the right figure was represented on the left by identifying what does P means in the system and then assigning it to be a process. Then, it will be appended to what parameter value does this process applies.

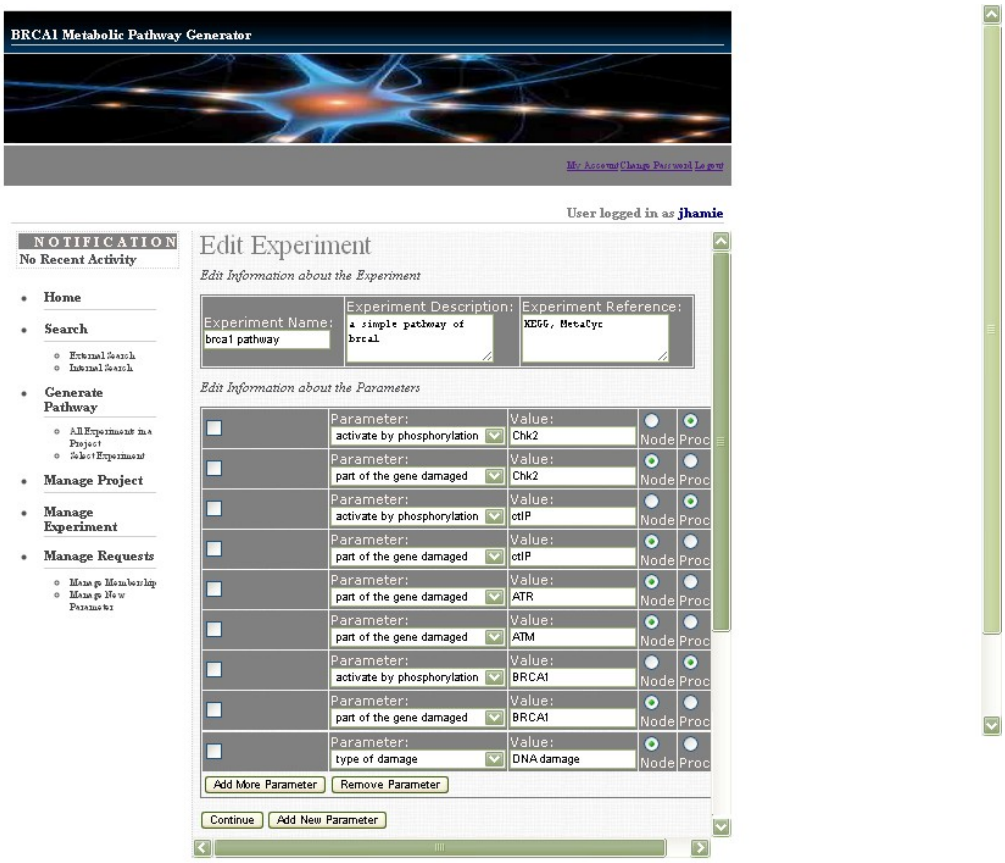
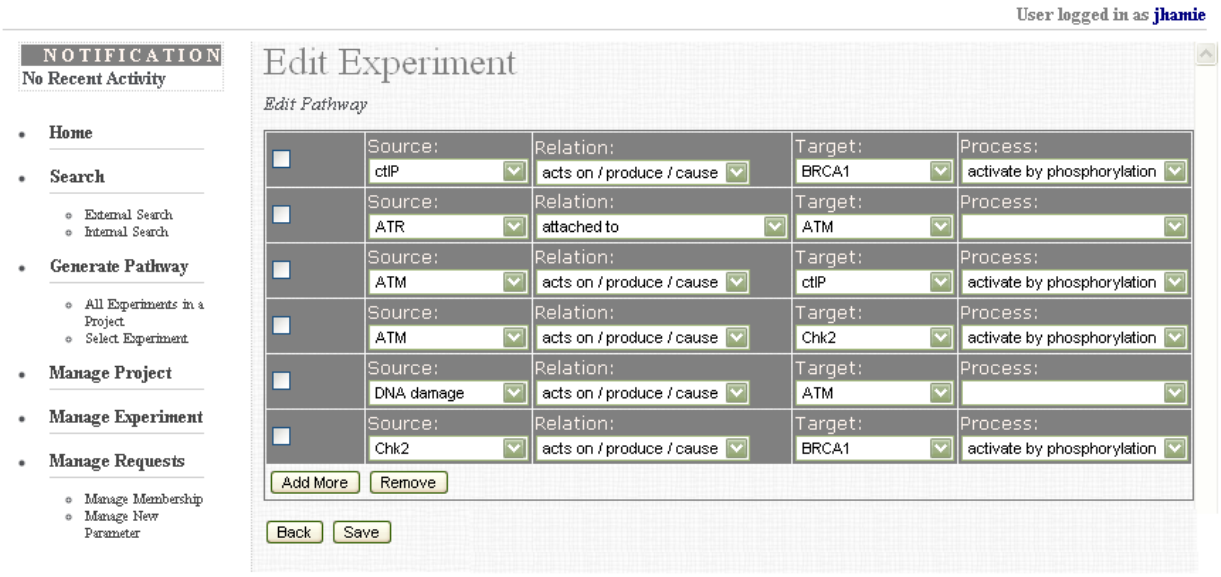
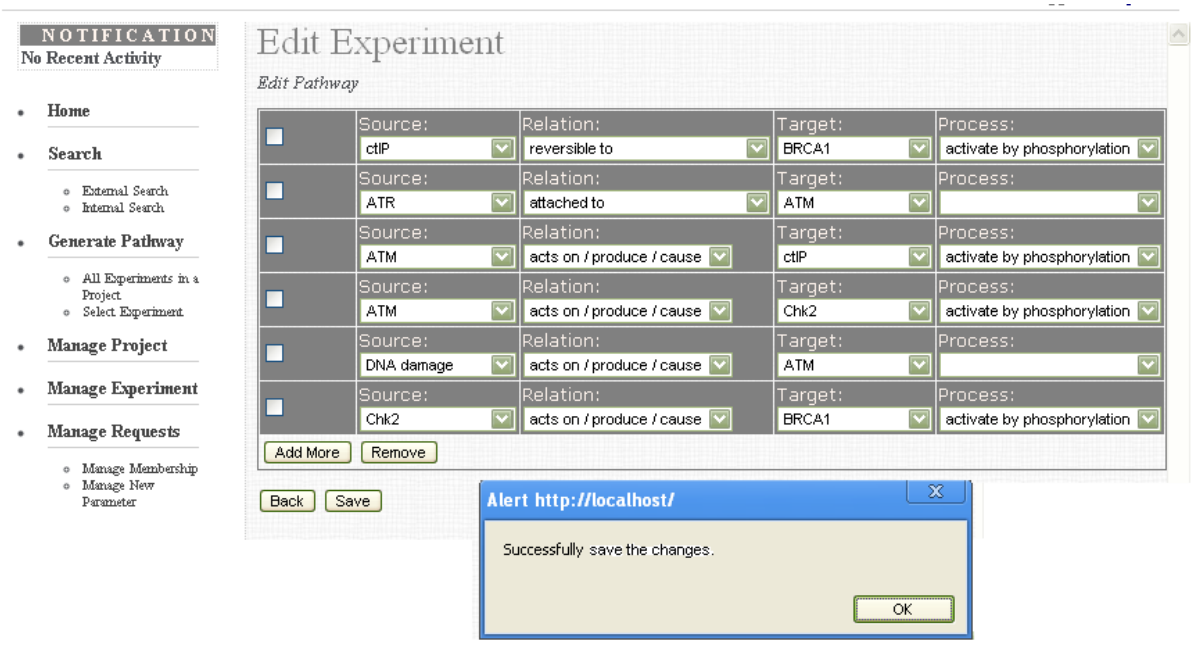


Figure 51 Manage Experiment – Edit Experiment

This figure shows the first part of editing an experiment. This section consists of information about the experiment's name, description, reference and the parameter's name and value as well as their category, either node or process.



This figure shows the second part of editing an experiment. This section consists of information about the pathway (i.e. source, relation, target and process). After saving the changes, the system will display an alert message to inform the user that the changes were successfully saved.



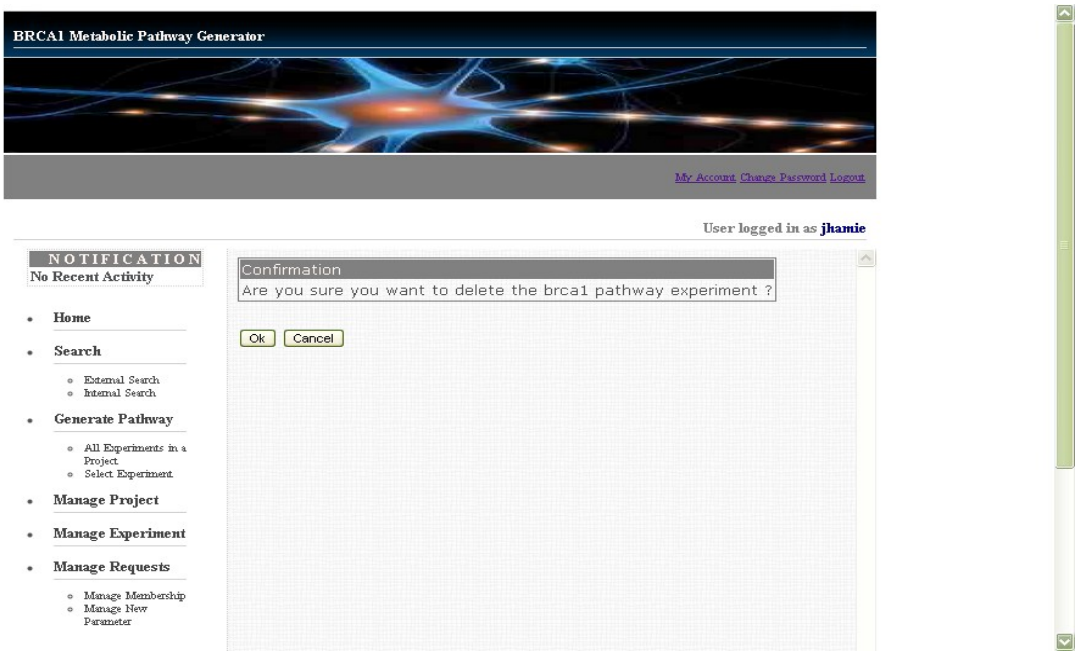


Figure 52 Manage Experiment – Delete Experiment

This figure shows the interface for deleting own experiment.

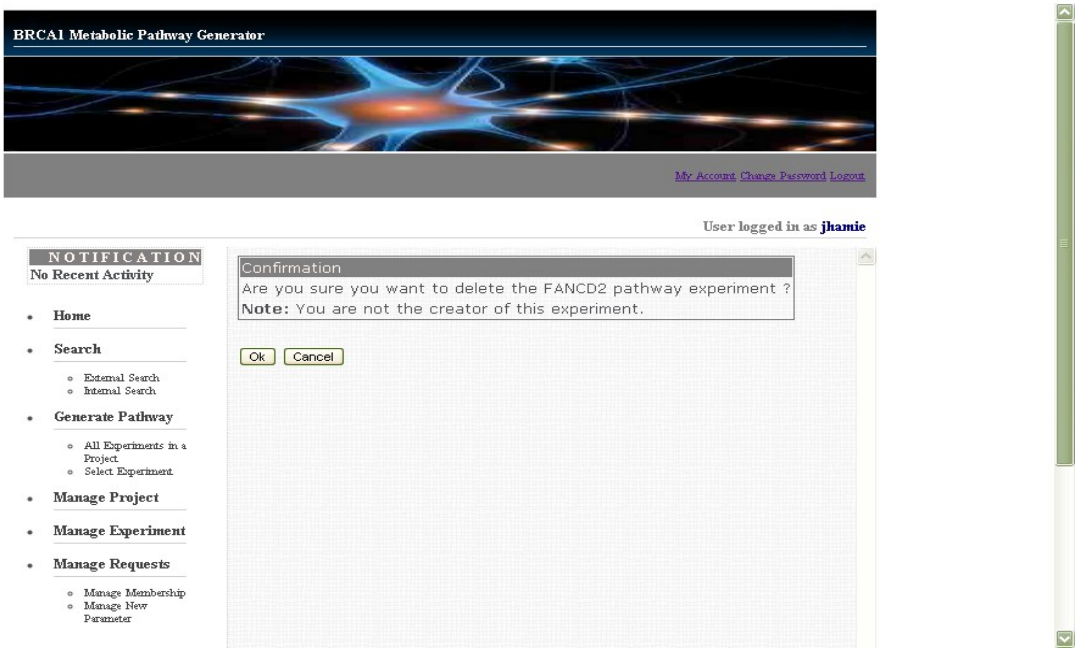


Figure 53 Manage Experiment – Delete Experiment

This figure shows the interface for deleting an experiment created by members.

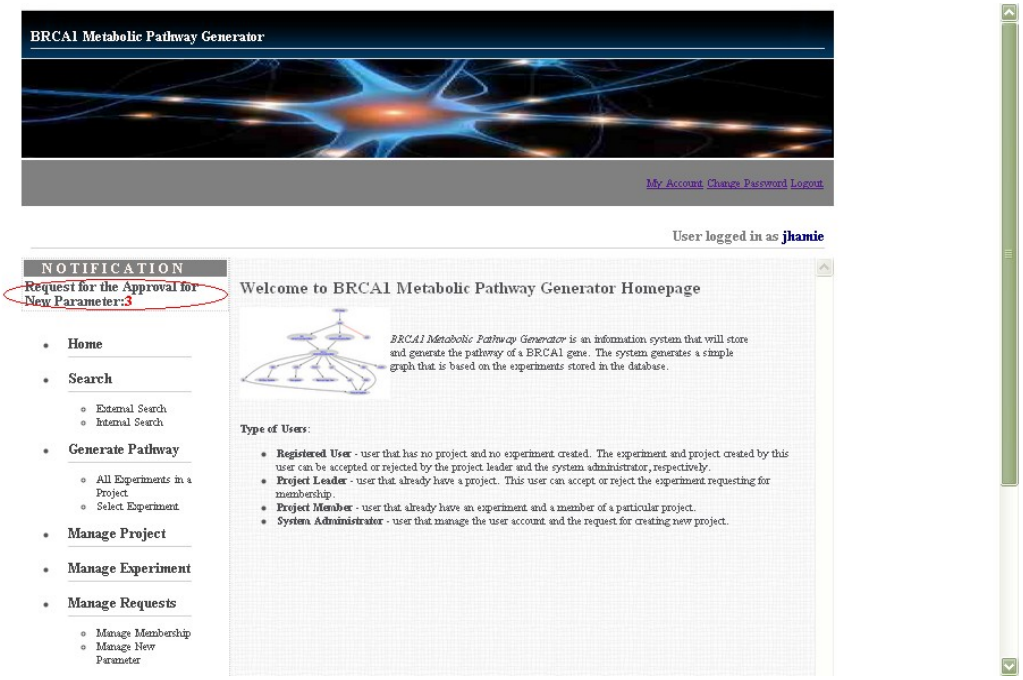
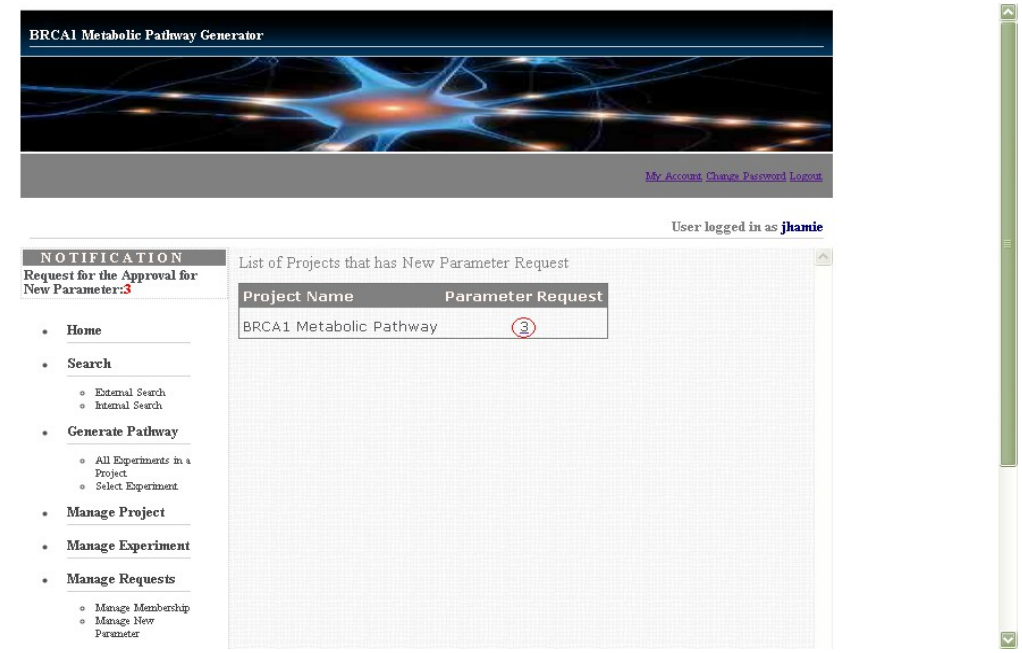


Figure 54 Manage Requests – Requests for new Parameters

This figure shows the interface for handling requests for new parameters. Clicking the number of requests for new parameter, the system will display the list of project names that has parameter requests.



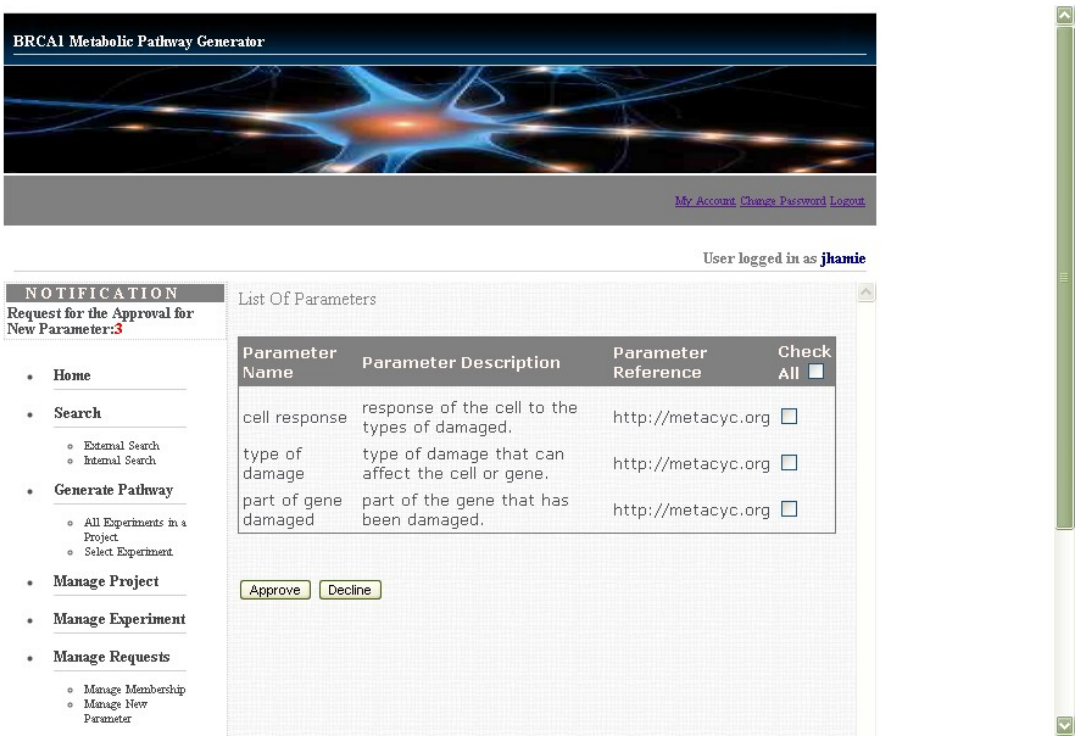


Figure 55 Manage Requests – List of Parameter Requests

This figure shows that by clicking the total number of parameter requests in a particular project allows the project leader to see the details about the parameters (i.e. parameter name, description and url) and enable him/her to manage it.

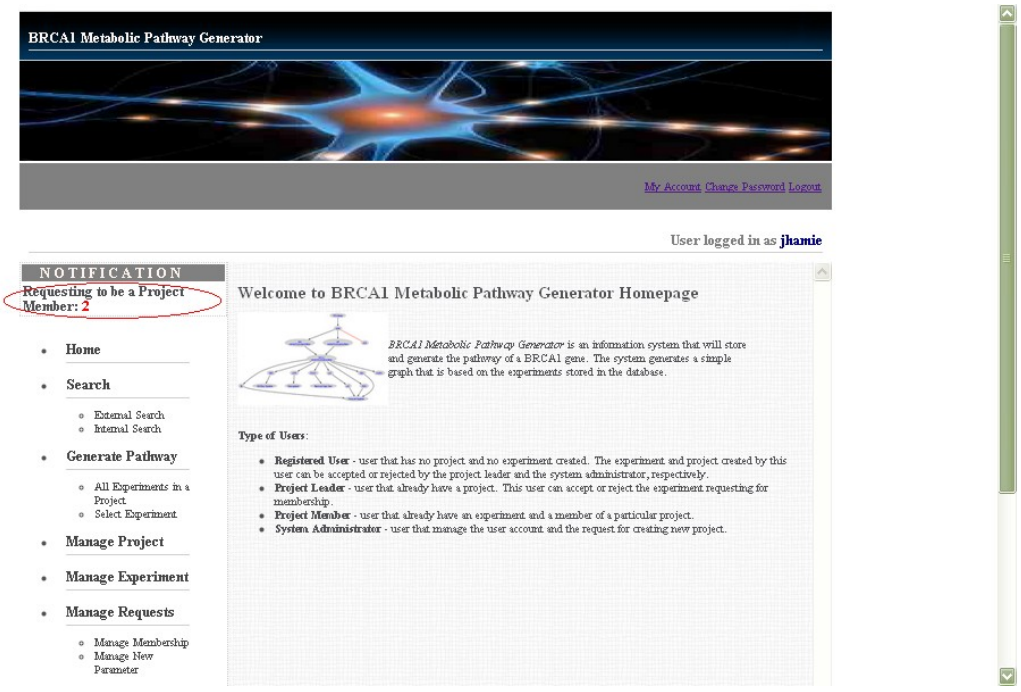
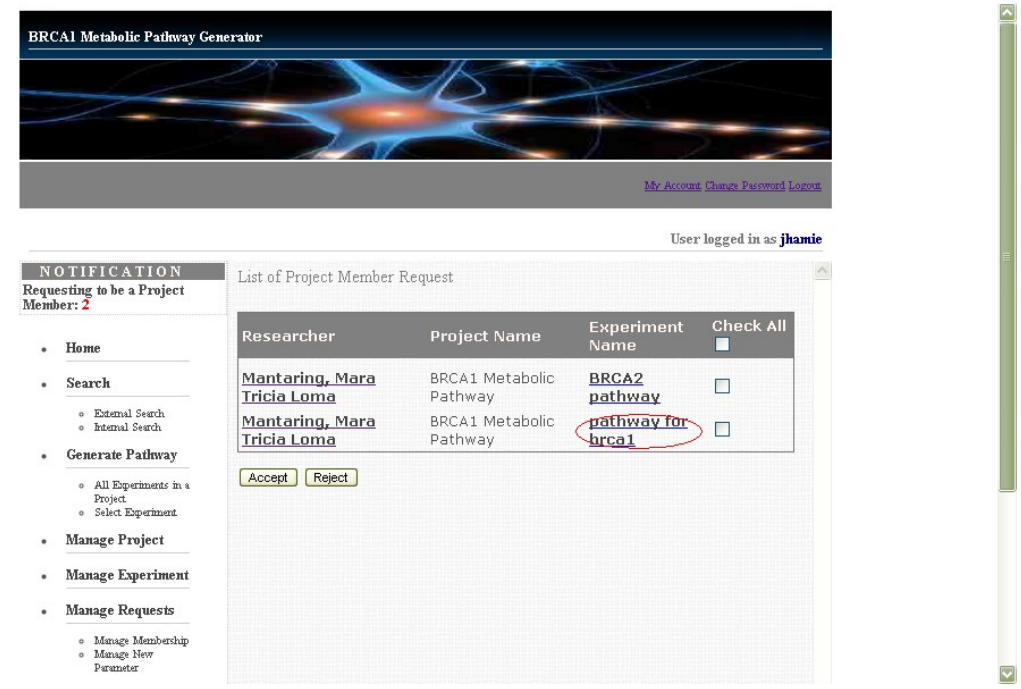
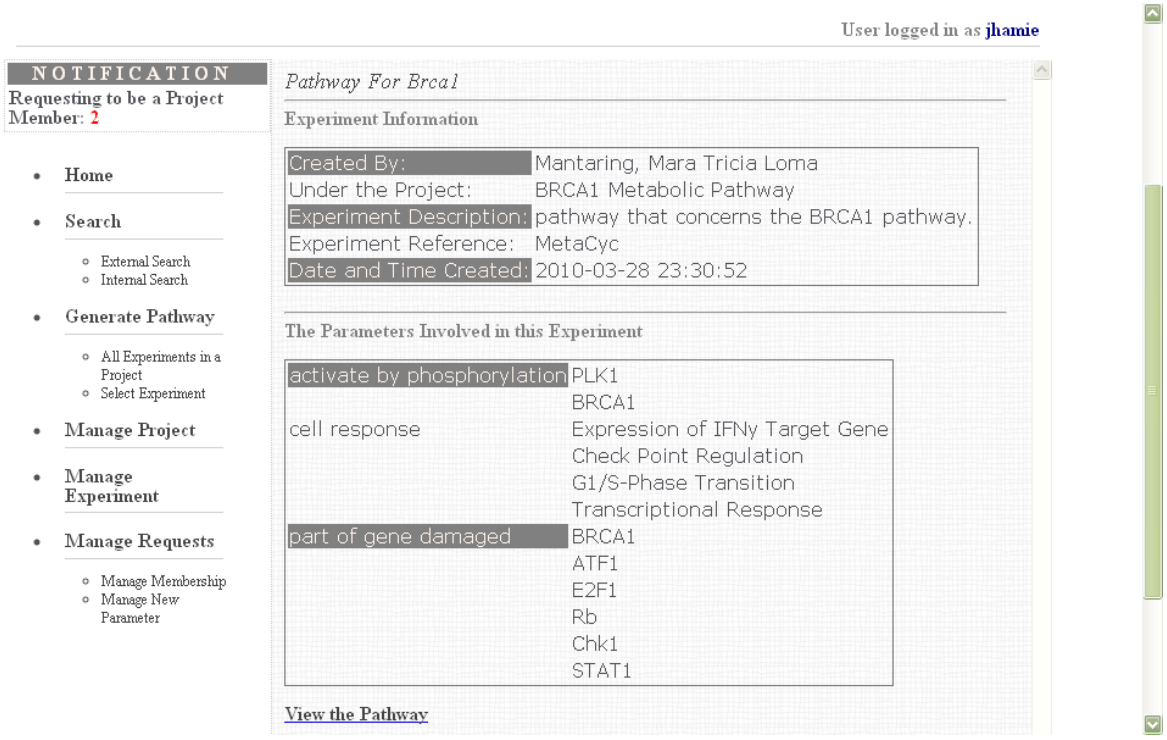


Figure 56 Manage Requests – Requests for new Project Membership

This figure shows the number of requests application for project member. Clicking the number of request, the system will show the list of experiment name and all the details about it.



Clicking the name of the researcher, the system will show the profile of the clicked name. On the other hand, clicking the name of the experiment, the system will show the details about the experiment's creator, name, description, reference, date and time created, and the parameters involved in that experiment.



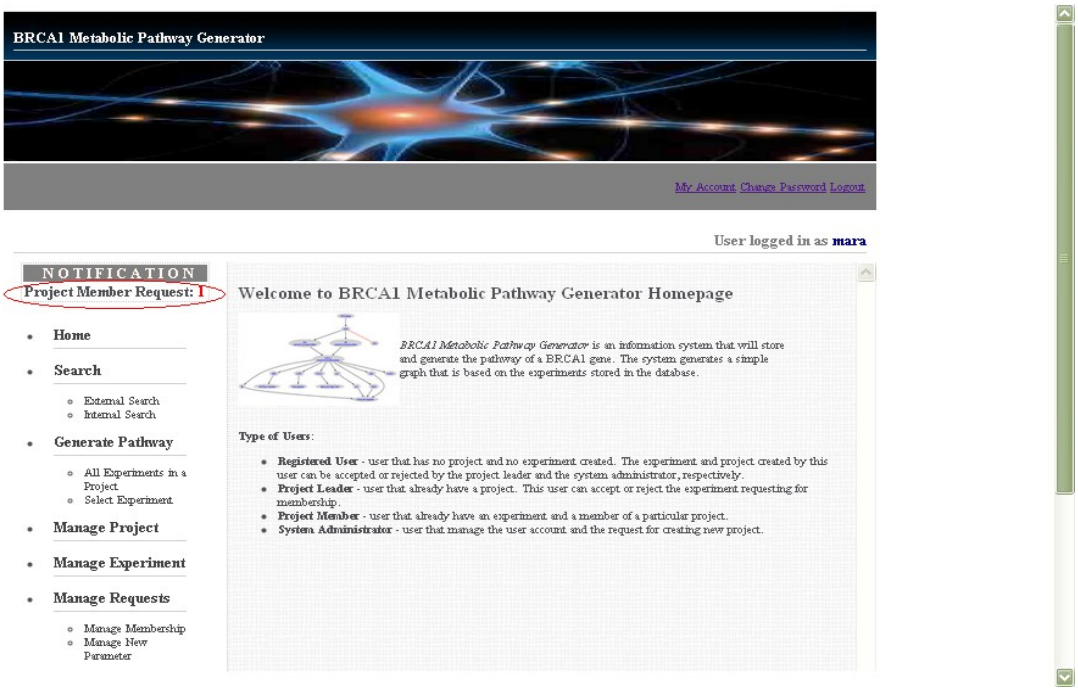
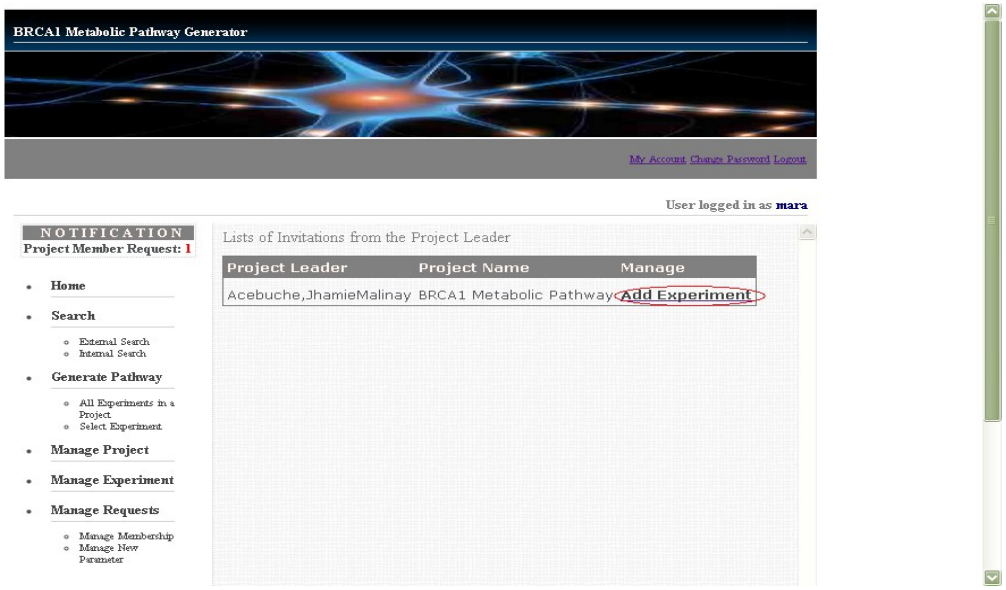
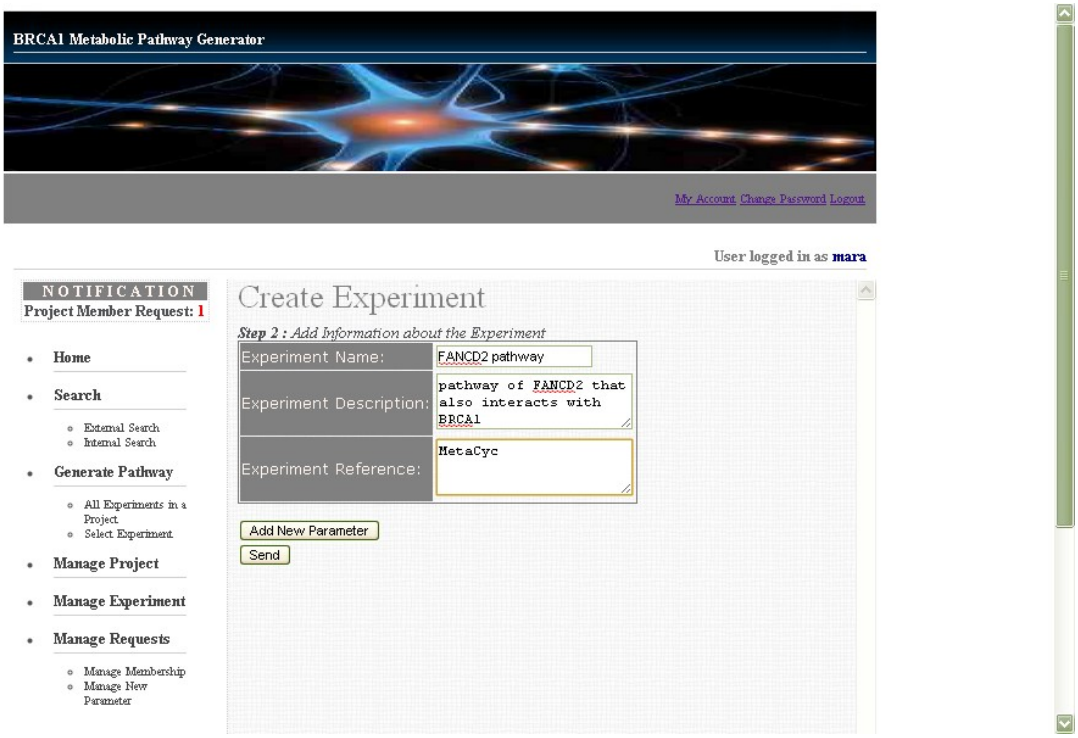


Figure 57 Registered User that was requested to become a Project Member of a Project

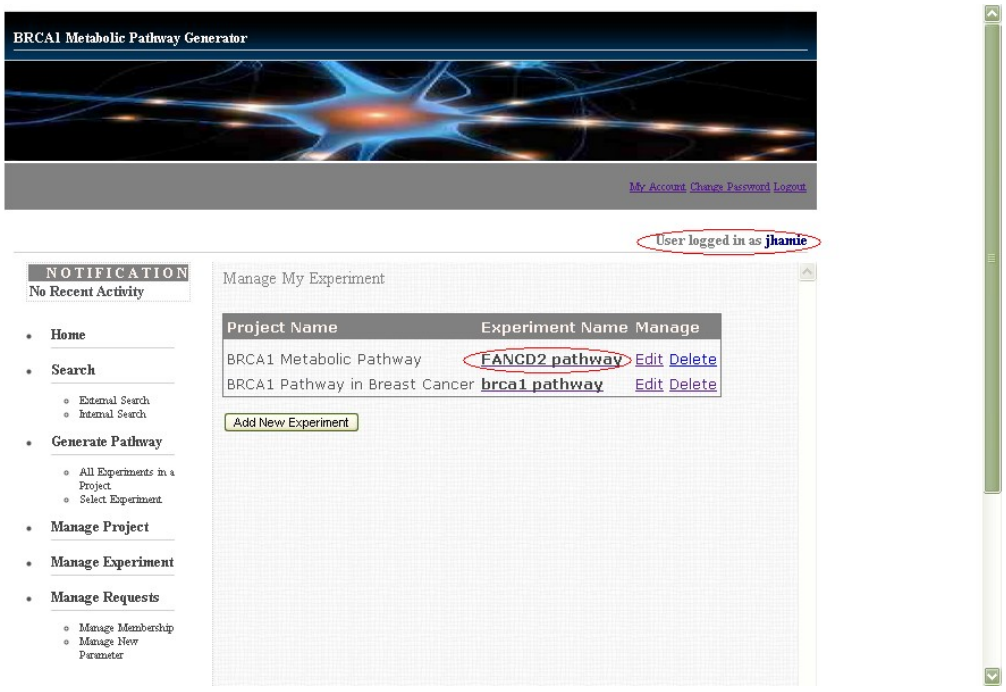
This figure shows the interface for handing request from project leader. The notification table displays the number of request from project leader requesting the registered user to be a project member. Clicking the number of requests, the system will display the name of the project leader, the name of the project and the "Add Experiment" function.



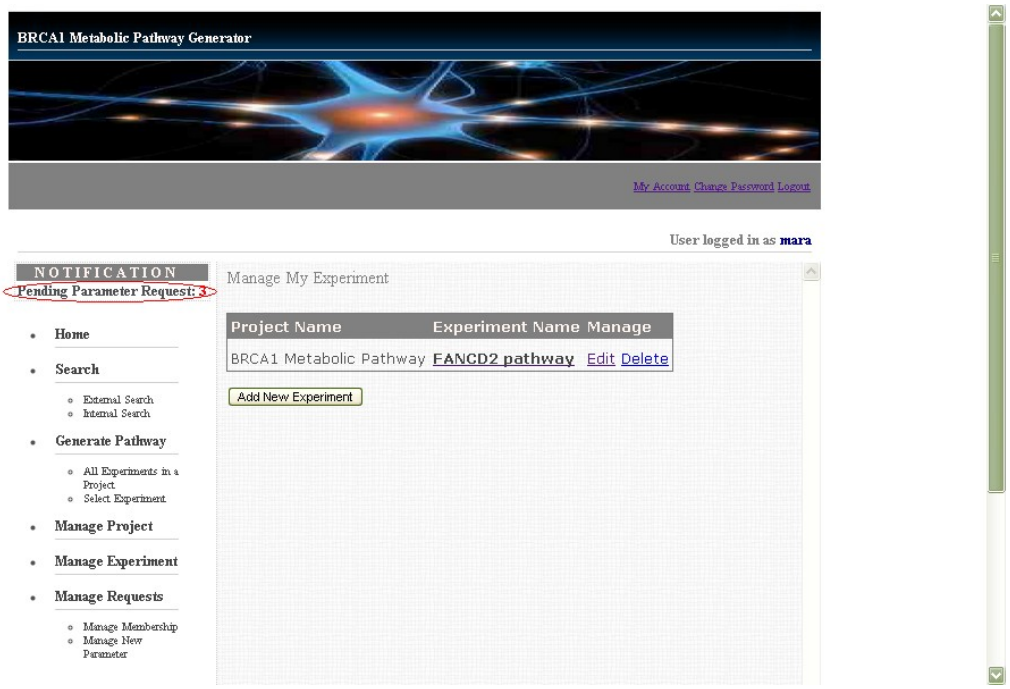
The "Add Experiment" link will enable the user to create an experiment to that project.



This figure shows the section of adding an experiment under a project in which the registered user was requested to become a project member. Also, this figure shows adding an experiment in a project that has no available parameters. Clicking the "Add New Parameter" button, the system will enable the user to request for new parameter to the project leader. On the other hand, clicking the "Send" button, the system will only add the information about the experiment (i.e. name, description and reference) under that project. After clicking any of these buttons, the system will display the added experiment with the two functions that can be done to that experiment. The system will also display the added experiment of the project member in project leader's list of experiments.

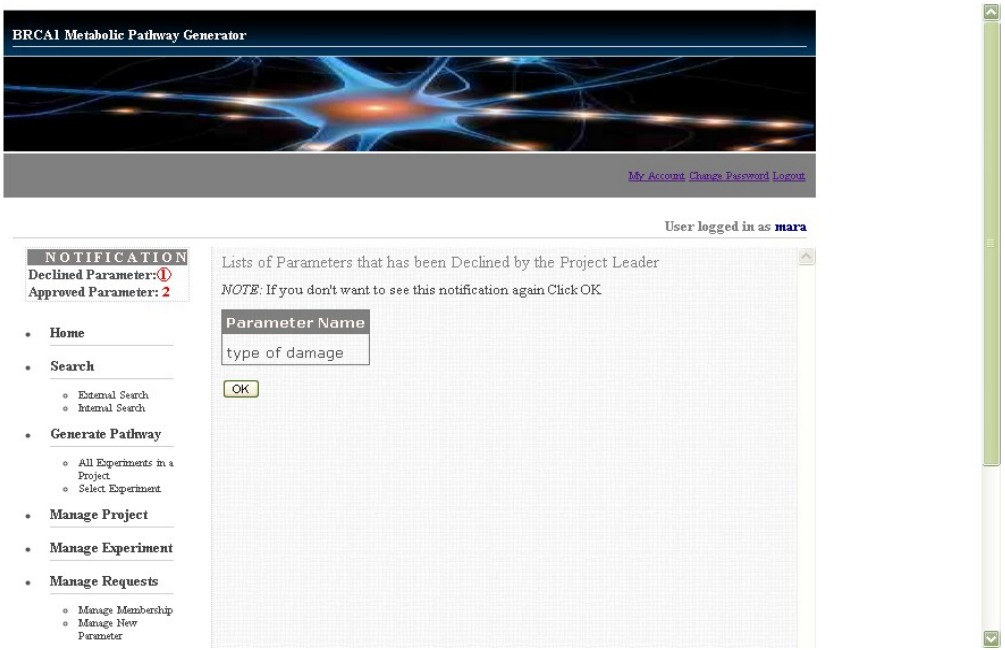


This figure shows that the project leader can edit or delete the project members' experiment.

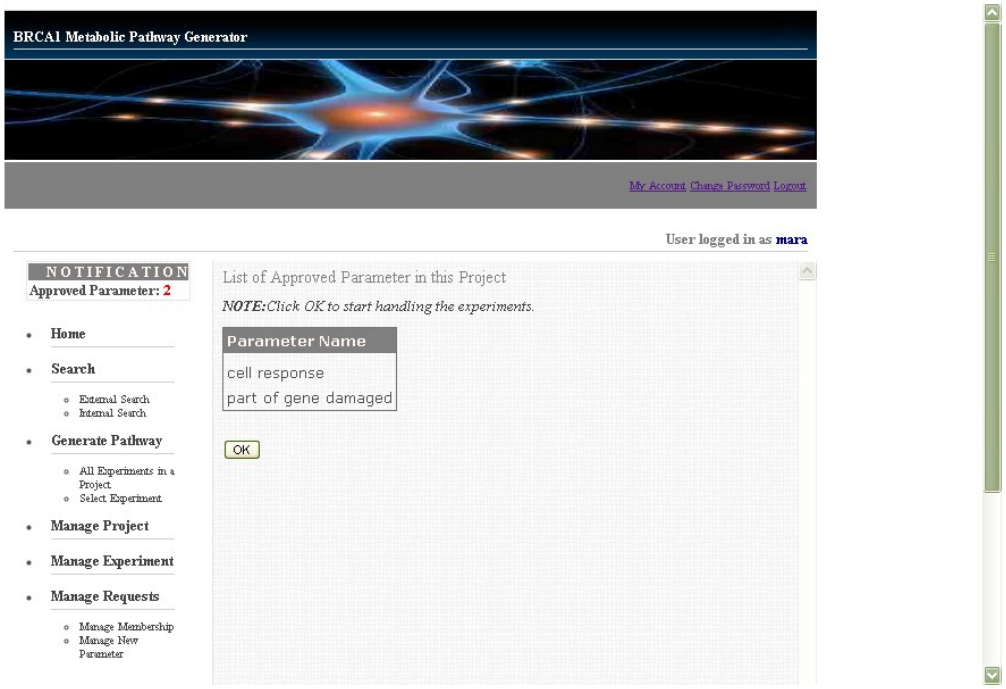


The system displays the number of pending request for new parameters in the notification table of the project member.

The notification table in this figure displays the number of parameters approved and declined by the project leader.



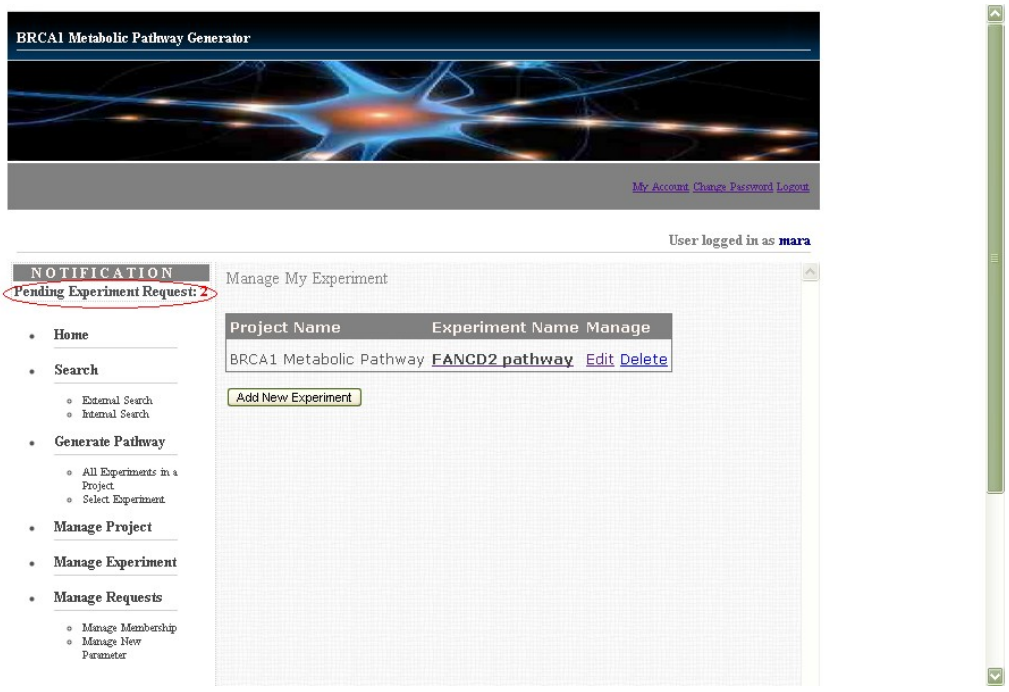
Clicking the total number of declined parameters will allow the user to view the names of rejected parameter.



Clicking the “edit” or add new experiment-> project name link under manage experiment will enable the user to view the list of approved parameter names. Clicking the “ok” button will allow the user to confirm the approved parameter and to continue handling the experiment.

Manage experiment menu in project members’ page that includes editing and deleting experiment is the same as the project leaders’ manage experiment. Except that the project member can only delete or edit the experiments he/she created.

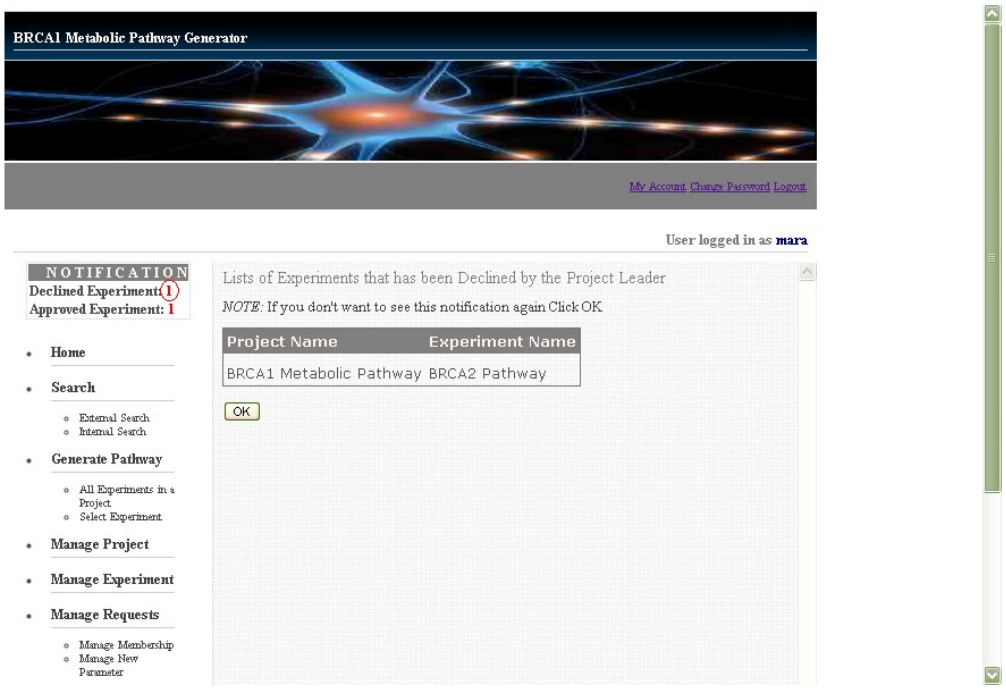
The process of adding new experiment of the registered user is similar to project leader except that the registered user needs the project leaders’ approval for the experiment he/she added.



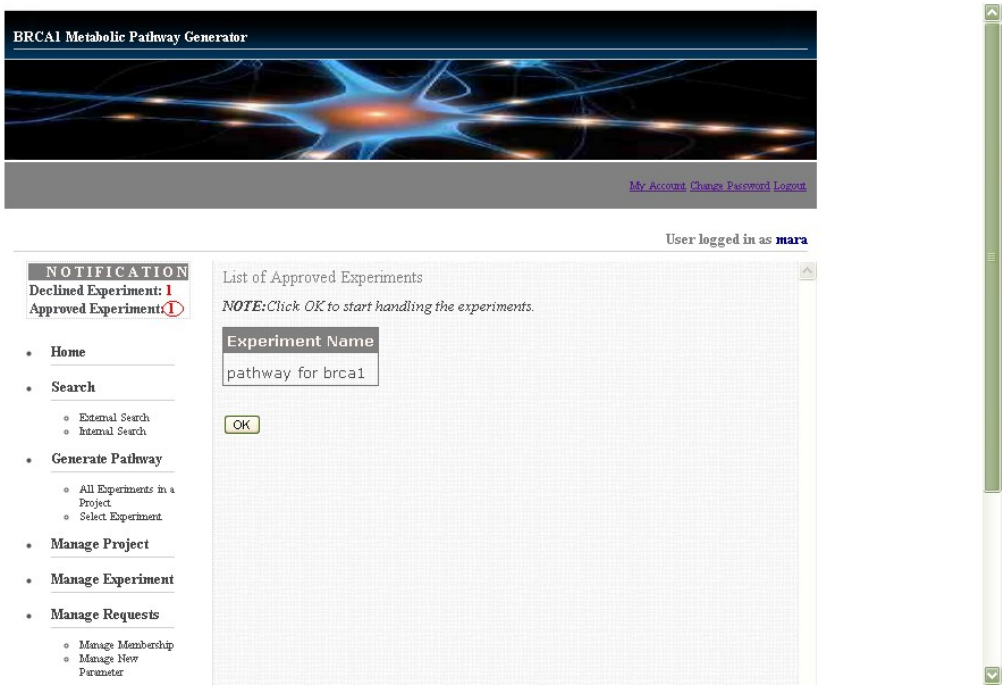
This figure shows the number of pending request for new experiment.

The notification table displays the number of approved and declined experiments. Clicking the number of declined experiment will display the list of declined experiment names and project name. On the other hand, clicking the number of approved experiment will display the list of

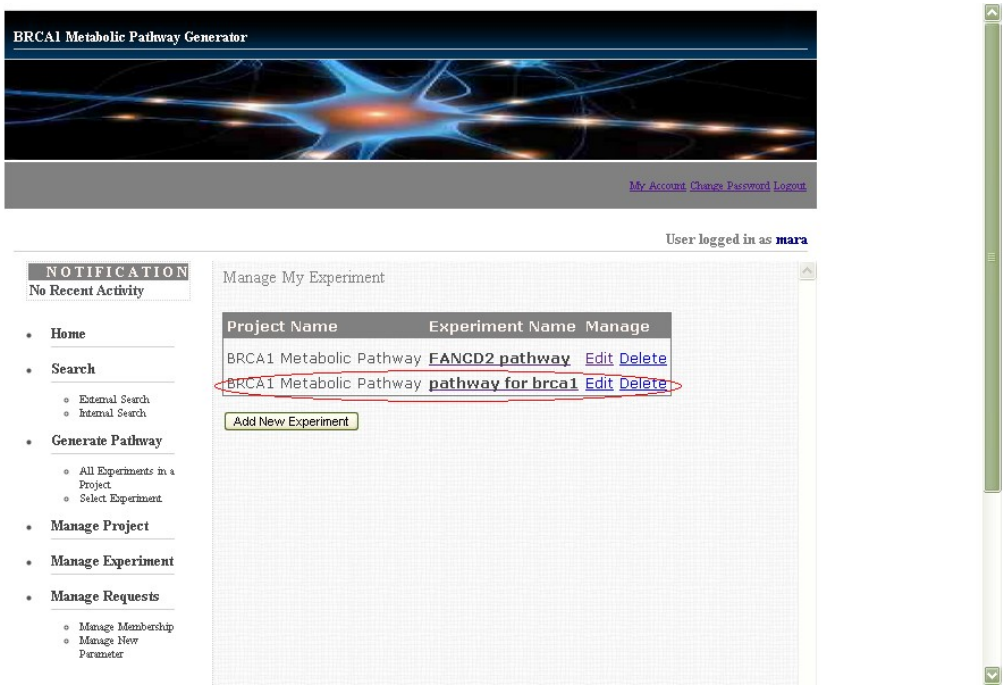
approved experiment names. If the experiment was approved by the project leader then the registered user would become a project member.



The figure shows the list of declined experiment(s).



The figure shows the list of approved experiment(s) name.



The figure shows that the approved experiment(s) is now included in the list of experiment(s) that can be manage.

The users have two options in generating the graph: choosing a project or choosing an experiment to be combined with other experiments stored in the database.

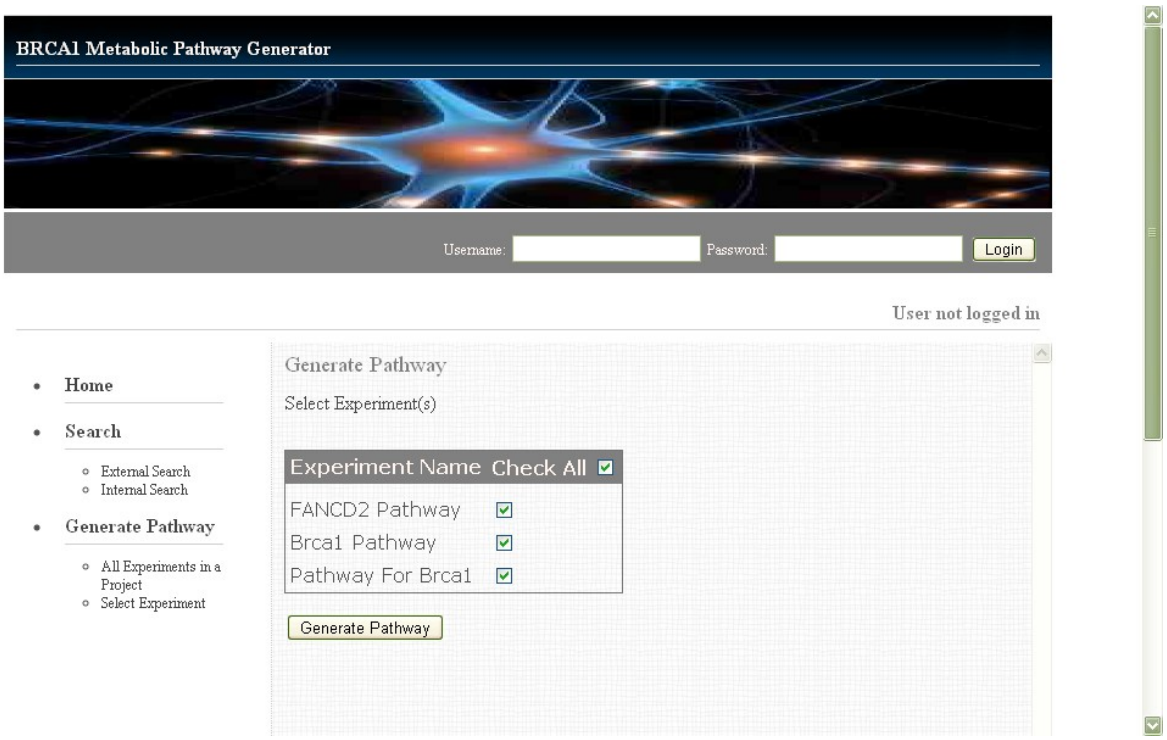
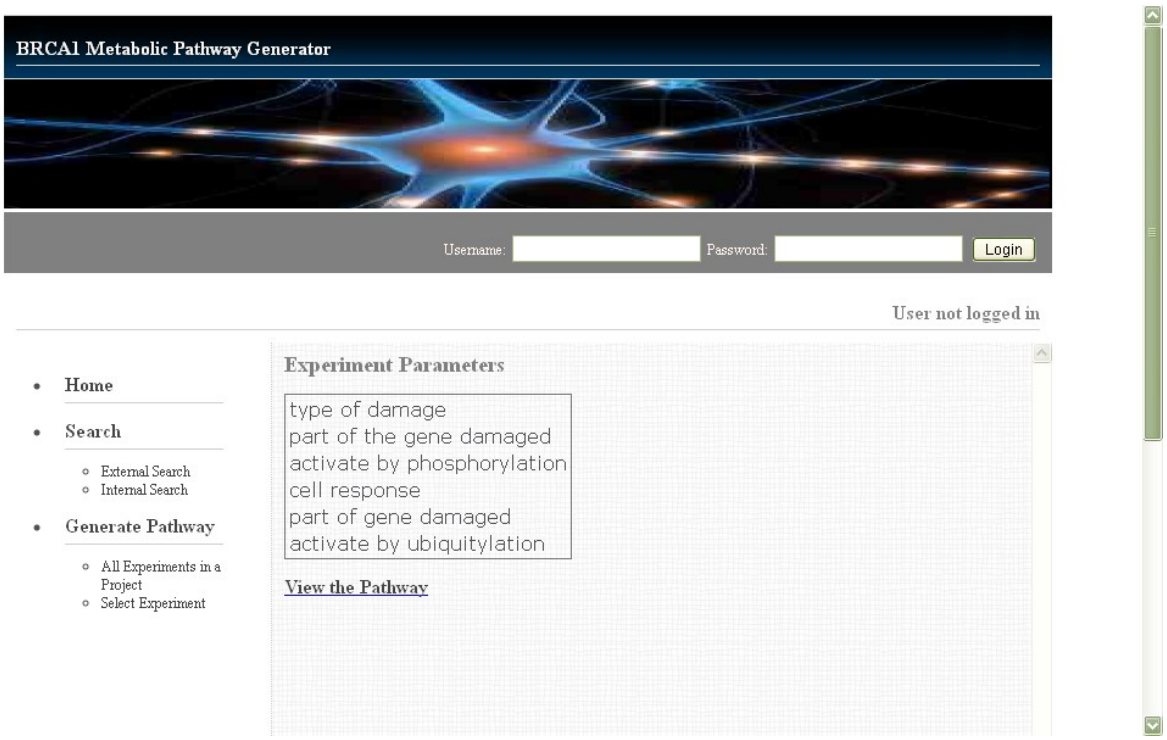


Figure 58 Generate Pathway – Select Experiment

This figure shows the interface for generating the pathway from selected experiment(s). The user selects an experiment to combine with other experiment.



The system will display common parameters in the experiment(s) that were selected.

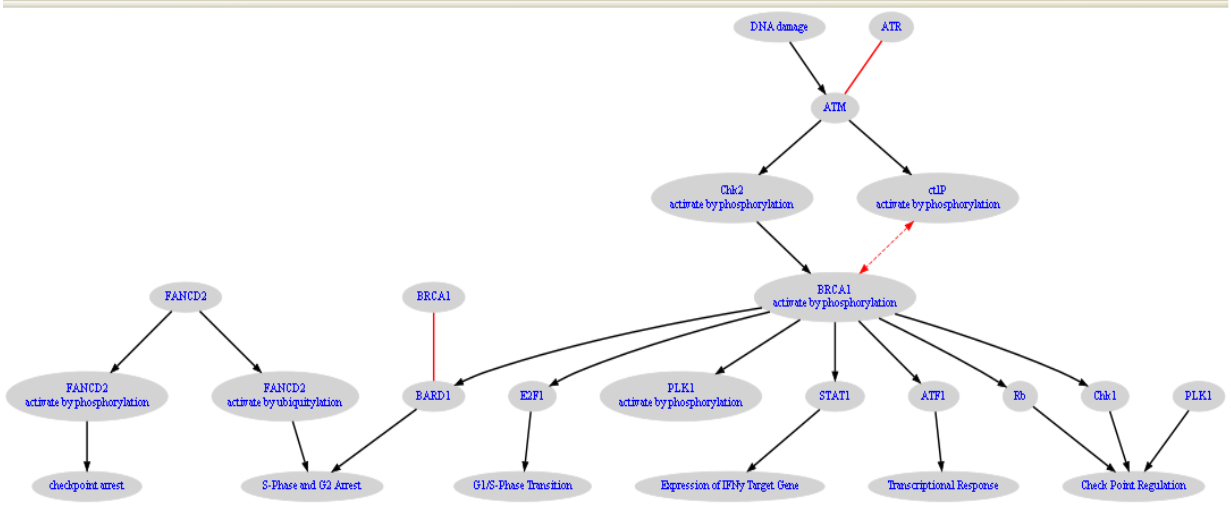
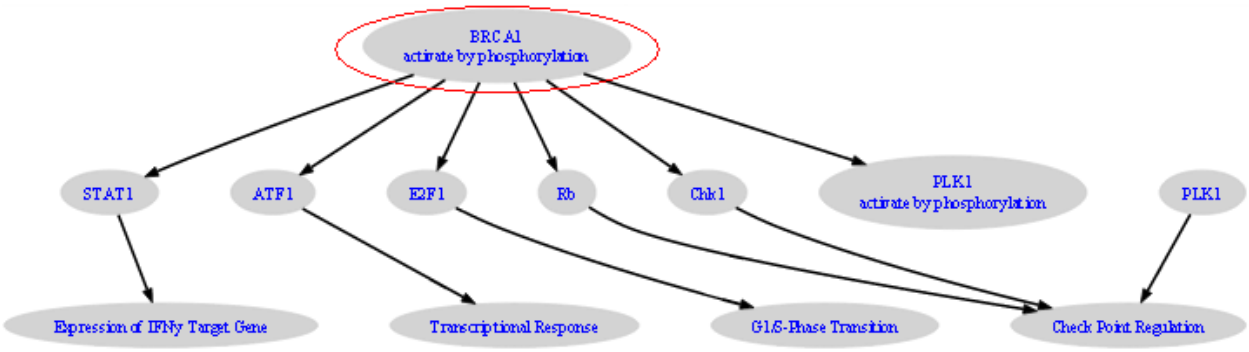
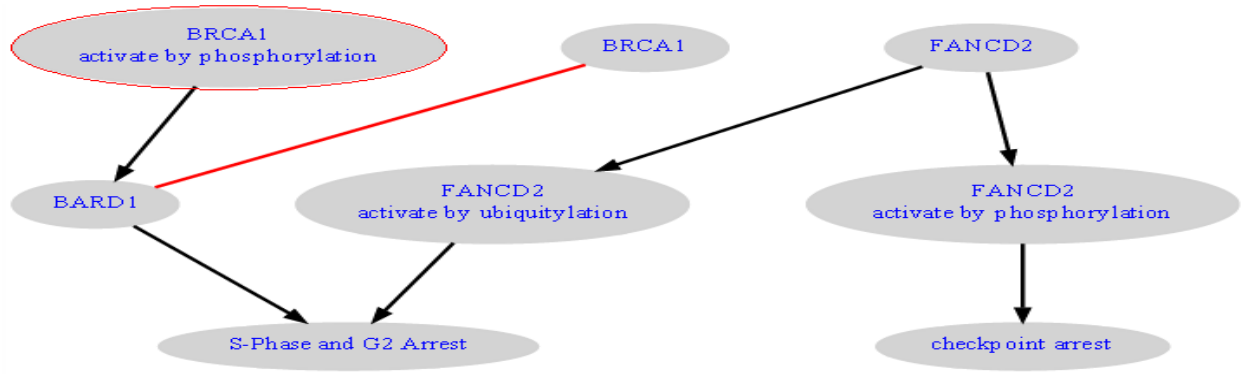


Figure 59 Sample Graph Generated from Selected Experiment(s)

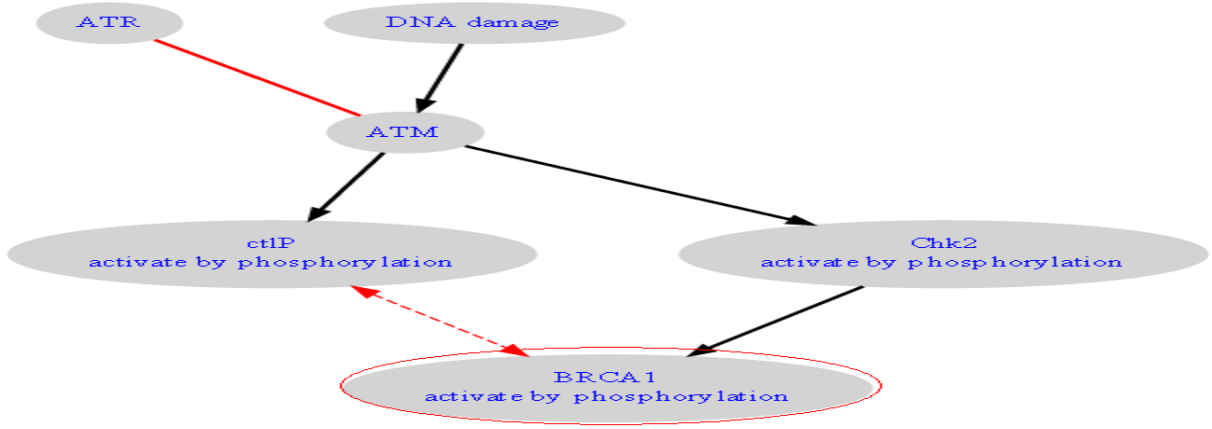
This figure shows the graph generated from the experiment(s) selected. The graph in this figure comes from the combination of the following experiments shown below.



Sample graph generated from experiment 1 stored in the database.



Sample graph generated from experiment 2 stored in the database.



Sample graph generated from experiment 3 stored in the database.

All graphs have a common node which is the “BRCA1 activate by phosphorylation”.

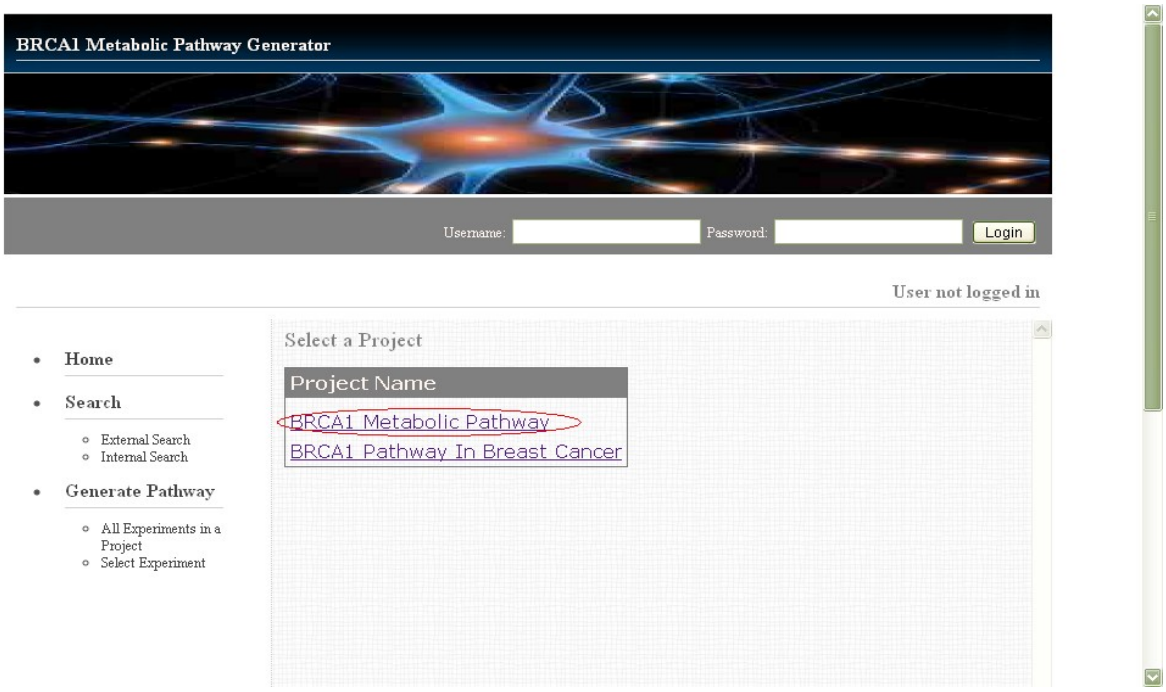
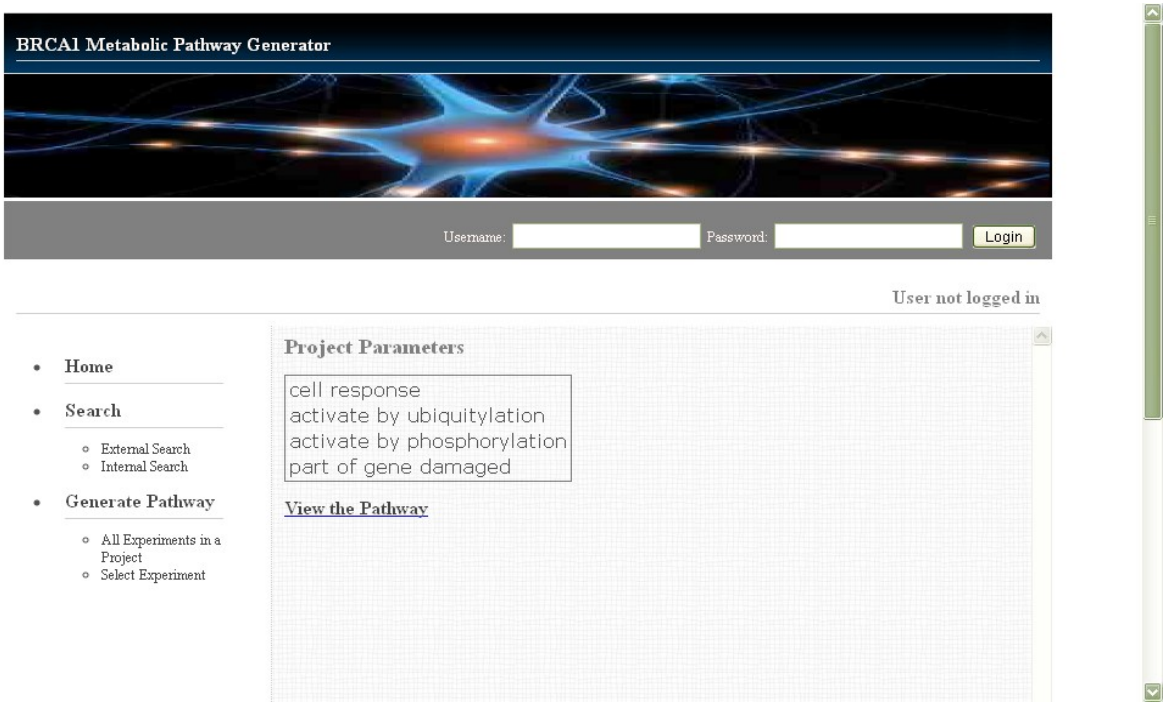


Figure 60 Generate Pathway – All Experiments in a Project

This figure shows the interface for generating the pathway from selected project. The system will generate the graph of all experiments in the selected project.



The figure shows the list of all parameters in the selected project.

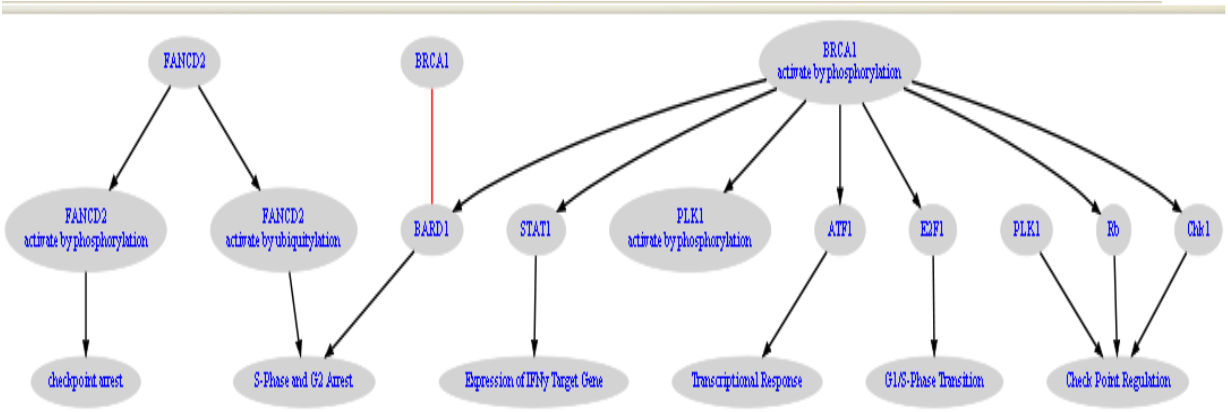


Figure 61 Sample Graph Generated from the Experiments in the Selected Project

This figure shows the graph generated from the selected project.

VI. Conclusion:

BRCA1 Metabolic Pathway Generator is an information system that store and generate the pathway of a BRCA1 gene. The system generates a simple graph that is based on the experiments created by an expert. The generated graph is greatly dependent on the values of parameters as well as the values of the rules. The rules consist of the source, relation, target and relationship that will consequently form the pathway. Any input value is case sensitive, for instance the string “brca1” is different from the string “BRCA1” and consequently it represents two different nodes in the graph.

The system also uses the graphviz tool to visualize the graph of the pathway in an experiment. It also creates a graphical output file specifically a .svg file to show each node and relationship with other node in a diagram to the user’s browser.

VII. Recommendations:

The system can be further improved if the user can view the pathway using larger images when there are lots of experiments involved in the pathway. It would be better if the user can save it as image files (jpg, png, etc.).

Another improvement would be if the user could view the pathway from the specified parameters.

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