EXAMPLE

1

Toward an Understanding of the Cuban-American Experience of Ambiguous Loss

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Abstract

If awarded, a Fordham Faculty Research Grant (FRG) will support my collaborative research[1] assessing the applicability of the concept of ambiguous loss to the experiences of older Cuban émigrés residing in New York and New Jersey.

Ambiguous loss is a contextually based chronic condition of unresolved grief related to trauma and stress that can affect individuals and families (Boss, 2010). Unlike more conventional concepts of loss, it is characterized by its unclear and indeterminate nature—rendering it difficult to know when to begin or end the grieving process (Boss, 1999). For example, an individual or family can suffer from ambiguous loss if a loved one is physically present but psychologically absent—as when a parent or spouse proceeds through the stages of Alzheimer's Disease—or, conversely, psychologically present but physically absent (Boss, 2010).

The principal investigators hypothesize that due to Cuba's traumatic history and conflicted U.S. relations, Cuban-Americans suffer from ambiguous losses; cut off from their country, they kept physically absent families left behind, psychologically present in the U.S. Following Cuba's 1959 communist revolution, thousands of Cubans granted refuge in the U.S. believed their stay would be temporary; however, 50 years later, their ability to return to their country is restricted and influenced by their home and adopted country's political relations. Furthermore, although the intervening half-century may not have lessened older Cuban-American émigrés' feeling the double-edged sword of loved ones' psychological presence and physical absence, time and the influx of Spanish-speaking immigrants from a wide variety of countries has dulled and diluted the plight of Cuban-American refugees in the U.S. national consciousness and presence of mind.

Therefore, the case of older Cuban-American émigrés is both an exemplary and overlooked opportunity to respond to recent calls for more culturally sensitive research to better understand the cross-

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[1] *with* Zulema E. Suárez, Ph.D., Adjunct Professor, Fordham University Graduate School of Social Service (*see* provided CV as a supplemental document to this application).

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cultural concerns related to this serious condition for which no closure exists (Boss, 2010). A high prevalence of depressive symptoms have been found among Cuban older adults (Perrino, Brown, Mason, & Szapocznik, 2009), suggesting the possible presence of ambiguous loss; however, few studies examine the relationship between psychological distress and ambiguous loss among Cubans. Consequently, this project will advance an understanding of culturally competent practice with Cubans as it relates to the experience of ambiguous loss in order to inform and influence social work practice, research, and policy.

We expect to begin the project pending IRB approval in April 2011 and to complete it by the end of 2011. This study will serve as a pilot study to help secure additional external funding such as from the Hartford Scholars Program (application due February 1, 2012), which aims to train researchers and practitioners to support the rapidly increasing needs of an aging population.

Background

Both investigators' research interests include understanding the psychosocial aspects of Latino immigrants adapting to life in the U.S. They were both born in Cuba and are bilingual / bicultural (Spanish and English). Dr. Rose M. Perez's dissertation explored the emotional experiences of Latino youth in relation to the contexts in which they engage (e.g. with families, schools, friends) (Perez, 2009). More recently, Dr. Perez wrote a conceptual paper (Perez, in press) elaborating on the acculturation issues that immigrants in the U.S. experience. Dr. Perez' work history includes project management skills and qualitative research interviewing participants, synthesizing data for analysis and writing final reports. The second investigator, Dr. Zulema Suárez, has published extensively in the area of Cuban-American family studies (Suárez, 1997, 1998, 1999; Suárez & McAdoo, 1993) and has experience working with qualitative grant-funded research. The investigators have previously collaborated on a book chapter on Cuban-American families (Suárez & Perez, in press).

Although ambiguous loss is an oft-discussed concept in psychology (Boss, 1999, 2006), and has been introduced into social work in relation to immigrant experiences (Falicov, 2005), there is little empirical research on this topic. Boss (2007), proposes that ambiguous loss is a social construction that

lends itself to qualitative assessment because the traumatic and stressful events that are the etiology of the condition occur outside of the person. In other words, they are contextual rather than psychological (Boss, 2007) with the consequent feelings of ambiguity characteristic of the condition being described as emanating from situations rather than intra-psychically. However, the lived experience—and the interpretation that is given to that experience by the person who has both lived through and lives with ambiguous loss—can create ambivalent feelings that affect their present and future relationships (Boss, 2007). Therefore, although the concept of ambiguous loss has existed for some time, the lack of empirical research regarding its applicability has prevented its full use to alleviate the syndrome it seeks to describe: an inability to say goodbye to the past that inhibits an individual's ability to engage in the present, sentencing them to a future filled with a continual sense of loss for which they may blame themselves or their loved ones, but never the actual culprit: ambiguity itself.

Contribution

Thus this project will make two primary contributions: first, it will advance scholarship on ambiguous loss as it relates to immigrants and refugees; and second, it will provide insight into issues faced by older Cuban-Americans who are linguistically isolated. Both contributions will prove significant to social work practice, research, and policy, and will be supported by rigorous research methods to produce these results.

In this study, a purposeful sample of older (ages 65+) Spanish-dominant Cuban-American refugees who immigrated to the New York / New Jersey area shortly after the 1959 Cuban revolution will be interviewed to better understand how their experiences leaving Cuba and resettling in the U.S. fits with the theory of ambiguous loss. Emphasis on the early waves of émigrés for this study is based on the difficulty of adapting to the sudden, life changing and traumatic events that occurred on the island, which justified leaving; later waves of émigrés grew up within the communist system and did not leave suddenly. Qualitative interviews focused on identifying and understanding ambiguous loss will provide a detailed description of the meanings attributed to the loss of homeland, how participants have coped with these

feelings, and how such feelings have varied over time since their arrival in the U.S. The work will consist of the interviews, transcription, and analysis of the data.

Ambiguous loss lends itself well to the social constructionist perspective, and therefore to qualitative assessment (Boss, 2007). The investigators will use a purposeful sampling method, in order to select the sample that in their judgment best represents the population of this study (Rubin & Babbie, 2009). Use of qualitative interviews, conducted in Spanish will help provide an understanding of whether the ambiguous loss theory does indeed fit the experience of Cuban-Americans, or, alternatively, how the theory may be adapted to their experience.

With this information, we will be able to assess how the ambiguous loss framework can be applied to Cuban American émigrés. Individual in-depth interviews, each lasting between 45 minutes and one hour, will be audio taped, transcribed, and edited to correct transcription errors. Recordings will be destroyed after verification of transcription. Spanish language data will then be transferred into Atlas.ti, or an equivalent qualitative data analysis software program, and will be independently coded by at least the two principal investigators using an inductive method and constant comparison between interviews to increase reliability. This preliminary analysis will proceed according to a modified grounded theory method (Glaser & Strauss, 1967) to identify any emerging themes that we may be missing given our a-priori theoretical bias of ambiguous loss.

Further analysis will use a qualitative description method to analyze the data to understand the theory-derived concepts (e.g., ambiguous loss, boundary ambiguity), patterns, themes, and emergent understandings (Faber, Willerton, Clymer, MacDermid, & Weiss, 2008; Sandelowski, 2000; Sullivan-Bolyai, Bova, & Harper, 2005). Grounded theory, a qualitative inquiry that seeks patterns or common themes, is the basis of this project; therefore, the research will be completed by coding or classifying the data according to the themes that emerge inductively from the data (Charmaz, 2006). Thematic conceptual categories are likely to contain descriptions of reported losses, role changes, life events, coping strategies, and general themes. In addition, the researchers' current and future scholarship plans to draw on the

methodological ideas of John W. Creswell, expert on qualitative research and mixed method designs. Because loss among Cuban-American older adults is not a well-established research area, the grounded theory, with the help of experts, will present the information in depth and lay a foundation for future studies. Creswell has offered to serve as a consultant on our future expansions of this work in which mixed methods are planned to assess both ambiguous loss and its concomitant construct "boundary ambiguity", which involves confusion over family roles and membership.

Budget

The $6,500 budget is planned to include a need for: (1) one research assistant for IRB development and recruitment (10 hours at $15/hour); tasks include assisting with development and execution of needed correspondence and coordinating logistics of participant recruiting and scheduling = $150; (2) Spanish to Spanish transcription of 20 in-depth interviews at $160 each = $3,200; (3) One non-Fordham research assistant for data analysis and management during summer months (30 hours at $15 per hour rate); tasks include assisting with the analysis of 20 interview transcripts = $450; (4) Training on Atlas.ti for analysis in Spanish language = $300; (5) Consulting fees for assistance with this project from Zulema E. Suárez, Ph.D = $800; (6) Spanish to English translation of transcript sections for inclusion into submitted manuscripts = $700; (7) Additional costs for equipment, travel, recruitment, and payments to participants = $900.

Conclusion

By conducting a qualitative study with a purposeful sample, this research will reveal new information about psychological distress among older Cubans in the United States. Increasing the understanding of mental health among Cuban-Americans will help clinicians and other mental-health professionals develop culturally responsive social services. Other expected outcomes of the research include the publication of findings in scholarly journals, and the application to external sources for additional funding for further research. The investigators will submit articles to gerontology journals, and to journals focusing on the well-being of Latinos. Dr. Perez plans to apply to the Hartford Scholars Program, February 1, 2012 and will explore additional external funding sources.

EXAMPLE

2

Title: Phototoxicity of drugs and nanoparticles in the human eye

Abstract

If awarded, a Faculty Research Grant would enable me to capitalize on a peer-reviewed invitation to conduct research this summer in collaboration with my two post-doctoral fellows (Albert Wielgus, Ph.D. and Baozhong Zhao, Ph.D) at the National Institutes of Environmental Health Sciences (NIEHS), a North Carolina located unit of the National Institute of Health (NIH). Fordham's support is critical for five reasons:

(i) I do not have laboratory space at Fordham, and this type of collaboration is essential if I am to access the multimillion dollar photophysical equipment and human ocular tissues my research requires;

(ii) Due to the untimely death of the PI (Colin Chignell, July 2008) at the NIEHS' Photobiology laboratory, I have become the scientific head of this laboratory, requiring my presence as current titular PI for the successful completion of the projects that are the subject of this proposal;

(iii) Due to Federal budget cuts, in 2010 the NIEHS will not be able to cover my costs of travel and stay at their facility as in past years, and I will also have to cover some of my cost of supplies;

(iv) The NIEHS has, however, donated HPLC [High Pressure Liquid Chromatogram] equipment with fluorescence detectors (valued at $20,000) to Fordham's Department of

Natural Sciences through my initiative, the cost for packing and shipping of which would also be covered under this grant;

(v) In addition to the two scholarly articles I intend to produce from this summer's research for submission [Toxicology and Applied Pharmacology, Photochemistry Phtobiology]the NIEHS also anticipates making external grants available in my area of "nanosafety' for 2011-12, for which my work at their facility this summer will place me in an advantageous position.

Background

Everyone over the age of 65 is susceptible to developing cataracts and macular degeneration. In the next 30 years over 24 % of the population of the United States will be over the age of 65 and are therefore at risk for these blinding disorders. Although sight may be restored by an operation to remove cataracts, there is currently no effective treatment for retinal or macular degeneration. My ongoing research is to identify environmental risk factors that lead to these age-related blinding diseases and examine ways to prevent such damage. In addition to environmental hazards, there are dyes, drugs, over the counter medications and nanoparticles that can dramatically enhance phototoxic reactions in the human eye leading to early development (i.e., at 40 years old) of cataracts and macular or retinal degeneration.

The NIEHS facility at which I have been conducting this research for the past 12 years is a multidisciplinary lab that allows me access to multimillion dollar laser and photochemical equipment. During the summer of 2008 and my Spring 2009 Faculty Fellowship I developed at NIEHS an *in vitro* system using human lens epithelial cells to define phototoxic properties of nanoparticles with potential to damage the human lens.

(Phototoxicity and cytotoxicity of fullerol in human lens epithelial cells. Roberts JE, Wielgus AR, Boyes WK, Andley U, Chignell CF. Toxicology and Applied Pharmacology 2008 Apr 1;228(1):49-58.

In previous years at NIEHS, I have proven that ocular exposure to UVA and UVB (lens) or Visible blue light (430 nm) (retina) alone or in the presence of drugs or herbs (St. John's Wort) increases the human risk for developing cataracts and retinal degeneraton **(Wielgus AR, Chignell CF, Miller DS, Van Houten B, Meyer J, Hu DN, Roberts JE. Phototoxicity in Human Retinal Epithelial Cells Promoted by Hypericin, a Component of St. John's Wort. Photochem Photobiol.** (**2007) 83(3):706-13)**

Summer 2010 I will investigate how nanoparticles (fullerols), used for drug delivery to the eye, may cause very early retinal degeneration. I am also examining the potential for fluoroquinolone (i.e. cipro) antibiotics to cause early damage to the human lens. The final purpose of my research is to remove, modify or quench these toxic agents in order to prevent the formation of early or late onset cataracts and macular degeneration. These *in vitro* experiments are currently in progress and are expected to be completed by September 2010.

Contribution

Cataracts and age-related macular degeneration (AMD) are the most common causes of visual impairment in the elderly. Although there is a genetic component to these blinding disorders, clinical and epidemiology studies have confirmed that environmental hazards (sunlight, phototoxic drugs and herbal medications) are major risk factors in initiating cataracts and AMD. All of these environmental hazards induce the formation of free radicals and reactive oxygen species (ROS) in the eye. The aged eye has limited protection against

free radicals and ROS, thus environmental hazards can put older people at severe risk of serious ocular damage. I have modeled this synergistic effect between environmental hazards and age by studying the interaction of sunlight with endogenous photoactive substances (xanthurenic acid, lipofuscin, A2E) whose production increases dramatically with age.

I have previously defined the damage to human ocular tissues induced by the endogenous agents. I am now defining the ocular damage induced by exogenous agents using *in vitro* and photophysical techniques. The ultimate goal is to develop appropriate strategies to ameliorate or prevent age related, environmental, drug and nanoparticle induced cataracts and macular or retinal degeneration.

Specifically, before attempting to define the effect of photoprocesses on biological systems, it is essential to get precise information about wavelength, photochemical yields/reaction rates, and biological targets. Mechanisms may be further defined through examination of the effects on the target molecules in live cells. This knowledge will facilitate risk assessment in humans and promote development of more sensitive ways to measure and screen for damage in individuals and in populations. Furthermore, once the mechanisms of damage are known, phototoxic agents can be modified to inhibit detrimental processes or to improve the efficacy of beneficial reactions.

Consequently, my research involves a multidisciplinary approach:

1) *in vitro***:**

i. Models for Cataract formation Human Lens Epithelial Cells:

An *in vitro* model system (using human lens epithelial cells from human eyes) has been set up to determine potential phototoxicity of fluoroquinolone antibiotics and demonstrate specific damage end points (oxidative DNA damage, lipid peroxidation , apoptosis/necrosis, membrane damage, mitochondrial damage).

ii. Models for Macular Degeneration Human Retinal Pigment Epithelial Cells:

An *in vitro* model system (using retinal pigment epithelial cells from human eyes) has been set up to determine the potential phototoxicity of nanoparticles used for drug delivery) and demonstrate specific damage end points (oxidative DNA damage, lipid peroxidation , apoptosis/necrosis, membrane damage, mitochondrial damage).

iii. Models for Prevention of Damage to Ocular Cells

The effect of non-toxic quenchers known to cross blood lenticular and retinal barrier in humans. (i.e. lutein, N-acetyl cysteine) will be studied for their potentioal to block photodamage end points from the above in vitro experiments. These quenchers of phototoxic damage have been shown to be available to the human eye with supplementation.

2) Chemical and Photophysical Techniques

Time resolved photophysical techniques will be used to define the precise free radicals and reactive oxygen species formed by fluoroquinolones and nanoparticles. This will define the mechanism of phototoxicity for each agent. Dynamic Light Scattering will also be used to further define the chemical and physical properties of nanoparticles.

Cost

As stipulated in the abstract at the outset of this proposal, the costs for which I am requesting funding are paramount to my being able to travel to, supply my effective use of, and retrieve from the NIEHS in North Carolina the laboratory equipment necessary to the proposed research, some of which will now reside in the Fordham's Department of Natural Sciences due to my long-term collaboration with this facility.

Conclusion

Cataracts and age-related macular degeneration (AMD) are the most common causes of visual impairment in the elderly. In the next 30 years over 24 % of the population of the United States will be over the age of 65 and are therefore at risk for these blinding disorders. As stated at the outset of this proposal, not only will a Fordham Faculty Research Grant prove pivotal in supporting my longstanding line of research during a critical juncture in its funding, bring needed resources to the University, and provide a platform for future external support, it will prevent interruption of work that is already proving integral to our fight to preserve the sight of millions of Americans.

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(A) List of essential titles

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Andley, U. P., Rhim, J. S., Chylack, L. T. Jr. and Fleming, T. P. 1994. Propagation and immortalization of human lens epithelial cells in culture. Invest Ophthalmol Vis Sci 35:3094-3102.

EXAMPLE

3

Faculty Research Grant Narrative:

A Variational Approach to Vesicle Membrane Modeling

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Abstract : This project is a mathematical study of vesicle membrane fusion and lipid membrane mechanics. The cell membranes of almost all living organisms, as well as the membranes that surround a cell's nucleus and many other sub-cellular structures, are comprised of two thin layers of lipid molecules–the bilipid layer or lipid membrane. Vesicles are small sacs that life uses to store and transport substances in and out of the cell. A critical component of the vesicle's transport function is the ability of the lipid layer to fuse with other lipid layers. However, the mechanism underlying vesicle membrane fusion is not well understood, despite how commonly it occurs in nature and how reproducible it is to great precision in experiment. Moreover, the membrane fusion mechanism is not directly observable as it happens at extremely small length and time scales. Hence, vesicle membrane fusion remains one the most basic open problems in biophysics. This project proposes to simulate and study the origins of fusion by casting vesicles in a sophisticated mathematical model based on simple physical principles. Constructing the model and performing detailed numerical simulations will give spatial and temporal information not accessible by experiment. The project goals are: establish long term collaborations with biologists; obtain funding from the NSF and NIH; and make contributions to understanding the fundamental physics of lipid membranes.

This project is running in collaboration with Robert Eisenberg, PhD and Fredric Cohen, PhD of Rush University Medical Center in Chicago. Initiated earlier this year, the investigator and collaborators have to date agreed on a preliminary model. The model, a complicated system of partial differential equations, is solved numerically. Preparations are being made to run large scale simulations in October in the Laboratory Computing Resource Center at Argonne National Lab. Preliminary results from these simulations will be reported in a paper to be submitted to *Physical Review E* by December 2010. A more physically sophisticated model will be introduced and simulated in the early Spring for presentation at the Biophysical Society meeting in March.

Two grant applications will result from this work. The first will be to the NSF's Applied Mathematics Division in November 2010 and the other to the NIH in the fall of 2011. The investigator's continual application to these national grants will greatly be aided by the support of a "1st Year at Fordham" Faculty Research

Grant (FRG). The FRG will also permit the investigator to increase his scholarship and visibility in the applied and interdisciplinary mathematics community. Funds would be used to cover travel expenses to the collaborators' university, bring the investigator's collaborators to Fordham for face to face planning and discussion, employ Summer Undergraduate Research Assistants and acquiring a workstation for undergraduate researchers to implement large scale numerical experiments.

The remainder of this narrative is divided into background on the investigator and the mathematical field within which this project is framed and expected contributions of the project. The mathematical methodology is then described, followed by an outline of project expenses and a conclusion.

Background: The mathematical formulation of problems involving fluids and structures–such as the formulation the investigator is proposing to lend to the study of lipid membranes and vesicle fusion–has a long history. Beginning with Van der Waals theory of phase transitions and Landau's description of magnetism, this history includes the DeGennes' and Erikson-Leslie's theory of liquid crystals before progressing to today's popular approaches of using mathematical field theories and numerical methods to describe the processes of multi-physics condensed matter. Studies of liquid crystals [14], polymer electrolytes [16], super condictivity [5], charged gels [18], blood clotting [9] and blood flow [10] are a few examples. The range of physics addressed in this field is equal to the analytical and numerical techniques used. Building upon the investigator's dissertation and prior published work (see bibliography and CV), a guiding principle of the investigator's work is formulating comprehensive theories capable of guiding mathematicians in multi-physics problems, [22, 23]. It is from this foundation that the investigator forged collaborations with Drs. Eisenberg and Cohen, whose respective roles as Chairman and Director of Rush University Medical Centers Division of Molecular Biophysics and Physiology places their collective left foot firmly in physics while the other falls in the field of biology, where there is an even greater need for the comprehensive approach mathematics provides for understanding otherwise irreducibly complex systems.

Contribution : Biological membranes rearrange themselves in many biological processes. Fusion is a phenomenon specific to lipid bilayers, enabling transport of waste and engulfing of molecules by cells. It is the means by which a virus infects a cell and by which a sperm fertilizes and egg. Fusion occurs thousands of times in a single synaptic transmission, the firing of a nerve cell, [3]. A fusion pore, typically nanometers[1] in diameter, forms in a few nanoseconds. Well below the wavelength of light in size and too fast to be captured by today's fast digital microscope cameras (which image at just below milliseconds), the full fusion dynamic cannot be observed directly, [11]. Although it is one of the fundamental mechanisms of all living organisms, the detailed pathway by which two bilipid layers connect is unknown ([4]) and the energy required to

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[1]nano is the SI prefix for 10^{-9}.

undergo those pathways presently proposed is prohibitive, [13]. Moreover, traditional membrane mechanics in use by biophysicists today is a conservative, equilibrium theory and so cannot, a priori, describe the time course and the evolution of a true system. It is precisely because of this apparently irreducible complex system at the nexus of biology and physics that mathematics–and precisely this proposal–is poised to make a critical contribution to our understanding, not only of vesicle membrane fusion, but how to pursue an interdisciplinary agenda. Therefore, this project's use of well established mathematical tools will have a four-fold impact.

First, the mathematical approach will enable investigators to predict dynamics of fusion by positing consistent physical energies and initial data. Therefore, in stark contrast to traditional approaches in biophysics where information is taken from static or a priori configurations (e.g. spheres), [1, 12], the mathematical model will calculate the cascade of bilipid layer energy, forces and configurations as consequence of the field theory and be able to quantify physical parameters from more well established experimental models, [1]. See figure 1. Because the calculations yield values of all key variables over time, movies that precisely illustrate the time evolution of the membrane configuration can be generated. This allows one to appreciate changes over time, without having to refer to the physics or equations that underlie the fusion processes. Second, by thus facilitating the comparison of simulation with experiment, this study will challenge researchers' current hesitation to use detailed partial differential equations to model biological phenomena simply because of their (biological) complexity. If successful, the investigator's study will demonstrate that such complexity yields to concise and elegant mathematical descriptions which are therefore essential for research in biology. Third–a related impact–the success of this study will provide further evidence that the future of science will be dictated by interdisciplinary work. This project–along with the investigator's other research involvements–require expertise in chemistry, biology, engineering, mathematics and numerical methodology. Fusion is an example of merely one problem where the constant and close relationship between researchers in these areas is essential to making real progress. For this reason the investigator is fortunate to already have relationships with Rush University Medical Center and will also seek to work with biologists local to Fordham University and at the Einstein Medical School. Working in the context of these collaborations will also prove formative for future generations of scholars as the study engages undergraduate and graduate researchers to conduct numerical experiments. Finally, many mathematical tools are used in the formulation of fusion. These include geometry, partial differential equations, functional analysis and numerical methods. Writing a mathematical formulation of fusion leads to several interesting mathematical questions related to stability [2], well-posedness and the plethora of the connections between geometry and differential equations, [6, 19, 24].

Methodology : The primary impact of this project is gaining an enhanced understanding of vesicle membrane fusion. We begin by positing a membrane energy, denoted by E, which is defined in terms of a continuum variable $u(x,t)$ encoding the location of the membrane. The definition of $E[u]$ must be relatively simple, yet detailed enough to capture the physical energies relevant to the system. Typically $E[u]$ is a functional defined over a space of functions with certain differentiablity. We use a functional motivated by the theory of phase transitions, [19], whose efficacy was demonstrated in [6, 8];

$$E[u] = \int \frac{\epsilon}{2} \left(\Delta u - \frac{1}{\epsilon^2} f(u) - \frac{c}{\epsilon} g(u) \right)^2 \, dx + \frac{M}{2s} \left(\int \frac{\epsilon}{2} |\nabla u|^2 + \frac{1}{\epsilon} F(u) \, dx - s \right)^2 + \frac{N}{2v} \left(\int u + u_0 \, dx - v \right)^2.$$

The energy includes the surface tension, incompressibility and curvature effects of the classical Helfrich model. The representation is, however, more flexible and can readily account for multicomponent systems, inhomogeneities, and changes in topology. By solving the gradient descent equation

$$u_t = -E'[u], \quad u(0) = u_0, \tag{1}$$

one may explore the space of stable, equilibrium configurations of the vesicle. Here $E'[u]$ is the Euler-Lagrange derivative of $E[u]$. Equation (1) alone is not sufficient to describe the dynamics of real physical systems, especially when fluid motion is involved (indeed vesicles typically are in an aqueous medium.) For our purposes it is sufficient to solve the Navier-Stokes equations

$$\begin{cases} v_t + v \cdot \nabla v + \nabla p = \lambda \Delta v + f, \\ \nabla \cdot v = 0, \end{cases} \tag{2}$$

for the velocity $v(x,t)$ of the fluid (in fact, it is sufficient to solve the simpler and well-posed Stokes system as the flow at the micron length scale is typically of low Reynolds number.) The vesicle moves with the fluid and imparts the force $f(x,t)$ in (2) on the fluid. Writing down the form of f from physical considerations alone is typically difficult. However, using a variatonal formalism from the calculus of variations, one defines $f(x,t) = -E'[u]\nabla u(x,t)$. In total, the system enjoys the following property; the total energy

$$\frac{1}{2}\|v\|_{\mathbf{L}^2}^2 + E[u] \tag{3}$$

is nonincreasing. In mathematics, this property–that the energy is nonincreasing–is called an energy law and is the basis of the mathematical existence theory for (2). Profound to experimentalists is the following fact; the exchange of energies, fluid and vesicle motion and forces are outputs from these equations.

These equations are carefully discretized, using finite differences, and the discrete equations are solved numerically. This step involves a Newton's method and solving a system of linear equations with 100,000 and plus unknowns. On a standard workstation, this takes a minimum of four hours. The results from the simulation are stored and then interpreted. The entire process of modeling biological systems in this way is time consuming and fraught with technical complexities. Solving a large system of linear equations,

especially the Stokes system, requires a great deal of sophisticated numerical linear algebra. Moreover, care must be taken in choosing the spatial discretization–so that the system is even solvable–and the temporal discretization so that the energy law (3) is preserved (and that the numerical method is stable). Numerical schemes, designed specifically for this field theory, are implemented. However, the advantage of modeling a biological system in this way is that, because the configuration of the system is known at all points in space and time, the results contain information not accessible by experiment. It is for this reason that this variational approach to vesicle membrane modeling holds such promise for solving one of the most basic open problems in biophysics: vesicle membrane fusion.

Cost : Because of the time consuming, technical complexities of the mathematical modeling at the core of this inherently interdisciplinary–and consequently cross-country collaborative–project, the investigator seeks expenses to: (i) facilitate face to face meeting with his co-researchers at facilities that can accommodate both their simulation and experimental methods; (ii) employ one to two Summer Undergraduate Researchers Assistants at Fordham in preparing and conducting simulations; (iii) presentation at the Biophysical Society meeting in March 2011, which will be necessary to obtain peer feedback in preparation for future NIH funding applications; (iv) purchase one workstation devoted to remotely running resource intensive, parallelized, multiday simulations. It will be necessary for implementing the numerical routines by undergraduate researchers, who otherwise do not have access to such computing resources.

Conclusion : The proposed project builds upon the investigator's training in applied mathematics – particularly fluid mechanics, complex fluids and numerical simulation–and a platform of publications on the mathematical framework for modeling vesicles using the classical Helfrich energies, the Willmore energy and Euler number, [6, 7] as well numerical methodologies for solving complex fluid problems involving interfaces and electrostatic effects, [20, 21, 22]. The mathematics this project will employ is largely based on these works, and as such it is a natural extension of his work to bring this expertise into collaboration with researchers in diverse disciplines. These collaborators steer the investigators work to design more detailed mathematical models which are directly relevant to the types of questions biologists are interested.

By cementing relationships already initiated with biophysicists at a premier research institution, the proposed paradigm of interdisciplinary scientific inquiry with mathematics at its core will enable the investigator as a junior scholar to establish a track record in conjunction with the support of senior experimentalists to increase funding opportunities for the investigator and Fordham. These goals are critical to attracting distinguished researchers and funding to Fordham, increasing the research profile of the University, promoting the investigator's grantmanship and engaging the next generation of researchers and education at the undergraduate and graduate level.
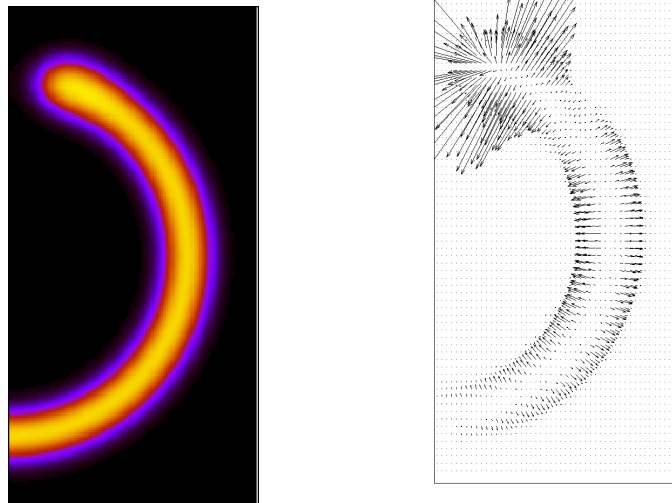
Figure 1: A calculated axially symmetric vesicle with pore (left) and the force it generates on the fluid (right). The concentration of the force at the rim of the pore–typically called line tension, an input in traditional membrane mechanics–as an output of the model.
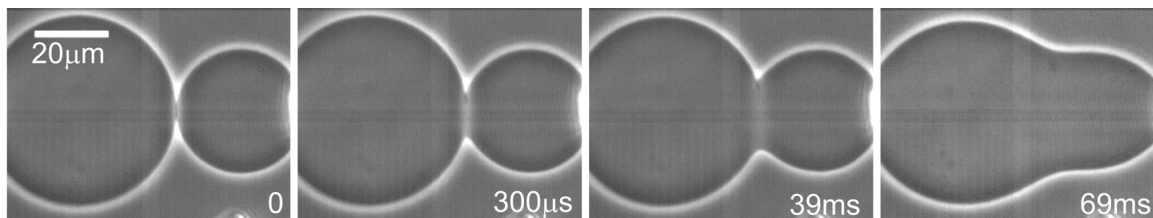

Figure 2: The merging of giant vesicles (taken from [11].) Fusion has already occurred in the first image frame.