Development and Usability Evaluation of an Android Application for Mobile Analysis of Microplate Assays: A Review of Literature

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ABSTRACT
Microplate assays are currently analyzed using large, expensive and cumbersome microplate readers in laboratories. This review identifies and critically analyzes current and inexpensive mobile phone solutions as well as other broadly relevant applications in order to identify gaps in current knowledge. Usability evaluation methodologies are reviewed and Mobile HCI challenges briefly discussed to give context for future analysis. It is found that although current research has produced accurate and portable microplate reader applications using smartphones there is no evident research conducted into whether there applications are user-friendly and no user evaluations have been conducted. There is also no academically agreed upon evaluation environment although a usability laboratory environment is suggested for this research.

Keywords
Usability, Life Sciences, Chemical Assays, Smartphone

1. INTRODUCTION
This research endeavors to find an accurate, effective method of analyzing chemical assay plates using only a smartphone and a small dark box. The solution aims to not replace but rather complement, or make more available, current analysis equipment such as microplate readers. Chemical assay plates are used in life science research such as cell cultures and the detection of antimicrobial activity and provide the user with an apparatus in which different concentrations of a drug are placed in order to determine effectiveness. The plates are analyzed using a microplate reader that makes use of the absorbance of light as it is shone through the assay plate's wells and the solutions they contain.

The analysis of assay plates is an essential part of the many life science operations and can currently only be carried out by microplate readers that are often far too expensive for remote or underfunded laboratories. These laboratories desperately need a solution that will in the least do a preliminary analysis that determines whether it is worth sending an assay plate away for more accurate analysis. Due to the size and weight of current microplate readers they are far from portable and are often too fragile and expensive to warrant frequent transport. There remains a gap to be filled by a solution that can be used in both an educational, preliminary testing and field context that is mobile and sufficiently accurate for providing useful observations. A smartphone solution could provide a more user friendly, cost effective way of solving the problems faced by conventional, current microplate readers.

Unfortunately many laboratories in South Africa suffer from poor quality testing and lab equipment, a problem caused mostly as a result of being isolated and poorly funded [1]. Mobile phones, however, are growing increasingly common with increasing penetration levels throughout Africa [2]. This opens up an opportunity to leverage the phone's camera and processing power for laboratory use. This research could provide a solution to these labs by providing a robust, inexpensive measure to increase underfunded, remote laboratories testing capabilities.

This review investigates current mobile applications in the healthcare and life sciences realm and aims to provide background into current microplate reader applications and their strengths and weaknesses. This will allow a guided approach into the development of a solution to the research question and allow us to borrow concepts and design patterns from current applications that contribute to their success. This review also briefly investigates current knowledge surrounding designing of interfaces and human interaction with mobile applications in order to assist in the critical analysis of current applications and as a way to discover where possible shortfalls occurred. Finally this review assesses the various methods researchers have taken to evaluate their applications. Evaluation techniques and their different aspects are important as they provide insight into the effectiveness and viability of a solution which will be required when determining whether our solution solves our research question.

2. HCI WITH MOBILE APPLICATIONS
Since the early developments of mobile devices there have been concerns about the way humans interact with these ubiquitous, portable forms of computing. This section will address the challenges faced by mobile devices and present research on possible solutions.

2.1 General Mobile HCI

2.1.1 Challenges
Designing mobile applications for human interaction is a difficult problem and one that has been thoroughly research for many years. The challenges associated with mobile HCI must be identified if more usable and successful applications are to be developed in the future. Research into such an area was conducted by Dunlop. M. and Brewster. S. [4] who identify challenges as users being mobile, users not having formal training, devices having limited input and output devices, incomplete and varying context information and users being unfamiliar to the frequency of interruptions during mobile device use. The causes of these issues are created as a result of mobile phones being small with limited

input devices and unreliable and expensive connectivity to other services [5]. These challenges have been investigated individually, largely confirmed and elaborated on further by a number of independent studies [6],[7]. Dunlop M. and Brewster S's. research presents a concise description of Mobile HCI problems but fails to provide in-depth solutions to the challenges presented. Their work nonetheless is both relevant and valuable as it provides an understanding of problems that will need thought and addressing if one is to build a mobile application that is considered user friendly and useful. There are limited gaps in mobile HCI research problems as the majority has been sufficiently investigated.

2.1.2 Solutions

Many solutions to the challenges presented are dependent on the context in which the mobile device will be used. Huang K.Y. [6] presents some general suggestions including the use of alternative keyboards to the standard QWERTY layout as well as the use of a stylus to make basic input more reliable and accurate. The limited screen size on mobile devices is a difficult problem to overcome with Huang proposing a 3D orientated interface as a viable solution. Overall Huang's research investigates different challenges and their respective solutions in a thorough study free of bias and is relevant to the research question as it demonstrates the limitations of mobile devices and guidelines to work around such limitations when designing interfaces for mobile applications.

2.2 Interface design patterns

Interface design is crucial for mobile devices and the design or lack thereof is often the cause of an applications success or failure. Nilsson E. [7] has been instrumental in his research into addressing design problems and the patterns that can be used to solve them. His research identifies 3 main problem areas containing sub sections of which 6 are selected to be fully addressed. Horizontal scrolling on mobile devices is identified as a main problem area and is largely addressed by ensuring the correct screen orientation. These problems and patterns are revealed to be only some of many interface problems as other research [8] presents conventional interface problems that are carried over to mobile devices such as enabling frequent users to use shortcuts and offering informative feedback. The above two studies are considered to be highly detailed, well motivated and descriptive however less impressive in the testing and evaluation of such interface problems and their solutions. Experiments would be difficult to replicate given just the papers and respondents are criticized as not being representative of all user personas. There is opportunity for future work to be conducted into the validation of interface solutions. Despite the criticism the research is highly relevant as all mobile applications require interfaces and often face the problems described by these studies. How these design problems are solved often determines an applications success and solutions will need to be implemented and considered in the development of application proposed by the research question.

2.3 Key usability factors of Mobile applications

Usability is a fundamental part of a user's needs and is identified, alongside aesthetics, as one of the major factors contributing to pleasure of using products [9]. There is a large field of research dedicated to investigating usability and producing guidelines for developing usable products but there is a distinct lack of research around usability with regards to designing mobile interface patterns. Designing interfaces for mobile phones is a unique problem that is not addressed in current usability studies which are more regularly done on mediums such as Webpages. When conducting research into usability factors of mobile devices Gundiz et al. [10] produce a concise and thorough literature review on current research around usability for mobile devices. They investigate usability factors when developing and testing a flight booking applications which, although not relevant to the chemical assays and the use of smartphone cameras, has some parallels and usability frameworks that are well defined and objective. Despite the study having a limited sample set of participants and its exclusion of the improvement of an applications functions the experiment is accurate and complete with valid conclusions being drawn from a set of interesting results. One such result showed that usability in design is not sufficient to achieve user satisfaction as users expect smart systems that are tailored to their needs. Usability is a central concept and metric that aids our understanding of how mobile applications are interacted with by users. Although understanding in depth usability issues is not essential to the proposed research question it is an important consideration. A more relevant and fundamental technique is that of evaluating usability which will be reviewed next.

2.4 Usability evaluation of Mobile applications

Usability evaluation is an integral procedure when determining where usability problems lie. This section will review different usability environments for evaluation, investigate techniques and usability measures and highlight challenges and recommendations for usability evaluations.

2.4.1 Field vs. Laboratory vs. Hands-on testing

Mobile application use in our daily lives is large and increasing dramatically. Determining the usability of an application is an important factor in judging whether an application will be successful and competitive against other mobile applications. We therefore require ways of evaluating usability of mobile applications for which are a number of techniques that describe ways of doing so. There is abundant research in this area and most papers agree on three principle methodologies for evaluating usability. There is, however, contention as too which technique yields more information to the researchers concerning usability. Nayebi et al. [11] conducted research which is less experimentation and more a review of the three methodologies (laboratory, field and hands-on environments) for evaluating mobile usability which they then survey and draw observations from. A failing point of the paper is their exclusion of laboratory experiments citing a number of vague reasons. They concluded that a combination of field studies and hands-on measurements could provide more significant usability information.

Betiol et al. [12], however, tested three different approaches to testing usability in both field and laboratory environments. Despite having limitations in its results due to not testing the users with explicitly concurrent tasks the research points to laboratory environments being the preferred environment for testing. A suitable evaluation environment for usability studies is clearly disputed and Kjeldskov et al. [13] help clear this up by providing a highly in depth and thorough review of Mobile HCI research and their choice of environment over a number of years. They found without bias that 49% of studies in 2009 used the laboratory approach, 35% of studies opted for the field study approach and finally applied studies accounted for 30% of all research with the deficit being methodologies that are less prevalent. Overall this demonstrates that a laboratory approach is the most commonly used approach a conclusion that is highly relevant to this research question as an appropriate evaluation environment will need to be implemented. Given the nature of the application that is to be developed a laboratory setting will be most suitable.

2.4.2 Evaluation Techniques and Usability Measures

Given a laboratory environment it is necessary to find an evaluation technique that produces valid results and highlights possible usability problems. There are a number of studies that create techniques and others that evaluates others proposed techniques. Kjeldskov et al. [14] produced an explorative study of two approaches namely an expert evaluation (heuristic inspection) and a user-based evaluation (using the think aloud protocol) both conducted from within a laboratory environment. The study found that the heuristic evaluation makes it harder to identify usability problems related to the support for collaborative work and in general fared worse than the think-aloud evaluation. This research is not completely relevant due to the collaborative aspect of their mobile application however the study was clearly motivated and described the two techniques in-depth. Although Kjeldskov et al. produce a logical study of the two methods there is very little research that confirms their findings and equally little research that evaluates other mobile usability studies approaches in laboratory environments with the majority of research focusing on one or the other approach individually.

Comparatively there is a sizable body of research around usability measures and there are a group of generally accepted measures to be used when evaluating usability. The ISO 9241 standard for usability classifies the measures into three groups notably “effectiveness”, “efficiency” and “satisfaction” [15]. These three groups are broken down into subgroups in a number of discussions and literature on the subject [16][17]. Deciding on what usability measures are to be incorporated in the usability study is important and is relevant as it provides a metric that indicates how usable the developed application is and what areas usability problems reside.

2.4.3 Challenges and Recommendations

As with many evaluation techniques there are challenges faced by the evaluator and decisions that will ultimately determine the studies success or failure. Svanæs et al. [19] conducted research into performing usability tests of mobile software in clinical settings and identified a number of key challenges and recommendations. The specifics of the experiment are not relevant but the study mentions that if the graphical user interface (GUI) is complex a separate desktop usability test is recommended before the full scale test is conducted. The study also highlighted the difficulties regarding the filming of participants and suggested a roof mounted camera to track the users interaction as “mirroring” (recording of the devices screen output) often loses the details of the users finger interaction with the display.

3. RELEVANT APPLICATIONS

This section will identify and analyze mobile applications that are relevant to the one required by the research. The aim is to provide an idea of what has been done in the area and what parts could be relevant to the research question. Applications that are broadly relevant with notable properties will be identified by field and analysed after which closely relevant or seemingly identical applications will be critically analysed.

3.1 Types of applications

There has been an increase in companies endeavoring to turn phones into lab equipment tools. Such companies include Holomic [19] and Sensorex [20]. Many of these applications have not been formally tested and there is a distinct lack of research on their methods however they remain relevant as many of them aim to either replace current laboratory equipment or leverage mobile devices processing power with the addition of custom sensors. This subsection investigates relevant applications that have been the subject of published studies. Applications are broken down by field, namely Chemistry and Medical, and discussed individually.

3.1.1 Chemistry

Chemistry is a field that has benefited substantially from the increase in mobile applications available. Educational tools such as periodic table explorers as well as chemical reaction applications are especially popular. Two relevant applications, which have been sourced from a review article [21] on mobile applications in drug discovery, will now be discussed after which two prominent healthcare applications will also be reviewed.

3.1.1.1 Optical Structure Recognition

A number of applications use optical structure recognition (OSR) which allows a user to take a picture of molecule that is drawn on a paper/whiteboard and use it as a query against a database of molecules to identify the correct molecule. This new technology is used by a number of publically available applications such as OSRA [22]. This type of application is relevant as it utilizes a mobile devices camera to process images in physical space.

3.1.1.2 Counting Molecules

A novel study done by Ayas et al. [23] produced an application for mobile devices that makes use of plasmonic enhancement in order to acquire Raman spectra at the single molecular level using just a smartphone and its image sensor. This research is relevant as it is essentially attempting to replace common lab equipment much like the research question at hand. This research is also relevant as it demonstrates the remarkable sensitivity of standard smartphone cameras and also makes use of a process similar to that which will be used by the application developed to solve the research question.

3.1.2 Medical

There has been sustained interest in medical applications (termed mHealth) from the medical sector over the past few years. This has resulted in the production of numerous applications to target growing markets.

3.1.2.1 Diabetes Applications

One such market that has experienced significant growth is the diabetes segment in which the number of mobile applications for self management of diabetes went from 60 in 2009 to 260 in 2011. [24]. One review [25] has carried out a systematic review of current diabetes applications giving insight into different interfaces, user ratings and usability evaluations. These applications are relevant as they represent similar applications that are interacted with frequently by users giving interesting information into what users want from these types of applications, what interfaces are successful and any usability recommendations.

3.1.2.2 Clinical Microscopy

While diabetes and similar applications focus on healthcare in urban environments and on a lifestyle level there are a number of projects involving mobile applications that are designed to analyze samples and make a preliminary diagnosis that provides a healthcare worker with information which aids them in decisions about further testing. One such project identified this need and leveraged a smartphones camera to implement a light microscopy solution for screening of hematologic and infectious diseases. They demonstrated their prototype's potential for clinical use by imaging red blood cells in samples using LED excitation. Although this project made use of a lens and phone mounted microscope setup the use of the smartphones camera and the inexpensive approach provides useful similarities especially as it is designed for use in third world regions and where laboratory facilities are scarce [26].

3.2 Analysis of current applications

This section will briefly discuss each previously mentioned application's strengths, weakness and overall impression of the conducted research.

OSRA [22] the first of our relevant applications was the first open source program for optical structure recognition and is an app that claims to be designed for a broad range of applicability. The application was originally a command line utility that has since been modified into a web-based interface that can be viewed via mobile devices. OSRA was tested by its developers in an objective and valid way given the difficulty of evaluating such an application. The accuracy was impressive and consistent with useful suggestions for future work to improve the imperfections such as noise. The research was unfortunately very focused on the algorithm and neglected to describe let alone test the web application with actual users. The program also had a few false negatives during testing however these instances were limited given the sample size.

The molecule counter [23] demonstrated a reliable and accurate solution to detecting single molecule events even with weak optical signals. The plasmonic substrates used in the observations can also be produced at a lower cost than the ones necessary for conventional tests. Most remarkable is the demonstration of a smartphones potential for analytical chemistry that this research provides. There is however a couple of failing points in the study. Firstly the application makes use of a modified commercial confocal Raman microscope which is far from portable and is not easy to acquire however the authors claim the equipment could potentially be easily miniaturized. The second failing is that the research yet again fails to mention the application used or any part of its design or interface save for a single picture.

Although the review of diabetes applications [24] did not review individual applications in detail it did provide some very useful insight into what users value including "comprehensibility" and "fault tolerance". The research also had some interesting conclusions regarding the correlation between the number of features and the perceived usability of an application. Overall the research made valid and logical conclusions and analysed a huge number of applications (656). It limited in terms of weaknesses however one weakness is that they sampled just 10% of the total applications to do an expert evaluation of. This may not be considered a large enough sample to draw significant general conclusions from. The research also considered only Android and IOs (Apple) operating systems perhaps unjustly ignoring other operating systems available to users.

The study into producing a light microscope that can accurately and reliably help identify malaria [26] is an impressive piece of research. It produced a solution that is comparatively inexpensive, portable and able to be used in rural environments. The research successfully demonstrates the light microscope adapted for mobile devices and its potential to improve diagnostic efficiency and relieve healthcare workers of time-consuming tasks. Despite these obvious strengths and accuracy claims the study did neglect to test the application and microscope device with actual users. The conclusions regarding actual use of the application are "suggestive" and "could prove" to be true. This research serves to be a very interesting proof of concept but further research needs to test the application in its envisaged environment of use. Additionally the automated counting of fluorescent TB images was processed on a laptop computer when the phones computational resources are more than sufficient to conduct this operation which would make the system more compact and efficient.

3.3 Analysis of assay reader type applications

There have been some notable projects that are largely similar to the one proposed by the research question. These similar studies are broken down into appropriate groups based on their focus, critically analyzed and discussed in the following sections.

3.3.1 Colourimetric

Vashist et al [27] noted that microplate readers are bulky and expensive and therefore there is a need for a portable and cheap smartphone based solution. The authors have formulated the problem correctly and identified important aspects however more evidence could be provided to demonstrate the need for such a solution. The authors provide a brief overview of previous research into using smartphones as colourmetric analysis tools and point out flaws in current research namely that their approaches were not validated by conventional procedures. There was however a lack of individual critical analysis of the work referenced. Overall the paper contained valid and sufficient basic components with the analysis of results appearing accurate although which type of analysis being conducted was not immediately apparent and insufficient conclusions were drawn. This research provides an original and useful contribution to current research as it demonstrates the potential that phone cameras have to analyze assays plates. The study also provides a useful comparison between the phone based solution and existing solutions using laboratory equipment but fails to mention how the phone based solution could complement as opposed to replace these existing solutions. The results achieved by their study were notable as they managed to provide a solution that is very close to the accuracy seen in current laboratory equipment. The only major downfall was yet again the lack of focus on the mobile application developed for this solution if there even was one. This research is relevant to the research question proposed here as the process followed to analyze the assay plates is near identical to the solution that will be developed.

3.3.2 Paper based

Guan et al. [28] conducted a study which produces a smartphone application that analyzed a paper based blood assay which was designed in a barcode-like fashion. The smartphone application would scan the bars of the paper assay using the smartphone's camera, process the data and produce information about the blood's type. The results of the application and barcode technique were highly positive as the application managed to correctly identify 98 blood samples, a result that is identical in accuracy to equipment used in Red Cross Australia's laboratories. Unlike previously discussed research in this review Guan et al. mentioned their application was developed for the Android operating system and briefly described the applications interface and usage process. Although the evaluation of the solution's accuracy of blood typing was notable and valid the research failed to investigate the usability of the application itself. The research presented is objective, void of emotion, has a logical flow and contributes to current understanding of effective, portable and inexpensive methods of determining blood types. This research is relevant as it provides useful guidelines as to which smartphone's have been successfully used in camera based applications and an example of a possible, although rudimentary, interface.

3.3.3 Assay plate based

Berg et al. [29] recently conducted very similar study to the research presented by our research question. They utilized a handheld piece of equipment consisting of a smartphone and a 3D printed mechanical attachment with a light emitting diode (LED) array to illuminate a 96 well assay plate. They also made use of a custom made application with machine learning algorithms in order to process the data which is then visualized and displayed to the user. Their research was notably well evaluated and the solution managed 99.6% accuracy. Not only was the solution accurate the hand held platform was cost effective and portable. At first glance this research seems to solve the research question proposed however although this study [29] briefly described the application and provided some use cases and screenshots there is no indication of any usability tests. The research claims the device could assist health-care professionals but no investigation has gone into whether this is true. The research also made use of a relatively complicated 3D printed mechanism and arguably would not get near the accuracy without it. This 3D printed mechanism may also be considered too expensive or difficult to acquire. Lastly the device only supports a 96 well enzyme-linked immunosorbent assay plate which although popular is only one of a number of different sizes of assay plates. Despite these flaws and a distinct lack of a thorough relevant literature analysis the research presents an objective, innovative and valid study with logical conclusions.

3.3.4 Previous research

Bellairs et al. [30] conducted research last year from which the research question proposed here is derived. Their primary goal was to develop an Android application that served as a mobile, portable, low cost solution for analyzing assay plates. Their study formulated the problem well giving it context and importance and presented a solution that was reasonably accurate and could be used with or without their DIY dark box solution. Critically their prototype also supported different size assay plates and allowed the user higher degrees of control of the variables than previously discussed mobile microplate reader solutions. The authors also noted that their mobile solution need not compete with current microplate readers but could also complement current lab equipment, a salient point. One weakness could be identified as the lack of testing on assays with actual lab assay samples. The way the user interacted with the Android application was described in detail with impressive well detection algorithms demonstrated however no description of the user interface was given. Finally the analysis and conclusions drawn were valid and accurate with no indication of bias.

4. DISCUSSION

This review first looked into mobile HCI problems facing mobile devices. While these problems are well analyzed in current research it is an area which is constantly innovating and discovering new technologies which makes for up to date research in the area difficult. Many problems identified remain useful however a number fall away and become irrelevant, a point that must be considered when working with very recent technological advances. Usability challenges conversely will almost always remain relevant and interfaces will consistently need to be designed with the user in mind. Most points made in the papers reviewed are ones that should be kept in mind when designing any application for use by many personas.

Of equal and perhaps greater importance is the type of usability evaluation that must be decided upon. While many of the reviewed papers recommend a specific type of usability evaluation environment it is my opinion only possible to be able to make such a suggestion if information is given on the context of the application's use. Each evaluation environment has its pros and cons and should be selected based on them. The most suitable environment for the proposed research question is without doubt the usability laboratory. This is because of the nature of the proposed application. The laboratory approach allows a more tightly controlled environment and given that the application will be used in actual laboratory the need for the testing in a noisy, mobile and distracting environment as proposed in field studies is diminished.

Similarly the usability techniques are context based and are tailored depending on the type of application. Many techniques proposed by the papers reviewed here are tailored to their individual applications and although they give good general guidelines they don't provide a perfect technique. One such guideline that as appropriate for the testing of this research question is the user based think aloud protocol. This is because with an expert evaluation you may find more general usability issues are solved that suit a wide target audience but the application proposed here has a specific persona in mind indicating that testing on actual users would be recommended.

Finally of all the relevant applications reviewed many achieved impressively accurate results and had innovative solutions but all studies failed to take their research further and test their applications on actual users leaving a huge gap in the research area. This gap is the one that the proposed research question here aims to fill. By conducting usability studies it will be determined whether users actually derive value from the many solutions described here and we will finally be able to answer those vague indications that these applications will be useful and usable.

5. CONCLUSIONS

This review aimed to analyze current solutions to mobile microplate reader applications and provide evidence of a gap and a need for the proposed research. This review has demonstrated the need to conduct usability evaluations on a fully functional mobile microplate reader application using a set of actual target users an order to determine their value and viability. This review also investigated appropriate usability environments, techniques and metrics in order to conduct valuable usability evaluations. The usability laboratory environment was deemed to be the most appropriate environment and the user based think aloud technique is recommended to be used for evaluating usability.

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