October 28, 2009

Iowa Association of Independent Colleges and Universities
Attention: Gary Steinke
505 5th Avenue
Des Moines, IA 50309
Phone: 515-282-3175

Dear Dr. Steinke,

On behalf of Clarke College, it is my pleasure to submit the enclosed application to the Iowa Association of Independent College and Universities for funding consideration in the FY 2010 Grow Iowa Values Fund administered by the Board of Regents. A grant of $93,046 over the period from June 2009 through June 2011 will assist our computer science and mathematics faculty to continue important research which has the potential for commercialization leading to jobs in the high-tech field of Bioinformatics.

This project is a continuation of a 2007 GIVF grant in which a HIV Web portal was created that provides relevant queries and analysis results for clinicians and medical researchers. This project will extend the research to include a clinical ontology design and implementation for other diseases using electronic medical records already available. It will produce an important tool to serve the medical community of the state as they care for patients. This project, housed at Clarke College, is a collaboration among faculty at the University of Iowa Hospitals and Clinics, the University of Wisconsin Hospitals and Clinics, Stanford University School of Medicine, and physicians at Dubuque Internal Medicine. The modest budget we propose will enable us to move forward on this project. We envision this project growing in the future to include other in-state sources identified by the Iowa Department of Public Health or similar agencies.

Clarke has been a leader in technology in higher education since the 1960s, when the college established one of the first computer science departments at a small liberal arts college. Today, this history of excellence continues and, combined with our recognized programs in natural sciences and mathematics departments, we are poised to excel in the grant project for which we are requesting funding.

Enclosed you will find the application as well as support letters from the collaborating colleagues. We look forward to the opportunity to work with you on this grant project and have it submitted to the Board of Regents for funding. Should you have any questions or need further information, feel free to contact Dr. Mary L. Caffery, Director of Grant Proposals, at (563)588-6363 or Dr. George Towfic, the principal investigator, at (563)588-6542.

Sincerely,

Joanne Burrows, SC, Ph.D.
President
Design and implementation of an Iowa clinical ontology

A proposal submitted to the Grow Iowa Values Fund
by George Towfic, Ph.D. Associate Professor of Computer Science
Clarke College, Dubuque, IA 52001

1. Executive Summary

Beginning in 2004, the Principal Investigator, Dr. George Towfic, and his co-investigators have worked to develop a Web-Based HIV Analysis Library. Using a sample set of patients’ records, they developed prototype mathematical models, Expert Systems and graphical tools to analyze patients’ reactions to HIV treatments provided in the State of Iowa and the State of Wisconsin. The developed analysis tools have been implemented on HIV patients’ datasets available at the University of Iowa, University of Wisconsin. The initial work was funded by previous grants including a GIVF grant, which has been awarded in 2007, to establish a web portal that stores and analyze HIV datasets obtained from the University of Iowa and University of Wisconsin-Madison. Using the 2007 GIVF and its matching funds, Dr. Towfic, with his colleagues and collaborators (hereafter referred to as we), were able to design and implement a web portal that provides relevant queries and analysis results for clinicians and medical researchers (www.datamining.com) (Towfic, et al., 2009-a).

Throughout the 2007 project’s development process, we were able, in collaboration with Stanford’s medical informatics department, The University and Iowa and Wisconsin-Madison’s hospitals and clinics, a Dubuque’s prominent physician, and Harvard medical school, to design and implement valuable Ontology tools. Details about these tools are provided below in the “Ontology components and structure” section. In addition to the designed and implemented tools, we used the GIVF grant fund to provide analysis servers and other hardware necessary for the software implementation. We published our research findings in three distinguished journals (Towfic et al., 2009-a; Towfic et al., 2009-b, Graziano et al., 2008). In this proposal, we plan to use our software, hardware, and research tools to design and implement an Iowa clinical oncology starting with the City of Dubuque. We are encouraged by the fact that we already established a close collaboration with a prominent Dubuque clinician, Dr. John Viner, who contributed to our publications and has provided invaluable consultations to our clinical research and projects. Dr. Viner will be working with other infectious diseases clinicians to provide our current proposal with clinical datasets and medical expertise. Another encouraging factor for the success of the current proposal is that the principal investigator has established a good relation with IBM in Dubuque and has been asked by IBM to teach four technology classes for IBM employees and more classes are scheduled on January 2010.
The long term objectives of the current proposal is to design and implement clinical ontology for Iowa’s clinics. The proposed ontology will provide the following services (more details are provided in the “Proposal Justification” section:

1. Provide a clinical vocabulary database for all health problems and associated treatments used by different hospitals and clinics in the state of Iowa (starting with the city of Dubuque)
2. Establish relations and rules between different patients’ health problems. The relations will categorize and identify patients with common health problems and provide major relations between one health problem and other related health problems.
3. Establish treatments’ rules under which a given treatment has provided successful or limited results. These rules will be generated using ontological machine learning algorithms to identify patients and environmental conditions that show successful or limited treatments’ efficiency.
4. Enable patients and clinicians to obtain statistical analysis related to patients’ health conditions. Such analysis will take advantage of the electronic medical records, currently available in the Iowa clinics, to provide patients and clinics with comparison charts that show patients’ reaction and adherences to treatments in comparison to patients with similar health and ecological conditions.

2. Organizational Background

Clarke College, founded in 1843 is recognized as one of the outstanding Liberal Arts Colleges in the Midwest. The pioneer spirit of its early founders has persisted as the college has moved into the 21st century. The founder’s mandate to be “progressive with the times” continues to inspire a faculty and staff of dedicated faculty to offer challenging and growth-producing education to all students. The college offers Bachelor degrees in 26 majors, Master’s degrees in Education, Business Administration and Nursing as well as the Doctor of Physical Therapy degree. Clarke's fall 2009 total enrollment of 1202 students includes students from 23 states, Puerto Rico and 14 foreign countries. The average ACT score of the 2009 freshman class is 23.2 and the average high school grade-point-average was 3.33.

Clarke is accredited by The Higher Learning Commission of the North Central Association. U.S. News & World Report consistently names Clarke College to its top tier of Midwestern colleges in the “Best Comprehensive Colleges-Bachelor’s” category. In a recent Forbes Magazine “America’s Best Colleges” listing, Clarke College was ranked among the best schools in the country. This year, in conjunction with the best colleges list, Forbes partnered with the Center for College Affordability and Productivity (CCAP) to develop a ranking of “America’s Best College Buys.” Clarke was named number four in the ranking of best college buys in the Midwest and was number 63 in the national best buy listing. It was the highest ranked school in Iowa for value.
The Computer Science department was the first at a liberal arts college in Iowa and is among the oldest in the Midwest. The pioneering spirit of the college and the department was demonstrated most recently when in 2004 it became the first college in Iowa to establish an undergraduate major in Bioinformatics. In collaboration with the natural sciences and mathematics departments, a total of 12 Ph.D. faculty members are involved in offering courses for this interdisciplinary major. The Isidore Laboratory, a molecular visualization lab for the Bioinformatics programs, was opened that year with support from the Dubuque Racing Association. Several Maytag Innovation Awards have supported ongoing faculty-student research projects related to this initiative.

3. Principle Investigator

Dr. George Towfic is an Associate Professor at Clarke College, Dubuque, Iowa. He taught many graduate and undergraduate courses related to the proposed project both during his time at Clarke College and in other national and international universities. These courses include Bioinformatics, Distributed Systems, Data Communication and Networking, Artificial Intelligence and Expert Systems, and Web Programming. Dr. Towfic works in close collaboration with IBM-Dubuque to teach technology courses (so far, he taught four courses and is scheduled to teach other courses on January 2010).

Dr. Towfic’s bioinformatics research has appeared in highly regarded journals including Bioinformatics, which is edited by Oxford and Stanford Universities and Journal of Proteomics and Bioinformatics. In addition to his academic research, Dr. Towfic’s scholarly achievements include his role as a reviewer for many NIH grant proposals, several textbooks, as well as peer reviewed transcripts. He is currently in collaboration with the HIV Medical Clinic at the University of Iowa, HIV Medical Clinic at the University of Wisconsin-Madison, Stanford Medical Center, and Harvard medical school to develop data mining tools and algorithms for the analysis of HIV drug resistance. Dr. Towfic has served as Principle Investigator for many research grants and has contributed and chaired national and international research conferences. Dr. Towfic is a member of the Institution of Electrical and Electronics Engineers (IEEE) and the Association for Computing Machinery (ACM).

4. Work objectives

The objective of this research project is to establish infectious diseases ontology that stores clinical datasets related to major infectious diseases Iowa. We will start with clinical datasets obtained from Dubuque clinics and expand this dataset to include other clinics from UIOWA and UW Wisconsin-Madison Hospitals and Clinics. The resulting ontology will be integrated with major infectious diseases ontology in collaboration with Clarke College (Dubuque, IA), the
University of Iowa, the Wisconsin (Madison-Wisconsin), and Dubuque clinics. We are encouraged by the fact that our collaborators are very interested in developing the proposed ontology (as stated by Dr. Viner’s letter of support and by our continual collaboration with prominent researchers and clinicians in the UIOWA and UW Wisconsin’s Hospitals and Clinics with whom we established our current web portal (www.hivdataming.com) and published the attached research papers).

5. Proposal Background

Although many clinical datasets (including electronic medical records) are currently available, offline and online, the last five years have witnessed a significant work by distinguished medical institutes to provide a unified ontology system to achieve the following advantages:

1. Provide clear definitions, associations, and classifications for major medical terms used by different clinics. Such definitions will eliminate major deficiencies currently involved in defining major medical terminologies such as: base and accepted RNA levels, initial and accepted CD4 count high and normal HDL, high and normal LDL, etc. Different countries and different medical institutes currently use different definitions and measuring rates to define each of the above medical terms. Such variant, which causes serious obstacles in understanding patients’ treatments progress, will be eliminated using standard definitions implemented in a unified worldwide ontology. With the increasing current interest in ontology, it is important that Iowa in particular, and the Midwest in general, contribute in this important medical project through projects such as the one we are currently suggesting.

2. Provide a machine learning system that enables computers to understand relations between different medical patterns. This will be provided using ontology’s machine learning query tools that enables computers to constantly locate new datasets and integrate it with existing datasets stored in a considered medical ontology. This will reduce the manual data collection process that currently dominates medical data analysis. It will also enable computers to identify related medical datasets by providing authenticated definition and descriptions of medical terms. Providing such definitions will collect all medical terms that have the same meaning into one group. This way, referring to initial viral load as initial viral load, base viral load, or basal load will provide the same set of medical data.

3. Provide an easy integration between related ontology. An example for this is that the ontology outcomes from this project can be easily integrated with other national ontology such that the components and tools developed by our ontology can be readily used by other national/international ontology. Standard definitions together with the ontology’s machine learning tools will ensure automated integrations between related medical ontology.
4. With the recent advances and popularity of semantic web, medical ontology will provide a natural implementation that can readily be integrated with current and future semantic web applications. This will eliminate data redundancies that dominate current web-based medical datasets.

In what follows, we will provide examples provided from our current HIV ontology tools (that we developed during our previous GIVF funding). We hope that these examples will demonstrate the advantages that ontology brings to the medical field in general and to the standardization and analysis of Iowa’s clinical trial datasets, in particular.

6. Proposal Justification

Electronic medical records are now available for physicians, nurses, insurances, and other medical institutions. However, due to data accessibility and processing restrictions, including Health Insurance Portability and Accountability Act (HIPAA) regulations, patients’ records have not been easily accessed by patients. Such access, if provided using recent computer technology that satisfies HIPAA regulations, would have many benefits not only for patients but also for physicians and clinical institutes. Although current medical records provides laboratory values for major health screening (such as total cholesterol, triglyceride, HDL, and LDL) and provide desirable, borderline, and high values for each attribute, these values are still calculated as a median value for a nationwide medical records approved by medical institutes such as American College of Cardiology (ACC), the American Heart Association (AHA), and the Physician Consortium for Performance Improvement (The Consortium), rather than categorized values based on the considered patient’s race, age, gender, related health conditions, and patients’ medical history.

Using the proposed web portal, patients would benefit from the availability of analysis tools that provide data mining analysis on real-life datasets, to obtain charts and tables that enable patients to contrast and evaluate their health conditions with respect to other patients with the same treatments, demographic conditions, and laboratory datasets. Patients will also obtain hypotheses validations regarding possible future laboratory outcomes obtained from contrasting the considered patient’s data with real-life data for patients with similar health conditions. In addition to statistical analysis and predictions, patients will be able, using a secure and encrypted servers, to obtain their historical datasets and will be able to access authenticated medical resources that provide scientific knowledge (obtained from official websites) regarding their health condition, symptoms, and medications. This will minimize misleading information obtained using poor online medical resources.

Hospitals and clinics will be able to provide this online service for their patients and will be better prepared for a future and unavoidable progress in the field of green technology and web-based medical services. Physicians and nurses will be able to obtain statistical analysis for
individual patients and for groups of patients classified according to their treatments type, health conditions, age, etc.

7. Selected examples from our current HIV ontology

Recently, through our previous GIVF grant, we worked with Stanford’s Medical Informatics department to develop HIV ontology for Iowa and Wisconsin hospitals and clinics (we have attached a copy of our contract with Stanford). Figure 1 depicts major components of the Iowa-Wisconsin HIV ontology. On the left hand side, under the class hierarchy menu, we show major ontology classes including the CD4 Count RNA level, Patients ID, Treatments, and clinical visits dates. The figure also shows that by selecting the Patients class, all 3197 patients IDs will be displayed in the PtID column (each with a diamond shape). More details about each patient are displayed in the individual editor menu (to the right). The figure shows that the selected patient has a CD4 count of 402, RNA level of 399, Sustiva-Combivir treatments which is prescribed on September 9, 2003. Figure 2 shows CD4 counts and RNA level for patient-ID 21 during seven laboratory tests. The following Semantic Query-Enhanced Web Rule Language (SQWRL) (O’Connor et al., 2009) ontology rule has been used to obtain the CD4 and RNA datasets for patient 21.

\[
\text{db:hasPtID}(?x, ?y) \text{ ^ swrlb:equal(?y, 21) ^ db:hasCD4_Count(?x, ?z) ^ db:hasRNA_Level(?x, ?w)} \rightarrow \text{sqwrl:select} (?y, ?z, ?w)
\]

The first term (db:hasPtID(?x, ?y) in the above rule obtains all patients IDs (using the hasPtID property), the second term (swrlb:equal(?y, 21)) selects datasets associated with patient 21 and the third and fourth terms select the CD4 count and RNA levels for patient 21 respectively. This rule-based query system provides fast query through a class association (in this case the PtID, CD4_Count, and RNA_Level classes). Figure 3 display all CD4 counts greater than 200 for patient 21 using the following SQRRL query:

\[
\text{db:hasPtID}(?x, ?y) \text{ ^ swrlb:equal(?y, 21) ^ db:hasCD4_Count(?x, ?z) ^ swrlb:greaterThan(?z, 200)} \rightarrow \text{sqwrl:select} (?y, ?z)
\]

8. Major advantages provided by medical ontology:

The above HIV ontology examples demonstrate the following advantages in using medical ontology:

1. Physician and clinical researchers will be able to obtain required patients information based on object oriented query system (provided via ontology classes such HDL and LDL cholesterol levels, diastolic and systolic pressure for hypertension, and a CD4-count and RNA-Level for HIV). Unlike, relational database systems, which use two dimensional tables through public keys, ontology establish relations between any
numbers of classes. This provides direct access from one class to another rather than indirect table access frequency used in relational databases.

2. Ontology and its association SQWRL query language, is designed to be used in the semantic web environment. This will provide two main advantages: 1. a considered ontology will be easily accessible through the web; 2. Medical institutes can easily add their datasets to a considered ontology through the semantic web.

3. Eliminating redundancies by ensuring that all medical terms and conditions are uniquely defined for a considered ontology. Since all medical institutes will use a unique ontology, they will have to agree on the definitions and clinical datasets included in the considered ontology. This will provide a universal definition for major medical terms including conditions under which a specified medication should be applied.

4. Unlike databases, ontology can be easily constructed and migrated from one server to another using a semantic web structure. Since Protégé (Robin et al., 2008) (the ontology IDE shown in Figure 1) and SQWRL are web based tools, it is easy to use available web browsers to download, construct, and navigate through a considered ontology.

5. Provides standard and relations between medical terms. For example, the properties definitions (shown in Figure 1 as hasCD4_Count, has RNA_Level, etc.), which are required in any ontological structure, provides relations between different medical components such as relations between HDL and LDL, diastolic and systolic pressure, and CD4 counts and RNA levels. Ontology will also provide relations between different treatments and patients’ reactions to different treatments, etc.

9. **Examples for ontology analysis available in our current web portal:**

Figure 4 depicts a screenshot that displays major analyses activities involved in our current data analysis web portal designed to provide analysis using the previously explained ontology. The web portal provides four major links:

1. Database Queries
2. Statistical Analysis
3. Clinical Rules
4. View available Hypotheses.

Our current database provides clinical datasets, depicted in Figure 5, on the following queries:

1. Obtain treatment and lab records based on a specific patient
2. Obtain patients' HIV dynamics associated with a drug regimen
3. Obtain distribution of patients' records for various treatments
4. Obtain RNA distribution among patients
5. Obtain CD4 distribution among patients
6. Obtain patients' IDs associated with a range of clinical records
7. Obtain distribution of patients' records within a considered initial CD4 range.

The Statistical analyses link provides the following analyses:

1. Obtain the rates of change of CD4 and RNA levels for one or many patients
2. Obtain summary graphs to evaluate relations between patients' CD4 count and RNA level
3. Obtain the rates of change of CD4 and RNA progression for a considered drug regimen
4. Obtain bar charts to evaluate the performance of different treatments
5. Obtain correlation and standard deviation analysis for a considered drug regimen
6. Obtain correlation and standard deviation analysis for a specific patient.

The clinical rules’ section includes:

1. Summary rules for the UIOWA and UW-Madison patients' datasets
2. CD4 and RNA classification criteria related to clinical treatments used at UIOWA and UW-Madison clinics
3. Cluster analysis that shows major features (mean and standard deviation) associated with UIOWA and UW-Madison clinics
4. Scatter plots that summarizes the CD4 count and RNA level associated with UIOWA and UW-Madison patient
5. Major criteria that distinguish patient response to different treatments
6. CD4 count and RNA level associated with different treatments
7. Groups of patients responding well to considered treatments
8. Groups of patients with similar response to considered treatments
9. Treatments with similar effect on HIV dynamics (such as CD4 count and RNA levels)

The available hypotheses section includes statistical tests to evaluate the following hypotheses:

1. Predict possible relations between two selected treatments with respect to CD4 count or RNA level changes
2. Predict possible relations between a group of patients treated with identical treatments
3. Predict possible relations between two groups of patients with respect to various parameters such as CD4 counts, RNA levels, and treatment type
4. Predict future CD4 count and/or RNA levels given patients’ historical datasets
5. Suggest possible future treatments given patients’ historical datasets

Each of the above sections provides a self explanatory outputs from the HIV ontology. Sample outputs are provides in Figures [6-9] whereby a physician can select one or many patients ID or drug regimens to obtain relevant datasets for selected patients IDs or drug
regiments. Figure 10 depicts the rate of change of CD4 and RNA levels during treatments. These data could be used to monitor treatment effectiveness and provide valuable inputs for physicians to study the overall effectiveness of a considered therapy. Figure 11 depicts a bar chart that shows the actual values of CD4 values, across all patients, for a selected therapy. This graphical output can be used to study the overall effect of a selected therapy under different patients’ conditions. Figure 12 depicts the standard deviation and correlation values for a selected treatment’s CD4 count and RNA levels. This figure’s standard deviation output can be used to estimate the performance of a considered drug. The standard deviation output will explain the spread of the CD4/RNA values. One standard deviation indicates that the considered treatment managed to keep the CD4/RNA values within 68% distance from the mean while 2 and 3 standard deviations indicate that the CD4/RNA values are within 95% and 97% distance from the mean, respectively. Treatments that provide less standard deviations are better used when the considered CD4/RNA values needs to be kept within a small controlled interval. Treatments with high standard deviations can be used to achieve major changes in the CD4/RNA values. The correlation value indicates the mutual effect between the CD4 count on the RNA level. High negative correlations indicate normal pattern between the CD4 count and RNA level where the RNA levels decrease as the CD4 count increase.

10. **Examples of expected services provided by the proposed project:**

   The following list provides analysis examples which will be provided by the proposed ontology development project:

   1. Compare individual patients’ data with groups of patients with similar lab readings (such as age, race, cholesterol, triglyceride, HDL, LDL, Sodium, Potassium, Chloride, CO2, Glucose, Creatinine, GFR, T-Cell CD4 count, and Viral load RNA level)
   2. Obtain statistical analysis for groups with similar treatments
   3. Obtain statistical analysis for possible future medical trends
   4. Obtain statistical analysis for possible future treatments
   5. Obtain predictions for change of medical data for the next one, two, three, four, five years
   6. Obtain possible change of treatments for the next one, two, three, four, or five years
   7. Obtain patients’ personal treatments and hospital costs
   8. Obtain medical explanations relevant to personal health conditions

11. **Main research and developments activities required for this project**

   The proposed project can be divided to the following modules:
Module 1:
Use the ontology datasets to obtain mathematical and statistical models to simulate:
   a. Over all changes in patients conditions with respect to one or many therapies
   b. Obtain treatment rules that govern the effectiveness of one or many treatments.
      For example, under what initial viral load/CD4 values would a given treatment perform better? What rules can identify the best drug regimen combination to be used with each treatment? What are the rules that classify patients to different groups according to their response to a considered drug regimen?
   c. How would patients correlate to each other with respect to their reaction to different therapies?

Module 2:
Research and implementation of in machine learning models:
   a. Predict possible relations between two selected treatments with respect to CD4 count or RNA level changes
   b. Predict possible relations between a group of patients treated with identical treatments
   c. Predict possible relations between two groups of patients with respect to various parameters such as CD4 counts, RNA levels, and treatment type
   d. Predict future CD4 count and/or RNA levels given patients’ historical datasets
   e. Suggest possible future treatments given patients’ historical datasets

Module 3:
Ontology design and implementation: This includes
   a. Protégé design
   b. Design of SQWRL rules
   c. Java implementation for SQWRL rules
   d. Database design and implementation

Module 4:
Computer networking: This research and development will be used to publish the resulting ontology and make it available through a client/server environment. This includes the following research area
   a. Performance analyses of different Client/Server designs and implementations
   b. Performance analyses of semantic webs
   c. Performance analysis of users’ inputs/outputs (human-machine interaction)
   d. Performance analysis of mass data storage

12. Impact
a. The proposed project will establish the first ontology software and analysis tools that takes advantage of the electronic medical records currently available most Iowa clinics. Upon the completion of this project, we will be able to integrate the resulting Iowa ontology with the ground national clinical oncology developed in many states.

b. This project will establish a close collaboration between Clarke College faculty and local physicians and clinics collaborating in this project by providing relevant clinical datasets and medical consultations.

c. Funding this project will guarantee the continuation of the current collaboration with national universities and clinics. Such collaboration will provide advanced technology and valuable expertise that will help providing better health services and an integrated clinical environment that provides standardizations in clinical terms and patients’ electronic medical records. We are pleased that our team suggested and is currently discussing the establishment of “The Midwest AIDS group”. This proposal to establish this team is supported by three prominent HIV clinicians (Dr. Jack Stapleton, Professor and Director, Division of Infectious Diseases, Dr. Frank Graziano (MD,PH.D. Department of Immunology, UW Hospitals and Clinics, and Dr. John Viner, MD, Dubuque Internal Medicine, Dubuque, IA)

d. This project will also provide undergraduate students at Clarke College with a good opportunity to be involved in significant scientific research that will encourage them to continue their graduate study.

e. Researchers at the state of Iowa will benefit from the collaborative nature of this project to exchange research ideas with their colleagues at the University of Wisconsin and Stanford University.

f. The hardware and software purchased and developed by this project will be available for researchers at the state of Iowa for further enhancement and optimization.

g. This project will provide jobs at the participating Iowa universities and colleges in the areas of medical analyses, mathematical modeling, computer networks, and Web design. In addition, we anticipate that one outcome of this collaboration is
to emphasize the importance of health informatics in the state of Iowa. This will
generate a job market in the area of medical informatics and will encourage local
companies to hire skilled personnel in this field. Another income source from this
project will be software product which will be available through licensing
agreements. The project use will incorporate network services including: Client-
server connection services, security tools and new clinical data input services.
Consultation services will also be available.

13. Proposed Budget

Funding for this project is requested for Salaries, computer and networking hardware, and
analysis and computer software. The principle investigator, CO-PI and the CO-Investigator
are on a nine months contract with Clarke College. The principle investigator is requesting
GIVF 0.15 of his salary for each the summer of 2009-2010 and 2010-2011 sessions. The CO-
PI is and the CO-Investigator are asking GIVF for 0.1 and 0.06 of their salaries for each of
the two summer sessions, respectively. Two students will be working full time in this project
for a total of eight weeks during the two summer sessions of 2009-2010 and 2010-2011.
Clarke College is respectively asking GIVF for a stipend of $4000 for each student during
each of the two summer sessions.

Permanent equipment required for the project includes four computers (two at the 2009-2010
academic year and two for the 2010-2011 academic year) provided by Clarke College to be
used for software development. Clarke College will also provide wireless network
connection network hubs, and network switches, and security certificates for the two
academic years ($10,334.00 for 2010, and $12,500.00 for 2011). Clarke College will also
provide storage devices to store the obtained clinical data.

Clarke college faculty participating in this project will allocate personal time to design and
implement ontology and machine learning software tools during the duration of this project.
We estimate our faculty members will allocate what extra time that would cost $25,280.00
for the 2010 academic year and $20,819.00 for the 2011 academic year. In addition to
software tools developed by the research group, we request that GIVF provide a total of
$11,336.00 required to purchase graphical and ontology software that will cost $7,300.00
for the 2010 academic year and $4,036.00 for the 2011 academic year. GIVF is requested to
provide $10,000.00 for the two academic years to be allocated for consultations, publications
and conferences. Clarke College will provide the amount of $3,000.00 for the same purpose.

The complete budget is shown on the next page.
**Budget for development of a domain specific clinical ontology**

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Figures and References
Fig. 1: HIV Ontology’s Protégé GUI interface

Fig. 2: Sample output from the HIV ontology. The output shows two rules used to display patient 21’s CD4 Counts and RNA levels
Fig. 3: Ontology rules to display patient 21's CD4 counts that are greater or equal 200
Fig. 4: The main page for the HIV/Analysis web portal

Fig. 5: The main page for the Database queries webpage
Fig. 6: Selection menu used to provide patient ID selection option to physicians and clinical researchers

Fig. 7: Sample output that displays the CD4 Counts and RNA levels for patient 38
Fig 8: Main menu for treatments selections to display relevant intonations for selected treatments

Fig: 9 Sample output the displays patients’ information related to the Sustiva treatments
Fig. 10: Statistical analyses that shows the rate of change of CD4 Counts and RNA levels for the Sustiva treatment

Fig 11: Graphical representation that shows patients response, in terms of CD4 count, to the Sustiva's treatments
Fig. 12: Statistical analysis that shows standard deviation and correlation analysis for patients taking the Sustiva treatment

References:


Attachments

1. Letter of support from Dr. Viner
2. Emails of support from UIOWA and UWISC
3. Contract with Stanford
4. Our Web Portal paper
Dear Mr. Donley,

Thank you for giving us the opportunity to explain more about the expected marketing plan and potential customers for our proposed medical informatics ontology tools. We hereby provide answers to your questions.

Again, we would like to thank you, and the review committee, for taking the time to review our proposal.

a. **What companies or institutions would be the primary potential customers**

   As part of our previous GIVF fund, we contacted major medical companies and institutions in the States of Iowa and Wisconsin. We hereby list potential customers and explain the type of expected collaboration with each of them:

   1. **Dubuque Internal Medicine**: We collaborate with two prominent physicians from Dubuque Internal Medicine. Dr. Ronald Iverson is a prominent Endocrinologist in Dubuque Internal Medicine. He is responsible for the management of electronic medical records related to Dubuque’s Internal Medicine branch. He coordinates with the McKesson Corporation in Dubuque. McKesson is a major international provider of health care information technology, providing information technology systems to over 70% of US hospitals with over 200 beds. Their Dubuque location specializes in systems software development and support. Another prominent physician and close collaborator in the Dubuque area is Dr. John Viner whose interest in our work is expressed in the letter of support attached with our application. Dr. Viner is directing us on how what would be most effective analysis tools that needs to be included in our ontology. He is working closely with us to make our tools usable by physicians and other medical institutions and communities.

   2. **Medical Associate and Finley Hospitals**: Although we don’t, yet, have collaborators from these hospitals, we are sure that when our software is in a more advanced stage, many physicians will be willing to encourage both hospitals to use our software. The Principle Investigator for this grant has taught Master degree classes in Nursing Informatics classes for nurses working in both Medical Associates and Finley hospitals. Students in these classes used real-life data from both hospitals and they often share their outcomes with experts in both hospitals and have provided us with positive feedbacks for possible collaboration. We don’t feel that we are ready yet for this step and prefer, at this point in time, to work with our physicians to develop our analysis tools before adding more collaborators for this project.
3. McKesson: As we mentioned above, one of our collaborators, Dr. Iverson, works closely with McKesson. Both he and Dr. Viner think that, if we obtain the GIVF grant, we can arrange a meeting the McKesson to discuss the type of collaboration that will benefit both parties (McKesson and our research work). We already discussed with Dr. Viner a broad collaboration plan with McKesson. Basically, the plan is that while McKesson is responsible for the Electronic Medical Records, we will use these medical records to implement our ontology and suggested analysis tools described in this grant proposal.

4. The University of Iowa and University of Wisconsin Hospitals and Clinics: Both universities have been close collaborators for the past eight years. We recently held a phone conference with Dr. Jack Stapleton (Professor and Division Director of the University of Iowa HIV Program, Director, Helen C. Levitt Center for Viral Pathogenesis and Disease) and Dr. Frank Graziano (Chair of the HIV Committee, University of Wisconsin Hospital and Clinics, and Past Chair of the HIV Committee American Academy of Allergy, Asthma, and Immunology (AAAAI)). During our phone conference, we discussed the establishment of the Midwest HIV group. The group will extend our recent collaboration to include other hospitals and clinics from different hospitals and clinics in the Midwest. We think that the establishment of such a group will provide a wide market for the analysis tools proposed in this grant. Dr. Stapleton wants to use the grant’s money to provide efficient patients’ treatments documentations that can use our suggested analysis tools. Dr. Graziano wants to use our tools to collaborate with many African countries that he often visits to encourage them to make better use and documentations of their treatments. We think that if this grant is approved, we will start extending our collaboration in both directions (Midwest and Africa). This will not only provide efficient analysis tools for our extended collaborators, but will also open a market to lease our software. Our collaborators also think that if this grant is approved, we should use the money to advertise our ontology tools and apply for NIH grants that will focus on the establishment and improvement of the medical analysis tools used in Iowa, in specific, and the Midwest in general.

b. Any estimates of the size of the potential market for the product

The American Recovery and Reinvestment Act of 2009 (the ARRA, also known as the Stimulus Bill) allocated $51 billion to healthcare. Although, as of yet, it has not been determined exactly how this money will be allocated to different sections related to the healthcare, it is known that medical informatics contributed significantly to the assigned fund. Two major funding sections are: Section 3015 - Demonstration Program to Integrate Information Technology into Clinical Education and Section 3016 – Information Technology
Professionals in Health Care. The assigned funding will undoubtedly have significant impacts on the medical informatics job market. Although major hospitals and clinics are already moving toward the adoption of electronic medical records, many hospitals in Iowa are still in the preparation phase toward moving in this direction. Final product from this proposal uses the medical records datasets to provide comparison analysis not provided by available medical records. Hence the market for our product will include the market already available for Electronic Medical Records in addition to growing market of Biostatistics, Bioinformatics, and Information Technology.

As far as Iowa and Wisconsin is concerned, our collaborators estimate the customer size for this project to be at least half the number of patients in major Hospitals and Clinics in addition to most physicians who would like to use our analysis tools. In addition, if we can provide user friendly interfaces to our analysis tools, we can expand our customers’ size to include other States. Our collaborators already have good relations with many Midwest clinics and therefore we think that including other Midwest hospitals and clinics is a doable goal. The market for our product can even be used internationally. In fact, Dr. Graziano (our collaborator from Wisconsin) already suggested that we can use our tools in many African countries that he visits. We think that this step can only be taken if we receive more government, for example NIH, funding. The principle investigator for this proposal is a frequent reviewer to many NIH grants (he reviews an average of three NIH grants every year). Based on what he reviewed, he thinks that we have a good chance to obtain funding to implement our tools internationally. We obviously intend to make Iowa the base for any job market extension related to our work.

As a final note on the job market related to Information Technology and Medical Informatics, we would like to refer to the latest Bureau of Labor Statistics report (http://www.bls.gov/oco/ocos103.htm) which states, in the occupational outlook handbook, that it projects a 37% growth in database administration jobs from 2006-2016 and that employment of medical records and health information technicians is expected to increase by 18 percent through 2016.

c. Description of efforts to be undertaken to market the product

If this grant proposal is approved, we have already planned different approaches to market the obtained clinical oncology tools. In what follows we list these approaches and what has already been done in their directions:

1. Once we receive our grant money, we will start designing a brochure to explain our available tools and their potential benefits. Our medical collaborators will participate in the content management process of this design and will help promoting our ontology tools to the medical community. The principal investigator and Dr. John Viner already started the publicity process in providing an interview with the Telegraph Herald newspaper (http://www.thonline.com/multimedia/?id=1353).
Upon the grant approval, the research group, collaborators, and Clarke College (through the public relations department) will put together a publicity plan that includes interviews with local media to explain the significance of our work and to encourage companies and institutions to use the developed tools.

2. We intend to work with Dubuque’s Small Business office to plan a strategy to promote a medical informatics support center in Iowa (starting in the Dubuque area). We already contacted Mr. Terry Sullivan from the Dubuque’s small business office and plan to meet with him to discuss the possibility of establishing such a support center. Clarke College has already provided a support letter toward the establishment of such medical analysis services.

3. We intend to offer lectures and presentations at local medical institutions and companies. We think that such presentations will provide a good dialog base to establish a marketing line for our ontology analysis tools. Medical associates, local health insurance companies, and local universities will be among the institutes and companies that can host such lectures.

4. Last year, we planned to hold local conference to promote our current HIV analysis tools (a draft brochure is attached). We then decided to postpone this conference to include more analysis tools (including our proposed ontology tools) and more medical datasets. We plan to start planning for this conference once our current proposal is approved. We think such a conference will promote the interest in medical informatics in Iowa and provide excellent marketing opportunities.

5. As stated in our explanation regarding the collaboration with local companies and institutes, we think that such collaboration will result in mutual contracts to implement our tools in local Hospitals and Clinics (to provide efficient analysis for doctors and nurses) and in local medical insurance companies (to provide better medical information and education to their patients).
Investigating the fluorescence of furans, dioxanes, and polychlorinated biphenyls (PCBs) in water: Developing a new technique to investigate the presence and levels of environmental pollutants

A proposal to the Grow Iowa Values Fund
Luther College
Decorah, IA

Principal Investigator: Olga Rinco, Ph.D.

October 2009

1. Summary

Water pollution and the health of our local water systems are of great concern to most global citizens today. We now know that many harmful processes, past and present, have led to contamination of our soil and water systems. Small organic compounds are among some of the most persistent (slowest to degrade) pollutants present in the environment. Because of their persistence, they remain a problem long after they have been deposited on the earth. Even at very low concentrations they can affect the organisms that live in the water or eat the vegetation containing the pollutants. Since these pollutants do not degrade and are very soluble in fat, they build up over time in the organisms ingesting them until they are present in concentrations high enough to pose serious health risks.

Furans, dioxanes, and polychlorinated biphenyls are three classes of organic pollutants that have been and continue to be deposited on our planet and are very harmful to living organisms if present in high concentrations. This study aims to explore whether it would be possible to detect fluorescent organic pollutants in water at low concentrations by complexing these molecules to cyclodextrins and observing an increase in fluorescence. Cyclodextrins (CD) are cyclic oligosaccharides that are commonly used in many fields of supramolecular chemistry.

Supramolecular structures are held together by non-covalent interactions, and this is the case for the organic pollutant-CD complex. Supramolecular structures are capable of changing the outcome of chemical reactions, or of having functions that cannot be achieved by the individual components of the system.

The goals of this study are as follows: 1) To determine which of the organic pollutants mentioned above could be detected by supramolecular photochemistry, 2) to characterize the key interactions between these molecules and the CD systems in an effort to develop a method for detecting these pollutants, and 3) to test local water systems for the presence of the pollutants in the study.

The work will be carried out using fluorescence spectroscopy to characterize the singlet excited state. Spectral and kinetic techniques will be used to develop an understanding of how the pollutant binds to the CD cavity.

Undergraduate students will be involved in all aspects of this work, and the research will enhance their education through an independent original project at Luther College. The project’s focus is in the area of environmental concerns and specifically water safety and purification. This research will look specifically for a method by which small organic pollutants could be identified by industry and government agencies, and thus there are potential benefits from this research for numerous local businesses as well as the Department of Natural Resources.
2. Project Description

The proposed research will use various techniques in both steady-state and time-resolved fluorescence spectroscopy. Fluorescence spectroscopy monitors the singlet excited state of a molecule. These species are very short lived (tens to hundreds of nanoseconds), and as such, the fluorescence studies give a snapshot of the system at a given moment. This study is basic research looking for a better method to detect organic pollutants in water systems, especially at low concentration limits. Complexing molecules (pollutants) to supramolecular architectures will give us a new way to investigate these pollutants in our water systems. This work aims to identify when water pollutants are present (even at low concentrations) and potentially develop methods for removing these pollutants from the water systems.

Background and Current Knowledge

Furans are a group of heterocyclic organic molecules derived from the thermal decomposition of cellulosic solids (i.e., pine wood). Furans are known to be toxic and carcinogenic.\(^1\) These molecules are known to be common byproducts of many common processes such as the incineration of municipal waste, forest or brush fires, and residential wood burning.

Dioxins are a group of chlorinated organic molecules with similar structure, including polychlorinated dibenzo-dioxins (PCDDs) and polychlorinated dibenzo-furans (PCDFs). There is a possibility of attaching up to eight chlorine atoms to the molecule, thus there are numerous molecules included in this family of compounds. Dioxins can have harmful health effects, depending on the number and placement of the chlorine atoms on the dibenzo rings. Dioxins are not very soluble in water, and as such do not pose a huge health hazard in water. However, other molecules that are soluble in water and pose risks (poly chlorinated biphenyls, PCBs) are related to the dioxin family of compounds, and thus studying both of these families is of interest.

PCBs are man-made and have a similar basic structure composed of carbon, hydrogen, and chlorine atoms. These atoms can be arranged in different structures leading to a family of 209 compounds. Some of these PCBs are more harmful than others. PCBs have been banned or severely restricted in many countries, but because they are very stable and slow to degrade, there are still many PCBs left in our environment today.

All three of these classes of molecules (dioxins, furans and PCBs) pose major health risks and exist everywhere in our environment. The stability of these molecules makes them persistent over long periods of time and allows the toxic nature of the molecules to be passed to organisms through the food chain. Even very small amounts of the compounds in water end up in fish and other organisms that live in water. As larger organisms (including humans) ingest the fish or other water organisms, they are in turn ingesting the organic pollutants as well.

Many studies have shown the harmful effects of these and other organic pollutants in water; this issue is undeniable. At Luther College, we are looking for a new way to detect these water pollutants at low concentrations in order to know if any water systems in the area have higher concentrations of these pollutants than they should. Very little work has been done on the fluorescence of these organic pollutants complexed to the host of cyclodextrins\(^2\), and no studies have been done to detect these pollutants by this method, as proposed in this research. The fluorescence of dioxins, furans, and PCBs is well documented\(^3\)\(^5\), so we are certain that we will be able to explore a relationship with this new host-guest system based in fluorescence studies.

Experimental Methods

The project will focus on environmental concerns, looking at new ways to identify furans and dioxanes (initially) and eventually polychlorinated biphenyls in aqueous systems. These and
many other fluorescent organic compounds are known as major pollutants of our water and soil systems. The supramolecular incorporation of the organic molecules in host systems often leads to changes in the fluorescence data obtained for the molecules.\(^6\) The idea behind this research project is to investigate how incorporating organic pollutants inside the more hydrophobic cavity of a host system increases fluorescence yields, causes shifts in the emission spectra, or alters the fluorescence lifetimes of the probe (environmental) molecules. Cyclodextrins (CDs) are very popular host molecules in supramolecular chemistry because of their defined shape and ready availability. Cyclodextrins are large cyclic oligosaccharides (Figure 1) that have an overall bucket shape and a hydrophobic cavity for incorporation of organic molecules. There are three common CDs (varying in size): \(\alpha\), \(\beta\), and \(\gamma\), which contain six, seven, or eight monomers, respectively. These have cavity sizes of 5.7, 7.8, and 9.5 Å, allowing for complexation of molecules of different sizes.

In this project, Luther students will be involved in studying the basic fluorescence of the target probes in homogeneous solvents and observing the changes in the fluorescence spectra based on polarities. Next, incorporation into a CD cavity of appropriate size will be attempted and monitored by fluorescence. The goal for this project is to be able to detect very low concentrations of environmental pollutants in water by adding a supramolecular host and observing the change in fluorescence data. There is substantial support in the literature for the changes in fluorescence upon the formation of a supramolecular complex (including the PI’s prior research)\(^7,\ 8\), but to the best of our knowledge, complexation has not been studied with the aim of eventually identifying trace organic components of environmental concern. This project will expose students to purification techniques, fluorescence studies, and an understanding of supramolecular complexation.

![Figure 1: Structure of \(\alpha\)-cyclodextrin](image)

Fluorescence spectroscopy allows us to study characteristics of target molecules (pollutants) as well as their surrounding environment, the supramolecular system. Various spectral and kinetic techniques can be used to monitor the singlet excited state. This study will undertake a comprehensive analysis of these environmental pollutants in hopes of seeing which may be identifiable by supramolecular interactions and host-guest photochemistry. The steady-state fluorescence technique makes it possible to investigate the fluorescence spectral properties, while the time-resolved technique focuses on the investigation of fluorescence lifetimes (\(\tau\)). The initial work focuses on characterizing the absorption spectra, fluorescence emission spectra, and singlet lifetimes for each of the selected probes in buffered solution, a series of homogeneous solutions, and then in solutions of cyclodextrins (CD). Spectral shifts and changes (or lack of) in fluorescence lifetimes gives an initial indication as to whether or not the organic molecules are included in the CD binding sites. Because the binding sites in the CD are less polar than bulk
water, if the organic molecule is bound to the CD, it would be expected to behave more like the non-polar solvent than the polar solvent.

Fluorescence polarization experiments add insight to the extent of interaction of the organic pollutant with CDs. Using polarizers in both steady-state and time-resolved fluorescence allows for the measurement of rotational lifetimes of the probe molecules. Rotational lifetimes are not affected by fluorescence emission shifts, and thus can be measured regardless of the location of the probe molecule. If the probe molecule is not bound tightly, it would be expected that it would be freely rotating, thus the rotational lifetime would be short. If the probe molecules are more restricted (whether interacting with the outside of the host system or bound within an interior binding region), the rotational lifetime will increase. This technique will allow us to investigate the extent of the inclusion of the various pollutants within the CD cavity.

Using standard quenching methodology (applied to both the steady-state and time-resolved techniques), information can be obtained about the probe’s environment and about host-guest interactions. In both cases, Stern-Volmer plots will be generated (\(A_o/A = 1 + K_{SV}[\text{Quencher}]\)) to calculate a quenching rate constant (\(k_q = K_{SV}/\tau_o\)) for the excited probe. If the probe is well protected from the aqueous quencher, the quenching rate constant (\(k_q\)) will be smaller than the rate constant for the probe in an aqueous system. Comparing the data obtained from the time-resolved technique to that of the steady-state technique allows for invaluable mechanistic information that cannot be obtained from steady-state measurements alone.

3. Principal Investigator

Olga Rinco, Assistant Professor of Chemistry, obtained her B.Sc. in Chemistry and Mathematics from McMaster University (Hamilton, On, Canada), a Ph.D. in Supramolecular Photochemistry from the University of Victoria (Victoria, BC, Canada), and postdoctoral training in Photochemistry and Photobiology from the National Research Council of Canada (NRC, Ottawa, On, Canada). Dr. Rinco has been a member of the Luther College Chemistry Department since 2003. Dr. Rinco’s research training includes expertise in both fluorescence spectroscopy and Laser Flash Photolysis. Her research has focused on intermolecular interactions between compounds in a field of study known as supramolecular photochemistry. She has published five articles in peer-reviewed journals related to both her Ph.D. and postdoctoral studies. Just this fall she has published her sixth journal article on the findings of her first research project in host-guest supramolecular photochemistry at Luther College in collaboration with seven undergraduate students. Since her appointment at Luther College, Dr. Rinco has mentored eleven undergraduate students in research projects (eight women and three men). Eight of her research students are chemistry majors, and three are biology majors. Dr. Rinco has secured external support from the R.J. McElroy Trust and the Monticello College Foundation. She is a member of the American Chemical Society and the Council on Undergraduate Research.

4. Organizational Background

Luther College, founded in 1861, is a Phi Beta Kappa institution acclaimed as one of the outstanding liberal arts colleges in the Midwest. Located in Decorah, Iowa (population 8,500), Luther is home to 2,519 undergraduates from 41 states and 47 countries, with the majority coming from the Upper Midwest (i.e., Iowa, Minnesota, Wisconsin, and Illinois). The college offers the bachelor of arts degree in more than 60 majors and pre-professional and certificate programs. The average ACT score of Luther’s first-year students is 26.3, and 34 percent come from the top 10 percent of their high school classes.
Luther College is recognized nationally for its membership in the prestigious consortium of the Associated Colleges of the Midwest, the National Association of Independent Colleges and Universities, the Annapolis Group, and the Pew Midstates Science and Mathematics Consortium. Luther continues to be recognized among the Top 100 colleges in the nation by the U.S. News’ annual ranking of America’s Best Colleges.

Reflecting the college’s commitment as a leader in sustainability initiatives, Luther is a member of the Association for the Advancement of Sustainability in Higher Education (AASHE) and was a charter signatory of the College and Universities President’s Climate Commitment. In Fall 2009, Sampson Hoffland Laboratories—Luther’s new science facility which houses the departments of chemistry and biology—received a gold certification from the Leadership in Energy and Environmental Design (LEED) green building certification system in recognition of its environmentally friendly design and construction features. Luther College has also recently been recognized as one of the nation’s Overall College Sustainability Leaders in the College Sustainability Report Card 2010 issued by the Sustainable Endowments Institute.

5. Collaboration

Dr. Rinco will only collaborate with undergraduate researchers at Luther College. All work will be carried out at Luther College and no further collaboration is necessary.

6. Proposed Budget

Luther College respectfully requests a grant of $39,465 from the Grow Iowa Values Fund. The funds are requested for salaries, supplies, and travel to scientific conferences. In addition, Luther College will provide $40,048 in matching funds to support the project.

Dr. Rinco is on a nine-month contract with Luther College. Dr. Rinco will be working on the proposed research project full-time during the summer months, thus she requests two months of summer salary during both project years. A key component of this project is the training of new scientists for the future, thus stipends for two summer undergraduate research students per year is also requested.

A new spectrofluorometer which will be used to do the research is being supplied by Luther College. Instrumentation for the time resolved measurements and UV Vis spectroscopy is also available at the college.
# Budget Table for GIVF (2 Year Proposal)

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| Fringe Benefits                                                          |               |             |               |             |                   |                 |
| • Principal Investigator (FICA 7.65%) (TIAA CREF)                        | $0            | $842        | $0            | $842        | $0                | $1,684          |
| • Undergraduate Students (2/year) (FICA 7.65 %)                          | $0            | $421        | $210          | $210        | $210              | $631            |
| **Total Salaries and Benefits**                                          | $0            | $18,863     | $2,960        | $15,902     | $2,960            | $34,765         |

| Permanent Equipment                                                      |               |             |               |             |                   |                 |
| • Jasco water jacketed spectrofluorometer                                | $16,604       | $0          | $0            | $0          | $16,604           | $0              |
| **Total Equipment**                                                      | $16,604       | $0          | $0            | $0          | $16,604           | $0              |

| Supplies and Indirect costs                                             |               |             |               |             |                   |                 |
| • Chemical Reagents, and solvents (including hazardous waste disposal)  | $1,000        | $1,000      | $0            | $1,000      | $1,000            | $2,000          |
| • Photochemical glassware and cuvettes                                   | $1,000        | $1,000      | $0            | $0          | $1,000            | $1,000          |
| • Indirect research costs (44.8 % of salaries)                          | $7,392        | $0          | $7,392        | $0          | $14,784           | $0              |
| **Total Supplies**                                                      | $9,392        | $2,000      | $7,392        | $1,000      | $16,784           | $3,000          |

| Travel Costs                                                             |               |             |               |             |                   |                 |
| • National meeting (of one of the major chemical societies)              | $850          | $850        | $850          | $850        | $1,700            | $1700           |
| • National Conference or other research travel expense                   | $500          | $0          | $500          | $0          | $1,000            | $0              |
| • Regional Physical Science Conference                                  | $500          | $0          | $500          | $0          | $1,000            | $0              |
| **Total Travel**                                                        | $1,850        | $850        | $1,850        | $850        | $3,700            | $1700           |

| Total Request From GIVF                                                 | $21,713       | $17,752     | $39,465       |
| Total Matching Funds                                                    | $27,846       | $12,202     | $40,048       |
7. Timeline

Dr. Rinco has just completed her first research project with undergraduate students at Luther College, and thus this project is the start of a new area of research. The methodology being employed in this project is similar to the one just published by the research group, so she is confident that progress will be made in this new area of host-guest chemistry.

The following timeline approximates the plan of work over the next two years:

**Project Year 1:**
We will explore the solubility and fluorescence trends of all three classes of compounds (representative molecules) and do homogeneous studies to see which are most promising. We will also try to discover which host-guest system will be most suitable for the identified most promising species to study (i.e., which cyclodextrins are most appropriate). We may start on preliminary work to characterize the interaction between the environmental guest and the CD host.

**Project Year 2:**
In the second year of the project, we will focus on the host-guest interaction. Having identified viable systems to study, we will look at using our fluorescence methodologies to characterize the interactions and see how well the pollutants interact with their hosts. We believe we can make excellent progress in two years time, present the work at scientific meetings, and be working toward a publication near the end of the project’s timeline.

8. Impact

At the heart of this project is training undergraduate students in basic research that can help with environmental water concerns we are all facing due to the pollution of the past and the present. This project will immerse undergraduate students in an original and industrially relevant research project. It has been observed by all members of the Luther College Chemistry Department that research experiences have a profound impact upon the career plans of undergraduate students. A large percentage of our graduating seniors (> 60%) continue on to graduate and professional degrees, many in the state of Iowa. Of the eleven research students Dr. Rinco has mentored while at Luther, ten are continuing their studies (five in Iowa, four in Minnesota, and one in Wisconsin), and one is doing volunteer work in Minneapolis.

The research looks to address an area of concern for all of us, and could very easily be applied to water treatment questions. We are proposing to study a system that may help identify environmental pollutants that cannot be easily detected due to their low concentration levels in water. Though the concentrations are low, these compounds persist for a very long time, and thus accumulate in the fat storage of plants and animals. Ingesting small amounts of the contaminants over a long period of time can lead to harmful health effects, including cancer, and thus detecting these pollutants even at low levels is very important. Fluorescence spectroscopy is easy to carry out and instrumentation is relatively inexpensive and readily available, thus this application could be used in industry. Furthermore the only additional chemicals that would be needed are cyclodextrins, which are likewise inexpensive and available for purchase.

It is therefore expected that this research could quite substantially impact the future of four undergraduates and potentially the health of our local water systems. When our methodology is developed, we will test local waterways and see if any of them exhibit high levels of these organic pollutants. If so, such findings will be passed on to the Iowa DNR. In turn, the DNR or local industry could use this methodology to test for presence of these contaminants using the methodology developed in this study.
9. Bibliography and References Cited

I. Executive Summary

Upper Iowa University (UIU) is a leader in capacity building infrastructure. In partnership with the Grow Iowa Values Fund (GIVF), this project would address the core components of business growth through entrepreneurship, marketing and business development efforts, and business growth in northeast Iowa. By building on the success of UIU’s entrepreneurial spirit the past five years, we are excited to present this application for consideration.

This project will potentially uplift a depressed community (Fayette) through the continued work of the Upper Iowa Business Development (UIBD) grant program. By providing limited start up funding to entrepreneurs, using UIU’s acclaimed master planners, local e-commerce websites, and support from the City of Fayette, this project will have long-lasting impact on the economy within both the City of Fayette and the County of Fayette.

In addition to this project, information will be disseminated to other interested organizations for similar projects throughout Iowa.

II. Project Description

Anyone associated with one of Iowa’s private, not-for-profit institutions of higher education knows the dramatic economic impact these institutions create for the communities in which they are located. According to the Iowa Association of Independent Colleges and Universities, Iowa’s private, not-for-profit institutions produced nearly $1.9 billion in economic activity in the State of Iowa last year. In many cases, these institutions are the largest and most significant economic engine in their communities.

This is certainly true for the City of Fayette and Upper Iowa University, a private, not-for-profit institution located in Fayette since 1857. Fayette is a community of approximately 1300 located in northeast Iowa. According to data from the Iowa State University Retail Trade Analysis Program, the community has seen economic decline in a number of categories during the past decade. Population has decreased 14% since 2000. Since 2001, retail firms are down 24%, retail sales have declined 30%, and per capita sales have
plummeted 37%. Perhaps most acutely diagnosing the City of Fayette’s dramatic economic decline is its ranking in State and National Median Household Income (NMHI), with Fayette’s now just over $28,000, or 68% of the NMHI.

During that same period, Upper Iowa University has experienced steady and consistent growth, with enrollments increasing on the Fayette campus by nearly 40% over the past five years. Upper Iowa University has a Fayette campus enrollment of 904 students and an enterprise wide enrollment (which includes academic extension centers, a robust online program, and external degree) of approximately 6,700 students. Partly due to its large academic extension program, the University employs 240 people at its Fayette campus, making it Fayette County’s largest employer.

While Upper Iowa University has always been an active member of the Fayette community, the Board of Trustees and the university’s current administration determined that UIU needed to take an even more proactive role in regional and community economic development during the institution’s strategic planning process in 2006. One of the nine initiatives outlined in the university’s strategic plan focuses solely on “enhancing the quality of Fayette as the residential, life-style, and economic center of UIU’s future.” Since adopting the strategic plan, several economic development initiatives have been established by Upper Iowa University to improve the vitality of the City of Fayette and the surrounding region. Nearly a half million dollars in federal funding has been secured to support the university’s efforts.

One of these initiatives is the Upper Iowa Business Development (UIBD) grant, a University endowed program established in 2007 through a gift by UIU Board Chair Bob Firth and his wife, Betty Firth, also a UIU board member. This endowment, presently valued at approximately $570,000, was established with the goal to award an annual grant of up to $40,000 to entrepreneurs interested in starting, expanding, or relocating a business in Fayette, Iowa.

Applicants must demonstrate a sound business plan, growth potential, and sustainability. Applications are reviewed by the UIBD Grant Advisory Committee, made up of local business owners, elected officials, economic development professionals, the Executive Director of the area regional planning commission, and University personnel. The committee
scores applicants on strength of the business plan, the impact the business will have on the
community (i.e. jobs created, sales and tax generated), symmetry with University objectives,
e-commerce elements of the business plan, and whether the business provides a new amenity
for the community.

Recipients, and in some cases unfunded applicants, are provided with business
development assistance and entrepreneurship mentoring. One success this initiative has had
is to create an e-commerce Web site for an applicant even though the business did not meet
the minimum requirements of the UIBD grant. Applicants are counseled about other possible
sources of funds, including historical tax credit opportunities and Iowa’s Targeted Small
Business program.

The first UIBD grant was awarded in August of 2008 to Fayette Flooring, a new retail
store specializing in flooring and concrete overlay. This $15,000 award enabled the business
to make interior and façade improvements to its newly purchased building, thereby
enhancing the physical appearance of the main street. During its first six months in
operation, Fayette Flooring did $73,363 in sales and employed one full-time and two part-
time employees. The business provided an internship experience for an Upper Iowa business
student. The new retail store contributed to the local tax base by paying $1,080 in property
tax to the City of Fayette.

In August of 2009, a $40,000 grant was awarded to S.K. Rogers Funeral Chapel to
support the construction of a new funeral chapel, also to be located on Main Street. The
business, currently under construction, will house a small real estate office. Both of the
UIBD grant awardees have worked with University master planners in the design of the
projects to help establish a common look and feel for new construction in Fayette’s business
district. Additionally, awardees are required to provide the UIBD Grant Advisory
Committee with financial statements to assist the committee in evaluating the success of the
grant initiative. Awardees are encouraged to work with the Upper Iowa University e-Center,
established in part to assist area businesses with development of e-commerce ready websites.

The UIBD grant initiative has already had a tremendous impact on the community.
Currently, five construction projects are underway in a three-block radius on Fayette’s Main
Street. These projects are two UIBD grant awardees and another UIBD applicant who is
receiving University master planning assistance. The latest project will move the
university’s flagship book and apparel store from campus to the downtown area. In the previous ten years, no new retail construction had occurred on Fayette’s Main Street. There is little question that this economic development initiative is creating growth in a city, and a region, that is desperately in need.

In order for the UIBD grant to continue to have the desired impact, the advisory committee believes that full $40,000 grants must be awarded annually to attract applications that will create renewed vitality and bring growth to the community. Toward this end, the University Advancement Office is seeking foundational and alumni support to increase this endowment from its present $570,000 level to $1 million so that interest income generated annually will allow for a $40,000 annual award. Currently, the endowment is not generating enough income to support a full award and there is concern that this successful program may stagnate.

In an effort to prevent this, Upper Iowa University is requesting Grow Iowa Values Fund support in the amount of $60,000 to allow this business development program to continue. Any GIVF funding received will not go into the endowment but instead will be used only to partially fund awards made to successful UIBD grant applicants during these two fiscal years. The Upper Iowa Business Development grant will provide economic growth and job creation in a county currently facing severe economic distress and an unemployment rate of 8.1%.

As written and passed into law during the 2005 session of the Iowa General Assembly, House File 809 appropriates $5 million annually to the Board of Regents for capacity-building infrastructure in areas related to technology commercialization, entrepreneurship and business development for the purposes of state economic development. The legislation also permits the Board of Regents to award funds to independent institutions for these purposes. Upper Iowa University embraces the core tenets of the GIVF, as demonstrated by its recent creation of the e-Center and establishment of the Heartlanding Information Technology Services Center, a faculty and student operated information technology service. Both of these initiatives are partially funded through two USDA Rural Development grants, a U.S. Department of Education grant, and also with University resources.

It is our hope that the Board of Regents will recognize the positive economic impact the UIBD grant has on the City of Fayette and the citizens of northeast Iowa. Although the
Grow Iowa Values Fund has previously supported primarily research and commercialization projects at private institutions of higher education, it is our belief that financial support for successful business development programs is a prudent investment. This is especially true considering the incredibly challenging economic times our state is experiencing. The grant advisory committee will continue to use established metrics to evaluate the performance of the grant program. These measurements will establish best practices and benchmarking that will be made available to other institutions considering similar programs designed to foster entrepreneurship and business development in their communities.

III. Principal Investigator/Project Manager

Andrew Wenthe is Chair of the Upper Iowa Business Development Grant Advisory Committee and is employed as the Director of External Affairs for UIU. Wenthe is the project manager for several grants received by the University relating to community and economic development, including a three-year, $139,500 USDA Rural Community Development Initiative grant, a two-year, $99,000 USDA Rural Business Enterprise Grant, and a $238,000 Congressionally-awarded appropriation through the Fund for Improving Post-Secondary Education.

The Office of External Affairs has oversight over Upper Iowa’s e-Center, an interdisciplinary, collaborative venture emphasizing practical “real world” application. The e-Center integrates three interrelated elements: web-enabled and computer assisted learning, the security of electronic data storage and transmission, and local and regional economic development through business incubation and support. The e-Center contains a faculty and student operated information technology service that provides website development and maintenance support to area business owners.

Additionally, Wenthe serves as the State Representative for Iowa House District 18, which includes parts of Fayette, Bremer and Black Hawk Counties. Wenthe serves as Vice-Chair of the Appropriations committee, and is a member of the Economic Growth, Transportation, Agriculture and Education budget committees.
IV. Budget

Upper Iowa University is seeking $60,000 from the Grow Iowa Values Fund to be used to partially support Upper Iowa Business Development (UIBD) grant awards for fiscal years 2010 and 2011. Any GIVF funding received will not go into the endowment but instead will be used only to partially fund awards made to successful UIBD grant applicants during these two fiscal years. The University has established an endowment valued at approximately $570,000 that generates interest income to fund UIBD grant awards. At present, the endowment is not generating sufficient income to offer full awards, which could weaken the quality of applications received and result in diminishing the economic impact the program has on the community. Money received from the Grow Iowa Values Fund will allow the UIBD Grant Advisory Committee to make $40,000 awards in 2010 and 2011. During this time, the university will continue to actively secure the additional $430,000 to create a sustainable funding source.

Upper Iowa University’s e-Center will offer technical assistance and business mentoring support to successful UIBD grant recipients. These initiatives have been established through nearly a half million dollars in federal grant support in addition to the allocation of University funds.

<table>
<thead>
<tr>
<th>GIVF Award</th>
<th>UIU cash match</th>
<th>UIU in-kind match</th>
<th>Endowment</th>
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<tr>
<td>2010 UIBD Award</td>
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<tr>
<td>2011 UIBD Award</td>
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<td></td>
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<tr>
<td>Staff time (2 years)</td>
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<td>Legal (2 years)</td>
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<tr>
<td>Advisory Committee time (2 years)</td>
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<td>(15 members x 10 annual hrs @ professional hourly rate of $35 = $5,250)</td>
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<tr>
<td>Endowment Principle</td>
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<td>$570,000</td>
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<tr>
<td><strong>Total</strong></td>
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<td><strong>Total UIU Match</strong></td>
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V. Project Timeline

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
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<td>Oct. ’10 – June ’12</td>
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VI. Collaboration with other Higher Education Institutions

The current UIBD Grant Advisory Committee is comprised of individuals representing the City of Fayette, Upper Explorerland Regional Planning Commission, Fayette County Economic Development, Oelwein Chamber and Area Development, Elkader Economic Development, and the UIU Board of Trustees. Upper Iowa University partners with Northeast Iowa Business Network on a USDA Rural Development grant. UIU collaborates with Northeast Iowa Community College, the University of Northern Iowa, and Kirkwood Community College in a number of initiatives. The diversity of the individuals and entities listed exemplifies the University’s widespread collaborative efforts.
VII. Research Activities

The research and benchmarking being done through the Upper Iowa Business Development grant includes the following measurable metrics: new retail firms, new retail sales, new property tax collected, new community amenities, new jobs created, and enhanced foot traffic in downtown Fayette. The Heartlanding Information Technology Services Center is also measuring the number of retail firms served, Web site activity, and e-commerce sales of businesses it is supporting. This data will provide Upper Iowa students with research opportunities and will lead to the establishment of best practices for future programs designed to foster entrepreneurship and business development in their communities.
Additional Information Request

Upper Iowa University Business Development Grant Program
Proposal submitted by
Andrew Wenthe
Vice-President for External Affairs
Upper Iowa University

1. Please provide more specific information about what the potential grantees are allowed to use the grants for.

Upper Iowa Business Development grants are made available to individuals wanting to start or expand a business in the City of Fayette. As part of their application, prospective awardees are required to submit a business plan (using a Small Business Development Center template provided to applicants) indicating for what purpose and at what stage in their project they would use UIBD grant funds. Normally, the committee will request that the applicant provide a Gantt chart that illustrates a project schedule. Dependent on the project and the needs of the business owner, UIBD grant awardees could use grant funds for research, development or commercialization of a product, marketing and advertising, or construction/renovation expenses. In the past, grant funds have been used to construct a new building, make façade improvements to an existing building, and convert a building’s interior to better suit retail needs. Grant funds are awarded on a reimbursement basis and can be used only for expenditures agreed upon and approved by the UIBD Grant Advisory Committee.

2. Are grantees required to provide cost share for the projects?

Yes, all UIBD grant applicants are required to provide a cost share for their project. The minimum cost share allowed is a 20% cash match (no in-kind allowed) of the amount of the total grant award. The UIBD Grant Advisory Committee uses criteria in awarding grants that considers the personal investment in a project by an applicant. The committee believes it is critical to a project’s long-term success that the applicant have sufficient “skin in the game” or investment in their project. In the first two years of this economic development initiative, both awardees have far exceeded the 20% minimum cost share requirement in the grant application.

3. Would the grants be focused on specific types of businesses or entities?

The UIBD grant is designed to foster economic growth, job creation, and renewed vitality in northeast Iowa. Applicants demonstrating impact in these areas are encouraged.
Although needs of the region and community will be considered, it is not currently the intent to specifically target types of businesses or entities.

All applicants for a UIBD grant are scored on the following criteria:

- **Strength of Business Plan/Experience** – 20 points
- **Impact** – 30 points
- **Quality of Life Improvements** – 5 points
- **Web-based Business Plan** – 25 points
- **Student Internship/Faculty Research Opportunity** – 10 points
- **Ability to Leverage Funds** – 10 points

4. **Please describe more specifically how this effort will be coordinated with any local, regional and state economic development efforts and how the project could potentially be of benefit as a demonstration to other areas of the state.**

   The UIBD Grant Advisory Committee was intentionally created to include individuals representing a wide array of interests and areas of expertise. State Representative Roger Thomas, Chairman of the House Economic Development Committee, is a committee member and has been helpful in providing guidance to awardees and applicants about sources of state funding. This has included opportunities available to entrepreneurs through the Iowa Department of Economic Development. Wendy Mihm-Herold, Executive Director of Upper Explorerland Regional Planning Commission, also serves on the advisory committee. Wendy and her staff actively investigate economic development opportunities available at the state, local and regional level and this input has been helpful. The Fayette County Economic Development Director and the Oelwein Chamber and Area Development Director serve on the advisory committee, both of whom have strong connections to and awareness of state and regional economic development programming. Additionally, we required one of our UIBD grant awardees to participate in the University of Northern Iowa’s MyEntreNet rural business development program which helped her become aware of challenges and opportunities that exist for a small business owner.

   The UIBD grant initiative has great potential to be used as a demonstration program for other private institutions of higher education. Private colleges and universities already have tremendous economic impact on their communities, often located in struggling rural areas of the state. A business development and entrepreneurship initiative similar to the UIBD grant can have a considerable impact on job creation and economic growth in these communities. Additionally, an institution’s alumni often have a vested interest in both their alma mater and its community. There is also much interest in entrepreneurship programs. As was the case with Upper Iowa, which received a $570,000 private gift to establish the endowment funding the grant program, this type of community development/entrepreneurship initiative is attractive to private as well as public investment.
5. **Please provide information about the potential for this project to create additional jobs.**

   Job creation is a major goal of the UIBD grant and therefore is one factor that is given serious consideration by the UIBD Grant Advisory Committee when reviewing applications. Each of the first two UIBD grants awarded has created jobs in Fayette, both permanent full-time positions and temporary jobs related to construction. The advisory committee is benchmarking just how many full-time, part-time and temporary positions will have been created because of this initiative.

   There is little question that job creation is one of the greatest strengths of the UIBD grant program. Several inquiries have been received in the Office of External Affairs about the next UIBD grant award cycle. Nearly all of these potential applicants are considering projects that will create new jobs in Fayette.