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# REPOSITORY OF MALARIA DRUGS AND INSECTICIDE RESISTANCE

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*Abstract*— **Resistance mechanisms are tactics deployed or developed by an organisms to suppress, skip or bypass the effects of treatments administered to render it action less. Several literature has shown that both the malaria parasite and her vector resists the effect of antimalaria drugs and insecticides respectively. The specie with the highest occurrence of resistance to insecticides and drugs are the West African *Anopheles gambiae* (A. gambiae) and her parasite *Plasmodium falciparum (Fp)*.**

**Two major resistance mechanism identified in *Anopheles gambiae* are the target site resistance mechanism and the detoxification enzyme-based resistance mechanism (Hemingway et al., 2000). *Plasmodium falciparum* secrets excess glucose to resist the effect of tetracycline while high rate of efflux is found to be responsible for Chloroquines, Artemisinin and resistance.**

**This research sought to build a repository that will house the computationally inclined work/ projects, thesis, models and/ or systems of *Pf* drug resistance and *A. gambiae* insecticide resistance. The repository involves three main activities which are uploading fresh *in-silico* projects, searching for projects of interest on the repository and downloading such data into hard or external disk drives or other storage devices. This kind of work provides easy access and insight to existing *in-silico* models and projects on *pf* and *A. gambiae* resistance, makes it interesting and easy to peruse and provides opportunity for users to mine Information including data collection, accumulation, assembling, compiling, formulating, deriving, reporting, producing as provided by the authors/ owners of the research in consideration.**

*Keywords* — ***in-silico*, repository, vector, resistance mechanisms, specie, *anopheles gambiae*.**

## I. INTRODUCTION

Resistance is the ability of something to be able to suppress or make ineffective the effects of external stimuli introduced into its environment (internally or externally).

Resistance in mosquito species and her parasite has posed a serious threat to their human host and the medical society at large has been trying to find solution to this challenge. This study focuses on the most common of all the malaria vectors and parasites in West Africa. The *Anopheles gambiae* and the *Plasmodium falciparum* are the most common resistant specie worldwide; due to the way the genes have adapted to the effect of chemical compounds on them. Several efforts have been made to control the spread of resistance.

Prevention of malaria and other mosquito-borne diseases depends in large part on vector control and usually involves the use of insecticides. Insecticide-based methods include insecticide-impregnated bed nets, as well as more obvious applications such as indoor or aerial sprays and water treatments. However, the emergence and spread of insecticide resistance poses a serious threat to the sustainability of current control efforts, with several insecticide classes already showing reduced efficacy in controlling disease vectors in the field. Thus, there is a clear and urgent need for improving the sustainability of current insecticide-based control interventions as well as for exploring alternative, non-insecticidal methods for controlling major vectors (Vontas et al., 2010). Creating a repository refers to making available a location for storage, for the safety or preservation of computationally inclined research work that has been carried out on resistance of *Pf* to antimalaria drugs and A. gambiae to insecticides.

Current molecular, cellular, and genomic methods are now applied to the mosquito because of its importance as the major vector of human malaria in the endemic areas. An important focus of such studies is the immune defense system of the mosquito, which may be implicated in the response to invasion by the *Plasmodium* parasite and, therefore, in the success or failure of malaria transmission (Dimopoulos et al., 2002).

## EVOLUTION OF INSECTICIDE RESISTANCE

The evolution of insecticide-resistant insects provides evolutionary biologists with ideal, contemporary model systems for studying how new adaptations can be very rapidly acquired. There is therefore great interest in the use of the tools of molecular biology to elucidate the mechanisms of insecticide resistance.

A few cases of insecticide resistance were investigated at the molecular level during 1990s to mid 2000s using 'traditional' molecular techniques. The number was limited because essentially only those cases involving known genes that could readily be cloned by heterologous PCR or reverse genetics were tractable. Three types of mechanism were revealed by these early studies, two involving enhanced detoxification of

the insecticide and one rendering the target site for the insecticide insensitive to its effects (Oakeshott et al., 2003).

## II. LITERATURE REVIEW

*Physiome model repository* is a convenient repository that aimed at improving collaboration in model development and dissemination amongst the scientific community**.**

Her objectives are to promote the sharing of models with their revision history intact. Furthermore, collaboration between several researchers is often required during the development of a model. Collaboration on a model can be greatly simplified by a tool which records the change history of a model, and makes that history available to other collaborators. Finally, once a model is ready to be published, it must be indexed and presented so that it can be easily searched for and viewed, thereby avoiding unnecessary duplication of modelling efforts.

The methodology adopted were use the Plone content management system to provide the indexing used for power searching: specific pieces of information are drawn/ pulled out of certain file types when making exposures and added to the searchable indexes like;

1. User access control for all workspaces in the repository: users who can read from and write to a given workspace, and also controls the visibility of exposure pages
2. Manages the interface workflows: state transitions (private to public to publish) and allows repository curators some level of oversight and control.

**Results:** PMR2 is accessible to the end user over a web interface. Exposure pages in a PMR2 based repository can be accessed simply by entering the URL of the repository into a web browser. PMR2 has been used to create the CellML Model Repository, which currently contains over 500 CellML models and can be viewed at http://models.cellml.org/

*Repository of antibiotic resistance cassettes* **aimed at making a knowledge repository of antibiotic resistance gene cassettes (an important mechanism for the spread of resistance) available to the wider research community and to allow researchers to annotate sequences containing gene cassettes using the system and contribute new entries to the repository as these are found.** **http://www2.chi.unsw.edu.au:8080/rac/**

Her objectives include constructing a central free repository of known cassettes conferring antibiotic resistance, using standard nomenclature systems where these have been established and listing alternative names where appropriate. Provision of accurate and consistent annotation of gene cassettes in DNA sequences containing cassette arrays using the nomenclature systems defined in the repository and a process for assignment of unique names for newly sequenced antibiotic resistance cassettes in MRI consistent, with existing nomenclature systems for adding new cassettes to the repository.

Methodologies adopted include:

1. Updatable RAC with newly identified cassettes, including those submitted by users, and offers a central location for the community to share knowledge.
2. The lexical recognizer uses BLASTn to identify occurrences of any feature from the FDB in a sequence.
3. Gaps in annotations are manually reviewed and those found to correspond to novel cassettes are assigned unique names.

**Result:** An online knowledge base for microbiologists studying antibiotic resistance was developed which provides convenient access to the Attacca automatic annotation engine that allows users to easily and accurately annotate cassette arrays in bacterial DNA sequences.

IRBASE is a system that aimed at becoming a global repository for insecticide resistance data. Her objectives are to make available a relational database based on the Mosquito Insecticide Resistance Ontology (MIRO) and to avail users to be able to use the website to search and retrieve data. Methodology include using free and open source software (FOSS) to develop and maintain IRbase.

Results: Data can be submitted to IRbase on-line by using a web interface or off-line by filling in a spreadsheet. Users may use the website to search and retrieve data using a single or a combination of search criteria (ontology terms & dates) can be used. Matching results can be displayed on screen, exported to a tab separated file for further analysis, or visualized using color coded Google maps.

## III. STATEMENT OF THE PROBLEM

Around the world, the malaria situation is serious and getting worse. Malaria threatens the lives of 40% of the world's population – over 2 200 million people. Each year, there are an estimated 300-500 million clinical cases. Malaria is estimated to kill more than 1 million people annually, the majority of whom are young children. Ninety per cent of malaria cases in the world occur in Africa south of the Sahara. Children under 5 years of age and pregnant women are most affected by malaria. It is one of the leading causes of death among young children. Together with pneumonia, diarrhea, measles and malnutrition, malaria is responsible for over 70% of deaths in young children especially in developing countries. Malaria during pregnancy causes severe maternal illness and anemia, and is also associated with low birth weight among newborn infants, a leading risk factor for infant mortality. Malaria's cost to human and social well-being is enormous. The mosquito-borne disease typically strikes its victims not once but repeatedly. As a result, workers' output is diminished, and children miss school, often for periods of a week or more at a time. The economic loss from malaria was estimated at US$2 billion in Africa alone in 1997. Malaria is a

major cause of poverty, and poverty exacerbates the malaria situation. Taken together, the effects of malaria on lives and livelihoods are devastating for economic progress in hard-hit countries (UNICEF, 2000). Therefore, more eradication and control strategies are needed to counter the effects and damages caused by these diseases. Thus, studying resistance mechanisms both in *Pf* and in *A. gambiae*, gathering all the mechanisms together as a bunch at a goal for the purpose of further studies and research on how to improve chemical combination for insecticides and merging cocktails of compounds in drug to target detoxification genes may require a system or a product which will eradication difficulties in accessing related research works and journals, articles, books and thesis of researches that have been carried out, concluded and published in this area which may be useful for researchers who aim at working in this research area.

We aimed at developing a web-based repository for *in-silico* models, thesis, projects, books and journals of resistance mechanisms of *Plasmodium falciparum* to drug and *anopheles gambiae* to insecticides.

The following objectives were used to achieve the aim of this project stated above:

1. Design of a web-based interface that can gather users' information in the repository for identification and authentication purposes.
2. Building a module that cater for upload of journals, thesis, books, articles and other relevant materials was implemented in the repository
3. Design a module where users can download related research paper and journals.
4. Development of a querying technique and interface that permits users to search keywords and subsequently mine Information. Such mining include data collection, accumulation, assembling, compiling, formulating, deriving, reporting and producing, as provided by the authors/ owners of the research in consideration.

## IV RESEARCH METHODS

1. Bundling of resources (articles, journals, books, thesis, chapters and term papers) together to enable sharing of knowledge and methods between different individuals.
2. We used Microsoft ASP.NET for the front-end design (interfaces and the appearance of controls on the web forms). This is one of the new tools around for web-based systems and it is easy to combine with VB.NET. Visual Basic.NET was used for coding the major functionalities when events are raised (middle ware). Microsoft SQL Server 2008 was used as the Database management software (back end). Internet Information Service version 7.5 (IIS 7.5) was also used as the web server to aid client-server communication.

## V RESULTS

The System developed has ten modules which takes care of download of related journals for work, registration of new users, resetting users' passwords, searching of uploaded articles present in the database, uploading, viewing of uploaded journals/articles and editing of users' profiles. Articles can be searched for in the repository either by the author(s) name(s) or the title of the work. Results are displayed from the database as a grid view on the page.

Figure 1: GUI for the Registration Page

Figure 2: GUI for searching stored articles in the repository.

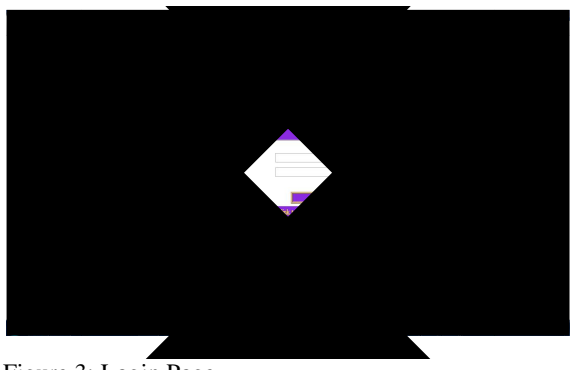

Figure 3: Login Page

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## V. TABLE DESIGN

TABLE 1: FILEDATA TABLE STRUCTURE

| FIELD | DESCRIPTION | DATA TYPE | KEY | ALLOW NULL |
|---|---|---|---|---|
| Uploader | Keeps the users who upload documents by their user names | Varchar(40) | | No |
| Title | Holds the record of the title of the article saved | Varchar(2000) | | No |
| Content_type | Captures the type of document saved which can be pdf file or doc file | Varchar(30) | | No |
| Filesize | The field where the file length in MB (approximated to 2 decimal places) of uploaded document is saved, files more than 150MB will not be saved. | Varchar(30) | | No |
| Filename | The name of the file generated by the system is stored in this field. | Varchar(100) | | No |
| Data | This stores the url (file path) of stored documents in the server folder for easy retrieval. | Varchar(500) | | No |

TABLE 2: REGISTRATION TABLE STRUCTURE

| FIELD | DESCRIPTION | DATA TYPE | KEY | ALLOW NULL |
|---|---|---|---|---|
| Name | Stores the full name of users for record purposes and for extra | Varchar(200) | | No |

***Registration:*** This table stores the necessary information of newly registered users. The basic structure of the table also consists of two basic fields necessary for login; the username field and the password field. The password field holds the encrypted password of users.

| | | | | |
|---|---|---|---|---|
| | identification | | | |
| Sex | Captures the gender of users (male or female) | Varchar(10) | | No |
| DOB | DOB field (meaning date of birth) stores the birthdays of users | Varchar(15) | | No |
| Nation | Captures the country where user has citizenship | Varchar(30) | | No |
| Stage | The academic level of users are stored in this field; the levels are masters, doctor, grad for a graduate, professor and student and others | Varchar(20) | | No |
| UserName | Captures the username of users required for logging in | Varchar(20) | | No |
| Email | Stores the email addresses of users; required for the reset of password. | Varchar(150) | | No |
| Password | Field for capturing the encrypted passwords of users | Varchar(15) | | No |

***Work*:** Work table stores the summarized detail about the work done by the researcher who uploaded the work; it also captures some description of what will be seen in the article.

TABLE 3 WORK TABLE STRUCTURE

| **FIELD** | **DESCRIPTION** | **DATA TYPE** | **KEY** | **ALLOW NULL** |
|---|---|---|---|---|
| Title | This field holds the title of uploaded articles | Varchar(500) | | No |

| | | | | |
|---|---|---|---|---|
| Author | This field captures the author(s) of the project work | Varchar(500) | | No |
| Abstract | Captures the short detail of the project work | Varchar(8000) | | No |
| Aims | The aim of the project is being captured in this field | Varchar(8000) | | No |
| Objectives | Captures the objectives of the research work | Varchar(8000) | | No |
| Methodology | Holds the information about how the project was executed most importantly, the methods adopted. | Varchar(8000) | | No |
| Results | Captures the results of the project | Varchar(8000) | | No |
| Conclusion | The conclusion of the project work being captured here | Varchar(8000) | | No |
| Upload_Date | Captures the date which work was uploaded | Varchar(50) | | No |
| Uploader | Captures the identity of the user that uploaded the article | Varchar(30) | | No |

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