Summary and Discussion of Research

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1 Introduction

My general interests include the application of partial differential equations, numerical analysis, lightning modeling and data analysis, and data modeling for rare genetic metabolic disorders to improve diagnostic process.

My earlier work focused on the development of a continuous approach for modeling a lightning discharge. A concrete mathematical model was developed that computes the change in the electric potential due to lightning. I have recently developed a different technique that computes the potential change in a spherical domain by using spherical Bessel functions. I have also been involved in lightning data analysis, by developing mathematical methods to compute the amount of charge transport during lightning. Both of these are major components of computation of lightning flash energy, which is one of the main ingredients in studying climate change.

Recently, I have been interested in analyzing and modeling clinical data regarding rare genetic metabolic disorders, in particular mitochondrial disorders. The research into these disorders are rather recent, and mostly focuses on pediatric patients with early onset. However, there are quite many older patients with late-onset forms of these disorders, and they have to endure years of struggle to get diagnosed. My goal is to determine patterns between the symptoms and other variants about the patients to help the diagnostic process. My initial work focused on late-onset Glutaric Acidemia Type-2 patients, and it revealed some interesting patterns that can be clinically useful.

2 Lightning Modeling and Data Analysis

2.1 Background

An important parameter in the Goddard Institute for Space Studies (GISS) General Circulation Model is the energy associated with a lightning flash. This parameter is closely tied to global lightning NOX production, important molecules to track in studies of our evolving climate. Currently, the parametrization of flash energy is very crude, therefore better estimates are necessary.

One way to estimate flash energy involves estimating the change in the cloud electric potential and the amount of lightning charge deposited by a flash. The electrostatic energy $U$ of a collection of charges above a flat conducting plane is, from electrostatic theory, given by

$$U(t) = \frac{1}{2} \int_V \phi(\mathbf{r}, t) \rho(\mathbf{r}, t) \, dV,$$  \hspace{1cm} (1)
where the volume integration is taken over the upper half space, \( \phi \) is electric potential, and \( \rho \) is charge density. When a lightning flash begins at time \( t_1 \) and ends at time \( t_2 \), the total change in electrostatic energy \( \Delta U \) is

\[
\Delta U = U(t_2) - U(t_1) = \frac{1}{2} \int_V \phi(r, t_2) \rho(r, t_2) - \phi(r, t_1) \rho(r, t_1) \, dV = \int_V \bar{\phi}(r) \Delta \rho(r) \, dV,
\]

(2)

where \( \bar{\phi}(r) = (\phi(r, t_1) - \phi(r, t_2))/2 \) is half of the change in the electric potential due to the lightning flash and \( \Delta \rho \) is the change in charge density due to all current flow in the atmosphere during the flash (for example, even the thunderstorm generator currents would be included here). The last step in (2) is obtained by using the standard (integral) definition of \( \phi \) in terms of charge density, and interchanging the orders of integration. Since the average lightning current during a flash is typically much larger than all other thundercloud currents, the total change in charge density is closely approximated by the charge density due to lightning: i.e., \( \Delta \rho \simeq \Delta \rho_L \), where \( \Delta \rho_L \) is the charge density deposited by the flash, i.e. charge transport due to a flash. Flash energy \( W \) then can be expressed as

\[
W = \int_V \bar{\phi}(r) \Delta \rho_L \, dV.
\]

(3)

My work concerns developing techniques to estimate \( \bar{\phi} \) and \( \Delta \rho_L \).

2.2 Computation of the Change in Cloud Potential, \( \bar{\phi} \)

We consider the evolution equation

\[
\frac{\partial \Delta \phi}{\partial t} = -\nabla \cdot (\sigma \nabla \phi) + \nabla \cdot \mathbf{J} \quad \text{in } \Omega \times [0, \infty), \quad \text{(4a)}
\]

\[
\phi(x, t) = 0, \quad (x, t) \in \partial \Omega \times [0, \infty), \quad \text{(4b)}
\]

\[
\phi(x, 0) = \phi_0(x), \quad x \in \Omega, \quad \text{(4c)}
\]

where \( \Omega \) is a bounded domain in \( \mathbb{R}^3 \), conductivity \( \sigma \in L^\infty(\Omega) \), and current density \( \mathbf{J} \in L^2(\Omega) \).

In the earlier work [8], (4a) was discretized, and integrated forward in time. Whenever the electric field reached the breakdown threshold in some region of the atmosphere, the associated conductivity parameter in the discrete equation was taken to infinity. An explicit formula for the limiting potential was obtained:

\[
\Phi(t^+) = \lim_{\Delta t \to 0} \Phi(t + \Delta t) = \Phi(t) - A^{-1} W_t (W_t^T A^{-1} W_t)^{-1} W_t^T \Phi(t)
\]

where \( W_t = [w_0 | \ldots | w_l] \) and each \( w_k \) is a vector whose entries are all zero except for a single 1 and \(-1\), and \( A \) is a discretization of the Laplacian.

My work concerns the development of a continuous approach to the lightning discharge where the solution to the large system of discrete equations is replaced by a continuous analogue. We consider (4a), and whenever the electric field reaches the breakdown threshold we replace \( \sigma \) with \( \sigma + \tau \Psi \) where \( \tau \) is a scalar and \( \Psi \) is the characteristic function for an open subdomain \( \mathcal{L} \) (lightning channel) with \( \bar{\mathcal{L}} \subset \Omega \). Here \( \bar{\mathcal{L}} \) is the closure of \( \mathcal{L} \). We define
\( \mathcal{L}^c = \Omega \setminus \mathcal{L} \). With this change in \( \sigma \) and using the substitution \( \phi = (-\Delta)^{-\frac{1}{2}} \Phi \), (4a) becomes

\[
\frac{\partial \Phi}{\partial t} = -A_\sigma \Phi - \tau A_\Psi \Phi, \tag{5}
\]

where

\[
A_\sigma = -(-\Delta)^{-\frac{1}{2}} (\nabla \cdot (\sigma \nabla)) (-\Delta)^{-\frac{1}{2}} \quad \text{and} \quad A_\Psi = -(-\Delta)^{-\frac{1}{2}} (\nabla \cdot (\Psi \nabla)) (-\Delta)^{-\frac{1}{2}}.
\]

It is shown by Auscher et al. in [6] that the domain of the operator \((-\Delta)^{\frac{1}{2}}\) coincides with the Sobolev space \(H^1_0(\Omega)\), and there exist constants \(c_1\) and \(c_2 > 0\) such that

\[
c_1 \|\nabla f\|_{L^2(\Omega)} \leq \|(-\Delta)^{\frac{1}{2}} f\|_{L^2(\Omega)} \leq c_2 \|\nabla f\|_{L^2(\Omega)} \tag{6}
\]

for all \(f \in H^1_0(\Omega)\). Utilizing this result, we show in [3] that the eigenproblem for \(A_\Psi\) reduces to the following generalized eigenproblem: Find \(u \in H^1_0(\Omega), u \neq 0\), and \(\lambda \in \mathbb{R}\) such that

\[
\langle \nabla u, \nabla v \rangle_{L^2} = \lambda \langle \nabla u, \nabla v \rangle_{\Omega} \tag{7}
\]

for all \(v \in H^1_0(\Omega)\), where \(\langle \cdot, \cdot \rangle_{\Omega}\) is the \(L^2(\Omega)\) inner product

\[
\langle \nabla u, \nabla v \rangle_{\Omega} = \int_{\Omega} \nabla u \cdot \nabla v \, dx. \tag{8}
\]

Our analysis in [3] exhibits four classes of eigenfunctions for (7):

1. The function \(\Pi\) which is 1 on \(\mathcal{L}\) and harmonic on \(\mathcal{L}^c\); the eigenvalue is 0.
2. Functions in \(H^1_0(\Omega)\) with support in \(\mathcal{L}^c\); the eigenvalue is 0.
3. Functions in \(H^1_0(\Omega)\) with support in \(\mathcal{L}\); the eigenvalue is 1.
4. Excluding \(\Pi\), the harmonic extensions into \(\mathcal{L}\) and \(\mathcal{L}^c\) of the eigenfunctions of a double layer potential on \(\partial \mathcal{L}\). The eigenvalues are contained in the open interval \((0, 1)\). The only possible accumulation point is \(\lambda = 1/2\).

In addition, we proved that these eigenfunctions form a complete orthonormal basis for \(H^1_0(\Omega)\):

**Theorem 1** If \(\partial \Omega\) is \(C^2\) and \(\partial \mathcal{L}\) is \(C^{2, \alpha}\), for some \(\alpha \in (0, 1)\) (the exponent of Hölder continuity for the second derivative), then any \(f \in H^1_0(\Omega)\) has an expansion of the form

\[
f = \sum_{i=1}^{\infty} \phi_i,
\]

where the \(\phi_i\) are eigenfunctions of (7) which are orthogonal relative to the inner product (8).

Using these results, we obtain an explicit formula for the limiting potential in [9]:

\footnote{Work leading to this result had been a 40-year-old unsolved mathematical problem originally posed by Tosio Kato in 1953. It has been solved by Ausher et al. in 2002, see [5]. The problem is often referred to as "Kato’s square root problem."}
Theorem 2 If \( \partial \Omega \) is \( C^2 \) and \( \partial L \) is \( C^{2,\alpha} \), for some \( \alpha \in (0,1) \) (the exponent of Hölder continuity for the second derivative), then the electric potential \( \phi^+ \) immediately after the lightning discharge is given by

\[
\phi^+(x) = \begin{cases} 
\phi_L & \text{if } x \in L, \\
\phi_0(x) + \xi(x) & \text{if } x \in L^c,
\end{cases}
\]

where

\[
\phi_L = \frac{\langle \nabla \phi_0, \nabla \Pi \rangle_\Omega}{\langle \nabla \Pi, \nabla \Pi \rangle_\Omega},
\]

and where \( \Pi \) and \( \xi \) are harmonic functions in \( L^c \) with boundary conditions as specified below:

\[
\begin{align*}
\Delta \Pi &= 0 \text{ in } L^c, & \Pi &= 0 \text{ on } \partial \Omega, & \Pi &= 1 \text{ in } L, \\
\Delta \xi &= 0 \text{ in } L^c, & \xi &= 0 \text{ on } \partial \Omega, & \xi &= \phi_L - \phi_0 \text{ on } \partial L.
\end{align*}
\]

2.3 Computation of Lightning Charge Transport, \( \Delta \rho_L \) or \( \nabla \cdot J \)

Sonnenfeld et al. [12] describe newly developed balloon-borne instrumentation, an Es- onde, which can be used to measure thundercloud electric fields within a frequency band from 1 Hz to 5000 Hz. The goal in this earlier work was to use electric field changes in conjunction with data from the Lightning Mapping Array (LMA) to gain insight into the transport of charge by a lightning stroke.

In [11], we introduced a filtering procedure that separated the background electric field associated with instrument rotation and cloud charging processes from the lightning-induced electric field change. By using polynomial fits, shift, and polynomial extrapolation, we computed the electric field change \( E_L \) due to lightning. The process is summarized in figure 1.

We have also developed techniques to estimate the amount of charge transport due to lightning. We consider both monopole and dipole approximations to the charge transport associated with a flash. In our analysis, we approximate the Earth as a flat, perfect conductor. Let \( E_1 \) be the measured electric field in a cloud-to-ground flash (CG, monopole). If
the sonde is at location $S$, then the measured electric field $E_1$ at $S$ associated with a point charge $q$ at location $P$ and image charge at location $\bar{P}$ is given by the following formula:

$$E_1(t) = q(t)F(P(t))$$

where

$$F(P) = \frac{1}{4\pi\varepsilon_0} \left( \frac{S - P}{||S - P||^3} - \frac{S - \bar{P}}{||S - \bar{P}||^3} \right)$$

The constant $\frac{1}{4\pi\varepsilon_0}$ has the value $9 \times 10^9$ when the electric field is in volts/meter, position is measured in meters, and the charge $q$ is in coulombs. A bar is placed over a vector to denote its image value. The image of $P$ is the point obtained by reflection across the plane defining the perfect conductor. If $E_2$ is the measured electric field in an intra-cloud flash (IC, dipole) with a positive charge $q$ at location $P$ and equal negative charge at location $P_+$, then the measured electric field $E_2$ at $S$ is given by the following:

$$E_2(t) = q(t)(F(P_-(t)) - F(P_+(t))).$$

To find the locations of charge centers and the amount of charge $q$, we minimize

$$||E_L(t) - E_1(t)|| \text{ or } ||E_L(t) - E_2(t)||$$

at each instant $E_L(t)$ is measured subject to the following constraints:

- $(C1)$ = Charges are centered on the lightning channel,
- $(C2)$ = Minimum distance for charge transport (CG),
- $(C3)$ = Charge is conserved (IC),
- $(C4)$ = Minimum distance between charge (IC),
- $(C5)$ = Charge centers are in the regions of high likelihood.

In [10], we modified this technique and used it to analyze all the flashes during a thunderstorm occurred on 18 August 2004 near Langmuir Laboratory in New Mexico. We also incorporated information from the radar data of the storm. As a result of this analysis, we were able to determine the entire charge structure of the storm, as seen in figure 2.

![Figure 2: Side view of the charge structure of 18 August 2004 storm near Langmuir Laboratory. Red dots represent the positive charge centers and blue dots represent the negative charge centers. The size of the dots is relative to the amount of charge transport.](image-url)
2.4 Potential Change in a Sphere

With the newly developed continuous model described in the Section 2.5, the goal is to be able to compute the change in the electric potential in a type of domain that would be suitable for a lightning channel. e.g cylinder, cylinder with a half-sphere attached to both ends, connected ellipsoids... However, our extensive studies, both theoretical and numerical, have shown that mathematical difficulties prevent this model from doing that. As a result, I wanted to look at a simpler three dimensional domain, namely a sphere. In [2], I studied the problem

\[
\frac{\partial \nabla^2 \phi}{\partial t} = -\frac{1}{r^2} (\sigma r^2 \phi_r)_r \quad (r, t) \in [0, 1] \times [0, \infty),
\]

(13a)

\[
\phi(0, t) < \infty \quad t \in [0, \infty),
\]

(13b)

\[
\phi(1, t) = 0 \quad t \in [0, \infty),
\]

(13c)

\[
\phi(r, 0) = \phi_0 \quad r \in [0, 1].
\]

(13d)

over the domain as a sphere of radius 1 centered at the origin, and developed a new technique utilizing spherical Bessel functions to compute the change in the electric potential due to lightning. Neglecting \(\nabla \cdot \mathbf{J}\) in (4a), using spherical coordinates, and utilizing spherical symmetry reduces the problem (4a) - (4c) to problem (13a) - (13d). The initial potential \(\phi_0\) lies in the space \(L^2([0, 1]) = \{ f \in L^2([0, 1]) | \lim_{t \to 0} \int_0^t s^{-1} |f(s)| ds = 0\}\),

where \(L^2([0, 1])\) is the usual space of square integrable functions on \([0, 1]\) and \(\sigma > 0\) lies in the space \(L^1([0, 1])\) of essentially bounded functions on \([0, 1]\).

In the moments after a lightning discharge, the conductivity along the lightning channel becomes infinitely large. In this domain, we assume lightning channel \(L = [0, \Delta r]\), with \(L^c = [0, 1] \setminus [0, \Delta r]\). Therefore, we write \(\sigma = \sigma + \tau \Psi\), where \(\Psi\) is the characteristic function of \(L\), that is \(\Psi = 0\) everywhere except on \(L\), and \(\tau\) is a large scalar. If lightning occurs at time \(t = 0\), then in the moments after lightning the electric potential is governed by

\[
\frac{\partial \nabla^2 \phi}{\partial t} = -\frac{1}{r^2} ((\sigma + \tau \Psi) r^2 \phi_r), \quad (r, t) \in [0, 1] \times [0, \infty),
\]

(14)

subject to the boundary conditions (13b) - (13d). If \(\phi^\tau(r, t)\) is the solution to (14), then the potential after the lightning is given by

\[
\phi^+(r) = \lim_{t \to 0^+} \lim_{\tau \to \infty} \phi^\tau(r, t)
\]

(15)

assuming lightning is very fast.

In calculating the limit, functions \(\{\kappa_i\}, i \geq 1\), where \(\kappa_i(r) = \sqrt{2}(i\pi r)j_1(i\pi r)\) and \(j_1\) is the spherical Bessel function of order 1, are utilized. These functions form a basis for \(L^2_0([0, 1])\). Utilizing this result to write the solution \(\phi\) as an eigenexpansion leads to the following ordinary differential equation

\[
\dot{\beta}(t) = -(S + \tau R)\beta(t).
\]

(16)
where

\[
(S)_{ij} = \langle \sigma(r) \kappa_i(r), \kappa_j(r) \rangle, \\
(R)_{ij} = \langle \kappa_i(r), \kappa_j(r) \rangle_{\mathcal{L}}.
\]

By using \( \{ \kappa_i \}, i \geq 1 \), the eigenvectors of matrix \( R \) are classified and they are used in calculating the limit in (15). In [2], we show that \( \phi^+ \) can be given by the following:

**Theorem 3**

\[
\phi^+(r) = \int_0^r \phi^+_s(s) \, ds = \begin{cases} 
\phi(\Delta r) & \text{if } r \in \mathcal{L}, \\
\phi(r) & \text{if } r \in \mathcal{L}^c,
\end{cases}
\]

where \( \phi^+_r(r) = (1 - \Psi(r)) \phi(r, 0) \).

### 2.5 Future Research

Application of the continuous model developed in Section gives way to two boundary integrals due to (11) and (12). I am currently working on this model in a two-dimensional domain and I am using the Boundary Element Method (BEM) to compute the boundary integrals. Boundary Element Method is rather new to me. I have studied them a few years ago and had a graduate student who worked on a project related to BEM computation. Therefore, I will initially experiment with this in two-dimension, and then I will move into three dimensional domains.

### 3 Data Modeling for Mitochondrial Diseases

#### 3.1 Background

Mitochondrial disorders are rare, genetic disorders of the mitochondria, which is the center of the energy production in the human body. Therefore the disorders of the mitochondria effects almost every system of the body. There are about 40 disorders that are due to different issues in the different steps of the mitochondria’s working process. A subset of mitochondrial disorders is fatty acid oxidation disorders. There are about 13 different fatty acid oxidation disorders depending on how and in which step the fatty acid metabolism is effected. People with fatty acid oxidation disorders cannot utilize fats for energy. When the body needs energy, it first uses the available glucose, and then it looks for fat. If fat cannot be utilized for energy, muscle breakdown begins, releasing toxins and putting the kidneys and the whole body in great danger.

Since these disorders are genetic, they often present themselves at birth or shortly thereafter. In that case, the initial onset is often severe, and quick medical attention, diagnosis, and treatment is crucial. Therefore many of the neonatal onset cases may be fatal. On the other hand, in the case of milder mutations of the effected gene, patients may develop adult-onset type of the disorder. In that case, patients develop symptoms over a longer time period, and they (and their doctors) often think that one symptom has nothing to do with the other. That is due to fatty acid oxidation disorders effecting many seemingly unrelated systems of the body. Hence, these late-onset adult patients do not receive treatment until their conditions get much worse and they end up needing serious and urgent medical attention.
Unfortunately, at that stage, the damage done to their body may no longer be reversible by
treatment, and their treatment would only help them to keep their condition from getting
worse. Most serious damage is done to the muscles. Patients may lose the use of their legs
or arms, their heart muscles may deteriorate, they may develop breathing problems, and
they might also develop seizures. Those are all very serious consequences for a disorder that
can have an onset with very common and not serious symptoms such as muscle weakness,
exercise intolerance, fatigue, hypoglycemia, and vomiting. Unfortunately, when one seeks
help with those symptoms, more common issues come to mind first. In addition, fatty acid
oxidation disorders are considered as pediatric disorders and doctors treating adults may not
even be knowledgable with them. As a result many patients end up in wheelchairs, or with
breathing tubes for life, or with a much lower quality of life than they could have had, had
they been diagnosed earlier.

The goal of my work is to utilize the available clinical data to develop a clinical model
for timely diagnosis of fatty acid oxidation disorders in late-onset patients, and expand the
analysis to the rest of the mitochondrial disorders.

3.2 Analysis of MADD Patient Data and Results

Having been involved with these disorders for family reasons, I have studied a lot of re-
search papers over time. A typical clinical research paper in this area looks at a group of
patients with a specific question in mind and tries to answer that question. Often times
the question is the possible existence of certain variants, like symptoms, test results, reaction
to certain medication...etc. The dissemination of the results is often in the form of
percentage-of-existence-per-variant. Such analysis does not cross-examine the existing vari-
ants, and therefore makes it impossible to see if there are any relations between the variants
themselves.

Multiple Acyl-CoA Dehydrogenation Deficiency (MADD), or Glutaric Acidemia Type 2
(GA2), is one of the fatty acid oxidation disorders. Grünert in [7] put together the clinical
information for all the late-onset MADD patients studied in literature to date. Study pro-
duced a big table including verbal clinical data of the patients and results in terms of the
same percentage-of-existence-per-variant structure. Having seen the need for the improve-
ment in the diagnostic process for late-onset patients, I wanted to study this big data and
see what I could do as a mathematician. In [4], I studied the data to see if there was a
correlation between the age at the time of the onset of the symptoms, age at the time of
diagnosis, and type of symptoms of these patients, along with their gender, related mutation,
and some other variants. I created a numerical data set with the variants I wanted to study
initially, and used different types of MATLAB plots to determine patterns between different
parameters. The most important and unexpected findings are summarized in figures 3 and 4.

As can be observed in figure 3, the diagnosis for patients experiencing muscle weakness can
take up to 30 years after the initial onset of the symptoms, making them very prone to losing
function of their limbs. More interestingly, all the females experiencing muscle weakness as
a symptom who received their diagnosis 10 or more years after the onset of their symp-
toms had their onset before their twenties, and such males had their onset after their late
teens. There is a nearly disjoint separation between males and females. As I have observed
Figure 3: Male and female patients having muscle weakness who are diagnosed 10 or more years after their onset. % 67 of all patients and % 80 of the patients who are diagnosed 10 or more years after their onset experienced muscle weakness, making it the most common symptom among late-onset MADD patients.

during my consultation with other medical doctors in a recent conference this is not something that was known or pointed out before. The reasons for this are still need to be studied.

Figure 4: (a) shows patients having vomiting as a symptom; (b) shows patients having hypoglycemia as a symptom.

The other two common symptoms I studied were vomiting and hypoglycemia. As can be seen in figure 4, both of these symptoms appear in patients having their onset before their thirties, with a single exception in hypoglycemia. In addition, we observe in 4(a) that females are more prone to vomiting than males. Similar to patients with muscle weakness, patients experiencing vomiting had to wait for a long time for a diagnosis. On the other hand, patients with hypoglycemia seemed to have received a rather timely diagnosis, as seen in figure 4(b). This might be due to hypoglycemia having a more serious outcome with
a possible emergency room visit following the episode, and hence patients receiving more
through evaluation.

In consultation with the pediatric geneticist Dr. Anthony Perszyk at the University of
Florida Jacksonville, we came to conclusion that since such meta analysis of data have never
been done before, the results were quite unique and could help the diagnostic process if more
work is done in analyzing the remaining parameters that are not analyzed yet. In addition,
since many fatty acid oxidation disorders share similar symptoms and presentations, it would
be a good idea to do a similar analysis for the remaining 10 or so fatty acid oxidation
disorders. Combining these results can result in a model that can be used in the diagnostic
process.

### 3.3 Future Research

One other parameter I will try to incorporate into this analysis is the mutation type. It
might be interesting to know if the type of mutation is any way related to the other param-
ters. Because mutation types are related to the geographical region of the patients, this
might lead to different diagnostic models for different regions, like different continents or
countries.

Next, I will start looking at the data for the remaining fatty acid oxidation disorders, one
disorder at-a-time. Depending on the results, all of the data might also be combined to get
an overall look at all the fatty acid disorders as a group. I am very positive that at that
point it will be quite possible to have a model that can be followed clinically. Remaining
mitochondrial disorders may have different results than this particular group. Therefore next
step will be to start looking at patient data for the rest of the mitochondrial disorders and
see if an improvement in the diagnostic process is possible for the late-onset patients in that
group.

### 4 Future Plans and Potential Collaborators

In addition to pursuing the ideas outlined under further research, there are three other
projects I am planning to commit to in the immediate future.

#### 4.1 NIH K25 Award for Mentored Training and Other Grants

K25 awards are NIH grants that provide mentored training for mathematicians or engi-
neers with absolutely no biological or medical background. The intention is to incorporate
more quantitative scientist into medical or biological fields. The grant provides funding for
necessary training in the field (1-2 years), followed by additional time (2-3 years) for estab-
lishing research in the field. I feel that such a grant will provide me the necessary medical
and biological background I am lacking, and it will enable me to pursue more serious math-
ematical studies in the field of mitochondrial disorders. I have been in contact with the
program officers at NIGMS and NICHD, two institutions of NIH who support my area of
research, and I am in the process of establishing a mentoring team at one of the leading
institutions in the area of mitochondrial disorders. The teams I am looking into are Dr.
Marni Falk and her team at the Children’s Hospital of Philadelphia, Dr. Vamsi Mootha and his team at Harvard Medical School, and Dr. Mary Kay Koenig and her team at the University of Texas Medical School at Houston. These teams each have a different area of research related to mitochondrial disorders. However, per my personal conversations with them, they all involve great deal of data modeling/future prediction, and they are in need of mathematicians/statisticians to work with them. The grant has 3 application cycles in a year. I am planning to submit an application by the end of Spring 2016.

In addition to strongly pursuing a K25 award, I will also pursue funding at other resources. Here are some possibilities:

- Other NIH research grants, such as R3, R21, or even R1 would be appropriate. In the case that a K25 is not possible, I will look into R grants more seriously, and apply for a suitable one.
- Recently, mitochondrial research has been included in the Congressionally Directed Medical Research Program (CDMPR) run by the Department of Defense, and my research falls under their program goals.
- United Mitochondrial Disease Foundation (UMDF) is a big supporter of mitochondrial research, and they have a strong funding mechanism providing both small and large grants.
- Muscular Dystrophy Association (MDA) also offers grants that support improvement in the diagnosis and treatment of disorders that effect muscle. Mitochondrial disorders, especially fatty acid oxidation disorders, fall under the focus of MDA.

4.2 Computation of Future Risk for a Disease

Pediatric Geneticist Dr. Cherly Garganta at the University of Florida in Gainesville is setting up a new metabolic laboratory. In addition to testing for metabolic disorders, like mitochondrial disorders, her goal is to be able to measure disease associated metabolites and be able to calculate a score that indicates the future risk for a disease. Effectiveness of lifestyle and medication changes will also be incorporated. Similar scoring is currently being used in newborn screening tests. I plan to study how this is accomplished for newborn screening, and try to adapt it to metabolic disorders.

The current and future techniques and patterns explained in Section 3.2 could also be incorporated in the calculation of this score.

4.3 Lightning Image Sharpening

Geostationary Lightning Mapper (GLM) will be launched in March 2016 as part of Geostationary Operational Environmental Satellite R Series (GOES-R) spacecraft. As described in [1], the Geostationary Lightning Mapper is a single-channel, near-infrared optical transient detector that can detect the momentary changes in an optical scene, indicating the presence of lightning. GLM will measure total lightning activity continuously over the Americas and adjacent ocean regions with near uniform spatial resolution of approximately 10 km. It is
anticipated that GLM data will have immediate applications to aviation weather services, climatological studies, and severe thunderstorm forecasts and warnings. However, there is a need to perfect GLM images to make them most useful. It is possible that we can use mathematical image sharpening techniques to eliminate background noise and sharpen GLM images. Dr. William Koshak of NASA Marshall Space Center, Huntsville, AL, a well-known scientist in the area of lightning research, has introduced me to this work. I plan to study the idea further and submit a proposal to NASA to pursue this research opportunity.

References


