Development of an electronic laboratory notebook for structure-based drug design.

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Abstract

Dissection of the 3D-structure of macromolecular targets for the design and synthesis of new drugs with high specificity, comprises a series of multi-disciplinary approaches *in vitro*, *in silico* and *in vivo*. Recording and maintaining an up-to-date file with the data derived from the methods applied is of great importance, especially, after the advanced instrumentation used nowadays and the vast amount of data generated [1].

Our work focuses on the development of a database and a software tool that follows the individual steps of a **structure-based drug design approach** (*Figure 1*) for the recording, storage and evaluation of the data produced at each stage.

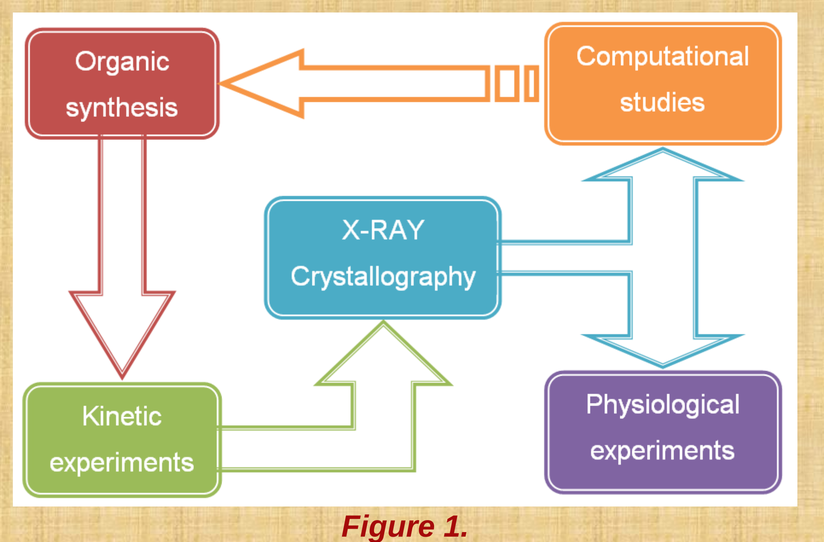

Figure 1.
The structure-based drug design approach used for the development of the electronic laboratory notebook.

System requirements

The software life cycle development process (*Figure 2*) was employed to record the needs of potential users. The requirements for the application were the following:

- **Experimental data entry**
  (e.g. organic compounds)
- **Data handling**
  (e.g. sorting, exporting)
- **Routine calculations**
- **Evaluation of results**
- **Targeted queries**
- **User management system.**

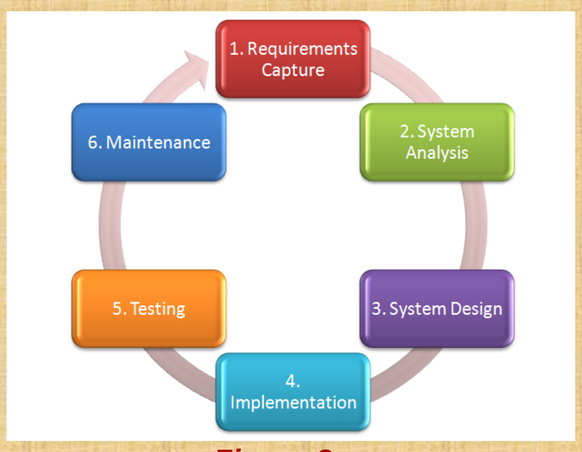

Figure 2.
The software life cycle.

The potential users and part of their requirements are summarized in UML diagrams (*Figure 3*).

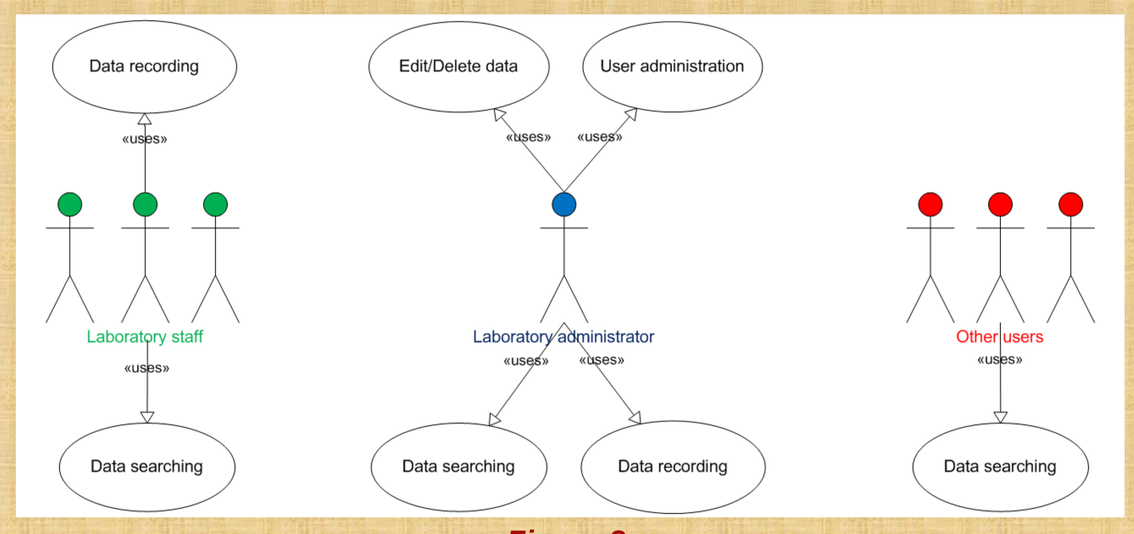

Figure 3.
Use case diagrams representing part of different users' needs.

System analysis & design

The application was developed in accordance with the aforementioned system requirements. It provides the users with the option to store data for:

- **Organic compounds to be tested as potential drugs**
- **Kinetic assays (IC_{50}, K_i)**
- **X-ray crystallographic experiments**
  (data collection, structure determination – structure refinement – structure analysis)
- **Information on synthesis**
- **Results from toxicological, physiological and clinical studies**
- **Drugs already launched in the market.**

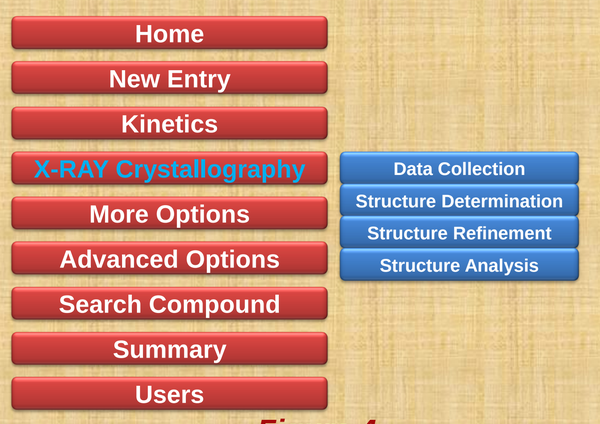

Figure 4.
Main menu of the application. The submenu of the X-RAY crystallography option is shown.

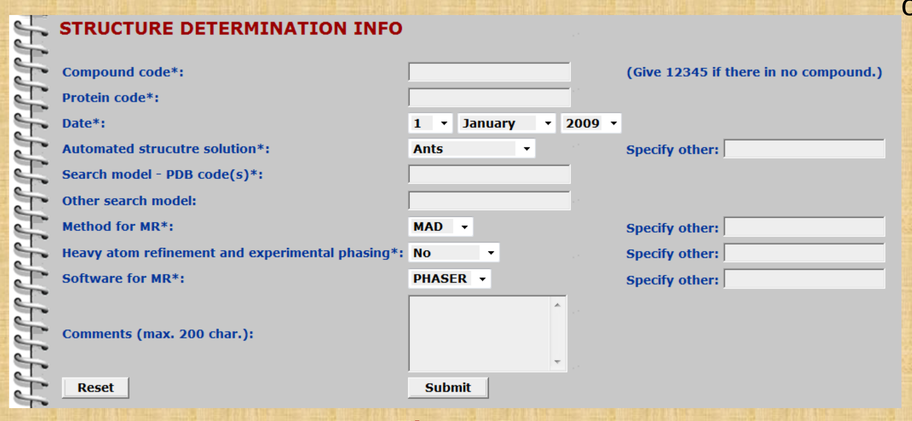

Figure 5.
Form used for structure determination info filing.

Data filing is organized in **forms** in which detailed information related to the samples to be tested as potential drug candidates is recorded.

Required fields, dropdown boxes, checking for numeric characters, uploading files, error messages, free text boxes make the application **user friendly** and easy-to-handle.

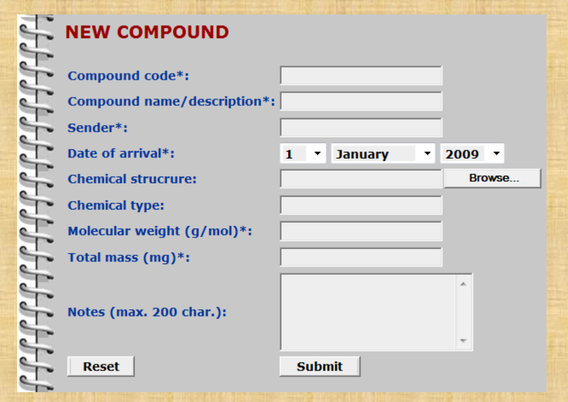

Figure 6.
Form used for new compound filing.

Previews of the individual forms are presented in *Figure 5, 6*.

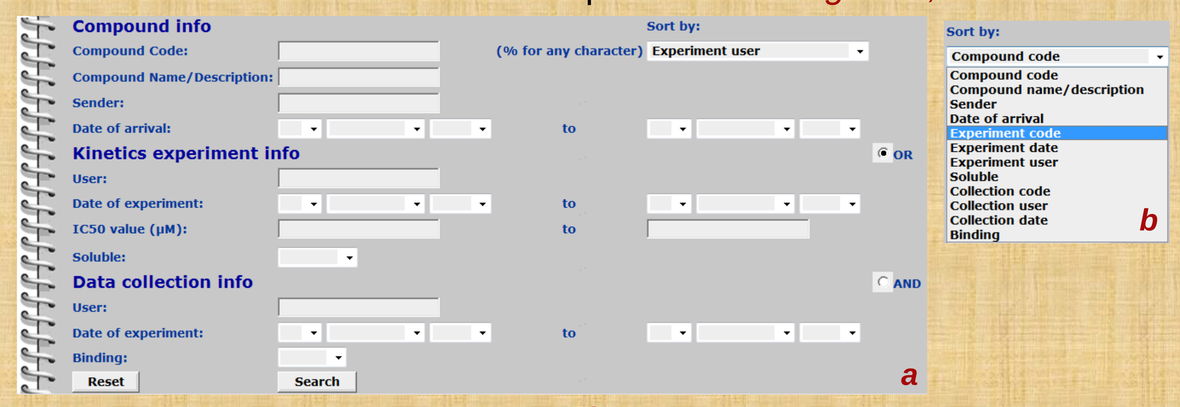

Figure 7.
Form for searching data with multiple filters, boolean operators and sorting parameters.

The electronic laboratory notebook gives user the option to:

- **Search with multiple filters (*Figure 7a*)**
- **Sort (*Figure 7b*) and export results (e.g. Excel files)**
- **Handle efficiently the available records (*Figure 9*)**
- **Connect to related online DBs for data mining**
- **Edit/delete data**
- **Manage the user system (*Figure 8*)**
- **Have access to online help**
- **Avoid routine calculations.**

Figure 8.
Preview of the form used for adding a new user.

Figure 9.
Preview of results for compounds filed in the database.

Technical characteristics

The database is called "lab_book" and consists of 15 tables that are associated through the fields "**compound_code**" and "**protein_code**", the primary keys of tables "sample" and "protein", respectively. Insert( ), update( ) and delete( ) are the main operations on the database tables. The application is **flexible** and **compatible** with multiple operating systems as it is web-based (opens in a web browser). In addition, it is implemented in PHP, HTML, SQL and JavaScript and runs on the Apache server.

Acknowledgements

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References

[1] C. Stephan et al. Proteomics 2010, 10, 1230-1249.