Laboratory information system for pharmacological data
Automated reporting feature

Jonas Berglund
### Title (English)
Laboratory information system for pharmacological data - Automated reporting feature

### Abstract
Development of cancer drugs is usually done in a highly automated process generating large amounts of data for potential drugs. The data is managed in a Laboratory Information System for processing and evaluation. Studying dose-response relationships is central in determining effective levels of dosages for these drugs. This degree project involved the implementation of various reports to study the dose-response relationship, as well as preparing a general system for data extraction to 3rd party applications from the Laboratory Information System.

### Keywords
Laboratory information system, reporting, IC₅₀, dose-response, data extraction, survival index

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### Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>BIRT</td>
<td>Business Intelligence and Reporting Tools</td>
</tr>
<tr>
<td>EC50</td>
<td>Half maximal Effective Concentration</td>
</tr>
<tr>
<td>IC50</td>
<td>Half maximal Inhibitory Concentration</td>
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<tr>
<td>FMCA</td>
<td>Fluorometric Microculture Cytotoxicity Assay</td>
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<td>HTS</td>
<td>High Throughput Screening</td>
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<tr>
<td>LIS</td>
<td>Laboratory Information System</td>
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<tr>
<td>ORCA</td>
<td>Optimized Robot for Chemical Analysis</td>
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<tr>
<td>RCP</td>
<td>Rich Client Platform</td>
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<tr>
<td>SI%</td>
<td>Survival Index Percent</td>
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1 Introduction

Chemotherapy, the use of drugs to kill cells, is a commonly used cancer treatment. It is usually used as a complement to surgery and radiation therapy. However, the utility of chemotherapy is limited by side effects and drug resistance, which demands the emergence of new drugs. Development of new drugs is performed via High Throughput Screening (HTS), an approach where several thousands of substances are tested regarding their cytotoxic effect.

At the division of Clinical Pharmacology, Uppsala University, compounds are screened for cytotoxic activity utilizing HTS; cancer cells are treated with tens of thousands of substances in order to find effective drugs[1]. This process generates vast amounts of information that must be recorded, such as biological sample characteristics, substance concentrations and cell survival measures. The information is handled by a Laboratory Information System (LIS). Purposes of a LIS are (among others) to facilitate the laboratory workflow by handling standards and keeping data consistent. To be adoptable to new circumstances and functionality requested by the users it needs to be highly configurable and extensible.

Today an in-house developed LIS called Brunn serves the screening activity at the department (see Figure 1). It rests on the Bioclipse software base, an application for bioinformatics projects. Brunn not only stores but also gathers screening results, and provides basic analysis functionality. Brunn's graphical user interface lets the user manage the microtiter plates used in the screening process, and also provides a general view of existing drugs and cell lines. However, it lacks more advanced graphical data compilations. It is for example common to test the activity at different concentrations of interesting chemical compounds to see the concentration dependency of the cytotoxic effect. The in vitro measured cytotoxic effect is predictive for the clinical drug response of the tumour[2]. Precious time would be saved if this dependency could be visualized in the LIS. Furthermore, results need to be exported, both to other functions in Bioclipse and also third-party applications like Matlab.

The aim of this degree project is to add this functionality to Brunn by enabling the generation of various reports and preparing a general system for extraction of data from the LIS. This report will initially go through some theory behind pre-clinical drug development and what kind of data is generated in the process, followed by a presentation of Brunn, the LIS handling this data. Accompanied by specifications for data extraction and report construction comes the design and implementation, the actual contents of this degree project. Finally a discussion about reporting as a concept will be made, after some possible future usage areas for Brunn has been explored.
Large libraries of chemicals are screened for their ability to modify a chosen target. Candidate compounds are reduced to hit compounds with target modifying propensities. These are further analyzed and reduced to the most promising lead compounds. Lead compounds are used as starting point for chemical modifications to improve certain features, i.e. potency and selectivity, before advancing to biological or clinical trials. The Brunn LIS supports the screening activity in this drug discovery and development process.

2 Pre-Clinical Drug Development

The first step in drug development is identification of compounds in a chemical library having the desired activity. In cancer drug development, cells are exposed to chemical compounds whereupon cytotoxicity is measured by estimating cell death via fluorescence. This is an automated high throughput process generating data that is processed and analyzed in the LIS. At the division of Clinical Pharmacology, the process is automated using a robotics system: Optimized Robot for Chemical Analyses (ORCA). The cytotoxicity assay used is called FMCA and is highly suited for HTS. Potential drugs are evaluated by testing several compound concentrations and analyzing the dose-response relationship. Typically the data analysis step aims to determine the IC50 value which is used to compare the efficacy of compounds.
2.1 ORCA and FMCA

The major instrument in the HTS process is an automated machine, an Optimized Robot for Chemical Analyses (ORCA) equipped with a reader (FLUOstar Optima) for Fluorometric Microculture Cytotoxicity Assay (FMCA). The assay (Figure 2) uses drug prepared 96- or 384-well microtiter plates to which cell suspension are added. Plates are prepared with drugs using the ORCA which transfers compounds onto the plate from a masterplate containing stock solutions of the compounds to be tested. Plates are identified by the assignment of a unique barcode by the ORCA. After 72 h incubation followed by washing, Fluorescein Diacetate (FDA) is added followed by an hour of re-incubation. Cytotoxicity is then measured by the fluorescent signal generated by hydrolysis of non-fluorescent FDA into fluorescent fluorescein by cells with intact plasma membranes after the drug exposure. From this measure a Survival Index (SI%) is calculated as the fluorescence in the wells in percent of control wells (untreated cells) with blank values (only drugs) subtracted. This is made in a few replicates for each concentration to get a reliable value. A successful assay relies on quality criteria based on these replicates.[3]

![Diagram of ORCA and FMCA process](image)

**Figure 2:** A masterplate with stock compound solutions are prepared based on one of many predefined plate layouts for the plate type; 96 or 384 wells. Drugs are transferred from the masterplate onto a set of plates which is then seeded with cell suspension. After incubation, centrifugation and washing, FDA is added. Yet another incubation lets the FDA take action and cell survival can be measured by fluorescence. The cell survival gives an idea of drug potency. Picture is reproduced with permission from Jonathan Alvarsson, Uppsala University.
2.2 Data Analysis

The data from the HTS is analyzed in the LIS to identify hit compounds for further evaluation. By testing several compound concentrations in the same assay an IC50 value is generated to assess the potency of the compounds. The IC50 value indicates what concentration is needed to inhibit a biochemical process by 50%, and is estimated from the observed effects of the different concentrations. Dose-response curves are generated to visualize the concentration-effect relationship and ease the selection of interesting compounds.

2.2.1 Definition

Drugs affecting receptors can do this in two ways; the agonistic or the antagonistic approach. An agonist has an ability to bind to and alter the activity of a receptor, which is known as the efficacy of an agonist. This property distinguishes them from antagonists that binds to a receptor but do not alter its activity, instead blocking the agonist-mediated response. When the potency of an agonist is defined, this is usually done by its EC50 value, while the potency of an antagonist is usually defined by its IC50 value. As this may indicate there is no fundamental difference between the terms, but rather purely a difference in what abbreviation is used. This becomes clearer as usually biological responses are measured and not direct receptor affinity, making the differences less important and the response more important.[4]

EC50 is the half maximal effective concentration and measures the effectiveness of a drug candidate. It is defined as the concentration for which 50% of the maximum response of an agonist is observed.

IC50 is the half maximal inhibitory concentration and measures the effectiveness of an antagonistic drug candidate that inhibits biological function of an agonist. It indicates what concentration is needed to inhibit a biochemical process by 50%.

2.2.2 Determination

Determining EC50 and IC50 values is useful for comparing potency of drugs with similar efficacies and are central to determining “safe” levels of dosages for drugs. Lower values of EC50 and IC50 indicates higher potency and is often associated with fewer side effects, something that is highly coveted in drug development. Measuring of these values involves observing responses in consecutive experiments with varying concentrations. If the concentration measures are transformed into a logarithmic scale they typically follow a symmetrical sigmoid curve, where the effect increases rapidly in a relatively short concentration interval. The inflection point of this curve, in which the effectiveness slows with increasing concentration, is referred to as the EC50 value. If an inhibitor is used the response decreases, creating a downhill dose-response curve, making the midpoint referred to as the IC50 value.[4] This project is based on such experiments, and I will henceforth exclusively use the term IC50. Figure 3 shows a dose-response curve for cell survival with IC50 value marked.
IC50 can be mathematically determined from the dose-response curve by fitting a parameterized model to the curve:

$$E = E_0 + \frac{E_{\text{max}}}{1 + (IC50/D)^{\text{Hill}}}$$

where E is the observed effect, E0 is the lowest observed effect, Emax is the highest observed effect, D is the dose and Hill is the largest absolute value of the slope of the curve. [5]

However, in these low resolution experiments (usually just five values) it is better estimated directly from the graph. This is done with linear interpolation that is not as prone to overfitting:

$$\frac{IC50 - D_1}{D_2 - D_1} = \frac{E_50 - E_1}{E_2 - E_1} \implies IC50 = (E_{50} - E_1) \cdot \frac{D_2 - D_1}{E_2 - E_1} + D_1$$

where E1 and E2 are the two consecutive values on each side of the value where the effect drops below 50% (E50), and D1 and D2 are the two consecutive concentrations corresponding to the E-values.
3 The Brunn LIS

The Brunn LIS serves the screening activity at the department by handling data from the ORCA. The reporting feature and data extraction tool implemented in this degree project are integrated into Brunn to further strengthen the plate analysis and evaluation. Brunn is a plug-in project to Bioclipse, an open source workbench aiming at providing all necessary functionalities for chemo- and bioinformatic projects in one application. The ability of Bioclipse to provide opportunities to create plug-in projects, comes from its inheritance of Eclipse functionality. Eclipse is an open source software development platform for developing Java applications. The Eclipse Rich Client Platform provides possibility to develop programs based on the Eclipse Platform, like Bioclipse.

3.1 Eclipse

Eclipse is an open source software development platform primarily made for developing Java applications, but has been widely used and grown to be much more since the original creation in 2001 by IBM. It has an extensive plug-in system that can extend its capabilities, and new projects are constantly developed by the Eclipse Community (individuals and organizations from the software industry developing Eclipse), adding new functionality. In 2004 the Eclipse Foundation was created and assumed the responsibility from IBM. The Eclipse Foundation also provides the Eclipse Rich Client Platform (RCP); an application framework for developing programs based on the Eclipse Platform.[6]

3.2 Bioclipse

Bioclipse is an open source workbench for chemo- and bioinformatics based on the plug-in architecture of Eclipse RCP. By these means the platform inherits the functionality and visual interface from Eclipse, just as any RCP-developed application. Bioclipse aims at providing all necessary functionality for a chemo- or bioinformatic projects in one application. For example it can handle sequence, structure and spectrum data. Via plug-in projects under development Bioclipse is constantly improving and providing additional functionality. It is being actively developed as a collaboration between the Proteochemometric Group in the department of Pharmaceutical Biosciences at Uppsala University and the Steinbeck Group at the EBI.[7][8]
3.3 Brunn

Brunn is an in-house made LIS developed by Jonathan Alvarsson (currently at the department of Pharmaceutical Biosciences). It serves the screening activity at the department by reading, processing and storing the plate data generated by the ORCA. In the graphical interface of Brunn (Figure 4) users can open individual plates from an overview for manual curation and quality assessment. Information about masterplates, cell lines and compounds are also available and can be treated in a similar manner.

![Image of Brunn GUI]

**Figure 4:** The GUI of Brunn. In the Brunn explorer view to the left, objects (e.g. masterplates, plates, cell lines) are created and maintained. These objects can be visualized in the right view, as a plate in this example.
4 Specification

The aim of this degree project is to add functionality to Brunn by enabling the generation of various reports and preparing a general system for data extraction. The project consists of three main parts with different requirements to be met. An API for data extraction should be able to transfer data between Java applications and web services. Experimental data is modeled in finer detail than is needed for further processing in third party application, thus an API that models data at a higher level is needed. The API should be a separate component of Brunn not relying on the processing made in Brunn, but directly access the database and extract necessary information. A report for each plate displaying dose-response curves and IC50 values for the compounds are also to be implemented, as is a report showing the masterplate layout. The latter should also provide a table to access compound names.

4.1 Data Extraction

The first task to be performed concerned an API for extracting data from Brunn to other software. Other software primarily refers to Bioclipe and Matlab. Today, only a simple copy to clipboard function is implemented in the GUI but a programmatic interface is needed as complement. The design should aim at a simpler structure with plates, wells, substances and functions; pure, basic and uncluttered. Figure 5 shows a prototype data model to be exported from the API. The 96 or 384 wells of a plate can contain one or more substances at different concentrations. Plate functions can be defined for a plate (e.g. average values of control and blank wells), and well functions can be declared for a well (e.g. survival index). The API should be used either directly in a Java application, or for network transfer via a web service. It accesses the database and extracts the data directly, i.e. without the need to launch a Brunn GUI.

![Class diagram](image)

**Figure 5:** Class diagram for a basic data extraction API. A plate holds many wells with any number of substances (usually one). Functions can be declared for plates (e.g. variation between wells with the same concentration of a compound) and wells (e.g. survival index).
4.2 Plate Report

Next in line after the data extraction task was the implementation of a mechanism in Brunn for automated report generation for evaluation of a plate. These are tasks that until now have been performed by manually transferring the data into excel and applying fixed macros. Time would be saved if this evaluation could be performed directly in Brunn. The report would desirably contain the functions declared for each plate with corresponding value, a chart showing the dose-response relationship and the IC50 value calculated from the values of concentration and cell survival. In Figure 6 an initial sketch of a plate report containing the desired information can be seen.

![Simple initial sketch of plate report content. A dose-response curve accompanied by underlying values and IC50 value for the compound.](image)

4.3 Masterplate Report

Plate preparation uses the ORCA robot which transfers compounds onto the plate from a masterplate containing stock solutions of the compounds to be tested, making it easy to produce a large number of plates from a single masterplate. Brunn models the masterplate as a template which specifies the type, location and concentration of drugs on the plates that will be examined. Since this layout is very important to know in the evaluation of each individual plate it would be convenient to get a visual view of this layout inside Brunn when a plate is accessed. Presenting it in a report makes it easy to print and bring to the laboratory as well as include as a complement to the printed plate report. The masterplate report should also list the compact compound identifiers (aka markers) and the corresponding real compound name, so markers on the plate can be identified as the correct drug.
5 Design and Implementation

This section thoroughly describes the design and implementation of the separate parts in the degree project. Possibilities, considerations and final solutions are presented. Data models and sample reports are supplied to visualize the results.

5.1 Data Extraction

Since Brunn rests on the solid ground of Bioclipse, a Bioclipse manager fitted the purpose of data extraction. A manager is a class responsible for handling persistent classes that contain the actual data stored in the database. The manager provides functionality for operations associated to the managed classes, such as creating them and establishing their relationships (a plate with wells with substances etc.), and has the comprehensive responsibility for them. This method of gathering the functionality in a few managers makes it easier to maintain the storage and retrieval processes with the database. The actual saving and loading of objects from the database is done with Data Access Objects (DAOs), also managed by the managers, which operates on one or a few persistent classes.

Via contact with Ola Spjuth from the development team behind Bioclipse I was provided with the basic structure for such a manager. The manager had to be extended with the desired functionality of reading data from the database and presenting it on a plate basis. This refers to the plate, its substances with concentrations and all declared functions for both the plate and the individual wells. This mainly involved a simplification and smaller rearrangements of the data, so that only the important data needed for the analyses were presented in a structured manner. The manager currently contains methods for extracting the barcodes for each plate stored in the database and extracting a plate with a specific barcode of those.

5.2 Reports

The software base of Eclipse was perfectly suited for developing the report in their own reporting tool BIRT. It provides an easy to use report design perspective inside Eclipse that lets developers easily design and integrate reports into applications. A predefined set of report templates are supplied to address a wide range of reporting needs, but reports can also be built from scratch.
5.2.1 BIRT

Eclipse Business Intelligence and Reporting Tools (BIRT) project is an open source software project providing reporting and business intelligence capabilities mainly for Java applications. Since 2004 it has been a top level software project within the Eclipse Foundation because of its ability to address a wide range of reporting needs. Its main purpose is to let developers easily design and integrate reports into applications. BIRT has two main components: a visual report designer based on Eclipse, and a runtime component that can be added to any application server. Furthermore an individual charting engine allows charts to be added to an application. Several data sources are supported such as JDBC¹, POJO², XML³, Web Services⁴ and Flat Files⁵. In this project the visual report designer was used for report layout (Figure 7). Report elements are basically dragged and dropped into the report and their properties changed in the graphical interface. The runtime component provides the same functionality but everything is done in a pure programmatic manner.⁹

Figure 7: Visual report designer perspective in Eclipse. BIRT reports are constructed using drag and drop technique from the palette of objects to the left. The large report view in the middle contains the constructed report layout. In the property editor view below the report, the object properties can be changed.

1 Java Database Connectivity; an API for accessing a database.
2 Plain Old Java Object; an ordinary Java Object.
3 Extensible Markup Language; user definable specification for creating custom markup languages.
4 Web APIs accessible over a network and executable on a remote system.
5 A database model as a plain text file.
5.2.2 Plate Report

Some design issues concerned what data to feed the report with, and where to get this data from. As previously mentioned there was a newly developed manager that could extract the data, and additional functionality could be implemented to process the data and present it to BIRT in a useful flavor. This would be convenient since BIRT supports JavaScript as data source format. However, the manager is designed to operate without having to open the desired plate in Brunn, which is very convenient if you are just interested in extracting the data. But this direct connection to the database implies a few drawbacks if used from inside Brunn to extract the data for the plate report. Namely, the same information is read twice; first by Brunn and then by the manager. The same inefficiency would of course arise if BIRT was fed directly from the database via JDBC. Instead of this double data extraction the report relies on data collected directly from Brunn, and does not use the manager to retrieve it. However, the manager will still be used to export data to other, third-party software.

What emerged as the best way to feed BIRT with data was that of storing to and retrieving it from flat files. This option meant processing of the data already read into Brunn and writing of it to flat files. BIRT can read the data into data sets that are represented by a header and corresponding values. Many data sets can be used in the same report, and they can come from the same data source but with different filtering and/or sorting applied. The processing primarily consists of rearranging already existing values into meaningful BIRT data set structures. However, the processing also included some calculations, the most important being the IC50 value that was calculated for each tested substance on the plate using linear interpolation.

The prepared data sets were then imported into the BIRT report and presented as side-by-side lists displaying name and IC50 value for each tested substance. A line chart with SI % plotted against concentration along with tables displaying the underlying values were also included. For easy-to-read purpose a line was drawn in the chart on IC50 to show where in the graph it can be read. Figure 8 shows the information in the report from one substance at a plate. Complete plate reports can be found in Appendix B and Appendix C.

![Figure 8: The entry for the substance tioguanin in a plate report. SI is plotted against concentration to obtain the dose-response curve. Where to read the IC50 value in the graph is marked by the red dashed line.](image)

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5.2.3 Masterplate Report

The implementation behind this report resembles the previous one for the compilation of individual plates, but no calculations are done. As before the data is written to flat files and read into BIRT datasets. To fit the look of a real masterplate this report is however in landscape format. Figure 9 shows the masterplate report for a 96-well plate, a report for a 384-well plate can be found in Appendix A. On the left is a list of marker names followed by the accompanying substance's real name. This is because the real names are often too long to fit in the grid layout representing the masterplate itself, which can be found to the right in the report. For each well on the masterplate the marker, its concentration and concentration unit are presented. For easier and faster overview the marker names are made bold.

![Masterplate layout](image)

**Figure 9:** A masterplate report showing the substance names and their layout on the plate. M denote markers which represent the substances on the plate, B denote blank wells (drugs, but no cells) and C denote control wells (cells, but no drugs).
6 Future Development Perspectives

There are two overall aims of the present research program in the research group; improving the efficacy of currently available pharmacological cancer treatment, and identifying new compounds with potentially improved efficacy[10]. Features in Brunn to help fulfilling these aims have been requested by the users.

6.1 Optimal Drug Selection for Treatment

The first problem is addressed by providing predictive information for selection of optimal drugs for individual treatment. For the integrity of patients the plates are anonymized during the analyses so no information can be directly related to individual patients. However, there exist a clinical database with patient information, into which data from the experiments should be integrated to function as decision base. This means that the combined information will be used to choose treatment for the patient. The API implemented for data extraction from Brunn will be used to perform this data transfer.

Figure 10: IC50 profile for finding resembling compounds. The y-axis holds the different cell types the compound has been tested against, and the x-axis represent the deviation from its average IC50 value for those cell lines.

6.2 Finding New Drugs

The second problem is addressed by the HTS approach previously described. From this large-scale screening for new compounds Brunn should be able to transfer IC50 values into a correlation database that holds IC50 profiles for the compounds. Study Figure 10 for example of an IC50 profile. An IC50 profile shows the effect of the compound on different cell lines and can be compared to profiles of known drugs to find resembling profiles. Supported by a dose-response curve comparison as seen in Figure 11, the profiles can be used to see which compounds resemble each other. Assuming similar dose-response curves and profiles represent similar mechanism of action, this may reveal the mechanism of action of new compounds where this is unknown[11][12].
Figure 11: Dose-response profile for comparison of compound actions. An IC50 profile alone can not distinguish between compounds with similar IC50 values but different dose-response relationships, but a dose-response profile can. NCI-H69 (purple) and CEM/VM 1 (orange) cell lines have similar IC50 values but completely different dose-response curves, indicating different mechanisms of action. This difference can only be established by consulting their dose-response curves.

6.3 Charting

An important aspect of HTS is quality control. Batch tests are performed to see if there are any systematic deviations in the screening system over time. It would be helpful if plate characteristics such as variation coefficients could be plotted over time as a support for the quality control process. Furthermore, in Brunn there exists the possibility for the user to define functions for plates. Instead of getting a chart displaying the dose-response curve for the drugs, it could be useful to see these user defined functions plotted instead. This could be accomplished by providing the user with the opportunity to choose which function to plot at runtime, something supported by BIRT.
7 Discussion

7.1 Environment
User feedback into the development process was easily obtained as the department not only hosts research people from the university, but also hospital employees; the end users of Brunn. Meetings with these people generated immediate feedback and requests for improvements and new features. This response was very useful, especially in the early phase of the project as it helped getting on the right track from the start.

7.2 Reporting
The use of BIRT for reporting was a new experience for both my supervisor and the people behind Bioclipse, so they followed it with interest to see if it really could be used for this purpose and how it would work. One implication of the Bioclipse team’s inexperience with BIRT was limited support from them, but an active development forum on the Internet provided answers to many questions that arose. Furthermore, the forum could be searched for already asked questions as well as tutorials for less experienced report designers.

According to contacts to the developers of Bioclipse in the industry, reporting is an important and coveted tool in analysis work. Thus, they are looking for a component to generate various reports. They have considered both JasperReports[13] and Crystal Reports[14], but consider BIRT as the most interesting alternative since it is based on Eclipse and is thus probably easy to integrate and run in Eclipse. For charting they have previously used JFreeChart[15], but will start using BIRT also for this purpose, much because of my positive experience with BIRT in this project.

7.3 Charting
Functionality for visualizing user defined functions for the plates has been suggested, but the actual need and desire in this statement remains unknown. After all the IC50 value and the dose-response curve is what is used for assessing drug potency. The BIRT report designer being used for creating the reports implies that functions must be declared before runtime in the report file. This makes it impossible to plot functions declared by the user unless they are manually added in the code. However, as previously stated, probably few functions will be used this way. Adding them in advance may be accomplished by investigating what functions may be used this way.
8 Acknowledgements

I would like to thank my supervisor post-doc Claes Andersson for providing the opportunity to conduct my degree project at Uppsala University Hospital in the research group Cancer Pharmacology and Informatics of the Department Medical Sciences. Thanks for your guidance and thorough examination of my report. Invaluable support and help has come from co-supervisor PhD student Jonathan Alvarsson regarding Brunn and programming, thanks for helping me when I got stuck. Special thanks to Ola Spjuth for providing manager code and discussions about BIRT and reporting in Bioclipse. Thanks also to professor Rolf Larsson for accepting to be my scientific reviewer, and laboratory technician Lena Lenhammar for introducing me with the laboratory workflow. A final thanks to other people at the department whose knowledge contributed to the formation of the reports, and to my opponents.
9 References


Appendix A  384-well masterplate report
Appendix B  96-well plate report

Dose-response report
for plate "96"

<table>
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<th>Function</th>
<th>Value</th>
<th>Function</th>
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<td>1440</td>
<td>ControlBlankRatio</td>
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Amuklein, IC50: 0.256 μM

C [μM] | 52%
0.02  | 82
0.1   | 57
0.5   | 39
2.5   | 13

Dosepencrin, IC50: 0.0489 μM

C [μM] | 52%
0.02  | 65
0.1   | 37
0.5   | 11
2.5   | 7

Tingnam, IC50: 31.6 μM

C [μM] | 52%
2     | 109
10    | 77
50    | 74
250   | 13

Melilirin, IC50: 11.8 μM

C [μM] | 52%
0.2   | 117
1     | 99
5     | 45
25    | 33

Viakrin, IC50: 0.083 μM

C [μM] | 52%
0.04  | 54
0.2   | 36
5     | 15
5     | 14

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Appendix C  384-well plate report